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Synthetic/Engineering Biology: Issues for Congress

September 30, 2022

Congressional Research Service
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R47265

CRS REPORT
Prepared for Members and
Committees of Congress

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Synthetic/Engineering Biology: Issues for Congress

Synthetic biology, sometimes referred to as engineering biology, is the application of engineering principles and the use of systematic design tools to enable the reprogramming of cellular systems at the genetic level for a specific functional output. It is one type of biotechnology. Since synthetic biology is still an emerging field, distinctions are not always clear between synthetic biology and related terms such as engineering biology, genetic engineering, genome engineering, and biotechnology. This situation can make it difficult to quantify trends in application areas, research funding, public investments, and economic impact, and it may complicate the application and oversight of federal regulations.

SUMMARY

R47265

September 30, 2022

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Synthetic biology may find use in multiple sectors, including biomanufacturing, medicine, consumer products, agriculture, smart materials, energy generation, conservation, and pollution remediation, among others. Its tools, processes, and products are part of the broader bioeconomy, which some suggest could be developed and deployed in a distributed and localized manner, offering opportunities for reindustrialization and new opportunities in rural regions of the United States that are more equitable and sustainable. Tracking federal investments in synthetic biology is difficult because of differences in how synthetic biology is defined; CRS analysis of data reported to a federal repository found that from FY2008 through FY2022 selected U.S. government research funding for synthetic biology increased from about $29 million to nearly $161 million, though these numbers may significantly undercount the total federal investment. Evaluating private investment and global markets in synthetic biology is similarly difficult to track, with estimates ranging from $37 billion to $100 billion by 2030.

New communities of practice, some of which are outside the traditional norms of scientific research, have emerged alongside, and sometimes because of, increased access to technologies associated with synthetic biology. These communities of practice are helping expand educational opportunities and impacting who can research and innovate with synthetic biology. Increased access could address some of the social and economic inequalities associated with emerging science and technology.

Advances in synthetic biology tools, access to genetic sequence information, and companies that synthesize DNA have raised certain biosafety and biosecurity concerns—for example, who should be able to access these capabilities and what limits might be placed on synthesis capabilities. Synthetic biology also enables applications intended to be released into, and engineer, natural environments. Some of these applications could cause irreversible effects on organisms and ecosystems, which could also have biosecurity implications. U.S. strategic competitiveness, particularly with China, and the potential implications for the U.S. military and international security have also been raised.

Some question whether the current U.S. regulatory system and research investments are sufficient to address the broad cross-cutting issues associated with synthetic biology and how to ensure U.S. competitiveness and leadership. As applications become more complex, novel, and designed for broader use in the environment, policymakers may consider whether the Coordinated Framework for the Regulation of Biotechnology, which currently guides U.S. biotechnology regulation, is sufficient to oversee current and future applications of synthetic biology. Congress may also consider whether additional oversight mechanisms are needed; specifically, whether agencies have the necessary expertise and adequate resources to evaluate proposals for funding or to adequately research and evaluate ecological impacts of applications seeking regulatory approvals.

Title IV of Division B of P.L. 117-167 sets forth, in part, a directive to improve the lay public's understanding of engineering biology and support greater evidence-based public discourse about its benefits and risks. Congress may choose to consider how public investments in public engagement might impact public acceptance and trust in synthetic biology and its applications and whether to require federal research and regulatory agencies to engage in periodic strategic assessments to identify research and coordination opportunities and potential biosafety/biosecurity concerns. Such assessments could be a part of broader efforts to assess the position of the United States in the bioeconomy and biotechnology in general. In addition, Congress may consider how it should engage with international deliberations on synthetic biology.

The impact of Executive Order 14801, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*, will face additional analysis once it is implemented, budget requests are submitted, and appropriations are potentially enacted. These activities could impact the issues mentioned above and other legislative and oversight functions of Congress as it relates to synthetic biology.

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Introduction

Synthetic biology is the application of engineering principles and the use of systematic design tools to enable the reprogramming of cellular systems at the genetic level for a specific functional output (e.g., the production of biofuels, the secretion of drug precursors, or acting as biosensors) and may also be referred to as engineering biology.[1] Sequencing technologies, which read DNA, make it possible to sequence entire genomes and transcriptomes[2] efficiently, in great depth,[3] and cost effectively. Collected sequences information is stored in databases, many of which are publicly funded and freely accessible. Gene synthesis technologies can take sequence data and "write" DNA, turning it into physical material which can then be designed or engineered for different purposes. The ability to both read and write DNA is a fundamental enabling technology of synthetic biology.

While humans have deliberately altered the genetic code of plants and animals for millennia through domestication and selective breeding, the relatively recent application of sophisticated tools to make direct changes at the cellular level to create novel genetic material (i.e., DNA and RNA) to obtain specific functions has led to the emergence of synthetic biology as a new field of research. Tom Knight, co-founder of Ginkgo Bioworks,[4] sometimes referred to as the "godfather" of synthetic biology,[5] said of it in 2005:

> In the same way that electrical engineering grew from physics to become a separate discipline in the early part of the last century, we see the growth of a new engineering discipline: one oriented to the intentional design, modeling, construction, debugging, and testing of artificial living systems.[6]

While genetic engineering tools and techniques are the primary methods used in synthetic biology, it is a multidisciplinary field that leverages a broad set of tools, techniques, and processes.[7] Disciplines that contribute to synthetic biology include systems biology, bioinformatics, molecular biology, microbial ecology, and plant virology.[8] It is a component of biotechnology—a broad term that dates back to 1919 referring to a process of producing products from raw materials with the aid of living organisms.[9] Additionally, synthetic biology relies on and builds upon advances in other fields such as nanotechnology, artificial intelligence, and robotics. The multidisciplinary aspects of synthetic biology, combined with its increasing accessibility,

[1] Geoff Baldwin et al., eds., *Synthetic Biology: A Primer*, rev. ed. (London: Imperial College Press; Singapore: World Scientific Publishing Co. Pte. Ltd., 2016).

[2] A transcriptome is the full range of messenger RNA (mRNA). mRNA is a single-stranded molecule of RNA that corresponds to the genetic sequence of a gene.

[3] S.A. Laird and R.P. Wynberg, *A Fact-Finding and Scoping Study on Digital Sequence Information on Genetic Resources in the Context of the Convention on Biological Diversity and the Nagoya Protocol*, U.N. Convention on Biological Diversity, Montreal, Canada, 2018.

[4] Ginkgo Bioworks is a synthetic biology company which began trading on the New York Stock Exchange in 2021 with a market cap of $2.5 billion.

[5] Leslie Mertz, "The Engineer's Take on Biology: The Godfather of Synthetic Biology Watched the Field Evolve and Continues to Expect Big Things," *IEEE Pulse*, vol. 7, no. 2 (2016).

[6] Thomas F. Knight, "Engineering Novel Life," *Molecular Systems Biology*, vol. 1 (2005).

[7] Kent Redford, Thomas Brooks, and Nicholas Macfarlane, et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019.

[8] National Academies of Sciences, Engineering, and Medicine, *Biodefense in the Age of Synthetic Biology*, Washington, DC, 2018, https://doi.org/10.17226/24890.

[9] Karl Ereky, *Biotechnologie der Fleisch-, Fett-, und Milcherzeugung im landwirtschaftlichen Grossbetriebe: für naturwissenschaftlich gebildete Landwirte verfasst* (Berlin: P. Parey, 1919).

have led to the establishment of new industries and the emergence of new communities of practice.

Since synthetic biology is still an emerging field, distinctions are not always clear between synthetic biology and related terms such as engineering biology, genetic engineering, genome engineering, and biotechnology. This situation can make it difficult to quantify trends in application areas, research funding, public investments, and economic impact, and it may complicate the application and oversight of federal regulations. (For more discussion of terminology and definitional issues, see the **Appendix**.)

Synthetic biology contributes to the broader bioeconomy—the share of the economy based on products, services, and processes derived from biological resources.[10] Many predict that the bioeconomy will be a driver of economic growth, estimated at up to $4 trillion per year globally over the next 10 years.[11] Specifically, many view the development of, and transition predominantly to, a bioeconomy as a means to address grand challenges such as climate change, food security, energy independence, and environmental sustainability.[12] Some suggest that technologies of the bioeconomy, including synthetic biology, could be developed and deployed in a distributed manner, offering opportunities for reindustrialization and new opportunities across the United States.[13] Estimates of the size of the global synthetic biology market, a component of the broader bioeconomy, vary—some suggest it will reach $37 billion by 2028[14] and others predict $100 billion by 2030.[15]

This report provides an overview of select synthetic biology application areas, current U.S. investment in synthetic biology, emerging communities of practice, and biosafety and biosecurity implications. Finally, it discusses a set of potential issues for Congress to consider, including regulations and international governance implications, ecological implications, transparency and public engagement, and strategic foresight to identify areas where federal policy may be deemed necessary.

Potential Applications

The tools and technologies associated with synthetic biology have the potential to develop a broad range of applications, including medicine, consumer products, agriculture, smart materials, energy generation, conservation, and pollution remediation (see **Figure 1**). Some of these potential uses have raised concerns over biosecurity, biosafety, and ecological impacts, as well as ethical, societal, and broader governance issues.[16] This includes concern among governments of

[10] For additional analysis on the bioeconomy, see CRS Report R46881, *The Bioeconomy: A Primer*, by Marcy E. Gallo.

[11] CRS Report R46881, *The Bioeconomy: A Primer*, by Marcy E. Gallo.

[12] Ibid.

[13] Philip Shapira, Nicholas E. Matthews, and Carrie A. Cizauskas, et al., "Building a Bottom-Up Bioeconomy," *Issues in Science and Technology*, vol. 38, no. 3 (2022).

[14] The Insight Partners, "Synthetic Biology Market Size Worth $37.85 Billion, Globally, by 2028 at 20% CAGR—Exclusive Report by The Insight Partners," press release, April 26, 2022, https://www.prnewswire.com/news-releases/synthetic-biology-market-size-worth-37-85-billion-globally-by-2028-at-20-cagr—exclusive-report-by-the-insight-partners-301532833.html.

[15] Coherent Market Insights, "Global Synthetic Biology Market to Surpass US$ 100.4 Billion by 2030, Says Coherent Market Insights (CMI)," press release, May 19, 2022, https://www.globenewswire.com/en/news-release/2022/05/19/2446967/0/en/Global-Synthetic-Biology-Market-to-Surpass-US-100-4-Billion-by-2030-Says-Coherent-Market-Insights-CMI.html.

