



Molecular Foundations for Biotechnology (NSF 22-554)

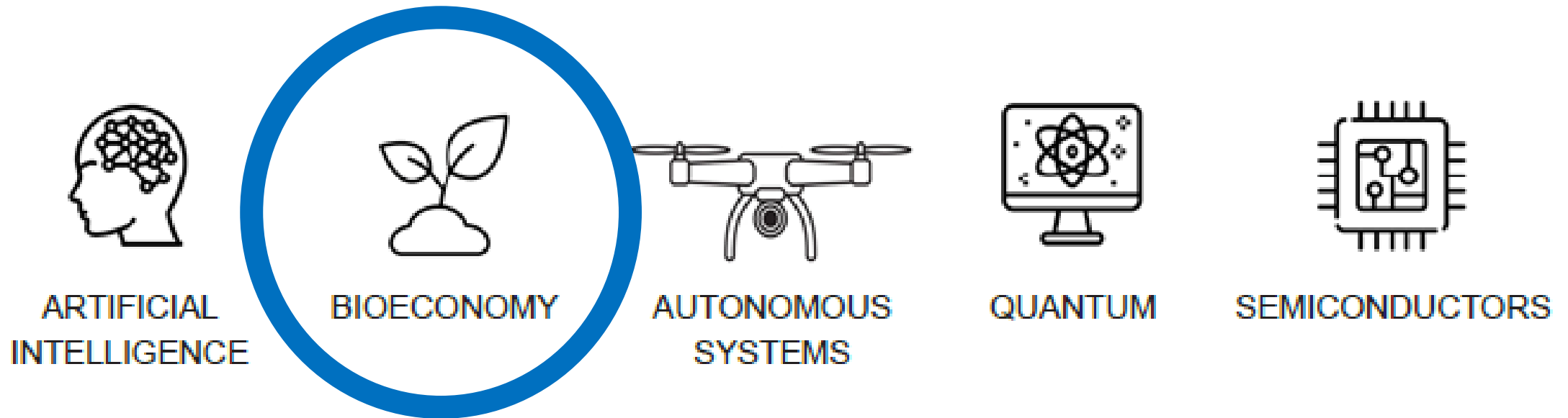
CISE Office Hour February 09, 2022

- **Catalina Achim**, Division of Chemistry, MPS Directorate
- **Krastan B. Blagoev**, Division of Physics, MPS Directorate
- **Zhilan J. Feng**, Division of Mathematical Sciences, MPS Directorate
- **Wilson A. Francisco**, Division of Molecular and Cellular Biosciences, BIO Directorate
- **Tingyu Li**, Division of Chemistry, MPS Directorate
- **Marcia E. Newcomer**, Division of Molecular and Cellular Biosciences, BIO Directorate
- **Steven W. Peretti**, Division of Division of Chemical, Bioengineering, Environmental and Transport Systems, ENG Directorate
- **Amarda Shehu**, Division of Information and Intelligent Systems, CISE Directorate

David Berkowitz, Division Director & **Lin He**, Deputy Division Director, CHE/MPS
Henry Kautz, Division Director & **Wendy Nilsen**, Deputy Division Director, IIS/CISE

Several US Technology Areas of High Priority

The Critical and Emerging Technologies are cross-cutting, convergent, and independent fields of research that collectively offer enormous economic potential and are critical to the Nation's long-term economic and national security.



Molecular Foundations for Biotechnology



- Response of the Division of Chemistry to Critical and Emerging Technologies
- Multi-year campaign with different annual themes
- **2021:** The development and deployment of fundamentally new techniques to modify the structure, function, and/or fate of proteins interacting with small molecules for important applications in biotechnology.
- Co-funding: PHY/MPS, MCB/BIO, CBET/ENG
 - **Ultra-Fast Development of Portable Small Molecule Sensor-Actuators** Tim Whitehead (U. Colorado Boulder)/Sean Cutler, Ian Wheeldon (UC Riverside)/Francis Peterson (Med Coll Wisconsin) - 2128287
 - **Bioorthogonal Chemistries Targeting 5-hydroxytryptophan for Biological Discovery and Biologics Development** Abhishek Chatterjee, Tim van Opijnen and Eranthie Weerapana (Boston College) 2128185
 - **Developing Next-Generation Approaches to Targeted Protein Degradation** Daniel Nomura/Thomas Maimone (UC-Berkeley) 2127788
 - **Deciphering the Logic of PTM Crosstalk via Novel Chemical Technology: Histones and Beyond** Philip Cole/Ben Garcia (Harvard/Wash U) - 2127882

2022 Solicitation



Synergistic scientific research collaborations that involve innovative machine learning (ML) methods to foster advances in research on the function of biomolecular systems and have the potential to drive innovation in biotechnology.

