BSE
Biological Systems
and Engineering

2022 - 2027

BIOLOGICAL SYSTEMS AND ENGINEERING DIVISION

STRATEGIC PLAN

FROM THE DIVISION DIRECTOR

Since 2016, I have had the great honor to lead the Biological Systems and Engineering Division in the Biosciences Area of Berkeley Lab. The best part of our division is the world-class talent of our people. Our expertise ranges wide; from cutting-edge technology in automation and the next generation of analytics-driven research, to the discovery of new biology-enhanced fuels and chemicals to reduce our dependence on fossil fuels and to absorb carbon from our atmosphere to life-saving advances in health research to protect energy workers and average citizens alike. Our research is enabled by operations professionals that design and maintain one-of-a-kind instrumentations, keep people safe through physical and psychological wellness initiatives, and open the doors of science to everyone including young learners, community members, and stakeholders. As part of Berkeley Lab's Biosciences Area, we are a part of a large National Lab mission dedicated to biological research in service to the Department of Energy mission and the needs of the United States.

In Winter 2021, I charged our intellectual community to devise a strategic plan to unify the diverse research foci and operations and technical strengths of our division. Our breadth and depth of research, operations, and technical abilities is a tremendous strength when organized and coordinated.

Our plan was envisioned by representatives from all types of roles and career stages. By examining what is possible in seven years, we have the opportunity to align programs between proposal cycles, focus our Laboratory Directed Research and Development (LDRD) funds toward coordinated goals, and work with our stakeholders and collaborators to deliver orchestrated mission-driven research. Seven years to take on the most pressing issue the world will face, climate change. Seven years to develop solutions that will benefit people and the planet.

Clearly, these are audacious goals, and we know we are not acting alone, both in the global community and here in the division. We can deepen our contributions to the Biosciences Area Strategic Plan and wholeheartedly participate in Berkeley Lab's mission and scientific goals. In that regard, we express our gratitude to those who work with us to improve and advance our discoveries and developments. Every member of the division involved in this process deserves appreciation, from the initial survey respondents who framed the scope of this work in the division, to the teams that developed ideas to move forward, and to the reviewers and editors who honed the ideas and the narrative. Involvement in this process allowed us to value our work in a wider context and exposed us to the brilliance of our colleagues.

Our ambitious goals will bear many types of fruit: some anticipated, others not. Through this plan, we set our intentions high to make a difference. This is our call to action.

Onward,

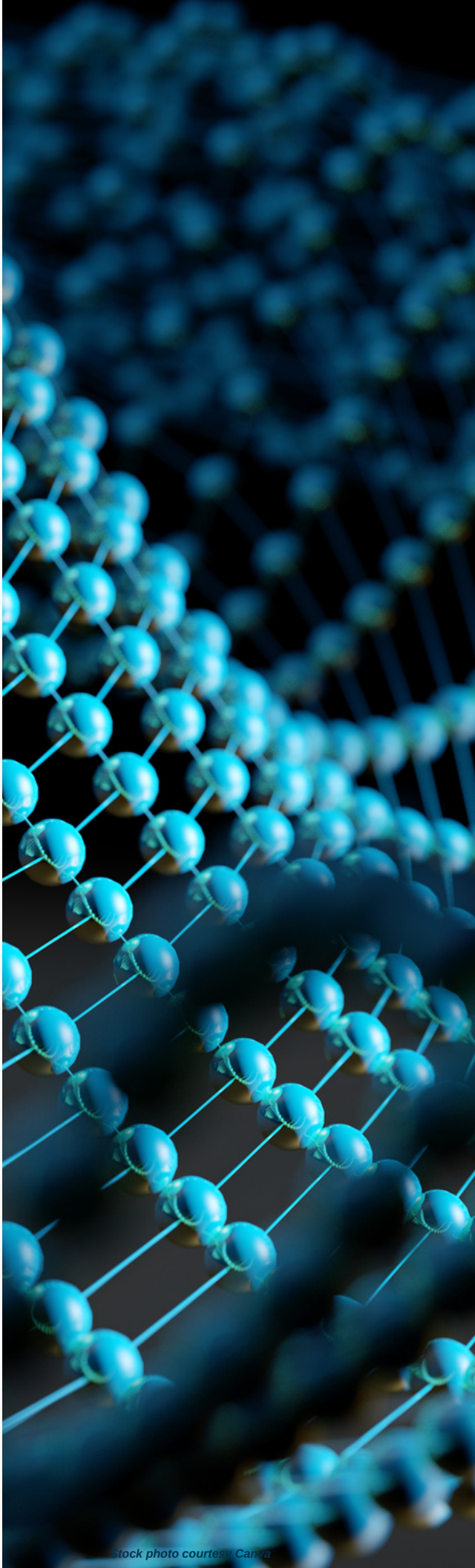
Blake Simmons

Blake Simmons, PhD
Division Director,
Biological Systems and Engineering
December 2022

