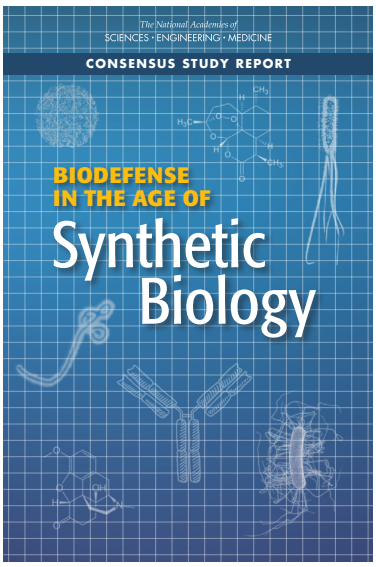
Consensus Study Report
HIGHLIGHTS
June 2018

Biodefense in the Age of Synthetic Biology



Synthetic biology collectively refers to concepts, approaches, and tools that enable the modification or creation of biological organisms. While the goals of synthetic biology are beneficial, these capabilities also could be used to cause harm. This report assesses the security concerns raised by synthetic biology in order to inform efforts to mitigate potential threats.

The age of synthetic biology has brought with it opportunities to transform approaches to treating disease, manufacturing chemicals, producing fuels, remediating contaminants, and numerous other applications with benefits to humankind. Some synthetic biology capabilities, however, have dual use potential—that is, they can be misdirected to cause harm to humans, animals, plants, and the environment. Synthetic biology makes possible new types of weapons and adversaries that the United States' approach to biodefense was not originally designed to counter.

Making informed decisions about whether and how to mitigate potential malicious uses of synthetic biology requires a realistic assessment of security concerns. To that end, the U.S. Department of Defense, working with other agencies involved in biodefense, asked the National Academies of Sciences, Engineering, and Medicine to develop a framework to guide an assessment of the security concerns related to advances in synthetic biology, to assess the levels of concern warranted for such advances, and to identify options that could help mitigate those concerns.

The resulting report considers how synthetic biology capabilities affect the biodefense threat landscape, identifies which capabilities presently pose the greatest concern, and notes ways in which future developments may affect these concerns. The report also discusses, from a broad perspective, some current approaches for mitigating concerns related to the malicious use of biotechnology, how synthetic biology may challenge those approaches, and conversely, how synthetic biology may help address challenges or bolster mitigation approaches.

FRAMEWORK FOR ASSESSING SYNTHETIC BIOLOGY CAPABILITIES

Synthetic biology concepts, approaches, and tools do not, in and of themselves, pose inherent harm. Rather, concerns derive from the specific applications or capabilities synthetic biology might enable. The report outlines a framework for assessing concerns related to synthetic biology-enabled capabilities (Figure 1). In its deliberations, the committee used this framework along with its members' subject matter expertise to analyze specific capabilities in terms of each of four factors: usability of the technology, usability as a weapon, requirements of actors, and potential for mitigation. In addition

to supporting the analysis in this study, the framework is intended to aid others now and in the future in order to, for example, evaluate the implications of new experimental findings or technologies, monitor developments that may lower current barriers, or predict potential future areas of concern.

The framework for assessing concern consists of four factors, along with descriptive elements within each factor. These factors delineate the information used to assess the level of concern for particular synthetic biology capabilities.

Using the framework, the committee holistically assessed the relative levels of concern across the full landscape of capabilities considered. Conclusions regarding the relative level of concern are summarized in Figure 2. Of the potential capabilities assessed, three currently warrant the most concern: re-creating known pathogenic viruses, making existing bacteria more dangerous, and making harmful biochemicals via in situ synthesis. The first two capabilities are of high concern due to usability of the technology. The third capability, which involves using microbes to produce harmful biochemicals in humans, is of high concern because its novelty challenges potential existing mitigation options.

