

## From BIOS to *bios*: bootstrapping openness in synthetic biology

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*bios*: 'life, course or way of living'<sup>1</sup>

The BIOS is boot firmware, designed to be the first code run by a PC when powered on. The initial function of the BIOS is to identify, test, and initialize system devices such as the video display card, hard disk, floppy disk and other hardware. The BIOS sets the machine hardware into a known state, so that software stored on compatible media can be loaded, executed, and given control of the PC.[3] This process is known as booting, or booting up, which is short for bootstrapping. <sup>2</sup>

### **Introduction**

In what sense is biology, or biological life, open? Synthetic biology offers one potent yet problematic answer to this ambiguous question. Synthetic biology places biological substance at the intersection of

software, microelectronics, post-genomic biology and network cultures. Little more than ten years old, synthetic biology wants to 'do for biology what Intel does for electronics' says George Church, Harvard.<sup>3</sup> In other words, synthetic biology promises that biological substance will look like BIOS, the code that sets the 'machine ... in a known state so that software stored on compatible media can be loaded, executed and given control.' In bringing the engineering and industrial design model of BIOS to biology, synthetic biologists necessarily mix together several different kinds of openness. The biological objects - and subjects - that synthetic biology imagines are affected by ideas of openness derived from the design economies of software and electronic hardware and the 'wikinomics' or 'crowdsourcing' of network cultures. These ideas, I will suggest, cannot be consistently, compatibly or stably booted up in biological work on biological objects.

Biological objects do not yet exist. Biological substance is difficult to objectify precisely because it is in many ways too open. Anyone who is interested in biological objects must continually close biological substance too. At the same time, synthetic biology relies on openness as the main pathway to objectification. Opening biological substance and biological work will make biological objects. Synthetic biologists say: 'the biological will become BIOS, if only we open it in the right ways.' However, this claim, iterated in countless accounts of synthetic biology, exists basically as a promise. In its own way, promise is a crucial way to initialise technoscientific things. Promise generates

speculative materialisations that help bootstrap things into existence. Synthetic biology is, I will argue, booting itself up on affective registers via contagions of belief and desire concerning the design of biological substance.

In order to explore the multiple forms of openness, and promise as bootstrapping materialisation, we might ask:

- How is opening and openness done in synthetic biology?
- What kind of openness do we value epistemically, aesthetically and pragmatically in biological objects?
- When biological objects exist as promises, what does that allow to happen? Conversely, how does the promissory mode inhibit what can happen?

In this paper, I explore these questions drawing on a range of scientific publications, items of mass media and policy, but above all, from the iGEM (international Genetically Engineered Machine) competition, an annual student synthetic biology competition held annually at MIT, Cambridge, since 2004. iGEM, it seems to me, encapsulates many of the conflicting, cross-cutting ideas of openness found in synthetic biology more generally. As an object of analysis, it documents itself in a range of wikis, in images, reports and video scattered across network media (wikis, youtube, twitter, blogs, websites, etc.).

***Two imperatives to open in synthetic biology: unfold and expand***

'The century of biology' <sup>4</sup>confronts problems of food security, global

health inequality and peak oil. The previous century, 'the century of silicon,' generated billions, if not trillions, of objects concerned with communication and movement. (For instance, in mobile communications alone, market research estimates there will soon be over a trillion mobile devices on the planet.<sup>5</sup>) If biology is to effectively and quickly address the planetary problems of energy, food and health, then, according to synthetic biologists, do better than molecular biology or related life sciences. Biological work desperately needs the design processes that electronics, software and other engineering disciplines developed in the industries of the twentieth century. It might then aspire to the delirious growth deified in Moore's Law – the doubling of the number of transistors on a chip every two years.

In the several hundred iGEM projects done since 2004, a rate of growth that seems comparable to electronics, and a range of topics, ambitions, interests and enthusiasms that go well beyond it. Many of the iGEM projects address health, and a substantial portion address energy and environmental problems. Many, if not all, explicitly or implicitly address problems of control, regulation and timing in biological substance or biological work.

