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Organism, machine, artifact: The conceptual and normative challenges of synthetic biology ☆

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ABSTRACT

Synthetic biology is an emerging discipline that aims to apply rational engineering principles in the design and creation of organisms that are exquisitely tailored to human ends. The creation of artificial life raises conceptual, methodological and normative challenges that are ripe for philosophical investigation. This special issue examines the defining concepts and methods of synthetic biology, details the contours of the organism–artifact distinction, situates the products of synthetic biology vis-à-vis this conceptual typology and against historical human manipulation of the living world, and explores the normative implications of these conclusions. In addressing the challenges posed by emerging biotechnologies, new light can be thrown on old problems in the philosophy of biology, such as the nature of the organism, the structure of biological teleology, the utility of engineering metaphors and methods in biological science, and humankind's relationship to nature.

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Synthetic biology is a new discipline that aims to apply rational engineering principles to the creation of biological organisms, subsystems and their components (Endy, 2005). Significant milestones achieved in the field to date include the de novo synthesis of functional viruses (Cello, Paul, & Wimmer, 2002), the creation of a novel lineage of bacterium from a wholly synthetic bacterial genome (Gibson et al., 2010), and the compiling of a registry of standard biological parts that synthetic biologists can draw upon as the building blocks for the construction of synthetic organisms designed for a wide range of human purposes (O'Malley, Powell, Davies, & Calvert, 2008). Techniques that are currently being developed in the synthetic life sciences will eventually enable humans to engage in the large-scale design and creation of novel organisms, and perhaps even radically different forms of life, that are exquisitely tailored to human ends.

Authors commenting on the philosophical implications of synthetic biology have often remarked on its tendency to blur boundaries between supposedly discrete ontological categories, such as between organism and machine, living thing and artifact, 'the natural' and 'the artificial'—ontological outcomes that many authors find ethically disquieting. Thus far, however, discussions of these ontological and normative issues have remained relatively underdeveloped in the literature. What precisely does it mean for an organism to be 'synthetic' or 'artificial'? How do the processes and products of synthetic biology differ from other means of modifying, deriving, and understanding the causal structure of living systems? Is the engineering approach that is characteristic of synthetic life science unique, or simply a rigorous application of the technological, artifactual and mechanicistic thinking that pervades much of modern biology? Does thinking of organisms (synthetic or otherwise) as 'living machines' enhance our abilities to understand, control, construct and predict the behavior of living things, or does it impede progress toward these goals? In what ways does our increasing technological stance toward the natural living world, as reflected in the achievements of synthetic biology, have the potential to transform humankind's relationship to nature, and does this transformation raise ethical concerns?

☆ The idea for this special issue emerged from a workshop held at the University of Copenhagen in January, 2011 as a part of the UNIK Synthetic Biology project in collaboration with the Oxford Uehiro Centre for Practical Ethics, University of Oxford.

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This special issue works toward answers to these questions by examining the defining methods and concepts of synthetic biology, detailing the contours of the organism–machine and organism–artifact distinctions, situating the products of synthetic biology vis-à-vis this conceptual typology and against the deep history of human manipulation of the living world, and exploring the normative implications of these conclusions. The issue is comprised of nine original research papers that engage the above philosophical questions through theoretical analysis and rigorous argumentation that is informed by the latest work in biological science. By reflecting on the conceptual and methodological challenges posed by emerging disciplines such as synthetic life science, new light can be thrown on traditional problems in the philosophy of biology, such as the nature of the organism, the utility of engineering metaphors in biological science and science education, accounts of biological function and teleology, and the ethical and social implications of the ongoing revolution in biotechnology.

1. The role of rational engineering principles in the understanding and design of biological systems

A defining feature of synthetic biology is its attempt to apply rigorous engineering principles to the design of biological systems. This involves drawing from an expanding catalog of standardized biological 'parts' (e.g., genetic sequences) with well-understood, predictable and reasonably isolatable properties that can be arranged in various combinations in the service of preconceived design goals. **Pablo Schyfter (this issue)** documents the importance of this engineering ideal for the demarcation and evolution of synthetic biology as an emerging field in its own right. Through a series of interviews with practicing synthetic biologists and an analysis of ethnographic data, Schyfter shows how the drive to make, build and create things—in contrast to the aim of producing knowledge claims per se—is a defining feature of the synthetic life sciences, with significant implications for the methods, organization, epistemology, and ontology of synthetic biological research and its demarcation from other closely related fields.

