Pharmaceutical Matters: The Invention of Informed Materials

Andrew Barry

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Introduction

IN COMPARISON to physics and biology, chemistry appears to be a science lacking in theoretical interest. Unlike physics, it does not claim to be concerned with the investigation of fundamental forces and particles. Unlike biology, it does not concern itself primarily with the properties and dynamics of living materials. Indeed, as Bernadette Bensaude-Vincent and Isabelle Stengers note in their *History of Chemistry* (1996), the discipline is often considered merely a 'service' science. In one common view, although chemistry did once play a leading role in the development of scientific thought, in the 20th century that role seems to have been displaced by other fields. To be sure, chemistry is a large field embracing a huge range of important topics and problems but it apparently no longer possesses the status that it once had in the hierarchy of scientific disciplines: 'chemistry may seem to be a kind of applied physics, whose focus is not on the progress of knowledge but technico-industrial utility' (Bensaude-Vincent and Stengers, 1996: 245). From this perspective, chemistry is doubly uninteresting. First, the direction of its development is determined by purely instrumental considerations. Second, the discipline no longer aspires to address any fundamental questions. At best, contemporary chemistry simply makes it possible for some of the fundamental scientific developments of the 20th century (quantum mechanics and genetics, in particular) to find fields of application. At worst, it remains tied to a naive and outdated ontology of atomism and mechanism. The received view that chemical thought is theoretically limited is not new. In his *Creative Evolution*, Henri Bergson had drawn a sharp contrast between the limitations of physics and chemistry and the philosophical importance of the sciences of life: 'those who are concerned only with the functional [as distinct from the creative] activity of the living

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being are inclined to believe that physics and chemistry will give us the key to biological processes' (Bergson, 1998: 36; Ansell-Pearson, 1999: 149).

In this article, I make four intersecting arguments, which contest this received view. First, I argue that chemistry is of general interest to social theory not because of its larger theoretical claims or ethical implications, but rather because, as Bensaude-Vincent and Stengers argue, it is an industrial, applied and empirical discipline. Indeed, part of the theoretical interest of chemistry is that it indicates the importance of research which is not primarily guided by theory, but is attentive to the singularity of the case. Second, focusing on a specific case of R&D in pharmaceutical chemistry, I develop Bensaude-Vincent and Stengers's claim that one of the key features of chemical R&D is that it is concerned with the invention of what they term *informed materials*. The article argues that molecules should not be viewed as discrete objects, but as constituted in their relations to complex informational and material environments. Third, drawing on the philosophy of A.N. Whitehead and the sociology of Gabriel Tarde, I suggest how we might make a distinction between the concept of invention, used by Bensaude-Vincent and Stengers, and the concepts of discovery and innovation. While we may or may not agree with Bergson's claim that chemistry does not provide an account of the creative activity of living materials, I argue that chemical R&D is not merely innovative, but is itself creative or inventive, in Tarde's sense of the term. Chemical R&D does not, among other things, discover or synthesize new molecules or new molecular structures but, as Bensaude-Vincent and Stengers argue, it invents informed materials. Fourth, I argue that an important feature of contemporary pharmaceutical chemistry is, to use A.N. Whitehead's terms, the invention of new methods for the invention of such materials. Although the materials produced by chemists have always been informed, the development of contemporary pharmaceutical research has fostered new forms and levels of informational enrichment. My suggestion is that the chemical molecules invented by chemical R&D are now so rich in information that the informational content of invented materials becomes easier to recognize. In part, the conduct of contemporary pharmaceutical R&D is of general interest precisely because it makes the informational content of invented materials more clearly visible. In sociology, as in chemistry, the general interest of the example derives from an attention to its specificity.

Chemistry

In their history, Bensaude-Vincent and Stengers do not deny that there is some truth in the received view of chemistry as merely a service science. But they offer two correctives, both of which suggest a richer account of the history of chemistry. First, they note some of the ways in which chemistry has continued to produce surprising and fundamental results in the 20th century. They point, in particular, to Prigogine's work in far-from-equilibrium physical chemistry and his analysis of self-organizing systems. Contemporary chemistry, in their view, points to the limitations of those

approaches that seek to deduce from first principles, but instead recognizes the possibility of learning from the contingent:

> What are the properties of a substance if one is interested only in deducing them without learning? And how does one learn from them if not by painstaking experiments of which they are an integral part or deciphering the temporal configuration of all the processes at work? (Bensaude-Vincent and Stengers, 1996: 264)

In this view, chemistry is not so much a positivist science, but a discipline which points to a new form of empiricism. It produces substances, the properties of which *cannot* be derived from general laws.[1]

Second, and relatedly, their history indicates that the 'technico-industrial utility' of chemistry cannot be understood simply as a process of application. On the one hand, once outside of the laboratory, chemists confront environments or open systems which necessarily do not correspond to the closed environments of the laboratory (Bensaude-Vincent and Stengers, 1996: 249). In these circumstances, the relation between the field of application (factory, urban environment, field) and the laboratory is necessarily one of translation, rather than application or diffusion (Latour, 1988, 1999). On the other hand, in so far as chemistry has played a critical part in the development of new materials, it has also given rise to a different notion of matter. Matter is not merely reshaped mechanically through chemical R&D but is, according to Bensaude-Vincent and Stengers, transformed into *informed material*:

> Instead of imposing a shape on the mass of material, one develops an 'informed material' in the sense that the material structure becomes *richer and richer in information*. Accomplishing this requires a detailed comprehension of the microscopic structure of materials, because it is playing with these molecular, atomic and even subatomic structures that one can *invent* materials adapted to industrial demands. (1996: 206, my emphasis)

Bensaude-Vincent and Stengers's argument raises two immediate questions, to which they do not provide answers in this text. First, what is implied by the idea that such materials are invented? What is at stake in using the term invention in describing what happens to chemical substances in the laboratory rather than, for example, the term discovery? Second, how are we to make sense of the idea that materials can somehow become 'informed' or, as they suggest, 'richer and richer' in information?

