EBRC Engineering Biology Research Consortium

January 22, 2021

Dear Ms. Plimpton:

The Engineering Biology Research Consortium (EBRC) is pleased to submit the attached response to the National Science Foundation's Request for Information seeking comments on elements of its 2022-2026 Strategic Plan (as published in the Federal Register Vol. 85, No. 238 pg 79529).

EBRC is a non-profit, public-private partnership dedicated to bringing together an inclusive community committed to advancing engineering biology to address national and global needs. EBRC members represent diverse perspectives within the engineering biology research community and include some of the nation's top scientists and engineers. At its core, EBRC's objective is to advance pre-competitive research in engineering biology through cross-sector coordination between industry, academia, and government.

NSF's recent Strategic Plans have emphasized increasing scientific knowledge and understanding through fundamental research and using scientific innovation to overcome societal and national challenges. We offer comments from our vantage point as a convener of academic, industry, and governmental perspectives in support of a continued pursuit of these broad objectives and suggest strategies NSF may employ toward these ends.

We appreciate this opportunity to comment on elements of NSF's 2022-2026 Strategic Plan and look forward to its release.

Sincerely,

Rebecca Mackelprang, Ph.D.
Postdoctoral Scholar, EBRC

Enclosures:
Engineering Biology Research Consortium Comment on NSF RFI on 2022-2026 Strategic Plan
Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy
Microbiome Engineering: A Research Roadmap for the Next-Generation Bioeconomy

Engineering Biology Research Consortium

Engineering Biology Research Consortium Comment
NSF Request for Information on 2022-2026 Strategic Plan

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1. What are the interests, values and emergent science and policy issues that the Strategic Plan should recognize?

We divide this response into three subsections: 1a) interests, 1b) values, and 1c) emerging science and policy issues.

<u>1a: Interests</u>

NSF's strategic plan should support and communicate that strong investment in fundamental research drives knowledge, innovation, and the health and well-being of the American populace forward. Engineering biology (or synthetic biology) is an important area of research, enabling rapid innovation through the design and construction of organisms, molecules, enzymes. It is an interdisciplinary field with research areas and applications woven throughout the NSF directorates, including Biological Sciences, Computer and Information Science and Engineering, Environmental Research and Education, Mathematical and Physical Sciences, Social, Behavioral, and Economic Sciences, and Engineering. Expertise across these disciplines can be leveraged through collaborative efforts that build on fundamental techniques of engineering biology to advance national health, prosperity, and welfare. EBRC has roadmapped the technical research themes and application sectors central to these interests in *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy* (2019, attached).

Below, we offer a description of the technical themes and their application sectors summarized from *Engineering Biology* (2019), and suggest to NSF they be incorporated as areas of strong strategic interest:

TECHNICAL THEMES

Engineering DNA: Breakthroughs in DNA editing and engineering have transformed biological research. Investments in precision genome engineering and editing, oligonucleotide synthesis, and DNA fragment assembly expand the experimental capacity of researchers across biology. More work is needed to refine DNA engineering techniques for specific applications across Kingdoms of life.

Biomolecular Engineering: Engineering biology labs using diverse organisms and systems are working to synthesize macromolecules for desired functions through the design of metabolic pathways and circuits. As this work progresses, gene expression, proteins, RNAs, and metabolites will be increasingly tunable to desired situations and able to incorporate environmental feedback.

Host Engineering: Previous investments from NSF have led to incredible advances in the technical ability to engineer plants, animals, and microbes and to engineer cell-free systems. Funding should support efforts to expand host engineering capabilities in diverse organisms, to microbial consortia, and to integrate and respond to environmental conditions.

Data Science**:** The previously described three technical themes are each more effective and efficient when supported by strong modeling and data science. Improvements in software and computation lower the experimental burden on researchers as modeling predictions and experimental outputs converge. Data science is also essential for addressing challenges associated with the transition from basic to applied research such as automation, characteristic changes at scale, data flow, and informatics.

APPLICATION SECTORS

Industrial Biotechnology focuses on technical challenges relevant to industrial use of synthetic biology and the establishment of the United States as a global leader in the bio-based economy. Advances in technical research themes could enable, for example, RNA or protein-based biosensors that measure and adapt to feedstocks, intermediates, or other side products in manufacturing.

