Emerging Frontiers in Research and Innovation 2025

Informational Webinar

August 30th, 2024

AGENDA

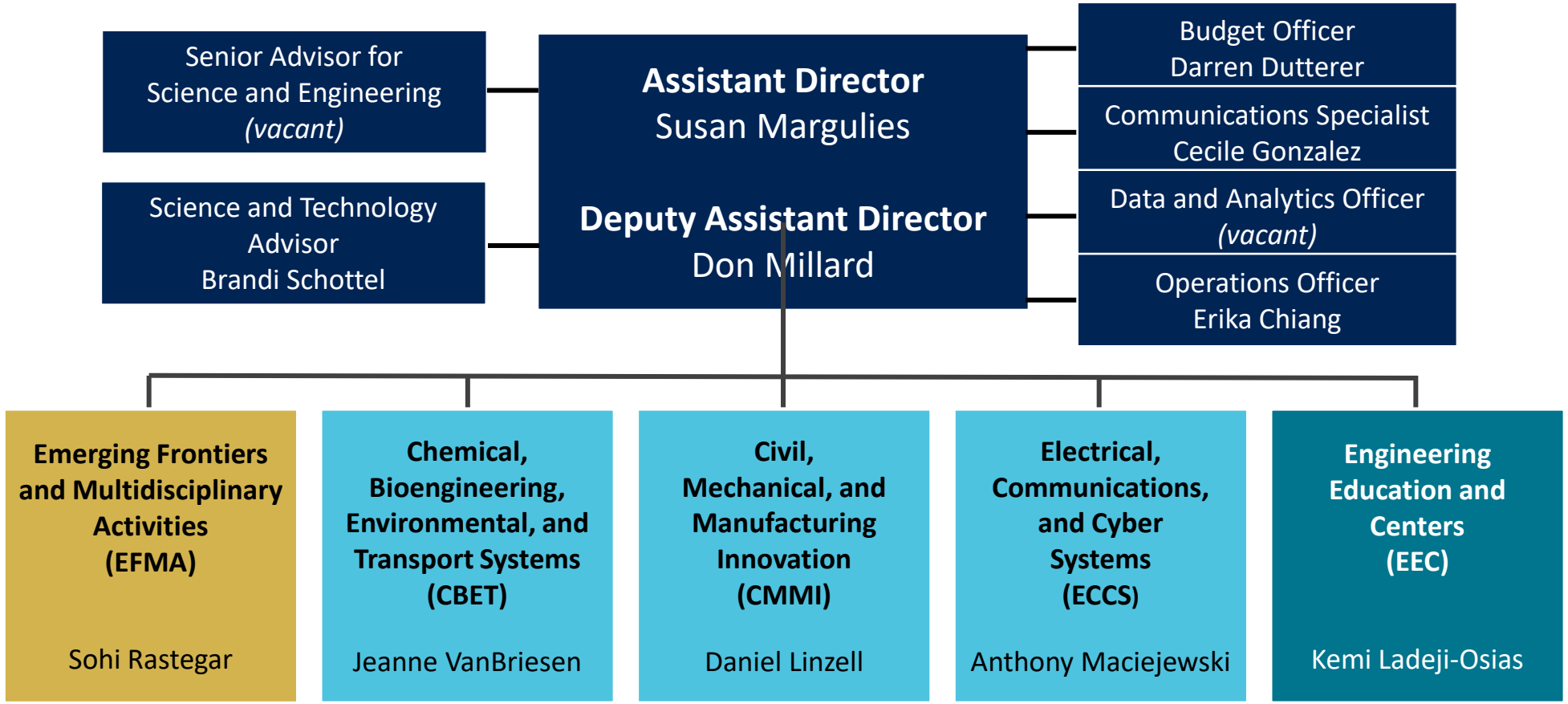
3:00 PM	Welcome from Sohi Rastegar, Office Head, NSF/ENG/EFMA
3:05 PM	Introduction of the Emerging Frontiers in Research and Innovation (EFRI) Team
3:10 PM	Overview of the EFRI Biocomputing Through EnGINeering Organoid Intelligence (BEGIN OI) Solicitation
3:45 PM	Questions

Webinar Housekeeping

1. The webinar is being recorded and the recording will be posted online
2. The webinar slides will be posted online
3. Questions will be addressed using the Q&A function
4. The Chat Function has been disabled
5. Send any questions not addressed in the webinar to efri2024-2025@nsf.gov