Invention

What is an invention? In *The Laws of Imitation*, Gabriel Tarde provides us with a starting point for a social theory of invention. For Tarde, invention was not the opposite of imitation, nor was the relation between invention and imitation analogous to the sociological distinction between agency and structure. Rather, invention involved the novel composition of elements

which were themselves imitations: 'all inventions and discoveries are composites of earlier imitations . . . and these composites are, in their turn, destined to become new more complex composites' (Tarde, 2001: 105). In Tarde's ontology there were no fundamental elements from which composites were invented. Even those objects which were often taken to be fundamental – such as chemical atoms and human individuals – were only fundamental from the point of view of specific scientific disciplines.[2]

As a composite, the properties of any invention were not reducible to the elements from which it was composed. At the same time, as Tarde argued, the process of invention provided a direction to history, although one that was neither linear nor predictable. Anticipating the conclusions of more recent economists and sociologists of technology, Tarde recognized that the process of invention was contingent, irreversible and path-dependent. In this way, Tarde conceived of inventions as events, not as mere moments in the progressive evolution of technology or the manifestation of the movement of societies from one form to another: '. . . to establish social science it is not necessary to conceive the evolution of societies . . . with a formula comparable to the type of itinerary planned in advance that the railroad companies propose to and impose on tourists' (1967: 93).

Some of Tarde's comments on invention seem to imply that he viewed individual genius as being of critical importance to the inventive process. Yet his account of invention was not psychological, nor did Tarde have a romantic conception of the individual creator. On the one hand, his account was based on a generalized social psychology of belief and desire, in which the notion of society applied as much to non-human as to human entities (Alliez, 1999). On the other, Tarde recognized that what he termed scientific geniuses (such as Cuvier, Newton and Darwin) mobilized the action of many obscure researchers whose contribution was often ignored (Tarde, 1999: 66). Invention, in Tarde's account, was accomplished not by an individual agent, but by lines of force which came to traverse the individual person. Moreover, for an invention to become irreversible depended on the extent of its subsequent imitation by others.

Tarde's conception of invention provides a corrective to two commonplace ways of conceiving of technological invention in general, and the inventive practice of chemistry in particular. In one view, chemical R&D is driven by social and economic forces. It is a service science, after all. In this way, the products of chemical innovation (such as molecules) become shaped by a social and economic dynamic which was external to them. In Tarde's terms, this form of socio-economic analysis operates with an excessively restrictive conception of society. In effect, the activity of chemical substances is simply rendered inert, excluded from the active realm of the social. In a second view, the chemist works to *discover* new materials. Indeed, the idea that new molecules are discovered is one apparently implied by pharmaceutical chemists themselves who write of research and development as a process of 'drug discovery'.[3] In this account, the fundamental properties of the finite set of chemical elements which make up the

periodic table provide a set of given possibilities out of which effective drug molecules can subsequently be synthesized. This view resonates with the 19th-century notion that nature exists as a repository of potential inventions, which are simply there waiting to be realized or discovered by the scientist or engineer (Macleod, 1996). For Tarde, such an account fails to recognize that an atomic element or a molecule is never just an element in isolation. Inevitably, the chemist, in discovering a new molecule, invents a new composite element. Invention leads to the actualization of the virtual, rather than the realization of the possible (Deleuze, 1988: 96–7).

Although Tarde does provide a starting point for a social theory of invention, his own historical analysis fails to recognize the significance of the industrialization of science and engineering that occurred in the late 19th century (Noble, 1977). In this respect, his image of invention was indebted to romantic notions of individual creativity. A.N. Whitehead's later remarks on the history of 19th-century science in *Science and the Modern World* are more suggestive. For Whitehead, 'the greatest invention of the nineteenth century was the invention of the method of invention' (1985: 120). This oft-quoted comment seems remarkable in a book that is primarily concerned with issues in the history and philosophy of science, rather than the sociology and history of technology. Yet it makes perfect sense in the context of Whitehead's philosophical project. In *Science and the Modern World*, Whitehead had little to say about the kinds of problem that traditionally preoccupy philosophers of science such as the relation between theory and evidence or the nature of scientific method. His concerns were metaphysical not epistemological, and at the heart of his philosophy was that 'the ultimate metaphysical principle is the advance from disjunction to conjunction, creating a novel entity other than the entities given in disjunction' (Whitehead, 1978: 21). As for Tarde, Whitehead's was a metaphysics of association. For Whitehead, the 19th-century invention of the method of invention made the production of novel associations a matter of *systematic* research and development. While fields concerned with the invention and investigation of materials such as chemistry and metallurgy have arguably played a merely supportive part in the development of many of the best-known developments in 20th-century scientific theory, from the point of view of the history of invention their role is absolutely critical.[4] To view such fields of science as merely instrumental, or simply driven by an economic logic, would fail to recognize their inventiveness. The notion of informed material, put forward by Bensaude-Vincent and Stengers, points to one way in which such sciences have been inventive, and to one way in which atoms and molecules come to exist, to use Tarde's terms, as 'complex composites'.

Informed Materials

How can we understand the idea that materials can be informed? Two views were commonplace among chemists in the late 19th century. First, in comparison to physics, which sometimes dealt with metaphysical abstractions, chemists prided themselves on the practical craft of their discipline.

In this period, 'chemistry's greatness consisted precisely in its not transcending the facts learned from its practice' (Bensaude-Vincent and Stengers, 1996). Chemistry was a discipline grounded in the controlled environment of the laboratory. Meeting the 'converging interests of academic research and industrial production', the chemistry laboratory both produced new entities and provided the space within which they could reliably be witnessed (Stengers, 1997: 95).

