About the Office of Technical Intelligence

The Office of Technical Intelligence (OTI) provides the U.S. Department of Defense Research and Engineering community and partners holistic, defense-relevant insights into emerging and potentially disruptive technology to enable U.S. and mitigate adversary technological surprise. To do so, OTI identifies emerging and potentially disruptive science and technology, recommends efficient research and development (R&D) strategies, and coordinates intelligence collection, analysis and dissemination to inform research and engineering activities. OTI accomplishes these missions through three complimentary efforts: technology watch and horizon scanning, technical assessments, and tailored intelligence support and coordination.

OTI technology watch and horizon scanning efforts are developing methods to identify nascent and disruptive science, technology, and capabilities through the exploitation of tailored approaches and tools, including analysis of scientific literature, patents, and worldwide investment using both open source and internal data.

OTI technical assessments provide decision-relevant R&D strategy inputs on emerging and potentially disruptive technologies to the Research and Engineering community by exploring opportunities and threats the technologies could enable, conducting data-driven analyses of drivers to forecast future trends and identify unique DoD needs, recommending specific investment and policy approaches, and developing and seed funding projects to leverage those opportunities.

OTI intelligence support activities are focused on coordinating efforts across the Research and Engineering community, ensuring timely and valuable analysis reaches users, and providing mechanisms to enhance communication between policymakers, researchers, and analysts.
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1 Cover photo courtesy of Yan Liang, Massachusetts Institute of Technology
Executive Summary
Synthetic biology is an emerging field in which scientists modify or ‘engineer’ DNA to improve their ability to understand, predict, design, and build biological systems. For more than a century, scientists have been applying knowledge of biology to agriculture, medicine, and some industrial systems, but advances over the past 20 years have enabled scientists to pursue research programs and to modify organisms in substantially more complex and targeted ways. These developments spawned the synthetic biology field. Thus, it is not a new field, but it is new in its approach – holistic engineering of biology – and its promise.

Bibliometric analyses of the synthetic biology field show a rapid rise in publications since the late 1990s. There have been more than 160 private synthetic biology companies operating since 2009 which have drawn more than $5.4 billion in private investment, and engineered organisms have spawned products worth more than $350 billion per year to the U.S. economy. Beyond economic impact, research has already demonstrated the potential for this field to have major effects on commodity and specialty materials, sensing, human performance, medical, and biological and chemical weapons threats and defense, all of which are of substantial importance to the U.S. Department of Defense (DoD).

Assessment Methodology
Considering the potential impacts, the goal of this study is to assess how – or if – DoD should invest in synthetic biology. We evaluate potential funding areas using 3 dimensions:

- **Impact and uniqueness of DoD needs.** The latter is important because if the Department has relatively similar needs to the private sector, private investment may satisfy DoD needs;
- **Funding from the private sector and other USG agencies.** These are also important to determine where other organizations may meet DoD needs and where DoD can leverage external investment;
- **Policy and regulatory challenges.** These inform our understanding of the ability of DoD to field technologies once developed and the timeline on which this might occur.

Based on this analysis, we outline practical steps DoD could take to generate the greatest value, including by leveraging external investment, committing basic research funding to areas which will push forward the broader field and DoD interests, engaging research leaders, and developing human capital.

Defense Applications & Opportunities
**Specialty Materials:** Synthetic biology research is already demonstrating breakthroughs from novel chemical production to nano-material assembly. Due to DoD’s unique missions, there are many special needs for advanced materials, and this area has low regulatory hurdles; however, it is receiving a relatively small amount of funding. The exception is an ongoing Defense Advanced Research Projects Agency (DARPA) program, which is focused on building synthetic biology infrastructure and using novel materials as a benchmark, the results of which can support future efforts. Thus, the specialty materials area is an attractive investment target. To leverage academic and private sector investment in this field, DoD should build future materials R&D funding opportunities with dedicated sections for biologically-produced materials. In conjunction, we propose an applied research effort to build on the 2014 Synthetic Biology for Materials prize to push the field to address DoD needs in the metamaterials area so as to demonstrate the potential for and explore the challenges and opportunities of using synthetic biology for materials.
Finally, each Service basic research organization should develop a program to support R&D of new platform organisms for producing various classes of materials. This would both meet a major need of the broader field and better position DoD.

**Sensing:** Natural and synthetic biological systems can already sense a wide variety of phenomena of interest, from specific chemicals to light and ionizing radiation. With DoD’s unique sensing needs and a paucity of private-sector funding, this is an area which will benefit from DoD funding and which appears to be a major opportunity in the medium-to-long term. Policy and regulatory hurdles for releasing highly-engineered organisms will be substantial, so policy development must accompany R&D. Similarly to specialty materials, the Services should build future competitions for sensing R&D with dedicated opportunities for novel approaches using synthetic organisms, and a challenge prize would further engage the field. Finally, ASD(R&E) should organize a working group to identify policy needs, to outline the research required to inform policy, and to support the development of both.

**Biological & Chemical Defense:** Synthetic biology may enable potential adversaries to develop chemical and biological threat agents with new characteristics. DoD has a responsibility to stay abreast of this field to enable protection for our military personnel, but because biological and chemical weapons defense is focused on threat mitigation instead of enhancing overall DoD capabilities, it is important to keep its size relative to its importance and not allow this aspect to overshadow the major opportunities provided by the field. The historical DARPA approach to protecting against novel bio-threats is appropriate. By developing the capability to respond to any new pathogen, R&D resources benefit DoD and the nation by improving emerging infectious disease preparedness while also enhancing defenses against novel threats.

**Other Applications:** Based on product, investment, regulatory, and policy factors, we find that the commodity materials, medical, and human performance application areas are not currently as ripe for DoD investment, although human performance applications have the potential to provide major benefits and some opportunities should be pursued when appropriate partners are available to lead testing.

**Human Capital:** In DoD, there are a limited number of highly-experienced program managers, leading scientists, and especially individuals in uniform with deep knowledge of the field. There is a lag time of 15-20 years between training junior officers and those individuals achieving senior ranks, so providing opportunities now is important for the future. To build human capital, the Services should tie generous grant funding to a requirement for leading researchers to spend 2-4 week sessions at Service laboratories. This would be a training opportunity and recruiting tool for DoD researchers. At the same time, the Services should institute bioengineering programs at each Academy. To expand their knowledge and relationships, students should be required to spend at least one summer at a major research university and to participate in the prestigious International Genetically Engineered Machine (iGEM) Competition.