Health & Medicine focuses on technical challenges relevant to the well-being of humans, animals, and populations through preventing and eradicating disease and supporting longevity and quality of life. The tools of engineering biology are being used extensively to develop new therapies, diagnostics, and vaccines, including COVID-19 vaccines.

Food & Agriculture focuses on the tools and technologies impacting how we feed the Earth's people and animals, including through the production of more food and increasing and improving nutritional content. Engineering biology is supporting development beyond traditional genetic engineering of plants and animals including precision host editing and engineering, development of microbial consortia that support soil or host health, and the production of lab-grown and plant-based meats.

Environmental Biotechnology focuses on the technologies and tools that enable deployment of bioengineered systems, ecosystem remediation, natural resource management, and environmental monitoring. As an example, the four technical themes could be used to design a microbial consortium that is able to metabolize harmful compounds for bioremediation (see *Microbiome Engineering: A Research Roadmap for the Next-Generation Bioeconomy*, attached)

Energy focuses on the application of engineering biology tools and technologies to advance clean and affordable energy sources and to reduce overall energy consumption. Engineering biology is being used to generate renewable biomass and feedstocks for energy generation and to reduce global energy consumption, for example, by making everyday enzymes, like those used in laundry detergents, more efficient.

1b) Values - The Strategic Plan should recognize that upholding key values facilitates the unencumbered pursuit of knowledge and leads to the greatest advances. Among these key values are fundamental discovery, risk-taking, open science, integrity and accountability, diversity, equity and inclusion, global collaboration, and sustainability (modified from *Beyond 2020: A Vision and Pathway for NIH*, https://www.coalitionforlifesciences.org/beyond-2020-a-vision-and-pathway-for-nih/):

Fundamental discovery: Transformational advances in human knowledge, technologies, and problem solving arise from basic studies undertaken without knowing the future utility of the research.

Risk-taking: Making breakthrough discoveries and transformative advances require that scientists and funders be willing to take calculated risks and be tolerant of failure.

Open science: Science progresses fastest when data and publications are openly shared among scientists and with the public.

Integrity and accountability: The ethical, responsible conduct of science is required to build public trust and to respond to societal concerns.

Diversity and inclusion: Scientists with different perspectives and life experiences broaden the questions being explored and improve team decision-making, as well as the potential impact.

Global collaboration: The complexity of science requires bringing together expertise from different disciplines and across sectors, both within our country and across national borders. Working together lowers the barriers to scientific discovery.

Sustainability of scientific enterprise: Ongoing, stable funding is essential for long term planning, bold initiatives, infrastructure needs, and workforce development.

1c) Emerging science and policy issues

Developing policy around emerging science and technology can be difficult; policy must seek to prevent misuse, enable beneficial use, and provide some means of debate, consensus-building, and regulation around emerging issues. Some emerging issues that NSF's Strategic Plan may address include gene editing, security, data sharing and integrity, privacy, intellectual property, environmental impacts, and health disparities. Here, we discuss policy issues related to gene editing and security.

Gene editing can be used for applications as simple as knocking out a gene in a laboratory bacterium or as weighty as editing the human germline. Its diverse array of potential applications include many that land in ethical gray areas. The challenge is, then, to support free and open research while placing safeguards that prevent its unethical use and to build mechanisms for consensus-building around applications that occupy gray areas. To meet this challenge, NSF should support interdisciplinary collaborations that bring together technical, social, and societal perspectives and expertise. They should include perspectives beyond a few elite researchers and should evaluate current and potential future directions and implications of developing technologies. They should generate actionable recommendations and support the integration of these considerations into researcher practice.

Security: Because of the wide range of beneficial and harmful potential applications of engineering biology research, EBRC supports a cultural shift to incorporate security analysis into every stage of the research and development lifecycle. Our Malice Analysis program, which trains graduate students and postdoctoral researchers to evaluate their own research for security concerns (https://ebrc.org/malice-analysis-assessing-biotechnology-research-for-security-concerns/), is one approach. While our program is targeted to practitioners of engineering biology, NSF should support efforts across STEM disciplines that highlight the need to incorporate security considerations into research design and implementation. In so doing, researchers will be prepared to engage appropriately with the government and policymakers to identify and mitigate the inevitable security vulnerabilities arising from advances in science and technology.

