This is a repository copy of *Modelling Systems Biology: Intertwinement and the 'Real'*.

White Rose Research Online URL for this paper:
http://eprints.whiterose.ac.uk/102888/

Version: Accepted Version

Book Section:
Carusi, A. (2016) Modelling Systems Biology: Intertwinement and the 'Real'. In: Whitehead, A. and Woods, A., (eds.) The Edinburgh Companion to Critical Medical Humanities. Edinburgh University Press , Edinburgh . ISBN 9781474400046

Reuse
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Annamaria Carusi, 'Modelling Systems Biomedicine: Intertwinement and the 'Real''. In A. Whitehead and A. Woods, Edinburgh Companion to Critical Medical Humanities, Edinburgh University Press, 2016.

Introduction

At a conference on developing the capacity of systems biology to transform itself in systems biomedicine, several of the scientists' presentations showcase the computational modelling methods they are developing. Drawing towards the end of his presentation, an experienced pharmacologist admonishes the audience to bear in mind that, despite the progress in modelling techniques that he has been discussing, a model is always just a representation and never reality. At this point, there is a PowerPoint slide showing Magritte's painting, This is not a Pipe, and chuckling from the audience. It will not have been the first time that they have seen it, as the painting is by now a trope running through these events, rivalled only by the quotation from George Box: 'Essentially all models are wrong, but some are useful.' Indeed, I have taken up this trope myself, but find that I need to judge my audience carefully when choosing what to move on with. Fairly unproblematic is the choice to follow up with Jorge Luis Borges's story about the unconscionable maps, 'On Exactitude in Science', but more problematic is to follow up with Picasso's portrait of Gertrude Stein, together with the quotation attributed to Picasso: 'Everybody says that she does not look like it but that does not make any difference, she will.'

The trope of Magritte's pipe/non-pipe foregrounds issues of representation for scientists, serving to make obvious the gap between models and reality. This analogy between art and science is based on a deficit model of concepts like 'fiction', 'metaphor' and 'narrative', which focus on what these modes of expression are not: not true, not real, not literal. In this chapter, I propose that one of the roles for the critical medical humanities scholar in this domain is instead to shift the conversation towards different analogies that are based on a generative and productive model of art: the world-making and world-collaborating modes of art.

The chapter starts by outlining the kind of modelling characteristic of systems biomedicine, an intricate hybrid of wetlab experiments, mathematical modelling and computational simulations. This hybridity brings with it a number of epistemic as well as social challenges, which are particularly evident in the visual displays that mediate observational and evidentiary styles and communications between the disciplines, and in the different attitudes around the matter of models and their targets. In the second section, I focus on the realism of models as a central focus of scientists' interest and disagreement, and discuss continuities between science and art forms with respect to realism and other ways of being 'world-directed'. Juxtaposing critiques of realism in the humanities and in science studies, I track a movement from anti-realism to non-dualist reconfigurations of the entire framework for thinking about the relationship between models and world. In the third section, I consider how these non-dualist frameworks open up different ways of thinking about systems biomedicine and the implications for ourselves as 'digital patients'. I conclude with a brief note about the responsibilities that this implies for the critical medical humanities scholar.

Systems Biomedicine and its Models

It is well known that models are pervasive in biomedical scientific practice; a wide range of organisms, animals and material artefacts are used to instantiate biological entities and processes or to stand proxy for broader or different classes. Models are a huge part of the mundane reality of biomedical scientists, who devote a large proportion of their research time and their energy to developing, constructing, using and refining specific types. Computational models are relative newcomers in this already jostling mix of models in biomedical research. Having arrived on the scene in the last few decades,[1] these models elicit a wide range of responses, from suspicion to optimistic confidence that they will be a major force in shaping biomedical research and its carry-through, or 'translation', to medical applications. Computational modelling is very broad, and could potentially be used in almost any strand of research. Systems biology as a new field and approach to biomedicine is entirely predicated upon the possibilities of modelling complex biological processes that advanced computational technologies and resources allow. In this sense, it is typical of technoscience, where science and technologies cannot be peeled off each other, the whole embedded in a complex network of social and institutional relations.

