CASA-Bio
Catalyzing Across Sectors to Advance the Bioeconomy

Unleashing the Power of Biology for Carbon Capture and Utilization

Further development into biological technologies that not only capture carbon emissions but also convert them into useful products will enable a circular U.S. bioeconomy that boosts domestic biomanufacturing, reduces environmental impacts, and fortifies supply chains.

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Executive Summary

Challenge

The reduction and capture of carbon emissions is a critical worldwide need for mitigating climate change. Biological systems offer a powerful, sustainable solution for capturing and converting single-carbon (C1) greenhouse gases, such as carbon dioxide, carbon monoxide, and methane, into valuable fuels, chemicals, and materials.

Opportunity

We envision a circular bioeconomy where biomanufacturing facilities--co-located with industrial emitters and producers of other waste and sustainable feedstocks--transform C1 emissions into valuable products to achieve climate goals and strengthen domestic supply chains.

Solution

To unlock the full potential of biological carbon capture and utilization, we propose a $1B investment to address three key areas:

- **Predictive Modeling:** Developing an accessible, AI-powered modeling framework will enable rapid assessment of economic viability and environmental impact for C1-based biomanufacturing processes.
- **Robust Organisms:** Expanding the suite of well-characterized, easily engineered organisms capable of efficient C1 conversion.
- **Scalable Infrastructure:** Bridging the gap between lab-scale research and industrial production by developing accurate scale-down methods and models and investment in C1-based pilot-scale facilities.

Cross-Cutting Advances

Innovation is needed to develop and accelerate deployment of affordable, reliable, and resilient clean technologies. Success depends on:

- **Collaboration:** Fostering partnerships between academia, industry, and government agencies is crucial. This includes establishing a Biomanufacturing Coordinating Committee.
- **Workforce Development:** Training a specialized workforce with expertise in engineering, life sciences, and computational biology is essential.
- **Open Access Data**: Standardizing data formats and supporting open strain collections will accelerate research and development.

Impact

By investing in these research and development priorities, we can unlock a future powered by renewable carbon, driving significant environmental and economic benefits while achieving a circular bioeconomy.

Motivation and Justification

The emerging bioeconomy includes harnessing the power of biology to create valuable services and products. The U.S. bioeconomy is currently valued at a trillion dollars and is predicted to grow globally to over $30 trillion over the next two decades [1,2]. The bioeconomy can play a major role in contributing to domestic supply chain security while at the same time achieving the U.S. climate goals of reducing greenhouse gas emissions 50-52% below 2005 levels by 2030 [3]. The bioeconomy enables the use of renewable resources to produce sustainable foods, fuels (including sustainable aviation fuels), chemicals, and other materials with an addressable market of over a trillion dollars [4–6]. Biological systems are uniquely suited for sustainably capturing and converting carbon. For example, abundant single-carbon (C1) greenhouse gases, such as carbon dioxide (CO_2) or methane, can be converted to useful molecules using renewable energy, such as light or hydrogen. Likewise, many C1 waste stream (including CO_2 and carbon monoxide emissions from steel or cement manufacturing or mixed gases generated from waste biomass and municipal solid wastes), which are not readily accessible for traditional conversion processes, could be good targets for conversion through biological processes. By harnessing such biological systems, we have the potential to remove 2-10 gigatons of CO_2 emissions annually [7–10].

To make a circular economy for C1 a reality, we need rapid and inexpensive scale-up of process that use renewable resources and produce little waste. In today's sugar-based bioprocesses, such as producing ethanol from corn, typically a third of the carbon is lost as CO_2. Efficient, novel C1 conversion processes are starting to be used commercially, but to scale up such efforts, additional strategic research and development (R&D) investments are needed to identify and optimize the most effective conversion pathways. This initiative focuses on R&D to overcome current barriers by industrializing efficient biological conversion of C1 to valuable products from existing and emerging feedstocks and processes. Success will enable significant reductions in industrial carbon emissions in support of the U.S. government's ambitious climate goals, thereby contributing to global climate change mitigation efforts and enabling a circular bioeconomy and robust domestic supply chains.

