Technical Objects in the Biological Century

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The kernel of the *Linux*/GNU operating system and the transcriptional regulatory pathways of the standard laboratory microbe, *escherichia coli (e. coli)* can both be understood as networks of control processes. In a paper recently published in the *Proceedings of the National Academy of the Sciences*, the authors compared the network of control functions in these two protean technical objects.[1] Their research was premised on the idea that the 4300 genes of the *e. coli* genome are like the several thousand functions programmed in a computer operating system. A genome, so the analogy runs, is the operating system of a cell. The genesis, however, of the two operating systems is quite different. The *Linux* operating system comes from coordinated, collaborative work on computer code, carried out at the interface between operating systems design and commodity computing hardware. *E.coli* epitomises an evolved control system, subject to many adaptive processes coming from its environment. The *PNAS* paper analysed the distribution of control functions in these two entities. Whereas *e. coli*, the product of substantial and deep-set evolutionary processes, displays a control hierarchy acting down through a great variety of low level functions, *Linux* could be characterised by a large number of middle-level control functions, governed from above by a small range of high-level controls, and acting down through a small number of low level controls.

In the so-called ›biological century‹,[2] technologies are likely to change. What kind of technical objects come from contemporary biology? In the interests of developing ways of accounting for our own implication in the emergence of biological technical operations, this paper discusses how synthetic biology is envisaging technical objects as it engineers *e. coli*, the most thoroughly studied species of bacteria. Synthetic biology lies at the intersection of molecular biology, genomics, computer science, software programming, microelectronics, and network cul-

1 Yan Koon-Kiu et al.: Comparing genomes to computer operating systems in terms of the topology and evolution of their regulatory control networks, in: Proceedings of the National Academy of Sciences 2010. Under: http://www.pnas.org/content/early/2010/04/28/0914771107.abstract (17. 10. 2011).

2 Kaushik Sunder Rajan: Biocapital: The constitution of postgenomic life, Durham, NC 2006. Under: http://www.loc.gov/catdir/toc/ecip062/2005030718.html (18. 11. 2011).

tures.[3] Synthetic biologists rarely speak of ›objects‹. They are much more prone to speak of devices, networks, circuits, constructs, pathways, systems and modules.[4] Little more than ten years into the life of the field, their apprehension of biology as modular, hierarchical, code-driven collectively invented technology is in some ways strikingly familiar: synthetic biologists say they want to »do for biology what Intel does for electronics«.[5] Synthetic biology aspires to create a pragmatic version of the much discussed twentieth century transformation of life into computer code.[6] It endeavours to arrange things such that biology will re-boot as 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«[7]. The aspiration to even make one type of cell to do this – *e. coli* for instance – is beyond reach at the moment. There are, however, many parts of an *e. coli* BIOS already in place.

If biology is to become a BIOS-like technology, what mode of existence will *biological technical* objects have? How will growth and reproduction, for instance, figure in the devices invented by synthetic biology? Writing before Intel, at a time when vacuum tubes had just begun to be replaced by solid-state semiconductor devices, the philosopher of technology and biology Gilbert Simondon contrasted the artificiality of technical objects with their concretisation. He writes in *Du Mode d'Existence des Objets Techniques* that »the essential artificiality of an object resides in the fact that man *[sic]* must intervene in order to maintain the object in existence by protecting it against the natural world, and by giving it the status of a part of existence«.[8] In concretisation, by contrast, the object, originally artificial, becomes »more and more like a natural object«.[9] In concretising, disparate functions are interlaced with each other; relations between parts or systems that were potential are actualised; and relations to the surrounding milieu are internalised such that the technical object can migrate into other settings and associate with other objects. Simondon's account of this process is complicated, since it ranges across technical

3 Cf. for a popular description Robert H. Carlson: Biology Is Technology, Cambridge, MA 2010.

4 Evelyn Fox Keller: What Does Synthetic Biology Have to Do with Biology? in: BioSocieties, 4/2–3 (2009), pp. 291–302.

5 Andrew Pollack: Custom-Made Microbes. At Your Service, in: The New York Times (17.01.2006). Under: http://www.nytimes.com/2006/01/17/science/17synt.html?_r=1 (18.11.2010).

6 Lily E. Kay: Who wrote the book of life? A history of the genetic code, Stanford, CA 2000.

7 Anonymous: BIOS, on Wikipedia, the free encyclopedia. Under: http://en.wikipedia.org/wiki/BIOS (25.03.2010).

8 Gilbert Simondon: Du mode d'existence des objets techniques, Paris 1958, p. 47, trans. A.M.

9 Ibid.

elements, technical individuals, and technical ensembles, and includes concepts such as technicity, associated milieu and recurrent (or recursive) causalities (some of which are discussed below). Importantly for our purposes, Simondon quite carefully distinguishes natural and technical objects. The concretised technical object has a mode of existence *analogous* »to that of spontaneously produced natural objects«.[10] No longer simply the application of scientific principles or results, the concretised technical object still possesses residues of abstraction that can lead to further concretisation, further confluence or growing together. By contrast, natural objects are concrete from the start.[11] In the *Linux* – e. coli comparison, the vast number of low level transcriptional processes regulating expression of genes in the cell suggests a greater degree of concretisation than the bulging middle manager control functions in Linux. As Yan et al. write, »biological evolution is building from the bottom to the top.«[12]