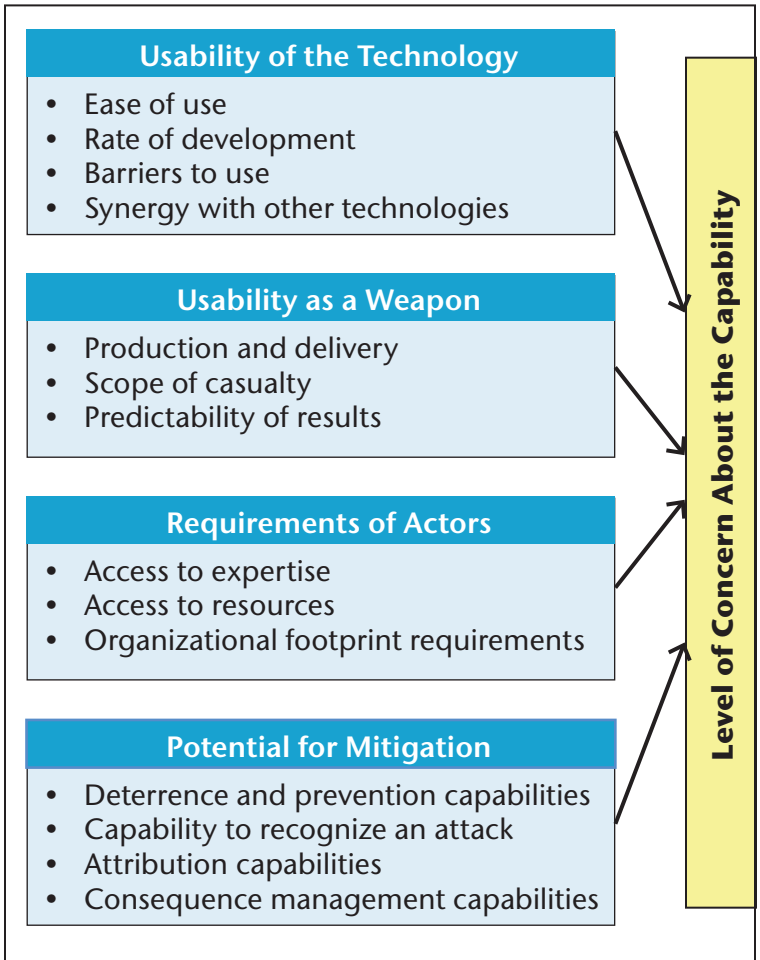


Figure 1. Framework for Assessing Concern. The framework consists of four factors, each with descriptive elements, used to assess the level of concern for particular synthetic biology capabilities.

Capabilities related to pathogens

These approaches could potentially be used to create disease-causing agents that infect and harm targeted individuals.

- ***Re-creating known pathogenic viruses:*** Constructing a known, naturally occurring pathogenic virus from the starting point of information about its genetic sequence.
- ***Re-creating known pathogenic bacteria:*** Constructing a known, naturally occurring pathogenic bacterium from the starting point of information about its genetic sequence.
- ***Making existing viruses more dangerous:*** Creating a modified version of a known virus in which one or more traits have been altered to make the virus more dangerous.
- ***Making existing bacteria more dangerous:*** Creating a modified version of a known bacterium in which one or more traits have been altered to make the bacterium more dangerous.
- ***Creating new pathogens:*** Constructing a pathogen from the novel combination of multiple parts.

Capabilities related to the production of chemicals or biochemicals

These approaches could potentially be used to engineer organisms such as bacteria, yeast, or algae to produce harmful substances such as toxins, drugs, or controlled chemicals.

- ***Manufacturing chemicals or biochemicals by exploiting natural metabolic pathways:*** Using an organism to synthesize a desired product by engineering it to contain a naturally occurring metabolic pathway.
- ***Manufacturing chemicals or biochemicals by creating novel metabolic pathways:*** Creating a new biosynthetic pathway that enables an engineered organism to produce a chemical that is not normally produced biologically.
- ***Making biochemicals via in situ synthesis:*** Engineering an organism to produce a desired biochemical and delivering this microorganism to the human body, where it releases the biochemical to cause harm.

Capabilities related to bioweapons that alter the human host

These approaches could potentially be used to enable bioweapons and means of attack that alter the physiology or function the human body itself.

