MODELING PROTEINS, MAKING SCIENTISTS:
AN ETHNOGRAPHY OF PEDAGOGY AND VISUAL CULTURES IN CONTEMPORARY STRUCTURAL BIOLOGY

by

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Abstract

This ethnography tracks visualization and pedagogy in the burgeoning field of structural biology. Structural biologists are a multidisciplinary group of researchers who produce models and animations of protein molecules using three-dimensional interactive computer graphics. As they ramp up the pace of structure determination, modeling a vast array of proteins, these researchers are shifting life science research agendas from decoding genetic sequence data to interpreting the multidimensional forms of molecular life. One major hurdle they face is training a new generation of scientists to work with multi-dimensional data forms. In this study I document the formation and propagation of tacit knowledge in structural biology laboratories, in classrooms, and at conferences. This research shows that structural biologists-in-training must cultivate a *feel for* proteins in order to visualize and interpret their activity in cells. I find that protein modeling relies heavly on a set of practices I call the *body-work of modeling*. These tacit skills include: a) forms of kinesthetic knowledge that structural biologists gain through building and manipulating molecular models, and by using their own bodies as mimetic models to help them figure out how proteins move and interact; and b) narrative strategies that assume a teleological relationship between form and function, and which figure proteins through analogies with familiar human-scale phenomena, such as the pervasive description of proteins as "machines." What I find is that these researchers are not only transforming the objects of life science research: they are training a new generation of life scientists in forms of knowing attuned to the chemical affinities, physical forces and movements of protein molecules, and keyed to the tangible logic and rhetoric of "molecular machines." This research builds on concerns in the feminist science studies literature on modes of embodiment in scientific practice, and contributes to studies of performance in science by examining visual cultures as performance cultures. In addition, I incorporate historical studies of the life sciences to map the making of the protein—this intricately crafted entity whose forms and functions, I argue, are recalibrating scientific expertise, reanimating biological imaginations, and reconfiguring the very contours and temporalities of "life itself."

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This dissertation was produced with the support of some of the most wonderful advisors a graduate student could hope to work with in the course of their degree. My dissertation committee, Stefan Helmreich, Joe Dumit, David Kaiser, and Donna Haraway each offered profound insight and encouragement.

In many ways this project started years before I arrived at MIT. In 1998 I was a graduate student in Environmental Studies at York University when I was introduced to Donna Haraway's work for the first time. I was fresh out of a molecular genetics laboratory where I'd been pursing graduate research, and her writing completely transformed my world. Buoyed by the possibilities for situated knowledge and embodiment in science, I committed myself to research in feminist science studies. In 2001 I attended a conference in Eugene, Oregon where Donna was a keynote speaker. When she showed up for my talk, and spoke to me after my presentation, I was stunned and in awe. When we happened to board the same plane and sit a row apart the morning after her keynote address, I gathered up the nerve to ask her where I should pursue my Ph.D. She told me I should study with Joe Dumit at MIT. I took careful notes. While we were mid-air between Eugene and Portland, an earthquake rattled the northwest coast. I took that as a good omen.

In 2002, when I arrived in the STS program at MIT to work with Joe Dumit, I was quickly swept up into a richly interdisciplinary environment that opened me up to new ways of thinking through my long-standing interests in embodiment and visualization in science. Joe was at the center of this world: he provided incredible intellectual and moral support, and committed truly amazing amounts of time mentoring me as I learned how—for the first time—to read social theory and philosophy, and begin the transformational process of "becoming anthropologist". Very early on, Joe enrolled me in numerous research projects on scientific visualization, each of which became sources of inspiration for the research that shaped this dissertation. Since his move to UC Davis, Joe has continued to closely mentor me on this project.

In 2004, shortly after he joined MIT's Anthropology program, I took a class with Stefan Helmreich. The depth and richness of his insights into the sciences of life profoundly inspired me, and I signed on to do a field with him for my general exams. In the course of our weekly meetings I was moved by his commitment of time and energy to mentorship, and I learned vast amounts from his careful and sharp analyses. As the primary advisor for this dissertation, Stefan has been an astoundingly careful reader and a constant source of inspiration. Taken together, Stefan and Joe's shared knowledge and commitments to critical scholarship, as well as their friendship and collegiality, have created a nurturing intellectual environment that has given me the courage to write passionately about a world for which I care a great deal. As I've moved through the many challenges of this degree, Stefan and Joe's collective generosity, care, and support have been extraordinary gifts.

In response to one of the first interviews I did with a protein crystallographer, I realized that I wanted to study the intersection of pedagogy and visualization in science. Dave Kaiser generously agreed to do a reading course with me on this topic. The reading list we

worked through together in the fall of 2004 was formative in my intellectual development. Meetings with Dave were wonderful, and the learning was rich. His expertise in pedagogy and modeling in science has given me much inspiration over the years.

In the spring of 2005 I had the opportunity to work with Donna as a visiting student in the History of Consciousness Program at UC Santa Cruz. In her graduate seminar that year Donna created an incredibly exciting environment for collective thinking. The community of feminist scholars that Donna fostered in that space was inspiring. I am exceptionally grateful to Donna for her generosity and careful reading of my work, and for her immense warmth and kindness.

In addition to my advisors, this study would not have been possible without the support and openness of the scientists with whom I worked. They gave me unquestioned access to their laboratories, group meetings, and classrooms, and the opportunity to watch them work and teach. I am grateful for all the time that they spent helping me to understand their research, and offering insights into their lives and worlds.

I want to thank the MIT HASTS community for their support over the last five years. I had the privilege of working closely with several faculty members. Susan Silbey was a constant and strong support, teaching me valuable lessons about ethnographic research and writing. I also worked closely with Susan on a collaborative NSF-funded project (with Sherry Turkle, Joe Dumit, Hugh Gusterson, Yanni Loukissas, and David Mindell) examining computation, visualization, and changing professional identities. Sherry Turkle's support through the research and writing of the reports to the NSF was invaluable. Michael Fischer was a generous reader of my papers throughout, and a great ally when we were out together in the field doing interviews with structural biologists. As a committee member for my general exams, Sheila Jasanoff taught me important lessons about the politics of science.

My cohort in STS, Candis Callison, Anita Chan, Richa Kumar, Jamie Pietruska, and Will Taggart helped create a nurturing community amidst what was a rather rough transition to MIT life. Many thanks to Etienne Benson, Nate Greenslit, Shane Hamilton, Eden Miller, Esra Ozkan, Rachel Prentice, Anne Pollock, Aslihan Sanal, Livia Wick, Rebecca Woods, and Anya Zilberstein for their friendship. Participants in the STS Writing Workshops, and members of Body Group offered lots of intellectual stimulation. Members of MIT's BioGroop, including Stefan Helmreich, Etienne Benson, Sophia Roosth, Sara Wylie, and, especially Rufus, created a lively community for life science studies. The MIT staff, including Kris Kipp, Debbie Meinbres, Karen Gardner, and Rosie Hegg offered invaluable support throughout. This research was generously funded by a four-year Social Sciences and Humanities Research Council of Canada (SSHRC) Doctoral Fellowship (Award No. 752-2002-0301) and by the National Science Foundation through both a Predoctoral Fellowship (Grant No. 0220347) and a Dissertation Improvement Grant (Award No. SES-0646267).

I want to thank my professors at York University for their encouragement in pursing this degree, in particular Leesa Fawcett, Adrian Ivakhiv, Rusty Shteir, Evan Thompson, and Joan Steigerwald. My intellectual community was expanded through international conferences, and I had the pleasure of meeting and working with numerous feminist scholars including

Aryn Martin, Rachel Prentice, Lucy Suchman, Annemarie Mol, Karen Barad, Catherine Waldby, and Nina Wakeford.

My dearest and oldest friend, Leah Cowen, created a most nurturing life for me in Jamaica Plain. In addition to her love and affection, our conversations on the sciences of life gave me new and inspiring insights into my research. Saara Nafici, Esra Ozkan, Maggie Crowley, and Peechaw and Alice the Cats, were wonderful friends and companions. In various combinations, we created a lovely home together at 7 Carolina. The Cambridge Dance Complex was an integral part of my life. I thank Joe Burgio and Shira Lynn for sharing dances that kept my heart and body moving, and especially Debra Bluth for her inspired teaching and healing arts. I am grateful to Clementine Cummer for creating a space for a dance collaboration that helped shape my thinking about this research, and to Jessica Rosenberg for being a caring companion and generous reader. By far, the place I spent most of my time conjuring ideas for this dissertation was the Arnold Arboretum in Jamaica Plain. I will always remember the Tall Pines, the Burr Oak, the Swooping Beech, and the Dancing Birches—they are truly inspired life-forms.

I lived and worked among some wonderful people at UC Davis while I was finishing this dissertation and teaching my first course. Many thanks to: Joe Dumit, Jim Griesemer, Moon Duchin, Chris Kortright, Andrés Barragan, Fabiana Li, Michelle Stewart, and Vivian Choi; participants of the Food for Thought writing workshop; and my wonderful students, Brigid, Ashley, Kylie, Katherine, and Megan, whose commitment to learning taught me so much about teaching and the anthropology of science.

In Santa Cruz, students in the History of Consciousness Program created an unparalleled intellectual home. From the bottom of my heart I thank Natalie Loveless, Mary Weaver, Maria Puig de la Bellacasa, Astrid Schrader, Sandra Koelle, Sara Bracke, and Sha la Bare for their brilliance, profound friendships, and generosity.

To my dear friends Geoff and Suzanne Bradley-Siskind, Ana Francisca de la Mora, Alorani Martin, Inge Tamm, Andrea Kohn, and Navin Nayak, I give many thanks for all your love and kindness. Above all, my family has been there for me every step of the way. To Mom, Dad, Stephanie, Maggie, Virginia, Kathie, Kyle, and Adam: thank you for everything, always. Your unconditional love and support mean the world to me.

This dissertation is dedicated to the memory of my Bubbies and Zaidies,

Ruth & Irv Mudrick
&
Saidie & Ken Myers

I will always remember your smiling eyes.

Biographical Note

Natasha Myers was born in Toronto, Canada. She spent fourteen years of her youth in dance studios, in an intensive pre-professional training program in classical ballet and modern dance. She continued dancing after she moved to Montreal, and earned her B.Sc. in Biology from McGill University in 1997. Lured by gestural, dancing forms of plants and flowers, that same year she started a PhD in biology at McGill, investigating the molecular genetics of flower development. She left the lab a year and a half later to begin a Masters in Environmental Studies at York University. Her thesis, *Body-fullness in Biology: Feminist Environmentalism Meets Merleau-Ponty's Philosophy* explored the possibility for embodied ethics in biological imaging and imagination. She received a Social Sciences and Humanities Research Council of Canada Doctoral Fellowship and joined the HASTS program at MIT in 2002. Her paper "Molecular Embodiments and the Body-work of Modeling in Protein Crystallography" (forthcoming in *Social Studies of Science*), won the 2006 Nicolas C. Mullins Award for outstanding graduate scholarship from the Society for Social Studies of Science, and her paper "Animating Mechanisms: Animations and the Propagation of Affect in the Lively Arts of Protein Modeling" (published in 2006 in *Science Studies*) received Honorable Mention for MIT's 2005 Benjamin Siegel Prize. The National Science Foundation has generously supported her research, in the form of a Predoctoral Fellowship, and a Dissertation Research Grant. For the past ten years she has collaborated with dancers and visual artists to create performances that explore the relationships between dance and science. In July 2007, she returned to York University, joining the Department of Anthropology as an Assistant Professor, teaching and conducting research in the anthropology of science and technology.

Chapter 1

Introduction

The gene and the cell are undoubtedly the central figures of twentieth-century biology.[1] However, as structural biologists intensify investigations into the forms and functions of biological molecules, it is the protein molecule that is coming into being as the star of the early twenty-first-century life sciences. Today, journals such as *Science* and *Nature* are publishing newly determined protein structures almost weekly, and as of May 2007 the atomic coordinates for over 43,300 protein structures have been deposited online in the Protein Data Bank (PDB). With the promise of novel insights into basic biological processes, and major contributions to biomedical research and drug development, biologists, chemists, physicists, engineers, mathematicians, and computer scientists are converging on the field of structural biology, turning protein structures into objects of multi-disciplinary interest and investment. In the process, their work is shifting the cusp of visibility for scientific studies of life.

These researchers apply computationally intensive, multidimensional visualization techniques to render the folds, forms and movements of otherwise "subvisible" (Sagan and Margulis, 1988) biological molecules in elaborate detail [See Figure 1.1].[2]

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[1] See for example Keller (2000), Landecker (2007), and Franklin and Lock (2003).

[2] Proteins are "macromolecules," large, complex biological molecules, often made up of thousands of atoms. Reduced to their constituent parts, they are made up of small molecular subunits called amino acids linked end to end to form long polypeptide chains. A protein may be made of a single polypeptide, or several folded together. Amino acids themselves are small molecules made up of varying amounts of carbon, nitrogen, oxygen and hydrogen and some contain other elements such

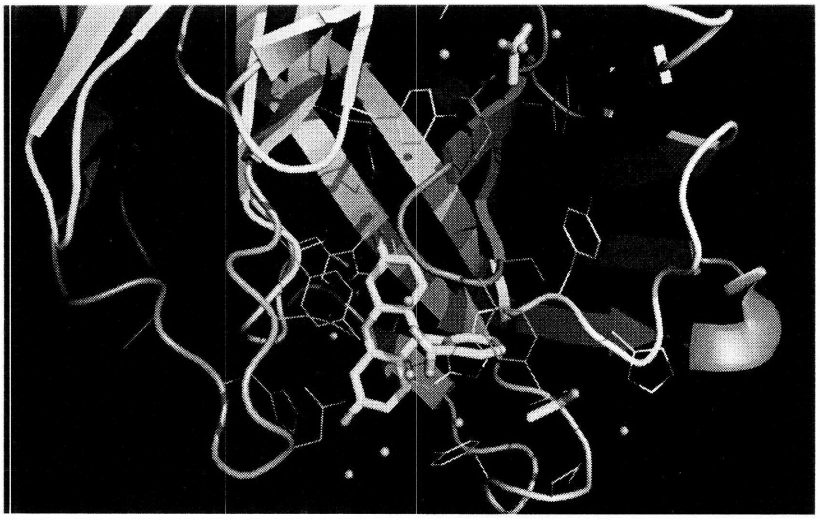

Figure 1.1: A Ribbon diagram of a protein molecule. Used with permission from an anonymous ethnographic informant.

They make use of high-energy forms of radiation, state-of-the-art interactive digital media, augmented computer power, continually upgraded software and automated techniques to craft atomic-resolution, three-dimensional models and animations of protein structures onscreen. These techniques enable them to amplify protein structure data as interactive digital models that they can manipulate and analyze. As they ramp up the pace of structure determination, making visible the structural properties of a vast menagerie of proteins, these life scientists can be seen turning from matters of code to matters of substance—that is, from spelling out linear gene sequences to inquiring after the multidimensional

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as sulfur. There are 20 different kinds of amino acids. While they all share a common carbon backbone structure, each bears a different chemical side chain that confers different chemical properties. Each species of protein has a unique sequence of these twenty amino acids, and polypeptide chains can vary greatly in length. For a peptide chain to acquire biological function in a cell, or a test tube, it must be folded correctly. Proteins fold into secondary structures, such as alpha-helices, and these secondary structures pack together to form the tertiary structures of the active form of the protein. The active forms of some proteins are made up of 2 or more polypeptides, and when these pack together, proteins acquire their quaternary structure, and fully functional form.

materiality of the protein molecules that give body to cells. In the process, structural biologists are not only collectively transforming the forms of data that populate life science laboratories and databases; they are also crafting new ways of knowing, new forms of expertise, and new narratives about what constitutes "life." In order to track these shifts, this ethnography explores pedagogy and training in the lively visual cultures of twenty-first century structural biology.

Currently, structural biology encompasses a number of distinct visualization traditions, each with unique histories, disciplinary convergences, and practical cultures. Thes include: X-ray crystallography; electron microscopy; nuclear magnetic resonance imaging (NMR); studies of protein folding; and predictive modeling and protein engineering. X-ray crystallographers build three-dimensional atomic resolution models of proteins from data gathered from X-ray diffraction experiments with proteins that can be coaxed to form crystals. Electron microscopists use high-energy microscopes to resolve low-resolution models of larger protein complexes, such as the massive protein assemblages that form membrane pores and channels. NMR researchers, on the other hand, apply their techniques to produce high-resolution models of small, soluble proteins. Protein folding researchers draw on a range of visualization techniques and biochemical analyses to map the elusive pathways through which polypeptide chains fold into their active conformations. Predictive modelers and biological engineers develop algorithms and run simulations in the effort to predict unknown protein structures from known protein sequences, to explore how molecules interact with each other, or to engineer new kinds of protein molecules. Members of each of these diverse practical cultures are trained in the full spectrum of scientific disciplines.

In order to comprehend the import of molecular visualization for contemporary life science research, I situate structural biology within the cultural milieu and practical horizon anticipated and actualized by biological engineers. Protein structure data has particular import for members of the biological engineering community. These investigators aim to reengineer biological systems at the molecular scale. Once frustrated by the opacity and recalcitrance of the gooey, proteinacious substances that constitute living systems, biological engineers are now employing atomic-resolution molecular visualization to produce protein models as physical objects they can measure, model, manipulate, and redesign. In the hands of biological engineers, proteins are figured most frequently as "molecular machines": like car parts, proteins become "biological parts," "components," and "devices"; mechanical objects that exert force and conduct "work" in order to "drive" cellular life. As these twinned desires for visualization and intervention are actualized through advances in structural biology, life science, as a practice and culture, is itself is being re-engineered.

This ethnography is based on four years of ethnographic fieldwork among multidisciplinary communities of structural biologists and their students. My primary fieldsite was a large, private university on the east coast of the U.S. There, I conducted in depth interviews with researchers working on projects in protein structure in the varied fields of protein crystallography, biological engineering, protein folding, electron microscopy, and mechanical engineering.[3] Many of my interviews lasted for up to two hours, and I had the opportunity to do follow up interviews with a number of informants, as well as observe

[3] The present study does not include NMR researchers.

them do laboratory work, and sit in on weekly group meetings. My informants were at various stages in their training and they included principal investigators, research coordinators, course directors, postdoctoral researchers, graduate students, teaching assistants, and undergraduate students. I also observed full semester-long graduate and undergraduate courses, including lecture courses on macromolecular crystallography, biomolecular kinetics, protein folding, introductory biology and biological engineering courses, as well as a hands-on laboratory for biological engineering majors. In addition, I attended several professional meetings, numerous public lectures on structural biology and biological visualization, and interviewed a number of structural biologists working at other institutions on the east and west coast of the U.S.

This introductory chapter serves a number of purposes. First, I provide a brief history of structural biology that locates contemporary practices in a history of inquiry into protein molecules and structural studies of life. Second, I introduce a very recent event that shook the field of structural biology from its foundations: the retraction of five major structural biology research papers after it was discovered that the models published were wrong. This event serves to demonstrate how hard it is both to produce structural models of proteins, and to train the next generation of researchers in the tacit and critical skills required for the task. In order to situate the challenge of molecular model building in context, I locate protein models within a history of three-dimensional modeling practices in the life sciences. In this inquiry I pose the question: what kind of scientific object is a protein model? In the process I aim to highlight how this study of protein modeling can contribute to theoretical debates on visualization, representation, and practice in the science and technology studies literature. I examine not just how protein modeling is reconfiguring the

visual cultures of life science; I ask how an analysis of protein modeling can reorient the STS literature on scientific visualization, and produce more lively accounts of life science practice. Finally, I outline the methodological innovations this study makes for anthropological studies of science, and provide an overview of the chapters that follow.

(Re)Folding the Threads of Life: A Brief History of Structural Biology

> Today the world is messages, codes, and information. Tomorrow what analysis will break down our objects to reconstitute them in a new space? What new Russian doll will emerge?
>
> Francois Jacob, *The Logic of Life,* 1973

As historians and anthropologists of the biosciences have shown for the cases of genes and cells, the identity and materiality of biological objects are transformed continuously with shifts in the technical and discursive practices that constitute biological visualization and interpretation.[4] Such is the case with proteins: as models of proteins are amplified through interactive digital media, and drawn into new stories about cellular life, the very nature of these substances is currently in formation. This ethnographic study thus incorporates historical studies of the life sciences to map the making of the protein—this intricately crafted "material-semiotic actor" (Haraway, 1997) whose forms and functions, I argue, are reanimating biological imaginations, and thus reconfiguring the very contours and temporalities of "life itself."

Proteins are of course not new to the life sciences, and they never actually disappeared from laboratories. Indeed, proteinacious substances have inhabited chemists' laboratories

[4] See for example Keller (1995, 2002), Kay (2000), Haraway (1997), and Landecker (2007).

and animated their imaginations since the late eighteenth century. Proteins have a particularly rich history in the late-nineteenth and twentieth century life sciences.[5] In the 1860s, TH Huxley popularized his "protoplasmic theory of life," proposing that the unifying basis of all life—the vital material which united the plant and animal kingdom—was the proteinacious substance of the cell that he called the "protoplasm" (Geison, 1969). It was the irritable and contractile capacity of the protoplasm that demonstrated the vital powers of the cell. Yet, Huxley was no vitalist: his protoplasmic theory proposed a mechanistic view of life, in which the "vital forces" of the cell could be reduced to mechanical, "molecular forces" (Geison, 1969: 280). By the late-nineteenth-century, the protoplasm was already figured as a molecular substance that adhered to mechanical laws. As Lily Kay (1993, 2000) has shown, by the 1930s Huxley's protoplasmic theory had given way to a widespread view that proteins were the "principal substances" of life. Indeed, through the 1930s and 1940s, and up until the determination of the structure of DNA in 1953, proteins were thought to be the material basis of heredity, and intensive effort was invested in determining their elemental composition, chemical specificities, and cellular activity (see Kay 1993).

Structural studies of life are also not new. Life scientists have long been interested in the forms and structures of living bodies. Historically, structural studies of life have included anatomy (e.g. Foucault, 1973, Kuriyama, 2002; Klestinec, 2004), developmental biology and embryology (e.g. Keller, 1996; Hopwood, 1999, 2002), systematics and evolutionary

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[5] See for example Abir-am (1987, 1992), Kay (1993), Cambrosio, et al. (1993), Rheinberger (1997), Creager (2002) and de Chadarevian (2002). Tanford and Reynolds' (2001) *Nature's Robots*, is a "scientists' account" of this history, and while problematic in its presentation of particular figures in the history of this field (particularly their scathing, gender stereotyping account of Dorothy Wrinch), it provides some valuable insights into the history of proteins in the life sciences.

biology (e.g. Bowler, 1989; Star, 1992), and more recently, the study of cellular "ultrastructure" with electron microscopy (Rasmussen, 1997). In ways similar to their predecessors, contemporary structural biologists understand visualization as the key to knowledge. Tethered to this understanding is their adherence to a mechanistic vision of molecular life in which a protein's function is given by its form. An enduring example of this mechanistic logic is Emil Fischer's 1885 lock-and-key model, which predicted that enzymes performed their chemical reactions and acquired their functional specificity by achieving "intimate contact" with substrates that had similar geometrical configurations (Fischer quoted in Clardy, 1999: 1826; see also Cambrosio, et al., 1993). Indeed, even today the lock-and-key model has conceptual currency in the field. As biological chemist Jon Clardy put it in a relatively recent issue of *PNAS*, "No analogy has so profoundly influenced our thinking about the joining of biological molecules as Emil Fischer's lock and key. After a century, it still serves as an appropriate introduction to the exquisite fit that small molecule keys have for large molecule locks" (1999: 1826). Visualizing a three-dimensional molecular structure is thus considered to provide the access to knowledge about its function, and the key to predicting how it "works" in the cell.

Studies that aimed to visualize protein structures were first initiated in England in the 1930s. These structural studies initially dominated the field of "molecular biology"; named as such by mathematical physicist Warren Weaver to designate an area of research that would bring physics to the study of life at the molecular scale (see Kay, 1993; Law, 1973). W.T. Astbury, a biophysicist and member of the growing "protein community" in the U.K. (Law, 1973), was among the first to popularize the field (Stent, 1968). In 1951, Astbury insisted that "molecular biology" was to be understood as the "predominantly three-

dimensional and structural" study of the biophysical and chemical properties of molecules (cited in Stent, 1968: 390). By 1967, however, the definition of molecular biology had already begun to change. In his widely cited lecture "That Was the Molecular Biology that Was," Gunther Stent (1968) forecasted the decline of the structural school of molecular biology. While Stent defended the structural school's "down-to-earth," "physical" approach, which promoted the "idea that the physiological function of the cell" could be understood "only in terms of the three-dimensional configuration of its elements" (1968: 391), at that time Stent did not see how these contributions could be "revolutionary to general biology." After all, by 1967, it had taken over twenty years to determine the structures of merely two "respiratory proteins": hemoglobin and myoglobin (ibid.). The revolution was, according to Stent, going to be led by the "one-dimensional" or "informational school," whose "intellectual origin" in the emerging computational cultures of cybernetics and cryptography in the1950s and 1960s was "diametrically opposite" to the physical understandings of molecules championed by the structural school (Stent 1968: 391; see also Kay 2000).

While structural biology did not disappear, the contributions of this field did lose traction during the sequencing craze of the molecular genetics and genomics revolutions (see for example Kay, 2000; Keller, 2000). During the 1980s and 1990s, in particular, a kind of "genetic fetishism" swept over the life sciences (Haraway, 1997). The "molecular vision of life" that took root in the wake of the determination of the genetic code was a vision that flattened life into thin threads of genetic "information" (see Kay, 1993; 2000). However, since the late 1990s, with the completion of the genomes of humans and other organisms, and the ramping up of post-genomic investigations, researchers are coming up against the

limitations of genetic sequence data for accessing the multi-dimensional problems that biology poses (Kirschner, 2000).

Structural biology research is fueled by the techniques, databases, and economies (Sunder Rajan, 2006) generated through the genomics and bioinformatics revolutions.[6] Yet proponents of a structural approach to the study of life are critical of the late-twentieth century obsession with genes. Encouraged by biologists' almost embarrassing admission that genes don't actually *do* anything in the cell,[7] structural biologists have invested intensive effort in delineating forms and functions of protein molecules—the substances genes are supposed to "encode". From a structural perspective, proteins are the enzymes that catalyze life-sustaining chemistry; the substances that transduce signals within and between cells; and the molecules that organize, transcribe, translate, and rewrite DNA to produce more proteins; and the dynamic—continually cycling, growing, and retracting—architectural support for cellular life. As structural biologists shift molecular biology research agendas to the elucidation of protein forms and functions, they challenge gene-centric conceptions of life, and recast the principal actors in the cell. For this new generation of researchers, it is proteins, rather than genes, that are the key agents enacting the story of life.

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[6] Large scale "proteomics" projects, modeled on the high-throughput, industrial scale technologies and logics that organize genomics research, have been launched to facilitate biomedical research and efforts in the area of rational drug design. See for example Abott (2000), Jones (2003), Smaglik (2000), and Wadman (1999).

[7] This assertion comes from several different camps: from practicing scientists based in major research institutes, see for example Coen (1999), Lewontin (2000), Kirschner (2000), and Harrison (2004); as well as from a group of scientists who no longer work in laboratories, but are dedicated to developing critiques of genetic centrism in the life sciences (see for example Goodwin, 1994; Holdrege, 1996; Ho, 1998).

Reconfiguring these narratives of life has required new visualization technologies to help flesh out the story. There is, however, a yawning gap in visibility between well-articulated DNA sequences and the pulsing vitality of protein-packed cells. Genes can be "decoded" as one-dimensional strings of information, and cells and their substructures can be brought to light through multidimensional microscopic techniques and genetic marker technologies.[8] However, the configurations of the large majority of the dynamic molecular events in the cell still remain largely subvisible. Molecular forms and interactions can be accessed indirectly through a vast array of in vitro biochemical assays and genetic dissection techniques. Protein forms and movements, however, have for the most part been conjectured indirectly, with the result that they are frequently rendered as amorphous blobs in cartoon diagrams that depict hypothetical scenarios for protein activity in the invisible depths of the cell. No longer satisfied by a reliance on genetic sequence data, or on microscopic images to interpret biological processes, contemporary life scientists want to visualize molecular events in the cell at atomic resolution.[9]

Diane Griffin,[10] a young and energetic, tenured professor of chemistry at the large, east-coast university where I conducted my research, is the head of a structural biology

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[8] See Keller (2002) and Myers (2005) on three- and four-dimensional cellular visualization through confocal microscopy.

[9] David Goodsell (1993, 2004) is a structural biologist employed at the Scripps Research Institute. He has published a series of illustrated books that flesh out his vision of the "molecular machinery" inside cells. He is also employed by the Protein Data Base to illustrate the "Molecule of the Month" (see http://pdb.org). Jacques Dubochet at the Université de Lausanne (Al-Amoudi, et al., 2005) and Wolfang Baumeister at the Max Planck Institute (Sali, et al., 2003) are electron microscopists who are independently attempting to develop new techniques to render proteins visible in cells at the atomic scale.

[10] I have changed the names of all participants in this study. Others whose work I have encountered in the literature or in public talks are named and cited.

laboratory that solves protein structures using the techniques of X-ray crystallography. In an interview exploring her choice to pursue a career in X-ray crystallography, she justified her pursuit of molecular visualization—in spite of the massive technical challenges it presents for researchers—as her desire to see into and make sense of molecular realms:

> I really liked the idea of trying to understand how enzymes formed. What did they do? How did they catalyze this reaction? What was the detailed mechanism involved? ... I figured out that I couldn't think of working on a project if I didn't understand *what it looked like*. I needed that first ... You have to have some kind of concrete thing to start with, even if its just one picture. At least there is something more tangible involved there. It was just that it seemed to me that that was the starting place for science. The first thing you ask is *"What does it look like?"*

According to Diane, making invisible protein structures visible turns them into "tangible," "concrete" entities with which she can think and work. Molecular visualization becomes a means of interpreting the role and significance of a particular molecule in a narrative of its biological function in the cell.

During one of her lab's weekly group meetings in the fall of 2006, Diane practiced a talk she was about to give at an upcoming Harvard symposium on a field of research the organizers called "chemical biology." Animated in front of her group of fifteen graduate and undergraduate students, and postdocs, she recounted a comical experience she'd had preparing for the talk. She knew the first thing that she had to do was to figure out what was this thing they were calling "chemical biology". She told the group what she found when she visited the website of a new journal, *ACS (American Chemical Society) Journal of Chemical Biology*, and looked at their mission statement: "So, it said, 'If you want to know what chemical biology is,' and I thought, yes I do! So I kept reading. But then it said, 'Well then, go to the Harvard symposium and hear the thirteen people at the leading edge

of chemical biology talk.' And I thought, 'Oh! This isn't good!'" A huge burst of laughter erupted from the group. Indeed, having been identified at the leading edge of this field, it became quite clear to her that it was actually her job to define its vision.

As she began her talk, she stood facing her students at the head of a long conference table, and gestured across the room towards a half-finished power-point slide. As she walked through the points she would make in her talk, she laid out her approach to the "incredible" chemistry that "nature has tailored" in living cells. Undeterred by the serious technical challenges X-ray crystallographers like herself face in visualizing molecular forms, she told the group that she wants to "think bigger about what we can accomplish":

> Instead of solving the structure of one enzyme from a pathway, we [want to] solve the structures of all the enzymes in the pathway, alone and in complexes. Instead of solving the structure of one protein from a superfamily, [we want to] solve structures of multiple members of that family—because in the comparison you can often figure out what is truly important in those molecules ... [We also want to use] what I call mechanistic crystallography to solve many structures of one enzyme and capture states as it proceeds through its reaction cycle.

Completely mapping the molecular events of even one reaction pathway for an enzyme would be no small feat. Indeed, it is only recently that such a dream could even have been imagined: it had taken Nobel Prize winner Max Perutz twenty-two years to determine the atomic structure of just one protein; and when the Protein Data Bank was first founded in 1971, fewer than a dozen protein structures had been deposited. Today the PDB houses tens of thousands of structures, "snapshots" of protein molecules at single moments of

time, and the number is growing at an exponential rate.[11] It offers what could be thought of as a rich "atlas of observables" (Daston and Galison, 1992) that life science researchers can use to compare and contrast protein structures within and between species; offering a powerful medium through which they can train their sensibilities around protein form and begin to piece together dynamic visions of molecular processes. But while automated techniques, faster computers, and other technologies have now made it possible to solve protein structures on the timescale of a PhD students' tenure in the lab, the work is still daunting.

In this sense, Diane's message was not meant just to inspire and delight the audience at the following week's symposium; this was a rallying call directed to the students in her laboratory, whose shoulders will carry the weight of these ambitious goals. If this field is to produce profoundly new visions of molecular life, Diane and her colleagues must invest their energies in training a new generation of scientists in the skills and practices of molecular visualization and interpretation. With this shift from reading and writing one-dimensional genetic codes to modeling and interpreting the functions of three-dimensional and temporally dynamic protein molecules come new practical and conceptual hurdles for researchers and their students. Thus, it is not just the objects of biology that are being reworked in structural biology laboratories; the scientists who constitute these objects must also be reconfigured.

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[11] For an inquiry into the production of models as "snapshots" and the narrative of "capture" in structural biology discourse, see Chapters 5 and 6.

The Great "Pentaretraction"

I approach this study from the premise that the production of protein models, and the training of body of experts who can build and interpret them, are remarkable achievements.[12] It is my aim to examine precisely how, in the rapidly shifting and multi-disciplinary terrain of life science research, structural biologists are finding new ways to "see into" molecular realms; and how they are teaching a new generation of scientists how to see what they see, work with multidimensional data forms, and interpret their findings. A recent scandal, characterized as "one of protein crystallography's greatest blunders" (C. Miller, 2007: 459), helps to illuminate just what kind of an achievement it is to produce and propagate sound structural knowledge of protein molecules.

In December 2006, Geoffrey Chang, a young and stunningly successful PI heading a protein crystallography lab in the Department of Molecular Biology at The Scripps Research Institute, published a letter in *Science* retracting five high-profile research papers in which he and his lab had presented novel structures of a series of membrane-bound proteins (Chang, et al., 2006: 1875). Three of the papers had been published in *Science* (one in 2001, two in 2005), one in *Nature* (in 2006), and another in *The Proceedings of the National Academy of Sciences* (in 2004). These retractions were in response to a paper

[12] I use the term "achievement" in the sense that philosopher of science Isabelle Stengers attributes to the notion (Stengers, n.d.) In a constructivist reading of Whitehead's philosophy, Stengers approaches the study of science with a kind of care that recognizes the profound and particular achievements of scientists, resisting attempts to debunk or deconstruct their approaches or findings.

published in September 2006 in *Nature* by a team of Swiss researchers who provided evidence that strongly suggested that the structures that Chang's laboratory had produced were wrong. When Chang investigated, he was "horrified to discover" that a "homemade data-analysis program" had "inverted" two columns of data, skewing the data and massively contorting the structures his lab had built. This piece of software, which had been "inherited" from another laboratory, had been used on four of the other structures he had published (G. Miller, 2006: 1856).

Three of the protein models Chang's group had botched belonged to an "ancient family" (G. Miller, 2006: 1856) of membrane proteins whose biological function—the active (energy dependent) transport of molecules across cell membranes—was the object of much scrutiny by biochemists. These proteins, in the MsbA family, are referred to as membrane pumps, because they pump unwanted molecules out of the cell. These molecular pumps are of "great clinical interest" (G. Miller, 2006: 1856) because they enable cells, like bacterial and cancer cells, to continually clear unwanted substances, like anti-cancer drugs and antibiotics, which pose a hazard to their viability. Drugs that can disable these membrane pumps, and prevent cells from clearing these potent toxins, thus have potential therapeutic applications for cancer treatment and for preventing the evolution of antibiotic resistance in bacteria (see Cowen 2002, 2005 for the role of these pumps in the evolution of drug resistance in fungi). As such they are targets for much pharmaceutical development. Getting the structure of these proteins right is clearly a high stakes game.

When Chang published the first MsbA structure, it caused a stir among the biochemists who had already been studying its biochemical mechanisms: the structures did not jive

with the available biochemical evidence. But the allure of Chang's visualizations blinded Chang's group and the reviewers in high-profile publishing industry to the "careful [biochemical] studies published in unglamorous workaday journals" (459). As reported in a news article that appeared with Chang's retractions in *Science,* Christopher Higgins a biochemist at Imperial College London admitted that: "When the first structure came out, we and others said, 'We really don't quite believe this is right.' It was inconsistent with a lot of things" (G. Miller, 2006: 1856-7). Others reportedly experienced difficulties "persuading journals to accept their biochemical studies that contradicted Chang's structure" (1857). David Clarke at the University of Toronto had served on funding panels were "Chang's work was influential." He suggested: "Those applications providing preliminary results that were not in agreement with the retracted papers were given a rough time" (ibid.). It appears as though when set next to a flashy visualization of protein structure, claims that challenged Chang's models were "dismissed as just old-fashioned biochemistry" (C. Miller, 2007: 459). Chang's peer-reviewed publications demonstrate the power of a "beautiful" picture to silence even expert critics. Once published and affixed in the literature, his structures stood unchallenged as *the* models of these proteins for six years.

In January 2007, Chris Miller (2007) published a letter in *Science* in response to what he called Chang's "Great Pentaretraction." He turns Chang's "devastation" (G. Miller, 2006: 1856) into a cautionary tale presenting a tough lesson in pedagogy and training for students in the seductive arts of molecular visualization:

> [W]hile an embarrassment to the authors, [it] nevertheless provides the rest of the field with some small measure of comfort beyond mere schadenfreude. The mistake so clearly illustrates two lessons that we aging baby boomer professors ram down the throats of our proteomically aroused

> graduate students: (i) that those lovely colored ribbons festooning the covers and pages of journals are just models, not data, and (ii) that you invite disaster if you don't know what your software is actually doing down there in the computational trenches. Students have a hard time subsuming these dicta into their souls for two reasons: the tyranny of authority (the vanity journals occupying the vanguard) and the inherent beauty of the macromolecular models that emerge, as if by magic, from the user-friendly crystallographic software accumulated over decades through the generous labor of the field's talented reciprocal space-cadets[13]... (C. Miller, 2007: 1875).

Miller points to two key challenges crystallographers currently face in training their excitable, easily enchanted students: how to teach them to be wary of the awesome and dangerous beauty of the visual "facts" produced through molecular modeling; and how to get them to think critically about how their labour-saving computer software helps them craft these structures. In this brief manifesto, Miller tethers the problems of visualization to problems in pedagogy and training and locates this knot at the central matter of concern for the future of his field. I think Miller has his finger on the pulse of what is at stake in structural biology today: how in the face of increasingly alluring graphics and augmented automation are crystallographers able to keep their critical, craft skills alive?

A generational transition is underway in structural biology labs today. Miller and his "aging" colleagues grew up in an era when they had to write their own codes: from the 1970s through to the late 1990s protein crystallographers developed their own algorithms to process and visualize crystallographic data. Though she looks quite youthful, Diane Griffin is also part of this generation: her students call her "an old school crystallographer," and she proudly dons this moniker. As a graduate student she wrote her own code using

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[13] "Reciprocal space" is a technical term for the space into which crystallographic structures are built.

FORTRAN: as such, she knows how her programs work, can anticipate the kinds of bugs that are hard to avoid when writing programs, and so understands how easy it is to introduce errors into crystallographers' massive data sets and iterative calculations. Like others of her generation, she does not trust software to handle the data correctly: she insists that crystallographers must be vigilant and constantly keep computed processes in check. Today, many of the crystallographic model-building programs have been standardized and entire suites of software have been made available to crystallographers to process and visualize their data. Master crystallographers' (who Chris Miller refers to as "reciprocal space-cadets") skills and labour have been "generously" given over to the software; once embedded, they are effectively hidden and can no longer play a pedagogical role in training future crystallographers. Working only on the surface of the user-friendly interface, students can no longer "dig in" to the "guts" of the code,[14] and thus have no idea how the models get churned out of their computers.

Diane, like Miller, is also concerned about the seductive potential of the "inherent beauty of the macromolecular structures," which seem to overpower students' critical faculties, making them forget that the structures they produce are just models, not the thing itself. In an interview about protein crystallography as a visualization practice, Diane and I discussed how crystallographers assess the truth claims of images, given the context of a culture in which they are constantly bombarded with visual facts. I asked her: "How do they become critical readers of images? How do they develop the skills to be able to assess something they are really interested in?" To this she responded:

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[14] See Turkle et al. (2005) for how researchers in a number of fields describe codes as the "guts" of the computer.

> Yes, yes. That is very, very important. And I've found too that people will take a picture as a fact in a way that they really shouldn't. Because it is just one image, and it can move and it can change. And people come and say, "But I thought this distance [between amino acids] was 3 angstroms[15] period." And like, that's the end of the world! "It's three point zero, zero." You know, a structure can be incredibly valuable, but it is a *model*! A model of something that *moves*! And that really you need to think about it, and think about where the data came from, the quality of the data and all these other things. And it sometimes can be too powerful, and kind of stops people from thinking about something that they still should be thinking about.

The seduction of visualizations was one of many themes that myself, Sherry Turkle, Joseph Dumit, Susan Silbey, Hugh Gusterson, Yanni Loukissas, and David Mindell explored in our collaborative NSF-funded study on computation, visualization, and changing professional identity across fields in science, engineering, and design (see Turkle, et al., 2005). In May 2005, Diane Griffin attended one of series of meetings that we had organized for this project. These meetings brought together life scientists, architects, nuclear weapons designers, materials scientists, and engineers in the fields of biological, aeronautical, astronomical, and marine research. We were interested in hearing from them how their computer-intensive technologies were transforming visualization in their respective fields, and where practitioners in these different fields were experiencing similar problems. In ways that resonated with the nuclear weapons scientists and others now relying on computer modeling, Diane expressed much anxiety over the "pretty pictures" that people in her field could generate so easily, with all their new, "fancy" software.

> The way that we usually present our X-ray data is by making Ribbon drawings of the protein structure [see Figure 1.1], just traces the backbone of the structure. It used to take a long time to make those pictures. If you were presenting the initial structure, say at a meeting, where it wasn't

[15] An angstrom is the measurement of the distance between atoms. One Angstrom is equal to 1.0×10^{-10} meters.

> published yet, it was kind of the original model and you weren't quite sure of everything yet. The picture you would show would represent that it wasn't really done. It wouldn't be a fancy picture yet because it would take such a long time to make it. Now you can make it in 2 seconds, you know...the program spits out pretty pictures and when you show that the people go "Oh! It's all done!" And you can stand up there and say, "These are sort of the distances but don't believe them. Big error bars! Not finished yet! Just a rough idea!" And they'll just hold on to it and go "This is done because look how pretty it is!" So we now on purpose make ugly figures to show its not really done yet. Because they don't listen to you: they see it with their eyes. [Laughing in the background] You have to show them something ugly if you don't want them to set on this and have it be the truth forever.

Here she spoke directly to Miller's concern with the students' seduction by the authority of visual images presented in "vanity journals." As she recounted, it "used to take a long time" to make pictures. Automated software now enables crystallographers sitting at computers to "spit out" "pretty pictures" at high speed. Once the labour of model and image making is hastened through the fast graphics capacity of contemporary computers, and pretty pictures are a dime a dozen, members in this field must recalibrate how they assess visual claims to truth.

The skills Diane Griffin and Chris Miller are trying to cultivate in their students is what could be called a *critical epistemology of visualization* (see Turkle, et al., 2005). Diane, for one, has put extensive effort into educating members of her laboratory and graduate students across her campus how to exercise their critical judgments over the data and images that computers churn out. She wants to make sure that structural biologists-in-training know the "dark dirty secrets of crystallography," so they can see "where structures can go wrong." As she told me in one of our first interviews:

> I do a recitation on how you evaluate a structure. And so I tell them all the ways that they can cheat. You know, what are good statistics, and how can you make your statistics look better when they are not good. And so, I go

> through this whole lecture on how to really evaluate a paper. And what are the important caveats in the structures? And, you know, how do you know what's real? How do you know what to believe? You know, part of me is on sort of a little bit of a crusade, because I think there is a lot of wrong information out there.

It is worth noting that it is not just the students who have to be trained to be critical visualizers. The reviewers of Chang's papers were apparently equally seduced.

So how are protein models built? And what precisely does a crystallographer contribute to the model building process to ensure its accuracy and prevent such blunders? It is in attempting to build their first structures that students begin to discover just what it is they have to bring to their data. Dehlia a fourth year PhD student in Diane's lab whose first structures were already published in *Nature*, told me: "And one thing I didn't realize when I started building is the extent that ... you have to start making executive decisions." Her lab-mate Amy, a fifth year PhD student who had been having incredible difficulty solving the structure of a new protein she was working on, confirmed this in a separate interview. She emphasized that:

> A lot of guesswork goes into [building a structure]. And guesswork isn't the best word to use; maybe subjective would be the best word to use to describe it. And that's not something you can understand until you actually have a structure that you have done yourself, or are in the middle of doing. The first structure I did was an easy one. I was really surprised that it was up to me to put in [amino acid] residues. It was up to me to put the [polypeptide] backbone in. I was just really surprised...That it was something that I could make a mistake and no one would know. Its kind of scary, and it makes you really wary about other structures sometimes.

Not only do they need to be able to discern where and when the computations are off, they need to make "executive decisions" about where amino acids go in the structure, which confirmations of atoms are energetically feasible, and which defy allowable bond

angles or inter-atomic distances. To do their work well students must cultivate sound judgments that demonstrate a respect for protein forms. This situation thus presents a very steep learning curve for crystallographers-in-training, and students often make mistakes when attempting to build their first structures. Producing sound structures requires what Diane calls "manual thinking," set of skills that can't be relegated to computers. As such she resists automation of what she sees as the crystallographer's irreducible contribution to model building (see Chapter 2). In other fields of visualization, such as PET (Dumit, 2004), automation is seen the best way to remove bias and produce objective results. In protein crystallography however, where the automated software can't be trusted, the only way to ensure quality data and prevent error is through constant human intervention with the computing processes. Thus for Diane and the students she trains, crystallographic model building continues to rely extensively on human labour. She has actually banned the use of some automated software in her lab. Angered when she discovered that one of her students had used this software to help build part of a model, she made the student repeat the modeling work by hand. Her mistrust of automation was vindicated when the student discovered that the computer program had indeed gotten the structure wrong. Automation amounts to cheating in some ways for Diane because it sidesteps the laborious training process necessary for crystallographers to cultivate this kind of "manual thinking," and to develop and exercise expert judgment (see also Turkle et al., 2005).

Where Chris Miller aims to tame naïve students' thirst for labour-saving automation and their appetite for stunning visuals, he stops short of identifying precisely what the skills are that these novices need to cultivate in order prevent bungling further structures. For me, the Chang debacle confirms what I have found repeatedly in my research: that

crystallographers' expert knowledge depends on a range of craft skills and tacit knowledge that have not been successfully automated. Chang's mangled models also show that cultivating these skills in a new generation of scientists actually constitutes a quite a significant achievement. It is the primary aim of this study, then, to identify precisely what these skills are, and to determine how they are propagated within structural biology communities.

Before I introduce my approach to the formation and transfer of tacit knowledge within this field, in the following sections I situate this ethnography within the context of an emerging literature on models in the visual cultures of science, and studies of pedagogy and training.

Models and the Visual Cultures of Science

Philosophers and historians of science Nancy Cartwright (Cartwright et al., 1995; Cartwright, 1997), Evelyn Fox Keller (2000b; 2002), Mary Morgan and Margaret Morrison (1999) have made vocal and well-heeded contributions to the literature on a wide array of scientific models, including two-dimensional diagrams, flow charts, and analogical models, among others. This work builds on movements in the history, philosophy, and sociology of science to reorient long entrenched assumptions about science as a theory-driven activity. These scholars aim to overturn a "semantic" view of theories which identify models as iterations of and therefore dependent on theory. This literature, thus joins forces with a larger body of work in the social studies of science that brings to the fore the tacit knowledges, social negotiations, moral economies, work cultures, and figural vocabularies

of scientific practice.[16]

If it is possible to make a generalization about scientific models, it is that they are ambivalent objects that are hard to pin down. Hacking suggests "models are doubly models": they are both representations of theories and of phenomena (1983: 216). Morrison and Morgan describe this dual function of models as their capacity to set up a "relation" to their two referents: both theories and the world (1999: 25). Yet a model can be a theoretical elaboration, an empirically informed abstraction, a "conceptual hallucination" (Gilbert and Mulkay quoted in Lynch, 1990), or all of these at the same time. Sergio Sismondo (1999) suggests that models and their kin (simulations) occupy a "messy category," one that we should not try to clean up (1999: 258). Models spread out across a "continuum" of possible forms and functions and "cut across boundaries of pure categories": they are "monsters necessary to mediate between worlds that cannot stand on their own, or that are unmanageable." (1999: 247).

Three-dimensional models are another species entirely. More than visual traces, marks or inscriptions, three-dimensional models explicitly blur the boundaries between automated machinic productions and the skilled work of scientists. Counter to the myths of disembodied "mechanical objectivity" that tend to pervade scientists' accounts of visualization practices (Haraway, 1991; Daston and Galison, 1992), three-dimensional modeling practices make explicit scientists' creative and embodied contributions to visualizing life. They also disrupt assumed binaries between the intellectual and physical

[16] See for example: Collins (1985), Shapin and Schaffer (1985), Lynch and Woolgar (1990), Kohler (1994), Galison (1997), Haraway (1997), Mol (2002), Prentice (2005), and Suchman (2007) among many others.

labour of research: in practice, three-dimensional models are improvised, handcrafted artifacts that articulate scientists' intuitions and observations; they are recursively made and remade in attempts to conceptualize and actualize new hypotheses and new modes of inquiry. Moreover, three-dimensional models—whether physical or virtual—are malleable, interactive objects. In other words, these models demand corporeal engagement; and it is in a modeler's entanglements with a model that both the model and the modeler's imagination are subject to continual transformation. I argue that modeling practices challenge narrow conceptions of "thinking" as a cerebral activity, and make visible how craftwork, creativity, and modes of embodiment are central to scientific reasoning. As I examine more closely below, models also open up new insights into the foundational role of teaching and learning in the making of both science and scientists.

Pedagogy and Cultures of Model-making

The problems of pedagogy and training in structural biology are salient at this moment when educators and researchers in this rapidly expanding field struggle to find ways to introduce protein structures into classrooms and innovate molecular visualization techniques in the laboratory. They are involved not so much in the task of "generational reproduction," as in a kind of generational innovation—training students in a body of knowledge and skills, and through pedagogical regimes that are distinct from those that characterized their own disciplinary formation.

Until recently, historians have largely regarded three-dimensional models as "mere"

"memory tools" or "mneumotechnical devices"[17] that aid in teaching and learning, with little to offer scientific research. The low status of models in the historical and social studies of science literature reflects a general lack of interest in pedagogy and training in science.[18] In an attempt to recuperate a lost history, recently several scholars have endeavored to resuscitate models as lively objects in research contexts.[19] These scholars have shown how scientists rely on models as objects-to-think-with: models are the skilled craft products of scientists' observations and intuitions; they are continually built and rebuilt in attempts to produce new insight and new ways of knowing.

And yet, with the notable exception of David Kaiser's (2005a) study of the dispersion of Feynman diagrams in postwar physics, few studies have cultivated an interest in the lives of models as pedagogical tools. With Kaiser, I assert that physical and virtual models, diagrams, analogies and animations are essential tools, not only for research, but also for teaching; and that pedagogy and training are vital to the scientific enterprise. There is much to learn from analyses of how life scientists teach each other how and what to see, and how to apply techniques and technologies to model and remodel life. It is insights

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[17] The term "mneumotechnical device" is used in Cambriosio, et al. (1993: 681), to describe models as tools used to aid the memory.

[18] For notable exceptions see Kaiser (2005a, b) and Warwick (2003). Other studies have shed much insight into this arena. In the STS literature, pedagogy studies have focused on various themes, including: trajectories of training (e.g. Traweek, 1988); the "moral economies" of laboratories and apprenticeship training (e.g. Kohler, 1994); disciplinary formation (e.g. Bourdieu, 1990; Fleck, 1979; Foucault, 1995; Kuhn, 1996; Keating et al., 1992; Maienschein, 1991); the stabilization and dispersion of knowledge and tools through pedagogical and institutional networks (e.g. Clarke and Fujimura, 1992; Kaiser, 2005a; 2005b); the physicality of scientific training and theoretical work (e.g. Kaiser, 2005a; Warwick, 2003); the inculcation of tacit and craft knowledge (e.g. Bourdieu, 1998, 2004; Collins, 1985; Latour, 2004; Olesko, 1993; Polanyi, 1958; Warwick and Kaiser, 2005); and the problems of generational reproduction (e.g. Gusterson 2005).

[19] See for example Francoeur (2000), Hopwood (1999), de Chadarevian and Hopwood (2004), Cambrosio, et al. (1993), and Keller (2002).

into pedagogy and training that can help shed light on the *formation* of the visual and practical cultures that give body to science.