In terms of the becoming of technical objects, the key difficulty is whether *e. coli*'s concretisation can be artificialised and then re-concretised in different ways. Crudely put, can the intricate pyramid of low-level *e. coli* control functions be re-configured into something that looks more like the *Linux* control flows? If this can happen, how will it happen? The confluence of ideas, values, practices and problems of digital-computational culture around contemporary biology is very broad, no doubt. If there is any way that biology will become technology, it seems that it must be engineered informationally. The *PNAS* article mentioned above directly posits a shared fundamental property of biology and software: »biological and software systems both execute information processing tasks.«[13] There are many analogies, convergences, overflows, and intersections between biology and information processing.[14] We could point to the vast databases and software interfaces for DNA and other sequence data, the extensive ontologies of genes, pathways, interactions, species, molecules and reactions, the abundant metaphors and figures of code, system, communication and program, the visual and mathematical models of structures, relations and networks in cells, species organs, and diseases found in systems biology, or even the many wikis, portals, software applications, and web services furnishing biological data, information and publications for various aspects of biology. Even knowledge, data and techniques concerning a single or-

10 Ibid. p. 48.
11 Ibid. p. 49.
12 Yan et al: Comparing genomes (as note 1), p. 5.
13 Ibid. p. 1.
14 Simondon too often invoked the concept of information as a way of thinking about processes of individuation and concretisation, especially in Gilbert Simondon: L'individuation psychique et collective à la lumière des notions de forme, information, potentiel et métastabilité, Paris 1989.

ganism such as *e. coli* are distributed across a large global information assemblage. While convergences between biology and digital cultures are manifold, synthetic biology presents interesting tensions between artificiality and concretisation, between the technical and the natural. In its emphatic attempts to couple engineering design principles with biological techniques, synthetic biology confronts many decisions about what is copied, what is transferred or transcribed from one domain to the other, from biology to engineering, from computational culture to biology. The sciences on which synthetic biology draws include cell biology, biochemistry, microbiology, genetics and late 20th century molecular biology in particular.[15] In drawing on molecular biology, it has to deal with the naturalness and artificiality of *e. coli*. It is easy to find evidence of *e. coli* naturalness. Strains of *e. coli* are found in every human gut. The artificiality of *e. coli* is equally striking. For much of the 20th century, biologists bred strains of *e. coli* that were defective in various ways in order to understand processes of mutation, evolution, selection, infection, reproduction, metabolic pathways, gene mobility, etc. As Carl Zimmer argues, *e. coli* has become engineerable because of the many ways in which the growth of *e. coli*, its naturalness and spontaneity, was interrupted, perturbed and artificed.[16] In Simondon's terms, we might say that *e. coli* has undergone an artificialisation that lifted it out of nature, and made it more like a ›part of existence‹ than an existing thing. The question that synthetic biology now addresses is how to re-concretise *e. coli* as a technical object.

This re-concretisation is in practice and principle conceived in terms of software systems and microcircuit hardware. A quick glance at the past decade's scientific publication in synthetic biology suggest that the metaphor of the algorithmic object has been worked up very explicitly and in many closely related varieties. For example, »we advocate the metaphor of the cell as an algorithmic machine, rather than a mechanical one, and the use of machine-orientated engineering language to implement synthetic biology«.[17] The commonness of terms such as ›logic‹, ›circuit‹, ›device‹, ›programming‹, ›interface‹ and the more interesting technical verb ›interfacing‹ in this literature indicates the rhetorical imprint of algorithms, digital devices and network media in this field.[18] What is at stake in this unsur-

15 Hans-Jörg Rheinberger: What Happened to Molecular Biology?, in: Biosocieties 3 (2008), pp. 303–310.

16 Carl Zimmer: Microcosm. E. coli and the New Science of Life, New York, NY 2009.

17 Victor de Lorenzo and Antoine Danchin: Synthetic biology. Discovering new worlds and new words. The new and not so new aspects of this emerging research field, in: Embo Reports 9/9 (2008), pp. 822–27, here p. 825.

18 For a review, cf. Priscilla E. M. Purnick and Ron Weiss: The second wave of synthetic biology. From modules to systems, in: Nat Rev Mol Cell Biol 10/6 (2009), pp. 410–22. But almost any publication in the field will say something similar.

prising desire to bring digital logic, algorithmic processes and machine-orientated engineering language into biology? The borrowing of an engineering control discourse from computer science is seen as crucial to the initialising or bootstrapping of *biological technical* objects in synthetic biology. Emulating Intel, synthetic biology places great stock in stable platforms, modularity, combinational logic, compatible standards, controllable programming interfaces, and computer-assisted design (CAD) processes. These are not just convenient tropes or metaphors: »The defining question of synthetic biology research moving forward will not be whether biology can be engineered, but how to develop engineering principles for biological systems.«[19] This is an interesting statement. The question of whether biology can be engineered seems to have a foregone conclusion: yes, it can be. The real question is: can it be engineered according to principles? In contrast to the many now familiar borrowings of notions of code, program, memory, etc. by biology, synthetic biology thus regards various engineering principles and practices – of electronic and software engineering, and particularly those associated with open source software – as the optimal way to normalise the making of *biological technical* objects. The real stake here, it seems, is not just a change in the direction of work on biological materials, but the construction of ›principles‹ that re-generate potential for change.