- ***Modifying the human microbiome:*** Manipulating microorganisms that live on and within humans (for example, to disrupt normal microbiome functions).
- ***Modifying the human immune system:*** Manipulating aspects of the human immune system (for example, to alter how the immune system responds to a particular pathogen or to stimulate autoimmunity).
- / ***Modifying the human genome:*** Creating changes to the human genome by adding, deleting, or modifying genes or by causing epigenetic changes that modify gene expression. While not of significant concern to the committee, a subset of this category is the concept of *human gene drives*, the incorporation of genetic elements into the human genome that are designed to pass from parent to child and spread through a population.

CONCLUSIONS

Though important for myriad beneficial applications, synthetic biology and related biotechnologies expand the landscape of potential biodefense concerns. These capabilities make possible new modes of attack, some of which may not be detectable or treatable with current approaches to disease containment and biodefense mitigation. The age of synthetic biology also lowers some of the barriers to developing and using biological and chemical weapons, potentially putting such weapons within the reach of adversaries with relatively low expertise, financing, and access to scientific equipment and resources.

Synthetic biology expands what is possible in creating new weapons. It also expands the range of actors who could undertake such efforts and decreases the time required.

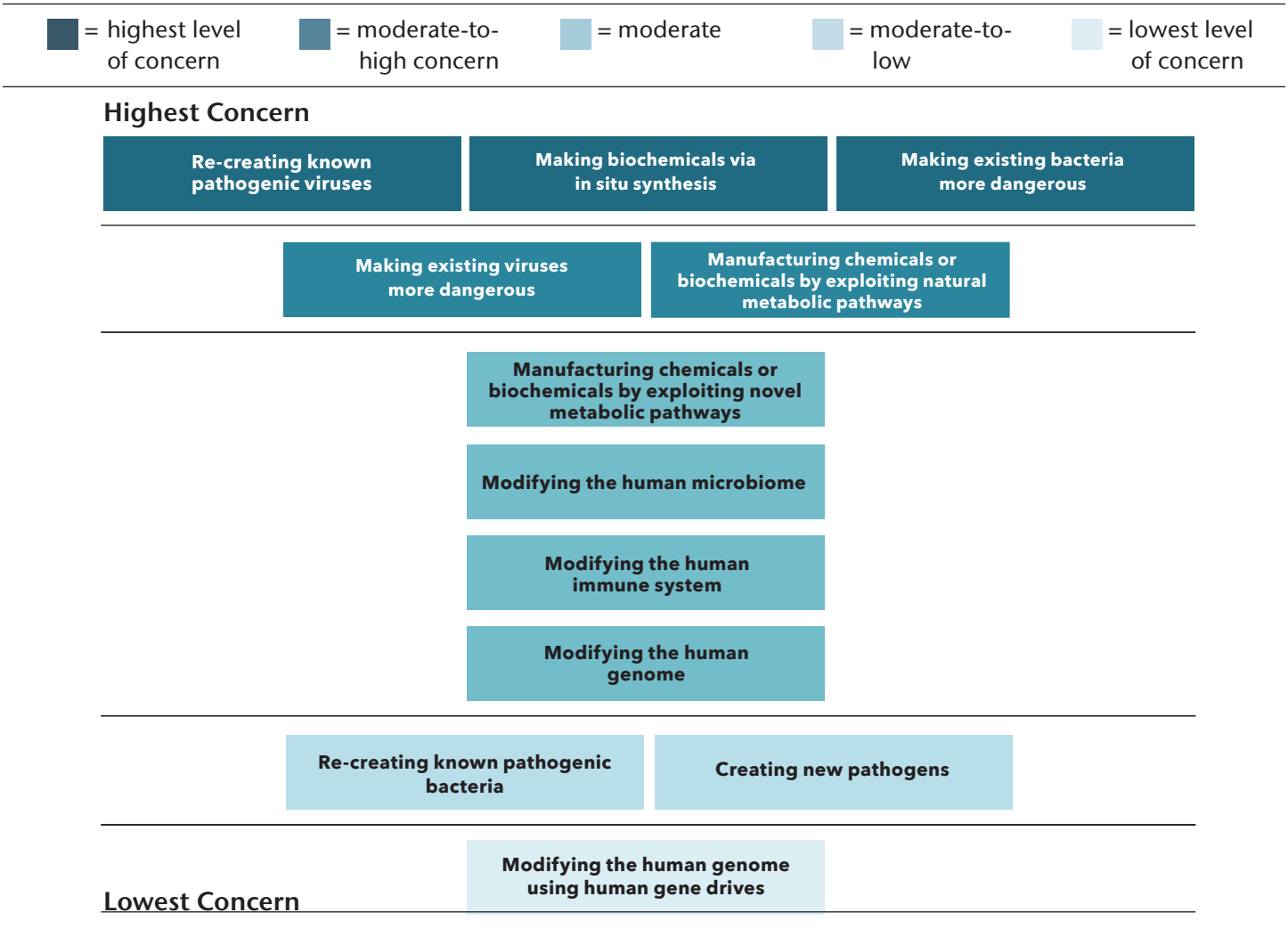


Figure 2. Relative ranking of concerns posed by the synthetic biology capabilities analyzed. At the present time, capabilities toward the top warrant a relatively higher level of concern while capabilities toward the bottom warrant a relatively low level of concern. Capabilities that are on the same horizontal line pose roughly the same level of concern, though often for different reasons.

The report's analysis necessarily reflects a snapshot in time, given understanding of current technologies and capabilities. As knowledge and biotechnology continue to evolve, it can be expected that current bottlenecks will widen and current barriers will be broken. The report identifies areas worth monitoring going forward and notes how related developments such as gene therapy, nanotechnology, automation, additive manufacturing, and health informatics may converge with synthetic biology and help overcome current barriers to the development or use of synthetic biology-enabled weapons.

Some malicious applications of synthetic biology may not seem plausible now, but could become achievable if certain barriers are overcome.

