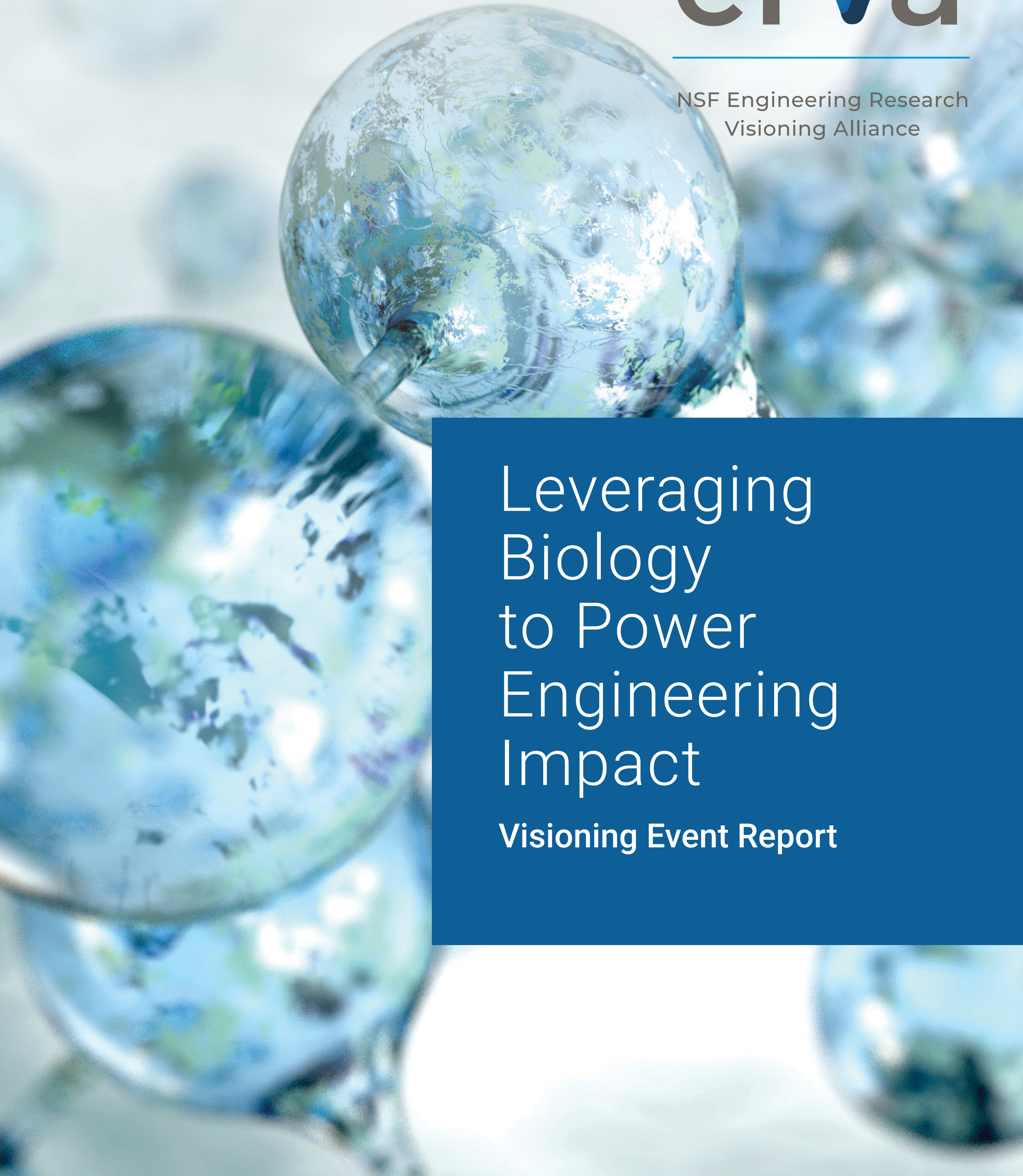

NSF Engineering Research Visioning Alliance

Leveraging Biology to Power Engineering Impact

Visioning Event Report

Leveraging Biology to Power Engineering Impact

A Visioning Report of the Engineering Research Visioning Alliance

Report Finalized October 25, 2022

Co-Hosts:

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The Engineering Research Visioning Alliance (ERVA) is a neutral convener that helps identify and develop bold and transformative new engineering research directions, directly supporting the nation's ability to compete in a rapidly changing global economy. Funded by the National Science Foundation (NSF) Directorate for Engineering, ERVA is a diverse, inclusive and engaged partnership that enables an array of voices to impact national engineering research priorities. The five-year initiative convenes, catalyzes and empowers the engineering community to identify nascent opportunities and priorities for engineering-led innovative, high-impact, cross-domain research that addresses national, global, and societal needs. Learn more at ervacommunity.org.

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ERVA visioning events enable the engineering research community to identify nascent opportunities and priorities for engineering-led, innovative, high-impact research that addresses global and societal needs. Each event relies on the efforts of organizations and individuals who volunteer to lead, guide, and participate in its activities.

Gratitude is extended to the event co-hosts who supported this workshop by providing leadership and recommendations for participants: the University of Delaware, led by Levi Thompson, dean, College of Engineering; University City Science Center, led by Heath Naquin, vice president, government and capital engagement; Johns Hopkins Whiting School of Engineering, led by Ed Schlesinger, dean; and the Waters Corporation, led by Steve Martin, vice president of research. Special thanks to co-host report writer Erica Brock.

The Thematic Task Force co-leads who developed the creative framework for this visioning event and contributed to the report development were Cato Laurencin, university professor and Albert and Wilda Van Dusen Distinguished Endowed Professor of Orthopaedic Surgery, University of Connecticut; and Jake Beal, engineering fellow, Raytheon BBN Technologies.

Thematic Task Force members contributed their time and expertise and were instrumental in framing and shepherding the workshop conversations:

- Simone Bianco, Altos Labs
- Jennifer Blain Christen, Arizona State University
- Douglas Friedman, BioMADE
- Michael Ibba, Chapman University
- Jeff Lievense, Lievense Bioengineering LLC
- Ellis Meng, University of Southern California Viterbi School of Engineering
- Maurine Neiman, University of Iowa
- Kiisa Nishikawa, Northern Arizona University
- Alison L. Sheets-Singer, Nike, Inc.
- Anup Singh, Lawrence Livermore National Laboratory
- Mehmet Toner, Massachusetts General Hospital, Harvard Medical School, and Harvard-MIT Division of Health Sciences and Technology

This visioning effort also benefitted from the expertise of facilitators and annotators in each of the event breakout sessions. These sessions were inspired by "8 Impossible Things," statements that envisioned an ideal future that could be made possible through research and innovation inspired by biology and engineering.

