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The Commodification of Emergence: Systems Biology, Synthetic Biology and Intellectual Property

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Abstract
In this article I address the interactions between biological knowledge and ideas about the kinds of entity that are suited to appropriation. I start by arguing that commodification and reductionism are closely linked, and that patenting suits entities that are discrete and isolable, such as those that are the focus of molecular biology. I then turn to the new field of systems biology, which recognizes that traditional reductionist approaches to biology are no longer adequate and attempts to provide a more integrative understanding of biological systems. In doing this, systems biology has to deal with emergent phenomena. But patenting does not suit the dynamic and interactive complexity that is the object of study in systems biology. If systems biology rejects reductionism where does that leave commodification? I examine attempts to commodify predictive computational models in systems biology. I then turn to systems biology's sister discipline, synthetic biology, which deals with emergence by reducing the complexity of biological systems. By factoring out messy contingencies, synthetic biology is, in theory, well suited to commodification. Drawing on both these examples I explore how ideas about appropriation, including open source, are influencing the nature and course of research in biology.

Keywords Commodification, Disentanglement, Emergence, Intellectual Property, Synthetic Biology, Systems Biology

My concern in this article is with the relationship between the regulatory and the epistemic. My focus is on the two new fields of systems biology and synthetic biology, fields which aim to integrate high-throughput molecular data to provide a more complete understanding of the operation of biological systems. Both fields have to deal with emergent biological phenomena. My interest is in how ideas about the kinds of entity that are suited to appropriation affect the nature and production of biological knowledge, and I pay particular

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attention to attempts to commodify the emergent objects of the biological sciences to make them fit with intellectual property regimes.

There has been a substantial amount of previous discussion of how commercialization pressures may be influencing scientific research (see Etzkowitz and Leydesdorff, 2001; Gibbons and Wittrock, 1985; Gibbons *et al.,* 1994; Hellström and Jacob, 2005; Mirowski and Sent, 2002; Nowotny *et al.,* 2001; Slaughter and Rhoades, 1996; Thackray, 1998). Some of this work has looked at the effects of commercialization on research practices (e.g. Behrens and Gray, 2001; Blumenthal *et al.,* 1996; Packer and Webster, 1996), but there are very few actual examples of how the *content* of the research itself is affected by these pressures, such as Balmer's (1996) discussion of the influence of patent policies in the choice of a particular DNA mapping strategy. This article aims to contribute to this relatively neglected area of investigation.

To outline the article, I start by discussing commodification, and how it requires that a commodity be objectified and isolable, which means that it must be reduced or fragmented. I draw on Callon's ideas about 'disentanglement' to make sense of how a commodity becomes extracted from the context in which it was previously embedded. Arguing that there are close links between commodification and reductionism, I then turn to reductionism in molecular biology. Patenting is heavily influenced by the molecular-biological view of the world, and molecular biology, in turn, is well suited to commodification. Systems biology, in contrast, attempts to integrate molecular-level data and produce new understandings of biological systems. A key feature of systems biology is its readiness to embrace emergence, a concept which can be understood in various ways (e.g. in terms of unpredictability arising from interactions or contextual influences). Because of its inherently unbounded and unpredictable nature, emergence would seem to be particularly difficult to commodify. Actual patents in systems biology show how the 'commodification of emergence' has operated in practice. After highlighting potential problems with the 'anticommons' that could arise in systems biology patents, because of the interconnectedness of biological systems, I show that most systems biology patents relate to computational models, which are predictive and delimit the number of entities that need to be taken into account. I then turn to synthetic biology, a related field which attempts to construct biological systems. Synthetic biology aims to develop components which are standardized and interchangeable by reducing biological complexity and 'disentangling' phenomena from their biological context. In this way it fits well with the requirements of commodification. I argue that in synthetic biology our ideas about appropriation may (albeit subtly and gradually) shape our ideas about the nature of living things. I conclude that systems biology and synthetic biology deal with emergence in different ways, and that the approach of synthetic biology is the one that is most likely to be taken up in public and policy debates.

This article grew out of a project focused on systems biology. This project involved 35 in-depth interviews with scientists working in systems biology institutes in the US and the UK (referred to with code names throughout), and extended visits to three systems biology laboratories. The comparison with synthetic biology was brought up during the interviews and was explored further in an epistemological analysis and survey of this emerging field (see O'Malley *et al.*, 2008). The synthetic biology material is also based on attendance at workshops and conferences on synthetic biology, membership of a UK synthetic biology network, and discussions with synthetic biologists. With the empirical material as background,

this article primarily draws on commentaries on these two fields from scientists, philosophers, lawyers and other theorists.

Commodification

At a very simple level, a commodity is something that can be bought or sold. For something to be a commodity it must be objectified (Sharp, 2000), that is, made into a 'thing' (Mirowski and Sent, 2007). As Marx (1887) famously said, a commodity is 'an object outside us'. For something to be a 'thing' it must be fragmented, or, as Jacob puts it: 'reduced to a format that makes it possible to make an exclusive package or artefact for which an exchange value may be established' (2003: 127). The use of the word 'reduced' here is interesting, and hints of the links between reductionism and commodification.

Since a commodity is a 'thing' or a 'package' which must be fungible, that is, interchangeable with other objects (Lind and Barham, 2004: 51), it must have clear boundaries: it must be obvious where it ends and where the rest of the world begins. Here it is helpful to draw on the idea, which can be found in Adam Smith (see Schaffer, 2003), that 'disentanglement' is necessary for commodification. Callon has provided helpful elaboration of 'disentanglement', which he describes as a process 'through which, with growing force and clarity, a world exists in which entities are transformed (and retransformed) into things and then goods ... that can circulate' (2007: 343). The notion of disentanglement makes it clear that commodities do not come ready-made, 'decontextualized, dissociated and detached' (Callon, 1998: 19), but instead that they must be first extracted from the network of relationships in which they are already embedded (Holm, 2007). This process of disentanglement requires the mobilization of resources, social and economic actors, and institutions (see Parry, 2008). It is only after these complex negotiations and iterations that we are left with a commodity, an apparently stable object. I will show how these ideas of disentanglement can be very helpful, particularly when it comes to understanding the practices of synthetic biology. But before turning to these issues, it is necessary to focus on the links between commodification and reductionism.

