

Since the inception of the modern atomic theory, chemists have used physical models to represent the structure of molecules. The goal of this paper is to bring molecular modelling into focus as a constitutive yet overlooked element of chemical practices. It begins with a short technical introduction to molecular models, and then moves into a participant-centred analysis of molecular modelling. Central points of this analysis include, first, a discussion of the dichotomy between graphical and material forms of representation, with suggestions about its consequences for a semiotically-centred view of scientific activity; and, second, a look at the problem of the interpretation of molecular models, as discussed in the chemical literature. The last section focuses on the design of modelling systems through two related historical case studies — namely, the production of two space-filling modelling kits developed in the United States between the late 1930s and the late 1960s.

The Forgotten Tool: The Design and Use of Molecular Models

Eric Francoeur

Most people are familiar with molecular models, having seen those strange ‘tinkertoy-like’ structures in the pages of the science section of daily newspapers, in popular scientific literature, or even in the publicity pages of *Science* and *Nature* (see Figures 1, 2 and 3). Often enough, the focus of the picture is not the model itself but the scientist observing it, holding it or simply standing next to it. Indeed, pictures of scientists with their models are very much part of Western scientific iconography.¹

In such a tableau, the model by itself is of little relevance (even though it can sometimes be aesthetically pleasing). It is what the model stands for that is of prime importance. It is the molecule: its secrets that the scientist has unravelled or is trying to unravel; its power that she or he has unleashed or is trying to unleash. The molecule is what everything is about. It seems fair to assume that, for the casual observer, the model is no more than a clever, practical, yet mundane contrivance not worth a second thought.

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Like other forms of representation, such as the familiar road map or the ubiquitous graph, one is usually more inclined to look through it than at it.

That molecular models are taken for granted is perhaps not surprising. Historically, there is nothing dramatically novel about the idea of using physical structures to represent the spatial arrangement of atoms in molecules (or crystals). This practice is strongly associated with modern atomic theory, although it arguably predates it.² In his lectures, John Dalton used atomic models composed of wooden spheres connected by metal pins. In the late nineteenth century, van't Hoff made extensive use of molecular models to illustrate his ideas on stereochemistry and, in the twentieth century, a number of major discoveries are associated with the use of models: the alpha-helix, the structure of DNA, myoglobin and haemoglobin.³ Models are also familiar for the role they play in the teaching of chemistry, but for all their widespread presence in the practice and the culture of chemistry, molecular models have

FIGURE 1



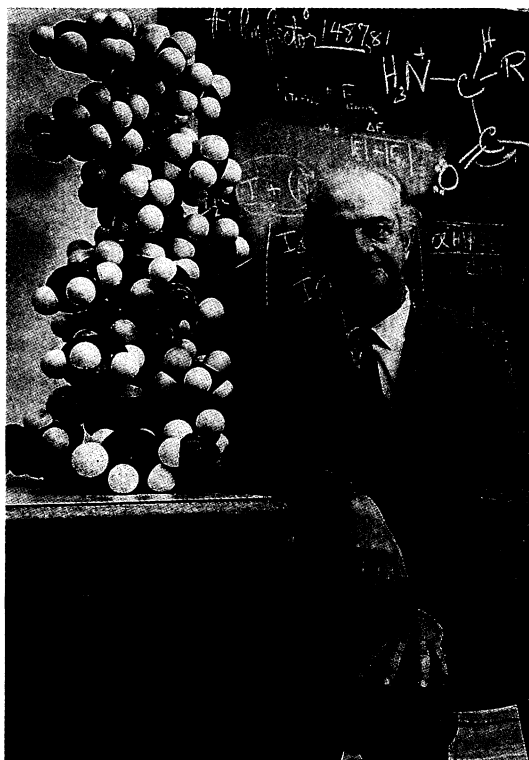
Dr Makio Murayama (ca. 1962), assembling a skeletal model of myoglobin. On each side of him are skeletal models of the alpha-helical structure of proteins (Courtesy of the National Institutes of Health, Bethesda, MD)

attracted little attention from the practitioners in the field of science studies.⁴

The goal of this paper is to bring molecular modelling into focus as a constitutive, yet overlooked, element of the practice of chemistry. It does not seek to present a single systematic argument, but is more of a preliminary exploration. The literature from two current areas of interest in science studies will serve as our guide for this exploration. The first is that of visual representation, which historians, sociologists and philosophers have approached in the past two decades, using a variety of perspectives to analyze a wide diversity of practices and devices.⁵ The second field is the 'science-as-practice' approach that has characterized the thinking of some authors in the same period.⁶

This paper is divided into two main sections. After a technical

FIGURE 2



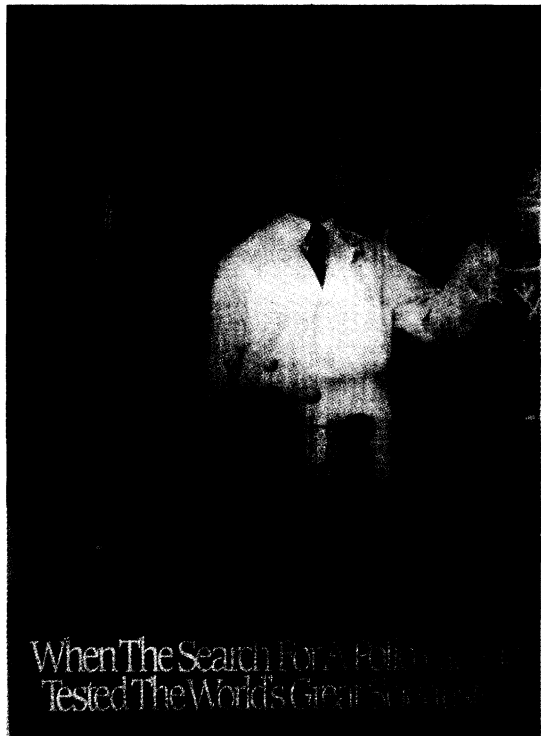
Dr Linus Pauling, sitting next to a space-filling model of the alpha-helical structure of proteins. (Courtesy of the California Institute of Technology)

introduction, the first section offers a participant-centred analysis of molecular modelling. A central point of this analysis is the apparent dichotomy between two-dimensional and three-dimensional forms of representation, with suggestions about its consequences for a semiotically centred view of scientific activity. This section concludes with specific examples of how models have been used in research settings. The second section focuses on the problems related with the designing of molecular models, through two related case studies.

Molecular Models: Unity and Diversity

Molecular models are basically three-dimensional structures that depict, more or less to scale, the three-dimensional position of

FIGURE 3



Detail of a photograph used by BioWhittaker for publicity purposes. The typical ball-and-stick in the foreground is part of the symbols commonly associated with chemistry (Photograph used with permission from BioWhittaker, Inc., 8830 Biggs Ford Road, Walkersville, MD 21793, USA)

atoms in a molecule and the bonds between them. Such structures often result from the assembly of basic components, which are referred to as 'atomic models'. Each atomic model is a 'building block' which incorporates some desired geometrical attributes of the constituent atoms (such as covalent or van der Waals radii, bond angle and bond length). As the configuration of a molecule is held to result from its constituent atoms, so does the configuration of a molecular model result from its constituent atomic units. Commercially available modelling kits consist generally of modular elements (atomic units and connectors) that allow representation of a vast, if not infinite, number of different structures.⁷ As we shall see in this paper, the practice of molecular modelling is directly linked to the interest in such structures as key elements in formal accounts of the witnessable properties⁸ of chemical compounds.⁹

It is interesting to note how a task seemingly as simple as rendering in three dimensions the structure of molecules has led to the proliferation of approaches and tools. Judging from the available technical surveys,¹⁰ one could estimate roughly that dozens of different types of atomic models are (or have been) available on the market, and that at least as many different types of modelling components have been designed and manufactured by laboratories and institutions to suit specific needs.

These same surveys offer useful classifications, descriptions and discussions of these different types of models. The most familiar and common types usually fall within one of two classes: the 'closed' models and the 'open' models.¹¹ The closed models, often referred to as 'space-filling' models, are assembled from spherical atomic units that come in contact and have diameters that are proportional to what is commonly referred to as the 'van der Waals radii' (see Figure 2). These models are particularly suited for the study of 'steric hindrance' — that is, the way in which the volume of atoms imposes constraints both within and between molecules. In open models, the atoms are represented by balls of arbitrary size, or are simply implied by the intersection of rods that represent the bonds. Typical representatives of that class are the 'ball-and-stick' models (see Figure 3), familiar to chemistry students, as well as the skeletal models (see Figure 1). These models are best suited to perform measurements of structural values such as inter-atomic distances and the rotational angles between atomic groups.