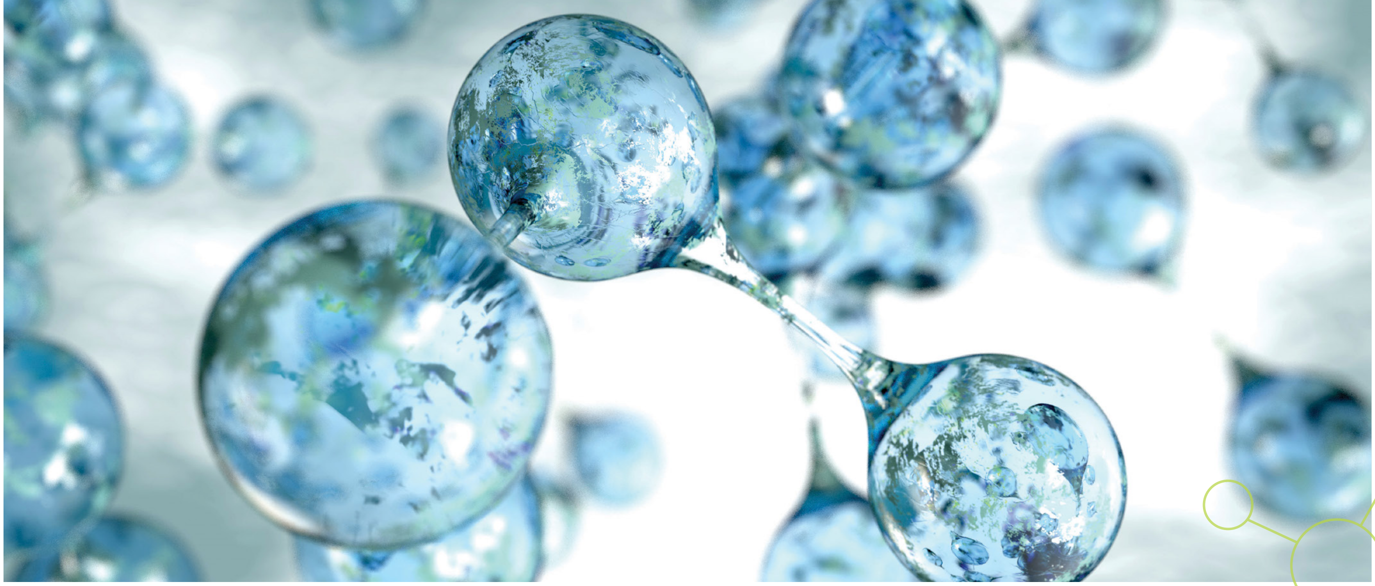
1. **Smartphones don't need a trade-in; they reproduce**: Jamie Phillips, University of Delaware; Thanh Nguyen, University of Connecticut; Scot Miller, Johns Hopkins University; and Rebecca Schulman, Johns Hopkins University
2. **A businesswoman flies to work using her new exoskeleton**: Kiisa Nishikawa, Northern Arizona University; Helen Lu, Columbia University; Alison Sheets-Singer, Nike
3. **Your bathroom mirror performs hospital-grade diagnostics**: Dave Martin, University of Delaware; Kenneth Barner, University of Delaware; Ellis Meng, University of Southern California
4. **There's never another "your child has been exposed to…" sign at daycare**: Jake Beal, Raytheon BBN Technologies; Julie Maresca, University of Delaware; and Anup Singh, Lawrence Livermore National Laboratory
5. **Any-town USA manufactures all the chemicals and materials it needs from plants grown nearby**: Doug Friedman, BioMADE; Jeff Lievense, Lievense Bioengineering LLC; Steve Martin, Waters Corporation
6. **Lifespans are no longer defined by ZIP code**: Jennifer Blain Christen, Arizona State University; Heath Naquin, University City Science Center; Larry Nagahara, Johns Hopkins University
7. **Central NYC residents breathe pristine mountain air**: Michael Ibba, Chapman University; Jason Gleghorn, University of Delaware; Rebecca Schulman, Johns Hopkins University; Scott Miller, Johns Hopkins University
8. **A 100-year-old breaks the 100-meter sprint record**: Cato Laurencin, University of Connecticut; Mehmet Toner, Harvard Medical School; Panagiotis (Panos) Artemiadis, University of Delaware

The event discussions were informed by the following speakers who contributed their expertise: NSF Assistant Director for Engineering Susan Margulies; Lynn Rothschild, NASA Ames Research Center; C. Brandon Ogbunu, Yale University; David S. Kong, MIT Media Lab; Sarah Richardson, MicroByre; and Eleni Stavrinidou, Linköping University.

ERVA is also grateful to all the workshop participants who contributed their time to create a valuable discussion and conference report and to their organizations for the liberty to share their expertise for this effort.

ERVA executive director Jennifer Carinci led the event planning, program development, and execution under the guidance of ERVA principal investigator Dorota Grejner-Brzezinska, The Ohio State University; and co-Principal Investigators Anthony Boccanfuso, UIDP; Barry Johnson, University of Virginia; Charles Johnson-Bey, Booz Allen Hamilton; and Edl Schamiloglu, University of New Mexico. Development of the visioning session theme was informed through input from the ERVA Standing Council, Advisory Board, NSF Engineering collaborators, and our research intelligence partner Elsevier.

Finally, staff and leadership from ERVA and UIDP, ERVA's administrative core partner, provided operational expertise for this event and report: Sandy Mau, ERVA communications director; and Mark McGill, ERVA program coordinator. UIDP staff Natoshia Goines, Abishai Kelkar, and Morgan Jones-King contributed to event execution, and Mike Brizek, UIDP program director, consulted on workshop facilitation.



Executive Summary

A phone that can regenerate itself. New York City with fresh mountain air. Plant-based, locally-grown manufacturing materials. All technical challenges seemingly impossible to execute, but incredible to imagine.

These are among the challenges presented to a diverse array of experts and practitioners with a clear objective: to envision bold engineering research priorities that can advance progress and address some of society's most pressing problems. Set in motion by the Engineering Research Visioning Alliance (ERVA), a Thematic Task Force with members from academia, industry, and the nonprofit sectors formulated "8 Impossible Things," each a statement accompanied by an image of an ideal future positively impacted through bold research--and subsequent innovation--at the intersection of biology and engineering. These eight challenges inspired more than 100 researchers to draw outside the lines and think outside the box to formulate research priorities not only imaginable, but achievable.

The NSF Engineering Directorate, led by Susan Margulies, set the course for discussions by framing three exploratory research domains at the intersection of biology and engineering:

01

Bio-Inspired/Bio-Informed
Inspiration from biology is used to engineer components and systems. Naturally occurring chemistry has driven advances in materials science. The design of engineered systems has been informed by nature-based mechanical solutions. Neuroscience is under scrutiny to provide inspiration for brain-based data storage and computational capabilities. In the future, we stand to learn much from biological mechanisms of resilience and adaptation to inform the design of engineering structures and systems.

02

Repurposing Biology
Biological constructs may be adopted and adapted for purposes beyond their existing biological function. A classic example of this is the use of DNA molecules for data storage, building on the remarkable integrity and potential for error-free replication of this macromolecule. Additionally, intense interest is focused on designer organisms, products of synthetic biology, that may afford functionalities from mining to agriculture, biofuels, to biofoundries. Engineered living systems may provide building blocks for next-generation sustainable engineering.

