# Biological and Environmental Research Biological Systems Science Division Update

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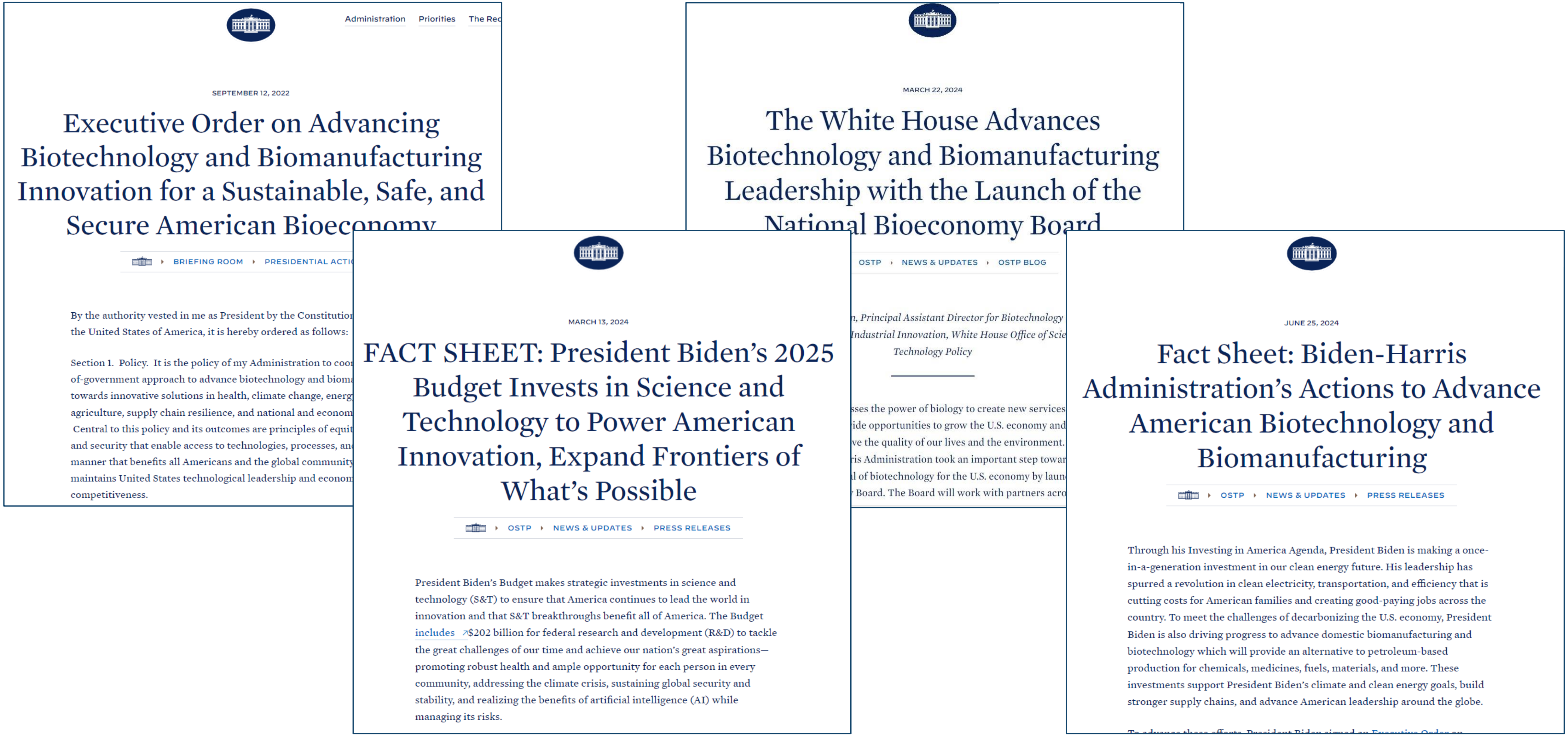
Director, Biological Systems Science Division
October 24, 2024

U.S. Department of ENERGY | Office of Science

Energy.gov/science/

# Bioscience is Still at the Forefront



Administration Priorities The Rec

SEPTEMBER 12, 2022

## Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy

BRIEFING ROOM ▸ PRESIDENTIAL ACTI

By the authority vested in me as President by the Constitution
the United States of America, it is hereby ordered as follows:

Section 1. Policy. It is the policy of my Administration to coor
of-government approach to advance biotechnology and bioma
towards innovative solutions in health, climate change, energ
agriculture, supply chain resilience, and national and econom
Central to this policy and its outcomes are principles of equit
and security that enable access to technologies, processes, an
manner that benefits all Americans and the global community
maintains United States technological leadership and econom
competitiveness.

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MARCH 22, 2024

## The White House Advances Biotechnology and Biomanufacturing Leadership with the Launch of the National Bioeconomy Board

OSTP ▸ NEWS & UPDATES ▸ OSTP BLOG

*n, Principal Assistant Director for Biotechnology*
*Industrial Innovation, White House Office of Scie*
*Technology Policy*

sses the power of biology to create new services
ide opportunities to grow the U.S. economy and
ve the quality of our lives and the environment.
is Administration took an important step towar
l of biotechnology for the U.S. economy by laun
Board. The Board will work with partners acro

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MARCH 13, 2024

## FACT SHEET: President Biden's 2025 Budget Invests in Science and Technology to Power American Innovation, Expand Frontiers of What's Possible

OSTP ▸ NEWS & UPDATES ▸ PRESS RELEASES

President Biden's Budget makes strategic investments in science and technology (S&T) to ensure that America continues to lead the world in innovation and that S&T breakthroughs benefit all of America. The Budget includes ↗$202 billion for federal research and development (R&D) to tackle the great challenges of our time and achieve our nation's great aspirations—promoting robust health and ample opportunity for each person in every community, addressing the climate crisis, sustaining global security and stability, and realizing the benefits of artificial intelligence (AI) while managing its risks.