Editorial Note: Every effort has been made to define acronyms upon first the usage in this document. A list of commonly used acronyms can be found at https://biosciences.lbl.gov/acronyms/

TABLE OF CONTENTS

BSE
Biological Systems and Engineering



INTRODUCTION

The goal of this strategic plan is to capture and align BSE's capabilities and strengths, to set audacious goals to address difficult challenges in the natural and built environment that threaten our nation and world, and to thoughtfully nurture the talent to do this work.

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

The Biological Systems and Engineering (BSE) Division discovers solutions using an interdisciplinary approach. We are a diverse division, with a broad portfolio of research areas and sponsors. The goal of this strategic plan is to capture and align BSE's capabilities and strengths, to set audacious goals to address difficult challenges in the natural and built environment that threaten our nation and world, and to thoughtfully nurture the talent to do this work. At BSE, we believe our greatest strength is our people and their talent. With contributions from the entire BSE community, this plan was developed through division-wide virtual meetings, surveys, focused sprint teams, and feedback sessions. These activities brought together groups to imagine and prioritize what is possible over the next seven years.

The BSE people first approach leads us to first present our Inclusion, Diversity, Equity, and Accountability (IDEA) goals. Continuous improvement in IDEA will enable the best science and technology to come to light, in BSE, in the Biosciences Area and at Berkeley Lab.

This strategic coordination plan is not intended to comprehensively list all the research conducted in BSE, but rather to highlight the most important themes to enable our division's success. The two science themes included are Carbon Negative Research and the Health/Energy Nexus Research. These topics represent the most urgent research we are uniquely qualified to address to mitigate the risks posed to people and the planet.

This urgency delivers our final goal of Automation and Self-driving Labs. Even with the capabilities of our talented staff and the capabilities they use every day, to fully meet our ambitious carbon negative and health/energy nexus goals the expedient development of automation and self-driving labs is necessary. To address these audacious challenges, we need state-of-the-art tools and approaches, including integrating dense data more fully in experimental iteration.

BSE has been integral to achieving the aims of the Biosciences Strategic Plan[1] (BSP) and building out the capabilities of the Biosciences Area since its creation seven years ago. For example, BSE is the home of nearly all of Biosciences' biomanufacturing research and development, which was in its early stages during the creation of the BSP in 2013. Through BSE strategic leadership, the Division is now home to premier Department of Energy (DOE) biomanufacturing capabilities that arose through those strategic planning efforts and is the significant contributor to that Area-wide and Lab-wide strategic goals. BSA researchers have leveraged capabilities for understanding the impacts of environment on human health into new research programs that support national security missions, the beginnings of which were envisioned in the 2019 BSP update. BSE's strong strategic contributions to Biosciences' leadership are demonstrated through its successes since 2015. This plan seeks to lay a foundation for the next seven years of BSE strategy and will be an important step in the process of visioning a new BSP in 2024.

1. https://biosciences.lbl.gov/strategic-plan/

To achieve our science and technology goals we must understand and address the needs of the BSE community and the people who are impacted from our discoveries.

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

Strategy Scope:

Simply put, we cannot achieve our science and technology goals without understanding and addressing the needs of the BSE community and the people who are impacted from our discoveries. We have a two-pronged approach for improving IDEA (inclusion, diversity, equity, and accountability) for BSE: internal and external impact. Internally, we will advocate for improving salary competitiveness, both locally and compared to sibling National Labs, with an eye towards equity within all pay ranges and strive to optimize personnel access to the extensive benefits and resources available at Berkeley Lab. BSE will serve as training-hub for many aspects of a successful bioeconomy workforce, including training in upskilling, leadership, program development and communications. External-facing goals include building a more vibrant network of external partners and supporting a culture of discussing and evaluating the positive and negative impact of our research and collaborations on underserved populations. We recommend improving recruitment, hiring, and retention of talent, including through approaches such as training managers for implicit bias and increasing outreach of paid advertising in journals and websites that reach underserved populations. Together, our goal for BSE as a diverse and inclusive Division is to expand access to research internally and externally to underserved groups.

