

Detailed analysis of bioengineering, including trends in CRISPR, -oomics, synthetic biology, biomachine interfaces and biocomputing.

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THIS YEAR REQUIRES FOCUS



In August 2017, a rare explosive event known as GW17817 took place in space. Two stars collided, unleashing a blast energetic enough to form an incalculable number of new stellar bits that continue to travel through interstellar space. Over time, this stardust will combine into small objects, evolve into large rocks, fuse with even more material, and form into planets. One incredibly violent disruption will someday lead to the formation of a new corner of the universe. This is how our own sun and Earth, and all of human existence, came into being.

Lately it's as if we've been living through the aftermath of cataclysmic explosions: the release of generative artificial intelligence systems like ChatGPT and Midjourney, a fusion breakthrough that could someday generate zero-carbon energy, Russia's ongoing invasion into Ukraine, deep uncertainty about a global recession, and AlphaFold's protein-folding algorithms that predicted structures for nearly all cataloged proteins known to science, to name a few. These and other forces of change are colliding, going supernovae, and resulting in an unfathomable amount of new signals—bits of change that, over time, result in the trends that shape society.

Now more than ever, it's important to carefully track new trends as they emerge. But that isn't easy, given the rapid pace of change. For that reason, the theme of our 2023 Tech Trends report is Focus. It is crucial to focus when new signals are forming because some may be lasting and develop into impactful trends, while others might burn out and fade away. In an increasingly complex and fast-paced world, leaders who focus on the trends that matter and adapt to changing circumstances make better decisions and see improved outcomes. Trends enable them to anticipate near-term change, understand the factors influencing their industries, and develop a point of view on the future.

Our research is presented in 14 in-depth reports that reveal the current state of play, a list of influencers to watch, key trends, detailed examples, expert perspectives and recommendations designed to help executives and their teams develop their strategic positioning. Some of the trends are new advancements on mature technologies, while others represent frontier technologies and areas of science. When we look at them collectively, new centers of gravity come into focus, and we can glimpse the impacts they will have on every sector.

Trends on their own cannot predict the future. Rather, future-focused organizations use them to deeply reflect on the tension between long-term and short-term goals and to reduce uncertainty. By understanding the trends and changes shaping the landscape, executives can make informed decisions and capitalize on new opportunities in the year ahead.

We invite you to join us in observing how the stardust settles into new signals and trends. Share your feedback with us at 2023trends@futuretodayinstitute.com.

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Amy Webb
Chief Executive Officer
Future Today Institute

SIAIE OFPLAY

Breakthroughs in bioengineering mean incredible opportunity for every industry, but could also pose new risks as the technology is developed and implemented.

The convergence of biological technologies, information systems, and next-generation platforms has the potential to fundamentally transform business and society. Breakthroughs in biology, combined with developments and innovations in other technologies, are unlocking vast new opportunity spaces for a diverse range of fields, including agriculture, health care, sustainability, energy, consumer products, and manufacturing.

In this section of our emerging tech trends report, we use bioengineering as an umbrella term to broadly encompass many biology-related technologies, including CRISPR, synthetic biology, DNA sequencing, and platform technologies such as cell therapy and precision medicine. The impact of bioengineering in the coming decade will be profound. The supply of raw materials will no longer be constrained by natural availability. Drought-stricken communities could produce animal protein and crops regardless of extreme climate events. New "living drugs," like yeasts that produce malaria defenses, could be deployed quickly and economically in impoverished communities. Cells might be reprogrammed to reverse their aging process and prolong the lifespans of living organisms, including humans.

Synthetic biology in particular stands to transform society and the global economy as the technology matures and a wide range of applications move into the mainstream. But game-changing, emerging biotechnology trends also mean new risks—some catastrophic—if not managed properly.

Bioengineering Domains

Innovations in biotechnology are currently defined by five key areas: biomolecules, biosystems, biomaterials, biocomputing, and biomachine interfaces. Major breakthroughs in one field either reinforce or accelerate breakthroughs in the others.

Biomolecules (or "Omics")

A group of biological sciences collectively known as omics—including fluxomics (metabolic reactions in cells), metabolomics (chemical species involved in the reactions in cells), proteomics (the decoded product, or proteins), transcriptomics (the RNA created from each piece of genetic code), and genomics (the DNA code that drives cellular processes)—is working to analyze the structure and functions of biological molecules that translate into the function and dynamics of an organism. Learning about and tinkering with the engineering of molecules (think: DNA, RNA) will lead to new therapeutics and innovative defenses against novel viruses, as well as alternatives to the ways we currently grow food.

Biosystems

Biology is complex. Scientists are applying engineering principles to understand and influence the pathways, connections, and interactions within biological systems. Developing new processes could lead to new opportunities to modify or even create cells, tissues, organs, and potentially complex networks like respiratory systems.

Biomaterials

It is now possible to replicate or improve upon raw materials using bioengineering technology. One example: a bioreplacement material that is produced sustainably, at a lower cost than traditional raw materials, and at no harm to the environment.

Biocomputing

Biology is made up of code—and the goal is to harness that code for computing. DNA and RNA can be used as mediums for storing information and data processing. While traditional supercomputers use a lot of energy, heat up quickly, and require costly cooling centers to function properly, biological computing systems can perform computations without burning excess energy—and are infinitely scalable.

Biomachine Interfaces

Innovative new interfaces are connecting living organisms to computers for many different purposes, including restoring a stroke victim's ability to walk or creating the opportunity to someday control external computers simply by using thought.



When will bioengineering disrupt you?

Advancements in bioengineering will disrupt every industry within the next two decades. Future Today Institute now thinks of bioengineering as the next critical general-purpose technology. Like the steam engine and the internet before it, bioengineering has the potential to influence entire economies and to alter society through political, economic, and social structures.

There are several factors driving the momentum of bioengineering trends and the probable timing of an industry's disruption:

Scaling: While the pace of innovation is fast across the spectrum of technologies, it takes time for a promising new biotech development to scale beyond the lab. Scaling also requires discipline, patience, and effort.

Costs: Bioengineering research is still costly, though the price of components, equipment, and materials drops every year. To be sure, it's still significantly cheaper to use old technology like existing chemicals, products, and systems that power everything from agriculture to textile manufacturing. Today, it's possible to grow, roast, and package a whole chicken for \$5, while a single cultured chicken patty costs more than \$20 to produce. Technological advancements will eventually bring down costs of production as we've seen in other fields, such as computing. Once a disruptor can make a product cheaper using bioengineering methods than using traditional ones, it will push faster into the mainstream.

Constraints on adoption: Even if a technology is maturing, constraints on its adoption can hinder its influence in an industry. For example, a business may refuse to adopt an alternative bioengineering technology because it challenges an existing successful strategy.

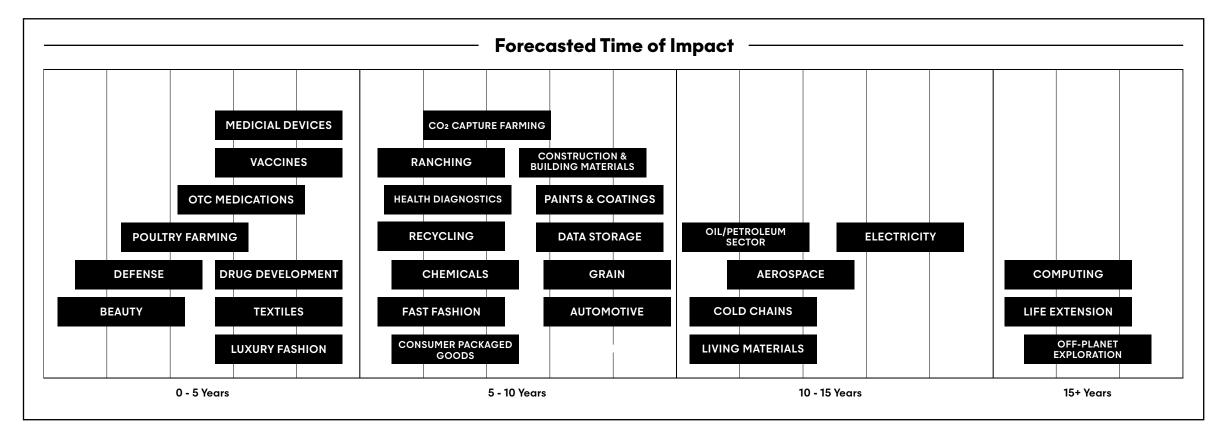
Regulations: The pace of technology advancement typically far exceeds any changes to regulation. Bioengineering is unique in that regulation exists, but products and processes are treated differently in every country. Regulatory and policy uncertainty could accelerate or stifle growth.

Media mentions: Increased awareness and enthusiasm can influence the momentum of a technology, even when there's been no real breakthrough. The metaverse, which few were talking about prior to Mark Zuckerberg's announcement about it in October 2021, is now ubiquitous thanks to intense media attention. Funding rounds followed, which accelerated development, testing, and commercialization. Media bursts related to bioengineering will drive momentum, especially if those stories are favorable and—importantly—easily understood by the general public.

Public perception: How the public understands, and responds to, bioengineering advancements will create or quell demand. This is especially true for food and beverage, consumer packaged goods, beauty and fashion, overthe-counter medicines and vaccines, and new therapeutics.

R&D developments: The pace of new research breakthroughs can't be scheduled to coincide with a board meeting or earnings report. Factors like funding, quality and size of staff, and access to resources can improve the likelihood and speed of new discoveries. We closely monitor R&D developments but treat them as wild cards.

When Will Bioengineering Disrupt Your Industry



Source: FTI research, expert interviews

Breaking Down the Bioeconomy

Advancements in related technologies, including artificial intelligence, will act as a force multiplier as bioengineering technologies develop, as will new policies that incentivize development and growth.

Economic Impact

Funding begets funding, and real-world use cases beget adoption and commercialization. Because bioengineering is an enormous field with a fast-moving collection of technologies, it's challenging to project its total economic impact. For example, the size of the global market for CRISPR genome editing is projected to exceed \$4 billion by mid-decade, while in the US alone it could reach \$18.9 billion by 2031. Transcriptomic technologies, which are used for drug discovery and development, cell biology, single cell analysis, and gene expression, are projected to exceed \$33 billion globally by 2031.

We do know that in the coming decade, as new products and services scale, all five anchors of bioengineering will create significant new value for the global economy. In 2023, the biomolecules arena will continue to develop faster than the others thanks to growing investor activity and a burgeoning field of viable startups.

Based on viable technologies and use cases that exist today, estimates of the combined total economic impact of bioengineering range from \$2 trillion to \$4 trillion per year beginning in 2030.

Emerging Risks

Increasing tensions between the US and China, as well as the unintended consequences of genetic manipulation, are ongoing risks.

Biology is Unpredictable

Biology is highly interconnected, and it tends to self-sustain, even when we don't want it to. Creating a minimal viable genome, or any other novel organism, could lead to a cascading effect and be impossible to manage in the wild. One concern has to do with what's called outcrossing, which is what happens when engineered genes mix with wild populations and native species. Outcrossing could lead to new types of weeds that could kill endemic plants, for example, or to a new pathogenic microorganism that could spread disease to insects, birds, and other animals. A lab accident, or a containment breach, could result in today's harmless laboratory bacterium becoming tomorrow's ecological catastrophe.

Novel Viruses

There is also the specter of personal viruses, engineered to deliver genetic code to just one person or group of people. A landmark 2021 study showed how CRISPR could be used to edit DNA while it's still inside patients' bodies, in that case restoring vision to people with a rare genetic disease that causes blindness. In people with this disease, a defect in the CEP290 gene slowly destroys light-sensing cells in the retina until little healthy tissue is left. Eventually, the retina becomes just a tiny porthole to the outside world (imagine the tip of a sharpened pencil). Because retinas are extremely complicated and fragile, doctors cannot replace them with a transplant; extracting cells to manipulate them in a lab is also too challenging. So instead, researchers built a beneficial virus to carry new genetic instructions that told the cells to perform CRISPR on their own inside the retina. (Viruses are just containers for biological code, so they can be beneficial or detrimental.) They injected billions of copies of this virus under the retinas of a small number of people with this form of blindness, and so far, the experiment seems to be a success. CRISPR has acted like a microscopic surgeon, editing the CEP290 mutation to produce a protein that can restore light-sensing cells and, eventually, the patients' vision. This is a thrilling, groundbreaking studybut given the propensity for dual use, other viruses could plausibly be engineered to cause mutations rather than correct them.