Reductionism is important for my argument, because the two new forms of biology that are my focus here—systems biology and synthetic biology—are both based on a belief that traditional reductionist approaches to biology are no longer adequate. If biology rejects reductionism where does that leave commodification? To help make sense of the issue, and to put the two new fields in context, it is useful to discuss reductionism in traditional molecular biology, and its links to commodification.

Reductionism and molecular biology

Reductionism in biology is the view that 'all complex entities (including proteins, cells, organisms, ecosystems) can be completely explained by the properties of their component parts' (Gilbert and Sarkar, 2000: 1). Molecular biology, as its name suggests, focuses on the molecular level and 'encourages the belief that a detailed understanding of individual molecular properties may be sufficient to account fully for cellular and organismic phenomena'

(Powell and Dupré, forthcoming: 6). The aspiration is that biology will ultimately be explainable in terms of physics and chemistry (Crick, 1966).

Molecular biology became consolidated as the dominant perspective in biology after the discovery of the structure of DNA in 1953 (Powell *et al.,* 2007), and still holds a huge amount of institutional and epistemic power. This is demonstrated by the fact that patenting is heavily influenced by the molecular biological view of the world. We see this in the understanding of the gene that is adopted in patent practice, where it is considered that '[a] gene is but a chemical, albeit a complex one' (*Amgen Inc.* v. *Chugai Pharmaceutical Co.,* 1991). In patenting it is seen as perfectly appropriate to think of a gene in this reductionist way as entirely explicable in terms of its chemical constituents. This approach to understanding genes becomes problematic, however, in the context of research which shows that genes are highly interactive, have many different biological functions and operate in diverse biological processes (Pearson, 2006). DNA's chemical nature seems insufficient to account for all the consequences of gene action, which depend on the biological context in which the gene is operating and on the presence of a large cast of supporting mechanisms, without which genes are impotent (Moss, 2003).

Reductionist understandings of the nature of biological phenomena fit very well with intellectual property regimes. McAfee argues that molecular-genetic reductionism supports certain kinds of economic reductionist arguments, and that this 'double reductionism', as she calls it, 'furthers the extension of the commodity realm to the molecular level' (2003: 203). She maintains that seeing genes as 'unitary objects with stable, predictable properties provides conceptual support for treating genetic constructs as tradable commodities which are subject to market exchange and to the assumptions of neoclassical economics' (2003: 204). In this way reductionism and patenting are mutually supportive.

But this reductionist perspective has limitations, and these limitations are being confronted in systems biology, which attempts to integrate diverse sources of molecular data and generate a more complete understanding of biological phenomena, an understanding which introduces the notion of emergence.

Systems biology

In brief, systems biology is an approach to biology that uses complex computational and mathematical tools to make sense of the vast amounts of data generated by genome sequencing projects and other molecular data-gathering exercises (Auffray *et al.,* 2003). It is based on the realization that the interactions between biological molecules and the networks that result are far too complex to be analysed without computational techniques. A key aim of the field is to produce dynamic *in silico* models of biological systems.

As with most new fields there is no consensus on the definition of systems biology. One derogatory way of describing it is 'physiology with advertising' (Interview 34). And it has been pointed out that the field fits conveniently into current fashions for network thinking (Bonneuil and Gaudillière, 2007). Systems biologists argue, however, that what makes the field new is the kinds of technologies that are being used to study biological systems, the accumulated molecular data, and, perhaps most importantly, the integration of many different types of data.

Systems biology and molecular biology

It is helpful to compare systems biology with molecular biology, to draw out some of the key differences. Systems biology is often portrayed as being the biological revolution which will replace molecular biology. For example, a scientist working in one of the new institutes for systems biology says: 'We're now going to have to create a new way of thinking about biology that's going to be as great a revolution as the molecular revolution was' (Interview 11).

Commentators such as Keller note that 'the reductionist phase of genetic research is now over' (2005: 103), and one of the central claims made by many systems biologists is that their field is not reductionist, and in fact is a reaction to 'the essential failure of the reductionist agenda' (Interview 20). One scientist says revealingly that systems biology is 'the name of the crisis; it's the name of the fright that everyone's gone into about having all the pieces and still not knowing how biology works' (Interview 34).

Some see molecular biology as a detour in the history of biology, and they portray it as the antithesis of systems biology (Interview 11 and Interview 34). A systems biologist, for example, says: 'It's still very much an ''us and them'' thing between the molecular and the systems people' (Interview 20). This can even influence scientific work, since 'practicing systems biologists are often hindered by paradigm battles with molecular biologists' (Boogerd *et al.,* 2007: 5). Others, however, argue for more of a continuation between the two: 'systems biology is based on the progress of molecular biology because we need to know components, but knowing components is not knowing life' (Interview 33).

Emergence in systems biology

According to some interpretations, a key feature of systems biology is emergence. Van Regenmortel says that '''emergence'' has appeared as a new concept that complements ''reduction'' when reduction fails' (2004: 1016). Some commentators 'maintain that the concept of emergence is destined to be associated with systems thinking in much the same way that reductionism has come to be regarded as molecular biology's philosophical counterpart' (Powell and Dupré, forthcoming: 9).

Emergence is a concept that is notoriously hard to pin down, and the brief attempt I make here will, I hope, serve my purposes of understanding the implications of emergence for intellectual property. The traditional idea of emergence is that something is more than the sum of its parts (which explains the comment of one systems biologist: 'Is the sum greater than the parts? If it's not, it's not systems biology', Inteview 34). Another way of explaining this is to say that the characteristic properties of the whole cannot be deduced from the most complete knowledge of the properties of the constituents (see Broad, 1925). In this way unpredictability is a key feature of emergence (Hodgson, 2000). An example of an emergent property is 'wetness'; a single molecule alone cannot be wet, only a collection of molecules can (Gilbert and Sarkar, 2000). Another evocative example of emergence is given in respect to systems biology:

> What is the difference between a live cat and a dead one? One scientific answer is 'systems biology'. A dead cat is a collection of its component parts. A live cat is the emergent behaviour of the system incorporating those parts. (*Nature,* 2005: 1)

This example is interesting not only for its colour but also because it links emergence to the idea of something being alive. Emergence is closely connected to notions of life, since: 'Living systems being nonlinear dynamical systems, have properties different from their constituents in isolation' (Boogerd *et al.*, 2007: 12). This point will become important in respect to the discussion of synthetic biology below.

