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Book review: Robert Carlson's *Biology is Technology: The Promise, Peril, and New Business of Engineering Life*

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Biology is Technology: The Promise, Peril, and New Business of Engineering Life. By Robert Carlson. Harvard University Press, Cambridge, MA. 2010. 279 pp., $39.95 (hardback). ISBN: 9780674035447

While the political plate is full of pressing global issues to contend with such as energy, global warming, healthcare, a recession, and international security, polling reveals the economy is the major concern of most American citizens. Failed macroeconomic policies have created the need for a new paradigm for economic growth.

These issues all have something in common, and that nexus is the success of technology. In free market, capitalist economies, markets eliminate obsolete technologies and utilize innovations to create new avenues for economic growth. The marketplace has a demand for industrial applications and useful products that will provide solutions to these issues.

Over the past several decades, several industrial revolutions took place including those in genomics, nanotechnology, and synthetic biology. In the 1990s, scientists sequenced the human genome in hope of providing medical cures through personalized medicine and DNA vaccines. However, genomic cures have yet to materialize, mandating more focus on translational genomics. An infrastructure to support nanotechnology is in place, and researchers are in various stages of product development.

Over the past decade, synthetic biology has caught the attention of venture capitalists in Silicon Valley, governments, foundations, and the private sector. In addition to job and wealth creation, synthetic genomics researchers will potentially create revolutionary products through modifying genomes, creating the next generation of plastics, agricultural products, bioremediation organisms, bioweapons, carbon neutral fuels that will reduce our dependence on oil, novel enzymes, and vaccines.

Biology is Technology is the most comprehensive overview to date of the state of the field of synthetic biology. Although Rob Carlson, a bioengineer and principal with Biodesic, has formal academic training

in physics, his fellowship with the Molecular Sciences Institute and expertise on biotechnology make him uniquely qualified to analyze the field's potential and the challenges to its future development.

A crucial step to ensuring the success of the field is the development of enabling technologies. This includes fast, powerful, and cost efficient computers. In addition, DNA sequencers and DNA synthesizers are necessary to identify genes and make synthetic DNA sequences.

Moore's Law reveals that computing power progresses and its costs decline at a predictable rate. Carlson calculated that the capabilities of sequencers and synthesizers have followed a similar pattern referred to as the Carlson Curve. The costs of reading and writing new genes and genomes are falling by a factor of two every eighteen to twenty-four months, and productivity in reading and writing is independently doubling at a similar rate. The Carlson Curve projects that scientists are approaching the ability to sequence a human genome for $1000, which should occur in approximately 2020. Consequently, we are now at the inflection point on the growth curve where scientific discoveries and inventions in synthetic biology will occur.

I find Carlson's thoughtful discussions of the major challenges to the field's development the major strength of the book. This is primarily due to his ability to explain simply what non-engineers can learn from engineers.

One major challenge is the complexity of biological systems. Bioengineers hope to mass produce bioengineered products similar to those of the microelectronics and computer industries. However, technologies require development, and industrial processes ultimately require a proof of concept – and they face engineering challenges in the process.

To simplify the complexity of systems, engineers separate complicated problems into simpler independent problems. Drawing on three engineering principles from Drew Endy's "Foundations for Engineering Biology" article (2005), Carlson elaborates on how these principles apply to synthetic biology. First, is the standardization of parts. This requires that researchers identify biological parts such as switches and promoters, and ultimately create a catalog of interchangeable parts. Second, bioengineers have abstraction hierarchies, a continuum from synthesized oligonucleotides made from 50-100 base pairs, to build parts, which make devices, which make a system. Third, it is necessary to decouple or separate the design and fabrication processes.

The vision of bioengineers is to build synthetic biological systems that exchange information from compatible standardized parts and behave predictably. Endy and Carlson use a Lego metaphor to describe synthetic biological parts; however, when parts are assembled, a problem with crosstalk or noise between signals in pathways occurs. Until researchers better understand these undesired interactions that nature has already worked out, applications such as gene therapy will have unwanted side effects. In addition, the effects of environmental and developmental interaction on gene expression and cell cycles are not fully understood. Currently, researchers must repeatedly use trial and error to create predictable systems. Craig Venter recently disclosed that 99 percent of his lab experiments failed before creating a synthetic cell.

To effectively illustrate the current limitations of designing biological systems, Carlson uses the aeronautical engineering metaphor of geese and early aircraft – both of which appear too heavy to leave the ground. While the solution to the weight and performance issue is resolved by evolution in geese, humans designed efficient systems for aircraft. When aeronautical engineers developed early aircraft, they used a flight model simulation for the interaction of aircraft and the environment. Carlson notes there is nothing similar in synthetic biology. Developing a similar testing environment will require the ability to

quantify relationships between variables in a model describing phenomena at the molecular level, such as protein bonding and chemical and physical reaction rates of molecular components.

Another major challenge is the development of a system that provides incentives to researchers while at the same time not creating barriers to the development of products for the public good. Carlson describes the incentives for several cutting edge researchers which vary based on their objectives, resulting in different intellectual property approaches.