EBRC believes that the best policy outcomes for emerging science occur when academic researchers, industry, and government work together to understand the implications of a technology and build consensus around a prudent way forward that does not stifle the pursuit of knowledge.

2. How can NSF help maintain US leadership in an evolving global research and education landscape?

Maintenance of U.S. leadership in research and education is dependent on a recognition that people are our greatest asset. Programs and support that encourage diversity, equity, and inclusion, that promote the overall well-being of researchers, that provide sufficient opportunities for early-career researchers, and that are agnostic to institutional and pedigree prestige will help ensure that the United States fully leverages its spectacular human capital. As it does, its researchers and workforce will be well positioned to lead global efforts, initiatives, and collaborations around research and education and take leadership positions in the science-based economy.

EBRC has identified four areas of focus for its own work that are critical for advancing engineering biology research and education, and believe that they are applicable across disciplines supported by NSF. First, a greater NSF emphasis on policy and international engagement (e.g., through expansion of the Office of International Science & Engineering) within the research community it supports could spur greater engagement of researchers with both domestic and international science and science-based policy. Second, the collaboration of diverse researchers across a discipline to roadmap the goals and challenges within their field can bring common goals into focus and reduce the time to achieve major milestones. Third, a coherent strategy on supporting STEM education and a strong workforce with a range of skill levels and abilities will ensure that the leadership built by the U.S. can be sustained. And fourth, progress in research can raise security issues. To truly lead, the U.S. must recognize and address such issues without suppressing research. Attention to each of these focus areas will underpin a responsive scientific enterprise capable of adapting to unexpected breakthroughs and evolving international political and scientific events in a manner consistent with the values described in question 1.

Policy & International Engagement

As other nations continue to build competitive science and technology research and development programs, the U.S. is at risk of losing its position as a global leader if it does not renew its commitment to excellence. The U.S. must invest internally and engage globally. It must actively support and be involved in collaborative efforts (e.g., The Global Biofoundries Alliance) to avoid duplicative efforts at home and to enable our own researchers to build upon the work of others. We must commit to attracting and retaining the most talented researchers without prejudice toward their Nationality.

Maintaining leadership in discussions around the ethical, legal, and social use of emerging technologies will help promote U.S. values internationally. The U.S. has an opportunity to lead international discussion and construction of ethical frameworks surrounding the development of engineering biology’s tools (e.g., genome editing) and applications (e.g., vaccine or drug development). Normalizing the incorporation of ethical, legal, and social considerations into basic research and supporting collaborations between social and technical scientists will push research in directions most likely to benefit society and will prepare the U.S. to lead the world in identifying the boundaries of ethical technology use.

Education & Workforce Development

A diverse STEM workforce benefits the entire research and development enterprise and is crucial to maintaining U.S. leadership. Different backgrounds and experiences compel people to ask different questions and approach problems with different perspectives. In the United States, science generally and engineering biology specifically continue to have an inexcusable overrepresentation of white males. Special consideration should be given to programs working to identify leaks in the diversity pipeline, the cause of the leaks, and repairs that promote an inclusive and respectful research enterprise. However, it's important to acknowledge that the terminal end of this "pipeline" has limited academic faculty positions and research funding available and that individuals may intentionally exit that pipeline for reasons of professional interest. Therefore, conduits to STEM-based positions in industry, teaching, policy, communications, and civil service should be recognized and supported along the STEM education pipeline. As an example of one area of focus, graduate students widely find that exploring opportunities outside of research is not supported by faculty advisors and mentors. Incorporating training opportunities for them that are sanctioned by faculty into graduate education is important for building a STEM workforce that is prepared to lead not only in scientific research, but in science policy, science education, and science communication.

Additionally, not everyone who can contribute to the STEM workforce can enter the pipeline through the same channels. Support for training opportunities outside of traditional higher education channels (e.g., training certification programs; retraining programs) could provide entry to the field for those transitioning from other industries or who have not followed traditional educational paths. To ensure that formal training prepares students for the jobs that actually exist in their geographic region, NSF can support partnerships between community or junior colleges and companies that align education and training to industry needs.