Some commentators distinguish between weak and strong emergence (Boogerd *et al.*, 2007). Weak emergence is where it is not possible to explain or predict the properties of an emergent object, because the components work differently together than they do apart, but such an explanation may be possible in the future, with increased knowledge and understanding of the phenomena. Strong emergence is where 'system behaviour cannot be inferred or predicted from the behavior of components in isolation' (Boogerd *et al.*, 2007: 330). In this case it is not possible in principle to predict emergent properties from first principles (Richardson and Stephan, 2007).

There is much discussion of the nature of emergence, which is not, of course, only found in biological contexts, but is also present in social life, and in law (Hodgson, 2000). But what is of immediate concern to me here is how the concept is used in scientific practice. Many biologists treat emergence as if it simply involves taking context into account (Powell and Dupré, forthcoming). If context is important in understanding a biological phenomenon then it makes sense to assume that an understanding of constituent parts isolated from their context will never lead to a complete explanation of this phenomenon (Gilbert and Sarkar, 2000). A corollary of this point is that environment, or context, becomes more important in systems biology than it was in reductionist molecular biology. As the boundaries of a biological system become looser and more permeable, and less causally decoupled from the environment, so the system becomes less amenable to commodification. Another factor which decreases the 'boundability' of biological systems is the fact that they are open: 'they exchange matter and energy with their environment' (Van Regenmortel, 2004: 1017).

It may be counter-productive to attempt to provide a precise definition of emergence. As Powell and Dupré show: 'emergence concepts remain relatively undeveloped, and it may even be that some of their contemporary utility stems from their ambiguity' (forthcoming: 18). What I am calling emergence others may prefer to call wholism, interactionism or organicism (see Gilbert and Sarkar, 2000). The concept of emergence is sufficiently ambiguous and vague to incorporate these different ideas.

Having emphasized the connections between emergence and systems biology it is necessary to note that some commentators argue that systems biology is not genuinely concerned with emergence, but is just reductionism writ large. For example, one critic says of certain varieties of systems biology: 'This is brute-force, geno-centric reductionism in the guise of entireness, rather than a novel integrative approach devoted to wholeness' (Huang, 2000: 471). Although this statement is intended as a criticism of the whole enterprise of systems biology, some systems biologists themselves are explicit about their own reductionist objectives, and do not see the label 'reductionist' as a slur (Interview 7). One, for example, thinks that: 'the systems stuff's really a starting point for the reductionist biology' (Interview 24). Another says: 'What we have got to emphasize is a molecular-level analysis, so we need to be able to trace back emergent properties or life or biology, phenotypes, whatever we're looking at, to the molecular underpinnings' (Interview 9). There is a truism underlying these points that 'science cannot proceed without some dissection and some analysis of

parts' (Hodgson, 2000: 73), and no one I interviewed would have denied this. It would be overly simplistic to imply that systems biology is only concerned with wholes and that there is no place for reductionist analysis in this field.

It remains the case, however, that the dominant discourse of systems biology is one of *anti*-reductionism, and this is something that systems biologists often draw upon when defining their work in opposition to previous molecular biology. This discourse is so pervasive that the BBSRC, the UK's largest funder of systems biology, recently felt the need to reassure the UK's scientific community that:

> BBSRC has not become anti-reductionist as a result of encouraging the uptake of systems biology approaches. BBSRC maintains a neutral position here.... It acknowledges that the molecular-level research it has funded—and continues to fund—is an important part of the picture. (BBSRC, 2006)

Patenting in systems biology

Attempts have been made to commodify systems biology, and it is helpful to examine the patents that have been granted in the field. As we have seen in the discussion of commodification above, patenting suits entities that are fixed, static and excluded from external intervention. This is far from the dynamic and interactive complexity that is the object of study in systems biology.

One systems biologist makes an important point about interactivity and its implications for patenting in systems biology. He says that since that the most important biological properties come from the operation of systems and not from the operation of individual genes: 'if you want to acquire intellectual property ... you can't do so by patenting individual genes, you've got to patent a system or a collection of genes' (Interview 3).

This is one strategy in systems biology patenting, and already there are patents on networks of interacting molecules, which Allarakhia and Wensley (2005) identify as systems biology patents. These patents have given rise to concern that patenting a whole system or network could have negative consequences for further research, since 'actions that result in the enclosing of large research terrains are more likely to have significant impact on technological opportunities available for follow-on developers' (Allarakhia and Wensley, 2005: 1485). The patent model is based on the idea that innovations are discrete and separable from their context. As we have seen, this is not the case with interconnected biological systems. The danger of 'enclosing of large research terrains' is an example of the 'tragedy of the anti-commons' (Heller and Eisenberg, 1998), which is the situation where the existence of patents leads to the neglect of large areas of research which would otherwise be ripe for innovation and exploitation.

There are dissenters to the 'tragedy of the anti-commons' argument (see Caulfield *et al.*, 2006). Adelman (2005), for example, argues that the redundancies of biological systems mean that 'work-arounds' will actually be easier in biology than they would be in other fields, and research questions will be approachable from several different directions. However, I think that Adelman underestimates the interactivity and complexity of biological systems. A 'work-around' in biology is very likely to have unintended and unforeseen knock-on effects on other parts of a biological system, and as a result it is unlikely that totally separate lines of research could be pursued.

Because of this interconnectedness of biological systems, there do appear to be some immediate difficulties with patents on interacting biological networks, which could be thought of as systems biology patents. It is necessary to note here that in attempting to identify systems biology patents there is a definitional problem. There is no class for patents in systems biology per se, so those that other sources have identified as systems biology patents (e.g. Allarakhia and Wensley, 2005; *Nature Biotechnology,* 2005; Russell, 2006) are based on assumptions about the kinds of patents that they think are representative of the field.

