

A nature with their nature

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Synthetic biology eludes conclusive definition. As an incipient field, discipline, project, or ambition, it takes no singular form, nor does its membership (which is heterogeneous) practice in a synchronized manner.¹ Nonetheless, synthetic biologists have clustered into semi-distinct factions, each of which has its own particular understanding of the field and its own particular ways of practicing. Among these is a group that promises to deliver a field of ‘true’ or ‘authentic’ engineering—a field that will carry on as do existing, established disciplines of engineering, but with a living substrate.² The group argues that achieving this aim demands the importing and deployment of principles, ideas, and forms of work from traditional engineering.³ These components, the synthetic biologists argue, will ensure ‘true’ engineering by shaping the new field using established engineering as a model.

This same group dedicates special attention and effort to one principle and practice: rational design. In laying out his vision for synthetic biology, Drew Endy proposes to replace the existing “expensive, unreliable and *ad hoc* research process” with what Tom Knight describes as “the intentional design, modeling, construction, debugging, and testing of artificial living systems.”⁴ Put simply, these researchers and others hope to make planning and building with living stuff as systematic and standardized as building with things like electronic circuitry. Rational design in synthetic biology hinges in part on simulations of living nature as technological artifice. These simulations in turn rely on representations of biology as something that carries an inherent potential for rational design.

In 2010 and 2011, an interdisciplinary, innovative project entitled “Synthetic Aesthetics” paired synthetic biologists with artists and designers in collaborative projects aimed at exploring just what design entails in synthetic biology.⁵ Each pair was given funds to support spending an equal amount of time in the lab and in the studio, along with freedom to explore design as they saw fit. One of these teams—synthetic biologist Fernan Federici and architect David Benjamin—placed rational design and digital simulation at the crux of their work. As already noted, rational design is central to the engineering faction of synthetic biology; digital simulation is one tool that these practitioners have proposed to assist their design work.⁶ The results of Federici and Benjamin’s project offer a useful perspective from which to examine many important aspects of synthetic biology’s pursuit of rational design. Federici and Benjamin’s digital simulations of plant cell growth rested on a collection of representations akin to many of those frequently used in synthetic biology. Most importantly, these representations all involve casting living things as entities carrying design potential. For Federici and Benjamin, plant cells were conceived as logical problem solvers; for synthetic biology, all manner of biological stuff is rationally designable material. In both cases, the practitioners do not capture a singular and freestanding ‘nature of nature’ but instead deliver a nature consistent with *their* nature.

From cells to buildings

Federici and Benjamin’s collaboration made use of their shared interests and combined abilities. In broad terms, the pair studied the self-organizing dynamics of

xylem cells using biological imaging tools and architectural computer simulations. Xylem cells form a part of plants' vascular system. The cells are curious due to their capacity to develop a form of exoskeleton, a structure that helps to give shape to the organism's vascular system. Federici and Benjamin set out to study the self-organizing abilities of xylem cells by simulating how the cells construct their exoskeletons in specific spatial conditions. Studying this phenomenon served a broader and bolder aim: capturing the cells' biological 'logic.'

Federici and Benjamin posited the notion of biological 'logic' as the driving mechanism underlying xylem cells' capacity to build. 'Logic' here refers to the problem-solving capability inherent in these plant cells. The two researchers believe that using imaging tools and computer simulations to identify and capture this 'logic' can serve both synthetic biology and architecture. The former may gain a tool for analyzing how biology organizes; the latter may find novel ways to engage with and harness the living world. For the architect, biological 'logic' might provide techniques for resolving structural problems in innovative and unexpected curious ways, and it could enlist biology as an aid to architecture as more than a reserve of forms to mimic.

To study how xylem cells self-organize and build their structures, Federici and Benjamin introduced artificial walls and boundaries into a colony of the cells, and they then tracked how the cells built their structures within the constrained spaces. In other words, they posed a structural quandary and watched as the xylem cells produced a solution, hoping that simulating the process digitally would reveal the 'logic' underlying the cells' growth. As the cells developed, they were photographed using confocal microscopy. The images of the exoskeletons were then transformed into a point-vector computer model and the growing process was quantified into a body of numerical data. Finally, the pair used Eureqa, a software tool, to develop equations approximating relationships between the data. Federici and Benjamin argued that these equations capture the cells' biological 'logic' in mathematical form.