Second, many (although not all) chemists viewed the discipline as a science of atomic elements and molecules. This identity was displayed clearly in the periodic table, a diagram that is still to be found on the walls of the present-day laboratory. Conceived in this way, chemistry appeared to make two assumptions. One was that atoms have given and invariant identities, an assumption which was (partially) undermined with the discovery of radioactivity at the beginning of the 20th century. The second was that chemistry is a science of combinations between these invariant entities. Despite the fact that chemists write of things such as carbon, water and iron all the time, such atoms and molecules are never studied in isolation. The chemist is interested in the fact that the properties of atoms and molecules vary considerably depending on the form and circumstances of their association with others.

For Whitehead, the discipline of chemistry had a particular importance in the exposition of his philosophy of organic mechanism. For Whitehead recognized that the image of matter as being composed of distinct atoms and molecules had come to inform contemporary understandings of reality. In this commonplace view, a molecule is thought of as something like a stone – a kind of stuff 'which retained its self-identity and its essential attributes in any portion of time' (Whitehead, 1978: 78; Stengers, 2002). Whereas Bergson wished to distance himself from what he viewed as the limitations of chemical thought, Whitehead's own criticism of this commonplace view drew some inspiration from chemistry. In his account, however, the identities of atoms and molecules were not distinct, nor were they invariant. Rather than starting out from the first assumption (the invariability of atoms and molecules), Whitehead began from the second (the variability of their associations). Viewing chemistry as a science of associations or relations, Whitehead argued that a molecule should be considered an historical rather than a physical entity. In his view, a molecule should not be understood as a table or rock, but rather as an event: 'a molecule is a historic route of actual occasions; and such a route is an event' (Whitehead, 1978: 80). Seen in these terms the endurance of a molecule through time cannot be taken for granted. Molecules certainly endure, but it cannot be assumed that they remain the same: 'physical endurance is the process of continuously inheriting a certain identity of character transmitted throughout an historical route of events' (Whitehead, 1985: 136).

Chemistry should not be understood then as a science of combinations between given elements that are nonetheless to be considered distinct and immutable. Rather, the identity and properties of atoms and molecules are

transformed through their changing associations. The properties of a hydrogen atom bound within a water molecule are different from the properties of a hydrogen atom bound within a hydrogen molecule. The properties of a water molecule are quite different at temperatures above and below 0ºC. The properties of a metal vary considerably depending on whether it contains trace impurities of other elements. In displacing the notion of the object by the notion of the actual occasion or actual entity, Whitehead suggested a different account of atoms and molecules. For Whitehead, actual entities, including molecules, are not bounded at all, but are extended into other entities, while folding elements of other entities inside them. As became clear with the development of quantum chemistry, apparently distinct atoms and molecules entered into the internal constitution of others through their association. This recognition was a central part of Whitehead's metaphysics: '[An] actual entity is present in other actual entities . . . The philosophy of organism is mainly devoted to the task of making clear the notion of "being present in another entity"' (1978: 50, see also Deleuze, 1993: 78; Halewood, 2003).

For chemists, the fact that molecules have changing properties depending on their associations is an everyday reality. The molecule that is isolated and purified in the laboratory will not have the same properties as it has in the field, the city street or the body (Barry, 2001: 153–74). The challenge, for the chemist, is to multiply the relations between different forms of existence of a molecule both inside and outside the laboratory (Latour, 1999: 113–14). It is impossible to establish an identity between the molecule in the laboratory and a molecule elsewhere, but it may be possible to establish a relation of translation. The problem is particularly difficult to address in thinking about the properties of drugs. Bensaude-Vincent and Isabelle Stengers note the challenge faced by chemists engaged in pharmaceutical research:

> The pharmacological chemist can certainly pursue the dream of an *a priori* conception of molecules to be synthesized for their pharmaceutical properties, but it is still the case that 60 to 70 per cent of medicines today are of natural origin . . . From this field the chemist takes the active molecules, which he isolates, purifies and copies, and modifies at leisure. But it is also 'on the field – on the ailing body' – that medicine designed in a laboratory must operate. Humanity delegates active chemical substances to act not in the aseptic space of a laboratory but in a living labyrinth whose topology varies in time, where partial and circumstantial causalities are so intertwined that they escape any *a priori* intelligibility. (1996: 263)

Bensaude-Vincent and Stengers pose the problem of the relation between the 'aseptic space of a laboratory' and the 'living labyrinth' of the body as an ontological one. Molecules necessarily do have different identities and effects in the laboratory and the body. But, for pharmaceutical research, the gap between the laboratory and the body is equally economic, regulatory and legal. Although pharmaceutical companies may be able to identify

potential drug molecules through a variety of methods, there is no guarantee that active molecules will work effectively and safely as drugs in living bodies.[5] During development many active molecules fail, whether because they are poorly absorbed or metabolized, or are subsequently shown to have toxic effects. Moreover, in the context of the growing concern of consumers, regulators have become more cautious about drug approvals and 'increasing post-marketing surveillance has led to an increasing number of withdrawals'.[6] The withdrawal of Bayer's Baycol™ is a well-known recent example.[7] In these circumstances, research and development costs have escalated. Pfizer, for example, the world's largest drugs company, has warned that its $5bn annual research budget will yield only about two major new drugs per year. The average pre-clinical trial development cost of new chemical entities is said to be $30m per molecule. Perhaps 90 percent of such molecules fail such trials. The cost of generating a single approved medicine is claimed to be over $600 million.