[16] Todd Kuiken et al., "Creating a Research Agenda for the Ecological Implications of Synthetic Biology" (Woodrow

many developing countries and indigenous and local communities over how synthetic biology may affect their cultures, rights, and livelihoods.[17]

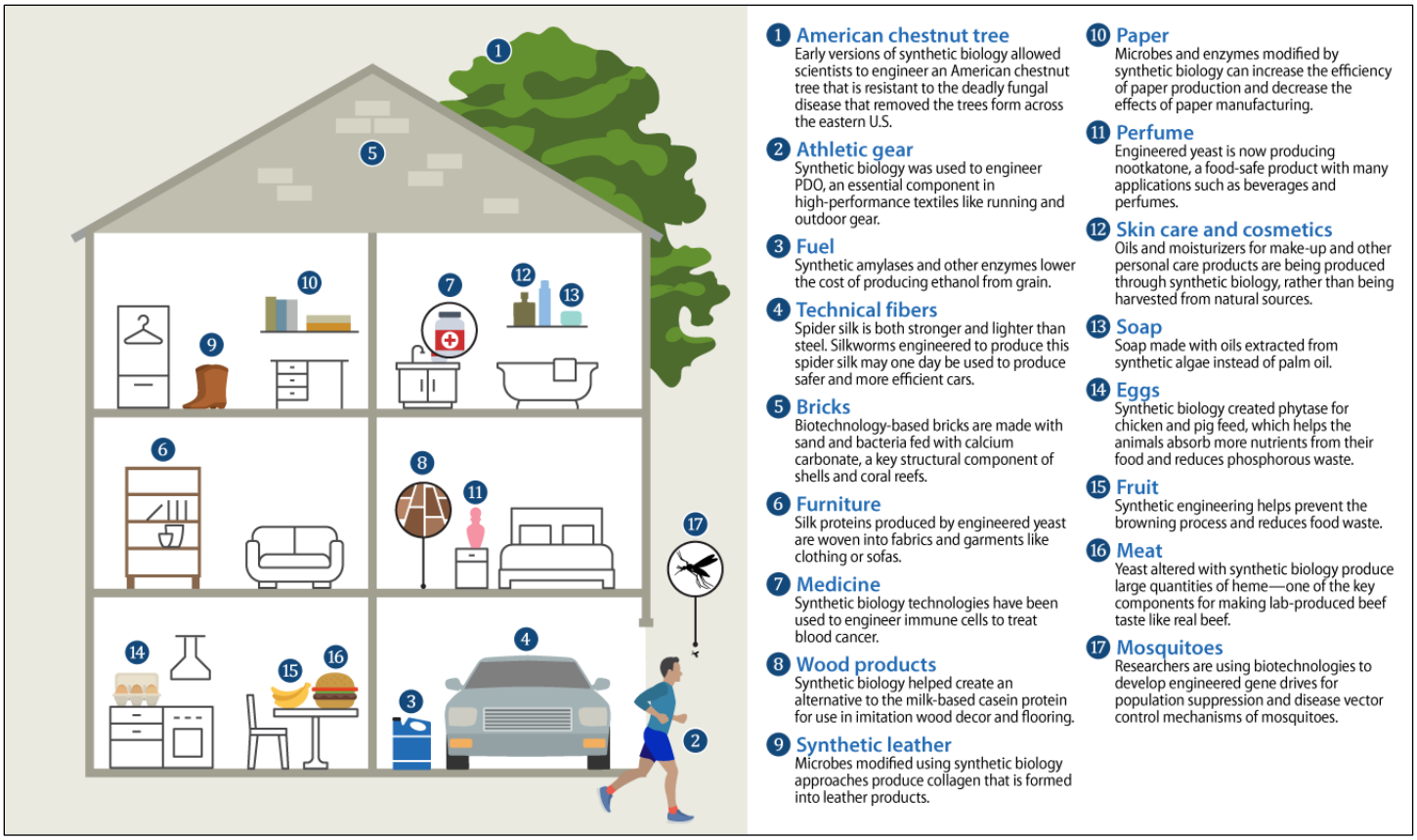
The list of selected applications discussed below illustrates the breadth of sectors impacted by synthetic biology.[18] This list is meant to be representative rather than exhaustive.

Wilson Center, 2014), https://www.wilsoncenter.org/sites/default/files/media/documents/article/SYNBIO_res_agenda.pdf; Todd Kuiken et al., "Shaping Ecological Risk Research for Synthetic Biology," *Journal of Environmental Studies and Sciences*, 2014, https://doi.org/10.1007/s13412-014-0171-2; Kenneth A. Oye et al., "Regulating Gene Drives," *Science* vol. 345, no. 6197 (2014), pp. 626-628, https://doi.org/10.1126/science.1254287; Kent Redford, Thomas Brooks, and Nicholas Macfarlane, et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019; Todd Kuiken, Rodolphe Barrangou, and Khara Grieger, "(Broken) Promises of Sustainable Food and Agriculture Through New Biotechnologies: The CRISPR Case," *The CRISPR Journal*, February 2021, pp. 1–7, https://doi.org/10.1089/crispr.2020.0098; National Academies of Sciences, Engineering, and Medicine, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* (National Academies Press, 2016); Jennifer Kuzma and Khara Grieger, "Gaps in U.S. Oversight Call for Community-Led Responsible Governance (CLEAR-GOV) for Gene-Edited Crops," *Science* vol. 370, no. 6519 (2021).

[17] Kent Redford, Thomas Brooks, and Nicholas Macfarlane, et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019.

[18] For select applications of gene editing see CRS Report R44824, *Advanced Gene Editing: CRISPR-Cas9*, by Marcy E. Gallo et al.

Figure 1. Examples of Currently Available and Proposed Synthetic Biology Applications



Source: Image recreated from Kent Redford et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019.

Notes: The products/applications shown in this figure are not exhaustive and could expand or contract based on technological developments, regulatory approvals, or public acceptance.

Biomanufacturing

Synthetic biology is currently being used as a platform technology. Synthetic biology plays a crucial role in biomanufacturing, which utilizes biological systems to produce commercially important biomolecules for use in the agricultural, food, material, energy, and pharmaceutical industries.[19] It can serve as a platform technology (a group of technologies that are used as a base upon which other applications or processes can be developed). For example, in a computer the hardware, or operating system, is the "platform" in which software applications can run. One analysis predicts that over the next 20 years, the direct annual global impact of biomanufacturing for materials, chemicals, and energy could be $200-$300 billion a year.[20]

[19] Yi-Heng Percival Zhang, Jibin Sun, and Yanhe Ma, "Biomanufacturing: History and Perspective," *Journal of Industrial Microbial Biotechnology*, vol. 44, no. 4-5 (2017).

[20] Michael Chui, Matthias Evers, and James Manyika, et al., *The Bio Revolution: Innovations Transforming Economies, Societies, and Our Lives*, McKinsey Global Institute, 2020, https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives.

A recent example of synthetic biology's impact in biomanufacturing was its role in producing COVID-19 vaccines more quickly than previous vaccine development methods.[21] The first doses of the vaccine were administered in human clinical trials 66 days after the genome of COVID-19 was released. Using the COVID-19 virus's gene sequence and the tools and technologies associated with synthetic biology, such as gene synthesis, scientists were able to chemically synthesize the genes that encode vaccine antigens to create a fully synthetic RNA-based vaccine.[22]

Another example is the production of hyaline—a family of films that are clear, flexible, and mechanically robust.[23] These properties enable them to be utilized in flexible circuits, touch screen displays, printable electronics, and other electronics that require flexibility, such as wearable devices and foldable smartphones. The films are produced by engineered organisms that are optimized using a suite of robotics and the iterative application of artificial intelligence.[24]

The combination of biology, computer-aided design, robotics, and engineering principles is typically conducted in biofoundries—facilities that provide integrated infrastructure enabling the rapid design, construction, and testing of engineered organisms for biotechnology applications and research. There are biofoundries spread across the globe, and a Global Biofoundry Alliance has recently been established to coordinate activities worldwide.[25]

Recent federal biofoundry initiatives include the Defense Advanced Research Projects Agency's (DARPA's)[26] Living Foundries program and the recent BioMADE initiative sponsored by Department of Defense (DOD). The DARPA Living Foundries program was developed to create a revolutionary, biologically-based manufacturing platform to provide new materials, capabilities, and manufacturing paradigms for DOD and the nation. The program seeks to develop the tools, technologies, and methodologies to transform biology into an engineering practice, speeding the biological design-build-test cycle and expanding the complexity of systems that can be engineered.[27] In 2021 DOD sponsored BioMADE, a new manufacturing innovation institute to "enable domestic bioindustrial manufacturing at all scales, develop technologies to enhance U.S. bioindustrial competitiveness, de-risk investment in relevant infrastructure, and expand the bio

[21] Elie Dolgin, "Synthetic Biology Speeds Vaccine Development," *Nature*, September 28, 2020, https://www.nature.com/articles/d42859-020-00025-4; and Jean-Nicolas Tournier and Joseph Kononchik, "Virus Eradication and Synthetic Biology: Changes with SARS-CoV-2?," *Viruses* 13, no. 4 (2021), https://doi.org/10.3390/v13040569.

[22] Elie Dolgin, "Synthetic Biology Speeds Vaccine Development," *Nature*, September 28, 2020, https://www.nature.com/articles/d42859-020-00025-4.

[23] John Cumbers, "Inspired by Nature, Zymergen Brews High-Performance Bio-Electronics," *Forbes*, April 12, 2020, https://www.forbes.com/sites/johncumbers/2020/04/12/inspired-by-nature-zymergen-brews-high-performance-bio-electronics/?sh=4b56024d2f18; and Christopher A. Voigt, "Synthetic Biology 2020–2030: Six Commercially-Available Products That Are Changing Our World," *Nature Communications* vol. 11, no. 1 (December 11, 2020), p. 6379, https://doi.org/10.1038/s41467-020-20122-2.

[24] Christopher A. Voigt, "Synthetic Biology 2020–2030: Six Commercially-Available Products That Are Changing Our World," *Nature Communications*, vol. 11, no. 1 (December 11, 2020), p. 6379, https://doi.org/10.1038/s41467-020-20122-2.

[25] Nathan Hillson, Mark Caddick, and Yizhi Cai, et al., "Building a Global Alliance of Biofoundries," *Nature Communications*, vol. 10, no. 2040 (2019).

[26] For information about DARPA, see CRS Report R45088, *Defense Advanced Research Projects Agency: Overview and Issues for Congress*, by Marcy E. Gallo.