In an illuminating analysis of the varied cultures of modeling in twentieth century biology, Evelyn Fox Keller (2002) demonstrates the historical instability of models as explanatory systems that aim to account for biological phenomena. She explores a number of model-making traditions in the history of biology, and shows how members of this diverse research community distinguished themselves by their use of particular kinds of models and explanatory frameworks. Her analysis shows that models have been at the center of debates among scientists struggling to assert the legitimacy of their techniques. Through an account of variations in modeling practices, she poses the question: What kinds of evidence could count as an explanation of a phenomenon at different points in the history of biology? She situates the wide diversity of models within the context of shifting explanatory frameworks that governed which kinds of models were accepted, contested or ignored. For Keller, it is the variability in the criteria of what could count as an explanation that is of historical and philosophical interest. For her, these criteria are determined by the specific "needs" of scientific communities, and it is this set of needs that circumscribe what she calls "epistemological cultures." For her, an epistemological culture is made up of "the norms and mores of a particular group of scientists that underlie the particular meanings they give to words like theory, knowledge, explanation, and understanding, and even to the concept of practice itself" (2002: 4). Epistemological cultures are then, distinct communities who share practices and knowledges, including visualization techniques and criteria for the adjudication of scientific evidence.

It is at this juncture, the branching off of distinct epistemological cultures, that questions of pedagogy and training gain import for social studies of science. What is the *process* by which researchers-in-training become oriented with an epistemological culture? In the present study of structural biology communities, I am interested in the *formation* of epistemological cultures and the forging of professional identities through training regimes that inculcate students in particular ways of seeing and knowing. In the present study, I examine the formation of epistemological cultures—cultures of seeing and knowing—around protein modeling techniques. I draw on Kaiser's (2005a) study of the introduction of new theoretical tools in physics as a guide for examining the introduction and disciplinary installation of new visualization practices in structural biology. As Kaiser shows, Feynman diagrams depended on pedagogical "dispersion" before they could attain wider use and consistent interpretation; and in the context of institutional expansion in cold-war physics education, science educators were actively involved in stabilizing and relaying these visual theoretical tools through pedagogical networks. Writing with historian of science Andrew Warwick, Kaiser proposes that Michel Foucault's (1973, 1995) insights into "institutional gazes, bodies, gestures, architectures, routines, incitements, examinations, and punishments" can be extended to examine regimes of training in the making of scientists (Warwick and Kaiser, 2005: 402-3). Foucault's articulation of the productivity of power makes it possible to track the "positive economy" of training and discipline—that is, how regimes of "institutionalized training" shape both the students' bodies and the very grounds of knowledge taught (399). New subjectivities and new knowledge, as well as new institutional forms, are produced in the process. My study in turn examines how protein visualizations and discourses are propagated and stabilized in classrooms and laboratories at a unique moment, when—enticed by the promise of drug

discovery and biomedical innovation, and fueled by a post-genomic funding regime that has boosted interest and investment in the life sciences—a multi-disciplinary group of researchers are converging on protein structures. As they render protein forms through multidimensional interactive digital media, they are also producing a new generation of scientists with a new vision and feel for molecular life.

Modeling Bodies: Three-Dimensional Models in the History of the Life Sciences

What kind of scientific object is a molecular model of a protein? I begin this inquiry by locating protein models in a growing literature on three-dimensional models in the history of the life sciences. Contemporary practices of molecular modeling can be included among older traditions of three-dimensional model-making which have thrived throughout the history of the life sciences. This long and varied history of the construction and use of three-dimensional models has recently captured the attention of scholars tracking the material cultures of the sciences (e.g. See for example Haraway, 1989; Daston, 2003; de Chadarevian and Hopwood, 2004; Hopwood, 1999; Francoeur, 1997; and Star, 1992). Three-dimensional models are essential visualization tools for teaching, learning and research in the life sciences. Familiar examples of these include models of animals and plants preserved in natural history museums, and those used for teaching and research in anatomy, embryology, and evolutionary biology. The enduring materiality of these models (and their stabilization through the institutional structure of museum culture) ensured maximal access to specimens not otherwise available. In the domain of natural history, the scientific purpose of these models was the precise characterization and display of natural forms in reproductions that could demonstrate taxonomic classification schemes, theories

of evolution, and morphological specificity. The kind of representational accuracy sought in such models of animals and plants was descriptive. It is assumed that it is by virtue of their power to replicate or simulate the likeness of a given phenomenon that these models functioned as scientific models. However, as I shall suggest below, it is also their representational power that rendered their status as scientific objects vulnerable.

Many of these three-dimensional models can be seen to fit within a tradition that some have called "mimetic modeling." In *Image and Logic*, Peter Galison (1997) describes how the "image tradition" in particle physics originated within a practice of "mimetic" experimentation. Physicists brought the "morphological sciences" of cloud formation into the laboratory through attempts to mimic the properties and processes of atmospheric phenomena, reproducing them in cloud chambers in the laboratory (1997: 80-91). In this particular permutation of physics culture, "seeing" and "believing" were intimately entwined. Providing what Galison calls a "homomorphic" representation of the process, these mimetic models evoked in the viewer a sense of equivalence between the model and phenomenon (106). Within the mimetic tradition that Galison describes, the measure of an effective model was its verisimilitude, its likeness to the phenomenon under investigation. Thus, the explanatory force of the cloud chamber experiments was bound up in its capacity to successfully mimic natural processes (69): it was in this "similarity relation" (Morrison and Morgan, 1999: 29) between world and model, that the cloud chamber could produce evidence for theories about cloud formation. As other examples of mimetic models show, it was the similarity relation of the model to the thing modeled that provided experimental proof of the theory in question (see also Keller, 2002).

In her study of the shifting institutional organization of natural history museums, Susan Leigh Star (1992) quotes a turn-of-the-twentieth-century taxidermist attesting that his task was "not to depict the mere outline of an animal on paper or canvas and represent its covering of hair, feathers or scales." This would imply a reduction or abstraction of the phenomenon. Rather, it was his work "to impart to a shapeless skin the exact size, the form, the attitude, the look of life" (quoted in Star, 1992: 262). Taxidermy is a good example of what James Griesemer calls "remnant modeling," where the skins of the very animals modeled are stuffed and posed to mimic lively bodies. He suggests that such models are able to "serve certain sorts of theoretical functions *more* easily than abstract formal [models] by virtue of their material link to the phenomena under scientific investigation" (1990: 80).

Lorraine Daston includes taxidermy in a larger modeling tradition she calls "extreme mimesis" (2003: 31), a tradition which, for her, is best exemplified by The Glass Flowers, an extensive set of exquisitely crafted botanical models produced by glassblowers Leopold Blaschka (1822-1895) and his son Rudolf Blaschka (1857-1939) between the years 1886 and 1936 under commission from Harvard University. As replicas of botanical forms, these models were nearly flawless. Daston, admiring their craftsmanship, remarks "though the actual deception of appearance taken for reality lasts only for a moment, the pleasure of potential deception lingers long" (2003: 8). It was this ability to deceive the viewer into believing that the model was the thing it represented that seems to have defined the potency of such models as scientific objects. However, these were also objects whose status as works of science had been most difficult to defend. Models that embody such extreme mimesis have tended to get caught between traditions of art and science, between

the designations of artisanal objects and scientific tools. Daston suggests that there was indeed a time in the history of biology when "the verisimilitude that is called illusionism in art" could become "scientific accuracy" (2003: 8). As I discuss below, it is partly because of their association as works of art, that mimetic models such as these now occupy the most ambiguous category of scientific models.

For Morrison and Morgan, effective models are "renderings," not mimetic "reflections" of phenomena (1999: 27). As their examples from physics and economics demonstrate, the measure of a model is not its approximation of reality: its legitimacy is derived from its usefulness, by how it "performs" in its applied context (1999: 28). Thus it is the use of a model as a tool in scientific research that determines its status as a scientific object; for them, the usefulness of a model is derived from its function of abstraction, its ability to eliminate extraneous details, to pare down the phenomena to its essential features.[20] As in physics and economics, examples of such renderings can be seen in wide use through the history of biology in the form of mathematical models, diagrams, flow charts, and cartoons. Such renderings are effective, in their view, because they balance representational and instrumental features. Thus as "realistic," multi-dimensional forms, mimetic models doubly defy the kind of abstraction, efficiency, and ease of movement that would make them useful as scientific tools. They do not conform to Bruno Latour's "immutable mobiles," that range of flattening inscription practices that promise efficiency in their movement through networks, and deftness in mobilizing allies to resolve arguments over scientific claims.[21]

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[20] See for example Lynch (1991); Morgan and Morrison (1999); Rheinberger (1997).

[21] For analyses of how the widespread practices of three-dimensional modeling in biology opens up a critique of Latourian analysis, see Hopwood (1999) and Francoeur (2000).

Mimetic modeling thus introduces a mutation into our contemporary expectations of the function of models. It would seem that a model as complex as the phenomena it stands in for would be counter-productive to the analytical work of science.

Indeed, mimetic models did not perform well under such demands. Star's exploration of taxidermy shows that the American life sciences underwent a dramatic shift at the turn of the century towards experimental, physiological research, moving "away from realist representations of nature, and away from concrete instantiations of nature's panopoly" (Star, 1992: 261). Because mimetic models could not parse phenomena into abstract elements, they were assumed to function primarily as memory devices or teaching aids. The models were deemed less useful as heuristic devices or tools in research; they worked better as demonstrations of preexisting theory or as physical instantiations of classification schemes. As such, they came to be seen as ineffective mediators within the context of experimental biology, and were relegated to the status of pedagogical objects for public instruction. Today they are more readily seen as curious objects of art. Star suggests that one of the reasons for this was the institutionalized division of labour between professionalized scientists and amateur modelers, a division of labour that rendered the producers of these models craftspeople and artisans, rather than scientists (1992: 261). While such divisions of labour may have represented the institutionalized status quo, they also served to elide the artisans' contributions to science.

How is it, then, that protein models have such high status in the life sciences today? Are structural biologists not merely glorified artisans caught up in the scientifically useless task of producing yet further instantiations of "nature's panopoly"? How can a model depicting

the precise location of thousands of atoms—a model as complex as the molecule it is supposed to represent—be used to do analytic work? I suggest that the answers to these questions require examining how model-building practices are themselves a kind of scientific work. I am particularly interested in what shifts when concerns about the representational status of these models are held in abeyance. Rather than adjudicating models according to their representational power, that is, how well they represent nature, I want to examine what else, other than likeness, is generated in the process of building models. How do these models do more then represent nature? How do they animate imaginations, and generate knowledge in their very construction and use? I propose approaching models through the idiom of "enactment" (see Mol, 2002; Barad, 2003) to explore what forms of life are brought into being in the process of building and using models. I do this by paying attention to how three-dimensional models are crafted, and the forms of knowing that are conjured in the process. My first step however, is to take a look at how discourses of representation tend to elide the work of the modeler, by focusing on the end product, rather than what is produced in the modeling process.

Representations or Renderings of Nature?

> [T]he term "model" is probably best understood as a verb, with the authors as subject, and the experiments and the conceptual schematic as a single, unparseable, composite object. Only at the end of the process do we have a separate entity—a model as a noun...
>
> Evelyn Fox Keller[22]

Is an atomic-resolution model of a protein also a mimetic model? Like the mimetic models

[22] See Keller (2000b: S82).

described above, molecular models are supposed to *represent* the precise configuration of atoms in a protein molecule. There is, however an important distinction: unlike the other three-dimensional models, protein models lack a visible referent. The atomic structures, textures, and other physical qualities of protein molecules are not visible in the same ways that macroscopic or even microscopic phenomena are available for inspection and corroboration. Even high-powered electron microscopes don't offer "direct" views of protein molecules.[23] Thus, there is no available visible referent, no tangible molecule against which the likeness of the model can be measured. Molecular models are thus, in many senses, "made up."[24]

Max Perutz, a Nobel Prize winning crystallographer recounted a fascinating moment of slippage when a molecular model was interpreted as a mimetic representation of molecular worlds. He recounts a story about how he and his colleagues from the Laboratory for Molecular Biology in Cambridge presented their famous molecular models of DNA and proteins to the Queen of England. "When we proudly showed [the models to] the Queen and her party, one of her Ladies-in-Waiting exclaimed: 'Oh, I had no idea we have all those little coloured balls inside us!'"[25] Seduced, this unwitting "Lady" mistook the models for life-like representations, as if they were true-to-life amplifications of the very material substances in her body. Perutz narrates a comedic scene that pokes fun at—and simultaneously solidifies—anxieties about the risks involved in producing models that

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[23] Direct vision, is of course a ruse. Ian Hacking (1983) for one insists that you can't actually see through a microscope: you see with it. Keller's (1996) essay "The Biological Gaze" develops Hacking's thesis of representation as intervention further for the field of biological microscopy.

[24] See Hacking's (1986) essay "Making Up People".

[25] Perutz (n.d.) "The Medical Research Council Laboratory of Molecular Biology."

could seduce unwary viewers into believing that they are mimetic representations. The Ladies-in-Waiting are like the naïve students and peer-reviewers that Miller wants to educate against the seductive power of visual facts. What he attempts to "ram down the throats" of his "proteomically aroused" students is that a protein model is only ever *just a model.* It is at its barest a set of atomic coordinates, points in space that are overlaid by a range of colourful diagrammatic conventions that instruct the viewer in how to look and how to interact with the data in different ways. So, while a protein model is supposed to accurately define the atomic coordinates of a molecular structure, it does not provide viewer seamless visual access to molecular realms.

Thus, where a mimetic model of an animal of plant could produce what Daston refers to as the "pleasure of potential deception" (the moment where a viewer might mistake the glass flower for the thing itself), this is not the case for molecular models of proteins. The pleasure is curtailed by rampant anxieties among members of the structural biology community about the dangers of potential *seduction*: their primary concern is that, like the Ladies-in-Waiting, naïve viewers could be seduced into believing that molecules actually resemble the model. Evaluating protein models within the idiom of representation thus leads invariably to a discourse bound up with anxieties about how molecular representations (including notational conventions, and the particular media used to model proteins) can overdetermine the look and feel of otherwise subvisible molecular worlds.

Though their status as research objects has been questioned, the mimetic models described above are indeed powerful representations of nature: they could, as proxies, stand in for otherwise absent living bodies, and re-present the artful forms of nature. Yet as

representations, they are what Keller calls "models as nouns", "separate entities" at the "end of the process" of modeling. In my view, protein models are more than *"representations of"* molecules, and more than *"representations of"* scientific knowledge. My aim is to theorize models outside of the idiom of representation, so that they can be seen, not just as objects that stand in for phenomena, but as *forms of knowing,* as knowledge in-the-making. I am interested in the way that three-dimensional models do not represent things, as much as *enact* them, and in the process produce new forms of knowing for the modeler. My first move, then, is to reexamine "models as verbs" rather than as end-state representations. One way to effect this move is to shift from a discourse of representation—which too easily slips into the realm of "model as noun"—to one of *rendering,* an idiom which can gather up the modeler and their media, and make tangible the very activity of modeling.

Thus, my sense is that if protein models are regarded merely as end-stage *representations of* molecules, then they certainly do have the power to seduce uncritical viewers. However, I'd like to re-read Perutz's account of his presentation of his models to the Queen outside of the idiom of representation. While his script perpetuates gendered roles for the uncritical, impressionable (female) viewer, and the expert (male) scientist, there is an important difference between the expert modeler and the novice viewer that deserves to be explored further. Where the Lady-in-Waiting mistook the model for the thing itself, it should be noted that "no chemist" worth their mettle "would propose that models, even in their more elaborate forms, are about what molecules 'really' look like" (Francoeur, 1997: 12). As historian of chemistry, Eric Francoeur (2000) suggests, in the hands of expert crystallographers, molecular models operate through "homology" rather than

"homomorphy" (64)[26]; that is, they indicate forms and relations between elements, rather than replicating the look and feel of the object. How, then, is it that these models can operate so differently in the hands of their makers? What might account for this difference? I propose that seen as verbs, as visualizations-in-the-making, models are not necessarily dangerous seductions, but powerful "lures" that can entangle and entrain their modelers' bodies and imaginations, and entice them into new visions of molecular worlds.[27] As such models are potent training devices; and modeling practices become, then, means for training novice researchers how to look, how to feel, and what to care about in the molecular realm.[28]

As my dictionary reminds me, the term *rendering* is multivalent. A rendering can indeed be a representation of something, as in a translation, a work of art, or a detailed architectural drawing. But a rendering is not just an object that can stand in for something else; rendering as a verb is also the activity of producing these representations. In this active sense of the term, a rendering can be a performance, as in the rendering of a play or musical score. In this sense, renderings can carry the mark of the artist, such that as the performer enacts it, a musical score is inflected with unique tones, textures and affects. Another use of the term is in the field of computer modeling, where a rendering is "the processing of an outline image using colour and shading to make it appear solid and three-

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[26] Francoeur develops Peter Galison's terms "homomorphy" and "homology" in relation to the representation function of molecular models. See Francoeur (2000).

[27] On abstractions as "lures" see Isabelle Stengers (1999; n.d.). For a fuller description of models as lures, beyond of the representational context of deception and seduction, see Chapter 2 of this study.

[28] See Maria Puig de la Bellacasa (forthcoming) on how "thinking with care" can transform feminist ethics and politics. I am particularly interested in tracking how scientists think and work with care, and how this approach can transform ethnographic accounts of their practice.

dimensional" (Oxford American Dictionary). In this sense, a rendering is the modeler's elaboration, addition, or augmentation of a simpler thing. To render is also to provide, hand over, or submit (as in to render up a verdict or a document), each of which are performative gestures that pass an object or communication from one person towards another. Heard in a different register, to render is also to tear, or rip things apart. In a lively discussion about rendering practices among an interdisciplinary gathering of life scientists, architects, engineers and anthropologists, Sherry Turkle interjected: "My grandmother used the term rendering to describe what she did to chicken fat!" Indeed, to render is also to "melt down," to process and separate, as in rendering fat from bone, and extracting proteins, and other usable parts from an animal carcass. What holds all of these diverse uses of the term together is that each refers not just to the object that is rendered, but also to the subject, the one who renders, and the activity of rendering.

As the skillful productions of highly trained craftspeople, mimetic models do more than just represent nature: they are renderings that refer back to their modelers. In this regard, Leigh Star (1992) is careful to document the intense and "messy" work involved in the production of the "look of life" in dead animals; and like Star, Daston (2003) also emphasizes the labour, artisanal skills and craftsmanship that went into constructing the Glass Flowers. Yet, precisely how does the modeler interact with their media? What kinds of insights and what kinds of learning are generated as the modeler works between objects, theories, modeling media, and machines in the model-building process? I ask: If a modeler who renders nature in three-dimensions aims to conjure likenesses of natural form, what else do they engender in the process?

Nick Hopwood's (1999) treatment of the history of late-nineteenth century embryological modeling practices provides a key to this question. Hopwood documents embryologist Wilhelm His's (1831-1904) techniques for sculpting scale models of embryos in wax. In defense of a mechanical theory of embryological development, His had developed a method for precisely reconstructing the form of embryos from the details derived from microscopic examination of tissue slices. Using a microtome (the invention for which His is most renowned), projective drafting techniques and freehand wax sculpture, His worked the sectioned images into exquisite three-dimensional form. This was a craft that demanded much artisanal skill. His promoted embryological research as active work that enlisted the scientist's eyes, mind, and hands. His scale models aimed for a "more direct bodily apprehension of form" (1999: 482); this would enable the modeler to build up a "three dimensional mental image," and the value in this for His was that "the pictures in the memory that have once made their way through the hand stick much more firmly in the head" (quoted in Hopwood, 1999: 483). Hopwood sees His's commitment to modeling as "a passionate argument for doubly embodied knowledge" (1999: 482). In Hopwood's reading, His's insight into the mechanical processes of embryogenesis was gained through the physicality of building models. His "had first to make his problem, to use his fingers", and it was by this method that he was able to "'to give body' to his views". In giving material form to the embryos he also "gave body" to his theory. In the process His developed an embodied knowledge of the phenomenon in the practice of making models, such that that the problem of development became familiar to his body. As Hopwood argues, it was "the experience of modeling" that was "the most compelling evidence of the importance of mechanical principles in development" (Hopwood, 1999: 466). His thus learned the mechanical forces of embryogenesis by working with the forces of physical

materials, and with the physics of his body.

Caught up in the interactive physicality of model building, His became *entangled* in the modeling media: he worked over the wax to sculpt embryological forms; and the media, in turn, worked over his body and his imagination. As Hopwood demonstrates, three-dimensional model building is a kind of corporeal and imaginative performance that trains the modeler's body. In this sense, His's models were not merely *representations of embryos,* or *representations of knowledge*; his models were *performances as knowledge*. In other words, His's models were *enactments*, which, in-the-making, engendered new forms of knowing.

Modeling Proteins, Making Scientists: Forms of Knowing in Structural Biology

Hopwood's insights into His's three-dimensional wax modeling techniques have import for thinking through the skills and knowledge structural biologists gain building protein models through interactive computer graphics. In this study I argue that protein crystallography, and structural biology more generally, are exemplary fields for tracking the formation and transfer of tacit knowledge and craft skills in science. The task of constructing models, and interpreting the structures and functions proteins is not straightforward. In interviews, structural biologists have emphasized that it is "hard" to "learn how to think intelligently about structure," and to acquire the skills to "see what the structure is saying." This kind of expertise is especially difficult to cultivate in novice students. While formalized chemical and physical laws do inform their work, structural

biologists must also draw on a realm of knowledge that has not been codified in order build and interpret structures. In addition to understanding how computer algorithms are crunching their data, students must learn how to visualize and analyze biochemical structures as objects that take up space and move in time. They have to learn how to make sense of these structures and hypothesize what it is proteins are up to in the cell: how it is that they perform their chemistry and physically interact with each other and with other molecules. This is a daunting task; these "massive," dynamic molecules are made up of thousands of atoms. Therefore, in their classrooms and laboratories, structural biologists must find ways to cultivate a *feeling for the protein* in their students (see Chapter 2).

In the present study, I explore how structural biologists acquire this feeling for molecular form. I examine three intertwined processes: the forms of knowledge generated as researchers build models of protein molecules; the modes through which this knowledge is propagated between and among researchers and their students; and the formation of professional identities around the construction and interpretation of these models as visual facts. I show how classrooms and laboratories are becoming sites for training a new kind of scientist whose forms of knowing are attuned to the chemical affinities, physical forces, and movements of protein structures, and keyed to the tangible logic and rhetoric of a mechanistic, though surprisingly lively vision of molecular life. I argue that protein visualization and interpretation relies heavily on a set of practices that I describe as the "body-work" of modeling in structural biology. I explore how researchers' bodies become key resources in producing knowledge about protein structure, and in propagating such forms of knowing between and among researchers and students. Several modes of body-work are at play in structural biology. They include forms of kinesthetic knowledge gained

in the process of building and manipulating molecular models through various media, including physical and virtual forms. Researchers also use their bodies as experimental media, performing not only thought experiments but what could be thought of as "body experiments": their bodies become mimetic media to help them figure out how proteins move and interact. A third mode of embodied reasoning includes researchers' application of narrative strategies that assume a teleological relationship between form and function, and which figure—and so give form to—proteins through analogies with familiar human-scale phenomena. Narrated and visualized within in the realm of physical, embodied experience, proteins take form onscreen, in language, and in experiment in two distinct, though often overlapping registers: as both "lively bodies" and as "machines." The body-work of modeling in structural biology, then, is an entwined "material-semiotic" practice (Haraway, 1997) for producing and propagating knowledge about molecular forms. By examining protein models as renderings, I can track the production of new forms of knowing and regimes of training to shed light on both the making of a new kind of science, and a new kind of scientist.

Ethnographic Forms of Knowing: Accounts of Gesture and Affect Among Protein Modelers

> If ideas cannot be comprehended without a history of the gestural knowledge and the objects through which they came to be expressed, and to which the terms of their expression most directly refer, then history of scientific ideas is a poor history indeed.
>
> James Griesemer, 2004

Philosopher and historian of biology James Griesemer (2004) notes that accounts of three-dimensional modeling practices must include a history of the "gestural knowledge" through which models are made and used. Studies of scientific representations, then, need to take into account the enactment of models: the "gestural as well as symbolic knowledge and the variety of means and modes of making, experiencing, and using models" (435). This concern with the kinesthetic knowledge generated by building and using three-dimensional models poses a methodological challenge for studies of pedagogy and visualization in structural biology. Protein structures and functions not only can't be reduced to metaphors of code for the scientist, their production and deployment can't be fully captured in the texts scientists write. Accessing the visual cultures of structural biology thus requires attending to the dynamics of researchers' bodies engaged in the enactment of molecular models.

I argue that visualization in structural biology is inherently performative.[29] Structural biologists communicate the fine structures of three-dimensional and temporal objects to their colleagues and students in several ways: by animating their models onscreen using interactive computer graphics; and by pulling the models off the screen and animating them through gestures and affects, using their bodies as mimetic models to articulate and relay the forms and movements of the molecule. Such extra-textual descriptions of molecules come alive in formal talks, class lectures and informal communication between researchers within and outside of the laboratory. These modes of body-work facilitate communication, and at the same time they provide a means by which researchers can use

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[29] On performance in science see Barad (2003), Doyle (2003), Mol (2002), Latour (2004), Pickering (1993), Herzig (2004), and Prentice (2005).

their bodies to "figure out" and hypothesize how proteins might fold and interact with each other (a practice that is both enabling and constraining for how they imagine molecular worlds). I suggest that molecules can become visible—and, indeed, palpable and thinkable—when structural biologists build and use models. Thus, structural biologists not only "do things with words," in the sense that Austin (1975) defined "the performative," they craft expert modes of communication and reasoning through gesture and body-work (on performativity see Butler, 1993; Goffman, 1959; Phelan, 1993; Rotman, n.d.; Sedgwick, 2003). Moreover, they enroll a new generation of life scientists in these forms of knowing, by tacitly and explicitly training their students in these subtle modes of communication through body-work.

This study offers a contribution to methodological innovations in the growing body of literature in the anthropology of scientific practice[30]. The central objects of life science research are no longer flat or static. As the objects in life science change, so must the methods of the analyst. Geertz's (1973) call to attend to the many layers of expression and communication in cultural practice, is especially salient for this study which aims for a "thick description" of the interpretive practices of structural biologists. For Bourdieu (1977), studies of practice require going beyond an "objectifying standpoint which grasps practices from outside, as a *fait accompli*" (1977: 4). He aims, rather, to develop an ethnographic technique that can emulate the "generative principle" of a practice by "situating" the ethnographer "within the very *movement*" of its "accomplishment" (ibid.).

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[30] See for example Downey and Dumit (1997), Dumit (2004), Franklin (1998), Franklin and Lock, (2003), Gusterson (1996), Hayden (2003), Heath (1998), Helmreich (1998, forthcoming), Knorr-Cetina (1999), Latour (1986, 1987), Lock (2002), Rabinow (1996), Sunder Rajan (2006), Thompson, (2005), and Traweek (1988).

Refusing "second order" abstractions that elide temporality and turn practice into an analytic object, such methods aim to account for the strategies, improvisations, and slips, and the rhythms, tempo, and orientations of practice "on the ground" (ibid.: 5-8). Such methods attune my attention to the performance or enactment of scientific knowledge in practices of teaching, learning, and visualization.

This study proposes a new approach for STS analyses of the performance of scientific knowledge—a method that can document and analyze the body-work of visualization, interpretation and communication among practicing scientists. Tracking the performance of models demands methods that can document the dynamic interplay of models, bodies, and imaginations. To communicate their multi-sensate molecular knowledge, structural biologists (including X-ray crystallographers, protein folding researchers, and biological engineers) often perform the structures and movements of their proteins through elaborate gestural forms. Using their entire bodies, including hands, arms, shoulders, head, neck, torsos, and even legs, they can articulate and relay their intimate knowledge of molecular forms and movements. Erving Goffman (2001) has suggested that conducting such a study would demand that the ethnographer "tune" his or her body "in" to the daily activities and practices of those they study; a practice that requires subjecting one's own body to gain a richer interpretation of the plays of affect, gesture and language in the field (154-155). In order to tune myself into and parse the dense thicket of "figural vocabularies," gestural knowledge, and tacit practices, I draw on over 25 years of training in classical and modern dance. This expertise gives me the skills to attend closely to others' corporeal techniques, and enables me to draw on my own affinity for movement in order to detect, recall, and relay researchers' subtle bodily affects, including the tempos, rhythms, and tones that

propagate through their performances of protein models. As a situated knowledge practice, my analysis thus makes no attempt to mask the ways in which I *move with* and am *moved by* the life scientists I study.

Chapter Overview

This study is laid out in six chapters, each of which builds on ideas fleshed out in the others, to address a range of themes on pedagogy and visual cultures in structural biology. Each chapter approaches the topic from a different angle, diffracting my ethnographic fieldwork in structural biology through a different crystalline array of histories and theories of modeling, embodiment, practice, and performance in science.

Following this introduction, Chapter 2 "Molecular Embodiments and the Body-work of Modeling in Protein Crystallography,"[31] builds on both ethnographic observations of contemporary protein crystallographers and historical accounts of early molecular modeling techniques to examine the *body-work* of crystallographic model building. In this chapter, I pay special attention to the media used for building crystallographic models and the corporeal practices through which modelers learn the intricate structures of protein molecules. I show how, in the process of building and manipulating protein models, crystallographers also sculpt *embodied models* alongside the digital renderings they craft onscreen. I explore how crystallographic modeling at the computer interface is thus not only a means of producing representations of proteins; it is also means of training novice

[31] This chapter is forthcoming as an article in *Social Studies of Science*. See Myers (forthcoming a).

crystallographers' bodies and imaginations. I examine how protein crystallographers' *molecular embodiments* offer a site for posing a new range of questions for studies of the visual cultures and knowledge practices in the computer-mediated life sciences.

Chapter 3, "Performing the Protein Fold: The Pedagogical Lives of Molecular Models,"[32] explores the relations among teaching, learning, and imagination in science. I examine how structural biologists approach teaching as a means to articulate their students' embodied imaginations of molecular forms. Moving from the emphasis on crystallographers-in-training in the laboratory (Chapter 2), this chapter shifts to examine pedagogical practices in the setting of an undergraduate classroom. In this chapter I am concerned with the formation of molecular imaginaries in those who have not yet gained access to expert knowledge. As an ethnographic observer in an undergraduate lecture course on protein folding, I show what the instructors must do in order to communicate their tacit knowledge of protein forms and movements to their students. I examine several pedagogical techniques, including: the instructors' use of human-scale analogies to lure students into molecular worlds; their performance of physical models in order to teach students what they must do with their bodies in order to learn how proteins fold; their projection and play with interactive computer graphics media; and their elaboration of molecular forms through the medium of their bodies. I develop the concept of gestural modeling as a form of mimetic modeling; by *becoming molecular*, I show how instructors can perform nuanced models of protein folding for their students. This chapter serves then, to show how pedagogy and training in science require that instructors remodel their

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[32] This chapter is accepted for publication as an article in Sherry Turkle's edited volume, *The Inner History of Devices: Ethnography and the First Person*, forthcoming with MIT Press. See Myers (forthcoming b).

students' bodies, not just inspire their minds.

Chapter 4, "Modeling Molecular Machines: Structural Biology, Biological Engineers, and the Materialized Refiguration of Proteins,"[33] makes the shift from the context of biology classrooms, to examine how structural knowledge of proteins is refigured within the cultural milieu of biological engineering education. In this chapter I explore how proteins have been figured and refigured in the historical and contemporary scientific literature and in current pedagogical discourses in biological engineering. In Chapter 3 I observed an oscillation between proteins figured as lively bodies and proteins figured as molecular machines. By contrast, in Chapter 4 I examine how, for whom, and in what contexts, structural biologists clamp down on the metaphor of molecular machines. I draw on Donna Haraway's cyborg feminist (1991; 1994; 1997) theory of "materialized refiguration," and treat the metaphor of molecular machines as an adept visualization technology that can render proteins visible, tangible, and workable as machines and also as an enticing *lure* that can to recruit biological engineers-in-training. Yet, I show how the material and semiotic labour structural biologists invest in constructing an amazing array of different kinds molecular machines inside the bodies of cells gets elided when the metaphor of machines is conflated with the molecule itself. Building on Haraway's (1997) elaboration of "genetic fetishim," I show how a kind of "machine fetishism" is operative in contemporary structural biology. And yet, by treating "materialized refigurations" like molecular machines as renderings, that is as forms of knowing that are enacted and performed, I show how the tropes that these investigators are constructing produce a kind

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[33] This chapter is accepted for publication as an article in Sharon Ghamari-Tabrizi's *NatureCultures: Thinking with Donna Haraway*, forthcoming with MIT Press. See Myers (forthcoming c).

of molecular machinery that is undeniably lively.

Chapter 5, "Animating Mechanism: Animations and the Propagation of Affect in the Lively Arts of Protein Modeling,"[34] is a sustained mediation on the performance of molecular mechanisms, and the nature of the media structural biologists use to animate their hypotheses about how proteins move and interact. Where mechanical models of life may seem, on first glance to parse living bodies in ways that deaden lively processes, I build on feminist contributions to the science studies literature to show how, rather than spelling the "death of nature", mechanistic reasoning in the life sciences can become a site for feminist inquiry into modes of embodiment and the role of affect in the performance of scientific knowledge. I re-read the interactivity of protein modeling through Karen Barad's formulation of "intra-action" to show how bodies, media, and machines are entangled in the production of animations of proteins in both virtual and embodied media. I demonstrate how, through their embodied animations of molecular movements, structural biologists enliven molecular mechanisms as a means to open up the mechanisms to understanding, and then propagate this lively knowledge among their colleagues and students in pedagogical and professional contexts. I argue that this mode of embodied animation is not an extra-scientific phenomenon, but an experimental practice that supports the work of mechanistic modeling. Though structural biologists may boast that they have captured "life itself" in the form of molecular machines, this chapter examines how their narratives of capture slip and slide into narratives forms that simultaneously express their affective entanglements, their passions, and desires that arise in responsive

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[34] This chapter has been published in a special issue on the Future of Feminist Technoscience in *Science Studies*. See Myers (2006).

relation to the proteins they lovingly model. In the conclusion to this study, I examine much more closely my own investments in transforming stories that script science as a practice geared towards the "capture of life itself"; and show how this study aims to *transduce* life scientists' narratives of liveliness by hitching a ride on the excitements and passionate forms of knowing structural biologists engender in their modeling work.

Chapter 2

Molecular Embodiments & The Body-work of Modeling in Protein Crystallography

Introduction

X-ray crystallography is one of the primary techniques used to generate structural data from which molecular models of proteins are constructed. Protein crystallographers use interactive computer graphics technologies to build three-dimensional, atomic-resolution models of the intricate molecular structure of proteins. I ask Diane Griffin, a professor of chemistry and biology, who heads a protein crystallography lab, about the challenges her students face learning to model proteins in three-dimensions (See Figure 2.1). She tells me that it is hard to learn how to "think intelligently about structure." She points to the steep learning curve her students face trying to master X-ray crystallographic techniques, and enumerates the challenges of building molecular models and interpreting the functions of proteins from molecular forms. Acquiring the skills to "see what the structure is saying" is "hard to do, and it takes time," she tells me, but eventually "you do get better at it." She describes what often happens when her graduate students show her computer graphic renditions of their molecules in the early stages of the building process. "Look I connected it!" they proudly declare, presenting their model to her. Yet, when she examines their models in detail, looking closely at the bond angles between the amino acids and the direction of the polypeptide chain that winds through the protein, her response is often anguished: "What did you do to that side chain? No! No! Let me move it back!"

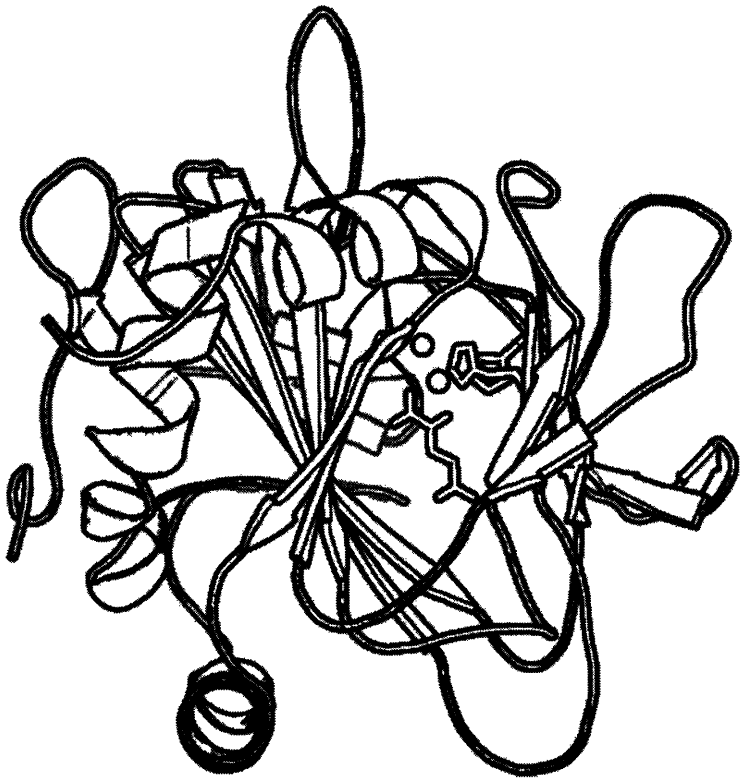

Figure 2.1: Ribbon diagram of a protein molecule. Close up detail shows the active site of the protein. Used with permission from an anonymous ethnographic informant.

As she tells the story, she contorts her entire body into the shape of the misfolded protein. With one arm bent over above her head, another wrapping around the front of her body, her neck crooked to the side, and her body twisting, she expresses the strain felt by the misshapen protein model. "And I'll just get this pained expression," she tells me. "I get stressed just looking at it... It's like I feel the pain that the molecule is in, because it just can't go like that!" She feels compelled to fix the model. She mimes a frantic adjustment of the side chain by using one arm to pull the other back into alignment with her body, tucking her arms in towards her chest and curving her torso over toward the core of her body, demonstrating the correct fold. With a sigh of relief she eases back into a

comfortable position in her chair. The comically anguished look on her face relaxes back into a warm smile.

Apparently, the students in her story had not yet acquired a *feeling for* the proper molecular conformation. In a mode evocative of what Evelyn Fox Keller (1983) has described as Barbara McClintock's "feeling for the organism," Diane expresses her feeling for the molecule. As her gestures and affects convey, corporeal knowledge appears to play a key role in her ability to "think intelligently" about protein structure. What she demonstrates here is that structural biology is a craft-practice that demands embodied knowledge.

This chapter examines how practices of protein modeling rework conventional understandings of the relationships between model and modeler, and mind and body. Ian Hacking (1983) makes a distinction between "models you hold in your hand"—material models made with "pulleys, springs, string and sealing wax"—and "models you hold in your head," conceptual models and mental images which function through analogy and imagination (Hacking, 1983: 216). Yet, if we take seriously Diane's experience of the pain of the misshapen molecule, such a distinction between "models-in-the-hand" and "models-in-the-head" does not hold. While Hacking draws these two kinds of models apart, I would argue instead for a deeper entwining of material and conceptual models in the *embodied imagination* of the modeler. Diane carries more than a "mental image" of what a molecule should look like in her head[35]: seeing, feeling, and moving with the

[35] The term "mental image" is widespread, and is often used to think through notions of the scientific imagination. See for example Meinel (2004) and Trumpler (1997). See also Sacks (2003)

chemical constraints of the molecule, she has *embodied* molecular forms. Maurice Merleau-Ponty's (1962) phenomenology of perception argues that sensation and movement are intimately tied to visual understandings of form. Diane demonstrates well how this coupled nature of seeing and feeling is played out in crafting structural knowledge.

As life scientists increasingly "give body" (Hopwood, 1999) to molecular biology, the methods of the ethnographer must keep pace. Diane's acquired feeling for the molecule clues us in to some of the complex corporeal practices that are involved in "thinking intelligently about structure." Crystallographic protein modeling is a time-consuming process of constructing models from experimental data using interactive materials, both physical and virtual. This chapter aims to show that it is through the "body-work" of crystallographic model-building, that is, through the labour of constructing, manipulating, and navigating through protein models onscreen, that researchers are literally able to come to grips with—and so make sense of—molecular forms and functions. In addition to the intensive labour required to conduct X-ray crystallographic experiments,[36] or the other tacit knowledges involved in the wet lab work of protein biology, three modes of body-work are brought into relief in the field of protein crystallography.[37] I term these the body-work of

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for an elaboration of the diversity and complexity of mental images.

[36] From the arduous calculation and analysis of crystallographic data, to the physical labour of operating the machinery of experimentation, crystallography is labour intensive practice. Diane, describing the intensely physical experience of conducting experiments and gathering data at synchrotrons, jokes that researchers need to train at the gym to ensure that they're fit enough to handle the heavy doors that protect them from the high-intensity X-ray beams. On the issue of the intensive labour of crystallographic calculation, and the allocation of this work to women in the early history of crystallographic computing see de Chadarevian (2002).

[37] On tacit knowledge see for example Collins (1985), Polanyi (1958), and Rheinberger (1997).

incorporation, communication, and *reasoning,* in order to foreground the role of researchers' bodies in learning, relaying and interpreting the specificities of protein forms and functions.[38] As I demonstrate in this chapter, the slow, reiterative, interactive work of crystallographic modeling enables researchers like Diane to incorporate molecular models into their embodied imaginations. Once embodied, these models come alive in researchers' performative gestures as they communicate the fine details of protein structures. They use this mode of body-work in conversations within and outside of the laboratory, and in conference presentations and classroom lectures. Throughout the chapter, I draw on Diane as an exemplar and as a guide to help pose new questions about the role of researchers' bodies in life science practice. While Diane may appear to be an exceptional case—she could be construed as an "expressive" scientist, having studied drama in addition to chemistry as an undergraduate at Vassar College in the 1980s—interviews with her male and female students and colleagues, and among researchers within the wider field of structural biology show that her "feeling for the molecule" is in no way exceptional, and, indeed, participates in a significant and wider phenomenon among experienced protein modelers. That a "feeling for the molecule" is widespread among experienced modelers raises significant questions for social studies of pedagogy in science, as the transfer of the tacit knowledges through modes of body-work in protein modeling pose challenges for training a new generation of structural biologists.

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[38] This is of course, an artificial parsing of what is a much more entwined process. My observations suggest, for example that the body-work of communication, the elaborate gestural expression of molecular form is intimately involved in the process of reasoning. In Chapter 4 I show how researchers conduct "body-experiments," much like "thought-experiments", where they use their bodies to work through and reason through such dynamic phenomena as intra-molecular forces or inter-molecular interactions. In Chapter 2 I show how these performative practices are also a mode that enables incorporation, a way for the modeler to learn possible molecular forms and movements.

Though the history of structural biology is rich with accounts of model-building, limitations in the historical record make it difficult to study model-building in practice. In addition to providing insights into contemporary protein crystallography, this ethnography offers a re-reading of historical accounts of early protein crystallographers. In historical and contemporary cases, I examine the role of corporeal knowledge in crystallographic modeling in both physical and virtual media, attending to how early developers of interactive molecular graphics sought to preserve the tangibility of virtual models. Throughout, I pay attention to what protein researchers have to do with their bodies in order first to acquire and then communicate this embodied knowledge of molecular structure. What I find is that crystallographic model-making is not only a means of building molecular models: it also offers a training ground for the modeler—a means of reconfiguring researchers' embodied imaginations with knowledge of protein forms and movements. Working with and building multidimensional models of proteins are practices that rearticulate researchers' bodies. Exploring the nature of such *molecular embodiments*, this chapter offers a contribution to the history and anthropology of science, with insights into the role of researchers' bodies in the visual cultures of the computer-mediated life sciences.

Fleshing out the Folds of Molecular Forms of Life

This shift in attention from reading and writing DNA sequences to modeling protein forms has methodological implications for social studies of scientific practice and visual cultures. Tracking the movements of the metaphor of code closely, analyses of molecular biology

have tended to focus their interpretations at the level of the language that scientists deploy in their texts (see for example Doyle, 1997). However, social and historical studies whose methods map too closely to this metaphor, and rely entirely on text-based readings of the rhetoric of code, miss out on a wider range of practices that have contributed to the making of molecular biology. The current intensification of protein structure research, with its elaborate modeling techniques that draw on intuition and trial and error, and which demand performative modes of body-work, makes it clear that an exclusively rhetorical analysis is inadequate to the task. The production and deployment of protein models by life scientists resist reduction to text for both scientists and social scientists. Accessing a "thick description" (Geertz, 1973) of the representational forms and practices in molecular biology thus requires more than decoding the textual productions of scientists; in addition to the semiotics of models, it requires attending to researchers' *corporeal* and *affective entanglements* with available concepts and modeling media, and with the visualization machinery they entrain on living substances.[39] Taking embodiment seriously in protein modeling demands the ethnographer attend to the subtle enactment of models in the process of building, using, and reasoning through their forms. In this sense, the ethnographer must, in turn, develop a *feeling* for scientists' movements, gestures, and affects, for how structural biologists work with their objects. These are practices that can be difficult to record and relate, and so to convey the subtler dimensions of the craftwork, tacit skills, and creativity of scientific practice ethnographers and historians need to develop new competencies for tracking bodies and embodiment. To remedy analyses that

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[39] Donna Haraway's (1991, 1997) theory of "material-semiosis" comes closest to an analytic modality that can account for the conjoined material and semiotic processes through which researchers combine words, gestures and materials to give body and meaning to proteins in their construction of molecular models.

flatten both molecules and practices, this chapter aims to flesh out the "liveliness," (Haraway, 1997: 137) and "body-fullness" (Haraway, 2001) that structural biologists perform through their work.

The Body-work of Molecular Model-Making: A Brief History

Some of the most striking features of the wide range of three-dimensional models used in biology are their tangibility, manipulability and amplification to a human scale. This is perhaps most apparent in the case of molecular models, those playful ball-and-stick "Tinker-toys" representing atomic structures familiar from high school chemistry laboratories (see Francoeur, 1997). Structural biologists have built and used models of protein structures from crystallographic data since the late 1950s (de Chadarevian, 2002; Francoeur, 1997). Eric Francoeur (1997, 2000, 2001; Francoeur and Segal, 2004) has documented the history of molecular models in chemistry and biochemistry, detailing how they have been improvised, standardized, and disseminated. Made from metal, plastic, cardboard, Styrofoam balls and toothpicks, balsa wood and elastic bands, three-dimensional models have amplified the molecular world to sizes and forms, and in styles, manageable and imaginable for their users and admirers (see also Bassow, 1968). And beginning in 1963, structural biologists produced molecular models that flickered on analog computer screens, creating an entirely new medium for molecular visualization (Levinthal, 1966; Francoeur and Segal, 2004).

While the media in which molecular models have been built has changed significantly over the years, modeling materials have consistently been selected for their tangibility and

manipulability. Francoeur shows that a special feature of molecular models is that that they "embody, rather than imply, the spatial relationship of the molecule's components" (1997: 14). Such models can be manipulated and analyzed:

> Like many other types of object handled by scientists in the field or the laboratory, they can be touched, measured, tested, dissected or assembled, and tinkered with in many different fashions. In other words, they act as a material analogy (14).

Building physical analogues of molecules thus requires handling and a mode of thinking and working that is spatial. As Francoeur notes, the "working out" and "sorting out" of structures with physical models is a kind of "thinking with the hands" that has long been an integral part of the work and knowledge of chemists and biochemists (2000: 6). This practice of "thinking with the hands" is well exemplified by a canonical story often told in the history of structural biology. Linus Pauling is remembered for his exceptional skills modeling proteins in three-dimensions: his "discovery" of the structure of the alpha-helix, while lying in bed with the flu in Oxford in 1948, has become legend (see also Nye, 2001). In an obituary for Pauling, Max Perutz, who was then competing to determine the same structure, describes how Pauling figured out the alpha-helix, "amus[ing] himself by building a paper chain of planar peptides" while laying in bed, until he "found a satisfactory structure by folding them into a helix" (Perutz, 1994: 670). This process of "discovery" required him to improvise with ready-to-hand materials. "Giving body" to molecular form, he fleshed the molecule out in order to figure out the spatial organization of atoms (see Hopwood, 1999).

In the history of three-dimensional modeling practices, such work has not been easy.

Molecular modeling in three-dimensions requires concerted effort and great patience. In his account of the "discovery" of the helical structure of DNA in the early 1950s, Watson (1969: 62) reminisced that his and Crick's "first minutes with the models" were "not joyous." "Even though only about fifteen atoms were involved, they kept falling out of the awkward pincers set up to hold them the correct distance from one another" (62). Indeed, he had to keep "fiddling" with the models to get them to hold together (122). As he and Crick got closer to determining the structure they sometimes spent whole afternoons "cutting accurate representations of the bases out of stiff cardboard" (123) to produce models of nucleotide pairs that could be shuffled in and out of different pairing possibilities. This was an improvisational practice that eventually enabled them to give form to the DNA molecule and figure out how the nucleic acids adenine and thymine, and guanine and cytosine could pair to form the double helix (ibid.). Molecular model-building with physical materials is thus a time consuming, trial-and-error ridden process that requires physical engagement and exploratory interaction with often finicky materials.

The models themselves were built in a range of different media, each of which afforded particular kinds of bodily interaction and manipulation. Some of the materials even revealed the work of their makers. In 1957, John Kendrew's laboratory in Cambridge, U.K., produced the first model of a protein. Made out of thick tubes of black Plasticine and supported on wooden pegs, it was nicknamed "the sausage model" (see Figure 2.2). As this frame, shot from an "in house" movie of the making of the sausage model at the Laboratory for Molecular Biology (LMB) reveals, the model builder appears not to have been Kendrew,

but one of the many women who were employed in his laboratory.[40] In addition to providing what was a shocking and "visceral" view into the molecular realm,[41] this model also offered a record of the performance of the modeler. That is, the pliable Plasticine medium recorded the movements and gestures of the modeler's handiwork.

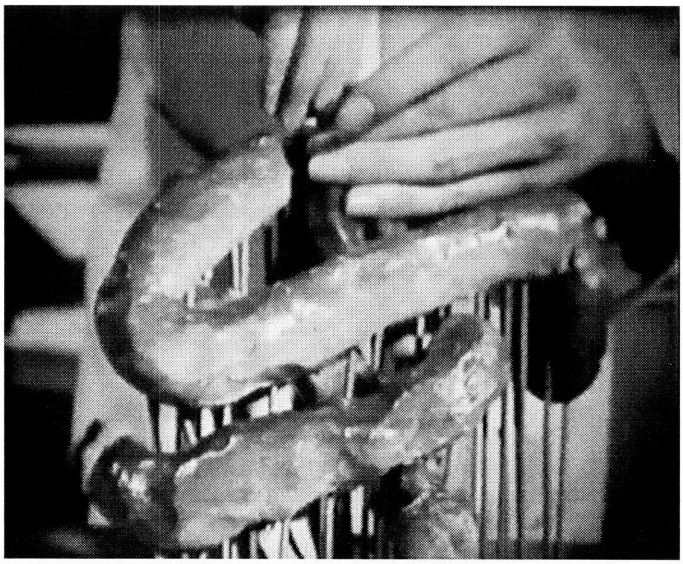

Figure 2.2: Building the "sausage model" of myoglobin. A screen-shot of the making of the first model of a protein molecule from a movie produced in Kendrew's laboratory at the LMB. Used with permission from the MRC Laboratory for Molecular Biology.

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[40] In *Designs for Life*, Soraya de Chadarevian (2002) examines the history of women in protein crystallography laboratories, in particular the women technicians, or "computors" who, before the advent of computer graphics, were responsible for most of the labour of computation in crystallographic experiments, measuring crystallographic data by hand and using punch-card computers. As this frame-shot shows, these women were apparently also involved in the craft of model-building.

[41] After the model had been built, people who viewed the model marveled at the "visceral" quality of the model. Kendrew and others expressed surprise at "unexpected twists the protein chain was performing" (de Chadarevian, 2002: 142). In Chapter 3, I explore further how biophysicists had expected proteins, substances that could form regular crystalline arrays, to be simple, symmetrical structures.

When attempting to build his earliest models of haemoglobin in the early 1960s, Max Perutz also tried Plasticine, but when this material proved too unstable for his more complex molecule, he resorted to cutting thermo-setting plastic into topographical sections that he stacked one on top of each other, baking the model to set it permanently into shape (de Chadarevian, 2002: 143) (see Figure 2.3).