The specific technologies that have made systems biology possible are, on the one hand, the sheer computational power for constructing and managing large databases, and for running simulations that once took days, if not weeks, in a few hours; and on the other, the devices and means for gathering data, the developments of algorithms for processing data, and the development of techniques for constructing simulations and visualisations. There are many different forms of computational model and modelling approaches.[2] One can make a rough distinction between (1) data-intensive modelling approaches that harness new technologies for generating, storing and integrating data, together with algorithms to discover patterns and interactions among data, which are taken as models of, for example, molecular interactions; and (2) computational science approaches that are based upon mathematical models and computational simulations of dynamical biological processes. In fact, these approaches are often closely associated. From the perspective of their construction, computational models are hybrids.[3] Ideally, in biomedical sciences, there is a very close connection between experiments (using cells, tissues, organs, non-human animals or humans), mathematical modelling and computational simulation. This is especially important the closer the research comes to medical applications, such as for diagnosis, drug safety testing or treatment. The hybridity of the models is both methodological and ontological. It is methodologically hybrid for two reasons. Firstly, there are clearly a number of methodologies involved in constructing the computational models: experimental, mathematical, computational. Secondly, during the modelling process, there is not a clear dividing line between experiment, equation and simulation, in the sense that they are all geared towards each other. Experimental techniques are used, but the nature of the experiment changes as it becomes geared towards producing data for models and for testing the output of the simulation. Mathematical modelling is notvalidated purely in the mathematical terms of deduction and proof but needs to be geared both towards experiments and towards the numerical techniques of simulation; the outputs of simulations are interpreted against the background of the interconnec- tion between experiments, equations and the simulation techniques employed. There- fore, not only methodologically but ontologically too, what is called a ‘computational model’ is a hybrid system of interconnected experiments, equations and simulations. An illustration of this sort of hybrid system can be seen in Figure 2.1. Constructed computational models cannot simply be compared with a target domain in order to see whether they successfully represent that target, since there are not necessarily sufficient grounds of comparability between them. Especially when computational models are being brought into medical and clinical contexts, they meet up with a wide variety of different types of data and accompanying instruments, techniques and typical research questions. Appropriate comparability is not given in advance, but needs to be worked at and produced through ongoing iterations of modelling and testing. In this process,

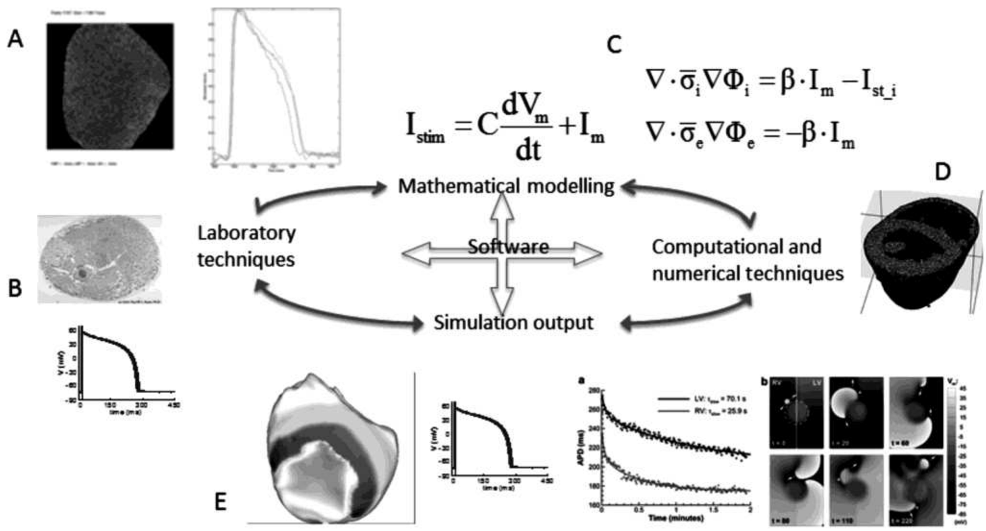

Figure 2.1 A hybrid system of modelling. Author’s own figure.

the model as entity, even as a hybrid entity, falls into the background, and it is just as well to talk about modelling as activity and process.

Each of the elements in the model system is a temporary moment in the process, materialised through apparatus (wetlab apparatus and instruments, the computers and computational infrastructure for the running of simulations), symbolic systems (language, mathematical and numerical symbols, graphs and diagrams) and different modes of observation, such as the output of tracking devices, microscopy and the visualisations generated by simulations.[4] The entire process is mediated through visual outputs, which are both materialisations of the ongoing modelling process and social junctures for the process.[5] The visual displays of outputs have the dual role of making accessible the observations afforded by the different techniques, and of communicating these to others.[6] Visual displays are occasions for researchers to gather together for data interpretations and discussions of the modelling process; they facilitate the integration and interplay of the different aspects of the process; and they mediate social interactions of the different disciplines involved. Considering how closely related visual displays are to the observational and evidentiary styles of different epistemic cultures,[7] their role goes far beyond being mere vehicles for communication. For example, the visualisations of computational simulations are often alien to microscopists, and the microscopical observations can be meaningless to computational scientists. Through the visual displays, there can be an alignment of methodologies: we see this when simulators and experimentalists start to adopt the same way of rendering their visual displays. Alternatively, the visual displays make the faultlines between disciplines stand out even more.[8] Thus the visual displays are active mediators throughout the negotiations and rapprochements or distances between communities.