Geopolitical Tensions

The US and China both see bioengineering as critical to the futures of their national security and economic growth. In September 2022, President Biden signed an executive order establishing a biotechnology and biomanufacturing initiative. Versions of the EO had been proposed during both the Obama and Trump administrations, but the COVID-19 pandemic created a new sense of urgency. Today, more than 70% of drug ingredient manufacturing facilities registered with the US Food and Drug Administration are outside the country, while 13% are in China, so reshoring the production of active pharmaceutical ingredients, fertilizers, and other agricultural materials has taken center stage.

That same month, the Biden administration announced a new biomedical research agency called the Advanced Research Projects Agency for Health, or ARPA-H, which is modeled after the storied Defense Advanced Research Projects Agency (DARPA). Around Washington, ARPA-H is being touted as a "Shark Tank" for biomedical research, and part of its mission is to break new ground on myriad untested

approaches. Congress has allocated \$1 billion for ARPA-H so far, and it's being led by DAR-PA alums and former bioengineering industry executives.

The policy and the new agency will spur domestic development, but they've also created new geopolitical tensions with China, whose drugmakers and biologic manufacturing companies were a central component of US manufacturing. Exploiting the learnings from the success of its rapid, global 5G expansion, China named biotechnology as an area of strategic importance, and its 14th Five-Year Plan specifically highlights the bioeconomy as part of its road map to the future.

Through policy and incentives, China is supporting a vast domestic biotechnology ecosystem. It is creating the world's largest colonies of genetically altered or replicated nonhuman primates, which will give it a strategic advantage in bioengineering research, testing, and new product development. China is also building the largest national genomic database in the world and restricting both the export—and outside use—of its data.

Why bioengineering trends matter to your organization

Future Today Institute research suggests that bioengineering is maturing into a disruptive force that will affect nearly every industry in the coming decade. By 2030, most people in developed economies will have likely eaten, been treated by, or worn a product created with a bioengineering technology. Businesses must gain an understanding of the promise and peril of bioengineering today so that leaders can develop new approaches to products and processes, improve materials, reduce costs, and ultimately remain competitive.



Bioengineering is a modern "general purpose technology" that has the potential to influence entire economies and to alter society through political, economic, and social structures.

Innovations in biotechnology are currently defined by five key areas: biomolecules, biosystems, biomaterials, biocomputing, and biomachine interfaces. Major breakthroughs in one field either reinforce or accelerate breakthroughs in the others.

Based on viable technologies and use cases that exist today, estimates of the combined total economic impact of bioengineering range from \$2 trillion to \$4 trillion per year beginning in 2030.

Advancements will result in optionality for carbon capture, plastics recycling, and biodiversity improvement.

INSIGHTS

Ethical concerns around genetic engineering have yet to be resolved; this could prove to be a challenge as new techniques, such as genetic surgery, become available to the public.

There is no singular global framework governing bioengineering. As a result, we can anticipate geopolitical conflict stemming from the development and use of emerging bio-based technologies in the years to come.

Emerging trends in synthetic biology, CRISPR, artificial intelligence, and engineering will result in new opportunities for health care, pharmaceuticals, agriculture, food and beverage, beauty, chemicals, sustainability, energy, and materials production industries.

Disruptions to conventional meat and dairy production, textile manufacturing, and pharmaceutical development are on the near-term horizon.

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IMPORTANT TERMS

Cas9 (CRISPR associated protein 9)

A special enzyme that can cut DNA sequences. Cas9 is part of the "molecular scissors" method of genome editing made possible by CRISPR.

Chimera

A living organism created by combining cells from at least two genetically different organisms.

Chromosome

A thread-like structure made up of a single length of DNA and found in the nucleus of each cell.

CRISPR (clustered regularly interspaced short palindromic repeats)

A naturally occurring genetic engineering tool found in bacteria that can be programmed to target specific areas of genetic code and to edit DNA at precise locations.

DNA (deoxyribonucleic acid)

A self-replicating two-stranded molecule, arranged as a double helix, that contains the genetic instructions used in the development, functioning, and reproduction of an organism.

Enzyme

A biological catalyst, usually a protein. Enzymes speed up the rate of specific chemical reactions in cells.

Ex vivo

Outside of cells or an organism.

Gain of function (GoF) research

Research intended to modify a biological pathway in a cell line or organism to enhance or increase certain biological functions.

Gene

The basic unit of heredity.

Gene editing

Intentionally altering cells or organisms by inserting, deleting, editing, or otherwise modifying a gene or gene sequence.

Genome

The complete set of DNA that makes up an organism.

Genome editing

Altering, inserting, deleting, or replacing a DNA sequence.

Heritable genetic change

Altering genes in a way that results in changes that pass down through generations.

In vivo

Inside of cells or a living organism.

Induced pluripotent stem cells (iPSC)

Cells that have been reprogrammed back into an embryo-like state with the potential to develop into other types of cells that can be used for therapeutic or reproductive purposes.

Mutation

A change in a DNA sequence.

Off-target effect

An unintended direct or indirect consequence of altering an organism.

Regenerative medicine

An emerging field seeking to repair or replace torn, defective, or missing tissue using stem cells, engineered cells, or biological processes.

RNA (ribonucleic acid)

A messenger chemical that carries instructions or translates the genetic code of DNA into structural proteins.

Stem cells

Nonspecialized cells that have the ability to develop into other types of cells with specialized functions.

Synthetic biology

A field of science rooted in both biology and engineering that seeks to redesign organisms, or design new organisms, to have new abilities.

ONES TO WATCH

Dr. Ali Nouri, assistant secretary for congressional and intergovernmental affairs at the US Department of Energy, for developing policies and initiatives to govern the future of biotechnology.

Dr. Amy Trejo, director of R&D, responsible materials innovation at Procter & Gamble, for leveraging bioengineering for sustainability in consumer goods.

Dr. J. Craig Venter, founder and CEO of JCVI and serial entrepreneur, for advancing the fields of synthetic biology and genomic research.

Dr. Drew Endy, associate professor of bioengineering at Stanford University, for his pioneering research in genetic logic, rewritable DNA data storage, and development of standard biological parts, among other innovations.

Eben Bayer, co-founder and CEO of Ecovative, for innovating business models to integrate mycelium technology into the production of food and materials.

Dr. Emily Leproust, CEO of Twist Bioscience, for breaking new ground in high-throughput synthesis and sequencing of DNA.

Dr. Emmanuelle Charpentier, co-founder of CRISPR Therapeutics, for her pioneering research on CRISPR and her current research and commercial projects.

Dr. Gaurab Chakrabarti, CEO and founder of Solugen, for his work applying synthetic biology to decarbonize the chemicals industry.

Dr. George Church, lead for Synthetic Biology at the Wyss Institute and serial entrepreneur, for advancing the field of synthetic biology into myriad research, industrial, and consumer application paths. In 2023, watch for updates on his de-extincting technology.

Dr. Hal Barron, Dr. Rick Klausner, and Hans Bishop, founders and CEO of Altos Labs, for leading a new effort on cellular rejuvenation programming to reverse the human aging process.

Dr. Demis Hassabis and Dr. Shane Legg, cofounders of DeepMind, for their groundbreaking AlphaFold AI program that predicts a protein's 3D structure.

Dr. Jason Kelly, co-founder and CEO of Ginkgo Bioworks, for scaling genetic engineering to produce bacteria with a wide variety of applications.

Dr. Jennifer Doudna, principal investigator at Doudna Lab at University of California, Berkeley, for her pioneering research on CRISPR and her current research and commercial projects.

Dr. Jianmin Fang, co-founder, CEO, and CSO of RemeGen, for overseeing one of the largest partnership deals between a Chinese biotech company and a Western company (Seagen) in history.

John V. Oyler and Dr. Xigodong Wang, co-founders of China-based BeiGene, for finding creative ways to comply with new US laws passed in 2022 requiring auditing and inspections.

Josh Tetrick, co-founder and CEO of Eat Just, for commercializing cultured meat. In 2023, watch as a new market develops for cultured meat production, distribution, and restaurants in Singapore.

Dr. Lisa Dyson, founder and CEO of Air Protein, for her work developing food from carbon dioxide.

Dr. Mary Maxon, executive director of BioFutures at Schmidt Futures, for developing and leading a new program to maximize the potential of biotech for a circular bioeconomy.

Dr. Michael Fisher, senior fellow at the Federation of American Scientists, for his work on science and technology policy, with a focus on the future of the bioeconomy.

Dr. Michelle Holko, principal architect for Google Cloud's Healthcare and Life Sciences solutions, for her work on the futures of biotechnology and cybersecurity.

Dr. Nikhita Singh, co-founder and chief product officer of Artificial, for building automation infrastructure and tools for the futures of biotech

Niya Gupta, co-founder and CEO of Fork & Good, for developing models to scale cultured meat while making it affordable to all.

Dr. Patricia Bubner, founder and CEO of Orbillion Bio, for her work in cell-cultured meats.

Dr. Yin Ye, vice chairman of the board of BCI Genomics, for scaling DNA sequencing.

Dr. Yves Falanga, entrepreneur in residence at EcoR1 Capital, for leading discovery immunology projects in biotech.

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BIOENGINEERING PIATEORNS

BIOENGINEERING PLATFORMS

CHEAPER GENOME SEQUENCING

The first human genome cost roughly \$2.7 billion and took 13 years to complete. In 2012, it cost about \$10,000 for researchers to sequence a full genome. Today, you can sequence your genome from the comfort of your home for less than you'd spend on a Black Friday TV deal. Late in 2022, genomics giant Illumina revealed its latest product: the NovaSeg X series, which the company says will slash the cost of sequencing to just \$200 per human genome at twice the speed of existing systems. This is a significant development: Faster, cheaper genome sequencing will lead to new genetically targeted drugs, diagnoses for people with rare diseases, and new diagnostics for cancers. As the cost of sequencing decreases, researchers will be able to diversify genomic data sets, which are primarily made up of DNA from people of European descent. Illumina has competitors: California-based Ultima Genomics came out of stealth with new technology that will sequence genomes for \$100 starting in 2023, and Chinese company MGI started selling lower-cost machines in 2022.

MAPPING THE HUMAN GENOME

When the first human genome was deciphered

two decades ago, it was not entirely complete. That's because roughly 200 million bases of DNA, or about 8% of the human genome, weren't yet readable. Many stretches of DNA weren't readable by sequencing machines because they had repeating segments or were simply too challenging to be recognized and cataloged. As technology improves, so will our ability to map a more detailed version of human life on a granular scale. The Telomere-to-Telomere Consortium, aptly named after the end caps of chromosomes, published a new set of papers in 2022 that identified all but five of the hidden areas of the map. Using various sequencing technologies, including a novel nanopore device capable of reading 100,000 bases at a time alongside a sequencer with improved accuracy, researchers discovered new areas for gene evolution. In 2023 and beyond, scientists will gain new insights into regions of the human genome that haven't been explored fully, which should in turn reveal discoveries about human evolution, longevity, and resiliency.

SEQUENCING ANCIENT GENOMES

Archaeology and genetics are merging, with insights about the history of life on Earth. Ar-

chaeogenetics, as the field is known, is working to extract DNA from ancient bones to reveal secrets about our ancestors. The 1000 Ancient Genomes project, led by Pontus Skoglund at the Francis Crick Institute in London, recently analyzed the DNA of a 10,000-year-old skeleton found in Somerset, England. The sequence showed that he likely had dark skin and blue eyes, a genetic combination that might have been common millennia ago but today is rare. Sequencing ancient genomes will help historians develop a more accurate understanding of what society might have been like thousands of years ago and how we compare today.

FASTER GENE SYNTHESIS

Synthesis transforms digital genetic code into molecular DNA, allowing scientists to design and mass-produce genetic material. This is what Twist Bioscience does to form as many as 300 base pairs of DNA. Joining these snippets, or oligos, forms genes. Both the price for oligos and time to produce them is decreasing—even while the length and complexity of base pairs is increasing. It now costs an average of just seven cents per base pair—a 22% decrease year over year. The DNA snippets produced by Twist can be ordered online and shipped to a lab within

days; the synthetic DNA is then inserted into cells to create target molecules, which are the basis for new food products, fertilizers, industrial products, and medicine.