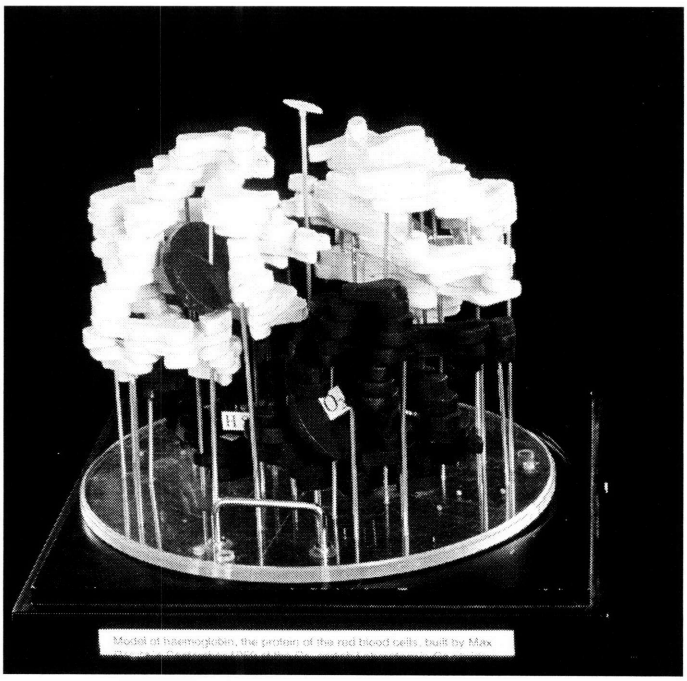

Figure 2.3: Max Perutz's low-resolution model of hemoglobin made with thermo-setting plastic. Used with permission from the MRC Laboratory for Molecular Biology.

However, this rather clunky, low resolution, model could not articulate the fine detail of hemoglobin's atomic structure, or be used to demonstrate the subtle movements of hemoglobin's molecular mechanism. Perutz was later able to produce atomic-resolution

models of hemoglobin using standardized, machined ball-and-stick parts (Francoeur, 1997). The adjustable links between atoms along the polypeptide chain made possible through such modeling kits provided the opportunity for the modeler to manipulate the model. The mechanical properties of these models could be engaged dynamically, and performatively, as a means to make arguments about molecular function.[42] In a video interview conducted towards the end of his life, Max Perutz can be seen moving a ball and stick version of his haemoglobin structure in and out of different conformations, demonstrating with delight the effect of oxygenation on the structure of the heme group (see Figure 2.4)[43]

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[42] It is significant that different levels of resolution and different materials rendered proteins in very distinct ways. The sausage model portrayed the myoglobin as a "rather vulgar" (Perutz, 1968) body, with an anatomy that could be "dissected" (see de Chadarevian, 2002). High-resolution models built from standardized machined parts made proteins look much more machinic, with clean lines and movable parts, and made them available to be manipulated as chemical mechanisms. As I show in Chapter 3, this shift has made it possible for proteins to be figured through the now pervasive metaphor of "molecular machines."

[43] See interviews with Max Perutz online. "Face to Face with Max Perutz" Vega Science Trust <http://www.vega.org.uk/video/programme/1> Also shown alongside Perutz and his mechanical model is a video clip of an interactive molecular graphics screen animating the same movements onscreen. Perutz's handling of the model is also described in de Chadarevian (2002).

Figure 2.4: Stills from a video of Max Perutz demonstrating the chemical mechanism of the oxygen binding heme group of his atomic-resolution model. Used with permission from The Vega Science Trust. Interviews with Max Perutz can be viewed at: http://www.vega.org.uk/series/facetoface/perutz/

Thus, it is important to take into consideration the various media used, not only to understand how modelers *represented* protein molecules—what they were fashioned out of and what they looked like—but also for understanding how as *renderings*, these distinct media engaged modelers bodies in different ways. Different materials afforded different modes of interaction and manipulation, and different kinds of insight into the molecular realm.

The Digital Materiality of Interactive Molecular Graphics

The contribution of researchers' bodies to model-building has not been lost with the

transition to virtual media. Indeed, interactive computer graphics aimed to facilitate modes of embodiment more conducive to model-building. As crystallographers improved their techniques, acquiring higher resolution data, and modeling increasingly complex proteins, the use of physical materials for molecular modeling became more difficult. Material models became far too large and cumbersome to build, subject as they were to the unfortunate effects of gravity and mechanical stress. This was a lesson learned by one group of molecular modelers based in Manchester, U.K. in the early 1960s. After their elaborate model of a protein made of balsa wood and elastic bands collapsed in the dry and dusty basement in which they were working, they went so far as to contemplate building their model underwater in a swimming pool to cancel the effect of gravity (see Francoeur and Segal, 2004: 412). Following his failures to model proteins in balsa wood at Manchester, C. David Barry, one of the members of this group, joined MIT biologist Cyrus Levinthal at Project MAC to help develop the first interactive computer graphics work station for visualizing, manipulating and predicting protein structures (Francoeur, 2002; Levinthal, 1966). Between 1963 and 1967, Levinthal, in collaboration with Barry and others, developed an interactive molecular graphics machine they jokingly nicknamed "The Kluge" (see Francoeur and Segal, 2004). This interface made use of a "crystal ball" (an early mouse) and light pen to enable control of rotation and the selection of specific coordinates of the structure. Offering an improvement over the swimming pool option, interactive graphics can be thought of as the first practical zero-gravity chamber for molecular modeling.[44]

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[44] Thanks to Stefan Helmreich for this analogy. Interactive graphics does seem to offer a gravity-free, buoyant environment for protein modeling. Indeed, as Donna Haraway reminds me, interactive computer graphics may in some ways reproduce the watery worlds that support protein structures in their cellular environments.

Once interactive graphics had already begun to take hold of the molecular modeling community, Robert Langridge, a key supporter of Levinthal's work at Project MAC, articulated the benefits of molecular graphics over working with physical models. In a 1981 paper reviewing advances in computer graphic modeling he wrote:

> Space filling or wire models are satisfactory up to a certain level of complexity, but purely mechanical problems cause serious difficulties since the model on the bench and the list of [atomic] coordinates in the computer are not necessarily closely related (*especially after the model is degraded by many curious hands*). Particularly difficult is the restoration of a structure after simple modifications. With computer graphics, the display and the data are directly related, storage of prior configurations is simple, and pieces do not fall off (Langridge et al., 1981: 661, emphasis added).

As it turns out, it was the very pliability of physical molecular models that was both their greatest virtue and greatest limitation as working tools. The haptic dimension involved in the manipulation and handling of physical materials was key for the production of models that could give modelers a sense of the structure and dynamics of the molecule, and offered a means for researchers to use their bodies to incorporate structural knowledge. However, once available to "curious hands," these toy-like structures tempted continuous reworking and tweaking, eventually leading to conformational distortion. Motivated to overcome the challenges faced in working with physical models, while inspired by the tangibility they offered, crystallographers and computer scientists collaborated to develop interactive computer graphics technologies for building protein models onscreen.

Early researchers' accounts of the development of computer hardware and software in

interactive molecular graphics reveal how they approached the problem of preserving the tangibility and manipulability of models in making the transition from physical to virtual modeling. What becomes clear from their accounts is that an intimate relationship between user and computer had to be engineered into a workstation interactive enough to keep the modeler physically engaged in model-building. With interactive computer graphic techniques the crystallographer is intimately coupled to the computer screen through an array of input devices that aim to mimic some of the aspects of physical model-building. Eric Francoeur and Jerome Segal's (2004) history of the emergence of interactive molecular graphics makes it clear that while this interactive technology offered a medium distinct from the physical models previously used to investigate structures, these tools preserved the tangibility of other media used in protein modeling. The embodied nature of this early interactive graphics technology was not, however, immediately obvious to the uninitiated. At a Gordon conference in 1965, Robert Langridge presented the Kluge system to an unenthusiastic audience. As he recalled, one crystallographer "objected that a graphics display would simply not do as a substitute for physical models, since he had to have his hands on something, something physical, so that he could understand it." For Langridge, "standing up at a conference and showing 16mm movies, in the early days, was really not a good substitute for sitting in front of the computer and actually using it. When you first got your hands on that crystal ball at Project MAC and moved the thing around in three dimensions it was thrilling. There was no question" (Langridge quoted in Francoeur and Segal, 2004: 418).

The early developers of these programs sought to generate the "smooth handling" of graphic models in "real time" on the computer screen. They aimed "to produce an illusion

(a hand-eye correlation) strong enough that the operation required to manipulate the model via the computer" could become "instinctive" (Barry, et al. 1974: 2368-9). In this way the molecular graphics "map and model" could be "manipulated almost by hand" (Tsernoglou, et al. 1977: 1379) For Langridge "smooth rotation of three-dimensional objects is one of the most important elements in making use of the display seem "natural" to persons used to handling "real" molecular models (Langridge, 1974: 2333). He explained that at the time there was, however, "no precise definition of the terms real-time and interactive": "The difference between interactive and noninteractive uses of computer graphics depends on how long you are willing to wait to see a result" (Langridge, et al., 1981: 666). "Satisfactory" interactions demanded advancements in the speed of computer processors, but also patience on the part of the user (ibid.).

In the hardware systems that emerged later, a whole new array of input devices were developed and used to enhance the human-computer interface in the simulation of a "real-time," interactive modeling experience.[45] Switches, knobs, joysticks, tablets—and a range of apparatuses to generate the experience of "3D vision" through stereoscopic technologies—connected the user to the maps and models they could manipulate on screen. By the early 1980s, a number of different technologies were available to produce these stereo effects. Robert Langridge and his co-workers (Diamond, et al., 1982) describe one stereovision system, where "left and right perspective views are presented alternately.

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[45] In an article called "The Human Interface," M.E. Pique (1986) writes: "Ideas spreading from Xerox PARC and Atari, through the Apple MacIntosh and the Commodore Amiga, will reach molecular graphics during 1986: pop-up windows, pull-down menus, more than one thing going on at a time. During the next 5 years, users and builders will make molecular systems more like video games, with mice and trackballs, some joysticks that are specialized by function, and the working system easier to use and more fun."

When they are viewed through a synchronized shutter, each of the observers' eyes sees only its associated image, and the result is perceived as a stereoscopic image with a strong sense of depth of field" (286). Creating the three-dimensional effects and the "illusion" of depth through stereoscopic techniques, however, assumes that the user has binocular vision. So attentive to the interaction between users' bodies and the graphics hardware, and convinced that "a good ten percent" of the population has difficulty seeing in stereo, a group of researchers at the Laboratory of Molecular Biology in Cambridge devised an elaborate optical system to simulate three-dimensional perception for "one-eyed guys." Reworking the physiology of vision for one- or two-eyed researchers, such innovations of stereoscopic techniques attest to their inventors' recognition of the embodiment of seeing.

Remarkably, what interactive computer graphics developers achieved was more than "an illusion" of connection between modeler and model: the interactive graphics workstation became a prosthetic extension of a physically engaged modeler into a very tangible world of graphic molecules. Ensuring that protein researchers experienced the physicality they had come to expect from their molecular modeling work, interactive molecular graphics developers offered a successful alternative to modeling with physical materials. In the process they also produced a new kind of tangibility for virtual objects.

In 1977, Tsernoglou and his collaborators (Tsernoglou, et al., 1977) reported the successful modeling of a protein entirely through interactive graphics technologies. The complete transition from physical to digital models did not however, take place overnight. Physical models retained pedagogical value. In the early days of protein crystallography, crystallographers like Perutz, Kendrew and Dorothy Hodgkin built large-scale three-

dimensional electron density maps out of physical materials. They would trace slices of electron density on transparency paper, and stack these between Plexiglas sheets, building up a physical model of the electron density map layer by layer (see Kendrew 1964; de Chadarevian, 2002; see below for a description of electron density maps).[46] In the 1960s, Diane's advisor Susan Fielding participated in building the first model of an enzyme using these early techniques. Diane trained in Susan's lab in the 1990s. At that time interactive computer graphics programs were already readily available for constructing three-dimensional electron density maps onscreen,[47] yet Susan insisted that her graduate students first learn how to build physical models of electron density using Plexiglas sheets. Diane explained Susan's rationale for this pedagogical exercise: digital graphics could only

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[46] Kendrew describes modeling from such stacks of electron density as a process of "dissection," such that "from the map it was possible to "dissect out" a single protein molecule" (Kendrew, 1964: 681). According to reviewers assessing developments in the field by 1975, this method proved "almost unbelievably cumbersome" (Collins et al., 1975: 1049). This is particularly true since many different maps would have to be constructed and compared. Collins and his colleagues (Collins et al., 1975) outlined how, in1968 at Yale University, Frederic M. Richards came up with an innovation that radically transformed the work of mapping and modeling. The Richard's "optical comparator," "Richard's box," or "Fred's Folly" as it came to be known, "revolutionized the interpretation of protein electron density maps" (1049). The device projected an optical illusion, making it appear as if a wire model was "embedded" within the three-dimensional electron density map through the use of a half-silvered mirror (ibid.). The model could then be manipulated until its projected image fit within the electron density. The coordinates of the atoms would then have to be measured and calculated from the model itself. And while this "arduous work" was both "highly tedious and inherently inaccurate," it was a step up from the method Kendrew first employed (ibid.). See also de Chadarevian (2002).

[47] Novel systems of interactive computer graphics overcame the practical limitations of the solid structures generated by Plexiglas electron density maps and wire models. For example, they enabled the "fitting" of a digital model directly into the electron density map, rather than having to "dissect out" a structure from a solid object (Collins, et al., 1975: 1049): "Electronic Richard's boxes" allowed variously sized volumes of electron density to be displayed on the computer screen in stereo, enabling the user to "superimpose" stereo images of atomic models "in such a way that the latter [could] be translated and rotated until an optimum fit of the model to the map [was] achieved" (ibid.). As such, "fitting model to map...can be far more convenient and faster than the mechanical operations in the Richard's box" (ibid.). An added benefit, and indeed what the developers saw as the most important feature of this interactive system, was that the coordinates of the constructed model could be recorded automatically. Replacing the time consuming and completely error prone work of trying to measure the atomic distances from scale models, the grid logic of the computer screen could accurately identify the location of each atom in the structure.

present small pieces of the map at a time, so that physical modeling was the best way to get a feel for the map and molecule as a whole. At the same time, this pedagogical training practice served to provide a material reference for novices just beginning to work in the digital medium, so that when the students went to use the virtual tools, they already had a sense of the physicality of the electron density topographies they were navigating onscreen (see Figure 2.5).

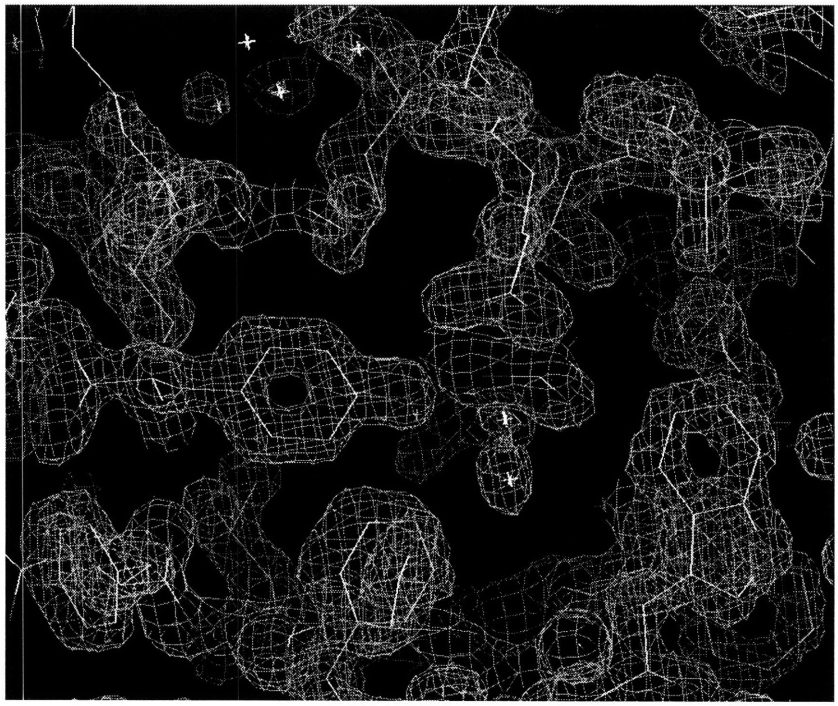

Figure 2.5: Digital electron density map. Note the model that is being built into the regions of electron density. Used with permission from an anonymous ethnographic informant.

While digital models are the primary medium for model-building today, physical models are still present in some labs. In her office, Diane shows me one small molecular model

she sometimes uses to make a particular argument about a chemical interaction. But the primary modeling media remains interactive graphics. Fernando, a fifth year PhD student in Diane's lab mourns this loss of physical models, which he sees as the best means to provide modelers-in-training with a tangible object that could stand as the primary referent for the graphics media. He would prefer that a culture of physical modeling be maintained alongside the computer graphics to help crystallographers-in-training gain experience manipulating three-dimensional objects. He has observed that molecular modeling kits are also less prominent in chemistry classrooms and tutorials in his department, and he sees this as the product of an intellectual culture that devalues physical models, treating them as "playful" tinker-toys rather than as serious tools.[48] His colleague Brent, for example is not so familiar with the use of physical models in his work. Brent, who is a postdoc in Diane's lab, expressed surprise when he saw his friend Tim, a skilled protein crystallographer, carrying around physical model. Brent pretended to be Tim and acted out how he was using the models: "See. It can only happen like this. I can't fit my active site here because my density is this big!" Brent called him a "dork" and told me that was "just funny to watch him thinking like that," playing with his models. He qualified his surprise with the explanation: "Well, he is a chemist." Brent, who was trained in microbiology before he moved into protein crystallography, tells me that he "thinks differently."

In some senses, interactive graphics reconstitute what it means for a virtual object to be tangible. In pedagogical contexts, novices do have a hard time experiencing this kind of

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[48] My observations of lecture courses and teaching laboratories in structural biology do show evidence of the use of some physical models, though these are often ancient artifacts and they are used in conjunction with interactive graphics, two-dimensional renderings, and rich rhetorical analogies (see Chapter 2).

tangibility. However, over time and with the experience of constant interaction with virtual objects they eventually acquire a feeling for the tangibility of interactive objects. Katherine Hayles (1999) argues against the prevailing assumption that users are drawn out of their bodies, or disembodied, in interactions with virtual media. What I have seen suggests that rather than "dematerializing" the molecule into some body-less virtual reality space, over time the interactive graphics workstation used for crystallographic model-building enables a particularly effective kind of handling for molecular models. Digital models acquire a materiality and tangibility through their manipulation on-screen. Diane makes the embodied nature of computer modeling work clear when describing her experience building crystallographic models onscreen. She invokes the same language and gestures one might use to describe model-building with physical materials:

> And physically you are sitting at your computer, often with the stereoglasses on. And you are *physically dragging* pieces of protein structure, like amino acids, and sticking them in. You drag it in and you stick it there. And then with your dials or your mouse, you are adjusting it, moving the pieces to get it to fit. So you are *physically building* with the stereoglasses and the mouse. You are physically building in a model into this electron density.

As Diane describes building the model, she stretches her arms out in front of her and reenacts the activity of modeling. She uses her hands to mime her work at the computer. Through elaborate gestures she carves out the space of the computer screen, the amino acids and the shape of the electron density map that she rotates in her hands. Her hands clasped and pulsing around invisible objects, she conveys the density and textures of the molecules, and their intermolecular associations, while in the open, gestural space in front of her she builds a model "onscreen" (see Figure 2.7 for an example of a model building

screen). Through this elaborate body-work she expresses how tangible the graphic model is for her.

When I observe crystallographers building protein models onscreen, the protein model is never left hovering in virtual space: it is kept in motion through rapid and restless gestures of the mouse and the quick paced, and sometimes clumsy, tapping out of keyboard commands that pull up new windows and views. In one window, data will be streaming up the screen, and in another, the crystallographer holds the skeleton-like interactive rendering of a model. She keeps it alive in space and depth, rotating it on screen and zooming in and out, keeping it visible at multiple angles, constantly shifting her visual and haptic relationship to it. This dynamic practice of seeing in motion appears to offer a means for the modeler to keep the three-dimensionality of the model visible and tangible. But more than the crystallographers' hands and eyes are in play. Though more subtle than their hand movements, their entire bodies become affectively entangled in the task of manipulating the model onscreen: with movements initiated at the head and neck, crystallographers move as they rotate the model, leaning in, pulling away, and even peering around behind obstructions in order to see and feel their way through the intricate structure. Moreover, as they parse the thicket of this dense visual field for another witness, either for a curious, novice onlooker or another expert viewer, they pull the model off the screen through elaborate gestural choreographies that animate the structure's intra-molecular forces, functional mechanisms and movements. Thus, for experienced users, virtual models become tangible interactive objects. For novices, who haven't experienced the embodied interactivity of the graphics interface, these models can be fleshed out and relayed through modelers' gestures and movements, which give body to otherwise virtual

objects.

The Human-Computer Lens

Protein crystallographers make use of an elaborate set of computer-mediated techniques in order to build atomic-resolution models of proteins. This practice is intensely time consuming, and physically and intellectually demanding.[49] According to Diane, to be a crystallographer you have to be "a molecular biologist and a protein biochemist, you have to be a little bit of a physicist, you have to be a computer jock, *and* you have to be an artist." The model-building process is itself a rite of passage towards becoming a protein crystallographer. The common lore in the lab is that even if well versed in the theory of crystallography, a crystallographer remains a novice until they have fully built their own structure. Working in the tangible medium of interactive computer graphics, modelers-in-training learn how to see, feel, and build protein structures through the embodied interactions with the data. Model-building is thus a kind of training ground for crystallographers to acquire their "feeling for the molecule," to develop the tacit skills and craft knowledge required to visualize proteins and "think intelligently about structure." As I show below, the well-trained crystallographer's molecular intuitions form an integral part of the technological "lens" that draws proteins into view.

Approaching crystallography as an optical system, that is, a technology for visualizing molecules, crystallographers often compare and contrast X-ray crystallographic techniques to microscopy (see Glusker, 1981; Glusker and Trueblood, 1985). Diane adapts this

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[49] For example, it took Max Perutz twenty-two years to produce a high-resolution model of hemoglobin.

canonical analogy in her introductory lecture to graduate students in her macro-molecular protein crystallography class, and presents a hand-drawn schematic on an overhead based on Glusker and Trueblood's diagram (see Figure 2.6 a and b).

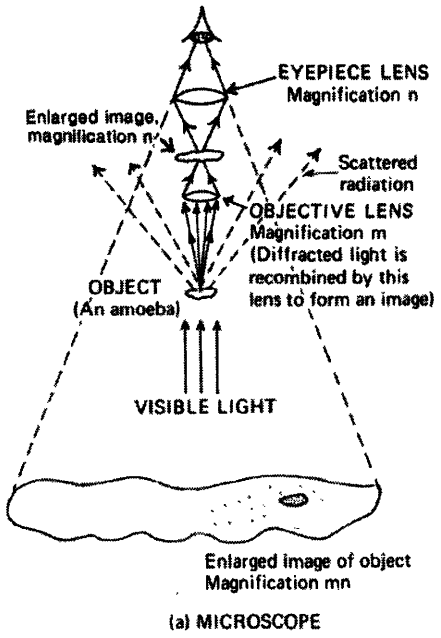

Figure 2.6 a. Microscopy

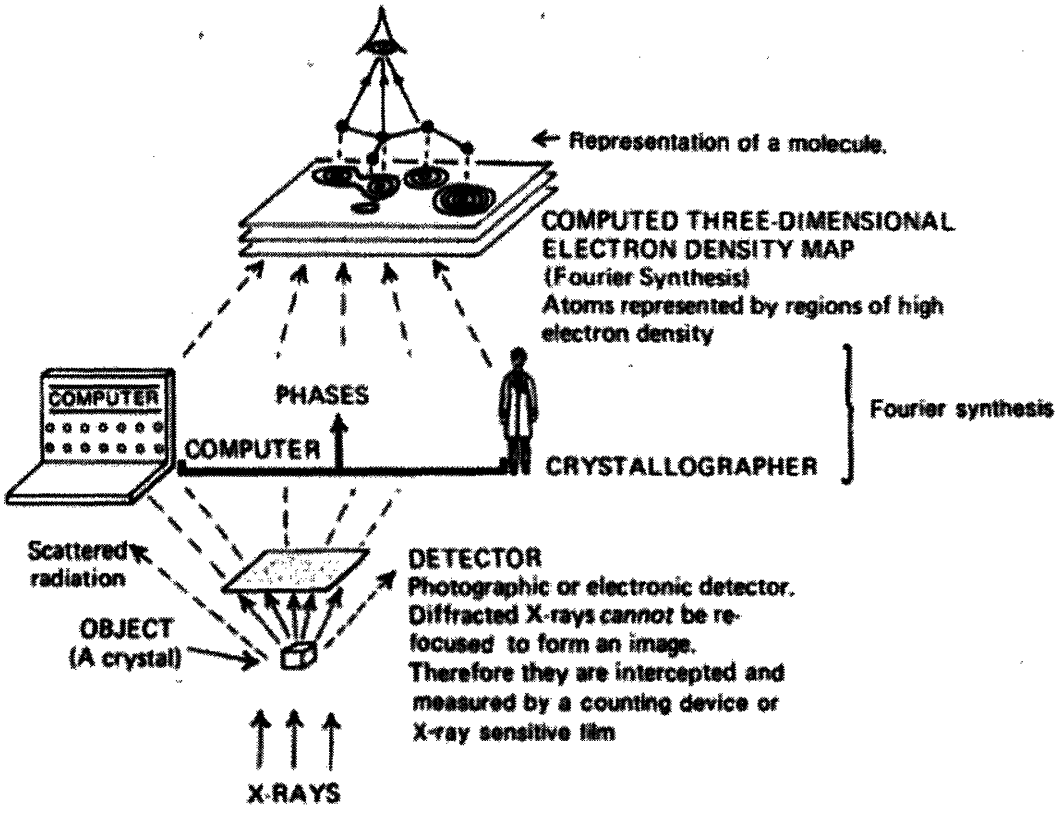

Figure 2.6 b: Crystallography. The Human-Computer Lens. Glusker and Trueblood (1985) use this diagram to create an analogy between microscopy and crystallography. Note the "crystallographer" and "computer" form a lens that can, with the aid of "Fourier synthesis" recombine the diffracted X rays into an electron density map, and produce a molecular model. Glusker and Trueblood's caption reads: "With X rays the diffraction pattern has to be recorded electronically or photographically...because X rays cannot be focused by any known lens. Therefore the recombination of the diffracted beams that is done by a lens in the microscope must, when X rays are used, be done mathematically by a crystallographer with the aid of a computer" (1985: 5). Used with permission from Oxford University Press.

As their diagram outlines, in contrast to the optical systems of microscopes that make use

of visible light, X-rays cannot be focused with the aid of lenses. In place of a microscope lens, crystallographers have devised an intricate system to couple the modeler with an assemblage of computer technologies and mathematical functions. This assemblage simulates the function of a "lens" that can actively resolve models of protein structure. This *human-computer lens* in effect provides the resolving power for an "X-ray microscope."

Crystallographic Vision: Getting Lost and Found In the Model

> Imagine sailing for years through uncharted water, and then suddenly you see land rising on the horizon. And this model emerging was like this. So one morning in September in 1959, our results came out of the computer at the Cambridge Mathematical Laboratory, thousands of numbers, which we plotted on sheets of paper. And then we drew contours round them, and there emerged a landscape of peaks and valleys. So, I built this model. And then, suddenly saw this thing, you know, which I'd been working on for twenty-two years. And it was a fantastically exciting moment. I always say it was like reaching the top of a mountain after a very hard climb and falling in love at the same time.
>
> Max Perutz[50]

In the many steps required to transform a protein from its *in vivo* form into models and animations of its structure and molecular movements, protein crystallographers make use of an array of computer-mediated visualization techniques including X-ray imaging, electron-density mapping, molecular modeling, and tools for producing publishable figures and generating animations. First protein molecules must be purified from cells, and

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[50] From an interview with Max Perutz by the Vega Science Trust, 2001. "Face to Face with Max Perutz" Streaming video of the interview available at http://www.vega.org.uk/series/facetoface/perutz/. Perutz was an avid mountain climber. http://www.vega.org.uk:8080/ramgen/face2face/perutz_haemoglobin_story.rm

crystallized. Forming viable crystals is often a major rate-limiting step, sometimes taking years in itself.[51] X-rays are then used to generate diffraction patterns of the crystal. The series of patterns that are produced as the crystal is rotated in the X-ray beam correspond to the positions of the atoms within the proteins packed into the crystal. In ways similar to other three-dimensional visualization systems like the Visible Human Project, PET scans, and confocal microscopy,[52] there is a "tomographic" logic to this X-ray imaging system which builds up a three-dimensional image by slicing through the object at precise intervals and stacking these slices. As the crystal rotates in the apparatus, detectors pick up images of the scattering of X-ray at every degree of rotation. Each spot on the diffraction pattern, and each X-ray image, itself a slice through the molecule, becomes a data point for generating a map of the approximate position of the electrons in the molecule.

As Dorothy Hodgkin recounted in her 1964 Nobel lecture (the award was given for work done in the late 1940s and 1950s), while the techniques of structure determination can be

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[51] These steps of protein purification and crystallization deserve careful ethnographic observation. According to Diane, even with today's technology, which greatly expedites the process, a graduate student may start a project and after four years still not have successfully crystallized a protein or built a model. In the history of protein modeling, particularly during wartime years, protein purification was a messy task. Slaughterhouses provided some of the cheapest and most abundant sources of tissue. Currently, most proteins are purified from bacteria that have been genetically engineered to over-express the gene for a protein of interest. Crystallization poses serious challenges for crystallographers as some proteins are notoriously difficult to crystallize, or just do not form crystals. Crystallographers regularly joke that protein crystallization is a practice requiring "voodoo magic." They develop all kinds of rituals to ensure that once they find the "magic potion" that can coax their protein to form crystals, they can reproduce their results. From playing techno music while they mix their biochemical media; to donning a special sweater; to not shaving one's beard; or to talking to their crystals: they will do anything they can to get them to grow.

[52] On the generation of three-dimensional images in confocal microscopy and the Visible Human Project, respectively, see Keller (2002) and Waldby (2000). Joseph Dumit's (2004) analysis of PET scans calls for detailed descriptions of the apparatus of visualization to facilitate understanding of the kinds of mediation that an object, such as a brain, must undergo in order to render images that can travel as facts beyond the laboratory.

"formally" represented as a cycle of mappings followed by "rounds of calculation" and modeling, "the outline hardly gives an accurate impression of the stages of confused half-knowledge through which we passed." (Crowfoot Hodgkin, 1972: 75-6). A key problem that the crystallographer faces is that the pattern of light scattering is extremely cryptic. Each spot on the diffraction pattern is a product of the interaction of every atom in the molecule, and every molecule in the crystal. The diffraction patterns produced must be analyzed and transformed through a series of complex mathematical functions, including Fourier transforms, in order to translate them into a form that is legible and interpretable. These conversions generate three-dimensional electron density maps of the molecule that indicate the approximate positions of the atoms within the proteins. These maps are read almost like three-dimensional topographical maps, where "peaks" of electron density mark the approximated positions of atoms (see Figure 2.5).

Indeed, working in between maps and models over the long duration of model-building is an elusive and piecemeal practice, involving much trial and error. Crystallographic models are built slowly through a recursive and iterative interplay between increasingly refined electron density maps and models. Moving back and forth between different kinds of electron density maps that correct for various errors, crystallographers actively cycle between techniques of mapping and modeling. As they build more amino acids into the electron density, they use the model as a means to generate more refined electron density maps. Calculating backwards, they can construct hypothetical electron density maps of the models they are building, as a means to test the model against the observed data. Thus they move through rounds of mathematical refinements, recalculating the density peaks, re-fitting the model, and continuously comparing calculated electron densities with

observed electron densities. Layered into this process is the corroboration of their model with the known sequence of the protein. Gradually a clearer and clearer image of the map and model emerges.

Much of the difficulty in this work lies in the fact that the model is never self-evident from the map. Faced with an electron density map, the crystallographer has very few clues as to which parts of the protein fit into which parts of the electron density. As Dehlia and Amy made clear to me in interviews with them, the crystallographer must make "executive decisions" (see Introduction). It is up to the crystallographer to recognize what amino acids fit into particular configurations of electron density: According to Diane, one can use what she calls "known knowledge" to "interpret what otherwise would be completely un-interpretable." Sculpting a best-fitting model into the map through a wayward and intuitive process, the crystallographer must draw on embodied knowledge of allowable molecular geometries, including the distances and bond angles between atoms within the poly-peptide chain, and intra-molecular forces that hold the whole molecule together. For Diane, model-building requires the modeler to be comfortable with the experience of meandering through the electron density map, never really knowing for sure "where you are." As crystallographers build, they must first get lost in the map, and feel their way around familiar and unfamiliar forms in order connect up the model atom by atom, doing work that the computer alone cannot achieve (see Figure 2.7).

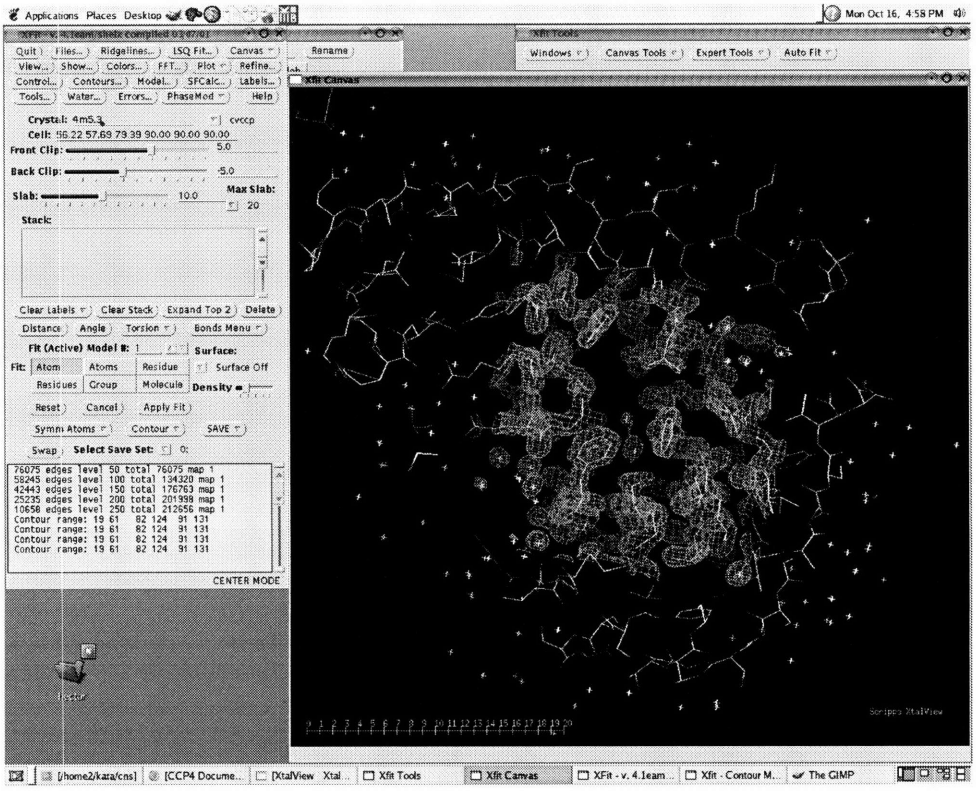

Figure 2.7: A screenshot of an interactive computer graphics interface used for building a model into the electron density. Used with permission from an anonymous ethnographic informant.

Best known for his articulation of the role of tacit knowledge in scientific practice, philosopher of science Michael Polanyi (1958) offers insight into crystallographic model-building. Indeed, as a physical chemist who had used X-ray crystallographic techniques in his experiments, he developed elements of his thinking about tacit knowledge with reference to crystallographic practice. Drawing on Gestalt psychology, Polanyi found "inarticulate manifestations of intelligence" beneath the surface of scientific practice, an intelligence that "falls short of precise formalization" (1958: 53), wherein experimental progress is made incrementally, by trial and error, and in such a way that researchers

"grope" their way toward insights (62-63). Diane's experience modeling maps onto this description well: for her, the structure can remain obscure for a long time, until a shift in perception opens it up to view. Once you have started building your model, she explained,

> Then you'll look at it and go, "Okay, there's a big side chain here." And three residues down there's something long. And this looks like an arginine [an amino acid] and down there [points] that looks like something big. And you'll go through your sequence, and go, "Okay, where are the arginines? What's four residues away? Oh, lysine [an amino acid]. That's no good." And you will work your way through. And you'll sort of build some of it, and then go, "Okay now I'm lost and I don't know where I'm going next"...
>
> And there are certain folds that people know. Like TIM barrels [see Figure 2.8]. One time I could see some helices in an early map, and I was putting a couple in, and I put a couple more in. And then, I think I got up for a minute and came back and just sort of saw from a distance what I had done. And I looked and there was a whole bunch of helices around in a row. And I said, "That's a TIM barrel!" And there's got to be strands in the middle. And then I pulled in a TIM barrel and went, okay, it's a little off, it needs some adjusting, but yeah, that's what it is.
>
> And so, sometimes it takes a long time to recognize the fold, because sometimes it's not a very standard fold. And other times it can come out relatively quickly, you'll all of a sudden see the connections by how things are, or you'll find a region where you can see the density of beta-strands. And you know that you can pull in the model and try to get it to fit.

Figure 2.8. A Ribbon diagram of a TIM barrel. Note the circular arrangement of alpha-helices. Used with permission from an anonymous ethnographic informant.

For Diane, building models is like a "detective story" where the crystallographer has to search for clues about their structures. She says, "that's why you never know you are done until you are *done*. Because at the end stage you go, "Okay if that's correct we should be able to connect [amino acids] five and six, and it's all there!" Here Diane's account suggests that there is a gestalt shift in seeing that occurs through the immersive work of modeling, where the form of the folds jump out at her, emerging whole from a piece-meal process of building. The interactive graphics systems that Diane uses can, as their early developers advertised, engage her in the "intuitive, trial and error" style used with mechanical models: these systems exploit an "interactive mode" which is "able to take advantage of the powers and versatility of the *"human computer"* for pattern recognition

and inductive thinking" (Barry, et al., 1974: 2368; emphasis added).

The Craft-work of Computer Modeling

> We decided to develop programs that would make use of a man-computer combination to do a kind of model-building that neither a man nor a computer could accomplish alone...It is still too early to evaluate the usefulness of the man-computer combination in solving real problems of molecular biology. It does seem likely, however, that only with this combination can the investigator use his "chemical insight" in an effective way.
>
> Cyrus Levinthal, 1966: 49, 52.

Interactive computer graphics technologies are just one of the many ways that computers figure in crystallographic work. Crystallographers were among the first life scientists to make use of computers, initially for alleviating the massive labours they faced with calculation, and later for reducing the physically labourious process of data collection and for facilitating computer graphic representation and manipulation (de Chadarevian, 2002; Francoeur and Segal, 2004; Siler and Lindberg, 1975; Tsernoglou, et al., 1977). In each case, computers introduced important changes in the ways modelers did their work; however, in none have computers completely replaced the modeler.

Until very recently, few steps of the crystallographic modeling process had been fully automated. Though many computer scientists and mathematicians aim to automate protein structure determination, the programs they have developed currently cannot, on their own, fully determine protein conformation from its sequence, or perfectly fit a model to a map. Thus the crystallographer is an essential component of this visualization technology. The "human" part of the human-computer lens—that is, the crystallographer—must sculpt a best fitting model into the map through a practice that requires intimate knowledge of

molecular form, keen eyes, intuition, and an intimate bodily engagement with the model as it is slowly built up over time.

As outlined in the diagrams comparing crystallographers and microscopists in Figure 2.6 (a and b), while they may assume that microscopists rely on the "mechanical objectivity"[53] of their technical apparatus to produce faithful microscope images of cells, crystallographers explicitly theorize an entwined human-technological agency in their practice of drawing proteins into view. In this sense, crystallographers are explicit about the contributions of their knowledge and labour to model-building. It is the embodied nature of crystallographic modeling that preserves for the crystallographer what might be called a "critical epistemology of visualization". Key here is that crystallographers value the intuitions and embodied knowledge they contribute to their work: they deem the craft nature of their practice a virtue that raises the epistemological status of their data (see Turkle, et al., 2005: Ch. 1, 2, 5). Recall the lesson learned from Chang's models which were mangled by a glitch in a computer program: without the careful, embodied attention to the model as it was being built, the machines left to their own devices produce garbage. By making so explicit their direct participation in model-building, protein crystallographers are very careful about qualifying the epistemological status of their various visual productions: their renderings are only ever "models," imperfect but powerful representations of otherwise invisible molecular worlds.

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[53] On "mechanical objectivity," see Daston and Galison (1992) and Galison (1998).

Molecular Embodiments

> To get used to [things] is to be transplanted into them, or conversely to incorporate them into the bulk of our own body. Habit expresses our power of *dilating* our being-in-the-world, or changing our existence by approaching fresh instruments.
>
> Maurice Merleau-Ponty[54]

> We may say that when we learn [a] probe, or a tool, and thus make ourselves aware of these things as we are of our body, we *interiorize* these things and *make ourselves dwell in them.*
>
> Michael Polanyi[55]

How do interactive molecular graphics technologies enable this physical experience of handling and manipulating structures? A phenomenological approach to the kinds of learning enabled within the training ground of crystallographic model-building draws out the fine details of this process. Exploring the prosthetic nature of tool use, Maurice Merleau-Ponty (1962) and Michael Polanyi (1958) offer insights into the intimate association of bodies and tools in learning. According to them, we learn to use new instruments by means of enveloping them within the folds of our flesh, and also by reaching our bodies outwards to meet the tool as an extension of ourselves. These insights into learning suggest that our bodies are open to the world, porous to new possibilities and adaptable to new kinds of tools. In this way, protein modelers can be understood to "dilate" and extend their bodies into the prosthetic technologies offered by computer graphics, and "interiorize" the products of their body-work as embodied models of molecular structure. In a key moment during an interview with Diane, she offered this insight into her experience incorporating molecular forms. She told me:

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[54] Merleau-Ponty (1962: 142).

[55] Quoted in Rheinberger (1997: 74).

> The person who builds a structure...they understand the structure in a way that I don't think anyone else ever will. And I try now as an advisor, I try to get inside the structure and really try to understand it at that level. And I have for a few of them, but it is really time consuming, I mean, to sort of have the structure in your head in *three dimensions*, which is how I felt about some of the other structures that I actually did build myself. And I would be at a meeting and people would be discussing a mechanism, and I would kind of close my eyes and try to think about it and go, "No. Too far away."
>
> And you know, it's really this vision that you have of the active site, and sort of this sense of how tightly packed it is and how much flexibility there might be and where those regions of flexibility are. To have this sort of sense that you have. And you can think about it then *moving* in a way because you sort of know something about what the density was, so that you know that part is definitely mobile right in there, but that this part would not be mobile. And this information is kind of like stored in your brain in some way, and it's not something that is easy to communicate, because, you know you can't explain something in three dimensions to someone...

A number of striking insights emerge from Diane's description. In order to really "understand" the protein model, she has to "get inside of it." As she describes in other conversations, by actively handling the model through interactive molecular graphics programs she can project herself "inside" of it and figure out "where she is" within the structure. She achieves this intimacy with the model by dilating her body-image to meet its form. But clearly, her learning body does not just extend outwards to meet it: she also envelops the model within her flesh. Although she indicates that she "stores it" in her "brain" and can rotate the molecule around in her "head," while she describes the model, her whole body is engaged in descriptions of its flexibility, intra-molecular forces, tensions and movements. Once inside her as an embodied model, she has both a "vision" of the active site and a "sense" or feeling for the forces within the molecule that exceed what

could be described as a "mental image." It is through the dimensionality of her body that she is able to appreciate the full three-dimensionality and movements of the protein model, so that she feels the spatiality and temporality of the molecule by virtue of the spatiality and temporality of her own body. While she mourns the limitations of language for the communication of three-dimensional, structural knowledge, Diane's body provides an articulate medium for vivid expression of the fine details of molecular structure: inflected and informed by the molecular models that inhabit her body, she demonstrates with clarity the twisting helices and the movements of the peptide backbone meandering through the molecule. Throughout our conversations, during class lectures, and in informal discussions with members of her lab, her gestures and affects animate the forms, textures, and tensions within the protein.

Diane's molecular embodiments are in no way exceptional. In depth interviews with her male and female students, and with other crystallographers, show that those who have made it through the rite of passage of model-building, those have "solved" their own structures, can carry specific knowledge of the configurations and chemical mechanisms of their proteins in their bodies. For example, an interview with Diane's postdoc Brent, who was a football player in college, revealed that molecular embodiments are not restricted to a stereotype of the "expressive woman scientist."[56] When I asked him to describe one of the proteins he had modeled before, he proceeded with an elaborate demonstration of its chemical mechanism. He leaned across the table between us, and drew his hands

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[56] I attended a reunion of structural biologists who had all trained under two well-known protein crystallographers in the U.S. In one talk, a male crystallographer joked that you couldn't trust anything that a particular female crystallographer said: she was too exuberant and prone to exaggeration. The sexism of his sentiment was loud and clear: he aligned expressiveness and femininity as excessive modality that threatened objective knowledge.

together, carving a small pulsing sphere out of the space in front of him. In order to describe the specific intra-molecular forces between a small cluster of amino acids in the active site of his protein he tenderly drew the middle finger of one hand across an invisible force field on the palm of the other, indicating the exact site where charged amino acids interact with each other. Throughout his demonstration he held a buoyant tension in his hands that extended through his arms, and into his whole body. He had cultivated a profound feeling for his protein in the course of building the model, and he performed what he hypothesized to be its chemical mechanism through gestures and affects that reflected the intimacy of his molecular knowledge.

The habituses of other students I interviewed had not yet been inflected with such precise molecular affects. These were the graduate students and postdocs who had not yet built their own structures, including: those who were new to the lab and to crystallographic practice; those who were still struggling to perfect what they often refer to as the "magic" of getting their proteins to crystallize; and those stalled at the stage of trying to, as they say, "massage" poor quality diffraction data into meaningful electron density maps. When I asked them to describe proteins they were at least familiar with, those that they hadn't modeled themselves, they rarely used gestures, and if they did, their gestures were vague and imprecise, as if their hands loosely circumscribed the general form of an object at a distance. They were familiar with the model from the outside, but it did not yet "belong" to them.

Among protein crystallographers there is a profound sense of investment of one's "self" in the model: seen as a craft product of labour and love, a crystallographic protein model is

an artisanal object. For Diane, and others, the sudden emergence of the model after the arduous "labor" of construction warrants a "birth announcement." In an interview, Diane described it this way:

> And so the process...I don't know, some other people say that they want birth announcements when the structure [is coming out]...because it is kind of like being in labour...And often a building process will take nine months. And it is, it's sort of as it's coming out...you're all of a sudden, "Oh! Look at where that conserved patch is...Yes! Oh! Oh! That makes so much sense! That other group was wrong about what those residues do." And so it's sort of this unveiling. And then you finally give birth to your molecule. And what I've started doing is putting our structures on refrigerator magnets and so then for Christmas you can share with your family and friends. [Natasha: Like an ultrasound?] Exactly. Right. Everyone sends out their pictures of their kids and you send out pictures of your kids. It is kind of like that in a way.

The product of a crystallographer's labour is always figured by the modeler as "my protein," "my molecule." As Brent described, it's not until you can produce crystals that diffract well, and start working on a model, that the protein becomes "yours." He explained that he always keeps a number of projects running and maintains a kind of emotional distance until a protein shows promise by forming "beautiful" and reproducible crystals that diffract well. For him, it is only once a project is well on its way that the protein becomes his own. He emphasizes his intense sense of ownership of the molecule and the model by drawing his arms powerfully into his chest and emphatically repeating the word "mine". This evocative gesture also served to remind me *how* the protein model belongs to him: the model is not the product of disengaged rationalization, and it does not hover in his head as a mental image. The model *belongs to his body* because in a sense, that is where his knowledge of it lives.

Thus the richest, most detailed model of the molecule resides in the modeler. Any rendering the modeler produces is merely an abstraction of this knowledge. Diane makes clear the frustration she feels about the limitations of the two-dimensional figures she must construct to communicate to others what she identifies as the most salient features of the structure. She insists that no one will ever understand the protein as intimately as those who built the model. And this is why, when new structures are presented in the literature or at meetings, she will never take the two-dimensional diagrams or descriptions of mechanisms at face value: she must go to the Protein Data Bank and download the coordinates of the model into an interactive molecular graphics program so that she can examine the model herself and get a feeling for its folds. The listing of a model's atomic coordinates in the PDB does not suffice: she must handle and manipulate the models as tangible, three-dimensional objects in order to acquire at least some of the knowledge that the crystallographer who built the model possesses.

Crystallographic modeling through interactive computer graphics is thus not only a practice that produces digital renderings as visual forms of data; it is also a pedagogical site for producing new protein crystallographers. The students who presented their misshapen models to Diane, and elicited from her a cry of pain, were crystallographers-in-training: they were in the process of acquiring a feel for the possible geometries, forces and movements within proteins. Of the advanced students I interviewed, all recognized Diane's skills but said they were still "nowhere near" her "level" yet. This was a skill they understood as her ability to look at a model and intuit what was right and what was wrong. However, Diane's skill, as she says, to "see what the structure is saying" does not merely rely on memorized mental images of what proteins should look like. Keen molecular vision

is, for her, an embodied practice of observation and manipulation, where seeing is also a way of *feeling* what the structure is expressing in its form.

A number of specific protein models inhabit Diane's body—those models she worked on herself. These *molecular embodiments* are the product of her intense involvement in the modeling process over long periods of time. *Becoming molecular*, she is able to give what is otherwise a virtual structure a physical body, a place for it to dwell. The practice of building protein models has thus *articulated* Diane's body with specific molecular knowledge (Latour, 2004; Prentice, 2005).[57] In other words, through an interactive practice of sculpting molecular models, the models themselves act recursively to sculpt and reconfigure the modeler's body. Crystallographic modeling is thus a practice of learning as incorporation, of building the model into one's body as it is sculpted piecemeal onscreen. In this sense, molecular embodiments are generated by "infolding" the model into the "flesh" of the modeler, where it comes to reside, as a part of the modeler her- or himself (on "infolding" see Haraway, 2006; Merleau-Ponty, 1968). Inflected and informed by the embodied models that get embedded in their tissues, researchers' bodies become expressive media for the expression of molecular forms.

Conclusion

Protein crystallography presents a visualization practice that challenges traditional notions

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[57] Bruno Latour (2004) interprets laboratory training as a process that articulates the novice researcher's sensory body. Drawing on Latour, Rachel Prentice (2005) develops the concept of "mutual articulation" to describe how computer scientists in collaborations with surgeons design effective computer simulations for teaching anatomy and surgery. In this case the designer must articulate the model-patient through codes that in turn articulate the body of the surgeon who uses this interface for training. There is also a form of "mutual articulation" going on between the molecular modeler, their computer, and the models they construct.

of knowledge. It is as if protein crystallographers celebrate Ian Hacking's (1983) famous reformulation of representation "as intervention": their visual facts are produced through techniques of manipulation, and they are candid about the contributions of some forms of tacit knowledge to their model-building practice. However, the human-computer lens of contemporary crystallographic modeling requires that crystallographers have more than "good hands" (e.g. Heath, 1997): they must also carry their knowledge of protein forms, forces and movements throughout their bodies. In addition to their hands, their arms, shoulders, torsos, necks, and even knees can be pulled into play. As they manipulate and build crystallographic models, they incorporate these unique and complex molecular forms into the folds of their flesh. In the process they rearticulate and so entrain their embodied imaginations. Thus, in addition to revising conventional notions of scientific vision as a practice of disembodied objectivity (see Haraway, 1991), crystallographers' model-making reworks the relations between subjects and objects of scientific knowledge. Modeler and model are intimately entangled and co-crafted in this practice. Indeed, as the very objects around which their professional identities are formed, protein models belong to their modelers in a way that goes beyond concerns over intellectual property and scientific priority. To become a crystallographer, the modeler must become their model.

A thicker ethnography of protein modeling must extend beyond the model-building phase. Once built, the structure of a protein model remains to be interpreted. "Thinking intelligently about structure," requires hypothesizing how a protein carries out its functions in the cell. This phase of research also depends on the trained intuitions and embodied knowledge of experienced crystallographers. As Diane demonstrates, the crystallographer carries the model within her body, but she also can "get inside of it" in order to "figure

out" how it "works." Her goal is to have a three-dimensional atomic-resolution understanding of "how nature has tailored" proteins to do chemical and biological "work" within the cell. To do this she uses her embodied knowledge of the specific molecular geometry and chemistry of the protein in order to reason through possible biological mechanisms. In this sense, *figuring out* protein mechanisms requires another form of "body-work," one that couples the body-work of incorporation to that of communication (see Chapter 5). This wealth of embodied knowledge in turn shapes how proteins come to be figured, both materially and semiotically within scientific papers and in pedagogical and professional presentations (see Chapter 4).

