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Safety, security, and serving the public interest in synthetic biology

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Abstract
This article describes what may be done by scientists and by the biotechnology industry, generally, to address the safety and security challenges in synthetic biology. Given the technical expertise requirements for developing sound policy options, as well as the importance of these issues to the future of the industry, scientists who work in synthetic biology should be informed about these challenges and get involved in shaping policies relevant to the field.

Introduction

Synthetic biology is ushering in a very exciting time for the biotechnology industry, filled with new applications, new products, and the potential for unprecedented growth. Yet, synthetic biology also raises important public policy considerations about whether the field is being developed in line with the public's interest, as well as biosafety and biosecurity concerns. *Biosafety* involves the safe handling and containment of infectious microorganisms and hazardous biological materials, and biosecurity pertains to the threats posed to human and animal health, the environment, and the economy by deliberate misuse or release of microbiological agents and toxins [4]. This article describes what may be done by scientists and by the biotechnology industry to address these challenges. While increasing safety and security often requires collective or governmental actions, given the technical expertise required to develop sound policy options, as well as the importance of these issues to the future of the industry, it is important for scientists who work in the synthetic biology field to be informed about policy matters that affect them and to get involved.

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Safety

To date there have been no reported safety problems resulting from synthetic biology research or synthetic biology products, adding to the excellent safety record for genetically engineered organisms (GMOs) or DNA recombinants. Complacency among scientists is not warranted, however, just because the experiences with these technologies have been positive does not mean that all synthetic biology products may be assumed to be safe into the future. The ability to use synthetic biology tools to produce new variants and new traits may yield much different organisms than would likely be developed through natural selection or through traditional bioengineering techniques, affecting safety [15].

In the biomedical sciences, individual biosecurity events and biosafety lapses have resulted in increases in regulatory burdens for legitimate scientists (for example, controls on regulated pathogens, or "select agents."). If an incident with synthetic biology occurs that is perceived to threaten public safety, political responses and regulations may soon follow (and they may not be proportional to the risks or even address them). Already, concerns have been raised in scientific journals and the popular press, such as the possibility of a biocontainment lapse with a contagious and genetically modified pathogen, or the potential for a gene drive to go awry [6, 19]. While not related to synthetic biology, that there were notable, high-profile biosafety lapses from US government laboratories in the last several years adds to general concerns about biotechnologies of all types [2, 3, 13, 16]. The "DIY Bio" community has been very proactive about safety and safety education, but there have also been concerns raised about what other amateurs working in synthetic biology may be able to do in their kitchens, including attempts at gene therapy [12, 14].

One way to reduce safety concerns in synthetic biology is to make sure that safety is given more prominent support in the synthetic biology field, and that research into improvements in safety is specifically funded [21]. Safe Genes, a DARPA program, is one example of needed safety research [24]. This program aims to develop tools and methodologies intended to control, counter, and reverse the effects of genome editing, including gene drives. However, there is room for more such efforts [24]. Synthetic biology also provides an opportunity to set norms for the safety of products, including environmental releases [10]. Reliable data about how often laboratory errors occur is lacking, including what might be done to reduce the human error rate for various laboratory techniques. Community laboratories and iGEM provide safety education to amateur biologists and should be supported in that work, but there are additional options to alert practitioners about potential risks, including supporting simplified biosafety instruction, or funding "ask a biosafety expert" programs so that amateurs can get their questions answered [7, 11]. Open Philanthropy Project, a relatively new foundation, has stepped into fund the creation of safety protocols for the DIY Bio community, as well as to enhance the study and inclusion of safety at the iGEM competition [17, 18].

Security

Concerns about the likelihood of bioterrorism and biowarfare ebb and flow depending upon world events. Since the anthrax letter attacks of 2001, there have been concerns that nonstate actors could misuse advanced biotechnologies to develop biological weapons, but this has not been reported to date. Scientists should know, however, that while the misuse of biotechnologies to produce weapons has been thankfully rare, it is not at all clear to experts why that is the case. It is certainly not because the technologies and materials are difficult to acquire. The twentieth century saw most major military powers with extensive offensive biological weapons R&D programs, before the US unilaterally disbanded its program in 1969, and the Biological Weapons Convention was signed in 1972. Whether the norm against biological weapons development is going to hold into the future is unknown, but the erosion of norms against chemical weapons use is alarming and does not bode well for the future.