**Conclusion**

This assessment presents a R&D strategy which aligns basic and applied research, develops human capital, and leverages existing investment where possible to engage the synthetic biology field in the most promising areas. In doing so, it would position DoD to benefit substantially going forward.
Introduction

Synthetic biology is an emerging field in which scientists modify or ‘engineer’ DNA to control living cells. While the definition of the field differs between organizations, the key aspect is the holistic, directed modification of organisms’ genomes which is allowing scientists to improve substantially their ability to understand, predict, design, and build biological systems. Current research in the field suggests that synthetic organisms will be useful as or produce inputs to a wide range of applications, from medicine to human performance, weapons, sensors, and high-performance materials. Because of the rapid growth of the field and the potential for it to generate significant tactical, operational, and strategic impacts, the Research Directorate, within the Office of the Assistant Secretary of Defense for Research & Engineering (ASD(R&E)), has designated it as a priority basic research area.

The goal of this assessment is to identify opportunities for the U.S. Department of Defense (DoD) in the synthetic biology field. To do so, it starts by briefly describing the history of and present state of the synthetic biology field; next, it examines the future direction of the worldwide research enterprise; and the third section discusses application areas relevant to defense along with regulatory and policy issues surrounding them. The final section synthesizes these parts into an analysis of which areas are best suited for DoD investment and offers concrete steps DoD can take to leverage opportunities in synthetic biology.

An Emerging Field with Mature Roots

For more than a century, scientists have been applying knowledge of biology to agriculture, medicine, and some industrial systems, but until more recently, they primarily identified and generated new microbes and products through slow, laborious processes that relied on trial and error. They collected samples from local and remote areas because they could only leverage the limited building blocks expressed in known organisms, and they relied on relatively undirected methods, such as breeding, when seeking to generate new traits. Altogether, these factors limited the speed of development and applications of biology-enabled processes and products.

In the 1970s and 1980s years, scientists developed the ability to perform limited direct modifications, such as adding a few genes, to organisms. These advances spawned the first genetically engineered organisms with commercial value, but more complex, directed changes were still not feasible; however, the past 20 years have seen rapid advances resulting from the development of technologies ranging from rapid gene sequencing to computational analysis and sensitive imaging. These

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have enabled scientists to pursue research and to successfully modify organisms in more complex, holistic, and targeted ways.

This work has generated new methods and collaborations and enabled new approaches, such as taking an engineering approach to biology by separating genes into their constituent parts, making catalogues of these parts, and using them to make novel combinations that do not exist in nature – similarly to how electrical engineers might use capacitors, resistors, and other interchangeable parts. These developments and new approaches spawned the field referred to as synthetic biology or engineering biology. Thus, it is not in and of itself a new field. The organisms synthetic biology is creating and seeks to create are the more complex and varied successors to earlier genetically engineered organisms. That is, synthetic biology builds on at least forty years of existing research and techniques, but it is new in its approach – holistic engineering of biology – and its promise. One of the leaders of the field, Drew Endy of Stanford University, describes his goal as “making living matter fully programmable.”

Research identified with synthetic biology has been growing since the late 1990s. A number of organizations and groups have conducted bibliometric analyses of the synthetic biology field, and all show a rapid rise since the early 2000s, with increases ranging from 6x to >100x depending on search terms. While only formed in 2002, Stanford University’s Department of Biological Engineering now has a budget of greater than half a billion dollars per year and is moving into a new, purpose-built facility in 2014 because it has outgrown the available space on campus. A series of recent analyses show that the U.S. is the leader in the field, with more than three times as many papers as the next most prolific country, the UK, and 8 or more times China.

Technology development has been especially rapid in the past 7 years, which is substantially decreasing the cost and timeline for engineering organisms. For example, DARPA’s *Living Foundries: Advanced Tools and Capabilities for Generalizable Platforms* program was able to generate a >7.5-fold acceleration and a >4-fold decrease in cost for the design-build-test cycle for generating new production strains of organisms.

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3 For example, see: “BioBricks Foundation.”
4 Discussion with Dr. Drew Endy.
5 Data courtesy of the Australian Defence Science and Technology Organization; McEntee and Stratman, *The US Synthetic Biology Landscape in 2010; Synthetic and Systems Biology*.
6 Discussion with Dr. Drew Endy.
7 Oldham, Hall, and Burton, “Synthetic Biology.”
between 2012 and 2014. Of course, this does not imply that synthetic biology has ‘fully arrived’ in terms of applications and economics. There are a number of technical and regulatory challenges holding the field back, which are discussed in depth later in this paper. Nonetheless, the field is moving forward, and one of the driving factors is government research and development (R&D) funding.

While it is difficult to separate funding specifically for synthetic biology research from larger biology R&D programs, the authors estimate that the U.S. government provides at least $220 million annually towards synthetic biology research and development. The U.S. Department of Energy leads funders, followed by the National Science Foundation, DoD, including DARPA, the National Institutes of Health, and the U.S. Department of Agriculture, along with other agencies.  

Outside of the US, it is even more difficult to gather data on synthetic biology funding; however, some useful highlights are available. The UK Science Minister recently announced a £60 million (~$100 million) multi-year investment in synthetic biology focused on medical applications, and the Chinese Academy of Sciences includes synthetic biology in its Innovation 2050: Technology Revolution and the Future of China roadmap. In 2008, the Chinese Academy of Sciences established the Key Laboratory for Synthetic Biology, which joins the Qingdao Institute of Bioenergy and Bioprocess Technology, the State Key Laboratory of Microbial Technology, and other government-funded state and academic laboratories in performing synthetic biology R&D.  

A confluence of factors, including the nascence of the field, the importance of government-funded research, and the emergence of synthetic biology from other academic pursuits, has created a landscape where academic institutions are at the leading edge of the field. The most prominent U.S. researchers primarily reside at MIT, Harvard, Stanford, University of California, Berkeley, and the Scripps and J Craig Venter Institutes. The synthetic biology commercial landscape also highlights this. Whereas typical startup communities are centered in Northern California, private companies in synthetic biology cluster around leading research institutions and often have professors as founders, as demonstrated by the largest hub being situated in Boston.  

Further advances in synthetic biology are likely to have tremendous value – both in dollar and societal terms. Organisms produced by traditional genetic engineering and by the first generation of synthetic biology have already spawned products worth $350 billion per year to the U.S. economy and are already in every room of the house. DuPont, Pfizer, Bausch & Lomb, Coca-Cola, and other Fortune 500 companies

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8 Data estimated by the author because official data does not exist.
9 Department for Business, Innovation & Skills, “Over £60 Million for Synthetic Biology”; Pei, Schmidt, and Wei, “Synthetic Biology.”
make or use packaging for products derived from engineered organisms, including food, clothing, medicines, and beauty products.\textsuperscript{10}

While this economic impact is substantial, it is mostly derived from simpler modifications to organisms and results in commodity products. In order to generate substantially more impact across a wider variety of fields, the complexity, precision, and scope of genome engineering must continue to increase; as the private company data in the following section demonstrates, investors are funding companies which are bringing or intend to bring these types of organisms to market. Thus, while there is still substantial need for basic research to enable the future development of this field, advanced commercial applications are emerging.