Yet, protein models also have a life that extends well beyond the immediate grasp of the modeler. Once a model is built, it is uploaded into the ever-growing Protein Data Bank, where it becomes available to researchers in such fields as biological engineering and rational drug design. Crystallographic models also feed into high-throughput proteomics initiatives that seek to amass catalogues of all proteins produced in a given cell, tissue, or species. Interactive graphics technology allows these researchers access to the folds and intricate chemical forms over which the crystallographer had long labored. As mobile, interactive objects, protein models can be manipulated and incorporated by a larger audience, instructing others in the ways of its folds. However, as the models move out from the crystallography laboratory, and enter wider circulation, crystallographers voice some anxieties. PDB entries list the atomic coordinates of the protein model, include relevant statistics and experimental data, and provide files that can be uploaded into interactive graphics programs. Yet they do not carry the "thickness" of the modelers' structural knowledge. For example, Edward, one of Diane's postdocs expressed concern

that others would regard his model as a "static structure," rather than, as he described it, a "breathing entity." His embodied knowledge is thicker and livelier than the data that can be transmitted through the PDB: in a sense it is he who keeps his model alive, both in his trained embodied imagination, and through his lively performances of its form. Thus, in the process of distribution, much of the crystallographers' artisanal labour is obscured as their craft-productions are, in a sense, picked off the shelf and swept up in capital-intensive economies among drug developers and biomedical researchers.

In conclusion, this chapter has aimed to articulate how attention to the "body-fullness" of protein modeling can transform historical and contemporary conceptions of life science practice. In this study I have not only aimed to refigure the role of scientists' bodies in their work, I have also sought new ways of making sense of the objects of biological research. As protein molecules come to be figured *in, through, and as* bodies, the flattening tropes of information and code are no longer adequate metaphors to describe the practices of life scientists or the substances of life. Rather, molecular models, and the scientists who make and are made by them, form exceptionally animate assemblages that demand interpretive strategies with equally dynamic modes of attention.

Chapter 3

Performing The Protein Fold
The Pedagogical Lives of Molecular Models

Models, Bodies and Imaginations

One of my classroom-based field sites for this study included a semester-long lecture course that examined the biology of protein structure and folding. "The Protein Folding Problem" was cross-listed in the departments of biology, chemistry, and chemical engineering and the students, both undergraduate and graduate, came to it from diverse disciplinary backgrounds, including physics, biological engineering, and computer science. The professors for the course were Jim Brady and Geoff Miller. Jim is a prominent protein scientist, who is also known for his commitment to science education. Geoff is a mechanical engineer who has recently taken an interest in protein structures.

Over the course of the semester I became acutely aware of the challenges these instructors faced in teaching a new generation of life scientists how to visualize complex three-dimensional models of proteins. In this course, students were asked both to imagine and render multidimensional models of otherwise invisible and intangible objects. In the first weeks of the course, students were encouraged to learn the intricate molecular structures of proteins "by heart." Jim told the class: "We want you to have it in your head. You need to know it cold." Throughout the semester, Jim worked hard to impart the skills students would need to get protein structures in their "heads" and "hearts" through commanding

performances of his knowledge of protein folding. Throughout his lectures, he leapt energetically between streaking biochemical equations and experimental data across the board, and demonstrating protein structures with colourful ball-and-stick models. Geoff, on the other hand, brought his engineering expertise to the classroom and lit up his lectures with slick interactive computer graphics displays to demonstrate the special features of these elaborate molecules. Getting a feel for how these researchers approached the challenge of training a new cohort of scientists requires some inquiry into the relations between imagination and learning.

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It is a truism that effective science teachers must awaken their students' imaginations. Yet the landscape of the imagination, its formation, and its role in learning and scientific research are little understood and seldom explored in the science studies literature. How do structural biologists envision molecular events in the cell? When they close their eyes, and imagine their proteins performing chemical reactions in the cell, what does that world look like? What are the forms, textures, and temporalities of the molecular worlds they imagine? This study examines biological visualization in the broadest sense: that is, visualization as a practice of rendering models of life, and visualization as a mode of conjuring imagined life-worlds. Where it is relatively straightforward to track the material culture of protein models, including the media and machinery through which they are constructed, it is more difficult for the historian or anthropologist to gain access to the fluid permutations of scientists' imaginations.

Historian of science Maria Trumpler (1997) has developed a wonderful approach to this challenging field of inquiry. She documents the generation and reproduction of protein scientists' rich imaginary worlds by inquiring into the changing representations of membrane channel proteins over several decades. She writes about the "importance of the scientists' own mental images," and how they "privately conceived" of "large, complex, three-dimensional molecule[s] moving in time and space" (1997: 55). No single model captures the full picture held in mental images. According to Trumpler,

> While any two-dimensional representation on paper shows only one aspect of the channel, the convergence of the different representations and the plasticity of imagination yield a complex mental image that can incorporate all perspectives simultaneously, reflect differing time scales at will, and be a collage of various molecular models (1997: 56).

For Trumpler, "complex mental images" of otherwise invisible substances help researchers pose experimental questions and communicate with each other.[58] For her, the successful mental image of proteins is dynamic: generated by means of the "convergence" of many distinct modes of representation, mental images are the cumulative product of different kinds of representations that shift as new visualization techniques and conventions are incorporated into and worked over by researchers' "plastic" minds. To access the history of this rich visual imagery, Trumpler examines the visual conventions of diagrams and models

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[58] Here Trumpler echoes the work of Cambrosio and his colleagues (1993) in their historical study of the role of Erlich's models in his research into antibodies. In this case, Erlich created cartoon diagrams that served as representations of what he imagined antibodies might look like and how they worked, which, in effect, served to materialize otherwise elusive substances. In both these studies, the role of imagination in scientific research is brought to the fore.

arrayed in molecular biology textbooks. She notes that textbooks often combine and juxtapose distinct visual representations in a single figure. She analyzes these figures as attempts to convey, to students, templates of the converging models that practicing scientists hold in their imaginations. She treats these as pedagogical devices that instruct students in how to conjure protein structures in their own minds.

Trumpler makes significant contributions to our understanding of the nature of scientific imagination: first by identifying the kinds of sources historians might use to find expressions of otherwise imagined entities; and second, by recognizing that scientific imaginations are produced through pedagogical processes, such that textbooks can be read as instruction manuals for producing converging images in students' minds. I am curious, however, how a methodological shift from accounting for the history of two-dimensional representations of proteins in textbooks, to ethnographic accounts of the performance of three-dimensional protein models in biology classrooms, can extend and refine the import of her work.

With Trumpler, I propose that three-dimensional models have both a rich material history, as well as lively inner life. As I showed in Chapter 2, X-ray crystallographers hold three-dimensional protein models "in their hands" and "in their heads." Such *embodied models* are both seen and felt in the tissues of the modeler. And yet, embodied imaginations do find outward expression: model-making practices involve modes of body-work for both the *incorporation* and *performance* of molecular knowledge. For glimpses into the inner life of protein models, I tune my inquiry into sites where what is at stake is the communication of embodied molecular knowledge. I examine how structural biologists perform embodied

models in the classroom context of a lecture course in the biology of protein folding as a means to demonstrate how models, bodies, and imaginations are entangled in processes of teaching and learning.

Infolding the Fold

In an interview on teaching practices in introductory biology courses, one of Jim Brady's former graduate students offered insight into her embodied experience of models of protein folding. As an undergraduate, Joanna had studied chemistry. Very early on she realized that she had a remarkable ability to visualize three-dimensional molecular structures and chemical interactions. She credits her ability to do so well in chemistry to her skills as "visual spatial learner." "I was never a memorizer," she told me. "But from the moment that they put Van der Waal radii on molecules...I could see it in my head"[59]:

> You know, when two molecules come together, or even unlike molecules that don't want to be next to each other, for whatever reason, I can see those electrons moving to the other side of the molecule. It made total visual sense to me. It didn't make sense on paper. It never made sense on paper. I wasn't a memorization reaction learner at all. But electron-pushing diagrams made so much sense. And I kept wondering, "why is everyone else having such a hard time with this?"

She laughed when I asked her to describe what these models looked like in her imagination:

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[59] Van der Waal's radii describe the volume that a particular atom occupies. Van der Waal's forces prevent atoms from occupying the same volumes.

> Natasha: Are they coloured?
> Joanna: Yeah! [Laughter] I've never thought about it this closely. Yeah, they're coloured! That's kind of bizarre.
> Natasha: Are they textured?
> Joanna: No, they are pretty smooth. Yeah, they're pretty smooth! [Laughs] My proteins are either Ribbon diagrams in my head or Van der Waals, depending on what I'm looking at. If I'm looking at a binding pocket, it'll be a Van der Waals image with just a surface that I see up there doing it. If it's a folding, if anything has to do with folding it's a Ribbon structure. It's always a Ribbon if it's a folding.

She recognized that the models "in her head" conformed to conventional representations that she had learned. Diagrams that render Van der Waal radii are a particularly interesting convention: they not only describe the volume that an atom will occupy, but they are flexible spheres that can also be used to model regions of attractive and repulsive forces between atoms. As in the example of Diane "feeling the pain" of the misshapen protein model, researchers feel Van der Waals forces viscerally: when they look at structures whose atoms defy allowable radii, they the sense the inter-molecular tension in their bodies. I asked Joanna if these were forces she could feel as well as see. "It's hard to describe. I just see it in 3D" she told me. But seeing for her appears to be a strongly corporeal experience: as she described proteins that she had worked on in the lab, her body came alive with articulate gestures that demonstrated molecular forms and forces.

She showed me how she communicates the complex forms and movements that are in her imagination. With her arms held out in front of her, her wrists touching, palms open and facing upwards, and her hands seeming to hold some invisible substance, she told me:

> I always do this. [Emphasizing the gesture]. Whenever I talk about the crystal structure...I always do this. 'Cause that's how the molecule kind of looks. It's like this [Emphasizing

> the gesture, she rotates her hands and body.] You know. And domain one unfolds and then it's flopping around. [She mimes this floppy domain with one hand]. You know. Always. Always. Even in my thesis defense talk. It was like this. And it was flopping around like this.

In attempts to communicate protein folding to her colleagues, she performs her embodied model of the protein, itself a convergence of many modeling efforts.

As a post-doc currently involved in developing new strategies for teaching undergraduate biology, Joanna has faced some major hurdles trying to teach others how to see molecules in three-dimensions. It has become clear to her that not everybody has the ability to visualize complex molecules:

> To me it is so intuitive. My hardest stumbling block is to rationalize that it's not like that for everyone else. So to me the hard part was actually stepping back, and realizing not everyone gets this. How can I get other people to understand what I see in my head automatically?

Like Joanna, I am also curious about how three-dimensional knowledge of protein structures gets into students "heads". Jim and Geoff's protein folding class offers some clues to explore this process in depth. What they demonstrate is that there is nothing "automatic" about the process.

In one of his early lectures Jim drew his students' attention to some confusion around a homework assignment. Some apparently had trouble with the wording of "Question 2". Directing the students to a Ribbon diagram of a protein structure found in the textbook[60]

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[60] The textbook for the course was Brändén and Tooze (1999).

the students were asked to:

> Draw, copy, or trace a version of Figure 2 (e) with the alpha carbons and nitrogen atoms clearly labeled or coloured.

Apparently some students had some trouble interpreting the meaning of "copy." Jim clarified: "This means *hand copy*! If you Xerox it, you don't assimilate it!" "You have to trace it!" he implored. He demanded that the students get involved in the structures: in order to learn *by heart* the form of the fold, they had to trace the direction of the poly-peptide chain *by hand*. He demonstrated for the class. Against the backdrop of larger-than-life projection of a Ribbon diagram of a protein structure, Jim swept his entire body up in the act of tracing the elaborate curvature of the fold (see Figure 3.1). He caught the curve of the winding backbone, and traversing the full visual space of the amplified model, he hitched a ride on its folds. As he folded his body to follow the direction of the poly-peptide backbone, he told the class: "You have to signal actively" in order to "get" the structure of the fold. He demonstrated how, in his words, "you can't not learn something" if you get your body involved. Here Jim clued his students into their bodies as resources that they could use to learn the fine structures of complex three-dimensional molecular forms.

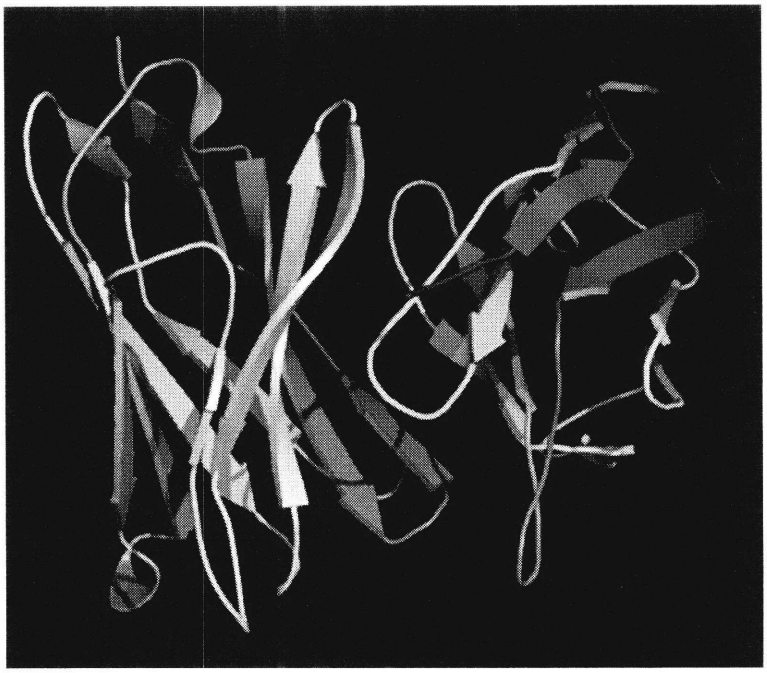

Figure 3.1: Ribbon diagram of a protein. Used with permission from an anonymous informant.

Joanna and Jim offer an instructive cue that has helped me figure out where and how to look for evidence of scientific imaginations in-the-making. In so doing, they also demonstrate how Trumpler's notion of a "mental image" does not fully convey the multidimensional textures of researchers' molecular imaginaries. Textbook images present models as representations—the end products of scientific work. Yet, researchers' molecular imaginaries are more than the convergence of *representations* in the form of "mental images"; protein models are also *renderings*, and their conception, construction, and elaboration have rich corporeal histories. Models don't just light up in their minds: they multidimensional objects that entangle scientists' bodies.

Rather than producing "mental images" of converging representations of proteins, I argue that structural biologists' imaginations are animated by the convergence of "embodied

models." The difference between these accounts—between imagination as the convergence of "mental images" or of "embodied models"—is that the latter pulls scientific representations off the page and opens up a space for recognizing the multi-sensorial, embodied nature of the formation of scientific imaginations. I see experienced researchers' imaginations as animations of a multidimensional array of visualizations, analogies, and data forms that they can both see and feel; over time, their embodied imaginations become repositories of the most textured and nuanced imagery of protein folding. As experienced researchers and teachers, Jim and Geoff face the serious challenge of communicating their embodied models of protein folding to their students. Tracking just how they articulate their embodied models requires that I attend to the body-work of teaching and learning; that is, to the performance of models in the classroom.

As I examine throughout this study, researchers' embodied knowledge of proteins animates classroom lectures, conference presentations, informal talks, and casual conversations. In this chapter I show how these otherwise tacit forms of knowing are made explicit in the classroom. In such sites, instructors teach students how to build their own embodied models of protein folding, layer by layer. Teachers encourage their students to engage three-dimensional models of protein structures kinesthetically (e.g. through physical models and interactive computer graphics interfaces), and to get hooked into their own bodies and experiences of other bodies *as analogues for* protein molecules through the use of human-scale analogies. My thesis is that teaching protein folding biology is a physically and conceptually demanding practice geared towards remodeling students' bodies and imaginations, in order to give them a feeling for the fold. I thus offer this ethnography of their teaching practices to provide a glimpse into the "infoldings" of bodies and models in

the formation of scientific imaginations and practices of learning (Haraway, 2006; Merleau-Ponty 1968).

The Protein Folding Problem

At the first meeting of Jim and Geoff's course, "The Protein Folding Problem," over fifty students cram into the classroom. In his first lecture, Jim recalled that just fifteen years earlier, when he first started teaching the course, only ten students signed up. "What has changed?" he asks the class. "Why so much interest in proteins?" The growing wave of interest in proteins among students appears to echo the interests of the pharmaceutical industry and researchers in biomedicine and public health. Protein folding research has attracted massive funding and a multi-disciplinary group of researchers (e.g. Smaglick, 2000; Wadman, 1999). In these arenas, there are currently major efforts underway to develop new understandings and new treatments based on knowledge of protein structure and protein folding pathways. For example, Alzheimer's, Huntington's, and CJD, the human form of mad cow disease, are all protein-folding diseases, in which proteins in the specific kinds of cells do not fold correctly. Misfolded proteins damage tissues by producing lethal aggregations inside cells. The problem as Jim defines it is that no one fully understands how "healthy" proteins "know how" to fold into the proper conformations, or what triggers them to misfold.

When protein folding fails, Jim is concerned that "we can't efficiently correct the problem." In a vivid example of the protein folding problem on an industrial scale, Jim describes Eli Lilly's Indianapolis fermentation plant that produces insulin for "10 million diabetics."

There they enlist *E. coli* bacteria into insulin production through genetic engineering. The proteins produced inside these bacterial cells are, however, not yet in the "active" form. The peptides that are produced must first be extracted from the bacteria, and then purified, unfolded, denatured, refolded and processed in vitro to get them to fold into their active conformations. Jim illustrates his point: "If insulin is not folded correctly, it forms scrambled eggs." Though researchers at Eli Lilly have, through trial and error, developed a series of steps to go from "scrambled eggs" to "native" (meaning active) insulin, the biochemical processes involved in getting insulin "folded" into the correct conformation, is itself is not fully understood. There is currently no coherent theory on which they can draw for the precise engineering of this process.

Jim believes that progress in this area requires the training a new cohort of scientists to tackle the problem. He advertises the course as a means to spur a generation of students to take on the task of "deciphering the second half of the genetic code." He presents a challenge to his students: "Hopefully one of you will solve this class of problems." Indeed, this course is not so much designed for the generational reproduction of a set of known facts, but as a way to equip students with the tools they will need to push the field forward. Jim organizes the course so that his students can acquire what he calls a "deep" knowledge of protein structure and folding.[61]

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[61] It should be noted that this chapter limits its focus to the activities of teaching and the techniques for learning that are introduced in the classroom setting. I have not included interviews with students or attempts to capture their "uptake" or incorporation of the structural knowledge of molecules. Further studies need to be conducted to examine students' individual and collective "memory practices" (Bowker, 2005). How do students "sign" molecular models to each other? How do they teach themselves and each other? How do they *learn "how to learn"* about molecular form within and beyond the classroom?

In class, Jim described the emergence of the protein folding problem for life scientists. The defining moment for him was when the first model of myoglobin was produced by John Kendrew's laboratory at the LMB in Cambridge, UK. In 1958, *Nature* published photographs of a more refined version of Kendrew's first "sausage" model (Kendrew, et al., 1958). Looking a little less like viscera than the sausage model, this model resembled sculptures of contorted bodies caught in an awkward embrace.[62] According to Jim, this model was "shocking" to the scientific community: "The moment that image hit the press, people wondered: 'How does this chain know where to go'?" Kendrew himself was surprised by the irregularity of the protein structure that emerged from his X-ray data. He had expected that proteins, able to organize themselves into highly ordered crystalline states, would have some form of internal symmetry (Kendrew, 1964). What gave this strange molecule its conformation? How did this polypeptide chain know how to fold?

Jim describes the challenge of the protein folding problem: "You can have a deep understanding of the end state, but have no clue how it got there." Proteins fold deep within the cell; this process occurs on the "subvisible" scale of atoms and at the speed of nanoseconds, and is thus, in practice, invisible. Visualizing protein folding thus presents a significant challenge to researchers, and they have responded with an array of imaging, modeling and simulation techniques drawn from chemistry, physics, biochemistry, crystallography, molecular genetics, computer science, and mathematics. Even still, protein folding has resisted definitive visualization and analysis. No single representation of protein folding satisfactorily captures the elusive behaviours of the polypeptide chain as

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[62] For a history of Kendrew's myoglobin models see de Chadarevian (2002).

it wriggles its way through a range of conformations in search of its "active" or "native" state. Computer scientists and mathematicians have attempted to build simulations to animate these dynamic processes (see Figure 3.2), but as I show in Chapter 5, the animations are approached cautiously and with much skepticism. Protein folding thus presents visualization and communication challenges for scientists and their students: what can they do to convey the full multidimensionality of this process?

The process of protein folding is not only difficult to communicate through pictures and words; it also presents a challenge to the ubiquitous application of cybernetic models of communication to cellular processes. If one follows the mechanism outlined by the increasingly shaky "central dogma" of molecular biology, polypeptide chains are the end product of a complex process that involves the reading and writing—the "transcription" and "translation"—of "information" stored within the genome.[63] In this rhetoric, DNA is transcribed into an RNA molecule, which, in turn, serves as a "messenger" that transports an RNA "transcript" of the nuclear DNA into the cytoplasm. It is in the cytoplasm that ribosomes, tiny macromolecular organelles, "read" the ribonucleic transcript, and "translate" it into a polypeptide chain of amino acids linked end to end.[64]

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[63] For critical readings of the history of the central dogma see Keller (1995), Kay (2000), Haraway (1991), Doyle (1997). For an example of how biologists are reworking the central dogma see Coen (1999).

[64] For a fabulous "animation" of the translation of RNA into protein, see "Protein Synthesis: An Epic on the Cellular Level." This re-enactment of protein synthesis was performed on a football field at Stanford University in 1971. Introducing the resulting film, Nobel Prize Laureate Paul Berg notes, "Only rarely is there an opportunity to participate in a molecular happening. You are going to have that opportunity. For this film attempts to portray symbolically, yet in a dynamic and joyful way, one of nature's fundamental processes: the linking together of amino acids to form a protein." The reenactment is set to a revision of Lewis Carroll's poem "Jabberwocky," and is produced in what Berg calls the "dance idiom": dancers in flamboyant costumes portray key molecules in the protein synthesis pathway, leaping about and calling out their molecular identities to animate the

It is at the point where the polypeptide chain is released into the cytoplasmic matrix that the protein folding problem emerges as a practical issue for the cell. This is also the point where the metaphor of cybernetic communication breaks down, and ceases to do productive work for illuminating what I call the *molecular practices of cells*. For a protein to acquire cellular activity, the long, floppy polypeptide chain must fold itself into specific conformations. In the process of forming active structures, the polypeptide chain folds, unfolds, and refolds dynamically. A single chain can form intricate secondary structures such as coils, helices, or sheets, each which depend on delicate hydrogen bonding between the side chains of the amino acids for their formation and structural integrity. There is no template or code that determines a protein's active form: many different amino acid sequences can produce similar tertiary structures, and similar sequences can even produce different folds. Somehow, the proteins, in their complex cellular environments, must *figure out* how to fold themselves into their active three-dimensional forms. It is in this interruption of the cybernetic model of information flow that protein folding has stumped researchers for the last fifty years.

"programming" and "assembly" of a polypeptide chain. If this is indeed a reenactment of the cybernetic metaphors of code and information flow, it is at least cybernetics on LSD. This movie has become a major hit on YouTube, with over 110,000 viewings as of June 2007. It is widely viewed in undergraduate biology classrooms, and has been repeatedly recommended to me by practicing scientists. See
http://www.youtube.com/watch?v=u9dhO0iCLww

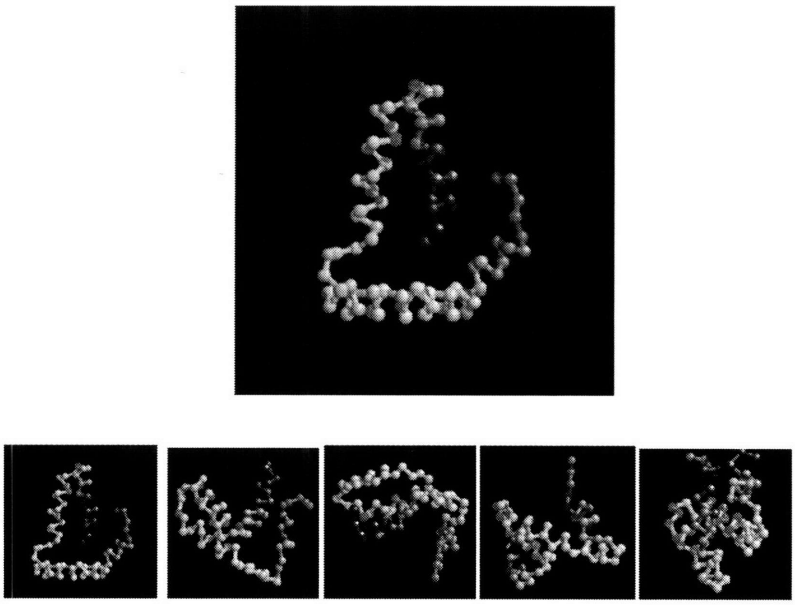

Figure 3.2: Screen shots from a hypothetical computer simulation of a protein folding. This simulation describes a theoretically feasible pathway for protein folding see the protein folding prediction simulations by David T. Jones at: http://www.cs.ucl.ac.uk/staff/D.Jones/

Since the early 1960s, researchers in biochemistry, biophysics, molecular biology, engineering and computer science have searched in vain for an algorithm to predict the protein folding pathway and the active structure of the protein from the amino acid sequence of a polypeptide chain. Cyrus Levinthal, working in collaboration with computer scientists and engineers at MIT's Project MAC, was the first to devise an ambitious project to use computer algorithms to predict complex protein structures (Levinthal, 1966; Francoeur, 2002; Francoeur and Segal, 2004). Working with the assumption that the biologically active conformation of the protein would be at its "lowest energy state," Levinthal developed computer algorithms that experimented with hypothetical forms of protein molecules. However, no matter how much he tweaked his computer programs, he

failed to predict the correct conformations for protein structures that had already been determined with X-ray crystallography. [65]

Today, Increasingly powerful computers are being applied to protein prediction. Computer modelers participate in competitions to test their algorithms for protein structure prediction. CASP, or "Critical Assessment of Techniques for Protein Structure Prediction," is a competition funded by NIH and the National Library of Medicine. This competition has now hosted a series of experiments, in which protein modelers apply their predictive algorithms to see which methods best predict the structures of proteins.[66] The biggest challenge these researchers face turns out to be modeling where and how water molecules interact with the polypeptide chain as it folds up in its wet, cellular environment. One of the problems is that this work requires extensive computer power to run protein folding simulations. This problem has been addressed by distributed computing. Folding@Home, for example, is protein prediction project that has been modeled on SETI (which searches for signs of extra-terrestrial life in the universe) by making use of volunteers' home computers to run predictive algorithms.[67] These projects continue, with marginal success, to devise algorithms in attempts to predict structure from protein sequence (e.g. Jones, 1997).

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[65] The failures of this assumption have led to what is known as the "Levinthal Paradox", whereby a single polypeptide chain can have multiple low energy states. Jim suggests that the assumption that the native conformation is at the lowest energy is "religious dogma," which is not based on empirical evidence.

[66] See http://predictioncenter.org

[67] For Folding@home see http://folding.stanford.edu

In 2004, Diane Griffin introduced the speaker at a university-wide lecture on protein folding hosted by the department of chemistry. The speaker was Barry Honig, a Howard Hughes Medical Institute researcher at Columbia University. Half joking, Diane introduced him as "the man who, if he's right," will put her and other crystallographers "out of work." A burst of nervous laughter rose from the audience as they sat with anticipation to hear the latest on computational advances in Honig's talk, titled "Protein Structure Prediction." Although he admitted current failures, Honig expressed his confidence that they will soon be able to predict folding pathways and structures, and in effect, replace the empirical work of crystallographers and other structural biologists (Honig, 1999). However confidant Honig's claims were, it was a tough sell for this crowd.

Jim Brady and members of his laboratory were in the audience at Honig's talk. I sat a couple of rows away from Jim and watched his reaction to the talk. He didn't ask questions at the end of the lecture, and when it was over promptly got up and left the room. As he had emphasized in his lectures, he is skeptical of those who believe they would find the answer to the protein folding problem with bigger and better computers. In his second lecture of his course he explained to the class that DNA "codes" cannot be treated as a proper language, and so, the rhetoric of informatics does not hold for proteins. If there is no algorithm to predict the fold, what then could be going on in the transformation of the linear peptide into the complex three-dimensional structure of the mature protein? For Jim, "protein folding is a deep problem." Refusing to flatten protein folding into a two-dimensional problem of reading or writing DNA sequences, he drew his students' attention to the depths and dynamics of the fold. If they are to become "true protein folders," as Joanna his former student identifies, they must learn how to embrace the "depths" of the

protein folding problem, and with this, the indeterminacy of the fold. I read this as an admission that protein folding doesn't readily lend itself to computation or automation, and as such, I see it as an invocation that researchers must go "deeper," and apply their bodies and imaginations to cultivating embodied models of proteins.

Over the duration of this lecture course, I was able to observe the layer-by-layer, real-time construction of what, after Trumpler, could be called "converging models" of protein folding. In his lessons, Jim scribbled a seemingly endless series of graphs and equations across the blackboard to illustrate the biochemistry of protein folding in relation to experimental data on molecular kinetics. He augmented these shorthand scrawls, diagrams and charts with several other visualization media. These included analogies and physical models. In addition, in his lectures, Geoff contributed to this rich visual culture by building physical models of protein structures, and conducting demonstrations with interactive computer graphics and virtual animations. Taken together, these various modeling media combined to give body to the folds and structures of protein molecules.

Modeling Molecular Bodies by Analogy

Models that function by means of analogy are useful for illustrating the intertwining of mind and body in scientific reasoning. Analogies can illustrate complex processes or otherwise inaccessible phenomena by enlisting imagination, experience and intuition (Morgan and Morrison, 1999). Peter Taylor and Ann Blum suggest that modeling by analogy and metaphor enable "associations from one field to animate a scientist's thinking about another field," and so make "research 'do-able'" (1991: 276). Analogies can be

thought of as producing their own form of "realism" (Lynch, 1990: 208). In this sense, analogies achieve a materiality that can often be more tangible than the thing being modeled (see Cambrosio, et al., 1993). In particular, conceptual analogies can connect familiar, embodied experience of the world to distant or invisible phenomena. Jim used analogies in his class to materialize the phenomena of protein folding in forms and at scales that made them tangible to his students. The use of analogies in the class demonstrates the material-semiotic practices involved in modeling students' bodies and imaginations with knowledge of protein folding.

Each time Jim introduced a new class of proteins, he offered the students what he called a "motivator" to capture their interest in the protein of the day. These motivators were analogies that got the students thinking about the everyday materiality of proteins. He used examples of cooking egg whites and making Jell-O to illustrate effects of heat and cooling on proteins like albumin and collagen: heat denatures proteins and promotes their aggregation, changing the state of a substance from fluid to solid. According to Jim, Jell-O is merely "unfolded collagen." To call up people's familiar experiences with collagen in its denatured form, Jim offers other examples such as glue, the congealing of chicken soup and the healing of wounds. He also used fever as an analogy to illustrate the temperature sensitivity of protein folding ("above 106 degrees, you're dead"). Beginning at the macroscopic scale he took the class on a journey from the familiar worlds of corporeal experience, down to the molecular realm. In this way he tapped into students' experience to help them get a richer feel for these substances.

These analogies gave texture to the molecular worlds that the students in the class couldn't

otherwise grasp. In some senses, these analogical models were *metonymic* in their nature. Metonymy, by connecting part and whole through association, acts by revealing contiguity through processes of scale-manipulation (Lanham, 1991: 101-2). However, rather than using a "part" of a thing to stand in for the "whole," Jim inverted this rhetorical form: he used the "whole," that is, large-scale phenomena to draw students into the molecular "parts". In other words, Jim employed human-scale phenomena like egg whites, hair, and gastric juices, processes like the curdling of milk, and the cooking of eggs to model the structures and states of proteins at the molecular scale.

These metonymic figurations were meant to hook students' imaginations. Yet, he also recognized that these motivators wouldn't always hook everyone. When he didn't get a rise out of the class from his description of leather as unfolded collagen, he muttered under his breath, "Nobody wears leather shoes anymore. We're moving into the modern age. I need to change the motivator!" And again, when no one could answer his question about what happens to blood when you heat it up, he felt compelled to provide washing instructions to the students so they would know what to do if they got bloodstains on their clothes:

> Let's say we want to look at denaturation versus temperature. Let's take a mixture of ovalbumin and lysozyme in egg whites. What happens when you heat that up? Does it denature? Yes. Can you establish an equilibrium between the denatured state and the native state? No? What about haemoglobin? Some of you are very familiar with haemoglobin. What happens when you heat up haemoglobin? Some of you must have had bloodstains? [No response.] You never had bloodstains? Wow. [A male student tentatively answers: "It loses colour?"]. It *changes* its colour. Right? And then is it easy to get out? You know? No! Once you heat up haemoglobin, right...if you make a mistake and you've got a bloodstain, and you put it in a washing machine with hot water, you are done, you'll never

> get it out. You are much better off washing it in cold water. [Laughter]. Let me tell you, you ever get a bloodstain you have to wash it with cold water [Jim gets louder]! If you wash it in hot water you will get thermal denaturation and aggregation!

This is, of course, a lesson the women, who make up about half the class, likely understood quite well, though were in no position to admit publicly.[68] Faced with an awkward silence from his students, Jim was forced to scrounge for hooks that could elicit recognition and produce an embodied understanding of the effects of heat on protein folding. When the hooks did work, however, their effect was visceral. I, for one, really got how collagen folds at the site of fresh wounds by contemplating the formation of my own scars.

For philosopher of science Isabelle Stengers (1999; n.d.), abstractions, such as analogies and models, are propositions "asking for, and prompting, a 'leap of imagination'; they act as a lure for feeling, for feeling 'something that matters.'" Effective models, like analogies, can produce what Stengers (n.d.) calls an "empirically felt elucidation of our experience":

> To define abstractions as *lures* and not as generalizations is something any mathematician would endorse. For a mathematician abstractions are not opposed to concrete experience. They vectorize concrete experience. Just think to [sic] the difference between the mute perplexity and disarray of anybody who faces a mathematical proposition or equation as a meaningless sequence of signs, and the one who, looking at this same sequence, experiments [sic][69] *sheer disclosure*, who immediately knows how to deal with it, or is passionately aware that a new possibility of doing mathematics may be there. In order to think abstractions in

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[68] During his lecture, Jim showed no sign that he recognized the gendered aspects of his inquiry into students' experiences with blood-as-hemoglobin.

[69] In translation from the French, there is a wonderful folding over between "experience" and "experiments" in Stengers' text.

> the constructivist sense I am presenting, we need to forget about nouns like "a table" or "a human being" and think rather about a mathematical circle. Such a circle is not abstracted from concrete circular forms, its mode of abstraction is related to its functioning as a lure for mathematical thought, luring mathematicians into *adventures* which produce into [sic] a mathematical mode of existence new aspects of what it means to be a circle (n.d., emphasis added).

Here, the metonymic motivators that Jim uses to traverse dramatic shifts in scale can be understood as "lures" that operate to "vectorize concrete experience": they move the students to feel the transformations the protein undergoes in its folding and unfolding, as movements they can sense with their own bodies. This is the "sheer disclosure" of insight, which suggests that understanding is a kind of bodily "concrescence" (see Stengers on Whitehead, 1999). I read concrescence as a material-semiotic convergence where "knowing" is a feeling that resonates in one's flesh. And yet, as I explore more thoroughly in Chapter 4, a lure is only effective in the hands of someone trained to use it; that is, trained in the nuances of the world a particular abstraction inspires. Stengers' example of the abstraction of a mathematical circle shows how a circle operates as a lure most especially for the trained mathematician, who is immediately pulled into a whole world of circles as mathematical objects. Seen in this light, it is Jim's job in the classroom to both generate lures that can hook his students in, and train them in how follow these lures so that they can "vectorize" their experience and make the Alice-in-Wonderland leap into molecular worlds.

The Body-work of Modeling

Three-dimensional models can be thought of as enactments of the intimate knowledge

their modelers engendered in their production. Yet models have a life that extends beyond the immediate grasp of their modelers. When molecular models leave the hands of their makers, the models themselves become teachers in their own right. They do this by attracting the active and "curious hands" of other users.[70] Models and modeling practices are mobile, they move from research into teaching contexts and back again as they are built, used, revised, remodeled, and reconfigured (see Hopwood, 1999; Francoeur, 1997). In this sense, models have a pedagogical life cycle as they move between the hands of their makers and users: in different contexts, these objects afford different kinds of interactions and different kinds of learning. Teaching, learning, and research thus become intertwined through practices of modeling.

During a lecture on the major folds or secondary structures that form in proteins, Jim demonstrated the structure of the alpha-helix with a well worn ball-and-stick model. He claimed that this relic was brought to this campus some fifty years ago from the LMB in Cambridge, England. The model Jim held up in front of his class *re-membered* the molecular structure that Linus Pauling "discovered" in 1948.[71] Indeed, the model that Jim held up was one of many replicas of the alpha-helix that had been produced to help other researchers grasp the fine details of this special fold. Elaborating this point, Jim recounted a story about his experience as a post-doctoral fellow at Cambridge University. There he worked with Cyrus Chothia and Arthur Lesk at the MRC when they were investigating Pauling's proposed structure in order to learn how alpha-helices might pack together to

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[70] On how models attract "curious hands" see Langridge, et al. (1981: 661).

[71] See Glusker (1981), Pauling, et al. (1951).

form larger tertiary structures within proteins. According to Jim, they spent "years and years and years just *looking* at this structure." This required re-building physical models of the alpha-helix and trying to figure out how multiple helices might pack together.

In this case, Pauling's original model of the alpha-helix was transformed. No longer an object whose intrinsic properties remained to be determined—what Hans Jörg Rheinberger (1997) might call an "epistemic thing"—the model became a "technical object" in an experimental system that posed a different kind of question: rather than inquiring into what this thing was, Chothia and Lesk was an inquiry into how this structure related to other similarly shaped things. Made over into an experimental tool, it became a means to produce new kinds of questions. In a sense these models became what Rheinberger might call "vehicles for materializing questions" (1997: 28).

Models of the alpha-helix also became instructive objects that taught their users how to look at molecular structures, and see in new ways. Jim reminisced:

> One thing was very clear in that group: some people were just able to sit and look at the structures. But most people could not do that. They had to get up and get a cup of coffee and do an experiment. Some people could just look at the structures. And finally they saw things that nobody else saw. Because that discipline of sitting and looking is something that is very hard. And it is something that has been lost. I worked with Aaron Klug who won the Nobel Prize for a three-dimensional structure. He used to sit there and say to us, he'd say, "You Americans you can't sit still long enough! You go off and do an experiment... You don't *look*."

Jim used the ball-and-stick model to teach his students how to see. In so doing, he offered insight into practices of looking and the corporeal discipline involved in working with and learning from molecular models. When Jim presented the alpha-helix to the class he made

it clear that "sitting and looking" is anything but a leisurely activity. You can't just gaze lazily at the model: "If you just *look* at it you don't see anything." Playing on the double meaning of the verb "to grasp", he told the class: "Now...This is not easy to grasp, and that's why it's so important to *grasp* these structures.[72] He picked up the model, which was two feet tall and a foot and a half in diameter, and rotated it around in his hands, assuring the class, "soon you will start to see." He demonstrated that "seeing" requires active handling. With his hands and eyes he showed the class how to "walk through" the model amino acid by amino acid. Examining it atom by atom, he used his hands to feel around the grooves and ridges formed by the side chains as they spiraled up the helix. For Jim, "sitting and looking" involved his whole body, and so he showed the students what they would have to do with their bodies in order to really get a handle on the intricate folds of protein models.

The protein folding problem demands that students develop keen spatial reasoning skills as well as the ability to "recall" instantly the form of a given protein structure. Jim made this requirement clear: "You must be able to see leucine [an amino acid] in three dimensions. You need to be able to see it immediately." When he demonstrated the structure of the leucine zipper, an important fold for protein-DNA interactions, Jim joked that students need to know it well enough so that "if your grandmother asks you for it, you could draw it." These instructors did not expect students to absorb this knowledge passively by just looking with their eyes. In his performance of the model of the alpha-helix, Jim's bodily involvement was essential. As demonstrated in his insistence on "hand copying" rather

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[72] For a description of embodied metaphors like "grasping" see Lakoff and Johnson (1999).

than photocopying the diagram in the textbook, he did not expect the students to absorb this knowledge passively: he insisted the students fold the structures into their bodies.

Building Molecular Models

In contrast to the gooey, proteinacious forms that Jim evoked through his body-based analogies, Geoff brought "engineering thinking" to the classroom. Able to think about the physicality, forces, and forms of protein structures, he also drew on a different logic than the linguistic and cybernetic metaphors that have dominated theories and practices in molecular biology over the last five decades. According to Jim, people who can think like Geoff are sought after by biologists to help them reason through the intricacies of structure. When Jim was first working on the lattice structure of a virus, he turned to Geoff: "No wet biochemist could deal with a lattice. Who knows about lattices? Engineers know." Indeed, while many of Geoff's lectures were illustrated with digital media, on several occasions he felt compelled to "bring home" the complex structures he was describing by using improvised physical models that he would pass around the class. In one case he passed around a soccer ball as a physical model of the icosahedral structure of a viral protein shell, and in another, he demonstrated the ways two helices come together in the formation of a special fold found in collagen microfibrils—the coiled coil—by using rolled transparencies marked with the locations of amino acid side chains as they would be positioned on the helix (see Figure 9). True to engineering form, during one lecture he rigged-up a model of collagen microfibrils with pencils, "magic tape" and a volunteer:

> Alright, so this is a diagram [of collagen, projected on the LCD screen, see Figure 3.3] to try and get in your head. And

> if you're like me...I couldn't quite visualize it. So if you don't mind, we're going to play a little game....Sparing no expense, what I have here...And this one takes some volunteers, so if you don't mind, I'll sign you up. [Points to a male student in front of him]. This is not a skill thing, it's just proximity. [Laughter]...Alrighty? And this is what we are going to do. I have very expensive materials. I have pencils, which are going to approximate little collagen triple helices. And this is absolutely the best. I don't know how you feel about the state of marketing ... I want you to know, this is "Magic Tape." It says right there "Magic Tape." ... Anyhow, here's what we are going to do...Everybody see the elements here? I'm going to do all the hard work. I'm going to put them down and then you get to hold it while I tape it together.

Each pencil represented a helical structure formed by three collagen peptides, and Geoff laid the pencils down, side by side, with their ends staggered with respect to each other. He used a transparency marked with a grid to define the stagger distances between each triple helix. In close negotiation with the student, he managed to roll the five pencils up to create a tube-like structure.

> Okay I'm going to pick this thing up, and I'm hoping you are going to tape this sucker everywhere you can. Nature does this in a flash. It doesn't need magic tape either. We are going to pass this thing around, lest they think we are fooling them ... Perfect. Alright. Give Chris a hand here [clapping] ... Starting with you, we'll pass this around. A collagen microfibril right before your very eyes!

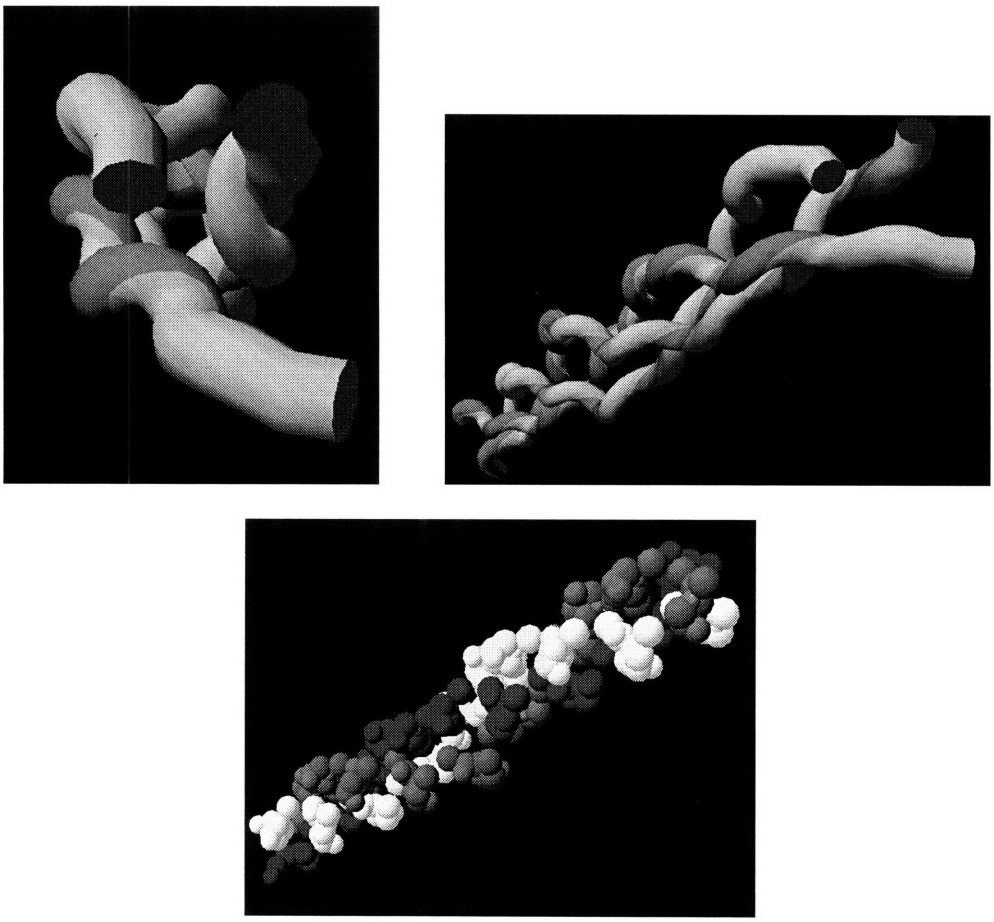

Figure 3.3: Three views of the coiled-coil structure of collagen microfibrils. I used Swiss PDB to produce this image by downloading the coordinates for a collagen microfibril from the PDB and experimenting with different views and visualization conventions. The original structure was deposited by J Bella, et al. (PDB ID 1cgd), and was published in *Structure* (1995) Volume 3(9): 893-906.

As the model was passed around, students examined it closely, rotating it in their hands, and looking down through the narrow channel formed at the center. They chimed in with

questions about what pencils represented, and how microfibrils packed together to form higher order structures of collagen fibrils. The demonstration was a success in that it got the students working with their hands and gave them a concrete structure to think with so they could begin to ask questions. As this example demonstrates, physical models were put into play where two-dimensional representations failed to get students bodies involved in the structural problem at hand.

Projection and Play with Virtual Models

Where models like the ball-and-stick alpha-helix seem to be relics of days gone by, this new cohort of students can download molecular graphics software onto their home computers in order to play in the molecular realm. There is indeed a playful element to the software, but a kind of play that's inherently pedagogical. In his lectures, Geoff took the students on "Hollywood tours" projecting protein structures using slick interactive molecular graphics and animation programs. "Just in case you haven't played with your Playstation today," he announced to the class, "This is a little fun ride." He invited the students into the game of interactive molecular graphics, playing up the magic show effect of these "nifty" tools.

Geoff walked the students through the main features of interactive graphics programs like SwissPDB, Chime, and Protein Explorer (see Figure 3.4). These tools enable the display and manipulation of the protein structure data that can be downloaded from the Protein Data Bank (PDB). In addition to leading students through the ins and outs of the programs, Geoff also instructed the students how to look and what to see in molecular molecules on-

screen. With his mouse and a few control keys, he demonstrated how one can zoom in on particular regions of the protein fold, highlight specific amino acid groups, rotate the molecule in digital space, and develop an eye for finding the right point of view to display particular structural features. The challenge, as he presented it to the class, was that molecular models are complex. There are a "whole lot of atoms," he explained, "what you want to look at is distributed through the molecule. There's not one single thing that you look at." "Looking" for Geoff, appears to involve as much "handling" as Jim's walk through of the physical model of the alpha-helix.

In one lecture, while Geoff was in the midst of projecting a virtual model for the class, Jim jumped in to help to narrate the biology of a particular fold. With Geoff at the controls of the interface, Jim called out requests for Geoff to display certain views, or highlight specific residues to emphasize certain features of the molecule. New, more dramatic views of the proteins were met with hushed "Oohs!" and "Ahhs!" from the students behind me. Collectively the instructors demonstrated how interactive molecular graphics software could be used to reveal otherwise hidden features, conceal some at the expense of others, and to move back and forth between viewpoints. According to Geoff, "You're going to find you spend 90% time spent fiddling to get the point of view correct." He told the class that they'll have to keep asking "Where did that disulphide bond go?" He advised the students to "pick a view that looks good to you and remember it."

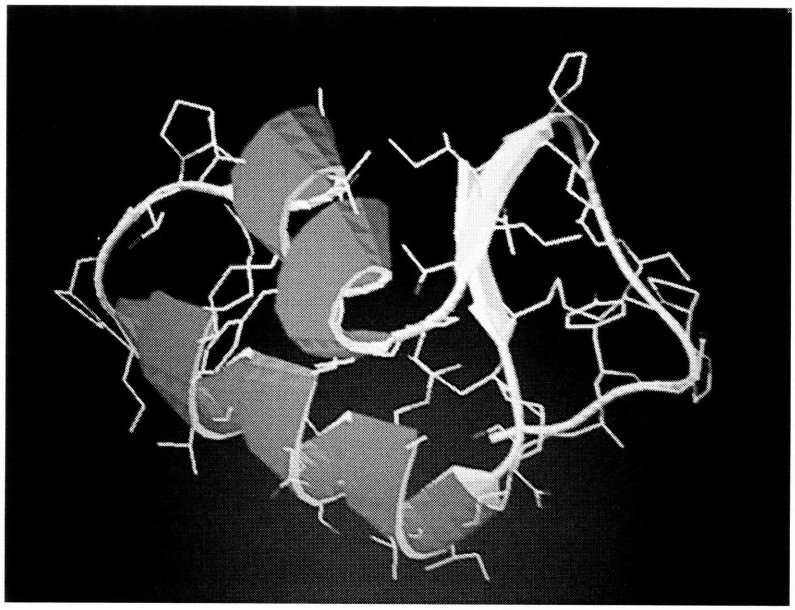

Figure 3.4: A screen shot of a protein model viewed through the SwissPDB graphics interface. To make this image, I downloaded the coordinates of a protein (beta-purothionin, a plant toxin) from the PDB (PDB ID 1bhp) and played with various visual conventions until I found a way to highlight the alpha-helices and beta sheets in the molecule. The original structure was deposited by M.M. Teeter, et al., and published in *Acta Crystallography*, Section D (1995), Vol. 51: 914.

Yet he was not totally swayed by what he called the "pretty pictures" that can be generated through these technologies, and warned the students against the "deception of animation." In a fly through tour of coiled coils, he paused to offer this:

> And let me just point out to you, if you were paying attention there, you'll notice the deception of animation. I can only pull on this [alpha-helix] as a rigid body. I only have at my disposal the means to translate this, to pull it sideways as a rigid body. If you look at it your intuition should tell you that you should not be able to do that.

> *Because these things are wrapped around each other.* The physics of the matter would require you to unravel [the coil]. And that's exactly the situation...And of course here [in this virtual medium] we can just ignore that. We can just let these things blithely interpenetrate! [Laughter] To hell with physics!

Both Geoff and Jim adopted what could be called a "critical epistemology of visualization."[73] Geoff pointed out a common misconception about models derived from crystallographic modeling: "Beware of the fallacy of false precision. You get the impression that these molecules are known rock solid....But there is a certain amount of judgment involved." He warned the students that crystallographers do a lot of what he calls "tweaking and jiggering" to get the best fit between the model and the data. "What you are seeing is someone's best guess." In line with numerous other research scientists across an array of disciplines (Turkle, et al., 2005), these instructors were faced with the challenge of assessing the possibilities and limitations of emerging virtual media. As such, they were adamant about teaching their students how to engage these tools critically. What is interesting here is that the measures against which virtual media are tested are based on

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[73] On critical epistemologies of visualization see Turkle et al (2005). In results emerging out of a collaborative NSF study on computation, visualization and emerging professional identities, myself, Sherry Turkle, Joseph Dumit, Susan Silbey, Hugh Gusterson, and David Mindell introduced the term *critical epistemology of visualization* to account for the ways that interactivity in virtual media allows practitioners to exercise their tacit skills, judgment, and skepticism with regard to computer mediation of their objects and experiments. This term refers to the many ways that researchers and designers assess the truth claims and scientific value of visual images, the kinds of criteria they invoke for evaluating images, and more generally, the ways they critique visualization and simulation practices. In my research for this project I found that today's life scientists approach visualization with a healthy skepticism. For crystallographers who determine the structures of complex molecules through a complicated, mentally and physically challenging set of imaging, mapping and modeling techniques, the model they produce is only ever "just a model." These researchers understand the representational and technical limitations of their visualizations and never confuse the model for the molecule itself. Even microscopists who work more directly with the material they visualize, tend to recognize the extent to which their images are mediated, abstract representations of the cells they study. In addition, all the cell and molecular scientists we worked with insisted on a critical pedagogy for visualization.

the physicality of corporeal experience.