03

Improving on Biology
It's also possible to envisage engineering components and systems that go "beyond biology." One example is manipulating the interactions between species in different kingdoms. This "interkingdom engineering" has breathtaking potential to improve human health, for example by manipulating the human microbiome to ameliorate obesity or interrupting interspecies virus transfer to diminish disease spread.

The 8 Impossible Things

This report casts the findings of this visioning event within the framework of the three domains, using the 8 Impossible Things as a device to inspire bold, new engineering research directions.

- Smartphones don't need a trade-in; they reproduce
- A businesswoman flies to work using her new exoskeleton
- Your bathroom mirror performs hospital-grade diagnostics
- There's never another "your child has been exposed to..." sign at daycare
- Any-town USA manufactures all the chemicals and materials it needs from plants grown nearby
- Lifespans are no longer defined by ZIP code
- Central NYC residents breathe pristine mountain air
- A 100-year-old breaks the 100-meter sprint record

Three common threads are woven through the ideation inspired by these concepts:

- Sustainable solutions that involve repurposed or recycled materials;
- Inclusive design and research to serve all populations equitably; and
- Affordable approaches that ultimately provide low-cost solutions.

The research priorities outlined in this report lay the groundwork for achieving solutions for each of the 8 Impossible Things. The task force identified topics ripe for exploration that promise significant advances in how the world tackles some of its biggest problems.

Photo credits (from top): Rodion Kutsaev on Unsplash; used with permission, Sarcos Technology and Robotics Corporation; Sharon McCutcheon on Unsplash and Sanibell Bv on Unsplash; Tanaphong Toochinda on Unsplash; Ricardo Gomez Angel on Unsplash; Conner Baker on Unsplash; Ajay Parthasarathy on Unsplash; Nicolas Hoizey Poa on Unsplash

Engineering Research Opportunities Inspired by Nature

Although separate disciplines, the convergence of biology and engineering has enormous potential to solve some of our greatest problems. Bulletproof vests. Solar panels. Exoskeletons. These advances once seemed impossible to create, but they are now a part of our lives.

The 8 Impossible Things provide fertile ground to envision distinct topics for engineering research. Framed within the three exploratory research domains proposed by NSF, disparate priorities converge as opportunities for cross-cutting impact.

Research priorities that could rapidly advance engineering solutions in the bio-inspired/bio-informed domain include:

- **Biomaterials and biodegradables** to replace components that fill landfills today and may offer further benefits, such as the ability to resist disease pathogens;
- **Next-generation sensors, monitoring, and reporting systems** that detect pollution and infectious disease on surfaces, in municipal effluent systems, in homes, and in the environment, at scales ranging from cellular to an entire city or region; and
- **Discoveries that leverage commonalities among animals and plants with beneficial capabilities** such as long lifespans, limb regeneration, or the ability to live in extreme environments.

Using biological entities as building blocks, the repurposing biology domain offers engineering priorities ripe for exploration, to include:

- **New materials** that can sequester carbon and filter, remove, or transform pollutants into benign alternatives;
- **Leveraging the brain-machine interface** and systems intelligence to improve communication and computing devices; and
- **Stronger, long-lasting bio-based materials** for buildings and other infrastructure.

Research priorities that can be framed as improving on biology include:

- **Regenerative engineering and improvements on human biology**, from lightweight, human-powered prosthetics to improving communication through better understanding of the brain-machine interface and innovation in wearables or implants that enable new human-to-device interfaces;
- **Advances in additive manufacturing** enabling custom bio replacement parts;
- **Models to understand aging and its effects** with an eye toward cellular reprogramming and rejuvenation, including ways to short-circuit senescence and exploring DNA repair mechanisms

Prioritized by the participants, the fundamental research topics, as well as estimated timeframes to bring envisioned results to fruition, are provided on the following pages.

Identified Research Priorities

#1 impossible thing — SMARTPHONES DON'T NEED A TRADE-IN; THEY REPRODUCE

2 YEARS	5 YEARS	10 YEARS
The brain-machine interface and systems intelligence, with a vision for what's next in personal communication and computing devices (beyond the smartphone). Identifying market drivers and conducting life-cycle analysis to determine which components hold the most promise for R&D.	Advances in additive manufacturing to generate custom bio replacement parts.	Regenerative engineering, building off research into self-healing infrastructure.

#2 impossible thing — A BUSINESSWOMAN FLIES TO WORK USING HER NEW EXOSKELETON

2 YEARS	5 YEARS	10 YEARS
Data-sharing and monitoring systems (for safety and to identify maintenance and repair needs). Applying new functionalities for existing prosthetic devices.	Ultra-lightweight, high-density propulsion and power systems. Two-way, human-to-device interfaces using wearables or implants. For internal systems, ways to boost the human body's resources to power implant or prosthetic systems. Strong, lightweight materials, with bone as the optimal model.	Bio-inspired principles for navigating, landing, and avoiding physical structures.

#3 impossible thing — YOUR BATHROOM MIRROR PERFORMS HOSPITAL-GRADE DIAGNOSTICS

2 YEARS	5 YEARS	10 YEARS
Efficient data-sharing using a "physician in the loop" model that also ensures patient privacy. Methods to integrate data from multiple samples and platforms and to analyze these integrated databases for the greatest benefit for individuals and population health.	New testing platforms and sensors that are accurate using tiny biosample sizes. Methods and models to detect baseline changes in key biometric measures from a variety of sensing technology mechanisms and biosample types.	Purpose-designed artificial intelligence (AI) conversational interfaces that could be leveraged to detect changes in voice, expression, and appearance that correlate with health changes.

#4 impossible thing — THERE'S NEVER ANOTHER "YOUR CHILD HAS BEEN EXPOSED TO..." SIGN AT DAYCARE

2 YEARS	5 YEARS	10 YEARS
Passive sensing and health risk prediction technology for in-home use. Biologically-inspired sensors and diagnostics to monitor at larger (population) scale. R&D inspired by naturally anti-pathogenic surfaces (e.g., shark skin) and natural systems in biology that protect organisms living in fetid environments.	New smartphone interfaces for automated disease tracking. Models to quickly predict vaccine efficacy for emerging diseases. Evaluation of biofilms that could be repurposed to develop invisible "bioarmor" or a barrier to prevent entry of pathogens. Multi-faceted, multiplexed, dynamic models, devices, and sensors to identify environmental factors that affect pathology from air, surfaces, and effluent sources.	Machine learning and AI models to collect, track, and analyze data to predict future pathogens. Novel approaches for wearable devices for detection combined with targeted therapeutics to enhance immune activity for targeted patient groups. Methods to enable identification of people vulnerable to particular pathogens and systems to mitigate transmission.