Apart from patents on biological networks, other examples given of systems biology patents are on computer-based models of biological systems. This is because most systems biology companies are attempting to simulate disease and drug action *in silico* (Mack, 2004). For example, the company Optimata has been granted a patent which allows 'virtual trials' of drugs on a computer (Russell, 2006). Other patents are on biosimulation tools with names like 'virtual patient', 'virtual human' or 'visual cell' (Uehling, 2003). There are similar patent applications pending on computer models, including a method of constructing a gene network from quantitative data, a biological network model, and a system for simulating the operation of biochemical systems (*Nature Biotechnology,* 2005). As well as bringing up issues about the legitimacy of patenting computer software (issues that I do not have space to discuss here), these patents raise interesting questions about what constitutes a model in systems biology.

A model is not simply a description of a biological system, because it is necessarily a simplification of the system (without this simplification it would not be a model, it would just be a representation of the system), and it also incorporates hypotheses about how the system is thought to work (Interview 23). Both of these features could be argued to make biological models amenable to commodification. Because a model limits what it is included within it, it becomes more bounded than the actual biological system. Furthermore, the incorporation of hypotheses about how the system is thought to work gives the model the facility to be predictive. Boogerd *et al.* explain how in systems biology: 'emergent properties are predicted by calculating how the model behaves *in silico* and compared to observations made on the system level' (2007: 6). We also saw above that commodification requires 'unitary objects with stable, *predictable* properties' (McAfee, 2003: 204, emphasis added). If models give us the facility to be predictive, then they may lend themselves to commodification.

One of the key features of emergent phenomena, however, is that it is *not* possible to predict their properties from the properties of the component parts. Here we see that the 'commodification of emergence' in the case of predictive computational models is actually the commodification of weak, rather than strong, emergence, because the definition of strong emergence is that prediction is not possible in principle, however advanced our knowledge of the phenomena. Wynne argues that this emphasis on predictive modelling in systems biology 'effectively deletes the issues of emergence' (2005: 76). This is the case if we think in terms of strong emergence, but not if we are concerned with weak emergence. We may want to conclude, however, along with Wynne, that in terms of strong emergence, the successful predictive modelling of a biological system means that it will come to be understood as something which does not possess emergent properties. According to systems biologists Westerhoff and Kell, systems biology does not embrace strong emergence because

it is guided by the hope that 'life is calculable and can therefore be captured in a computer model' (2007: 64). The research programme that is grounded in this hope that 'life is calculable', and that it is possible to eliminate the unpredictable characteristics of biological phenomena, is systems biology's sister discipline: synthetic biology.

Synthetic biology

The objectives of synthetic biology are to construct novel biological systems and to redesign existing ones. Some see synthetic biology as providing an empirical test of the models in systems biology by trying to build them as functioning biological systems (Barrett *et al.,* 2006). Others see synthetic biology as a distinct field with autonomous aims (Endy, 2005). Nevertheless, synthetic biology and systems biology have much in common. They both developed in the 2000s and they are both concerned with understanding the operation of biological systems by making use of modelling and systems design (Brent, 2004). Both frequently draw analogies between biological systems and electronic circuits, and endorse approaches which draw on engineering and the physical sciences. Synthetic biology can be conceived of as 'the other side of the coin of systems biology' (Victor de Lorenzo in Breithaupt, 2006: 21), or 'systems biology in reverse' (Interview 30), because rather than learning about a biological system, going on to model it *in silico* and then perhaps attempting to build it, synthetic biology *starts* with the construction of the biological system. Most importantly for my purposes, synthetic biology has been called 'a reductionist approach to systems biology' (James Collins in Ferber, 2004: 158).

Synthetic biology is a disparate field and incorporates a range of different activities, from attempts to create protocells (by inserting molecular components into lipid vesicles), to attempts to strip away excess DNA from existing genomes. The disparate nature of the field means that it would be inappropriate to generalize about its approach to emergence (see O'Malley *et al.,* 2008). Some strands of synthetic biology, for example the protocell school, make the complexity and emergence of biological systems explicit topics of investigation. Benner and Sismour, scientists who engage in DNA synthesis, also embrace emergent properties, saying that the aim of synthetic biology is 'to create in unnatural chemical systems the emergent properties of living systems' (2005: 533). But here I will focus on the most well-known and well-funded strand of synthetic biology which aims to make biology into an engineering discipline (Endy, 2005). To this end, these synthetic biologists draw on the engineering principles of standardization, decoupling and abstraction (Brent, 2004) with the objective of developing biological components which are interchangeable, functionally discrete and capable of being combined easily in a modular fashion (i.e. 'plug and play', see Isaacs and Collins, 2005). My argument here is that the attempt to reduce complexity conveniently makes this flavour of synthetic biology well-suited to commodification and to existing appropriation regimes. This is because:

> ... the more dramatically researchers can reduce the complexity of biological organisms, the better they can turn these organisms into instrumentalizable media and simultaneously reduce the difficulties ... of the encounter between biotechnologies and patent law. (Pottage, 2007: 330)

If a biological entity is made into one that it is discrete then it becomes amenable to patenting, and also to open source. My point is that ideas about appropriation, including open source approaches, are influencing the course of research in this branch of synthetic biology. Franklin (2003) observes a similar phenomenon in cloning, a technique which makes reproduction more exact and replicable than it would be otherwise. Drawing on Franklin's (2003) work, Hoeyer notes that it was developments in patenting which made animal cloning into a viable industry because 'cloning circumvents the heterogeneity introduced by sexual reproduction and thus *stabilizes the object of ownership in accordance with the rules of the property regime*' (2007: 341, emphasis added). As in synthetic biology, in cloning scientific and technological developments make the biological entity more stable, less heterogeneous and more suitable for commodification.

