Testimony to the House Committee on Energy and Commerce
on Advances in Synthetic Biology and Their Potential Impact

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Given by Drew Endy of Stanford, CA

Good Morning, Chairman Waxman, Ranking Member Barton, and Members of the Committee.

My name is Drew Endy. I am an Assistant Professor in the Department of Bioengineering at Stanford University, President of the BioBricks Foundation, and Director of the BIOFAB: International Open Facility Advancing Biotechnology (BIOFAB). I serve on the Committee on Science, Technology and Law at the National Academies and am a recent nominee to the National Science Advisory Board for Biosecurity. My own work and that of my students is the direct result of sustained public funding for basic science and engineering research from the NIH, NSF, and DOD, and for which we are grateful.

Synthetic biology has been called "extreme genetic engineering" by civil society organizations. This label is true but only in relation to the past 35 years of biotechnology that follow the invention of recombinant DNA technology and other early tools. Speaking as an engineer, the facts today suggest that we are extremely bad at engineering biology.

For example, in my own lab we are working to understand and engineer how cells make decisions, store information, and communicate. One current "holy grail" is to implement a genetically encoded 8-bit information storage system. Our deliverable is similar to a computer's memory chip or a USB flash drive that you might use with a digital camera, except for two major differences. First, our system will only store 8 bits, which is 8 billion times less than what you could store on an electronic memory stick available today from Walmart for $20. Second, our system is made from proteins and DNA that function inside living cells. The system works by controlling enzymes that flip DNA back and forth; a stretch of DNA pointing "left" means "0" while "right" means "1". We will use our system to study and control cancer, aging, and development. For example, we plan to create combinatorial counters that track the number of times cells divide, and explore the possibility of building into cells additional "fail-safes" that prevent out-of-control replication, such as during cancer. Practically, the design of our first 8-bit combinatorial counter requires that we combine the DNA sequences for at least 48 genes encoding the various DNA flipping enzymes with as many more control elements. In total we need to design, build, and test about 100,000 base pairs, or letters, of highly engineered DNA. Using the best tools available it has taken us over one year to get the molecular pieces that comprise our first bit working.

The high cost and uncertainty of doing genetic engineering research has big impacts. For example, ~99% of all engineered genetic "programs" today are encoded by less than 20,000 base pairs of designer DNA. As a second example, the NIH is thought to spend ~5% of its total annual budget supporting researchers who then spend up to 50% of their time manipulating DNA by hand. Thus, while most of the attention is focused on the applications or ethics of biology and biotechnology, it is also important to look at the tools, processes, and human practices that comprise the work itself. This is where synthetic biology has a powerful role to play.

For example, we have heard today how researchers at the J. Craig Venter Institute (JCVI) reconstructed a 1 million base genome using DNA synthesis. As a related example, in 2005, researchers in Japan constructed a composite genome approaching 8 million base pairs in length, starting from natural DNA fragments. The scale of these genome construction projects is ~10 to 100-fold beyond what's required by most research projects. Very simply, today, if every publicly funded biomedical or biotechnology research team had direct access to a gene or genome printer, most researchers could focus their full attention on the challenges of understanding and applying biology to solve problems instead of spending the majority of our time "bashing" DNA.

As a second example of synthetic biology in practice, just because we have DNA printers does not mean that we will have much useful to say. We need to also discover or invent the languages and grammars that enable us to write more powerful genetic programs, moving from today's simple declarative statements – "synthesize lots of insulin" – to tomorrow's short stories and novels – "identify, attack, and destroy the tumor in this patient, and then differentiate and re-grow into healthy replacement tissue." Here is where old but powerful engineering ideas based on standardization and abstraction are starting to have an impact. For example, the public-benefit BIOFAB facility in Emeryville CA has a two-year goal of producing a first "operating system" supporting large-scale and reliable genetic programming in the bacterium *E. coli*, which is a well-studied model organism and "workhorse" of industrial biotechnology. We estimate our first cellular operating system will include ~3,000 standard biological parts encoding different cellular control functions. We intend to make this cellular operating system freely available so that all researchers can more quickly and reliably engineer useful genetic programs.

