## SCIENCE AT THE CROSSROADS

## Synthetic Biology: Life as App Store

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Since the early 19<sup>th</sup> century, scientists have proposed a variety of naturalistic explanations for the organization of matter in living systems, particularly its origin and propagation from parent to offspring. Some biologists (selectionists; adaptationists) favor the idea that such organization arises by natural selection exerted on living materials with little intrinsic structure of their own. Others (structuralists; physicalists) say the complex materials that living creatures are made of have inherent self-organizational properties that determine what the life forms are and how they develop. The lack of conclusive answers despite decades of research and tens of thousands of published studies has allowed empirically unfounded creationist beliefs to persist in broad sectors of the population (Newman 2008). The still primitive understanding of the material basis of living systems also continues to instill awe in scientists, most of whom probably consider the notion of rationally designing organisms an impractical dream. However, the new field of synthetic biology now aims to change this. As I describe below, with its modus operandi of sidestepping biological origins and complexity in favor of simplification and application, ironically—and despite the intentions of the majority of scientists involved—the synthetic biology enterprise verges uncomfortably close to the metaphysics of creationism.

Synthetic biology is a collection of techniques and agendas (both research and business) that includes (i) the construction of DNA sequences that encode protein or RNA molecules which assemble into complex entities (macromolecular complexes, circuits, networks) with previously defined or novel functions; (ii) the substitution of chemically synthesized DNA or DNA analogues for their natural counterparts in order to change cell behavior and/or produce novel products; and (iii) attempts to define and construct basic living systems from minimal sets of molecules. These programs have been termed, respectively, *DNA-based device construction, genome-driven cell engineering*, and *protocell creation* (O'Malley, et al. 2008).<sup>1</sup> Synthetic biology has been termed "extreme genetic engineering" (ETC Group 2010; Tucker and Zilinaskas 2006) in contrast to earlier recombinant DNA techniques that sought mainly to modify and refine existing types of organisms by altering or inserting individual genes.

Before the emergence of modern science, the acquisition of useful technical knowledge in the absence of theoretical understanding had a rich history (Bernal 1965). The Neolithic revolution saw the domestication and breeding of plants and animals millennia before the formulation of a science of inheritance. Bronze and Iron Age metallurgy flourished without the atomic theory, and bridges and pyramids were built in societies ignorant of the laws governing tensions and loads. Synthetic biology, however, has emerged in a world in which the sciences either have sound theoretical frameworks (e.g., chemistry,

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<sup>&</sup>lt;sup>†</sup> I thank Eric Hoffman for helpful comments and suggestions.

<sup>&</sup>lt;sup>1</sup> Protocell creation is a program of basic science research that is largely peripheral to the applications and commercial ferment around synthetic biology.

physics),<sup>2</sup> or if they do not (e.g., ecology, climatology, seismology), are striving to acquire them. For some proponents of synthetic biology, though, its lack of theory is a matter of indifference or even a virtue.<sup>3</sup>

The cellular systems of concern to synthetic biology are, in fact, even more complex than ecological, atmospheric, and geologic systems whose behaviors continue to elude precise forecasting. Notwithstanding the field's conceptual thinness, however, the ambitions of many of the prominent figures in synthetic biology extend beyond prediction, or even control, to genesis. In the words of a sociologist of science, "synthetic biology does not simply aim to describe or to represent life; it aims to create it" (Calvert 2008, 394). I argue below that this goal, though probably espoused by many synthetic biologists, is based on erroneous assumptions and thus highly suspect as an industrial technology.

## The Registry of Standard Biological Parts (RSBP; see

<u>http://partsregistry.org/Main\_Page</u>) associated with the non-profit BioBricks<sup>4</sup> Foundation (see <u>http://biobricks.org/</u>) promises "a collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems." But current understanding of molecular genetics and cellular biochemistry guarantees that many such parts will not exhibit the same activity in different assemblages (see below). This goes unmentioned in the online materials the Foundation has prepared for outreach to the public and business communities. According to a recent report in the journal *Science*, participants at a synthetic biology meeting in July 2010 concluded that of the 13,413 items then listed in the RSBP, 11,084 didn't work. One presenter noted, "Lots of parts are junk" (Kean 2011).

