Moonshots for the 21st-Century Bioeconomy

A Policy Paper by the Engineering Biology Research Consortium

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Engineering biology has the immense potential to revolutionize our economy, further our societal goals, and ensure products, technologies, and solutions that benefit all Americans. A number of consumer products and solutions that we see everyday integrate engineering biology-based technologies, helping Americans and people worldwide to live healthier and happier lives. For example, in the healthcare sector, many biologics, like insulin, have been produced via biomanufacturing for over 40 years and more recently, CAR T-cell immunotherapy is being used to treat complex cancers with improved effectiveness. Engineering biology was also responsible for the rapid development of the vaccines to fight the COVID-19 pandemic. Engineering biology has the potential to make these healthcare solutions more equitable and accessible, and to treat many of the diseases and illnesses that impact hundreds of thousands of lives. Engineering biology will also be pivotal to tackling the climate crisis and global sustainability challenges. Over the last 50 years, ethanol, biofuels, and sustainable chemicals have been successfully produced through the engineering of biology and expanding the use of these technologies will be critical for energy and supply chain security. Innovations in engineering biology are making possible carbon-negative manufacturing using microbes to convert carbon from the atmosphere into the products we use every day, from packaging materials to clothing and laundry detergent. The agriculture sector has long employed engineering biology tools and technologies to accelerate breeding and develop agronomically valuable traits, and is gaining steam with sustainable, climate-friendly fertilizers and crops resilient to drought and pests. And for the dinner table, numerous companies are providing alternative and plant-based meats, dairy, and other sustainable foods developed with engineering biology to consumers, helping to secure the food sector and combat climate change.

Commercial Products and Solutions	***Engineering Biology Technology***
COVID-19 vaccines (e.g., Pfizer, Moderna)	mRNA designed to trigger an immune response to the SARS-CoV-2 spike protein.
Alternative meats (e.g., Beyond Meat, Impossible Foods)	Engineered proteins and enzymes to look, taste, and feel like meat.
Sustainable, climate-friendly fertilizers (e.g., Pivot Bio)	Engineered microbes designed to increase nitrogen availability for crops.
Bio-based, renewable chemicals and materials (e.g., BASF, LanzaTech)	Biobased chemicals, enzymes, and proteins for nutrition, personal and home care, medical and dietary nutrition, and cleaning detergents.
Synthetic DNA (e.g., Twist Bioscience)	Customized synthesis of genes and genomes at various scales for use in research and industry.

Looking forward, engineering biology will enable new products and technologies that catalyze the transition from fossil fuels into renewable and sustainable materials and solutions for nearly every sector and industry. The federal government has already shown a dedication to bio-based manufacturing through the establishment of the biology-centric Manufacturing Innovation Institutes BioMADE, BioFabUSA, and NIIMBL. But to make the bioeconomy a reality, the field needs funding, infrastructure, and policies that support the development of foundational tools, the transition of technologies, and processing and scaling to commercialization.

Here we envision moonshots for achievements in engineering biology across five sectors, highlighting the promise and potential of biotechnology. We also link to our interactive EBRC roadmaps, which provide more expansive visions of the innovations that are possible through engineering biology research and application.

Health care and medicine

Short-term Moonshot - New, decentralized manufacturing that does not rely on billion dollar manufacturing facilities, thereby reducing the costs of drugs, accelerating treatments, and benefiting patients across the board. This distributed infrastructure would enable on-demand production of therapeutics and biopharmaceuticals (including seasonal development and manufacturing, such as vaccines against flu), increasing the availability of treatments and therapies for rare diseases and hardening domestic defense against emerging biothreats. Requires capacity for rapid design, discovery, generation, and/or manufacturing in multiple bio-platforms (nucleic acids, proteins, and cells) and incentives (policy and financial) for physical infrastructure and workforce development.

Long-term Moonshot - Commercial deployment of smart, programmable biotechnologies. This will include therapeutic cells, probiotics for detecting and curing diseases, devices at scale for personalized medicine, and platforms or organisms for disease control or eradication. Such technologies leverage the dynamic and unique properties of biology (e.g. innate biosensing and actuation and output of biological circuits) within the therapeutic or device to treat diseases like auto-immune disorders or cancer, for wound healing or countering persistent environmental damage, or for combatting vector-borne diseases like malaria or West Nile virus.

EBRC roadmap resources - *Engineering Biology* (2019), see Health & Medicine; *Engineering Biology & Materials Science* (2021), see Health & Medicine

Climate and energy

Short-term Moonshot - Domestic capacity to accelerate year-by-year declines in atmospheric greenhouse gas (GHG) emissions from agriculture, transportation and industrial sources. Biotechnologies can enable carbon capture from the highest GHG emitting industries (cement, steel) to produce value added chemicals and materials. Federal policies and incentives can accelerate and expand current technologies in practice that enable carbon capture and conversion with engineered microbes and plants.

Medium-term Moonshot - Displacement of today's commodity chemicals produced from fossil resources that have the largest GHG footprint (ammonia, ethylene, propylene, etc.) with biomanufacturing using engineered organisms and renewable feedstocks. Large-scale bioconversion of atmospheric carbon dioxide (gigatons per year) into value-added chemicals (bio-oil) and agricultural supplements (bio-char).

Long-term Moonshot - Eliminate the need for fossil resources for energy, chemicals, fuel through use of engineered organisms and biosystems, providing every consumer – regardless of where they are from or how much they earn – with a sustainable choice of products.

EBRC Roadmap Resources - *Engineering Biology for Climate & Sustainability* (2022); *Engineering Biology & Materials Science* (2021), see Energy, Environmental Biotechnology, and Industrial Biotechnology; *Engineering Biology* (2019), see Environmental Biotechnology, Industrial Biotechnology, and Energy; *Microbiome Engineering* (2020), see Energy, Environmental Biotechnology, and Industrial Biotechnology.