For pharmaceutical companies the costs of clinical trials and the even greater costs of withdrawing drugs after they have been marketed pose a clear problem: how is it possible to maximize the chances that a drug will be both effective and safe prior to the conduct of such trials and, thereby, to increase the productivity of pharmaceutical R&D? How can reliable relations be established between the 'aseptic space of a laboratory' and the 'living labyrinth' of the body without the presence of real bodies? In brief, how can innovation be speeded up?[8]

Bensaude-Vincent and Stengers indicate one solution to the problem. Pharmaceutical R&D can be directed to the extraction and purification of active molecules from naturally occurring substances. This practice can give rise to a series of legal and ethical questions concerning the ownership of intellectual property, for example, regarding indigenous knowledge of the medicinal properties of plants, or the ownership of viruses which are present in particular populations (Pottage, 1998). Such an approach is of continuing importance, but it is only one possible research strategy open to pharmaceutical companies. A more general understanding of pharmaceutical R&D is suggested by the notion of informed material.

One way of understanding the idea that a material entity (such as a potential drug molecule) could be informed or 'rich in information' would be to say that the material *embodies* information. In this view, the design process builds information into the structure of the molecule. But this view would not make sense if we understood the molecule to be simply a discrete and bounded entity. For if molecules were simply discrete entities, how could one then distinguish between a molecule which embodies little information and the 'same' molecule with the same structure of elements that embodies a great deal of information? In Whitehead's and Stengers's terms it is possible to give a different and more precise meaning to the idea of a material object being rich in information. This would acknowledge that material objects (such as molecules) exist in an informational and material environment, yet this environment cannot, as Whitehead argued, be

considered as simply external to the object. An environment of informational and material entities *enters into* the constitution of an entity such as a molecule. Nor can this environment be perceived from a viewpoint which is external to it. The perception of an entity (such as a molecule) is part of its informational material environment (Whitehead, 1985: 87; Fraser, 2002).

Thus defined, the notion of an informed material makes sense of what pharmaceutical actually do. Pharmaceutical companies do not produce bare molecules – structures of carbon, hydrogen, oxygen and other elements – isolated from their environments. Rather, they produce a multitude of informed molecules, including multiple informational and material forms of the same molecule. Pharmaceutical companies do not just sell information, nor do they just sell material objects (drug molecules). The molecules produced by pharmaceutical companies are more or less purified, but they are also enhanced and enriched through laboratory practice. The molecules produced by a pharmaceutical company are already part of a rich informational material environment, even before they are consumed. This environment includes, for example, data about potency, metabolism and toxicity and information regarding the intellectual property rights associated with different molecules. In this way, pharmaceutical laboratories have similarities to other laboratories. As Karin Knorr-Cetina argues, laboratories: 'invent and recreate . . . objects from scratch . . . creat[ing] new configurations of objects that they match with an appropriately altered social order' (1999: 44).

Drug Discovery

Consider the case of a medium-sized pharmaceutical company called ArQule which, towards the end of the 1990s began to transform itself into a 'drug discovery company' – a company oriented toward the development of new chemical entities. Although ArQule was unusual in some respects, its approach to drug discovery is indicative of broader shifts in the conduct of contemporary pharmaceutical R&D. These centred on the introduction of new technologies, including high-throughput screening, combinatorial chemistry, genomics, and computer modelling (Bailey and Brown, 2001).[9] In this way, elements of the drug discovery process, which had hitherto been based on craft laboratory skills, became increasingly industrialized (Augen, 2002; Handen, 2002). At the same time, the introduction of new technologies involved alliances between companies working in distinct areas of technology, and also the formation of so-called virtual pharmaceutical companies which managed such alliances (Cavalla, 2003: 267).

ArQule made its name as a pioneering company in combinatorial chemistry, a set of techniques that made it possible to produce a huge number of potential drug molecules cheaply and quickly.[10] Instead of being the product of specific synthetic pathways of the kind associated with traditional synthetic organic chemistry, combinatorial chemistry enabled new molecules to be mass produced (Hird, 2000; Thomas, 2000: 69–88).

> Synthetic chemistry: A + B + C -> AB + C -> ABC (an individual compound)
>
> Combinatorial chemistry: A_n + B_n + C -> A_nB_n + C_n -> $A_nB_nC_n$ (combinatorial library of 10,000–1,000,000 compounds)

For the traditional organic chemist the problem was to find the most efficient way of synthesizing a given molecular compound (ABC) from a finite set of building blocks of existing compounds (A, B, C, D . . .) which were either readily available in the laboratory or could be purchased from chemical suppliers. Indeed, the discovery of solutions to particular synthetic problems was central to the field of organic chemistry, as it was once taught in university courses. In the laboratory, organic chemists had to deal with all the difficulties of translating formal solutions to synthetic problems into practice. As Bensaude-Vincent and Stengers explain:

> organic chemistry texts usually present the classic, conventional reaction chains. But to the student or researcher falls the problem of directing the actors in a play, so to speak, and creating the situations they need to achieve the desired goal. (1996: 159)

By contrast, combinatorial chemistry performs synthesis through mass production. Through combinatorial chemistry a large number of different but chemically similar building blocks (A_a, A_b . . . A_n) can be reacted with sets of other building blocks (B_a, B_b . . . B_n) and (C_a, C_b . . . C_n) to produce huge numbers of synthetic compounds. In this way, molecules come to exist not as the product of individual synthetic pathways, as was previously the case, but in conjunction with a multitude of other molecules produced through combinatorial pathways. Physically, molecules produced through such techniques are dissolved in standard solutions and stored, for example, in arrays of test-tubes. These arrays collectively form what in the industry are termed *libraries* of compounds (Beno and Mason, 2001). The metaphor of a library of molecules is appropriate because not only do such mass-produced molecules have a material existence, but they are also held in an informational form in catalogues and databases. Without further research, individual molecules produced through combinatorial chemistry have little commercial value. In practice, combinatorial chemistry companies, such as ArQule, sold whole libraries of molecules to those larger pharmaceutical companies that had the resources to investigate and exploit them.