As already noted, computational modelling is still fairly new in these domains; it has yet to prove itself, and often even has yet to show itself worthy of the time, energy and resources that are required to test it. It needs an intricate set of interdisciplinary relations between experimentalists, mathematicians and computer scientists to get off the ground, which will (if successful) ultimately produce a different transdisciplinary space where both the entities researched and the researchers are not quite the same as at the outset. Forging the collaboration network is not easy. Adopting a methodology as different as computational modelling implies a very deep shift for researchers. For example, a biological process observed through microscopy is a very different entity to a biological process (even ostensibly the same one) computationally modelled. It positions the researcher in a very different way with respect to the research process, involving a different research identity. A question might even arise as to whether what is seen is still a biological process, and whether one is still involved as a witness to a currently occurring biological process, as one is in a wetlab experiment.[9] What is seen, observed and explored and who sees, observes and explores are defined in terms of each other. There are ontological stakes for researchers too, and this is manifested in a recurring concern in encounters around computational modelling between different disciplines. This is a concern with what is real or realistic. For experimentalists, in the laboratory or in the clinic, computational models often evoke responses that put into doubt the reality of what they seem to show, and there are often disagreements or tensions over what counts as realistic.[10] Loosened from the material experimental setting of in vivo or in vitro models and all the apparatus around them, computationally generated visualisations are not perceived (literally) as showing something that is a 'real' process. Mathematicians instead hold a quantitative representation of a biological process to be more realistic than a qualitative one, because it represents mechanisms – that is, mechanisms quantitatively rendered rather than observed. Models are most often described as representations or descriptions in the everyday language and in the publications of biomedical modelling, even though the meaning of 'representation' is rarely made explicit. Thus, in the discourse of scientific modelling, the terms 'realistic' and 'representation' are frequently and unself-consciously used, and demands made on each other in the interdisciplinary negotiations and dialogues (and breakdowns) are frequently couched in these terms. To doubt whether something is a representation is at the same time, in this discourse, to doubt whether it is a model at all. Even though computational modelling is heralded by some to be a new paradigm of modelling (and hence science), there are also sceptical questions raised about whether they are still models in the same way as the accepted forms of models of biomedical research: organisms, non-human animals and humans, and material models. Whether or not they are accepted as models betrays deeply held expectations about the processes and criteria whereby something becomes a model in the different scientific communities implicated in the demand, by computational modelling, to be recognised as such.

What is behind this scepticism has in part already been discussed; beyond the visual differences between the different displays, there is also the matter of matter. That is, the observations afforded by these different displays are in different material modalities and of very different material entities. Experimentalists understand themselves to be observing the process they are investigating in a particular model organism. This is an indirect and often highly stylised and constructed process, but yet they take themselves to be in 'causal contact' with the process, through their visual displays: looking through a microscope, or looking at images of different kinds, or graphs produced through some form of automated tracing. Ultimately, even if only through long and intricate chains, these visual displays bear the traces of familiar equipment and lead back to something organic, something actually biological: that is, the wet stuff of a wetlab. Often the wonder of being a biologist is that these organic things can be coaxed into visibility at all.[11] In a computational visualisation, however, what is seen is something that is not itself organic or 'wet'; moreover, its relation to equipment connecting it indirectly to the organic cannot be 'read off' it. In fact, what is seen is a mathematical–computational entity that yet appears as more vividly, concretely present than the organic thing that is often so tenuously visible.[12] In systems biomedicine, there is a preference for models that are 'of the same matter' as the target domain – such as cell, tissue or animal models: these often count as more realistic, and as epistemologically privileged.[13] A response from systems biomedicine is to try to position their models in the same terminology – in vivo, in vitro, in silico. Rhetorically, this addition of 'in silico' in a parallelism with 'in vivo' and 'in vitro' suggests a seamless continuity between these modalities of experimental models, a parallelism of matter to match the parallelism of form. It counters the perception that computational models are abstract, and gives them a matter – silicon – that is rhetorically suggested as being analogous to the matter of other models in biology. The very use of this rhetorical device in characterising experimental models already points to the crucial importance of sociability in constructing systems biomedicine: others must be persuaded, and, as we shall see, models must be constructed in accordance with the rhetoric, trying to make the parallelism as close to a reality as possible.

Realism, Really?

There are several parallels between the enterprise of modelling in science and in art (by art, I mean art in the broad sense: including visual, performance and literary arts), starting with the difficulty of getting new modes of modelling accepted, which is analogous to getting new styles accepted in art. In both art and science, there are negotiations, tensions, rifts over what is to count as art, as science, as representation (or whatever label is thought to be at stake) in the face of rupture or difference with existing styles. In the case of models, the parallels with art go even deeper because what is at stake is precisely the same issue: the relationship whereby something – an organism, an equation, a portrait and so on – gains meaning or significance in virtue of appearing to 'stand in for', 'point towards' something else – another organism, a biological process, a particular person. Science and art are both domains where this relationship cannot be taken for granted; they both experiment with new ways of establishing the relationship, struggle to establish it, question the way it is currently or traditionally made, and try new ways of making it repeatedly.

This insight into the continuity between science and art is not a new one. In the philosophy of modelling, the analogy between art and science falls into two camps. 'Models as fictions' accounts focus either on the accuracy of models or on their reference: for example, on questions concerning whether the idealisation of models results in inaccurate representations of the real world phenomenon modelled, just as in fiction events and characters are not depicted as they 'really' are; or on questions concerning whether the referents of models exist, and if so, whether their mode of existence is akin to that of fictional entities.[14] 'Models as metaphors' accounts focus instead on the question 'how do models work', and their answer is: 'in the same way as metaphors'. These accounts are not as immediately concerned with semantics and truth as they are with understanding something about how models in science are put together: the arrangement of elements that allows them to gain a particular purchase on the domain they are targeting.[15] With these approaches, a different set of questions about truth and models emerges: this time, the questions emerge in the terms of the opposition between the metaphorical and the literal, and whether, on the 'models as metaphors' account, it is possible, finally, to literalise models, so that their truth (or not) can be evaluated.