The field's implicit and sometimes explicit view of cells and multicellular organisms is that they are devices that implement sets of defined tasks or functions, or if they are not inherently so, they can be engineered to fit this description.<sup>5</sup> The field thus encourages an ethos of hacking and gamerism. (A recent profile of the Harvard synthetic biology researcher, George Church, is titled "The Life Hacker.") A good sense of the frame of mind of many of the principals can be gleaned from a 2005 article by the physicist Freeman Dyson, who is something of a godfather to the synthetic biology movement:

In the post-Darwinian era, biotechnology will be domesticated. There will be do-it-yourself kits for gardeners, who will use gene transfer to breed new varieties of roses and orchids. Also, biotech games for children, played with real eggs and seeds rather than with images on a screen. Genetic engineering, once it gets into the hands of the general public, will give us an explosion of biodiversity. Designing genomes will be a new art form, as creative as

<sup>&</sup>lt;sup>2</sup> While always, in principle, subject to revision, quantum theory, molecular dynamics, relativity theory, and thermodynamics and statistical physics have provided conceptually coherent accounts and quantitative prediction of the behavior of matter on multiple scales.

<sup>&</sup>lt;sup>3</sup> One highly touted strategy involves mass production of billions of variant *E. coli* genomes that can be scrutinized for favorable phenotypes; see Bohannon (2011). In most scientific disciplines massive trial-anderror protocols would be antithetical to theory-guided research, but in some Darwin-inspired interpretations of biology, it is the essence of the theory (Dennett 1995).

<sup>&</sup>lt;sup>4</sup> The term "BioBricks" is trademarked by the BioBricks Foundation.

<sup>&</sup>lt;sup>5</sup> A 2004 News Feature in the journal *Nature* quotes Tom Knight, a senior computer scientist in the MIT School of Engineering and an originator of the BioBrick notion as stating "An alternative to understanding complexity is to get rid of it." See Ball (2004).

painting or sculpture. Few of the new creations will be masterpieces, but all will bring joy to their creators and diversity to our fauna and flora. (Dyson 2005).

Dyson's vision of unbridled, human-conducted biological manipulation is already underway (strikingly echoing that of the English philosopher and political figure Francis Bacon [1561–1626] in his posthumously published utopian novel, *The New Atlantis*, written nearly 400 years ago).<sup>6</sup> Some of the incubators are the International Genetically Engineered Machine (iGEM) undergraduate competition, held yearly at the Massachusetts Institute of Technology (MIT), and venues of the do-it-yourself biology (DIY bio) movement (Kean 2011).<sup>7</sup> The genetically modified microbes and animal and plant cells generated by these activities (as well those in ostensibly more accountable academic and industrial settings) could potentially invade and establish themselves in surrounding ecosystems in a disruptive and destabilizing fashion.

When much milder sorts of DNA manipulations were first performed in the U.S. in the 1970s, these very concerns led to frank discussions by the scientists involved in venues such as the influential 1975 conference on recombinant DNA in Asilomar, California. Several years of deliberation by the Recombinant DNA Advisory Committee (RAC) followed, resulting in a set of National Institutes of Health (NIH) Guidelines for the performance of gene manipulation research (Wright 1994), which still remain in place. These guidelines are binding for all academic institutions that accept federal funds and are observed voluntarily by many private biotechnology companies (Erickson, Singh, and Winters 2001).<sup>8</sup>