**Future Directions**

The Office of Technical Intelligence funded Quid, Inc., a San Francisco-based data-analytics firm, to carry out a study of the private company landscape in synthetic biology to gain a better understanding of the direction of the commercial field. Because private companies tend to be at an earlier stage of development, trends in their formation, foci, and ability to attract investment are all signals which may provide insights into future trends in the commercial world. The data supporting the study covers the period from the first quarter 2009 until the third quarter 2013 and is most representative of activity in the U.S. and Europe because of disparities in the use of venture capital and reporting of investment events in other parts of the world.

The first finding is that there is substantial activity in the synthetic biology area, both in terms of number of companies and investment. This analysis identified 162 private synthetic biology companies operating from 2009-2013 which drew $5.4 billion in investment from 281 distinct investors, including many of the best-known venture capital firms (Khosla Ventures; Draper, Fisher, Jurvetson; Kleiner Perkins; TPG) and corporations (Chevron, Unilever, Novartis). Intrexon, a synthetic biology company that designs and produces organisms for agricultural, medical, and industrial applications, conducted an initial public offering (IPO) this year that valued the company at more than $2 billion.

The graphic on the following page depicts a network of the private companies in the field that have received venture capital or other private investment. The companies are clustered based on the language with which they describe themselves in investment documents and on their websites.

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\textsuperscript{10} Carlson, “The U.S. Bioeconomy in 2012 Reached $350 Billion in Revenues, or about 2.5% of GDP”; Solomon, “Industrial Views on Synthetic Biology.”
Company descriptions divide the field into three main application areas, materials, services, and medical applications. These break down into 7 distinct communities structured around application areas, as shown in the above graphic, in which links represent the use of similar language and the size of the dot represents the number of links a company has. Of particular note is the fact that there is no community focused on sensing applications, which is an area that may be of defense interest.

In addition to the automated analysis which grouped companies based on the language they use to describe themselves, we analyzed the companies by product category, dividing companies into five groups:

- **Commodity Materials**: pure commodity companies, comprised of biofuels and industrial chemical makers.
- **Specialty Materials**: pure specialty materials companies, which produce fine chemicals, personal-care products, and nutritional additives, in addition to hybrid specialty and commodity materials companies. We included hybrid companies in this group because the current business strategy of many in the area suggests that they find the specialty materials application more promising and are shifting resources to it.
- **R&D Services**: providers of biological design, testing, process development, and consulting that run the gamut from optimization of biological molecules to design of entire organisms.
- **Laboratory Supply**: providers of customer-specified DNA, RNA, enzymes, and cell-cloning services; these companies tend to be more focused on process and known products than design or innovation.
- **Medical**: Drug development and pharmaceutical companies working with engineered antibodies, proteins, nucleic acids, and other therapeutics generated by biological engineering.

Analyzing by product area, we are able to classify the state of private-company activity. First, the Commodity Materials area appears to be on a downtrend. High, but falling investment, only a moderate number of companies founded after 2006, and relatively few IPOs or buyouts relative to investments suggest that the market is either saturated or investors and entrepreneurs no longer see it as attractive, and highly unequal investment suggests that investors have already picked winners. Altogether, this suggests that the commodity materials field is poised for relatively lower growth (see graphs, next page).
In contrast, while the Specialty Materials area has attracted substantially less investment, companies are much younger and investment is much more equal. When investment is more equal, this suggests that the market has not yet picked winners. Altogether, specialty materials appears to be an emerging area with the potential for substantially larger growth. In this case, the lower number of buyouts and IPOs emphasizes its youth, as companies may be too new and the market too uncertain to attract larger moves.

The R&D Services group is similarly young and has received lower levels of investment, with the exception of one big winner. Intrexon, which has attracted $500 million dollars in investment, was omitted from the analysis above because of the degree to which it skews this group. When removed for analysis, the group has low investment, but many newer companies. Even without Intrexon in the analysis, the market is starting to make larger investments in some companies in this area, as noted by the higher inequality in investments. Taken together, R&D services is an area in the early stages of growth with the potential for substantially more.

In contrast, the Laboratory Supply area has more companies which tend to be older, unequal investment, and a larger number of buyouts and IPOs. This suggests that there are established leaders and that it is more mature segment with less room for growth.
Finally, the Medical segment has a large number of companies, many relatively small investments, a moderate level of inequality, a moderate proportion of young companies, and a large number of buyouts and IPOs. This describes a sector that is going through cycles of renewal, has a steady stream of new entrants, and sees small investments in companies, most of which fail or take a long time to reach maturity, but that receive buyouts when they are successful (as is common with purchases of successful biotech companies by large drug companies). This suggests a steady sector that is neither emerging nor mature. This is best understood in the context that many of the companies in the medical space are developing engineered protein and antibody drugs, which are established markets in the pharmaceutical industry. As a result, the uncertainty about this application is lower.

While investment data are indicative of future developments in the field, the novelty of most of the synthetic biology approaches means that the speed with which the field will develop is still uncertain due to the need for future technical advances and as-of-yet unclear regulations. The following section discusses these areas to better illuminate the character of the field and to inform later discussion of opportunities for DoD.

Factors Holding the Synthetic Biology Field Back
Despite the promise – and even some commercial success – of synthetic biology, generating high performance and predictable operation of engineered biological systems is still a challenge. During a workshop earlier this year, a group of leading synthetic biologists agreed that there is still a substantial need for fundamental engineering research, tool development, cheaper DNA prototyping, and a wider range of well-characterized platform organisms. Furthermore, for applications which would require releasing living synthetic organisms into the environment, there is substantial uncertainty about whether this should go ahead – or will be allowed to by regulators and policymakers, especially in the global context.

The synthetic biology field still has a ways to go before reaching the ability to abstract rules about genes and gene components that predict function inside a wide range of organisms. To accomplish this will require a substantial amount of new research, new tools, and different approaches to analyze gene function in the complex environment presented by living organisms outside the lab. While commercial applications continue to grow, some leading synthetic biologists argue that the research necessary to generate leaps forward from today in these areas has a fragile funding stream and that this is jeopardizing advances. One program that has benefited this area is DARPA’s three year, $35 million Living Foundries: Advanced Tools and Capabilities for Generalizable Platforms that began in 2012. As noted above, it has funded research and tool development that, for one performer, enabled a >7.5-fold acceleration and a >4-fold decrease in cost for the design-build-test cycle of an industrial organism.