Rationale for this goal:

- As a community of diverse individuals, we affirm that the joy of discovery is for everyone and improving IDEA goals is the right thing to do. The complex challenges that BSE has undertaken, require input and participation of a diverse group of researchers and team members. Our goal is to make BSE and DOE resources available to a wider swath of people, both locally and nationally, for improved transparency and public service.
- BSE has the opportunity to be a leader at Berkeley Lab. IDEA improvements will keep BSE competitive in the job market.
- Psychological safety for all employees is important to enable all to bring their authentic

selves to work and share their ideas. This is essential to support the best team science at BSE in current and future programs.
- The timing is right because there have been many changes in IDEA due to changing ways of work; the pandemic's impacts; and the national reckoning with social, racial, and environmental justice. These movements and changes have been codified to impact DOE through President Biden's Justice40 Initiative[2] goals, which aims to deliver at least 40 percent of the overall benefits from Federal investments in climate and clean energy to disadvantaged communities.

Needs to achieve the goal:

- Ongoing analysis of non-represented and represented employee salaries to address pay equity.
- Improve iterations on exit surveys, analyze survey results, and disseminate survey data for a deeper understanding of how to support our workforce.
- Improve transparency on the skills, experience, milestones, core competencies required to be considered for promotion.
- Build and maintain a resource of direct connections between BSE and Historically Black Colleges and Universities (HBCUs), Minority Serving Institutions (MSIs), community colleges, and other organizations focused on underserved populations. Aim to keep and enhance partnerships and build new partnerships.
- Develop a historical understanding of the impact of BSE on underserved groups, or current interactions. Use iterative cycles to set goals, implement strategies and document both outcomes to understand impact and learn from mistakes.

Measurements of success:

- Quantity and quality of answers in the IDEA section of the performance management process. Supervisors are held accountable for reviewing employee IDEA efforts and commenting appropriately. The Berkeley Lab performance management process is a valuable tool to leverage for this objective.
- Anticipate and reduce employee turnover by ensuring maintenance of high overall job satisfaction, mental and physical wellbeing across the BSE community, and communication of Berkeley Lab resources to benefit their career.
- Number of students reached, and staff engaged in outreach or change.
- Specific and real research engagements with communities.
- Advancement of BSE's involvement in Science, Technology, Engineering and Math (STEM) education and workforce development through involving high school and college students in training and internships.
- BSE's readiness to meet and exceed Justice40 criteria.

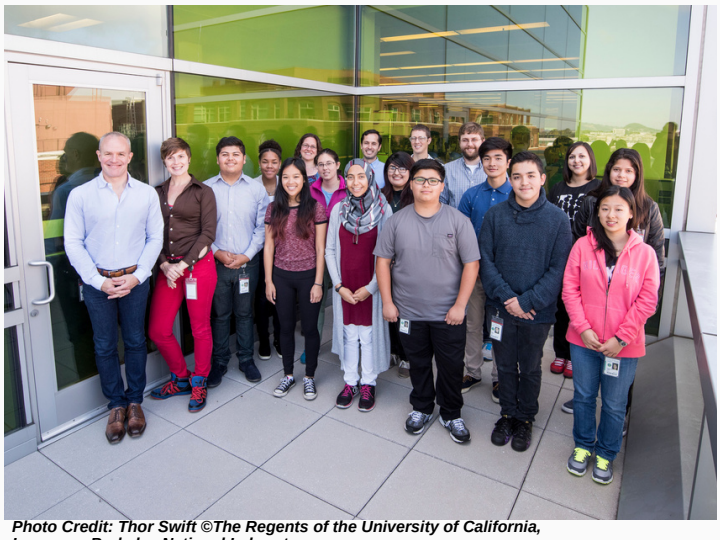


Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

2. https://www.whitehouse.gov/omb/briefing-room/2021/07/20/the-path-to-achieving-justice40/

DECARBONIZATION AND CARBON NEGATIVE RESEARCH

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

As a community, we need to mitigate and reduce atmospheric carbon for climate stabilization, and develop and increase biomanufacturing to enable decarbonization, create jobs, and expand the economy.

