October 1, 2010

Office of Science and Technology Policy (OSTP)
Executive Office of the President
Dr. John P. Holdren, Director OSTP
725 17th Street Room 5228
Washington, DC 20502

cc Thomas Kalil, Deputy Director for Policy

Comments for OSTP from BIO on Synthetic Biology – J Craig Venter Announcement "Synthetic Cell"

Dear Dr. John P. Holdren,

The Biotechnology Industry Organization (BIO) is the world's largest biotechnology organization, providing advocacy, business development and communications services for more than 1,100 members worldwide. Our mission is to be the champion of biotechnology and the advocate for our member organizations - both large and small. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology technologies. Corporate members range from entrepreneurial companies developing a first product to Fortune 100 multinationals. We also represent state and regional biotech associations, service providers to the industry and academic centers. BIO member companies apply synthetic biology technology to help resolve important challenges in synthesizing new products, whole cell systems and other biologic processes to improve all types of manufacturing and chemical processes.

Background

A revolution occurred in the field of chemistry between 1930 and 1960, referred to as the "synthetic chemistry revolution." It was during that period that methods for producing novel organic chemicals, including polymers, such as nylon and Teflon™, were invented. This revolution extended into agriculture and pharmaceuticals, creating tremendous economic value, and significant employment in the regions that led this revolution, in particular the United States, Europe and Japan. We are in the early period of a new revolution referred to as the "synthetic biology" revolution. Engineered microorganisms are being used to synthesize chemicals and polymers that are used in our everyday lives. Similar to the past revolution in chemistry, this new revolution in biology will broadly impact the chemical industry, and will extend into agriculture and pharmaceuticals. In the chemicals sector, production of chemicals using engineered microorganisms and enzymes could generate global revenue of $1 trillion and create 1.2 million direct jobs. Additional revenue and job creation will occur as synthetic biology delivers advanced biofuels, pharmaceuticals and new engineered crop species.

A group of pioneering chemical companies is using synthetic biology to engineer specific routes/paths in the microbe to enable them to produce new molecules. For example, Genencor, a division of Danisco is collaborating with The Goodyear Tire & Rubber Company to develop engineered microorganisms that produce a biochemical, BioIsoprene ™ product that can be used to manufacture synthetic rubber. The rubber manufactured using this process will substitute for synthetic rubber and natural rubber that is currently derived from plants such as the rubber tree, which are not indigenous to the United States. This

project is of fundamental importance on a variety of levels. First, by applying synthetic biology to the production of tires, this 21st century technology is revitalizing a traditional sector of the U.S. manufacturing industry. Second, students of history will appreciate that nations cannot defend themselves without access to rubber. Rubber is a critical material for both air and land transportation. Our nation will be more secure if we are able to utilize microorganisms to produce this critical material domestically.

Synthetic biology is being used to invent solutions to the most urgent problems of our time, and given the speed and efficiency of these new methods, potential solutions can be designed and tested rapidly. The recent oil spills in the Gulf of Mexico, Michigan and China underscored the need to develop new technologies to protect health, property and the environment as we transition away for our dependence on petroleum. For example, there is a need for new oil dispersants that are less toxic than those available today. The recent oil spills motivated Modular Genetics, Inc. (Modular) to join forces with a consortium of scientists and engineers at three major U.S. universities to develop new "bio-dispersants" that are effective and less toxic than traditional chemical dispersants. The National Science Foundation (NSF) awarded a RAPID Response Grant to this group, and Modular has already produced new engineered microorganisms that synthesize bio-dispersants that are being tested for their effectiveness and potential toxicity. Significantly, this industry/university partnership is providing hands-on training to students at three universities on strategies and methods for using synthetic biology to create new chemical products aimed at addressing serious unmet needs. These students will soon be among the young leaders who use synthetic biology to build a sustainable chemistry industry, which combines three areas of U.S. strength: biotechnology, agriculture and chemical manufacturing. Synthetic biology offers the United States the opportunity to establish a leadership position in a growing sector that can revitalize our traditional industries and at the same time stimulate economic growth in rural America.

Landscape

Synthetic biology is a transformative technology that has the potential to fundamentally change the way we make and use chemicals and materials, and it has the potential to accelerate and transform our economy. Synthetic biology is an extension of recombinant DNA technology, which was invented in the 1970s, and draws extensively from the heritage of safety that was a fundamental element of the culture of the scientists and engineers who developed these methods. The early period of the modern revolution in biology started with the development of recombinant DNA technology. At the dawn of this new era, researchers in the field agreed to develop guidelines to ensure the safe practice of the technology. Given that synthetic biology has its roots in a culture that values safe practice of the technology, it is no surprise that, as the field continues to advance; many of the strongest cautionary messages originate from within the synthetic biology community itself. Below, we discuss recent advances in the field that have attracted significant attention, and provide perspective on the potential implications of these advances with regard to safety and the regulatory considerations.

The advancing field of synthetic biology offers us in this century the chance to make a significant change in our product development paradigm. As often occurs during dramatic change, the initial phases are marked by use of metaphors to help individuals and society grasp the potential for the differences offered in the new field. They do so by exploiting effective, yet still imperfect, similarities in something more familiar to the audience to show how the newer thing might work. We are at that juncture in the field of synthetic biology, which is ripe with illustrations based on "parts" or "electronics" or systems that have the property of being modular and open to reconfiguration. In this scenario, the potential impact of synthetic biology in research and product development speaks directly to the ability to make and test prototype biological systems with a speed and complexity not presently feasible, or not presently cost effective. As with most product development, innovation and competitiveness can often be tied to the ability to rapidly and predictably iterate through a solution space to obtain optimum performance outcomes. Synthetic biology offers this promise to academic research groups, government technology institutes, and to public and

private corporations seeking to develop biological solutions to today's challenging needs in fields such as biofuels, renewable chemicals and polymeric materials, agriculture, environmental science and pharmaceutical product development for the health care industry.