The team's next experiment involved more direct engagement with architecture and architectural simulations. Federici and Benjamin again created a model based on photographs of the cells. However, rather than quantifying growth and deriving equations, the two treated the model as one of a human-scale structure (such as a building). They explain:

We applied architectural scale, materials, and loading conditions to the 3D model. Then, we supposed that our goals for the architecture-scale exoskeleton were to use the least amount of materials to achieve the least structural displacement. We ran an automated algorithm to generate, evaluate, and evolve multiple design permutations.⁷

Federici and Benjamin argue that the shape of the xylem cells' exoskeleton is one optimized for the conditions under which these cells grow—microscopic spaces and biological materials—and *not* one optimized for the scale, materials, and goals of human design and construction. However, by using architectural optimization software, the team framed xylem cells and their 'logic' as design collaborators and as a design tool, respectively. The cells offer solutions different from those typically proposed by the human architect.

Simulations, representation and the 'out-there'

Methodologically, Federici and Benjamin's work was an exercise in simulation. The pair's models simulate cells and human structures, along with how those cells and structures behave in particular situations. Federici and Benjamin's simulations were of course representations. In fact, the project produced and employed many types of representations, such as photographs, models, numerical data, and equations. These representations, including the computer simulations, were deployed for the purpose of making biological logic something observable and usable. Two key underlying presuppositions drove the project, namely, the beliefs that biological 'logic' exists in itself and that it can somehow be captured—in other words, that it is out there and that we are capable of discovering it.

Commonplace understandings of representation rely on the premise that some 'out-there' must exist to be represented in the first place. Thus, simulations are facsimiles or portrayals of something independently present in the world. However, as Steve Woolgar and Michael Lynch (among others) argue, the supposition of a free-standing 'out-there' is often wrong.⁸ In some instances, the idea of a self-standing entity that representations replicate or approximate fails because without representational tools, the entity cannot be witnessed at all.⁹ Federici and Benjamin's xylem cells are not accessible to us without instruments like microscopy and photography. In other cases, representations are the only reality at hand. The pair's biological 'logic' does not exist in the sense in which we typically use the term; rather, it is present only by way of mathematical equations, not independent spatio-temporal being. This is also the case with synthetic biology's view of a free-standing design potential in living nature; outside this field and its pursuit of a 'true' engineering, there is no assumption of rationality or design potential in biology. Rationality is a matter theorized by synthetic biology, just as biological 'logic' is something of Federici and Benjamin's doing and is characterized by the particularities of their specific collaboration. The idiosyncrasies of the team molded both the process by which the purported biological 'logic' was made 'witnessable' and the form that the resulting representations took. Crucially, this work rested on a particular view of the living things under study—a view that in turn relies on conceptions of design. Specifically, synthetic biology's view of a rationally designable biology rests on an understanding of design that is imported from established engineering.

Federici and Benjamin's work cast the cells as logical entities engaged in rational design, and it did so by way of three interlinked depictions. First, xylem cells are problem solvers (like architects); they practice skillfully. Second, their behavior is ordered (like architectural work); their practice has procedure. Third, this order can be systematized (as is the case with architectural work); the procedure can be arranged. The three suppositions are abstractions of architectural agents, practices and orders, respectively. Thus, in trying to 'find' the 'logic' of biology Federici and Benjamin framed the xylem cells and their growth as agents practicing a vocation that involves systematic practices.

The three depictions support the team's search for 'out-there' biological 'logic.' For Federici and Benjamin, biological 'logic' may not exist materially as do the cells themselves, but nonetheless it is something that the cells 'have.' 'Logic' is not

something *postulated*, but something captured with photography and simulation. Crucially, the pair's concept of 'logic' exists as one part of an overarching depiction of xylem cells as living things engaged in systematic practices. Federici and Benjamin rendered the cells 'logical' by treating them as logical entities.

The potential for rational design

Federici and Benjamin examined and simulated this biological 'logic' by exploring instrumental links between architecture and synthetic biology and by approaching xylem cells as if they are structural problem solvers. Making the cells' 'logic' into something witnessable and functional for epistemic and design practices was a project particular to the pair. The objects under study and the things being produced were *by* and *of* the pair, and they reflected the idiosyncrasies of the collaboration. Synthetic biology presents a similar case.

Representations in synthetic biology seek to draw out what the discipline views as an inherent potential for rational design. As I noted above, one of synthetic biology's most vocal factions champions a view of the field as 'true' or 'authentic' engineering. Synthetic biologists in general promise to deliver innovative technologies using the stuff of living nature, and many argue that such technologies will have positive economic and environmental ramifications. Those who aim at engineering authenticity supplement these promises with visions of particular forms of design and fabrication. Authenticity, they argue, will follow from importing and employing so-called 'engineering principles' such as standardization of parts, decoupling of processes, design-build-test cycles, and rational design.¹⁰ Practitioners hope that such principles can structure engineering work with a biological substrate, just as effectively as the same principles have structured civil engineering work with metal and concrete.