On these views of models as fictions, parallels between science and art are encouraged and enjoyed up to the limits of questioning the reality of scientific objects. If scientific models can be understood as fictions, it is only to the extent that, like fictions, their relation to reality is not straightforward. If they can be understood as operating like metaphors, it is only to the extent that, like metaphors, they are not literally true. The assumption, though, is generally that science is directed towards the real and the literal in ways that fictions and (for example) poetic metaphors are not and need not be. But this deep and long-standing assumption is precisely what we need to contest.

The deficit account fails to take into consideration the different ways in which art and literature can be world-directed. The realist movement that reached its apogee in the late nineteenth century, and continued in various forms long after it was a specific movement, is but one expression of this. This form of realism often sought to elide any trace of process of production, and to deliver to the receiver a finished product, to be consumed rather than to interact with. A long tradition of critical theory has subjected realism to critique from several different perspectives: post-structuralism and deconstruction; broadly Marxist and historical materialist; and psychoanalytic, to name but three main trends. These are all accounts that refuse to accept at face value realism's account of itself as producing works whose features are determined by the real or actual perceptual, social or moral world that they purport merely to convey. A classical critique of the pretensions of literary realism is Roland Barthes's S/Z.[16] Barthes proposes an entirely different picture of the realist text: one where the making of the text comes to the fore, and the interweaving of codes as being responsible for the production of an illusion of reality, a realist effect, which far from allowing real society to stamp itself on the work, forms what counts as realist. There are many other critiques in a similar vein, a whole movement of anti-realism, which has made any form of straightforward realism an impossible theoretical position. For a humanities scholar steeped in post-structuralism, deconstruction and postmodernism, it is difficult not to consider scientists' use of terms like 'realism' and 'representation' as hopelessly naïve, and as evidence of a positivism that stubbornly lingers, or paradoxically becomes even more robust. Yet even across all artistic forms, it cannot be said that realism has succumbed before these critiques, and it continues as a more or less robust form, particularly in film and literature. At the same time, it is not necessary to be a card-carrying realist to be 'world-directed' in some way, and this impetus has taken on a huge variety of aesthetic forms and modalities. Whatever realism might be, univocal it certainly is not. But that is the point: world-directedness has different modes, different styles.

Critiques of realism in critical theory began before similar moves in science studies and have several similarities. Typical of the critique of realism in critical theory is the demonstration of the constructed nature of realist works, bringing to the fore the processes of production involved in them. We see a very similar trend in science and technology studies (STS), starting out with a work that could be considered the STS counterpart to Barthes's S/Z: Latour and Woolgar's Laboratory Life.[17] Science is described by Latour and Woolgar as a massive, concerted literary endeavour. Science's objective is the persuasion of readers rather than the discovery and revelation of facts;

hence it is mobilised around literary inscriptions. The influence of semiotics is evident in many key passages of the book, in particular the treatment of scientific discourse as a form of fiction, which, through textual characteristics, gives rise to a 'truth effect'.[18] The attention to inscriptions has continued to be developed within science and technology studies, with continued strong emphasis on the sociality within which inscriptions are embedded.[19]

A difference between STS as it would go on to be defined and practised, and the critical theory/semiotics from which Latour and Woolgar took inspiration, is the extent to which critical theory, in its various forms, gave precedence to the productive capacity of the matter of textuality – the writerly, the painterly, the grain of the voice: écriture, sémeiosis, the trace, among others. An example of an approach in science studies that stands out for developing and extending ideas in critical theory is Hans-Jörg Rheinberger's use of Derrida's notions of différance, trace and grafting to talk about experimental systems.[20] He writes that

> to see experimental systems as pervaded by différance [. . .] stresses that the system undergoes a play of differences and oppositions governed by its own operator-time, and at the same time that it decalates or displaces what at any given moment appear to be its borders.[21]

When the borderlines around systems are seen to be constantly displaced, experimental systems appear as grafts of other experimental systems in an ongoing grafting of one upon the other, in what is often a meandering path. The scientific enterprise is seen as essentially temporal, and not necessarily structured with the narrative coherence that a traditional history might give it (for example, from origins in the form of a problem to be solved or question to be investigated to the solution of the problem or the answering of the question). It may be seen to be 'groping blindly', or to be empirically meandering rather than having definitive goals determined by preset hypotheses. 'The significance or, better, the significant units of the experimental system concatenate into a constantly changing signifying context. There is no direct progress toward a definite "meaning"—whatever "meaning" might mean here.'[22] Episodes of discovery, or of definitive claims, are post hoc narrative reconstructions. This is the power of narrative to give form to episodes in time, and to demarcate the boundaries of a progress story. When the question of 'faithfulness' between scientific claim and real-world entity or process actually comes up, therefore, it cannot be considered apart from the narrative that draws the borders within which faithfulness can even be considered. Modelling is part of an experimental system; in fact, in the case of systems biomedical modelling, it is part of hybrid experimental systems. Whether 'a model' accurately represents its target domain is similarly a question of where the borders of its system are drawn, and through which narrative reconstructions they are drawn.