Topics of iGEM entries	2004	2005	2006	2007	2008	2009
Communication and control processes	3	7	8	4	11	14
Computing devices	0	1	6	3	5	11
Environment	0	1	8	9	14	12
Ethics and social impacts	0	0	0	0	0	1
Health and medicine	0	0	2	10	16	20
Imaging and visualisation	1	0	5	1	0	3
Laboratory techniques	1	1	3	2	16	19
Manufacture and industry	0	1	1	5	5	11
Software design	0	0	0	2	1	2
Transforming life	0	0	1	12	8	0

iGEM has been growing rapidly in terms of numbers of participants, in numbers of participating institutions, and countries. (See tables for this.) Each iGEM project makes use of publicly available biological parts, BioBricks, and sometimes constructs new BioBricks that it makes available to others through an online registry, the Registry of Standard Biological Parts.<sup>6</sup> The skills, ambitions, and enthusiasm for synthetic biology displayed in the many student teams confront two basic problems.

First, biological substance is frustratingly diverse and historically contingent. Second, biological engineering is a difficult activity to coordinate.

In relation to the first: despite a half-century of attempts to express life in material-semiotic terms such as 'program,' 'code' and 'machine,' biological substance does not adhere to the form-matter, or coding-coded, distinctions of most industrial design techniques. Even the overreaching promise of genomics - to finally unfold an exhaustive sequential specification of the ground-plan of any organism - has inadvertently dismantled the important control concept of the gene as program, and proliferated ever more intensive and extensive attempts to sequence everything in sight (epigenomics, metagenomics, etc.). Faced with the radical historical contingency of biological substance, and unremitting flows of biological data, synthetic biologists advocate several approaches. Biological substance needs to be pared down. Genomes are tangled in redundancies, copies, and seemingly unused sequences that echo evolutionary events. It therefore makes sense to prune back the genome to the minimal set of elements needed for life (hence a BIOS), and then, and only, add functionality to that. The 'minimal genome' approach to synthetic biology associated with J. Craig Venter attempts to devise biological firmware on which many different applications could be developed.<sup>7</sup> Alternately, in iGEM, biological standard parts based on relatively short sequences of DNA attempt to bring the component approach that has been so successful in

software and electronics industries (and many other industrial production processes) to biological engineering.