From this standpoint, objects themselves matter less than the process of making them. In many different ways, synthetic biology is an organised belief in the idea that engineering principles – in the form of models, standards and design techniques – can produce *biological technical* objects of great logical and material complexity in the 21st century, just as in the 20th century engineering principles manifestly produced objects of great logical and material complexity: computer operating systems or very large-scale integrated circuits. This belief in sophisticated engineered biological objects, iterated in innumerable accounts of synthetic biology, is largely prospective. While there are many technical objects under discussion in synthetic biology (biosensors, biofuels, biomaterials, synthetic vaccines, drug-delivery systems), we see a plethora of models, standards,[20] design processes,[21]

19 Patrick Boyle and Pamela Silver: Harnessing nature's toolbox. Regulatory elements for synthetic biology, in: Journal Of The Royal Society Interface, 6 (2009). Under: http://rsif.royalsocietypublishing.org/content/6/Suppl_4/S535.full=18 (16. 11. 2011), p. 543.

20 Thomas Knight: Draft standard for BB-2 Biological Parts (2010). Under: http://hdl.handle.net/1721.1/45139 (16. 11. 2011).

21 Michael A. Fisher et al.: De Novo Designed Proteins from a Library of Artificial Sequences Function in Escherichia Coli and Enable Cell Growth, in: PLoS ONE 6/1 (2001), p. 15364; A. Cortajarena et al.: Designed Proteins To Modulate Cellular Networks, in: Acs Chemical Biology 5/6 (2010), pp. 545–52.

biological part repositories,[22] software prototyping platforms and above all devices. Many synthetic biologists turn to mathematical and statistical models as they seek to develop objects of diverse technicity.[23] The mathematical and computation models that are being built, however, are partial, hedged realizations of objects-to-come.

1. Part biological objects

If the engineering principles have yet to be invented or agreed, do any *biological technical* objects exist? We might say there are *parts* of such objects. In trying to engineer biology, synthetic biologists very often talk about parts. The globally publicised announcement in June 2010 »Venter boots up first synthetic cell«[24] echoed the words »boots up« of the *enfant terrible* of genomic science, Craig Venter, to headline the technical achievement of synthesising a minimal whole genome in vitro and then persuading an organism to regard it as its own.[25] Venter's whole genome work – and the scale of his team's achievements – cover over the fact that as a field, synthetic biology has largely produced *parts, components* and *devices*. In many respects, the titles of other synthetic biology publications suggest much less ambitious achievements: »a synthetic oscillatory network«,[26] »reconstruction of genetic circuits«,[27] »combinational logic design«.[28] Rather than pointing to a concretised technical object, each of these titles designates a part or component: an oscillatory network, a circuit, or some logic. They remain, slightly modifying Simondon's terminology, abstract *technical elements*, parts of a technical ensemble to come. The key question is, given that these parts and modules are being made, how can these parts put be together?[29]

22 Anonymous: Welcome to the Registry of Standard Biological Parts, under: http://partsregistry.org/Main_Page (18.11.2011).

23 Yizhi Cai, Mandy L. Wilson and Jean Peccoud: GenoCAD for iGEM. A grammatical approach to the design of standard-compliant constructs, Nucleic Acids Research 38/8 (May 2010), in: pp. 2637–44.

24 Patrick Walter: Synthetic biology Venter ›boots up‹ first synthetic cell, in: Chemistry & Industry 11 (2010), p. 5.

25 Carol Lartigue et al.: Creating Bacterial Strains from Genomes That Have Been Cloned and Engineered in: Yeast. Science 25/325 (2009), p. 1693–96.

26 Michael. B. Elowitz and Stanislas Leibler: A synthetic oscillatory network of transcriptional regulators, in: Nature 403/6767 (2000), pp. 335–38.

27 David Sprinzak and Michael B. Elowitz: Reconstruction of genetic circuits, in: Nature 438/7067 (2005), pp. 443–48.

28 Douglas Densmore and John Anderson: Combinational Logic Design in Synthetic Biology, in: Iscas 2009 Ieee International Symposium On Circuits And Systems, Vols 2009, pp. 301–04.