<sup>6</sup> In The New Atlantis, the father of Salomon's House (a kind of research institute) describes its accomplishments in organism modification as follows: "[W]e practice...all conclusions of grafting, and inoculating, as well of wild-trees as fruit-trees, which produceth many effects. We make them also by art greater much than their nature; and their fruit greater and sweeter and of differing taste, smell, color, and figure, from their nature. And many of them we so order, as they become of medical use. We have also means to make divers plants rise by mixtures of earths without seeds; and likewise to make diverse new plants, differing from the vulgar; and to make one tree or plant turn into another...We have also parks, and enclosures of all sorts, of beasts and birds; which we use not only for view or rareness, but like-wise for dissections and trials, that thereby may take light what may be wrought upon the body of man. Wherein we find many strange effects: as continuing life in them, though divers parts, which you account vital, be perished and taken forth; resuscitating of some that seem dead in appearance, and the like. We try also all poisons, and other medicines upon them, as well of chirurgery as physic. By art likewise we make them greater or smaller than their kind is, and contrariwise dwarf them and stay their growth; we make them more fruitful and bearing than their kind is, and contrariwise barren and not generative. Also we make them differ in color, shape, activity, many ways. We find means to make commixtures and copulations of divers kinds, which have produced many new kinds, and them not barren, as the general opinion is. We make a number of kinds of serpents, worms, flies, fishes of putrefaction, whereof some are advanced (in effect) to be perfect creatures, like beasts or birds, and have sexes, and do propagate. Neither do we this by chance, but we know beforehand of what matter and commixture, what kind of those creatures will arise" (Bacon 1979). The anticipation of the ethos of synthetic biology in these proto-Enlightenment passages is made poignant by the last sentence, which strikes a rationalist chord entirely abandoned in the modern (or postmodern). See Newman (2009b).

<sup>&</sup>lt;sup>7</sup> DIY bio consists of hobbyists, some with professional training, who convene in studio-like laboratories such as GeneSpace in Brooklyn, New York and BioCurious near San Francisco, California, or even in their own garages or basements.

<sup>&</sup>lt;sup>8</sup> Significantly, however, in 2011 certain synthetic biology-related manipulations of organisms were excluded from coverage by the NIH Guidelines at the request of the pharmaceutical industry. See http://www.selectagents.gov/resources/13.Jacqueline\_Corrigan-Curay%20CDC%20FINAL%20Talk.pdf.

The synthetic biology hacker culture is only voluntarily regulated despite the potential and intention to produce increasingly exotic life forms (Kean 2011).

Molecular biologists, and particularly bioentrepreneurs (the two categories now greatly overlapping), have often expressed frustration with the regulatory inconveniences that were set in motion because the public and governmental agencies took seriously the concerns of an earlier generation of scientists. Many are determined to weaken or eliminate the existing rules and prevent further restrictions on emerging technologies in the field. In the present U.S. climate of regulatory deconstruction, "self regulation" is the watchword, and the bureaucratic tendency is to subsume the microbes and other organisms prospectively created by synthetic biology under the NIH guidelines, even though the technology addressed by those guidelines is very different from that currently available with synthetic biology. The Presidential Commission for the Study of Bioethical Issues was charged by President Barack Obama in May 2010 to prepare a report on the ethical implications of synthetic biology, and by December of that year the report had been submitted. Important issues such as the possibility of escape of novel, disruptive microorganisms into the environment appear to have been set aside with minimal exploration. This is the relevant discussion in the report:

Synthetic biology's critics and proponents alike worry that creating new organisms that have uncertain or unpredictable functions, interactions, and properties could affect ecosystems and other species in unknown and adverse ways. The associated risks of escape and contamination may be extremely difficult to assess in advance, as such novel entities may have neither an evolutionary nor an ecological history.<sup>[56]</sup>...Countering these concerns, at least somewhat, is experience showing that synthetic cells and systems in research settings have tended to be short-lived by comparison to those that have evolved in nature. Scientists have observed that synthetic organisms allowed to develop in the laboratory have consistently evolved toward nonfunctionality.<sup>[57]</sup> (*New Directions* 2010, 70).