Rheinberger's strategy does not collapse the construction of scientific facts upon social construction; instead, he retains the typical humanities concern with textual forms of meaning-making, where processes of meaning that hinge upon the materiality of meaning systems (differing, tracing, grafting) are focused upon in their own right.

The result is not so much an undercutting of objectivity for scientific claims as a different framing of this objectivity in an account that shows how it comes about that some scientific claims come to be endowed with a 'scientific object' and to be considered 'within the truth'. For Rheinberger, textual processes of meaning are an ineliminable aspect of this:

> At a given moment and in a given research process, what, say, a microsome or a virus 'represents' – in the sense of how it is 'produced', how it is 'brought forth' – is an articulation of graphemes traced and confined by the procedures of the research process.[23]

The narrative elements of Rheinberger's account are not a form of fictionalism. To adopt Rheinberger's perspective on models does not lead to the conclusion that the entities they target are fictional rather than real, or that they are somehow inaccurate or only approximations of the truth. Textual and narrative processes produce experimental systems, together with the domain that they investigate: models, together with their targets. The question of whether they are 'realistic' can only be asked within bounded systems produced and constructed through these processes, and only at certain points of the 'historiality' of the science. The demand for realism made across disciplines in systems biomedical modelling may be premature, since what can be 'realist' in the current stage of ongoing hybridisation of models – or of grafting of experimental systems, in Rheinberger's terms – is as yet undefined and indeterminate. However, that the demand plays such a prominent part in the interactions among disciplines also points to it as an important site of grafting, where the meaning of what it is to be realistic will be worked out at the same time as the experimental systems become interwoven.

Beyond Dualism

These ways of addressing questions of realism, and related notions of faithfulness, representation and so on, lead to a disintegration of any neat dualism of model and target. We have already seen that talking about models as though they are clearly bounded things is highly problematic in the case of the models typical of systems biomedicine, since there is no single element that is a model, but rather a series of inter-related modelling processes with different objects, tools, techniques and visual displays. This view may lead to the temptation to overemphasise the active role of models in constructing the target domain. On this view, agency is seen as being all on the side of modelling, whereas the object that is modelled is passive. Modelling as agent forges the relationship whereby models can be said to be 'of' a target domain, and at the same time constitute the target domain. Different forms of constructivism (social, historical or post-structuralist/writerly) lead to variants on this view. Increasingly, however, the stark opposition between constructivism and realism is giving way before a number of different proposals for overcoming the persistent dualisms between subject and object, nature and culture, matter and meaning that have dogged Western thought for so long. A good example is Karen Barad's agential realism, discussed in the Introduction to this volume, which locates agency in science's objects as well as in science, in the non-human as well as the human.[24] For Barad, the 'subjects', 'objects' and instruments of science are co-constituted through their intra-actions with each other. Far from being independently constituted and externally related, these are entangled with each other.

Drawing upon the later work of Maurice Merleau-Ponty, Aud Sissel Hoel and I have proposed a non-dualist ontology around the notion of the measuring body.[25] The measuring body is an instantiation of what Merleau-Ponty calls 'flesh', something that is neither subject nor object, neither consciousness nor substance, but rather 'the formative medium of the object and the subject'.[26] Our approach focuses on the mediation of scientific domains that occurs through the measuring body as an interconnection of perceptual, symbolic and technological modalities of expression in multi-dimensional environments. The measuring body is not the body of a discrete being, but a particular way of intertwining modalities of expression, entities and environments, specifying what counts as the 'real' things and processes of an environment – for example, a scientific domain. People, as well as other objects, are caught up and operate in the measuring body, to be measured as well as measuring. By measuring we mean a kind of standard setting, a system of equivalences and differences between modalities and things; such systems have distinctive styles of parsing and interconnecting things. They emanate from a particular way of opening out onto the world – a particular stance, one might say; but they are never unidirectional, as the things that are specified through such stylised systems are intertwined in reciprocal, mutual relations. Whatever opens onto things is also opened onto by other things with which they are intertwined. There is a complicity between seers and seen, between interrogators and interrogated. We underscore the continuities between science and art as expressive modalities of meaning, in that they do not merely communicate pre-existent meanings or represent in an external way, but forge new styles of meaning and knowing, and new domains (or environments), where words like 'real' and 'realistic' come to have determinate – or at least working – meanings. If scientific domains are specified through their measuring bodies, then trying to cross or connect them – for example, through interdisciplinarity – entails encountering and grappling with different styles, in an encroachment of styles upon each other that reshapes and respecifies that domain, and everything, everyone, implicated in it.[27]

The positions that I have outlined – Barad's, Hoel's and my own – are just a small sample of current attempts to break out of the dualisms of subject and object, mind and matter, knower and known. These dualisms are deeply entrenched in Western thought and difficult finally to push out and have done with: hence, the many different attempts at building a non-dualist framework for thinking, from different angles and perspectives. Having started off with critiques of realism, we are now at a point where our main concern is not to deconstruct ideas about faithfulness and accuracy of representation. Rather, we need to understand how the enterprise of rendering the world, knowing and acting in it, in its intertwinement of bodies, technologies, expressivities, forms ourselves and our world, and what may be the forms of responsibility that flow from that.[28]