Strategy Scope:

Addressing and mitigating climate change is, without reservation, a present and looming threat to the wellbeing of people and the planet. Our goal is to explore and develop technologies, methods, and processes to use waste streams and new feedstocks/starting materials for the production of drop-in and new replacements to petrochemicals and other carbon-intensive materials. Starting materials will include gaseous feedstocks (CO_2, methane, syngas, etc.), solid/liquid waste streams (plastic, agricultural, municipal, etc.) and bioenergy crops. Criteria for development include low-impact production, local resources, and processes that are well-matched to end-products or scale-up. Material criteria will include carbon impact of waste streams and the value or market size of end-products. Target products will include (but are not limited to) sustainable aviation fuels, marine fuels, organic acids, recyclable biopolymers, clean energy relevant critical materials, durable goods/construction materials, and high-value chemicals (flavors, fragrances, cosmetics, pharmaceuticals). Our research will incorporate DBTL (design, build, test, learn), data integration, and scaling to engineer our ideas more efficiently. and translate them to high-impact, real-world solutions. Finally, we recognize policy will play an integral role in carbon negative efforts central to DOE and Berkeley Lab initiatives and will identify how our research impacts policy and vice versa, particularly in relation to how waste is treated and to circularize the economy.

Rationale for this goal:

- As a community, we need to mitigate and reduce atmospheric carbon for climate stabilization, and develop and increase biomanufacturing to enable decarbonization, create jobs, and expand the economy.
- BSE is well positioned to take on this complex challenge with our established research programs in biomanufacturing, expert diverse staff, instrumentations and facilities, and a local biotech talent pool. We know how to engineer organisms and have expertise in scale-up and de-risking.
- The time is ripe for this research because of the critical environmental concerns - we cannot wait any longer to develop solutions and deploy them to the world.

Needs to achieve the goal:

- Personnel and culture: A staff skills analysis to identify sets that can be filled through collaborations and new hires, with an emphasis on differing perspectives (likely material science, environment engineering, process economics, microbial ecology) and diverse backgrounds. We should continue to build diverse relationships with private, academic, philanthropic, and government collaborators.
- Discoveries: High throughput methods for strain engineering to survey a wide range of CO_2 or C1-gas consuming organisms and/or microbial communities for genetic tractability. Improved synthetic biology of plants and microbes to improve carbon uptake and conversion. Investigation of co- and multi-culture consortia for efficient and robust conversion of waste streams, including CO_2 and methane. Development of hybrid technologies and biobased critical materials for other forms of renewable energy generation is needed.
- Technology: A framework for using a diverse range of feedstock inputs, including lignocellulosic and algal biomass, waste gasses and direct air capture to implement carbon negative biomanufacturing. A deeper understanding of market-product analysis (e.g., market size, profit margin, and competitive technologies) likely in collaboration with Berkeley Lab's Intellectual Property Office (IPO). Integration of biomanufacturing with non-biological direct air capture technologies. Inception for a nexus that expands the application of biotechnology towards other renewable energies. Advances in life cycle assessment (LCA) and techno-economic analysis (TEA) benchmarking software and improved translation of LCA/TEA findings for both researchers and policy makers. Additional methods in soil carbon analysis to target soil carbon.
- Operations and Capabilities: A better understanding of the role of carbon negative research in the mission of the Biological Genome Engineering and Manufacturing Facility (BioGEM) building and working closely with colleagues in the Advanced Light Source (ALS), and Molecular Foundry, and the upcoming Biological and Environmental Program Integration Center (BioEPIC). Expansion of the resources of Advanced Biofuels and Bioproducts Process Development Unit (ABPDU) and Agile BioFoundry (ABF) to expedite the bench to industrial scale pipeline, along with a robust TEA/LCA system to evaluate the technologies. Keeping well informed in industrial scale biotechnology through field trips and workshops. Appointment of a working group to generate a clear flow chart of BSE prioritized substrates, in particular waste. Develop close relationships with the Berkeley Lab Foundation and partner with Small Business Innovation Research (SBIR) and Technology Commercialization Fund (TCF) grantees to expedite tech commercialization.

Measurements of success:

- The numbers: patents, publications, awards and recognition, startups, industrial clients (for ABPDU and ABF in particular), press news, international events hosted by BSE, personnel trained and continuing to work in the field (as part of workforce development).
- Setting international standards or policy for biological carbon negative production routes.
- Carbon negative consortia participation and leadership.
- Synergies with a broader set of research being done in the Biosciences Area and Berkeley Lab as part of the Carbon Negative Initiative.