29 Cf. for instance Anonymus: Welcome to the Registry (as note 22).

While there are various kinds of parts in synthetic biology, primarily these parts are pervasively conceived in terms of genetic elements: »We define a biological part to be a natural nucleic acid sequence that encodes a definable biological function, and a standard biological part to be a biological part that has been refined in order to conform to one or more defined technical standards.«[30]

As is well-known, molecular biology has for over a half-century attempted to describe genetic elements in cells in material-semiotic terms such as ›program‹, ›code‹ and ›machine‹.[31] From the mid-1950s on, nucleic acid sequences (DNA), genes, and subsequently, genomes became the primary locus of biological attention. Four decades of recombinant DNA biology have yielded a wide variety of practical techniques for cutting, copying and pasting DNA – mainly using enzymes isolated from various bacteria.[32] The sophisticated techniques for *in-vivo* and *in-vitro* manipulation of DNA largely function as ways of making biological parts in synthetic biology. That is, synthetic biology views molecular biology's repertoire of techniques of DNA manipulation from the perspective of parts. DNA comes nowhere near complying with the form-matter, or coding-coded distinctions that are layered into most industrial and engineering concepts of a *part*. Even the heavily invested promise of the genomic sciences starting in the 1990s – to unfold an exhaustive sequential specification of the DNA 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 and resequence every genome in sight (epigenomics, metagenomics, etc.) in pursuit of elusive variations, subtle interactions and inordinately complicated regulatory mechanisms.[33]

For its part, synthetic biology responds by saying that this super-saturated diversity, generated by the fluxing, differentiating mass of reactions, signals and criss-crossing feedback paths, needs to be pared down to something more layered, hierarchical and ordered, and that can be modelled in terms of parts in logical combination. Here the model of digital integrated circuits comprising logical elements such as gates and switches closely interconnected on semiconductor wafers seems to be almost ineluctable. Almost without exception synthetic biologists promote and indeed insist on engineering biology using parts, most quintessentially and reductively, in the form of BioBricks.[34] The descriptions, design and use of BioBricks

30 Reshma P. Shetty, Drew Endy and T. F. Knight: Engineering BioBrick vectors from BioBrick parts, in: J Biol Eng 2/1 (2008), p. 5.

31 Kay: Book of life (as note 6).

32 James D. Watson: Recombinant DNA. Genes and genomes. A short course, New York, NY 2007.

33 Evelyn Fox Keller: The century of the gene, Cambridge, MA / London 2000.

34 The BioBricks Foundation. Cf. http://biobricks.org/ (18. 11. 2011).

explicitly predicate *biological technical* objects comprising parts tailored to a »standardized interface technology«.[35] BioBricks are made from DNA sequences. These sequences conform to a standard proposed by the MIT computer scientist Tom Knight.[36] The BioBricks standard says nothing about the specific function of the biological parts. It really only addresses how parts can be put together. The standardisation concerns only those aspects of the biological part that pertain to assembly, or linking together. Obviously, parts that cannot be connected or interfaced easily are not engineerable. The BioBricks standards documents (BBF 2010), a RFC (Request for Comments) modelled on the grass-roots standardisation of internet protocols undertaken by the Internet Engineering Task Force in the 1970–80s,[37] is quite brief. It lists the DNA sequences with which every BioBrick must begin and end, and lists the sequences that may not appear in the BioBrick. With the right start and end sequences, some well-known and widely used laboratory techniques of DNA assembly can be applied to bring BioBrick parts together in a given order. The connection of several parts together will perhaps make a device with a particular function (a logic switch, an oscillator, a sensor, an actuator, etc.).

Importantly, putting several parts together makes something that is still a BioBrick. This is a key requirement since it opens, in principle, the door to many further compositions: »The key innovation of the BioBrick assembly standard is that a biological engineer can assemble any two BioBrick parts, and the resulting composite object is itself a BioBrick part that can be combined with any other BioBrick parts«.[38]

For instance, the device might be concerned with vision. In the biochemistry of animal vision, molecules such as beta-carotene are broken down into retinal, a form of vitamin A, by an enzyme called beta-carotene monooxygenase. Retinal forms the chemical basis for vision. So a simple BioBrick device could couple a part that synthesises beta-carotene with a part that produces retinal from beta-carotene. Such a device might be useful in building things that respond to light. In fact such a device exists in the Registry of Standard Biological Parts (Registry of Standard Biological Parts 2010), along with several thousand others.

Synthetic biologists, influenced by computer science, say that the process of putting parts together must be, in principle, »*idempotent*«.[39] The term, borrowed

35 Thomas Knight: Idempotent vector design for standard assembly of biobricks, Massachusetts Inst Of Tech Cambridge Artificial Intelligence Lab (2003), http://dspace.mit.edu/handle/1721.1/21168 (18. 11. 2011).

36 Tom Knight: Draft standard for BioBrick biological parts (2007). Under: http://hdl.handle.net/1721.1/45138. (18. 11. 2011).