Building the STEM workforce that the U.S. needs to reach its potential as a global leader in research and innovation may require evidence-based, fundamental shifts in how we view and perform science education and training. As described in our response to question 1, our values support undertaking bold ideas with big potential benefits to move beyond a stagnant status-quo. Within the field of engineering biology, the potential benefits include a dominant bioeconomy led by a diverse workforce. But to achieve this robust bioeconomy workforce, its members must be trained with agile skills and flexibility to adjust to quickly evolving demands and landscapes. Investments must be made in not only supporting the fundamental research contributing to biotechnologies, but also in support of the necessary spectrum of skills and knowledge for careers in industrial biotechnology and biomanufacturing.

Roadmapping Research Advancement and Innovation

Roadmapping research goals and associated challenges and milestones can highlight priority research areas, unite research fields, facilitate collaboration and coordinated efforts, and efficiently advance ambitious research agendas. Partnerships across academia, industry, and government are best-suited to capture the breadth of a field and present a realistic picture of what research can accomplish on given time horizons and the barriers that must be overcome to do so. The EBRC's 2019 *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy* (attached) leveraged the expertise of more than 80 members of the field to articulate and share short- and long-term opportunities and challenges. EBRC has since released *Microbiome Engineering: A Research Roadmap for the Next-Generation Bioeconomy* (attached) and *Engineering Biology & Materials Science: A Research Roadmap for Interdisciplinary Innovation* (https://roadmap.ebrc.org/2021-roadmap-materials/). Roadmaps present policymakers (e.g., funders), companies, and academics with holistic views of a field and can facilitate collaboration and unity behind achieving research milestones. The roadmap developed by our engineering biology community supports U.S. leadership in the field both by its creation and by the research and applications to which it calls attention. Roadmapping may be successfully used in other disciplines to support unifying, goal-oriented, holistic approaches to US-led scientific advancement.

Security in Research

Advances in engineering biology and many other STEM fields have associated security implications. This is one of the most important areas in which the U.S. must provide leadership, as an influence vacuum here could steer global practice away from our own National interests and deprioritize our societal values.

To achieve this, NSF should support community-building security and associated issues. For example, iGEM (International Genetically Engineered Machine) competitions place an emphasis on the incorporation of security considerations into all phases of the research life-cycle. The consideration of security issues must not be limited to research funded by DHS and/or DoD. NSF's broad reach enables it to support the introduction of security into the awareness and education of researchers and trainees across diverse specialties. Attention and support should be given to efforts that seek to foster interdisciplinary training and collaboration such as those between technical researchers and social scientists.

3. How can the plan best underscore the importance to the Nation of fundamental research and its broader impacts?

The NSF 2022-2026 Strategic Plan should, as it has in the past, highlight how fundamental research supported by the NSF has been formative to advances across all aspects of human life and the environment. It has supported such leaps in human knowledge, enabled the digital revolution, grown a burgeoning bioeconomy, increased our national security, saved human lives, and is crucial to climate repair.

Fundamental research in engineering biology develops tools to build up the field's capabilities to, for example, design biological circuits, metabolic pathways, biological nanostructures, and cell-free biological systems that can be applied to meet diverse challenges. Here we offer three examples of how fundamental research can have a broad impact on society:

Cell-free systems are one powerful example of leveraging fundamental research to solve real world problems. They are well suited for use as sensors because compounds do not have to overcome the challenges of cell walls and membrane transport to be detected. Scientists are using a synthetic cell-free system to build modular, specific, sensitive, and deployable water quality test kits (see Jung, *et al*., *Nat Biotechnol* **38,** 1451–1459 (2020)).

Fundamental research on tiny, gas-filled nanostructures found in some photosynthetic microbes is now being applied to medical imaging through engineering biology. Because of their unique properties, these gas vesicles are able to stay dry and stable in aqueous solutions. Researchers are leveraging these properties to improve some biological imaging techniques, including for optical coherence tomography (OCT), where it serves as a needed genetically programmable contrast agent (see Lu, *et al., ACS Nano* 2020, 14, 7, 7823–7831).

Bio-based alternatives to products reliant on petroleum-based manufacturing are also a powerful use of engineering biology. Fundamental research has enabled scientists to build metabolic pathways and enzymes that yield desired products. Some of these products do not just replace their petroleum-based counterparts but improve upon them. For example, Zymergen's recent release of Hyaline, a thin biofilm that can be used on electronics, touch sensors, and optical filters, is the result not just of the industry researchers who developed it, but of the fundamental research on host engineering, metabolic programming, and data science that came before.

End of response