Molecular Gestures

Joanna and her colleagues in the biology department have recently developed a series of workshops and lesson plans using specially designed three-dimensional models and interactive computer graphics to help students learn to visualize the structures and movements of biological molecules. Through this work, Joanna has come to recognize that teaching these concepts places extra demands on her body to perform the multi-dimensionality of biological phenomena. While she is wary of what she calls "anthropomorphizing the molecule" (see Chapter 5)—she worries that students might take her too literally—she tells me that in class she actively animates molecules with her body:

> I probably like the dancing and movement so much [in the classroom] because I do see these things rolling around in 3D in my head. And yeah, its like, if I could get my body to do this [As she curves her body around an imaginary fold, voicing the movement with a "Schwooo!"], and have this little arm flapping in the breeze. I don't know. It just makes more sense.

As she talks, her body comes to life, and I can see her delight in communicating the details of the fold. But what kind of anthropomorphism do her proteinacious choreographies perform? Need she be so wary of ascribing agency to the molecule? As I investigate below, it may well be this very mode of *becoming molecule* that Joanna is able to communicate to her students in ways that facilitate their learning.

Drawing on an array of representations, including biochemical assays, crystallographic structures, computer generated models and simulations, as well as metonymic models that hook students into molecular phenomena, Jim and Geoff moved through a wide array of media in order to generate a collage of converging models of protein folding in the imaginations of their students. And yet, like Joanna, perhaps the most vivid medium that Jim had available for communicating the forms and movements of proteins was his own body. Inflected and informed through his own practice of modeling molecular forms, Jim's body had itself become a pedagogical model.

Bumping up against the limits of language for articulating the qualities of three-dimensional things, Jim struggled to find the right words to paint a clear picture of protein structure:

> It is clear from the X-ray diffraction patterns that proteins are objects with space in them. This is very different from packed polymers. So, we can ask: What is the character of the interior? Is it oily? Is it patchy with regions of solvent? But patchy is a two-dimensional word. I can't think of a three-dimensional word that gets at this.

Where language falls short, and where two-dimensional images fall flat, Jim used his body to get at the otherwise elusive texture, tensions, forms, and movements of proteins. Expressive throughout his lectures, he used his body to convey special features of a given fold. When describing the folding of a globular protein, he often drew his arms into the core of his body. Curving over and tucking inward to create a concave form, he used the shape of his arms to mimic the internal organization of helices and sheets. When describing the packing of two helices in a protein, he repeatedly drew his arms in towards each other, crossing them at the forearms to specify the precise angle at which they are

associated. The flexibility or inflexibility of this association was made clear through the tension he held in his muscles.

Several studies have recently taken up the question of the role of gesture in scientific reasoning (Alac and Hutchins, 2004; Ochs et al., 1994; Goodwin, 2000) In "Interpretive Journeys: How Physicists Talk and Travel Through Graphic Space," Elinor Ochs (1994) and her colleagues have approached the study of gesture in the performance of scientific concepts. They describe the gestures that mediate communication among physicists who attempt to convey their research to each other in weekly lab meetings. In this paper, they apply ethnomethodological conversation analyses to video recordings in order to track how bodily gestures help physicists narrate and dramatize their scientific stories. They observe what they call "understanding-in-progress" and show how "scientists can take seemingly immutable transcriptions such as published graphic displays, and, over narrative time, transform them into highly mutable, highly intertextual and symbolic narrative spaces through which they verbally, gesturally, and graphically journey" (1994: 158).

In their example, physicists' gestures are seen as explicitly discursive; gesture for the physicists offers a "dynamic grammar," a means of supporting their language, and helping them to make statements about mathematical relations and two-dimensional graphic displays (1994: 161). By contrast, in the protein folding class, Jim's gestures are performances of forms that take up space and move through time.

Rather than using movement to animate language, Jim used his body to perform substances, forms, and textures that are hard to relate through words. Jim's gestural

choreography was thus less a "grammar" than a form of *mimetic modeling*. Three-dimensional molecular models of proteins find expression through *mimetic gestures*; that is, gestures that render the form and movements of the molecule through the form and movements of the modeler's body. Brian Rotman (n.d.) approaches mimetic gestures as the most "primitive" gestural form. I would like to argue, however, that such mimetic gestures offer sophisticated modes of model-making and reasoning for these researchers. Mimetic gestures of molecular embodiments can themselves be considered species of mimetic models: they are renderings that articulate forms of knowing and performatively sculpt imagined worlds.[74]

In this sense, Jim's body *became molecular* (Deleuze and Guatari, 1980) in order to perform the protein fold. In the process his body became a model and pedagogical tool. Key here is that in this performative idiom, the boundary between the scientist and their object breaks down. This appears to be a productive form of anthropomorphism—where human bodies become resources for communicating the otherwise inexpressible molecular forms, textures, and tensions.

Though Jim looks nothing like a protein molecule (!), his molecular gestures are precise. During an in-depth demonstration of the packing of helices during protein folding, Jim held his arms out in front of him, crossed at the forearms to mimic how it is that the "side chains are talking to each other." His stance strong, and holding his arms in position, he began to

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[74] Through mimetic gestures, I also hope to challenge the assumed binary between the visual and the discursive. These gestures are not quite rhetorical devices, nor are they purely visual cues. They are material-semiotic modes of communication. In this sense mimetic gestures operate somewhere between discursive and non-discursive modes of expression. See Deleuze's (1988) *Foucault.*

describe his body as the model: "Now when two helices are packing against each other they form a junction..." All of a sudden he paused and looked up. He called on Geoff. "I want you to stand up." "Alright," Geoff agreed, and stood up. Jim gave him instructions: "Now, point to the junction." Geoff pointed vaguely at Jim's crossed arms. "No, not there!" With his "helices" still packed together, Jim used his voice and eyes to redirect where Geoff was pointing: "Right between ... Yeah, okay."

Jim carried on with his description while Geoff stood by his side, pointing at the junction. In this moment, Jim made explicit that *he* was the model. By asking Geoff to point to the junction where his arms meet, he demanded and received Geoff's confirmation that his arms really were helices. In this way, the class could also come to see Jim as the model of interdigitating helices. Moreover, Jim required Geoff to point, not to any place where his arms meet, but to a specific site on his body-as-molecular model. There was a specificity in this mimetic gesture that demanded Geoff locate the exact site of the junction. Becoming molecule, Jim made the model tangible and thinkable for himself, Geoff, and his students.

Conclusion

In this course, teaching protein folding became a practice of modeling students' bodies and imaginations. This pedagogical work is an example of what Bruno Latour (2004) has described as the "articulation" of the scientists' sensorial body as they get trained in laboratory instruments and techniques. After Latour, Rachel Prentice (2005) has developed a concept of "mutual articulation," which acknowledges the recursive nature of model building: in the process of building models, the models can then act recursively to

rearticulate the modeler's body. In the case of improvising new models for teaching protein folding, modeling becomes a pedagogical practice that produces new "molecular embodiments," by reconfiguring the bodies and imaginations of students.

Collectively Jim and Geoff worked hard to create a learning environment where each student could experience the convergence of models, images, diagrams, and analogies, and so develop a feeling for the elusive nature of protein folding. The aim of their teaching was to hook their students' bodies and imaginations into the fold. The course gave students a mission ("Hopefully one of you will solve this class of problems.") and a method ("First you must master the structure, then you can move on to experiments."). By invoking mastery, Jim was not asking for definitive knowledge, but a willingness among the students to let models instruct their bodies: in other words, he had to train his students how to use models as lures that can pull them into the subvisible worlds of protein folding. The skills they would need included the ability to *become molecular*, to inhabit the model, and perform the fold. In a sense, the course elaborated just how models are material-semiotic actors "built to be engaged, inhabited, lived" (Haraway 1997: 135). It was in this process of learning how to model their bodies and imaginations, that Jim's students, in turn, were ushered into the fold of an emerging professional identity skilled in the lively arts of molecular visualization.

Chapter 4

Modeling Molecular Machines: Structural Biology, Biological Engineers & the Materialized Refiguration of Proteins

> Late twentieth-century machines have made thoroughly ambiguous the difference between natural and artificial, mind and body, self-developing and externally designed, and many other distinctions that used to apply to organisms and machines. Our machines are disturbingly lively, and we ourselves frighteningly inert.
>
> Donna Haraway, "Cyborg Manifesto," 1991: 152

> I am convinced that technoscience engages promiscuously in materialized refiguration; that is, technoscience traffics heavily in the passages that link stories, desires, reasons, and material worlds. Materialized refiguration is an eminently solid process, even to the point of the practice of objectivity, not some merely textual dalliance.
>
> Donna Haraway, 1997: 64

Introduction

"Who here has taken a biology course before?" Dan Hijiko, a professor of biological engineering looked up at the eighty or so students who had crowded into a too-small lecture hall on the first day of spring semester classes at this private, east coast university. They had arrived for a freshman seminar aimed at recruiting a new cohort of students into the school's brand new biological engineering major. Save one or two, all the students put up their hands. "Good," he responded. "But this will be a little different from what you

learned in your other courses." Dan was the coordinator for this half-semester course that featured lectures by biological engineers drawn from departments across the institution. He turned to introduce the director of the program, Stan Graham, who offered the students a taste of what this new major would offer. "Biology has changed," Stan told the class. "When I was your age biology was *just starting* to be on the verge of being quantitative and designable." According to him, the molecular and genomics revolutions transformed biology by making biological "parts" and "components" available to manipulation at the molecular scale. "Biology today is at the point where getting the parts and manipulating them is relatively easy. Now, the hard part is: How do they *work*? Now that you know what the components are, how do they *work*? Well," he announced to the class, "they work as machines."

Stan turned to the projection screen that displayed a black-and-white, time-lapse movie of a cell migrating across a slide. He and the students watched its magnified, animal-like body undulate as it pulled itself across the screen.

> If you look at a picture of a cell here migrating across a surface, you want to know how to make that cell migrate faster, to colonize a biological material, or slower to prevent a tumor from metastasizing. You have to look *inside the machine* for how the molecular components work together as a machine to transmit forces to the environment; to pull on the environment, pull the rest of the cell along. There's the actin cytoskeleton, and all sorts of proteins that link the actin cytoskeleton to receptors across the cell membrane. These all work as an exquisite, *many, many, many, many* molecule machine.

This moving image was juxtaposed against other projected images, including colourful cartoons of the "molecular machinery" of the cell, and engineering-styled electrical circuit

diagrams that traced the intra-cellular "regulatory circuits" that "govern" the cell's large machine "assemblages." "Now that we have the components," he explained, "biology needs to be studied the way engineers look at things." These freshmen, interpellated as would-be biological engineers ("*you* have to look inside the machine"), were instructed to see this cell as engineers engage their objects. The classroom became a training ground for new students to learn see through the obscuring density of the seething cellular masses that constitute living bodies. At the same time the instructors aimed to instill in them the desire to get at the underlying parts, components, and devices that "do work" in the cell to "drive" cellular life.

"These are very appealing metaphors and this is engineering language," Stan explained. Indeed, molecular machine metaphors are alluring to many, and this is a language that has become pervasive in contemporary scientific texts, where proteins are ubiquitously figured as "molecular machines," "the machinery of life," (Goodsell, 1993), and even as "nature's robots" (Tanford and Reynolds, 2001). Proteins are rendered as the mechanical levers, hinges, switches, motors, gears, pumps, locks, clamps, and springs that "transduce" forces, energy, and information (e.g. Hill and Rich, 1983; Bourne, 1986; Hoffman, 1991; Krieisberg, et al., 2002; Harrison, 2004; Chiu, et al., 2005). These components are seen to assemble and reassemble into complex interlocking devices that act to build and maintain the cell as a higher order machine. It appears that the metaphor of molecular machines is on the rise, both in the scientific literature, and in the rhetoric that prevails in teaching and research contexts. In this sense, life science is rapidly becoming a discipline in structural engineering.

Yet, sitting in this introductory biological engineering class I was struck by the distinction that Dan had pointed out between what students in this class would learn that was different from what they got from their biology courses. This distinction quickly became clear to me. In Jim Brady and Geoff Miller's course, "The Protein Folding Problem," protein molecules were narrated in a range of registers. While Geoff did bring an engineer's aesthetic to protein molecules, rendering them similarly to Stan's "molecular machines," Jim's animated body-work and analogical scale-manipulations modeled proteins as gooey, lively bodies. One key difference here is that "The Protein Folding Problem" was first and foremost a biology course, and Jim, the primary instructor, a classically trained biologist. In that course, figurations of protein molecules were allowed to oscillate between molecule as lively body and molecule as machine; and yet, the prevailing tropes for protein folding in that course were dynamic, dancing forms that could render the subtle movements and textures of the folding process. In this chapter I am interested in those researchers who put the metaphor of molecular machines to work. I want to understand what is at stake when researchers attempt to keep protein metaphors from oscillating between the figures of lively bodies and machines, and how researchers clamp down on machines as principal figurations for these molecules. To do this I first examine how the metaphor of molecular machines has operated in the history of cell biology and biophysics, and in the contemporary contexts of biological engineering and structural biology communities. In this inquiry, I am not admonishing the use of machines as an analogy for molecules. On the contrary, following Isabelle Stengers (n.d., 1999), I see the production of "molecular machines" as an exquisite achievement. This chapter examines the many layers of this achievement. In what follows I track *how* these machines are constructed; *what kinds* of machines are constructed inside cellular bodies; and the *forms of expertise* that must be

engineered in order to put these machines to work in living organisms.

Machine Vision

Protein modelers and structural biologists increasingly apply molecular visualization technologies such as X-ray crystallography, cryo-electron microscopy and computer algorithms to the task of building three-dimensional atomic-scale models of protein molecules and interpreting their cellular activities. The interesting thing is, the closer they look with these visualization technologies, the more machines they seem to discover in the cell. But, let us pause for a moment here. Are structural biologists and biological engineers merely applying their visualization tools to reveal protein machines at work in what is fast becoming the factory floor of the cell?

As I hope to show in this chapter, visualization technologies are not such neutral devices: machinic discourses and aesthetics play a major role in how these invisible substances are brought into view. By *figuring* the very objects of biology through machine tropes and stories, biological engineers are not just artfully describing cells and molecules through appealing language. Their metaphors transform how they make proteins visible, tangible, and workable as objects. A key element of this process, which I examine below, is that this also transforms what kinds of investigators are recruited to do this work. So, while for the uninitiated, machinery may not be an obvious or self-evident descriptor for the writhing form that crawls across the microscope slide, or the gooey substances that churn within it, in practice, the seething cellular body is not merely *like* a machine for the biological engineer, in their hands, it *becomes* one. Figuring molecules and cells as machines through technoscientific narratives is for Donna Haraway (1997) an "eminently solid

process" (64) through which things and words "implode" (97), crystallizing new kinds meanings and forms of life for both scientists and their objects. My aim in this chapter is to show how structural biologists and biological engineers learn how to build and use the metaphors of molecular machines.

From Informatics to the Mechanics of "Life Itself"

In the context of the sequencing craze of the genetics and genomics revolutions and the rise of corporate biology and genetic engineering, Donna Haraway has suggested that "the living world" became a "command, control, communication, intelligence system," or "C^3I in military terms" (1991: 150; 1997: 97). For her:

> These issues are about metaphor and representation, but they are about much more than that. Not only does metaphor become a research program, but also, more fundamentally, the organism for us is an information system and an economic system of a particular kind. For us, that is, those interpellated into this materialized story, the biological world *is* an accumulation strategy in the fruitful collapse of metaphor and materiality that animates technoscience (1997: 97).

Key to Haraway's concerns here is that rendering through metaphor is a practice of *worlding*. She writes that, "We act in and are inside this world, not some other. We are subject to, subjects in, and accountable for *this* world" (ibid.). From the vantage point of a feminist science studies model of accountability, we must take responsibility for how our renderings cut into and so *rend* the world.

In 1985, when Haraway wrote the "Manifesto for Cyborgs," she remarked: "The new machines are so clean and light"; "cyborgs are ether, quintessence" (1991: 153). In the era

of C^3I, materiality was disavowed, and the "depths" of the organism were elided by the glinting "surfaces" of silicon chips and body-less codes. In the 1980s and 1990s "life itself" had become a problem of coding to be solved in the language of informatics (see also Kay, 2000). However, in these early days of the twenty-first century, our machines and economies are morphing (Franklin and Lock, 2003; Sunder Rajan, 2006; Waldby and Mitchel, 2006), and so too is the machinery that has come to constitute "life itself" (see Fujimura, 2005). In this post-genomic era of computer-intensive, atomic-scale, 3D molecular visualization and simulation, "life itself," can no longer be flattened into the thin threads of information scripted into genetic sequences: structural biologists are involved in the work of re-membering the materiality of cells and molecules.

Stephen Harrison, a prominent protein crystallographer whose Harvard-based laboratory builds atomic-resolution models of protein molecules, has suggested in recent years that there are

> hints that specific kinds of control logic are embodied in specific kinds of molecular architecture ... Thus, structural biology must seek to understand information transfer in terms of its underlying molecular agents by analyzing the molecular hardware that executes the information-transfer software ... The architectural principles of the cell's control systems and the dynamics of their operation are no less proper studies of structural biology than are the organizational and dynamical properties of the molecular machines that execute the regulated commands (Harrison, 2004: 15).

Harrison remains invested in the model of the cell as a computing command, control, communication system, and yet, he is convinced that there is another level of analysis. As the techniques of structural biology that he and other crystallographers employ become more widespread, the code-cracking analysis of the "informatics" of life is being buttressed by the structural analysis of the "architecture" and "hardware" of life. In Harrison's

articulation, the key actors in the cell are no longer the genetic code-scripts read as software. He looks to the structures of the "molecular agents" that underlie the transfer of information, and the "transduction" of forces and energy in the cell. It is the proteins that have been figured as the cell's hardware, and it is their properties that are to be measured, modeled, and manipulated as machines in order to flesh out the story of "life itself."

"Captured in" the hands of twenty-first-century structural biologists, it has become evident that "life itself" is denser than code: it has a three-dimensional material body whose textures, structures, internal forces and intricate movements carry out the regulated, well disciplined work of the cell. Researchers are no longer satisfied reducing the organism to the software of a coding system; the organism now has a mechanical architecture, and its molecular mechanisms have come to resemble the many kinds of machines with which we currently live and work (see also Fujimura, 2005). These include: the cogs and wheels of industrial capitalism, like those pictured on a recent cover of *Cell* (Figure 4.1); computer hardware; electrical circuits; and the springs, locks, and clamps of modern day mechanical devices. If, as Haraway entreats, we are to be accountable for the worlds we craft, we must try to understand the models of life into which we—including our kin, those fresh-faced would-be biological engineers—are being interpellated.

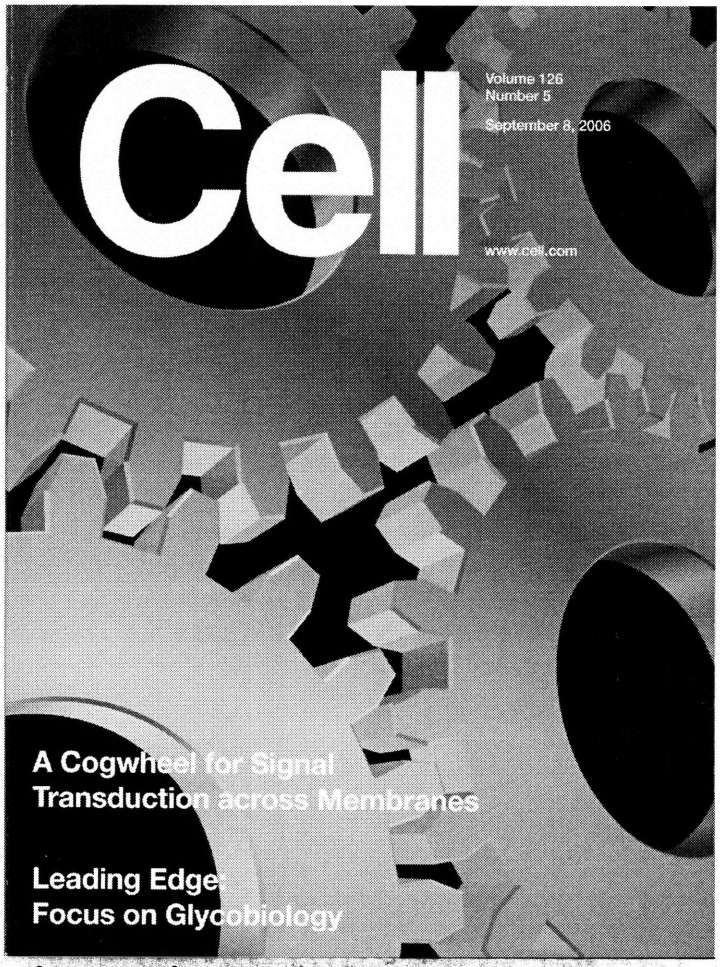

Figure 4.1: The cover of *Cell* September, 8, 2006: 126 (5). "A Cogwheel for Signal Transduction across Membranes." [75]

[75] Inside the journal, the caption for the cover reads: "The mechanism by which receptors transduce signals across membranes remains an important open question in molecular biology. Various models have been proposed, involving association/dissociation and piston and pivot motions. In this issue, Hulko et al. (pp. 929–940) describe the NMR structure of HAMP, a widespread domain of prokaryotic transmembrane receptors, which forms a parallel, four-helical coiled coil. Based on the interdigitation of the side chains in this structure, the authors propose a cogwheel model for signal transduction, which involves the concerted rotation of the helices in a plane perpendicular to the membrane. The model is illustrated conceptually on the cover by a gear box with four cogwheels. The image is by Martin Voetsch (Max Planck Institute for Developmental Biology)" (Anonymous, *Cell*, 2006).

Materalized Refiguration

> Nature is...about figures, stories, and images. This nature, as *trópos*, is jerry-built with tropes; it makes me swerve. A tangle of materialized figurations, nature draws my attention.
> Haraway, 1994: 60

Donna Haraway invites her readers to take a closer look at rich tropes and stories that shape knowledge and practice in technoscience. She asks: "How do we learn *inside the laboratory and all of its extended networks* that there is no category independent of narrative, trope, and technique" (1997: 161, emphasis in the original)? Haraway explains that in Greek, "*trópos* is a turn or a swerve; tropes mark the nonliteral quality of being and language" (1997: 135). For her, metaphors are tropes, but they are not merely immaterial utterances, they are "material-semiotic actors" (1991: 200). To use a biophilic analogy, metaphors can be thought of as proteinacious catalysts: they are dense, fleshy substances that can activate, congeal, crystallize, and precipitate new kinds of bodies and new kinds of meanings. For her, scientific models are also kinds of tropes, but tropes that are "instruments" that can be "built, inhabited, lived" (1997: 135). I extend this definition of scientific models as tropes to three-dimensional models of protein molecules and ask: How are molecules *turned* into machines in the hands of life scientists? How are models of molecular machines built, inhabited, and lived by biological engineers and structural biologists?

Haraway also attends to the many *figures* that participate in the production of technoscientific stories. The term "figure," of course, has many meanings. The Oxford English Dictionary suggests it can signify a person or character, a body or object, or a trope, model or other form of representation. As a verb, "to figure" also implies the act of

reasoning, as in "to figure something out." I animate three multi-valent figures in this story: machine-inspired protein modelers; the otherwise subvisible proteins to which they give body through practices of molecular modeling; and the machinic tropes they enlist to make sense of these molecular structures. As persons, objects, metaphors, and modes of reasoning, these figures each have long histories in the life sciences. And yet today, they have become increasingly potent catalysts, producing and propagating new scientific objects and forms of life in both laboratories and science classrooms.

The molecular machines so important to biological engineers and structural biologists are the products of what Haraway would call *materialized refiguration*. This is a practice through which scientists can turn "tropes into worlds" (1994: 60), conjuring new scientific practices, material possibilities, and forms of signification. For her, this "collapse of metaphor and materiality" is a question of "modes of practice among humans and nonhumans that configure the world—materially and semiotically—in terms of some objects and boundaries and not others" (1997: 97). In the hands of differently trained researchers, distinct tropes can be used to catalyze some models of life and not others.

The materialized refiguration of cells and proteins as machines hinges on the productive meeting of biologists and engineers. Joanna, who conducted her PhD research in Jim Brady's laboratory, told me a story about one particularly productive meeting. Geoff Miller had been invited into Jim's lab to begin collaborating on protein structure projects[76]. On his first day at the group's lab meeting, Geoff completely refigured how Joanna thought

[76] In Chapter 2, I describe how Jim Brady sought out Geoff to get his help working on the lattice structure of viral coat proteins. According to Jim: "No wet biochemist could deal with a lattice. Who knows about lattices? Engineers know."

about a protein with which she was already very familiar. In the meeting, he performed a form of model building that echoed how he had approached modeling collagen with pencils and "Magic Tape" for the protein folding class:

> Just as we were all sitting around the table describing [the protein], and talking about [it], all Geoff did was take a paper clip that was sitting at the table...and he took the paper clip and he's like "Okay. I need to understand what you guys are talking about." And he just folded the paperclip into a three-dimensional representation of what we were talking about. And we were all sitting there going, "Wow." It was just kind of so bizarre that after twenty some odd years of working on [this protein], [we] had never thought about it in this way. And Geoff, as soon as we started talking about the structure, he wanted to see a model of it. It was like, immediately, "Let's make a model." He came back the next day with more elaborate wire that he had taken and molded at his house...And he came in and said, "Oh! There's a clamp! This is a lock. I mean this is lockin' that molecule right in place." And now there're all these papers they've published on the molecular clamp. It's a lock! It's a clamp! And it's so exciting. And its funny, his whole approach was entirely different...I'd looked at that structure a million times. You know. And I was like, "Oh yeah. It's a lock! I mean that's a clamp!"... I wasn't working on that project, but it opened a whole door of experiments that would have not happened otherwise. An entire postdoc was hired to work on this. And it hadn't been called a clamp until Geoff came to the meeting.

A modeler by nature, this engineer needed to hold the structure in his hands. Simple modeling tools would suffice: a paper clip or wire that he could turn and twist. But he also had other tools at his fingertips that were integral elements of his visualization apparatus: he had a facility and a familiarity with clamps as mechanisms, and the analogy of the molecular clamp came easily to him. As Haraway (1997) suggests, a metaphor can even drive an entire research program (97). In this sense, the livelihood of a postdoc, the scientific significance of a protein, and the productivity of a research laboratory all *turned* around the figures of the clamp, the engineer, and his jerry-built model.

When viewed as a practice of materialized refiguration, it becomes possible to see that the

visualization technologies researchers engage do not merely "unveil" fully functional molecular machines within the body of the cell. Machine analogies are also not merely aesthetic flourishes of language, or just "attractive" figures of speech. The application of machine metaphors is itself both a penetrating visualization technology, and a *lure* that draws its users into other possible worlds, with world-changing effects for both the scientist and their objects.

The figures of the biological engineer, the protein, and the machine are all entwined in processes of materialized refiguration. Fulfilling their desire to see into and manipulate molecular worlds, protein modelers produce practical cultures that can refigure protein molecules through machine analogies. In turn, these machine analogies reconfigure the practice of life science. In effect, this process remodels the scientists themselves: as the molecule becomes a machine, the biologist must become an engineer. Moreover, as biologists' molecular imaginations become increasingly machinic, engineers' machines are becoming increasingly biological, and surprisingly lively. As Haraway has shown in the context of genetics and genomics, it took work to refigure "life itself" as informatic code. As I show here, it takes work to build machines into the body of organisms. Haraway's call to attend to the materiality of language is thus also a call to make visible how technoscientific tropes are put to work, for whom, and at what cost. I examine the rendering of molecules as kinds of machines, and thus the worlding of new kinds of bodies, models of life, and livelihoods, all of which protein modelers have found ways to propagate and sustain.

A Brief History of Molecular Machines

In the late-nineteenth-century, Thomas Henry Huxley argued that life must be analyzed according to its chemical and physical properties. In the 1870s he developed a mechanical theory of the cell that he peddled as the "protoplasmic theory of life" (see Geison, 1969; Huxley, 1878). In 1880, the Encyclopedia Britannica published Huxley's definitive entry on "Biology." It was here that Huxley took the opportunity to display his new way of thinking about the stuff of life. He explained:

> A mass of living protoplasm is simply a molecular machine of great complexity, the total results of the working of which, or its vital phenomena, depend, on the one hand upon its construction, and, on the other, upon the energy supplied to it; and to speak of vitality as anything but the name of a series of operations, is as if one should talk of the 'horology' of a clock (Huxley, 1878: 15; and cited in Beale, 1881: 297)

In light of contemporary biological engineering, Huxley's parsing of the protoplasm, and indeed, the phenomenon of life, as a working machine whose parts must be supplied with energy, would probably not make today's audiences swerve. Huxley's contemporaries, however, took great exception to the analogy and its implications for vital phenomena. Lionel Beale, a vitalist who argued against the mechanization of life, was the president of the Royal Microscopial Society, and one of Huxley's most prominent opponents (see Gieson, 1969). In his annual address to the society in 1881 he voiced this strong objection to Huxley:

> This is the sort of teaching that has long retarded the progress of thought, and affords an example of the puerile objections palmed off on the public as scientific criticism, and supposed to be sufficient to controvert evidence founded upon observation, and arguments based on facts which any one may demonstrate. It is not most wonderful that Professor Huxley can

> persuade himself that a single reader of intelligence will fail to see the absurdity of the comparison he institutes between the *invisible, undemonstrable, undiscovered* "machinery" of his suppositious "molecular machine" and the *actual visible works of the actual clock, which any one can see and handle, and stop and cause to go on again* (Beale, 1881: 297. Emphasis added).

Similarly for JW Dawson, then the outgoing president of the American Association for the Advancement of Science, it would "scarcely be possible" in the space of Huxley's Encyclopedia entry, "to put into the same number of words a greater amount of unscientific assumption and unproved statement" (Dawson, 1883: 195). Their primary complaint was that, given the limits of microscopic vision at the time, "molecular machines" could be no more than an elaborate fantasy. To identify invisible and intangible substances as machines represented at best a kind of catachresis: in this sense, a metaphor that lacks a concrete referent (see Kay, 2000 on catachresis). For Huxley's opponents, machines were real, but molecule-sized machines a fiction. For molecular machines to exist they had to have, like a clock, "actual visible" workings into which one could intervene. According to Beale:

> Magnify living matter as we may, nothing can be demonstrated but an extremely delicate, transparent, apparently semi-fluid substance... [O]bservations...favor the conclusion that living matter should be regarded as consisting of infinite numbers of infinitely minute particles, varying much in size, and possibly capable of coalescing, free to move amongst one another, as they exist surrounded by a fluid medium which contains the materials in solution for their nutrition and other substances (Beale 1881: 279).

Beale refused to entertain the existence of machines within the transparent, fluid bodies of living cells. In his commitment to objective empirical observation, Beale rejected the use of what he saw as figurative language. His qualitative description of the cell was however, not free of tropes: indeed, his description conjures a kind of molecular society of freely

moving bodies. Haraway warns her readers to be aware of the denials of the rich metaphoricity and figural craft of scientific vision. To deny the material-semiosis of vision is a ruse: all scientific vision depends on troping. The irony is that Beale did not recognize the genius of what might be called Huxley's "working conceptual hallucination."[77] In contrast to Beale's intractable, free moving bodies, Huxley's machinery was able to produce an alluring object of analysis for the exact scientist. By conjuring machines within the body of the cell, Huxley conceived of a biological object whose properties could, theoretically at least, be quantified. The metaphor of machinery offered Huxley a bridge he could traverse in his imagination between the visible, tangible and manipulable world in which he lived, and the invisible, intangible world of biological molecules. In light of the recent dominance of machine figurations in biology, this would become the enduring and alluring metaphor that could do the work of luring would-be-engineers into the sciences of life.

While Huxley's theory of molecular machines was not vindicated in the late nineteenth century, these debates between vitalists and mechanists show that a struggle over effective metaphors to visualize biological molecules—as kinds of free roaming bodies or inanimate machines—was already in place before molecules could ever be seen. In 1885, for example, Emil Fischer proposed a mechanical theory to explain the intimate specificities and forms of interaction between molecules, such that "enzyme and substrate" would "fit together like a lock and key" (Fisher cited in Clardy, 1999). In 1900 Paul Erlich elaborated on this model of protein specificity to develop his own theory of molecular association between antibodies and antigens. However, rather than rendering these molecular

[77] Gilbert and Mulkay quoted in Lynch (1991).

associations as the mechanical interlocking of keys and locks, he animated antibody proteins in a comic strip narrative that rendered them in the form of animal bodies, which some suggested resembled "hungry pollywogs" (Cambrosio, et al., 1993: 676). As Alberto Cambrosio and his collaborators show, in spite of the fact that no one knew how these molecules looked, Erlich's "tangible diagrams" became effective research tools that enabled him to conceptualize and materialize a successful experimental program (676). Though controversial in their time, these "imaginative diagrams" provided a richly figurative medium through which Erlich was able to imagine, and experimentally intervene in, molecular associations, and so, in the process, "give body" (Hopwood, 1999) to otherwise invisible antibodies.

Whether proteins are figured as machines or animals, it is clear that those who practice molecular visualization have never relied exclusively on visual evidence in order to construct models of these subvisible worlds. That is, visualizing molecules has always involved imagination: the *conjuring* of figural vocabularies—such as metaphors and models—that could provide at least tenuous, tentative links between that which could be seen, that which could be imagined, and that which—in the context of the particular culture of life science at the time—could be said (see Foucault, 1973). Materialized refiguration is thus, a creative material-semiotic practice of conjuring some forms of life and not others.

Resolving Molecular Machines with X-Ray Crystallography

As I showed above, in the history of protein science, there had been a continuous oscillation between the figure of the protein as an animate body, and the figure of the

protein as machine. However, with mounting evidence of the chemical and physical basis of vital phenomenon, at the turn of the twentieth century the mechanistic model of life began to gain ground and trump vitalist accounts (see for example Jacob, 1973; Lenoir, 1982; Kay, 1993; Keller, 1995). This was facilitated in part by efforts already well under way among chemists to figure molecules as the mechanical building blocks of life.

In the history of chemistry the machine aesthetic has long had quite a hold over scientists' imaginations. Christof Meinel (2004) has produced an insightful history of the earliest construction of physical models in chemistry. He links the aesthetics of the earliest molecular models to those of architecture and engineering. To do this, he traces three-dimensional modeling practices in chemistry back to a period in the nineteenth century before chemists had even fully theorized the spatiality of atomic structures.[78] One of the earliest forms of these models, called "glyptic formulae," was first presented to a distinguished audience the Royal College of Chemistry in London by the then head of the College, August Wilhelm Hofmann, in 1865. According to Hofmann, the "combining powers" of atoms were demonstrated by joining painted croquet balls to each other by

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[78] Henricus van't Hoff published the first theory of three-dimensional molecular structure in his *Arrangement of Atoms in* Space, in 1874. However, because molecular structures could not be visualized directly, this concept took much time to be absorbed. In 1892, John W. Caldwell (1892) published an article in *Science* titled "Some Analogies Between Molecules and Crystals," that confessed his earlier skepticism with regard to this structural theory. He writes:

> A fifth analogy [between molecules and crystals]...bases upon the hypothecation of actual molecular structural form—configuration according to Wunderlich's proposed term to express stereo-chemical relations. The subject of molecular configuration is comparatively new; still we are becoming familiarized with diagrams and models intended to represent such relations. Many of us may have been at first indisposed to accept these views as anything more than visionary and fantastic; but the more we have pondered them, the more we have been impressed with their significance and beauty. Shape, form and volume must be attributed to molecule as well as to mass; the only trouble has been in regard to the former, the apparent audacity and hopelessness of any attempt to penetrate matter to such depths (89).

means of metallic tubes and pins. The models, assembled as vertical and planar branching structures, were mounted on stands to "rear in this manner a kind of mechanical structure in imitation of the atomic edifices to be illustrated" (Hofmann cited in Meinel, 2004: 250). Though they were not intended to depict the actual structure of atoms, they closely resembled the ball and stick models still in use today. Meinel astutely asserts that it was not chemical theory these models were meant to convey:

> What Hofmann delivered in front of the powerful and the leisured was not meant as an introduction to organic chemistry. Instead it was a most carefully composed performance primarily meant to convey the idea of the chemist as someone who knows how to manipulate matter according to his will, and who will eventually be able to build a new world out of chemical building materials that could be assembled and disassembled *ad libitum* (252).

Meinel links the aesthetics of early molecular models with other kinds of modeling kits already in wide circulation in the nineteenth century. Construction kits that enabled "children to create a variety of polygonal forms by connecting peas or coloured balls of wax by means of toothpicks" (267) were instruction devices to inculcate children into the "conquest of space" made possible through the engineering and architectural "culture of construction" that dominated aesthetics in the nineteenth century (266). Once made over into mechanical objects that could be assembled, disassembled, and rebuilt, chemists could re-imagine themselves as engineers synthesizing mechanical molecular structures. Thus, long before Huxley had proposed the notion of molecular machines, chemists had developed a "symbolic and gestic space" (Meinel, 2004: 270) in which molecules could be imagined and manipulated as mechanical devices.

I jump ahead now, in this brief history, to 1957, when John Kendrew's laboratory in

Cambridge, UK completed the first ever X-ray crystallographic model of a protein molecule. At that point, protein crystallography had been in development for over twenty years, as biophysicists struggled to visualize and build atomic-resolution models of these complex molecules by diffracting X-rays through crystallized protein (see Law 1973, de Chadarevian, 2002).[79] Since proteins could be coaxed to form "beautiful" crystals, biophysicists expected proteins to be highly symmetrical chemical entities. The scientific community was thus not prepared for what Jim Brady referred to as the "shock" of Kendrew's model when photographs of it hit the press (see Figure 2.2) Those who viewed this early model—its convoluted structure molded out of thick tubes of black Plasticine and supported on wooden pegs—remarked that it looked like "abdominal viscera" (de Chadarevian, 2002: 142) and had a "rather repulsive" appearance (Perutz, 1968: 45). The "sausage model" defied all expectations: it looked nothing like the symmetrical forms proteins were hypothesized to have. As Max Perutz recounted in a collection of essays on molecular biology put together by *Scientific American*:

> It was a triumph, and yet it brought a tinge of disappointment. Could the search for ultimate truth really have revealed so hideous and visceral-looking an object? Was the nugget of gold a lump of lead? Fortunately, like many other things in nature, myoglobin gains in beauty the closer you look at it. As Kendrew and his colleagues increased the resolution of the X-ray analysis in the years that followed, some of the intrinsic reasons for the molecule's strange shape began to reveal themselves. The shape was found to be not a freak but a fundamental pattern of nature (Perutz, 1968: 45).

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[79] It wasn't until methods for X-ray diffraction were under development by Bragg in 1913, that molecular form could begin to be determined from a crystal. Indeed, when Caldwell wrote on analogies between crystals and molecules, X-rays had not even been discovered yet. W.C. Roentgen discovered this potent form of radioactivity in 1895, and it wasn't until 1912 that crystals were first contemplated as good material for diffracting X-rays. In a remarkable inversion of technology, in 1913 W.L. Bragg discovered that he could turn this X-ray diffracting property of crystals into a technology for investigating the molecular structures within the crystal itself. For Bragg, the discovery of X-rays "increased the keenness of our vision over then thousand times and we can now 'see' the individual atoms and molecules" (Bragg quoted in Crowfoot Hodgkin, 1964: 71). It took until the 1930s and 1940s until protein crystallography was developed.

It seems as if the crude low-resolution Plasticine model offended these biophysicsts' molecular aesthetic. Curiously enough, however, the closer they looked the more beautiful the protein model became. As they intensified their X-ray beams, applied augmented computer power to calculate the atomic map of the structure, and swapped their Plasticine modeling materials for standardized molecular modeling kits with machined parts, the protein molecule became a mechanical object, with clean lines, precise angles, and movable elements that could be clicked in and out of functional conformations (see de Chadarevian, 2002; Francoeur, 1997). In the process, it became possible to analyze complex molecular structures as mechanical objects.

Figure 4.2: Max Perutz and John Kendrew in 1962. A close up view of Perutz model is pictured in Figure 2.3 of Chapter 2.

A photograph taken in 1962 of John Kendrew and Max Perutz eyeing each other's models captures well how different modeling materials and scales of crystallographic resolution

produce very different molecular aesthetics (Figure 4.2). Kendrew, with his later, more delicate, wire-frame atomic-resolution model of myoglobin, stands at the right, while Perutz with his dense, lumpy, low-resolution model of hemoglobin made of thermo-setting plastic is on the left. It was not until 1968, twenty-two years after he initiated the project, that Perutz attained an atomic-resolution model of hemoglobin. In a video interview conducted by Vega Science Trust towards the end of his life, Perutz can be seen animating one part of an atomic-resolution model of hemoglobin, clicking the oxygen-carrying heme group in and out of its active conformation (see Figure 2.4.).

As they increased the resolving power of their tools and applied standardized, machined parts to the task of building their models, the figure of the molecule-as-grotesque-body was eventually superceded by the figure of molecule-as-mechanical structure. Unsatisfied with the irregularity of the visceral sausage model as the symbol of "life itself", they disciplined their tools and their craft—including the resolving power of their visualization technologies and their mechanistic aesthetic—to make their molecules visible, tangible, and manipulable as machines. The figure of the mechanical molecule seems to have provided a tacit framework through which they evaluated the representational status and aesthetic value of their models. Indeed, their narrative quest to make the stuff of life visible could only be resolved, that is, come to full resolution, once molecules could be modeled on the aesthetics of machined parts.

Cultivating A Feeling for Machines in Structural Biology

It took great effort for Kendrew and Perutz to model proteins as mechanical structures with

movable, machinic parts. Today, structural biologists use a vast range of interactive computer graphics media and multiple conventions for depicting molecular structures (as wire frame models, Ribbon structures, space filling models, etc.). These distinct media produce numerous opportunities for modelers to express their own molecular aesthetic. Modelers can render proteins in a range of aesthetic forms: in ways that make them appear to have glinting, metallic architectures; or as globular, gooey bodies that wriggle when they are animated onscreen. Thus, while the rhetoric of the molecular machine is pervasive, it is by no means the only way proteins are figured. Edward, a postdoc in Diane Griffith's laboratory surprised me during one of our conversations. As we sat in front of his computer, he explained why it is so difficult to use off-the-shelf software to predict how proteins might bind, or "dock" with one another. It is hard to predict the shape of a protein because, as he told me:

> Edward: You know, proteins are breathing entities...
> Natasha: Did you say proteins are...breathing?
> Edward: Breathing entities... I don't know sounds a bit romantic, doesn't it.

He is what he calls a "well-trained" crystallographer. As such, Edward does not see proteins as the static molecular structures that are published in scientific papers. These models are effective lures for him, pulling him into a lively world of molecular forms. He has a feeling for the intra-molecular forces within a protein, for the ways that they move and "breathe" as they interact with other proteins, folding and unfolding in their watery, intracellular worlds. Edward is moved to enact the breathing qualities of his molecule, which he mimes by wrapping his hands around an invisible, pulsing sphere. I remark on how different this lively language sounds from the ways he had just been describing what he called his "mechanistic approach" to molecular analysis. "I can see there is a bit of a

paradox in there, isn't there," he admits. In a single breath he shifts from figuring the protein as a breathing body, to modeling it as a molecular machine. In this, he seems to straddle with ease the chasm that once separated Beale's and Huxley's models of the substance of life. In what follows, I examine how, and for whom, proteins cease to oscillate between lively body and machine. When do life scientists' discourses and practices *clamp down* on the molecule as a machine? When, and for whom do proteins, at least, temporarily cease to be "breathe"?

Edward's colleague, Fernando, is a fifth year PhD student also working in Diane's lab. In one of our several interviews I asked Fernando if he ever used metaphors other than machines to talk about his proteins. I remarked to him that often I heard structural biologists talk about proteins as kinds of bodies. This suggestion put him on edge a little, and his response was firm: "A protein by itself is not a living thing," he tells me. "It is...it is a machine. And it will break down, just like machines do. Okay? And if something is not there to repair it, another machine, another piece of machinery," the whole system will "break down." At the suggestion that proteins had lively qualities, Fernando clamped down firm on the metaphor of molecular machines. [80]

Fernando is fluent in the rhetoric of molecular machines. Yet machine metaphors are not just pedagogical devices for him. He likes to use the metaphor in part because he has a

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[80] For some insight into what might be at stake for structural biologists in affirming the machine metaphor over body metaphors, in Chapter 5 I describe this interview in more depth, and show how figuring molecules as "breathing entities" creates a serious problem for teaching concepts in evolutionary theory. Molecular machine metaphors, in this respect, act like a kind of public relations campaign to keep lay people from thinking that molecules themselves could be driving evolution through their affinities and "desires."

particularly nuanced feel for machines and their parts. He is a latecomer to science, and at forty, he is significantly older than most of the graduate students in his cohort. He grew up in a working class Hispanic family and spent his twenties working as a plumber, manual labourer, and pizza delivery boy, and took much pleasure in building cars. He later went back to school, and started teaching CAD drawing to architecture and engineering students at a community college. Machines are familiar to Fernando: they are, like Beale's clock, "actual visible works" into which he can see and intervene. He understands how they work, how their parts fit together, and what keeps them ticking. In the middle of our interview he got up to show me how door hinges work, how you can look at them, handle them and know which way the door should swing. I smiled and nodded when he resorted to the example of the hinges on "ladies' makeup compacts," which he thought would really drive his point home to me, in particular. Our conversation produced dizzying Alice-in-Wonderland effects of scale as we zoomed along what seemed to be a continuum of visibility, from human-scale machines, down to the scale molecular machines and back again.

As a protein crystallographer he builds models of proteins to *figure out* what the "machinery" of the cell looks like, and how it works. For him, X-ray crystallography is a visualization tool that he uses to get a "snapshot of the machine." He describes his job as a protein modeler through an allegorical tale that took us to the factory floor of a robotics-mediated automotive assembly line:

> So you know, you are talking about the machine that screws in the fender at the Ford car plant. We're studying that machine because we are trying to find out what it does. And without [the X-ray crystal] structure we are just *feeling* it, just tentatively, sometimes with big thermal gloves. So we can't really get to *feel* the intricacies or the nuances of the drill bits. And all of a sudden crystallography is a snapshot of the machine. Okay. It [the

> machine] can even be in multiple states. Standing still turned off. In a state when there is a screw being drilled into the fender. You know, it can be somewhere in between. Alright? But because we've seen a similar machine in another company, we kind of have an idea of what the machine does. We've seen the individual parts and stuff like that. I'm not going to mistake the machine for drilling for the machine for welding. Okay. What crystallography allows you to do is to say, "Hey that is a drilling machine, not a welding machine." Okay. And by looking at certain parts of the machine you can tell whether the drill bit is six inches long or two inches long or whether it has a the neck that moves up and down, or whether the neck is static. That's the sort of stuff you get in a crystal structure that you don't have before.

Intense in his delivery, Fernando successfully sustained the analogy of the cell as the factory floor of the Ford car plant throughout his story. He had such a strong grip on the analogy that there was eventually a slippage from the machine as a metaphor for the molecule, to the molecule that had actually become a machine; in this case a (robotics-mediated) machine that could do highly specialized kinds of work in (a capital-intensive) cell.

Fernando's image of a human worker whose tactile and visual acuity is dampened by wearing big thermal gloves is an effective analogy to demonstrate how hard it is for the structural biologist to make sense of molecules without the resolving power of both X-ray crystallographic vision and an elaborate figural vocabulary to make sense of the substances they draw into view. Crystallographic modeling gives Fernando both a three-dimensional visualization of the molecule and a "nuanced" "feeling" for its "intricate" structure. As he made clear during another interview, crystallographic modeling with interactive computer graphic interfaces is, for him, a craft practice through which he has been able to develop what he calls a kind of "touchy-touchy-feel" for the molecular model as he builds it onscreen: "I don't want to say touchy-touchy-feely like that, but that sort of holding on to

something and getting a feel of it."[81] Taking off his thermal gloves, so to speak, he uses the interactive computer graphics interface to bring molecules into haptic sensation, as well as into view. And yet, he goes a step further: he draws on his feeling for machines to complete his mechanistic model of the molecular structure.

In an interview about how mechanical engineering contributes to biological understanding, Geoff Miller suggested that protein researchers are working "in the dark". He explained: "Imagine yourself in a pitch black room. Your job is to figure out what's in the room. You have three or four flashlights. Each has a different frequency of light, and is a different shape and size. One light will show you a spot this big around [Makes a gesture with his hands]. Another will only show flat objects of certain size. Another shines a little bitty spot." Molecular visualization could, in this sense, be understood as a practice of groping around and fumbling in the dark with objects at the limits of the visible, tangible, and imaginable world. As such it is a process of shining select beams of light, grabbing hold of small parts of a larger phenomenon, and collecting up this data to form more coherent picture of the whole. As protein modelers struggle to give form to molecules and figure out how they work, they also model the cell and its substances through tangible analogies, tropes that are ready-to-hand, and familiar to the touch. These are analogies that enable modelers to grasp—to make sense of, to imagine, and to intervene in—otherwise invisible realms. For Fernando, this entails modeling molecules figuratively and materially as those objects most familiar to him; that is, as machines.

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[81] As I examine more closely in Chapter 5, when I asked him whether he found that he relied on his body to help him understand molecular form, he very nearly blushed, and got quite uncomfortable, as if asking him about his body had overtly sexual or at least overly sensual implications. This to say that invoking bodily knowledge makes my informants uneasy.

Though he is quite taken by the tools X-ray crystallography affords his curiosity, Fernando is ambivalent about his future in the field. "You can get so fascinated by the intricate gear work of a particular piece," he told me, "that you never learn how to operate the whole machinery." He finds he's very attracted by developments in biological engineering today, which do promise the possibility of "operating" the "whole machinery" of the cell. These are same kinds of promises that have enticed a new generation of students to sign up for the new biological engineering major at his university, the one directed by Stan Graham. The "molecular machine" is thus a powerful lure, an alluring recruiting device for rallying would-be engineers into life science practice. The materialized refiguration of the molecule as a machine gives the engineer something they can get their hands on, something they can literally grasp. And it is through this metaphor that biology has become quantifiable, manipulable and re-designable, in ways that, for the first time, have enabled engineers to *re-work biology*; literally and figuratively they have *put life to work* at the molecular scale.

Engineering Biological Engineers

Like proteins, metaphors left to their own devices don't automatically crystallize into forms that can produce new meanings and material effects. Like crystallographers' efforts to coax proteins to form "living, breathing" crystals, metaphors must be nourished and sustained within the context of a practice and a culture that can keep them alive. This raises a problem for the emerging discipline of biological engineering. While machines are prominent companions in daily life, as expert technical objects they tend to fall outside of

the domain of the classically trained biologist, and more to the point, outside the experience and expertise of many freshmen, and sophomores taking a seat in introductory biological engineering courses. Few would likely have had as much experience with machinery as Fernando. In order to *work the machine into the cell*, life scientists' ways of thinking and imagining biological worlds must be reconfigured. Biological engineers must enlist and train a new generation of scientists to think and work like engineers. They do this by *luring* new recruits with the technological promise of "direct access" to biological worlds at the molecular scale. In order to make the machine analogy do work, however they must *engineer biologists* who not only have a "feeling for the organism," but who also have a feeling for the machine. Biological engineers must be trained to cultivate and deploy machinic analogies, and entrain their visualization techniques and technologies, their language, tacit knowledges, and practices to lively substances in such a way as to make machines visible and tangible within the cell.

During my observations of a semester-long undergraduate biological engineering teaching laboratory, I learned that cultivating a feeling for machines is not an easy task. This was a required laboratory course for sophomores who, through a lottery, had won a coveted seat at the laboratory bench and an opportunity to major in biological engineering. The third of this four-module course focused on what the instructors called "systems engineering." Over the course of six labs, students helped fine-tune a "bacterial photography" system; that is, they optimized the conditions under which bacteria, engineered to induce colour changes when exposed to light, could be deployed to take photographs using the simple principles of pinhole camera technology. In order to analyze how it was that their bacteria were being put to work, they needed to understand the principles of the regulating

machinery controlling the engineered bacteria's cellular "circuitry." Their laboratory manual offered this insight:

> Biology is particularly well suited to model building since many natural responses appear digital...The digital responses of cells to perturbations, combined with lab techniques for moving DNA parts around, allow logic functions and circuits to be constructed in living cells.

