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The cognitive life of mechanical molecular models

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ABSTRACT

The use of physical models of molecular structures as research tools has been central to the development of biochemistry and molecular biology. Intriguingly, it has received little attention from scholars of science. In this paper, I argue that these physical models are not mere three-dimensional representations but that they are in fact very special research tools: they are cognitive augmentations. Despite the fact that they are external props, these models serve as cognitive tools that augment and extend the modeler's cognitive capacities and performance in molecular modeling tasks. This cognitive enhancement is obtained because of the way the modeler interacts with these models, the models' materiality contributing to the solving of the molecule's structure. Furthermore, I argue that these material models and their component parts were designed, built and used specifically to serve as cognitive facilitators and cognitive augmentations.

1. Introduction

Up to the 1960s, biochemistry and molecular biology were profoundly influenced by the deployment and diversity of a peculiar kind of *research tool*: mechanical molecular models[1] (Francoeur, 1997, 2000). Although such physical models of molecular structures have been replaced by simulated or virtual models in modeling tasks (Francoeur & Segal, 2004), the building of scale models of molecular structures from tangible components was once an important part of the practice of biologically oriented chemists. This model-building strategy directly served the scientist's research interests. The construction and manipulation of plastic, wooden and metallic models of possible molecular structures played a central part in an informed trial-and-error research strategy that proved especially useful in elucidating complex molecular structures such as those of organic macromolecules. In the late 1940s and early 1950s, chemist and biochemist Linus Pauling pioneered the *systematic* use of these "tinker toys" for the structural determination of compounds (e.g. Corey & Pauling, 1953), a research strategy historian of science Lily Kay has characterized as a "molecular architecture epistemology" (Kay, 1993, p. 262). This pervasive research strategy led to new scientific knowledge, including major breakthroughs, by stimulating the scientist's imagination and pointing to new research avenues (Laszlo, 1993, 2000). Certainly the most famous example of such successful use of molecular models is James Watson's and Francis Crick's use of this research strategy in discovering the basic structure of the DNA molecule. The metallic model they used was not simply a dramatic display in an extravagant showcase: it was itself a tool for research and served as a locus for discovery. And this case is no anomaly—the use of such models for complex structural determination was typical rather than exceptional (Francoeur, 1997).

Although nowadays these tangible models are seldom encountered outside undergraduate biochemistry courses, their historical importance as research tools guarantees their place in the standard iconography of science, making them familiar even to the layman. The role these physical models have played in scientific discovery has received little attention,[2] with most scholarly focus being aimed to their supporting roles as pedagogical devices manipulated for

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[1] Although the first use of such material models to represent molecular structures can be dated back at least to John Dalton, father of the atomic theory of matter, they were mainly used as demonstration apparatuses (Petersen, 1970; Ramsay, 1975). The use of such models as research tools began to be mainstream in the late 1930s (Francoeur, 1998).

[2] Two notable exceptions can be found in the work of sociologist of science Éric Francoeur, which focuses primarily on the use and development of such models as part of the material culture of science, and in the work of Baird (2004), which focuses on giving material artifacts and scientific instruments an epistemic status, accessible, amongst other means, through active material manipulations. I see this paper as a continuation of their respective work.

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better learning/memorization of a selected molecule's structure or used as visual support in classrooms (e.g. Coll, 2006). Though the historian Olby (1974) does mention here and there the use of such models, and describes in detail Pauling's paper-made alpha-helix model (Olby, 1974, pp. 208–201; see Section 3.2.1 below), there is no systematic discussion of the importance and role these physical models played—even though they did play a central role in paving the way for contemporary molecular biology. Philosophers have paid even less attention to these models but, when attended, the discussion centers on the more general aspects of representing and modeling (e.g. Giere, 2012), such as the scientists' struggle with visualizing three-dimensionality by a two dimensional media (e.g. de Chadarevian & Hopwood, 2004; Francoeur, 1997; Gooding, 2006)). More generally, in the SEP entry on *Models in Science*, Frigg and Hartmann write about physical models that they "[...] do not give rise to any ontological difficulties over and above the well-known quibbles in connection with objects, which metaphysicians deal with." (Frigg & Hartmann, 2012, Section 2.1). From this latter perspective, there seems to be little more to physical models of molecular structures than a means to represent more accessibly the three-dimensional structure of a given molecule.

The trouble with this view is that it does not account for the actual practice of using physical models as research tools nor for the manner by which new scientific knowledge is produced when doing so. When a modeler aims to solve a molecule's structure with the aid of such physical models, she explores different combinations of model parts, makes measurements, often disassembling and reassembling the models built. These interactive manipulations exploit the mechanical properties of the models, properties which are not reducible to matters of visualization. Moreover, the use of these physical models has often replaced the deployment of mathematical calculations in molecular modeling contexts. This introduces a pragmatic dimension that cannot be ignored: when compared with geometrical drawings and mathematical calculations, physical models appear to be costly (in time, energy and money) and cumbersome replacements for clean paper work. I argue here that mechanical molecular models are not just static representations, equivalent to flat geometrical and mathematical calculations with a three-dimensional twist; they have something more that makes them non-trivially different from their inscriptional counterparts.

The main claim of this paper is that mechanical molecular models (henceforth, '*M-models*'[3]) were used as research tools that, through their mechanical properties, augment and extend the modeler's cognitive capacities and performances. Moreover, I argue that their component parts were *designed, built and used* to serve such cognitive functions. By an intelligent use of M-Models' material properties, the molecular architect's manipulations of the model parts enhanced her cognitive performances by facilitating the modeling task. This shows that, contrary to Frigg and Hartmann's summary, there is more to the ontology of physical models than what has been led to believe by current philosophical investigations. Recasting M-models as cognitive augmentations opens the way for a new horizon of research in the philosophy of science about the scientific uses of physical models.

The following discussion can only be partial due to the immense diversity in the design and application of M-models. My discussion will be limited to ball-and-stick models and CPK space-filling models, and to the context of informed "trial-and-error" research strategies.[4] Most of the history of the development and integration of M-models as scientific research tools will also be ignored.[5] The present paper is organized as follow: Section 2 sets the stage by describing molecular modeling activities and the representational capabilities of M-models. In Section 3, I argue that the very materiality of physical models is what interests molecular architects, since it allows them to embody the geometrical properties of molecular structures directly. Moreover, the materiality of M-models provides mechanical properties that can be exploited both representationally and as constraints on model building. These material affordances and constraints are central in allowing M-models to serve as cognitive augmentations, since the effective cognitive use of M-models arises from the interaction between the modeler and her model.

