Synthetic Biology, So What?

BRIEFING PAPER

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"What is synthetic biology and what impact has it had on daily life? In other words, so what?

Introduction

Synthetic biology enables the engineering of biological systems to help solve some of society's foremost challenges. The field is already delivering innovations that touch our lives and is poised to deliver transformative solutions that help people and the planet flourish.

With a growing world population comes growing demands: for food, for healthcare, for energy, for natural resources. In the face of these global challenges, synthetic biology has enabled transformative solutions.

Biology is fundamentally programmable. Over the past several decades, scientists have figured out how to manipulate biology; in essence, to read, write and edit the very code of life: DNA. As life's genetic code becomes increasingly decipherable, biology can be configured to do what we need it to do. Cells can be coaxed to produce life-saving medicines and fuel, to generate commodities such as materials, dyes and chemicals in ways that are more environmentally friendly, and to grow and produce food. It may sound like science fiction, but these efforts are happening *today* and are available to consumers worldwide.[1] There have been many achievements to date, but we are just at the tip of the iceberg for what synthetic biology can help us achieve.[2]

Many reports have been written about what synthetic biology might deliver.[3] Here we highlight ways that synthetic biology is already being incorporated into our lives in a variety of application areas. The examples provided *are already commercially available* and were curated to elevate the concept of synthetic biology from a hypothetical phenomenon to what it really is – a real-world discipline providing unparalleled outcomes for humans and planet.[4] While several examples are recent, some may be older, reflecting the earliest forays into engineering biology that have since led to commercial successes – and demonstrating the continuum in design learning and technological progress that is the field of synthetic biology.

Application highlights

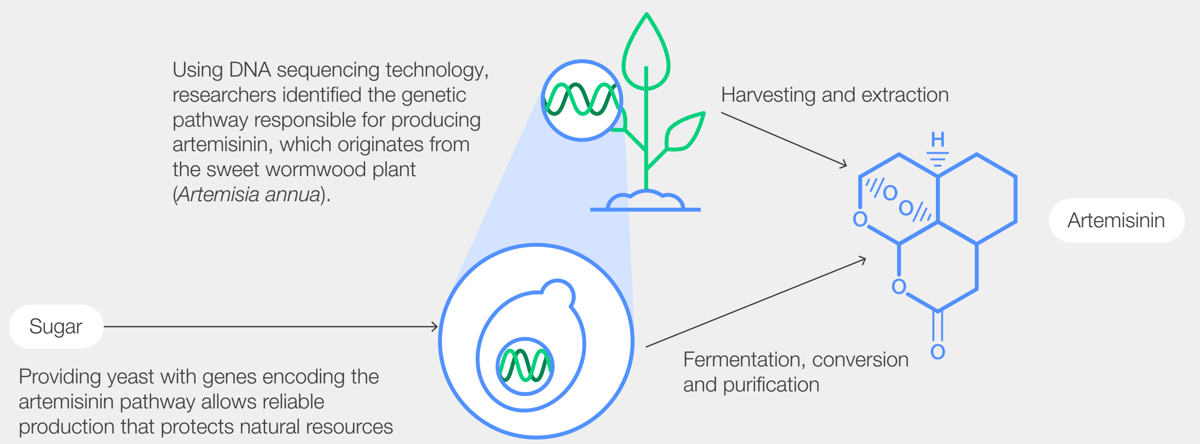
Medicine

Did you know? The mRNA COVID-19 vaccine was a triumph of synthetic biology. From designing the nucleic acid sequence to scaling up production and manufacturing, advances in synthetic biology were fundamental to our ability to respond to the global pandemic.

The world faces persistent challenges in health and healthcare[5] and synthetic biology has enabled solutions for a range of these challenges, from designing novel biomedicines to lowering the cost of manufacturing in the health supply chain. One recent example of synthetic biology's contribution to medicine is the synthetic mRNA vaccine, which saved lives and livelihoods and stabilized societies and economies during the COVID-19 pandemic. This new class of biomedicines holds much promise to address other infectious diseases as well as non-communicable health challenges such as cancer. A new mRNA vaccine against respiratory syncytial virus (RSV) – a virus that causes mild, cold-like symptoms in most but can become serious for babies and the elderly – received regulatory approval earlier this year.[6] Furthermore, roughly $250 million in venture investment flowed into optimizing mRNA technology in 2022,[7] indicating market interest in designer mRNA as a platform for vaccines.