The solicitation seeks to catalyze synergistic and innovative work at the interface of ML/AI on one hand and the biological, physical, and mathematical sciences and engineering on the other hand that goes beyond sequence-structure relationships and addresses standing challenges in biology.

- The Directorates for MPS, CISE, BIO and ENG are participating in this solicitation, highlighting the importance of partnerships across disciplines.

Targeted Areas



The solicitation will give support for interdisciplinary research endeavors that:

1. Bring together computer science expertise in ML/AI on one side and chemistry, biology, physics, engineering, and/or mathematics on the other side,
2. Focus on integrated, convergent research projects that create new mechanism-guided machine learning frameworks for the prediction and detailed characterization of the function of biological macromolecules (e.g., protein, nucleic acids, and macromolecular assemblies of both protein and nucleic acids),
3. Test the validity, specificity, and generalizability of the proposed ML frameworks with robust experimental platforms.

The novel, interdisciplinary approaches could focus on current challenges such as:

- a. Predict and characterize the interactions of intrinsically disordered proteins (or proteins that contain disordered regions)
- b. Expand our understanding of the dynamic relationship between biopolymer function and the environment
- c. Gain insight in the assembly of biomolecules into higher order complexes, including understanding, building upon, and/or disrupting protein-protein interactions
- d. Design, synthesize, and characterize natural and synthetic polymer hybrids
- e. Predict RNA (structure and) function



Merit Review Criteria for MFB Proposals

- Intellectual Merit
- Broader Impacts
- Additional Solicitation-Specific Criteria
 - *How the proposed ML methods will be validated by planned experiments*
 - *The potential of the new prediction methods to be applied or generalizable to systems beyond the specific biomolecules/biopolymers on which the project focuses*
 - *The use of interdisciplinary approaches that develop new knowledge in both computer science and in biological, physical, and/or mathematical sciences*
 - *Need for the proposed interdisciplinary collaboration to meet the goals of the proposed project and plans that enable synergy and effectiveness of the proposed collaboration*

Required Letter of Intent



1. Project Title

The title should describe the project in concise, informative language that is understandable to a technically-literate reader.

Proposal titles should begin with "MFB:" then the title of the project.

Titles of collaborative proposals should begin with "Collaborative Research: MFB:" followed by the title of the project.

2. Project Information

i) Synopsis (2500 characters)

The Synopsis should include a statement on the intellectual merit of the proposed activity and a statement on the broader impacts of the proposed activity. Include the specific goals of the research and testable hypotheses for each goal.

ii) Other Comments (2500 characters)

Explain how the project will address each of the four Additional Solicitation Specific Criteria identified in the Solicitation.

3. Optional Data Fields

i) Research disciplines (255 characters) - Identify the disciplines in which the research is grounded

ii) Key references (255 characters) - DOI and/or ISBN for key references cited in the Letter of Intent

4) List Senior Project Personnel and Participating Organizations

Submission of the Letter of Intent must be done by an Authorized Organizational Representative.

Submission of multiple Letters of Intent is not permitted.

Other Information



- **Budget** up to \$1.5 million/3yr; Up to 6 awards expected.
- **Timeline**
 - Letter of intent (LOI) is required; due date **February 14, 2022**
 - Full proposal: due on **April 14, 2022**
 - Review process: panel/ad hoc review
 - Funding decisions: Summer 2022
- **For more information**
 - Email contact: mfb@nsf.gov
 - Website: <https://beta.nsf.gov/funding/opportunities/molecular-foundations-biotechnology-mfb>

Questions and Answers