These different classes of models, as well as the diversity within each of these classes, reflect the wide variety of needs and purposes

chemists face in their exploration of chemical structures.¹² What features of a molecule are to be represented? With what degree of accuracy? On what scale? There are, in principle, no holds barred. In some circumstances, objects as trivial as ping-pong balls can be turned into a perfectly acceptable model of a given molecule; while at other times, as we shall see, only dedicated components resulting from the finest craftsmanship are considered acceptable. The following comment from Robert Corey, a long-time collaborator of Linus Pauling at the California Institute of Technology, captures vividly the spirit of this diversity:

All models involve so many compromises that it is generally difficult to get more than a few persons to agree to what features should be incorporated and what ones should be omitted. It is my impression that most of the research workers who make their own molecular models might well continue to do so regardless of models that were commercially available, just as so many chemistry teachers prefer to write their textbooks regardless of the hundred or more good texts that are already available.¹³

Molecular models can be considered a mode of visual representation, in the sense that they allow us to visualize molecular structure. Yet, arguably, no chemist would propose that models, even in their more elaborate forms, are about what molecules 'really' look like. In fact, any argument to that effect is bound to be considered technically moot, since, as a prominent biophysicist has noted, 'for something smaller than the wavelength of light, there is no such thing as showing how it really looks on the molecular level'.¹⁴ From a more sociological point of view there is no such thing as comparing a molecular model to the 'real' thing, since it is through the model itself, or through other forms of representational work, that a molecular structure becomes coherently visible.¹⁵ In fact, the concept of molecules as having static, discrete structures reducible to the limit forms of geometry can be considered in itself a 'model' — a formal gloss mobilized in the process of accounting for the properties of matter at the molecular level. As a result, the molecular realm is not only amenable to a variety of visual formulations (both graphical and material) and to the language of descriptive geometry, but it is also imbued with mathematical order, and thus made inherently measurable and reportable.¹⁶ The importance of this last point will become obvious in the discussion of models as research tools. Molecular models constitute, in a literal sense, the integration and reification of a heterogeneous set of discrete, normative, structural values assigned to the constituents of molecules

(atoms or groups of atoms) on the basis of theoretical and/or empirical considerations.¹⁷ This integration and reification as a practical accomplishment will be explored in the last part of this paper.

Representation, Practice and the Nature of Molecular Models

Over the years, chemists have developed and adopted a number of techniques and conventions to represent the structure of molecules on a two-dimensional graphical surface. The simplest graphic structural formulas are highly abstract and elliptical. They contain very little explicit information about three-dimensional configuration.¹⁸ Nevertheless, a trained reader is usually assumed to be able to infer the configuration of a molecule from this limited information and, in general, the lack of detail increases not only clarity but also the ease of production and reproduction. Alternatively, some techniques can be called upon when more details about configuration are deemed necessary. These include perspective, shading, special projections and stereoscopy. It is not difficult to find in the chemical literature references to the limits of two-dimensional graphical representations. As the biochemist Robert A. Harte pointed out:

Limitations in the technology of graphic arts impose on the scientist the practical necessity of studying and communicating most of his ideas about the three-dimensional world of molecules either in words alone or in two-dimensional pictures or diagrams. The relative size of substituent groups, constraints on free rotation, essential interchangeability of certain groups, and the spatial relations within and between molecules cannot be entirely adequately represented in this way. As a consequence, numerous systems of molecular models have been devised and used for such studies.¹⁹

A similar argument, made thirty years earlier, can be found in the pages of the *Journal of Chemical Education*:

The various types of isomers and other features of stereochemistry require more than empirical formulas, particularly for the purpose of instruction. Likewise the nature of the valence bonds and the spatial relations of atoms to each other in chemical combination are not clearly shown even by two-dimensional graphic formulas. Wherever it is desired to illustrate direction and extent in molecular structure three-dimensional models obviously possess great advantages.²⁰

Similar quotes recur in the chemical literature. The argument is not

only widespread, but also, as pointed out above, considered obvious: models are very good at expressing and illustrating the structure of molecules, and in some cases are much better than graphical forms of representation.

The discussion of models as didactic tools is a fixture of chemistry education. The *Journal of Chemical Education* is filled with dozens of papers on the design and use of models in the classroom. Their use is discussed and encouraged by textbook authors,²¹ and modelling kits are even distributed by textbook publishing companies. Some even claim that one's capacity for seeing the intended three-dimensional structure of a 'flat' chemical formula ensues from observing and manipulating molecular models in the course of one's education.²²

Thus, a central feature of all these discussions is the way in which models are often defined in opposition, or contrast, to graphical representation. There is a sense that, relative to graphical structures, models are closer to the 'real' thing, almost as if models constituted a sudden about-face on the Latourian path that leads from complex three-dimensional objects to simple, less confusing, two-dimensional images — a return to the 'objects' scientists had left behind by resorting to graphs, diagrams and similar inscriptions.²³ Yet it cannot be anything of the sort. Relative to the kind of empirical evidence with which chemists are confronted daily, both graphics and models are equally 'eidetic representations'.²⁴ As such, they are to some extent similar. Like the graphical formulas used by chemists, molecular models are organized, artefactual visual displays. Things such as the division of a model into discrete physical components and the use of colour coding, for example, help in the definition and identification of what are considered to be the relevant basic constituents of a molecule. An important and obvious difference is that models embody, rather than imply, the spatial relationship of the molecule's components. As a result, the observer is freed from the constraints of perspective: free to embrace, at leisure, many points of view. Models can also be manipulated. 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.²⁵

Physical models are to some extent mobile, immutable and readable, but they are far from sharing all the extensive attributes of two-dimensional inscriptions.²⁶ For example, in *The Double Helix*,

James Watson describes how the DNA model he and Crick assembled acted as a powerful device to convince close collaborators of the validity of their conclusions about DNA structure.²⁷ Of course, it could not be easily reproduced and passed around,²⁸ nor could the whole research community be brought into the lab to peek at it. Models do constitute, as Tufte puts it, a most direct method to display three dimensions;²⁹ but the model-builder's work, like the work of the surveyor, needs to be 'mapped out', reduced to a two-dimensional plane, if it is to acquire the power of an inscription.³⁰

It seems quite clear that a semiotically centred study of physical modelling, no matter how sophisticated, is bound to be at best incomplete. At worst, it could relegate models to the status of 'proto-inscriptions'. One could see the recourse to physical models as a symptom of an 'immature' discipline which has not yet achieved complete 'semiotic reductionism' (with the inevitable comparison of chemistry with physics). Alternatively, models could be depicted as a cognitive crutch for students with a limited capacity for abstraction. Such a position leads to a number of problems. First, it would completely ignore evidence which suggests that the development and use of increasingly refined techniques of physical modelling is historically parallel to, and contiguous with, the appearance of the 'many small, unexpected and practical sets of skills to produce images, and to read and write about them' which, according to Bruno Latour, characterize modern scientific culture.³¹ Second, it would be tantamount to engaging in the same kind of hierarchical assessment characteristic of debates on the validity or desirability of physical modelling. Ramsay's historical studies remind us, for example, how in the 1860s the use of models and graphic formulas was viewed with wariness by many chemists, and sparked off controversies concerning the validity of the atomic theory. Stereochemical theories and the use of structural models gave atoms, entities considered at once useful and highly hypothetical, a 'reality' that numerous chemists felt was unwarranted. The following passage, from an 1867 editorial note describing 'glyptic formulae' models sold in London at the time, vividly captures this uneasiness:

The figures that may be formed by the combination of these coloured balls are very striking and are more likely to rivet the attention of students than chalk symbols on a blackboard. Whether they are calculated to induce erroneous conceptions is a question about which much might be said.³²

Interestingly, this uneasiness related to the use of molecular models survived the entrenchment of the atomic theory and the development of stereochemistry. In a 1970 paper, Quentin Peterson, designer of the Cenco-Peterson models, reports biting criticisms of the simplistic 'wire models and ping-pong balls' conceptualizations of the molecular realm.³³ Exactly a century after they had been associated with a revolutionary, if highly questionable, vision of chemical reality, molecular models symbolized for some a simplistic vision that threatened to hinder the development of chemistry.³⁴ This questioning even led to proposals of changes in the way the world of molecules is represented:

In contrast to discrete particle atom models, which I have always viewed as a sort of glorified tinkertoys, a model of the substanceless field atom might resemble an exquisite, three-dimensional lacelike structure, with larger holes representing where the particles once were, and the other voids in the lace demarcating binding, valency, and like energy fields and levels, all at a point in time. Of course, the real atom would lie somewhere between the two.³⁵

It is quite clear that if one is to make sense of physical modelling, one needs to step back from a view of scientific activity as strictly rhetorical and look at it in terms of manipulative practice and material culture.³⁶ Two key concepts seem particularly relevant here: namely, the idea of material manipulation, in the sense of an embodied interaction with the physical world; and the related concept of interaction between human and material agency.³⁷

The idea of manipulation is central to the process of mechanical molecular modelling. At the constitutive level, most models will allow only the correct number of connections (bonds) to be formed for each type of atom. Furthermore, and more interestingly, the way models mechanically resist or yield when one tries to have them adopt some configuration constitutes a physical, embodied experience of 'allowed' or 'non-allowed' spatial configurations — as warranted by such factors as bond length, bond angles, the free rotation about single bonds and steric hindrance (hindrance resulting from the contact between atoms). In short, models mimic, mechanically, some of the important physical properties attributed to molecules. The following passage illustrates how some types of models can be valued as haptic (or tactile), rather than visual, display:

CPK [space-filling] models are very informative during the process of putting them together, but the completed models all look alike. Computer versions of

CPK models have successfully imitated their appearance and most of their disadvantages (the fact that the inside is completely hidden and the difficulty of identifying an atom or group), without, so far, imitating the real virtue of CPKs, which is *the physical 'feel' for the bumps, constraints, and degrees of freedom one obtains by manipulating them.*³⁸

On the other hand, discussion of the limits of three-dimensional structures are as prominent as, and often contiguous with, discourse about their advantages. The 'gap' between molecular models and other representations of molecules appears particularly evident when the latter are grounded in a quantum-mechanical understanding of chemistry. In the following passage, for example, the fact that molecular models are classical systems is presented as both a limiting and an enabling feature:

Clearly a model for a quantum mechanical system such as a molecule cannot itself be quantum mechanical. So models for chemical structures are bound to be classical systems, besides which models of this sort are the only ones we can handle visually or tactually.³⁹

But one does not need to mobilize quantum mechanics in order to point to the limits of models. More 'traditional' mechanical considerations can do the trick. Indeed, it is not uncommon for textbook authors to follow discussion of the benefits of models as a didactic tool with a *caveat emptor* about the ways in which models can also mislead the uninformed user:

Despite their great help in visualizing molecules, models can be deceptive. As we learn more about the responses of real molecules to deformation forces, we will recognize that models do not respond in parallel ways and thus can lead users into false impressions about molecular strains. In general, models are too stiff in resisting angle bending and too loose in rotation about single bonds, and the space-filling variety are inflexible in responding to compressions of nonbonded atoms. Rarely will any model fall into the correct conformation by itself, as does the molecule it represents.⁴⁰

In some cases, the warning can indeed be quite substantial. For example, in his *Introduction to Stereochemistry*, Kurt Mislow dedicates two sentences to the usefulness of models, followed by a detailed two-page discussion of how models constitute 'oversimplifications'.⁴¹ Another author provides a thorough comparison of the 'idealized geometry' of models with the 'actual geometry' of organic compounds.⁴² The shortcomings of models have also been discussed by Pierre Laszlo in the following terms: 'It is difficult to represent flexibility: in space-filling models, atoms are interlocked

in a total and non-realistic rigidity; open models use for bonding, if they are precise, metal rods which are much too rigid'.⁴³ For Laszlo, computer-modelling systems have a distinct advantage over mechanical models, since they do not allow manipulation, in the strict sense of the word. This, he argues, reduces the illusion, and 'this illusion was dangerous'.⁴⁴ Yet, he concedes, mechanical models do allow one to 'think with the hands', a practice he considers central to chemistry.⁴⁵

These passages illustrate how models are, like their graphical counterpart, essentially a non-reflexive form of representation — that is to say, the connection, the similarities and differences they have with real molecules cannot be specified through the models themselves.⁴⁶ Through generalizations or specific examples, authors try to convey to the neophyte user some of the ways in which the behaviour of a model does or might depart from what is considered proper molecular behaviour. Nigel Gilbert and Michael Mulkey observe that scientific texts (including textbooks) usually offer few instructions to guide readers' interpretation of pictures.⁴⁷ It seems that, in the case of models, authors often adopt quite an opposite attitude, making an overt effort to provide such instructions. Of course, no set of rules can cover all the possible molecular structures in their different states and authors have finally to appeal, explicitly or implicitly, to the user's judgement and knowledge. In the end, the 'correct' use and interpretation of a model is ultimately a practical, skilful accomplishment.⁴⁸ In short, we can see at work in molecular models (or more precisely, in discourse about models) the tension between the two different aspects of 'realizing', as defined by David Gooding.⁴⁹ On the one hand, models allow a direct, palpable, materially circumscribed observation and exploration ('realizing') of a phenomenon referred to as 'molecular structure'. On the other hand, it appears clearly that this apparent directness of observation conceals, in fact, an 'historical process in which the ontological status of observable things is worked out as observational techniques are developed and disseminated through the mastery and transfer of skills'.⁵⁰

Molecular Models as a Laboratory Technology

Historically, molecular models have played an important role not only as didactic tools, but also as research instruments. The use of

models in the development of stereochemistry and conformational analysis has been well documented by Bertrand Ramsay, a chemist and historian of chemistry. His work provides specific examples of the different ways in which a model can be mobilized: as a tool to make measurements; as a heuristic tool for development and discussion of hypotheses about molecular structure; or simply to illustrate, in themselves or through photography, proposed structures and conformations.⁵¹ Although mechanical models can still be found in research settings, many of their roles and functions have been slowly taken over in the past decades by computer modelling systems, coupled with graphic displays.

The role of molecular models as a research tool is well exemplified in the field of molecular-structure determination. Basically, standard structural determination methods (such as X-ray crystallography) cannot reveal the exact position of atoms in a molecule, due to problems of resolution and of inherent disorder in molecular structure. On the other hand, chemists have, over time, developed a set of rules describing how atoms 'behave' in a molecule. These are called 'stereochemical rules' and include, among other things, bond lengths, bond angles and non-bonded interatomic distances. Ideally, these rules circumscribe a finite number of structures with a given sequence or set of atoms.⁵² Molecular models designed to incorporate some or all of these constraints have been typically used in two ways. The first method, known as the 'model-building' or 'trial-and-error' approach, consists in building plausible structures, which are then compared with the empirical evidence at hand. Unlikely structures can be discarded and the most probable structure can then be chosen. The use of this method is exemplified by the work of Pauling, Corey and Branson on the basic structure of fibrous proteins (which led to the structure known as the alpha-helix),⁵³ and the work of Watson and Crick on the structure of DNA.⁵⁴ In the second case, models are used to refine crystallographic data, which take the form of electron-density maps. The work of John Kendrew on the structure of myoglobin, as well as the work of Max Perutz on the structure of haemoglobin, are prominent examples of this approach.⁵⁵

In view of the numerous constraints, or 'rules', they had to work with to solve structural problems, especially in the study of macromolecules, some scientists have considered molecular models not simply as one option among other types of possible graphical or

mathematical representations, but as a sheer necessity. As Linus Pauling stated in his 1953 Nobel Prize address:

These requirements [constraints] are stringent ones. Their application to a proposed hydrogen-bonded polypeptide chain cannot in general be made by the simple method of drawing a structural formula; instead, extensive numerical calculations must be carried out, or a model must be constructed. For the more complex structures, such as those now under consideration for the polypeptide chains of collagen and gelatin, the analytic treatment is so complex that it resists successful execution, and only the model can be used.⁵⁶

These are but a few examples of how molecular models have been used in the research process. Yet they show clearly how they constitute a practical embodiment, a surrogate for something that can neither be directly experienced, seen nor measured. They allow an invisible, dynamic and fuzzy phenomenon — the structure of molecules — to be turned into a ‘static’ phenomenon that is both directly witnessable and discretely measurable. Models allow us, quite literally, ‘to create an artificial and normalized situation within which tinkering with the model can parallel tinkering with the situation it models’.⁵⁷ This is achieved, as discussed above, by merging the spatial and mechanical properties of models with the properties of molecules, guided, though not directly determined, by an elaborate set of theoretical assumptions and empirical findings. An interesting aspect of the use of models in research is that they somehow seem to blur the distinction between the representational and the experimental. Molecular models could easily be considered a special case of what Martin Krieger calls the diagrammatic or picturing tools used by physical scientists as part of their ‘paper-and-pencil problem-solving activities’.⁵⁸ On the other hand, it is quite obvious that they are sometimes treated as tools of empirical investigation through simulation. This point certainly merits further attention, although it will not be pushed further here.

Designing Molecular Models

So far, molecular models have been treated as most scientists usually do in their daily practices, as ‘ready made’ artefacts or instruments: This section will focus on the initial design and production of specific types of modelling kits. It will examine two specific space-filling modelling kits developed in the United States

between the late 1930s and the mid-1960s — namely, the Fisher-Hirschfelder-Taylor models and the Corey-Pauling-Koltun models.

The idea that atoms have a volume was first proposed in the late nineteenth century by the Dutch physicist J.D. van der Waals, to explain the deviations of gases from ideal behaviour. This atomic volume is expressed as the value b in the van der Waals equation of state.⁵⁹ This value is often referred to as the ‘van der Waals radius’ of an atom, and over time this phrase came to express (incorrectly, some argue) the volume of atoms, regardless of whether the molecules they compose are in the gaseous, liquid or solid (crystalline) state. The basic idea is that the van der Waals radius expresses the distance between the centre of two non-bonded atoms as the attractive and repulsive forces between these atoms achieve an equilibrium. On the other hand, when two atoms are bonded, the distance separating the two nuclei will be shorter. The distance at which an atom will allow a bonded atom to approach its centre, or nucleus, is known as the ‘covalent radius’.