#5 impossible thing: ANY-TOWN USA MANUFACTURES ALL THE CHEMICALS AND MATERIALS IT NEEDS FROM PLANTS GROWN NEARBY

2 YEARS	5 YEARS	10 YEARS
Life-cycle analysis and techno-economic analysis to determine what processes are the best targets for future engineering research and development and what specific communities need, as well as predictive models for technology transfer and process scale-up. Biological systems for biomanufacturing potential (biomining the full periodic table). Low-cost infrastructure development for local data-sharing that is cybersecure.	Novel, low environmental impact methods (e.g., net zero carbon intensity and low-water consumption) to process and purify finished materials. Methods to prioritize production of chemicals and materials based on technical and economic feasibility for their use and projected societal benefits.	New, truly low-cost methods to cultivate and process local lignocellulosic feedstocks as a sustainable source to replace fossil feedstocks. Improved real-time monitoring, including better imaging for collecting data in large-scale systems to facilitate high-fidelity scale-up and more efficient large-scale equipment design and operation.

#6 impossible thing: LIFESPANS ARE NO LONGER DEFINED BY ZIP CODE

2 YEARS	5 YEARS	10 YEARS
Improving the methods and models to collect, mine, analyze, and visualize integrated datasets and data infrastructure to make information more usable, accessible, and accurate using AI and machine learning. Enhancing capabilities in data access, management, and security, working in collaboration with stakeholders and communities to ensure the design meets their needs.	Developing new types of targeted sensors and monitoring systems that can collect multiple endpoints and generate maps to track data over time.	Collaborative efforts to prioritize collection of data with the strongest connection to positive clinical outcomes that can be leveraged for targeted follow-up studies and analyses.

#7 impossible thing — CENTRAL NYC RESIDENTS BREATHE PRISTINE MOUNTAIN AIR

2 YEARS	5 YEARS	10 YEARS
Improving devices for air quality monitoring and source identification to determine the causes of pollution at a more granular level (e.g., pollution from indoor heating systems; automobile exhaust; industry, agriculture, etc. New materials inspired by biology that sequester carbon, filter pollutants, or make pollutants benign. Bio-based materials for civil infrastructure that maintain strength and longevity.	Rapid adaptation and scaling of existing technologies and solutions for pollution capture or mitigation. Methods for upgrading existing infrastructure to accommodate sustainable, efficient power grids. Understanding the role of carbon capture in improving air quality. Filters and other technology that can sense, capture, and remove pollutants directly from the air.	New bioremediation materials that can remove pollutants on contact.

#8 impossible thing — A 100-YEAR-OLD BREAKS THE 100-METER SPRINT RECORD

2 YEARS	5 YEARS	10 YEARS
New ways to test how human performance relates to aging, nutrition. and physical training, with an eye toward longer-term research to develop devices such as biomimetic chips to empower muscles or optogenetic chips to promote regeneration or repair.	Advances in lower-cost prosthetics and mobility solutions to enhance wearable devices and materials to improve athletic performance.	Models to better understand cellular aging and promote cellular health through reprogramming and rejuvenation, as well as testing ways to short-circuit senescence, targeting DNA repair mechanisms in particular. Effective models to discover and assess commonalities among animals and plants that are long-lived, have special capabilities (such as limb regeneration), or that inhabit extreme environments.

Research in these areas can move the 8 Impossible Things that inspired this visioning report into the “possible” column. Advances in biomanufacturing, in turn, will move research discoveries from the laboratory into the hands of industry and society. This report identifies a number of engineering research priorities to enable this important technology transfer mechanism.

Taking Action

The full ERVA report provides a unique look at transformational priorities where engineering and biology can have impact while contributing to an inclusive research community. The aim is to inspire researchers and sponsors (public, private, and nonprofit) to support aligned research leading to innovation and pursue these priorities. ERVA challenges readers to disseminate this report and prioritize areas with potential for the greatest return on investment.

These priority research directions can build momentum to innovate and create meaningful solutions. Sensors can be improved to capture accurate data and diagnostics. Robotics can be leveraged to improve and extend human performance. Materials can be developed to enable local manufacturing and resolve supply chain issues. Pursuing these research endeavors highlights the synergy between engineering and biology to advance technologies that ultimately create cost-saving, equitable, and sustainable solutions for society.

> “Engineers must lead the biotechnology revolution by unleashing biology’s potential and fueling transformative impacts on society, the economy, and our planet.”
>
> SUSAN MARGULIES
>
> NSF Assistant Director for Engineering

Leveraging Biology to Power Engineering Impact

Taking inspiration and knowledge gained from nature, engineers from diverse disciplines regularly identify creative and impactful solutions to complex, global challenges. The Engineering Research Visioning Alliance (ERVA) convened a diverse group of more than 100 technical experts representing the academic, corporate, government, and nonprofit sectors to consider future research opportunities for tackling eight "impossible things."

Background

From advances in genome editing with CRISPR to new robotic designs that take inspiration from the animal kingdom, innovations at the interface of engineering and biology have transformed modern life and impacted a range of fields such as health care, agriculture, and technology.

Despite this rapid progress, the sheer number and complexity of challenges facing the world—from climate change to infectious diseases—require bold, new, creative strategies.

To identify fundamental research gaps and nascent opportunities, specifically in areas where engineers can take the lead, 128 experts met in March 2022 for a two-day virtual visioning event, "Leveraging Biology to Power Engineering Impact." Convened by ERVA and co-hosted by Johns Hopkins University, the University City Science Center, the University of Delaware, and the Waters Corporation, the event inspired creative thinking around complex topics as participants were presented eight "impossible things." Each is a snapshot of an ideal future positively impacted through bold research--and subsequent innovation--at the intersection of biology and engineering. The essential question the event put forward to be addressed:

What are the questions that researchers working at the intersection of biology and engineering should explore to improve the human condition?

Inspiring Creativity While Identifying Key Research Needs in Engineering
ERVA's visioning events gather interdisciplinary groups of researchers to discuss, strategize, and prioritize innovative, high-impact ideas in engineering research.

NSF Assistant Director for Engineering Susan Margulies began the event by sharing her perspective on how engineers can use three approaches—bio-inspiration and bio-informed thinking, repurposing biology, and re-shaping the interaction between biological forms—to design and build new and impactful systems using biology.

Participants were invited to the visioning event based on their areas of expertise and with considerations for diversity across discipline, geography, sector, gender, race and ethnicity, and career stage. Eight breakout groups were tasked with addressing an "impossible thing," a specific challenge posed by the event's leadership (the Thematic Task Force) to provoke bold thinking about future possibilities that can be tackled by research at the interface of biology and engineering.

> "Rapid progress requires convergent approaches. The seamless integration of engineering and biology will drive discovery and inspire innovation."
>
> SUSAN MARGULIES
> NSF Assistant Director for Engineering

With a focus on research directions where engineering approaches and solutions are paramount, attendees proposed avenues for further study and discussed research directions necessary to achieve each goal.