2. Molecular architecture epistemology

> "I soon was taught that Pauling's accomplishment was a product of common sense, not the result of complicated mathematical reasoning. Equations occasionally crept into his argument, but in most cases words would have sufficed. [...] the essential trick, instead, was to ask which atoms like to sit next to each other. In place of pencil and paper, the main working tools were a set of molecular models superficially resembling the toys of preschool children." (Watson, 1980, p. 50)

Molecular modeling is a central activity in the chemical sciences, including biologically oriented ones. Molecular structures are composed of atoms held together by covalent bonds. Different types of atoms have different valences (which determine the number and type of possible bonds with other atoms) so molecular structure is determined by the pairing sequence, length and angles of these interatomic bonds. Chemical compounds are substances consisting of at least two different elements that come in fixed proportions. Compounds with the same constitutive elements but with different atomic structures are called isomers. Molecular structure, the three-dimensional arrangement of a molecule's constituents in space, is thus a central aspect of molecular modeling since isomers may not share the same chemical properties. Isomers may differ in the bonding sequence of their elements or may share the same sequence but differ in the spatial orientations of their constituents. Thus given a single formula spelling out the relative proportions of the atomic constituents of a compound (such as H_2O), the chemist still requires knowledge of the molecule's three-dimensional conformation in order to explain the compound's behavior and properties. Hypothetical molecular structures can be compared to explore their differing impact on chemical properties and, with biomolecules such as proteins and enzymes, their differing functional roles.[6]

[3] A note on the nomenclature: There is no standard expression to refer to the vast diversity of physical models of molecular structures. The simplest expression, 'molecular models', is too broad, since this often refers to an abstract structural (and sometimes dynamical) characterization of a given molecule. So a structural formula of a molecule is a molecular model of that molecule. Material molecular model, although it explicitly points to the materiality of the models, is a term already in use in materials science. Eric Francoeur (1997, 1998, 2001) uses the expression "mechanical molecular models", which is my preferred appellation, that I will abbreviate as 'M-models' (capital M for "mechanical material molecular"-models). I will refer to these scientists as modelers, molecular architects or simply as architects, but usually restricting the last two to cases where actual manipulation is implied.

[4] For other forms of M-models, model kits, and research applications see Smith (1960), Walton (1978) and Francoeur (1998). Scientific contexts in which M-models are used also include, for instance, the study of protein folding, enzyme catalysis and other forms of molecular mechanics (Walton, 1978).

[5] See the work of Éric Francoeur, especially his (1998), and Marie-Jo Nye (1993) for the setting and development of the use of M-models.

[6] In order to alleviate the discussion of unnecessary details, I will not discuss the experimental means for determining the different elements in a compound (e.g. spectrography) nor those for determining empirically if an hypothesized molecular structure is indeed empirically valid (e.g. X-ray diffraction). The discussion will rather focus on means of constructing a viable structural hypothesis given empirical data and the principles of stereochemistry.

Chemists have devised many ways to represent structural properties, using these methods to generate hypothetical molecular structures and derive empirical predictions from them. I will first discuss the representational capabilities and limitations of M-models and then examine the different representational trade-offs of M-model kits. With these notions in hand, it will become clear that these physical models were more than mere surrogates for more accessible and cheaper mathematical tools such as structural formulas and geometrical drawings. This will open the way for an investigation of the advantages of using material props in molecular modeling.

2.1. Physically representing a molecule

In this paper, two general types of M-model kits will be discussed: ball-and-stick model kits (see Fig. 1) and space-filling ones (see Fig. 2). These M-model kits are specialized in representing what Ollis (1972) calls *constitution* and *configuration*. A molecule's *constitution*, i.e. which atoms are part of the molecule and how these atoms bond together, is usually represented by the building blocks of molecular model kits: atom models. In ball-and-stick model kits, balls represent the atom's nucleus position, the valence of the element and angles between the covalent bonds are represented by the number of holes and their arrangement, holes in which connectors (the sticks) are inserted. In space filling model kits (such as CPK models), the volume of the atom—its van der Waal's radius, a zone of exclusion for other non-bonded atoms—is represented by the volume of the atom model (a sphere or quasi-sphere). Connector slots are included in the atomic components, allowing the modeler to attach these components together.

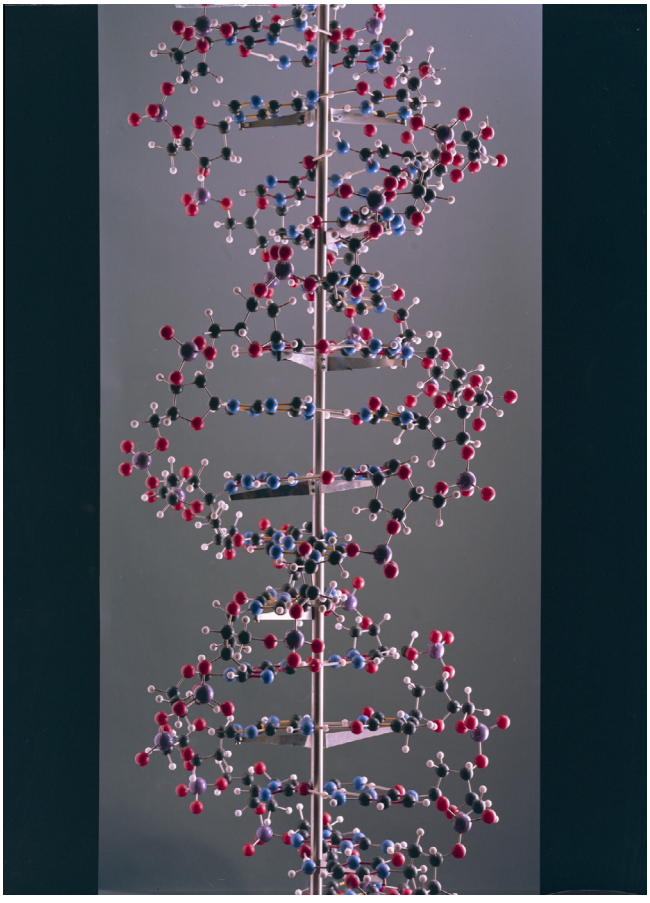

Fig. 1. A ball-and-stick model of the DNA molecule. Built for the International Science Pavilion, Brussels World Exhibition, 1958. Picture courtesy of MRC Laboratory of Molecular Biology.