The van der Waals and covalent radii are essentially what space-filling models were designed to represent. The diameter of each spherical atomic unit is proportional to the van der Waals diameter of the atom it represents, and a plane cut in that sphere intersects the covalent radius. Models are assembled by ‘bonding’ the atomic units along their plane surfaces. In units designed to represent atoms forming multiple bonds, the planes are cut at the appropriate angle to represent the bond angle.

The historical narrative that follows is based on a variety of recently unearthed archival documents. While it sheds light on specific events and developments of interest to the historian of chemistry or early structural biology, its principal purpose is to underline and illustrate the specific problems confronting the designers of these models. These problems are basically of a dual, overlapping nature. The first, ‘conceptual/theoretical’ problems, centre around defining the set of numerical values the models have to embody. In the case of space-filling models, for example, we will see in particular how the apparently straightforward notion of ‘atomic volume’ demands that specific choices and compromises be made in the process of designing models.

The second set of problems stems from the obvious fact that models evolve in a physical realm that is not identical to that of molecules themselves. The properties of models, *qua* technical artefacts, are linked to things such as gravity, frictional forces,

tensile strengths and the rigidity or flexibility of the specific materials used. These are the types of forces invoked by investigators seeking to account for the physical properties of mechanical models. They differ greatly from the type of forces typically invoked to account for the physical properties of molecules. While some of these properties are considered helpful in modelling adequately some of the behaviour attributed to molecules, they are just as easily, on occasion, said to conspire against this goal. Molecular modelling is thus linked to a mastery of these 'macrophysical' properties. The task confronting the designer/user is one of creating and maintaining the link between the macrophysical properties of models and the microphysical properties of molecules, all the while recognizing that a complete overlap of properties is impossible. As with literary analogies, the creation of material analogies is predicated upon decisions of what can count as 'relevant' and what can be dismissed as 'irrelevant'; of what is 'acceptable' and what is 'not acceptable'.

Luckily, for most scientists and students, these problems can be circumvented by relying on commercially available modelling kits, with the hope or conviction that their designers have done an adequate job. This introduces the realm of down-to-earth financial and commercial considerations and, more importantly, it leads to a situation in which the solutions to these problems is delegated to others. To use *standard* models means to be able to steer clear of numerous technical problems, their solutions being prepackaged in the models.

The FHT models

In 1937, Joseph Hirschfelder, a theoretical chemist at the University of Wisconsin in Madison, felt he needed space-filling molecular models to continue his research on intermolecular forces in small molecules. How he intended to use these models is not very clear, since none of his subsequently published work made direct mention of their use. Comments he made twenty years later, although referring to biological molecules, offer a glimpse of how he would have used such models in practice:

The geometrical structure of two biological molecules is the most important factor in determining their intermolecular forces. It is very helpful to construct molecular models With these models one can make preliminary estimates of

the separation between each atom in molecule A and each atom in molecule B when the two molecules are held in a particular orientation. Knowing these separations we can turn the theoretical cranks to determine the energy of interaction corresponding to this orientation.⁶⁰

A few years earlier, in 1934, the German chemist H.A. Stuart designed what are now considered to be the prototypical space-filling models.⁶¹ These Stuart models, as they became known, were commercialized around 1934 by a German company, Leybold. Hirschfelder was well aware of the availability of such models;⁶² he showed no dissatisfaction with their design, but rather with their price. At one US (1937) dollar per atomic unit, he considered them to be too expensive. So he made his own models in the university machine shop out of fishing cork and meat skewers. The machine shop mechanic, Lee Henke, designed a device for holding the spherical corks in place, while cutting slices out of them at any angle and any distance. The cost of such models was about fifteen cents per atomic unit. However, Hirschfelder found cork still too expensive and not totally satisfactory. He then tried moulding the models out of plaster of Paris. These efforts resulted in requests from other laboratories for his models.⁶³ It is probably such requests that spurred him to approach scientific supply companies to commercialize his design. He first tried 'to get Central Scientific Company to market this type of model cheaply [T]hey thought anybody interested in such things was crazy, but Fisher Scientific then made them [in] 1939'.⁶⁴

The Fisher-Hirschfelder models were presented as a collaboration between Hirschfelder and Fisher's Development Laboratory, and as having been 'developed primarily at the earnest request of a group of workers in the field of theoretical chemistry who believe that such models will be of primary importance to the advancement of their researches'.⁶⁵ Education and industrial chemistry were also mentioned as other potential fields of use. The kit was composed of colour-coded wooden balls representing different atoms. Holes drilled in each face allowed units to be assembled through the use of double-taper brass pegs. Single holes allowed free rotation around single bonds.

According to company literature, such a kit allowed the accurate representation of spatial relationship and steric hindrance in molecules. It was presented as a flexible standardized tool able to help chemists over a wide range of approaches and problems. Suggested uses included comparing putative structural formulas for a given

molecule, locating electrical charges and dipole moments, examining valence and van der Waals forces, and extracting space coordinates for the benefit of mathematical calculations.⁶⁶

Interestingly, Hirschfelder never received any royalties from Fisher, simply a 'few free sets'. Hirschfelder commented later that all he wanted was something cheap 'so we could make up big molecules', but added that 'Fisher did not cooperate in this regard'.⁶⁷ In fact, the original cost of the FH models was about ten cents per atom, cheaper than the original cork models and ten times cheaper than the Leybold-Stuart models. Hirschfelder's original goal was to lower the cost to about three cents per atom.⁶⁸ He was not the only one concerned with price. In a letter to him shortly after the models were marketed, Linus Pauling stated that 'we would like very much to have a large set of them for use in connection with our researches on molecular structure and, in fact, I feel that it would be desirable for us to have about twenty-five kits, which sell at \$12.00 apiece. The cost of this large set is, however, too great to handle'.⁶⁹

So far no documentary evidence has been found to suggest that Pauling's laboratory did acquire FH models. It is quite likely that Pauling intended to use them, among other things, in ongoing studies on the basic structure of fibrous proteins. The field of polypeptide structure research was quite distant from Hirschfelder's own work and initial purposes in designing the models. Nevertheless, this field had not escaped Fisher's publicists' attention, as they stated that '[p]lans are already under way at a large university for testing the Wrynch [sic] and other possible structures for proteins with these models'.⁷⁰

Despite the fact that they did not completely live up to the expectations of their inventor and initial supporters like Pauling, the FH models were bound for a long career. They are still sold today by the Fisher Scientific Company and, in fact, their catalogue description has changed very little from the early days. Interestingly, though, at some point in the late 1970s, the kit was dropped from Fisher's main research equipment catalogue, to be offered in its educational material catalogue.

Through the years, some changes were made. The brass connectors, which proved to offer poor tensile strength and resulted in unstable models, were replaced in the 1940s by a special patented snap connector designed by Hugh Taylor of Princeton University, who used the models in studies of the structure of polypeptide

chains.⁷¹ The early statement that '[t]here seems to be no limit to the complexity of the molecules which may be constructed other than the number of atoms available and the size of the workroom'⁷² proved, with time, to have been over-enthusiastic. Taylor's contribution was considered important enough for his name to be added to the eponymous label of the models. From that moment on they became the Fisher-Hirschfelder-Taylor (or FHT) models, as they are known today. At some point in the 1950s, special metal-coordination kits, as well as silicon and fluorine models, were made available, and in 1959 the wooden balls were replaced by moulded plastic ones.⁷³

Beyond price and other practical considerations, from the chemist's point of view, the interest of the FHT models was linked to the structural values that were embedded in them. The models, in other words, had to represent 'valid' or 'adequate' values of bond angles, covalent radii and van der Waals radii. Only then would an elaborate 'tinkertoy' be turned into a valuable research tool allowing the investigator to produce, on the basis of what was already known, new and unknown results.

The structural values embedded in the FHT models, as specified by Hirschfelder,⁷⁴ came from different sources. Covalent radii and bond-angle values came principally from the electron diffraction work of Pauling and Brockway on a dozen small organic molecules, published in 1937,⁷⁵ though other sources were also used. The assumption was that specific values resulting from research on a finite subset of small organic molecules could be extended unproblematically to the wider realm of organic molecules. This idea was never openly challenged, and these values were never changed through the years; FHT models are still sold today using the same numbers. Such an inductive generalization is of course based on the assumption that molecular structures are additive — that they are literally the sum of their parts.⁷⁶ We will see later how it is sometimes difficult to maintain this assumption of additivity.