How does existing and emerging energy including fossil, nuclear, solar, wind, geothermal, and bioenergy production impact human and organismal health?

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

Strategy Scope:

Our overall research question is: How does existing and emerging energy including fossil, nuclear, solar, wind, geothermal, and bioenergy production impact human and organismal health? A similar set of challenges exists around development of drop-in and new materials using sustainable biological routes. Our goal is to quantify health effects, both positive and negative, with an emphasis on understanding health equity and community spread. Research targets include the feedstock impact (waste gas and solids/recycling, agricultural, mining/drilling), processing impact (manufacturing, transportation, installation), use- and end-phase impacts (emissions, disposal, degradation), and secondary effects (climate change, heatwaves, extreme weather events, fire, impacts to food systems). These deeper understandings of the health/energy nexus have important implications for benchmarking (i.e., LCA) and policy. As we prepare for these types of energy-related research questions, we see potential cross-over in our research approach to biodefense topics, including evaluation of biological and chemical agents, and other threats such as radiological threat agents.

Rationale for this goal:

- Communities living in close proximity to energy production facilities or those exposed occupationally need to understand health risks associated with exposures and develop preventive response strategies.
- BSE is well positioned to take on this challenge with our long-standing expertise in exposure science using *in vivo* and *in vitro* model biological and spatial systems to study observable changes and biological big-data pipelines to delineate molecular mechanisms and identify biomarkers.
- With DOE's stated dedication to energy justice for underserved communities while balancing the immediate need for renewable energy and carbon negative manufacturing, the timing is right.

Needs to achieve the goal:

- Personnel and Culture: Build a relationship between diverse health and energy research teams to establish a common vocabulary. Inclusion of health markers in biomaterial/fuels design or LCA. Establish collaboration agreements with other divisions and units for equipment sharing. Build clinical partnerships for translational research.
- Discoveries: Explore the fate and life cycle of toxic molecules in the human body. Overlay multi-omics data into systems pathways. Deeper understanding of how scale-up of renewable energies impacts community waste streams and human exposures.
- Technology: Investment in infrastructure that spans cell to organism to macro health-impacts through visualization, measurement, and modeling, such as real time biosensors, automation, clinical proteomics, microscopy tools, and advancements in single cell methods (e.g., novel Fluorescence-activated Cell Sorting (FACS) technologies)
- Operations and Capabilities: Equipment sharing agreements and improved system for recharge/investment in tech support/ microscopy and exposure environments.
- Deeper connection to other departments in BSE and other areas at Berkeley Lab to draw expertise in emerging energy technologies and products with potential health impacts. Tap into energy, in particular bioenergy and biomanufacturing, research at Berkeley Lab to front load human health and safety in the research pipeline.
- Integration of automation tools to improve workflows for testing impacts on human health.

Measurements of success:

- Program development with DOE or other stakeholders in this research area.
- Development of a forum to learn about other funding agencies, for example guidance and leadership in Office of National Homeland Security (ONHS), that have touch points to health-energy nexus research.
- Improved access to research infrastructure (automation, imaging, process development units, computing) and development of core facilities (single cell technologies).
- Establishment of biological model platforms evaluating energy-related health risks (i.e. biomanufacturing products and byproducts).
- Development of Artificial Intelligence/Machine Learning (AI/ML) platforms for risk assessment.
- Cross-education of health scientists on new biomaterials and bioproducts and LCA benchmarking and health impacts/toxicology approaches for biomanufacturing researchers to improve collaboration and shared vision.

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

AUTOMATION AND SELF-DRIVING LABS

Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

Our goal is to expand automation tools and software development for biosciences applications, establish a metric by which to measure progress, and improve strain and microbiome engineering efficiency for stability or a desired function.

Strategy Scope:

The accelerated pace of discovery needed for the science goals requires speed enabled through automation and self-driving labs. Our goal is to expand automation tools and software development for biosciences applications, establish a metric by which to measure progress, and improve strain and microbiome engineering efficiency for stability or a desired function.

Automation refers to automated experiments and data analysis. Self-driving labs refers to AI-driven experiment planning and hypothesis generation, coupled with automation. In the latter case, the expectation is to eventually converge to a mode of operation in which no human intervention is required.

