# How synthetic biology can help the environment

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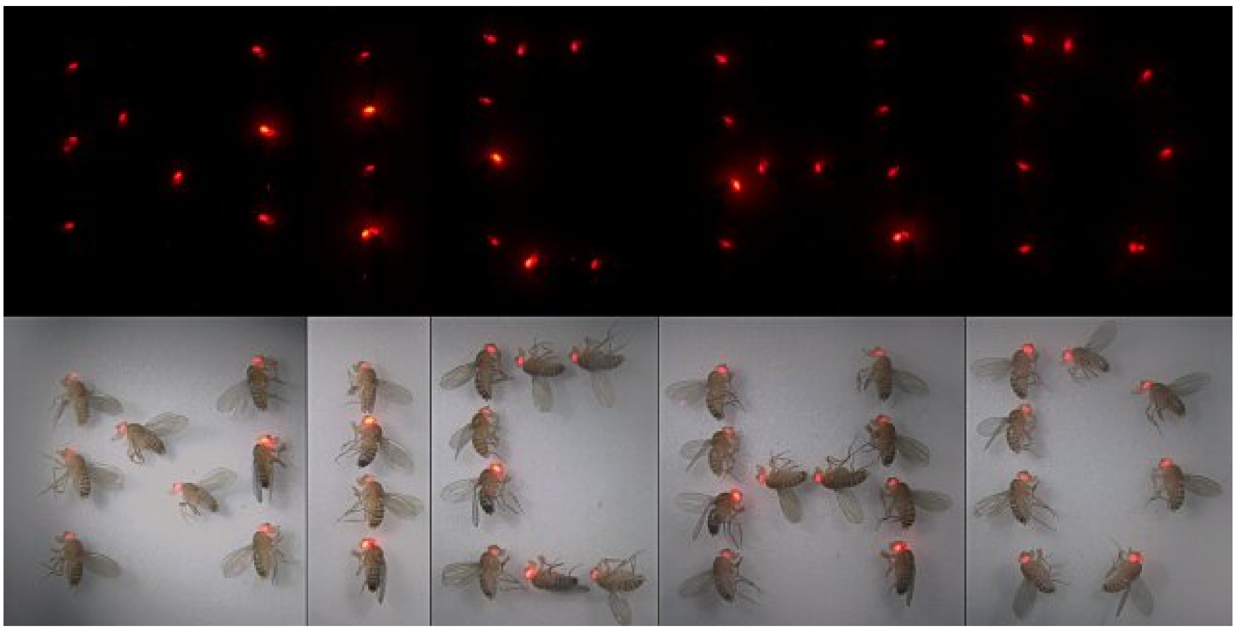

CRISPR was used to give fruit flies red fluorescent eyes. Credit: [Photo: NICHD]

Most environmental science is focused on how to turn back the clock, not push it forward, says Ben Bostick, a geochemist at Lamont-Doherty Earth Observatory. "We think about how we can roll back our footprint, and not so much about how can we make our footprint bigger in a positive way," he said. "But there are many examples of synthetic biology that I think actually have a lot of potential in the environment. Think of how we can help our environment just by doing things like improving the materials we make using synthetic biology."

Synthetic biology (synbio) is the construction of biological components, such as enzymes and cells, or functions and organisms that don't exist in nature, or their redesign to perform new functions. Synthetic biologists identify gene sequences that give organisms certain traits, create them chemically in a lab, then insert them into other microorganisms, like E. coli, so that they produce the desired proteins, characteristics or functions.

Since 2011, when I wrote a general introduction to synbio, the field has grown rapidly.

One reason for this is the development of the gene editing tool CRISPR-Cas9, first used in 2013, that locates, cuts and replaces DNA at specific locations. Another reason is how easy it has become to use the Registry of Standard Biological Parts, which catalogs over 20,000 genetic parts or BioBricks that can be ordered and used to create new synthetic organisms or systems.

In 2018, investors poured $3.8 billion and governments around the world invested $50 million into synbio companies. By 2022, the global market for synbio applications is projected to be $13.9 billion. But synthetic biology is still controversial because it involves altering nature and its potential and risks are not completely understood.