But although combinatorial chemistry, in conjunction with high-throughput screening techniques, reduced the costs of producing and analysing the properties of new molecules, it did not solve the problem of how to determine whether they would work in living bodies. According to industry reports, combinatorial chemistry companies faced the problem that the new technology was not yielding the kinds of dramatic improvements in the productivity and efficiency of drug discovery that had been anticipated by investors and partners. The danger was that ArQule would end up simply

providing the bulk material for drug development, but not playing any significant role in the subsequent informational enrichment of its product. It would not be able to engage in either what researchers term 'lead generation' (developing a set of molecules which have the potential to become drugs) or 'lead optimization' (refining this set). In these circumstances, ArQule's strategy was to reinvent itself as a 'drug discovery company' and, at the same time, to attempt to create a new form of informed material. Value could be realized by enriching molecules with information.

In broad terms, ArQule's attempt to do this had two elements. One was to integrate elements of the existing 'drug discovery process'. To work as a drug, a molecule did not merely have to be potent; it also had to be absorbed by (and eliminated from) the body, it had to be non-toxic, and metabolized neither too slowly nor too quickly. Traditionally, major pharmaceutical companies had performed tests for these properties in sequence. First, potential drug candidates were tested for potency against specific targets, then the other properties of those molecules that were likely to be potent were investigated. ArQule's aim was to perform them in parallel, thereby dramatically reducing the time taken to optimize the design of a potential drug molecule:

> In the traditional drug discovery process, physico-chemical properties, selectivity, potency and ADMET (absorption, distribution, metabolism, elimination, toxicity) parameters are evaluated in a sequential manner, extending the time required to identify a lead candidate and increasing costs. Key information provided by ADMET profiling is historically obtained *at the end of the discovery process*. Adverse results at this step can eliminate compounds that have already progressed for many years, at a substantial cost (Arqule, 2001) . . . [Instead, the] sequential process with late failures must be replaced by a multi-parameter filer at every stage of the drug discovery process. (Hill, 2001)

This strategy was called Parallel Track™ drug discovery: the trade mark is an indicator that this method of invention itself had a market value and public visibility. As a brand, ArQule did not address itself to consumers (Blackett and Robins, 2001), but to the network of potential investors, collaborators and researchers necessary to maintain an innovative company.

The second element of ArQule's approach to the problem of drug discovery involved a proliferation of the forms of existence of molecules. Molecules increasingly existed in ArQule not merely as material and informational objects in laboratories and libraries, but also as the objects of computer modelling. To be sure, computational methods had already established a place in the drug discovery process, however, this place had been a limited one:

> [In drug discovery a] team must come up with a drug which will interact with a novel target for therapeutic intervention in an important disease. The team will have access to data on related targets and existing drugs which interact

> with them. They may have a crystal structure of a target protein. And using a library of computational tools, with their inherent sets of chemical rules, the team can make an informed assessment regarding the shape of molecules that might interact with the target. In modern companies, they will then be able to enumerate a focused library of possible actives using these methods. But this is where their 'simulation' ends. (Beresford et al., 2002)

ArQule's approach was to extend the use of computer models to the simulation of ADMET. Through computer models, the libraries of molecules generated through combinatorial chemistry could be subject to what pharmaceutical researchers called *virtual screening* (Manly et al., 2001). In this way, it would become much easier, and cheaper, to deal with the size of library generated by combinatorial chemistry. In principle, huge libraries of molecules could be enriched through computer modelling, reducing the need for costly laboratory experiments. In practice, however, the development of computer models which might be of use to the laboratory chemist is far from straightforward. Models themselves can be derived, in part, from general quantum mechanical principles. But, as Bensaude-Vincent and Stengers argue, chemistry can rarely rely on general principles, perhaps particularly in the case of the pharmaceutical industry. Necessarily, the development of computer models relies on data derived from earlier laboratory and clinical trials on molecules that may be more or less different from the molecules that the chemist is interested in. However sound the theoretical bases of models are, their reliability depends on the quality and breadth of the data sets on which specific calculations are based.

In discussions between chemists, the term *chemical space* has particular importance. Why is this term so significant? One reason is that it provides a way of thinking about the distance between the properties of the molecules they are interested in and the properties of the molecules that have been used to derive the models. The quality of the models depends on the volume of chemical space they are able to operate within with some degree of reliability. As one team of chemical modellers explained: 'Any primordial models in the past were invariably poor in their predictability because they were based on a very small data set of tens of compounds' (Beresford et al., 2002). In this way, the concept of chemical space is both important, but difficult to operationalize. It is not a Newtonian space, governed by particular coordinate axes which exist independently of the entities which exist within the space. Rather, chemical space is a relational space, the coordinates of which are governed by the particular medical chemical process under investigation. Two different molecules which exist in close proximity to each other in relation to one specific process, for example, may be distant from each other when viewed in relation to a different process. Different pharmaceutical companies, research teams or projects may temporarily occupy different regions of chemical space. But, at the same time, they are likely to conceive of the structure of chemical space in quite different ways.