Deliverables

As economics are tied directly to carbon and energy efficiency at industrial scales, this initiative aims to understand how biological systems can be optimized and implemented and where C1-based biomanufacturing strategies can be leveraged to best advantage over other approaches. While a few processes using biological systems that convert CO_2 and other local C1 feedstocks into valuable products are being commercialized, further investment to expand these technologies are needed to simultaneously grow the bioeconomy while also meeting climate objectives. The most pressing R&D needs to realize this vision, summarized in Figure 1, include: (1) new computational models to predict and help develop bioprocesses that

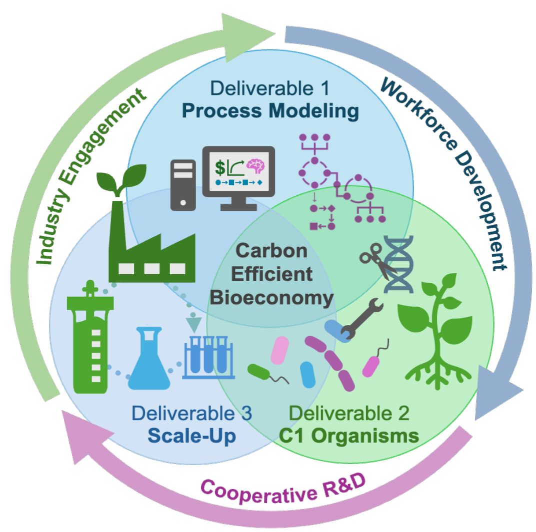

Figure 1. Diagram depicting the deliverables and enabling activities for this initiative.

are economically and environmentally viable; (2) standardized sets of organisms with robust C1 conversion capabilities and readily available genetic engineering toolboxes, and (3) scalable infrastructure for optimized conversion of C1 to a wide range of chemicals, fuels, materials, and nutrients. **Below, we describe three R&D deliverables, which with a $1B investment over the next five years, we envision would enable broad commercialization of expanded C1 conversion biotechnologies to foster a circular carbon efficient bioeconomy.**

Deliverable 1: An Accessible Modeling Framework for Biological C1 Conversion Process Development

Rationale/Critical Gaps

Biomanufacturing uses organisms as 'cellular factories' to produce commercially important products. Historically, the majority of biomanufacturing processes have used well-characterized bacteria or yeast cells grown in simple tank fermenters to convert plant-derived sugars into products. Data from decades of research on these sugar-based processes have enabled process modeling that can predict resource requirements, economic viability, and environmental impacts in a way that can inform and guide their development toward commercialization.

However, for C1-based conversion, traditional biomanufacturing processes fall short in two main ways: the C1 material being converted is often gaseous (unlike the sugars used in traditional bioprocessing), which necessitates unique bioreactor design and configuration, and the organisms for converting C1 materials are poorly characterized. These differences make modeling C1-based bioprocesses much more complex than modeling their sugar-based counterpart. Whereas some of the modeling tools and databases developed for sugar-based processes can be applied to C1 processes, there is currently no accessible, accurate modeling framework to predict the economic and environmental viability and thus the impact of C1 processes. This shortcoming severely limits development and deployment of these important technologies.

Key Goals and Milestones

To overcome barriers in understanding and modeling of the key biological systems needed to advance C1 conversion processes, we suggest the following Goals and Milestones:

- **Create a large-language model (LLM)**, similar to ChatGPT, and other artificial intelligence/machine learing (AI/MI) tools to integrate information from multiple, disparate sources, with the milestone of identifying viable product targets, processes, and places in the production pipeline that could benefit from adjustments.
- **Ensure that the modeling tool is accessible and easily usable** by researchers, educators, entrepreneurs, and policymakers who may not have extensive computational experience, with the milestone of enabling widespread adoption for assessing economic feasibility and environmental impact of new C1 bioprocesses.