Bostick, who works on remediating arsenic contamination of groundwater by stimulating natural bacteria to produce substances that arsenic sticks to, explained that, in fact, the entire biological community that works on organisms alters biological systems all the time, but don't change genetic material or organisms. Scientists delete enzymes, insert new ones, and change different things in order to understand the natural world "Those are standard techniques now but they're done mechanistically," he said. "If you want to see how a protein works, what do you do? You actually change it—that's exactly how we have studied our environment. They are synthetic and they are biological alterations but they're just not done with the purpose that defines synthetic biology." Synbio is more controversial because its purpose is to build artificial biological systems that don't already exist in the natural world.

Nevertheless, synthetic biology is producing some potential solutions to our most intractable environmental problems. Here are some examples.

## Dealing with pollution

Microbes have been used to sense, identify and quantify environmental pollutants for decades. Now synthesized microbial biosensors are able to target specific toxins such as arsenic, cadmium, mercury, nitrogen, ammonium, nitrate, phosphorus and heavy metals, and respond in a variety of ways. They can be engineered to generate an electrochemical, thermal, acoustic or bioluminescent signal when encountering the designated pollutant.

Some microbes can decontaminate soil or water naturally. Synthesizing certain proteins and transferring them to these bacteria can improve their ability to bind to or degrade heavy metals or radionuclides. One soil bacterium was given new regulatory circuits that direct it to consume industrial chemicals as food. Researchers in Scotland are engineering bacteria to convert heavy metals to metallic nanoparticles, which are used in medicine, industry and fuels.

CustoMem in the UK uses synthetic biology to create a granular material that attracts and sticks to micropollutants such as pesticides, pharmaceuticals, and certain chemicals in wastewater. And Australian researchers are attempting to create a multicellular structure they call a "synthetic jellyfish" that could be released after a toxic spill to break down the contaminants.

## Preserving biodiversity

American chestnut trees dominated the East Coast of the U.S. until 1876, when a fungus carried on imported chestnut seeds devastated them, leaving less than one percent by 1950. To make blight-resistant trees, scientists have inserted a wheat gene into chestnut embryos, enabling them to make an enzyme that detoxifies the fungus. This chestnut tree is likely to become the first genetically modified organism to be released into the wild once it is approved by the Department of Agriculture, the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA).

Revive & Restore, an organization that uses genetic techniques to preserve biodiversity, is attempting to rescue the endangered black-footed ferret, which is susceptible to sylvatic plague. Because the domestic ferret is not, scientists are studying the possibility of finding the genes that give the domestic ferret resistance and editing them into the black-footed ferret's genome. The research will begin with cell cultures in the lab.

Gene drives are mechanisms that spread a desired genetic trait through a population to control invasive species. A gene drive was recently under consideration to control the golden mussel, which has invaded South American and Latin American waters. After identifying the genes related to reproduction and infertility in golden mussels, scientists proposed using CRISPR-Cas9 to edit the mussel's genome to make the females infertile. The genetically modified mussels would then be bred with wild mussels in the lab, creating modified embryos that could be released into the wild to spread infertility throughout the population. A gene drive to eliminate mosquitoes that carry malaria has worked in the lab, but no engineered gene drive has been tried in the field as yet.

Some scientists are also working on modifying coral genomes to give them more resistance to warming ocean temperatures, pollution and ocean acidification. Others have proposed modifying the genes of cyanobacteria that affect moisture in the soil crust of semi-desert ecosystems so that the soil retains more water and more vegetation can grow.

The Impossible Burger. Credit: Dale Cruse

## Feeding the world

With the world population expected to hit 10 billion by 2050, global demand for food could increase by 59 to 98 percent. Climate change impacts—higher temperatures, extreme weather, drought, increasing levels of carbon dioxide and sea level rise—are jeopardizing the quantity and quality of our food supplies.

## Improving agriculture

Researchers at the University of California, San Diego discovered that when plants encounter dry conditions, they release a hormone that closes the plant's pores in order to retain water, slows its growth and keeps the seeds dormant. That hormone is expensive to synthesize, however, so scientists worked with synthetically developed receptors in tomato plants that responded in a similar water-conserving fashion to a commonly used fungicide instead, making the plants more resilient to drought.

The Salk Institute's scientists have identified the genes that encourage a plant's root system to grow deeper into the soil. They plan to engineer genetic pathways to prompt deeper roots, which will enable crop plants to resist stress, sequester more carbon and enrich the soil.