For more information, please read solicitation NSF 24-508

NSF Directorate for Engineering



Emerging Frontiers and Multidisciplinary Activities Office

Sohi Rastegar, *Office Head*

Louise R. Howe, *Program Director*

Alias Smith, *Program Director*

Greg Rorrer, *Program Director*

Sydney Schroeder, *Program Assistant*

Lanita Thomas, *Panel Assistant*

Ebun Ogunsusi, *Panel Assistant*

Biocomputing through EnGINeering Organoid Intelligence (BEGIN OI) Team

Topic Leads: Steven Peretti, *Program Director, ENG/CBET*
Steven Zehnder, Program Director, ENG/CBET

- Jason Borenstein, Program Director, SBE/OAD
- Dwight Kravitz, Program Director, SBE/BCS
- Edda Thiels, Program Director, BIO/IOS
- Kenneth Whang, Program Director, CISE/IIS
- Stephanie Gage, Program Director, CISE/CCF
- Jordan Berg, Program Director, ENG/CMMI
- Krastan Blagoev, Program Director, MPS/PHY
- Vishal Sharma, Program Director, CISE/CNS
- Alias Smith, Program Director, ENG/EFMA

Goals of the Webinar

- To inform the community about the EFRI FY 2025 Program Solicitation
- Respond to questions from potential applicants

Key website

Office of Emerging Frontiers & Multidisciplinary Activities (EFMA) Website:

http://www.nsf.gov/eng/efma

Please refer to this website for up-to-date information.

The Emerging Frontiers in Research & Innovation (EFRI) Program

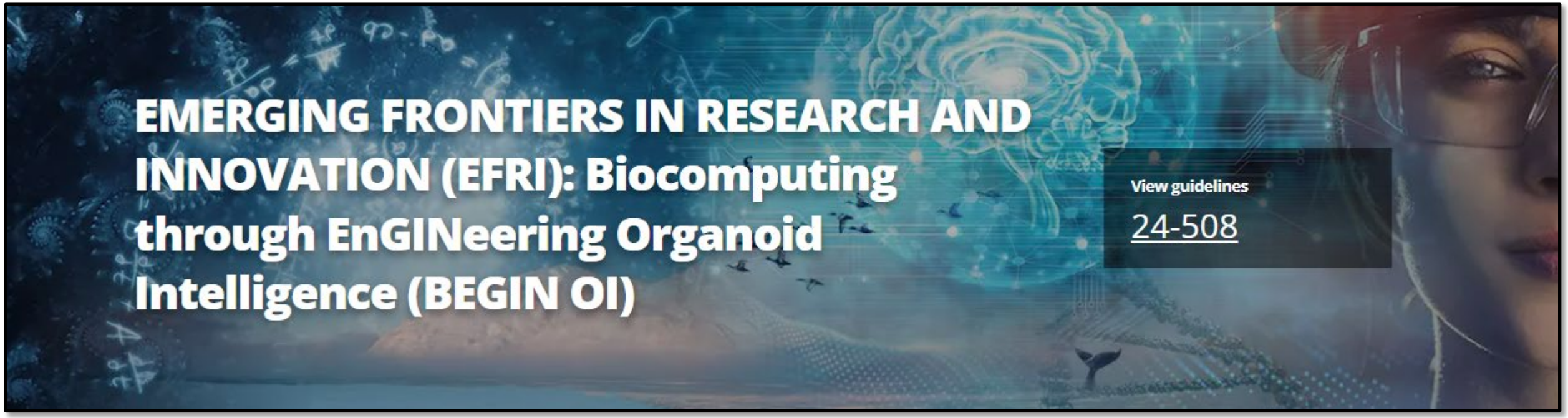
The EFRI Program serves a critical role in helping the Engineering Directorate to focus on important emerging areas in a timely manner.