The determination of the van der Waals radii that give the models their space-filling properties was a completely different story. Even their taxonomy is uncertain, for they are referred to by both Hirschfelder and the Fisher company alternatively as the 'kinetic theory diameters', 'our old friend "*b*" in the van der Waals equation' and 'collision diameters'. According to Hirschfelder, the values adopted for hydrogen and carbon (respectively 2.13 Å and 2.67 Å) were taken from Stuart.⁷⁷ These values are very close to the

ones on which Stuart based the design of his own models. In fact, in the description of his models, Stuart quotes the values 1.8 Å and 2.9 Å as being the correct ones, while he in fact used the values 2.10 Å and 2.70 Å so that the covalent faces would be of the same diameter in both hydrogen and carbon, resulting in a smooth transition from one to the other.⁷⁸ It is difficult to say if Hirschfelder's choice was driven by the same concern, but the values he adopted had the distinct advantages of corresponding, respectively, to balls of 1" and 1.25" in diameter. For oxygen and nitrogen, Hirschfelder seems to have partly heeded Pauling's advice that all first-row atoms be given a diameter of 2.40 Å, while for the other atoms he made use of the rule, also proposed by Pauling, of adding 0.8 Å to the single bond covalent radius of an atom in order to obtain the correct radius.⁷⁹ The space-filling 'properties' of the models were discussed in a pamphlet issued by Fisher:

When two molecules collide in a gas they can come together until they reach a separation defined by their 'collision diameters' The sizes of the atoms in these [FHT models] are proportional to the kinetic theory collision diameters corresponding to gentle collisions. The diameters have been made somewhat smaller than called for by theory so that it will be certain that when neighbouring atoms in the models of molecules touch the situation would correspond to a condition in the real molecule where the atoms are squeezed together with great force. Thus configurations *impossible* with the models correspond to molecular configurations which are energetically *improbable*.⁸⁰

One can see in this passage how the values chosen for the atomic radii of the models are presented as a compromise between theoretical requirements and the necessity of providing safeguards against 'false negatives' (that is, reducing the likelihood of artefactual steric hindrance). While there is an attempt to define 'the actual situation' to which these values correspond, the last sentence is an implicit warning that the models in themselves cannot determine what are actually possible configurations. The user is ultimately left not only with the task of distinguishing between the probable and the improbable, but also of figuring out how to operate this distinction.

The CPK models

Approximately seven years after the original request to Hirschfelder, Pauling's laboratory at the California Institute of Technology

finally had its own space-filling models, designed and manufactured on the premises. Work on these models began after the war, as Pauling and his collaborators returned their full attention to the problem of protein structure. As stated in a 1947 report to the Rockefeller Foundation, the development of these models was considered a key element of this research programme:

Determinations of the structures of amino acids and peptides could be greatly expedited, and insight into many of the problems of protein structure could doubtless be significantly extended, by the use of precisely constructed molecular models. Models of this sort, embodying bond angles and atomic radii in accord with most recent structural data, have been designed by Dr Corey in collaboration with Professors Linus Pauling, Verner Schomaker and J.H. Sturdivant and some of these models have already been built in the shops of the Department of Chemistry.⁸¹

At this stage, cost was no longer an object. Despite the extra costs it must have entailed, the decision to custom-build models on site was justified by discrepancies in the values used in commercial sets, such as the FHT, and what was considered the appropriate values for the task at hand:

... models designed for studying probable molecular configuration and intermolecular packing the van der Waals radii of the atoms should conform to the intermolecular distances found in crystals and in noncrystalline solids rather than to gas collision radii or even smaller radii commonly used in models of organic molecules.⁸²

These latter values are of course used by the FHT model, even though they are not named specifically. The difference in the radii values of both models proved to be as high as 0.30 Å. Emphasis was on accuracy:

If the models are intended for use as a substitute for calculation in the examination of structures, they must be accurately built and capable of retaining their bond angles and other configurational features.⁸³

On the other, the desired accuracy could not always be achieved and room had to be made for compromise:

The bond angles around the nitrogen and the carbon atoms [of the amid group] are probably not so accurate, both because experimental data are still insufficient to establish them with certainty and because compromises have been made to increase the simplicity and to extend the usefulness of the models.⁸⁴

The only time they were mentioned in a research article, the models are simply said to 'conform to the accepted van der Waals

of the atoms',⁸⁵ without further details. Although it is not mentioned explicitly anywhere, the structural values used in the design were based on the work of Corey and his collaborators on the structure of specific peptides and amino acids (namely, by 1946, diketopiperazine, glycine and DL-alanine).⁸⁶ Work on these relatively simple substances related to proteins was initiated at CalTech in the late 1930s, based on the assumption that knowledge about their structures could help solve the structure of the more complex polypeptide chains.⁸⁷

The CP models were never available commercially, but the workshop blueprints were made available to any researcher, who could then have them made by his or her own workshop. In the 1950s, Caltech's Department of Chemistry instrumentation shop even produced and sold a limited number of sets 'as an accommodation to selected research laboratories'.⁸⁸ It would be more than a decade before models partially based on the CP design became commercially available. Work on these models, later known as Corey-Pauling-Koltun models, or CPK for short, started in the early 1960s, an era of growth for a field that later became known as 'molecular biology'. Around that period, the structure of biologically active molecules, such as proteins or nucleic acids, became of particular interest to a great number of researchers. Given these circumstances, molecular models became an ever more useful, if not essential, laboratory implement.

The CP models had opened the door to the modelling of macromolecules, but had an important drawback. It seems that they, like other equivalent types of models, proved to be too expensive for most laboratories, as well as for research and teaching institutions. John Platt, a biophysicist, sounded the alarm in a 1960 report to *Science*, stating that models available commercially were either too expensive or clumsy, and 'as a result, the advanced research laboratories in molecular biology commonly make their own macromolecular models in their own shops, often at a cost of thousands of dollars for so elementary a model as a single turn of a DNA double-helix'.⁸⁹ As for less fortunate centres, he continued, they simply have to do without, which he considered a serious hindrance to the development of the field and its proper teaching.

For a time, Platt led an effort within the National Academy of Sciences to remedy the situation. The task was taken over, later in 1960, by the National Institutes of Health (NIH) Biophysics and Biophysical Chemistry Study Section (BBCSS), and especially by

one of its consultants, Walter Koltun, also a biophysicist. In July 1960, Koltun assembled a group of eight scientists, mainly chemists and biochemists, in Berkeley, California. The purpose of this meeting was to initiate discussion on the design of a set of models that would be both practical and economical for macromolecular research, and whose commercialization would be sponsored and subsidized by the NIH, through the BBCSS. The BBCSS had good reasons to support this project financially. First, it helped promote the development of molecular biology, which was part of the Section's mandate at the time. Second, and probably more importantly, there were potential savings in stock for the NIH:

. . . [C]ertainly the Pauling [CP] models are a good example and there are other models available which apparently are quite satisfactory for many purposes; but the expense of these is so great that the National Institutes of Health, when they evaluate research grants, end up with quite a bill for each lab to get not only the Pauling model, but people start making their own for their own particular specific purposes, and this begins to run into money . . .⁹⁰

An interesting element of the ensuing discussion on what type of models would better suit the needs of researchers is the topic of 'foolproofing' — that is, protecting the less-than-competent or absent-minded user from mistakes by incorporating the necessary competence in the models themselves. For example, the committee members agreed readily that there is never really free rotation around carbon-carbon single bonds, but rather rotation between 'preferred' states. A system that would allow single-bond rotation only between these states, it was argued, 'would . . . bring to mind something that most people tend to overlook, and make mistake in doing'.⁹¹ In the same vein, it was argued that space-filling models might be 'safer' than skeletal models:

And there is a hazard to these that most biochemists don't appreciate, namely, they don't have the concept of space of van der Waals radii, and with these you can make essentially an infinite number of possible structures. There is nothing to prevent you. Here because you have a van der Waals representation the number of impossible structures becomes diminished strongly.⁹²

Yet, specifying the values of the van der Waals radii would require more than looking in the nearest textbook:

Dr. Koltun: Is there any available description for the van der Waals [radii] that you would like to see?

Dr Rich: You mean a set of numbers?

Dr Koltun: A set of numbers, right.

Dr Rich: That is the whole thing. There are too many.

Dr Marsh: Everybody has their own opinion.

Dr Rich: I have been more pleased, I would say, by the Pauling core set than any other, although I would guess that they were designed in 1952 or 1953, and I would think now that they could be tightened up a bit — I mean changed slightly.

Dr Marsh: My general observation is whenever you find a structure where they are touching they are too small for inter-molecular purposes.

Dr Rich: Unfortunately I think one will have to make a compromise that you will never end up with an ideal set, just in the nature of things, *because in fact the electronic distribution around the atom is influenced by the other atoms, and to say that there is such a thing as van der Waals radius represents a sort of first approximation. On the other hand, because we can't afford to build an atom for each environment, we in fact have to make this compromise*, and the artful thing to do is make that compromise, which leaves the most flexibility and minimizes the number of errors you make, but that minimization will never go to zero. I have models with this where every connection was made, and it made a nice tightly packed unit, and when I build it carefully out of these models on a much bigger scale I found that clearly it was impossible. But on the other hand, it is better to have an error on that level, which gives us a spurious result, than an error on the level where you cannot build something which is possible, and you miss something that is quite important⁹³

This passage is followed by a cautionary tale of Pauling himself being led to believe that a certain molecule had only four possible conformations, when it was later found that there were in fact five. This passage shows how the additivity of atomic volumes is imposed on molecular structure as part of a practical generalizing strategy, in the face of an intractable (and expensive) complexity. As was the case earlier with the FHT models, there is an emphasis again on avoiding 'false negatives'.