Modelling Systems Biomedicine and its Patients

Going beyond a critique of realism to accounts of world-directedness that attempt different frameworks for non-dualist thinking opens possibilities for considering systems biomedicine as a domain that is modelled as it uses models to investigate biological and physiological processes. The models and the domain modelled are not externally constituted entities that are in a face-off with each other, as in a positivistic realism; rather, they are inextricably intertwined with each other, through, for example, the materiality and visuality of the different processes and activities involved in it. Systems biomedicine emerges as a grafted, entangled and intertwined domain, in which all of the elements are mutually defined, in complicity with each other, defining a style of realism. Implicated in this style are people, as well as other entities: for example, the patients and the public of systems biomedicine.

Systems biomedicine promises a reconfiguration of disease, diagnosis and treatment that will better serve patients and 'consumers'.[29] In fact, in its data-intensive form, systems biomedicine must implicate us, not at the end of a pipeline that starts with science and ends with the diagnosis and treatment of people. As a mode of research, data-intensive systems biomedicine requires the active participation of individuals to provide data, either through consenting to their data being used and reused, or through self-monitoring on a variety of applications on their mobile devices, computers and different kinds of kit, and donating data. With this is born the idea of the patient or person as medical data generator. The whole enterprise of developing systems biomedicine frequently invokes the 'digital patient'. This is conceived as an individualised model of each person, constructed from the 'trillions of data points' that an individual data generator could generate over a lifetime.[30] However, the data from one person, as abundant as it might be, could not by itself be used to model the progression of a condition or disease, or be used to target diagnoses and treatments specifically to that person. For this, whole populations of data generators are required, so that statistical processes and computational methods can be used to make accurate predictions. Therefore this is both an individual and a community effort. On an individualist rhetoric, one's 'reward' is that one receives one's own personalised model on which to test the outcomes of different treatments. For example, on the website of the 'Digital Patient Project' there is the following patient-directed statement:

> The Digital Patient is an envisaged super-sophisticated computer program that will be capable of generating a virtual living version of yourself. When this is achieved, it will be possible to run 'simulations' of health and disease processes on the virtual or 'digital' you, and use the results to make predictions about your real health. It will also be possible to determine the best treatment specifically for you. This is termed 'personalised medicine', and is intended to be the future of healthcare.[31]

Here we find the familiar dualisms around the virtual and the real, which run like a red thread throughout the project's ongoing deliberations concerning what visualisations could be used to engage individual users. This is a challenge for the project, and in newsletters and other project reports there are traces of different solutions put forward at different times. The idea of an avatar as the main interface between 'real' and 'digital' patients is proposed; taking up prominent gaming devices such as Microsoft Xbox Live, it is suggested that it should be made to look like individual patients for 'emotional intensification'.[32] Although this idea does not find its way into the final project report, a further trace of it is an animated film showing a scenario of what such a consultation might be like. A patient is shown an avatar, which is at first of a generic human that (in the patient's voice) is described as 'breathing and moving its eyes', and when made to jog, 'started to sweat'. We hear the patient say that he does not understand what this has to do with his check-up, but he is then asked to stand on a platform and is scanned by a laser, and 'suddenly the model on the screen changed and it was me . . . it even had my face,' down to 'all my skin blemishes'.[33]

As yet, we do not know what form something like the digital patient might take. This is a context where what 'realism' means will be as political a question as it is a representational one. With the extension of the modelling of systems biomedicine beyond science, into the clinic and well into the public space, we become part of that world that will become intertwined with modelling; those biological and physiological processes modelled are 'ours', in us, and our own being will be co-defined and co-constituted along with that of the models. What modelling and its relationship to the world become is a topic urgently requiring critical engagement on the part of the humanities scholar. Not only the science, but also the material, textual and visual interfaces – that is, the familiar territory of the humanities scholar – are crucial to the imaginary of science and public alike. This is an engagement that needs to work alongside modelling from as early as possible; we cannot wait until models are defined and entrenched to the point where they are too heavy to shift. This engagement with modelling is at the same time technoscientific, biological and social; it demands from us epistemic, aesthetic and ethical awareness and readiness in order to participate in the making of knowledge, the forms and styles of modelling and representing, and the ethico-political stakes in the enterprise. The complicity between modelling and world here takes on a political overtone, but tracing our way back to when science seemed to be 'just science', we will find it was always there.

Conclusion

I opened this chapter by suggesting that one of the roles of the critical medical humanities scholar in a field such as systems biomedicine is to bring into the conversation about models a greater range of ways in which artefacts like models express and enact their world-directedness. Bringing forward examples such as Picasso is a way of opening up different perspectives on world-directedness, as this is experimented with in art as well as in science. When we do bring forward such examples with confidence and without accepting that the only thing that science might learn from art are the limitations of the relationship to the real (as in the deficit account of fictions), we are also able to acknowledge that modelling is productive and formative in just the ways that art has long known itself to be; that being 'world-directed' implies not representational accuracy between a model and its target, but an intertwinement of modelling apparatuses, languages, techniques, biology and people. The ontology of intertwinement, or other forms of non-dualism, does not neatly distinguish representers, representations and their objects; neither does it allow for neat parcellings-out of science and society; rather it focuses on the specific intertwinements that engender the worlds we inhabit and ourselves as inhabitants. Responsibility does not come after science 'captures' reality; if anything, it is even more pressing than science in its realist mode, since the logic of intertwinement brings a responsibility for the form that systems biomedicine takes across laboratory, clinic and world. For humanities scholars, taking on board the ontology of intertwinement implies accepting to participate in this responsibility, in the forming of the reality of something like systems biomedicine.