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JUNE 25, 2024

## Fact Sheet: Biden-Harris Administration's Actions to Advance American Biotechnology and Biomanufacturing

OSTP ▸ NEWS & UPDATES ▸ PRESS RELEASES

Through his Investing in America Agenda, President Biden is making a once-in-a-generation investment in our clean energy future. His leadership has spurred a revolution in clean electricity, transportation, and efficiency that is cutting costs for American families and creating good-paying jobs across the country. To meet the challenges of decarbonizing the U.S. economy, President Biden is also driving progress to advance domestic biomanufacturing and biotechnology which will provide an alternative to petroleum-based production for chemicals, medicines, fuels, materials, and more. These investments support President Biden's climate and clean energy goals, build stronger supply chains, and advance American leadership around the globe.

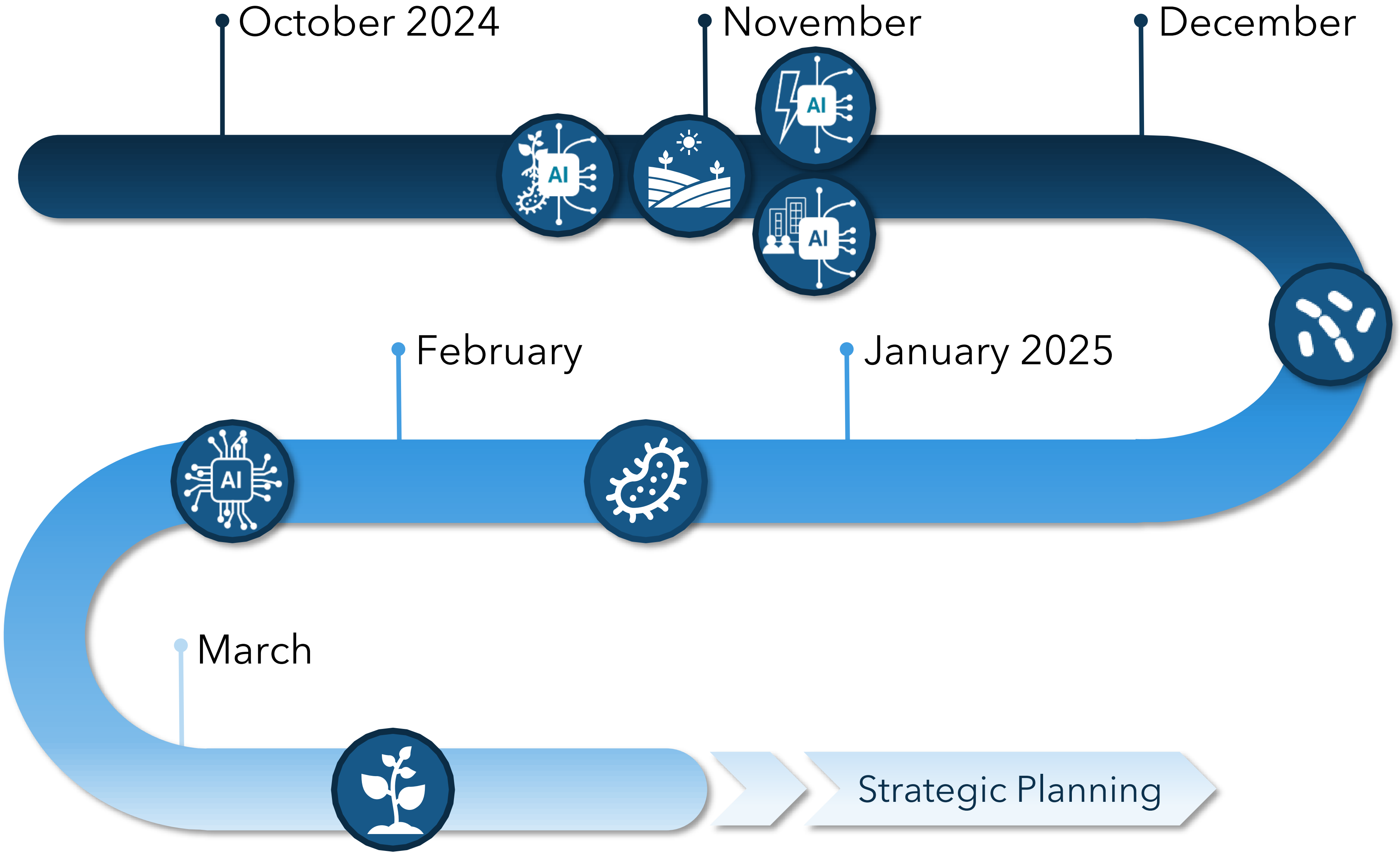
# BSSD – Change Agent for a Sustainable Future

- Microbial Conversion
- Computational Biology
- Biosystems Design
- Plant Genomics
- Sustainable Bioenergy
- Environmental Microbiology
- Enabling Capabilities

## Holistic Understanding of Genome Function

- Fuels and Chemicals
- Predictive Biology
- Engineered Biosystems
- Robust Models
- Scientific Leadership
- Enhanced Biosecurity

# BSSD Upcoming Workshops and Strategic Planning



October 2024

November

December

January 2025

February

March

Strategic Planning

- Biology and Environment AI Roundtable
- Resilient Bioenergy Crop Production Workshop
- Foundational Energy AI Roundtable
- User Facility Science and Ops AI Roundtable
- Engineering Microbial Communities Workshop
- Microbial Design Workshop
- ASCR/BER AI for Biology Workshop
- Plant Design Workshop

# Frontier Science for the Bioeconomy Workshop Series

## Resilient Bioenergy Crop Production – October 30-November 1, 2024

*Determine, predict, and improve both plant and plant microbiome response to a changing environment to optimize biomass feedstock production.*

## Engineering Microbial Communities – December 16-18, 2024

*Understand the assembly, function, and behavior of microbiomes and how to manipulate them to facilitate microbial solutions to challenging environmental problems and advance their utility across the bioeconomy.*

## Microbial Design for a Developing Bioeconomy – January 28-30, 2025

*Harness and leverage the diverse genetic and metabolic potential of microbes as platforms to efficiently produce biofuels, biproducts, biomaterials for a thriving and sustainable bioeconomy.*

## Plant Design for a Developing Bioeconomy – March 12-14, 2025

*Understand and manipulate potential bioenergy crops to efficiently generate clean, renewable, and sustainable biofuels, bioproducts, and biomaterials under variable abiotic stresses.*

# Office of Science Roundtables on Transformational Science Enabled by AI

**GOAL:** Identify and prioritize aspirational opportunities to address significant scientific challenges aligned with SC Program science through AI-enabled transformations.