8 impossible things

1. Smartphones don't need a trade-in; they reproduce
2. A businesswoman flies to work using her new exoskeleton
3. Your bathroom mirror performs hospital-grade diagnostics
4. There's never another "your child has been exposed to..." sign at daycare
5. Any-town USA manufactures all the chemicals and materials it needs from plants grown nearby
6. Lifespans are no longer defined by ZIP code
7. Central NYC residents breathe pristine mountain air
8. A 100-year-old breaks the 100-meter sprint record

Opportunities to Leverage Biology to Power Engineering Impact

Impossible Thing 1: Smartphones don't need a trade-in; they reproduce

Instead of waiting in line to pick up the latest smartphone model each year, could a phone simply upgrade itself? While participants agreed that a self-reproducing cell phone in a pure, biological sense is likely impossible, rethinking the relationship between technology and biology sparked bio-inspired ideas for engineering new kinds of sustainable, adaptable, and repairable electronic devices in the future.

A key first step would be to explore biological systems that could effectively perform tasks a cell phone does electronically. Specific research areas include how systems in biology adapt, replicate, heal, produce power, and communicate, as well as how they store and process information.

Engineers could apply engineering principles to develop "design rules" and propose practical and cost-effective designs followed by rapid prototyping. Attendees discussed ways that engineers can leverage their expertise to ensure that prototypes meet specific requirements for mass production and are made from durable, replicable materials and processes.

Participants recognized the value of focusing on one component or specific materials. Another avenue is creating modular hardware units that can produce or be connected to biological components that perform a specific task.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- **Biomaterials and biodegradables** to replace a substantial amount of materials used for cell phone design and manufacture;
- **The brain-machine interface and systems intelligence**, with a vision for what's next in personal communication and computing devices (beyond the smartphone);
- Advances in **additive manufacturing** to generate custom bio replacement parts;
- **Regenerative engineering**, building off research into self-healing infrastructure; and
- **Identifying market drivers and conducting life-cycle analysis** to determine which components hold the most promise for further research and development.

Advantages to developing a new, engineering-driven perspective in this area include reducing electronic waste and use of raw materials, and potential downstream research impacts in areas such as regenerative engineering. By digging deeper into potential communication devices and bio-enhanced delivery channels, this work can create new avenues for future study, such as bio-inspired devices that have more memory, can learn faster, and use less energy, enabling equitable access to new devices and reducing environmental impacts.

Impossible Thing 2: A businesswoman flies to work using her new exoskeleton

Is a commuter-friendly suit the future of transportation? Creating a strong, lightweight, and reliable personal flying device is a highly technical challenge, but leveraging the progress made in similar technologies makes this task possible to achieve in the future. The components required—materials, prosthetics, and organic power generation--could have broader applications for enhancing human capabilities.

A crucial component of this challenge is connecting existing technologies and devices into a single system. Using a human-centered design approach, engineers can leverage their expertise and the latest research in material science, actuators, batteries, sensors, joint replacements, prosthetics, and space suits to design a personal commuter suit that meets the lift, load, and protection requirements needed for human flight.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- For external systems, **new ultra-lightweight, high-density propulsion and power systems**;
- For internal systems, new ways to **boost the human body's resources** to power implant or prosthetic systems;
- Applying **new functionalities for existing prosthetic devices**;
- **Two-way, human-to-device interfaces** using wearables or implants;
- Bio-inspired research into **principles for navigating, landing, avoiding physical structures**, etc.
- **Biobased strong, lightweight materials**, with bone as the optimal model; and
- **Data-sharing and monitoring systems** (for safety and to identify maintenance and repair needs).

Participants noted that relevant technologies are ripe for progress now in several areas, including materials science, actuators, batteries, sensors, and prosthetics. Research progress on such a device would have beneficial applications in other areas, such as personal mobility enhancements and transportation that is both affordable and practical. There is substantial potential for financial and environmentally positive impact on research and development in this area. This also feeds naturally into progress in aerospace engineering, where novel methods of control engineering and the physics of flying objects should be developed.

> "The combination of an eagerness to think boldly, take risks, embrace interdisciplinary collaborations and partnerships, and a commitment to translating our innovations into technologies that improve the human condition, is what I see happening here."
>
> ED SCHLESINGER, dean of the Whiting School of Engineering at Johns Hopkins University

Impossible Thing 3: Your bathroom mirror performs hospital-grade diagnostics

Participants agreed that a future where individuals can perform screenings and monitor their health on a daily basis from the comfort of their home is within technical reach. Bringing the necessary device (or devices) into the home would require significantly more production and availability of diagnostic tests, sample types, and new platforms to launch, monitor, and manage such devices in an economically feasible, accessible, equitable, and secure way. Privacy concerns will need to be addressed as technology is developed.

As a starting point for early integration into an in-home system, participants recommended that efforts focus on optimizing existing devices, such as personalized health trackers, medical patches, toilets and sinks that test samples for disease, and smart home health devices such as scales.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- New **testing platforms and sensors** that are accurate using tiny biosample sizes;
- **Efficient data-sharing** using a “physician in the loop” model that also ensures patient privacy;
- Methods and models to **detect baseline changes in key biometric measures** from a variety of sensing technology mechanisms and biosample types;
- Methods to **integrate data from multiple samples and platforms** and to analyze these integrated databases for the greatest benefit for individuals and population health;
- **Purpose-designed artificial intelligence (AI) conversational interfaces** that could be leveraged to detect changes in voice, expression, and appearance that correlate with health changes.

Participants noted that evaluating future prototypes in a research hospital or other health care facility would allow opportunities for refinement before the device is produced for home use. Such a device could integrate advances in both computing power and diagnostic tools and align with other research efforts to detect disease early to reduce health care costs.

Impossible Thing 4: There's never another "your child has been exposed to..." sign at daycare

As the COVID-19 pandemic moves into the next phase, is it possible to hope that exposure notifications could become a thing of the past? While participants agreed that completely eradicating all infectious diseases is likely impossible, discussions targeted creative ways to reduce a disease's impact on daily life.

To tackle this impossible thing, engineers should bring control theory to management of the microbiome as a whole rather than focusing on disease-causing elements alone. Engineers are well positioned to collect and analyze data to create better models and predictions, define the overall problem's parameters, test new platforms and technologies using rapid prototype development cycles, and bring their problem-solving thinking to this complex issue. For all three research priorities identified—disease monitoring, efforts to boost immune systems, and disease ecology—developing effective, low-cost ways to manage and share data with infectious disease and clinical experts is critical to ensure wide adoption and equitable access.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- Solutions to improve **disease monitoring** with a focus on development of low-cost, large-scale, automated platforms to rapidly detect, identify, and preemptively address new pathogens and model risks on a global basis, including:
  - » **Biologically inspired sensors and diagnostics** to monitor at larger (population) scale, e.g., connected to waste treatment, air handling systems, etc.;
  - » **Passive sensing and health risk prediction technology** for in-home use;
  - » **Machine learning and AI models** to collect, track, and analyze data to predict future pathogens; and
  - » Creating **new smartphone interfaces** for automated disease tracking.