37 Janet Abbate: Inventing the Internet, Cambridge, MA 2000.

38 Shetty et al.: Engineering BioBrick vectors (as note 30), p. 2.

39 Ibid. p. 5.

from mathematics and computer science, describes operations that can be applied to something (a number, a data structure, etc.) multiple times without changing the kind of result that it yields. Idempotency has been demonstrated in certain mathematical techniques and implemented in certain computational processes, especially in software architectures. Searching a database for an address is said to be an idempotent operation on the data in the database since it does not change that data (although such a search might itself cascade into many other changes). The principle of idempotency has previously only been implemented in software-based systems. The GET and PUT operations in the Hyper Text Transfer Protocol (http), for instance, are idempotent, because whether a specific GET operation is executed once or a thousand times on a given resource (URL), the result will be the same. Idempotency basically means that something changes state without any side-effects. In its application to synthetic biology parts, the principle of idempotency has a different function. It becomes a way of thinking about how parts relate to each other. In synthetic biology, no matter how many BioBricks are combined, the result will still be a BioBrick. No matter how many parts make up the device, the device will still be a part. This idempotency of BioBricks promises certain design and production potentials. From an engineering perspective, the process of design becomes a matter of functional composition, perhaps guided or automated by various rules; the process of fabrication becomes a matter of synthesis of DNA sequences. If idempotency holds, »cultures of circulation« similar to those seen in software[40] can begin to accrue and coalesce around the parts, assembling and combining them in many different ways, in layered and hierarchical architectures, similar to those seen in operating systems. Practically, in the engineering of devices, the opacity and convoluted interiority of living cells is replaced by lines of BioBricks, neatly concatenated in clear and distinct diagrams that can be manipulated and automated using engineering techniques of recomposition and ›abstraction hierarchies‹.

2. Putting parts together: the problem of pluripotent composition

Idempotency brings incredible restriction in the context of technical objects in general, let alone in the context of living things. It may turn out to be too restrictive. While there are thousands of BioBricks in the Registry of Standard Biological Parts, the engineering ideal of putting things together from idempotent parts, often described in the introductory chapters of software engineering textbooks as

40 Benjamin Lee and Edward LiPuma: Cultures of Circulation. The Imaginations of Modernity, in: Public Culture 14/1 (2002), pp. 191–213.

modularity,[41] is hard to realize in practice. Like all regulatory ideals, the attribute of idempotency synthetic biology ascribe to biological parts can only be guaranteed through *pluripotent* engagements with things. These engagements constantly undermine the notion that objects have attributes or stable properties, including the attribute of idempotency. In other words, idempotency as an engineering principle of change risks running against the processes of change that would allow technical objects to mediate nature-cultures anew.

Again, Simondon's account of parts and components is useful here. At the core of his account of how technical objects change, lies an analysis of parts or ›technical elements‹ in terms of *technicity*. Technical elements, like technical individuals and technical ensembles, have a technicity, »the capacity to produce or to undergo an effect in a specific way«.[42] The degree of technicity of an element refers to the degree of concretisation it embodies. As mentioned above, concretisation brings with it autonomy, mobility and capacity to enter into new associations. »The more the technicity of a technical element is raised,« writes Simondon, »the more the conditions of employing this element are wider by virtue of the high stability of the element«.[43] The availability of technical elements of high technicity affords the possibility of invention of technical objects. While the action of humans in the advent of technical objects is quite a complicated matter for Simondon (this will be discussed below in the context of models), what happens in invention depends on the technicity of technical elements. Invention »discovers an individual being capable of incorporating«[44] the technicities of different elements. A technical object organises and combines not the materiality of its elements, but their technicities. If technicity is a prerequisite for invention, as Simondon maintains, then locating the technicity of biological elements will be important for synthetic biology.

Does the principle of idempotency bring a high degree of technicity? It could be seen as implying a high degree of technicity since it abstracts away from the materiality of DNA. Simondon, however, is careful to point out that technicity of elements or parts arises from the technical ensembles they are invented and made in. That is, the potential of a technical element to move and recombine in new technical objects comes from the way in which a technical ensemble thoroughly blends or fuses considerations of form and matter in a technical element. Only a technical ensemble can span the geographies, techniques, and materials needed to achieve this fusion.[45] This is precisely *not* the case in the BioBricks notion of

41 Harold Abelson: Structure and Interpretation of Computer Programs, Cambridge, MA 21996.
42 Simondon: Mode (as note 8), p. 74.
43 Ibid. p. 75 et seq.
44 Ibid. p. 75.
45 Ibid. p. 72.

idempotency, where a notion of form derived from mathematics and computer science completely overshadows the ensemble of techniques for working with the materiality of DNA.

Molecular biologists have for several decades routinely assembled DNA sequences using many different methods and materials. As Christine Smolke, a leading synthetic biologist, observes, »many laboratories build up their own assembly methods and constructs and will have a laboratory-specific catalog of parts that are incompatible with any proposed standard.«[46] The BioBricks standards, however, imply one way of putting parts together. As the realisation dawned that parts need to be put together in different ways, various modifications of the BioBricks standard appeared, such as the BioFusion standard[47] and the BioScaffold standard.[48] Variations in technique are nothing unusual in the evolution of technical objects. Standards often replace each other in quick succession, especially in the early ferment of change associated with technologies. The crucial question is what kind of technicity of biological parts would be needed so that technical objects – objects that have an individual existence, that are open to change, that carry some charge of virtuality or duration – can come into existence? If we treat Simondon's account of the mode of existence of technical objects as a guide, we would have to say that the current framing of biological parts in terms of idempotent assembly may well be highly limiting. It would be »hypertelic« in Simondon's terms since it is adapted solely to the process of assembling parts, a process that pertains mostly to the »technical milieu«[49] in which BioBricks are made and used. This hypertelic tendency is quite deep-seated in synthetic biology. The premise of all BioBricks and most of the other parts produced by synthetic biologists is the Central Dogma of molecular biology:[50] information flows from DNA-encoded genes to RNA and then to proteins which direct cell metabolism through their activity as enzymes. Ideally, technical function is programmed in DNA, and via the transcription and translation processes of the cell assembled into proteins. Unlike the exhaustively designed materiality of microchips, themselves fabricated in a high-intensity glo-

46 Christine D. Smolke: Building outside of the box. iGEM and the BioBricks Foundation, in: Nature biotechnology, 27/12 (2009), pp. 1099–1102, here p. 1100.