The development of a transparent, standardized, and open access AI/ML-driven modeling tool would help researchers and others design and test models for C1 bioprocesses, to gather information from existing databases and present it in a user-friendly way for researchers, educators, entrepreneurs, policymakers, and others. The tool would consider various factors, such as the materials and organisms used in the process, the design and size of the bioreactor, and how to separate and purify the final product to allow users to quickly identify product targets and production processes that are both environmentally friendly and financially viable. The tool would also incorporate information on the resources required, key cost factors, estimated cost of producing the final product, and greenhouse gas emissions associated with the process, as well as availability and location of the specific resources and workforce. Together, these capabilities of the modeling tool would help ensure that new technology can be effectively designed and deployed.

5-year and Ongoing Impact

A broadly available and usable modeling framework driven by AI/ML would enable the development of C1 conversion bioprocesses that are most likely to be environmentally and economically sustainable. Putting this framework into practice will generate additional data that can be used to continually refine the modeling, such that its predictive power grows over time. Ultimately, this tool could accelerate the development and deployment of biotechnologies that use C1 to create valuable products, leading to significant environmental and economic benefits.

Deliverable 2: A Suite of Robust Organisms for C1 Conversion Bioprocesses

Rationale/Critical Gaps

The well-studied, easily engineered organisms that have proved to be so beneficial for traditional biomanufacturing do not have the ability to use C1 directly. Thus, implementing industrial-scale C1 bioconversion has had to rely on a handful of less-studied species for which genetic tools are lacking and knowledge banks are sparse. This deficiency has made it difficult to engineer these organisms for improved, robust growth at the scale needed for C1 bioconversion. Moreover, the time and cost of developing these genetic tools and biological understanding has hampered the exploration of potentially superior, uncharacterized organisms with desirable industrial traits. This holds true across all C1-converting organisms, including non-photosynthetic bacteria, algae, cyanobacteria, and engineered plants.

Therefore, there is a critical need for development of a suite of robust, well-characterized organisms that are easy to engineer for industrial C1 conversion bioprocesses. There is also a critical need for development of advanced genetic tools and fundamental research in systems biology to improve understanding of metabolic pathways for product production and feedstock utilization. These efforts must be supported by centralized, open-source databases of genetic information, metabolic pathways, and organismal cultivation conditions that can be used for accurate predictive modeling (see Deliverable 1).

Key Goals and Milestones

To overcome barriers in our ability to engineer an expanded set of organisms suitable for advanced C1 conversion processes of a wider range of feedstocks and chemicals, fuels, and materials, we suggest the following Goals and Milestones:

- **Develop open-source genetic tools and high-throughput, automated pipelines** for exploring gene and pathway function, with the milestone of enabling modeling and engineering of a wider array of robust, novel organisms capable of C1 conversion and thus production of a wider array of target compounds.
- **Establish an open-source facility for preservation and distribution** of natural and engineered strains and genetic tools, with the milestone of enabling a more cohesive, shared community effort to accelerate R&D advances for industrializing C1 bioprocesses.
- **Increase efforts to study and develop engineering tools for current and new organisms**, with the milestone of developing an expanded suite of well-characterized chassis organisms suited for atom- and carbon-efficient C1 conversion at an industrial scale.

The development of tools to evaluate and engineer a wider range of organisms for C1 conversion process development would leverage and build on existing and emerging genetic tools and databases to advance understanding of these systems and effectively engineer efficient scalable bioprocesses. These endeavors would align with current efforts to expand Biofoundries, incorporating automation to accelerate throughput for data generation and genetic engineering of a broader range of biological systems. Concomitant open-source collection of organisms and tools could enable researchers, with database and modeling efforts in Deliverable 1, to both access and deposit relevant organisms, tools, and data into a single, accessible system that will be instrumental for accelerating scale-up of C1-based processes, as described in Deliverable 3.