But what is a circuit? Electrical engineers are of course quite familiar with circuits; the concept of a cellular circuit is drawn directly from electrical engineering, and uses the same iconography and nomenclature as electronic circuit diagrams (see for example Gilman and Arkin, 2002). In the lab, the students were introduced to an analogue—what could be considered a materialized figuration—of their photo-sensitive bacteria. This analogue was a circuit board. The students were expected to apply electrical engineering concepts, and to complete an electronic circuit in order to demonstrate their understanding of the engineered circuitry in their bacterial cells. Each pair of students had at their desk a partly assembled electronic "solderless breadboard" that included a photodiode and an LED, which, if the circuit was completed correctly, would turn on and off in response to changes in light intensity sensed by a light-sensitive photodiode (Figure 4.3). Students were asked to complete the circuit by connecting resistors of varying strength to appropriate sites on the breadboard.

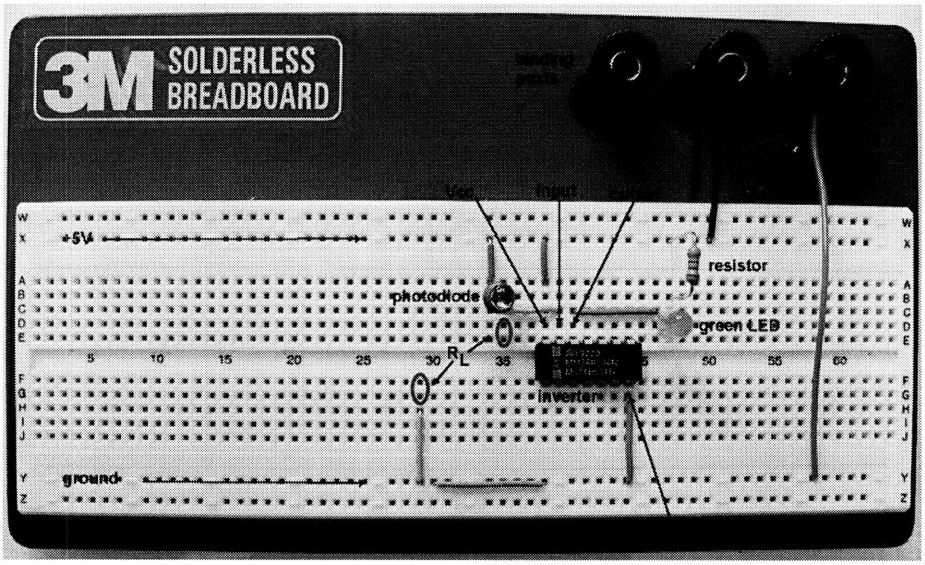

Figure 4.3: A "breadboard" wired up as an analogue of the bacterial photography system. Used with permission from an anonymous ethnographic informant.

Some of these sophomore biological engineering students, however, struggled with basic electrical engineering concepts. Meera, who was trained in computer science before coming into biological engineering, was the TA for this module of the lab. She had to run a remedial tutorial in electrical engineering several times over for small groups of students. Looking rather confused, they gathered around her at the white board. The laboratory director, herself not trained as an engineer, but as a molecular biologist, also joined the lesson. Current flow, resistors, converters, photodiodes, signal matching and ground all had to be explained. Meera, who had assembled all the circuit boards herself, seemed a little surprised by how hard it was for the students to get the concepts: "Inverters ... you all know what that is? ... Okay? ... Does it make sense when I say current flows through a

wire? ... Does that make sense? ..."

The students' blank stares, and repeated questions gave the lie to the excited statement in their lab manual: "Notice how much easier it is to assemble electrical circuits as compared to biological circuits. It takes seconds to swap in a new resistor into your circuit but a few days to assemble," a couple biological parts together. Apparently, it was not that easy: what they were being asked to do was make sense of what was a rather dense material-semiotic tangle. Modeled on a circuit diagram, the bacteria had been engineered from "standardized biological parts"; that is, proteins and genetic sequences that had been modeled as input, output, and signal matching devices, resistors, inverters, terminators, and protein generators. Thus the bacteria themselves were an analogue, or materialized refiguration, of an electronic circuit. The circuit they fumbled with at their lab benches was therefore a materialized refiguration of a materialized refiguration: it was an analogue of the cell, which itself had already been designed and built on the model of the circuit board. Their attempts to wrap their heads and hands around this did indeed give them cause to swerve.

One might expect that analogies are most useful when they draw on knowledge of a familiar realm to illuminate another, less well-known realm. The use of the language of circuitry for inscribing cellular signaling and regulation had already become standard language in the lab and in classroom lectures, yet the students did not have an appreciation for its full import. The bacterial system they had been using throughout the module depended an in-depth understanding of electrical circuits. However, the students were not yet fluent in the terminology and techniques for electronic circuit construction or

analysis. The circuit building exercises were, in this regard, quite productive: they were diagnostic of where students' understanding of the analogy of the cellular circuit had broken down, and offered to remedy the situation by enabling them to cultivate a feeling for the circuit as a tangible machine. The lesson learned by the students, their instructors, and their ethnographer was, then, that the circuit is not a self-evident figure for the cell, and that its effective use must be cultivated. It takes work to build the machine into the organism, and this work must be supported by a practical, conceptual, and material culture. This involves engineering a new generation of biological engineers who can be lured by the metaphor of molecular machines.

Machinic Fetishism or Lively Machines?

> "Life itself" depends on the erasure of the apparatus of production and articulatory relationships that make up all objects of attention, including genes, as well as on denial of fears and desires in technoscience.
>
> Haraway, 1997:147

In an article that appeared in *Nature* in 1986, "One Molecular Machine Can Transduce Diverse Signals," Henry Bourne remarked astutely that in the life sciences, "argument by analogy, like gambling, was once practiced behind closed doors" (814). Bourne was claiming that by the mid-1980s, analogical reasoning in biology had finally been "elevated into respectability" with rich "payoffs" (814). In this article Bourne could be said to have "outed" analogy as an integral practice in the work of science. What is curious, however, is that just as he put the rich productivity of some kinds of analogy on display, he simultaneously obscured others. Most notably he made no reference to the analogy that most promiscuously populated his essay: the figure of molecular machines. No longer an

animating figuration, the molecular machine had, for him, already become a dead metaphor, an unremarkable thing-in-itself. Yet, as Emily Martin suggests, "far from a dead metaphor," it had become "a sleeping metaphor" that must be "woken up so we can examine the work it is doing" (Martin, 1998: 39).

One hundred years after Huxley first introduced the machine metaphor, it seems to have lost its punch. Some might weave this tale into a Whiggish historical narrative that reads molecular visualization technologies as having finally vindicated what could only now be seen as Huxley's daring and provocative *premonition* of the underlying nature of molecular life. Once molecules' "works" were made as "actual" and tangible as Beale's clock, this history could be trumpeted in a triumphalist tone: "Lo and behold! The invisible protein molecule has been made manifest—and look for yourself, it really is a machine!" In this move, machines are no longer animating figures that enable the scientist to take a leap across the divide between the visible and the invisible; with atomic-resolution molecular vision, molecular machines have been forged into technoscientific fact.

In this light, the work that has gone into producing molecular machines is at risk of being made invisible, and drawn back behind closed doors. Following Haraway, I am wary of such moments in which the richly "tropic" and figurative nature of technoscientific vision is erased or denied (See 1997: 133-137). Drawing on Marxist, psychoanalytic, and feminist analyses Haraway offers crucial insight into how tropes are sedimented, or "corporealized" (141) into technoscientific objects. She examines how, in the name of objectivity and neutrality, technoscience denies the tropic nature of its visual and material productions, and in effect produces a literalization that gives fixed form to the trope as a "fetish" object

(1997: 141-148). In her reading of the "genetic fetishism" of late-twentieth century life sciences, she shows that "life itself" was corporealized into the flattened forms of information and code, tropes whose powerful figurations have shaped biology since the 1960s (Haraway, 1997: 141; see also Kay, 2000). But biology today, as Stan Graham told his students, is changing, and I would hazard to say that this "genetic fetishism" is giving way to a kind of "machinic fetishism" in structural biology.

For Haraway, fetishes are "substitutes," that "obscure the constitutive tropic nature of themselves and of worlds. Fetishes literalize and so induce an elementary material and cognitive error. Fetishes make things seem clear and under control" (1997: 136). She reminds us that "fetishism is about interesting 'mistakes'—really denials—where a fixed thing substitutes for the doings of power-differentiated lively beings on which and on whom...everything actually depends" (135). In the case of commodity fetishism, "things are mistakenly perceived as the generators of value, while people appear as and even become ungenerative things, mere appendages of machines, simply vehicles for replicators" (ibid.). By naturalizing and literalizing machines in the bodies of organisms, asserting the neutrality of visualization technologies, life scientists risk giving the impression that they are merely unveiling the underlying machinery of life. In so doing they disavow the power of their own inventive analogies and the work they put into crafting their models. In the case of protein modeling, I want to draw attention to structural biologists' labour, their conceptual and practical dexterity, as well as their creativity and desires; these are investigators who, in their productive application of the machine as a metaphor, have been able to turn their molecules into visible, tangible, and workable objects. I remain curious, however, about those moments when molecular machines get

naturalized as nature's tools, rather than recognized as the elaborately constructed *figural machinery* of the investigator.

In the all-too high stakes game of contemporary US creationism-evolutionary debates, in which proponents of both Intelligent Design[82] and neo-Darwinian evolution deploy the metaphor of molecular machines with serious deadpan literalism, the question of who made these molecular machines anything but a trivial matter. The joke, at which neither the creationists nor the evolutionists are in a position to laugh (their silence revealing the depth of their investments), is that these are neither God's clever little devices, nor evolution's sometimes-clumsy concoctions. From the vantage point of materialized refiguration, molecular machines can be seen as neither Nature's nor God's handiwork: they are none other than the marvelous conjurings of creative scientists and engineers, who have figured and materialized them through the techniques, aesthetics, and desires of their technoscientific arts. What is ironic is that both sides continually defer the responsibility for engineering these machines to higher powers, evolutionary or otherwise—to the extent that they don't take any credit for this crafty work. In the end, it is the biological engineers, more than other life scientists, who fess up to the absurdity of this denial. For, though they might muffle their laughter, they do get the joke: as they struggle to reassert the respectability of "design" and "designers" in the realm of life science, they

[82] See the website http://www.arn.org/mm/mm.htm for insight into how molecular machines are used by proponents of Intelligent Design. Access Research Network hosts a "Molecular Machines Museum," which provides "an introduction to molecular machines and irreducible complexity," complete with animations of all kinds of molecular machines in the cell, in particular the bacterial flagellum, whose mechanism, ID proponents suggest is just far to complex to have evolved through Darwian processes. The site quotes ID proponent Michael Behe: "A man from a primitive culture who sees an automobile might guess that it was powered by the wind or by an antelope hidden under the car, but when he opens up the hood and sees the engine he immediately realizes that it was designed. In the same way biochemistry has opened up the cell to examine what makes it run and we see that it, too, was designed."

do, after all, want recognition for their labours—those massive, micro-scale engineering projects that they have rigged up within living cells. They are keenly aware of how the analogy of molecular machines has been productive of new objects, meanings, lines of research and forms of life. In particular, they understand well how it has sustained their very livelihoods.

If, as Haraway suggests, materialized refiguration is a practice of "worlding" that gives substance and significance, body and meaning, to emerging technoscientific objects, then how technoscience refigures the stuff of life matters: this is a practice that materializes some kinds of bodies and meanings rather than others. Refusing to take responsibility for crafting these figures and models is what Haraway calls an "avoidance of the tropic...tissue of all knowledge" (1997: 137). Such a denial emerges from a misplacement of "error," where scientists are trained to assume that error is located in the "zone of culture," (137) that is, in what are assumed to be unscientific practices of storytelling and figuration. However, as she shows, the actual error "inheres" in the assertion of the "literalness" of models of "life itself," in this case, the deadpan literalism of the molecular machine (137).

As I hope I have made clear in this chapter, scientific visualization is ripe with materialized refiguration, and this process is anything but straightforward. As Jim Brady's evocative body-work demonstrates, machines are not the only figures that populate molecular imaginaries. With ethnographic attention to materialized refiguration *in practice*, to the "enactment" of the metaphor of molecular machines, it is possible to see that the machine analogy does not resolve fully mechanical objects in the bodies of organisms. In spite of attempts to clamp down on figural vocabularies of proteins, to render them as deterministic

machines, life scientists' animating performances of the analogy produces biological machines that are undeniably *lively*.

The biological engineers that designed the laboratory course really did get this when they found themselves at the limits of their metaphor of the electrical circuit. After describing the "easy" features of the circuits they had engineered in bacterial cells, their laboratory manual provided this caveat:

> In practice, spatial and temporal factors hamper even simple designs. The *cell is a messy circuit board* without the static physical separation you could find between electronic circuit elements. Proteins are made and roam the cell, invariably interacting with nucleic acids and with other proteins in unpredictable and unspecified ways (emphasis added).

Proteins in this "messy circuit board" "roam the cell," and in their meanderings, (which seem to evoke Beale's "freely moving bodies") escape full characterization and predictive analysis. In practice, biological engineers' machines are indeterminate and unpredictable. Like the cyborgs that propagate through Haraway's texts, these molecular machines are "queer" figures that do not produce a straight story or picture of life that comes to any determinate resolution (on "queer" science see Franklin, 2006, and 2007). As I show in the next chapter, the machinic fetishism maintained in scientific texts breaks down the moment that proteins are *performed* by structural biologists as simultaneously machinic and lively. It is in the moment when the modeler enacts these machines as if they were also breathing, desiring, writhing bodies with chemical affinities and anthropomorphized affects, that the craftwork and creativity of their figurations are made palpable. Thus

biological engineers and structural biologists perform a far more "wily biology" (Dumit, 2003) than their machinic fetishism avows.

The practice of modeling the stuff of life is, then, akin what Haraway (1997) might call the "unapologetic swerving of liveliness" of "worldly bodies-in-the-making" (137). To literalize or fetishize the machine in the body of the cell is thus to refuse to recognize machine analogies as animating and enlivening tropes. It is also to deny their roles as penetrating visualization technologies; as the integral components of the "apparatuses of observation" (Barad, 1996) and "bodily production" (Haraway, 1991) that draw molecular structures into view. It is also to ignore their role as powerful "lures" that enable both a "leap" of imagination (Stengers, 1999), and an attractive and tractable means for engineers to finally get a grip on "life itself" as a quantifiable, manipulable, and designable substance. Taken as a profound achievement, in Stengers sense, it is possible to track the "intense pleasure in skill," of modeling molecules as machines, such that "machine skill," and the skill to use machine analogies, is not a threat to feminist knowledge practice (Haraway, 1991: 180). In Haraway's (1991) cyborg figuration: "The machine is not an *it* to be animated, worshiped, and dominated. The machine is us, our processes, an aspect of our embodiment" (180). There is, afterall, "no fundamental, ontological separation in our formal knowledge of machine and organism, of technical and organic" (Haraway, 1991: 178). Molecular machines can in this way be made visible as the potent, material-semiotic substances they are: that is, as the catalysts that have, in the hands of researchers, worked efficiently and effectively to crystallize matter and meaning, practices and cultures, and ways of life for both molecular substances and their scientists.

Chapter 5

Animating Mechanism: Animations and the Propagation of Affect in the Lively Arts of Protein Modeling

Introduction

In the summer of 2005, anthropologist Michael Fischer and I were both pursuing research the field of structural biology. We were invited by a mutual friend to jointly conduct a series interviews with structural biologists based in a group of laboratories at a privately funded cancer research institute on the east coast of the U.S. There we met with Andrés, a protein crystallographer doing his postdoctoral research in an immunology lab. During our interview, Andrés demonstrated a molecular mechanism he had worked out for intercellular adhesion. This is a mechanism that operates between cells, and makes use of inter-locking proteins to maintain the structural integrity of developing tissues. His structural study of a group of cell surface proteins determined that these molecules are long and straight. One part of the protein is embedded in the cellular membrane, while the other extends out into the extra-cellular environment where it is available to bind to similar molecules on adjacent cells. The binding end of the protein has three short protrusions that give it a ratcheted structure. He hypothesized that this ratcheted structure provides a mechanism to strengthen binding between adjacent cells.

Andrés, Mike, and I were seated facing each other on tall stools next to a workbench in

the lab. Andrés was telling us how his protein works, and I was busy scribbling notes in my notebook while he was talking, with barely enough time to watch how he was demonstrating the structure. "Here, take my hand", he said. With this, I looked up. "As if we were shaking hands." I had to drop my notebook and pen in my lap, so that I could reach out my hand, apologetic for having been so distracted by my note taking. He wanted to convey the strength of the associations made between molecules whose binding holds two adjacent cells together. We clasped hands in a firm handshake, but he leaned back. I was unprepared for this, and our hands slipped apart. "How would we make our grip stronger?" he queried. "Suppose we are climbing a mountain, what kind of grip would we need?" Still holding hands, he eased me into an answer by gripping me at the wrist. I followed along, and clasped his wrist in turn. We both leaned away. Our grasp was decidedly stronger. "Right", I confirmed. Molecules binding at their first and second hooks would form a stronger bond. "And how would we make it even stronger?" He extended his grip further up my arm, clasping me at my elbow. I followed suit and we tested the strength. Together, Michael Fischer, Andrés and I, acknowledged the augmented stability of this third hold.

Ratcheting up the grip, from binding at the hands, to the wrists, to the elbows, Andrés sculpted a model for strong molecular association by using the physical intuition of his body. By enlisting my participation in this performance of his model he interrupted my note taking and redirected my ethnographic attention towards the body-work of reasoning in structural biology. His own body had become a key resource for him to be able to make arguments about molecular mechanisms: his body was invested in his interpretation of protein structures, and the forms and potential functions of these proteins animated his

imagination. He in turn animated his hypothesis by entangling us both in this demonstration of his model. More than a pedagogical trick, I argue that that his bodily intuition has contributed to his scientific questions and committed him to several years worth of research into these intermolecular interactions. Despite little evidence to support his theory—that these proteins bind to each other using all three hooks—he still holds out hope that he might one day find the crystal structures that can validate this feeling he has for the strength of these molecular associations.

His animation of the mechanism of inter-cellular adhesion seems at first to contradict the tropes and registers in which proteins are typically figured in the scientific literature. As I showed in Chapter 4, the metaphor of molecular machines is pervasive in structural biology and biological engineering communities.[83] In some ways, protein modelers' mechanistic rhetoric could be read as an attempt to eradicate vestiges of vitalism from biological explanations. Indeed, as I demonstrate in this chapter, many I have interviewed and observed teaching express concern about the ascription of agency to proteins. They invest much effort into policing what they see as rampant anthropomorphisms that ascribe forms of human desire to proteins. In some ways, it's plausible to interpret researchers prevalent use of machine metaphors as an attempt to quell this tendency to slip into animistic language. It appears as if they are operating with the assumption that machines

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[83] Mechanism has held a prominent place in the history of biological modeling and theory-making more generally. This mode of reasoning builds on a long history of theories and metaphors that inscribe living bodies as machines (see for example Gieson, 1969; Hopwood, 1999; Keller, 1995; 2002; Lenoir, 1982; Pauly, 1996). Researchers working in the broad field of the life sciences have deployed mechanical theories of biological function at many scales of the organism, and in ways that have shaped knowledge in such fields as embryology and development (see Hopwood, 1999, 2002), as well as cell biology (see Landecker, 2003, 2007).

are predictable and tractable entities, and that their machine metaphors will reduce otherwise messy systems to the deterministic logic of physical and chemical laws.

Andrés's performance of this molecular mechanism, however, forces me to take a closer look at the nature of mechanistic reasoning and machine metaphors in biology. As he performed them, his mechanistic model does not fully de-animate living processes. Indeed, there is something curiously *lively* about his molecular mechanism. I aim to show how, rather than spelling the "death of nature" (see Merchant, 1983), mechanism in the life sciences might be an interesting site for feminist analyses of scientific practice. In this chapter, I examine modes of learning and communication among protein modelers in research and teaching contexts, paying special attention to how they use a variety of media, including their own bodies, to animate chemical and physical processes at the molecular scale. Paying attention to the expressive body-work of molecular modeling, I show how researchers' affects and embodied performances inflect mechanistic knowledge in structural biology. Rather than deadening living processes in order to make them more tractable, and so available to analysis, my informants' expressive performances show up what Donna Haraway has called the "unapologetic swerve of liveliness" that animates both bodies and knowledge in-the-making (1997: 137).

In this chapter, I draw on a diverse array of tools from ethnographic, historical, and philosophical literatures that have a bearing on visualization, embodiment, and modeling in the sciences. I draw on feminist science studies scholar Karen Barad's (1996, 2003, 2007) theory of "intra-action"; Chris Kelty and Hannah Landecker's (2004) "theory of animation"; Michael Taussig's (1993) exploration of "mimesis" as a form of modeling; and

Deleuze's (1986) Bergsonian mediations on movement. I develop the notion of "liveliness," not as an immaterial vital force that imbues matter with the properties of life, but as a narrative form that shapes life scientists' stories about living bodies. "Liveliness," in this sense is a performance that taps into the excitability of all kinds of bodies (human, nonhuman, and machine) that are swept up in the act of crafting compelling narratives of life. Throughout this chapter, and in the conclusion to this study, I examine how narratives of liveliness present a narrative form that is distinct from that which scripts scientific visualization as the "capture of 'life itself'." I argue that stories of molecular liveliness inflect structural biologists figurations of molecular machines, and enable them to enact a kind of biophilic resonance that helps them make sense of the substances they lovingly model. This chapter thus aims for an account of mechanistic reasoning that does not elide the passions that are so alive in practices of making of scientific knowledge.

Intra-action, Response-ability, and Excitation

I am interested in how protein modeling practices can extend feminist theories of performativity in science, in particular how these practices make visible relations among modes of embodiment, learning and communication, and the role of affect in the propagation of scientific knowledge. My hope is to expand the category of what counts among the central practices to be tracked in ethnographic analyses of the visual cultures of science. Feminist scholars have made major contributions to the literature on performance and performativity in science.[84] These include Judith Butler's (1993) analysis of the

[84] On the role of performance in scientific experiments, and in the production of scientific knowledge, see Pickering (1993) and Sibum (1995).

relationship between biological sex and gender performance in her extension of Austinian theories of performativity, and Donna Haraway's (1991; 1997) theory of "situated knowledges", which takes seriously the "material-semiotic" production and performance of scientific knowledge. Karen Barad (1996, 2003, 2007) makes significant contributions to the long-standing debates in the science studies literature on human and nonhuman agencies. She draws on both Butler and Haraway to propose a feminist theory of "agential realism" that can account for the "enactment" of scientific knowledge through the multiple material and conceptual agencies involved in its production. Barad's theory calls for an account of knowledge production at the scale of the "phenomena" that are produced in experimental configurations, and so she pays particular attention to the specific configurations scientists set up between themselves, their apparatuses for observation, and the things they observe.

In order to think through the dynamic relations between all kinds of agents in a laboratory configuration, Barad distinguishes *interaction* from *intra-action*. For her, interaction "presumes the prior existence of independent entities", and builds on a "Cartesian cut" that assumes an inherent distinction and division between subject and object in a given situation. Intra-action, on the other hand, "enacts an *agential cut*", that is, "a local resolution within the phenomenon" (Barad, 2003: 815). To elaborate her theory, Barad extends Neils Bohr's philosophy-physics and his treatment of the wave-particle duality of light to account for the impossibility of separating an experimental object from the "agencies of observation" that are enlisted to draw it into view. Bohr was concerned with how different laboratory configurations could be used to enact distinct properties of light. Light could be detected in the form of either waves or particles, but never both forms at the

same time. In Barad's framework of intra-action, light becomes one of two possible experimental objects – either a wave or a particle – through precise intra- actions between the scientist, their agencies for observation, and the substance subjected to experimentation. Thus, for her, laboratory observations refer not so much to the object as such, but to the phenomena performed at the scale of whole experimental configurations (Barad, 1996).

For Barad, this means that "phenomena do not merely mark the epistemological inseparability of 'observer' and 'observed'; rather, *phenomena are the ontological inseparability of agentially intra-acting 'components'*" (Barad, 2003: 815, emphasis as in the original). Barad shows how subjects and objects precipitate out, as such, from their experimental configurations. In other words, the "agencies" which participate in experiments are themselves formed by each other in their intra-action. She is thus able to expand the frame for analysis of scientific experimentation to include the experimental configurations of objects and apparatuses, as well as the material and discursive agencies enacted by the scientist.

This inseparability of objects and other agencies directs attention to issues raised in the feminist science studies literature, in particular the question of accountability in the production scientific knowledge. In *Human-Machine Reconfigurations,* Lucy Suchman (2007) reviews theories of agency in the STS literature. In this context, she grapples with the legacy of actor network theory (ANT) and "its aftermath", drawing Barad's theory of intra-action into a long-standing conversation among scholars concerned with the "mutual constitution" of human and nonhuman agencies in scientific practice. Suchman quotes

Michel Callon to show that ANT's "network" is not one "connecting entities which are already there, but a network which configures ontologies. The agents, their dimensions, and what they are and do, all depend on the morphology of the relations in which they are involved" (Callon cited in Suchman, 2007: 261). Yet, as Suchman's genealogy of theories of agency in STS makes clear, Barad's formulation takes a further step to articulate a feminist account of power, knowledge and responsibility in science. Extending ANT to the embodiment and performativity of the scientists, Barad's agential realism poses the question: Where do scientists' bodies end and experimental instruments and objects begin? For me, this means that they do not simply interact, or mutually produce each other, but are profoundly *entangled*. It is the form of such entanglements—including the modes of embodiment and forms of knowledge performed—that remain within the purview of the scientist. While taking seriously material constraints—how matter matters—Barad's theory of intra-action also aims to account for the *responsibilities* invested in those who configure experimental arrangements. Her theory insists that scientists (and analysts) account for the roles they play in circumscribing phenomena, making the cuts that locate subjects and objects, and producing and performing knowledge.

I extend Barad's work to understand how, in the entangled configurations of life science laboratories and classrooms, knowledge is enacted through affect and feeling as well as through instruments and objects. So, while intra-actions can be seen to morph the object in order to produce experimental data, I do not assume that the human observer is left untouched. I aim to understand how, in their intra-actions with experimental objects and visualization media, scientists affect, and are affected by, scientific knowledge as they produce and perform it. I read intra-action as a call for attention to the intimate, partly

choreographed, partly improvised contact-dance[85] between human and nonhuman bodies and machines in scientific practice. I argue that scientists must learn how to *move with* and *be moved by* the objects they investigate, and that this elastic, intra-active push and pull between bodies is key to how they engender knowledge. I suggest that scientists get entangled in a contact dance with the objects they study, as well as with the malleable media and metaphors they get use to model these bodies; and I aim to show how the knowledge they gain depends on their own bodies' *response-ability* to the bodies they model. In what follows I explore how scientists themselves could be conceived of as *excitable tissues*[86] who can respond intra-actively to their molecular objects and the media they use to model them. Through their intra-actions with each other and with their models, protein modelers *transduce* and so *propagate* the molecular affects and gestures they have cultivated in order communicate their feeling for protein forms and mechanisms. The aim of this exploration is to develop an inquiry into how scientists and their analysts might become more accountable for the passionate forms of knowledge produced and propagated within and beyond laboratories.

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[85] Contact improvisation is an improvisational dance medium in which two or more dancers engage in a tacit conversation between bodies. Dancers keep close physical contact while exploring the conversational interplay between their bodies and experimenting with balance, gravity, weight tension, gesture and tacit modes of communication. It is a viable metaphor to capture the improvised and choreographed entanglements enacted between bodies (human, nonhuman and machine) at work within biological laboratories. I am looking for a way of theorizing the relations between bodies that holds on to their affects, unpredictability, and multiplicity, and which allows room for seeing how bodies can move with and be moved by each other. The metaphor of contact improvisation, which invokes bodies in motion and in conversation, does this work for me.

[86] The history of life science abounds with the language of "excitation", "irritability", and "sensitivity." These are terms deployed in cell biology and neuroscience in the nineteenth century. In *Matter and Memory*, Bergson (1991) writes: "living matter, even as a simple mass of protoplasm, is already irritable and contractile...it is open to the influence of external stimulation, and answers to it by mechanical, physical and chemical reactions" (28). See Gieson (1969) for a taste of the language of irritability and excitation in history of the protoplasmic theory of the cell and studies of muscle tissue. I develop this notion of excitable tissues towards the end of the chapter.

Sites of Intra-action in Protein Modeling

Barad's notion of intra-action is particularly useful in thinking through the production of visual facts in science. Visualizations, like protein models, can be regarded as the products of intra-actions between scientists, their objects of analysis, and their visualization machinery – which includes the material and semiotic technologies they deploy both to parse and propagate their data. I investigate the intra-actions that produce structural knowledge of protein molecules. The primary objects, the "epistemic things" in Hans-Jörg Rheinberger's (1997) terminology, are the proteinacious substances being modeled. Yet, as invisible entities, molecules as such are inextricably bound up with the agencies of observation that draw them into view. In this case, these agencies include X-ray crystallographers' extensive assemblage of machines—including metaphors and interactive digital visualization media—collectively geared to produce and interpret atomic resolution models of proteins *as molecules*. Living substances are thus *made molecular* through these techniques and practices. The primary phenomena produced out of these intra-acting assemblages of human and nonhuman bodies and machines are, then, interactive computer graphic renderings of the atomic structures of proteins.

As I showed in Chapter 2 and summarize below, these digital models are interactive: they can be handled, manipulated and modified. As such, they enable multiple sites of intra-action, not only for those who build them, but also for their extended users, including those who attempt to pull these models off the screen and communicate the fine details of protein structures to wider audiences. As this chapter aims to show, such intra-actions

produce another range of phenomena, in particular the *animations* that bring mechanistic models to life. I examine ways that protein modelers animate their models and mechanistic theories through a range of excitable media[87] including their own bodies. I explore how such "active" media enable researchers to communicate more than just the configuration of a molecular mechanism. They also relay a range of affects and sensibilities that inflect the model they perform. In order to examine how molecular expertise is propagated, I show how these gestures and affects comprise a form of mimetic communication through which knowledge of protein structures and mechanisms is relayed in both professional and pedagogical settings.

Crystallographic modeling is a fine example of intra-action in the production of visual facts in science. The human-computer interface that crystallographers use to build protein models offers an exceptional site to examine the intra-actions that shape knowledge of protein structures and mechanisms. This visualization practice involves active and

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[87] This is a term that is already in use in the scientific literature. Current uses resonate nicely with the ways I want to use the term here. Gil Bub, a researcher in physiology working on pacemakers at McGill University defines excitable media as follows: "Excitable media are spatially distributed systems which have the ability to propagate signals without damping. For example, a forest fire travels as a wave from its initiation point, and regenerates with every tree it ignites. This is in contrast to passive wave propagation, which is characterized by a gradual damping of signal amplitude due to friction. An example of passive wave propagation is sound waves passing through air. An impulse over a certain threshold initiates a wave of activity moving across the excitable media. As each element undergoes an excursion from steady state, it causes its neighbors to move over threshold at a rate determined by the diffusion coefficient (a `passive' property of the media), and the rate of rise of the diffused species of the excited element (a `active' property of the media). The propagation of electrical activity in cardiac muscle involves the interaction of different ion species across a combination of active and passive ion channels and diffusion of charge through a heterogeneous substrate with dynamically changing conductances. Despite complexity inherent in conduction at microscopic scales, the heart can be approximated as a continuous excitable media. A variety of cardiac tachycardias have been attributed to formation of large scale patterns of excitation such as the formation and break up of spiral waves." See http://www.cnd.mcgill.ca/bios/bub/excitablemain.html

prolonged handling and manipulation of experimental data throughout what is an often-arduous process of constructing the model by hand (de Chadarevian, 2002) or onscreen (see Chapter 2). As I outlined in Chapter 2, Eric Francoeur and Jerome Segal (2004) have shown how a series of computer hardware and software innovations in the 1960s and 1970s enabled protein modelers to transition from building molecular models with physical materials to using interactive computer graphics systems for the display and analysis of structural data. Although modeling materials have changed dramatically between the early days of physical modeling with mechanical ball and stick parts (Francoeur, 1997), early computer graphics developers were able to preserve the materiality of physical models by engineering workstations interactive enough to give users the sensation that they were directly manipulating virtual molecules "with their hands" (Langridge, 1974, 1981; Francoeur and Segal, 2004).

Yet, once built, crystallographic protein models can also travel: as digital objects, they become available to many other users. For example, once a crystallographer builds a protein model, she uploads the structural data into the Protein Data Bank (PDB). In so doing, she makes it available to a wider range of researchers, including biological engineers, predictive modelers, and drug designers who are always on the lookout for new protein structures. A curious researcher will download the coordinates of a protein structure and manipulate it onscreen. As I described in Chapter 2, these tools prosthetically couple the researcher to the model so that as they navigate through the intricate folds of the protein, zooming in on atomic details, and rotating it through virtual space, it becomes a tangible object (see also Francoeur and Segal, 2004). For me, this practice constitutes a kind of intra-active body-work that enables the researcher to learn the structure by

incorporating the form of the protein into their body as an "embodied model."

The intra-actions that produce molecular knowledge also exceed the computer interface: the details of a molecular structure, and hypotheses about how it functions, must be communicated among researchers and their students. Key here are sites of *social intra-action*. As I showed in Chapter 3, my observations of the pedagogical lives of models show that once a researcher has cultivated converging embodied models of proteins, he or she may then be able to perform these models for others off-screen, so to speak. In addition to teachers' and students' performances of protein forms and movements in classrooms and teaching laboratories, researchers also readily enact their embodied knowledge of molecular structure in professional contexts. They do this in formal and informal research settings, including in weekly lab meetings, in presentations at meetings and conferences, and even as they chat with each other at the laboratory bench. Additionally, ethnographic interviews offer another site for researchers to express molecular knowledge through their bodies. In each of these sites, structural biologists may perform their knowledge of a protein alongside graphic renderings in order to elaborate a structure or its movements; or, in the absence of other visual media, researchers' may rely on their bodies to render the protein.

I argue that performative modes of body-work are intra-active in the sense that they require others who can *move with* and be *moved by* these molecular gestures—in both the physical and affective senses of the verb "to move"—so that the details of the structure and hypotheses about molecular mechanisms to be relayed. That is, for these embodied models to become effective *lures*, they must be able to draw others into new forms of

understanding. This demands that structural biologists and biological engineers be attuned to the figural vocabularies and molecular affects that are alive and in play in their communities. I return to this point in later sections of this chapter.

Modeling Biological Mechanisms

Brian Found is a biological engineer based at a computer science and artificial intelligence research center at the same institution where Jim Brady and Diane Griffin teach. In the fall of 2005, Brian Found co-taught a course on biomolecular kinetics and cellular dynamics with Stan Graham, the director of the school's new biological engineering major. The course was geared towards biological engineers-in-training. In one of his lectures Brian defined "mechanism" as the parsing of a living entity, such as a cell, into discrete, interconnected units. For him, a mechanism is an abstraction that severs a larger entity into parts and orders them by their functionality, affording an effective means for manipulation. As a biological engineer, he is invested in garnering as much mechanistic knowledge about his system as possible. He told the class:

> You have to get a mechanistic understanding of everything. Because that's where the true power comes from. If you have a mechanistic understanding you really know how it works and you can change how it works. If you have kind of a philosophical understanding you can describe it after the fact. You can wrap some pretty words around it, but that understanding isn't sufficient to empower you to make the system do something different; that is, what you want it to do. So that's our mantra. The question is how deep into the mechanism do you need to know?

The "true power" that Brian invokes is the ability to engineer new kinds of molecular mechanisms that perform predictable functions in living systems. He desires a level of understanding that makes living processes tangible at the scale of intra- and inter-

molecular forces and energies. The biological engineering "mantra" that he and Stan frequently recited in their lectures was "measure, model, manipulate, and make". They aim towards building quantitative models of cellular and molecular processes that enable intervention and re-engineering. In one sense, their designs on life serve as a not so subtle reminder of the ways that mechanistic thinking has historically alarmed feminist theorists concerned with the exploitation of nature (e.g. Merchant, 1983; Griffin, 1984; Plumwood, 193). I would, however, like to read their desire for mechanistic knowledge more generously.

I want to draw attention to the kind of understanding that Brian gestures towards, even while he dismisses its merit. Though he is not convinced it will get you very far as an engineer, he does see that it is possible to "wrap some pretty words" around a model to aid in "describing" the mechanism, if only "after the fact". My fieldwork in Brian's lectures, and in group meetings among members of his laboratory show that often a protein is modeled as a body at the same time as it is made over into a mechanical object. Indeed, it is not only words, but bodies too, that get "wrapped around" the model as the mechanism is conceptualized and performed. My observations suggest that modeling molecules as complex molecular machines that take up space and move through time has enlisted these researchers' own moving bodies as resources to "give body" (Hopwood, 1999) to the mechanisms they investigate, and to animate their theories.

Mechanisms, or things that operate mechanically, have three-dimensional, temporal structures, in ways similar to living bodies. A biological mechanism, by definition, involves some kind of movement or change: biological substances are transformed chemically and

physically in the process of conducting "work" in the body. The development and application of a mechanical theory to a biological process is a practice that requires postulating an internal teleology of things; that is, relationships between the part and the whole, between structure and function, and between form and purpose. Mechanistic reasoning involves ascribing a narrative teleology to how the parts and forms of an object change and move over time. In this sense, determining how molecules work, how they perform their functions and interact with each other in the cell (with the assumption that they in fact perform a kind of work), is an act of interpretation: the researcher must form a hypothesis by piecing together partial snapshots of an otherwise dynamic process.

The framework that structural biologists draw on to make such interpretations is clearly shaped by chemical and physical laws and theories. But, as I have shown in previous chapters, it is also shaped by their experience working with models, and by analogies that produce metonymic shifts between the scale of human experience and that of molecular life. As I showed in Chapter 4, in order to interpret the functions of molecules, protein modelers draw on (among other things) their embodied experiences with human-scale mechanisms and machines (both within and beyond the laboratory) as sources of practical logic and reasoning. Machines work well as analogies in part because they are also three-dimensional and move through time. Practical knowledge of machines shapes how structural biologists produce and disseminate knowledge of protein structures and functions. Viewed from this perspective, mechanistic modeling appears to rely on researchers' application of experiential knowledge as well as with their dexterity with

language.[88] In this sense, I see mechanistic reasoning is an intra-active, material-semiotic practice. I propose that gestural and verbal descriptions of molecular mechanisms are more than the aesthetic flourishes of expressive scientists: they are integral to the very conception and development of mechanical models. And while structural biologists insist on mechanical analogies, their renderings do not actually deaden living processes. Indeed the renderings that they produce through the animating media of their bodies are exceptionally lively.

Animating Mechanisms

Mechanisms, by definition, move. Animating media that can pull phenomena into time, are especially useful for playing through the temporal forms of mechanical objects and theories. Such media are particularly useful as visualization tools in the life sciences, as they have the capacity to render the temporal forms of living organisms. What I hope to show in this section is how, when scientists craft animations that pull a parsed process into time, the mechanisms they engender can acquire rather lively properties.

Here I examine animations rather than simulations in life science. I do this for several reasons. First, the term simulation is in wide use in the life sciences, and it has several connotations many of which are beyond the scope of this study. Not all simulations are animations: some simulations remain "in code" and do not have visualization features that animate processes visually in time. For my purposes here, term animation keeps in play the

[88] For an account of the cultivation of metaphors and "muscular" knowledge situated in the context of imagery prominent in Victorian science, see Jordi Cat's (2001) account of Maxwell's methods of "illustration".

connection between visualization practices that pull static entities into time, and animation as the act of breathing life into, or re-animating static objects. I also want to move away from the primary association that simulations have with representation, where simulations call attention to the resemblance or similarity they produce between the world and the model. In similar ways to the term rendering, animation maintains focus on the scientist as the creator, the conjurer, or animator, of otherwise invisible worlds. Where I see animation as an intra-active practice, it is in the end the scientist who is accountable for crafting such visions of the world.

All kinds of animations have been developed in the history the life sciences. For example, embryologist Wilhelm Roux (1859-1924) employed everyday materials to create an experiment that could defend mechanical theories of organismal development against Hans Driesch's vitalist theories. By incubating balls of dough containing varying quantities of yeast, joining them together in cellular formations, and observing the patterns they formed as they rose, Roux effectively produced an "animation" of the differential growth of cells in embryogenesis (see Hopwood, 1999). Keller (2002) documents another early form of animation, which she describes as a kind of "simulation."[89] Stéphane Leduc (1853-1922), a biophysicist working at the Nantes Medical School drew on the persuasive powers of mimicry to simulate the mechanical processes governing life forms. In the laboratory Leduc produced "artificial" cells and organisms from osmotic gradients generated by salt crystals and dyes. These chemical creatures seemed strangely alive, their growth patterns and forms mimicking those of dividing cells, sporulating mushrooms,

[89] In this context, simulation captures well how Leduc's technique produced a "similarity relation" between the model and the world it represented (Morgan and Morrison, 1991).

blooming plants, and free swimming algae. As mimetic animations, they worked marvelously. According to one observer: "these mineral growths are not mere crystallizations as many suppose...They imitate the forms, the colour, the texture, and even the microscopic structure of organic growth so closely as to deceive the very elect."[90] Through his strange "methods of imitation," Leduc conjured the semblance of living entities in "materials chemically unlike but physically resembling the cells and tissues themselves" (Keller, 2002: 15). Leduc's animation was a temporally dynamic model: by moving through time it could evoke a living process.[91]

Leduc produced these animations in an attempt to demonstrate a link between living and non-living matter, to generate evidence for his belief that living entities were governed by nothing more than the same physical laws that acted on chemical substances. As a means to stamp out vitalist tendencies which still haunted biology at that time, Leduc's "artificial organisms" were meant to prove that no external vital forces were required to enliven matter; that physical materials could, left to their own devices, acquire the characteristics most closely associated with living substances. Leduc, then, was able to make use of the temporality of this animating media in order to demonstrate the physical basis of living processes, and as a means to evoke support for his mechanistic theory.

Chris Kelty and Hannah Landecker (2004) have proposed a "theory of animation" that examines the relations between moving image technologies and the production of knowledge in the life sciences. Alongside contemporary modes of digital animation, they

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[90] W. Deane Butcher quoted in Keller (2002: 15).

[91] Rheinberger (1997) describes a simulation as a model in *"precession"* (113).

treat early-twentieth-century microcinematography (Landecker, 2005) as a form of animation. In its joining of biological and filmic techniques, micro-cinematography was a form of animation that brought cells to life on film screens. For them, "media that represent the living organism over time, such as time-lapse microcinematography, not only demonstrate the life of the organism in question, they also *animate* it in relation to other, often dominant, modes of static representation" (Kelty and Landecker, 2004: 45). Kelty and Landecker are less interested in the ways that animations simulate life than their "*status as images in relation to knowledge*" (32, emphasis as in the original). They read animations as the playing of theories or models forward in time, that is, as the animation of otherwise static abstractions or ways of seeing that have already been systematized in scientific research. Thus, it is the theories themselves that are animated through time-based imaging technologies.

Kelty and Landecker provide a crucial contribution to situating time-lapse imaging and animation within the history of theories and models in life science. To extend their work further, I foreground the ways that animations not only embed ways of seeing, but also, how, in pulling static models into time, animations refigure these ways of seeing and the very theories they enact. Seen in the framework of intra-action, it is in their very performance that animations also transform knowledge. As I show in the following section, Kelty and Landecker's approach works well for graphic animations, including the computer animations that structural biologists are currently producing. However, as I examine later in the chapter, there is an important difference between Kelty and Landecker's "theory of animation"—as the animation of scientific theories—and what I propose, which is a *model of animation* concerned with the *animation of models*. This

difference can be seen most clearly by exploring how structural biologists use their bodies as animating media.

Computer Graphic Animations

Today, protein crystallographers and protein folding researchers make use of the spatial and temporal possibilities of digital media to build and manipulate their protein models as time-based renderings onscreen. In the process they animate the molecular mechanisms they hypothesize and intuit. Such animations are proudly displayed and available to be downloaded from laboratory websites, frequently projected to awed audiences in conference presentations and in undergraduate classrooms, and they circulate widely through informal networks on the Internet. Some make use of high-end graphics, while others use much simpler imagery.

One of the more elaborate molecular animations currently circulating among life science researchers and students was developed for teaching core biological concepts to Harvard undergraduates. The "Biovisions" project employed character animators and state of the art computer graphic animation systems in its aim to offer a glimpse into the "Inner Life of the Cell."[92] Building directly on protein structure data, the creators saw this as a "completely

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[92] The animation is available to view online at http://www.studiodaily.com/main/technique/tprojects/6850.html. It was produced out of a collaboration between Harvard University and the Howard Hughes Medical Institute Biological Sciences Multimedia Project. Alain Viel and Robert A. Lue directed the conception and scientific content, and the animation was produced by John Liebler at XVIVO Studios. See the "Multimedia Production Site" for descriptions of other projects, guided tours through contemporary innovations in the life sciences, interviews with scientists, and clips of other animations, at http://multimedia.mcb.harvard.edu/ . Currently clips of this video are widely circulated on YouTube. As of June 2007, just one of the many clips of this

accurate rendering" (Marchant, 2006). However, set to ambient, orchestral music this 3D flythrough animation does more than just pull mechanical objects into time: these animations also provide glimpses into the scientists' and animators' molecular imaginations. Animations like this could be described fairly as "working conceptual hallucinations"; that is, "hybrid combinations of schematic, iconic and even fantastic features" (Gilbert and Mulkay quoted in Lynch, 1991: 209). I propose that such animations are renderings that combine researchers' practical knowledge with imagined forms: they are temporally dynamic tracings of researchers' physical intuitions—their *feeling for*—protein forms and movements. Animating media thus afford protein modelers a medium through which they can express their molecular imaginations and intuitions in time. Moreover, if these are expressions of researchers' embodied imaginations, what is remarkable is that rather than following through on the aesthetic of their machine analogies, these animations are surprisingly lively. As one reviewer comments, the molecules and organelles "move with bug-like authority, slithering, gliding and twisting through 3D space" (Marchant, 2006). It is possible to parse a phenomenon into discrete elements and configure it as a mechanism. However, by pulling these static elements into human time, protein modelers narrate biological mechanisms through lively figurations, endowing molecular mechanisms with animistic, even wily behaviours. In this sense, modelers use malleable media, and apply temporal structures such as musical scores and story lines, in ways that inflect their molecular knowledge with a range of animistic affects. Biological machines, and their modelers' fantasies, are expressed through what I am calling a narrative of liveliness (see Chapter 6). These animations thus make clear the

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animation people have posted on YouTube has been viewed over 500,000 times; is accompanied by 2663 posted comments; and has been listed as a "favorite" 4202 times.

etymological relations among the terms *animation*, *animal*, and *animism*.

However effective they are as pedagogical lures, many researchers are quite skeptical about using these animations as anything more than entertainment. Lynn and Joanna are postdocs who had been hired to work with professor of biology George Fraser on an HHMI funded program to transform the introductory biology curriculum for undergraduate students. I interviewed them about how they use visualizations when teaching an introductory biology course. In the midst of our conversation, I asked Joanna, who had been a graduate student in Jim Brady's laboratory, how she felt about computer animations that attempt to visualize protein folding. Her response, and the conversation that ensued between her and Lynn are quite telling. I offer an extended excerpt below:

> Joanna: I've always hesitated [to make animations of protein folding]...maybe it's because I'm from Jim Brady's lab. I have always really hesitated trying to put what I see on my head onto paper. I was always the one in the lab up there who was able to make beautiful models for people. Not 3D models. But I was the one who was easily able to take the data, and make the 2D cartoon to see that "Okay this step goes first, then its got to be this step, then this step." I could do that very easily. But I always hesitated to actually put anything amorphous, [like] the simulations together. Because from day one joining the lab, Jim was like "You can't make a simulation of protein folding. You can't do it! It's not going to be accurate!"
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> I can give you the steps that I know happen. I have no problem describing or creating representations that make people understand that very easily. But making an animation that goes from one to the other...It's that ingrained Jim Brady thing that says: "No you can't do that it'll be wrong!"
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> For instance the molecule I was studying when I was there: It's got two sections. And we—myself and another grad student—we determined that yes, in fact, without a question, what happens is that one section folds before the other. We could see it and we know it happens. And we have lots of data that shows that's how it happens. But I would never try to model a...

Lynn: A continuous process?

Joanna: Yes, a continuous process out of that. I could say yes, I can give you a model that shows that this guy is solid, this guy is loose. But I would never [animate it]. It's the Jim Brady in me ... It's very difficult because so little is known. That's what makes protein folding is so hard to describe to people. Cause, everyone seems to want to put a time sequence on things, to make a simplified animation. There's so few cases where we can say a simplified animation, oh, that's right. We just don't know.

Lynn: That's interesting. I just realize that's what irks me about the tRNA folding movie that [we] show in class. It's precisely that. You don't know that's what happens.

Joanna: You don't know the directionality, you just don't know ...

Lynn: ... that that's the order of the steps.

Joanna: From a protein folding background, to me its infinitely frustrating when people do that. I've seen more graduate students spend their careers trying to make animations and simulate folding when there's no experimental basis for what they are doing...And it's very difficult as a true protein folder—I can't buy it. I don't believe it. I can see the desire to represent that, or to get at those steps. But there is just not enough data to support [it].

One thing that is very interesting here is that Joanna kept repeating that her resistance to animation is the Jim Brady "in her". It appears that as much as molecular forms have been folded into her embodied imagination, so has her teacher. In this sense, her embodied knowledge of protein folding is not just about scaling between the dimensions of the human and the molecular, but a kind of *transduction* of knowledge from one human to another (for more on transduction, see later sections of this chapter). More to the point of here, however, is that Joanna and Lynn are concerned that animations overdetermine the temporal sequence of what is for them a dynamic and complex process. Joanna "knows"

how a protein folds, and she can "see" it; she even understands the "desire to represent" the forms and movements of the folding process. However, she is very concerned that animations overdetermine the temporal form of the dynamic processes she studies. She is anxious about how animations *rend* time.

Looking at the BioVisions project as a *rendering*, it is possible to see how computer graphic animations shed insight into the embodied imagination of their makers. However, when these animations are treated as end-stage *representations of* a process they produce a kind of closure: by putting a time stamp on a process, by directing how others see and experience the temporality of a process, animations are risky because they can seduce lay audiences by overdetermining the viewer's experience of temporality.

My reading of this is that computer animations, seen as representations, cut off the possibility intra-action between the viewer and the model. This was evidenced quite strongly when Jim Brady (apparently against his better judgment) presented a computer graphic animation of a "molecular machine" in his protein folding course. During one of his lectures he projected an animation of GroES, a chaperonin molecule, doing its work in the cell. "It really is a molecular machine; the structure was solved," he told the class as he stood in front of the projection screen that animated the molecule through its movements. "We are seeing a cycle. You see what happens to the machine. Charges up with ATP, recharges, cap binds. There's rotational motion." Jim started to try and describe what was happening, but he suddenly stopped, stood in front of the screen, with his back to the students, and just stared up at the movement, as if he'd gone into a trance. He eventually pulled himself away, and told the class: "You can look at this quietly in your own home.

We'll let that go." He paused again, and then said, "You've got the sense of a real machine there." At this he shut down the LCD projector, and went back to his lecture.

The animation produced a kind of stunned silence. Projected as a representation, this animation left no room for intra-action. In this sense, animations are distinct from the static models that Jim animates and brings to life for his class. Static models seem to leave much more room for intra-active play, opening up to a kind of exploration that enables the viewer to *participate* in figuring out the temporal form of a process. Computer animations, while they do provide a window into how molecular worlds are imagined, do not entangle their viewers in the same ways, and so tend to cut off the kinds of embodied participation that students need in order to really get a feel for molecular forms and movements.

As I examine in the following sections, it is through modelers' intra-actions with models, that they are able to animate and propagate their tacit knowledge of molecular structures and mechanisms. Moreover, entangled with this tacit knowledge is a range of affects that turn out to be central to how researchers learn and communicate molecular knowledge.

Embodied Animations and Molecular Affects

There are many viable media for animating life science data and hypotheses, including physical (e.g. rising dough), celluloid (e.g. film), and virtual (e.g. computer graphic) media.[93] These are all malleable materials that can be used to pull abstract concepts—like

[93] See Eugene Thacker's, *Biomedia* (2004) for an exploration of the various ways "media" comes

mechanical theories—into space and time. Researchers bodies, it turns out, are also exceptional media for producing animations. The body-work involved in protein modeling and mechanistic reasoning demonstrates vividly what protein researchers must do with their bodies in order to bring molecular models and mechanisms to life. In many ways, they rely on gestures and affects to communicate structural knowledge of proteins amongst themselves and their colleagues, and to students and their wider publics. With an interest in examining the role of affect in the performance and propagation of knowledge in science, I extend the study of animations to include modes of animation that excite the bodies and imaginations of scientists.