The committee agreed to come up with a set of compromise values after 'judicious consultation'. Unfortunately, it is not clear at this point how this consultation was performed. In a description of the finished models, published in 1966, Koltun states that the 'covalent and van der Waals radii and bond angles are intended to be representative of those occurring in most structures; they agree with those used in the Corey-Pauling Models, but incorporate a number of changes, reflecting more recent data'.⁹⁴ This statement is followed by a footnote that lists, not published research, but the names of eighteen scientists, whose suggestions were elicited by the Committee and are reflected in the chosen value. These individuals were located in eleven institutions, including Purdue, Caltech, Harvard, Yale and Columbia. Not surprisingly, one finds in there

famous names such as Linus Pauling, Robert Corey and Robert B. Woodward, the grand master of chemical synthesis. Whether or not they were meant simply as an acknowledgement, this list of names certainly gave considerable weight to the proposed values. Furthermore, the potential user could find comfort in the knowledge that, whatever compromise was achieved, the models would represent it with an accuracy equivalent to 0.03 \AA .⁹⁵

Conclusions

Much remains to be said about the history of the three types of models discussed here. Yet these first insights into the complex processes by which these models came into being certainly allows a few general conclusions.

First, it should be obvious that the models discussed were not the result of the passive contemplation of nature, nor for that matter the passive reflection of the results of the active investigation of nature (that is, data-inscriptions), even though *post hoc* accounts do tend to concentrate on issues of empirical accuracy when justifying specific choices. On the contrary, it appears that models could very well fit into Barnes's definition of representations as 'actively manufactured renderings of their referents, produced from available cultural resources'.⁹⁶ Of course, such a definition begs the question of the referent itself. It traps the analysis into a pictorial account of representation which relies on a 'one-on-one mapping relation' between a representation and its referent,⁹⁷ and seems to assume an *a priori* ontological or theoretical closure. The cases discussed have illustrated how, as Cambrosio and his colleagues suggest, the 'theoretical, experimental, and representational elements' of scientific practices 'are best understood as a series of concurrent, mutually constitutive events'.⁹⁸ In short, the history of molecular models is part of the history of how scientists have not so much represented as actively defined (and redefined), for all practical purposes, the molecular realm.

Second, the picture thus provided clashes with the notion of models as 'glorified tinkertoys'. Time, energy and financial expenditures underlying the design process indicate that at least for some scientists, and for some particular tasks, molecular models constituted a *bona fide* and essential tool. That some other scientists balked at this approach to the molecular realm, as we have seen

earlier, removes nothing from this fact. How these particular designs were received, adopted and adapted *in situ* for different lines of scientific enquiries is certainly a question for future research.

On an historical note, we can see how the development of the CPK models is contiguous with the development and diffusion of structural thinking in biochemistry.⁹⁹ In some ways, their origin could be traced to the familiarity with modelling techniques Pauling developed through his early work on the structure of crystals.¹⁰⁰ In their early version, they are an example of how a familiar technique is actively adapted to 'fit' a new substantive area (in that case, protein structure). On the other hand, the final version of the CPK models is the result of a concerted effort to transfer this expertise and knowledge from a number of limited local settings across to the whole domain of biochemistry.¹⁰¹

I hope that this paper has at least achieved the goal of bringing molecular models to the forefront, as worthwhile objects of investigation. This has been done mainly by focusing, thematically and historically, on scientists' discourses concerning the representation and modelling of the molecular world, and on some of the problems and domains in which modelling has been used. Obviously, molecular models have played a direct and important role in the ways we talk about, think and look at molecules (and vice versa). They have shaped our direct sensory experience of something that by definition can neither be touched nor seen. In most cases, they have been treated as simple windows to the molecular world. They can also become windows to the history of how we make sense of the world around us.

• NOTES

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chives. I am especially grateful to Dr Walter L. Koltun for giving me access to his personal papers; to Alberto Cambrosio and Michael Lynch for their advice, comments and suggestions; and to Martin (Ted) Hermary for editorial comments.

1. Although an in-depth analysis of the iconographic style of these pictures is not the objective of this paper, a few remarks seem to be in order. As pointed out, for instance, by Michael Lynch (personal communication), parallels can be drawn between these and other forms of portraiture. In *Ways of Seeing*, John Berger draws attention to the 'analogy between *possessing* and the way of seeing which is incorporated in oil painting', and illustrates this analogy with a classical portrait of art lovers surrounded by the paintings they own. At play is a double-possession; the possession of the paintings as objects, and the possession of the objects in these paintings. This double-possession is also present in Figure 1, showing the chemist surrounded by models — objects which he owns (or rather masters), thus evoking the chemist's mastery of the molecular realm. One is also reminded here of Holbein's famous 1533 painting, *The Ambassadors*, showing two men in rich surroundings, standing on opposite sides of shelves filled with scientific instruments, mainly instruments of navigation. Similarly, the objects in Figure 3 could be considered instruments of navigation, of exploration, with the notable exception that they are designed to exploit the riches of a microscopic universe, not of far-away lands: see John Berger, *Ways of Seeing* (London: British Broadcasting Corporation & Penguin Books, 1972), 83ff. Figure 2 brings to mind the 'Great White Hunter' of colonial times, a pose endlessly replicated in popular fishing and hunting magazines and in the snapshots of weekend anglers and hunters. This similarity is emphasized by the relaxed pose of Linus Pauling, leaning slightly towards his 'trophy', his facial expression reflecting a mix of mild pride and contentment. For a discussion of the portrayal of scientists with their instruments, see Gregg DeYoung, 'Postage Stamps and the Popular Iconography of Science', *Journal of American Culture*, Vol. 9 (1986), 1–13.

2. It has been suggested that the use of models for depicting atomic arrangements dates back as far as Kepler, in 1611: see Deane K. Smith, *Bibliography on Molecular and Crystal Structure Models* (Washington, DC: US National Bureau of Standards, 1960), 1.

3. These are perhaps the most perspicuous and famous examples of the use of molecular models. In fact, the use of these models extends to all disciplines that have interests in molecular or crystalline structures (such as chemistry, biophysics, biochemistry, molecular biology and even geology). Furthermore, models have been used within these disciplines to address a vast array of different problems. To my knowledge, there has not been any systematic survey of the different uses of molecular models.

4. There are of course noticeable exceptions. O.B. Ramsay, a chemist and historian of chemistry, has done interesting historical analyses of the role of molecular models in the development of stereochemistry and in the development of conformational analysis: see O. Bertrand Ramsay, 'Molecular Models in the Early Development of Stereochemistry', in Ramsay (ed.), *Van't Hoff-Lebel Centennial*, ACS Symposium Series No.12 (Washington, DC: American Chemical Society, 1975), 74–96; and Ramsay, 'The Early History and Development of Conformational Analysis', in James G. Traynham (ed.), *Essays on the History of Organic Chemistry* (Baton Rouge, LA: Louisiana State University Press, 1987), 54–77.

5. No attempt will be made here to synthesize these contributions, if only because such a task would be endless. But see, for example: Martin Rudwick, 'The Emergence of a Visual Language for Geological Science, 1760–1840', *History of Science*, Vol. 14 (1976), 149–95; Michael Lynch and Steve Woolgar (eds), *Representation in Scientific Practice* (Cambridge, MA: The MIT Press, 1990); Karin Knorr-Cetina and Klaus Amann, 'Image Dissection in Natural Scientific Enquiry', *Science, Technology, & Human Values*, Vol. 15 (1990), 259–83; Bruno Latour and Jean de Noblet (eds), *Les 'vues de l'esprit': Visualisation et connaissance scientifique*, Special Issue of the Monograph Series *Culture Technique*, Vol. 14 (1985).

6. The corpora of these two fields of enquiry overlap extensively but, for specific examples, see: Ian Hacking, *Representing and Intervening* (Cambridge: Cambridge University Press, 1983); Joseph Rouse, *Knowledge and Power* (Ithaca, NY: Cornell University Press, 1989); David Gooding, *Experiments and the Making of Meaning* (Dordrecht: Kluwer, 1990); Andrew Pickering (ed.), *Science as Practice and Culture* (Chicago, IL: The University of Chicago Press, 1992).

7. In technical terms, the aspects of molecular structures that can be represented by molecular models fall into four categories: 'constitution' denotes the atoms present in a molecule and the bonds between them; 'configuration' denotes the spatial arrangements of atoms and bonds in a molecule of a given constitution; 'conformation' denotes the possible different spatial arrangements in a molecule of known constitution and configuration; and, finally, 'chirality' denotes the property of three-dimensional structures that are not superimposable upon their mirror images: see W. David Ollis, 'Models and Molecules', *Proceedings of the Royal Institution of London*, Vol. 45 (1972), 1–31, at 2.