[27] Defense Advanced Research Projects Agency (DARPA), "Living Foundries," https://www.darpa.mil/program/living-foundries.

manufacturing workforce to realize the economic promise of industrial biotechnology."[28] Biomanufacturing and developing the U.S. science and technology workforce was the focus of a November 2021 President's Council of Advisors on Science and Technology meeting.[29]

Agriculture

Synthetic biology has a range of possible agricultural applications both for crops and livestock.[30] For example, it may increase the precision with which changes can be made in plant genomes and expand the number of characteristics that can be changed or introduced.[31] These advances have shown potential for designing plants with new and enhanced traits,[32] enabling plants to be used as biosensors to detect pollutants, [33] and in water purification applications.[34] Synthetic biology can also be applied in ways that harness a plant as a "toolbox," using it to produce other types of outputs, such as chemical precursors for vaccines.[35] Synthetic biology is also utilized to engineer livestock for particular traits, such as polled (hornless) cattle.[36]

Synthetic biology techniques coupled with recent advances in understanding the important role the microbiome[37] plays in plant health and overall agricultural productivity has led to the development of fertilizers that improve crop yield. One aspect of the microbiome relates to nutrient uptake, particularly nitrogen. Certain bacteria can fix nitrogen (a chemical process that converts nitrogen into ammonia or other nitrogenous compounds) from the air and are used as a biological fertilizer. However, these bacteria are not naturally compatible with cereal crops (corn, wheat, rice).[38] Pivot Bio, a synthetic biology start-up, developed a genetically modified nitrogen-fixing microbial community, ProveN, that associates with corn roots.[39] This biological fertilizer proves a reliable source of nitrogen for corns plants and can reportedly reduce the need for liquid fertilizer by 25 lbs./acre while increasing yields by 5.8 bushels/acre.[40] Reducing the amount, or

[28] For information on DOD's BioMADE program, see https://biomade.org/.

[29] President's Council of Advisors on Science and Technology (PCAST), "Biomanufacturing, the Federal Science and Technology Workforce, and the National Nanotechnology Initiative," November 29, 2021, https://www.whitehouse.gov/pcast/meetings/2021-meetings/.

[30] CRS Report R46737, *Agricultural Biotechnology: Overview, Regulation, and Selected Policy Issues*, examines additional applications and select policy issues associated with agricultural biotechnology.

[31] National Academies of Sciences, Engineering, and Medicine, *Genetically Engineered Crops* (Washington, DC: National Academies Press, 2016), https://doi.org/10.17226/23395.

[32] June I. Medford and Diane M. McCarthy, "Growing Beyond: Designing Plants to Serve Human and Environmental Interests," *Current Opinion in Systems Biology*, vol. 5 (October 1, 2017), pp. 82–85, https://doi.org/10.1016/j.coisb.2017.08.008.

[33] Matthew J. Bick, Per J. Greisen, and Kevin J. Morey, et al., "Computational Design of Environmental Sensors for the Potent Opioid Fentanyl," *eLife*, vol. 6, no. e28909 (2017).

[34] Based on preliminary research and conversation with June Medford, Professor, Colorado State University; https://medford.colostate.edu/, 2020.

[35] James Reed, Michael J. Stephenson, and Karel Miettinen, et al., "A Translational Synthetic Biology Platform for Rapid Access to Gram-Scale Quantities of Novel Drug-Like Molecules," *Metabolic Engineering*, vol. 42 (2017).

[36] Alison L. Van Eenennaam, "Application of Genome Editing in Farm Animals: Cattle," *Transgenic Research*, vol. 28 (2019).

[37] The microbiome consists of all the microorganisms that live on, or in, other living things (e.g., skin, gut, or soil).

[38] Christopher A. Voigt, "Synthetic Biology 2020–2030: Six Commercially-Available Products That Are Changing Our World," *Nature Communications*, vol. 11, no. 1 (December 11, 2020), p. 6379, https://doi.org/10.1038/s41467-020-20122-2.

[39] Ibid.

[40] Karsten Temme, *Pivot ProveN Performance Report,* Pivot Bio, 2019, https://info.pivotbio.com/2020-performance-

need, for liquid fertilizer can potentially reduce environmental harms associated with fertilizer production, application, and subsequent runoff.

An additional agricultural application of synthetic biology is the engineering of yeast to produce food additives. One such example is the Impossible Burger, for which the yeast *Pichia pastoris* was engineered to produce soy leghemoglobin, which adds a "meat" flavor to the plant-based burger and enables it to "bleed." Other products produced from engineered yeast include vitamin E, stevia, and milk whey.[41]

Environmental and Conservation Applications

Synthetic biology is being explored as a potential tool for environmental protection, conservation, and invasive species control. In addition to optimism about synthetic biology's potential, there is also concern about whether risk assessment tools and methods exist to evaluate the environmental impacts of synthetic biology and whether appropriate policies and regulations exist.

Gene Drives

An engineered gene drive is a system of biasing inheritance to increase the likelihood of sexually-reproducing species passing on a modified gene to offspring. Offspring inherit one copy of a gene from each parent. Normally, this limits the total incidence of mutations over generations. An engineered gene drive system combines the ability to insert a gene of interest (e.g., a sex biasing gene) into the genome of a parent along with the gene drive itself, which causes the inserted gene to copy itself into the DNA from the unmodified parent.[42] The result is a preferential increase in a specific trait from one generation to the next and, in time, possibly throughout a species population. Gene drives have been suggested as a way to eliminate or reduce the transmission of disease,[43] eradicate or suppress invasive species and agricultural pests,[44] reverse pesticide resistance in agriculture, and aid in species conservation efforts.[45]

Cell-Free Systems

Cell-free systems, which some suggest can be thought of as programmable liquids,[46] enable the activation of biological processes without the use of living cells and have been used as a research

report.

[41] Christopher A. Voigt, "Synthetic Biology 2020–2030: Six Commercially-Available Products That Are Changing Our World," *Nature Communications*, vol. 11, no. 1 (December 11, 2020), p. 6379, https://doi.org/10.1038/s41467-020-20122-2.

[42] For additional information on gene drives and other gene editing tools, see CRS Report R44824, *Advanced Gene Editing: CRISPR-Cas9*, by Marcy E. Gallo et al.

[43] CRS In Focus IF10401, *Genetically Engineered Mosquitoes: A Vector Control Technology for Reducing Virus Transmission*, by Tadlock Cowan.

[44] John L Teem, Luke Alphey, and Sarah Descamps, et al., "Genetic Biocontrol for Invasive Species," *Frontiers in Bioengineering and Biotechnology*, vol. 8, no. 452 (2020).

[45] CRS Report R44824, *Advanced Gene Editing: CRISPR-Cas9*, by Marcy E. Gallo et al. Kent H. Redford et al., eds., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation: Technical Assessment*, International Union for Conservation of Nature, Task Force on Synthetic Biology and Biodiversity Conservation, Gland, Switzerland, 2019.

[46] Aidan Tinafar, Katariina Jaenes, and Keith Pardee, "Synthetic Biology Goes Cell-Free," *BMC Biology*, vol. 17, no. 64 (2019).

tool for more than 50 years.[47] They can remove the constraints of living organisms to develop simpler, more streamlined versions of biologically inspired systems that can be engineered efficiently for practical uses.[48] In a cell-based system, genetic instructions need to be assembled and imported into the cell, and then the cell must be maintained in order for the desired functions and outputs to occur.[49] Cell-free systems typically contain enzymes that are necessary for transcription and translation, which enables the process of producing proteins from DNA and RNA. These enzymes can be freeze dried and activated with water.[50] The merger of cell-free systems with the tools of synthetic biology is enabling biological platforms that can be used for biosensors, on-demand and portable biomanufacturing, and educational kits that can alleviate the need for expensive laboratory facilities and equipment.[51]

Cell-free systems could potentially contribute to decentralization of some aspects of health care through the development of portable diagnostics and localized drug manufacturing.[52] It has also been argued that the design and use of cell-free systems for production of high-value commodities, such as proteins or small molecules for pharmaceuticals and biologics, could avoid some of the challenges with current biomanufacturing methods. In particular, it could reduce the conflict between maintaining the life of the cells used for the production of chemicals and the economic goal of maximizing production capacity.[53] However, the practical and economic considerations of industrial-scale cell-free system biomanufacturing have not been tested, and challenges still remain.[54]

Addressing Climate Change

Some research suggests that synthetic biology may address issues associated with climate change, though it is difficult to predict whether such applications could be realized and what their impact on climate change could be.

One study reports that researchers were able to increase a plant's ability to fight off infection, which can be impaired when the production of salicylic acid is reduced due to short periods of hot weather above the normal plant growth's temperature range.[55] Other research groups are focused

[47] Adam D. Silverman, Ashty S. Karim, and Michael C. Jewett, "Cell-Free Gene Expression: An Expanded Repertoire of Applications," *Nature Reviews Genetics,* vol. 21 (2020).

[48] James U. Bowie, Saken Sherkhanov, and Tyler P. Korman, et al., "Synthetic Biochemistry: The Bio-Inspired Cell-Free Approach to Commodity Chemical Production," *Trends in Biotechnology,* vol. 38, no. 7 (2020).

[49] Aidan Tinafar, Katariina Jaenes, and Keith Pardee, "Synthetic Biology Goes Cell-Free," *BMC Biology,* vol. 17, no. 64 (2019).

[50] Aidan Tinafar, Katariina Jaenes, and Keith Pardee, "Synthetic Biology Goes Cell-Free," *BMC Biology,* vol. 17, no. 64 (2019).

[51] Adam D. Silverman, Ashty S. Karim, and Michael C. Jewett, "Cell-Free Gene Expression: An Expanded Repertoire of Applications," *Nature Reviews Genetics,* vol. 21 (2020).

[52] Aidan Tinafar, Katariina Jaenes, and Keith Pardee, "Synthetic Biology Goes Cell-Free," *BMC Biology,* vol. 17, no. 64 (2019).

[53] James U. Bowie, Saken Sherkhanov, and Tyler P. Korman, et al., "Synthetic Biochemistry: The Bio-Inspired Cell-Free Approach to Commodity Chemical Production," *Trends in Biotechnology,* vol. 38, no. 7 (2020).

[54] Adam D. Silverman, Ashty S. Karim, and Michael C. Jewett, "Cell-Free Gene Expression: An Expanded Repertoire of Applications," *Nature Reviews Genetics,* vol. 21 (2020). James U. Bowie, Saken Sherkhanov, and Tyler P. Korman, et al., "Synthetic Biochemistry: The Bio-Inspired Cell-Free Approach to Commodity Chemical Production," *Trends in Biotechnology,* vol. 38, no. 7 (2020).

[55] Jong Hum Kim, Christian Danve M. Castroverde, and Shuai Huang, et al., "Increasing The Resilience of Plant Immunity to a Warming Climate," *Nature,* vol. 607 (2022).

on increasing yields of biofuel crops, an important economic driver in the viability of biofuels. One study examined the potential for increasing plant growth and seed yield in the biofuel crop *Camelina sativa* by engineering the plant to utilize the CO_2 produced from photorespiration.[56]

Synthetic biology has also been proposed as a conservation tool to aid species impacted by climate change. For example, certain aspects of coral bleaching result from sea temperature rise. There are genetic traits in certain species of coral that provide resilience to ocean warming. Researchers have explored mechanisms to assimilate those traits into the genomes of other coral species in order to build resilience to the impacts of sea temperature rise.[57] While early research suggest these manipulations are possible, considerable technological development,[58] governance framework planning, and public engagement efforts would be required before synthetic biology could be applied to corals.