It is valuable for the U.S. government to pay close attention to rapidly advancing fields such as synthetic biology, just as it did to advances in chemistry and physics during the Cold War era. However, approaches modeled after those taken to counter Cold War threats are not sufficient to address potential new types of weapons in the age of synthetic biology. The potential unpredictability related to how a synthetic biology-enabled weapon could manifest creates an added challenge to monitoring and detection. To account for the broader capabilities enabled by synthetic biology, the U.S. government could, among other actions, evaluate existing infrastructure for disease surveillance and identification and consider strategies for preventing misuse of biology that manage emerging risk in addition to current approaches focused on restricting access to specific pathogens and toxins.

The U.S. Department of Defense (DoD) and its partnering agencies should continue to pursue ongoing strategies for chemical and biological defense; these strategies remain relevant in the age of synthetic biology. DoD and its partners also need to have approaches to account for the broader capabilities enabled by synthetic biology, now and into the future.

While addressing the potential concerns posed by synthetic biology in the age of biotechnology will remain a challenge for scientists and for the nation's defense, there is reason for optimism that, with continued monitoring of biotechnology capabilities and strategic biodefense investments, the United States can foster fruitful scientific and technological advances while minimizing the likelihood that these same advances will be used for harm.

COMMITTEE ON STRATEGIES FOR IDENTIFYING AND ADDRESSING POTENTIAL BIODEFENSE VULNERABILITIES POSED BY SYNTHETIC BIOLOGY

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For More Information . . . This Consensus Study Report Highlights was prepared by the Board on Chemical Sciences and Technology and the Board on Life Sciences based on the Consensus Study Report *Biodefense in the Age of Synthetic Biology* (2018). The study was sponsored by the U.S. Department of Defense. Any opinions, findings, conclusions, or recommendations expressed in this publication do not necessarily reflect the views of any organization or agency that provided support for the project. Copies of the Consensus Study Report are available from the National Academies Press, (800) 624-6242; http://www.nap.edu or via the Board on Chemical Sciences and Technology web page at http://www.nationalacademies.org/bcst.

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