8. Witnessable properties refer to properties that are accessible to the senses either directly, or through recorded instrumental measurements.

9. This idea is often expressed in biochemistry by the structure/function trope. For a clear *exposé* of the importance of structure in accounting for the properties of chemical compounds, see Robert B. Woodward, 'Art And Science in the Synthesis of Organic Compounds: Retrospect and Prospect', in Maeve O'Connor (ed.), *Pointers and Pathways in Research* (Bombay: CIBA of India Limited, 1963), 23–41.

10. See, for example: Smith, *op. cit.* note 2; Douglas G. Nicholson, 'Modelling Molecules', *Chemical and Engineering News*, Vol. 30 (1952), 3164–67; and Anne Walton, *Molecular and Crystal Structure Models* (Chichester, Hants: Ellis Horwood, 1978).

11. This classification is borrowed from Smith, *op. cit.* note 2.

12. For a related discussion of the diversity of conventions in graphical representations in chemistry, see Roald Hoffmann and Pierre Laszlo, 'Representation in Chemistry', *Diogenes*, No. 147 (1989), 23–51.

13. Robert B. Corey, letter to John R. Platt, 8 March 1960 (California Institute of Technology Archives, Robert B. Corey Collection, Folder 3.2).

14. Jane S. Richardson et al., 'Looking at Proteins: Representations, Folding, Packing and Design', *Biophysical Journal*, Vol. 63 (1992), 1186–209, at 1186.

15. Here I am paraphrasing Michael Lynch, 'Science in the Age of Mechanical Reproduction: Moral and Epistemic Relations Between Diagrams and Photographs', *Biology and Philosophy*, Vol. 6 (1991), 205–26, at 208.

16. On the concept of mathematization, see Michael Lynch, 'The Externalized

Retina: Selection and Mathematization in the Visual Documentation of Objects in the Life Sciences', in Lynch & Woolgar (eds), op. cit. note 5, 153–82, at 169.

17. For a related discussion of the relationship between the two-dimensional visual traces or signatures of microscopic entities and three-dimensional graphical models in biology, see Lynch, op. cit. note 16, 167–68.

18. Even constitutive details, such as hydrogen atoms, for example, are also often left out.

19. Robert A. Harte, *Molecules in Three Dimensions: A Guide to the Construction of Models of Biochemically Interesting Compounds with CPK Models* (Bethesda, MD: American Society of Biological Chemists, 1969), 1.

20. Thomas H. Hazlehurst, Jr and Harvey A. Neville, 'New Models of Old Molecules', *Journal of Chemical Education*, Vol. 12 (1935), 128–32, at 128.

21. See, for example: Alan Bassindale, *The Third Dimension in Organic Chemistry* (Chichester, Hants: John Wiley and Sons, 1984), 5; Ernest L. Eliel, *Stereochemistry of Carbon Compounds* (Tokyo: McGraw-Hill Kogakusha, 1962), 13; Kurt Mislow, *Introduction to Stereochemistry* (New York: W.A. Benjamin, 1966), 42; Stanley H. Pine et al., *Organic Chemistry*, 4th edition (New York: McGraw-Hill, 1980), 91.

22. Hoffmann & Laszlo, op. cit. note 12, 42.

23. For a discussion of the production, inspection and transformation of inscriptions as a central laboratory research activity, see Bruno Latour, 'Drawing Things Together', in Lynch & Woolgar (eds), op. cit. note 5, 19–68, at 39.

24. 'Eidetic representation' is used here in the same sense as Lynch's 'eidetic image', that is, the generalized or idealized portrayal of an object. The term 'eidōs' was first proposed by Husserl, but is used in a different way by Lynch: see Lynch, op. cit. note 16, 162.

25. The use of material analogies is not exclusive to the field of chemistry. Other examples can be found in the domain of biology and the health sciences, such as plastic skeletons and 'dissectible' plastic models used in teaching anatomy, or silicone models used to teach lump-detection skills in breast self-examination. This last case is particularly interesting, since such models are designed to convey exclusively tactile information.

26. Latour, op. cit. note 23, 20–21.

27. James D. Watson, *The Double Helix* (New York: Atheneum, 1968), Chapter 27.

28. As we shall see later, the capacity of other research sites to assemble models similar to the original (or, rather, the lack of such capacities) rapidly became an issue for the scientific community.

29. Edward E. Tufte, *Envisioning Information* (Chichester, Hants: Graphics Press, 1990), 16.

30. A myriad of techniques are used to render graphically the structure of molecules. These include the photography of models and various forms of drawings, based on specific graphical or chemical conventions. Stereoscopy is commonly used to convey the three-dimensional structure. The structure can also be rendered textually, by simply writing down, for example, the space-coordinate of each atom.

31. Latour, op. cit. note 23, 22. For a short historical discussion of the use of models in engineering, see Eugene S. Ferguson, *Engineering and the Mind's Eye* (Cambridge, MA: The MIT Press, 1992), 102–07. For a short but telling analysis of

the role of models in Renaissance architecture, see the exhibit brochure *Italian Renaissance Architecture* (Washington, DC: United States National Gallery of Art, 1994). This brochure points out, in particular, how the development of the use of models as an architectural tool parallels the development of modern architecture. See also Robert B. Harmon, *Architectural Models: A Selected Bibliography* (Monticello, IL: Vance Bibliographies, 1980).

32. Quoted in O. Bertrand Ramsay, *Stereochemistry* (London: Heyden, 1981), 62–63.

33. Quentin R. Peterson, 'Some Reflections on the Use and Abuse of Molecular Models', *Journal of Chemical Education*, Vol. 47 (1970), 24–29.

34. Laurence E. Strong, 'Against Trivial Research' (Letter to the Editor), *Chemical & Engineering News*, Vol. 45 (6 March 1967), 7–8.

35. Jack De Ment, 'Intriguing New Ideas on Atoms' (Letter to the Editor), *Chemical & Engineering News*, Vol. 45 (24 April 1967), 7.

36. See David Gooding, 'Putting Agency Back into Experiment', and Andrew Pickering, 'From Science as Knowledge to Science as Practice', in Pickering (ed.), *op. cit.* note 6, 65–112, 1–26.

37. Gooding, *op. cit.* note 36, and Andrew Pickering, 'The Mangle of Practice: Agency and Emergence in the Sociology of Science', *American Journal of Sociology*, Vol. 99 (1993), 559–89.

38. Richardson et al., *op. cit.* note 14, 1186 (our emphasis). In order to transcend this limitation of computer modelling systems, researchers at the University of North Carolina (Chapel Hill) coupled a powerful computer modelling system to a mechanical arm that feeds back to the operator the attractive and repulsive forces of the virtual molecules she or he is working on: see 'Molecular Docking Arm', *Popular Science* (November 1991), 24.

39. David W. Theobald, 'On Visualizing Chemical Structures', *Education in Chemistry*, Vol. 5 (1968), 99–100, at 100.

40. Pine et al., *op. cit.* note 21, 91.

41. Mislow, *op. cit.* note 21, 42–46.

42. Bassindale, *op. cit.* note 21, 3–10.

43. Pierre Laszlo, *La parole des choses ou le langage de la chimie* (Paris: Hermann, 1993), 77 (my translation: original in French).

44. *Ibid.*

45. Attempts to state that models are conventional illusions and yet capable, in some circumstances, of being interpreted realistically, is reminiscent of what Gilbert and Mulkay have dubbed 'Trubshaw's dilemma'. They describe this dilemma as growing out of scientists' use of both realist and fictional repertoires to characterize their pictures': see G. Nigel Gilbert and Michael Mulkay, *Opening Pandora's Box* (Cambridge: Cambridge University Press, 1984), 160.

46. For a discussion of non-reflexivity in scientific illustrations, see Gilbert & Mulkay, *op. cit.* note 45, 147.

47. *Ibid.*, 148.

48. In a short discussion of 'mock-ups' as a glossing practice, Garfinkel and Sacks suggest that the interpretative problem finds its solution in the user's willingness, whenever discrepancies between the model and the 'actual situation' crop up, to pay full authority to the latter. It should be obvious in this case that the models are in themselves a component of the process through which what counts as the 'actual situation' is defined in practice, leaving the interpretative problem open.

See Harold Garfinkel and Harvey Sacks, 'On Formal Structures of Practical Actions', in John C. McKinney and Edward A. Tirykian, *Theoretical Sociology: Perspectives and Development* (New York: Appleton Century Crofts, 1970), 337–66, at 363.

49. Gooding, *op. cit.* note 36, 71–72.

50. *Ibid.*, 72.

51. Ramsay, *op. cit.* note 4.

52. As the size of molecules grows, so does, exponentially, the number of possible conformations. In the case of macromolecules such as proteins, it is for all practical purposes impossible to test all possible conformations in order to decide which is the most probable.