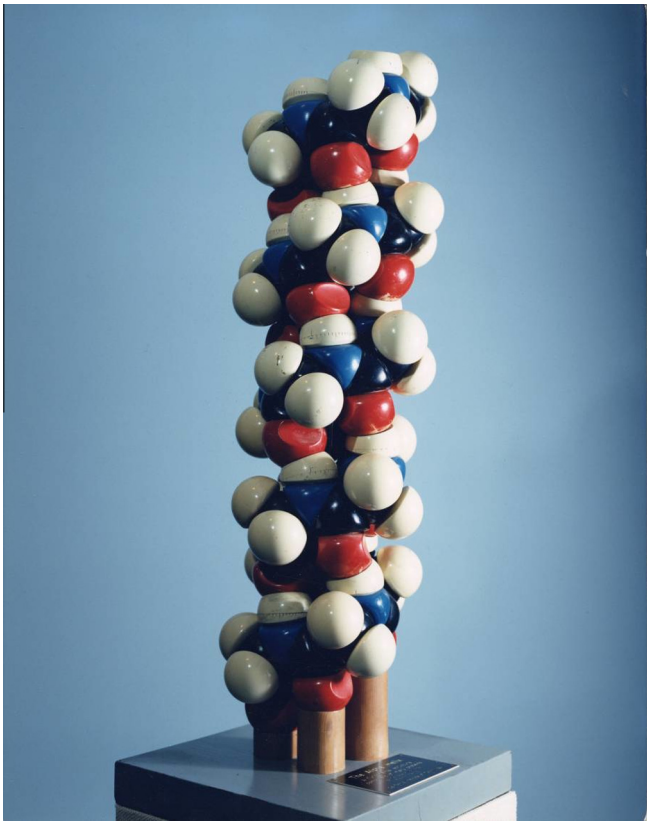

Fig. 2. A space-filling model of the alpha helix, built by Linus Pauling in 1951. Courtesy of Ava Helen and Linus Pauling Papers, Oregon State University Libraries.

Given what an atom model stands for, e.g. an atom of hydrogen or one of carbon, the geometrical properties of the atomic components (number and angles of possible connections) will differ accordingly in both model kits. In the case of space-filling models, the atom's "volume" will also vary according to atomic type. The element an atom model is associated with is often represented by the color of the model. In most ball-and-stick and space-filling models, the same color code (white for hydrogen, black for carbon, red for oxygen, etc.) allows the architect to easily recognize which element is represented by each atom model.

M-models represent the chemical bonds structuring molecules by mechanical connectors connecting atom models one to another. Connectors are the key constituents for representing a molecule's *configuration*, that is, the structural and spatial relationships of the interatomic constituents of the molecule. These connectors, piecing the atom models together, can either be embedded directly into the atom models (as in CPK space-filling models) or they can be separate parts that must be carefully chosen to build the M-model (as in ball-and-sticks models).

The ball-and-stick M-models' connectors are separate tubes and rods used as intermediaries between atom models (the sticks in "ball-and-stick") and can have different lengths, thus serving as representations of interatomic bonds and bond length. These protuberant connectors allow easy visualization of the molecular structure since connectors force space between atom models, allowing the modeler to see through the whole structure and thus easily measure interatomic relative position. Ball-and-stick connectors can also be either rigid or flexible, depending on whether the interatomic distances is relevant for the modeler's aim or not (see next section). The holes into which rigid connectors fit often

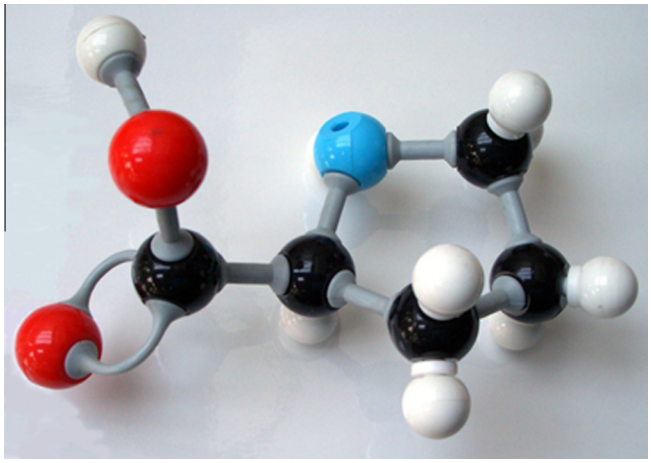

Fig. 3. A ball-and-stick model with flexible connectors. Interatomic distances are not represented. Picture by Peter Murray-Rust / CC BY-SA 2.5.

allow rotation, and depending on the model kit, bending can be excluded by making connectors in rigid materials (often wood or metal). In contrast, flexible connectors made, for instance, of metallic springs or twistable plastic, can be bent and writhen. The latter are often used in M-model kits for chemistry undergraduates, allowing the student to focus their learning on the topological properties of the molecules (the sequence of atomic catenation) by abstracting away the interatomic spatial relationships (see Fig. 3). In molecular modeling tasks, interatomic spatial relationships are central, so rigid connectors are mostly used.

In space-filling M-models, the connectors are integrated directly into the atom models which, in combination with the atom model's volume, make them functionally analogous to specific-length rigid connectors in ball-and-stick models.[7] The rigidity or flexibility of connectors play a central role in molecular structure solving tasks (see Section 3.2) as they impose constraints on molecular configurations that can be obtained by the use of a specific model kit. Finally, space-filling model kits are more opaque than ball-and-stick ones because the connectors are directly integrated into the atom model, leaving no or little space between the constituents. This characteristic is responsible for the compact globular shape of space-filling models.