Federal Synthetic Biology Funding and Initiatives

Tracking federal investment in synthetic biology is difficult, in part because of the variety of terminology used, sometimes interchangeably, to describe research and development in this area (see the **Appendix**). A 2015 report from the Woodrow Wilson Center estimated that U.S. research agencies invested about $820 million in public funding between 2008 and 2014.[59] **Figure 2** shows selected U.S. research funding in synthetic biology from FY2008 through FY2020[60] as reported in the Federal RePORTER repository.[61] Two of the earlier and largest investments into synthetic biology came from the National Science Foundation (NSF) and DARPA.

The first major NSF investment was made in 2006, when the agency provided over $37 million for the Synthetic Biology Engineering Research Center (SynBERC).[62] SynBERC was a multi-university research center funded for 10 years to develop a foundation for synthetic biology. Following the conclusion of SynBERC, the Engineering Biology Research Consortium was founded by members of SynBERC to continue the research that had been started and help

[56] Jyoti Dalal, Harry Lopez, and Naresh B. Vasani, et al., "A Photorespiratory Bypass Increases Plant Growth and Seed Yield in Biofuel Crop *Camelina sativa*," *Biotechnology for Biofuels*, vol. 8, no. 175 (2015).

[57] Madeleine J. H. van Oppen, James K. Oliver, and Hollie M. Putnam, "Building Coral Reef Resilience Through Assisted Evolution," *PNAS*, vol. 112, no. 8 (2015); Rachel A. Levin, Christian R. Voolstra, and Shobhit Agrawal, et al., "Engineering Strategies to Decode and Enhance the Genomes of Coral Symbionts," *Frontiers in Microbiology*, vol. 8 (2017); and Phillip A. Cleves, Marie E. Strader, and Line K. Bay, et al., "CRISPR/Cas9-Mediated Genome Editing in a Reef-Building Coral," *PNAS*, vol. 115, no. 20 (2018).

[58] Kent Redford, Thomas Brooks, and Nicholas Macfarlane, et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019.

[59] Todd Kuiken, *U.S. Trends in Synthetic Biology Research Funding*, Woodrow Wilson Center, Washington, DC, 2015, https://www.wilsoncenter.org/publication/us-trends-synthetic-biology-research-funding.

[60] Data from 2008 to 2020 was obtained via a search of the Federal RePORTER system for the term "synthetic biology" in the grant project titles and abstracts. Not all agencies use the same terminology or definitions for funding categories, which could impact the choice of words used to describe a project in grant applications. Some projects that might be considered synthetic biology therefore could be missing from this analysis.

[61] Effective March 1, 2022, the Federal RePORTER system has been retired and is no longer available. To view the archived content, see https://wayback.archive-it.org/18816/20220223125200/https:/federalreporter.nih.gov/FileDownload.

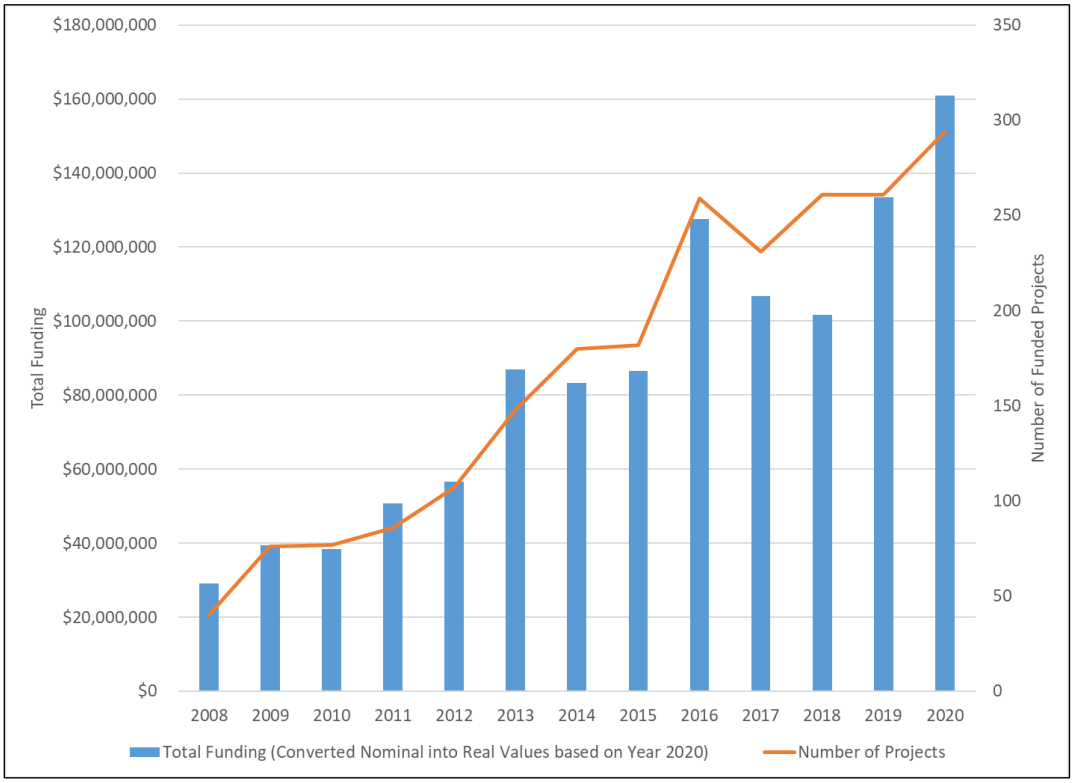
[62] Synthetic Biology Engineering Research Center (SynBERC), Award Abstract #0540879, 2006, https://www.nsf.gov/awardsearch/showAward?AWD_ID=0540879.

facilitate "interactions between academic and industry members, and broad-impact activities to support socially responsible innovation."[63]

DARPA has created multiple programs around synthetic biology, including Living Foundries,[64] Biological Robustness in Complex Settings,[65] Safe Genes,[66] and Insect Allies.[67] DARPA does not report its funding to the Federal RePORTER system. According to one report, nearly 60% of all funding for synthetic biology in the United States has come from DARPA.[68] This suggests that the numbers in **Figure 2** may significantly undercount the total federal investment in synthetic biology. The overall trends, however, suggest a significant increase in federal research funding since FY2008, from about $29 million in FY2008 to nearly $161 million in FY2020.

Figure 2. Selected U.S. Federal Funding of Synthetic Biology, FY2008-FY2020

in U.S. dollars, adjusted for inflation



Source: CRS analysis of Federal RePORTER data. Effective March 1, 2022, the Federal RePORTER system has been retired and is no longer available. To view the archived content, see https://wayback.archive-it.org/18816/20220223125200/https:/federalreporter.nih.gov/FileDownload.

[63] Engineering Biology Research Consortium (EBRC), "About," https://ebrc.org/about/.

[64] Defense Advanced Research Projects Agency (DARPA), "Living Foundries," https://www.darpa.mil/program/living-foundries.

[65] Defense Advanced Research Projects Agency (DARPA), "Biological Robustness in Complex Settings (BRICS)," https://www.darpa.mil/program/biological-robustness-in-complex-settings.

[66] Defense Advanced Research Projects Agency (DARPA), "Safe Genes," 2018, https://www.darpa.mil/program/safe-genes.

[67] Defense Advanced Research Projects Agency (DARPA), "Insect Allies," 2018, https://www.darpa.mil/program/insect-allies.

[68] Todd Kuiken, *U.S. Trends in Synthetic Biology Research Funding*, Woodrow Wilson Center, Washington, DC, 2015, https://www.wilsoncenter.org/publication/us-trends-synthetic-biology-research-funding.

Notes: The numbers represented in this figure underestimate the total U.S. funding in this space. Data was obtained via a search of the Federal RePORTER system for the term "synthetic biology" in the grant project titles and abstracts. Agency projects identified in the search included HHS, NSF, NASA, USDA, and some programs within DOD. Not all agencies use the same terminology or definitions for funding categories, which could impact the choice of words to describe a project in grant applications. Therefore, some projects that might be considered synthetic biology could be missing from this analysis if the term synthetic biology was not used. In addition, DARPA funding is a large component of total U.S. funding for synthetic biology, but the agency does not report its funding directly to the Federal REPORTER system, and is not captured in this figure.

National Engineering Biology Research and Development Initiative

Title IV of Division B of P.L. 117-167 (commonly known as the CHIPS and Science Act; Division B is the Research and Development, Competition, and Innovation Act) directs the President, through the Office of Science and Technology Policy (OSTP), to implement a National Engineering Biology Research and Development Initiative to "advance societal well-being, national security, sustainability, and economic productivity and competitiveness."[69] The Initiative's goal is to advance research and biomanufacturing in engineering biology, including through the support of social, behavioral, economic, and risk research. The Initiative also is to focus on accelerating the translation and commercialization of such research while also improving interagency planning and coordination of research programs. As discussed previously, synthetic biology is included within the context of engineering biology.

While the legislation prescribes certain objectives for OSTP and the participating agencies, it does not authorize specific appropriations to meet those objectives. Budget allocations and future requests from individual agencies to meet their own objectives, as well as the prescribed interagency coordination and funding of research, await additional analysis once the initiative commences.

White House Executive Order on Advancing Biotechnology and Biomanufacturing Innovation

On September 12, 2022, the White House released Executive Order 14081 on advancing biotechnology and biomanufacturing innovation for a sustainable, safe, and secure American bioeconomy.[70] The executive order prescribes a "whole-of-government approach to advance biotechnology and biomanufacturing towards innovative solutions in health, climate change, energy, food security, agriculture, supply chain resilience, and national and economic security."

The executive order focuses on 10 areas:

- harnessing biotechnology and biomanufacturing research and development to further societal goals;
- data for the bioeconomy;
- building a vibrant domestic biomanufacturing ecosystem;
- biobased products procurement;
- biotechnology and biomanufacturing workforce;
- biotechnology regulation clarity and efficiency;
- reducing risk by advancing biosafety and biosecurity;

[69] H.R. 4346, 117th Congress; became P.L. 117-167 on August 9, 2022.

[70] Executive Order 14801, "Advancing Biotechnology and Biomanufacturing Innovation," vol. 87, no. 178 *Federal Register* 56849-56860, September 15, 2022.

- measuring the bioeconomy;
- assessing threats to the united states bioeconomy; and
- international engagement.

The Assistant to the President for National Security Affairs (APNSA), in consultation with the Assistant to the President for Economic Policy (APEP) and the Director of OSTP, is tasked with coordinating the overall effort.

Emerging Communities of Practice

New communities of practice, some of which include individuals and groups outside of university, industry, and government research institutions, have emerged alongside, and sometimes because of, increased access to technologies associated with synthetic biology. According to NASEM, science education, which is crucial for the future workforce and the pursuit of living wage jobs, "is not the national priority it needs to be."[71]

These communities are helping expand educational opportunities and the scope of who can research and innovate with synthetic biology, which may lead to new discoveries, investments, the development of a diverse and representative bioeconomy workforce, and strengthening U.S. leadership and competitiveness in the field. These types of communities may also help address resource, training, and mentorship barriers that underserved communities commonly face in science, technology, engineering, and math (STEM) fields. Below is a brief description of three of these communities which have shown rapid growth and leadership alongside the development of synthetic biology.