**Topics include:**

- **Biosciences and environmental sciences (BER, BES) – October 28-29**
- **Fundamental energy research (BES, BER, FES) – November 7-8**
- **User facility science and operations (All SC Offices) – November 7-8**
- High energy and nuclear physics, including accelerator and detector research (HEP, NP, BES, FES)
- Materials and chemical sciences (BES)
- Fabrication science, combining microelectronics, plasma science and manufacturing (FES, BES, HEP, NP)

**Roundtables will identify:**

- Significant and potentially impactful scientific challenges that could be dramatically accelerated by AI
- Potential broad scientific and DOE mission impact
- Experimental and compute capability needs
- Near-term pathways to advancements in the field, including the need for new tools or methodologies
- Opportunities or gaps in workforce development
- Barriers to application of AI to solve important challenges

# Envisioning Frontiers in AI and Computing for Biological Research ASCR-BER Workshop

## PURPOSE

To identify the priority research directions for transforming the field of biology by new developments in applied mathematics, computer science, and computational science including new tools that leverage artificial intelligence (AI).

## Potential Themes

- New Mathematics and Computer Science to Advance Biology Research
- Integration of High-Resolution Imaging and Experimentation with Computational Advances
- Digital Twins and Bio-Inspired Design for Discovery and Translation
- Application of automated lab systems to catalyze biological discovery and design

**Planned for February 2025 in Washington, DC**

# Planning for the Future – Plant Transformation Capability (PTC)

## SC Mission Need - Capability gap to support plant genomics research

- Plant transformation is a critical step in bioengineering, and it is a bottleneck for bioenergy crops.
- The U.S. risks falling behind in a race where other nations are aggressively aiming to corner and control key technologies including plant-based biotechnology and synthetic biology.

## Proposed Plant Transformation Capability (PTC) will:

- Provide the infrastructure, technical resources, and leadership to efficiently engineer a broad range of mission-critical bioenergy crops, essential for global leadership in bioeconomy.
- Position the U.S. to take a competitive lead in addressing plant functional genomics and plant biotechnology.
- Enable a next generation of bio-workforce addressing technical challenges developing new and efficient genomic tools for bioenergy crops transformation.

| **Critical Decisions (CD)** |
|---|
| CD-0, Approve Mission Need |
| CD-1, Approve Alternative Selection and Cost Range |
| CD-2, Approve Performance Baseline |
| CD-3, Approve Start of Construction |
| CD-4, Approve Start of Operations |

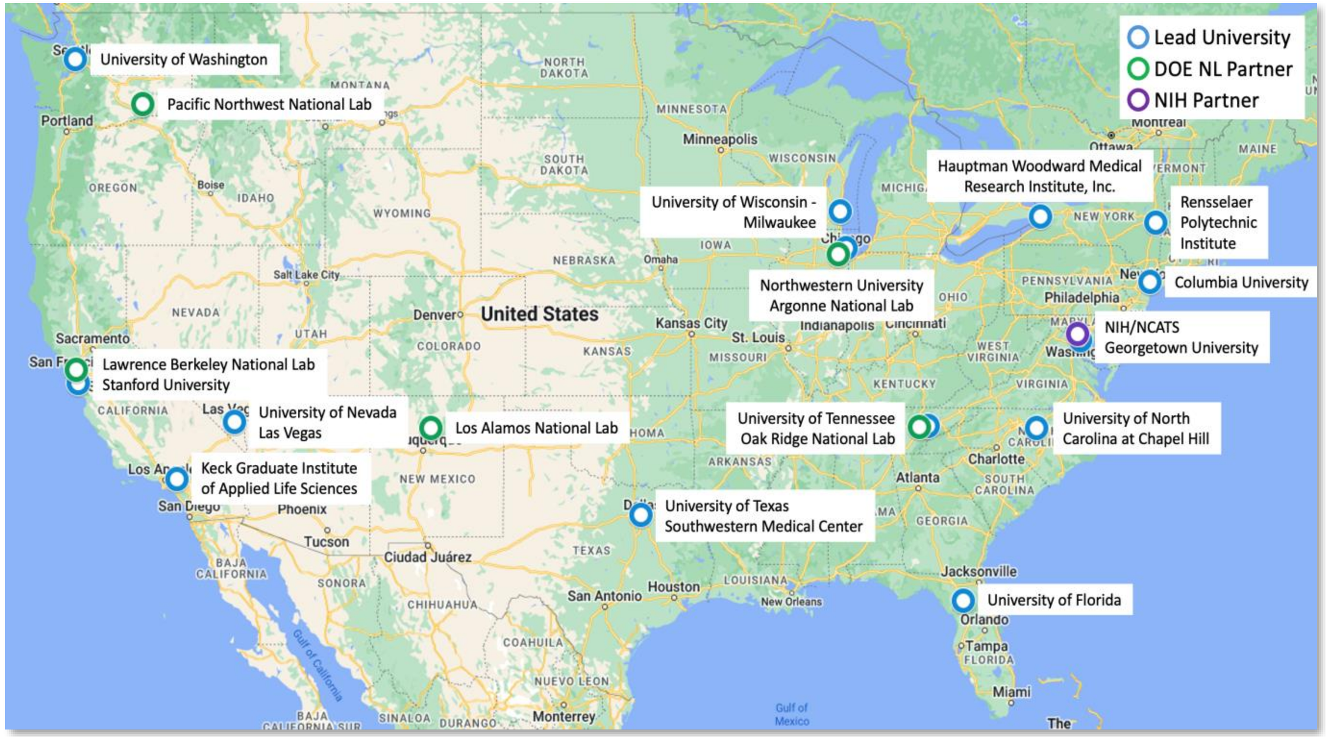
## Current Status

- **August 2024 CD-0 achieved→ ESAAB-E approved Mission Need Statement (MNS)**
- **Requesting Congressional approval to start the project.**