- Community Driven – Engages the research community (through a DCL) as well as NSF Program Directors to identify and fund a portfolio of projects in strategic emerging, interdisciplinary areas that may not be supported through current NSF programs, and in which ENG research plays the leading role.
- Uses Potentially Transformative / High risk, High reward and Interdisciplinary as criteria for project selection.
- Signature midscale project-funding mechanism in ENG ($2M / 4 year projects)

EFRI Topics – 07-25

FY07	**ARES:** Autonomously Reconfigurable Engineered Systems **CBE:** Cellular and Biomolecular Engineering
FY08	**COPN:** Cognitive Optimization and Prediction **RESIN:** Resilient and Sustainable Infrastructures
FY09	**BSBA:** Biosensing and Bioactuation **HyBi:** Hydrocarbons from Biomass
FY10	**SEED:** Science in Energy and Environmental Design **RESTOR:** Renewable Energy Storage
FY11	**M3C:** Mind, Machines, and Motor Control **MIKS:** Engineering based on Multicellular and Interkingdom Signaling
FY12/13	**BioFlex:** Flexible Bioelectronics Systems **PSBR:** Photosynthetic Biorefineries **ODISSEI:** Origami Design for Integration Of Self-assembling Systems For Engineering Innovation
FY14/15	**2-DARE:** 2-Dimensional Atomic-Layer Research and Engineering
FY16/17	**ACQUIRE:** Advancing Communication Quantum Information Research Engineering **NewLAW:** New Light and Acoustic Wave Propagation: Breaking reciprocity and time-reversal symmetry
FY18/19	**CEE:** Chromatin and Epigenetic Engineering **C3 SoRo:** Continuum, Compliant and Configurable Soft Robotics Engineering
FY20/21	**DCheM:** Distributed Chemical Manufacturing **E3P:** Engineering the Elimination of End-of-life Plastics
FY22/23	**BRAID:** Brain-Inspired Dynamics for Engineering Energy-Efficient Circuits and Artificial Intelligence **ELiS:** Engineered Living Systems
FY24/25	**BEGIN OI:** Biocomputing through EnGINeering Organoid Intelligence **PEL:** Ideas Lab: Personalized Engineering Learning (NSF 23-627)

EFRI FY 2025 Topic



Biocomputing through EnGINeering Organoid Intelligence (BEGIN OI)

- The objective of BEGIN OI is to harness the novel discoveries and advancements in biological sciences, engineering, material sciences, and computer sciences toward designing 3D *in vitro* biological systems that are capable of information processing and actuation.

- Supports foundational and transformative research to advance the design, engineering, and fabrication of organoid systems that are capable of processing information dynamically while interfacing with non-living systems

BEGIN OI

- Supports a broad interpretation of *in vitro* biological "intelligent systems" to include capture of real-world input, autonomous processing in an engineered biological construct, and generating an output that drives an engineered system

- Asks investigators to define the bounds of "intelligence" and "learning" needed to achieve responsive and adaptive biological computing and control

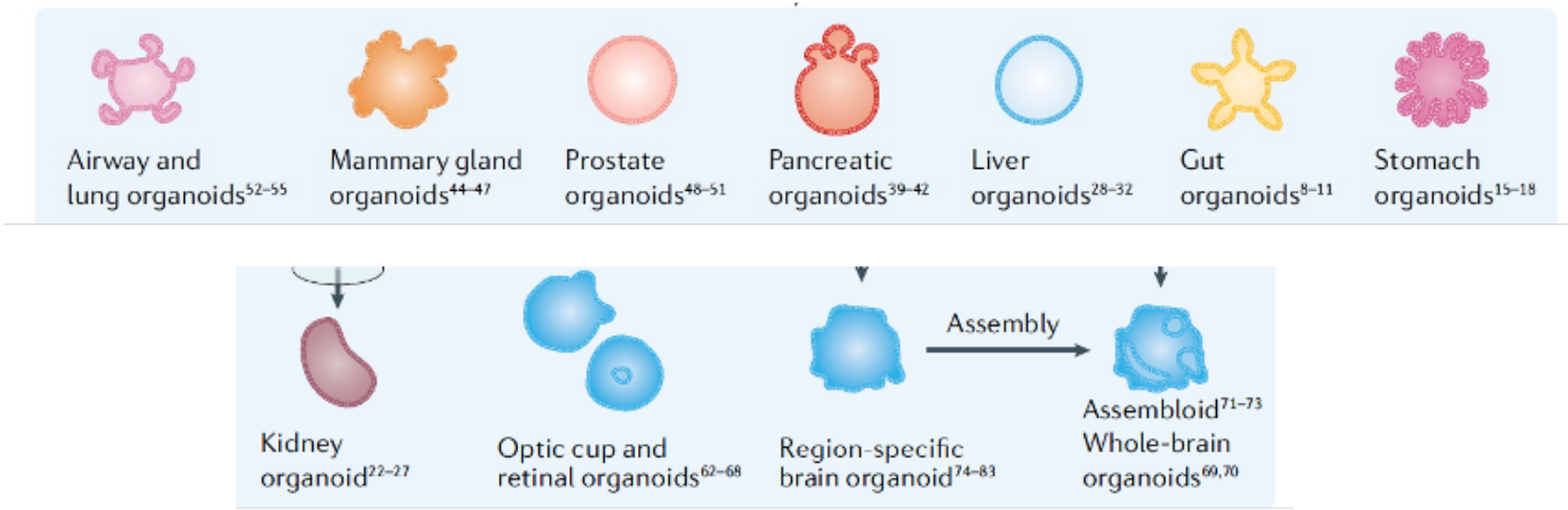
- Requires a convergent research approach that engages engineers, biologists, computer scientists, social scientists, ethicists, and others