MACHINE LEARNING-POWERED DRUG **DISCOVERY**

COVID-19 accelerated the use of machine learning (ML) in drug discovery. Computer-modeled simulations and pattern recognition have led to new insights about molecular behavior, while groundbreaking discoveries from DeepMind's AlphaFold last year provided a new window into protein structure prediction. A few technical challenges have limited the broader use of ML, including a lack of massive, quality data sets. Some biotech startups are addressing the gaps using generative algorithms that can custom-design a molecule from scratch (think: Lensa, the mobile app that makes AI selfies, but for biology). South Korean startup Standigm uses AI to generate novel chemical compounds with desired properties. Once it identifies candidates, it runs simulations to discover therapeutic patterns and to prioritize potential targets. (See our Artificial Intelligence trend report for additional research for AI-enabled drug discovery.)

experts in both fields hoping to surface new

BIOENGINEERING PLATFORMS

NEW CRISPR TOOLS

Though it makes the most headlines, CRIS-PR-Cas9 isn't the only gene-editing tool available to researchers. In fact, Cas9 is just one of many CRISPR-Cas systems. Late in 2022, a massive audit of viral genomes surfaced a treasure trove of potential CRISPR-based genome-editing tools. Some of the systems appear to be able to edit mammalian and plant genomes, which could make them attractive as next-gen gene-editing tools. Viral Cas enzymes could soon join a growing toolkit of gene-editing tools discovered in microbes. Some biotech startups have used machine learning to reveal how novel Cas nucleases (Cas12 and CasX) might improve CRISPR editing. MIT researchers designed a new CRISPR-based tool capable of snipping out faulty genes—as long as 36,000 DNA base pairs—and inserting large DNA sequences at desired sites in cells. This new technique, known as PASTE (programmable addition via site-specific targeting elements), could target hard-to-treat diseases caused by defective genes with a large number of mutations.

CELL THERAPY 2.0

For more than a decade, researchers have transplanted healthy, viable cells to replace or repair damaged ones. Most notably, cellular therapy has shown promise in helping a person's immune system fight cancer. But cellular therapy carries associated risks ranging from flu-like symptoms to death. The field is evolving, and two emerging techniques are pushing cell therapy into its next era. One is in vivo cell therapy, which helps patients produce cells that can bind to specific proteins on the surface of cancer cells. Researchers at the Department of Health and Nursing in Nanfang College of Sun Yat-sen University and at Huazhong University of Science and Technology, both in China, loaded nanocarriers with a new set of genetic instructions and successfully regressed leukemia in a mouse. The second technique involves engineering synthetic gene circuits to protect healthy cells when delivering cellular therapy. CAR T-cells can be lethal to cells they encounter, whether they're cancerous or not. A new method of controlling cell therapy using engineered networks would offer doctors better precision.

PROGRAMMABLE GENE-EDITING PROTEINS

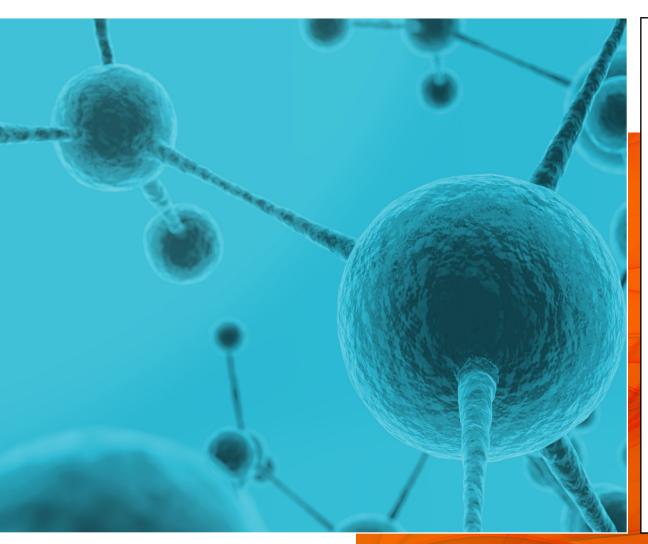
Scientists at MIT's McGovern Institute and the Broad Institute of MIT and Harvard have discovered a new class of programmable DNA-modifying systems called OMEGAs (Obligate Mobile Element Guided Activity), which could move small bits of DNA throughout bacterial genomes. A new editing enzyme among a family of proteins called IscB is a potential ancestor of Cas9. IscBs were the first proteins in an OMEGA system. In nature, these genes might be performing a wide variety of functions that scientists are only starting to understand; inside a lab, this opens a host of new possibilities to adapt biology for different tasks. Think of OME-GAs as accelerators for the next generation of genome-editing tools.

PRIME EDITING

A new technique called prime editing could make the gene-editing process much more precise and result in more accurate modifications. As impressive as CRISPR is, it can sometimes change the wrong genes or accidentally break apart strands of a DNA's double helix. The refinement to CRISPR affords more precision and versatility. One obstacle to making use of prime editing is that it requires a large protein, but in 2022 researchers at Massachusetts General Hospital created a system called Split Prime Editing, which improves on existing techniques. This should accelerate the optimization and application of prime editing for research and therapeutic uses and enable more researchers to access this technology in the near future.

BIOMOLECULES

BIOMOLECULES



ON-DEMAND MOLECULES

Scientists now use synthetic biology to discover and produce molecules on demand. DARPA and the MIT-Broad Institute Foundry proved that new molecules can be rapidly generated for practical use. In a research challenge, teams used artificial intelligence and synthetic biology to deliver six out of 10 requested designer molecules in just 90 days. That length of time will shorten as more efficient methods are used to discover different molecule types and produce materials as needed. Boston-based startup Generate Biomedicines has trained an AI called Chroma to invent proteins with structures that, as far as we know, don't exist anywhere in nature. Inspired by DALL-E 2, the powerful textto-image AI system from OpenAI that allows anyone to create photorealistic images based on short text prompts, Generate's system asks the user to describe the shape, size, and function of a protein they'd like to see. It then uses diffusion modeling to generate a structure with the right amino acids folded correctly to meet the description.

QUANTUM BIOLOGY BREAKTHROUGHS

Quantum biology seeks to investigate processes in living organisms that can't be described by the classical laws of physics. Electrons, protons, and chemical bonds are quantum, and to understand their dynamics we need quantum mechanics. Physicists know that a single particle can interfere with itself because of a famous experiment years ago in which scientists passed the same particles simultaneously through two different slits in a wall. Although there were two spaces open for particles to pass through, each individual electron formed into a pattern that looks like the interference pattern of a wave. Researchers at the University of Vienna wondered if this physics experiment might inform biology. They watched a chain of amino acids interfere with itself in molecules of gramicidin, a natural antibiotic made up of 15 amino acids. This discovery has paved the way for scientists to study the quantum properties of biomolecules—and will lead to new research exploiting the quantum nature of enzymes, DNA, viruses, and more.



Humans can be better than they are, so let's do that.

JAMES S.A. COREY, CALIBAN'S WAR

BIOSYSTEMS

BIOSYSTEMS

ORGANOIDS

It's difficult and dangerous for scientists to study how living human tissue responds to viruses, medications, or other stimuli: Brain or heart tissue can't be removed from a living person. As an alternative, scientists are creating organoids tiny three-dimensional, multicellular clusters grown from human stem cells that resemble complex tissues like those of major organs. One of the fastest-moving areas is brain research. Since 2008, when researchers created the first cerebral organoids to provide more understanding of brain functions, cerebral organoids have been used in research on autism and on diseases such as the Zika virus. Researchers at Stanford University and the Chan Zuckerberg Biohub created human forebrain organoids (the forebrain is the part of the brain responsible for thinking, perceiving, and evaluating our surroundings). There are two current schools of thought on how to create organoids: Grow them from human tissue, or create animals with human-derived neurons in their bodies. Research is underway elsewhere that would transplant bits of human brain organoids into rats, which raises both complex ethical concerns and, perhaps, fears of super rats that process information as well as humans do. Organoids

aren't conscious (yet), and as experimentation progresses, scientists must develop ethical standards.

COVID-19 ORGANOIDS

Lab-grown lung and brain tissues are being used to research the lasting effects of SARS-CoV-2, the COVID-19 virus. Miniature guts and livers are also being grown in high-security labs and infected with the virus, as are combinations of different organs to test therapies and the lasting effects of long-haul Covid. In 2022, scientists at the Karolinska Institute in Sweden infected brain organoids with SARS-CoV-2 and discovered that brain fog could be caused by the destruction of connections between neurons. Neurobiologists at the UK's MRC Laboratory of Molecular Biology in Cambridge used organoids to learn that SARS-CoV-2 damages the protective barrier of the brain.

ORGAN-ON-A-CHIP

Picture something like a computer chip, but with a transparent circuit board that's connected to a biological system pumping a blood substitute through tiny blobs of tissue. Organ-on-a-chip systems (OoCs) are synthetic organs made of multichannel, three-dimensional microfluidic

cell culture technology that promotes organ functions, processes, and physiological responses. It turns out that these chips are better at predicting real-world responses in humans than the use of conventional lab animals. Researchers in South Korea developed an artificial nervous system that can simulate a conscious response to external stimuli. It includes an artificial neuron circuit, which acts like a brain; a photodiode that converts light into electrical signals; and a transistor that acts as a synapse. All of these components are connected to a robotic hand. More hardware than wetware at the moment, this type of a system could help people with certain neurological conditions regain control of their limbs. It could eventually be worn or even embedded. In 2022, Emulate, a company that makes OoCs, tested 870 human liver-chips across a blinded set of 27 drugs with known toxicity issues—and the chips did a better job of predicting drug safety than the usual methods of studying drug interactions. A team of bioengineers at Harvard University used donated vaginal cells to make a vagina on a chip in late 2022. The chip successfully mimicked the vaginal microbiome and is actually more accurate than other existing models being used in labs. OoC academic research and startups are

attractive to both venture funding and foundations, which view the technology as foundational to new drug discovery.

MICROBE ENGINEERING-AS-A-SERVICE

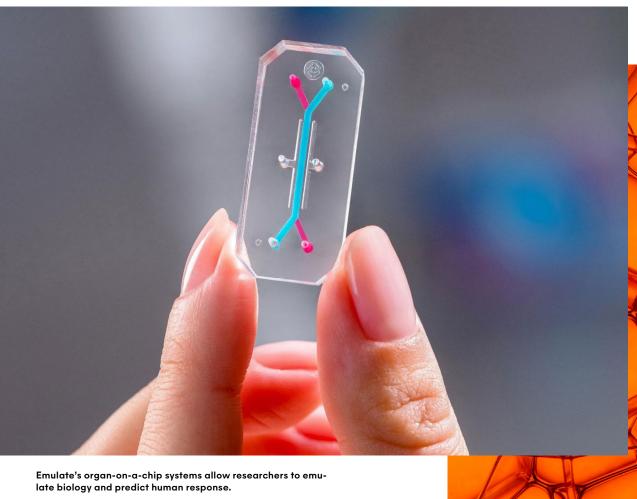
Synthetic biology is an emerging field that builds new life, including replacement organs and soft tissue as well as entirely new kinds of organisms never before seen on Earth. At the end of 2022, Ginkgo—which is now the leading platform for cell programming—launched a new division to develop custom enzymes. By using machine learning-guided protein design and proprietary bacterial and fungal host strains, researchers hope to soon develop myriad applications, like fabrics that dissolve after one wear to reduce washing, which requires water and environmentally unfriendly detergents.