The International Genetically Engineered Machines Competition (iGEM)

The iGEM competition is an annual synthetic biology event where global undergraduate, graduate, and high school students and community biotech labs compete to build genetically engineered systems using standard biological parts called BioBricks.[72] Team projects have ranged from building simple biological circuits to developing solutions to local and global agricultural and environmental conservation issues.[73] iGEM began in 2003 as an independent study course at the Massachusetts Institute of Technology (MIT) and is now an independent non-profit foundation. The course became a summer competition with five teams in 2004, growing to 350 teams in 2021 (see **Figure 3**), highlighting the growth of synthetic biology. Since 2004, over 60,000 students from 46 countries have participated in iGEM. Many student participants have gone on to form companies, including the founders of Ginkgo Bioworks, a synthetic biology company which began trading on the New York Stock Exchange in 2021 with a market capitalization of $2.5 billion.[74]

[71] National Academies of Sciences, Engineering, and Medicine, *Call to Action for Science Education: Building Opportunity for the Future*, The National Academies Press, Washington, DC, 2021, https://doi.org/10.17226/26152.

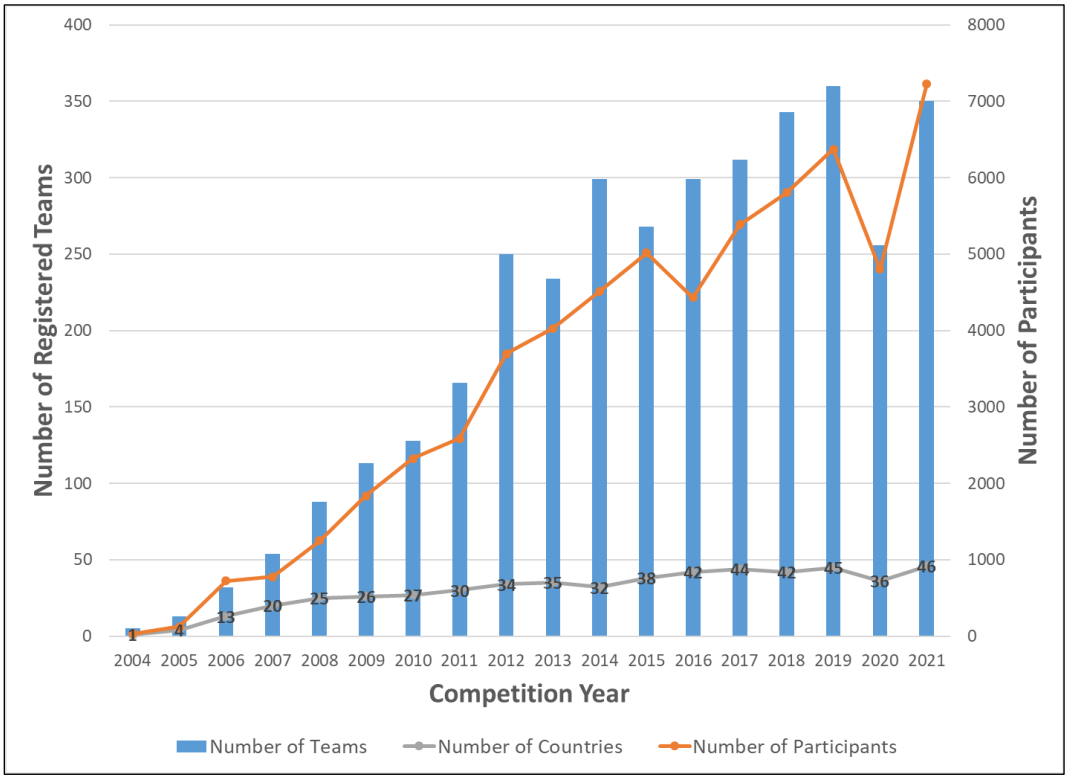
[72] International Genetically Engineered Machines Competition, "Registry of Standard Biological Parts," http://igem.org/Registry.

[73] International Genetically Engineered Machines Competition, "Competition," https://igem.org/Competition.

[74] Riley de Leon, "Ginkgo Bioworks Begins Trading on the NYSE after Completing SPAC Merger," CNBC, September 1, 2021, https://www.cnbc.com/2021/09/17/ginkgo-begins-trading-on-the-nyse-after-completing-spac-merger.html.

Some have argued that iGEM is a valuable component of the broader bioeconomy[75] by helping to build the bioeconomy workforce.[76] In 2017, the number of teams from China surpassed the number of U.S. teams for the first time while U.S. participation declined, contributing to concerns about U.S. competitiveness in synthetic biology and biotechnology more broadly.[77] The iGEM competition moved its headquarters and annual jamboree from Boston to Paris in 2020.

Figure 3. Global Participation in iGEM 2004-2021



Source: International Genetically Engineered Machines Competition, "Previous Competitions," https://igem.org/Previous_Competitions.

Biodesign Challenge

The Biodesign Challenge is an annual competition that offers opportunities for art and design students to develop projects around potential biotechnology applications.[78] Started in 2016 with 9 teams from the United States, the competition has grown to 56 teams from 18 countries in 2022.

[75] For more information on the bioeconomy and iGEM, see CRS Report R46881, *The Bioeconomy: A Primer*, by Marcy E. Gallo, and http://www.igem.org.

[76] Kelsey Lane Warmbrod, Marc Trotochaud, and Gigi Kwik Gronvall, "IGEM and the Biotechnology Workforce of the Future," *Health Security*, vol. 18, no. 4 (August 1, 2020), pp. 303–339, https://doi.org/10.1089/hs.2020.0017.

[77] For a more in-depth analysis of China's role in biotechnology and its implications for U.S. policy, see Scott Moore, "China's Role in the Global Biotechnology Sector and Implications for US Policy," The Brookings Institution, 2020, https://www.brookings.edu/wp-content/uploads/2020/04/FP_20200427_china_biotechnology_moore.pdf; Mark Kazmierczak et al., *China's Biotechnology Development: The Role of US and Other Foreign Engagement*, Gryphon Scientific, 2019, https://www.uscc.gov/sites/default/files/Research/US-China%20Biotech%20Report.pdf.

[78] Biodesign Challenge, "Biodesign Challenge," http://biodesignchallenge.org/.

Students are connected with a team of synthetic biologists and experts to guide them as they develop their ideas. The competition is based upon a theory that design plays an integral role in the development of any technology and that a designer's vision can both anticipate and inspire new applications, which in turn can influence the research community and shape societal attitudes toward technologies. Some students have taken their Biodesign Challenge projects and developed them into start-up companies. For example, the 2016 winner from the Fashion Institute of Technology (NYC) founded AlgiKnit,[79] which develops renewable yarns from kelp and recently raised $13 million in venture capital investment.[80]

Do-it-Yourself Biology (DIYbio)

Do-it-yourself biology, or DIYbio, is a global movement to spread the use of biotechnology and synthetic biology tools beyond traditional academic and industrial institutions to other communities.[81] Practitioners include a broad mix of citizen scientists, amateurs, enthusiasts, students, and trained scientists, some of whom focus their efforts on using synthetic biology to create art, explore biology, create new companies, or simply to tinker. The concept of amateur biotechnologists—that eventually became DIYbio—began to take shape around 2000, after a working draft of the human genome was completed by the Human Genome Project.[82] People began setting up home laboratories,[83] which evolved into dedicated laboratories in commercial spaces. Organizers pooled resources to buy, or take donations of, equipment, and began what have become known as "community labs." The first community labs opened in the United States in 2010 (Genspace[84] in New York City and BioCurious[85] in California's Silicon Valley), growing into a global research and innovation community. Most DIYbio groups operate under the community lab model, where the goal is to support local community education and experimentation in the biological sciences through the facilitation of independent and collaborative projects and classes that are open to the public. There are also startups, community groups, and other incubator spaces that identify as practicing DIYbio.[86]

Questions have been raised surrounding the DIYbio community's ability to address the biosafety and biosecurity concerns associated with conducting biological research outside traditional research facilities, which have certain biosafety and biosecurity related trainings and procedures in place—particularly the potential release of biological materials, as well as certain biosecurity concerns related to increased access to biological materials and technologies.

To address safety, security, and ethical concerns, the DIYbio community has been involved in a number of initiatives, including conversations and workshops with the FBI's Weapons of Mass Destruction Directorate. These activities focused on building trust and relationships between the

[79] AlgiKnit. https://www.algiknit.com/.

[80] AlgiKnit, "Materials Innovator AlgiKnit Closes $13 Million Series A to Transform the Textile Industry's Environmental Impact," press release, June 29, 2022, https://www.prnewswire.com/news-releases/materials-innovator-algiknit-closes-13-million-series-a-to-transform-the-textile-industrys-environmental-impact-301577657.html.

[81] Daniel Grushkin, Todd Kuiken, and Piers Millet, *Seven Myths and Realities About Do-It-Yourself Biology*, Woodrow Wilson Center, Washington, DC, 2013, https://www.wilsoncenter.org/publication/seven-myths-and-realities-about-do-it-yourself-biology-0.

[82] Ibid.

[83] Rob Carlson, "Splice It Yourself," *Wired*, May 2005.

[84] Genspace, https://www.genspace.org/.

[85] BioCurious, https://biocurious.org/.

[86] For a list of DIYbio labs and projects, see https://sphere.diybio.org/.

FBI, law enforcement, other first responders, and the DIYbio community to address potential biosafety and biosecurity issues. In addition, the DIYbio community, in partnership with ABSA International, the Association for Biosafety and Security, developed a certified biosafety training course[87] and an open access biosafety handbook.[88]

Potential Biosecurity Implications[89]

The biosecurity concerns of synthetic biology are part of a larger policy debate on how best to manage biosafety and biosecurity associated with emerging technologies and life sciences research. The United States has multiple, overlapping policies that provide guidance and oversight for life sciences research, depending on the types of experiments and biological agents used. While some oversight mechanisms are required by law, others are guidance issued by funding agencies and are mandatory only if the research is funded by the U.S. government. Privately funded research, or research conducted outside the United States, may therefore not be covered by certain U.S. oversight mechanisms. One analysis suggested that the U.S. life sciences research biosafety and biosecurity policymaking process is reactive, leading to inconsistent policies that limit U.S. ability to address emerging threats.[90]

Some of synthetic biology's associated technologies and applications have raised specific concerns. While the ability to read and write DNA has led to positive outputs, such as the development of COVID-19 vaccines, the relatively free access to genetic information and the increased ability to have it synthesized by private companies has raised safety and security concerns.[91] These concerns include questions about who should be able to access synthesis capabilities and what limits might be placed on the services that may be provided. The National Institutes of Health (NIH) recently updated its gene synthesis screening guidelines in order to address some of the biosecurity related issues associated with access to sequences of concern.[92]

Some synthetic biology applications and outputs are intended to be released into, impact, and engineer environments, which are sometimes referred to as the built environment. Some of these applications for the built environment could have biosecurity implications. The potential for gene drives to spread and persist throughout the environment could cause irreversible effects on organisms and ecosystems.[93] These potential ecological impacts could have biosecurity and strategic implications for the United States. For example, if a staple crop or ecosystem were impacted by a synthetic biology application, deliberately or by accident, it could affect U.S. food and water supply chains and global food security systems.