It is difficult to evaluate this statement. Note 57 in the original document contains an inactive link to a presentation before the commission by a prominent synthetic biology researcher. If the original text contained evidence for the reassuring conclusion, it was probably anecdotal, since an attempt to identify relevant studies on PubMed in November 2011 using the search terms "synthetic biology" + "nonfunctional" failed to turn up any. But even if escaped microbes are short-lived, transfer of their novel genes and genetic networks to environmentally established counterparts remains a possibility (Heuer and Smalla 2007).

Critical scrutiny of synthetic biology and demands for more adequate regulatory regimes for the more than 200 academic and commercial laboratories now engaged in synthetic biology research in the U.S.<sup>9</sup> have therefore fallen to civil society groups. Shortly after the release of the Presidential Commission's report, a letter of protest drafted by Friends of the Earth U.S. (FOE), the Erosion, Technology and Concentration (ETC) Group, and the International Center for Technology Assessment (ICTA) that was signed by 58 environmental, public interest, and religious groups from 22 countries was issued. The letter cited the report's ignoring of the precautionary principle (Newman and Raffensperger 2000), lack of adequate concern for the environmental risks of synthetic biology, reliance on

<sup>&</sup>lt;sup>9</sup> Mapping the Emerging Synthetic Biology Landscape (Synthetic Biology Project, Woodrow Wilson International Center for Scholars, Washington, DC, 2011), <u>www.synbioproject.org/library/inventories/map/</u>.

unsubstantiated technologies for environmental safety, and reliance on the chimera of self regulation. A set of governance principles for synthetic biology, which include synthetic biology-specific regulations to protect the environment and ensure worker safety, was released jointly by FOE, ICTA, and ECT Group in early 2012.

Interest in synthetic biology by major corporations in the energy, chemical, and agricultural sectors has been immense, with corresponding activity by venture capitalists determined to recruit publicly funded academic scientists into startup operations. The submission by the International Civil Society Working Group on Synthetic Biology (consisting of the ECT Group, FOE, ICTA, EcoNexus, and the Sustainability Council of New Zealand) to the Convention on Biological Diversity's Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA)<sup>10</sup> cites a 2009 estimate of the market for synthetic biology products at \$233.8 million in 2008 with predictions of growth to \$2.4 billion in 2013 and \$4.5 billion by 2015. According to one industry analyst, synthetic biology startups in the biofuels and bio-based chemicals sector received \$1.84 billion in private funds between 2004 and 2010. According to sources in the same report, four of the top five energy companies (Royal Dutch Shell, Exxon Mobil, British Petroleum, and Chevron), three of the top five chemical corporations (BASF, Dow, and Exxon Mobil), and the top three grain trading companies (Cargill, Archers Daniel Midland, and Bunge) had established partnerships with synthetic biology companies by 2011.

As might be expected, the U.S. military has taken a keen interest in the technology as well. A report in *Nature* recounts (with unacknowledged Orwellian touches) discussions at a 2011 conference convened by the Department of Defense (DOD)'s Defense Threat Reduction Agency at which synthetic biologists were asked to look for "more environmentally friendly ways to manufacture explosives." One University of Texas researcher who holds grants from several DOD agencies asserted, "You can have someone die because of the way we currently prepare munitions, or you can put in proposals to try to make it easier and safer and greener to make munitions." Another bioengineer, from Boston University, was awarded \$1.5 million a year for five years by the DOD's Office of Naval Research to develop "microbiorobots"—reprogrammed bacteria that are able to sense materials in the environment. Such robots could potentially be repurposed to deliver poisons or explosives, but the Geneva Conventions (the ones that also prohibit torture) forbid signatories from funding work that could facilitate the development of biological weapons (Hayden 2011).