47 Ira Phillips and Pamela Silver: A New Biobrick Assembly Strategy Designed for Facile Protein Engineering (2006). Under: http://dspace.mit.edu/handle/1721.1/32535 (18. 11. 2011).

48 Julie Norville, Angela Belcher and Tom Knight: A New BioScaffold Family of BioBrick Standard Biological Parts to Enable Manipulations such as Protein Fusions, Library Construction and Part Domestication (2008). Under: http://openwetware.org/wiki/The_BioBricks_Foundation:BBFRFC15 (18. 11. 2011).

49 Simondon: Mode (as note 8), p. 52.

50 Francis Crick: Central dogma of molecular biology, in: Nature 227/5258 (1970), pp. 561–63.

bal technical ensemble, BioBricks have to be not only assembled in design software, but fabricated either using laboratory techniques or increasingly, by online DNA synthesis services such as DNA2.0 or GeneArt.[51] Only then can they be introduced into microbes such as *e. coli*. Although they grow quickly, and have relatively simple architectures compared to animal and plant cells, *e. coli* are not amenable to the ›digital discipline‹ of binary voltage levels and constant clocked repetition on which algorithmic processing implicitly depends and which most contemporary electronics design simply takes for granted. Despite a century of laboratory manipulations,[52] the temporal dynamics of cells are difficult to tune because the regulatory processes taking place there are incredibly interwoven on many different time-scales ranging from micro-seconds to months. While synthetic biology imagines life as a set of processes that can be disaggregated into useful functions, the regulatory mechanisms operating in cells are sensitive to many different reactions and interactions. Through metabolic fluxes, DNA, RNA, proteins, carbohydrates, lipids and many other molecules come together and come apart in ways that blur the discreteness of *biological technical* functions, even as they embody the concretised life of *e. coli*. Again, *e. coli* as a technical object suffers from the more or less full concretisation is has undergone in evolution.

3. The geography of biological parts

The geography of control functions in *e. coli* is crucial here. In order to skirt around the massive evolutionary concretisation of microbes, synthetic biologists have concentrated on making parts that stay close to the DNA-related processes of the cell, especially the transcriptional and translational mechanisms that control when and how DNA sequences become RNA and then proteins. Most of the work in synthetic biology to date is focused on the transcriptional machinery that synthesizes RNA molecules from nuclear DNA. (Indeed, the PNAS paper discussed above only took into account the transcriptional processes associated with the *e. coli* genome.) The parts, modules and devices that have been made

51 GeneArt AG: GeneArt Supports iGEM Contest for the Third Year in a Row. GenAart – Excellence in DNA Engineering and Processing: Gene Synthesis, Directed Evolution, Plasmid Services (2009) Under: http://www.geneart.com/english/events-press/press/latest-press-releases/pressdetail/article/geneart-supports-igem-contest-for-the-third-year-in-a-row-1/index.html?no_cache=1&cHash=e0ab0227e2 (18. 11. 2011). DNA2.0: Synthetic Genes – Gene Synthesis Overview – DNA2.0. (2009) Under: https://www.dna20.com/index.php?pageID=17 (18. 11. 2011).

52 Hannah Landecker: Culturing life. How cells became technologies, Cambridge, MA 2007.

nearly all seek to utilise, modify or control cells via the transcriptional processes that synthesize RNA from DNA templates. Transcription is of such central importance that many descriptions and definitions of biological parts or modules take it as axiomatic. For instance, the definitions of parts or module in synthetic biology is intrinsically transcriptional: »We define a module as the simplest element of a gene regulatory network, consisting of a promoter, the gene(s) expressed from that promoter, and the regulatory proteins (and their cognate DNA binding sites) that affect the expression of that gene.«[53] The promoter, the gene, the DNA binding sites: all of this refers to parts of the regulatory mechanisms for transcription of DNA into RNA. By making transcription into the foundation of biological parts, synthetic biology can combine DNA sequences according to a combinational logic, as typified in BioBricks. It has been quite productive, and yielded, with varying degrees of viability, several hundred devices, for instance, made by teams in the iGEM competitions.

Yet the potential for logical combination of biological parts based on transcriptional processes comes at a cost. Both the geography of the cell and the technical milieu in which *e. coli* cells are worked on remain largely unthought. The design of idempotent parts largely regards the many interactions between environment, cell and genome as a background or platform for combinational logic. It presents combinational logic as platform-neutral. Actually, platform-neutrality, a term that refers to software that can execute on different computing hardware, is a highly specific achievement. The timing and the fluxing variability of these processes is much harder to deal with. In contrast to digital devices, where increasingly rapid synchronised clocking has been a regulatory constant that allowed many different kinds of automated design to take root (computer assisted circuit design, the many layers of software ranging from microcode to scripts), regulation in synthetic biology remains an ongoing problem in several senses.