MINIMAL VIABLE LIFEFORMS

To understand how new organisms might be created, scientists have long pursued developing an MVP—minimal viable product—for biology. In 2010, scientist J. Craig Venter and his team announced an astonishing discovery: They could destroy the DNA of an organism called Mycoplasma capricolum and replace it with DNA they had written on a computer that

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BIOSYSTEMS



Source: eurekalert.org/multimedia/750904

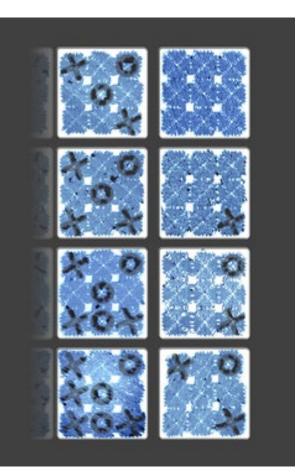
was based on a similar bacterium, Mycoplasma mycoides. Venter's team named their 907-gene creature JCVI-syn1.0, or Synthia, for short. It was the first self-replicating species on the planet whose parents were, technically, computers, and the project was designed to help the team understand the basic principles of life, from the minimal cell up. In 2016, Venter's team created JCVI-syn3.0, a single-celled organism with even fewer genes-just 473-which made it the simplest life-form ever known. The organism acted in ways scientists hadn't predicted. It produced oddly shaped cells as it self-replicated. Scientists came to believe that they'd taken away too many genes, including those responsible for normal cell division. They remixed the code once again, and in March 2021 announced a new variant, JCVI-syn3A. It still has fewer than 500 genes, but it behaves more like a normal cell. Now, researchers are working to strip down the cell even further, and have developed a new synthetic organism, M. mycoides JCVI-syn3B, which evolved for 300 days, proving that it could still mutate. There were many significant developments in 2022. Researchers at Osaka Metropolitan University created a synthetic bacterium capable of swimming by introducing seven proteins into it. With minimal genetic information,

the spherical synthetic bacteria are thought to be the smallest mobile life-forms to date. These minimal viable organisms will help researchers design the future of life from first principles.

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BIOMACHINE INTERFACES

BIOMACHINE INTERFACES



Researchers at the California Institute of Technology made the world's smallest Tic-Tac-Toe game board out of DNA. (Artist rendering.)

Image courtesy of Caltech

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LIVING ROBOTS

In 2020, a cluster of stem cells from an African clawed frog served as the base for a fortuitous experiment involving a supercomputer, a virtual environment, and evolutionary algorithms. Researchers created 100 generations of prototypes before they had a tiny blob of programmable tissue called a xenobot. These living robots can undulate, swim, and walk. They work collaboratively and can even self-heal. They're tiny enough to be injected into human bodies, travel around, and—maybe someday—deliver targeted medicines. While xenobots are technically made up of living cells, researchers are quick to point out that they lack the characteristics of a traditional biological life-form. In 2021, xenobots got a design upgrade and new capabilities. While they previously needed the contraction of heart muscle cells to move forward, upgraded xenobots can self-propel using tiny hairs on their surfaces. In 2023, a third generation of xenobots will live longer and be able to sense what's in their environment. They will also be able to operate in robot swarms to complete a collaborative task. Xenobots are being used to help researchers understand how defects in the hairlike structures in our lungs, called cilia, can result in diseases. Also in progress: xenobots that

can travel to a damaged spinal cord and repair it with regenerative compounds. Meanwhile, another type of living robot, the anthrobot, was developed in 2022 from donated human tracheal cells. Covered in cilia, these anthrobots harnessed the structures like flexible oars to propel themselves around. When the bots were grown in a petri dish, scientists discovered they could be assembled into super-anthrobots to perform tasks; a team at Tufts University grew a sheet of human neural cells and scratched a few off to create a defect roughly a millimeter wide, and super-anthrobots on the other side catalyzed healing.

LIVING SENSORS

Research is already underway to develop biosensors that can detect deadly bioweapons on the battlefield and harmful chemicals in factories. What's new for 2023: biosensors that can detect the presence of specific DNA sequences. Researchers at the University of California, San Diego created a bacterium called Acinetobacter baylyi capable of detecting a single DNA letter mutation in a gene that's present in many cancers. With a focus on the microbiome, they engineered the bacterium to detect mutated DNA sequences while living inside of the gut. While

still very early in development, living sensors could someday be used to detect viral outbreaks in a community's sewage system, cholera in drinking water, and other pathogens.

NANOMACHINES

Molecular robotics will someday be used on all life-forms to provide targeted therapies as well as genetic augmentation. Scientists at Harvard's Wyss Institute discovered that both robots and our DNA can be programmed to perform tasks. Molecules can also self-assemble and react to their environments. A team of scientists at Arizona State University and Harvard created single-stranded DNA that can self-fold into origami-like shapes. It turns out that RNA can be used, too—and both can be produced inside living cells. Scientists at the California Institute of Technology built a DNA-based version of tictac-toe with self-assembling DNA origami tiles. In 2022, researchers designed proteins that can self-assemble into a molecular engine (think: axles and rotors, but for biology). Programmable molecular machines could be used to repair damaged cells and unclog arteries. Dozens of projects to create DNA or protein-based nanomachines are now underway.

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BIOCOMPUTING

BIOCOMPUTING



Microsoft's DNA Storage project enables molecular-level data storage into DNA molecules by leveraging biotechnology advances to develop archival storage.

BIOLOGY PLAYS GAMES

In 2022, scientists at the Spanish National Research Council genetically modified a strain of E. coli called Marionette so that it could sense different chemicals and respond to them. This version of the strain could be controlled by the research team; if they altered the activities of genes, the E. coli would behave as directed. The researchers also modified the strain so that its plasmids each encoded for a different fluorescent protein (red and green). The ratio of the red and green wasn't predetermined, and it could be altered with future chemical inputs. Without inputs, the ratio would simply stay constant and, in a way, was a form of memory. When there was a new input, the resulting color would be determined by the previous ratio. Here's where things got interesting: The researchers taught the Marionette strain how to play tic-tac-toe. They grew the bacteria in eight wells that correspond with the outer squares of a grid, and instructed the bacteria to play the game. Initially, they played randomly, but the Spanish National Research Council team trained the bacteria by adding chemicals to the squaresand after eight sessions, the bacteria played at an expert level. While the bacteria haven't yet beat humans at tic-tac-toe, there's an interesting analogy worth remembering: The benchmarks in computing, and specifically in artificial intelligence, have always been gameplay. This isn't the only biological computer. Last year, a biocomputer called DishBrain learned how to play the 1980s video game "Pong." DishBrain is made of about 1 million live human and mouse brain cells grown on a microelectric array that can receive electrical signals. The signals tell the neurons where the pong ball is, and the cells respond. The more the system played, the more it improved. In 2023, we expect to see further demonstrations of new, simple forms of neural networks made from biology.

BIOLOGICAL CIRCUITS

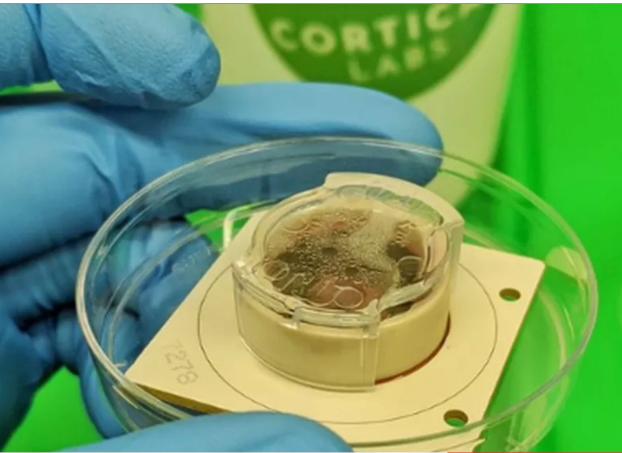
Scientists are in the process of building biological circuits, made of synthetic DNA, and the software that operates them. A program called DNAr, developed at the Federal University of Mato Grosso do Sul in Brazil, simulates chemical reactions, while another called DNAr-Logic enables scientists to design circuits. A high-level description of a logical circuit is then converted into a chemical-reaction network, which can be synthesized into DNA strands. By dramatically speeding up the design process for biological circuits, scientists could also speed up the time

it takes to discover health treatments and new drugs.

USING DNA TO STORE DATA

In 2018, scientists from Microsoft Research and the University of Washington achieved a new milestone: They discovered how to create random access memory on DNA at scale. They encoded 200 megabytes of data on human DNA—including 35 video, image, audio, and text files ranging from 29 kilobytes to 44 megabytes. In 2021, the team built a molecular controller and DNA writer on a chip, with a PCIe interface. Microsoft used the system to store a version of the company's mission statement in DNA: "Empowering each person to store more!" The Intelligence Advanced Research Projects Activity, a group within the Office of the Director of National Intelligence, intends to store an exabyte of data—roughly a million terabyte-size hard drives—in a blob of DNA. It's a weird branch of biological science, yes, but human computing has practical purposes: DNA could solve our future data storage problems. It's durable, too: Evolutionary scientists routinely study DNA that is thousands of years old to learn more about our human ancestors. Chinese scientists at Tianjin University stored 445KB of data in an

BIOCOMPUTING



Cortical Labs created DishBrain to push the boundaries in biological computing.

Photo courtesy of Cortical Labs

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E. coli cell. Twist Bioscience discovered how to make hyperdense, stable, affordable DNA storage. By depositing microscopic drops of nucleotides onto silicon chips, Twist's robots can create a million short strands of DNA at a time. The end result will be a tiny, pill-size container that could someday hold hundreds of terabytes of capacity. Now, a consortium called the DNA Data Storage Alliance is developing an interoperable storage ecosystem using DNA as a data storage medium. Founders include Microsoft, as well as Western Digital, Twist, and Illumina. Members of the consortium, including Los Alamos National Laboratory, Seagate, FujiFilm, Dell Technologies, Lenovo, IBM, and the University of Arizona's Center for Applied Nanobioscience and Medicine, are hoping to write megabytes of data per second on synthetic DNA that will be readable for thousands of years.

MANAGING THE LOOMING **GENOME STORAGE PROBLEM**

One of the fastest-growing data sets in the world comprises human genetic data. By 2025, we may be out of data storage space for human genomes, according to estimates by the University of Illinois at Urbana-Champaign. As precision medicine, CRISPR, and gene therapy technologies continue to advance, our storage needs will explode, along with the computing power and requirements for acquiring, distributing, analyzing, encrypting, and safeguarding our genomics data. As technology increasingly intertwines with biology, inadequate storage capacity and insufficient technology workflows for storing all that data become ever more urgent issues—and the lack of planning so far becomes ever clearer. Australia's Garvan Institute of Medical Research is looking into processes and workflows to reduce the genomic data footprint.

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In 10 years, there will be organ printers in the finest hospitals around the world.

PROFESSOR TAL DVIR,

WHO LED A RESEARCH TEAM THAT 3D-PRINTED THE FIRST VASCULARIZED HEART

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PATHOSEN TRENDS

PATHOGEN DETECTION



Environmental DNA (eDNA) is used to identify living organisms present within an ecosystem.

Image courtesy of FISHBIO/fishbio.com.

CRISPR DIAGNOSTICS

In addition to making edits, CRISPR also allows fast detection of pathogens by identifying sequences in their DNA or RNA. In many diagnostic systems, human pathogens are found using real-time polymerase chain reactions, which is an accurate—but time-consuming and expensive—method. Special enzymes, known as Cas enzymes, can be used to diagnose pathogens such as SARS-CoV-2. Researchers at the University of California, San Diego developed a rapid diagnostic technology that detects SARS-CoV-2 using CRISPR. In early tests, detection took less than an hour.

eDNA DETECTION

Environmental DNA, or eDNA, is genetic material found in the environment. Feces and fur from animals, as well as hair and saliva from humans, are just some of the organic matter found in soil, seawater, snow, and air. As a fish moves through water, it is continuously shedding bits of itself. Likewise, when a cyclist rides on a trail, her sweat, mucus, and dead skin cells wind up mixed into the gravel and dirt. These fragments of nuclear or mitochondrial DNA can reveal invaluable insights about an environment. Sci-

entists from the United States Geological Survey and the Monterey Bay Aquarium Research Institute are developing a new mobile eDNA sampler that can float through rivers and streams collecting material and detecting pathogens or invasive species autonomously. As detection systems advance, eDNA detection will serve as an early warning system for potential outbreaks of diseases. But there's another interesting use for eDNA: reconstructing ancient ecosystems. In 2022, scientists excavated eDNA from frozen soil in the Arctic desert and were able to piece together a lost world nearly 2 million years old. The eDNA revealed a coastal forest with conifers, black geese and horseshoe crabs, lemmings and mastodons—a natural wonderland unlike any in existence today.