Foundational Concepts

- No organ is an island, entire of itself, every organ is a piece of the body, a part of the main. (apologies to John Donne)
- Intelligence: "the ability to acquire and apply knowledge and skills"
- Biomimetics: "principles from engineering, chemistry and biology are applied to the synthesis of materials, synthetic systems or machines that have functions that mimic biological processes"
- Bioethics: biological research activities are fundamentally intertwined with Ethical, Legal, and Social Implications

No organ is an island, but is independently “intelligent”

- Organoids can be developed from a variety of sources, and embody varied aspects of intelligence



Adapted from https://doi.org/10.1038/s41578-021-00279-y

Biomimetics

- **Interoception:** bidirectional signal processing between the brain and the organs that generates a representation of the internal state of an organism

  - Mediated by vagus nerve and endocrine systems
  - Therefore, organs convert physical or chemical signals into electrical signals. How do we capitalize on/mimic those processes?
  - How does the nervous system learn to interpret those signals?
  - Can we create an analogous learning process for organoids?

Ethical, Legal, and Social Implications (ELSI)

Responsible development requires embedding ELSI considerations into the project.

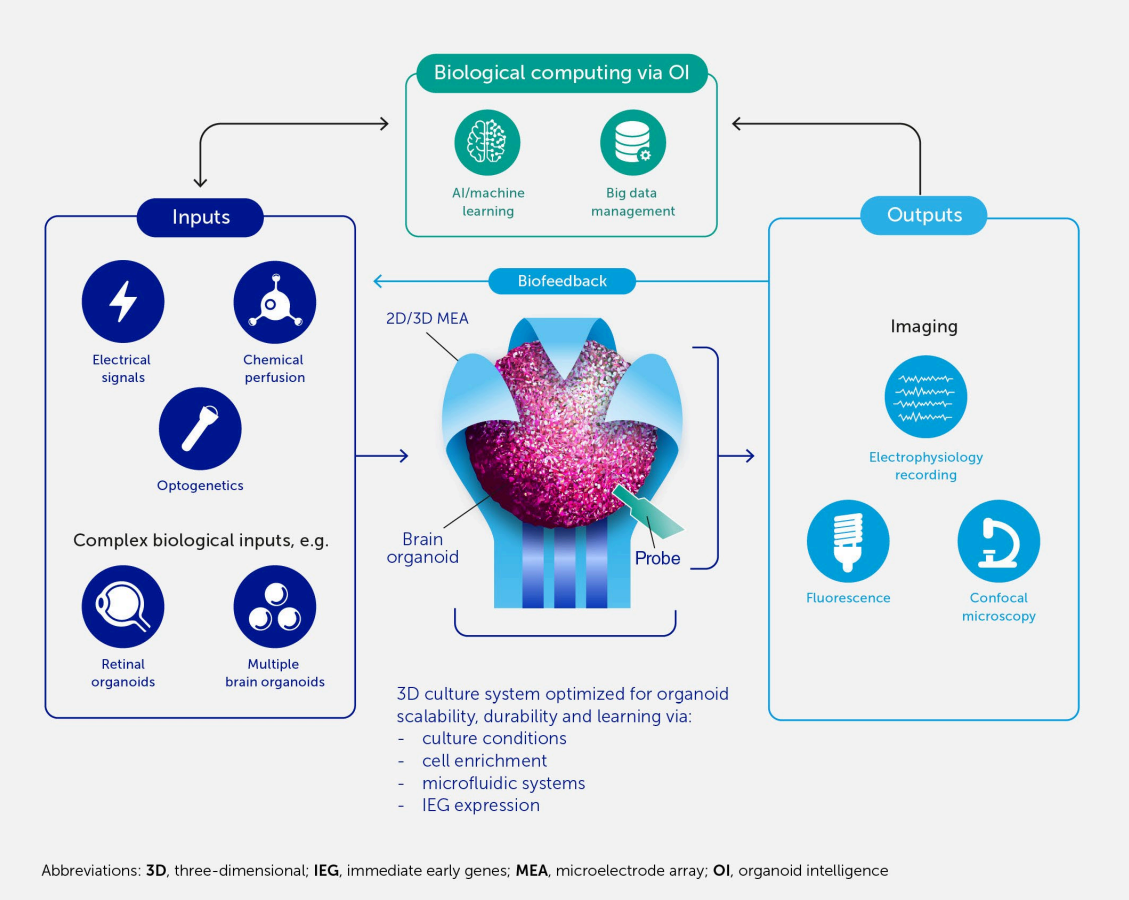
A variety of approaches in ethics could influence how ELSI considerations are framed. These include but are not limited to:

- Principlism (for example, applying principles such as beneficence or respect for persons)
- Case-based reasoning
- Ethical theories or frameworks (such as Utilitarianism or Virtue Ethics)
- Codes of ethics (for example, from professional organizations)

Proposals must include a plan the describes the project's ELSI research activities

An INTEGRATED ELSI Component is Critical

Research Thread 1: Biocomputing Theory and Modeling



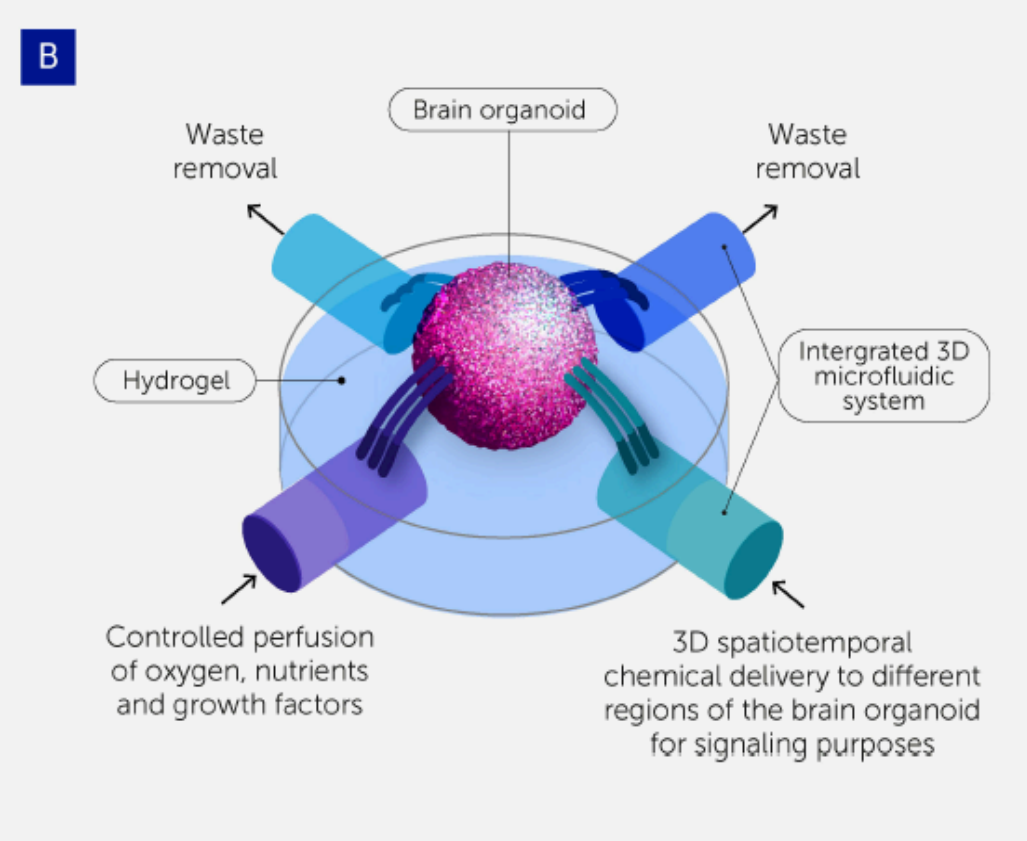
- New computational models/AI approaches that describe the ability for storage and retrieval
- Effectively interpret the complex biological outputs into meaningful information
- Computational strategies may be highly reliant on nature of inputs and outputs; which in turn depends on the sensing and signaling systems employed