# New – Integrated Biological and Computational Low Dose Radiation Research Awards
## *Characterizing cellular responses to low dose radiation exposures* – DE-FOA-0003281

## *14 new projects in FY24*

**Generate precise experimental datasets in model systems to characterize cellular and molecular mechanisms underlying low dose/low dose-rate (LDR) ionizing radiation (IR) exposure health risks using AI and ML approaches**



- Human **bone marrow** model for **response network** studies of low dose/low dose-rate radiation exposures
- Combined dosimetric and toxicological contributions to **bone marrow** response in mice from low-dose strontium exposure using **AI-driven mouse model and digital twins**
- Automated HT screening of the effect of low dose radiation on **breast** using fibroblasts incorporated **mammographic density models**
- Combined experimental and AI-based **deep learning** approach to low dose and dose-rate **breast** cancer radiation risk prediction
- Evaluation of the cellular and molecular responses of **human skin** fibroblasts and neurons derived from iPSCs with varying intrinsic radiosensitivity to low dose radiation
- Exploring **T cell** functional dynamics following low-dose radiation exposure: insights into metabolic and other regulatory alterations using a **multi-omics systems biology** approach
- Modeling the circadian effects of low dose radiation on immunometabolism and its effect on **liver organoid** physiology
- ***Ab initio* modeling** capabilities for simulating **DNA damage** under ionizing
- Bridging the gap between low dose exposures and **emergent physiology** using **integrative modeling** and experimentation from epigenome to cell phenotype
- **AI-facilitated** assessment of **exosome-mediated** bystander effects of low-dose ionizing radiation
- Understanding the mechanism and health consequences of low-dose radiation at a **molecular level**
- Single-cell level elemental signatures of low dose radiation exposures in **mammalian model** systems
- Genetic diversity of **human heart** responses to low-dose radiation
- Quantitative **protein signatures** of low dose radiation exposure

# New – Bioimaging Research and Approaches for the Bioeconomy and the Environment Awards

## *Novel Techniques or Biological Utility of Quantum and Bioimaging – DE-FOA-0003231*

## *6 new projects in FY24 (+6 more coming in FY25)*

**Research to enhance resolution, speed, stability, sensitivity, or chemical specificity of bioimaging and sensing; includes quantum enabled approaches.**

- 3D imaging of microbial biofilm architecture in opaque porous media to assess responses to stress
- Genetically encoded anaerobic fluorescence reporters, nanobody and quantum dot (QD) probes, and automated anaerobic liquid handling and multi- modal imaging

PI: Vasdekis, Andreas
University of Idaho
Moscow, ID

PI: Shor, Leslie
U Connecticut
Storrs, CT

PI: Wildenschild, Dorthe
Oregon State U.
Corvallis, OR

PI: Schuck, Peter
Columbia University
New York NY

PI: Theis, Thomas
North Carolina State U.
Raleigh, NC

PI: O'Malley, Michelle
UC Santa Barbara
Santa Barbara, CA

- Apply coherent diffraction imaging techniques and computational algorithms to reconstruct high-resolution images (coded ptychography) for label-free gigapixel microscopy with intrinsic molecular contrast in soils and the rhizosphere
- RASER (Radiofrequency Amplification by Stimulated Emission of Radiation) MRI for non-invasive molecular imaging of plant metabolism and plant-soil-microbe interactions
- Deeply subwavelength metabolic imaging with avalanching nanoparticles
- Entanglement-Enhanced Visual Metabolomics applied to single cells and populations

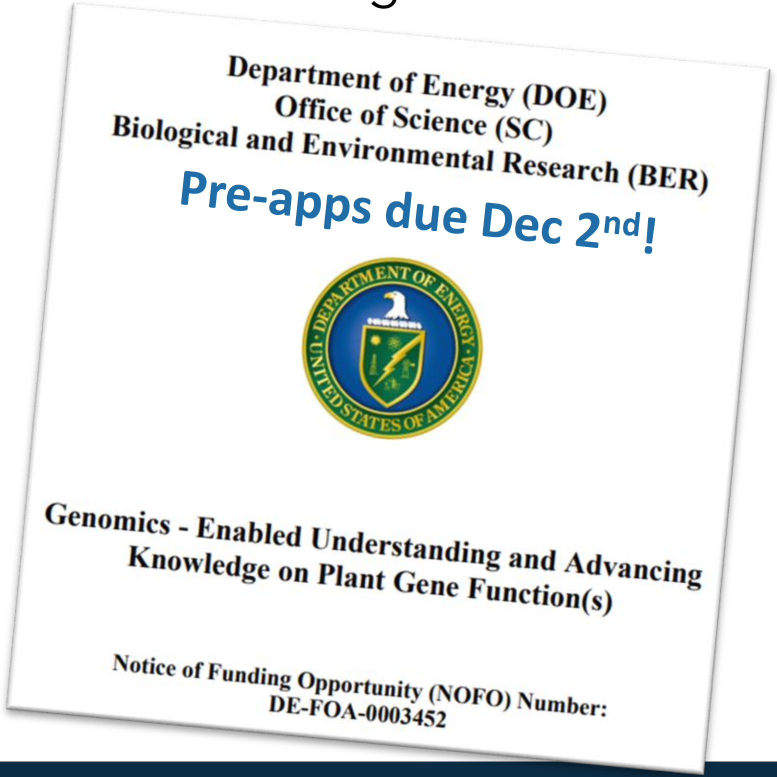
# FY25 Upcoming Reviews/Activities

- ❑ Annual Bioenergy Research Center (BRC) Reviews – Nov, Dec, Jan, Feb
- ❑ SC Roundtables on Transformational Science Enabled by Artificial Intelligence
  - ❑ Biology & Environment – Oct 28-29
  - ❑ Foundational Energy Research – Nov 7-8
- ❑ Frontier Science for the Bioeconomy Workshop Series (previous slide)
- ❑ UCLA-DOE Institute for Genomics and Proteomics Virtual Review – Nov 4-5
- ❑ JGI On-site Triennial Review – Dec 4-6
- ❑ Low Dose Virtual Kickoff Virtual Meeting – December 11-12
- ❑ ASCR/BER Envisioning Frontiers in AI and Computing for Biological Research Workshop – February 2025
- ❑ LBNL Enigma SFA Review – Feb 26-27
- ❑ 2025 BSSD PI Meeting – March 31-April 2
- ❑ LLNL Microbes Persist SFA – late Spring-early Summer
- ❑ PNNL Phenotypic Response of the Soil Microbiome SFA – late Spring-early Summer