2.2. Representing and misrepresenting with M-models

In a guidebook on commercial M-models, Anne Walton (1978) describes over 50 different kits for building M-models, falling under 6 broad categories individuated by general representational capabilities. Such diversity is directly related to the many aspects of a molecule's structure and behavior that a molecular architect might need to model, and the trade-offs between various model kits in terms of the ability to represent different of these aspects. There are no standard model kits for the simple reason that there are no standard molecules. The choice of model kit depends on the architect's interests (what properties she is aiming at modeling) and which trade-offs the modeler is willing to accept. These trade-offs may be understood in two general different ways. First, as Éric Francoeur notes, M-models are theory-laden representations of molecules:

> 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. [...] 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. (Francoeur, 1997, pp. 12–13)

For instance, ball-and-stick models use a Daltonian model of atoms (as points or spheres) while space-filling models take into account van der Waals forces by representing atomic volumes. M-models also usually represent molecular structures at room temperature and do not depict atomic excitation (Walton, 1978). Although questions of realism, idealization and truth are important for an exhaustive analysis of the nature of the representational capabilities of M-models, these considerations go beyond the aim of the present discussion.

The second way of understanding trade-offs—the one that I will focus on here—consists in the intrinsic limitations of the representational capabilities of these material props. As I will argue in Section 3, it is the very materiality of M-models that makes them powerful research tools. But this materiality comes with a cost: there are limits in what one can do with materials, and thus every materialized model comes with its very own inherent representational limitations and mechanical constraints. These limitations point to the fact that M-models represent some aspects of a molecule's structure, but may ignore others, and, even more importantly, may dramatically misrepresent others. These trade-offs must be taken into account and mastered by the architect's skillful and stereochemically[8] informed use, coupled with a familiarity with the model kit's misrepresentational capabilities so that artifacts and valid representations can be distinguished. For instance, some molecular conformation may be built with a ball-and-stick model kit, but since the atomic "volumes" are not represented in such model kits, the conformation may be energetically impossible because of the atoms van der Waal's radii.

The trade-offs imposed by the material constitution of M-models can be informatively organized on at least two different dimensions by which model kits can be classified. The first of these is the *dynamical capabilities* of a model kit. There are *static models*, where no deformation or transformation of the overall shape of a molecule is possible, and dynamic ones, where rotations, inversions, and other forms of structural transformations are possible (Walton, 1978, p. 14). So M-models may misrepresent dynamical properties of molecules in two ways: allowing deformations that are not possible at the molecular level or forcing stasis where there are possible deformations at the molecular level. These misrepresentational possibilities are directly related to the design of the atom models and their connectors, and on the type of material(s) model kits are built of. For instance, rigid metallic rods may not bend where plastic ones would, so the modeler must be aware of these potential misrepresentations since a particular conformation of a M-model may not be realizable at the molecular level (or the reverse).

[7] See Corey & Pauling (1953) for technical specs and detailed diagrams of CPK space-filling models connector's logic. CPK model kits are but one kind of space-filling models. See Walton (1978) for other forms of space-filling model kits.

[8] Stereochemistry is the subdisicipline of chemistry that studies the three-dimensional properties of stereoisomers, molecules with the same constitution but that differ in their conformation (form). Stereochemical principles identify the space of possible three-dimensional shapes of a given molecular conformation can take, for instance by identifying which bonds can rotate and how much.

The design and development of different model kits were in part directed by the use of such mechanical affordances (or lack thereof). For instance, Platt (1960) complained that the limited deformability and fragility of space-filling M-model become problematic when studying conformational changes induced by chemical reactions. Although Klotun connectors (Klotun, 1965) allowed more freedom in bending bond angles and strengthen M-models' overall structural integrity when using the Corey–Pauling space-filling model kit (thus becoming the popular Corey–Pauling–Klotun (CPK) model kit), chemists mostly interested in studying molecular deformation preferred to work with open ball-and-stick models. However, at that time, the ball-and-stick model kits that were available had limited usefulness because of their inadequate rotational capabilities of specific bonds and their overall inability to distort bond angles without tensile strength breaking the model apart (Petersen, 1970). To cope with these mechanical problems, Petersen designed a special connector-type that would allow the molecular architect to decide whether a specific bond would be rigid or allow free rotation. Moreover, it would also allow the modeler to use the tensile strength between model parts to represent chemical strain between atoms, thus allowing the model to deform in the same configuration as the represented molecule would (Petersen, 1960).

A second kind of trade-off is linked to the very materiality of M-models. Depending on the visual perspective taken, some model parts will be in the front, masking those "behind" either visually or by making measurements of "internal" components' relationships more difficult. Visual and manual accessibility to the overall structure of a M-model is thus relative to the openness or transparency of the model kit. It is important to note that M-models do not look like molecules in any way for the simple reason that atoms (and some molecules) are smaller than a light wave and thus do not have a visual appearance. Openness and closeness are thus properties of M-models that do not represent any real properties of molecular structures (Walton, 1978). On one end of the spectrum, we find open-models, models that allow a visual and manual access to the position of the atoms by abstracting away their volume. Ball-and-stick models are paradigmatic open-models since connectors force space between the atom models, thus opening windows into complex molecules internal structure. On the other end, with closed models, such as CPK space-filling models that represent the volume of the atoms, the atomic relative positions are often masked by the volume of the atom models and this makes the access to "inner" molecular components more difficult. This is particularly obvious when modeling macromolecules such as proteins, because the intricacy of structures makes access to the interior components arduous, whether or not the model is opened or closed (Smith, 1960).[9]

I have briefly summarized two sorts of representational trade-offs that apply to some degree to all types of model kits. Of course, each model kit has its very own set of trade-offs, and the commercial availability of model kits has been sometimes insufficient for some modeling task, leading the molecular architect to design her own model kit. Some models are the result of compromises between representing different structural aspects of the molecule, others are designed to represent one aspect "supremely well" (Walton, 1978, p. 12). An important point is that all M-models kits are inaccurate in some respects, simply because of their design and the properties of the material in which they are embedded. The modeler is thus always committed to choosing which aspects need to be more or less accurately represented for the task at hand.

2.3. M-models and mathematical tools

Until Linus Pauling's insistence in the 1950s on the systematic use of M-models for both teaching and research purposes, a pencil-and-paper approach was the common usage in structural and behavioral research (Klein, 1999; Nye, 2001). In contrast with M-models, pencil-and-paper approaches consist in working out a given molecule's structure by means of quantitative and structural formulas and drawings of the three-dimensional structure of the molecule. A compound's constitutive atoms, their relative proportions and, in the case of expanded structural formulas, their bonding sequences can be represented by means of an artificial language specially made for these purposes. As mentioned in the introduction, one important limitation of these modes of representation is their limited capacity in visually representing the molecule's three-dimensional structure, a key structural component of large macromolecules. Nonetheless, complex mathematical calculations *can* be made to establish interatomic distances, bond length, steric hindrance, and other relevant properties. Thus by computing the different parameters of a hypothetical structure, the chemist can analytically establish if a molecular structure is possible or not, given the established principles of stereochemistry.