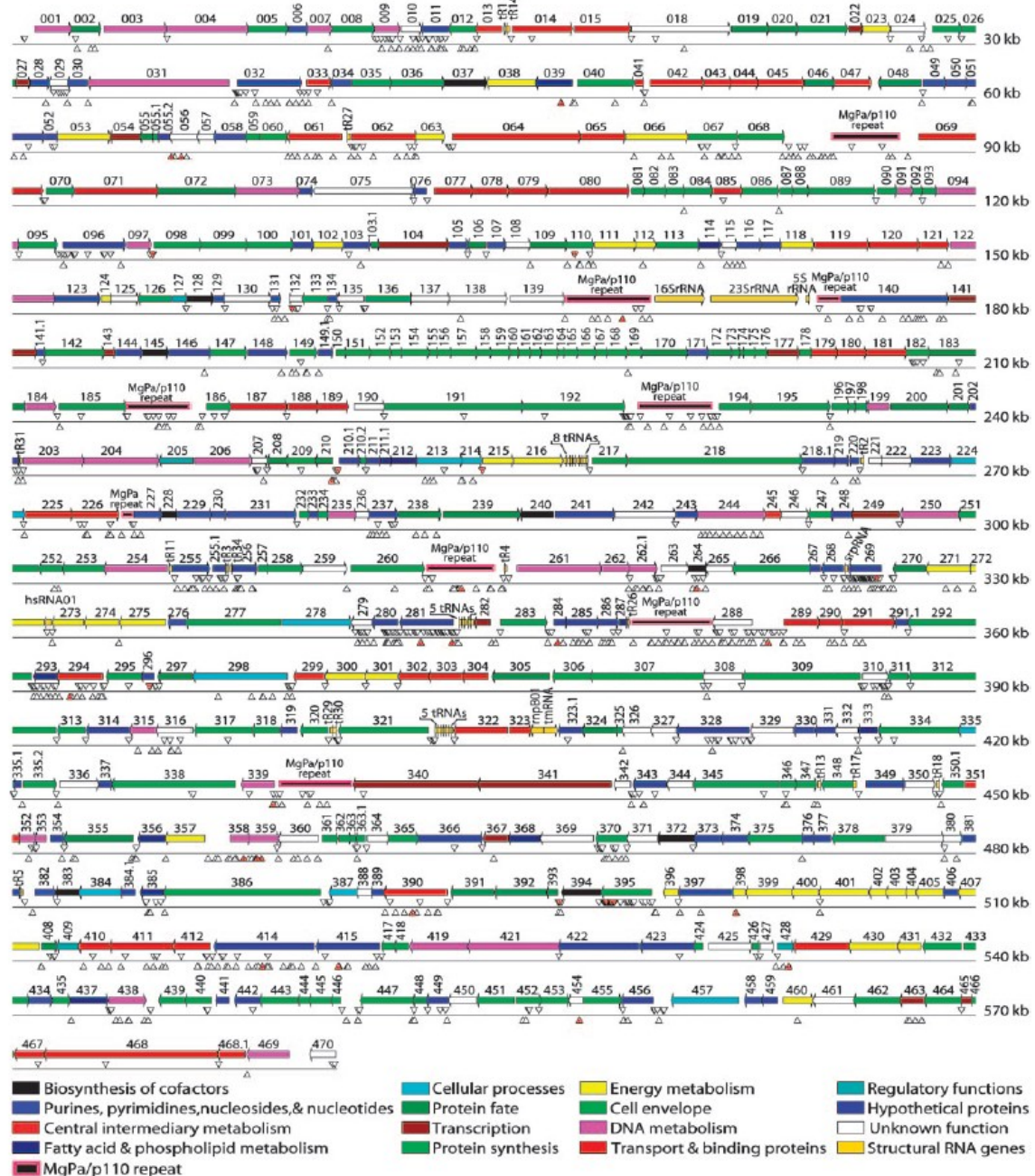


Fig. 2. Global transposon mutagenesis of *M. genitalium*. The locations of transposon insertions from the current study are noted by a  $\Delta$  below the insertion site on the map. Insertions mapped in our previous study (4) are noted with a  $\nabla$ . Sites with 10 or more insertions are noted by a red filled triangle ( $\blacktriangle$ ).

Both the minimal genome and BioBricks share a commitment to the openness of biological substance. Both imagine biological substance as a set of processes whose most relevant features can be rendered in terms of pathways, networks, graphs, block or circuit diagrams (with temporal dynamics expressed in, for instance, differential equations). Both minimal genome and modular approaches to synthetic biology seek to minimise opacity and to evacuate the interiority of biological substance by creating clear and distinct forms that can be graphed, modelled and automated using fairly familiar visual devices. Of these, pathways and networks might be the most salient.

As to the second obstacle to Moore's Law rate of progress in making biological objects – the difficulty of effectively coordinating biological work – synthetic biologists recognise that they need each other. Synthetic biologists are not in the same position as Intel's circuit designers, who can draw on a layered, distributed, and heavily automated production system to design chips in Cupertino and see them fabricated in Singapore. The lack of coordination in work on biological substance makes turning biological function into objects or products repetitive and time-consuming. Many more people need to be involved. In the response to this, networked collaboration as seen in open source software, in collaborative filtering or 'crowd-sourcing' on the web seems a more effective way of proceeding. It is no accident that when the first synthetic biology publications appear in *Nature* in 2000,<sup>8</sup> the *Nature* editors were also writing about the merits