# FY25 Potential Funding Opportunities

**Funding Opportunities for FY 2025 (dependent on appropriations)**

- ☐ Genomics-Enabled Understanding and Advancing Knowledge on Plant Gene Function(s) FOA (Posted!)
- ☐ Systems Biology Research to Advance Bioenergy Crop Production FOA (real soon!)
- ☐ Bioimaging Research and Approaches for Bioenergy and the Environment targeted DOE National Laboratory Call (TBD)
- ☐ Early Career Research Program (ECRP) (TBD)
- ☐ Reaching a New Energy Sciences Workforce (RENEW) (TBD)
- ☐ Funding for Accelerated, Inclusive Research (FAIR) (TBD)



Department of Energy (DOE)
Office of Science (SC)
Biological and Environmental Research (BER)

Pre-apps due Dec 2nd!

Genomics - Enabled Understanding and Advancing Knowledge on Plant Gene Function(s)

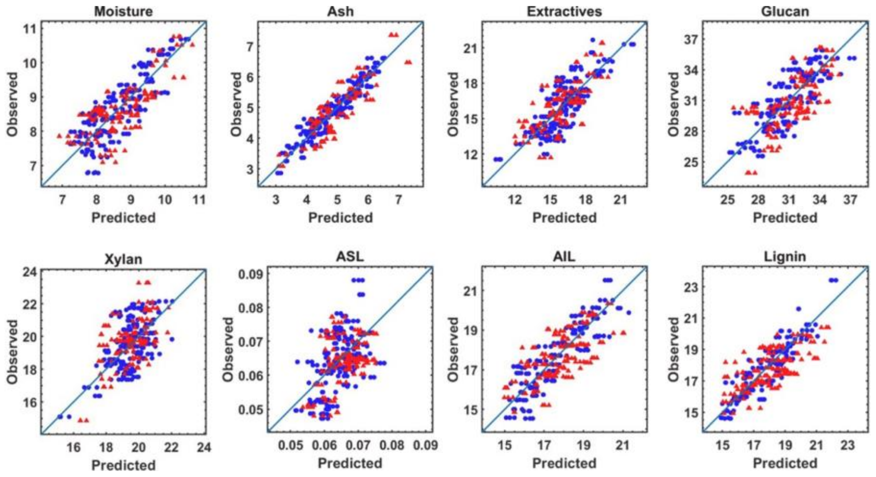
Notice of Funding Opportunity (NOFO) Number:
DE-FOA-0003452

# Rapid and High-Throughput Determination of Sorghum (Sorghum bicolor) Biomass Composition Using Near Infrared Spectroscopy and Chemometrics

CABBI
CENTER FOR ADVANCED BIOENERGY AND BIOPRODUCTS INNOVATION

## Background/Objective

- Compositional characterization of biomass is vital for the biofuel industry. Traditional wet chemistry-based methods for analyzing biomass composition are laborious, time-consuming, and require extensive use of chemical reagents as well as highly skilled personnel.
- In this study, the specific objectives were to develop full spectral range partial least squares regression (PLSR) models and robust PLSR models based on selected important wavelengths for rapid and high-throughput characterization of sorghum biomass. Near-infrared (NIR) spectroscopy was used to quickly assess the composition of above-ground vegetative biomass from 113 diverse, photoperiod-sensitive, biomass-type sorghum (Sorghum bicolor) accessions cultivated under field conditions in central Illinois.



Prediction of sorghum biomass composition using selected bands.

## Approach

Biomass samples were analyzed using NIR spectra collected in the spectral range of 867–2536 nm, with their chemical compositions determined following the National Renewable Energy Laboratory (NREL) protocol. Advanced spectral pre-treatment and band selection techniques were utilized to develop calibration models using PLSR.

## Results

The prediction ability of PLSR models using selected wavelengths was better than that of PLSR models using full raw spectra. The developed PLSR models with a few selected wavelengths showed excellent model performance for moisture, ash, extractives, glucan, acid-insoluble lignin (AIL), and lignin contents. Compared to full wavelength models, the models based on a few selective wavelengths reduced RMSE by 29%, 33%, 17%, 29%, 9%, and 8% for moisture, ash, extractives, glucan, AIL, and lignin, respectively.

## Significance/Impacts

This study demonstrated the potential of NIR spectroscopy as a rapid, real-time, and high-throughput analytical tool for the characterization of sorghum biomass for biofuel and biochemical production. The predictions for moisture, ash, extractives, glucan, xylan, acid-soluble lignin (ASL), AIL, and total lignin were accurate and reliable, demonstrating the capability of NIR spectroscopy to provide rapid and precise characterization of sorghum biomass.

Ahmed et al. 2024. *Biomass and Bioenergy*. DOI:10.1016/j.biombioe.2024.107276

# Overexpression of Heterologous Laccases and Peroxidase Leads to Increased Biomass Yield and Reduced Recalcitrance in *Populus*

## Background

Laccases (LAC) and peroxidases (PRX) are the major phenyl-oxidases that play an important role during the polymerization of monolignols into lignin during secondary xylem development. The gene functions of various laccases and peroxidases in woody plants are poorly understood.