- **Engineering research supporting efforts in biology to boost the immune system**, including:
  - » **Passive, low-cost, effective ways to collect useful data during clinical trials** to inform precision prevention and therapeutics development;
  - » R&D inspired by **naturally anti-pathogenic surfaces (e.g., shark skin) and natural systems in biology** that protect organisms living in fetid environments;
  - » **Models to quickly predict vaccine efficacy** for emerging diseases;
  - » Evaluation of **biofilms that could be repurposed to develop invisible "bioarmor"** or a barrier to prevent entry of pathogens; and
  - » Novel approaches for **wearable devices for detection combined with targeted therapeutics** to enhance immune activity for targeted patient groups.

- Research in **disease ecology**, how transmission occurs, and methods for mitigation, including:
  - **Multi-faceted, multiplexed, dynamic models, devices, and sensors** to identify environmental factors that affect pathology from air, surfaces, and effluent sources; and
  - Methods to **enable identification of people vulnerable to particular pathogens** and systems to mitigate transmission.

New tools and technologies are developing rapidly, such as the ability to quickly detect, sequence, and track new disease variants and the highly programmable and rapidly deployable mRNA vaccines. With heightened public awareness of the impacts of pandemics, there is increased interest in enhancing disease monitoring, tracing, and mitigation efforts to slow the spread and reduce the effects of new outbreaks.

> "I encourage all of us to make this the start of a conversation and a collaboration building to a future. If we use this opportunity to connect, to go outside of our traditional boundaries, powerful stuff can happen here."
>
> HEATH NAQUIN, vice president of government and capital engagement at University City Science Center

Impossible Thing 5: Any-town USA manufactures all the chemicals and materials it needs from plants grown nearby

Supply chain disruption initiated by the pandemic and exacerbated by war and other factors make the prospect of empowering communities to produce their own critical resources and raw materials increasingly attractive.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- **Life-cycle analysis and techno-economic analysis** to determine what processes are the best targets for future engineering research and development and what specific communities need, as well as predictive models for technology transfer and process scale-up;
- Novel, **low environmental impact methods (e.g., net zero carbon intensity and low-water consumption) to process and purify finished materials**;
- **Biological systems for biomanufacturing potential** (biomining the full periodic table);
- **New, truly low-cost methods to cultivate and process local lignocellulosic feedstocks** as a sustainable source to replace fossil feedstocks;
- Improved real-time monitoring, including **better imaging for collecting data in large-scale systems** to facilitate high-fidelity scale-up and more efficient large-scale equipment design and operation;
- **Methods to prioritize production of chemicals and materials** based on both technical and economic feasibility for their use and projected societal benefits; and
- **Low-cost infrastructure development** for local data-sharing that is cybersecure.

New advances and technical capabilities in fields such as biomanufacturing can accelerate advances to achieve this “impossible thing.” With increasing pressures on global supply chains and the desire to transition from reliance on petroleum products to locally available, economically sustainable energy sources, finding new ways to produce materials for daily life close to home should be prioritized.

Impossible Thing 6: Lifespans are no longer defined by ZIP code

The year 2020 brought renewed attention to the role of social and geographic factors in a person's health and well-being, and to the disproportionate impact of these factors for underrepresented populations. While addressing this particular impossible thing remains a large-scale challenge because of the many complex variables at play and potential causative factors involved, there is an opportunity for engineering research to take a leading role in addressing this issue. This topic is ripe for rapid R&D advancement when engineering researchers leverage recent advances in biotechnology, data science, and renewed recognition of the relationship between geography and health.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- **Improving the methods and models to collect, mine, analyze, and visualize integrated datasets** and data infrastructure to make information more usable, accessible, and accurate using AI and machine learning;
- Collaborative efforts to **prioritize collection of data with the strongest connection to positive clinical outcomes** and that can be leveraged for targeted follow-up studies and analyses;
- Developing **new types of targeted sensors and monitoring systems** that can collect multiple endpoints and generate maps to track data over time; and
- **Enhancing capabilities in data access, management, and security** working in collaboration with stakeholders and communities to ensure design is appropriate to meet their needs.

> "As the pandemic showed us, when there is a critical unmet need and when those involved in fundamental research and commercialization work side by side, we can make what appears to be the impossible possible. It's great to be challenging mindsets to convert these eight topics into something that's possible, but it would be equally impressive if we can disrupt the paradigm that delivers these solutions to society."
>
> STEVE MARTIN, vice president, global research, Waters Corporation

Impossible Thing 7: Central NYC residents breathe pristine mountain air

Can megacities enjoy air that's as clean as a nature preserve? This challenge was seen as "very possible" to meet. However, the complex nature of air quality and the sheer economic scale of reducing emissions and remediating unclean air presents a massive challenge.

Where can engineers take the lead? As a first step, the attendees recommended that engineers determine if air quality can be improved using existing technologies and, if not, how bio-inspired approaches could assist. For the latter, a next step would be to develop a research framework that applies effective processes from biology and then designs a viable, affordable, and scalable way to leverage those processes within the context of engineering principles.

IDENTIFIED TOPICS POSSESSING THE GREATEST RETURN ON INVESTMENT AND TO BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- **Rapid adaptation and scaling of existing technologies and solutions** for pollution capture or mitigation (e.g., electric cars, gas fermentation at heavy industry sites);
- Improving **devices for air quality monitoring and source identification** to determine the causes of pollution at a more granular level (e.g., pollution from indoor heating systems, automobile exhaust; industry, agriculture, and waste management emissions; pollution sources outside the immediate region);
- Developing methods for **upgrading existing infrastructure** to accommodate sustainable, efficient power grids;
- **New materials inspired by biology** that can sequester carbon, filter pollutants, or be engineered to make pollutants benign;
- Research in new **bioremediation materials** that can remove pollutants on contact;
- **Bio-based materials for civil infrastructure** that maintain strength and longevity;
- Better understanding of the **role of carbon capture in improving air quality**; and
- Filters and other technology that can **sense, capture, and remove pollutants directly from the air**.

Another specific approach includes establishing testing sites and prototypes locally in cities so residents and other interested partners can see the effects that different devices have on air quality. Engineers can work with social scientists to engage multiple stakeholders and partners at all stages and engender community buy-in by demonstrating how devices and prototypes help reduce air quality disparities between communities.

Recent technological progress is a springboard for scaling up, and further progress holds the promise to advance solutions for other challenges, such as biological remediation. This topic is of high interest to U.S. government agencies because of negative and unevenly distributed impacts of poor air quality that are likely to be further exacerbated by climate change. As a global health issue, air quality is poised for multinational collaboration.

Impossible Thing 8: A 100-year-old breaks the 100-meter sprint record

Can advances at the nexus of engineering and biology research help a 100-year-old person break a world record? Participants chose to recast this "impossible thing" as a challenge to sustain peak athletic performance and stamina rather than retain world-class speed into old age. With a combination of anti-aging tools, new training accessories and prosthetics, and regenerative medicines that prevent senescence entirely, a future where a centenarian can break records is certainly within reach.