5-year and Ongoing Impact

Investments in the study and development of new organisms for C1 bioconversion, together with the resources for storing and sharing these resources, would progress towards a future powered by renewable carbon. Collaboration across academia, industry, and government agencies would foster availability of a broadly accessible collection of strains and genetic tools. These biological resources and technologies, along with databases and modeling capabilities in Deliverable 1, would enable the accelerated development of economical and scalable C1 conversion bioprocesses with expanded community involvement in R&D efforts.

Deliverable 3: Infrastructure To Accelerate Translation and Scale-Up of Industrial C1 Bioprocesses

Rationale/Critical Gaps

There is a critical need to bridge the gap between laboratory-scale research and industrial-scale biomanufacturing to achieve rapid translation to meet current climate targets. Limited pilot scale infrastructure exists for traditional sugar-based biomanufacturing, but there are virtually no support systems for biological C1 capture and conversion processes. Consequently, companies must build costly pilot and demo scale facilities that are often underutilized after a process has been commercialized. Thus, there is a need for accessible user facilities, biofoundries, pilot/demo facilities, and contract development and manufacturing organizations in the U.S. to de-risk barriers to scale-up and support the growing number of R&D labs and companies in this space.

Carbon capture and utilization requires specific needs beyond the challenges of working with non-model organisms discussed in Deliverable 2. For example, efficient fermentation of poorly soluble C1 gases requires reactors designed for high gas mass-transfer rates with low power input; conversion of toxic substrates (e.g. methanol and formic acid) requires carefully designed feeding strategies; and aerobic utilization of highly reduced substrates (e.g., methane and methanol) requires exceptionally high cooling capacity. Altogether, C1 processes are fundamentally different from traditional biomanufacturing and are currently not supported by existing facilities. Thus, they require further infrastructure and R&D efforts.

An additional and significant hurdle lies in transitioning lab-scale successes (a few liters) to industrially viable processes (500,000+ m^3). This gap makes securing investment challenging, with limited examples of successful commercial ventures. Demonstration-scale facilities are needed to de-risk and attract more investment in these processes.

Key Goals and Milestones

To address key challenges for scale-up of C1 conversion bioprocesses required for overcoming barriers to industrialization, we suggest the following Goals and Milestones:

- **Develop simulation (e.g., scale-down) systems** that enable accurate prediction of large-scale C1 conversion bioprocesses, with the milestone of optimizing the ability to test factors affecting growth and production in industrial scale environments prior to investing in pilot facilities.
- **Develop facilities for demonstration-scale C1 conversion** bioprocesses, with the milestone of de-risking technologies, attracting investment from industry, and fostering more public-private partnerships toward innovation for C1 conversion bioprocesses.

Expanded infrastructure for developing accurate scale-down experimentation and models and for demonstrating feasibility are key opportunities to foster collaboration among academia, government labs, and industry for tackling existing challenges in C1 conversion bioprocesses. Facilities for bioprocess development and demonstration would address a critical and costly gap for virtually all commercialization efforts aimed at C1 conversion. Unlike a pilot system that a company might build at great cost and that could go underutilized once they have moved beyond pilot demonstration, a publicly-funded facility to scale processes with multiple industrial partners successively could have more perennial value toward the establishment of a circular bioeconomy.

5-year and Ongoing Impact

Collaboration among academia, national labs, and industry is crucial for sharing knowledge, streamlining technology transfer, and fostering innovation. While some aspects of C1 bioprocess development and scale-up are unique to the challenges of individual substrates and the organisms that consume them, we anticipate that many of the lessons learned will be applicable to other bioprocesses and vice versa. The development of improved modeling and technologies at multiple scales across R&D and industry efforts will serve to de-risk and accelerate time to industrialization for new commercially viable C1 bioprocesses.

Cross-Cutting Opportunities

Key Goals and Milestones

To achieve these ambitious goals, we envision a series of cross-cutting opportunities and innovation targets that will also be needed to develop, de-risk, and accelerate deployment of affordable, reliable, and resilient clean technologies.