While the electronics metaphor is attractive to grasp, and useful for many of the scientists driving innovation in the field of synthetic biology, other biological or chemical metaphors can color the potential positive impact synthetic biology can offer to industries that adopt it. One of the fundamental shifts afforded by synthetic biology is the ability to "write" genetic information on a scale heretofore impossible. The example of "writing" an entire genome *de novo*, as exemplified by the recent work at the J. Craig Venter Institute, culminates an evolutionary development of technology started when humans first understood that breeding for traits is, in effect, causing genetic information to assemble in a manner more conducive to man's interests, say in animal or crop domestication. At that time, science lacked the ability to cause DNA to assemble in a new manner, but it did understand the benefits of selecting for that assembly. As time and technology advanced, the ability to manipulate DNA at an increasingly direct level led to molecular cloning and for the first time, to our ability to directly compose DNA in a sequence of our choosing. This started 40 years ago with small genes, such as that for human insulin, but has moved to pathways, chromosomes, and now to entire genomes. The ability to solve problems/challenges through technology, that otherwise would not have a solution, causing the production of something like human insulin in a controlled, renewable system has brought direct benefit to mankind, and was part of the tremendous biotechnology revolution that spawned entire industries, and changed forever the way one thinks about discovery of or production of a product.

So in a sense, last century's technology accelerated in the chemical and pharmaceutical industries when we learned to "write" complex molecules synthetically, instead of relying solely on finding and extracting them from nature. The biotechnology revolution allowed us to begin the process of deliberate assembly of still relatively small amounts of DNA into systems that produced important products or facilitated fundamental research. Today, synthetic biology holds the promise of allowing us to write entire pathways, or genomes, to create routes to production of valuable biochemicals, biopolymers, therapeutics, and performance materials. As with prior technology revolutions, it also should spawn entire new industries (as was the case with companies created to supply restriction enzymes or pcr kits), or drive innovation in adjacent space, such as in computational and information sciences, automation technologies, and analytical science, to name a few. A truly remarkable concept to consider is that with the success of synthetic biology, it stands actually to converge with one of its driving metaphors. For instance, it is entirely conceivable that synthetic biological "circuits" will one day be found operating the underlying computational systems used in the labs and companies building new products with synthetic biology.

BIO Recommendations

The ethical and regulatory issues raised by the development, use, and potential misuse of synthetic biology have initiated multiple studies, reviews and recommendations by interested parties in academia, industry, concerned citizens and government agencies, both domestically and in other countries. Voluntary regulatory guidelines have been established and industry is responsibly adhering to these guidelines. BIO members are aware of the potential low levels of risk associated with synthetic biology technologies and would welcome opportunity to work with other stakeholders to evaluate these voluntary guidelines to determine whether they should become mandatory.

Individual academics as well as focus groups have recently published reports and papers that provide excellent summaries of the technical, legal, and ethical issues as well as options for governance. (References include: Synthetic Biology, Michele S Garfinkel, Drew Endy, Gerald L Epstein, Robert Friedman, Hastings report (2007), Synthetic Biology, Social and Ethical Challenges, Andrew Balmer and Paul Martin, BBSRC report (2008), and Synthetic Biology: Navigating the Challenges Ahead, Arjun

Bhutakar, Genome Biol. Nov 8; 8(11) (2007)). Numerous groups (both US and European) have been formed and chartered with addressing the challenges and concerns of synthetic biology. We propose formation of a single federal interagency working group to insure all federal agencies involved with synthetic biology are operating with a coordinated approach. Recommendations from these groups have been in general agreement that synthetic biology does not pose significant novel threats or overarching concerns. The regulatory framework that has been shaping recombinant DNA technology for the past 40 years is generally applicable and relevant for the products of synthetic biology, and we should continue to develop the technology and products under that framework. However, any additional regulation in specific areas should be carefully designed and established in consultation with industry and academia. For example, the current voluntary guidelines that several leading synthetic gene providers have agreed to operate under, ensures that potentially hazardous genes and gene fragments are being provided in a responsible fashion. Moreover, in the future, the need may exist to develop proactively, in consultation with the biotechnology industry, a regulatory framework, as overarching federal policy.

At the recent (July 8-9, 2010) Presidential Commission for the Study of Bioethical Issues, George Church and Craig Venter (two pioneers in the field of synthetic biology) among others stated that there is a need for government regulation. BIO would endorse the formation of an interagency group that would seek to coordinate all federal activities related to synthetic biology. Our member companies and organizations are concerned with safety and public perception, and would work with such an interagency group to help develop strategies that would ultimately provide a high degree of safety and security at all levels (from individual researchers to national safety concerns), as well as robust support of biotechnology innovation.

BIO is appreciative of the opportunity to submit comments and would be pleased to engage further in the discussion of an interagency oversight working group for synthetic biology.

Sincerely,

Brent Erickson
Executive Vice President
Biotechnology Industry Organization