Intellectual property in synthetic biology

It is not yet clear how the intellectual property issues in the dominant strand of synthetic biology will play out. At the moment the information needed to build the functional and interchangeable parts (called 'biobricks') that are the focus of much current effort in systems biology is freely available on the web, although there is much discussion about whether it should remain so (see Henkel and Maurer, 2007; Kumar and Rai, 2007; Maurer, 2006; Rai and Boyle, 2007). More complicated constructed networks and systems are the subject of patent applications (e.g. Keasling *et al.*, 2007), and patents on the technology for gene synthesis have recently been the focus of litigation battles between companies (see *GenomeWeb Daily News*, 2008). In contrast to these proprietary strands, the 'biobricks' school often make a point of articulating their open source aspirations (e.g. Keasling, 2005), not least because they explicitly attempt to make synthetic biology more similar to software code, which is modular, standardized and re-useable (explaining why some people think a better name for the field would be 'modular biology', see De Vriend, 2006: 25). Modular entities are ideal for open source because they can be worked on simultaneously by a large community of both users and producers, and this can speed the development of the field.

We should not be lulled into thinking that because this field models itself on open source it is removed from the pressures of intellectual property. Although there are several different understandings of open source in circulation (Stallman, 2007), in its most familiar incarnation—open source software—it relies on copyright and uses open source licences (such as copyleft) to compel inventors to share their intellectual property. A self-consciously open source initiative in the biosciences (Biological Innovation for Open Society [BIOS]) produces biological licences where members agree not to assert their intellectual property rights against one another (BIOS, 2008). In these cases, open source itself depends on the existence of prior property rights. Rather than being a substitute for intellectual property, open source is perhaps more correctly conceived of as a mosaic of private property (Biagioli, 2007). For this reason appropriation is just as important in open source as it is in more conventional property rights (Kumar and Rai, 2007; Rai and Boyle, 2007).

In forcing biology into the mould of engineering, by developing discrete and substitutable parts, synthetic biology is simultaneously making biology better fit intellectual property regimes. This is not a coincidence, because patent law developed in the context of industrial manufacturing (see Pottage and Sherman, 2007). It is also consistent with the direction of

biotechnology more generally, which can be seen as 'relentlessly pursuing the program of making every element of the world programmable or susceptible to engineering' (Pottage, 2007: 340).

The reduction of complexity

For some, the reduction of complexity needed to make biology into an engineering discipline is not merely an instrumental aim, but is based on a faith that synthetic biology will ultimately lead to 'the elucidation of the underlying simplicity' of nature (Palsson, 2000: 1149). Many synthetic biologists hope that the complexity of biological systems, a key concern in systems biology, might be an eliminable accident of historical accumulations over evolutionary time (Balaram, 2003). Programmatic statements along these lines are common. For example, Heinemann and Panke say: 'As the complexity of existing biological systems is the major problem in implementing synthetic biology's engineering vision, it is desirable to reduce this complexity' (2006: 2793).

The reduction of complexity may not be achievable, however. Synthetic biologists such as those in Ron Weiss's group advise that: 'it may be prudent to treat some biological uncertainties as fundamental properties of individual cell behavior' (Andrianantoandro *et al.*, 2006: 13). They continue in a way that reminds us of the understanding of emergence as dependence on context:

> A biological device has no meaning isolated from a module; a module has no meaning isolated from a cell; a cell has no meaning isolated from a population of cells. This contextual dependence is an essential feature of living systems. (2006: 13)

The concern here is that by attempting to eliminate complexity and contingency, synthetic biologists might end up losing sight of the emergent properties that define living systems, which are themselves historical accumulations, being the result of billions of years of evolution (Balaram, 2003; Dupré, 2007). Andrianantoandro *et al.* stress that a recognition of the contextual dependence of living systems is necessary to engineer them successfully, and that the 'notions of standardization, decoupling, and abstraction must therefore be recast to better reflect the complexity of the cellular contexts' (2006: 12). In this way they acknowledge that biological systems may not be fully susceptible to engineering goals. Marguet *et al.* (2007) also worry that if synthetic biology's standardization agenda is pushed too far, this will remove the flexibility that is needed for engineered systems to be useful, which will result in the design of synthetic systems that will ultimately fail. Wimmer predicts this in saying that 'the engineers will find out that the bacteria are just laughing at them' (quoted in Breithaupt, 2006: 23).

If the complexity of biological systems is inescapable, then commercialization will have to adapt to this. Andrianantoandro *et al.* suggest that, rather than producing standardized parts, synthetic biologists could take into account uncertainty and context-dependence and engage in 'on demand, just-in-time customization of biological devices and components, which need not behave perfectly' (2006: 13). But this goes against the grain of the field overall, which is optimistic that it will succeed in making biology more like engineering, and hence more easily commodifiable.

Perhaps the most (in)famous synthetic biology patent application is Craig Venter's application, filed in May 2007, for the smallest genome needed for a living organism (Glass *et al.,* 2007). On a superficial level, this patent could be seen to be founded on reductionist assumptions, because it is a patent on DNA as the essential constituent of a living organism. However, closer analysis of the patent shows that the context is a crucial constituent. The genome will only work if implanted into a 'rich bacterial medium', which possesses properties that are undefined in the patent. Since the environment is a crucial part of the patent, there is scope for emergence in this 'patent on life'.

Synthetic biology tries to avoid the problems associated with emergence by eliminating all the messy contingencies and complexities of biological systems, in this way making them amenable to certain reductionist visions of commodification (perhaps sneaking in some context by the back door, as in the Venter patent). Whether attempts to reduce biological complexity and commodify emergence will succeed is an empirical question, but it is one whose answer will have important implications for intellectual property. If biological systems can be shaped into the form necessary for them to be exchanged in the market economy, we may have to change our understanding of what 'life' is in the process.

This point brings us back to the issues of 'disentanglement' raised at the start of the article. In attempting to reduce the complexity of biological systems, and shape them into exchangeable parts well-suited to commodification, synthetic biology is itself engaged in 'disentanglement'. Furthermore, this process of disentanglement is contaminated with pre-existing ideas about which forms of intellectual property would be most appropriate for the developing technology. This is particularly important because synthetic biology does not simply aim to describe or to represent life; it aims to create it. We do not merely have an example of 'intervening' here, where scientific effects are found only in the context of a certain experimental situation (see Hacking, 1983). In synthetic biology the intervention into nature is more profound, because synthetic biology is the deliberate attempt to design living organisms. Synthetic biology, like other biotechnologies that have preceded it, works by 'extending the reach of human manufactures into the texture of life itself' (Pottage, 2007: 324). The fact that our creations of potentially new life forms are heavily influenced by certain preconceptions about appropriation may be worrying to some.