The gee-whiz aura that pervades most press coverage of synthetic biology plays into a glorification of gimmickry in modern society, which in recent years has been embodied in the products of Apple Inc., developed under the supervision of the late Steve Jobs. Craig Venter, the principal private entrepreneur behind the Human Genome Project of the 1990s, has become an iconic figure in science journalism where he is frequently pictured astride his personal yacht, *Sorverer II*, collecting previously uncharacterized microorganisms from poorly accessible sites to use in his commercial synthetic biology projects. One is a \$600 million project sponsored by Exxon to engineer the genome of algae, using trial-and-error strategies such as mass production of randomly mutated genomes, in an attempt to solve the global

<sup>&</sup>lt;sup>10</sup> http://www.cbd.int/doc/emerging-issues/Int-Civil-Soc-WG-Synthetic-Biology-2011-013-en.pdf.

climate and food crises.<sup>11</sup> The ETC Group, in its synthetic biology report cited above, summarizes its well-referenced discussion of such plans as follows:

Since [algae] are very common in the environment, there is a possibility of outcrossing with natural species and contamination of microbial communities in soil, seas and animals, including humans. Microbes propagate and mutate quickly and also move through soil, waterways and other routes, so it may be especially difficult to track escapes. Synthetic biologists contend that their lab-made creations are probably too weak to survive outside the optimized conditions in which they were developed; however, this assumption has been proven wrong before [for transgenic corn and soy]. . .Reengineering algae's biology, or altering global algal stocks on any large scale. . .may directly impact the global oxygen cycle, carbon cycle, nitrogen cycle and ozone production—potentially in unpredictable and harmful ways. (ETC Group 2010, 38, 49.)

Beyond new kinds of fuels and foods, the ambitions of the field's visionaries might be expected to turn toward production of "improved" humans, as occurred over the past century with the successive rise of selective eugenic, transgenic, and cloning technologies (Newman 2010). Thus, Harvard's George Church confided to a reporter, "I wouldn't mind being virus-free," which elicited the comment: "It may be too late to reengineer all of his own cells to prevent viral infections, but Church doesn't rule out the possibility of rewiring the genome of a human embryo to be virus-proof" (Bohannon 2008). This proposal might not pass muster with Harvard's Institutional Review Board for human subjects research, particularly if evidence of benefits of endogenous retroviruses in human evolution came to its attention (Nelson, et al. 2003). However, Church's style of thought, which is shared by fellow life hackers<sup>12</sup> and abetted by journalistic hype, suggests that other ill-conceived transhumanist stratagems may be in the offing.

Apart from the potential damage to the environment, the food chain, and to human individuals and the gene pool, some commentators have expressed concern about detrimental effects that synthetic biology and related engineering approaches to biology may exert on the scientific and broader culture.<sup>13</sup> Scholars associated with the field of "science and technology studies" (STS), which took form in the decades since the original recombinant DNA debate, are often more critical of the conceptual frameworks within which scientists perform, report, and publicize their work than the social scientists and bioethicists of the previous period, many of whom served as enablers of researchers' reductive models and exaggerated claims (Stevens 2000; Newman 2009b).

Questions raised and problematized in the recent literature include the validity of the engineering paradigm for synthetic biology, the doctrine (which can be traced back as far as the Italian political philosopher Giambattista Vico [1668-1744]) that we can only truly understand that which we can construct, that a single component of a complex system (e.g.,

<sup>&</sup>lt;sup>11</sup> See the online interview of Venter in *Scientific American*, subheaded: "The geneticist and entrepreneur hopes to use synthetic biology to transform microscopic algae into cells that eat up carbon dioxide, spit out oil and provide meals." (Biello 2011).

<sup>&</sup>lt;sup>12</sup> Another prominent synthetic biology researcher, Drew Endy, formerly at MIT and now at Stanford, asked, in an interview with a *New Yorker* reporter, "What if we could liberate ourselves from the tyranny of evolution by being able to design our own offspring?" (Specter 2009, 61).