Microbes that live with legumes give them the ability to convert nitrogen from the atmosphere into nutrients the plant needs to grow. However, because other plants cannot naturally assimilate nitrogen, farmers have traditionally used chemical fertilizers. The production of fertilizer, made mainly from fossil fuels, results in greenhouse gas emissions and eutrophication. As an alternative, Pivot Bio, a California company, engineered the genes of a microbe that lives on the roots of corn, wheat and rice plants to enable the microbe to pull nitrogen out of the air and feed it to a plant in exchange for nutrients. In field tests, its nitrogen-producing microbe for corn yielded 7.7 bushels per acre more than chemically fertilized fields.

## New foods

Agriculture, including raising livestock, is responsible for about 8 percent of U.S. greenhouse gas emissions. Genetically modified microbes are being used to produce food that is more sustainable, ethical and potentially healthier. Motif Ingredients is developing alternative protein ingredients without animal agriculture. It uses engineered microbes to produce food proteins that can be tailored to mimic flavors or textures similar to those found in beef and dairy.

Impossible Foods' plant-based burger contains synthesized heme, the iron-containing molecule found in animals and plants that gives meat its bloody flavor. To make it, scientists added a plant gene to yeast, which, after fermentation, produced large quantities of the heme protein. Impossible Burger uses 75 percent less water and 95 percent less land than a regular beef burger, and produces 87 percent fewer greenhouse gas emissions.

As the demand for seafood grows globally (fishing stocks are already 90 percent overfished), so does the need for fishmeal, the protein pellets made of ground up small fish and grain that feed farmed fish as well as livestock. California-based NovoNutrients uses $CO_2$ from industrial emissions to feed lab-created bacteria, which then produce protein similar to the amino acids fish get by eating smaller fish; the bacteria replace the fishmeal, providing the fish with protein and other nutrients.

## Creating greener products

## Fuels

Burning fossil fuels for energy accounted for 94 percent of total U.S. anthropogenic $CO_2$ emissions in 2016, so a lot of research is aimed at creating better biofuels that don't compete with food production, soil nutrients or space. The latest generation of biofuels focuses on engineered microalgae, which have high fat and carbohydrate content, grow rapidly and are relatively robust. Altering their metabolic pathways enables them to photosynthesize more efficiently, produce more oil, absorb more carbon, and be hardier so that their numbers can be scaled up.

LanzaTech in Illinois identified an organism that naturally makes ethanol from industrial waste gases. After the company engineered it with "pathways" from other organisms to improve its performance, the organism is able to produce unique molecules for valuable chemicals and fuels. LanzaTech's first commercial plant in China has produced over seven million gallons of ethanol from steel mill emissions that can be converted into jet fuel and other products.

## Materials

165 million tons of plastic have trashed the oceans, with almost 9 million more tons being added each year. Synbio could provide a solution to this pollution problem, both by degrading plastic and replacing it.

In 2016, researchers in Japan identified two enzymes in a bacterium that enable it to feed on and degrade PET plastic, the kind used for water bottles and food containers. Since then, researchers around the world have been analyzing how the enzymes break down the plastic and trying to improve their ability to do so.

Textile mill in Bangladesh. Credit: NYU Stern BHR

California-based Newlight Technologies is using a specially developed microorganism-based biocatalyst (similar to an enzyme) to turn waste gas captured from air into a bioplastic. The biocatalyst pulls carbon out of methane or carbon dioxide from farms, water treatment plants, landfills, or energy facilities, then combines it with hydrogen and oxygen to synthesize a biopolymer material. The biopolymer, called AirCarbon, can replace plastic in furniture and packaging.

Lignin is a key component of plants that, like other types of biomass, could be used for renewable fuels and chemicals. Since very few bacteria and fungi can break it down naturally, scientists have been trying for years to develop an efficient way of doing so. Now some have engineered a naturally occurring enzyme to break it down, which could eventually make it possible to use lignin for nylon, bioplastics and even carbon fiber.

The manufacturing of complex electronic devices requires toxic, rare, and non-renewable substances, and generates over 50 million tons of e-waste each year. Simon Vecchioni, who recently defended his Ph.D. in biomedical engineering at Columbia University, is using synthetic biology to produce DNA nanowires and networks as an alternative to silicon device technology.