Adapted from DOI 10.3389/fsci.2023.1017235

Research Thread 2: Biology Integrated Culture Maintenance and Hardware Systems

To create an organoid-based computer, one must:

- Keep it alive and fully functional – this may require, for example, the development of a digital twin of the organoid to effectively control the culture environment
- Develop a robust signaling interface that allows for appropriate inputs to be introduced and outputs to be sensed and quantified



Adapted from DOI 10.3389/fsci.2023.1017235

Research Thread 3L Ethical, Legal, and Social Implications

The objective of this thread is to investigate ELSI issues raised by the proposed research project.

Proposals must include a **research plan within the project description** that describes the project's ELSI research activities.

The plan should identify ELSI research questions that complement the development in Threads 1 and 2. ELSI scholars must be integrated as active collaborators within the research team, helping shape research directions during the lifecycle of the project.

Solicitation Requirements

Award Size and Information

- Team Proposals Only:
  - 3-5 PIs/co-PIs
- Up to 4 years in duration
- Up to $2M over grant lifetime (including both direct and indirect costs)
- Up to $30M total for awards in FY 2024 and FY 2025 combined, subject to availability of funds

Eligibility: PIs and co-PIs

- PI Limit:
  - Principal Investigators (PI) must be full-time tenured or tenure-track faculty as determined by the submitting organization; or meet requirements described in the solicitation if the proposal is submitted by a non-profit, non-academic organization.
  - A minimum of one PI and two co-PIs must participate.
  - Maximum number of PI plus co-PIs: 5
  - At least one PI or co-PI must be full-time faculty in a College or Department of Engineering
- Limit on Number of Proposals per Organization: None Specified.
- Limit on Number of Proposals per individual (PI or co-PI): One per fiscal year

  Individuals may participate as either PI or co-PI in only one proposal submitted to this solicitation in a single fiscal year. It is the responsibility of the submitting organization to ensure that the PI and all co-PIs are participating only in one proposal as either PI or co-PI and not in any others submitted in response to this solicitation in a single fiscal year.

Eligibility: Organizations

- Organization Limit:
  - EFRI proposals may be submitted by a single organization or by a group of organizations consisting of a lead organization in partnership with one or more partner organizations.
  - Proposals may be submitted by:
    - Institutions of Higher Education: universities and two- and four-year colleges (including community colleges) accredited in, and having a campus located in the United States, acting on behalf of their faculty members.
    - Non-profit, non-academic organizations: Independent museums, observatories, research labs, professional societies and similar organizations in the U.S. associated with educational or research activities.
  - Only U.S. organizations are eligible to be the lead organization.
  - For interaction with industry, when appropriate for the proposed research, the GOALI mechanism (Grant Opportunities for Academic Liaison with Industry) may be used. https://new.nsf.gov/policies/pappg/23-1/ch-2-proposal-preparation#2F5

No Collaborative Proposals

- For each proposed project, a single proposal should be submitted by the lead institution with subawards to partners institutions
- No “Collaborative Proposals” are permitted
    - *The proposal will include a budget for each of the four years proposed.*

Broadening Participation Plan

- ENG promotes diversity in all aspects of its programs.
- As part of the EFRI 2024/25 Solicitation, EFRI requires all projects to include a Broadening Participation Plan.
- The goal is to broaden the participation and include the full spectrum of diverse talents in Engineering.
- Expand the diversity of thought, ideas, and approaches to defining and solving important research questions.

Broadening Participation Activities: Examples

- Inclusion of persons from underrepresented groups as PI, Co-PI, and/or other senior personnel, as appropriate for the project
- Inclusion of persons from underrepresented groups as graduate students, undergraduate students, and post-doctoral researchers
- Plans to diversify EFRI research teams through post-award supplements engaging persons from underrepresented groups including undergraduate researchers and teachers, such as REU, RET, or REM supplements
- Engagement of faculty and/or student researchers at minority-serving institutions, community colleges, technical schools, and/or high schools in the research project
- Enhancement of/collaboration with existing broadening participation programs at your home institution and/or nearby institutions
- Outreach activities that will interest and attract K-12 students from underrepresented groups to engineering undergraduate programs