The small number of linked facilities to rapidly design, prototype, and test new organisms is also slowing the field. Receiving DNA from synthesis companies can take 3 or more weeks, which slows the research process, and testing is still labor intensive. There are currently 4 major facilities in the world with integrated capabilities to design and prototype synthetic organisms and a similar number dedicated to testing and disseminating standard parts. The shortage of these represents a bottleneck that slows research; however, the follow on to DARPA’s initial Living Foundries program described above, Living
**Foundries: 1000 Molecules**, will invest approximately $110 million over 5 years to fund several design, prototype, and test facilities in the US, with the goal of enabling these facilities to generate synthetic organisms to produce 1000 molecules of industrial and defense interest, including dozens that are “effectively unattainable through synthetic chemistry and cannot be synthesized using existing biological chemistry.”

Beyond technical and infrastructure bottlenecks, the synthetic biology field is hampered by the limited range of organisms it can utilize. Out of the tens of thousands of organisms on the planet, there are fewer than 20 that are used in synthetic biology research, and the vast majority of research and commercially important work uses 5-7 ‘model’ organisms as chassis. This is the result of the challenge of adapting findings from one organism to another. New organisms typically require different methods to get DNA into cells, process DNA differently, require DNA placement in different parts of their genomes, are not compatible with existing genetic ‘parts,’ and require new assays. This explains the reliance on a small number of organisms, but the extension of synthetic biology to a wider range of ‘chassis’ organisms would enable new functionality and applications. According to Dr. Chris Voigt of MIT, a leading synthetic biologist, the challenge of working with new organisms is the primary reason he does not take on projects that are otherwise exciting and well resourced.

Another challenge specific to U.S. commercial development is limited access to repositories of organisms that allow samples to be used commercially. While there are large collections of organisms in the US, these restrict their samples for non-commercial applications. Singapore, Thailand, and India have or are developing repositories to support their biotechnology industries, but there is not currently such an organization or plan in the US.

Finally, regulatory and policy factors will play an important role in the future of synthetic biology and may restrict the field’s development. There is already substantial concern in a variety of interest groups and the popular press about the impact of releasing synthetic organisms into the environment. Environmental groups are challenging the concept, and a number of books and movies have used unintended consequences of the release of synthetic organisms as the basis for apocalyptic scenarios, even if many of these are not well-founded scientifically. The outcry over the use of genetically engineered crops in some countries provides a sense of the real-world political challenges that utilizing synthetic organisms in the environment would create, although this will develop differently in different countries; while a large proportion of crops grown in the U.S. are genetically engineered, most European markets bar crops created using this technology.

The European approach is driven by public perception of high risk from engineered organisms and the application of a different regulatory framework – the precautionary principle, which requires restraint unless there is proof of safety – than the US, which primarily relies on risk minimization and cost-benefit analysis. The result of these opposing approaches – one requiring a proof of safety and the other requiring proof of harm – is that synthetic organisms will meet substantially higher regulatory burdens in European

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12 Discussion with Dr. Chris Voigt.
13 Lawrence, *I Am Legend*. 
countries. In the past, Asian countries have largely relied on Western regulators’ approval or disapproval of products as a starting point for regulation, but it is unclear how they will proceed when local companies begin bringing more cutting edge technologies to market. Importantly, this discussion primarily applies to organisms intended for release. In contrast, groups using synthetic organisms in controlled, factory- and refinery-type settings tend to have a much smaller regulatory burden, as they can typically control the release or distribution of the organism.\(^{14}\)

While substantially more severe in Europe, there is still regulatory uncertainty in the US. There are at least 5 sets of policies and regulations emanating from different agencies, which may or may not have regulatory jurisdiction over various applications of synthetic biology depending on the technologies and applications involved. Future laws and regulations may also hinder synthetic biology, especially if an individual or group utilized it for nefarious purposes to large effect.\(^{15}\) Thus, while regulations will not have a major impact on all applications of synthetic biology – especially industrial uses – others will feel large effects, and an organization like DoD might find substantial legal, regulatory, political, and public relations challenges, even from allies, especially if it seeks to deploy ‘living’ organisms into the environment abroad. While perhaps less substantial, these same issues will also be present domestically.

While these challenges are important to a holistic understanding of the field, the sum of the data presages a bright future for synthetic biology. In some areas, development will be relatively slow, but it is worth recognizing that engineering microprocessors took many decades and billions of dollars before computers reached a level of sophistication where they changed both society and warfare. While the timeline for synthetic biology is unclear, there are a range of applications of synthetic biology that may have substantial defense implications. This assessment now moves from a broader look at the field to focus on the potential defense applications.

**From Nano to Mega: Potential Defense Applications of Synthetic Biology**

Synthetic biology has the potential to produce major advances in materials, sensing, and human health and performance. To better understand current efforts, potential future applications, and implications of R&D in synthetic biology, we break these broad areas into five application areas that academia, militaries, the private sector, and other groups may pursue: commodity materials, specialty materials, sensing, medical and human performance, and biological and chemical threats and defense.\(^{16}\) This discussion is based on current worldwide R&D and discussions of how the natural world presages the ability to develop capabilities. It also discusses the degree to which applications of potential DoD interest are distinct from private-sector applications and the likely regulatory burden for each application area from the U.S. perspective. These factors inform whether DoD investment is critical to the development of an application and whether there are non-technical roadblocks that may prevent even successful technology development from generating fieldable capabilities.


\(^{15}\) Ibid.

\(^{16}\) This discussion is intended to capture applications from a range of actors, so while the U.S. will not pursue offensive biological or chemical weapons applications, we include it because potential adversaries may.
Natural and engineered biological systems are effective at producing commodity materials. Forests provide a non-trivial proportion of the world’s building materials, and the food that we eat every day starts as living plants, animals, and microorganisms. In the US, genetically engineered crops already provide the majority of animal feed and some food products. Companies are also engineering biology to produce industrial chemicals successfully and at large scale, including biofuels, butanol, used as a solvent and chemical intermediate, lactic acid, used to make plastics, and 1,3 propanediol, which DuPont uses to make its near billion-dollar Sorona fiber for carpets and clothing.\textsuperscript{17}

However, while commodity applications of synthetic biology may have important economic effects, the role of these materials and the structure of commodity markets suggest that there will be few major effects on DoD. Commodities, by definition, are fungible, so the driving factor is price not performance. While synthetic biology appears likely to bring down the price of some commodities, it does not appear poised to substantially change the economics of areas in which DoD spends enormous amounts of money, such as fuels. At the same time, if there are opportunities to substantially decrease the price of a material such as gasoline or a direct substitute, the private sector will have enormous incentives to invest in R&D in this area because even a penny saving per gallon of fuel is worth billions of dollars.