## Approach

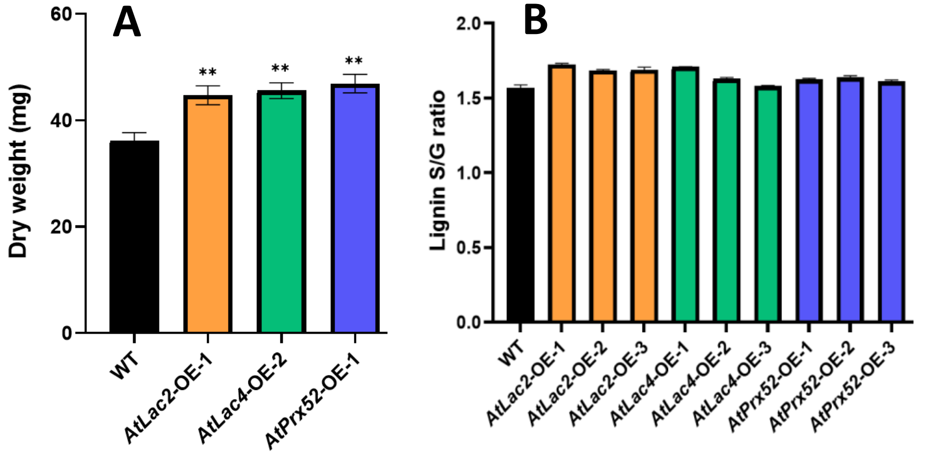
- The goal of this study is to understand the function of LAC and PRX in *Populus* (poplar) wood formation, plant growth, and biomass recalcitrance.
- Used the developing-xylem tissue-specific promoter DX15 to individually overexpress (OE) *Arabidopsis laccase2* (*AtLac2*), laccase4 (*AtLac4*), and peroxidase52 (*AtPrx52*) genes in poplar. Greenhouse-grown transgenics were assessed for growth phenotypes, gene expression, lignin analysis, and biomass saccharification efficiency.

## Results

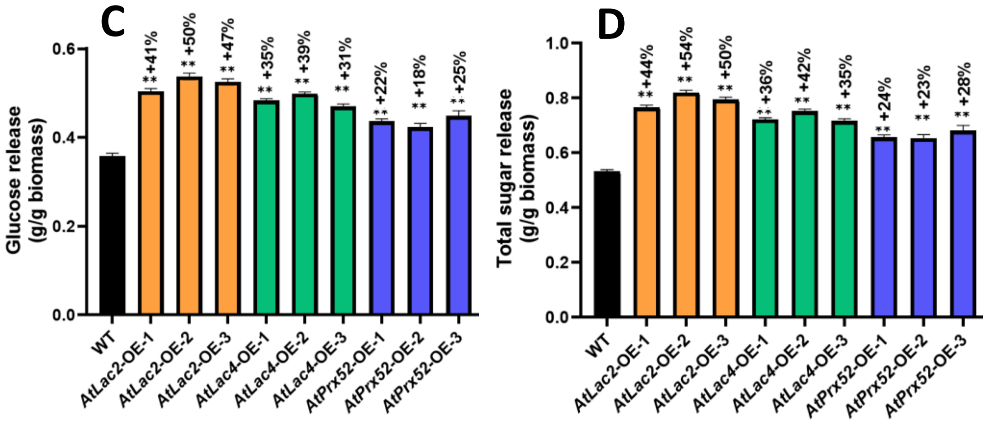
- Dry biomass yield increased by 24-30% across all OE transgenic lines compared to wildtype control (WT).
- No changes in lignin content were observed among the over expression lines, but all transgenic lines had higher lignin S/G than WT.
- Saccharification efficiency increased by 35–50%, 21–42%, and 8–39% in *AtLac2*-OE, *AtLac4*-OE, and *AtPrx52*-OE transgenic poplar lines, respectively, as compared to WT.
- Expression network analyses indicate that these laccases and peroxidases are important regulators in the biosynthesis of specific secondary cell wall components.

## Significance

Over-accumulation of LAC and PRX enzymes impacts plant cell wall structure and represents a promising strategy to improve ethanol production through improvement of saccharification efficiency in poplar bioenergy feedstocks.



Dry biomass (A) and S/G ratio (B) of wildtype control (WT) and transgenic poplar lines (OE).



Glucose (C) and total sugar (D) release from wildtype control (WT) and transgenic poplar lines (OE).

Ahlawat YK et al. *Biotechnology for Biofuels and Bioproducts, (2024) 17, 5.* (https://doi.org/10.1186/s13068-023-02452-7 )

# Enormous Diversity and Biogeochemical Potential within the Soil Virosphere

SOIL MICROBIOME
SFA @PNNL

## Objective

Explore the viral diversity and genes associated with soil biogeochemical cycles and create a public database of soil viruses.

## Approach

- Coordinated a global consortium, representing nearly 50 organizations worldwide, to generate the first-of-its-kind Global Soil Virus (GSV) Atlas.
- Collated the GSV Atlas from 2,953 soils, including 1,552 samples that were unavailable previously.
- Grouped 616,935 uncultivated virus genomes into 38,508 unique viral operational taxonomic units.
- Explored genetic diversity and functional potential of soil virosphere with statistical approaches.

## Results/Impact

- Provides the most extensive characterization of soil viral diversity to date, including an open database.
- Reveals soil viral genes with the potential for carbon and nutrient cycling.
- Offers a foundation for testing hypotheses regarding the role of the virosphere in the soil microbiome and global biogeochemistry.

Graham, E.B., et al. 2024. *Nature Microbiology*.
DOI: https://doi.org/10.1038/s41564-024-01686-x

Graham E.B, et al. 2024. [Data Set] PNNL DataHub. https://doi.org/10.25584/2229733