M-models may well offer better means of visualizing complex three-dimensional structures, but this function of M-models becomes especially relevant once the model has been completed. Using M-models as research tools implies that they are used to *solve* structures and not only to visualize them once the structure has been solved. This is a rather intriguing phenomenon considering the pragmatic implications of using M-models instead of their pencil-and-paper counterparts. M-models are expensive and require complex and precise manufacturing, as well as time- and energy-consuming familiarization and mastering of different model kits. They are also unpublishable in their full three-dimensionality, difficult to build, fragile, and hard to transport (especially models of macromolecules), while structural formulas and geometrical drawings of molecular structures are easy to publish, communicate, store and conserve, and are exceedingly cheap. M-models should thus offer something mathematical tools cannot.

I know of no published explanation of this phenomenon. The closest thing to an explanation can be found in the work of sociologist of science Éric Francoeur. Francoeur's work on M-models focuses primarily on visualization in scientific representations and on the material culture of the chemical sciences. Following an analysis of the differences between two-dimensional depictions of three-dimensional molecular structures (such as perspective drawings) and M-models as visualization tools, Francoeur concludes that M-models are much more: they are genuine research tools (Francoeur, 1997, 1998, 2000). Nonetheless, Francoeur's analysis does not offer any explicit explanation of why M-models were used as research tools *instead of*—or *in addition to*—mathematical tools and 2D representations. Rather, his analysis is focused on the design and engineering problems related to the trade-offs in building model kits, which ground the requirement for diversity in model kits.

Francoeur does point to some important dissimilarities between two-dimensional representations of molecular structures and M-models. While pencil-and-paper strategies can be construed as analytical instruments, Francoeur argues that M-models are better understood as "laboratory technology" (Francoeur, 1997, pp. 18–20). By embedding different geometrical properties of the atoms and interatomic bonds (as discussed above), a M-model

[9] Richardson et al. (1992) offer a neat picture of a strategy used by molecular modelers to circumvent part of this problem. Different visualization experiences can be obtained by introducing special dyes (such as fluorescent ones) on the model parts and then changing the kind of light (e.g. room light, UV light) used to illuminate the M-model. In case of complex macromolecules such as enzymes and proteins, one can dye some model parts in such a way that the primary and tertiary structure show under one light and the secondary and quaternary structure under another.

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." (Francoeur, 1997, p. 19) Because the molecular architect can actively explore the properties of a M-model and take notice of previously unknown emergent properties that were not obvious when locally assembling the atomic parts, the M-model itself can serve as a locus of discovery. Although Francoeur is right in contrasting the "experimental" status of M-models with flat representations used in the context of scientific publications, the distinction does not hold with mathematical tools in research contexts. Indeed, there are no suggested reasons why M-models would not be mere surrogates to mathematical tools since one could accomplish these different tasks (measurement, heuristic and illustrative uses) by using geometrical calculations and drawings instead. This remains to be done.[10]

In the following section, I will argue that the reasons for the popularity and success of M-models and their non-equivalence to mathematical tools when modeling macromolecules require us to construe M-models as cognitive augmentations.

3. The materiality of models

3.1. Physical models

Physical models, such as plastic organs, animal models, Watson and Crick's metal plated model of DNA, etc., are physical objects serving as representations of something else. There are many kinds of such models used in scientific research, differing greatly with respect to their representational capabilities, but also by the part they play in scientific investigations. Although physical models share a set of important similarities with abstract models (e.g. Bohr's atomic model), the most important difference is that they are material objects. This difference is not a superficial one—physical models are not simply abstract models reified; it is their very materiality that is exploited by scientists using them in research endeavors, and which constrains the ways they can be used.

The materiality of physical models is exploited in very different ways depending on their origin (natural or artificial), representational capabilities and the nature of the inquiry soliciting their services. For instance, fluid turbulence models exploit the materiality of their constituent parts in order to study their dynamical properties, whereas architectural models exploit the three-dimensionality of our material world (versus flat blue prints) to allow easy access to multiple three-dimensional visual perspectives (see de Chadarevian and Hopwood (2004) for more examples). Animal models are also material models, and their materiality is exploited by intervening on their constitutive mechanisms. One might agree that this materiality is an important dimension of physical models without appreciating this difference with abstract models as a deep one (e.g. Frigg & Hartmann, 2012; Giere, 2012). While it may seem trivial, we can already appreciate that not all physical models are the same type of material entity: some are alive, others inert; some are natural, others are artificial, etc. In the case of M-models, their materiality is exploited for cognitive purposes.

3.2. M-models as cognitive augmentations

3.2.1. Intermezzo—A stranger in Flatland[11]

What difference does the materiality of M-models make? A small detour through a singular episode in the history of molecular biology will illustrate what materiality can add to molecular models. In 1948, after falling ill and being confined to stay in bed, a bored Linus Pauling set out to occupy his mind by exploring possible configurations for polypeptide chains. Other models for such chains were already available, such as William Astbury's model for the alpha-keratin molecule (unstretched wool fiber). The constitution of the residues of the chain was known but its conformation was not. Pauling assumed that the peptide bond would remain planar and so that there could be no rotation at either end. Instead of working out this modeling problem by calculations and geometrical drawings, Pauling made use of a new form of "paper tool". As Olby puts it:

> "Pauling simply drew a polypeptide chain across a sheet of paper, with the peptide bond in the plane of the paper and the aC atom rotated so as to bring all the carbonyl groups on the same side of the chain. Then he drew lines through the aC atoms at an arbitrary angle to the chain and folded the paper along these lines through the dihedral angle (109°). This operation twisted the chain into a helix. It was then a matter of trial and error to find the orientation of the fold which brought carbonyl and amino groups into line for acceptable hydrogen bonding. In fact, *changing the orientation of this fold within the plane of the paper was equivalent to altering the pitch of the helix*. The result was that as early as 1948 Pauling had arrived at a rough approximation to the 3.7 residue helix now known as the α-helix." (Olby, 1974, pp. 208–281; emphasis added)

In order to explore possible conformations, Pauling exploited the material basis of his structural formula rather than relying on symbol crunching. With a basic set of assumptions, he was able to use the mechanical properties of the paper fibers (by folding and twisting them, and by preserving planarity where needed) not only to represent different pitches but to explore the range of possible pitches with a single material object. Indeed, had Pauling restricted himself to solving the structure by conventional methods, every "trial" leading to an improper structure would have required him to start anew by redrawing a new chain with a different pitch. On the other hand, with his improvised physical model, Pauling was able to simply unfold the paper and try new folding angles with the same piece of paper.