Rationale for this goal:

- The research community wants to target science questions that are too labor intensive to investigate without automation or self-driving lab capabilities. Some examples include systematic strain engineering for renewable biomanufacturing and carbon capture, predictive design of microbiomes, protein engineering, and chemical analysis.
- With BSE's history of multidisciplinary teamwork, significant expertise in synthetic biology, a good blend of biological and automation/software capabilities, proximity to the biotech industry and cloud labs (existing Experimental Data Depot (EDD) capabilities) and a diverse team, the division is well positioned to take on this challenge
- The timing is right because there is an intensifying conjunction of new synthetic biology tools (e.g., clustered regularly interspaced short palindromic repeats (CRISPR)-based), more high-throughput phenotyping tools (both sequence and mass spec-based), commercially available technologies (e.g., liquid handlers, cloud labs), and emerging, potentially disruptive, techniques (e.g., microfluidics, AI/ML).

Needs to Achieve the goal:

- Personnel and Culture: Addressing the unicorn recruitment challenge: staff must be knowledgeable in both biology and software/robotics. BSE is a world leader and can train people in this intersection, but it requires a large time and energy investment, while also managing competitive recruitment from the industry. The goal of automation and self-driving labs thrives when directed towards the most labor- and resource- challenging experiments. A shift of culture to incentivize ambitious experiments, where topic-area and automation and self-driving lab researchers partner early and there are clear benefits to both, is needed. Establish BSE-wide forums to analyze and evaluate different systems and the development of new pipelines to increase access to automation for more BSE researchers
- Technology: High-throughput miniaturized sensors, algorithms designed for synthetic biology data, microfluidics advances, ability to link together existing automation capabilities, robotic arms, cloud labs. Engage a technology scout for the existing automation and self-driving labs in industry/other national laboratories/academia.
- Operations and Capabilities: Emphasis on pipelines over one-offs, drop-in pipelines to expedite workflows, site visits at places (e.g., microbial communities, library screens, and strain engineering) at Berkeley Lab that could benefit from more automation.

Measurements of success:

- Demonstrable success stories with industry/ other National Labs/ academia/ cloud labs.
- Progress through automation levels for self-driving labs (customize level definitions to biological context).
- A cultural shift to default to automation instead of manual methods with intense use of automation systems - define a pilot study. Widespread sharing of automation tools across the area.
- A continuously increasing size of the average experiment performed in BSE using automation. Decrease in overall time, labor time and automation time to go from experimental design to results.
- Partnerships with researchers at HBCUs, MSIs, community colleges, and other organizations that would otherwise not have access to automation equipment.
- Emphasis of bioeconomy workforce development and enrichment of staff core competencies, with onsite industry or government supported training programs in automation and self-driving labs.

CONCLUSION

We want to define the core of our diverse, inclusive work environment to unite and inspire the talent of the division.