\textsuperscript{17} “About Butamax Advanced Biofuels”; “FAQS.”
One area in which DoD may have different needs for commodity materials production arises when including the cost of logistics in the price of the materials. While it is possible to buy gasoline or diesel fuel in the U.S. for $3-4 per gallon, it cost the U.S. military over $400 per gallon at some forward operating bases in Afghanistan due to delivery costs.\(^{18}\) Thus, some small-scale or light-footprint production of commodity materials at costs much higher than the open market rate may be valuable in special circumstances.

In general, commodity materials applications do not face a challenging regulatory environment. Producing a material (besides food) usually does not require the release of a living organism – which stays within the factory or refinery, and most materials are regulated based on their properties and not their origin. As such, using engineered biology does not typically trigger extra regulatory approval for the entrance into the market or use of a material.\(^{19}\)

**Potential Defense Applications:** Cheaper inputs to textiles and other products; at best, cheaper fuels and higher-performance lubricants.

Organisms naturally produce nano-scale particles and extremely complex molecules with tight tolerances. For example, there are a variety of bacterial species that naturally produce ferromagnetic crystals in the 50 nanometer range with very small size distributions.\(^{20}\) Using synthetic techniques, researchers from Cal Tech were able to leverage the folding properties of DNA to create precise carbon-nanotube junctions which demonstrated field-effect transistor-like behavior at the nano-scale, which might be useful for small-scale and low-power applications.\(^{21}\) These examples demonstrate the ability of biological systems to produce **specialty materials** which are difficult, expensive, or impossible to generate through traditional means.

In addition to producing and assembling well-known materials, biological systems produce high-performance materials not found elsewhere on earth, some of which we have no other way to produce. Bacteria which live in the mud at the bottom of the Black Sea metabolize ammonium into toxic products. To prevent damage to the rest of the cell from these metabolic products, the bacteria produce a molecule called a ladderane, named due to its ladder-like chemical structure, to create tight membranes that prevent diffusion of toxic chemicals outside of specific cell compartments. These molecules had not been described until their discovery in these bacteria, and their unique chemical structure may prove useful as a building block for novel materials. Further demonstrating the diversity of potential synthetic biology products, one of the toxic byproducts these bacteria produce is hydrazine, which DoD already uses to fuel rockets and in other applications as a high-performance propellant.\(^{22}\)

\(^{18}\) CBSNews.com Staff, “Real Cost of Gas at Afghan Bases.”
\(^{20}\) Chen and Bazylinski, “Bacteria That Synthesize Nano-Sized Compasses to Navigate Using Earth’s Geomagnetic Field.”
\(^{21}\) Maune et al., “Self-Assembly of Carbon Nanotubes into Two-Dimensional Geometries Using DNA Origami Templates.”
\(^{22}\) van Niftrik and Jetten, “Anaerobic Ammonium-Oxidizing Bacteria” and discussion with Dr. Alicia Jackson.
Finally, synthetic biology is already producing biological constructs and techniques to compute and to store information, such as a Harvard team that recently coded a book in DNA at an information density 6 orders of magnitude better than current hard disks and 3 better than quantum holography.23 These examples demonstrate the type of unique and useful molecules and processes which biological systems can generate. In contrast to commodity materials, DoD has many unique requirements for high-performance materials that do not have large private-sector demand, so the development of specific materials may be very sensitive to DoD R&D investment. Specialty materials also benefit from the relatively low regulatory barriers for the same reasons as commodity materials, namely that using biology to produce a material rarely creates an increased regulatory burden.

Potential Defense Applications: Sensor active materials; high-strength polymers for armor; stealth materials; corrosion-resistant coatings; biological computing; data storage and cryptographic materials.

To survive, organisms are constantly sensing the environment and tailoring their biological processes based on changes in conditions. These same mechanisms can be used to engineer useful biological sensors and to enable novel sensing and read-out capabilities for organisms. For example, the bacteria described earlier in this paper that produce ferromagnetic crystals do so to orient themselves, allowing them to maintain their position in precise aquatic microenvironments.24 Finely sensing magnetic fields is important to a range of military applications, showing that engineered biological pathways and systems might enable or replace DoD systems. Existing biological systems can also naturally and synthetically sense a wide variety of other phenomena of interest, from the presence of specific chemicals to light and ionizing radiation.25 Organisms can also produce physical and chemical signals which scientists could leverage to read-out living sensors. The Office of Naval Research (ONR) is supporting research into the development of a variety of electromagnetic ‘readout systems’ which would be compatible with the typical input/output signals of traditional military and civilian sensors. This work ranges from the development of a network of genes that enables cells to produce electrical current at their surface in proportion to activity within the cell to research on producing magnetic nanoparticles as outputs.26 In combination with these properties, biological sensors have a range of potentially advantageous characteristics, including their small size, the difficulty in distinguishing synthetic organisms from the ubiquitous biological systems in the environment, their exquisite sensitivity, the opportunity for multi-modal sensing, and their ability to self-replicate. Research into organisms that live in extreme environments, from boiling sulfur pools to jet-fuel tanks (a current problem for the Air Force), will also enable scientists to improve the durability of organisms in the environment.27

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23 Ratner et al., “Biologically Relevant Molecular Transducer with Increased Computing Power and Iterative Abilities”; Church, Gao, and Kosuri, “Next-Generation Digital Information Storage in DNA.”
24 Chen and Bazylinski, “Bacteria That Synthesize Nano-Sized Compasses to Navigate Using Earth’s Geomagnetic Field.”
25 Levskaya et al., “Synthetic Biology”; Bacterial Dosimeter.
26 “Scientists Engineer Bacterial Live Wires.”
Like specialty materials, DoD has a range of unique needs in the sensing field, but unlike specialty materials, sensing using synthetic organisms will trigger much higher regulatory hurdles. Introducing synthetic organisms into the environment typically triggers requirements for review, and many questions that regulators might reasonably ask, such as the extent to which organisms will persist and transfer genes, will require additional science to understand well. Deploying biological sensors would likely encounter even more complicated regulatory and political challenges abroad.

As a note, this paper defines the ‘sensing’ application as using living organisms to sense. As such, the use of biologically-produced compounds in traditional sensors fits in the specialty materials area. This distinction is important because of the regulatory implications of introducing living organisms into the environment and the technical and operational differences between using organisms in controlled facilities versus in the field.