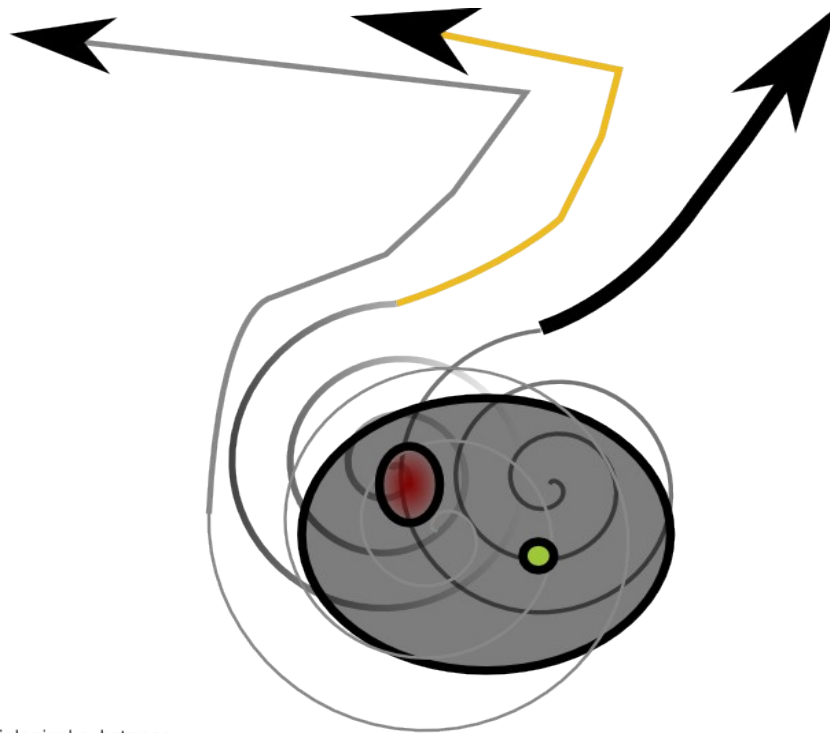
of 'open software,'<sup>9</sup> open source software was becoming highly visible as a major dynamic of network cultures, and the economics of open networked collaboration were being hotly debated ( see the 'wealth of networks' arguments proposed by Benkler; or the 'wikinomics' argument of Tapscott<sup>10</sup>). Network collaboration brings with it certain quite complex demands or requirements for openness. In synthetic biology and in the global iGEM competition in particular, which dates from 2004, these demands are sometimes framed in terms of democratisation of science. More usually, they are framed in almost Fordist engineering principles such as layered abstraction and modularity that will allow many people to work together efficiently. This doesn't necessarily sit easily with the 'crowd-sourcing' public ethos of iGEM.<sup>11</sup>

In this light of these two gestures or attempts at opening- techniques aimed at the opacity of biological substance; techniques aimed at the managing exorbitant biological work - iGEM and synthetic biology more generally can be seen as driven to bring together two different forms of openness. Synthetic biology needs to *unfold* biological substance in order to make biological objects. Unfolding affords forms of re-definition, re-ordering, re-composition and representation that curtail and harness the opacities and differences produced by evolution. On this score, we can see why there are so many synthetic biology projects concern counters, logic gates, times and switches. Simultaneously, because the re-organisation of biological substance is so complicated, and because there are exponentially different ways

that it might be done, synthetic biology needs to expand to include to as many participants as possible. Moreover, given the disappointments of the genetic engineering revolution already promised in the 1970s, this expansion must be marshalled in productive workflows. Even issues of intellectual property can be largely put to one side for the sake of *expanding* participation in biology. (This is also exemplified in iGEM but also in *OpenWetWare*.<sup>12</sup>) On this score, we see why so many aspects of iGEM begin to look more like popular culture than science: YouTube.com videos, colourful logos and graphics, photostreams on Flickr.com, etc. All of this revolves around the workflows and design principles implemented in the registries and standard parts.

### ***How to unfold biological substance?***

Both kinds of openness remain to be achieved. Both the unfolding of biological substance in diagrams, pathways and networks, and the expanded participation in design workflow present many problems. Since neither fully exists, they have to be done provisionally. How can this work of opening as unfolding and expanding begin? How can it initialised?



expanding and unfolding biological substance

At first glance, the answer to this question seems fairly straightforward. Biological substance undergo carefully controlled biological work. But what kind of work, and how will this work differ from what molecular biology or the life sciences more generally do? No doubt, synthetic biology must rely heavily on results of molecular biology and genomics of the last five decades. The biology of the second half of the 20<sup>th</sup> century is raw material for the century of (synthetic) biology. Unfolding biological substance requires the techniques of molecular biology as well as the very detailed information about pathways, signals, transcription, translation, activation, inhibition, binding and other cellular processes produced by increasingly automated sequencing projects associated with genomics. The 'unfolding' of biological substance in synthetic biology

depends on this accumulated knowledge.

That knowledge, because it is now so extensive yet intricate, poses problems for synthetic biology. How can it be assimilated and made readily available for use? Several aspects of synthetic biology address this problem. First of all, there is a heavy reliance on modelling, and particularly the forms of modelling developed by that other post-genomic life science discipline, systems biology. The models and simulations developed by systems biology already absorb a great deal of intricate biochemical detail about rates of reactions and the interactions between large numbers of metabolic processes in cells. While the metabolic complexity of even a single cell still eludes systems biology, nearly all of the the iGEM team pages have a modelling section dedicated to simulating some aspect of the biological construct they work on. These models and simulations integrated from systems biology only allow prediction of what some part of biological substance will do. Although they assist in the objectification of biological objects, the models cannot be exhaustive or complete in themselves. Not everything can be modelled. Even a single cell of e.coli, the standard biological organism in synthetic biology, cannot be fully modelled. Hence, the unfolding of biological substance in diagrams, models and graphics can only be partial. Conversely, the biological constructs produced by iGEM teams and other synthetic biologists must be limited in their interactions with biological substance more generally.