[87] Yong-Bee Lim, "Checking Ourselves Before Wrecking Ourselves: Co-Evolving Innovation and Safety in the DIYBio Community," Baltimore Underground Science Space, https://bugssonline.org/community/diybio-biosafety/.

[88] Genspace, "Community Biology Biosafety Handbook," 2020, https://www.genspace.org/community-biology-biosafety-handbook.

[89] For additional analysis on U.S. oversight of biological sciences research, see CRS Report R47114, *Oversight of Gain of Function Research with Pathogens: Issues for Congress*, by Todd Kuiken.

[90] Diane DiEuliis, Venkat Rao, and Emily Billings, et al., "Biodefense Policy Analysis—A Systems-Based Approach," *Health Security*, vol. 17, no. 2 (2019), pp. 83-99.

[91] Kai Kupferschmidt, "How Canadian Researchers Reconstituted an Extinct Poxvirus for $100,000 Using Mail-Order DNA," *Science*, July 6, 2017.

[92] Department of Health and Human Services, "Screening Framework Guidance for Providers and Users of Synthetic Oligonucleotides," 87 *Federal Register* 25495-25499, April 29, 2022.

[93] National Academies of Sciences, Engineering, and Medicine, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research*, The National Academies Press, Washington, DC, 2016.

These and broader issues around strategic competitiveness and how that can impact biosecurity have been recognized in recent initiatives, legislation, and reports. For example, Executive Order 14801 prescribes a set of provisions to address certain biosecurity related issues that synthetic biology may impact. Section 9 describes a biosafety and biosecurity innovation initiative, which seeks to reduce biological risks associated with advances in biotechnology, biomanufacturing, and the bioeconomy. Section 11 directs the Director of National Intelligence (DNI) to lead a comprehensive interagency assessment of ongoing, emerging, and future threats to U.S. national security from foreign adversaries against the bioeconomy and from foreign adversary development and application of biotechnology and biomanufacturing, including acquisition of U.S. capabilities, technologies, and biological data.

The National Security Commission on Emerging Biotechnology, established in Section 1091 of the FY2022 National Defense Authorization Act (P.L. 117-81) is tasked with evaluating emerging biotechnology's potential implications for U.S. strategic competitiveness, particularly with China, and for the U.S. military and international security writ large.

CRS Report R46458, *Emerging Military Technologies: Background and Issues for Congress*, by Kelley M. Sayler, examines issues in which Congress has expressed interest related to the biosecurity and national defense implications of synthetic biology and engineering biology. A 2018 National Academies of Sciences, Engineering, and Medicine report, *Biodefense in the Age of Synthetic Biology*, examined a range of biosecurity issues related to synthetic biology.[94]

Issues for Congress

As the tools and technologies of synthetic biology advance, applications become more complex, novel, and designed for broader environmental use, policymakers may consider whether the current U.S. regulatory system and research investments are sufficient to address the broad cross-cutting issues associated with synthetic biology (e.g. biosafety, biosecurity, and ecological impacts) and how to ensure U.S. competitiveness and leadership.

The recent Executive Order 14801, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*, sets forth various timelines (100 days to 18 months) for federal agencies to evaluate and report on progress towards meeting the goals of the executive order, which includes clarifying and streamlining biotechnology regulations, focusing on biological risk management, and "assessing and anticipating threats, risks, and potential vulnerabilities."[95] These activities could impact the issues specifically discussed below and other legislative and oversight functions of Congress as it relates to synthetic biology.

Regulation of Synthetic Biology Research and Applications (Status Quo)

Federal guidance for regulating biotechnology products, including those developed using synthetic biology tools, is conveyed through the Coordinated Framework for the Regulation of Biotechnology (the Coordinated Framework), published by OSTP in 1986.[96] The Coordinated

[94] National Academies of Sciences, Engineering, and Medicine, *Biodefense in the Age of Synthetic Biology*, The National Academies Press, Washington, DC, 2018.

[95] Executive Order 14801, "Advancing Biotechnology and Biomanufacturing Innovation," vol. 87, no. 178 *Federal Register* 56849-56860, September 15, 2022.

[96] Executive Office of the President (EOP), Office of Science and Technology Policy, "Coordinated Framework for

Framework holds that biotechnology products should be regulated according to their characteristics and unique features, not their production method—that is, whether or not they were created through specific processes or tools associated with biotechnology. The Coordinated Framework provides regulatory authority to evaluate and ensure the safety of biotechnology products to three primary agencies—the Environmental Protection Agency (EPA), the U.S. Department of Agriculture (USDA), and the Food and Drug Administration (FDA).

- EPA protects human health and the environment by regulating genetically engineered products that qualify as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. §136 et seq.); sets guidelines on the amount of pesticidal residue that may be present in food under Section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §301 et seq.); and regulates new chemical substances derived from microbial biotechnology under the Toxic Substances Control Act (15 U.S.C. §2601 et seq.).
- FDA protects human health and safety by regulating human and animal drugs, human and animal foods derived from genetically engineered plants, and genetically engineered animals under the authorities of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act (42 U.S.C. §201 et seq.).
- USDA regulates biotechnology products that may pose a risk to agricultural plant and animal health under the Plant Protection Act (7 U.S.C. §7701 et seq.) and the Animal Health Protection Act (7 U.S.C. §8301 et seq.).

In 2015, the Obama Administration issued a memorandum to update the Coordinated Framework to ensure that the regulatory structure is capable of meeting future biotechnology risks,[97] and the update by EPA, FDA, and USDA was published in January 2017.[98] It discussed the roles of the three agencies and the coordination of oversight responsibilities. The update generally concluded that the existing structure of regulation among the three agencies remained sound with respect to protecting health and the environment. The update also noted that certain factors imposed costs on small and mid-size companies and academic institutions, including uncertainty with respect to agency jurisdiction, and a lack of predictability of timeframes for review. [99]

The tools and technologies associated with synthetic biology raise questions about how (or whether) the products resulting from these technologies are to be regulated under the Coordinated Framework. A 2017 National Academies of Sciences, Engineering, and Medicine (NAS) report found that "regulators will face difficult challenges as they grapple with a broad array of new types of biotechnology products—for example, cosmetics, toys, pets, and office supplies—that go beyond contained industrial uses and traditional environmental release." As applications become more complex, novel, and designed for broader use—with deliberate spread and genetic alterations of species through gene drives—policymakers may consider whether the updated

Regulation of Biotechnology," 51 *Federal Register* 23302, June 26, 1986. For more information on OSTP, see CRS Report R43935, *Office of Science and Technology Policy (OSTP): History and Overview*, by John F. Sargent Jr. and Dana A. Shea.

[97] Memorandum for Heads of Food and Drug Administration, Environmental Protection Agency, and Department of Agriculture, "Modernizing the Regulatory System for Biotechnology Products," Executive Office of the President, July 2, 2015. https://www.epa.gov/sites/production/files/2016-12/documents/modernizing_the_reg_system_for_biotech_products_memo_final.pdf.

[98] Increasing the Transparency, Coordination, and Predictability of the Biotechnology Regulatory System, January 2017, https://obamawhitehouse.archives.gov/blog/2017/01/04/increasing-transparency-coordination-and-predictability-biotechnology-regulatory.

[99] See CRS Report R44824, *Advanced Gene Editing: CRISPR-Cas9*, by Marcy E. Gallo et al.

Coordinated Framework is sufficient to oversee current and future applications of synthetic biology or whether additional oversight mechanisms are needed.

There are different views on whether the current Coordinated Framework is sufficient for federal regulation of certain areas of synthetic biology research and resulting applications and products. Those in favor of maintaining the status quo view additional oversight costs as anticompetitive or inhibiting innovation, potentially leading to research shifting to more permissive oversight environments, such as overseas. Critics of the status quo, on the other hand, argue that the current regulatory system is insufficient to address the complexity and breadth of synthetic biology applications and does not address public trust and acceptance of the regulatory decision making process (see "Transparency and Public Engagement").[100]

Research Funding and Oversight for Ecological Risk Assessments

The potential release of synthetic biology applications into the environment, either deliberately or accidentally, has raised ecological and broader societal concerns, along with debates over how to govern such applications both domestically and internationally.[101] One particular example is the development and potential release of a gene drive that has been researched in mosquitos to address the spread of malaria.[102] The gene drive research community has recommended that a combination of stringent confinement strategies for laboratory—including molecular, ecological, reproductive, and physical—be implemented for gene drive research whenever possible to help prevent the unintentional release of gene drive systems into natural populations.[103] Subsequent measures could be investigated further if and when the research progresses to the stage where experimental field trials were to be proposed.

Progress in gene drive research has increased the potential for field trials to study the release of gene drive organisms into the environment,[104] raising questions on how to conduct ecosystem dynamic studies sufficient in size and scope to understand the complexities of a gene drive application and how it operates within the environment. Key challenges identified by one multidisciplinary group of gene drive experts include clarifying the appropriate roles of developers and others actively engaged in work with gene drives in decisionmaking processes, and establishing partnerships with relevant authorities and other stakeholders. The expert group outlined a series of commitments it suggests are critical for responsible conduct of a gene drive field trial to ensure that it would serve the public interest.[105] These commitments include fair

[100] Brian Allan, Chris Stone, and Holly Tuten, et al., "Genetically Modified Mosquitoes Could Be Released in Florida and Texas Beginning This Summer—Silver Bullet or Jumping the Gun?," *The Conversation*, 2020; and Natalie Kofler and Jennifer Kuzma, "Before Genetically Modified Mosquitoes Are Released, We Need a Better EPA," *Boston Globe*, 2020.

[101] National Academies of Sciences, Engineering, and Medicine, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values*; Oye et al., "Regulating Gene Drives"; Kent Redford, Thomas Brooks, and Nicholas Macfarlane, et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation*, IUCN, Technical Assessment, Gland, Switzerland, 2019; and Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment, "Report of the Ad Hoc Technical Expert Group on Risk Assessment." See https://www.cbd.int/doc/c/2074/26e7/a135b1b57dabe8e8ed669324/synbio-ahteg-2019-01-03-en.pdf.

[102] Michael Le Page, "Mosquitoes Are Being Genetically Modified So They Can't Spread Malaria," *New Scientist*, September 21, 2022, https://www.newscientist.com/article/2338948-mosquitoes-are-being-genetically-modified-so-they-cant-spread-malaria/.