53. Linus Pauling, Robert B. Corey, and Herman R. Branson, 'The Structure of Proteins: Two Hydrogen-Bonded Helical Configurations of the Polypeptide Chain', *Proceedings of the United States National Academy of Sciences*, Vol. 37 (1951), 205–11. Interestingly enough, reliance on mechanical models was mentioned specifically only once in the long series of articles published by Pauling and Corey on protein structure in 1951 and early 1952. This was in the last article of the series, a study of the configurations of polypeptide chains with *cis* amide groups: see Linus Pauling and Robert B. Corey, 'Configurations of Polypeptides Chains with Equivalent *Cis* Amide Groups', *ibid.*, Vol. 38 (1952), 86–93, at 86. A short discussion of the use of models by Pauling and Corey can be found in Lily E. Kay, *The Molecular Vision of Life* (Oxford: Oxford University Press, 1993), 261–64.

54. Watson, *op. cit.* note 27.

55. For a discussion of the use of models to refine X-ray crystallography data, see John C. Kendrew, 'The Three-Dimensional Structure of a Protein Molecule', *Scientific American*, Vol. 208 (December 1961), 97–110.

56. Linus Pauling, 'Modern Structural Chemistry', *Science*, Vol. 123 (17 February 1956), 255–58, at 257–58.

57. Rouse, *op. cit.* note 6, 40.

58. Martin H. Krieger, *Doing Physics* (Bloomington, IN: Indiana University Press, 1992), 117–19.

59. Linus Pauling, *General Chemistry* (New York: Dover, 1988), 196. Appropriately, *b* is expressed in l or ml mole.

60. Joseph O. Hirschfelder, 'Intermolecular Forces', in Linus Pauling and Harvey A. Itano (eds), *Molecular Structure and Biological Specificity* (Washington, DC: American Institute of Biological Sciences, 1957), 84–90, at 84.

61. Herbert Arthur Stuart, 'Über neue Molekülmodelle', *Zeitschrift für Physikalische Chemie (B)*, Vol. 27 (1934), 350–58.

62. Joseph O. Hirschfelder, letter to O. Bertrand Ramsay, 30 October 1978 (Division of Archives, University of Wisconsin in Madison).

63. Joseph O. Hirschfelder, letter to Linus Pauling, 23 September 1938 (Ava Helen & Linus Pauling Papers, Oregon State University).

64. Joseph O. Hirschfelder, undated manuscript (Division of Archives, University of Wisconsin in Madison).

65. Fisher Scientific Company (Pittsburgh, PA), 'New Molecular Models Conform with Modern Theories', *The Laboratory*, Vol. 10, No. 5 (1939), 94–96, at 95. This journal was published by Fisher Scientific.

66. Fisher Scientific Company, *New Molecular Models Conform with Modern Theories*, Company Brochure (ca. 1939).

67. Hirschfelder, op. cit. note 62.
68. Hirschfelder, op. cit. note 63.
69. Linus Pauling, letter to Joseph O. Hirschfelder, 16 May 1939 (Ava Helen & Linus Pauling Papers, Oregon State University). Pauling goes on to suggest that the Fisher company might make these models available to his laboratory at a nominal price, 'because of the fact that the work in our laboratory provides to some extent the basis for the models and because the use of the models in our researches on molecular structure might be of some value in advertising'.
70. Fisher Scientific Company, op. cit. note 66, 5. On Dorothy Wrinch and her cyclol theory of protein structure, see Kay, op. cit. note 53, 116.
71. Hugh S. Taylor, 'Large Molecules Through Atomic Spectacles', *Proceedings of the American Philosophical Society*, Vol. 85 (1941), 1–12, at 1.
72. Fisher, op. cit. note 66, 5.
73. Fisher Scientific Company, 'Molecules in 3-D', *The Laboratory*, Vol. 27 (1959), 112–13, at 112.
74. Joseph O. Hirschfelder (ca. 1938), *Specifications of Atomic Models*, undated manuscript (Division of Archives, University of Madison-Wisconsin). This short document also points out that the values specified by Hirschfelder were corrected by John Youngs Beach, a Caltech graduate and research physical chemist with the California Research Corporation.
75. Linus Pauling and Lawrence O. Brockway, 'Carbon-Carbon Bond Distances', *Journal of the American Chemical Society*, Vol. 59 (1937), 1223–36.
76. For a discussion of additivity in the physical sciences, see Krieger, op. cit. note 58, 44. Two of the features of additivity, as discussed by Krieger, seem particularly relevant here. The first is 'marginalism', or how the addition of small parts result in small effects. The second is 'invertibility' or 'decomposability', or how 'something big may be analyzed into smaller parts, parts that when added up compose that big thing': *ibid.* An interesting difference is that while Krieger insists that physicists do not put together 'actual objects', but rather add up numerical values derived from these objects, we can see that chemists do rely readily on the first strategy.
77. H.A. Stuart, *Molekulstrukturen* (Berlin: Springer, 1934).
78. B.M. Wepster, 'Stuart's "Atomkalotten"', *Recueil des Travaux Chimiques des Pays-Bas*, Vol. 65 (1946), 318.
79. Linus Pauling, letter to Joseph O. Hirschfelder, 26 September 1938 (Ava Helen & Linus Pauling Papers, Oregon State University). In this letter, Pauling, contrarily to Hirschfelder, explicitly uses the expression 'van der Waals radius' (even when he obviously means a diameter).
80. Fisher, op. cit. note 66, 6 (emphasis added).
81. California Institute of Technology, *Progress Report to the Rockefeller Foundation on Development of Chemistry-Biology Program at the California Institute of Technology* (1947), 16–17 (Rockefeller Foundation Archives, Rockefeller Foundation Collection, Record Group 1.2, Series 2050, Box 4, Folder 24).
82. Robert B. Corey and Linus Pauling, 'Molecular Models of Amino Acids, Peptides, and Proteins', *The Review of Scientific Instruments*, Vol. 24 (1953), 621–27, at 622 (emphasis added).
83. *Ibid.*, 622.
84. *Ibid.*, 625.
85. Pauling & Corey, op. cit. note 53, 86.

86. Robert B. Corey, 'X-Ray Studies of Amino Acids and Peptides', *Advances in Protein Chemistry*, Vol. 4 (1948), 385–406.

87. Linus Pauling (1939), *The Molecular Structure of Proteins* (Rockefeller Foundation Archives, Rockefeller Foundation Collection, Record Group 1.1, Series 205, Box 6, Folder 82).

88. California Institute of Technology, *Plastic Models* (23 March 1956), 1 (California Institute of Technology Archives, Robert B. Corey Collection, Folder 3.2).

89. John R. Platt, 'The Need for Better Macromolecular Models', *Science*, Vol. 131 (29 April 1960), 1309–10.

90. Biophysics and Biophysical Chemistry Study Section of the National Institutes of Health, *Conference of the Committee on Atomic and Molecular Models (Verbatim Report)* (Berkeley, CA, 25 July 1960), 6.

91. *Ibid.*, 51.

92. *Ibid.*, 58.

93. *Ibid.*, 53–55 (emphasis added).

94. Walter Koltun, 'Precision Space-Filling Atomic Models', *Biopolymers*, Vol. 3 (1965), 665–79, at 665.

95. In the end, selecting the van der Waals radii for this new set of models proved to be probably one of the less difficult tasks. By the time commercial production started in 1966, they had required the involvement of the US National Science Foundation (which paid for the very expensive plastic moulds) and of the American Society of Biological Chemists, as well as some ingenious design work from Walter Koltun, who patented a strong yet flexible plastic connector to assemble the models. A complete description of the CPK models, as well as a short story of their design can be found in Koltun, *op. cit.* note 94.

96. Barry Barnes, *Interests and the Growth of Knowledge* (London: Routledge & Kegan Paul, 1977), 7.

97. For a criticism of Barnes' mapping analogy, see Paul Tibbetts, 'Representation and the Realist-Constructivist Controversy', in Lynch & Woolgar (eds), *op. cit.* note 5, 69–84, 81–82.

98. Alberto Cambrosio, Daniel Jacobi and Peter Keating, 'Ehrlich's "Beautiful Pictures" and the Controversial Beginnings of Immunological Imagery', *Isis*, Vol. 84 (1993), 622–99, at 61.

99. On this topic, see Joseph F. Fruton, *Molecules and Life: Historical Essays on the Interplay of Chemistry and Biology* (New York: Wiley-Interscience, 1972), and Robert C. Olby, *The Path to the Double Helix* (Seattle, WA: University of Washington Press, 1974).

100. On Pauling's early career, see Robert Paradowski, *The Structural Chemistry of Linus Pauling*, unpublished PhD dissertation, University of Wisconsin (Ann Arbor, MI: Xerox University Microfilms, 1974).

101. Not surprisingly, a majority of the scientists who participated actively in the development of the CPK models had been at some point or other collaborators of Linus Pauling. I discuss this issue more in depth in 'Holding Macromolecules in Focus: A Socio-Historical Analysis of the Development of the CPK Models' (paper presented at the 1994 Annual Meeting of the Society for Social Studies of Science [4S], New Orleans, LA, 12–16 October 1994).

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