**Potential Defense Applications: Distributed tag, track, and trace systems; persistent clandestine sensors.**

Because of biological constructs’ and organisms’ ability to interact with human and microbial systems, synthetic biology has the potential to generate major medical breakthroughs, from cures to a wider range of diseases to the ability to treat disease with fewer side effects. A current research thrust is seeking to develop bacteria that can sense tumors, invade malignant cells, and produce anti-cancer molecules that do not harm healthy cells. The successful implementation of this approach would revolutionize cancer treatment, sparing patients the serious side effects of chemotherapy.²⁸ Scientists may also be able to use engineered organisms to combat a wide variety of other illnesses, from auto-immune to infectious diseases. In addition, synthetic biology is also already being used to produce complex small-molecules, such as the malaria drug described in the first section, new proteins, and vaccines which are being developed or used to treat diseases including influenza.²⁹

Synthetic biology also appears likely to open up opportunities in the human performance modification field through the potential to make regulatory molecules in laboratories or, more directly, inside the body. For example, bacteria that live in the human digestive system already convert food into neurotransmitters and other molecules that influence performance;³⁰ by engineering these organisms to sense the levels of compounds in the body and to supplement or counteract them when needed, it may be possible to enhance physical, cognitive, and socioemotional (or interpersonal) performance.

Although it has a greater emphasis in trauma, DoD has few truly unique needs in the medical space; in contrast, DoD has many unique human performance needs. A large proportion of developments in human performance technology would be relevant to medicine as well, and there is likely to be interest in broader society for effective enhancements. Nonetheless, military personnel must perform at a high level across the cognitive, physical, and socio-emotional spheres of performance through extreme stressors over long...
durations. This unique set of circumstances means that military personnel both require different levels of
performance and might benefit from different interventions.

Both the medical and human performance areas will have significant regulatory barriers, especially if
researchers intend to develop living organisms to use in these applications. Successfully bringing new
drugs to market requires approval by the U.S. Food and Drug Administration (FDA), but introducing
synthetic organisms into a person would potentially trigger two sets of ethical and legal regimes –
governing both human protection through the FDA and release into the environment (i.e. excretion from
the human) which might be regulated by the U.S. Environmental Protection Agency or another agency
depending on technical characteristics.31 Furthermore, the FDA does not approve treatments purely for
enhancement; rather, it requires that the preparation treat a disease. As such, both medical and human
performance applications of synthetic biology will have substantial regulatory hurdles to overcome.

In the case of human performance, these hurdles will be even higher because appropriate testing of a
performance enhancing preparation would require studies in relevant environments and populations,
which for DoD would mean military personnel. Human testing in military personnel has important
additional ethical restrictions due to the coercive nature of the military command structure and past
abuses, so the full development of synthetic biology-enabled human performance enhancements would
be particularly fraught with regulatory challenges. There is already widespread use of supplements in
military units, but nonetheless, from an ethical point of view, Defense researchers would need to balance
potential harm with the potential benefits to warfighters, especially those in combat situations, where
enhanced performance might mean the difference between life and death.32

Potential Defense Applications: Prophylactic application of bacteria on the skin to prevent infections and
to help heal wounds; probiotics that mitigate the effects of stress and enhance mental performance.

The same characteristics that make synthetic biology of interest for medicine and human
performance provide both a challenge and an opportunity in terms of biological and
chemical threats and defense. Synthetic biology may enable potential U.S. adversaries to
develop biological weapons with new characteristics that enhance their threat to U.S.
forces. Biological engineers could also seek to develop organisms that produce traditional and novel
chemical agents. Of course, the U.S. will not develop biological or chemical weapons, but potential
adversaries might choose to do so.

In contrast, organisms could be used to produce treatments for biological or chemical agents. For
example, academic researchers, funded by the Defense Threat Reduction Agency, were able to engineer
a human enzyme which deactivates G-series nerve agents (e.g. sarin) in the blood to be more than 340
times more effective.33 Medical synthetic biology research may enable the development of organisms
that can combat biological agents and produce treatments inside the body. Thus, synthetic biology will

31 Bar-Yam et al., The Regulation of Synthetic Biology: A Guide to United States and European Union Regulations,
Rules and Guidelines.
33 Goldsmith et al., “Evolved Stereoselective Hydrolases for Broad-Spectrum G-Type Nerve Agent Detoxification.”
likely enable both threats and countermeasures; however, it is critical to note that, while synthetic biology may enable biological and chemical threats, focus on potential threats often overwhelms discussions about other aspects of the field, such as materials and sensing, that are almost certain to offer tremendous opportunities to DoD and the broader U.S. economy. As such, it is important to keep the threat from synthetic biology in perspective compared to other applications.

Despite the need not to overstate any potential threat, DoD has unique needs in protection of military personnel from biological and chemical weapons, although in the age of terrorism, these increasingly overlap with domestic preparedness, response, and public health requirements. Protection against synthetic biology-enabled weapons also need not necessarily use synthetic biology, although many proposed routes to broadly applicable treatment platforms do utilize elements of biological engineering. Of course, the U.S. will not develop offensive weapons, but we will need to continue to monitor and to be prepared for adversary developments. From the U.S. perspective, biological and chemical defense has many of the same regulatory requirements as medical treatments, with the caveat that some treatments do not require human testing if there is no naturally occurring human disease (e.g. smallpox).

*Potential Defense Applications: Adversary development of novel threat agents; biological treatments for traditional and novel biological and chemical weapons.*

**Industrial Base Benefits**

In addition to the specific application areas, synthetic biology also has the potential to benefit the defense industrial base. As described in the case of bacterial production of hydrazine, organisms can sometimes produce important materials with fewer toxic byproducts than traditional chemical engineering approaches. DoD’s Strategic Environmental Research and Development Program is already examining the use of bacteria for the nitration of explosive compounds with the goal of decreasing the toxic waste generated by traditional processes.  

Beyond environmental benefits, synthetic biology may enable common infrastructure to produce a variety of products. By changing the organisms, feedstock, and conditions, it may be possible to produce a high-value chemical, to clean the bioreactors and perform a modest reconfiguration, and then to produce a therapeutic mostly using common equipment. While the importance of maintaining sterile conditions and proper reaction parameters typically complicates this, the ability to build infrastructure which can be utilized for various outputs means that synthetic biology can enable a more flexible and potentially more efficient industrial base.

Thus, synthetic biology has the potential to affect a wide range of areas relevant to DoD, from the materials that allow for the production of high-technology systems to the sensors that provide leaders information and the industrial base underlying our defense needs. Based on the potential impacts and integrating analysis from this entire paper, the following section assesses where DoD investments are likely to generate the greatest returns.