- **Technologies for C1 Capture from Existing and Emerging (Bio)manufacturing Processes**
  Most biomanufacturing converts plant-derived sugars that are derived from photosynthesis, which makes them lower-carbon-intensive than most fossil-based processes, but there is considerable potential to tune these bioprocesses to further minimize C1 emissions. We envision microbial bioprocessing facilities that are co-located with existing carbon-emitting industrial facilities and infrastructure to reduce costs. Developing modular bioprocess units that can be “bolted-on” to existing facilities will allow for flexible and rapid deployment, reduced need for large-scale equipment, and increased accessibility. In addition, diversifying energy sources, use of variable feedstocks, and improving process efficiency can significantly lower both emissions and cost for industrialization.

- **Coordination Among Researchers and Industry**
  Collaboration of industry with academia and national labs can have many benefits, including acceleration of development, scaling of biomanufacturing processes, and sharing of data and lessons learned. Too often, such collaborations become forestalled by intellectual property and licensing concerns. To promote more facile collaboration, we propose establishment of a Biomanufacturing Coordinating Committee composed of funding agency representatives, academic researchers, industrial scientists, investors and other stakeholders. This group could help foster direct interaction and collaboration while also providing feasible business case studies that consider real-world feedstocks, logistics, and regulations to advance the most promising technologies and bioprocesses. Providing economic incentives might additionally support the high initial costs associated with developing and scaling up new technologies. Incentivizing private sector investment through public-private partnerships and other funding mechanisms would serve to drive market pull, foster innovation, promote sustainable industrial practices, and motivate public demand to support early markets for new and emerging low- and zero-carbon industrial goods.

- **Workforce Development and Educational Outreach**
  The development of a specialized workforce is important for advancing a biomanufacturing revolution. This workforce could span multiple fields of engineering, life sciences, process engineering, computational biology, and economic modeling across a spectrum of education, training, and outreach programs [11]. Interdisciplinary workforce training will be essential to bridge the gaps between academia and industry by emphasizing initiatives across engineering and physical and life sciences. Incorporation of systems thinking and AI/ML concepts at all levels will also be vital as these technologies become increasingly pervasive. In order to achieve these goals, it is important to enhance science literacy and sustainability understanding among K-12 students and the general public. Social media campaigns and marketing can enhance outreach efforts, and social scientists should be included in these initiatives to effectively reach the general public.

- **Data Accessibility, Sharing, and Infrastructure**
  As outlined in Deliverables 1 and 2, there is a critical need for open, accessible, and standardized organism, tool, and data sharing to accelerate R&D and commercialization, not only for organisms important for C1-based bioprocesses, but also those for conversion of other waste and sustainable feedstocks to valuable products. To complement the initiatives outlined in Deliverables 1 and 2, we suggest expansion of the following tools for the broader community:
  - **Standardize Genetic Part Design and Rapid Sharing of New Tools.** A standardized design tool based on current state-of-the-art engineering parts and methods should be established with interoperability and standardization as forefront considerations as new biomanufacturing organisms are onboarded. Funding agencies supporting genetic tool development should also require researchers to make research products and related data available to the community as soon as possible after their validation, for example through mandatory deposition in strain and/or plasmid collections (see next bullet). Along with this, traditional barriers to rapid technology transfer need to be streamlined.
  - **Develop and Support Open Strain Collections and Databases for Key Biomanufacturing Organisms***.* Existing repositories should be expanded to include more novel organisms for biomanufacturing, as well as derivative engineered strains. Further, government funding should support maintenance and distribution of these resources. This will require the research community to focus their efforts on a set of keystone organisms to prioritize the generation and analysis of the necessary engineered strains and -omics data. Funding agencies, advised by the

Biomanufacturing Coordinating Committee, can facilitate development of such collections through financial support of R&D efforts generating these data and the facilities and staff housing strain collection databases. It will also be critical to mandate deposition of strains and data by funded researchers in standardized, machine-readable formats to facilitate integration of knowledge (see next bullet).