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APPLICATIONS

HEALTH APPLICATIONS

GROWING BLOOD

For people who live with rare blood types (AB negative, AB positive, B negative) or who have blood disorders, access to blood for surgery or a transfusion can mean the difference between life and death. Scientists have for decades attempted to grow blood cells in a lab at scale, but the process has until recently failed to produce enough to make an impact. Late in 2022, scientists at the National Health Service Blood and Transplant in the UK announced that they had grown red blood cells in a lab and successfully transfused them into a living person, a world first. It took 500,000 stem cells to generate 50 billion red blood cells, which then needed to develop. (A normal range of red blood cells is 3-5.65 million per microliter of blood in a healthy adult.) In 2023, a new study will determine whether lab-grown cells last longer in the body than donated blood cells, and if that's the case, patients who need regular blood transfusions could go longer between treatments. After that, researchers will set their sights on manufacturing lab-grown blood for rare blood types that don't typically have large donor pools.

MRNA VACCINES

The world's most powerful drug manufacturing factory may already be inside you. As genetic material that contains instructions for making proteins, messenger RNA is revolutionizing vaccine development. Unlike traditional vaccines, which use weakened bits of a live virus or bits of dead virus, the Pfizer-BioNTech and Moderna COVID-19 vaccines instead used mRNA to inject updated code in our cells. Long before they were making Covid vaccines, both Moderna and BioNTech were researching immunotherapies for cancer. After analyzing a tissue sample from a cancerous tumor, the companies ran genetic analyses to develop custom mRNA vaccines, which encode protein-containing mutations unique to the tumor. The immune system uses those instructions to search for and destroy similar cells throughout the body, which is similar to how the Covid vaccines work. BioNTech is running clinical trials for personalized vaccines for many cancers, including ovarian cancer, breast cancer, and melanoma. Moderna is developing similar cancer vaccines. In December 2022, the company announced that its personalized cancer vaccine, when combined with Merck & Co's immunotherapy treatment Keytruda, cut recurrence of and risk of death from the most deadly skin cancer compared with immunotherapy treatment alone. In the trial, the mRNA vaccine revved up the immune response. Also in 2022, Pfizer and BioNTech began recruiting volunteers to participate in a Phase 3 clinical trial for an mRNA flu vaccine candidate. The hope is that in 2023, scientists might develop a more accurate flu vaccine to match the virus circulating.

CRISPR-BASED ANTIBIOTICS

Antibiotic resistance is on the rise due to overuse and incorrect application. But a new approach could enable us to tackle antibiotic-resistant infections. CRISPR can be programmed to kill certain bacterial cells that contain specific DNA. Researchers at Canada's University of Sherbrooke demonstrated that a CRISPR-edited bacterium can be used to target an antibiotic-resistant strain of E. coli. When the edited bacteria were given to infected mice, they expelled 99.9% of the E. coli bacteria within four days. In the near future, CRISPR-edited probiotic bacteria could be used to treat bladder and skin infections.

CRISPR THERAPIES

Last year, an experimental CRISPR therapy successfully treated a 13-year-old girl with aggressive leukemia. After receiving a dose of immune cells genetically altered to attack her cancer, the girl, who had not responded to other treatments, showed no detectable cancer cells. It's a preliminary result as of this writing in late 2022, but an extremely promising example of the power of CRISPR therapies. This year, many trials will begin to test the efficacy and range of CRISPR. In some trials, CRISPR is being used to edit T-cells, a type of white blood cell essential for immune system response. T-cells kill foreign or dangerous cells. In CAR-T immunotherapy, researchers genetically engineer a patient's T-cells to have a receptor that recognizes the patient's cancer cells, telling the T-cells to attack. Therapies for eve disease, chronic infection, and even urinary tract infections are in development. CRIS-PR-Cas3, combined with three bacteriophages, successfully killed the strain of E. coli responsible for 95% of UTIs.

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REPRODUCTION & LIFE EXTENSION APPLICATIONS

REPRODUCTIVE AND LIFE EXTENSION APPLICATIONS



AGE REVERSAL

As we age, the sequence of our DNA might stay constant, but chemical changes do occur. Observing those changes could lead to new techniques to halt or even reverse age-related disease. Columbia University researchers discovered that it might be possible to record and store information about cells as they age. The technique, a sort of biological DVR, uses the CRISPR-Cas system over a period of days. In the future, if we can quantify aging at a cellular level, we might be able to reverse it. Synthetic biologist George Church and a team at Harvard's Wyss Institute combined three gene therapies related to cellular decay into a single compound. The intent: reverse obesity and diabetes while also improving kidney and heart function. Remarkably, the technique seemed to work (in mice, at least). Maybe that's why last year there were so many funding and partnership announcements. The Saudi royal family launched the Hevolution Foundation, a notfor-profit with an annual budget of \$1 billion to support basic research on the biology of aging. Meanwhile, the startup Altos Labs is developing biological reprogramming technology. In 2022, Altos, which raised a staggering \$3 billion in funding over just one round, announced a partnership with the Center for iPS Cell Research and Application (CiRA) at Japan's Kyoto University to study cellular rejuvenation programming.

GROWING SEX CELLS

For couples suffering from infertility or for individuals desiring to have a baby without a partner, acquiring donor sperm or eggs can be an expensive, overwhelming process. But what if you could make a baby using only your own genetic material? Thanks to groundbreaking work by Japanese scientist Shinya Yamanaka in 2006, it's now possible to create gametes derived from human-induced pluripotent stem cells. Cells are harvested from a skin biopsy or taken from a blood sample (both quick and relatively painless). Those cells are turned into stem cells, grown in a medium that resembles what would exist in a human womb, and developed into precursor sex cells, which mature into sperm or stem cells. Then, in vitro fertilization kicks in, and those cells are used to create an embryo. One or more of the healthiest embryos are then implanted into the uterus and, if all goes well, develop into a healthy, viable fetus. In 2019, the Japanese government approved research on human-animal embryo experiments, and in 2021 a team of researchers in Israel used an artificial

REPRODUCTIVE AND LIFE EXTENSION APPLICATIONS

womb to grow engineered mouse embryos that lived for 11 days.

SYNTHETIC WOMBS

In 2022, a viral video made some people think they were living in "The Matrix." The video, intended to spark a conversation about engineering life, depicted an artificial womb facility called EctoLife that could produce up to 30,000 babies every year. EctoLife isn't a real company, but synthetic and artificial wombs have already been used in science experiments. In an experiment at Northwestern University's Feinberg School of Medicine, researchers printed and implanted synthetic ovaries in mice that resulted in successful pregnancies. Researchers at the Children's Hospital of Philadelphia created an artificial womb called a biobag and used it to successfully keep premature lambs alive and developing normally for 28 days. For now, synthetic wombs don't look like silicon versions of the real thing—they tend to be pressurized, rotating devices attached to sterilized bottles of nutrients. We are still years away from synthesizing and growing a full-size organic womb, but the biobag represents an intervention that could help the thousands of premature babies born before 25 weeks each year. Or biobags

could eliminate the need for a person to carry a pregnancy at all.

GENETIC SCREENING FOR PREGNANCY

New genetic screening techniques that test embryos before implantation are making their way into fertility centers. California-based MyOme and New Jersey-based LifeView use the genetic sequences of parents, along with cells retrieved during a biopsy, to generate an embryo's entire genome. Next, they use algorithms to calculate the probabilities of certain ailments. Couples can then select embryos based on those results. LifeView provides genetic report cards to would-be parents: They can determine whether the embryo has the right number of chromosomes and review risk-assessment grades for heart attacks, certain cancers, and diabetes. While both companies are disease-focused for now, it is also possible to calculate scores and optimize for other genetic traits such as height and intelligence.

GENE SURGERY

Some diseases don't respond well to drugs. An emerging technique aims instead to fix errors in biological code. Gene surgery replaces defective or missing genes with properly functioning

ones. In 2022, researchers at the University of California, Irvine used precision genome-editing agents to correct inherited retinal diseases. In the lab, these agents, including base editors and prime editors, have successfully targeted the exact genes for correction. Several teams of researchers in California, funded through the Innovative Genomics Institute, are advancing this new type of surgery to tackle genetic blood, immune system, kidney, eye, and nervous system disorders. Today's surgeons slice open the body to remove faulty organs and repair blood vessels; tomorrow's surgeons might instead use CRISPR and other tools to fix, remove, or replace faulty genes.

PREDICTIVE GENETIC MODELS

Researchers are developing a new technique that might someday enable people to upgrade their children before birth. Using algorithms to understand the tiny variations in DNA—single nucleotide polymorphisms, or SNPs—these researchers hope to make accurate gene-based predictions about an individual's future. SNPs are important markers of genomic variants at a single base position in the DNA—and these single letter changes to our genetic code are contributors to conditions like diabetes. If SNPs

were read in vitro, before embryos were implanted, they could reveal whether that genetic combination had a higher probability of developing diabetes or even heart disease. If an embryo was edited using CRISPR, embryos could also be optimized with the best possible traits, given the raw genetic material. Theoretically, parents could influence myriad traits for their offspring, including hair texture, resistance to a virus such as HIV, or protection against Alzheimer's disease. This intervention, like the gene drive edit in mosquitos, would have a permanent, heritable effect. It could eradicate certain diseases passed from parents to children, and in the process improve the entire gene pool.

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FOOD APPLICATIONS

FOOD APPLICATIONS

PRECISION FERMENTATION

Precision fermentation is an advanced version of a very old technology: brewing. For hundreds of years, it's been used to multiply microbes to create specific products, from beers to medicines. Today, precision fermentation can be used for a host of purposes. Food technologists can use genome sequencing and gene editing as part of a precision fermentation process, which results in microbes engineered for specific purposes. For example, feeding engineered microbes into a precisely tuned fermenter could create synthetic coconut oil or palm oil. Genetically altered microbes, which are already in use to produce plant-based meat substitutes, could soon form the basis for nondairy cheeses. With more consumers seeking out vegan options and climate change affecting dairy production, Nestlé, Danone, Mars, General Mills, and Unilever are developing precision fermentation platforms to meet future supply chain constraints and market needs. Precision fermentation can also produce new forms of stabilizers and preservatives.

CULTURED PROTEINS

In 2020, Singapore approved a competitor to the slaughterhouse by allowing a bioreactor—a high-tech vat for growing organisms—run by a US company to produce cultured chicken nuggets for its residents. The company, Eat Just, manufactured chicken meat in bioreactors using cells taken from healthy, live chickens. In 2023, the company will open a 30,000-squarefoot facility in Singapore, and its bioreactors will have the capacity to produce tens of thousands of pounds of slaughter-free meat. By 2030, Eat Just plans for cultured meat products to cost the same as or less than the current price points for chicken, beef, and pork. Eat Just's successful entry into Singapore, a highly regulated country that's also one of the world's most important innovation hotspots, is accelerating interest in cultured meat's startup ecosystem. On the infrastructure side, Turkey-based Biftek is working on new technologies and serums to reduce the cost of lab-grown meat, and in Mexico, Micro Meat creates technologies to scale up production. In Israel, MeaTech uses 3D printing to produce whole cuts of cell-based meat, while Israel-based SuperMeat has developed what it calls a "crispy cultured chicken." Several

startups are bringing cultured meat to market. Finless Foods, based in California, is developing cultured bluefin tuna meat from the sought-after species now threatened by long-standing overfishing. Other companies, including Mosa Meat (in the Netherlands), Upside Foods (in California, formerly known as Memphis Meats), and Aleph Farms (in Israel), are developing textured meats, such as steaks, that are cultivated in factory-scale labs. Unlike the existing plant-based protein meat alternatives developed by Beyond Meat and Impossible Foods, cell-based meat cultivation results in muscle tissue that is molecularly identical to that of animals grown for our consumption. In some cases, it's improved; labgrown meat doesn't require the hormones and antibiotics used at conventional facilities.

SYNTHESIZED DAIRY

Soon, milk substitutes won't require soy-based products, oats, or nuts. Synthetic cow's milk, cultivated by artificially reproducing the proteins in casein and whey, will offer a dairy alternative that matches conventional dairy's mouthfeel, texture, and temperature resistance. Casein genes are added to yeast and other microflora to produce proteins, which are purified and

transformed using plant-based fats and sugars. Perfect Day makes lab-grown dairy products—yogurt, cheese, and ice cream—that are now sold in thousands of US grocery stores. New Culture is developing animal-free cheeses for pizza that stretch, melt, and taste like what you'd find at your favorite local restaurant. Nestlé and Danone, two of the largest food and beverage corporations, have been on an acquisition spree, buying lab-grown dairy startups around the world. In the next few years, the focus will be on scaling cultured dairy operations and lowering costs of production.