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34 Graham, *Nitration Enzyme Toolkit for the Biosynthesis of Energetic Materials.*
Assessing R&D Opportunities and Responsibilities for DoD

This section evaluates the five defense application areas using three dimensions:

- **Impact and uniqueness of DoD needs.** The latter is important because private investment may satisfy DoD needs and vice-versa if the Department has relatively similar needs to the private sector;
- **Funding from the private sector and other U.S. Government agencies.** These are also important to determine where other organizations may meet DoD needs and where DoD can leverage external investment;
- **Policy and regulatory challenges.** These inform our understanding of the ability of DoD to field technologies once developed and the timeline on which this might occur.

Based on this analysis, we outline practical steps DoD could take to generate the greatest value, including by leveraging external investment, moving towards funding applied research for specific needs, committing basic research funding to areas which will push forward the broader field in conjunction with DoD interests, engaging research leaders, and developing human capital. Each section describes the factors affecting the application area and provides a recommendation regarding R&D in that area.

The discussion of applied research opportunities is particularly important because, while companies are developing a range of products using synthetic biology, almost all U.S. Government funding for synthetic biology focuses on basic research. These basic research efforts have clear benefits in terms of progressing the overall science, but they do not focus researchers on solving specific needs or send companies signals that could drive private investment in these areas. Without a robust mix of basic and applied research, U.S. Government organizations miss an opportunity to gain insights into how difficult various specific targets are to achieve, which would undoubtedly inform basic research needs. Leaders from the synthetic biology community also regularly remark that they see a great opportunity to demonstrate to DoD that synthetic biology can provide it major benefits, and DoD should capitalize on this to solve identifiable challenges.

1. **Commodity Materials**

Broadly speaking, DoD does not have special requirements for the makeup of commodity materials. Even in traditional areas of distinction, such as jet fuel, military JP-8 fuel differs from commercial Jet-A in the additives, not the basic fuel. In the agriculture subset of commodity materials, growing food is not a core research area for DoD, even if combat feeding is. Where basic and applied research support to commodity materials work is required, the U.S. Department of Energy is a substantial funder and has a substantially larger budget for fuels R&D than DoD. In addition, the private company data analyzed above shows that commodity materials firms received substantial investment in the past 5 years.

A caveat to this discussion is that the production of fuels in austere locations is a potentially unique value proposition for DoD; however, the R&D needed is primarily engineering the physical production systems,

35 Fabara, “Edwards ‘Fuel’-ing up for New Conversion.”
36 It is worth emphasizing that this discussion is focused on R&D opportunities. There is an ongoing discussion within policy arenas about the value of DoD purchasing major quantities of fuels from synthetic and other renewable, domestic sources to support the industry attaining economies of scale; however, this is a separate questions from whether DoD should fund synthetic biology research in this area.
as opposed to the organisms, many of which are already available to produce fuels. As such, this need is more of a systems and industrial engineering challenge, as opposed to a synthetic biology challenge, although of course these must work hand-in-hand for the finished product.

**Assessment:** At present, resources should be directed elsewhere.

### 2. Specialty Materials

Due to the rigors of combat and demands for exquisite performance, DoD has unique needs for high-performance materials that are not present in civilian applications; however, this area is receiving relatively small amounts of private and government funding – both the specialty materials application area and the R&D services field which supports it – with the exception of the ongoing DARPA Living Foundries efforts, which are generating infrastructure and charging teams with producing challenging molecules. Living Foundries is not, however, incentivizing specific materials. Nonetheless, the intended outputs of this project, organisms that can generate 1000 molecules, can serve as inputs to specialty materials R&D. This area is also attractive because using synthetic biology for materials applications does not create a large regulatory burden.

**Assessment:** The specialty materials application area represents a major opportunity for DoD, both in terms of basic and applied research. Applied research dollars are likely to generate leverage in the lightly-funded commercial sector by orienting leaders in the field towards DoD challenges and thereby bringing substantial value to DoD. Basic research to characterize new platform organisms well-suited to producing a given type of material (e.g. metals, polymers, or alkaloids) would supplement applied R&D to enhance long-term benefits.

**Concrete Steps:** (1) Focus Service short- and medium-term synthetic biology funding on specialty materials R&D. Build future grants, Broad Agency Announcements (BAA), Small Business Innovation Research (SBIR), and other funding opportunities for materials R&D with dedicated sections for lower-performing, but novel materials produced using synthetic biology. Because most of these materials and processes will not have the same degree of optimization enjoyed by traditional materials and processes, those that initially underperform may substantially improve with focused R&D. Where possible, the funding opportunities should incentivize biologists to team with individuals and organizations that have experience developing high-performance materials for DoD. This will educate biologists about some of the pitfalls other fields have experienced in materials development and will create valuable networks.

One effort towards these ends is the ongoing Synthetic Biology for Materials prize, which was released in late 2014 as a result of the initial conclusions of this assessment. The Office of Technical Intelligence (OTI), within the Office of the Assistant Secretary of Defense for Research & Engineering, partnered with the Materials and Manufacturing Directorate of the Air Force Research Laboratory to present a prize for the best research and development plans to address specific metamaterials manufacturing needs using synthetic biology. This effort targeted metamaterials because it was possible to identify specific materials needs that would feed specific capabilities and because a range of desirable components are prohibitively expensive or impossible to manufacture at scale. Because of organisms’ ability to operate precisely at the nano-scale, biology – and synthetic biology in particular – offers a potential solution. The prize successfully
attracted valuable plans, which DoD has the opportunity to use to develop an applied research program because the prize structure gives DoD a license to use the submissions. DoD should take advantage of an applied research program in this area.

(2) Develop a program within each Service basic research organizations to support basic research into the characterization and development of new platform organisms well-suited to various specialty material types.

3. Sensing
DoD has a range of unique needs in the sensing area resulting from the value of high-performance sensors, the need to sense unusual signatures, and the benefits of clandestine sensing. Sensing is also a cross-cutting research topic within the synthetic biology field because it plays a role in almost any application—for example anti-cancer bacteria under development sense low oxygen levels and crop-enhancing bacteria benefit from sensing soil characteristics, but as the private company data show, there is no dedicated market segment working on this challenge. In addition, there are substantial policy challenges to the introduction of synthetic organisms into the environment in addition to the technical challenge inherent in using organisms in the ex-laboratory environment. Thus, sensing is likely to require a longer-term research program than specialty materials for it to come to fruition, but nonetheless, the benefits could be substantial, and sustained development towards DoD needs appears unlikely without DoD intervention.

Assessment: While further away from fielding, the sensing application holds substantial promise for future DoD applications. With DoD’s unique applications and a paucity of private-sector funding, this is an area which will benefit from DoD funding and which appears to be a major opportunity for DoD in the medium to long term. As such, DoD should build on existing ONR research efforts in the sensing field, both in basic and early applied research. To maximize the likelihood of being able to deploy sensing organisms, research should go beyond technical development of sensing organisms to develop the science necessary to inform policy on release of organisms into the environment. This should happen in concert with the engagement of policymakers to develop policy frameworks.