Food and agriculture

Short-term Moonshot - Consumer-scale production of sustainable protein and meat alternatives through cellular agriculture technologies to meet the needs of a growing population while maintaining a smaller ecological and physical footprint. This level of production will rely on our ability to scale-up processes cost effectively and on the development of clear and effective standards and product regulation.

Short-term Moonshot - U.S. agriculture producers' widespread adoption of enzyme- and cell-based sustainable fertilizers for more efficient nutrient cycling in agriculture. This will help reduce waste and run-off that cause environmental damage.

Short-term Moonshot - Deployment of engineered crops with higher nutrient density. Such crops can improve food security and human and animal nutrition, particularly in regions with resource scarcity. One of the key challenges in achieving this is the translation of foundational knowledge into diverse crop systems.

Medium-term Moonshot - Implementation of alternative crops and methods for biomass generation for use in chemical and energy production, without competing with food production. This includes strategies like the use of marginal lands and fallow season to sustainably increase biomass production.

Long-term Moonshot - Agriculture that is resilient to climate change and disease. By engineering crops and soil systems to respond to and withstand stress from climate extremes and threats posed by pathogens, we can increase the availability and capacity of agricultural yields around the world.

EBRC Roadmap Resources - *Engineering Biology for Climate & Sustainability* (2022), see Food & Agriculture; *Engineering Biology* (2019), see Food & Agriculture; *Microbiome Engineering* (2020), see Food & Agriculture

Industrial biomanufacturing and supply chain security

Short-term Moonshot - Reuse and upcycling of wastes, including plastics, agricultural wastes and GHG emissions across the U.S. through controlled application of engineered microbes and consortia. The biotechnologies to recycle and upcycle waste materials are becoming increasingly mature, including strategies to ensure their biocontainment, enabling a circular bioeconomy. Adoption into municipal waste management systems would help to eliminate bottlenecks in recycling and, perhaps more importantly, can help to recover valuable commodity chemicals and materials that can be transitioned back into the supply chain.

Medium-term Moonshot - Transition/adaptation of current petroleum infrastructure to accommodate production and processing of biobased fuels and chemical manufacturing. This includes establishing an expanded network of biorefineries specifically designed to process regional sources of biobased and/or GHG feedstocks. These biorefineries will need to address the specifications for either the subsequent bioprocess including fermentation and down-stream processing or meet the specification as a feedstock for chemical conversion at existing chemical manufacturing facilities.

Long-term Moonshot - Net exportation of renewable chemicals, fuels, and materials. Biobased production, extraction, recycling, and upcycling of supply chain staples is not only possible with engineering biology, but necessary for a sustainable future and healthy planet. Investment in biomanufacturing could make the U.S. a forerunner in producing, and exporting, these commodities.

EBRC Roadmap Resources - Engineering Biology for Climate & Sustainability (2022), Engineering Biology & Materials Science (2021), Engineering Biology (2019)

Foundational research to support biotechnology advancements

Short-term Moonshot - Widespread capacity across research and development enterprises to produce designed genomes, biomolecules, and cells. Technologies have advanced such that most laboratories can routinely engineer genes and genomes, proteins, and (non-natural) biomolecular circuits, and to customize cells, organisms, and cell-free systems, all bolstered by the integration of advanced data analysis, computational design, and data modeling. These advancements highlight the transformative potential of integrated biological data models, design frameworks for biomolecules, hosts, and organismal communities, and the promise of automating the design-build-test-learn process; however, bottlenecks exist in risk assessment and translation of fundamental tools to economically-viable technologies.

Medium-term Moonshot - Frameworks for FAIR (findable, accessible, interoperable, and re-usable) data. Engineering biology and biomanufacturing are increasingly model and data driven. To ensure a robust bioeconomy, widely accessible, quality data about biological systems, as well as scalable approaches to generate such complex data, are necessary. For biomanufacturing, creation of a publicly-available database of model and non-model production host organisms, their growth characteristics, genomics and other -omics data, predictive models of gene regulation, and genetic tools and protocols for each organism is necessary to enable growth and scale-up of the industry. Incentives are needed to encourage research and industry to develop and leverage FAIR data.

Medium-term Moonshot - Design, predict, evolve, and generate genetically-encodable biomolecules, such as proteins and RNAs, with user-specified complex molecular structures and functions. Genetically encoded macromolecules such as proteins and RNAs carry out myriad molecular functions at the heart of life. Understanding how a macromolecule's sequence maps to its function and developing new abilities for navigating the high-dimensional sequence space controlling macromolecular function will allow us to generate custom macromolecular sequences with custom functions. This will vastly expand the range of structural and material properties, catalysis, and molecular recognition that we can routinely engineer into biology, which will drive innovations across all sectors of the bioeconomy.

Medium-term Moonshot - Design, predict, and construct microbial consortia for specific niche environments and/or complex functions. Robust communities of organisms exist everywhere on Earth and are responsible for the health and wellbeing of entire ecosystems. Understanding the interplay between organisms in nature, and being able to capitalize on how different components of the system generate different reactions and responses, will help researchers to innovate on biotechnologies for all sectors across the bioeconomy. While developing engineered organisms, biocontainment strategies should be considered and developed to ensure their safe deployment.

Long-term Moonshot - Harness the tools and capacity to engineer any biomolecular, organismal, or cell-free system on Earth. While engineering biology should proceed with an inclusive depth of engagement from the research community, other science and engineering disciplines, government leadership, and the general public, the ability to understand, and the tools to safely, securely, and ethically engineer biology could have monumental advantages for the planet and would ensure continued success and growth for the bioeconomy.

EBRC Roadmap Resources - Engineering Biology (2019)