Second, there is an increasing tendency to rely on computer assisted

design software that embodies distillations of molecular biological techniques and results. Several hundred software packages related to synthetic biology have appeared (GenoCAD, SynBioSS, TinkerCell, etc.<sup>13</sup>), and a significant proportion of iGEM teams do software-related projects. At the same time, synthetic biology relies directly on commercial online DNA synthesis services such as DNA2.0, Blue Heron and Geneart.<sup>14</sup> In both settings- the design software and the commercial online services - biological knowledge is accessed, without the synthetic biologists needing to practically grapple with its intricacies. Rather than reading scientific articles, and then trying to use their results, the computer assisted design software promises synthetic biologists the possibility of wielding biological knowledge without needing to assay or reproduce experimental results themselves. Similarly, the commercial DNA synthesis services not only obviate skills in certain experimental techniques, they permit synthetic biology to work on a different scale and at a different rate in the laboratory. Both the CAD software and the commercial DNA synthesis seek affect the rate at which biological substance can become unfolds.

Third, the main approaches to synthetic biology, especially those embodied in iGEM and the minimal genome approaches, imagine design, standardisation and modularisation as the only ways in which biological substance can become biological object. The very notion of the BioBrick, the basic biological material that all iGEM projects conveys an image of biological work as something done by many

people in networked collaboration using standardised components. A BioBrick specified as a sequence of DNA, usually between several hundred and several thousand base pairs long, starting and ending with sequences specified by the BioBrick standards. A BioBrick embodies a designated biological function as a part or device. The expression of biological substance in a sequence of DNA literally unfolds temporal and topological contingencies in a line of letters or a block diagram that can be sequenced, synthesised, and above all, concatenated with other BioBricks to form devices and systems.

In these three principal respects – use of modelling to simulate and isolate biological constructs from the multiplicity of metabolic processes occurring in organisms; reliance on software automation to capture past biological knowledge; and insistence on standardised modules or platforms as the foundation of widened participation – synthetic biology unfolds biological substance onto a graphic plane of diagrams susceptible to the click, drag and drop style of work associated with network media. Furthermore, it is not hard to see how this unfolding of the folded topological and temporal complexity of biological substance entails different forms of participation in biological work. What remains somewhat to be explained is how these forms of opening can engender affective resonances. How does the promise of synthetic biology materialise?

### ***Initializing openness: the promise of design***

On this point I would argue much pivots on the open futures of

design. Design engenders the contagions of belief and desire that the promise of synthetic biology needs in order to materialise biological objects, and to realise itself as a discipline.

How are design promises made in synthetic biology? Like BIOS, they work on a bootstrap process. The three most visible applications of synthetic biology to date illustrate something of the promissory character of synthetic biology: anti-malarial compounds produced by re-engineered yeast;<sup>15</sup> synthetic biofuels produced by marine algae;<sup>16</sup> and the many accounts of biological counters, oscillators, clocks, switches, logic gates and circuits that have been published in journals such as *Nature*, *Science* and other major scientific journals.<sup>17</sup> These three promissory applications connect synthetic biology and global health inequality, synthetic biology and climate change, and synthetic biology and network cultures. The most advanced commercial instance of synthetic biology to date is probably the engineering of yeast to cheaply produce the important anti-malarial drug, artemisinin, or artemisinic acid. Funded by the William and Melinda Gates Foundation, the key scientist, Jay Keasling, became *Newsweek's* 'Scientist of the Year' in 2008.<sup>18</sup> As for synthetic biofuels, according to J. Craig Venter, there are currently at least 200 companies at work on algal biofuels in the United States.<sup>19</sup> Finally, the extraordinary proliferation of logical devices in synthetic biology connects biological objects to software cultures and microelectronics, perhaps the most highly valorised meta-field of technological change today. None of these three leading synthetic biology applications

exists as an object or product (although the anti-malarial compounds are said to close to commercial production). On the contrary, they function as vectors of pragmatic, epistemic and aesthetic values.