A thicker account of how *biological technical* objects come into existence would need to bring the geography of the cell together with the control functions and transcriptional logics. As Simondon writes, »the technical object lies at the point of encounter of two milieu, and it must be integrated into two milieux at once«.[54] Every technical object effects a reciprocal relation between geographical and technical milieux. Simondon's examples usually come from manufacture, transport or communication, where geography and technology are much more tangible than in a biological laboratory. The general point that a technical object brings different worlds into relation is, nevertheless, quite compelling since it allows us

53 M. Kaern, W.J. Blake and J.J. Collins: The engineering of gene regulatory networks, in: Annual Review of Biomedical Engineering 5/1 (2003), pp. 179–206, p. 180.

54 Simondon: Mode (as note 8), p. 52.

to comprehend how technical objects become more lively. The virtuality and the becomings of technical objects arise, on this account, from the fact that in bringing two worlds or milieux into relation, in adapting and concretising, technical objects embody a process »which conditions the birth of a milieu, in place of being conditioned by an already given milieu«.[55] In other words, the genesis of every technical object gives rise to a mixed reality, a techno-geographic milieu, an »associated milieu«.[56] This associated milieu allows the object at the same time to function technically. The process of becoming a technical object is neither progress towards a fixed technical function (this would be dis-adaptive and hypertelic according to Simondon), nor a humanisation of nature, a subjection of the nature to human interests or functions. Rather, geographical and technical milieux come together in a way that allows a technical object come into being.

In the engineering of *e. coli* via transcription-based control functions implemented as parts, it is not clear how this auto-conditioning process can take place. It is possible that the parts or module-based approach actually prevents this encounter between geographic and technical milieux from taking place. The recurrent, auto-conditioning, discontinuous advent of a technical object may actually be blocked by the ready translatability of combinatorial logic into transcriptional processes. Synthetic biologists are aware of the problems of reliance on transcriptional logic implemented as parts and modules. First, transcription is relatively slow in relation to other biological processes. As authors of one review write, »transcriptional and translational devices are easy to connect and are capable of great logical complexity, but such devices cannot be assembled into systems that respond in seconds«.[57] Transcription and translation take place over minutes through a process of successive elongating synthesis. As a result, synthetic biologists have been compelled to also begin to develop devices that are not reliant on the processes of DNA transcription into RNA, and RNA translation into proteins. There is no space here to describe how they have done this, but sometimes it involves engineering RNA, sometimes engineering proteins. In either case, these alternatives alter the part-based composition of *biological technical* objects.

Second, even if transcription is fast enough as a control process, transcription may produce many side-effects. The products of transcription may themselves be inhibited or thwarted by other forms of metabolic interaction in the organism.

55 Ibid. p. 55.

56 Ibid. p. 57.

57 Ernesto Andrianantoandro, Subhayu Basu, David K. Karig and Ron Weiss: Synthetic biology. New engineering rules for an emerging discipline, in: Mol Syst Biol 2 (2006), Art. Nr. 2006.0028, p. 4. Under: http://www.nature.com/msb/journal/v2/n1/full/msb4100073.html (18. 11. 2011).

An »endogenous protein network«[58] affects almost everything that takes place in the cell. Hence some authors speak of the »ultra-sensitivity of transcriptional cascades«.[59] Others discuss the inherent ›noisiness‹ or ›stochasticity‹ (tendency to behave as if the product of random processes) of synthetic gene networks.[60] These other interactions need to be understood and taken into account somehow. Behind all of these difficulties lie broader issues of the geography of heat, light, humidity, nutrients and other stimuli affecting growth.

4. Device physics, crystals and the model as associated milieu

Acutely aware of these problems that threaten the very ambition to make *biological technical* objects, synthetic biologists have responded by developing models and simulations.[61] Indeed, the comparison between Linux and *e. coli* discussed at the beginning of this paper is a sign of this rethinking of the conditions of possibility of *biological technical* objects. This work is taking place in advance of the existence of the technical objects as such. The results of such modelling are quite varied. They may be models that express a gene network for a device (clock, oscillator, switch, etc.); systems of ordinary differential equations that convey the response signals produced by a biological device over time; as well as models that lay down formal specifications for how biological parts should be put together. Each of these models involves visual and mathematical forms that can be treated as the basis of engineering principles while the patterns shown in the plots and images suggest the presence of regularities, these regularities themselves are tuned by varying the parameters of mathematical models, and by conducting model analysis in support of design of synthetic circuits. The development of the models is perhaps just as important as the things that are made, for only the models offer the possibility of predicting the behaviour of parts and collections of parts. These models owe much more to chemical engineering than they do to software or microelectronics. They are almost always expressed in terms of changes in the concentrations of metabolites, and they rely on the techniques developed by chemists and chemical engineers to describe the rates of reactions.

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58 Boyle and Silver: Harnessing nature's toolbox (as note 19), p. 359.

59 Sara Hooshangi, Stephan Thiberge and Ron Weiss: Ultrasensitivity and noise propagation in a synthetic transcriptional cascade, in: Proceedings of the National Academy of Sciences of the United States of America 102/10 (2005), p. 3581.