Synthetic biology tools are making it possible to produce therapeutic molecules via more reliable supply chains at lower costs and with less environmental impact. For example, artemisinin, an anti-malarial drug that is extracted from a rare plant,[8] is now able to be produced in the same microbes used to brew beer, making use of a fraction of the landmass and achieving economies of scale well beyond inefficient plant extraction processes (Figure 1).

FIGURE 1: Traditionally harvested from plants, the genes encoding the anti-malarial drug artemisinin can be ported into yeast to produce this valuable drug through fermentation, a process that uses sugar instead of fossil inputs. This alternative process allows reliable and customizable production that protects natural resources.



In medicine, synthetic biology innovations extend well beyond bioproduction of drugs and have also delivered customizable or personalized therapies.[9] For instance, our own immune cells ("T cells") can be removed from the body, outfitted with new genetic instructions to target and kill cancer cells, and then reintroduced into our bodies to fulfil that obligation. These types of engineered cells are commercially available today to treat several cancers.[10] A study in 2004 demonstrated that gene therapy in humans was possible, paving the way for editing T cells.[11]

Environment and green energy

Did you know? Synthetic biology is being applied to remove pollutants and repurpose waste, even turning waste and industrial "sidestreams" into valuable products. Millions of tons of waste have been diverted from landfills annually using synthetic biology approaches, particularly in the production of biofuels and bioplastics.

An increase in industrialization and urbanization has resulted in accumulation of anthropogenic byproducts, including fuel, plastics and other wastes. In addition to harming the natural environment, the World Health Organization indicates that

FIGURE 2A: **Repurposing CO_2 and sidestreams into products with synthetic biology.** Carbon dioxide is captured and through a series of processing steps, the carbon is repurposed via fermentation into high-value materials such as protein and fuel. Synthetic biology is applied during the fermentation step whereby microbes are programmed to transform various inputs into valuable molecules.