<sup>&</sup>lt;sup>13</sup> A range of these views is contained in a special issue on synthetic biology of the journal *Biological Theory* (<u>http://www.mitpressjournals.org/toc/biot/4/4</u>).

the genome of a cell or organism) can be sufficient to account for the properties of the whole, and that there is a unique viewpoint from which to comprehend the nature of a multiscale, hugely data-rich (e.g., biological) system (O'Malley 2009; Moya 2009; Callebaut in press). The relation of the new landscape of synthetic biology to prospects for patenting and commodification of life forms and their components has also garnered attention (Calvert 2008).

Synthetic biology derives from several strains of  $20^{\text{th}}$  century biological research that are conceptually very different (Calvert and Fujimura 2011; O'Malley 2009). The term, though first used as a book title by the French biophysicist Stéphane Leduc a century ago (1912), came into currency at the beginning of the present century to describe two specific, independent scientific programs heralded by two key papers. In one, an artificial gene-based circuit designed to have a novel dynamical property (a clock-like oscillation in the production of a protein) was introduced in the bacterium *E. coli* (Elowitz and Leibler 2000); in the second, a few years later, a naturally occurring genome (of a bacterial virus) was synthesized and shown to function in *E. coli* (Smith, et al. 2003).

The first of these research agendas, the prototype of the "device" paradigm described at the beginning of this article, arose within the scientific field of "systems biology." This is a multifaceted program that in its most sophisticated versions involves not only genes, but also the physics and chemical dynamics of interacting gene products and cells on multiple spatial and temporal scales (Newman 2003). To understand the range of behaviors of even the simplest of synthetic biology devices, mathematical and computational models are typically employed, and the results may indicate that "partition of a network into small modules. . . could in some cases be misleading, as the behavior of these modules is affected to a large extent by the rest of the network in which they are embedded" (Isalan, et al. 2008). In fact, simple genetic networks with minuscule changes can give rise to qualitatively different, or even opposite effects (Isalan 2009). Furthermore, many proteins—fundamental molecular components of every biochemical circuit or device—change their structure and function depending on the context (Uversky 2011).

The second research agenda, the prototype of "genome-driven cell engineering," is an extension of the older recombinant DNA technology, which has yet to live up to the enormous promises that accompanied its development.<sup>14</sup> The new methods are more powerful: by brute-force replication and selection protocols (see note 2) or more directed biosynthetic pathway engineering, they could potentially yield novel fuels or foodstuffs, or new means of manufacturing scarce pharmaceuticals (e.g., the antimalarial herbal derivative, artemisinin; Tsuruta, et al. 2009). Alternatively, they could be used to endow familiar and manageable organisms with new capabilities (e.g., as scavengers of or sentinels for toxics). But the experience of earlier genetic engineering initiatives suggests that the profit motive rather than broad human needs will be the driving force of the majority of these efforts (see Newman 2009a and references therein). Of all the areas of synthetic biology, the reductionist DNA-driven approach is the one most hospitable to business models based on patents, which strengthens its appeal to investors (Calvert 2008).

<sup>&</sup>lt;sup>14</sup> The evolutionary biologist John Avise wrote in 2004, "Despite nearly three decades of experience with recombinant DNA techniques, the ultimate contribution to the broader human enterprise remains uncertain" (Avise 2004, 177).

As a means for understanding the nature of living systems, none of the agendas within synthetic biology can take us very far, since they all ignore or marginalize evolution. When ancient protocells first arose more than 3 billion years ago from nonliving components (a process still shrouded in obscurity), they were likely to be based on some of the dynamical processes mobilized by synthetic biology device construction. But the world that engendered the first life-like systems contained no DNA, RNA, protein, or membraneforming lipid (i.e., water-insoluble) molecules; different molecules provided the material substratum for ancient life (Budin and Szostak 2010). The present-day components of cellular life evolved over time from the primitive ones. DNA-based genomes could not have existed in the first life-like systems, and the genomes of present-day cells are overwritten scratchpads recording the billions of years of evolution since DNA became the primary repository of molecular continuity. Fundamental cellular mechanisms are therefore impossible to decipher by reading any modern organism's DNA sequence.