While computer modelling can be used to select molecules from the libraries generated through combinatorial chemistry, modelling also generates and tests molecules that may not necessarily have any material existence at all. Molecules can be synthesized on screen – even more easily than through combinatorial chemistry. As well as combinatorial libraries, it is now possible for pharmaceutical companies to hold virtual libraries of molecules that have never been synthesized. However, it should not be thought that such computational experiments are necessarily less real than those tested in a traditional laboratory. For some pharmaceutical researchers and managers, all techniques are viewed more or less instrumentally in terms of how quickly and efficiently they yield molecules with a potential to become drug molecules. Others point out that computational experiments are closer to external reality than traditional laboratory experiments as they are likely to be based on data derived from trials on living bodies, whereas laboratory experiments will be conducted in standard solutions.[11] Linguistically, researchers establish equivalence between experiments conducted through computer models by computational chemists and experiments conducted using chemical materials by laboratory chemists. The former experiments are *in silico*, the latter are *in vivo* or *in vitro* (Leach and Hann, 2000). For the chemist it would not make sense to say that the experiment that takes place through computer model is simply a representation of the kind of experiment traditionally carried by the organic chemist or biologist in the laboratory. *In silico*, *in vivo* and *in vitro* experiments are all considered as distinct events that constitute their own objects, relations and forms of measurement, and their own strengths and weaknesses. The problem for a pharmaceutical research group is to translate between the different forms of experiment and different forms of existence of molecules, so that they enrich each other. In practice, this translation is likely to be difficult.

ArQule did not produce molecules that could be sold directly to consumers. The company did not have the resources to invest in expensive clinical trials, nor the political and legal expertise with which to manage its relations with the regulatory authorities, nor the infrastructure required for marketing and distribution. In this context, measurements of the properties of molecules, in their various material and immaterial forms, are critical to the formation of the market for potential drug molecules for companies such as ArQule (cf. Callon et al., 2002: 198–9). For along with other pharmaceutical companies, ArQule had to develop new materials that were sufficiently rich in information that they could provide both the basis for claims to intellectual property, and that would also be likely candidates for further development. Potential purchasers of ArQule's research did not purchase molecules, but molecules the properties of which had, in various forms, been measured, and that were, thereby, uncertainly predictive of their clinical existence. The economics of the pharmaceutical industry revolve around an extraordinary level of investment in measuring equipment – including computer modelling technology, laboratory tests and clinical trials – which produce uncertain results.

Thus specific molecules exist in the informational and material environment of the laboratory. But they also exist in a legal and economic environment of other molecules developed by other companies. Necessarily, in formulating research strategies chemists take into account the existence of prior patents.[12] This information, updated daily, is available on commercial databases. The importance of this informational environment accounts for a second sense in which chemists use the term chemical space which refers to the distance between patented drug molecules and the set of molecules they are investigating. In the context of this information, chemists may seek to buy into the legal-chemical space owned by other companies through collaboration. But they may also try to develop molecules that exist just outside of the space defined by a patent,[13] or colonize unexplored volumes of chemical space, or attempt to re-design drug molecules which have been patented, but which have failed clinical trials.[14] Moreover, in developing computer models, chemists make use of publicly available data on patented molecules. In these ways, intellectual property law should not be considered as simply a part of the external environment within which pharmaceutical companies operate and drug molecules are developed. In a number of different ways, information about existing patents enters into the life of molecules, even during the earliest stages of their development. The molecules produced by the pharmaceutical laboratory are rich in information about their (global) legal and economic, as well as their chemical relations to other molecules. The pharmaceutical laboratory is not a closed system, but a space which itself includes its external legal and economic environment (cf. Mitchell, 2002: 303; Strathern, 2002).

Conclusion: Chemical Invention

Does it make sense to describe pharmaceutical R&D as an inventive practice, rather than merely a practice of discovery? Are the kinds of entities produced through pharmaceutical companies novel? Certainly, the molecules developed by pharmaceutical R&D do not exist 'in nature'. But nor can they be designed simply on the basis of fundamental chemical principles. Nor are they merely structures of atomic elements that always had the potential to be discovered or realized. As we have seen, the development of new drugs involves the multiplication of forms of existence of molecules. But, at the same time, the multiplication of forms of existence of molecules is associated with their progressive informational enrichment.

Thus, the kinds of entities that are produced by pharmaceutical R&D are not simply bare molecules. Rather, they can be understood as 'societies' of different elements, as long as we understand that societies are associations of non-human as well as human entities. The idea of chemical space, which is used so frequently by pharmaceutical chemists, conveys precisely the way in which chemists understand that molecules are societies, in Tarde's sense of the term. As I have argued, the kinds of societies produced by pharmaceutical R&D take specific historical forms. The molecules produced in the contemporary pharmaceutical laboratory certainly are more

or less purified as chemicals, but they are also enriched in new ways. They are part of increasingly dense, spatially extended and changing informational and material environments formed not just through laboratory syntheses and tests, but through virtual libraries, computational models and databases. The notion of 'informed materials', introduced by Bensaude-Vincent and Stengers, describes such novel entities very well.[15]

For Whitehead it was a mistake to imagine that material objects (such as molecules) ever had a concrete existence. Rather than imagine that there are concrete material objects to which social meanings and uses are then added, he argued that objects themselves take historical forms. Whitehead himself was preoccupied by the problem of how, despite the historicity of things, things didn't change that much. Things endured. One of the key assumptions of chemistry is, of course, endurance. Atoms and molecules are never exactly the same as they were before, depending on their changing environments, but they also have an amazing capacity for endurance. Within the drug discovery process, the forms of existence of molecules proliferate. Molecules have characteristics and properties depending on their existence in different informational material forms (in laboratory tests, clinical trials, computer models, patent databases, etc.). But this does not mean that the identities of molecules are fluid. On the contrary, pharmaceutical research can only proceed on the basis that molecules actually endure across different sites, through different parts of the laboratory, throughout their life as products. In the pharmaceutical laboratory, the generation of enduring novel entities depends upon the multiplication of different forms of informed material.