Vecchioni ordered synthesized DNA from a company, used it to create his own custom BioBrick—a circular piece of DNA—and inserted it into the bacterium E.coli, which created copies of the DNA. He then cut out a part of the DNA and inserted a silver ion into it, turning the DNA into a conductor of electricity. His next challenge is to turn the DNA nanowires into a network. The DNA nanowires may one day replace wires made of valuable metals such as gold, silver (which Vecchioni only uses at the atomic scale), platinum and iridium, and their ability to "self-assemble" could eliminate the use of the toxic processing chemicals used to etch silicon.

"A technology for fabricating nanoscale electrical circuits could transform the electronics industry. Bacteria are microscale factories, and DNA is a biodegradable material," he said. "If we are successful, we can hope to produce clean, cheap, renewable electronics for consumer use."

## Building materials

The production of cement (a key ingredient of concrete) is responsible for about eight percent of global greenhouse gas emissions because of the energy needed to mine, transport and prepare the raw materials. bioMASON in North Carolina provides an alternative by placing sand in molds and injecting it with bacteria, which are then fed calcium ions in water. The ions create a calcium carbonate shell with the bacteria's cell walls, causing the particles to stick together. A brick grows in three to five days. bioMASON's bricks can be customized to glow in the dark, absorb pollution, or change color when wet.

## Dressing more sustainably

Fast fashion has a disastrous impact on the environment because of its dyes and fabric finishes, fossil fuel use and microfiber pollution. About three-fourths of the water used for dyeing ends up as toxic wastewater, and over 60 percent of textiles are made from polyester and other fossil fuel-based fibers that shed microfibers when washed, polluting our waters.

French company Pili synthesizes enzymes that can be tailored to produce different colors, then integrates them into bacteria. The bacteria are then able to create pigments. Pili's dye is produced without petroleum products or chemicals, and uses one-fifth the water of regular dyes.

Spider silk, considered one of nature's strongest materials, is elastic, durable and soft. Bolt Threads, based in San Francisco, studied spider DNA to figure out what gives spider silk its special characteristics, then engineered genes accordingly and put them into yeast, which, after fermentation, produce large quantities of liquid silk proteins. The silk protein is then spun into fibers, which can be made into renewable Microsilk.

## The risks of synbio

In the U.S., synbio chemicals and pharmaceuticals are mainly regulated by the Toxic Substances Control Act of 1976. Other synbio commercial products and applications are regulated by the EPA, Department of Agriculture, and the FDA. But do these agencies have the capacity and effectiveness to monitor synthetic biology as fast as it's developing and changing?

As some syn bio applications are starting to move out of the lab, there are worries about its potential environmental risks. If an engineered organism, such as those used in gene drives, is released into nature, could it prove more successful than existing species in an ecosystem and spread unchecked?

Bostick noted that each synthetic biology project today is usually focused on one very specific modification. "It's adding or altering a single enzyme, possibly putting in a series of enzymes so that it can do one thing," he said. "Very seldom do you tweak the rest of the organism, so it's not critical to the success of the organism and it's not likely to run rampant. From a scientific standpoint, it's hard to change more than one thing."

Moreover, according to Vecchioni, most synbio research is being done by student groups through iGEM's International Genetically Engineered Machine Competition, and every iGEM project must have a safety component—some way to turn off the gene or regulate it if it gets out.

Another concern is that the creation or modification of organisms could be used to create a disease for the purpose of bioterrorism. Vecchioni explained that the FBI is on the lookout for this. "They walk in nicely and say 'hi, we're watching,'" he said. "They also go to conferences and just make sure people are being smart about it." He added that DNA synthesis companies are also on alert. "They have a library of known dangerous pieces of DNA, so if you try to order something that is known to create disease in any organism, the FBI will come knocking on your door."

A more recent concern is that research institutes have begun setting up biofoundries, facilities that rely heavily on automation and artificial intelligence (AI) to enhance and accelerate their biotechnology capabilities. Jim Thomas, co-executive director of the ETC Group, which monitors emerging technologies, is concerned about the tens of thousands of organisms that AI is being used to create. "It raises a real safety question because if you have something go wrong, you potentially don't understand why it went wrong," said Thomas. "With AI it's a bit of a black box." He noted that most experts agree that there has to be a process for monitoring and assessing new developments in synbio.

Despite the potential risks of synbio, its potential benefits for the planet are huge. And as our environment is battered by the impacts of climate change and human activity, we need to explore all options. "We need every possible solution to even remotely get to the magnitude of change that we need to improve our world," said Bostick.