The Gates Foundation, a non-profit, granted US$42 million to UC Berkeley professor Jay Keasling to make a synthetic vaccine for malaria. He hopes to place the genes that produce a precursor to the drug artemisinin in bacteria and yeast which are used as factories for production. This is a unique and innovative solution to provide a cure to victims who typically can not afford the treatment. So, Keasling is not only interested in treating the disease, but can also use the principles learned from the process to make profits from other products in the future.

Using a similar bioengineering process, Craig Venter's Synthetic Genomics has partnered with ExxonMobil which provides $600 million to produce low carbon synthetic fuels using algae. This partnership to develop biofuels seeks a return on investment and profits, and will also benefit society by providing a solution to energy independence and reduce carbon emissions that are accelerating global warming.

Stanford bioengineer Drew Endy created the International Genetically Engineered Machines (iGEM) competition coordinated by MIT for undergraduates from around the world to make novel bioengineered products. In addition, Endy created the BioBricks Foundation where the oligonucleotides from the competition are placed in a Registry of Standard Biological Parts which uses Open Source licensing. Currently, over 5,000 parts are available for researchers to order. Endy is taking this approach because synthetic DNA products are typically made of a number of parts that may each have intellectual property. Although biotech start-ups rely on income through patents, too many patents on required parts will make it cost prohibitive to make a product.

In order to prevent a future "patent mess" in the field, Carlson provides a rigorous discussion of the merits and pitfalls of a solution-oriented approach using patent pools. Patent pools are a contractual arrangement agreed on by patent holders for licensing inventions that are used for other products made up of numerous patented products, such as sewing machines, radios, aircraft, and automobiles. The underlying principle is that cooperation between patent holders, through sharing research and its costs, will accelerate product development. Patent pools also provide an efficient method of obtaining numerous licenses at once through a streamlined process.

In theory, this is a win-win situation. However, Carlson cites the work of patent law professors James Boyle and Arti Rai of Duke Law School who are pessimistic about the success of patent pools for synthetic biology. Given the complexity and existing problems with the intellectual property of the enabling technologies, computers and biotechnology, they fear the issues relating to both industries will come together as a perfect storm (Rai and Boyle 2007).

In addition to infrastructural problems, patent pools are vulnerable to patent abuse and require effective government regulation. During World War I, patent holders in the aviation industry were reluctant to license their products, which slowed the innovation of new products. In 1975, several major patent holders in the industry established a patent pool and colluded to exclude competition and fixed prices, forcing the federal government to intervene and dismantle the arrangement.

In spite of these major challenges, Carlson predicts this field will have profound social and economic implications. He ends the book by posing the question, "What makes a revolution?" Currently, the primarily Western based pharmaceutical and biotech industry, makes hundreds of billions of dollars annually from domestic and international sales, and is growing faster than other sectors of the economy. New technologies can incrementally overhaul industries. A transition can also involve a radical transformation. In 1942, Joseph Schumpeter introduced the term "creative destruction" to describe this change (Schumpeter 1975).

In the past, creative destruction has revolutionized communications, electronic gadgets, transportation, health care, medicine, weapons, and agriculture. If the synthetic biology industrial revolution is successful, it could create a trillion dollar bioeconomy. Carlson discusses in depth the history of the military, beginning with organized land troops and the development of conventional weapons, then nuclear weapons, and the potential military adoption of pathogens as weapons making conventional militaries obsolete.

Carlson rightly focuses more on solution oriented approaches to problems in the field's development rather than civil society activism. But, in addition to a successful industrial revolution leading to a Schumpeterian revolution, is a cultural revolution in terms of how we see ourselves as humans also necessary?

Rather than viewing synthetic biology as a means for mankind to develop products for the public good, civil society activist groups such as ETC Group are attempting to slow progress in the field by publishing numerous articles and white papers, and most recently a press release calling for a moratorium in response to the publication of Venter's synthetic cell (ETC Group 2010). Carlson doesn't downplay the seriousness of bioterrorism, but dismisses their scare tactics as saying "boo."

Similarly to the introduction of genetic engineering, bioengineers are self regulating the field. Bioengineers are using precautions such as professional certification and monitoring the sales of synthetic DNA to prevent bioterrorism. ETC Group focuses on creating the "boo scenarios" and calling for global governance rather than self regulation. But, given the complexity of biological systems that Carlson describes, it remains difficult to create synthetic pathogens. Besides, should the risk assessment of biotechnology be held to a different standard? Over 40,000 deaths occur annually from automobile accidents in the United States alone.

In the book's opening paragraph, Carlson briefly discusses the title, "Biology is Technology." He makes the observation that biology is not just a scientific discipline; rather, it is a technology and has been for millions of years. Life as we see it today began as organisms exploited each other to survive and make energy in the Earth's newly formed atmosphere. Animals utilized mitochondria and plants chloroplasts acquired through symbiosis. I find the relevance of the title enigmatic and subsequently challenging to the reader.

While nature is a tinkerer and has limited tools to work with, mankind is a designer. With this advantage, we can create and redesign to optimize. During the Great Leap Forward, early modern man utilized farming and breeding resulting in the desired traits of temperance and musculature, and directed evolution began. In this regard, my own interpretation is that "biology is technology" makes the moral objection to synthetic biology less credible.

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