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Notes

1. In the sense given to the idea of empiricism by Whitehead and taken up by Deleuze: 'the abstract does not explain, but must itself be explained; and the aim is not to rediscover the eternal or the universal, but to find the conditions under which something new is produced' (Deleuze and Parnet, 1987: vii).

2. 'The final elements that every science ends up with – the social individual, the living cell, the chemical atom – are final only with respect to their particular science. They are themselves composite' (Tarde, 1999: 36, cited in Alliez, 1999: 10).

3. One of the leading trade journals of the industry is called *Drug Discovery Today*, and chemists speak of pharmaceutical companies as 'drug discovery companies'. The frequent use of the term discovery does not mean, however, that chemists understand the term literally.

4. Whitehead noted the critical importance of metallurgy to the development of physics in the early 20th century:

> The reason why we are on a higher imaginative level is not because we have finer imagination, but because we have better instruments. In science, the most important thing that has happened over the last forty years is the advance of instrumental design. This advance is partly due to a few men of genius such as Michelson and the German opticians. It is also due to the progress of technological processes of manufacture, particularly in the region of metallurgy. (1985: 143)

5. I leave aside here the critical question of the politics of clinical trials and the relations between pharmaceutical companies and regulatory agencies. For further discussion of these issues see Abraham (1995).

6. *The Financial Times*, nd, 2001.

7. In August 2001 Bayer voluntarily withdrew Baycol from the US market because of reports of sometimes fatal rhabdomyolysis, a severe muscle adverse reaction (Food and Drug Administration, 2001).

8. Macdonald and Smith (2001: 947) give an indication of the pressures placed on pharmaceutical R&D for increased productivity in the late 1990s:

> In 1998 GlaxoWellcome embarked upon a new enzyme-inhibitor programme . . . [featuring] an aggressive timeframe of seven years, from the start of medicinal chemistry through to drug launch. This period, dominated as it was by the constraints of the clinical programme [i.e. of testing on human patients], translated into a lead-optimization phase [i.e. the period in which likely potential drug molecules are identified prior to clinical trial] of no more than 12 months.

9. While the ethical and political implications of genomics have been a key focus for research in the social sciences, the development of genomics has seldom been placed in the context of other related trends in research and development. At the same time, elements of the drug discovery process, which had hitherto been based on craft laboratory skills, became increasingly industrialized (Augen, 2002; Handen, 2002).

10. Later commentators indicate that combinatorial chemistry became, for a period, an industrial fashion, just as genomics was later in the 1990s:

> the launch of combinatorial chemistry onto an unsuspecting pharmaceutical industry in the early 1990s resulted in several frantic efforts as companies tried to maintain a competitive edge through the generation and screening of compounds in unprecedented numbers and at an unprecedented rate. (Everett et al., 2001: 779)

The importance of speed in the commercial development of chemistry is not new. Synthetic chemists have often been concerned with the question of the speed and productivity of reactions and the whole field of catalysis derives from this concern.

11. In a pharmaceutical laboratory, potential drug molecules will generally be tested in solution. The solutions used by different laboratories need to take standard forms in order for results of different experiments to be comparable (Cambrosio and Keating, 1995: 82). Such standard solutions can never correspond to the more complex and variable conditions found in a living body. For examples of the

presentation of results of computational experiments see http://www.documentarea.com/qsar/a_beresford2002.pdf

12. See, for example, *The Investigational Drugs Database,* which

> is a daily-updated, enterprise-wide competitor intelligence and R&D monitoring service. It provides validated, integrated and evaluated information on all aspects of drug development, from first patent application to launch or discontinuation. Subscribers include most major pharmaceutical and biotechnology companies the world over. In addition, more and more companies servicing the pharmaceutical and biotechnology sector are subscribing. Chemical companies, CROs, consultants and media providers find the IDdb3 invaluable in locating lucrative new business partners. (http://www.iddb3.com/cds/solutions.htm)

13. A patent is likely not to apply to one molecule but to a set of molecules with similar structure (the 'scaffold') and similar biological activity.

14. This strategy is termed 'drug rescue' by researchers. On the relation between the dynamics of innovation and the occupation of technological space more broadly, see Barry (1999/2000).

15. Scott Lash argues that information should be understood as more than merely a collection of signals or data:

> The constant bombardment by signals, the ads of consumer culture and the like does not constitute information. It is chaos, noise. It only becomes information when meaning is attached to it. Information only happens at the interface of the sense-maker and his/her environment. (2002: 18)

Lash's analysis of information has parallels with my analysis of chemical material. The molecules produced through the industrial process of combinatorial chemistry can be thought of as material forms of noise that need to be filtered before they become useful. Individual molecules only become progressively informed in the assemblage of pharmaceutical research.

References

Abraham, J. (1995) *Science, Politics and the Pharmaceutical Industry: Controversy and Bias in Drug Regulation*. London: UCL Press.

Alliez, E. (1999) 'Tarde et le problème de la constitution', introduction to G. Tarde *Monadologie et Sociologie*. Paris: Institut Synthélabo.

Ansell-Pearson, K. (1999) *Germinal Life: The Difference and Repetition of Deleuze*. London: Routledge.

ArQule (2001) ArQule corporate website, http://www.arqule.com

Augen, J. (2002) 'The Evolving Role of Information Technology in the Drug Discovery Process', *Drug Discovery Today* 7(5): 315–23.

Bailey, D. and D. Brown (2001) 'High-Throughput Chemistry and Structure-Based Design: Survival of the Smartest', *Drug Discovery Today* 6(2): 57–9.

Barry, A. (1999/2000) 'Invention and Inertia', *Cambridge Anthropology* 21(3): 62–70.

Barry, A. (2001) *Political Machines: Governing a Technological Society*. London: Athlone Press.

Barry, A. and D. Slater (2002) 'The Technological Economy', *Economy and Society* 31(2): 175–93.