Three specific areas of research were identified where engineering could take the lead: 1) robotics and related technology, 2) decelerating the aging process, and 3) research on animals and plants with long life spans. Better understanding of aging as a biological process is a foundational knowledge gap that engineering research can address by applying systems-level thinking to the complex biological matrix that underlies the aging process.

IDENTIFIED TOPICS THAT COULD HAVE THE GREATEST RETURN ON INVESTMENT AND SHOULD BE PRIORITIZED BY THE BIOLOGY AND ENGINEERING RESEARCH COMMUNITY INCLUDE:

- Advances in lower-cost prosthetics and mobility solutions to **enhance wearable devices and materials to improve athletic performance**. Forward movement in this area can inform R&D efforts on more complex devices, such as **full-body exoskeletons**, as well as **passive technologies to improve athletic performance or slow the effects of aging**, such as shoes or clothing.
- **Models to better understand cellular aging and promote cellular health through reprogramming and rejuvenation**, as well as testing ways to short-circuit senescence, targeting DNA repair mechanisms in particular;
- New ways to **test how human performance relates to aging, nutrition, and physical training**, with an eye toward longer-term research to develop devices such as biomimetic chips to empower muscles or optogenetic chips to promote regeneration or repair; and
- **Effective models to discover and assess commonalities** among animals and plants that are long-lived, have special capabilities (such as limb regeneration), or inhabit extreme environments. This will provide findings to leverage in future research to reverse or retard aging.

Participants noted that although this research was framed as focusing on increasing athletic prowess in old age, this research has the potential for great societal benefits far beyond this domain, including improved quality of life

> "As we continue our 'wild thinking,' I wanted to encourage you to draw on this sense of discovery that fueled the many advances that have allowed us to live long and prosper. Academic institutions have a special responsibility to focus on practical outcomes that make a difference for the diverse communities that we serve here in our country."
>
> LEVI THOMPSON, dean, University of Delaware College of Engineering

Overall Assessment and Moving Forward

Bio-replacement is well-known territory to leverage biology to inform the design of engineered replacements. But three other research domains at the intersection of biology and engineering offer myriad opportunities to expand the boundaries: *bio-inspired/bio-informed; repurposing biology, and improving on biology*. This report identifies promising research priorities where engineering is needed for impact and where vision is required to pave the way for progress.

Bio-inspired/bio-informed research uses functional-structural mechanisms from biology for engineered system design, leveraging an understanding of systems within the bodies and organisms to inspire engineered constructs. Research priorities that could rapidly advance engineering solutions include

- **Biomaterials and biodegradables** to replace components that fill landfills today and may offer further benefits, such as the ability to resist disease pathogens;
- **Next-generation sensors, monitoring, and reporting systems** that detect pollution and infectious disease on surfaces, in municipal effluent systems, in homes, and in the environment, at scales ranging from cellular to an entire city or region; and
- **Discoveries that leverage commonalities among animals and plants with beneficial capabilities** such as long lifespans, limb regeneration, or the ability to live in extreme environments.

Using biological entities as building blocks, repurposing biology leverages molecules, cells, and other structures to perform new functions. Engineering priorities ripe for exploration include:

- **New materials** to sequester carbon and filter, remove, or transform pollutants into benign alternatives;
- **Leveraging the brain-machine interface** and systems intelligence to improve communication and computing devices; and
- **Stronger, long-lasting bio-based materials** for buildings and other infrastructure.

NSF Assistant Director for Engineering Susan Margulies challenged visioning event participants by asking whether engineering can “best” biology. This nascent research domain offers enormous opportunities for new functions and systems. Research priorities that can be framed as improving on biology include:

- **Regenerative engineering and improvements on human biology**, from lightweight, human-powered prosthetics to improving communication through better understanding of the brain-machine interface and innovation in wearables or implants that enable new human-to-device interfaces;
- **Advances in additive manufacturing** enabling custom bio replacement parts;
- **Models to understand aging and its effects** with an eye toward cellular reprogramming and rejuvenation, including ways to short-circuit senescence and exploring DNA repair mechanisms

Research in these areas can move the 8 Impossible Things that inspired this visioning report into the “possible” column. Advances in biomanufacturing, in turn, will move research discoveries from the laboratory into the hands of industry and society. Several priorities identified in this report are envisioned to enable biomanufacturing, including:

- **Biomining the full periodic table** by leveraging biological systems for biomanufacturing potential;
- **Identifying market drivers and conducting life-cycle analysis** on processes, materials, and technology to prioritize those with the most promise for production and scale-up; and
- Leveraging new discoveries—from improved materials to bio-informed power sources and bio-inspired communication systems—to **rapidly adapt and scale existing technologies and solutions**.

From these 8 Impossible Things, a roadmap emerges with action steps to make significant impacts on our nation's most vital resources, including health care, transportation, and manufacturing, and inspire new technology to improve the lives of citizens. The priority research areas outlined in this report point to immediate steps to pursue research-based advances at the intersection of biology and engineering. From solutions to minimize exposure to infectious diseases and data tracking to make health information more accessible, to bio-based materials with the promise to increase sustainability and reduce reliance on fossil fuels, engineering and biology have a role to play in making the impossible possible. We call on researchers and sponsors (public, private, and nonprofit) to support aligned research leading to innovation and pursue these priorities. ERVA challenges readers to disseminate this report and prioritize areas with potential for the greatest return on investment.

Appendix A: Visioning Event Participants

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Ishwar Puri, University of Southern California

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Will Richardson, Clemson University

Michael Roberts, International Space Station National Lab

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Appendix B: Event Presentation Summaries

Leveraging Biology to Power Engineering Impact

Presented by NSF Assistant Director for Engineering Susan Margulies; Lynn Rothschild, Research Scientist, NASA Ames Research Center; and C. Brandon Ogbunu, Assistant Professor, Yale University

Susan Margulies opened the visioning event with remarks that transitioned to a lively panel discussion with Lynn Rothschild, a research scientist at NASA's Ames Research Center, and C. Brandon Ogbunu, an assistant professor from Yale.

Ogbunu, who studies the intersection of evolutionary biology, genetics, and epidemiology, shared his perspectives on how seeing biology as an "information science" has shaped his lab's thinking and work. He also discussed ways to get diverse groups of students and faculty engaged in a wide variety of topics.

Rothschild shared how NASA's structure and focus on problem solving catalyzes "revolutionary solutions" and highlighted the importance of fostering creativity in students and early career researchers.

Three other talks also took place during the two-day event. First, David S. Kong, Director of the Community Biotechnology Initiative at MIT media lab, discussed how researchers can ensure representation and participation in technology and how including diverse perspectives and backgrounds will increase the likelihood of producing unique and creative solutions.

Sarah Richardson, CEO of MicroByre, challenged participants to question their assumptions and how engineering principles and frameworks can distort what one assumes is possible. Her take-home message? "Impossible is a heavy word, so what did you assume that led you there?"