60 Kaern et al.: Engineering (as note 53), p. 188.

61 Chris Barnes et al.: Bayesian design of synthetic biological systems. Proceedings of the National Academy of Sciences 108/37 (2011), pp. 15190–15195.

What is at stake in these models? We might approach them in two ways. First, we might see these models in terms of how they bring biology closer to other technologies. In attending to the specificities of reactions, dynamics, networks and fluxes, synthetic biologists sometimes claim that the models deliver information about »device physics«.[62] But the term ›device physics‹, borrowed from semiconductor engineering, covers over the significant differences in underlying ›physics‹. The development of semiconductors in the 1950s could draw on a century of solid-state physics, models of the regular structures of crystals, some statistical mechanics (and later quantum mechanics), electromagnetic field theory, and apply them to a well-established lineage of electrical and electronic communication technologies (telegraph, telephone, radio, radar, television) in order to bring together ›device‹ and ›physics‹. By contrast, the distance between the crystals of solid-state electronics and the cells of synthetic biology is much greater. There is as yet no biological equivalent to the detailed mathematical models of crystal structures or statistical models of conductivity and electron transport that animated the development of semiconductors. It may be that solid-state crystalline devices – the Intel model – rigidify the device-based approaches to synthetic biology and thwart the emergence of technical objects that incorporate the ongoing instability, the developmental cascades and the openness to events of living things.

There is consequently something else at stake in these models, and in thinking about these models. The practical problem that the models address is: how to bring scientific knowledge of something like *e.coli* together with technical mediation? Optimistically we can regard these models as a form of thinking that could introduce new margins of indeterminacy in technical objects. If technical objects only come into being through the creation of an associated milieu that conditions their technical function, we might re-appraise the very extensive modelling and simulation work going on in and around synthetic biology. It may be that in the 21st century, models are the terrain on which such mixed realities can be concretely thought. That is, the epistemic constructs and aggregates taking shape in models might well support the margin of indeterminacy, the background or basis on which the discontinuous event of technical invention can occur. Models are a form of thinking, and increasingly, models are the place where existing forms (logic, networks, devices, systems) draw on the almost overwhelming background of biological data. At least in cases, models stand at the confluence of the encyclopaedic drive of genomic research and the design imperative of industrial innovation.

In a certain way, technical objects share the same mode of existence as thinking itself. They can only come into being or take place discontinuously. They cannot be invented progressively. In order for a technical object with its associated milieu

62 Andrianantoandro et al.: Synthetic biology (as note 57).

to come into being, something living is needed, according to Simondon. For *biological technical* objects to come into existence, the real stake is here the synthetic biologists themselves as form of life. The vitality of technical objects, their potential for becoming, depends on the imaging and imagining of invention. Processes of imagining and inventing, and indeed human lives more generally, are essentially transductive: they are neither potential nor actual energy, but mediations between them two.[63] What happens in inventive thought is analogue to what happens in the object itself as it comes into being. The actuality of existing forms come into new relations on the basis of a ground of virtualities, potentials and forces: »[I]nvention is the taking charge of a system of actualities by a system of virtualities.«[64] Invention can only happen to the extent that existing forms are transformed by virtualities. Such virtualities can come from many different sources, but in invention they happen in thought, from that in thought which is not yet explicit, formalised, imaged, represented or perceived. As Simondon puts it, it entails »a recurrence of the future on the present, of the virtual on the actual«.[65] The fact that thought has an associated milieu, that it is itself an individuation in process, makes invention possible. As Simondon writes, »we can create technical beings because we have in us a play of relations and matter-form rapport that is very closely analogous to the one we institute in a technical object«.[66] The real stake for *biological technical* objects is not engineering principles, but forms of life, ways of operating invention, of thinking, that generate the kind of recurrent, auto-conditioning causalities that give rise to technical objects that can undergo concretisation.

Perhaps it would be good if synthetic biology attributed less potency to the machines – computers – that it seeks to emulate. It may be that these machines have less substance, less essential stability, less potency than synthetic biologists sometimes imagine. Wanting to do what Intel does for electronics may well entail somewhat different models of responsibility. The combination of Intel-inspired idempotency and electronics engineering-inspired modelling of devices might well limit the margins of indeterminacy that allow machines to compose ensembles, to form associations, and to embody technical cultures. To re-think how things come to exist more generally along the lines suggested here would involve taking into account the »free plurality of relations, or […] the open series of possible relations with other machines inside the technical ensemble«.[67] When things exist synthetically at the interfaces between different scientific disciplines, economic, industrial, media and cultural settings, the tensions between abstraction

63 Cf. Simondon: Mode (as note 8), p. 143.
64 Ibid. p. 58.
65 Ibid. p. 144.
66 Ibid. p. 60.
67 Ibid. p. 146.

and concretisation, and between the technical and the natural, become particularly acute. Rather than either identifying *e. coli* and *Linux*, or seeing them radically differently, the technical objects of the biological century might come into existence when their genomes, their operating systems, are articulated together. Philosophical, critical and empirical work has a role here too. Simondon describes the process of thinking about technical action as letting oneself be shaped or formed by the »material crystallisation of … thinking that has resolved a problem«[68] Our descriptions of biology as technology participate in opening biotechnical objects to further thought and invention.

68 Ibid. p. 247.