Concerns have been expressed for many decades about the potential influence of commercialization pressures on the content of scientific research, but it has proved difficult to give specific examples of how the content of the research is itself influenced by commercial pressures. In the case of synthetic biology we can see economic considerations about the nature of property influencing the direction of the development of the field, and influencing it in a way that could have profound future implications.

This is not to argue for some kind of economic determinism, where intellectual property concerns dictate the course of scientific research. We clearly have a case of 'co-production' of the scientific and the social/legal here (Jasnaoff, 2004). For examples of influence in the other direction, we have seen how gene patenting has been heavily influenced by the molecular biological idea that genes are a kind of chemical molecule, and how patenting as an institution was itself strongly influenced by the engineering and manufacturing paradigm of the early nineteenth century (Pottage, 2007). It is also likely that intellectual property regimes will be further influenced by the developments in systems and synthetic biology that I have been addressing here. But being aware of the interactions between biological and

patenting spheres is not to take force away from the point that our ideas about appropriation may come to shape our ideas about the nature of living things.

Emergence in policy debates and public discourses

My examples of synthetic and systems biology show that there are two different regulatory paths that could be taken in response to the integrative life sciences. On the one hand, as discussed in respect to synthetic biology above, effort may go into shutting down the unpredictabilities and complexities associated with emergence so that life fits better into existing ownership regimes. On the other hand, the problems with commodifying the emergent objects of systems biology, as well as the views of those synthetic biologists who doubt that biological complexity can ever be successfully 'reduced', may lead us to acknowledge that it is not possible to commodify emergent phenomena. This could lead to new ways of thinking about appropriation in the life sciences in general and could take regulation in new directions.

For example, we saw above how the appropriation of interconnected and networked biological systems could lead to the tragedy of the anti-commons. In situations such as this, an argument which is often made is that it is more economically efficient to keep these biological systems in the public domain (Allarakhia and Wensley, 2006) and 'outside the world of property' (Rai and Boyle, 2007). Doing this would involve giving up on the attempt to commodify emergence. There is also Andrianantoandro *et al.*'s (2006) suggestion that with emergent systems all we can aspire to is bespoke customization of biological components, the results of which would be imperfect and retain elements of unpredictability. This just-in-time customization would not demand the reductionism associated with commodification.

A recognition of the irreducibility of biological systems could perhaps have broader consequences. Thinking of the objects of biology in this way could lead to a shift in mind-set to incorporate context and indeterminacy. It could even be the case that the discourses of emergence and complexity we find in systems biology will be taken up more broadly (perhaps tying into popular forms of holistic thinking). This may lead to the development of new and as yet unimagined forms of regulation more aligned with these ways of thinking in the biological sciences. This, in turn, could change the tone of discussions about the implications of new biotechnologies.

Alternatively, and probably more realistically, the pressures to reduce complexity may dominate, and the route taken by synthetic biology may come to dictate regulatory thinking. We saw above how the engineering approach that synthetic biology adopts is historically tied to intellectual property regimes, and the combination of the instrumental power of engineering approaches and the economic pressures to commodify may prove irresistible. Additionally, in comparison to systems biology, synthetic biology's reductionist agenda may relate more easily to culturally pervasive notions of the importance of DNA (Ashcroft, 2003). Even though it is a newer and less cohesive field, synthetic biology is already receiving much more public, media and policy attention than systems biology. Nature's subtlety and recalcitrance may appear to be an obstacle at the moment, but in the future we may see life being reshaped in a way that fits better with economic imperatives.

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References

Adelman, D.E. (2005). A fallacy of the commons in biotech patent policy. *Berkeley Technology Law Journal, 20*, 985–1030.

Allarakhia, M., & Wensley, A. (2005). Innovation and intellectual property rights in systems biology. *Nature Biotechnology, 23*(12), 1485–1488.

Amgen Inc. v. *Chugai Pharmaceutical Co.* (1991). URL (accessed October 2008): http://vlex.com/vid/37355922

Andrianantoandro, E., Basu, S., Karig, D.K., & Weiss, R. (2006). Synthetic biology: New engineering rules for an emerging discipline. *Molecular Systems Biology*, URL (accessed October 2008): http://www.nature.com/msb/journal/v2/n1/full/msb4100073.html

Ashcroft, R.E. (2003). The double helix 50 years on: Models, metaphors, and reductionism. *Journal of Medical Ethics, 29*: 63–64.

Auffray, C., Imbeaud, S., Roux-Rouquié, M., & Hood, L. (2003). From functional genomics to systems biology: Concepts and practices. *Compte Rendus Biologies, 326*(10), 879–889.

Balaram, P. (2003). Synthesising life. *Current Science, 85*(11), 1509–1510.

Balmer, B.L. (1996). Managing mapping in the human genome project. *Social Studies of Science, 26*(3), 531–573.

Barrett, C.L., Kim, T.Y., Kim, H.U., Palsson, B.Ø., & Lee, S.Y. (2006). Systems biology as a foundation for genome-scale synthetic biology. *Current Opinion in Biotechnology, 17*(5), 1–5.

BBSRC (2006). Towards a vision and road map for systems biology. Report from the BBSRC Vision for Systems Biology Workshop, Exeter, 16–17 March.

Behrens, T.R., & Gray, D.O. (2001). Unintended consequences of co-operative research: Impact of industry sponsorship on climate for academic freedom and other graduate student outcomes. *Research Policy, 30*(2), 179–199.

Benner, S.A., & Sismour, A.M. (2005). Synthetic biology. *Nature Reviews Genetics, 6*, 533–543.

Biagioli, M. (2007). Denaturalizing the public domain: How to use science studies to rethink IP. Talk at the University of Edinburgh, 10 December.