# Environmental Stress Mediates Groundwater Microbial Community Assembly

Environ. Microbiology Highlight

## *Objective*

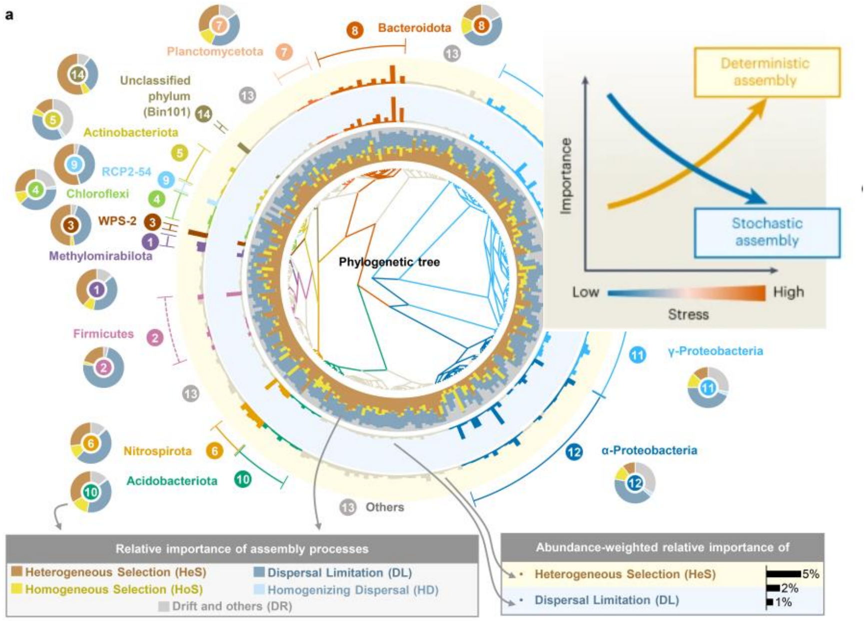
- Develop a general framework to understand relationships during microbial community assembly along stress gradients
- Understand how assembly processes of the groundwater communities differ across different microbial lineages?
- Reveal which environmental factor(s) are most important in mediating changes in community assembly processes in response to stressors

## *Approach*

- Examined planktonic communities in groundwater of Oak Ridge field site contaminated with U, NO3, Tc and heavy metal
- Sampled 100 wells and characterized community structure and >200 biogeochemical variables

## *Result/Impacts*

- Stochasticity, dispersal limitation and 'drift' decrease in importance in shaping microbial communities, but determinism and heterogeneous selection increase with environmental stress.
- This provides a general framework to capture the general relationships among community assembly processes and environmental stresses,



Nature Microbiology 9, pages490–501 (2024)
DOI:10.1038/s41564-023-01573-x

*Now Top 1% highly cited paper in Web of Science in the field of Microbiology!*

# SANS provides evidence for covalent complexes between lignin and pectin in plant cell walls Bio-SANS – Center for Structural Molecular Biology

Structural Bio Highlight

## Objective

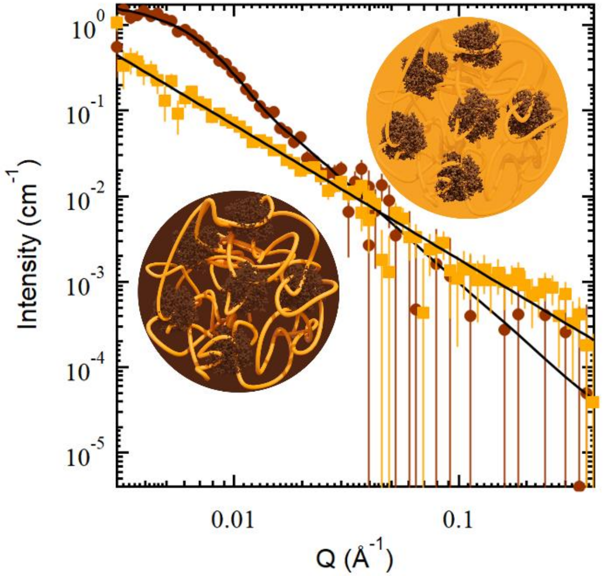
Understand lignin–carbohydrate complexes (LCCs), thought to be a significant source of biomass recalcitrance, to improve biomass conversion to biofuels and bioproducts.

## Approach

- LCCs formed between lignin and the pectin homogalacturonan (HG) were investigated by Small Angle Neutron Scattering (SANS) to characterize structural changes in HG deficient transgenic switchgrass after hot water pretreatment compared to wild-type (WT) plants.
- SANS revealed the structural differences in how lignin distributes during thermochemical pretreatment suggesting the presence of lignin-pectin complexes.
- Additional analysis of a model composite composed of pectin and lignin using contrast matching SANS showed that pectin and lignin form a highly interconnected polymer network and evidence of an ester bond between the polymers, providing strong evidence that pectin forms an LCC with lignin.
- Biophysical techniques included Fourier transform infrared spectroscopy and Solid-state nuclear magnetic resonance (NMR)

## Result/Impacts

Engineering plants to reduce pectin-lignin interactions that contribute to LCCs could decrease biomass recalcitrance for biofuel production.



SANS of a lignin – homogalacturonan (pectin) composite at the contrast match points for pectin (40% $D_2O$, brown curve) and $d_5$-lignin (80% $D_2O$, yellow curve). Inset schematic depicts match points:

- lignin-brown particles,
- pectin-orange chains.

R Shah, M Senanayake et. al. (2023) *ACS Sust Chem Eng* 11:15941-15950. https://doi.org/10.1021/acssuschemeng.3c04322

Visualization of Solvent Disruption of Biomass and Biomembrane Structures in the Production of Advanced Biofuels and Bioproducts

# Multi-omics analysis reveals the dynamic interplay between host chromatin structure and function during viral infection

BRaVE Project Highlight

## Objective

- Viruses often hijack host epigenetic processes for their benefit, but their impact on genomic structure is not well characterized
- Genomic structural changes may be an early signal of viral infection, but empirical evidence is lacking