Unlike systems biology, which has largely epistemic ends insofar as it aims to understand the causal structure of 'naturally occurring' biological systems, synthetic biology endeavors to construct, out of a harvestable biological substrate, novel entities with desired functional properties. And unlike the manipulation of naturally occurring systems as effected by (e.g.) genetic engineering, synthetic biology aims to design organisms wholesale through the application of rational engineering principles, promising unprecedented control over organisms and their properties. This control can be achieved either from the 'ground up' through the rational composition of basic building blocks (such as BioBricks™), or from the 'top down' by stripping existing organisms to the bare functional necessities—creating a 'minimal microbe'—and then adding specialized capacities on top of this basic functional platform.

Although the engineering orientation serves to demarcate the field of synthetic biology in the eyes of many of its practitioners, do the actual practices of synthetic life science vindicate the rational engineering ideal as applied to the design and re-design of living systems? Several contributors to this issue are skeptical that rational engineering principles will prove fruitful in the design of organisms to human specification, given the nonlinear and emergent complexity of living systems and the ubiquity of developmental constraints (due, e.g., to epistatic and pleiotropic interactions). The complexity of the genotype–phenotype map presents serious epistemic and causal obstacles to modular biological design—and may help to explain why the actual practice of synthetic biologists departs significantly from this engineering ideal (see O'Malley, 2009).

In illustrating this point, **Tim Lewens (this issue)** draws upon an example from the field of evolutionary electronics to show how irrational (or nonrational) evolutionary processes can be harnessed to produce better design than would be possible through the use of rational engineering methods alone. Blind mechanisms of variation and natural selection can be used to explore regions of design space that are causally invisible or otherwise epistemically off-limits to forward-looking rational engineers. If nonrational design processes have proven their mettle in the development of non-living artifacts like computer circuits, they are likely to play an even more central role in designing the far more complicated causal interactions that comprise living systems. In fact, Lewens offers reasons to think that nonrational evolutionary processes will in many cases produce biological design that is functionally superior to that generated through rational engineering approaches (for a counterpoint to this view, see Powell and Buchanan (2011)).

Maartin Boudry and Massimo Pigliucci (this issue) also stress the importance of recognizing the limited value of engineering concepts, methods and principles in the understanding and design of biological systems. Whereas Lewens takes a somewhat salutary view of the rational engineering methods deployed in synthetic biology in light of our epistemic limitations and the programmatic demands of the discipline, Boudry and Pigliucci are skeptical of the use of engineering concepts, metaphors and methodologies in biology full stop, including in synthetic biology. They see rational engineering-type approaches to organismic design as a hindrance to the creative goals of synthetic biology and as an obstacle to biological knowledge, communication and education more generally. At bottom, their worry is that "the systematic application of engineering metaphors to a domain that is fundamentally different from the world of human artifacts may send scientists on a wild goose chase" (p. X).

While Boudry and Pigliucci concede that engineering metaphors may be of some heuristic value, they contend that such metaphors break down at the molecular level, and emanate from an excessive penchant for molecular-genetic reductionism, a commitment to unwarrantedly strong forms of adaptationism, and a vastly over-simplified view of the genotype-phenotype map. Engineering analyses in evolutionary biology can help us to discern the function (and hence the 'ultimate' explanation) of a given organismic feature, and perhaps contribute to an understanding of how certain biomechanical 'design problems' were solved. But unlike intentionally designed artifacts, which are constructed with some human end (and perhaps good) in mind, naturally evolved design will often solve ecological design problems in ways that fail to make sense to a rational engineer.

The upshot is that there are significant limitations on the engineering paradigm as a conceptual and methodological framework for designing organisms and understanding their causal structure and evolution. There are also strong indications that processes of blind variation and natural selection can tap into subtle causal interactions that are invisible to our best models of development. Our ability to guide these nonrational evolutionary processes may prove critical to the success of synthetic biology for the foreseeable future.

2. Machine thinking and artificial teleology

Rational engineering approaches in biology are closely connected to the machine conception of the organism, which has its origins in Cartesian natural philosophy. Although biologists are well aware of the limitations of 'machine thinking' and its tensions with our current understanding of developmental systems, machine metaphors continue to pervade contemporary biological