In its work with engineering principles, synthetic biology relies greatly on representations of living things as objects *of* and *for* engineering. Segments of DNA are discussed as discrete 'parts.' When such parts are linked functionally, they become 'devices.' When devices are combined, the result is a 'system.' Systems can then be inserted into a supporting cell, or a 'chassis.' Experimenters comprehend, design, and build their biological artefacts using analogies, many of which are taken from electronics. Practitioners often represent genetic constructs as circuits of logic gates; a string of nucleotides becomes an AND gate, another an OR gate.¹¹ Such depictions cast the relationships and behaviors of living stuff in the mold of human artifice.

Laboratory work based on these representations has delivered biological equivalents of electronic devices like oscillators, switches, and counters.¹² This work and its depictions of living nature are bound by an essential commitment: if synthetic biologists are to design rationally, as do those in established engineering professions, the material which they employ must be *rationally designable*. Researchers argue that "general 'design principles'—profoundly shaped by the constraints of evolution—govern the structure and function of [biological] modules."¹³ Both the modular organization of living things and the rational, designable character of such parts are found in living things themselves. As such, one mission of synthetic biology is "uncovering biological design principles."¹⁴ Doing so is congruous with the

field's ambition to carry out 'authentic' engineering with a living substrate, since "a number of the design principles of biological systems are familiar to engineers."¹⁵ A 2011 publication on techniques and constructs that support "digital-like synthetic biology" states that just as "Boolean logic gates are widely used in electronic circuits to build digital devices, logic operations are encoded in gene regulatory networks that cells use to cascade and integrate multiple environmental and cellular signals and to respond accordingly."¹⁶ The authors do not simply employ an analogy to electronic systems based on Boolean logic. Like other synthetic biologists, they argue that the dynamics underlying electronic circuitry are already present in the biology itself, housed in "biological control modules"¹⁷ that can be exploited and re-engineered. That is, rational behavior—and consequently the potential for rational design and re-design—is a quality of the biology itself.

Federici and Benjamin rendered 'logic' as something inherent in xylem cells, usable by people but ultimately free-standing. Synthetic biology effectively does the same for rationality. This representation is indispensable to a group that aims to create a new type of engineering in the mold of prior forms of engineering. Representations of nucleotides as components that can be disconnected and reconnected in rational and functionally predictable ways serve to render a potential for rational design.¹⁸ As with Federici and Benjamin's 'logic,' this potential is cast as an independent 'out-there.' Synthetic biology can find it, make it witnessable, and harness it to accomplish rational design with biology.

Nonetheless, the potential for rational design is no more an independently existing 'out-there' than is Federici and Benjamin's 'logic.' Synthetic biology's 'out-there' potential exists through the field's representations, and is thus something *by* and *of* that field. Casting living nature as something that carries within it a potential for rational design requires ignoring properties that do not fit the picture of synthetic biology as 'true' engineering, such as irrationality and unpredictability. Doing so allows the potential for rational design to become witnessable and usable. By portraying a capacity that can be exploited by engineering, representations of potential make the stuff of living nature something that synthetic biology can use to design and to build. Moreover, the potential becomes something that helps to authenticate the field, its ambitions, and its work.

Representations are often seen as facsimiles of something else – facsimiles that lack the original's wholeness and that often distort its free-standing truth. In both the specific case of Federici and Benjamin's project and the ongoing case of synthetic biology, representation is not an imperfect journey toward an indelible reality. Instead, representation is an attempt to render things in particular ways for particular ends.

Federici and Benjamin simulated xylem cells as things enrolled for architecture, as instruments for and partners in design. The pair's biological 'logic' is *their* 'logic,' and outside their partnership it does not exist. The entities that Federici and Benjamin studied possess a 'logic' because they were situated in a particular partnership. The living things of synthetic biology carry design potential because they are situated in a particular field with specific ambitions. The field's rational design potential is similarly *its own* vision: a capacity to plan and build with biology and situate synthetic biology in the tradition of engineering.

Representations of biology as mechanical or electronic are not false depictions that are detrimental to some pursuit of truth, but consciously selected portrayals that satisfy a vision of rational design and construction. Synthetic biologists are working to create an identity for 'authentic engineering' that they can enlist as useful for their field. Casting living things as entities that carry a potential for rational design serves that mission. As such, these researchers are not working to capture the single, conclusive 'nature of nature.' Rather, they are seeking to deliver a nature consistent with *their nature—living stuff of engineering and for engineering.*

¹ Adam Arkin, et al., "Synthetic Biology: What's in a Name?" *Nature Biotechnology* 27, no. 12 (2009).