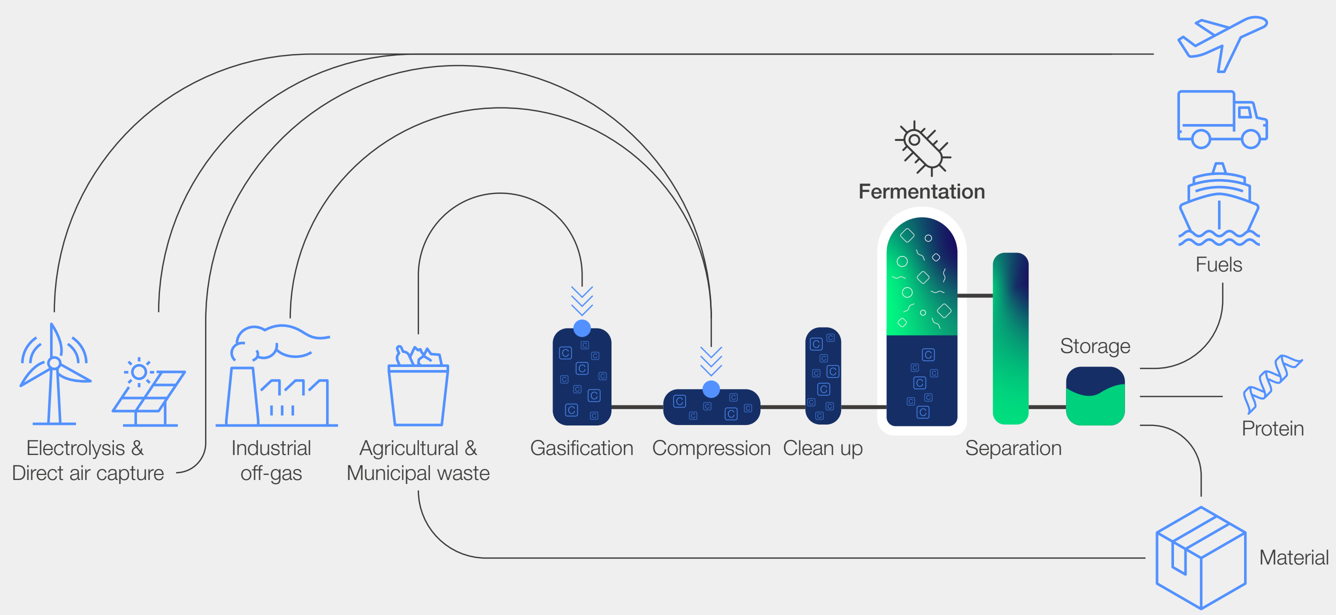
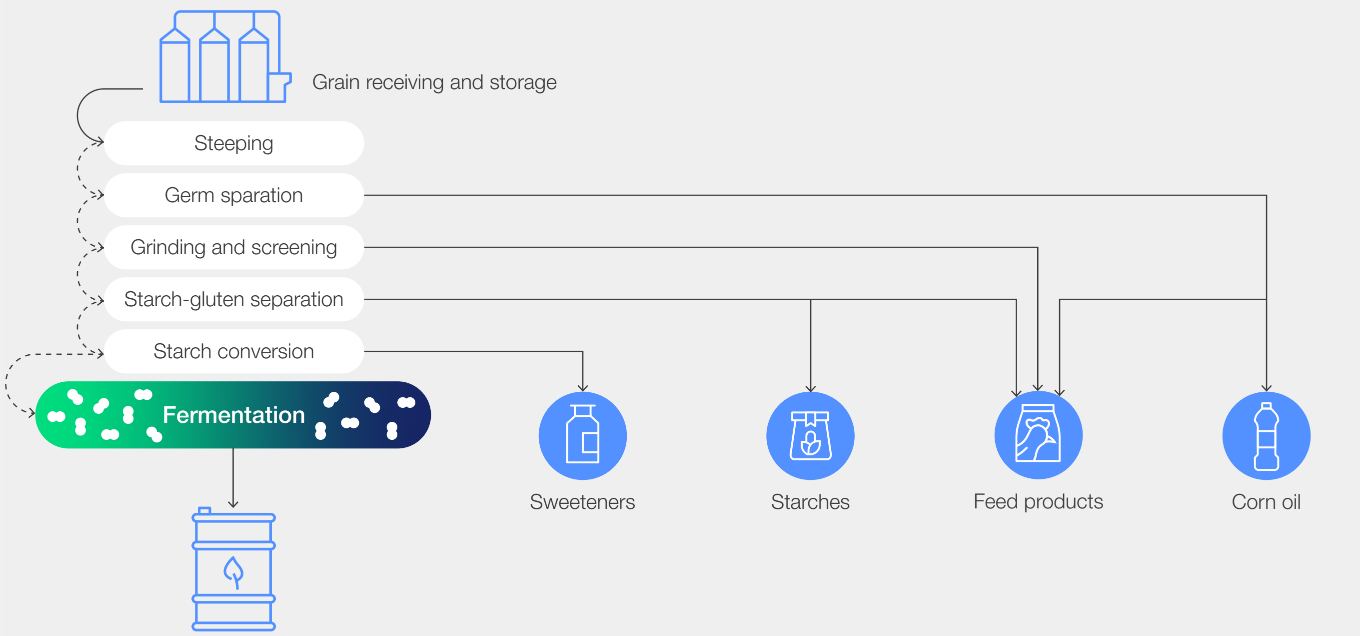


FIGURE 2B: **Corn is harvested and processed into sweeteners, starches, feed products and corn oil, with synthetic biology valorizing resuidual byproducts into bio ethanol.** After sidestreams are separated to make these products, the remaining residual material is further processed into bioethanol through fermentation with an engineered yeast that secretes powerful, highly optimized starch-processing enzymes.



environmental risk factors cause approximately 25% of human deaths.[12] For the majority of pollutants, cost-effective and scalable remediation approaches do not yet exist.