TRENDS A P L L A L S STENDS TRENDS

MATERIALS APPLICATIONS



DURABLE BIOFILMS

Several companies are developing bio-based, ultra-durable biofilms and coatings so that chipped nails, scratched paint, and cracked screens become yesterday's problem. In 2022, Ginkgo Bioworks acquired the biotech company Zymergen, which develops and produces molecules, microbes, and materials for diverse end markets, for \$300 million. Zymergen developed a transparent biofilm that is thin, flexible, and durable enough to be used to transmit touch on a variety of surfaces, including smartphones, TV screens, and skin. Other possible applications include nearly invisible printed electronics that flex and move as needed. Imagine a football covered in a biofilm that could reveal, in real time, the ball's spin rate and velocity, along with the quarterback's precise hand placement.

MYCELIUM LEATHERS

Mycelium is a root-like mushroom structure, and its fast-growing fibers form what looks like a white, fluffy tuft of material. Mycelium is easy to cultivate and harvest, and it can be processed into sheets of material that resembles leather. Hermès created a mycelium version of its classic luxury Victoria bag, while Adidas launched a pair of Stan Smith shoes made out of the leather alternative. In 2022, Bolt Threads and Ginkgo Bioworks announced a multi-project collaboration to optimize the production efficiency of mycelium leathers and to develop novel proteins for biomaterials.

INTELLIGENT PACKAGING

Smart packaging will drive agricultural advances and investment. Biopolymers such as polysaccharides, proteins, and lipids can be used to fabricate edible films or coatings as packaging so that rather than throwing away the packaging for your strawberries, you can eat it. University of Minnesota researchers are developing polymers that self-destruct or "unzip" when exposed to light, heat, or acid. Saltwater Brewery designed biodegradable and edible plastic rings for six-packs of beer—so sea turtles can eat them rather than get tangled in them. Infarm created a renewable plastic that folds around objects. It uses seaweed-based agar-agar gel to grow microgreens and herbs that don't need water. At the end of 2022, Prince William awarded a \$1.2 million Earthshot Prize to Notpla, a startup that uses seaweed to produce naturally biodegradable packaging. Researchers at the NOVA School of Science and Technology in Portugal are developing bio-based sensors made from natural extracts and biopolymers that can act as smart food packaging, with indicators showing various factors such as freshness.

SUSTAINABILITY TRENDS APPLICATIONS

SUSTAINABILITY APPLICATIONS

BETTER PLASTICS RECYCLING

In 2015, an environmental engineer at the University of Georgia named Jenna Jambeck published a groundbreaking study that used available data to estimate that 8 million tons of plastic enter the world's oceans every year. The amount of plastic produced is carefully safeguarded within companies, meaning that the actual amount of plastics filling up the oceans and landfills is likely much higher than Jambeck's estimate. Despite global efforts to recycle plastic products, there are numerous barriers: Consumer-facing plastics come in different varieties, they're often coated with labels or print, and they have colors and other features added. The mess of waste—used iPhone cases, empty shampoo containers, soda bottles-can't be easily managed at scale, so a lot of it piles up. An emerging chemical process to break down a wide variety of plastics into usable propane offers a new solution to recycle plastic en masse. Researchers at SLAC National Accelerator Laboratory and the National Renewable Energy Laboratory used a microporous material called a zeolite that contains cobalt nanoparticles as a catalyst to break down different polymer molecules. The majority could be turned into propane. At the University of Texas at Austin,

researchers used a machine learning model to generate novel mutations to natural enzymes that allow bacteria to break down the plastics found in soda bottles and most consumer packaging. The enzyme, called FAST-PETase (functional, active, stable, and tolerant PETase), could operate efficiently and work at an industrial scale. The first real-world application: setting the enzyme loose to clean up landfills.

ENGINEERING PLANTS FOR CARBON CAPTURE

Carbon dioxide is the undisputed culprit when it comes to climate change. What if we could just suck it out of the air? Trees do that naturally, but with deforestation, there aren't enough of them to make a sizable impact. The Salk Institute's Harnessing Plants Initiative is developing an innovative approach that relies on our existing carbon storage mechanisms to help solve climate change. It's developing engineered crops that can store more carbon in the ground for long periods of time. The crops have a larger root mass, are deeper, and contain more suberin, a plant tissue that already relies on CO2 and can store significant amounts without causing harm to the plant. Salk researchers are hoping to develop strains of rice, wheat, corn, and other

crops that both produce edible yields and store carbon for improved soil health. Meanwhile, an artificial leaf developed at Harvard harnesses solar energy. When connected to a strain of bacteria, it converts atmospheric CO2 and nitrogen into organic forms that can benefit living organisms. Those hungry, solar-fed bacteria essentially overeat, to the point where 30% of their body weight is excess energy-stored CO2 and nitrogen. These microbes then get mixed into soil, and near the roots of plants they release all that nitrogen, which acts as an organic fertilizer. At that point, they also release the CO2, where it remains trapped underground. The result: enormous crop yields without the environmentally poisonous side effects typically associated with chemical fertilizers.

GREENING FASHION

The textile and clothing industry is a notorious polluter but is making steps toward more sustainable practices. Transforming cotton into fibers and textiles for clothing still relies on coal, and the process contributes 10% of global carbon emissions. Producing clothing requires a tremendous amount of water, and washing clothes made of polyester releases 500,000 tons of microfibers into the oceans each year.

That's the equivalent of 50 billion plastic bottles. Roughly 85% of textiles end up in landfills annually. Plus, there are all those unwanted clothes that get discarded, by both retailers and consumers, to make way for the new season's replacements. That's enough to fill Sydney Harbor—the biggest and deepest natural harbor in the world-every year. So, consider if microfibers could instead be grown in a biofoundry. Bolt Threads developed a synthetic fabric called Microsilk that's engineered from spider DNA and was used by Stella McCartney in a 2017 fashion show. A Japanese startup, Spiber, synthesized enough fibers to manufacture a limited-edition parka. The company now develops microbially fermented materials for the apparel and fashion industry. Synthetic biology processes can transform mycelium—the fuzzy, fibrous structures that help fungi grow-into rugged material resembling leather. Whereas it takes years for a cow to mature to slaughter for its hide-during which time that cow must be fed, housed, and cared for-it takes just a few weeks for a spore to grow into mycelium leather. If fibers are designed and grown, rather than harvested and processed, then other opportunities could open up. For instance, bio-based pigments used to dye textiles could be edited to deposit the opti-

SUSTAINABILITY APPLICATIONS

mal amount of color with less water (or none at all), and be fully biodegradable.

DE-EXTINCTING LOST SPECIES

Woolly mammoths were once a keystone species, one that other species in the ecosystem depended on in many ways for stability. They stomped around in herds, knocking down trees and packing down snow layers as they searched for dead grasses to eat, and that helped keep the permafrost layer stable. Once the mammoths, and other large grazing animals, stopped compacting the snow and eating dead grasses, the ecosystem began to change: The snow melted more easily, which allowed the sun to reach the permafrost. The permafrost layer is now melting at an alarming rate and releasing greenhouse gases into the atmosphere, which creates a vicious cycle: Hotter temperatures lead to more melting, which releases more gases, which causes hotter temperatures, and on and on it goes. Researchers can help to de-extinct the woolly mammoth and other species using synthetic biology techniques: Starting with a fully intact healthy cell from a closely related species and working backward with genetic fragments from preserved specimens, they could develop a version of the extinct animals.

REWILDING BARREN TERRAINS

Rewilding is a direct human intervention into nature using technology and science; this holistic approach to conservation focuses on restoring the natural phenomena of wilderness ecosystems, providing connective corridors between wild spaces, and reintroducing keystone species to their natural habitats. A term coined more than 30 years ago, rewilding has gained renewed attention in the past few years as the climate crisis has grown more dire and new technologies have promised to protect and rehabilitate ecosystems. In 2017, researchers plunged into the waters off Lizard Island on the northeastern coast of Australia with some unexpected equipment in tow: a set of underwater loudspeakers. Their destination was a coral reef that had been all but abandoned by a once-thriving population of sea life. The researchers hoped that by broadcasting the telltale sounds of a healthy reef, they might lure back some of its vital inhabitants. Remarkably, it worked. In 2022, four bison were released in a woodland near Canterbury—the hope is that over time, the herbivores will revitalize a stretch of southeast England and allow vegetation to flourish again, which should in turn boost biodiversity.

ENGINEERED MOSQUITOES

In 2021, biotech company Oxitec launched a controversial field test of specially engineered mosquitoes in Florida as a move toward reducing the spread of deadly diseases such as dengue, yellow fever, and the Zika virus. Its tiny capsules contain an engineered form of the Aedes aegypti mosquito, called OX5034. Because only female Aedes aegypti bite and spread disease, Oxitec engineered males to pass on a gene that kills female offspring before they mature. Male offspring then continue mating and passing on the altered gene. The US Environmental Protection Agency said this pilot poses no human threat, while local authorities, who have been dealing with steadily growing cases of dengue fever and West Nile virus, hope that a smaller mosquito population will curb those diseases without insecticides or poisonous chemicals. Last year, the EPA approved an expanded plan to release 2.4 million genetically engineered mosquitoes in more US sites, including some in California. Similar experiments are underway in Malaysia and Panama. And what if in the future mosquitoes are flying syringes capable of delivering vaccines? Since mosquitoes can transmit malaria, University of Washington scientists are

working on a weakened form of malaria-causing Plasmodium parasites that won't get people sick, but will cause the body to create antibodies.



Synthetic biology is about to explode. It is the next frontier for innovation.

ERIC SCHMIDT,

CO-FOUNDER OF SCHMIDT FUTURES AND FORMER EXECUTIVE CHAIRMAN OF ALPHABET INC.

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CONSUMER

CONSUMER APPLICATIONS

SKIN CARE AND BEAUTY

Synthetic biology-derived compounds are producing improved ingredients in skin care products. Amryis, one of the first commercial synthetic biology companies, used biosynthesis to create a suite of products containing squalene, a key antioxidant found in moisturizers and traditionally found in shark livers. The Bay Area startup Geltor is engineering animal-free collagen for use in serums and creams designed to plump skin and reduce the appearance of fine lines and wrinkles; conventional collagen is usually drawn from bovine sources, but modern bioengineering means it can be grown in a lab. Skin care brand Algenist uses biofermented microalgae in its anti-aging products, and it developed alguronic acid that makes skin look more youthful. One Ocean Beauty, founded by former Burberry Beauty President Marcella Cacci, produces a bio-fermented exopolysaccharide isolated from brown kelp, an elasticity-promoting glycoprotein, and a blue light-repellant microorganismall from cells found naturally in the ocean.

MICROBIOME TEST KITS

The human microbiome is a mini-universe of the genetic materials living on and inside our bodies, inherited from our gestational mothers. The number of genes in the bacteria, fungi, protozoa, and viruses that make up our microbiomes is 200 times the number of genes in the human genome. That microbiome weighs nearly 5 pounds, and it lives mostly in your gut and on your skin. Microbiomes differ greatly from person to person, even if you're comparing siblings who live in the same city. How well you digest lactose, how vulnerable you are to skin cancer, how well you sleep, your probability of developing anxiety or becoming obese—all of these traits are linked to the microbiome and influenced by what you eat and drink, whether you smoke, what chemicals your body comes into contact with, and what medications you take. That data once was collected over several visits to an allergist, but today, at-home tests can determine the genetic makeup of your microbiome. Some companies will mix together special probiotic compounds to mitigate conditions or optimize the symbiotic relationship your body has with all those microorganisms.

IMPROVING GUT BIOMES

A mass extinction event is happening right now in our guts and in the environment. The widespread use of antibiotics, along with diets rich in processed foods, have led to a staggering decline of microorganisms in wealthy nations. During the past 12,000 years of human evolution, we've shifted nature's balance—our diets are now relatively narrow compared to those of our far-distant ancestors. Recently, scientists studied modern hunter-gatherer tribes in Tanzania, Peru, and Venezuela, and found that their microbiota had 50% more bacterial species than those in the West today. Unlike those tribes, we no longer hunt and eat wild flora and fauna. Those from wealthier countries now eat very little dietary fiber, a limited variety of fruits and vegetables, and only four species of livestock: sheep, poultry, cattle, and pigs. Worse, widespread use of antibiotics in farm animals used not necessarily to prevent disease but to increase weight gain and therefore the volume of meat available—means that we're ingesting compounds that are helping to destroy our own microbiomes. Humans are complex, composite organisms, made up of layers and layers of cells. Researchers now think that our gut microbiome is directly linked to our metabolism, our immune systems, our central nervous systems, and even the cognitive functions inside our brains. It's an inherited problem: Most of our microbiomes come to us from our mothers as we pass through the birth canal. A number of researchers are now looking at the future of our microbiomes. Vedanta Biosciences is making gut bacteria that can be turned into drugs, and counts the Bill & Melinda Gates Foundation as one of its investors. The American Gastroenterological Association and OpenBiome will track 4,000 patients over 10 years to learn about fecal microbiomes.