This hybrid case of an M-model/mathematical tool is simple and does not offer the whole range of complexities available in full-blown M-models, but it does point to a simple yet legitimate illustration of how materiality can be exploited in ways that mathematical tools alone cannot. In the example above, Pauling solved his modeling problem by augmenting the representational capabilities of his drawn structural formula through the exploitation of the very materiality of the medium on which the abstract formula was inscribed. The folding of the sheet of paper is not trivial for it puts at work a different set of cognitive capacities such as visuo-spatial reasoning and haptic reasoning (see below). Note that in

[10] Francoeur recognizes that the model kits, in all their diversity, "reflect the wide variety of needs and purposes chemists face in their exploration of chemical structures." (Francoeur, 1997, pp. 11–12). Francoeur also rightly points out that M-models are not mere surrogates *for two dimensional representations of complete molecular structures*, for M-models have empirical usages that extend beyond an "inscriptionistic" understanding of scientific visualization. However both these point do not explain why M-models were actually used *instead* of pencil and paper approaches. This is the question I set to answer here.

[11] In Edwin Abbott's classic 1884 novella *Flatland: A Romance in Many Dimensions*, a creature living in a two-dimensional world meets a three dimensional one, the stranger, which tries to expands the flatlander's world view by showing how to think about a three-dimensional world while only using two-dimensional concepts. Linus Pauling's paper model analogously extracts the third dimension of a flat inscriptional representation by exploiting the medium on which it is inscribed.

principle the same result could have been obtained by means of more complex mathematical/geometrical representations without relying on the paper's disposition to fold and unfold easily. Thus this augmentation is not one of Pauling's representational capabilities *per se* (since mathematical tools could have done the job) but rather one of performance in molecular modeling tasks.[12]

3.2.2. Cognitive facilitation

The materiality of M-models can only be exploited by external *mani*pulations (literally understood as active engagement *with the hands*). When using M-models as research tools, the architect engages in a form of distributed cognition that exploits both internal-to-the-brain and external representations to solve some task. M-models are cognitive facilitators for molecular modeling when the molecular structure sought is itself rather complex, such as the macromolecules studied by biochemists and molecular biologists. I will discuss in turn three aspects of cognitive augmentation that M-models' materiality confers to the molecular architect: (1) working memory offloading, (2) simplification of three-dimensional visualization, and (3) replacement of extensive mathematical calculations by the mechanical work done by the M-model.

As discussed above (Section 2.1), the geometrical properties of atoms and molecular structures that are represented by M-models are directly embedded into the model's parts. Thus a first obvious performance advantage is that once the model is built, the modeler needs not to keep in mind the modeled properties of the constituent parts for they are already embedded into them. For instance, in the case of space-filling models, the van der Waal's volume of an atomic part is already embedded into the quasi-spherical shape its corresponding atom model. The correct model part needs to be chosen by the architect but most of the relevant calculations have already been made by the model kit designers. Thus the modeler can decide, given the constraint of her problem space—determined by available empirical data, plausible hypothesis and the principles of stereochemistry—which model kit to choose with respect to the geometrical properties she can be confident will hold. The choice of a model kit allows the architect to ignore some properties and focus on those aspects that are more problematic.

In the assembly process, the modeler's focus is on local connections, working on one covalent bond at a time. Given some time, this building block strategy allows the molecular structure to slowly but surely emerge from the recursive assembly of connectors between atom models. This is due to the embodiment of the geometrical properties of the atomic components and interatomic bonds into the model parts themselves. The modeler is not required to track mathematically every new relationship that emerges from the addition of some atomic component to the incomplete structure being built, which would imply greater calculation time and higher probability of calculation errors. In M-models, the relationships are instantaneously produced by the material assembly of the component parts themselves. This also means that the modeler does not need to keep track of all possible emerging local conflicts for such conflicts may simply impede the whole assembly process (see below). Both aspects, the selection of geometrical properties that can be ignored while modeling and the holistic emergence of spatial relationships while constructing the model, alleviate the modeler's cognitive load. By delegating to the M-model part of the work in representing, the molecular architect can free her working memory to focus on the scientifically problematic aspects of the molecular structure under study and be relieved of those that can be taken for granted.

In cases of organic macromolecules, the three-dimensional structure is often so complex and constituted of so many different atomic parts that flat models rapidly become intractable. Representing the third dimension on a flat paper surface has always been a difficult task (Gooding, 2006, 2010), a task that physical models such as M-models implicitly solve by being material objects. M-models stand ready, easy to access in their very complexity either by means of manipulations or by moving around them. Indeed, one great advantage with physical models is that the best way to change one's visual perspective is to simply walk around it. Not only is this not possible on paper, but perspective drawings deform the spatial relationships between the atomic parts disposed on the artificially suggested third dimension. On the other hand, the M-model stands ready to be measured—with a ruler or with specially designed measuring tools for M-models (e.g. see Apsimon, Craig, Demayo, and Raffler (1968))—in all its three-dimensionality (Francoeur, 1998). Moreover, the exponential accumulation of interatomic relationships is latent in the material structure, waiting to be directly measured rather than calculated. Linus Pauling recognizes this great advantage of using M-models instead of mathematical tools:

> "These requirements are stringent ones. Their application to a proposed hydrogen-bonded structure of a 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 that are now under consideration for the polypeptide chains of collagen and gelatin, the analytical treatment is so complex as to resist successful execution, and *only the model method can be used*." (Pauling, 1964, p. 436, emphasis added)

A third form of cognitive augmentation conferred to the molecular architect consists in the replacement of extensive mathematical computations by the mechanical work done by the physical model itself. Indeed, the mechanical properties of M-models serve as both affordances and constraints to the modeling activity. The affordance of or resistance to some transformations and manipulations are often exploited in model kits in order to reflect the dynamical properties of molecular structures. Put differently, the macroscopic mechanical properties of the M-model represent molecular properties at the microscopic level. Space-filling models illustrate this point well. Taking atomic volumes into account means that one must systematically verify that every atom's electronic cloud is not in an energetically implausible overlap with the others. In ball-and-stick models, where atom models represent the atoms' relative positions, it is difficult to see on the M-model itself if the atoms' volumes overlap in some energetically unrealistic manner. By contrast, in space-filling models, the atomic parts explicitly embody into their material constitution the relative volume of the atoms they represent. The mechanical resistance and overlapping exclusion of atom models is thus an analog to steric hindrance at the level of the molecule.[13]

Such mechanical properties can be very specific to a given model kit or may be generalizable to most kits. M-models with atom

[12] It is tempting to suggest that the use of the paper folding strategy may have opened the door for Pauling to explore non-integral numbers of residue per turn. At that time, integral numbers were the norm and this expectation may have constrained the models if mathematical calculations had been used instead (Olby, 1974). The paper strategy would allow easy testing of the non-integral hypothesis.