Concrete Steps: (1) Apply Service medium- and long-term synthetic biology funding to sensing R&D. Build future grants, BAA, SBIR, and other funding opportunities for sensing R&D with dedicated opportunities for lower-performing, but novel approaches using synthetic organisms. As with specialty materials, those that initially underperform may substantially improve with focused R&D because these approaches will not have the same degree of optimization enjoyed by traditional sensors.

As part of these efforts – and similar to the design of the Synthetic Biology for Materials prize – offer a substantial financial prize for ideas to drive forward the production of a sensor relying on synthetic organisms that can detect exposure to 500 specific chemicals and record the order of exposure over a period of 12 hours. The stretch goal for an eventual applied research program should be to achieve a sensor that is smaller than 20 cm on each side with which scientists should be able to read out the total exposure in less than one hour and the order of exposure in less than 6 hours.
(2) Develop a program within each Service basic research organizations to support basic research into the characterization and development of new platform organisms well-suited to sensing in operational environments.

(3) Organize a working group within ASD(R&E) to examine what organizations and processes would need to be involved to approve the release of a synthetic organism into the environment and what science and metrics policymakers will likely need to make these decisions; begin to fund the science to support future policy by tying policy-supportive projects to more general sensing R&D funding.

4. Medical & Human Performance Modification

DoD’s medical needs are mostly consistent with broader, civilian needs, albeit concentrated more in certain areas, such as trauma. At the same time, the National Institutes of Health (NIH) dwarfs DoD’s biomedical research budget; the private sector is also investing in this area, and both the private sector and NIH are in a substantially better position to support novel therapeutics through the regulatory system. Because of the novelty of synthetic biology and the extra regulation required when using viable organisms in medical treatments, the regulatory burden will probably be even heavier than for existing treatments when using live organisms.

DoD has unique human performance applications, and the private sector is only investing in a limited way through relevant medical R&D. In the same way, medical funding is generating some relevant R&D at NIH and in other basic research organizations, but it is usually not targeted at human performance. This field has what is probably the largest regulatory challenge, especially when contemplating DoD research in this area. Where enhancement is concerned, the FDA does not currently have a mechanism for approving new ‘treatments,’ as it requires them to treat a disease to be considered, and research in military populations has additional hurdles.

Assessment: At present, resources should primarily be directed elsewhere, with some exceptions in the human performance field, which represents a major opportunity for DoD and would substantially benefit from R&D investment; however, the regulatory hurdles and potential communications challenges from the interaction between synthetic biology and human performance suggest that it is too early for DoD to move into this area unless DoD can identify civilian medical researchers as early partners who will carry developments through testing and regulatory approval. Research should also focus away from modifying the human genome and instead work on areas such as synthetic probiotics.

5. BW/CW Defense

Despite claims about the risks from synthetic biology often inappropriately drowning out discussions of other applications, DoD has a unique responsibility to protect military personnel from the use of biological or chemical weapons, and the private sector does not adequately address countermeasures to potential synthetic biology-enabled weapons. There is some private sector investment in synthetic biology to produce treatments for traditional agents, and the U.S. Department of Health and Human Services along with the National Institutes of Health supports some of this research. The regulatory environment for treatments is also on par with or somewhat less stringent than for medical applications.
**Assessment:** Because biological and chemical weapons defense is focused on threat mitigation instead of enhancing DoD capabilities to accomplish a wider range of tasks, it is important to keep its size relative to its importance and to structure R&D in such a way as to generate the greatest spillover benefits. The historical DARPA approach to novel biological threats is appropriate in both these regards. Programs such as 7-Day Biodefense sought to develop the capability to respond to any novel pathogen, whether naturally occurring or synthetic, on a militarily relevant timeline. This benefits DoD and the nation by improving pandemic and emerging infectious disease preparedness, while also enhancing DoD capabilities to respond to novel biological threats. Importantly, because of the regulatory challenges described above, the most promising opportunities for short-timespan successes are in programs to rapidly treat with small molecule or biologic treatments, but not living synthetic organisms.

**Concrete Steps:** The broad scope and challenge of this type of research suggest that it should primarily reside in DARPA. Where programs mature, the Defense Threat Reduction Agency should serve to finish applied research and transition solutions to the Services, as the BW/CW mission is inherently cross-Service. Because it is not possible to know what organism or characteristics a sophisticated attacker might use, funding should be reserved for projects that are agent-agnostic and are likely to generate spillover benefits for healthcare, such as improving responses to emerging infectious diseases of natural origin.

**Beyond R&D Investment – Human Capital**

While the focus of this paper up to this point has been R&D opportunities, human capital will affect the ability of DoD to operate effectively and efficiently in a synthetic biology-enabled world. At present, the Department has limited human capital in this area. There are few highly-experienced program managers in the Department, few leading scientists, and even fewer individuals in uniform with deep knowledge of the field. The lack of uniformed expertise is particularly troubling. There is a lag time of 20 years between training junior officers and those individuals achieving senior ranks, so providing opportunities now is crucial and would bear fruit well into the future.

**Concrete Steps:**

1. Tie generous grants to a requirement for leading researchers to spend 2-4 week sessions at Service research laboratories. Use these as a training opportunity for existing researchers, as a draw for post-doctoral students, and as a recruiting tool to attract high-performing talent.

2. The Services should institute bioengineering programs at each academy to train a cadre of uniformed military personnel. Each academy could target its program to coincide with other focus areas or strengths, such as systems engineering.

3. To improve their knowledge of and interaction with the field, the academies should require students in these majors to spend at least one summer at a major civilian research university working in a synthetic biology group, and each academy should send a team of students to participate in the International Genetically Engineered Machine (iGEM) Competition.

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37 “7-Day Biodefense.”
Conclusion
The synthetic biology field is not, in and of itself, new, but the degree to which the synthetic biology community seeks to engineer biology and the promise of the field are important. Because of the existing and promising future capabilities of engineered organisms, this assessment finds that the synthetic biology space presents a major opportunity for DoD. Targeted basic and applied R&D investment in specialty materials and sensing is likely to generate substantial short- and long-term value, especially in combination with programs to build human capital in DoD. Finally, while DoD should not ignore the biological and chemical weapons implications of synthetic biology, it should not allow these to dominate the conversation. R&D directed at this potential threat should be limited and targeted towards areas likely to generate spillover benefits for DoD’s and the world’s fight against emerging and established infectious diseases. The synthetic biology field appears likely to ‘take off’ in the next decade, and DoD should leverage this momentum towards its needs instead of being left by the wayside.
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