DNA-BASED MARKETING

Some companies are offering direct-to-consumer DNA testing kits with the promise of recommendations for skin care products and foods all based on the person's individual DNA profile. DNAnudge makes a diagnostic analysis of saliva samples and then issues users a wristband and app. When users shop, the wristband nudges them toward optimal choices, while the mobile app makes DNA-based product recommendations.



CONSUMER APPLICATIONS

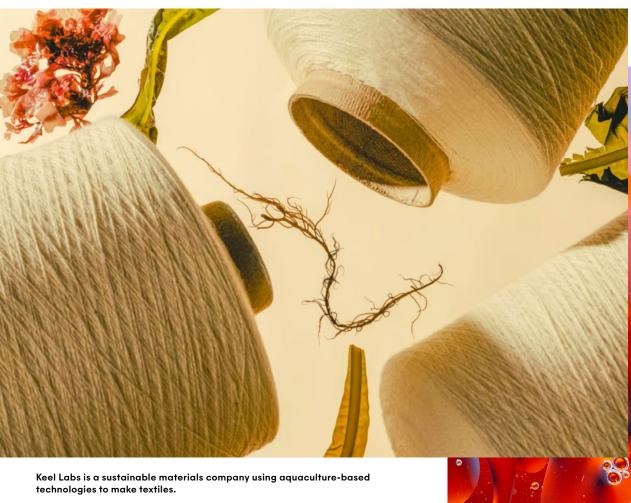


Image courtesy of Keel Labs

OPTIMIZING RECREATIONAL DRUGS

When it comes to recreational drugs like marijuana, genetic factors can determine whether someone feels pleasantly relaxed or anxious and listless. New diagnostic tests promise to optimize recreational drugs for someone's unique genetic profile. Atai Life Sciences, based in Berlin, is researching genetics, depression, and small molecules within cells in an effort to repurpose psychedelics as therapies for depression and PTSD. MindMed in New York is developing a platform to help patients determine which drugs to take—therapeutics based on MDMA and DMT-depending on genetic and other data.

DIY BIOHACKING PROJECTS

Biohacking is a socio-technological movement bringing together citizen scientists, academic researchers, technologists, data scientists, and others interested in life sciences. Biohackers are developing DIY solutions for diseases and illnesses, and they're driven by disenchantment with consolidation in the pharmaceutical industry, long regulatory processes, and slow product development. Some create novel enhancements. Openness and collaboration are valued; biohackers share their protocols, research, and materials online, much as technologists share their code on GitHub. A group of Bay Area biohackers launched the Open Insulin Foundation, a project based on the idea that insulin should be free. Diabetes affects 422 million people worldwide, and the project aims to develop the "first freely available, open organisms for insulin production that will be practical for small-scale, locally based groups to use." Biohacking also seeks new ways to engineer food and fabric. A team of biohackers created vegan cheese from engineered yeast. They used it to develop milk proteins, which they combined with water and vegan oil to make vegan milk, and then proceeded with a more traditional cheese-making process. The recipe is open source and free. Keel Labs (formerly AlgiKnit) uses kelp to make apparel and footwear and has developed yarn for a number of different textiles. Its product Kelsun is a seaweed-based varn that's an alternative to conventional materials. Modified yeasts, proteins, and other bits of DNA could be hard to control, however. Novel organisms ingested or released into the world could violate the United Nations Biological Weapons Convention, even if the biohack isn't itself intended to be a weapon. Some worry that the opensource ethos of biohacking could accidentally lead to a new class of biological weapons.

APPLICATIONS

TRENDS

AGRICULTURAL APPLICATIONS

UPGRADING PHOTOSYNTHESIS

Genetically modifying crops with upgrades could dramatically increase yields without needing to increase the other resources required for cultivation. Photosynthesis is the biological process green plants and some organisms use to harness sunlight to produce energy out of CO2 and water, and researchers are working on several projects to upgrade it. Simply over-exposing plants to sunlight doesn't have the same effect-more light can damage cells unless they turn on a biological system called quenching that's capable of flushing out the excess energy. On cloudy days, plants turn off quenching so they can hold on to the excess energy. This process of turning quenching on and off takes time, can be unpredictable, and creates enormous inefficiencies. Scientists hope that with genetic engineering, they can speed up the guenching process. In 2022, modified soybean plants were shown to yield 20% more thanks to a supercharged photosynthesis system. Researchers are also working on cowpeas and rice.

FASTER FLOWERING

Using the CRISPR gene-editing tool, researchers at the University of Georgia Warnell School

of Forestry and Natural Resources and at Franklin College of Arts and Sciences figured out how to make trees mature faster. They applied CRISPR to edit a flower repressor gene and drastically shortened the time it takes a poplar tree to flower—from 10 years down to just three months. It would typically take the plant a year to develop the systems to even produce flowers, and the team engineered the plant to mature in just a few days. The promise of this research is an accelerated time frame for tree breeding, as well as enhancement of trees' natural defenses against extreme heat, cold, and drought.

REGENERATIVE AGRICULTURE

Regenerative agriculture describes farming and grazing practices that rebuild soil's organic matter and restore degraded soil biodiversity. There's a clear need for this technology-led practice: Decades of using chemicals, salt-based fertilizers, carbon mining, and harsh insecticides deplete soil. Planting multiple types of crops together, rotating crops, cutting back on tilling, and reducing reliance on harsh chemicals can revitalize depleted soil, leading to improved yields, nutrient-rich crops, and improved resistance to flooding and drought. In 2017, the Rodale Institute launched the Regener-

ative Organic Certified program to start creating an official standard. It builds on the USDA-certified organic seal by adding requirements for soil health, animal welfare, and human rights. General Mills announced that it would advance regenerative agriculture on 1 million acres of farmland by 2030. Meanwhile, several brands, including Patagonia, Timberland, Allbirds, Gucci, and Balenciaga, have launched efforts to promote regenerative agriculture.

INDOOR FARMS

New technologies allow growers to produce plants and insects using alternative techniques, which include aquaponics, hydroponics, and vertical farming. Many countries lack the land mass or infrastructure to grow high-quality produce, so they're bringing traditional agriculture indoors and underground, using hightech robotics, irrigation, and lighting systems to cultivate food. In the US, 80 Acres Farms is building a fully automated indoor farm, nearly the size of two football fields, just outside of Cincinnati. In Bethlehem, Pennsylvania, vertical farming company Bowery Farming is laying the groundwork for an expansive, sustainable food supply system. Globally, Japan has emerged as a world leader in indoor farming. Many of the

country's 200 plant factories are subsidized by the government, but they thrive thanks to Japanese consumer demand for fresh, local, pesticide-free food. Near Kyoto, the Kansai Science City microfarm uses AI and collaborative robots to raise seedlings, replant them, water them, adjust their lighting, and harvest fresh produce. In nearby Kameoka, Spread uses machines and robots to cultivate plants that produce 20,000 to 30,000 lettuce heads per day. Plants mature in just 40 days before being shipped to nearby Japanese supermarkets. Last year, Spread raised \$30 million in Series A funding, making it the largest round in Japanese foodtech. In California, IronOx's fully autonomous, hydroponic indoor farm uses two robots to plant, maintain, and harvest produce. In just a single indoor, automated acre, those two bots can produce the equivalent of 30 acres of outdoor farming. In the past, the expense of robots, artificial light, and other equipment made vertical farms difficult to scale. But that's changing as the ecosystem matures and technology improves. Today, thanks to brighter, cheaper LED light bulbs, cloud-based Al systems, and more available agricultural sensors, vertical farms can now cultivate lettuce. spinach, basil, garlic, and snow peas. They tend to deliver 10 to 20 times the total yield of

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conventional farms with far less waste. Vertical farming projects now span the globe, settling mostly in urban centers such as Baltimore and Chicago.

ENHANCING THE FOOD CHAIN

Researchers are harnessing synthetic biology to produce better feed for animals. The startup KnipBio engineers fish feed from a microbe found on leaves, editing its genome to increase carotenoids important to fish health and using fermentation to stimulate its growth. The microbes are then pasteurized, dried, and milled. Other agricultural projects underway include synthetic organisms that can produce vast quantities of vegetable oil, and nut trees that can grow indoors using a fraction of the water the thirsty trees normally require, while also producing twice as many nuts.

CRISPR CROPS

CRISPR promises to enhance the nutritional value of produce, increase crop yields, and extend freshness. It has increased the level of omega-3s in plants and aided the creation of non-browning apples, drought-resistant rice, and mushrooms that can withstand jostling during transportation. (In most markets, product labels identify such products as genetically modified.) In 2021, the first CRISPR-edited tomatoes went on sale in grocery stores in Japan. The big question now is whether CRISPR-edited crops will be labeled "genetically modified organisms" and become subjected to the same regulations. The USDA has said that some edited crops—some varieties of soybeans, corn, and potatoes—don't fall under current regulations. In 2022, the agency approved the cultivation of a tomato engineered for enhanced nutritional value and color (it's purple). This year, regulatory agencies will continue to review guidelines for CRISPR crops, which could have an impact on their production in years to come.

ACELLULAR MEAT PRODUCTION

Unlike cellular-derived meats, which are made from living or once-living organisms, acellular meats are created with organic molecules that don't contain any living (or once-living) material in the final product. Acellular products don't require starter cells extracted from muscle biopsies. If the molecular structure of an acellular chicken nugget is the same as a nugget made of tissue harvested from an animal, is it still considered meat? The US beef industry is petitioning to bar nonanimal products from the definition of

AGRICULTURAL APPLICATIONS



meat, which could have implications on funding and advertising in 2023 and beyond as acellular startups start to scale.

SUPER ANIMALS

In 2019, a major outbreak of swine fever devastated China's stock and killed nearly a quarter of the global pig population. Though the disease was first reported in August 2018, it took the Chinese government a long time to act. Paradoxically, the disease spread because the Chinese government had taken positive steps to curb pollution. After new regulations went into effect, industrial pig farmers couldn't upgrade their facilities fast enough, which led to farm closures and a rerouting of the pork supply. Sick pigs were shipped throughout the country, fueling the disease spread. China consumes a tremendous amount of pork, and it will take years to rebuild the swine population. Enter genome editing: Dozens of gene-editing experiments and research projects are now underway in China to develop new breeds of disease-resistant, climate-acclimating super pigs intended for consumption. The research could have a spillover effect into other areas of agriculture and medicine, and could ultimately speed along new regulations.

SPACE-BASED FARMING

The Advanced Plant Habitat is a fully automated plant growth facility that was installed in the International Space Station in 2018. Rigged with cameras and more than 180 sensors, the data it gathers is sent back down to Earth for study. Scientists are learning how organic material grows differently in space. For example, germinating peppers takes an average of two weeks longer than it would on Earth due to fluid challenges in microgravity. Space agriculture is quickly becoming a multibillion-dollar industry, with startups including Square Roots, founded by Elon Musk's brother Kimbal Musk. NASA and Germany's space agency are now investing in a variety of space agricultural projects that could someday support off-planet habitats.

TERRAFORMING

Terraforming—literally, "earth shaping"—is a concept from science fiction in which people re-form another planet to resemble Earth and support human life. But as humans begin serious off-planet exploration, we must develop new agricultural techniques suitable for space. Our current microbes may be key to terraforming, because they can survive such harsh environ-

ments as the Atacama Desert. Of course, we may invent entirely new life-forms using synthetic biology. To advance from theory to reality, terraforming requires a host of robots to mine for resources and build an ecosystem capable of sustaining human life, as well as hybrid-skilled researchers with backgrounds in biology, botany, agriculture, robotics, and physics.



The power to control our species' genetic future is awesome and terrifying. Deciding how to handle it may be the biggest challenge we have ever faced.