[13] Given that atoms have electronic clouds occupying a certain space (their van der Waal's radius), they act as compressible spheres with van der Waal's repulsive forces limiting the manner by which they can be compressed together. Nonetheless, there are important disanalogies between the mechanical resistance of atom models and steric hindrance. Atomic parts are usually macroscopically incompressible while van der Waa"s volume can be microscopically compressed. Moreover, the van der Waal's volume is a probability distribution (electron cloud), while the atom model is not.

models and connectors all share a basic constraint space specified by the number of connectors an atom model possesses. Indeed, the connectors mechanically limit the number of bonds one can make with an atom model. The angles between the connectors play a similar role. While building a M-model, the molecular architect often faces mechanical limitations when assembling atomic parts together, limitations that inform her about the plausibility or aptness of the model under construction. Two atom models may not be linkable to one another because of interfering model parts, or because of a too large or narrow gap between them preventing the completion of the M-model. This form of mechanical limitation of M-models is often exploited by the architect; if a model cannot be constructed, then, given the assumptions in play, the molecular structure it represents cannot exist.[14] Again, it is the *macroscopic material resistance* of the atom models to be assembled to one another that allows one to infer that the molecular level analog is impossible. The M-model allows this form of representation by relying on the material properties of its parts to represent the properties of the parts of the target system—the atoms in the molecular structure. Francoeur underlines this mechanical aspect of M-models:

> "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." (Francoeur, 1998, p. 53)

Note that with mathematical tools, the possibility space is restricted by the laws of stereochemistry and not by the material properties of the mathematical tools themselves. One can draw too many bonds for an atom, or draw the wrong angles, etc. In contrast, the mechanical affordances and limitations of the M-model kits are not just structural nor are they abstract constraints given by the laws of stereochemistry that must be remembered in order to use the M-model correctly. They are embodied in the model parts' materiality and they can be exploited directly by attempting to build a given structure. The interaction between the M-model and the architect thus allows her to exploit the mechanical space of her physical model and directly infer from such exploratory manipulations implications at the molecular level (rather than relying on complex computations with the aid of mathematical tools). The "allowed" and "non-allowed" spatial configurations are not inferred by pondering geometrical relationships in an analytical manner. Rather, and this echoes Francoeur's understanding of M-models as "laboratory tools", the modeler experiments with them directly by actively manipulating model parts. The refusal of the model parts to connect, or their resistance to torsions, representing microscopic implausible/impossible molecular configurations, are thus perceived through the architect's hands. This form of direct inference from tactile sensations can be understood as a form of haptic reasoning.[15]

These examples may seem somewhat artificial in the sense that the mechanical properties of M-models must always be interpreted in a theoretical context, meaning that unconstructable M-models do not always imply the impossibility of the molecular structure. Of course, the architect must be guided in the construction of the M-model by the principles of stereochemistry, and thus may retain a candidate molecular structure even if the M-model is not constructable or reject one even if it is constructable. For instance, she might use another model kit to build the structure, one that trades off its representational capabilities in the right way for the construction of a model of the molecule under study. One may be tempted to downplay the importance of such mechanical properties by arguing that they do not play an important role in *actual* modeling activities. However, this would be historically false as the design, development and use of the original Corey–Pauling space-filling model kit in the early 1950s can serve to attest.

The development of the Corey–Pauling space-filling model kit (the Klotun connectors were added to the kit a decade later) came from the dissatisfaction with both the representational and mechanical properties of the Fisher-Hirschfelder-Taylor (FHT) model kit (Francoeur, 1998). As a research tool, the FHT model kit had been designed to aid in structural examination of small molecules' interatomic spatial relationships and steric hindrances, embodying van der Waal's radii of the gaseous form of molecules. However, after the war, biochemists started to work on more complex biomolecules and the limitations of the FHT model kit were felt. Solving proteins' structure with the aid of X-ray crystallography, a model kit's atomic constituents would have to embody van der Waal's radii in the crystal form of the protein rather than the gaseous form (Corey & Pauling, 1953). Corey and Pauling devised a new model kit embodying state of the art measurements of atoms' van der Waal's radius in crystal form. Moreover, the new model kit incorporated general assumptions about atomic bonding in crystal forms of peptides, proteins and amino acids. Atomic models of carbon, nitrogen and oxygen atoms were specifically devised to incorporate common biomolecular bonding relationships, completed with different adapters and connector links that allowed or constrained rotations at bonding sites.

Two sets were built but at different scales. The larger set (1 inch = 1 Ångström) was useful in examining steric hindrances of specific structures and in making precise coordinates measurements, which could then be compared with the data obtained through X-ray crystallography (Corey & Pauling, 1953). The larger set of space-filling model kit allowed Linus Pauling and Robert Corey to work out 36 possible configurations for polypeptide chains, of which they rejected all but four because of steric hindrance (Pauling & Corey, 1951). Although the manner by which these structures were tested and their geometrical properties established is muted in the paper, a press release of CalTech explains that it was done by building M-models of each chain:

> "Professor Pauling, working with data supplied by researchers and with a molecular model, was attempting to determine the possible structures for a new combination of polypeptide chains. He calculated mathematically that 36 structures were theoretically possible. The question then remained: Which of these were actually possible in nature? He attempted then to place "atomic billiard balls" in various positions on his special protein model and found that 32 of his theoretical possibilities actually were impossible in nature. *The balls did not fit properly*.
> [...]
> All of this work required only two hours, with the use of the molecular model. Without it, the problem would have required

[14] Such inferences are fallible, see below.