Synthetic biology is enabling new solutions in remediation, waste management and resource conservation and conversion. Some applications focus on sequestering carbon directly from the air and repurposing it into valuable products.[13] Microbial cells in particular can be rewired to convert carbon into useful commodities, including fuels, materials and chemicals (Figure 2a). The resulting engineered microbes are then deployed, via fermentation, near an emission source, such as a mill or landfill site, to capture carbon and subsequently convert it.

Beyond using carbon dioxide as an input, synthetic biology has been operating at scale for over a decade to valorize waste and sidestreams, repurposing them into high-value and commodity products. In one example, residual starch from corn milling is fermented with a yeast strain that has been programmed to convert starch into bioethanol[14,15] (Figure 2b). Not only does this process make use of sidestreams from corn processing but it also benefits the planet: on a per-gallon basis, bioethanol can reduce GHG emissions by up to 50%-60% compared with gasoline. While it is important to note that the sustainability of bioproducts depends on several factors and varies considerably,[16] utilizing waste and sidestreams as inputs to biological processes provides one approach to reducing emissions.

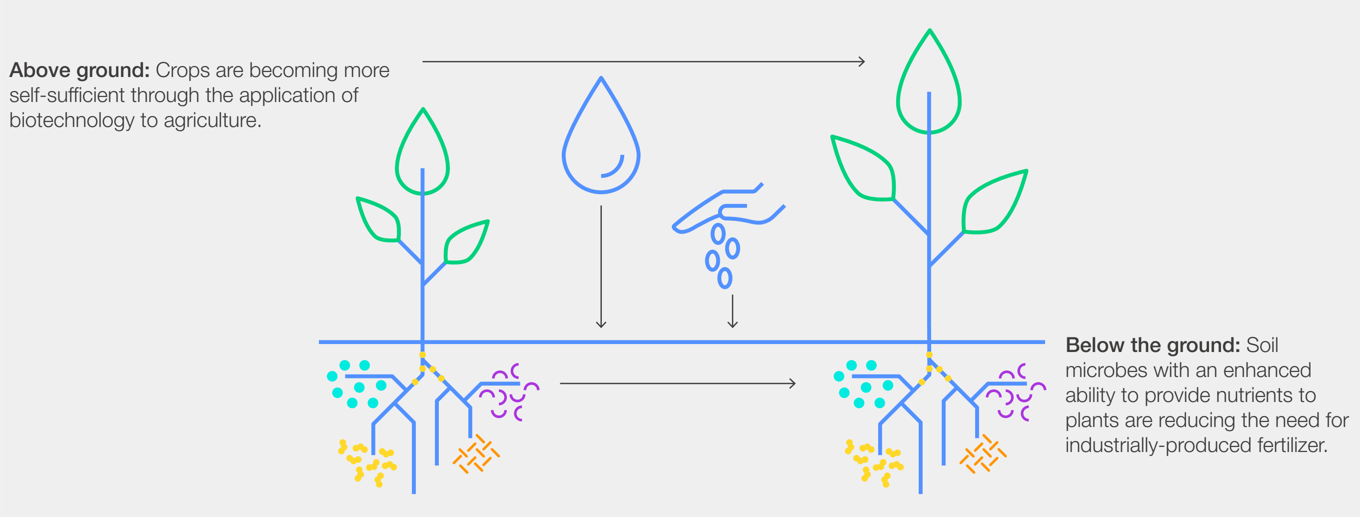
Agriculture and food production

Did you know? Over decades of innovation, synthetic biology is enabling crops to become more self-sufficient, stabilizing our food supply in the face of increasingly unpredictable climate conditions.

By 2050 the Food and Agriculture Organization estimates that nearly 9% of the world's population will be chronically undernourished, putting enormous pressure on land and natural resources and setting the stage for more ecological and climate disasters.[17] Furthermore, currently feeding and sustaining the world, agriculture and food production account for more than 30% of GHG emissions and 70% of all freshwater usage, and one-third of all food production is estimated to be wasted along the value chain.[18]