JENNIFER A. DOUDNA,

A CRACK IN CREATION: GENE EDITING AND THE UNTHINKABLE POWER TO CONTROL EVOLUTION



BIOENGINEERING TRENDS IN SOCIETY

GENETIC PRIVACY

The pandemic accelerated widespread use of infectious disease surveillance techniques, from saliva tests at airports and border crossings to nasal swabbing at testing centers. To ease testing bottlenecks, which sometimes resulted in hours-long lines, alternative testing centers opened up: Private companies dispatched workers, who often had no medical training, to vans or small tents to administer PCR or rapid-response tests. It wasn't immediately clear where the test results would be sent, or who might also gain access to the data. With the growing size and scale of third-party test results and genetic databases, anyone with the right skills could identify individuals—and we don't yet have safeguards against widespread genetic surveillance. In 2022, police used a baby's DNA to investigate its father for a crime. As of this writing, two commercial DNA databases can be accessed by law enforcement: GEDmatch and FamilyTreeD-NA, but state and local laws are in flux. For now, there are few restrictions on private companies buying and selling genetic data in the US and in many places around the world.

ARTIFICIAL HUMAN GENOMES

Genetic privacy will be increasingly difficult to safeguard—yet big genetic data sets are required to perform the kind of research that leads to new therapeutics. Scientists at the University of Tartu in Estonia use neural networks to develop novel segments on human genomes. The hope is that an artificial human genome will allow researchers to study DNA without infringing on anyone's privacy.

BIOBANK RELEASES

The UK Biobank (UKBB) made 200,000 DNA sequences available to scientists for research projects in 2021. This enormous trove of anonymized genetic data, primarily from Europeans taking part in a long-term study, includes 3 billion base pairs of human DNA. The UKBB also launched a secure, cloud-based computing environment, making it easier for scientists to collaborate and integrate different types of data. More biobank data were made available in 2022 from government-sponsored research, including the National Institutes of Health's All of Us project and the Million Veteran Program. The All of Us Researcher Workbench now includes health data from more than 372,000 participants,

including information from nearly 20,000 people who have been infected with SARS-CoV-2 and more than 57,600 initial responses to a broad health survey.

RESOLVING BIAS IN GENOME RESEARCH

Fewer than 2% of people who have had their genomes sequenced are from Africa. Overwhelmingly, the majority of sequences come from affluent Caucasian Americans and Europeans. This excludes an enormous number of people from the benefits of genetic research. There is now increased attention to and funding for diversifying genomic research. H3Africa works with African investigators to determine genomic and environmental determinants of common diseases. The Non-Communicable Diseases Genetic Heritage Study consortium, based in Nigeria, is creating a comprehensive catalog of human genetic variation among Nigerians. A decade-long Three Million African Genomes project is underway to locate missing genetic variants from ancestral genomes in Africa and build an African biobank of clinical information.

ETHICS IN INDIGENOUS GENOMICS

Biological materials from Indigenous peoples are still missing from genetic databases, basic research, and clinical studies. Here's one reason why: Late in the 20th century, the Havasupai were grappling with an increase in diabetes. They allowed researchers from Arizona State University (ASU) to collect blood samples for a 1990 study, hoping the research would help them eradicate the disease. But then, unbeknown to the Havasupai, the researchers expanded the scope of the project to encompass genetic markers for alcoholism and various mental disorders. They went on to publish multiple papers in academic journals highlighting their results, which led to news stories about inbreeding and schizophrenia among tribe members. The Havasupai were, understandably, horrified and humiliated, and filed a lawsuit against ASU in 2004. ASU eventually settled the suit in 2010, returned the blood samples to the tribe, and promised not to publish any more research. The Navajo Nation, the second-largest group of Indigenous peoples in the US, subsequently banned all genetic sequencing, analysis, and related research on its members. Although their objections were absolutely warranted,

BIOENGINEERING TRENDS IN SOCIETY



there was an unforeseen consequence: The pool of genetic data in the US now doesn't include Indigenous peoples. New initiatives could make genetic data sets and research more inclusive. The Summer Internship for Indigenous People in Genomics trains budding scientists, while the Center for the Ethics of Indigenous Genomic Research works to promote Indigenous-led research in biobanking and precision medicine. Canada and New Zealand are both working on governing frameworks and libraries to include Indigenous peoples, relying on direction from local communities.

DEVELOPING NEW LEGAL FRAMEWORKS

In 2022, famed Harvard geneticist George Church announced that one of his startups, Colossal, was aiming to bring back the woolly mammoth—but without tusks. His idea is to help combat climate change using the mammoth, which millennia ago were critical to keeping the northernmost regions of the planet balanced, but he also knew that once resurrected, the mammoth could result in poachers and an underground trade in tusks. With or without tusks, what's clear is that there are no current legal frameworks to assist countries in determining where—and whether—to allow genetically mod-

ified species to be set loose. As bioengineering advancements progress, governments will need to collaborate on a shared vision of the future, not to mention harmonized policies and regulations.

DECISIONS TO ALLOW OR PREVENT GERMLINE EDITING

He Jiankui, the Chinese biophysics researcher who used CRISPR to edit embryonic DNA, performed a trailblazing type of surgery—on genes. Jiankui is said to have edited the embryos created from the egg of a healthy woman and the sperm of an HIV-positive man. A set of healthy twins was born, making them the first known case of gene-edited children. Jiankui stunned the scientific community in 2018 when he presented his work and immediately faced global criticism for experimenting with human life. Jiankui and two collaborators were found guilty of "illegal medical practices" in China and spent three years in prison. Part of what made Jiankui's edits so concerning was that the changes would be heritable-meaning the new traits engineered in the twins could be passed on to their offspring. A dozen countries have banned germline engineering in humans, though their ranks do not include China. For

now, US federal law prohibits the use of federal funds for research on human germline gene therapy—regulations in this arena are notoriously politicized and have changed a few times in the past decade. The European Union's Convention on Human Rights and Biomedicine said tampering with the gene pool would be a crime against human dignity and human rights. But all those condemnations were made before CRISPR made it possible to precisely engineer the germline.

CHINA'S NATIONAL DNA DRIVE

Over the past decade, China has quietly created a scaled, national DNA drive to collect, sequence, and store its citizens' genetic data. DNA repositories are part of a wider panopticon, aided by the Chinese Communist Party's ambitions for artificial intelligence, that allows the government to continually surveil its constituents. In Xinjiang, the program was billed as "Physicals for All," and nearly 36 million people took part, according to China's official news agency, Xinhua. Much of the government's early DNA initiatives centered on the Uyghur population, whose data was reportedly being collected to help distinguish among China's many ethnic groups. Human rights groups have widely condemned

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this program. (China also faces widespread condemnation for targeting Uyghurs. For more on this subject, we recommend the Council on Foreign Relations' summary, at https://www.cfr.org/backgrounder/china-xinjiang-uyghurs-muslims-repression-genocide-human-rights.)

Chinese government researchers contributed the data of 2,143 Uyghurs to the Allele Frequency Database, an online search platform partly funded by the US Department of Justice until 2018. The database, known as Alfred, contains DNA data from more than 700 populations around the world. This sharing of data could violate scientific norms of informed consent, because it is not clear whether the Uyghurs volunteered their DNA samples to the Chinese authorities, and it's very unlikely that everyone involved knew that their DNA was being collected or understood the implications. Human rights activists say a comprehensive DNA database could be used to chase down any Uyghurs who resist conforming to the campaign, and Chinese officials have cited tracking down lawbreakers and criminals as a key benefit of the genetic studies.

China continues to collect wider swaths of genetic data from Uyghurs and other minority

ethnicities, as well as from Han Chinese (who make up 91% of the country's population). Soon it will have a comprehensive, powerful genetic data set unrivaled by that of any other country. The United States, Canada, the European Union, and the United Kingdom are debating the merits of genetic privacy. China, which collects massive amounts of information, and whose citizens seem untroubled by government surveillance, will face far less resistance to genetic studies and experimentation.

INTERNATIONAL COLLABORATIONS TO ADVANCE BIOENGINEERING

Researchers are building the first-ever comprehensive map of all 37.2 trillion human cells in the body. The effort includes 130 software engineers, mathematicians, computational scientists, biologists, clinicians, and physicists hailing from Israel, the Netherlands, Japan, the UK, the US, and Sweden. Although a cell atlas has long been theorized, new biological tools and more powerful computers have turned this one time vision into a reality. Scientists believe the mapping will give the medical community a new way of understanding how our bodies work and will help diagnose, monitor, and treat disease.

SCENARIOS

WHAT IF CONVENTIONAL MEAT CARRIED A WARNING LABEL LIKE CIGARETTES?

Scenario Year: 2033

Now that cultured meat is affordable and widely available, the consumption of conventional meat from slaughtered animals is considered distasteful and unethical. In many countries, conventional meat is packaged with a graphic warning label, just like cigarettes and alcohol. Images of discarded lamb carcasses or blood-soaked processing plant tables covered in chicken parts are printed in full-color and attached to the clear plastic packaging, revealing the meat inside and a bit of the story about how it was made.

WHAT IF ANIMALS WERE GROWN FOR JUST ONE PURPOSE—TO REPLACE HUMAN ORGANS?

Scenario Year: 2029

Genetically engineered pig hearts are now routinely produced for cardiac patients, thanks to the lifestock farms that raise animals for the purpose of organ donation. Unlike the commercial facilities where animals intended for consumption are pumped full of hormones and antibiotics to speed their growth and spend the entirety of their short lives in cramped warehouses, lifestock farms are bucolic resorts. Pigs raised for organ donation receive close, personalized attention from caring attendants. They receive the highest-quality food and water, comfortable accommodations, and the opportunity to socialize in pods. All stressors are removed, to ensure strong mental and emotional health, as a calm environment has been proven to aid in optimal physical development. Come harvest day, animals are euthanized humanely. While some argue lifestock farms are gruesome, they've not only created new opportunities for farmers but have saved countless lives that would otherwise have been lost within the former human organ donation system.

HOW TO PREPARE

What should your organization do now to prepare for these trends?

Bioengineering is a long-horizon collection of technologies that will continue to develop and mature over the next several decades. It may feel premature to take action today; however, advancements in this field will have a compounding effect. Al offers a useful analogy here: The entire field of AI developed largely unnoticed by the business community, until suddenly it seemed to be both ubiquitous and a necessary part of daily operations. Leaders who were tracking AI developments and had developed a point of view wound up with valuable first-mover advantages.

In the coming decade, bioengineering technologies will force leaders to confront their cherished beliefs about their core products and services, and they will challenge existing business models. Leaders will need to seek out new partnerships, develop new pipelines for talent, and align stakeholders on the moral and ethical uses of engineered biology.

We advise businesses to prepare for the bioengineering age as they would for any other transformational technology:

FAMILIARITY

Get to know the science, history, ecosystem, and players. Read books on synthetic biology and CRISPR. Cultivate relationships with experts. Attend a few conferences, just to learn. Follow VC funding and learn about their startups.

TRENDS

Prioritize the trends that are most critical to the organization in the near term, and project the likely business impact.

WHITE SPACES

Explore white spaces to gain new insights. Where are there opportunities for innovation and growth? What might threaten the organization's ability to thrive? Where are there downstream risks to partners or customers?

REHEARSE THE FUTURES

Generate scenarios that reveal plausible future worlds where bioengineering technologies have reached critical mass. Where can the organization play and win? What challenges can be identified up front?

VISION

Develop a long-term vision on bioengineering technologies to drive investment, M&A, product development, talent acquisition, and planning decisions.

KEY QUESTIONS FOR YOUR TEAM

6 Are we adequately In what ways will How could How could What new How could Do we have the What will it take bioengineering bioengineering bioengineering knowledge, to socialize the prepared for the opportunity spaces we leverage experience, and bioengineering era? influence our bioengineering affect our business can bioengineering make our company opportunities model in the next 2 unlock for our vulnerable? and risks of manufacturing to give us a talent in place? competitive years? business? bioengineering process? advantage over our inside our Does this change competitors? organization? Our supply chains? 5 years? Where does this our perspective on open a new market? risk? How can we Our product lines? If our typical create a sense of product urgency among our development cycle stakeholders? takes 5-10 years, what do we need to do differently starting today?

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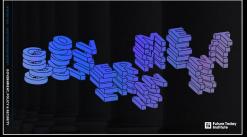


















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