[15] By haptic reasoning I mean the active use of the sense of touch as a part of a reasoning process (in contrast with visual reasoning, for instance). This can be obtained by directly manipulating objects, such as in solving a puzzle by feeling if the pieces fit together, or indirectly through the manipulated objects, such as the white canes (Hoover canes) used as a mobility tool by visually impaired people. This form of reasoning is also available in virtual models through haptic technology, where the materiality of the virtual models is indirectly recreated through artificial resistance (see Francoeur & Segal (2004) for a brief survey).

> so much mathematical calculation that the task would have been overwhelmingly laborious." (CalTech press release, 1951, quoted from Francoeur (1998, pp. 164–165); emphasis added)[16]

This case illustrates clearly that the inability of a M-model to adopt some configuration has been used both as source of *evidence* for the impossibility/implausibility of a molecular structure and as a motivation to develop new model-kits with different mechanical properties (Petersen's invention discussed in Section 2.2 also illustrates this last point).

I have argued here that M-models serve as cognitive facilitators by allowing the molecular architect to replace complex mathematical calculations by embedding in its very materiality geometrical and mechanical properties. These properties can be exploited through active manipulations of the model parts. Thus modeling problems can be solved by interactive manipulations with props rather than extensive pencil-and-paper mathematical computations. The manner of exploitation of the materiality of the M-models is determined by many factors, ranging from the design choices in the model kit's representational capabilities (and choice of material), the selection of the kit deemed to offer the best trade-offs given the problem at hand, and the architect's skills. Moreover, the M-model's materiality is itself an active participant in the modeling task because their mechanical properties produce effects when interacted with. When manipulating the M-model, the architect forces the model parts through some transformations to which the materials of which the model parts are made feedback some information on the feasibility of the assemblage. Torsions and other possible deformations, the degree of their feasibility and M-models aptness or resilience to construction are mechanical properties that result from the *interaction* of the modeler's hands with the model parts. The exploitation of these mechanical properties is informative, lending new knowledge about the aptness of a hypothesized molecular structure. While mathematical calculations rely on the analytical skills of the modeler and computation *over* inert symbols, a different deployment of cognitive capacities is exploited by the molecular architect when *interacting* with her M-model's mechanical properties.

I have used the term 'cognitive *augmentation*' to suggest that molecular modeling with M-models is quicker, easier and simpler than using mathematical tools, so that the difference M-models make in respect of mathematical tools is quantitative. This is true—for instance, Watson and Crick intentionally used M-models to beat Pauling in the race for solving the DNA molecule's basic structure (Olby, 1974; Watson, 1980). Nonetheless, there are reasons to believe that the difference can also be qualitative, and that therefore M-models are more than just surrogates for mathematical tools. Their materiality allows for, not just *better* performance of the same tasks, but performance of different tasks altogether. Let us return to Pauling's quote above. I have underlined a segment where Pauling claims that M-models can not only complement or even supplement mathematical tools in molecular modeling tasks, but that they also become *necessary* tools when the molecule's structural complexity is above some threshold. Put differently, there are modeling problems that resist solutions by mathematical tools because the complexity of the problem exceeds the architect's limited analytical capacities. Just what level of complexity is not mentioned, and it goes beyond the aim of this paper to attempt a definite answer. Nonetheless, this suggests that M-models (and nowadays their computerized analogues) may be exemplars of what Paul Humphreys (2004) has termed "epistemic enhancers", that is tools that extends the reach of our epistemic capacities and sometimes even augment them in such a way that we come to know what was unknowable with our natural cognitive capacities alone. M-models are such epistemic tools for they extend the architect's performance and the realm of solvable problems.

4. Conclusion

In this paper I have argued that an informed use of M-models allows these material props to serve as cognitive augmentations which facilitate the molecular modeling tasks biochemists and molecular biologists confront. Mechanical molecular models are research tools that bolster the molecular architect's cognitive performances. Instead of relying on mathematical tools or solely on internal cognitive capacities, the architect manipulates these material props in such a way as to become more efficient in her problem solving. This is done by replacing extensive mathematical calculations by a different set of cognitive capacities such as visuospatial and haptic reasoning. Moreover, exploitation of the materiality of the M-model by informed manipulations on the part of the architect allows the M-model to take an active part in the cognitive work required to solve a complex molecule's structure. M-models thus facilitate and extend the architects performances by integrating the inherent causality of the M-models materiality to serve as part of the cognitive process required to solve molecular modeling tasks.

One contribution that the present paper makes to the general philosophy of science is that it expands the representation-centered discussions about the use of models in science by offering an analysis where physical models serve as research tools that enhance the scientist's cognitive capabilities and facilitate scientific discoveries. This understanding of physical models thus opens the way for a new horizon of research about the scientific use and ontological statuses of material models. It also puts stress on the claim that physical models pose no special philosophical problem outside those concerned with object ontology since M-models mechanical properties allows them to serve as cognitive tools. Moreover, as the contrast between M-models and paper-tools shows, physical models are not embodied equivalents of their linguistic analogs.

Molecular structure solving tasks, with the aid of M-models, also show that these material props, when adequately used, can be integrated with the architect in order to form a larger cognitive system. This is done by distributing the cognitive load and processes across the modeler, the model and their interactions (Nersessian, 2008). It facilitates the modeling tasks by both augmenting the cognitive capabilities of the molecular architect and reorganizing the problem space by replacing abstract mathematical computations by visuospatial and haptic reasoning processes. The integration of the materiality of the models as parts in the cognitive processes of the modeler allows us to better understand the reasons for the popularity, diversity, and time, energy, and material investments in using these physical models as research tools.

This is but a first attempt at understanding the role of M-models as cognitive research tools. Further interdisciplinary research is required. A more detailed comparison of the different trade-offs between model kits, their impacts on cognitive performance, and a closer examination of historical uses of M-models as cognitive tools could allow a more complete understanding of how these tools scaffold scientific research. It may also open the door for a specific framework to understand the transition from tangible M-models to virtual ones (Francoeur & Segal, 2004).

[16] See also Pauling's notebook 28 for his research notes while modeling collagen with M-models. Many configurations are deemed "not constructable", "or can't be made", etc., and are thus discarded on such this basis. Francoeur (1998), especially in chapter 4, offers more examples.

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