## Approach

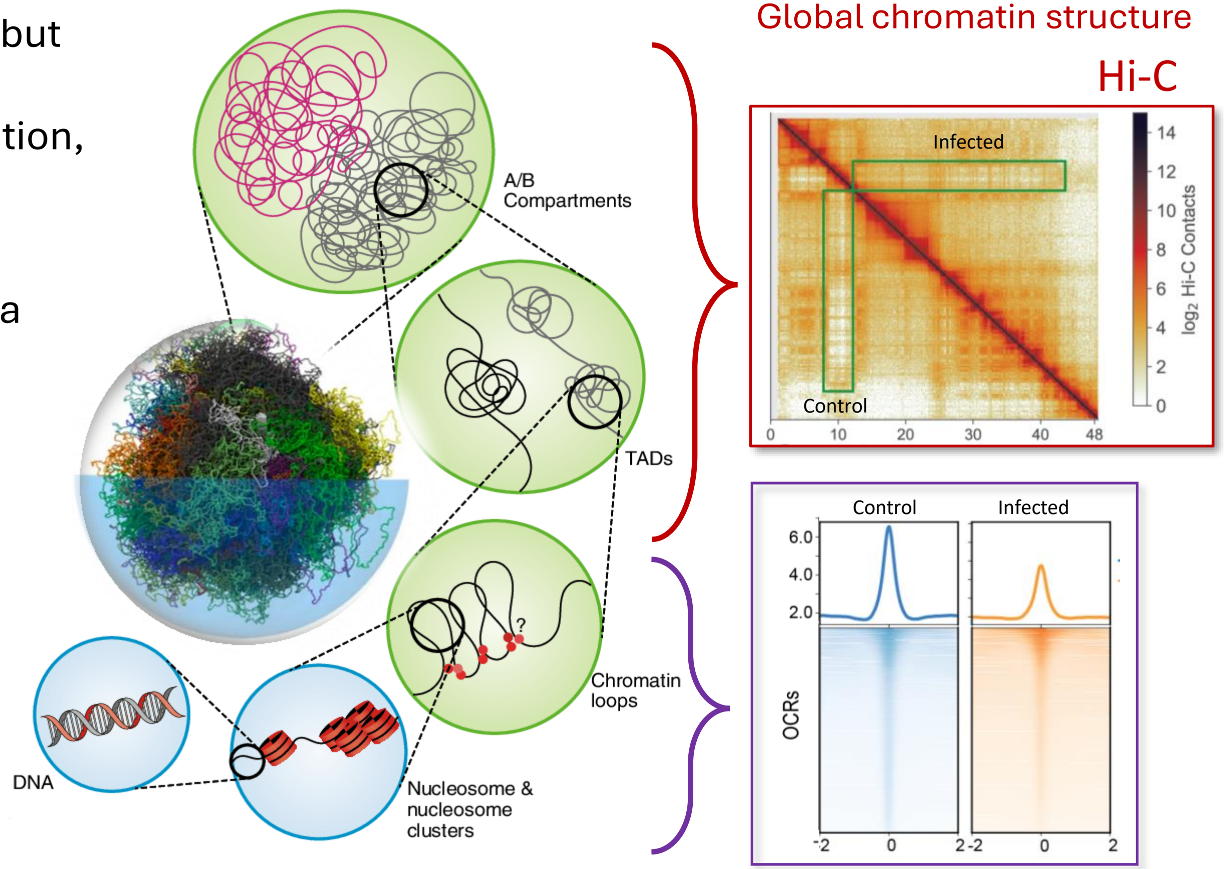
- Developed a non-cytotoxic model of viral infection using vaccinia virus and Vero cells
- Conducted paired, time-matched analyses of global to local chromatin structures and associated gene expression over time as infection progressed using sequencing modalities
  - Hi-C, ATAC-seq, and RNA-seq

## Impacts/Results

- Viral infection alters host 3D genome architecture, which becomes more condensed and loses accessibility
- Local nucleosome structure is a better indicator of gene expression, which is bidirectional
- While the genome structure-function relationship is non-linear, viruses have a significant impact early in infection which becomes more substantial over time, suggesting predictive use of chromatin structural information

Global chromatin structure

Hi-C



ATAC-seq

Local chromatin structure

Venu et al. *Communications Biology* 7, 721 (2024) [https://doi.org/10.1038/s42003-024-06389-x]

# Two-Dimensional Spatial Map of Gene Expression in Plant-Fungal Interactions

## *Objective*

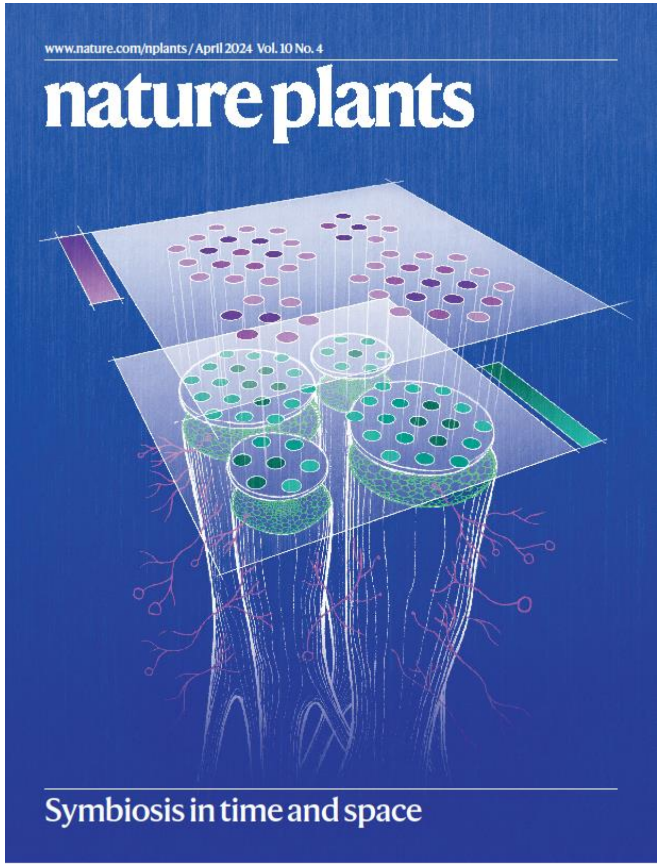
- Combine spatial transcriptomics with single-cell expression profiling to gain new insights on plant-arbuscular mycorrhizal interactions.

## *Approach*

- Single-nucleus RNA sequencing that allows the identification of novel cell types and cellular developmental trajectories was combined with spatial transcriptomics to add tissue context to gene expression data to two-dimensional map of plant and fungal transcriptomes during symbiosis.

## *Result/Impacts*

- The spatial transcriptomics map sheds light on coordinated gene expression in key root cell types that interact with mycorrhizae.
- Cortex cells exhibit distinct transcriptome profiles during different stages of fungal colonization.
- The approach demonstrates a new paradigm for multi-omics analysis of complex organismal interactions.



Serrano *et al.*, *Nature Plants* 10, 673–688 (2024)

# Thank you!