The application of synthetic biology across the food and ag value chain has delivered promising alternatives at scale with proven benefits to the planet, with gene-editing technologies being applied to make crops more self-sustaining. Certain drought-resistant varieties of maize, for example, have demonstrated up to 62% increased yield compared to conventional varieties in Uganda, Kenya and South Africa for decades (Figure 3).[19] Furthermore, biotech crops have reduced grower reliance on insecticides and improved their water use efficiency in Australia, reducing pesticide use by up to 85% and herbicide use by about 52%.[20] But the benefits of ag biotech extend even further; from 1996 to 2020, the application of gene-editing technologies to crops is estimated to have reduced global agricultural emissions by 23.6 million metric tons of carbon dioxide.[21]

FIGURE 3: **Synthetic biology is changing agricultural paradigms by enabling plants to become more self-sufficient.** Above the ground, genes such as those conferring increased vigour, reduced sensitivity to drought and/or protection from pests and herbicides are introduced into crops to make them more self-sufficient and capable of withstanding harsher climate conditions. Below the ground, soil microbes are engineered to enhance their ability to produce nitrogen fertilizer, thus reducing application of industrially-produced fertilizer.



Synthetic biology innovations in agriculture also focus on providing better nutrition to crops. By enhancing a microbe's natural ability to pull nitrogen out of the air and configure it into fertilizer, microbial fertilizer is providing a much needed alternative to industrial fertilizer production. In particular, the application of microbial fertilizer has avoided more than 315,000 megatons of CO_2 emissions since 2022.[22] Innovations with agricultural livestock are also making a dent in reducing the 100 teragrams of methane gas (CH_3) produced by dairy and beef cattle each year (rivalling what is generated by the oil and gas industry) through the development of synthetic biology-derived food additives that optimize bovine metabolism to emit less methane.[23]

Advanced manufacturing and value chains

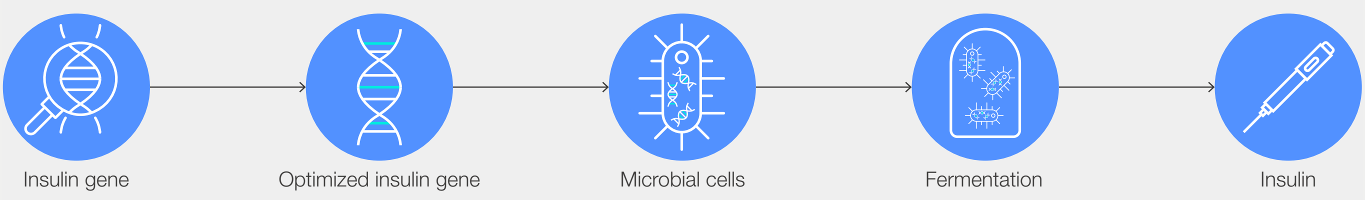
Did you know? Semaglutide is produced using biomanufacturing. In this process, the gene encoding the desired GLP-1 analogue is inserted into micro-organisms such as yeast or bacteria that are cultured to produce semaglutide in large quantities.

Biomanufacturing is a $1.4 trillion industry in the United States alone and contributes significantly to various sectors such as pharmaceuticals, industrial biotechnology, agriculture and environmental chemicals.[24] Biomanufacturing is leading to a future where everyday products – dyes, flavours, drugs, textiles – are produced using biology, generating fewer greenhouse gases and less hazardous waste than traditional manufacturing methods. Unlike conventional processes that rely on petrochemicals, biomanufacturing utilizes cells and microbes combined with diverse feedstocks, such as biomass, industrial by-products and food waste, to produce goods at commercial scale. By using non-fossil inputs, biomanufacturing plays a crucial role in advancing the net-zero transition in manufacturing and supply chains, making it a global priority as we continue on our journey to net zero.

The cells or microbes central to a biomanufacturing process are genetically optimized to produce desired outputs at commercial scale. Products such as insulin, growth hormones, antibodies, vaccines , polymers including bioplastics, and industrial enzymes have been commercially produced via biomanufacturing for several decades. Biomanufacturing is even being used to produce protein fibres for sustainable clothing[25]; resulting bioproducts have had a significant impact on healthcare and industrial biotechnology, demonstrating the lasting importance and success of biomanufacturing across various applications.

Biomanufacturing is also revolutionizing supply chains, as exemplified by one early example, the production of insulin.