A Letter of Intent (LOI) is Required
Due Date: September 12, 2024

- One Page
  1. TITLE - Title of the EFRI proposal preceded by the words “EFRI BEGIN OI:” as appropriate
  2. TEAM - Names, departmental and organizational affiliation, and expertise of the PI and at least two co-PIs
  3. SYNOPSIS (GOALS) - Brief description of the specific goals of the proposal (maximum 250 words)
- Additional Requirement:
  - Submission by an Authorized Organizational Representative (AOR) is required
  - A Minimum of 2 and Max. of 4 Other Senior Project Personnel (co-PIs)
  - A Minimum of 0 and Max. of 4 Other Participating Organizations
- LOIs are non-binding. They are not merit reviewed and no feedback is provided to the submitters
- **Submission of multiple LOIs by a PI is NOT permitted**

Full Proposal Submission
Due Date: December 12, 2024

- Follow NSF Proposal & Award Policies & Procedures Guide or Grants.gov Application Guide
- Project Summary (one page limit)
  - Proposals that do not separately address both intellectual merit and broader impacts in Project Summary will be returned without review
- Project Description (15 page limit)
  - Must include under Broader Impacts: Key Anticipated Outcomes; Broadening Participation Plan
- Additional Sections include:
  - References Cited; Biographical sketches; Budget; Current and Pending Support; Facilities, Equipment, & Other Resources
- Proposed budget must include funds for travel by at least one PI and one graduate student or researcher to attend an annual EFRI grantees' meeting. Awardees will be required to attend and present their research annually at an EFRI grantees' conference for the duration of the award.

Full Proposal Supplementary Documentation

Supplementary Documentation:

- List of Key Personnel: Provide a succinct description of what each person uniquely brings to the project and how their expertise will be integrated to foster synergy (3 pages max)
- Detailed management plan (3 pages max)
- Mechanisms for sharing the outcomes of the research with the scientific community (2 pages max)
- Post-doctoral researcher mentoring plan, if requesting support for post-doc(s)
- Student Mentoring Plan, describing mentoring activities for undergraduate
- Broadening Participation Plan – additional information up to 5 pages
- Data management plan (2 pages, plus additional document if needed)
- Single PowerPoint slide summarizing the vision of the EFRI proposal
- Cloud Computing Resource Request, if requesting support for CloudBank computing resources

Single Copy Documents: Collaborators & Other Affiliations

- NSF requires the use of a specific spreadsheet template for identifying COA information.
- This document must be submitted for each PI, co-PI, and every other senior project personnel member.

Review Criteria

- NSB-approved Merit Review Criteria
  - Intellectual Merit
  - Broader Impacts

- NSF Program Staff will also give careful consideration to the following:
  - Integration of ELSI within the project
  - Broadening Participation in Engineering and Science

Review Criteria
EFRI Solicitation Specific

- THREADS - Does the proposal address ALL three Threads?
- TRANSFORMATIVE - Does the proposed research represent an opportunity for a significant leap or paradigm shift in fundamental engineering knowledge?
- NATIONAL NEED/GRAND CHALLENGE - Is there potential for making significant progress on a current national need or grand challenge?
- Is the proposal responsive to the Programmatic Considerations for EFRI-BEGIN OI?
- Broadening Participation Plan - Does the plan actively promote, increase, and enhance participation and inclusion of the full spectrum of diverse talents in Engineering?
- Effectiveness of the proposed Management Plan.
- Ethical, Legal, and Social Implications (ELSI) - Does the proposal address the ethical, legal, and social implications of the proposed research?
- Student Mentoring Plan - Does the proposal present a description of the mentoring activities that will be provided for supported undergraduate?