Eleni Stavrinidou, an associate professor at Linköping University and PI of the Electronic Plants group, shared how engineers have historically been inspired by natural systems, typically by mimicking what plants and animals can do, and recommended that researchers embrace different approaches that unite technology and biology into a more symbiotic relationship.

Recordings of the inspirational panel and motivational talks are available at ervacommunity.org/event/visioning-event-biology/2022-03-09/

Diversity & Agency at the Multidisciplinary Frontiers of Technology

Presented by David Kong, MIT Media Lab, Synthetic Biologist

Innovation comes from exploring the intersection of different creative domains. Thus, the most innovative solutions in biology are unlikely to come from biologists. Instead, the best ideas come from people far away from the discipline. This distance ensures diverse perspectives and technical and social backgrounds, and it is more likely that they will generate more innovative, exciting, and disruptive ideas. Examples of this phenomenon in synthetic biology include Drew Endy, a civil engineer who suggested scientists could engineer living systems the same way they can a jet plane or a bridge. Tom Knight, a computer scientist, suggested that scientists could program cells just as computer scientists program computers.

The context and the form in which we use technology are important. When technologies mature, they are available to a more diverse group of people across more geographic locations. In life sciences, this approach has led to "Do It Yourself Biology." There are now community-driven laboratories in public libraries, a "bio fab lab" floating down the Amazon River, nomadic "bio busses," and MIT's Global Community Bio Summit. These extensions of the traditional lab increase access and participation in biology.

David Kong has been teaching an MIT and Harvard graduate synthetic biology class that enables students from around the world, many of whom are from diverse disciplines and have never been in a wet lab, to create innovations related to biology. To overcome problems of physical accessibility to the lab, the instructors taught the students how to program in-lab robots with Python so they could work on their experiments from anywhere in the world.

Science and technology can be inaccessible, especially for young people. One way to increase accessibility is to use music, a universal art form. Kong created a record player that translates data about microbes into sound and music. Young people swabbed objects in their communities, then Kong had the data sequenced, and a creative team created music based on the microbial content of these different objects.

KEY TAKEAWAYS

- Bringing together different types of disciplines and creative backgrounds can enable innovation.
- Increasing the distance between the solvers' field of technical expertise and the focal field of the problem leads to more innovative solutions.
- When technologies become available to more people, the people who use the technology and the geographic area in which they use it expand.
- Technology can make life sciences accessible to diverse populations around the world.
- One effective way to increase accessibility to technology is to use music because it is a universal art form.

Plant-Based Biohybrid Systems

Presented by Eleni Stavrinidou, Associate Professor and Principal Investigator at Electronic Plants Linköping University

Background

Engineers and innovators have been inspired by nature to bring technological solutions. Many of these efforts focus on trying to mimic the natural structures with artificial materials to reproduce the functionality, a process called "biomimicry." One such example is the gecko-inspired adhesive that mimics the nanostructure of the gecko to an adhesive surface. Scientists can also strive to repurpose natural processes and functions for technological solutions. For example, bioluminescent algae can be incorporated into an urban environment to light up a walkway. Biology itself offers inspiration when organisms use other organisms as their technology; for example, plants and legumes form mutualistic symbiosis with nitrogen-fixing bacteria. Symbiosis with algae can change how a sea slug gets its nourishment: Instead of consuming the chloroplasts in the algae as food, the slug integrates them into its own cells, enabling the animal to undergo photosynthesis and eliminating the need for external food sources.

Recent research further shows that it is possible to have symbiosis between technology and biology, with bi-directional communication between the two. Plants are energy converters; they sense their environment, and they synthesize surrounding materials. An example of using the energy conversion properties of plants is converting the products of photosynthesis, sugars, and oxygen into a form of energy. As another example, Michael Strano at MIT has shown the ability of plants to signal changes in their environment via a readable fluorescent signal in the plant leaves.

Eleni Stavrinidou, associate professor and principal investigator at Electronic Plants Linköping University, has developed a plant root that, over time, became an electronic conductor. When she induced a rose to take up a molecule called ETE-S, it created threads throughout the plant that conduct electricity. These biohybrid electrified plants continued to thrive: the electrical threads did not affect the plant's biological processes. These plants continue to grow and could also charge a battery.

KEY TAKEAWAYS

- Nature can inspire engineering solutions for society.
- Engineers can view plants from a technological perspective.
- It is possible to have symbiosis between technology and biology, with bi-directional communication between the two.
- A plant-technology hybrid can continue to grow and develop while functioning as an electricity conductor.

Impossible is a Matter of Perspective

Presented by Sarah Richardson, MicroByre, CEO

Background

Breakthroughs in science come from the re-evaluation of assumptions in a different context. Someone from a different technical or ethnic background or with orthogonal expertise can see things in a new context and then pick up the thread, leading to new insights. They do not invent a new technology: they create a new perspective that changes the ground assumptions and the idea of what is possible. Examples of negating long-held assumptions include questioning:

- the accurate formula for determining melting temperature that had been accepted for 20 years (led to a more accurate formula);
- whether a person could build a billion-dollar company based on the idea that people would pay to sleep in a stranger's home (led to creation of Airbnb);
- whether machines must involve something that simulates a bird's flapping wings (led to the creation of airplanes).

Synthetic biology is frequently described as bringing engineering principles to biology. The language describing the field, which uses analogies of programming and circuits, is borrowed from control theory in computer science and electrical engineering. Unfortunately, many assumptions are built into the language, which has greatly influenced what is thought possible or impossible. Language matters because the synonyms scientists use speak volumes about their attitudes. Connotation exposes the speaker's philosophy. When scientists talk about cells being controllable or programmable, their framework has made it too easy to accept assumptions that distort their perception of what is possible or impossible. Scientists must consider word choice when trying to understand someone else's work. Doing so can shift the paradigm cemented by unexamined assumptions masquerading as technical limitations.

The properties of biology can make something impossible. If an organism is resistant to the task scientists assign to it, it will not do it well (if it does it at all). A scientist who understands this law of biology would not accept the control analogy used by computer scientists and would have a very different idea of what is possible.

Impossible is a heavy word. If a plan is "impossible," does that mean it is impractical but possible? Or impractical but hard to achieve? Does it mean it is feasible but will not scale? Does it mean it is realistic but violates the laws of man? Or does it mean impossible, i.e., violates the laws of physics or biology? Scientists cannot afford to let their biases become their evidence, and they must ask what assumptions led them to decide something was impossible in the first place.

KEY TAKEAWAYS

- Breakthroughs in science come from re-evaluating assumptions in a different context.
- When people change their perspective, formerly "impossible" tasks become mundane.
- The synonyms scientists use in describing their work speak volumes about their attitude.
- Understanding word choice can shift the paradigm cemented by unexamined assumptions rather than actual technical limitations.
- There are different meanings of "impossible." Many of these meanings do not indicate that a thing cannot be done.

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