² Drew Endy, "Foundations for Engineering Biology," *Nature* 438, no. 24 (2005); Endy, "Synthetic Biology: Can We Make Biology Easy to Engineer?" *Industrial Biotechnology* 4, no. 4 (2008); Susanna C. Finlay, "Engineering Biology? Exploring Rhetoric, Practice, Constraints and Collaborations within a Synthetic Biology Research Centre," *Engineering Studies* 5, no. 1 (2013).

³ Ernesto Andrianantoandro, et al., "Synthetic Biology: New Engineering Rules for an Emerging Discipline," *Molecular Systems Biology* 2 (2006); Vincent De Lorenzo & Antoine Danchin, "Synthetic Biology: Discovering New Worlds and New Words," *EMBO Reports* 9, no. 9 (2008).

⁴ Endy, "Foundations for Engineering Biology," 449; Tom Knight, "Engineering Novel Life," *Molecular Systems Biology* 1 (2005): 1.

⁵ Daisy Ginsberg, et al., *Synthetic Aesthetics: Investigating Synthetic Biology's Designs on Nature* (Cambridge, MA: MIT Press, 2014).

⁶ Priscilla E. M. Purnick & Ron Weiss, "The Second Wave of Synthetic Biology," *Nature Review Molecular Cell Biology* 10, no. 6 (2009).

⁷ David Benjamin & Fernan Federici, "Bio-Logic," in Daisy Ginsberg, et al. (eds) *Synthetic Aesthetics: Investigating Synthetic Biology's Designs on Nature* (Cambridge, MA: MIT Press, 2014), 148.

⁸ Michael Lynch, "Science in the Age of Mechanical Reproduction: Moral and Epistemic Relations between Diagrams and Photographs," *Biology & Philosophy* 6, no. 2 (1991); Steve Woolgar, "Struggles with Representation: Could It Be Otherwise?" in Catelijne Coopmans, et al. (eds) *Representation in Scientific Practice Revisited* (Cambridge, MA: MIT Press, 2014).

⁹ M. Norton Wise, "Making Visible," *Isis* 97, no. 1 (2006).

¹⁰ Adam Arkin, "Setting the Standard in Synthetic Biology," *Nature Biotechnology* 26, no. 7 (2008); Endy, "Foundations for Engineering Biology."

¹¹ Harvey Lederman, et al., "Deoxyribozyme-Based Three-Input Logic Gates and Construction of a Molecular Full Adder," *Biochemistry* 45, no. 4 (2006); Keller Rinaudo, et al., "A Universal RNAi-Based Logic Evaluator That Operates in Mammalian Cells," *Nature Biotechnology* 25, no. 7 (2007); Jerome Bonnet, et al., "Amplifying Genetic Logic Gates," *Science* 340, no. 6132 (2013).

¹² On oscillators, see Michael B. Elowitz & Stanislas Leibler, "A Synthetic Oscillatory Network of Transcriptional Regulators," *Nature* 403, no. 6765 (2000); David McMillen, et al., "Synchronizing Genetic Relaxation Oscillators by Intercell Signalling," *Proceedings of the National Academies of Science* 99, no. 2 (2002); Jesse Stricker, et al., "A Fast, Robust and Tunable Synthetic Gene Oscillator," *Nature* 456, no. 7203 (2008). On switches, see Timothy S. Gardner, Charles R. Cantor, & James J. Collins, "Construction of a Genetic Toggle Switch in *Escherichia coli*," *Nature* 403, no. 6767 (2000); Mariette R. Atkinson, et al., (2003). Development of Genetic Circuitry Exhibiting Toggle Switch or Oscillatory Behavior in *Escherichia coli*," *Cell* 113, no. 5 (2003); Azi Lipshtat, et al., "Genetic Toggle Switch without Cooperative Binding," *Physical Review Letters* 96, 188101 (2006). On counters, see Ari. E. Friedland, et al., "Synthetic Gene Networks That Count," *Science* 324, no. 5931 (2009).

¹³ Leland H. Hartwell, et al., "From Molecular to Modular Cell Biology," *Nature* 402, no. 6761 supp. (1999): 47.

¹⁴ *Ibid.*, 51.

¹⁵ *Ibid.*, 50.

¹⁶ Baojung Wang, et al., "Engineering Modular and Orthogonal Genetic Logic Gates for Robust Digital-Like Synthetic Biology," *Nature Communications* 2 (2011), doi:10.1038/ncomms1516.

¹⁷ Ibid.

¹⁸ Steve Benner & Michael Sismour, "Synthetic Biology," *Nature Reviews Genetics* 6 (2005), doi:10.1038/nrg1637.