Genome-driven cell engineering also deliberately ignores many of the features of cells and organisms that have emerged from systems biology, including a determining role for physics. What are not conceptualized in this framework are realities such as nonlinear responses to small internal or external variations, causality at multiple spatial and temporal scales, and many-to-many mapping between genotypes and phenotypes. In their report on the replacement of the entire genome of a bacterium by a laboratory synthesized molecule with a virtually identical sequence, Craig Venter and his colleagues described it as the creation of a synthetic cell (Gibson, et al. 2011). But the experiment required an actual cell minus its DNA to serve as the host of the synthetic genome, and the genome was copied, not designed. No new insights into the nature of cellular life emerged from this study.

DNA-based device construction and protocell creation, in contrast, can actually provide some insights into the physics and chemical dynamics of the living state. Since these synthetic biology programs typically either manipulate and modify molecular components that are the products of life's long history rather than the conditions of its emergence, or introduce artificial ones, they do not (nor do they claim to) elucidate how and why cells function as they do.<sup>15</sup> While some synthetic biology researchers have begun to draw lessons from evolution, the goal has been to circumvent and engineer around ancient constraints to achieve their practical objectives (Skerker, Lucks, and Arkin 2009; Nandagopal and Elowitz 2011).

In a real sense, synthetic biology treats cellular life as a programmable "black box" within which ingenious functionalities can be constructed. This is reminiscent of the iPhone and other Apple-manufactured mobile devices, which their supervising creator, Steve Jobs, contrived to be black boxes, by making the hardware difficult to access and the software closed source, but simultaneously to be highly amenable to the development of "apps" (Isaacson 2011). Strangely, this is also how the Intelligent Design (ID) variety of creationism sees organisms—as unfathomable black boxes that evolution can modify and embellish, but not produce (Behe 1996).

<sup>&</sup>lt;sup>15</sup> An analogy is the impossibility of understanding how the U.S Constitution functions without any knowledge of U.S. history.

The creationist connection has more than incidental relevance to the progress (and potential setbacks) in our understanding of nature. In an influential essay, the Soviet physicist and historian of science Boris Hessen showed how, during the formation of Newtonian mechanics, the relation to a particular set of practical industrial and military agendas foreclosed certain avenues of basic inquiry (Hessen 1931). Thus, even Newton himself failed to conceptualize the notion of conservation of energy, implicit in his equations of motion. Such cases of uneven development are all but inevitable as a new science is taking form in a particular technological setting. What we are experiencing with the rise of synthetic biology, however, is a reversal in the advance toward a comprehensive understanding of living processes. In the context of the rise of anti-science ideologies in the social and political realms, even scientists seem willing to black-box nature and occupy themselves with widgets. The evolutionary biologist Carl Woese has written that "a society that permits biology to become an engineering discipline, that allows that science to slip into the role of changing the living world without trying to understand it, is a danger to itself," warning us not to imagine that tinkering and manipulation are the same as knowledge and understanding, even in the strictly scientific realm (Woese 2004).

If developed subject to the precautionary principle and implemented in reversible ways with appropriate safety monitoring and controls, synthetic biology can potentially contribute in a modest fashion to science, medicine, and the preservation of nature. Some of the apps devised by synthetic biologists are already useful as tools for genetic research (Constante, Grunberg, and Isalan 2011), and others show potential as diagnostic sensors for abnormal blood proteins and environmental toxins, and as therapeutics against cancer (Huang, et al. 2008; Haynes and Silver 2011; Ausländer, Wieland, and Fussenegger 2011). But, as indicated above, there continues to be a lack of proper oversight and risk assessment, and the field remains an open terrain for the corporations and military, which are avidly pursuing new apps, including ones for problems they have created, for the new problems they will create on the way to fixing the old ones, and for killing people. This dark side can only be held in check by recognizing the credulous techno-utopianism and distancing from actual scientific engagement that contribute to the coolness of the app culture.

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