FIGURE 4: **Biomanufacturing transforms supply chains.** Earlier scientific breakthroughs enabled researchers to isolate, optimize, and insert the gene encoding human insulin into microbial cells for commercial scale production, thus overhauling insulin supply chains and enabling an animal-free production process.



Previously, insulin was extracted from the pancreas of pigs and cows, a labour-intensive method with limited supply and the potential for allergic reactions. With recombinant DNA technology, researchers inserted the human insulin gene into bacteria or yeast (Figure 4), enabling large-scale, consistent production of insulin identical to that made by the human pancreas. This shift dramatically increased supply, reduced costs and improved patient outcomes, setting a new standard for biomanufactured products. With biology underpinning the production of essential medicines and their foundational components, synthetic biology can solve future drug supply shortages and create greener, more sustainable global supply chains.

Co-creating our biofuture: What is Needed Now?

The progress to date in synthetic biology has laid a foundation that will continue to transform sectors.[26] From food to manufacturing of materials and beyond, synthetic biology is the backbone of the future bioeconomy. However, to realize its full promise – at scale – will require overcoming significant barriers.[27] Spanning innovation and commercialization, long-term and sustained investments of resources from both government and the private sector, and the development of catalytic and supportive policies, the challenges are not unique to synthetic biology, and include the following:

Key challenges and opportunities

- Countries committing to sustained and long-term investments in digital and physical infrastructure, as well as the training of the skilled workforce required to implement synthetic biology approaches
- Private sector organizations committing to deploying and developing bio-produced ingredients and processes
- The enabling role of governments and larger corporations to support regional start-ups and synthetic biology ecosystems through value chain incorporation of biobased inputs and processes
- Regulatory innovations within and across countries that can accommodate new types of bio-based products and enable applications beyond containment
- Continued commitment by all stakeholders to responsible innovation in synthetic biology and safeguarding the responsible transition to a bio-based economy
- Lowering costs of products made using synthetic biology to increase accessibility as well as viable competitors to existing, non-bio-based products
- Development of technical standards and metrics that can be applied across the innovation pipeline to support the bioeconomy's growth[28]
- Developing bold new foundational and applied research programmes that integrate with emerging and converging technologies, such as machine learning and artificial intelligence, to enable new opportunities for biology to grow economies and tackle global challenges in health, environment, agriculture and beyond
- Tackling challenges with scale including infrastructure, workforce, supply chains and market receptivity

Learn more and get engaged: Key organizations and initiatives

There is a growing ecosystem of organizations seeking to co-create a better biofuture. While not exhaustive, below are examples of initiatives spearheaded by international organizations that are helping to create new coalitions tackling the challenges and opportunities highlighted above.

- **World Economic Forum:** The Forum's Bioeconomy Thematic, including the Global Future Council on Synthetic Biology, gathers global leaders across public and private sectors to accelerate the tech-driven bioeconomy.
- **The Engineering Biology Research Council:** this US council organizes a biannual forum of countries and convenes and publishes foundational reports. In 2023, the EBRC gathered 24 countries to discuss their national plans and roadmaps.
- **International Genetically Engineered Machines (iGEM) Competition:** What has been likened to the "Olympics of synthetic biology" catalysed the field over the past 20 years and remains the premier training ground for students in high school through post-graduate studies. To date, students from more than 65 countries are participating in this event with over 70,000 alumni across the globe.
- **The Organization for Economic Development (OECD) Global Forum on Technology:** Synthetic biology has been established as a strategic focus area for this effort whereby the OECD body is developing recommendations for leaders.
- **The International Advisory Council on Global Bioeconomy:** an independent think tank that facilitates international collaboration and mutual exchange for sustainable and circular bioeconomy development.
- **ASEAN (Association of Southeast Asian Nations):** ASEAN is developing bioeconomy strategies and synthetic biology is being considered as a potential key technological driver in this effort.
- **ASBA (Asian Synthetic Biology Association):** ASBA is an international organization dedicated to fostering partnerships and collaboration in synthetic biology in Asia. Founded by the synthetic biology communities of China, Japan, Republic of Korea and Singapore, ASBA comprises over 300 practitioners in the field across the region.

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