- **Standardize Data Formats to Enable AI/ML-Based Analysis.** We anticipate that a wide range of multi-omics datasets will be generated in Deliverable 2 and across other initiatives will be of broad utility to the research community. However, all data must be made easily accessible and deposited in standardized, machine-readable formats for downstream analysis and incorporation into existing open-source bioinformatics resources such as KBase (funded by the Department of Energy). The Biomanufacturing Steering Committee could play a role in helping to develop community-wide best practices for data deposition in publicly available databases.

Other Bioeconomy-Related Considerations

There are important ethical and environmental considerations for C1 bioprocesses, as there is for all biomanufacturing, which must be addressed to promote societal acceptance and responsible development of industry. Building public trust and acceptance of these emerging technologies is necessary for successful deployment, requiring strategies for engaging with stakeholders, addressing concerns, ensuring the implementation of robust safety protocols, and communicating the potential of biomanufacturing to address climate change and promote sustainability by replacing inefficient processes and replacing/reusing products. There is also a critical need to consider factors like water and energy use, land use change, energy justice, and potential environmental impacts of biomanufacturing processes.

Concluding Remarks

To accelerate towards the expanded industrialization of biological conversion of C1 to valuable products, we believe the most impactful R&D will focus on 1) comprehensive and accessible multi-scale models for prediction of the most economically viable bioprocesses for industrialization, 2) characterization of and genetic tool development for diverse and robust organisms for C1 conversion bioprocesses to expand the range of feedstocks and products, and 3) development of small-scale systems and models that accurately mimic large-scale systems as well as C1 conversion pilot scale facilities to de-risk bioprocess scale-up for production of a wide range of chemicals, fuels, and materials. Key considerations include the need for industrial involvement across the R&D process, providing “lessons learned” and feedback on the most promising bioprocesses to pursue, as well as the need for incentives to drive industrial investment in C1 conversion processes. Integration with existing and emerging (bio)manufacturing processes is also needed to minimize carbon emissions. There are also broad reaching implications across the bioeconomy including workforce development, data, sharing and infrastructure, and general consideration for scalable processes and community safety and education that must be addressed. Well supported R&D efforts to industrialize efficient biological conversion of C1 to valuable products and collaboration across disciplines, sectors, and technologies will significantly reduce industrial carbon emissions in support of U.S. climate mitigation goals, while accelerating the development of a prosperous and circular bioeconomy.

Authorship and Acknowledgements

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References

Sources accessed October 8, 2024.

1. Cumbers, J. (2022) White House Unveils Strategy To Grow Trillion Dollar U.S. Bioeconomy. *Forbes* https://www.forbes.com/sites/johncumbers/2022/09/12/white-house-inks-strategy-to-grow-trillion-dollar-us-bioeconomy/.
2. The White House. (2022) Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy.
3. The White House. (2022) National Climate Task Force. https://www.whitehouse.gov/climate/.
4. Teter, J. & Voswinkel, F. Transport. IEA https://www.iea.org/energy-system/transport.
5. Sanchez, D. P., Collina, L. & Voswinkel, F. Chemicals. IEA https://www.iea.org/energy-system/industry/chemicals.
6. Deal, H. (2024) State of the Industry Reports. The Good Food Institute https://gfi.org/state-of-the-industry-reports/.
7. Summary for Policymakers. in *Climate Change 2022 - Mitigation of Climate Change* 3–48 (Cambridge University Press, 2023). https://doi.10.1017/9781009157926.001
8. Net Zero by 2050. IEA https://www.iea.org/reports/net-zero-by-2050
9. Aurand, E. R. *et al.* Addressing the climate crisis through engineering biology. *npj Clim. Action* **3**, 1–4 (2024). https://doi.org/10.1038/s44168-023-00089-8
10. Biological Carbon Capture and Conversion. https://ebrc.org/publications-2022eo-carbon-capture/.
11. The White House. (2023) Building the Bioworkforce of the Future.