BIOS (2008). URL (accessed January 2008): http://www.bios.net/daisy/bios/licenses/398.html

Blumenthal, D., Causino, N., Campbell, E., & Lewis, K.S. (1996). Relationships between academics institutions and industry in the life sciences—An industry survey. *New England Journal of Medicine, 334*(6), 368–373.

Bonneuil, C., & Gaudillière, J.-P. (2007). Navigating post-Fordist DNA: Network, regulations and variability in genomics and society. Presentation at the International Society for the History, Philosophy and Social Studies of Biology, University of Exeter, 25–29 July.

Boogerd, F., Bruggeman, F.J., Hofmeyr, J.-H.S., & Westerhoff, H.V. (Eds) (2007). *Systems biology: Philosophical foundations*. Amsterdam: Elsevier.

Breithaupt, H. (2006). The engineer's approach to biology. *EMBO Reports, 7*(1), 21–24.

Brent, R. (2004). A partnership between biology and engineering. *Nature Biotechnology, 22*(10), 1211–1214.

Broad, C.D. (1925). *The mind and its place in nature*. London: Routledge & Kegan Paul.

Callon, M. (Ed.) (1998). *The laws of the markets*. London: Blackwell Publishers.

Callon, M. (2007). What does it mean to say that economics is performative? In D. MacKenzie, F. Muniesa, & L. Siu (Eds.), *Do economists make markets? On the performativity of economics*. 311–357 Princeton. NJ: Princeton UP.

Caulfield, T., Cook-Deegan, R.M., Kieff, FS, & Walsh, J.P. (2006). Evidence and anecdotes: An analysis of human gene patenting controversies. *Nature Biotechnology, 24*(9), 1091–1095.

Crick, F. (1966). The influence of physics on molecular biology (Cherwell-Simon Lecture), URL (accessed October 2008): http://profiles.nlm.nih.gov/SC/B/B/D/H/_/scbbdh.pdf

De Vriend, H. (2006). *Constructing life: Early social reflections on the emerging field of synthetic biology*. The Hague: Rathenau Institute. Working Document 97, URL (accessed June 2008): http://www.rathenauinstituut.com//showpage.asp?steID=2&item=2644

Dupré, J. (2007). Is it not possible to reduce biological explanations to explanations in chemistry and/or physics. Egenis working paper.

Endy, D. (2005). Foundations for engineering biology. *Nature, 438*(24 November), 449–453.

Etzkowitz, H., & Leydesdorff, L. (2001). *Universities and the global knowledge economy: A triple helix of university–industry–government relations*. London: Continuum.

Ferber, D. (2004). Microbes made to order. *Science, 303* (9 January), 158–161.

Franklin, S. (2003). Kinship, genes, and cloning: Life after Dolly. In A. Goodman, D. Heath, & S. Lindee (Eds.), *Genetic nature/culture: Anthropology and science beyond the two-culture divide*, 95–110. Berkeley: U California Press.

GenomeWeb Daily News (2008). Codon Devices, Blue Heron settle litigation. *GenomeWeb Daily News* 31 March, URL (accessed July 2008): http://www.genomeweb.com/issues/news/145956-1.html

Gibbons, M., & Wittrock, B. (Eds) (1985). *Science as a commodity*. Essex: Longman.

Gibbons, M., Limoges, C., Nowotny, H., Schwartzman, S., Scott, P., & Trow, M. (1994). *The new production of knowledge*. London: SAGE.

Gilbert, S.F., & Sarkar, S. (2000). Embracing complexity: Organicism for the 21st century. *Developmental Dynamics, 219*(1), 1–9.

Glass J.I., Smith H.O., Hutchinson III C.A., Alperovich N.Y., & N. Assad-Garcia (Inventors); J. Craig Venter Institute, Inc. (Assignee). 2007, October 12. Minimal bacterial genome. United States patent application 20070122826.

Hacking, I. (1983). *Representing and intervening: Introductory topics in the philosophy of natural science*. Cambridge: Cambridge UP.

Heinemann, M., & Panke, S. (2006). Synthetic biology—Putting engineering into biology. *Bioinformatics, 22*(22), 2790–2799.

Heller, M.A., & Eisenberg, R.S. (1998). Can patents deter innovation? The anticommons in biomedical research. *Science, 280*(1 May), 698–701.

Hellström, T., & Jacob, M. (2005). Taming unruly science and saving national competitiveness: Discourses on science by Swedish strategic research bodies. *Science, Technology, & Human Values, 30*(4), 443–467.

Henkel, J., & Maurer, S.M. (2007). The economics of synthetic biology. *Molecular Systems Biology* 3: 117, URL (accessed October 2008): http://www.nature.com/msb/journal/v3/n1/full/msb4100161.html

Hodgson, G.M. (2000). The concept of emergence in social science: Its history and importance. *Emergence, 2*(4), 65–77.

Hoeyer, K. (2007). Person, patent and property: A critique of the commodification hypothesis. *BioSocieties, 2*, 327–348.

Holm, P. (2007). Which way is up on Callon? In D. MacKenzie, F. Muniesa, & L. Siu (Eds.) *Do economists make markets? On the performativity of economics*, 225–243. Princeton, NJ: Princeton UP.

Huang, S. (2000). The practical problems of post-genomic biology. *Nature Biotechnology, 18*(5), 471–472.

Isaacs, F.J., & Collins, J.J. (2005). Plug and play with RNA. *Nature Biotechnology, 23*(3), 306–307.

Jacob, M. (2003). Rethinking science and commodifying knowledge. *Policy Futures in Education, 1*(1), 125–142.

Jansanoff, S. (Ed.) (2004). *States of knowledge: The co-production of science and the social order*. London: Routledge.

Keasling, J. (2005). The promise of synthetic biology. *The Bridge, 35* (4), URL (accessed July 2008): http://www.nae.edu/NAE/bridgecom.nsf/weblinks/CGOZ-6KJTMT?OpenDocument

Keasling, J., Vincent, M., Pitera, D., Kim, S.-W., Sydnor, W.T., Yasuo, Y. *et al.* (2007). USPTO Patent Application 20070166782: Biosynthesis of isopentenyl pyrophosphate.