Takeaways from 2024

2422333	EFRI BEGIN OI: Implantation of Dense Associative Memory through CArdiac muscle cell-based Reprogrammable Bio-Oscillatory Neural Networks	University of Notre Dame	**Pinar Zorlutuna**, Suman Datta, Daniel Schmidt, Nikhil Shukla, Meghan Sullivan
2422149	NSF-BSF:EFRI BEGIN OI: Integrated human brain organoid systems for adaptive reservoir computing	University of Michigan	**Jianping Fu**, Insoo Hyun, Feng Guo, Jonathan Kadmon, Orly Reiner, Omer Revah
2422412	EFRI BEGIN OI: Feasibility of 3D Biological Neurocomputers for Intelligent Biomedical Motor Control Systems	University of California Irvine	**An Do**, Hung Cao, Charles Liu, Zoran Nenadic, Leigh Turner
2422340	EFRI BEGIN OI: Reservoid Computer - Intelligent and Evolving Mechano-Reservoir Computing with Living Spheroids on Fibers	Virginia Tech	**Suyi Li**, Gil Hersch, Benjamin Jantzen, Amrinder Nain, Noel Naughton
2422352	EFRI BEGIN OI: Spatiotemporal Learning in 3D Neuronal Organoids	University of Maryland College Park	**Pamela Abshire**, Marc Dandin, Timothy Horiuchi, Erika Moore Taylor, Katherine Shilton
2422348	EFRI BEGIN OI:Neuron-Soft Organoid-Computer Interfaces for Long-Term Three-Dimensional Neural Network Computing	Harvard	**Jia Liu**, Petros Koumoutsakos, Na Li, Nanshu Lu, Jeantine E. Lunshof
2422282	EFRI BEGIN OI Teaching non-brain organoids how to think: PRogrammable OrGanoid intElligence using neuronal Networks implemented by gene Circuits (PROGENIC)	MIT	**Ron Weiss**, Calin Belta, Sambeeta Das, Laurie Zoloth

1. Address all threads!

To harness the power of biocomputing, holistic frameworks, driven by real-world applications, are needed that combine experimental, theoretical, computational, and engineering approaches while considering the ethical challenges throughout the project life cycle. With that in mind, ***addressing all three of the Threads*** *is critical to making significant advances in biocomputing and is required of each proposal submitted in response to this solicitation.*

Reviewers are instructed to look for all three Threads in your proposal

2. Organoids are 3D

*Harnessing the mechanisms behind complex biological behavior is critical for the development of "smart" technologies that integrate custom **3D in vitro biological systems** with engineered sensors and device interfaces to enable biological computing with superior power and data efficiency.*

Reviewers are on the lookout for 3D systems

3. ELSI is not separate. It's INTEGRATED

*Integrating social scientists, ethicists, and educators in the interdisciplinary teams **will be critical** for addressing the associated ethical, legal, and social implications of using living systems as building blocks for bio-enabled computing.*

*The [ELSI research] plan should identify **ELSI research questions** that complement the development in Threads 1 and 2. **ELSI scholars must be integrated as active collaborators** within the research team, helping shape research directions during the lifecycle of the project.*

Reviewers will evaluate your integrated ELSI research plan *as a research plan*

EFRI-2025 (NSF 24-508)
Important Solicitation Dates

Aug 30th, 2023	Informational Webinar
Sept 12th, 2024	Letter of Intent Due (required)
Dec 12nd, 2024	Full Proposal Deadline

Questions

efri2024-2025@nsf.gov

Program Guidance: Participation Limit

Each investigator may participate as either PI or co-PI on only a single proposal submitted in one fiscal year.

Program Guidance: Co-PI Limit

Each proposal *must* have a minimum of 2 co-PIs and a maximum of 4 co-PIs

Program Guidance: Engineer PI/co-PI

The Lead PI or one of the project co-PIs *must* be full-time tenured or tenure-track faculty within a College or Department of Engineering

Program Guidance: Co-PI from National Lab

NSF does not normally support research or education activities by scientists, engineers or educators employed by Federal agencies or Federally Funded Research and Development Centers (FFRDCs).

Preliminary inquiry must be made by sending an email to **efri2024-2025@nsf.gov** that explains the unique capability of the FFRDC or national laboratory. If permission is granted, a written statement from the cognizant NSF PD must be included as part of the proposal submission.

Program Guidance: Co-PI from non-US Institution

US-Israel Binational Science Foundation (BSF) – NSF 20-094

Provides for an international collaboration arrangement whereby U.S. researchers may receive funding from the NSF and Israeli researchers may receive funding from the BSF

Foreign Organizations *– NSF rarely provides direct funding support to foreign organizations. NSF will consider proposals for cooperative projects involving U.S. and foreign organizations, provided support is requested only for the U.S. portion of the collaborative effort. (PAPPG NSF 231, Chapter I.E.2c)*

Preliminary inquiry must be made by sending an email to efri2024-2025@nsf.gov that explains the unique capability of the FFRDC or national laboratory. If permission is granted, a written statement from the cognizant NSF PD must be submitted as part of the proposal submission.