Beno, B. and J. Mason (2001) 'The Design of Combinatorial Libraries Using Properties and 3D Pharmacophore Fingerprints', *Drug Discovery Today* 6(5): 251–8.

Bensaude-Vincent, B. and I. Stengers (1996) *A History of Chemistry*. Cambridge, MA: Harvard University Press.

Beresford, A., H. Selick and M. Tarbit (2002) 'The Emerging Importance of Predictive ADME Simulation in Drug Discovery', *Drug Discovery Today* 7: 109–16.

Bergson, H. (1998) *Creative Evolution*. Mineola, NY: Dover Publications.

Blackett, T. and R. Robins (2001) *Brand Medicine: The Role of Branding in the Pharmaceutical Industry*. Basingstoke: Palgrave.

Callon, M., C. Méadel and V. Rabeharisoa (2002) 'The Economy of Qualities', *Economy and Society* 31(2): 194–217.

Cambrosio, A. and P. Keating (1995) *Exquisite Specificity: The Monoclonal Antibody Revolution*. New York: Oxford University Press.

Cavalla, D. (2003) 'The Extended Pharmaceutical Enterprise', *Drug Discovery Today* 8(6): 267–74.

Deleuze, G. (1988) *Bergsonism*. New York: Zone.

Deleuze, G. (1993) *The Fold: Leibniz and the Baroque*. London: Athlone.

Deleuze, G. and C. Parnet (1987) *Dialogues*. London: Athlone Press.

Everett, J., M. Gardner, F. Pullen, G.F. Smith, M. Snarey and N. Terrett (2001) 'The Application of Non-Combinatorial Chemistry to Lead Discovery', *Drug Discovery Today* 6(15): 779–85.

Food and Drug Administration, Center for Drug Evaluation and Research (2001) 'Baycol Information', http://www.fda.gov/cder/dru/infopage/baycol/default.htm

Fraser, M. (2002) 'What Is the Matter of Feminist Criticism?', *Economy and Society* 31(4): 606–25.

Halewood, M. (2003) 'Materiality and Subjectivity in the Work of A.N. Whitehead and Gilles Deleuze: Developing a Non-Essentialist Ontology for Social Theory', unpublished PhD thesis, University of London.

Handen, J. (2002) 'The Industrialization of Drug Discovery', *Drug Discovery Today* 7(2): 83–5.

Hill, S. (2001) 'Biologically Relevant Chemistry', *Drug Discovery World* Spring: 129–30.

Hird, N. (2000) 'Isn't Combinatorial Chemistry just Chemistry?', *Drug Discovery Today* 5: 307–8.

Knorr-Cetina, K. (1999) *Epistemic Cultures: How the Sciences Make Knowledge*. Cambridge, MA: Harvard University Press.

Lash, S. (2002) *Critique of Information*. London: Sage.

Latour, B. (1988) *The Pasteurization of France*. Cambridge, MA: Harvard University Press.

Latour, B. (1999) *Pandora's Hope: Essays on the Reality of Science Studies*. Cambridge, MA: Harvard University Press.

Leach, A. and M. Hann (2000) 'The *In Silico* World of Virtual Libraries', *Drug Discovery Today* 5: 326–36.

Levere, T. (2001) *Transforming Matter: A History of Chemistry from Alchemy to the Buckyball*. Baltimore, MD: Johns Hopkins University Press.

Macdonald, S. and P. Smith (2001) 'Lead Optimization in 12 Months? True Confessions of a Chemistry Team', *Drug Discovery Today* 6(18): 947–53.

Macleod, C. (1996) 'Concepts of Invention and the Patent Controversy in Victorian Britain', in R. Fox (ed.) *Technological Change: Methods and Themes in the History of Technology*. Amsterdam: Harwood Academic.

Manly, C.J., S. Louise-May and J. Hammer (2001) 'The Impact of Informatics and Computational Chemistry on Synthesis and Screening', *Drug Discovery Today* 6(21): 1101–10.

Mitchell, T. (2002) *Rule of Experts: Egypt, Techno-Politics, Modernity*. Berkeley: University of California Press.

Noble, D. (1977) *America by Design: Science, Technology and the Rise of Corporate Capitalism*. New York: Oxford University Press.

Pottage, A. (1998) 'The Inscription of Life in Law: Genes, Patents and Bio-Politics', *Modern Law Review* 61(5): 740–65.

Shapin, S. and S. Schaffer (1985) *Leviathan and the Air-Pump: Hobbes, Boyle and the Experimental Life*. Princeton, NJ: Princeton University Press.

Stengers, I. (1997) *Power and Invention: Situating Science*. Minneapolis: Minnesota University Press.

Stengers, I. (2002) *Penser avec Whitehead: Une libre et sauvage création de concepts*. Paris: Seuil.

Strathern, M. (2002) 'Externalities in Comparative Guise', *Economy and Society* 31(2): 250–67.

Tarde, G. (1967) *On Communication and Social Influence*. Chicago, IL: Chicago University Press.

Tarde, G. (1999) *Monadologie et Sociologie*. Paris: Institut Synthélabo.

Tarde, G. (2001) *Les Lois de l'imitation*. Paris: Seuil.

Thomas, G. (2000) *Medicinal Chemistry: An Introduction*. New York: John Wiley & Sons, Ltd.

Whitehead, A.N. (1978) *Process and Reality*. New York: Free Press.

Whitehead, A.N. (1985) *Science and the Modern World*. London: Free Association Books.

Andrew Barry is Reader in Sociology at Goldsmiths College, University of London. He is the author of *Political Machines: Governing a Technological Society* (Athlone, 2001) and co-editor of *Foucault and Political Reason* (UCL Press, 1996) and *The Technological Economy* (Routledge, 2004).