Keller, E.F. (2005). The century beyond the gene. *Journal of the Biosciences, 30*(1), 101–108.

Kumar, S., & Rai, A.K. (2007). Synthetic biology: The intellectual property puzzle. *Texas Law Review, 85*, 1745–1768.

Lind, D., & Barham, E. (2004). The social life of the tortilla: Food, cultural politics, and contested commodification. *Agriculture and Human Values, 21*(1), 47–60.

Mack, G.S. (2004). Can complexity be commercialized? *Nature Biotechnology, 22*(10), 1223–1229.

Marguet, P., Balagadde, P., Tan, C., & You, L. (2007). Biology by design: Reduction and synthesis of cellular components and behaviour. *Journal of the Royal Society Interface*, URL (accessed October 2008): http://www.duke.edu/~you/publications/marguet_etal.pdf

Maurer, S. (2006). Reporter notes on Synthetic Biology/Economics Workshop: Choosing the Right IP Policy. UC Berkeley Goldman School of Public Policy, 31 March 2006. URL (consulted): http://gspp.berkeley.edu/iths/SynBio%20Workshop%20Report.htm

Marx, K. (1887). *Capital, vol. 1: The process of production of capital*. Trans. S. Moore and E. Aveling, Ed. F. Engels. Moscow: Progress Publishers. URL (accessed December 2007): Marx/Engels Internet Archive http://www.marxists.org/archive/marx/works/1867-c1/

McAfee, K. (2003). Neoliberalism on the molecular scale: Economies and genetic reductionism in biotechnology battles. *Geoforum, 34*(2), 203–219.

Mirowski, P., & Sent, E.M. (2002). *Science bought and sold: Essays in the economics of science*. Chicago: U Chicago Press.

Mirowski, P., & Sent, E.M. (2007). The commercialization of science and the response of STS. In E. Hackett, O. Amsterdamska, J. Wajcman, & M. Lynch (Eds.), *Handbook of science and technology studies*, 635–689. Cambridge, MA: MIT Press.

Moss, L. (*2003*). *What genes can't do*. Cambridge, MA: MIT Press.

Nature Biotechnology (2005). Recent patent applications in systems biology. *Nature Biotechnology, 23*(8), 939.

Nature (2005). In pursuit of systems. *Nature, 435* (5 May), 1.

Nowotny, H., Scott, P., & Gibbons, M. (2001). *Re-thinking science: Knowledge and the public in an age of uncertainty*. London: Polity Press.

O'Malley, M., Powell, A., Davies, J., & Calvert, J. (2008). Knowledge-making distinctions in synthetic biology. *BioEssays, 30*(1), 57–65.

Packer, K., & Webster, A. (1996). Patenting culture in science: Reinventing the scientific wheel of credibility. *Science, Technology, & Human Values, 21*(4), 427–453.

Palsson, B. (2000). The challenges of in silico biology. *Nature Biotechnology, 18*(11), 1147–1150.

Parry, B.C. (2008). Entangled exchange: Reconceptualising the characterisation and practice of bodily commodification. *Geoforum, 39*(3), 1133–1144.

Pearson, H. (2006). What is a gene? *Nature, 441*(25 May), 399–401.

Pottage, A. (2007). The socio-legal implications of the new biotechnologies. *Annual Review of Law and Social Science, 3*, 321–344.

Pottage, A., & Sherman, B. (2007). Organisms and manufactures: On the history of plant inventions. *Melbourne University Law Review, 31*(2), 539–568.

Powell, A., & Dupré, J.A. (forthcoming). From molecules to systems: The importance of looking both ways. *Studies in the History and Philosophy of the Biological and Biomedical Sciences*.

Powell, A., O'Malley, M.A., Müller-Wille, S., Calvert, J., & Dupré, J.A. (2007). Disciplinary baptisms: A comparison of the naming stories of genetics, molecular biology, genomics and systems biology. *History and Philosophy of the Life Sciences, 29*, 5–32.

Rai, A., & Boyle, J. (2007). Synthetic biology: caught between property rights, the public domain, and the commons. *PLoS Biology, 5*, URL (consulted October 2008): http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.0050058

Richardson, R.C., & Stephan, A. (2007). Emergence. *Biological Theory, 2*(1), 91–96.

Russell, J. (2006). Optimata, Entelos win simulation patents. *Bio-IT World*, 26 January. URL (accessed October 2008): http://www.bio-itworld.com/newsitems/ 2006/january/01-26-06-news-biosimulation?Itemid=19924&terms=optimata

Stallman, R. (2007). Why 'open source' misses the point of free software. Philosophy of the GNU Project, Free Software Foundation, 24 September. URL (accessed October 2008): http://www.gnu.org/philosophy/open-source-misses-the-point.html

Schaffer, S. (2003). Enlightenment brought down to earth. *History of Science, 41*(3), 257–268.

Thackray, A. (Ed.) (1998). *Private science: Biotechnology and the rise of the molecular sciences*. Philadelphia: U Pennsylvania Press.

Sharp, L.A. (2000). The commodification of the body and its parts. *Annual Review of Anthropology, 29*, 287–328.

Slaughter, S., & Rhoades, G. (1996). The emergence of a competitiveness research and development policy coalition and the commercialisation of academic science and technology. *Science, Technology and Human Values, 21*(3), 303–339.

Uehling, M.D. (2003). Model patient. *Bio-IT World* 15 December. URL (accessed October 2008) http://www.bio-itworld.com/archive/121503/trials.html?terms=Uehling+2003

Van Regenmortel, M.H.V. (2004). Reductionism and complexity in molecular biology. *EMBO Reports, 5*(11), 1016–1020.

Westerhoof, H.V., & Kell, D.B. (2007). The methodologies of systems biology. In F. Boogerd, F.J. Bruggeman, J.-H.S., Hofmeyr, & H.V., Westerhoff (Eds.), *Systems biology: Philosophical foundations*. Amsterdam: Elsevier.

Wynne, B. (2005). Reflexing complexity: Post-genomic knowledge and reductionist returns in public science. *Theory, Culture & Society, 22*(5), 67–94.