In order to understand how embodied animations are enacted, I follow Kelty and Landecker (2004) to examine techniques in which living substances are first fixed or frozen, and then re-animated. In this way I can track how static renderings are pulled into time through the animating media of researchers' bodies and imaginations. And yet, the embodied animations I am interested in are distinct in important ways from the cinematic forms and the mathematical formalism of L-systems described by Kelty and Landecker (2004). In *Cinema 1,* Deleuze (1986) examines Bergson's 1907 theses on movement from his text *Creative Evolution*. Deleuze defines a kind of modern cinematic movement that is produced through a mechanical recomposition of "real" movement. This modern form of cinematic movement is the "mechanical succession" of "snapshots" (what Deleuze calls "immobile sections") that cut movement into equidistant moments of time ("any-instant-whatever"). He associates this concept of movement with the achievements of the

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into play in contemporary computer mediated sciences.

Scientific Revolution, which were able to abstract time as an independent variable. According to Deleuze:

> The determining conditions of the cinema are the following: not merely the photo, but the snapshot (the long-exposure photo belongs to another lineage); the equidistance of snapshots; the transfer of this equidistance on to a framework which constitutes the 'film'...; a mechanism for moving on images. It is in this sense that the cinema is the system which reproduces movement as a function of any-instant-whatever, that is, as a function of equidistant instants, selected so as to create and impression of continuity. Any other system which reproduces movement through an order of exposures (*poses*), projected in such a way that they pass into one another, or are 'transformed', is foreign to the cinema (1986: 5).

Snapshots are produced through an apparatus of capture that sections and immobilizes "real" movement into "closed sets" of cinematic movement. Deleuze includes the "cartoon film" (5)[94] in this cinematic lineage, which may also include the computer graphic animations I described above. However, this is not the same kind of animation that I am observing in structural biologists' body-work: what I am seeing in their performances are forms of animation in which gesture itself the animating media (see Agamben, 2000). Where time in a time-lapse moving image can be sped up or slowed down, pulling fast or slow movements into human time, and so into perception (see Landecker, 2005; Myers, 2005), time is not mechanized in the embodied animations I see performed. Their animations are lively narrations whose temporality is elastic: they pull at and bend molecular time by acting out the attractive and repulsive forces and tensions between

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[94] Deluze on "cartoon films": "This is clear when one attempts to define the carton film; if it belongs fully to the cinema, this is because the drawing no longer constitutes a pose or a completed figure, but the description of a figure which is always in the process of being formed or dissolving through the movement of lines and points taken at any-instant-whatevers of their course. The cartoon film is related not to a Euclidean, but to a Cartesian geometry. It does not give us a figure described in a unique moment, but the continuity of the movement which describes the figure" (Deleuze, 1986: 5).

atoms in molecules; their body-work engenders an exploratory rendering, a kind of *reaching towards*, without producing a representation. Deleuze's definition, then, embodied animations are "foreign to the cinema," and appear to suggest a form of movement much more along the lines of Bergson's "open whole" of "duration" (Deleuze, 1986: 3-11), a kind of movement "cannot be divided without changing qualitatively at each stage of the division" (10). The models that structural biologists perform are explorations of the character of the protein, its habit, and its desires in a way that inflects it with their own character, habitus, and desire. Thus, I treat gestural movements differently than the animations produced through computer graphics.[95]

Protein crystallography offers an illuminating example of how embodied animations are generated. Fit squarely within a tradition of biological imaging and modeling that fixes or freezes substances in order to bring them into view, crystallography produces static models of protein structures. This practice offers a fitting comparison to Kelty and Landecker's example of microcinematography as a mode of animation, because it also begins with a technique that produces snapshots. The difference is that embodied animations reconstitute movement in a much more open way.

To gather data on a protein structure, a crystallographer first must concoct an appropriate biochemical medium that will encourage their particular proteins to crystallize into large, organized forms that can diffract X-rays. Before they even begin visualization, crystallographers have already cultivated an imagination of their proteins as lively. They

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[95] This is one reason that video ethnography poses a challenge to my research. To make movies, or isolate snapshots of modeler's mid-gesture, is to cut into what I see as a larger social and semiotic context for expression and meaning making.

treat crystals as living, breathing entities: once successfully "seeded" in the proper media, their crystals "grow." They conceive the proteins themselves in lively ways: even though the molecules are packed within the ordered array of the crystal lattice, they imagine that individual protein molecules vibrate energetically.

Diane Griffin produced a vivid demonstration of the nature of molecular excitations during a guest lecture for students in an advanced biology course. Taking on the job of instilling critical visual skills among the next generation of scientist, she instructed them in how to read protein crystallography papers, helping them to navigate the data and statistics they would need to understand in order to evaluate crystal structures published in papers and housed in the PDB. Pictures of ducks are commonly used to teach the concept of resolution in crystallography textbooks. Diane would like to use dogs to teach the concept of B-factors, which are a statistical measure of how much movement a molecule has inside of the crystal lattice. The more movement there is in a molecule, the more "disordered" the structure and data are, and thus the more that the crystallographer must make what Dehlia, Diane's student called "executive decisions" about where the atoms and the polypeptide backbone go in the structure. Molecules that have "floppy" side chains are disordered; and this raises the B-factors in particular regions of the structure, which the critical reader must use as guides to determine how good a fit there is between the model, the data, and the molecule:

> This is my favorite example. Those of you who know me, know that I'm not a fan of the duck. I'm a fan of the dog. And so I've decided that crystallographers should use dogs as examples rather than ducks. So anyway, this is my former dog, who passed away recently, Remy. He was a great dog.

Diane points to a picture of her dog on the beach, projected on the screen behind her. The

waves crashing up against the beach are vivid in the picture. Remy, however, appears as an indistinct blob in the center of the image. Diane continues:

> I don't really know if you can make out that this is a dog, cause there's a shadow. But this is a leg, there's another leg. This is the tail. Ah, that's an ear. Here's the nose. And so, this is what always would happen when I'd go out and try and take a picture of my dog. And the minute the camera would come out...the dog is like sitting nice, and you know smiling, and looking all happy and very calm. And then the camera comes out, and whoop! He's on his back and then his legs are going like this [Arms flailing in the air]. So I have a series of pictures, high resolution in the background, you know really good camera, really good developing, focus, everything, fantastic really high over-all resolution picture. But the thing I was trying to capture, ummm...If this [points to Remy] is like the molecule in the active site, it's completely disordered. And so this is one thing to keep in mind. It's not the overall resolution of the structure but it's the B factors [which is a measure the relative mobility of the atoms] of the things you are most interested in that you have to pay specific attention to. Because it could be the part of the structure you care about. You know. [If it's like this (points to Remy)] it's not very good information about where those atoms are located.[96]

Diane demonstrates how molecules move like her dog, and in so doing she animates both dog and molecule, flapping her arms around emphatically. By figuring the protein molecule as a dog, Diane produces an account of molecular movement that goes so far as to connote, that like her dog Remy, the molecules get all excited and perform for the camera when you take their picture. She has storied molecules, in particular those growing into crystalline form and exposed to high-energy radiation, as a lively, excitable media. It is

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[96] Just after Diane finishes, a student asks, "Do you have a new dog yet?" Diane responded: "I don't have a new dog yet. But I've narrowed down some of the available dogs to about 6 or 7 of them. I've decided that Remy would have wanted me to adopt a hurricane victim dog. I've heard that there are 50,000 pets that are gong to be needing homes as a result of the hurricane. My husband is definitely trying to convince me that one new dog would be the way to go. 50,000 would be too many...Alright. So other things you want to pay attention to is completeness of data...." Diane got a puppy named Jeb several months later. Like Remy, the puppy is a constant companion to her in the lab. When Jeb is not with Diane, he's with her grad students who spend their break time walking her, and making sure he doesn't pee on the carpet or chew the molecular models during lab meetings.

this narrative of liveliness, a kind of "molecular vitalism" (Kirschner, 2000) that already animates crystallographers' imaginations about what is going on in the world of molecules not only in crystals, but also *in vitro* and *in vivo*.

Starting with a lively substance, their visualization practice thus must find ways to fix or freeze this movement in order to get a good, clear (unblurred) "snapshot" of the structure of the proteins packed within each unit cell of the crystal. This movement must be dampened; and cryofixation is a widely used technique in which the crystal is dipped in liquid nitrogen just before it is subjected to X-ray diffraction. X-ray crystallography is thus a kind of freeze-frame technique. What is interesting is that given the amount of movement within the crystal at any one moment, each molecule may be frozen in a different position; thus crystallographers must render best-estimate models by averaging out the dynamic movements and subtle differences in conformation between all the molecules arrayed in the crystal. This practice produces a single structure, a static snapshot of the calculated average of all the protein molecules, frozen in time.

Edward, a crystallographer conducting his postdoctoral research in Diane Griffin's protein crystallography lab, told me that this snapshot can be challenging to interpret for those not trained in the structural biology. "Molecular biologists are notorious", he emphasized. "The main criticism crystallographers have about molecular biologists is that they don't think about the structure as a *breathing entity*. [For them] it's just a rigid body." For non-experts who don't have a feel for the physics and chemistry of protein molecules, the structures available to download from the PDB just don't convey how dynamic proteins "really are." While he has a mechanistic understanding of protein function, the aliveness of

his protein is a tangible concept for him: as he described the protein he was working on, he held his hands out in front of his body, as if holding a pulsing substance. The invisible object in his hands appeared to breathe like lungs. It is important to note here that in this moment Edward performed a well-rehearsed gesture that has propagated widely among structural biologists since Perutz solved the structure of hemoglobin. Hemoglobin is one of the principal molecular structures that life science students learn, almost as a rite of passage into studies of biochemistry, molecular form, and protein function. This is the molecule that carries oxygen in blood, and conveniently it is often taught and remembered as a "breathing molecule." In my interviews with biological engineering students enrolled in biochemistry classes, they often re-enacted the hemoglobin structure that they learned in class by making a gesture similar to Edwards,' though the students' renderings were less articulated and nuanced.[97]

His animated gesture does not necessarily suggest that he's tapping into some mysterious vital energy in the molecule. Edward "knows" how the protein moves in part from his close study of chemical laws and the physical properties of proteins. But he also has a tacit, kinaesthetic knowledge of the form of molecule that he did not learn from books—a knowledge he has gained intra-actively from having spent tremendous effort and extended periods of time building and navigating through protein structures onscreen. It is through the laborious work of modeling, manipulating the three-dimensional graphic space on his

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[97] In a video interview accessible online, Max Perutz can be seen animating the mechanism of hemoglobin, demonstrating with delight the form and movements of the molecular structure as it captured and released oxygen. See video interviews with Max Perutz online: "Face to Face with Max Perutz," Vega Science Trust. See Figure 2.4.
http://www.vega.org.uk/video/programme/1.

computer screen, that he was able to sculpt a fleshed out twin of the model, not just in his mind, but also in his body. In the intra-active process of building crystallographic models, working with X-ray diffraction data, and sculpting the model using interactive graphics, he has found a way to animate hypotheses about these static structures in his embodied imagination.

As I showed in Chapter 2, Diane, like Edward, has a multi-sensory, kinaesthetic sense of how the protein moves. In the process of modeling the protein *in silico*, she cultivates an affective, kinesthetic knowledge of the possible forms and movements of the protein *in vivo*. In this way, she can get "inside" the model. In many ways, however, the model also gets inside of her; and this is a key step if she is to use her structural intuition. Once the details of the model are embedded in her tissues, she has a way to feel her way around inside the protein and figure out how it works. In an interview (also recounted in Chapter 2) she described it this way:

> And you know, it's really this vision that you have of the active site, and sort of this sense of how tightly packed it is and how much flexibility there might be and where those regions of flexibility are. To have this sort of sense that you have. And you can think about it then *moving* in a way because you sort of know something about what the density was in each part, so that you know that that part is definitely mobile right in there, but that this part would not be mobile.

Through expressive gestures and affects she conveys her feeling for the molecule's intra-molecular tensions and forces, its chemical attractions, repulsions, affinities, and the possible ranges of motion across its chemical bonds. These are forces that she feels in her own body, to such an extent that when students present her with half-built protein models

whose configurations defy allowable bond angles and produce clashes between the radii of atoms, she cringes bodily and audibly. Embodied models or proteins are thus inflected with affects, with modelers' feelings for the elastic forces and movements within and between molecules.

Embodied animations excite structural biologists articulations of their molecular mechanisms frequently, and in all kinds of settings. In Diane's lab, many of the advanced graduate students and postdocs (particularly those who had successfully built crystallographic models) were delighted to tell me all about the molecular movements they could intuit, but couldn't otherwise see. In interviews where I asked them to explain how they conducted their experiments and how their proteins worked, they performed the vibrations of molecules embedded in growing protein crystals, and waved their arms about to emulate the floppy ends of polypeptide chains that would come out blurred in crystallographic snapshots. They also contorted their bodies into sometimes-awkward configurations to demonstrate the conformational changes of the molecule, and to show how it does its work mechanically and chemically in the cell.

Thus, in ways similar to cinematic forms of animation, these embodied animations originate with snapshot images; that is, freeze-frame crystallographic snapshots of proteins. However, these embodied animations are not mechanical reconstitutions of movement captured and visualized at equidistant time points. Already *lured by a narrative of liveliness* (see later in this chapter, and Chapter 6), these researchers tap into their stories of excitability and their own embodied imaginations, using their bodies to conjure possible molecular forms and movements. As renderings that conjure subvisible worlds, embodied

animations—unlike the computer graphic animations of which Jim, Joanna, and Lynn are so wary—do not overdetermine the forms and temporalities of molecular movement. These animations resonate with, rather than attempt to represent molecular movements. As exploratory movements reaching towards a sensate knowing, embodied animations are open to interpretation, and are, as I examine in later sections of this chapter, inviting for others to *try on* for themselves. In this sense, embodied animations socially intra-active, and participatory, offering an opportunity for modelers and their colleagues to learn how to move with and be moved by molecular excitations.

Risky Affinities: Dancing Molecular Desire

> Affinity: related not by blood but by choice, the appeal of one chemical nuclear group for another, avidity
>
> Donna Haraway, "Cyborg Manifesto", 1991: 155

> **af·fin·i·ty (noun)**
>
> 1. a natural liking for or inclination toward somebody or something, or a feeling of identification with somebody or something
> 2. somebody to whom somebody else is attracted
> 3. a similarity or likeness that connects persons or things
> 4. a relationship by marriage rather than blood
> 5. a similarity in structure between groups that may suggest a common origin
> 6. a measure of the likelihood of a chemical reaction taking place between two substances.
>
> *Also called avidity*
>
> 7. the attraction between an antigen and an antibody
>
> Encarta English Dictionary

Diane's affinity for her dog and dog metaphors to describe the excitability of protein

molecules suggests that there is an underlying molecular vitalism at play among structural biologists. Interviews with structural biologists were revealing for how lively narratives of molecular agency were negotiated and managed in pedagogical and professional contexts. The following is an extended excerpt from an interview I did with Joanna and Lynn, which illuminated how this is in fact a risky practice of figuration. This is the conversation that ensued after Joanna recounted the story of how Geoff Miller had produced the analogy of the molecular clamp in her laboratory:

> Natasha: So, analogies are so powerful they actually change the way you manipulate a system, the way that you operate on it?
>
> Lynn: And that's why you have to be so careful!
>
> Natasha: Do you use analogies like molecular machines a lot? Because I see that a lot in the biological engineering classes.
>
> Lynn: We use ... I tend to use analogies when I explain things. But I try to make sure that I don't go too far because if you start making things that don't correspond ...
>
> Joanna: ... Then they will believe the non-corresponding thing. George tends to use them more than the two of us ... But I don't necessarily like making too many engineering analogies. Number one: I don't know enough about engineering. Number two: I'm always afraid that I'm going to say something that makes them remember something inaccurately. And make them really believe a molecule is a machine, as opposed to a molecule. You know?
>
> Lynn: The thing that is the number one problem with how we talk about biology, the expert scientists, I mean by that, is that we anthropomorphize our molecules. And when we do that we, you know, literally, "If I was a DNA polymerize what would I want to do?" [Laughing] And that's fine between us, because we have this underlying, deep, ingrained appreciation of the fact that we're talking about what is energetically favorable for a molecule to do! [laughs]

Joanna and Lynn (in unison): *As opposed to what a molecule has a desire to do!*

Joanna: That's what's so difficult about evolution.

Lynn: And our students just so don't get that. And it's just...And I try not to ever say what the molecule wants to do, anymore. And if I catch myself, I always stop and ask my students to tell me exactly what did I just mean. And this year I am better at it than last year. [Laughs] I have not used it nearly as many times.

Natasha: So you're talking about the attribution of agency?

Lynn: Yeah. But our professors do it all the time. *All the time.*

Joanna: Yeah. And they don't...

Lynn: ... catch themselves ...

Joanna: ...catch themselves *at all.* Yeah! I mean, and it's very difficult. And it's very problematic. I was going to say, like for instance, with the sake of evolution, it's *very* problematic, because then the students will really believe that this molecule or *some other thing* decided that this molecule needed to change...and it's...

Lynn: Right, in terms of evolution, it's important for them to understand that the order isn't the environment changed and then therefore something arose that could deal with it; but the other way around, something was there that happened to exploit this changing environment. That's a huge, sort of huge concept in there that they don't necessarily get and can't get, unless they are entirely free of any *illusions* of the...

Joanna: [interrupts] Human characteristics of their molecule—that it's selecting to change itself! And it's just....I mean it's a little thing. As experts we can say, well "it's the chemistry in the molecule." But as intro to biology students, these guys don't see that it's...

> Lynn: George tells this story in class every f'ing year. Where—he likes to make the scientists human, which is a good thing. But then he tells a story about [a protein researcher] when he was at a conference and got asked a question, that he was pondering right in the middle of that. He literally stopped and said, "Well if I was this molecule, *what would I want to do*?" And you know, it's funny, you know, and it's a characteristic of a person. But it is a great disservice to an introductory biology student to hear that. Because it doesn't even... From George, it never comes with a disclaimer. What he actually meant to say was, "What would be evolutionarily advantageous for an organism to have in terms of the system."
>
> Lynn: It sounds little but it makes a huge difference.

Lynn and Joanna recognize that analogies are potent devices that can produce risky, unwanted effects for their rather impressionable students. They don't want their students to come away with the idea that molecules actually are miniature machines—they're not comfortable enough with their knowledge of what machines are, never mind what machines can do, to really develop those analogies with any level of precision. But they also don't want students to come away with the "illusion" that molecules have "human characteristics" and "desires." They are approaching introductory biology education as a kind of public relations effort to produce properly aligned supporters of evolutionary theory. As they see it, the risk in using anthropomorphisms to describe molecular behaviors is not that they will necessary instill creationist ideas in their students' minds; equally problematic is that by suggesting that molecules have desires—that they "want" to do things—they may seduce their students into conceiving Lamarckian views of evolutionary progress. Yet, what is so fascinating is that while they ardently police their anthropomorphizing analogies, they do recognize that experts—those who really get it about the affinities and energetics of chemistry—carry in them a kind of molecular vitalism. It's as if their own desires to become molecule, to figure out the tensions, forces,

and affinities of life as a molecule might, are so strong that despite all their best efforts to cut out their anthropomorphic animisms, they keep slipping up.

In our conversation, I told Lynn and Joanna about Diane Griffin's expression of pain when students present her their misshapen protein models. They laughed as I told the story about how she performed the correction of the molecule to set it right, in a way that suggested that they really got how Diane could feel the strain of the molecule. Joanna responded, "Yeah, absolutely." And Lynn interjected "Well, you see, Diane feels the pain of the molecule. She anthropomorphizes it, which is fine, for *her*, as long as she doesn't imply...you know." And yet, this story elicited their own accounts of how they act out molecular in class. Joanna fessed up to her rampant "anthropomorphisms" and got right into it, demonstrating for us what she does in class to teach about how molecules move through a gel in an electrophoresis apparatus. She tells her class: "You know, this little molecule needs to move through the gel. And it's a net, and it's stuck like this. And now I'm a big long molecule," she said as she danced out the wriggling bodies of the molecules as they move through the gel.

For them, the problematic anthropomorphisms include the body-work involved in performing molecular movements, that endow them with human (and animal) forms and desires. This conversation points to a number of important themes that I address in the following chapter. Namely, how, in spite of these ardent attempts to eradicate anthropomorphic analogies, do experts continually rely on their bodies and affects to perform molecular behaviors? Where and when do biologists slip up and enact molecular desires? When can't they help themselves? How might dancing molecules as if they were

full of desires, wants, and needs, not be such a terrible thing for these scientists? How, for experts, might this constant slippage into the practice of *becoming molecule* produce effective lures that draw them and their students into rich worlds full of converging embodied models of molecular life? I explore these questions later in the chapter, and in the Conclusion I examine more closely the nature of the narrative form they perform through these molecular affects. In what follows, however, I look at where embodied expressions of molecular desire are too risky to perform.

Truncating Molecular Body-work

Most of the time, in both pedagogical and professional settings, the researchers I interviewed and observed were uninhibited with their molecular gestures. However, in contexts where I called attention to their bodies, and to their practice of embodied modeling, they became visibly uncomfortable. In such situations, rather than focusing on what it is they cared about (e.g. the protein and its mechanism), I was drawing attention to what it was that their bodies were doing. When I asked Lynn and Joanna how they used their bodies in teaching, they giggled, waving their arms about, performing for me some of their most frequently used molecular gestures. But, reflecting on what it was they were doing in class, Lynn was visibly embarrassed: "We're making fools of ourselves is what we are doing!" During one of our interviews, just after Fernando demonstrated to me how hinges work on doors, I started to ask him if he ever used non-mechanical metaphors to talk about his proteins. In the midst this exchange I drew attention directly to his body. His first response took an interesting swerve that conflated his body as animator of molecular motions, with the animated proteins that make up his body:

Natasha: To what extent are these metaphors...more than metaphors. Do

you think about the protein outside of...

Fernando: Of my computer? Yeah.

Natasha: Yeah. Yeah. Okay. But a couple of things [I laugh]. You are using your body very expressively to describe the protein structure and its movements. So in some ways the protein is being described like a body.

Fernando: Yes it is. I am moving my arm. I am moving a set of proteins. Okay. You have a set of muscles that glide against each other and allow me to pull my arm and extend my arm and my fingers. I am moving my body. I'm having electrical impulses traveling at pretty much diffusion rate from the tips of my fingers to my brain, and then out to my eye to my brain that tell me that I am now closing my hands. So it is very physical, very *motional* relationship to the world. Things are always in change. Okay. When things reach stasis, equilibrium. They die. That's basically death. You have reached equilibrium. Nothing comes in nothing comes out. So how can you not describe molecules and life as a set of motions, as tensions. Okay. Someone described this to me once as: "Life is a constant struggle between the hydrophobic and the hydrophilic." [Natasha: A constant?] *Struggle* between the hydrophobic and the hydrophilic... I mean...You can't....It's nice to draw little cartoons with arrows, and triangles, and put in for the substrates. And it's great for initially visualizing things. But if you really want to think about these things, you've got to think about [pauses] everything that's happening.

Fernando apparently didn't get where my question was coming from. However, his response provided a stunning description of how he sees the relationship between life and movement. His response suggested that in addition to his highly mechanical approach to the study of living systems (note how he turns his own proteinacious body into a Cartesian machine for perception), he has cultivated a keen sensibility for molecular movements, and recognizes that conveying the tensions and movements that inhere in these phenomena demands more than static diagrammatic renderings. The second time I try to pose the question, I direct his attention to his body as a potential medium for conveying molecular forms. This time he gets what I'm trying to say, but his initial response,

particularly how his voice changes, suggests that what I just asked him had crossed the line into his personal space:

> Natasha: Do you think your body, your own body, is a useful resource for thinking about these things?
>
> Fernando: [Laughs. Voice goes up high. Pauses awkwardly.] Umm....I think you do it unconsciously. You relate to things that you know, and most people know their body pretty well. You know? As in my case, I've had a lot of time to hang out with myself. [Natasha: Laughing] And you know. I get to know myself pretty well. I know what hurts. I know what doesn't hurt. I know about how many drinks I should have before I cross the line. So, yeah, I think people use their bodies in a sense. You know, you are familiar, you talk with, you express to people. I use ideas in architecture and building because I've done it for so long. You look at the plumbing inside of a house. You look at the electricity. You know...People cannot talk about anything that they are not familiar with.

Andrés also experienced discomfort when I drew attention to his body-work. Michael Fischer and I were at an annual meeting for structural biologists. I was off looking at student posters, when Mike told Andrés that I was studying how structural biologists "danced" their molecules. Andrés confessed to Mike that he had choreographed "a little dance" for one of the molecules that he had modeled. When I rushed up to him having just heard the news, he told me: "I hate dancing, but there was just no other way to communicate the mechanism. I had to dance it." I asked him to show me his dance, but he declined, almost blushing. He had been quite comfortable enlisting my participation to perform his model of a cell adhesion molecule when I asked him how his protein worked. However, when I asked him to "do his dance," I apparently skipped over the part that was crucial to him. What I should have asked was what it was about the molecule that demanded he perform the mechanism with his body? How did this molecule work? While he refused to show me his "secret" dance as we stood in the lobby at the scientific

meeting, he had performed it before for a small group of colleagues. This is to say that researchers do not perform their molecular gestures on command, as much as I wouldn't do a pirouette if someone asked me to do one out of the blue. Structural biologists gestures are a crucial part of their practice, but singling out their body-work as the element of interest leaves them feeling vulnerable, as if they are standing up in front of you stark naked.

Other scenes of social intra-action that do not support expression of embodied models include those skewed by differential relations of gender and power. Zeynep, a protein crystallographer conducting her postdoctoral research in a lab based at the same institute where Andrés works, recounted a story that brought these issues to the fore. We were at a cocktail party held by a mutual friend when she told be about an incident that occurred when she was talking with the PI of her lab, describing for him a molecular mechanism she had hypothesized. We were standing in the corner of the kitchen, and she cleared space to show me the elaborate choreography she had used to convey this molecular mechanism to her professor. The mechanism involved one part of the protein making an upward, twisting, piston-like movement into another part of the protein. She demonstrated this with zeal, making a large upward gesture with one arm to enact the piston, while using her other arm to show the space occupied by the rest of the protein. Apparently her professor read her molecular dance as an overtly sexual performance, and teased her about making such rude gestures in public! By calling attention to her body, in that moment he gendered and sexualized her body-work, rendering it as an excessive and improper expression of knowledge. She took this warning seriously, and told me that she'd become much more self-conscious about how she moved when relating molecular mechanisms.

Except where body-work is made explicit, and encouraged as a pedagogical exercise, such as in Jim Brady's protein folding classroom, the examples of Fernando, Zeynep, and Andrés demonstrate that researchers' expressions of their molecular gestures depend on a condition in which this body-work remains tacit. The body-work of reasoning in structural biology seems then to operate most frequently just below the surface, as a kind of gestural vocabulary that supports and orients both the modeler and their interlocutors in their articulations of molecular mechanisms. As I have learned from these encounters, in order to be propagated effectively, molecular gestures must be kept alive; and this can only happen in social intra-actions that elicit and sustain them as tacit modes of knowledge.

Body-Experiments & the Social Intra-Actions Mimetic Modeling

I have conducted ethnographic observations in both Diane Griffin's and Brian Found's weekly group meetings. In these meetings, I have watched graduate students, postdocs and PI's fumble and correct the models they perform through their bodies, sometimes realizing mid-gesture that they have the structure wrong. In these situations they are quick to correct their own gestures as a means to correct the model that they are simultaneously figuring out in their heads. In the process, they learn new things while they play through possible molecular configurations and movements with their own bodies. Not so much a kind of thought experiment, the body-work of reasoning in protein modeling could be considered as a kind of body experiment. In this sense, I treat embodied models as tools that researchers can use in their experimental practice. Like Andrés, who ratcheted up his grip to demonstrate the binding of cell adhesion molecules, I see embodied models as "vehicles

for materializing questions" (Rheinberger, 1997: 28); that is, as means that can propel scientists into new kinds of conceptual and corporeal understandings of their research objects. As much as they are inflected with affect, I propose that these embodied models can be thought of, in Rheinberger's terminology, as "technical objects" that are employed in the investigation of "epistemic things." Very often structural biologists attempt to communicate embodied models as technical objects in order to produce shared understanding.

Members of Brian's group specialize in designing new protein structures. At one of their meetings, Kabita, a fifth year PhD student, presented her recent progress. The protein Kabita works on is complex: it forms a dimer, which means that it is made up of two similar molecules bound together. It also has intracellular and extra-cellular domains, with parts of the protein that must traverse the lipid bi-layer of the cell membrane. In the midst of this presentation her colleagues interrupted her with a constant stream of questions, asking her to clarify the structure of the protein she was describing. Even with intricate computer graphic renderings of the molecule projected on the screen behind her, they demanded more detail, and she was compelled to articulate the structure with her own body.

To communicate this intricate structure to the group she used her body to paint a Ribbon diagram of the molecule.[98] She proceeded to lift both her hands over her head and trace

[98] Ribbon diagrams, one of the most frequently used schemas for rendering protein structures, have an instructive quality about them. Arrows in the model indicate the direction of the polypeptide backbone (from the first amino acid in the chain to the last) as it winds through the structure. As Kabita's performance indicates, these are not just visual guides for the eye, but are also useful for

the winding backbones of the twinned molecules, one with each hand, following them as they traversed extra-cellular and intra-cellular spaces. Her gestures were large and sweeping as she brought her arms from high up, over her head, all the way down in front of her body. Her molecular dance ended with her fully bent over, hands touching the floor. Yet, questions still surfaced from the group, and Kabita was asked to describe the mechanism that bound the molecules together. "I like to think of it this way", she said, and repeatedly crossed her arms at the forearms, fists clenched, demonstrating with the tension in her musculature the binding energy between the molecules. A visiting professor, still confused, leaned over the table, and repeated this gesture over and over as he asked questions, inquiring and confirming with her that this was indeed the form of the molecular interaction she was describing. In a follow up email, Kabita told me that I had had the "misfortune of coming to what was probably my most contentious group meeting in at least two years. Brian still refers to it as 'that disastrous group meeting', because I didn't succeed in conveying my concepts, apparently." What is interesting is that even amidst such contention, she was comfortable to fully animate her hypothetical mechanisms with her body, and moreover, others used theirs to relay back to her both their understandings and missed understandings.

As this story suggests, researchers' bodies become animating media, both for figuring out how molecular mechanisms work, and for relaying knowledge about their structure to

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learning of forms kinesthetically. Ribbon diagrams could be compared to the tracers and tailings of a rhythmic gymnast's ribbon if she were to trace the winding back bone of a protein as she dances. One animation available online treats a Ribbon diagram as if it were a rollercoaster, by taking the viewer on a rather dizzying ride along the strands of the Ribbon backbone of a protein model. See http://streaming.wi.mit.edu/?sub=protein_rollercoaster&vid=X11_001_220K_256x199.mov.

others. Such forms of *social intra-action* show how bodily movement plays a role in how researchers learn and communicate structural knowledge. In the back and forth communication between Kabita and her interlocutors, her embodied model of the protein (itself a mimetic model) was re-enacted in an intra-active exchange until shared understanding (and even misunderstanding) was acknowledged. Here we can see these researchers trying to tune their bodies in to each other's figural vocabularies and molecular affects as a means to enable fuller communication of the forms and functions of particular molecules. In this sense, they not only have to embody the models they build, they have to learn how to *move with* and *be moved by* each other's mimetic gestures. This practice demands social intra-actions for shared knowledge.

I see a kind of mimesis at play in protein modelers' entrainment to molecular movements, and in their teaching, learning and communication. This relay of forms and gestures can be seen as an intra-active process aimed at achieving mutual understanding. As the above examples show, certain social intra-actions enable researchers to propagate their embodied models. They do this by communicating to their colleagues and students through a kind of iconic and indexical "gymnastics" (Bourdieu, 1977: 1). Pierre Bourdieu has likened such performances to a kind of "mimesis" that is similar to a "rite or dance" in which there is "something ineffable", something that "communicates, so to speak, from body to body, i.e. on the hither side of words or concepts" (Bourdieu, 1977:1). It may be through this mimetic, gestural language that biological molecules become intelligible, manipulable and workable as objects for the researcher, their colleagues and students.

Michael Taussig's (1993) multi-sensate theory of mimesis captures some of this movement

and participation that I see at play in the communication of molecular knowledge.[99] Reading Benjamin, Taussig develops the notion of an "optical tactility", in which movement, sensation and perception are woven together. Mimesis has two layers for Taussig: it contains both an element of copy or imitation, as well as the "palpable, sensuous connection between the body of the perceiver and the perceived" (Taussig, 1993: 21). This mimetic faculty nourishes and sustains shared understanding and knowledge within a larger cultural milieu. On this, he suggests that the mimetic faculty is "the nature that culture uses to create second nature". It is "the faculty to copy, imitate, make models, explore difference, yield into and become Other" (Taussig, 1993: xiii). To mime is thus to cultivate a model of another entity within one's own body—a model that can be shared with others.

For Taussig, "[to] ponder mimesis is to become sooner or later caught in sticky webs of copy and contact, image and bodily involvement of the perceiver in the image" (Taussig, 1993: 21). Mimesis involves perceptual and physical intra-actions between participating bodies. It is this intimate contact between scientist and substance—a contact mediated through prosthetic devices and visualizing machines—that helps me think through the body-work of protein modeling, reasoning and communication. Moreover, it is through a kind of mimesis that a researcher's body and their model can begin to fold into one another, producing not a mirror-image reflection or representation, but a kind of

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[99] Lucy Suchman (2007) and I (Myers, 2006) have both combined Michael Taussig's (1993) multi-sensate theory of mimesis and Karen Barad's (1996, 2003) theory of "intra-action" to explore human-machine entanglements. This convergence in our readings is not just a happy coincidence. It suggests to me that, as feminist scholars committed to exploring situated knowledges in human-computer interactions, we are seeing very similar kinds of phenomena emerging in our respective fields of study.

resonance. Self and other, modeler and model are thus not so readily separable from their relation: models and bodies become entangled in intra-active mimetic exchange. Below I investigate modes by which such infoldings are made to propagate.

Propagating Molecular Affects through Mimetic Transductions

Transduction is a term used widely in the field of structural biology. Proteins are figured as working machines that transduce force and energy within the cell (see for example Bourne, 1986; Harrison, 2004). The term transduction has at least three lineages in the history of science: one in acoustics and the other two in biology. It refers both to the "action or process of transducing a signal", such as sound through one medium to another, and "the transfer of genetic material from one cell to another by a virus or virus-like particle" (Oxford English Dictionary). In addition, "signal transduction" is frequently used in molecular biology to describe the transmission of extra-cellular signals into the cell and the propagation this signal as biophysical molecular events (see also Mackenzie, 2002). I incorporate each of these aspects of the term in my use here. Transduction, in this latter sense, describes a process for moving and transforming signals between molecules; in a signaling network, molecules propagate chemical energy and mechanical forces in a kind of contact-dance enacted between molecular bodies. The specificity of the media through which the signal moves, in this case, the physics and chemistry of the protein and watery cellular environment, morphs the signal into different registers as it moves between molecules. In this sense, the signal itself is not code, but gesture. Transduction is thus, not so much a transmission of information, but the propagation of a gesture through moving, responsive bodies.

I extend transduction to describe the propagation of movements and affects in between and among scientists. Through their intra-actions with each other and with their models, protein modelers can be seen to transduce and so propagate the molecular affects and gestures they have cultivated in order to communicate their feeling for protein forms and mechanisms. As I related in Chapter 3, Jim Brady demonstrated how protein models could entangle their users in participatory intra-actions that were geared towards learning. He showed his students how to look and learn by tracing the polypeptide backbone of a Ribbon diagram with his whole body. As he followed the peptide, his whole body got swept up the fold. This act of tracing is nothing like photo-copying. Tracing enables Jim to *transduce* the form of the polypeptide chain through his body, not to delegate the task to a replicating machine. The aim here is not to replicate, but to emulate. Like Kabita, who danced the Ribbon diagram of her molecule for her colleagues, the tracer's moving body, following the fold of the chain, renders the fold with their body, without producing a replica or a copy. In so doing, Jim and Kabita show how one must *move with and be moved by* the fold in order to learn the structure.

Coupling transduction and intra-action enables me to account for the specificity of the modeling media, and the kinds of bodies involved in these mimetic exchanges. Protein modelers communicate molecular forms within the range of motions available to their bodies: their contortions never actually look like the graphic models they project onscreen. Refusing any simple theory of representation, embodied models and animations render and so emulate modelers' feeling for the tensions, forces, and movements of molecules. In this sense, protein modelers' embodied animations extend and expand assumptions about what

counts as a model or scientific visualization: as we learn to see how bodies become models, the visual cultures of science become more and more recognizable as cultures of performance.

Embodied animations also require that theories of representation and communication in science account for the role of affect in the propagation of scientific knowledge. I draw on Henri Bergson's (1991) *Matter and Memory*, which animates a theory of perception based on nineteenth-century physiology. In this work he bundles perception and movement together in the nervous tissue of the body, exploring how affect and responsive action are produced through a "kind of motor tendency in a sensory nerve" (55-56). Diffracting Bergson through Deleuze (1986), I've been lured to think of living bodies as fleshy antennae whose physiologies act as a kind of resonating media that oscillates between conduction and resistance, as tissues for gathering up the energetics and movements of the world, and manifesting these as perception, affect, and action. Thus, as responsive and relational bodies, we hitch rides on the movements of others' in the world. In this vein, I treat bodies as *excitable tissues* with the capacity to collect up and relay these excitations by transducing them through their flesh. In this way, bodies can be figured as responsive and receptive entities capable of affecting and being affected, that is, bound up in affective entanglements with other bodies in the world.

By shifting to a language of "hitching onto" and "getting caught by", I want to put some pressure on readings of scientific visualization that build on the concept of visualization technologies as "apparatuses of capture" (Deleuze and Guattari, 1980). There is a tendency in theories of visualization to render visualization technologies as powerful tools

that can "capture" objects, where the objects themselves are rendered as passive captives of the apparatus. In an intra-active account of how scientists render the world, I pay attention to scientists' capacity to be moved by the forms and movements of the entities they attempt to draw into view. Their apparatuses of capture can never fully contain or constrain. Indeed, it is possible to think of scientists as attempting to entrain their bodies, imaginations, and instruments to the movements of their objects, which are never fully captured, and which continually evade. In the realm of protein modeling, I see researchers hitching a ride on the molecular forms they conjure, getting pulled along, and lured into radical intra-action.

Conclusion

As I hope I have showed in this chapter, protein models are not the only phenomenon (in Barad's sense) produced in the protein modeling laboratory. Protein models are embodied and performed in ways that propagate more than structural information. Embodied animations transduce affects, emotions, and feelings that inflect knowledge about protein structure. Through their animated bodies, researchers perform their knowledge in a register that both feeds into and exceeds the discourse of mechanism in structural biology. In spite of their continuous attempts to police animistic language through mechanistic logic, and indeed, in some cases to actively truncate their body-work, I detect an intra-active excitability in structural biologists' performances of their models. Molecular mechanisms are quickened, that is, enlivened through these intra-actions, recasting the trope of "molecular machines" within which proteins tend to be figured. I read structural biologists' excited gestures as performances that express their affective entanglements in knowledge making practices.

Going beyond Barad's call to account for the multiple agencies through which scientific knowledge is produced, this chapter has aimed to document how such knowledge is inflected and transformed in its very performance. I propose that the intra-actions between participating bodies (human, nonhuman and machine) produce a second order phenomenon that could be called *intra-animacy*.[100] This is not some immaterial "animism" that imbues matter with some external force, nor is it built up from a networked collection of individual agencies modeled on liberal notions of subjectivity. Intra-animacy is a phenomenon that is engendered through modelers' intra-actions with each other, and with their objects and machines. In turn, it animates their imaginations and narratives about the substances of life. I observe that intra-animacy performed as a range of affects and gestures that make visible structural biologists' intimate sensibilities with regards to molecular forms, their chemical affinities and physical movements.

As I have shown, these performative affects are not extra-scientific phenomena; they appear to be intrinsic to the conceptual and material work of producing and propagating structural knowledge. As such, the mechanical theories of protein function that researchers produce can be seen to depend on this affective enlivening of mechanisms for the effective production and deployment of mechanistic theories. Left to gather dust on the pages of elementary school textbooks or reduced to dead metaphors that fail to hail bodily participation, mechanistic models of protein function may indeed be "deanimations" of living substances (on modes of deanimation see Haraway, 1998). If these models are disentangled from the intra-actions that produce and sustain them, they may appear

[100] Thanks to Joe Dumit for first suggesting that what I was observing was a kind of "inter-animacy."

deadening and inert. However, if these visualizations can be drawn back into Barad's expanded framing of experimental phenomena, and observed within the assemblages through which they are enacted, then the "machinery of life" can be narrated in much livelier form. Enlivened models animate imaginations, techniques, experimental strategies, research questions and pedagogical interactions. Embodied animations are thus more than aesthetic flourishes: they are intra-active lures that pull scientists and their colleagues into imagined molecular worlds and so "vectorize" bodily experience to produce new forms of knowing. I suggest that it is protein modelers' capacity and willingness to *move with and be moved by* their models and animations—to conjure and mimetically transduce the excitability of proteinacious forms—which enables lively narratives thrive inside of the mechanistic logic life scientists avow. In the conclusion to this study that follows, I look much more closely at how such narratives of liveliness inflect life scientists' knowledge and practice.

Chapter 6

Liveliness

Beyond Automation and Inscription: Body-fullness in Biology

This study has examined how contemporary structural biologists learn to "give body" to molecules through a diverse array of media. The account I have provided highlights a range of visualization practices that don't conform to, or confirm standard accounts of life science practice. Two analytic schema developed in the context of social and historical studies of molecular biology laboratories break down, I argue, in view of the practices I have here described. These schema are 1) the reduction of laboratory work to practices of "inscription" (e.g. Latour, 1990; Latour and Woolgar, 1986), and 2) the rendering of the researcher as a "blind" "automat" plugged into the other machinery of the laboratory (e.g. Knorr-Cetina, 1999).

In his essay "Drawing things together," Latour (1990) attempts to account for the massive shift in knowledge associated with the scientific revolution. He suggests that it was the simple tools of the printing press, paper, pencils, and other inscription technologies that produced this transformation. These technologies generated inscriptions that were both *immutable* and *mobile*, both unchanging and able to circulate widely, to achieve "translation without corruption" (28). For Latour, the power embodied in two-dimensional inscriptions or images was that they could be collected, enabling scientists to "gather up

the world" (31) in one place at one time to generate a synoptic view over otherwise absent or distant things.[101] Latour emphasizes the power wielded by mobile and immutable inscriptions that are manifest on paper. He draws attention to the flat surfaces on which many distant and otherwise unrelated things can be drawn together in tables, charts, graphs, texts, and images. Flat surfaces, he asserts, are much easier to dominate than the things themselves, where "realms of reality" that appear distant become "inches apart once flattened out on the same surface" (54).

Examining the histories of three-dimensional modeling in the sciences, Hopwood (1999) and Francoeur (1997) take issue with Latour's "immutable mobiles." Counter to Latourian doctrine, three-dimensional models demonstrate that the "visual worlds of science" aren't so "flat" (Hopwood, 1999: 491).[102] Significant here is that three-dimensional models of complex forms are not legible in the same ways as flat inscriptions: building and using three-dimensional models cannot be reduced to practices of reading and writing. Hopwood (1999), for example, shows that anatomists valued His's waxes over flatter, more

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[101] The key to his theory is that, once available, these "immutable mobiles" could become recruitment devices which proponents of a theory could use to win arguments and challenge dissenters in the ongoing contests of knowledge and power, which, in Latour's (1990) view, are at the heart of the history of scientific progress. "Inscriptions allow *conscription*" (50) through a political process of mustering allies. Immutable mobiles therefore contribute to the stabilization of scientific fact through competing claims to truth. Counter to intuition, stabilization in Latour's formulation requires a kind of mobility. He draws attention to institutions that have the power of synoptic vision over cascades of files and records, such that the "bureau" becomes a "small laboratory in which many elements can be connected together just because their scale and nature has been averaged out." (54) He suggests that "in our cultures, 'paper shuffling' is the source of an essential power, that constantly escapes attention since its materiality is ignored" (55).

[102] His's waxes, for example, "did not fail to travel": in addition to their use in teaching embryology students at Cambridge, they were so well promoted that by the 1880s many embryologists began to make their own models, and new techniques flourished (1999: 462). And while Francoeur (1997) documents the challenges modelers faced in the construction, design and manufacture of molecular modeling kits, these kits eventually became widely dispersed and commonplace tools in both laboratories and classrooms.

abstract means of representation because, because "they could view them from all sides, feel their surfaces with their fingers, and cut them up. Having given three-dimensional 'body' to their representations, they could more readily work on them as though they *were* bodies" (491). Model-building requires that the user engage the model physically: the modeler must interact with, handle, and manipulate the model, in order to generate insight.

In Latour and Woolgar's (1986) *Laboratory Life*, inscriptions are frequently identified as two-dimensional markings on flat surfaces, and "inscription devices" are identified as machines that measure, mark, and draw traces out of biological phenomena. Karin Knorr-Cetina (1999) extends the idiom of machinic inscription in *Epistemic Cultures*, a comparative study of high-energy physics and molecular biology cultures. In this major study, she pays careful attention to researchers' sensory bodies. However her account renders the scientists and the organisms they work with fractured along the familiar fault lines of the Cartesian body. In her words:

> By the scientist's body I mean the body without the mind. If the mind were included, hardly anyone would deny the presence of the body. The *body*, as I use the term, refers to bodily functions and perhaps the hard wiring of intelligence but not conscious thinking (1999: 95).

Knorr-Cetina asserts that the body is essential to laboratory practice, but the body that she narrates is blind, silent, mind-less, and mechanical. Here she actively configures the body as a hard-wired mechanism that underlies, and in a sense holds up, the higher faculties of consciousness. The researcher's body reconfigured by and through the "epistemic machinery" of the laboratory becomes an "automat," a "black-boxed" "information-

processing machinery" running routine manipulations in the laboratory (97). She makes clear that while scientists do rely heavily on their senses, "if anything is irrelevant to the conduct of research in molecular biology, it is the sensory body as a primary research tool" (95). What is problematic here is that she perpetuates a "myth of body-lessness" (Haraway, 2001) that already saturates many scientists' and theorists' accounts of molecular biology practice. As such, she layers her reading of corporeal practices with a set of unquestioned Cartesian assumptions about the workings of perception, sense experience, and action. Knorr-Cetina's ethnography of the automated protocols and practices of inscription leave little room to account for passion, affect, and sensory engagement in laboratory life.

In this study, I have examined a range of visualization practices in molecular biology that are not produced through machinic inscription. Renderings like three-dimensional interactive computer graphic models of protein molecules, for example are not direct machinic inscriptions of the signature of a substance: forms of three-dimensional modeling explicitly involve the active input of the researcher. Modelers contribute their corporeal knowledge and conjure a range of narrative forms to help them parse relations between molecular form and function. A very different model of researchers' engagement in their work is rendered through accounts of structural biologists' physical, imaginative, and affective entanglements in multi-dimensional model-building practices. Distinct from the reading and writing practices involved in interpreting machinic inscriptions as legible texts, modeling practices require researchers' corporeal entanglement with their objects, modeling media, and machines in the production of scientific facts. Rather than turn researchers' bodies into yet another laboratory instrument, I treat the machines of the laboratory—in this case the physical models, computing devices and graphics interfaces of

structural biology labs—as prosthetic extensions of the researcher's sensory body. Far from silent and mechanical, the bodies I observe in the laboratory are open systems, affectively entangled with their objects, modeling media, and machines. The field of structural biology demonstrates how laboratory work is itself an ongoing practice of training and retraining the bodies and imaginations of scientists: researchers continually learn and adapt within the experimental apparatus, and reenact what they have learned.

These models and their associated forms of knowing are mobile, yet they do not move through a process of translation—as in the horizontal movements of flat images and texts across paper surfaces. Rather, they propagate through a kind of transduction of forms and movements relayed in multiple dimensions through gestures enacted between bodies and objects. Key here is that transduction of modeling knowledge is not impervious to "corruption," it is open to mutability: forms and gestures are diffracted through the modeler's tissues, and so inflected and transformed as they move between bodies. Model building thus generates local, partial knowledge; and yet, through the performance of models in the ongoing face-to-face interactions that constitute scientific training and communication, such forms of knowing can be made to propagate (Kaiser, 2005a). As I demonstrated throughout this study, tracking the mobility of models and modeling knowledge demands ethnographic attention to modes of embodiment, affect, and performance, aspects of laboratory life that are otherwise often hidden from view (see for example, Rose, 1983; Heath, 1997). It is the multidimensional practices of modeling in structural biology that make these aspects of science visible, and thus serve as a site for revising assumptions about the nature of laboratory life, and refiguring role of pedagogy and training in scientific work.

My aim in this study has been to produce an ethnographic account that hitches a ride on the liveliness, passion, and creativity that I see animating life science practice. In what follows, I take a closer look at how two distinct, and intertwined renderings of life science practice have shaped both scientists' and theorists' accounts.

Life Science, Liveliness, and Life Itself

> Life itself is the psychic, cognitive, and material terrain of fetishism. By contrast, liveliness is open to the possibility of situated knowledges, including technoscientific knowledges.
> Haraway, 1997: 137

In *On Beyond Living: Rhetorical Transformations of the Life Sciences*, Rich Doyle (1997) explores how the rise of a one-dimensional rhetoric in molecular biology in 1960s flattened living bodies into one-dimensional code. In this period, the primary object of biological interest, deoxyribonucleic acid, became over-coded in the rhetoric of informatics. In Doyle's formulation, molecular biologists effectively reduced bodies to a kind of thinness and transparency, with nothing left lurking secretly beyond or behind DNA's codes. Doyle suggests that in this move molecular genetics evacuated "life itself" from biology. For Doyle, once depth had been sucked out of bodies, biologically ordered bodies became "postvital," beyond living; in other words, life had left the building. It is in the flatness of the rhetoric of "body as code" that the enigmatic force of "life itself" was simultaneously squeezed into a molecule, and spread out into the thinness of legible text. In the case of the helically coiled DNA molecule, "life itself" got unraveled, unzipped. For Doyle, the emblematic moment in this history is when one molecular geneticist could look

down at the transparent body of a cell-fate- and genome-mapped body of a laboratory worm (*C. elegans*) and shrug and say, with maps at hand, "That's all there is" (Doyle 1997: 17). Here Doyle narrates a moment in the history of molecular biology where a kind of "boredom" settles in among scientists involved in genomics projects. Once reduced to legible codes, "life itself" and the labour of life science turned out to be not so lively.

Evelyn Fox Keller (1995; 2002) has shown, however, that a kind of vitalism has continued to lurk and linger just below the surface of life scientists' words. In her historical examination of the rhetoric of genes, she describes how geneticist J.H. Muller identified early concepts of the gene as "betraying a subconscious adherence to 'the ancient lore of animism'" (Keller, 2002: 127). Despite attempts by Muller and his colleagues to repress the "vital forces" with which the concept of the gene was imbued, a vitalist tendency continued operate in the ways that the gene was figured as an agential "entity embodying the capacity to act within its own being" (Keller, 2002: 127). As she demonstrates, such forms of "animism" were never fully eradicated from the concept of the gene. Keller unearths a liveliness that lingers in spite of attempts to de-animate life through mechanistic language and models in molecular biology.

In the short excerpt above, Haraway (1997) points to what could be thought of as two animating discourses in the history of life science practice: "liveliness," and "life itself." "Life itself" might be best thought of as a narrative of capture that produces scientific objects by pulling bodies out of time, while liveliness is a narrative form that keeps bodies in time. In this sense "life itself" and "liveliness" do not reside in any given living substance, or its representation—they are ways of storying and so, making sense of life.

Haraway helps me to see how Doyle's and Keller's accounts are distinct, though intimately entangled narrative forms, or kinds of story telling, that have long animated life scientists' imaginations. In the excerpts I offer here, Doyle focuses on a prevailing narrative form organized around the "capture" of "life itself," while Keller finds alive vestiges of a narrative of "liveliness" in life science practice.

In Foucault's formulation, "life itself" is that nonplace inhabiting the ever-receding depths of the modernist body, with all its associated techniques of visibility, legibility, and speakability (see Foucault, 1971). According to Foucault, "life itself" became seeable and say-able through new configurations that demarcated, distinguished, organized, and arrayed living things according to the logic of the table. "Life itself" in this sense is produced through an "apparatus of capture" (Deleuze and Guattari, 1980) that can catch living things and turn them into objects available to scientific scrutiny. For Haraway, the very notion of life itself "depends on the erasure of the apparatus of production and articulatory relationships that make up all objects of attention" (1997: 147). Thus in their search for life itself scientists erase their creative work, elide their apparatus, and in so doing produce fetishes. In Chapter 4 of the present study, I have shown how structural biologists attempt, through a kind of cryo-freezing, to capture life itself in the form of "molecular machines," and so, in the process produce a kind of machinic fetishism that disavows the exquisite skills they have cultivated in order to build machines inside the bodies of cells and organisms. And yet, in spite of their best efforts, the entities that structural biologists and biological engineers actually produce through their modeling practices are quite unlike deterministic machines: they are undeniably lively. It is this slippage into the realm of lively machines that clues me in that there is something out of

the ordinary going on in this work of modeling molecular life. It is in the production of lively machines that structural biologists and biological engineers are beginning to create new forms of life; and in doing so they undo the very binary between machines and organisms that initially constituted the study of biology (Haraway, personal communication; Foucault 1971). I return to this theme below to show how lively narratives escape the grip of this dualism.