Further Reading

Annamaria Carusi and Aud Sissel Hoel, 'Towards a New Ontology of Scientific Vision', in Catelijne Coopman, Janet Vertesi, Michael Lynch and Steve Woolgar (eds), Representation in Scientific Practice Revisited (Cambridge, MA, and London: MIT Press, 2014), pp. 201–22.

Annamaria Carusi, Blanca Rodriguez and Kevin Burrage, 'Model Systems in Computational Systems Biology', in Juan M. Durán and Eckhart Arnold (eds), Computer Simulations and the Changing Face of Scientific Experimentation (Newcastle-upon-Tyne: Cambridge Scholars Publishing, 2013), pp. 118–44.

Diana Coole and Samantha Frost (eds), New Materialisms: Ontology, Agency and Politics (Durham, NC, and London: Duke University Press, 2010).

Lorraine Daston and Peter Galison, Objectivity (New York: Zone Books, 2007).

Evelyn Fox Keller, Making Sense of Life: Explaining Biological Development with Models, Metaphors and Machines (Cambridge, MA, and London: Harvard University Press, 2002).

Evelyn Fox Keller, 'Models of and Models for: Theory and Practice in Contemporary Biology', Philosophy of Science 67 (2000), pp. 72–86.

Mary S. Morgan and Margaret Morrison, Models as Mediators: Perspectives on Natural and Social Science (Cambridge: Cambridge University Press, 1999).

Denis Noble, The Music of Life (Oxford: Oxford University Press, 2006).

Hans-Jörg Rheinberger, Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube (Stanford: Stanford University Press, 1997).

Franck Varenne, Formaliser le vivant: lois, théories, modèles (Paris: Hermann, 2010).

Notes

1. Although there are earlier precursors, systems biology is a postgenomic science. See Maureen A. O'Malley and John Dupré, 'Fundamental Issues in Systems Biology', BioEssays: News and Reviews in Molecular, Cellular and Developmental Biology 27.12 (2005), pp. 1270–6.

Systems approaches are also currently being deployed in research into 'holistic' medicine; see, for example, Volker Scheid, 'Holism, Chinese Medicines and Systems Ideologies', in this volume, pp. XX–XX.

2. See Olaf Wolkenhauer, 'Why Model?', Frontiers of Physiology 5 (2014), p. 21.
3. See, for example, Tarja Knuuttila and Andrea Loettgers, Modeling and Experimenting: The Combinatorial Strategy in Synthetic Biology, in Philosophy of Scientific Experimentation: A Challenge to Philosophy of Science (Pittsburgh, 15–17 October 2010); and Annamaria Carusi, Blanca Rodriguez and Kevin Burrage, 'Model Systems in Computational Systems Biology', in Juan M. Durán and Eckhart Arnold (eds), Computer Simulations and the Changing Face of Scientific Experimentation (Newcastle-upon-Tyne: Cambridge Scholars Publishing, 2013), pp. 118–44.
4. These are movies that show the outcome (in a qualitative modality) of running the simulation of a dynamical process, as it occurs through time. They can take many different forms, from highly 'realistic' to highly abstract; which form they do take is dictated by a combination of epistemic and social factors. See Annamaria Carusi, 'Scientific Visualisations and Aesthetic Grounds for Trust', Ethics and Information Technology 10.4. (2008), pp. 243–54; and Annamaria Carusi, 'Computational Biology and the Limits of Shared Vision', Perspectives on Science 19.3 (2011), pp. 300–36.
5. As in most scientific contexts, vision is dominant; different sensory modalities and different perspectives on vision enlarge our understanding of the role of sensory modalities in medical knowledge. See, for example, Jennifer Richards and Richard Wistriech, 'The Anatomy of the Renaissance Voice', in this volume, pp. XX–XX; and Heather Tilley and Jan Eric Olsén, 'Touching Blind Bodies: A Critical Inquiry into Pedagogical and Cultural Constructions of Visual Disability in the Nineteenth Century', in this volume, pp. XX–XX.
6. See also Soraya de Chadarevian, 'Models and Molecular Biology', in Soraya de Chadarevian and Nick Hopwood (eds), Models: The Third Dimension of Science (Stanford: Stanford University Press, 2004), pp. 339–68.
7. See Karin Knorr-Cetina, 'Culture in Global Knowledge Societies: Knowledge Cultures and Epistemic Cultures', Interdisciplinary Science Reviews 32.4 (2007), pp. 361–75.
8. For detailed discussion and examples, see Carusi, 'Computational Biology and the Limits of Shared Vision'.
9. See Evelyn Fox Keller, Making Sense of Life: Explaining Biological Development with Models, Metaphors and Machines (Cambridge, MA and London: Harvard University Press, 2002).
10. For more detailed discussion, see Carusi, 'Computational Biology and the Limits of Shared Vision', and Annamaria Carusi, 'Personalised Medicine: Visions and Visualisations', Tecnoscienza 5.1 (2014). For the contrast between images and diagrams, see Michael Lynch, 'Discipline and the Material Form of Images: An Analysis of Scientific Visibility', Social Studies of Science 15 (1985), pp. 37–66.
11. Evelyn Fox Keller, 'The Biological Gaze', in George Robertson, Melinda Mash, Lisa Tickner, Jon Bird, Barry Curtis and Tim Putnam (eds), Future Natural (London: Routledge, 1996), pp. 107–21; for how life processes are interconnected with the visual, see Hannah Landecker, 'The Life of Movement: From Microcinematography to Live-Cell Imaging', Journal of Visual Culture 11.3 (2013), pp. 378–99.
12. Augustin A. Araya, 'The Hidden Side of Visualization', Techné 7.2 (2003), pp. 27–93.