The security of synthetic biology has been in question by policymakers for several years. Gene-editing technologies were added to the annual worldwide threat assessment report of the US intelligence community in 2016 [22]. In May, 2017, the statement from the Director of National Intelligence included that genome editing was an emerging and disruptive technology "central to economic prosperity and social well-being, but it is also introducing potential new threats…. Research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increase the risk of the creation of potentially harmful biological agents or products." [5]. Though the DNI statement was almost certainly referring to gene editing advances enabled by CRISPR, there were no specific bioweapons scenarios identified in the statement.

Security concerns were the major concern for the US governmental advisory committee, the National Science Advisory Board for Biosecurity (NSABB), when they recommended against the publication of the H5N1 influenza "gain of function" papers in 2013 [9]. The NSABB was concerned that the genetic sequence information described in the research, which would enable H5N1 influenza to become transmissible from mammal to mammal, could give a nefarious actor a shortcut to developing a contagious biological weapon. In response to these synthetic biology advances which could lower barriers to biological weapons use, the US National academies has developed a framework to analyze new developments in synthetic biology for security risks. Their interim framework has already been published [15]. Using this framework, an analyst may examine factors useful for assessing the capability of a new technical advance to be used maliciously. For example, various factors to be examined include the potential of an advance/technology to be used as a weapon, and the attributes of actors who could command such a capability. This must be weighed against the capability for mitigation of misuse, including factors that lead to deterrence and prevention, the ability to recognize an attack, the ability to achieve attribution, as well as consequence management. Scientists need to be aware of the potential threat of misuse of legitimate biotechnology.

The FBI has introduced this topic to campuses and biotech companies as part of a "see something, say something" campaign for biology [1]. It is also critically important for scientists to appropriately communicate work that may lower barriers to biological weapons development. It is not always possible to avoid work that is the so-called "dual-use" but it is possible to communicate that the risks have been carefully considered and that the work was important enough to pursue.

Public interest

After the 2010 announcement that scientists at the J. Craig Venter institute had synthesized and "booted up" a viable bacterial cell, the Presidential Commission for the study of Bioethical Issues was tasked to examine the ethical implications of this work and to look more broadly at how synthetic biology was governed [8, 23]. The Commission was asked to consider the potential medical, environmental, security, and other benefits and risks of synthetic biology, so that "America reaps the benefits of this developing field of science while identifying appropriate ethical boundaries and minimizing identified risks." [23]. Fortunately, the Alfred P. Sloan Foundation had been funding research into this very question, and so there were many experts well-prepared to give the Commission the information it needed to make decisions about synthetic biology. Dr. Amy Gutmann, the chair of the commission and president of the University of Pennsylvania stated, "We considered an array of approaches to regulation—from allowing unfettered freedom with minimal oversight and another to prohibiting experiments until they can be ruled completely safe beyond a reasonable doubt. We chose a middle course to maximize public benefits while also safeguarding against risks." [23]. The commission concluded that no new regulations for synthetic biology were needed at the time [20].

In the future, there are likely going to be additional public examinations of the ethics and governance options for synthetic biology—but whether there will be a similar group of scholars to discuss the risks and governance of the field is an open question. Communities of well-informed people that include scientists, ethicists, and the public do not form by accident: they need to be cultivated and maintained. Without support for scholarly analysis of the ethics and governance implications of synthetic biology, credible scholars may not be able to comment, which would be a disservice to the public.

Conclusion

Synthetic biology is an exciting new field with the potential to bring about new products and benefits, and the tools brought by synthetic biology will open new directions for research, as well. However, practitioners of synthetic biology also need to attend to concerns about the safety and security of the field, as well as work to ensure that the work is conducted in the public interest.

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