I agree with science studies scholars that the "capture of life itself" is a pervasive narrative form through which scientists tell conquest stories about their encounters with the living world. The structural biologists and biological engineers that I interviewed and watched at work talked about "busting open" and "smashing apart" living cells in order to get at the molecular machines inside; and they described crystallographic snapshots as means of "capturing" states of chemical change in a protein. However, if "capture" is an alluring narrative modality for them, it is also an enticing way for theorists to tell stories about science. Inquiring into how scientists produce narratives of life itself, STS scholars have (re)produced an account that makes it seem as if the "capture of life itself" is the only kind of story scientists know how to tell. I see "life itself" in this sense as a powerful *lure* that has drawn both life scientists and their critics into their respective investigations. As story told by scientists, life itself appears to promise objectivity, distance, clarity, and power. As a story told about science by theorists standing at a distance, it serves as a device to expose a kind of denial that bolsters critics' claims to the fallibility of objective knowledge. I argue that there is something missing in this analysis. As Keller (2002) hints above, there is another alluring narrative modality in life science practice. I see what Keller calls the "vestiges of vitalism" in Muller's gene-talk as part of a narrative of liveliness that

continues—in spite of harsh policing against its use—to animate life scientists' stories about living bodies.

It is all too easy to produce and reproduce narratives of capture in the conventions of scientific writing. Yet there are other narrative forms that are not so visible in the texts scientists write. While writing is undeniably a fleshy, material-semiotic practice for scientists, their texts are often read as end-stage representations, such that the embodied enactments that give them form are elided in translation. With this in mind, it is necessary to remember that narratives have both textual *and* gestural forms. A narrative, as mimes and dancers remind me, can be enacted through movement; and a figure is not only a form of speech or writing, it is also a dance.[103] Structural biologists' figural vocabularies—their gestural stories—convey forms and qualities (textures, tensions, and forces) of molecular forms of life. While liveliness is most often edited out in the conventions of scientists' textual accounts, it comes alive and is readily performed through gestural media.

Gestural figurations also communicate scientists' relationships with their objects. If there is posture or habitus emblematic of—and I would argue co-constitutive with—the narrative of life itself, it is the gesture of the scientist pointing at a dissected, dismembered object-at-a-distance, and declaring, "That's all there is." On the other hand, the gestural form that best evokes a narrative of liveliness would be the excited resonance of the modeler performing the vibrational energy of the molecule she arduously and lovingly models. In contrast to narratives of the "capture of life itself", narratives of liveliness operate through

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[103] According to the Oxford English Dictionary, a figure is also "one of the evolutions or movements of a dance or dancer; also, a set of evolutions; one of the divisions into which a set dance is divided."

the idioms of excitability, desire, and excess. Stories of liveliness gesture towards and so conjure a living world that escapes capture. Through gestural media, living bodies take on forms that look much less like deterministic machines. "Lively" stories in this sense are those that narrate living bodies as wily, unpredictable, excitable tissues. These are also stories that betray how passion and desire structure scientists' knowledge; telling their stories through gestures, scientists relay their affinities for their objects. The stories they produce in and through their bodies could be thought of as biophillic, or what, after Haraway, Maria Puig de la Bellacasa (forthcoming) might call biological "love stories."

There are several ways to interpret the relationship between life itself and liveliness as I parse them here. Life itself and liveliness could be understood as two ways for scientists to render their *encounters* with the objects they study: one tells a story about objectivity at a distance, a story that denies the encounter; the other situates knowledge, performing a form of knowing that recognizes scientists' affective entanglement with their objects. And yet, this is not to say that liveliness and life itself are necessarily two opposing poles of a dyadic system of story telling. If I were to make this move, life itself—with its structure of denial that produces a story of conquest—could be read as an oppressive regime that aims to stifle, silence, or suppress liveliness in service of objectivity. The recovery or resuscitation of lively narratives would then, as Joe Dumit (personal communication) astutely points out, appear to be a liberatory move. And yet, that is not my aim here. By making liveliness visible, my intention is to set this story side by side with the story of life itself, to understand more deeply how they feed off of and into one another in the daily practices of laboratory life.

In this vein, this ethnography could be read as an attempt to track how structural biologists navigate the tensions between these narrative forms, how they struggle between different, sometimes conflicting, sometimes co-constitutive forms of knowing and communication in order convey what they learn from building and using models. Liveliness and life itself operate in parallel. A science that only told lively stories would not be recognizable as science; lively stories can't survive alone. For example, sometimes modeling molecules as bodies can lead researchers astray: though structural biologists may be skilled animators, as Dave Kaiser (personal communication) reminds me, "proteins presumably have *many more* degrees of freedom along which they can wiggle, bend, and fold than even the most agile dancer." While it would be an undeniably lively practice, if structural biologists just danced their molecules they wouldn't be doing science (or, for that matter, making art). At the same time, life itself already depends on liveliness: without an underlying narrative of liveliness, there would be nothing to capture in the story of life itself.

As I have shown in Chapter 4, narratives of molecular liveliness are constantly in play, but often once they are performed, they are quickly disavowed. One reason for this may be that these lively stories are risky: in the hands of naïve students and lay people, narrative forms that awaken imaginations to notions of molecular agency, or those that ascribe intentionality and desire to molecular interactions, have to potential to mutate neo-Darwinian evolutionary theory. And yet, experts—those who seem to have their fingers on the pulse of what is "really going on" in proteinacious worlds—are the ones performing lively narratives most frequently. In this way, expert structural biologists perform a kind of secret knowledge, available only to the initiated.

It is important to note here that liveliness is not vitalism; it is not a kind of vital force that infuses matter with life; and it is not the opposite of mechanism. Lively narratives are not positioned *against* machines. Machines, as I showed in Chapter 5, can be quite lively. Machines are more and other than what they get reduced to in discourses that operate at the divide between the machine and the organism. As Donna Haraway (personal communication) helps me see, lively machines and machinic life are the cyborg forms made possible through stories that don't get mired in the opposition between vitalism and mechanism that has haunted biology since its inception. I would argue that liveliness is a way of telling stories that refuses to make clean distinctions between organisms and machines: both organisms and machines can be lively. Indeed, liveliness does not operate within discourses made possible by the mechanism-vitalism divide; a dualism that has for too long constrained what is possible to say about life. If lively narratives are liberating at all, it is because they break out of this dualism, and open onto a new world in which thrive barely recognizable forms of life for which we currently have few words. Lively stories are open to the possibility of finding new ways to figure life and reconstitute the relations between machines and organisms. For this reason, the current surfacing of liveliness among the stories life scientists tell, bodes a transformational shift for the sciences of life.

As a means to situate my interpretive practices in this study, I must account for how "liveliness" operates not only as a lure for practitioners I track; it is also a potent lure in my own narration of life science practice. Rather than constraining my study to an account of the constitution of "life itself," I'm hitching onto the lure of liveliness in an attempt to provide an account of life science that would otherwise be obscured. In this ethnography I make no attempt to mask how I *move with and am moved by* life scientists lively practices

and narratives: in this sense, my work diffracts and transduces[104] scientists' pleasures and passions, their winces and cringes, along with my own.[105] As Stefan Helmreich (personal communication) reminds me, transduction does not promise complete or perfect translation. Movements and gestures diffract through tissues, and are inflected, producing interference patterns; signals get torqued as they are transduced. This ethnography is not only a representation of scientific practice; it is a rendering that keeps the modeler-ethnographer's contribution in full view. I conclude below with a meditation on Rich Doyle's (2003) ecstatic reading of alife research, as a means to explore of how narratives of liveliness are engendered and propagated through the kinds of intra-active practices I have documented in this study.

The Lure of Liveliness

> [A]life's power emerges not out of the barrel of a gun, but from the gestures of mouse and pixel, signifying and asignifying grapples with the machinic phylum. To be sure, the familiar seductions of alife are rhetorical, but they involve the sculpted, *implicitly choreographed movements of bodies as well as the affects provoked by the encounter with alife creatures.*
>
> Rich Doyle, 2003:41 (emphasis added)

Doyle's (2003) *Wetwares* offers a lively reading of life science research that goes beyond narratives of the capture of life itself. In the chapter "Representing Life for a Living," he

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[104] On transductive ethnography, see Stefan Helmreich (2007) "An Anthropologist Underwater: Immersive Soundscapes, Submarine Cyborgs, and Transductive Ethnography," *American Ethnologist* 34(4).

[105] In June, 2006, I collaborated with visual and movement artist Clementine Cummer to produce "Cellular Practices and Mimetic Transductions: A Dance in Four Scores." We performed at Close Encounters, the European meeting for the Society for Literature, Science, and the Arts, in Amsterdam. This piece built on my ethnographic work, and used text, movement and live video-feed to tap into and propagate scientists' affects and excitability in relation to their techniques and objects. In many ways, we attempted to transduce through our bodies the affects which we saw animating life scientists in their work.

looks into an area of research practitioners call "alife," in which some investigators claim to be able to "evolve" artificial organisms and worlds through algorithms (see also Helmreich, 1998). In light of his 1997 reading of the postvital turn in contemporary life sciences, Doyle is puzzled. He asks: "If life seems to have disappeared as a sovereign entity and joined the ranks of all those other relational attributes ... then it seems odd that it should reappear, so visibly on my screen" (23). It should be reasonable to ask where "life" has gone as *in silico* practices in the life sciences propagate and expand.[106] Biological laboratories are increasingly populated, not with the techniques and apparatuses of the wet lab and its visceral substances, but with the clean lines, codes, and colours of computer graphic models and simulations. Even in protein crystallography, the fleshy materiality of proteins eventually gets crystallized and diffracted and digitally rendered in stylized folds and flashy colours. The fleshy bodies and lively substances of organisms are indeed becoming rare. Rendered *in silico*, the stuff of life in the life sciences might start to appear a little aseptic, inert; even a bit cold. Yet, as Helmreich (1998: 134) shows in *Silicon Second Nature*, something life-like does appear on the screen, particularly when alife creatures perform behaviours culturally legible as "cute" or "primitive." For Helmreich:

> The cuteness of Artificial Life creatures is produced by *and* produces a sense that they are primitive entities, a sense that they are capable of miming—perhaps even parodying or burlesquing—advanced behaviour, a sign taken to demonstrate not that they are alive but only that they are simpler forms of life. The laughter at Artificial Life is the spark of life for these simulated creatures (134).

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[106] Organisms are being replaced by algorithms in new research arenas such as "computational physiology" (which aims to engender whole experimental organ systems on screen, see for example, http://pizza.cs.ucl.ac.uk/grid/ biobeacon/php/index.php), projects such as "BioSpice" (which promises quantitative analytic tools to parse life's "circuitry" with computational approaches to systems biology, http://biospice.lbl.gov/), and simulating technologies built to analyze protein folding and dynamics (see for example D.T. Jones' simulator, http://www.cs.ucl.ac.uk/staff/D.Jones/).

The animator, the one who breathes life into these creatures, is for Helmreich, the one who laughs, who recognizes life in alife. And yet, Helmreich leaves the aliveness of these artificial organisms as an open question: "Is it alive, or is it mimesis?" Doyle goes a little further. He asserts that alife creatures not only seem alive, they are alive.

There are important differences between alife organisms and the interactive computer models and animations of proteins. In structural biology and biological engineering the question is not whether the protein animations are alive, but rather if the renderings are lively; that is, whether they resemble deterministic mechanisms, or wily, animal-like bodies inflected with intentions, desires, and affects. So, while I'm not concerned with whether life, as such, appears on structural biologists' computer screens, I am interested in how liveliness gets generated and propagated through their computer interfaces. With Doyle, I suggest that there are three key features of in silico models and animations that enable liveliness to thrive onscreen: 1) the fluid and malleable capacity of computer graphics media to render temporality and movement; 2) the intra-activity of the interface; 3) and the capacity of animations to interpellate viewers into narratives of liveliness through their interactivity and movement.

One key quality of something lively is that it moves. In the history of the concept, life has long been associated with movement. In Chapter 4, I showed how Fernando, a structural biologist whose habitus had been inflected by his engineering expertise, performed a "motional" well-rehearsed reading of "life as movement":

> Things are always in change. Okay. When things reach stasis, equilibrium. They die. That's basically death. You

> have reached equilibrium. Nothing comes in nothing comes out. So how can you not describe molecules and life as a set of motions, as tensions. Okay. Someone described this to me once as: "Life is a constant struggle between the hydrophobic and the hydrophilic."

Life, for Fernando, inheres in the affinities and desires of molecules; in this, he conjures an alchemical notion of life. In his reading, bodies have an affinity for movement: it keeps them alive; and so to stop moving is to stop living. As he demonstrates, movement calls into play our stories about life (which are themselves narratives that lure us in through their play with time). And yet, any demarcation between the animate and the inanimate, the lively and the inert, already performs a narrative fold informed by one's predilections for what can count as alive (see also Helmreich, 1998). This of course depends on who participates in the interaction; not every party gets a chance to give name to this effect.[107] Life gets recognized *as such*, for Doyle, "only through the complex of translation mechanisms that render it articulable as something 'lively'" (23). Doyle draws on Peirce's notion of "abduction," which is a kind of reasoning through which a prediction is made in the absence of an assurance that it will succeed; abduction is the formation of a hypothesis that moves out into an unknown future. Doyle uses abduction to think about the ways that alife creatures propose (and so lure their users and viewers into notions of) other possible lives as kinds of hypothetical life. Indeed it is in the Austinian pronouncement "It's alive!" that "life" gets "corporealized," to use Haraway's term (1997: 141). As Doyle emphasizes in the passage above, the life effect of liveliness operates also at a nondiscursive level. That is, at the tissue level, as a kind of affect in the intra-acting, narrating perceiver, which could

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[107] As I emphasized in Chapter 5, a feminist model of accountability (such as Barad's "intra-action") recognizes such asymmetrical power relations, and never forgets the scientists' responsibilities for modeling, naming, or narrating, and circumscribing the forms of their intra-actions with their objects.

be understood in terms of Haraway's (1997) "material semiosis."

In this vein, Doyle insists that "the success of alife organisms in their virtual ecology is tied to their success in an actual interactive visual ecology, an ecology also populated by humans" (29): "Allowing oneself to be solicited by a screen entails a seduction in which humans interact with, rather than act on, an entire bramble of technological infrastructure" (59). What Doyle names as the "radical interactivity" and "complicity" of human-computer grapplings, is for me a both a carefully choreographed *and* improvisational contact-dance between humans and their machines, substances and models. Alife creatures produce "the life effect" by interpellating their viewers; and they do this through their capacity for intra-action. Lured into affective entanglements, and so "unable to look away," those interpellated by alife creatures are in some senses "abducted by silicon" (Doyle, 2003: 24-25).

My hypothesis is that if a model (imagined, computer graphic, or embodied) moves and can be interacted with, then its users and makers *can move with and be moved by it.*[108] In a Deleuzian-Bergsonian (1986) model of perception, affect, and action, living bodies are readily entrained to the movements (imagined, embodied, and otherwise) of others: bodies are porous and have capacity to be moved by movement; we are hailed by each other; and hitch rides on the movements of others. I suggest that life and liveliness are *effected* (and *inflected*) because of a kind of responsiveness in our tissues. It is through their excitable

[108] I draw this phrase from my master's thesis "Body-fullness in Biology," in which I examined an ethic of *seeing with feeling* in life science imaging techniques that move through time with developing organisms. For this I drew on Haraway's (1991) situated knowledges, Barad's (1996) intra-action and Merleau-Ponty's (1968) phenomenology of the flesh. See Myers (2005).

tissues that scientists are pulled into responsive relation with other moving bodies. It is in such entanglements with others that we find ourselves able to *move with and be moved by* other bodies. Excitability, it would appear, is the grounds for, or condition of possibility for intra-action. This is the excitability, that when enacted in lively stories, betrays scientists' affective entanglements with their objects, machines, and modeling media.

If laughter, for Helmreich, is the spark that gives life to alife creatures, I would step back to suggest that it is the capacity to be *moved to laughter*, and to produce *a laugh that moves*, or animates, is what makes possible this recognition of life onscreen. There is an excited contact-dance between the user and the screen; and this contact-dance hails an *affective response-ability* in participating bodies. That we are able to pronounce, "It's alive!", or "It's lively!" is related to our response-abilities, our ability to be moved by others. The "event" that we name "life happening now" is thus a material-semotic production: it does not just play out before our eyes: it is a participatory encounter, one that requires intra-activity and responsiveness between bodies. Thus, an ethic of responsibility comes into play precisely because of the power invested in the performative act of so naming this human-machine entanglement, this very relation, "life".

My sense is that structural biologists are viscerally abducted by intra-active movements and lively stories. It is through their computer graphic and social intra-actions that they become entrained to protein forms and movements; and it is through their bodies and language that they conjure and hitch themselves on to the movements of subvisible bodies, and catch the ride. Like alife, structural biology also "thrives on" a "complex ecology of brains, flesh, code, and electric grids," (23) and it is in this "bramble" of such intra-acting human-

machine ecologies that these scientists get drawn in (despite serious risk of censure) by the lure of liveliness.

In this study I have attended to the material-semiotic modes through which structural biologists *interact with, incorporate,* and *perform* their models and animations. These human-computer-substance intra-actions produce excitations in excess of the speech and writing, at the same time, entail a range of modeling practices demand more than an analysis of representation in scientific practice. Though proteins, the "principal substances of life," have been compressed, coded, and diffracted into digital form, there appears to be space in the human-computer assemblages of structural biology laboratories for a narrative other than the capture of life itself. As excitable tissues, these scientists are lured into intra-actions with their digital objects, and in so doing sustain and nourish narratives of liveliness. Where the search for "life itself" might just be the *lure* that gets scientists deep into such entanglements with molecules, cells and organisms in the first place, it is the intra-actions between scientists, their substances, and machines that sustains and nourishes lively stories, and animates biological imaginaries. Liveliness becomes a story scientists perform through their ecstatic interactions with other moving bodies. This is the liveliness that becomes visible and tangible in the expressive performances of life scientists and their models, and which calls this ethnographer's attention to the subtleties of body-machine practices and the layers of affect and expression so vital to life science research.

Bibliography

Abir-Am and Pnina G. (1992) 'The Politics of Macromolecules', *Osiris, 2nd Series* 7: 164-91.

Abir-Am, Pnina G. (1987) 'Synergy or Clash: Disciplinary and Marital Strategies in the Career of Mathematical Biologist Dorothy Wrinch', in Abir-Am, Pnina G. and Dorinda Outram (eds), *Uneasy Careers and Intimate Lives: Women in Science, 1789-1979* (New Brunswick: Rutgers University Press): 239-80.

Abott, Alison (2000) 'Structures by Numbers', *Nature* 489: 130-32.

Al-Amoudi, A, D Studer and J Dubochet (2005) 'Nanostructure of the Epidermal Extracellular Space as Observed by Cryo-Electron Microscopy of Vitreous Sections of Human Skin', *J Invest Dermatol* 124: 764-77.

Alac, Morana and Edwin Hutchins (2004) 'I See What You Are Saying: Action as Cognition in Fmri Brain Mapping Practice', *Journal of Cognition and Culture* 4/3: 629-61.

Anonymous (2006) 'A Cogwheel for Signal Transduction across Membranes', *Cell* 126/5.

Austin, J. L. (1975) *How to Do Things with Words* (Cambridge, Mass.: Harvard University Press).

Barad, Karen (1996) 'Meeting the Universe Halfway: Realism and Social Constructivism without Contradiction', in Nelson, Lynn Hankinson and Jack Nelson (eds), *Feminism, Science, and Philosophy of Science* (Boston: Kluwer): 161-94.

Barad, Karen (2003) 'Posthumanist Performativity: Toward an Understanding of How Matter Comes to Matter', *Signs* 28/3: 801-31.

Barad, Karen (2007) *Meeting the Universe Halfway: Quantum Physics and the Entanglement of Matter and Meaning* (Durham: Duke University Press).

Barry, C. D., H. E. Bosshard, R. A. Ellis and G. R. Marshall (1974) 'Evolving Macromodular Molecular Modeling System', *Federation Proceedings* 33/12: 2368-72.

Bassow, H. (1968) *Construction and Use of Atomic Molecular Models* (New York: Pergamon Press).

Beale, Lionel S. (1881) 'The Address of the President of the Royal Microscopial Society', *Science* 2/52: 294-97.

Bergson, Henri (1991) *Matter and Memory* (New York: Zone Books).

Bourdieu, Pierre (1977) *Outline of a Theory of Practice* (Cambridge: Cambridge University Press).

Bourdieu, Pierre (1990) *The Logic of Practice* (Stanford, Calif.: Stanford University Press).

Bourdieu, Pierre (1998) *Practical Reason: On the Theory of Action* (Stanford, Calif.: Stanford University Press).

Bourdieu, Pierre and Jean Claude Passeron (1990) *Reproduction in Education, Society, and Culture* (London: Sage).

Bourne, Henry (1986) 'One Molecular Machine Can Transduce Diverse Signals', *Nature* 321: 814-16.

Bowker, Geoffrey C. (2005) *Memory Practices in the Sciences* (Cambridge, Mass.: MIT Press).

Bowler, Peter J. (1989) *Evolution: The History of an Idea* (Berkeley: University of California Press).

Brändén, Carl-Ivar and John Tooze (1999) *Introduction to Protein Structure* (New York: Garland Pub.).

Butler, Judith P. (1993) *Bodies That Matter: On the Discursive Limits Of "Sex"* (New York: Routledge).

Cambrosio, Alberto, Daniel Jacobi and Peter Keating (1993) 'Erlich's 'Beautiful Pictures' and the Controversial Beginnings of Immunological Imagery', *Isis* 84: 662-99.

Cartwright, Nancy (1997) 'Models: The Blueprints for Laws', *Philosophy of Science* 64, Supplement. Proceedings of the 1996 Biennial Meetings of the Philosophy of Science Association: S292-S303.

Cartwright, Nancy, Towfic Shomar and Mauricio Suárez (1995) 'The Tool Box of Science', *Poznian Studies in the Philosophy of the Sciences and the Humanities* 44: 137-49.

Cat, Jordi (2001) 'On Understanding: Maxwell and the Methods of Illustration and Scientific Metaphor', *Studies in the History and Philosophy of Modern Physics* 32/3: 395-441.

Chang, Geoffrey, Christopher Roth, Christopher Reyes, Owen Pornillos, Yen-Ju Chen and Andy Chen (2006) 'Retraction', *Science* 314/5807: 1875.

Chiu, Wah, Matthew Baker, Wen Jiang, Matthew Dougherty and Michael Schmid (2005) 'Electron Cryomicroscopy of Biological Machines at Subnanometer Resolution', *Structure* 13: 363-72.

Clardy, Jon (1999) 'Borrowing to Make Ends Meet', *Proceedings of the National Academy of Sciences* 96: 1826-27.

Clardy, Jon (1999) 'Borrowing to Make Ends Meet', *Proceedings of the National Academy of Sciences* 96/5: 1836-999.

Clarke, Adele and Joan H. Fujimura (eds) (1992) *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences* (Princeton, N.J.: Princeton University Press).

Coen, Enrico S. (1999) *The Art of Genes: How Organisms Make Themselves* (Oxford: Oxford University Press).

Collins, D. M., F. A. Cotton, E. E. Hazen, E. F. Meyer and C. N. Morimoto (1975) 'Protein Crystal-Structures - Quicker, Cheaper Approaches', *Science* 190/4219: 1047-53.

Collins, H. M. (1985) *Changing Order: Replication and Induction in Scientific Practice* (London: Sage Publications).

Collins, Harry (1992 [1985]) *Changing Order: Replication and Induction in Scientific Practice* (Chicago: University of Chicago Press).

Cowen, Leah, J.B. Anderson and L. M. Kohn (2002) 'Evolution of Drug Resistance in Candida Albicans', *Annual Review of Microbiology* 56: 139-65.

Cowen, Leah and Susan Lindquist (2005) 'Hsp90 Potentiates the Rapid Evolution of New Traits: Drug Resistance in Diverse Fungi', *Science* 309: 2185-89.

Creager, Angela N.H. (2002) *The Life of a Virus: Tobacco Mosaic Virus as an Experimental Model, 1930-1965* (Chicago: Chicago University Press).

Crowfoot Hodgkin, Dorothy (1972) 'The X-Ray Analysis of Complicated Molecules, Nobel Lecture, December 11, 1964', in, *Nobel Lectures, Chemistry 1963-1970* (Amsterdam: Elsevier Publishing Company): 71-86.

Daston, Lorraine (2003) 'The Glass Flowers', *Things that Talk, Max Planck Institute for the History of Science* Preprint 233: 5-32.

Daston, Lorraine and Peter Galison (1992) 'The Image of Objectivity', *Representations* 40: 81-128.

Dawson, J.W. (1883) 'American Association for the Advancement of Science: Address of the Retiring President, Dr. J.W. Dawson, at Minneapolis, August 15, 1883', *Science* 2: 190-99.

de Chadarevian, Soraya (2002) *Designs for Life: Molecular Biology after World War II* (Cambridge: Cambridge University Press).

de Chadarevian, Soraya and Nick Hopwood (eds) (2004) *Models: The Third Dimension of Science* (Stanford: Stanford University Press).

Deleuze, Gilles (1986) *Cinema* (Minneapolis: University of Minnesota).

Deleuze, Gilles (1988) *Foucault* (Minneapolis: University of Minnesota Press).

Deleuze, Gilles and Félix Guattari (1980) *A Thousand Plateaus: Capitalism and Schizophrenia* (Minneapolis: University of Minnesota Press).

Downey, Gary Lee and Joseph Dumit (eds) (1997) *Cyborgs & Citadels: Anthropological Interventions in Emerging Sciences and Technologies* (Santa Fe, N.M.: School of American

Research Press).

Doyle, Richard (1997) *On Beyond Living: Rhetorical Transformations of the Life Sciences* (Stanford: Stanford University Press).

Doyle, Richard (2003) *Wetwares: Experiments in Postvital Living* (Minneapolis: University of Minnesota Press).

Dumit, Joseph (Year) 'How to Do Things with Science: Facts as Forces in an Uncertain World', in, Book How to Do Things with Science: Facts as Forces in an Uncertain World (City.

Dumit, Joseph (2004) *Picturing Personhood: Brain Scans and Biomedical Identity* (Princeton, N.J.: Princeton University Press).

Fleck, Ludwik (1979) *Genesis and Development of a Scientific Fact* (Chicago: University of Chicago Press).

Foucault, Michel (1971) *The Order of Things: An Archaeology of the Human Sciences* (New York: Pantheon Books).

Foucault, Michel (1973) *The Birth of the Clinic: An Archaeology of Medical Perception* (New York: Pantheon Books).

Foucault, Michel (1995) *Discipline and Punish: The Birth of the Prison* (New York: Vintage Books).

Francoeur, Eric (1997) 'The Forgotten Tool: The Design and Use of Molecular Models', *Social Studies of Science* 27: 7-40.

Francoeur, Eric (2000) 'Beyond Dematerialization and Inscription: Does the Materiality of Molecular Models Really Matter?' *International Journal for Philosophy of Chemistry* 6/1: 63-84.

Francoeur, Eric (2001) 'Molecular Models and the Articulation of Structural Constraints in Chemistry', in Klein, Ursula (ed), *Tools and Modes of Representation in the Laboratory Sciences* (Boston: Kluwer Academic Publishers): 95-115.

Francoeur, Eric (2002) 'Cyrus Levinthal, the Kluge and the Origins of Interactive Molecular Graphics', *Endeavour* 26/4: 127-31.

Francoeur, Eric and Jerome Segal (2004) 'From Model Kits to Interactive Computer Graphics', in de Chadarevian, Soraya and Nick Hopwood (eds), *Models: The Third Dimension of Science* (Stanford: Stanford University Press): 402-29.

Franklin, Sarah (2006) 'Keynote Lecture: Queer Science: Transbiological "Facts"'. European Association for the Study of Science and Technology (Lausanne, Switzterland, August 23-26, 2007).

Franklin, Sarah (2007) *Dolly Mixtures: The Remaking of Genealogy* (Durham: Duke University Press).

Franklin, Sarah and Margaret M. Lock (2003) *Remaking Life & Death: Toward an Anthropology of the Biosciences* (Santa Fe: School of American Research Press).

Franklin, Sarah and Helene Ragoné (1998) *Reproducing Reproduction: Kinship, Power, and Technological Innovation* (Philadelphia: University of Pennsylvania Press).

Fujimura, Joan H. (2005) 'Postgenomic Futures: Translations across the Machine-Nature Border in Systems Biology', *new Genetics and Society* 24/2: 195-225.

Galison, Peter (1997) *Image and Logic: A Material Culture of Microphysics* (Chicago: University of Chicago Press).

Galison, Peter (1998) 'Judgment against Objectivity', in Jones, Caroline A. and Peter Galison (eds), *Picturing Science, Producing Art* (New York: Routledge): 327-59.

Geertz, Clifford (1973) *The Interpretation of Cultures*: Basic Books).

Geison, Gerald L. and Manfred D. Laubichler (2001) 'The Varied Lives of Organisms: Variation in the Historiography of the Biological Sciences', *Studies in the History and Philosophy of Biolomedical Science* 32/1: 1-29.

Gieson, Gerald (1969) 'The Protoplasmic Theory of Life and the Vitalist-Mechanist Debate', *Isis* 60/3: 272-92.

Gilman, Alex and Adam Arkin (2002) 'Genetic "Code": Representations and Dynamical Models of Genetic Components and Networks', *Annual Review of Genomics and Human Genetics* 3: 341-69.

Glusker, Jenny Pickworth (1981) *Structural Crystallography in Chemistry and Biology* (Stroudsburg, Pa.: Hutchinson Ross Pub. Co.).

Goffman, Erving (1959) *The Presentation of Self in Everyday Life* (Garden City, N.Y.: Doubleday).

Goffman, Erving (2001) 'On Fieldwork', in Emerson, Robert M. (ed), *Contemporary Field Research* (Prospect Heights, Ill.: Waveland Press): 153-58.

Goodsell, David (1993) *The Machinery of Life* (New York: Springer-Verlag).

Goodsell, David S. (1996) *Our Molecular Nature: The Body's Motors, Machines, and Messages* (New York: Copernicus).

Goodwin, Brian C. (1994) *How the Leopard Changed Its Spots: The Evolution of Complexity* (New York: Charles Scribner's Sons).

Goodwin, Charles (2000) 'Action and Embodiment within Situated Human Interaction', *Journal of Pragmatics* 32: 1489-522.

Griesemer, James R. (1990) 'Material Models in Biology', *PSA: Proceedings of the Biennial Meeting of the Philosophy of Science Association*, Volume Two: Symposia and Invited Papers: 79-93.

Griesemer, James R. (2004) 'Three-Dimensional Models in Philosophical Perspective', in de Chadarevian, Soraya and Nick Hopwood (eds), *Models: The Third Dimension of Science* (Stanford: Stanford University Press): 433-42.

Griffin, Susan (1984) *Woman and Nature: The Roaring inside Her* (London: Women's Press).

Gusterson, Hugh (1996) *Nuclear Rites: A Weapons Laboratory at the End of the Cold War* (Berkeley, Calif.: University of California Press).

Gusterson, Hugh (2005) 'A Pedagogy of Diminishing Returns: Scientific Involution across Three Generations of Nuclear Weapons Scientists', in Kaiser, David (ed), *Pedagogy and the Practice of Science* (Cambridge, MA: MIT Press).

Hacking, Ian (1983) *Representing and Intervening: Introductory Topics in the Philosophy of Natural Science* (Cambridge: Cambridge University Press).

Hacking, Ian (1986) 'Making up People', in Heller, Thomas, Morton Sosna and David Wellberry (eds), *Reconstructing Individualism* (Stanford: Stanford University Press).

Haraway, Donna J. (1991) *Simians, Cyborgs, and Women: The Reinvention of Nature* (New York: Routledge).

Haraway, Donna J. (1994) 'A Game of Cat's Cradle: Science Studies, Feminist Theory, Cultural Studies', *Configurations* 2/1: 59-71.

Haraway, Donna J. (1997) *Modest_Witness@Second_Millennium.Femaleman_Meets_Oncomouse: Feminism and Technoscience* (New York: Routledge).

Haraway, Donna J. (1997) *Modest-Witness@Second-Millennium.Femaleman-Meets-Oncomouse: Feminism and Technoscience* (New York: Routledge).

Haraway, Donna J. (2001) 'From Cyborgs to Companion Species: Kinship in Technoscience'.Taking Nature Seriously: Citizens, Science and Environment (University of Oregon, Eugene, February).

Haraway, Donna J. (2006) 'Crittercam: Compounding Eyes in Naturecultures', in Selinger, Evan (ed), *Postphenomenology: A Critical Companion to Ihde* (Albany: SUNY Press).

Haraway, Donna J. (1989) *Primate Visions: Gender, Race, and Nature in the World of Modern Science* (New York: Routledge).

Harrison, Stephen (2004) 'Whither Structural Biology?' *Nature Structural Biology and Molecular Biology* 11: 12-15.

Hayden, Corinne P. (2003) *When Nature Goes Public: The Making and Unmaking of Bioprospecting in Mexico* (Princeton: Princeton University Press).

Hayles, N. Katherine (1999) *How We Became Posthuman: Virtual Bodies in Cybernetics, Literature, and Informatics* (Chicago, Ill.: University of Chicago Press).

Heath, Deborah (1997) 'Bodies, Antibodies, and Modest Interventions', in Downey, Gary and Joseph Dumit (eds), *Cyborgs and Citadels: Anthropological Interventions in Emerging Sciences and Technologies* (Santa Fe: School of American Research Press): 67-82.

Heath, Deborah (1998) 'Locating Genetic Knowledge: Picturing Marfan Syndrome and Its Traveling Constituencies', *Science, Technology and Human Values* 23/1: 71-97.

Helmreich, Stefan (1998) *Silicon Second Nature: Culturing Artificial Life in a Digital World* (Berkeley: University of California Press).

Helmreich, Stefan (2007) ' An Anthropologist Underwater: Immersive Soundscapes, Submarine Cyborgs, and Transductive Ethnography', *American Ethnologist* 34/4.

Helmreich, Stefan (forthcoming) *Alien Ocean: An Anthropology of Marine Microbiology and the Limits of Life.*

Herzig, Rebecca (2004) 'On Performance, Productivity, and Vocabularies of Motive in Recent Studies of Science', *Feminist Theory* 5/2: 127-47.

Hill, Robert and Peter Rich (1983) 'A Physical Interpretation for the Natural Photosynthetic Process', *Proceedings of the National Academy of Sciences* 80/978-982.

Ho, Mae-Wan (1998) *The Rainbow and the Worm : The Physics of Organisms* (Singapore ; River Edge, NJ: World Scientific).

Hoffman, Michelle (1991) 'An RNA First: It's Part of the Gene-Copying Machinery', *Science* 252/5005: 506-07.

Holdrege, Craig (1996) *Genetics and the Manipulation of Life: The Forgotten Factor of Context* (Hudson, NY: Lindisfarne Press).

Honig, Barry (1999) 'Protein Folding: From the Levinthal Paradox to Structure Prediction.' *Journal of Molecular Biology* 293: 283-93.

Hopwood, Nick (1999) '"Giving Body" To Embryos: Modeling, Mechanism, and the

Microtome in Late Nineteenth-Century Anatomy', *Isis* 90: 462-96.

Hopwood, Nick (2002) *Embryos in Wax: Models from the Ziegler Studio* (Cambridge: Whipple Museum of the History of Science University of Cambridge).

Huxley, Thomas Henry (1878) *A Manual of the Anatomy of Invertebrated Animals* (New York: D. Appleton and Company).

Jacob, Francois (1973) *The Logic of Life: A History of Heredity* (Princeton: Princeton University Press).

Jones, David T. (1997) 'Successful Ab Initio Prediction of the Tertiary Structure of Nk-Lysin Using Multiple Sequences and Recognized Supersecondary Structural Motifs', *Proteins* Suppl. 1: 185-91.

Jones, David T. (2003) 'Learning to Speak the Language of Proteins', *Science* 302 (November 21, 2003): 1347-48.

Kaiser, David (2005a) *Drawing Theories Apart: The Dispersion of Feynman Diagrams in Postwar Physics* (Chicago: Chicago University Press).

Kaiser, David (ed) (2005b) *Pedagogy and the Practice of Science: Historical and Contemporary Perspectives* (Cambridge, MA: MIT Press).

Kay, Lily E. (1993) *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the Rise of the New Biology* (New York: Oxford University Press).

Kay, Lily E. (2000) *Who Wrote the Book of Life?: A History of the Genetic Code* (Stanford, Calif.: Stanford University Press).

Keating, Peter, Alberto Cambrosio and Michael Mackenzie (1992) 'The Tools of the Discipline: Standards, Models, and Measures in the Affinity/Avidity Controversy in Immunology', in Clarke, Adele and Joan H. Fujimura (eds), *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences* (Princeton, N.J.: Princeton University Press): 312-49.

Keller, Evelyn Fox (1983) *A Feeling for the Organism: The Life and Work of Barbara Mcclintock* (New York: W.H. Freeman).

Keller, Evelyn Fox (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology* (New York: Columbia University Press).

Keller, Evelyn Fox (1996) 'Drosophia Embryos as Transitional Objects: The Work of Donald Poulson and Christiane Niesslein-Volhard', *History of Studies in the Physical and Biological Sciences* 26: 313-46.

Keller, Evelyn Fox (1996) 'The Biological Gaze', in Robertson, George, Melinda Mash, Lisa Tickner, Jon Bird, Barry Curtis and Tim Putnam (eds), *Futurenatural: Nature, Science, Culture* (New York: Routledge): 107-21.

Keller, Evelyn Fox (2000) *The Century of the Gene* (Cambridge, Mass.: Harvard University Press).

Keller, Evelyn Fox (2000 b) 'Models of and Models For: Theory and Practice in Contemporary Biology', *Philosophy of Science* 67, Supplement. Proceedings of the 1998 Biennial Meetings of the Philosophy of Science Association. Part II: Symposia Papers: S72-S86.

Keller, Evelyn Fox (2002) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines* (Cambridge, Mass.: Harvard University Press).

Kelty, Christopher and Hannah Landecker (2004) ' A Theory of Animation: Cells, L-Systems, and Film', *Grey Room* 1/17: 30-63.

Kendrew, J.C., G. Bodo, H.M. Dintzis, R.G. Parrish, H. Wyckoff and C. Phillips (1958) 'A Three-Dimensional Model of the Myoglobin Molecule Obtained by X-Ray Analysis', *Nature* 181: 662-66.

Kendrew, John C. (1964) 'Myoglobin and the Structure of Proteins. Nobel Lecture, December 11, 1962', in, *Nobel Lectures, Chemistry 1942-1962* (Amsterdam: Elsevier Publishing Company): 676-98.

Kirschner, Marc, John Gerhart and Tim Mitchison (2000) 'Molecular "Vitalism"', *Cell* 100 (January 7, 2000): 79-88.

Klestinec, Cynthia (2004) 'A History of Anatomy Theaters in Sixteenth-Century Padua', *Journal of the History of Medicine and Allied Sciences* 59/3: 375-412.

Knorr-Cetina, Karin (1999) *Epistemic Cultures: How the Sciences Make Knowledge* (Cambridge, MA: Harvard University Press).

Kohler, Robert (1994) *Lords of the Fly: Drosophila Genetics and the Experimental Life* (Chicago: University of Chicago Press).

Kreisberg, Jason, Scott Betts, Cameron Hasse-Pettingell and Jonathan King (2002) 'The Interdigitated Beta-Helix Domain of the P22 Tailspike Protein Acts as a Molecular Clamp in Trimer Stabilization', *Protein Science* 11: 820-30.

Kuhn, Thomas S. (1996) *The Structure of Scientific Revolutions* (Chicago, IL: University of Chicago Press).

Kuriyama, Shigehisa (2002) *The Expressiveness of the Body and the Divergence of Greek and Chinese Medicine* (New York London: Zone).

Lakoff, George and Mark Johnson (1999) *Philosophy in the Flesh: The Embodied Mind and Its Challenge to Western Thought* (New York: Basic Books).

Landecker, Hannah (2005) 'Cellular Features: Microcinematography and Film Theory', *Critical Inquiry* 31/4: 903-37.

Landecker, Hannah (2007) *Technologies of Living Substance: Cellular Life in the Twentieth Century* (Cambridge, Mass.: Harvard University Press).

Langridge, R., T. E. Ferrin, I. D. Kuntz and M. L. Connolly (1981) 'Real-Time Color Graphics in Studies of Molecular-Interactions', *Science* 211/4483: 661-66.

Langridge, Robert (1974) 'Interactive Three-Dimensional Computer Graphics in Molecular Biology', *Federation Proceedings* 33/12: 2332-35.

Latour, Bruno (1987) *Science in Action: How to Follow Scientists and Engineers through Society* (Cambridge, MA: Harvard University Press).

Latour, Bruno (1990) 'Drawing Things Together', in Lynch, Michael and Steve Woolgar (eds), *Representation in Scientific Practice* (Cambridge, Mass.: MIT Press): 19-68.

Latour, Bruno (2004) 'How to Talk About the Body? The Normative Dimensions of Science

Studies', *Body and Society* 10/2-3: 205-29.

Latour, Bruno and Steve Woolgar (1986) *Laboratory Life: The Construction of Scientific Facts* (Princeton: Princeton University Press).

Law, John (1973) 'The Development of Specialties in Science: The Case of X-Ray Protein Crystallography', *Science Studies* 3/3: 275-303.

Lenoir, Timothy (1982) *The Strategy of Life: Teleology and Mechanics in Nineteenth Century German Biology* (Boston: D. Reidel Pub. Co.).

Levinthal, Cyrus (1966) 'Molecular Model-Building by Computer', *Scientific American* 214: 42-52.

Lewontin, Richard C. (2000) *It Ain't Necessarily So: The Dream of the Human Genome and Other Illusions* (New York: New York Review of Books).

Lock, Margaret M. (2002) *Twice Dead: Organ Transplants and the Reinvention of Death* (Berkeley: University of California Press).

Lynch, Michael (1990) 'The Externalized Retina: Selection and Mathematization in the Visual Documentation of Objects in the Life Sciences', in Lynch, Michael and Steve Woolgar (eds), *Representation in Scientific Practice* (Cambridge, Mass.: MIT Press): 153-86.

Lynch, Michael (1991) 'Science in the Age of Mechanical Reproduction: Moral and Epistemic Relations between Diagrams and Photographs', *Biology and Philosophy* 6: 205-26.

Lynch, Michael and Steve Woolgar (1990) *Representation in Scientific Practice* (Cambridge, Mass.: MIT Press).

Maienschein, Jane (1991) *Transforming Traditions in American Biology, 1880-1915* (Baltimore: Johns Hopkins University Press).

Marchant, Beth. 'Cellular Visions: The Inner Life of a Cell' (http://www.studiodaily.com/main/technique/tprojects/6850.html, Accessed July 1, 2007).

Martin, Emily (1998) 'Anthropology and the Cultural Study of Science', *Science,*

Technology and Human Values 23/1, Special Issue: Anthropological Approaches in Science and Technology Studies: 24-44.

Meinel, Christoph (2004) 'Molecules and Croquet Balls', in de Chadarevian, Soraya and Nick Hopwood (eds), *Models: The Third Dimension of Science* (Stanford: Stanford University Press): 242-75.

Merchant, Carolyn (1983) *The Death of Nature: Women, Ecology, and the Scientific Revolution* (San Francisco: Harper & Row).

Merleau-Ponty, Maurice (1962) *Phenomenology of Perception* (New York: Humanities Press).

Merleau-Ponty, Maurice (1968) *The Visible and the Invisible* (Evanston [Ill.]: Northwestern University Press).

Miller, Greg (2006) 'Scientifiic Publishing: A Scientist's Nightmare: Software Problem Leads to Five Retractions', *Science* 314/5807: 1856-57.

Mol, Annemarie (2002) *The Body Multiple: Ontology in Medical Practice* (Durham: Duke University Press).

Morgan, Mary S. and Margaret Morrison (eds) (1999) *Models as Mediators: Perspectives on Natural and Social Science* (Cambridge: Cambridge University Press).

Myers, Natasha (2005) 'Visions for Embodiment in Technoscience', in Tripp, Peggy and Linda Muzzin (eds), *Teaching as Activism: Equity Meets Environmentalism* (Montreal: McGill-Queen's University Press): 255-67.

Myers, Natasha (forthcoming a) 'Molecular Embodiments and the Body-Work of Modeling in Protein Crystallography', *Social Studies of Science*.

Myers, Natasha (forthcoming b) 'Performing the Protein Fold: The Pedagogical Lives of Molecular Models', in Turkle, Sherry (ed), *The Inner History of Devices: Ethnography and the First Person* (Cambridge, MA: MIT Press).

Myers, Natasha (forthcoming c) 'Molecular Machines: Structural Biology, Biological Engineers and the Materialized Refiguration of Proteins', in Ghamari-Tabrizi, Sharon (ed), *Thinking with Donna Haraway* (Cambridge, MA: MIT Press).

Nye, Mary Jo (2001) 'Paper Tools and Molecular Architecture in the Chemistry of Linus Pauling', in Klein, Ursula (ed), *Tools and Modes of Representation in the Laboratory Sciences* (Dordrecht: Kluwer): 117 - 32.

Ochs, Elinor, Sally Jacobi and Patrick Gonzales (1994) 'Interpretive Journeys: How Physicists Talk and Travel through Graphic Space', *Configurations* 2/1: 151-71.

Pauling, Linus, Robert Corey and H.R. Branson (1951) 'The Structure of Proteins: Two Hydrogen Bonded Helical Configurations of the Polypeptide Chain', *Proceedings of the National Academy of Sciences* 37: 205-10.

Pauly, Philip J. (1996) *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology* (Berkeley: University of California Press).

Perutz, Max F. (1968) 'The Hemoglobin Molecule (November 1964)', in Haynes, Robert and Philip Hanawalt (eds), *The Molecular Basis of Life: An Introduction to Molecular Biology (Articles from 1948-1968)* (San Francisco: WH Freeman and Company): 39-51.

Perutz, Max F. (1994) 'Obituary: Linus Pauling', *Structural Biology* 1/10: 667-71.

Perutz, Max F. 'The Medical Research Council Laboratory of Molecular Biology' (http://nobelprize.org/nobel_prizes/medicine/articles/perutz/index.html, Accessed July 01, 2007).

Phelan, Peggy (1993) *Unmarked: The Politics of Performance* (London ; New York: Routledge).

Pickering, Andrew (1993) 'The Mangle of Practice: Agency and Emergence in the Sociology of Science', *American Journal of Sociology* 99/3: 559-89.

Pique, M.E. (1986) 'Technical Trends in Molecular Graphics', in Fletterick, Robert J. and Mark Zoller (eds), *Computer Graphics and Molecular Modeling* (Cold Spring Harbor, NY: Cold Spring Harbor Laboratory): 13-19.

Plumwood, Val (1993) *Feminism and the Mastery of Nature* (New York: Routledge).

Polanyi, Michael (1958) *Personal Knowledge: Towards a Post-Critical Philosophy* (Chicago,: University of Chicago Press).

Prentice, Rachel (2005) 'The Anatomy of a Surgical Simulation: The Mutual Articulation of Bodies in and through the Machine', *Social Studies of Science* 35: 867-94.

Puig, de la Bellacasa (forthcoming) 'Thinking with Care' in Sharon Ghamari-Tabrizi, *NatureCultures: Thinking with Donna Haraway* (Cambridge, MA: MIT Press).

Rabinow, Paul (1996) *Making Pcr: A Story of Biotechnology* (Chicago: University of Chicago Press).

Rasmussen, Nicolas (1997) *Picture Control: The Electron Microscope and the Transformation of Biology in America, 1940-1960* (Stanford, CT: Stanford University Press).

Rheinberger, Hans-Jörg (1997) *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube* (Stanford: Stanford University Press).

Rotman, Brian 'Gesture, or the Body without Organs of Speech', in.

Rotman, Brian. 'Gesture, or the Body without Organs of Speech' (http://accad.osu.edu/~brotman/gesture.html, Accessed March 16, 2004).

Sacks, Oliver (2003) 'The Mind's Eye: What the Blind See', *The New Yorker* (July 28): 48.

Sagan, Dorion and Lynn Margulis (1988) *Garden of Microbial Delights: A Practical Guide to the Subvisible World* (Boston: Harcourt Brace Jovanovich).

Sali, A, R Glaeser, T Earnest and W Baumeister (2003) 'From Words to Literature in Structural Proteomics', *Nature* 422: 216-25.

Sedgwick, Eve Kosofsky (2003) *Touching Feeling: Affect, Pedagogy, Performativity* (Durham: Duke University Press).

Shapin, Steven and Simon Schaffer (1985) *Leviathan and the Air-Pump: Hobbes, Boyle, and the Experimental Life* (Princeton: Princeton University Press).

Sibum, Otto (1995) 'Reworking the Mechanical Value of Heat: Instruments of Precision and Gestures of Accuracy in Early Victorian England', *Studies in the History and Philosophy of Science* 26/1: 73-106.

Siler, William and Donald A. B. Lindberg (1975) *Computers in Life Science Research* (New York: Plenum Press).

Sismondo, Sergio (1999) 'Models, Simulations, and Their Objects', *Science in Context* 12/2: 247-60.

Smaglik, Paul (2000) 'Genomics Initiative to Decipher 10,000 Protein Structures', *Nature* 407 (5 October 2000): 549.

Star, Susan Leigh (1992) 'Craft Vs. Commodity, Mess Vs. Transcendence: How the Right Tool Became the Wrong One in the Case of Taxidermy and Natural History', in Clarke, Adele and Joan H. Fujimura (eds), *The Right Tools for the Job: At Work in Twentieth-Century Life Sciences* (Princeton, N.J.: Princeton University Press): 257-86.

Stengers, Isabelle (1999) 'Whitehead and the Laws of Nature', *Salzburger Theologische Zeitschrift (SaThZ)* 2: 193-207.

Stengers, Isabelle (n.d.) 'A Constructivist Reading of Process and Reality'.

Stent, Gunther (1968) 'That Was the Molecular Biology That Was', *Science* 160/3826: 390-91.

Suchman, Lucy (2007) *Human-Machine Reconfigurations: Plans and Situated Actions, 2nd Expanded Edition* (New York: Cambridge University Press).

Tanford, Charles and Jacqueline Reynolds (2001) *Nature's Robots: A History of Proteins* (Oxford: Oxford University Press).

Taussig, Michael T. (1993) *Mimesis and Alterity: A Particular History of the Senses* (New York: Routledge).

Thacker, Eugene (2004) *Biomedia* (Minneapolis: University of Minnesota Press).

Thompson, Charis (2005) *Making Parents: The Ontological Choreography of Reproductive Technologies* (Cambridge, Mass.: MIT Press).

Traweek, Sharon (1988) *Beamtimes and Lifetimes: The World of High Energy Physicists* (Cambridge, Mass.: Harvard University Press).

Trumpler, Maria (1997) 'Converging Images: Techniques of Intervention and Forms of Representation of Sodium-Channel Proteins in Nerve Cell Membranes', *Journal of the History of Biology* 30: 55-89.

Tsernoglou, D., G. A. Petsko, J. E. McQueen and J. Hermans (1977) 'Molecular Graphics - Application to Structure Determination of a Snake-Venom Neurotoxin', *Science* 197/4311: 1378-81.

Turkle, Sherry, Joseph Dumit, Hugh Gusterson, David Mindell, Susan Silbey, Yanni Loukissas and Natasha Myers (2005) 'Information Technologies and Professional Identity: A Comparative Study of the Effects of Virtuality', Report to the National Science Foundation.

Wadman, Meredith (1999) 'US Plans Giant Effort on Protein Structure', *Nature* 400 (5 August, 1999): 494.

Waldby, Cathy (2000) *The Visible Human Project: Informatic Bodies and Posthuman Medicine* (New York: Routledge).

Waldby, Cathy and Robert Mitchell (2006) *Tissue Economies: Blood, Organs, and Cell Lines in Late Capitalism* (Durham, N.C.: Duke University Press).

Warwick, Andrew (2003) *Masters of Theory: Cambridge and the Rise of Mathematical Physics* (Chicago: The University of Chicago Press).

Warwick, Andrew and David Kaiser (2005) 'Conclusion: Kuhn, Foucault, and the Power of Pedagogy', in Kaiser, David (ed), *Pedagogy and the Practice of Science* (Cambridge: MIT Press): 393-409.

Watson, James D. (1969) *The Double Helix: A Personal Account of the Discovery of the Structure of DNA* (New York: Penguin Books).