At this point, let me acknowledge that one characteristic of synthetic biology is how quickly some of the core tools continue to change. For example, over the past five years, the length of the longest genome synthesized from scratch has increased by a factor of ~100. Thus, five years from now, we might expect that further advances in synthetic biology will enable the construction of ~100 million base pair genomes, a length nearly sufficient to encode worms and flies. To be clear, the capacity to construct genomes at such scales will not mean that we know how to "weave a worm" or "fly a fly." Rather, it guarantees that we will remain challenged to become orders of magnitude better at the basic science and engineering of biology for the foreseeable future. We will also be challenged to keep pace with developments and to sustain constructive dialog and policy-making across a diversity of concerns, values, and perspectives.

Regarding the impact of synthetic biology on national energy policy generally let me make two points. First, in very rough terms, life on Earth is thought to handle 100 terawatts of energy; human civilization uses 20 terawatts. Although it might appear that biology presents us with a 5-fold surplus as a potential energy source, we depend on the energy flowing through biology to provide for many other obviously essential needs, from ecosystems to ourselves. Thus, future large-scale deployments of synthetic biology-based technologies will need to be proactively coupled to the constructive resolution of matters involving resource utilization and land use politics.

Second, from an energy perspective, the ultimate value of biology as a manufacturing platform that addresses our nation's energy needs goes beyond the production of bulk commodity products such as liquid fuels. For example, by the early 1980s, the enzymes used in laundry detergents to treat stains had been engineered to work at cold-water wash temperatures by companies such as Genencor, Inc., resulting in the potential reduction of hot water heating bills amounting to 100,000 barrels of oil per day, nationwide. Stated differently, the "energy impact" of a single engineered protein integrated upstream into our daily lives via a laundry detergent is greater than the current oil spill in the Gulf of Mexico, and is roughly equivalent to the volume of biofuel that could be produced using $1/2000^{th}$ of our crop land. Synthetic biology brings us many more opportunities to better partner with biology in reducing our energy needs and net impact on the natural environment.

In closing, let me return to the work that has brought us here and briefly sketch some of its significance from a policy and governance perspective. What changes now that it is possible to construct a replicating cell from a synthesized genome?

From a safety perspective, we inherit a tradition of practical success from the genetic engineering generation. Via synthetic biology many more people will seek to work with and use biotechnology. For example, thousands of young engineering students now labor to design and synthesize simple DNA programs via the iGEM competition. We must renew and advance our understanding and teaching of best practices regarding biosafety.

From a security perspective, many people are concerned that it is now possible to directly construct harmful pathogens from DNA sequence information. This seems to me a real but remote possibility, and is likely best addressed by improvements in our capacity to respond to emerging infectious diseases, natural or otherwise, and to our public health systems. The more pressing security concern is to ensure that the tools and policies defining the future of biotechnology do not directly or inadvertently lead to a remilitarization of biology by nations.

Finally, synthetic biology advances are challenging the existing application of property rights in biotechnology. Stated plainly, as our capacity to engineer biology increases, so does the number and combinations of uses of genetic functions that will be deployed. Such novel uses and combinations are typically protected via patents. However, via synthetic biology, we are already experiencing situations in which the cost and time required to use a patent-based approach does not match the scale or pace of work. This emerging situation is likely to be exacerbated via an increased capacity to "compile" genetic material from sequences distributed via computer networks, in a fashion that should be familiar to anyone who has used or uses Napster, the Pirate Bay, or iTunes. Our capacity to explore and craft any improved ownership, sharing, and innovation frameworks underlying the future of biotechnology will have direct impacts on the development, application, and ultimate utility and acceptance of synthetic biology.

Thank you.

END OF TESTIMONY

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