[103] Omar S. Akbari, Hugo J. Bellen, and Ethan Bier, et al., "Safeguarding Gene Drive Experiments in the Laboratory," *Science*, vol. 349, no. 6251 (2015).

[104] Ethan Bier, "Gene Drives Gaining Speed," *Nature Reviews Genetics*, vol. 23 (2022).

[105] Kanya C. Long, Luke Alphey, and George J. Annas, et al., "Core Commitments for Field Trials of Gene Drive

partnership and transparency, product efficacy and safety, regulatory evaluation, risk/benefit assessment, monitoring, and mitigation. Others have proposed a code of ethics for gene drive research based upon scientific responsibility, ecological stewardship, public engagement, and benefit sharing.[106]

Congress may consider whether these and other initiatives set forth in Title IV of P.L. 117-167 and Executive Order 14801[107] are sufficient. Congress could also consider whether agencies have the necessary expertise and adequate resources to evaluate proposals for funding or to adequately research and evaluate ecological impacts of applications seeking regulatory approvals.

For example, while NIH is one of the leading authorities on disease research, questions remain as to whether the NIH mission, research budget, and expertise are appropriate for conducting field trials of gene drives. To examine the agency's role in conducting field trials of gene drives for disease vector control, NIH commissioned a study through the Novel and Exceptional Technology and Research Advisory Committee (NExTRAC).[108] The resulting report stresses that NIH should "ensure it supports research to address gaps in knowledge and implementation, and has the proper guidance and requirements for research proposals and applications in place to continue to fund contained laboratory research and to consider funding future field release research."[109] It makes a series of recommendations on biosafety, ecological risk, and strategies for conducting field trials. One such recommendation is for NIH to utilize an independent board to provide input on the assessments of potential benefits and harms, milestones, and any associated recommendations for potential field release studies. The report stresses that any final decision on whether there is approval to release a gene drive modified organism into the field should ultimately be made by regulators and local authorities.

In 2018, DARPA's Safe Genes Program invested $65 million to "develop a suite of versatile tools that can be applied independently or in combination to support bio-innovation and combat bio-threats" associated with gene drives.[110] However, this program did not address the ecological risk research needed to evaluate the release of a gene drive, particularly regarding the research infrastructure that may be needed to conduct staged field trials.

In 2021, EPA awarded over $3 million to five institutions to develop science-based approaches to evaluate the potential human health and environmental impacts of new biotechnology products.[111] None of this funding was directed towards facilities or research to conduct field trials of gene drives, nor was it coordinated with any of the research programs conducted at other agencies. Section 10402 of the Research and Development, Competition, and Innovation Act (P.L. 117-167; Division B of legislation often referred to as the CHIPS and Science Act) prescribes support for a national network of testbeds that would "enable scale up of laboratory engineering biology

Organisms," *Science*, vol. 370, no. 6523 (2020).

[106] George J. Annas, Chase L. Beisel, and Kendell Clement, et al., "A Code of Ethics for Gene Drive Research," *The CRISPR Journal*, vol. 4, no. 1 (2021).

[107] Executive Order 14801, "Advancing Biotechnology and Biomanufacturing Innovation," vol. 87, no. 178 *Federal Register* 56849-56860, September 15, 2022.

[108] NExTRAC was authorized by 42 U.S.C. 282(b)(16), Section 402(b)(16) of the Public Health Service Act.

[109] National Institutes of Health, Novel and Exceptional Technology and Research Advisory Committee, *Gene Drives in Biomedical Research Report*, 2021.

[110] Defense Advanced Research Projects Agency (DARPA), "Safe Genes," 2018, https://www.darpa.mil/program/safe-genes.

[111] U.S. Environmental Protection Agency, *Assessment Tools for Biotechnology Products*, 2021, https://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/recipients.display/rfa_id/663.

research." It is not clear whether this provision could allow for the development, construction, or designation of research facilities or test beds to conduct ecological risk research of certain synthetic biology applications, such as gene drives. Congress may consider whether specific appropriations, research programs, and joint coordination among agencies for developing and managing such research facilities is needed.

A perceived lack of coordination among federal research and regulatory agencies has raised concerns by some as to whether the United States is situated to harness the investments made into synthetic biology research and evaluate certain synthetic biology applications designed for release into the environment.[112] Congress may consider whether existing agency coordination is sufficient to identify research funding needs, along with agency expertise and authority to conduct ecological risk assessments. Section 10402 (P.L. 117-167) directs OSTP to improve interagency planning and coordination of engineering biology activities as well as support projects funded under joint solicitations by a collaboration of not fewer than two agencies participating in the initiative. No specific appropriations were provided in the legislation for these activities.

Transparency and Public Engagement

There has been limited public engagement around synthetic biology. This could be due, in part, to the multitude of definitions used to describe it (see the **Appendix**) as well as its place in the larger discipline of biotechnology, both of which make it difficult to distinguish certain applications from others. Public polling of U.S. citizens suggests that there are general concerns around biodiversity, human health, and bioterrorism.[113] Moral concerns that synthetic biologists are creating organisms and DNA from scratch were also identified. At the same time, additional polling suggests that members of the U.S. public are generally uninformed about synthetic biology (74.9%) and do not believe it is personally important to them (60.6%); 31.2% support both its use and federal funding for it.[114] These data suggest that there may be a disconnect between the U.S. public's views towards synthetic biology and the levels of public and private investment in synthetic biology, as well as the breadth of current and proposed applications (see **Figure 1**).

The *National Strategy for Modernizing the Regulatory System for Biotechnology Products*, released in 2016 by the National Science and Technology Council's Emerging Technologies Interagency Policy Coordination Committee, suggested that the complexities of the U.S.

[112] Todd Kuiken et al., "Creating a Research Agenda for the Ecological Implications of Synthetic Biology" (Woodrow Wilson Center, 2014), https://www.wilsoncenter.org/sites/default/files/media/documents/article/SYNBIO_res_agenda.pdf; Todd Kuiken et al., "Shaping Ecological Risk Research for Synthetic Biology," *Journal of Environmental Studies and Sciences*, 2014, https://doi.org/10.1007/s13412-014-0171-2; Kenneth A. Oye et al., "Regulating Gene Drives," *Science*, vol. 345, no. 6197 (2014), pp. 626–628, https://doi.org/10.1126/science.1254287; Redford et al., *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation: Technical Assessment*; Todd Kuiken, Rodolphe Barrangou, and Khara Grieger, "(Broken) Promises of Sustainable Food and Agriculture Through New Biotechnologies: The CRISPR Case," *The CRISPR Journal*, February 2021, pp. 1–7, https://doi.org/10.1089/crispr.2020.0098; National Academies of Sciences, Engineering, and Medicine, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* (National Academies Press, 2016); and Jennifer Kuzma and Khara Grieger, "Gaps in U.S. Oversight Call for Community-Led Responsible Governance (CLEAR-GOV) for Gene-Edited Crops," *Science*, vol. 370, no. 6519 (2021).

[113] Hart Research Associates, *Awareness and Impressions of Synthetic Biology: A Report of Findings Based on a National Survey Among Adults*, Woodrow Wilson Center (Synthetic Biology Project), Washington, DC, 2013.

[114] Heather Akin, Kathleen M. Rose, and Dietram A. Scheufele, et al., "Mapping the Landscape of Public Attitudes on Synthetic Biology," *BioScience*, vol. 67, no. 3 (2017).

regulatory systems make it difficult for the public to understand how the safety of biotechnology products is evaluated.[115] While Title IV Section 10402 (d)(4) of the CHIPS and Science Act (P.L. 117-167) directs the agencies and departments that participate in the National Engineering Biology Research and Development Initiative to ensure that "public input and outreach are integrated into the Initiative by the convening of regular and ongoing public discussions," specific appropriations were not included. Congress may consider its oversight authority to evaluate whether agencies meet this directive or whether additional appropriations to support public dialogues are needed. Initiatives like iGEM, the Biodesign Challenge, and community biotech labs (DIYbio) could serve as public engagement opportunities to better understand how the public views synthetic biology, particularly as the field advances and terminologies evolve. They may also address certain aspects of U.S. competitiveness concerns by expanding access to the tools and technologies of synthetic biology.

Engagement with International Deliberations

Synthetic biology products developed in the United States would need to meet international regulatory requirements if companies seek to compete on the global market. However, global differences in regulatory systems and lack of agreed-upon definitions have created a patchwork of international regulations (see **Figure 4**). Genome editing is sometimes equated with synthetic biology. While crops created through genome editing are tightly regulated in some countries, in others they are treated similarly to plants developed through traditional plant breeding techniques and remain unregulated.

While previous iterations of biotechnology products have been used in the environment, they have typically been designed to terminate after one life-cycle or been contained in a particular area. Some applications of synthetic biology such as gene drives are being designed to spread throughout the environment. These applications are challenging for international oversight as the introduction of a synthetic biology organism may not be contained within the border of a particular country and may raise cross-border ecological and biosecurity concerns.

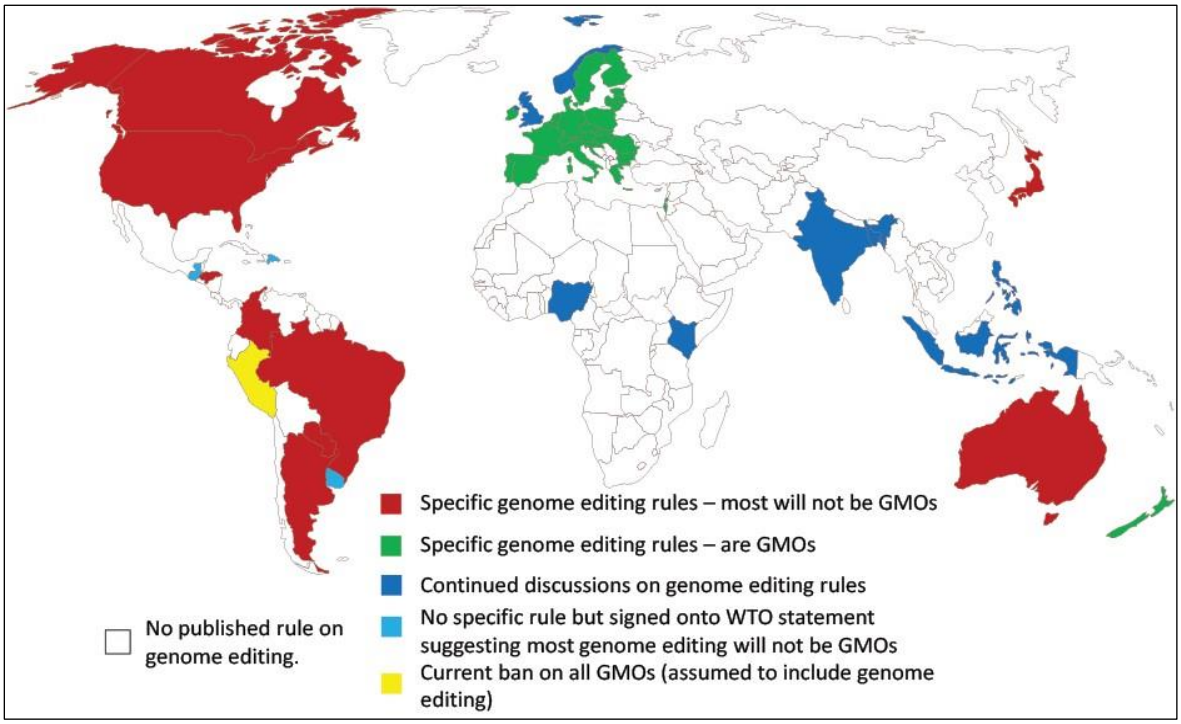
International deliberations examining potential impacts from, and governance of, synthetic biology products are occurring through various mechanisms, including the U.N. Convention on Biological Diversity, the International Treaty on Plant Genetic Resources for Food and Agriculture, the Biological and Toxin Weapons Convention, World Health Organization, the World Trade Organization, and the International Union for Conservation of Nature.