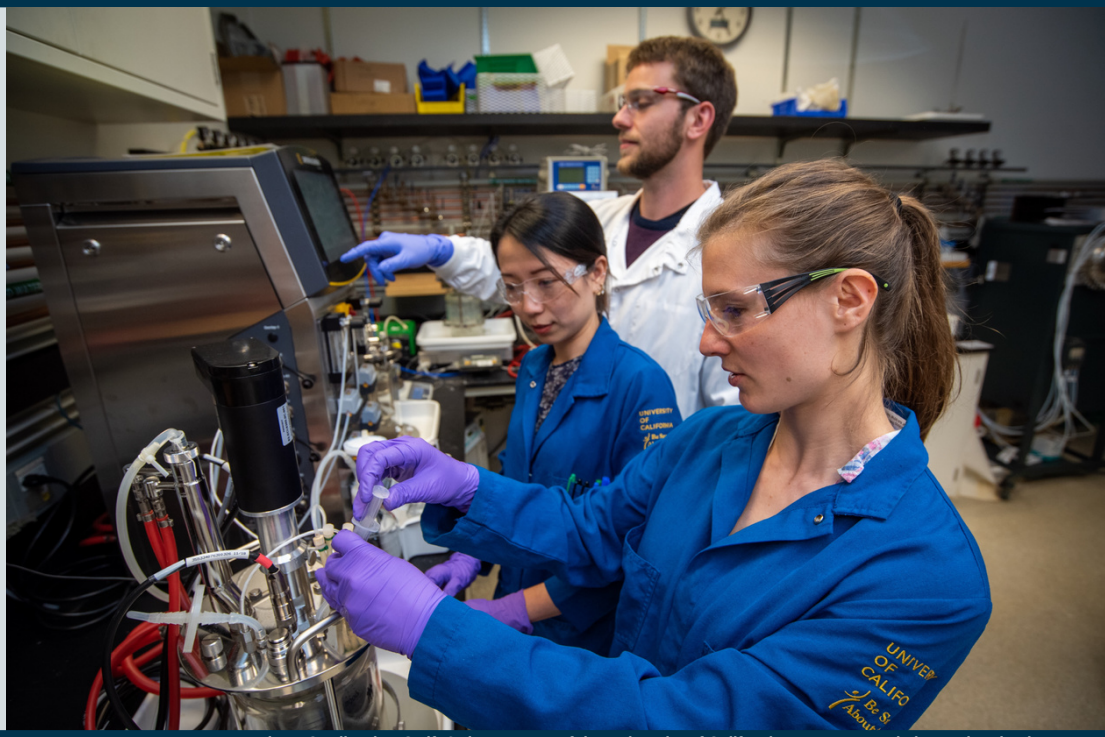
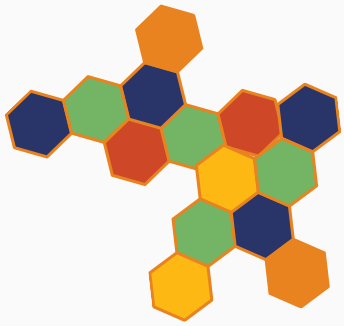


Photo Credit: Thor Swift ©The Regents of the University of California, Lawrence Berkeley National Laboratory

We offer a vision of BSE in the next seven years where our people and the communities we serve are well resourced to address the most pressing science challenges in carbon negative and health/energy nexus research and supported through increased automation. The strategic plan outlines several prioritized goals, however we expect small divergences and inspired offshoots, given the nature of our multidisciplinary research environment. While no single document can, or should, capture all of BSE's projected activities, this strategic plan sets the framework to focus the BSE division. It represents a set of ideas that best applies our talent, capabilities, and infrastructure, assists in bringing together groups of BSE researchers in new ways, and positions us strategically to outline and address future investment opportunities. We want to define the core of our diverse, inclusive work environment to unite and inspire the talent of the division. We commit to revisiting these goals annually and hope to use this framework to inspire our stakeholders and colleagues at Berkeley Lab and outside Berkeley Lab. We will also use our internal forums such as town halls to continually reiterate and use this document to assist team science in the division.

Our multi-disciplinary division is both a strength and a challenge - this plan aligns the division's capabilities to take on the most pressing of issues: environmental health (including climate change) and human health. In essence we seek to address key aspects of a robust bioeconomy; develop and build a thriving, diverse workforce, generate carbon negative routes to a vast range of commodities, assess the risk associated with these new technologies, and conduct the research in a systematic broadly usable manner.



ACKNOWLEDGEMENTS

This strategic coordination document represents the entire BSE division. The individuals listed below are the representatives that engaged in focus groups, sprint teams, and writing.

Jamie Acosta
Carolina Araujo Barcelos
Deepika Awasthi
Deepanwita Banerjee
Baishakhi Bose
Rosanne Boudreau
Susan Celniker
Hang Chang
Katy Christiansen
Henrique De Paoli
Alex Degg
Chang Dou
Thomas Eng
Hector Garcia Martin
Aindrila Mukhopadhyay
James Gardner
Sara Harmon
Justin Heady
Nathan Hillson
Kristen Hunter-Cevera
Lauren Jabush
Robin Johnston
Zack Jones
Jay Keasling
Dupeng Liu
Jian-Hua Mao
Joshua McCauley
William Morrell*
Chris Petzold
Diane Pierotti
JP Prahl
Tijana Radivojevic
Shilva Shrestha
Blake Simmons
Simone Giacometti
Steven Singer
Antoine Snijders
Ning Sun
Eric Sundstrom
Deepti Tanjore
Sara Tejedor Sans
Will Toomey
Miaw-Sheue Tsai

*Primary affiliation is Sandia National Laboratories

BSE
Biological Systems and Engineering

https://biosciences.lbl.gov/bse/

BioSciences

BERKELEY LAB

Stock photo courtesy Canva