13. For more on the epistemic weighting of experiments and models, see Mary S. Morgan, 'Experiments Versus Models: New Phenomena, Inference and Surprise', Journal of Economic Methodology 12.2 (2005), pp. 317–29; and for application to systems biology, see Sabina Leonelli and Rachel A. Ankeny, 'Re-Thinking Organisms: The Impact of Databases on Model Organism Biology', Studies in History and Philosophy of Biological and Biomedical Sciences 43.1 (2012), pp. 29–36.
14. For example, see John Woods (ed.), Fictions and Models (Munich: Philosophia Verlag, 2010).
15. The best-known example is Mary B. Hesse, Models and Analogies in Science (London and New York: Sheed & Ward, 1963).
16. Roland Barthes, S/Z (New York: Hill & Wang, 1974) [French original 1970].
17. Bruno Latour and Steve Woolgar, Laboratory Life: The Construction of Scientific Facts (Princeton: Princeton University Press, 1986).
18. Ibid., p. 184.
19. See, for example, Catelijne Coopman, Janet Vertesi, Michael Lynch and Steve Woolgar (eds), Representation in Scientific Practice Revisited (Cambridge, MA, and London: MIT Press, 2014), which follows upon the now classic Michael Lynch and Steve Woolgar (eds), Representation in Scientific Practice (Cambridge, MA: MIT Press, 1990).
20. Hans-Jörg Rheinberger, 'Experimental Systems: Historiality, Narration, and Deconstruction', Science in Context 7.1 (1994), pp. 65–81.
21. Ibid., pp. 71–2.
22. Ibid., p. 76.
23. Ibid., p. 77.
24. Karen Barad, Meeting the Universe Halfway: Quantum Physics and the Entanglement of Matter and Meaning (Durham, NC, and London: Duke University Press, 2007). For more on the notion of entanglement, see Des Fitzgerald and Felicity Callard, 'Entangling the Medical Humanities', in this volume, pp. XX–XX; and on human–non-human entanglements, see David Herman, 'Trans-species Entanglements: Animal Assistants in Narratives about Autism', in this volume, pp. XX–XX.
25. Aud Sissel Hoel and Annamaria Carusi, The Measuring Body, forthcoming.
26. Maurice Merleau-Ponty, Visible and Invisible, trans. A. Lingis (Evanston: Northwestern University Press, 1968), p. 147.
27. For more detailed discussion and applications to computational biology, see Annamaria Carusi and Aud Sissel Hoel, 'Towards a New Ontology of Scientific Vision', in Coopman et al. (eds), Representation in Scientific Practice Revisited, pp. 201–22; and for neuroscience images, see Annamaria Carusi and Aud Sissel Hoel, 'Brains, Windows and Coordinate Systems', in Annamaria Carusi, Aud Sissel Hoel, Timothy Webmoor and Steve Woolgar (eds), Visualization in the Age of Computerization (London: Routledge, 2014), pp. 145–69.
28. Martyn Evans explores similar themes on dualisms, non-dualisms and the articulations of a critical medical humanities in 'Medical Humanities and the Place of Wonder', in this volume, pp. XX–XX.
29. See, for example, Leroy Hood and Mauricio Flores, 'A Personal View on Systems Medicine and the Emergence of Proactive P4 Medicine: Predictive, Preventive, Personalized and Participatory', New Biotechnology 29.6 (2012), pp. 613–24.
30. Ibid.

31. This is a sub-project of the Virtual Physiological Human Network of Excellence, a major European computational modelling for systems biomedicine project. The project website is at: <http://www.digital-patient.net/> (accessed 14 July 2015). For a more detailed discussion, see Carusi, ‘Personalised Medicine: Visions and Visualisations’.
32. Digital Patient Project, Discipulus News: First Draft: Roadmap <http://www.digital-patient.net/files/discipulus_first_draft_roadmap_newsletter.pdf> (accessed 14 July 2015).
33. <http://www.youtube.com/watch?v=JijSCaVrYhw> (accessed 14 July 2015).