Congress may consider the most effective ways to engage with these international deliberations in order to maintain U.S. strategic interests and competitiveness. For example, whether current U.S. membership and participation is sufficient in order to effectively participate in deliberations on whether changes to, or development of new, treaties or agreements is appropriate.

participation in the deliberations, membership of the organizations involved, and whether changes to, or ratification of, resulting treaties is appropriate in order to maintain U.S. strategic interests and competitiveness.

[115] Emerging Technologies Interagency Policy Coordination Committee's Biotechnology Working Group, *National Strategy for Modernizing the Regulatory System for Biotechnology Products*, White House Office of Science and Technology Policy, 2016, https://www.epa.gov/sites/production/files/2016-12/documents/biotech_national_strategy_final.pdf.

Figure 4. Comparison of International Genome Editing Regulations



Source: Image recreated with data from Sarah M. Schmidt, Melinda Belisle, and Wolf B. Frommer, "The Evolving Landscape around Genome Editing in Agriculture," EMBO Reports: 21, no. 6 (June 2020), https://doi.org/10.15252/embr.202050680; and Jennifer Kuzma and Todd Kuiken, *Genome Editing in Latin America: Regional Regulatory Overview*, Genetic Engineering and Society Center, 2021, p. 7, https://research.ncsu.edu/ges/files/2021/08/Kuzma-Reg-IDB_Final_July2021.pdf.

Notes: 1. GMO = genetically modified organisms; WTO = World Trade Organization.

2. Products regulated as GMOs are typically required to go through a risk assessment (i.e., field trials) and a regulatory review process before being allowed on the market. Products classified as non-GMOs are not required to go through a risk assessment and can move directly into the market.

3. The genome editing rules for countries listed in red may still require certain products developed using genome editing tools, depending on specific types of edits made, to be regulated as a GMO. See Jennifer Kuzma and Todd Kuiken, *Genome Editing in Latin America: Regional Regulatory Overview*, Genetic Engineering and Society Center, 2021, p. 7, https://research.ncsu.edu/ges/files/2021/08/Kuzma-Reg-IDB_Final_July2021.pdf for additional detail.

4. Map current as of February 2021.

Strategic Foresight

USDA conducts annual vulnerability assessments to identify biotechnology products in other countries that are in the development pipeline and could be imported into the United States.[116] Section 1091 of the FY2022 National Defense Authorization Act (P.L. 117-81) established the National Security Commission on Emerging Biotechnology, which is to "consider the methods, means, and investments necessary to advance and secure the development of biotechnology, biomanufacturing, and associated technologies by the United States to comprehensively address

[116] Emerging Technologies Interagency Policy Coordination Committee's Biotechnology Working Group, *National Strategy for Modernizing the Regulatory System for Biotechnology Products*, White House Office of Science and Technology Policy, 2016, https://www.epa.gov/sites/production/files/2016-12/documents/biotech_national_strategy_final.pdf.

the national security and defense needs of the United States." The commission is to deliver its interim findings and recommendations to the congressional defense committees and the President no later than January 26, 2023, and its final report no later than January 26, 2024.[117] A report from the National Academies of Science, Engineering, and Medicine is expected in late 2022 advising EPA's Office of Research and Development on emerging scientific and technological advances it could use in support of the agency's mission for protecting human health and the environment over the coming decades.[118]

Regularly identifying what issues and applications synthetic biology may introduce in the short, mid-, and long term could be useful to highlight areas where federal policy may be needed to address strategic competitiveness, biosafety, biosecurity, ecological, economic, and public use and acceptance concerns. Strategic foresight can also aid in identifying broader economic and societal issues, including job market shifts and training needs.[119] Executive Order 14801 suggests that in order to secure and protect the U.S. bioeconomy the U.S. should adopt, in part, a forward looking, proactive approach to assessing and anticipating threats, risks, and potential vulnerabilities.[120] Congress might consider whether to require periodic horizon-scanning assessments across federal research and regulatory agencies to identify research and coordination opportunities, potential biosafety/biosecurity concerns, U.S. strategic positioning, and associated policy implications associated with emerging technological advancements in synthetic biology. Such assessments could be a part of broader efforts to assess the position of the United States in the bioeconomy and biotechnology.

[117] A list of the eight commissioners appointed by the Armed Services Committees is available at https://armedservices.house.gov/press-releases?ID=5806E52B-95BB-4921-9F92-D1A5BC2DA8C4. One additional commissioner is to be appointed by the Speaker of the House, House Minority Leader, Senate Majority Leader, and Senate Minority Leader, respectively.

[118] National Academies of Science, Engineering, and Medicine, *Anticipatory Research for EPA's Research and Development Enterprise to Inform Future Environmental Protection: The Road Ahead*, 2022, https://www.nationalacademies.org/our-work/anticipatory-research-for-epas-research-and-development-enterprise-to-inform-future-environmental-protection-the-road-ahead.

[119] Philip Shapira, Nicholas E. Matthews, and Carrie A. Cizauskas, et al., "Building a Bottom-Up Bioeconomy," *Issues in Science and Technology*, vol. 38, no. 3 (2022).

[120] Executive Order 14801, "Advancing Biotechnology and Biomanufacturing Innovation," vol. 87, no. 178 *Federal Register* 56849-56860, September 15, 2022.

Appendix. Terminology and Definitional Issues

The term *biotechnology* has been defined as the application of biological components or processes to advance human purpose,[121] and it is used as the overarching framing for the U.S. Coordinated Framework for the Regulation of Biotechnology.[122] Since the Coordinated Framework was first published in 1986, new terms have emerged to describe fields within biotechnology, including genome engineering and synthetic biology. However, since synthetic biology depends on advances from multiple disciplines and has a wide range of potential applications in multiple industries and research areas, there is no single agreed-upon definition of the field.[123] The term *synthetic biology* has more recently been used interchangeably with, and other times incorporated into, a broader description of engineering biology.[124]

This confluence of terminologies can pose challenges when attempting to analyze the field of synthetic biology in relation to application areas, research funding, public investments, or its broader impacts on the economy.[125] For example, complications can arise when trying to evaluate the applicability of current regulatory systems and oversight capabilities to these emerging and overlapping areas.

[121] National Academies of Sciences, Engineering, and Medicine, *Biodefense in the Age of Synthetic Biology*, Washington, DC, 2018, https://doi.org/10.17226/24890.

[122] Executive Office of the President (EOP), Office of Science and Technology Policy, "Coordinated Framework for Regulation of Biotechnology," 51 *Federal Register* 23302, June 26, 1986.

[123] Philip Shapira, Seokbeom Kwon, and Jan Youtie, "Tracking the Emergence of Synthetic Biology," *Scientometrics*, vol. 112, July 1, 2017, pp. 1439–1469, https://link.springer.com/article/10.1007/s11192-017-2452-5.

[124] Section 10402 of P.L. 117-167, National Engineering Biology Research and Development Initiative, includes the term synthetic biology when referring to certain federal agency research programs in the context of engineering biology.

[125] For additional analysis on the bioeconomy, see CRS Report R46881, *The Bioeconomy: A Primer*, by Marcy E. Gallo.

Select Terms and Definitions Associated with Synthetic Biology

Biotechnology: The application of biological components or processes to advance human purpose.

Genetic Engineering: A process that uses laboratory-based technologies to alter the DNA makeup of an organism. Can also be referred to as genetic modification.[126]

Engineering Biology: The "application of engineering design principles and practices to biological systems, including molecular and cellular systems, to advance fundamental understanding of complex natural systems and to enable novel or optimize functions and capabilities."[127]

Synthetic Biology: A further development and new dimension of modern biotechnology that combines science, technology, and engineering to facilitate and accelerate the understanding, design, redesign, manufacture, and/or modification of genetic materials, living organisms, and biological systems.[128]

Genome Engineering: A process where the sequence(s) of DNA are designed and modified.[129] Two techniques used for genome engineering are genome editing and gene editing, both of which refer to the incorporation of site-specific modifications into genomic DNA using DNA repair mechanisms. However, gene editing typically refers to focusing only on one gene, [130] while genome editing generally refers to targeting multiple genes simultaneously. Additionally, genome editing can refer to the targeted changes in non-gene regions in the hopes of inserting new genes or modifying gene-regulatory regions to manipulate the functions of existing genes, such as with CRISPR-Cas9.[131] Genome editing has also been compared to other breeding methodologies such as conventional breeding.[132]

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Acknowledgments

Contributors to this report included Alexandra Kosmidis, Research Librarian; and Mari Lee and Jamie Hutchinson, Visual Information Specialists.

[126] See the National Human Genome Research Institute definition of genetic engineering at https://www.genome.gov/genetics-glossary/Genetic-Engineering.

[127] P.L. 117-167, §10002.

[128] Convention on Biological Diversity, Ad Hoc Technical Expert Groups on Synthetic Biology, "Report of the Ad Hoc Technical Expert Group on Synthetic Biology" (Montreal, 2015), https://www.cbd.int/doc/c/aa10/9160/6c3fcedf265dbee686715016/synbio-ahteg-2017-01-03-en.pdf.

[129] G. Brett Rob, "Genome Editing with CRISPR-Cas: An Overview," *Current Protocols Essential Laboratory Techniques*, vol. 19, no. e36 (2019).

[130] A.M. Khalil, "The Genome Editing Revolution: Review," *Journal of Genetic Engineering and Biotechnology*, vol. 18, no. 68 (2020). G. Brett Rob, "Genome Editing with CRISPR-Cas: An Overview," *Current Protocols Essential Laboratory Techniques*, vol. 19, no. e36 (2019).

[131] G. Brett Rob, "Genome Editing with CRISPR-Cas: An Overview," *Current Protocols Essential Laboratory Techniques*, vol. 19, no. e36 (2019).

[132] For a comprehensive review of gene editing, see CRS Report R44824, *Advanced Gene Editing: CRISPR-Cas9*, by Marcy E. Gallo et al.

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