The ways in which synthetic biologists appeal to each of these domains – the biopolitical, the geopolitics of climate change, the biodigital – are worth further exploration in their own right. These appeals offer openings to futures that attract many different scales and types of speculative investment, ranging across public and private, institutional and non-institutional, military and civil, commercial and non-commercial, individual and collective settings. It seems that this highly transmissible form of openness, promissory openness, runs under the other kinds of openness in engendering fluxes of belief and desire in biological objects. If so, biological objects will owe more to what Melinda Cooper has called 'biological promise itself, ... a state of nascent transformability'<sup>20</sup> than to any attributes of biological substance or biological work.

The specific promise of synthetic biology concerns how design can manage transformation in both biological substance and biological work. In other words, the promise of design predicates the coalescence of the two forms of openness – unfolding and expanding – that I have just been discussing. In the promissory opening of synthetic biology, the two forms of openness – unfolding and expanding – bootstrap each other. The unfolding of biological substance pivots on expanded participation in biological work. At the same, the unfolding of biological substance in expanded biological

work folds biological work on itself. This last point seems to me crucial to the promissory mode of existence of biological objects. Every unfolding is a folding; every expansion is a contraction.

Evocative biological objects such as biofuels, synthetic antimalarials or biodigital artefacts like oscillators, switches and gates engender wide-ranging contagions of subjectification. The students who come to iGEM provisionally enrol themselves as synthetic biologist doing synthetic biology. The biological objects they make attest to their becoming biological subjects. Yet, they come to iGEM and synthetic biology only insofar as it promises something open, something visible to the world, something of epistemic, pragmatic or aesthetic value. Here the values of openness, the practices and forms of openness in iGEM matter greatly.

This reliance on existing forms of openness means synthetic biology can seem both familiar, and yet at the same time be marked by intense excitement and investment. The borrowing of the practices of social network media – wikis, youtube videos, rss feeds, etc. – would be one instance of a rendering of open. Moreover, the glory of prizes, medals, and the sometimes spectacularly ambitious applications and experiments exhibited in iGEM attract a degree of public interest that other more established sciences would either not risk or would struggle to attain. Finally, it is in the *bios* of iGEM teams that we might glimpse the promise of design in play most directly. Work on images, annotations, descriptions, diagrams, and proposal over time in groups is where the promise runs into the problem of realization.

The Registry of Standard Biological Parts is a simple and direct test of the promise of synthetic biology. By putting parts there, and by using parts from there, synthetic biologists change biological work. Here, the folding of biological work takes the form of uploading, linking, logging, submitting, transforming, and coding using the conventions of wiki editing.

### ***Conclusions***

BIOS, the first code run by a digital device when switched on, supports a proliferation of devices, applications and variations. In rendering biological substance subject to design in the form of products such as drugs, seeds or other biotechnologies, biological functions offer immense potential. Yet, the conditions under which such potentials become actual are highly contingent.

Openings bring people and things into fresh proximities or conjunctions. In any opening, people and things come closer to each other in some ways and not others. Any feeling of being open, or of things being open, is bound to be complicated and unstable. Things don't stay open. We need to understand synthetic biology as existing in a promissory bootstrapping mode. In bootstrapping, different kinds of opening entwine. Opening as unfolding of biological substance through pathways, networks, circuits and signals looks very different to opening as expanding the field of participants through networked engineering design workflows. The former concerns the folds of biological substance and its unrelenting topological intricacies; the

other concerns expanded workflows, collaboration, competition, and inclusion – who can do synthetic biology and how. Both unfolding and expanding carry epistemic, pragmatic and aesthetic values associated with opening. Yet the different values of openness feed into each other in particular ways in synthetic biology, and they allow the unfolding of biological substance and expanding of biological work to mingle. Furthermore, this mingling or entangling of different forms of openness supports the temporally open form of promise. Attachment to the design of biological objects for health, energy, food and climate is crucial to the initialisation of synthetic biology. BIOS needs biological work as *bios*, way of life, in order to boot biological substance.

In its temporally open framing, synthetic biology seeks to bootstrap biological substance into biological objects. The promise, as an opening of future, marshals all the others forms and values of openness I have been discussing. Yet, at the same time, it is forced to borrow extensively, to cite, and invoke other forms of in order to propagate itself, in order to attract attachments and investments. as well into the emerging promises that articulate synthetic biology with.



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