



U.S. NATIONAL SCIENCE FOUNDATION
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ALEXANDRIA, VIRGINIA 22314

NSF 24-112

Dear Colleague Letter: UKRI/BBSRC- NSF/BIO Lead Agency Opportunity in Biological Informatics, Systems Understanding of Host-Microbe Interactions, Synthetic Cells and Cellular Systems, and Synthetic Microbial Communities

July 31, 2024

Dear Colleagues:

SCOPE

The U.S. National Science Foundation (NSF) and UK Research and Innovation (UKRI) have a Memorandum of Understanding (MOU) on Research Cooperation. The MOU provides an overarching framework to encourage collaboration between U.S. and U.K. research communities and sets out the principles by which jointly supported activities might be developed. The MOU provides for a Lead Agency Opportunity whereby proposals may be submitted to either NSF or UKRI.

Through this Dear Colleague Letter (DCL), the NSF Directorate for Biological Sciences (NSF/BIO) and the UKRI Biotechnology and Biological Sciences Research Council (BBSRC) are pleased to announce 2024/2025 topical areas associated with this Lead Agency Opportunity.

The goal of this activity is to promote transatlantic collaborative research by reducing some of the barriers that researchers may encounter. The NSF/BIO-UKRI/BBSRC Lead Agency Opportunity allows U.S. and U.K. researchers to submit a single joint proposal that will undergo a single review process. This document provides guidelines for the preparation, submission, review, and award of joint NSF/BIO-UKRI/BBSRC proposals.

2024/2025 TOPICAL AREAS

Under the NSF/BIO-UKRI/BBSRC Lead Agency Opportunity, 2024/2025 proposals will be accepted for collaborative research in the areas of intersection between NSF/BIO and UKRI/BBSRC as set out in this DCL.

Proposals must address the priorities of both UKRI/BBSRC and participating NSF/BIO Divisions. Proposers must provide a clear rationale for the need for a U.S.-U.K. collaboration, including the unique expertise and synergy that the collaborating groups will bring to the project. Proposers should note that the Lead Agency Opportunity does not represent new funding. Proposals will be assessed in competition with all others submitted to the priority areas and agency programs identified in this DCL, and outcomes will be subject to both success in merit review and the availability of funds from both UKRI/BBSRC and NSF/BIO.

Proposers are invited to submit proposals to the Lead Agency Opportunity in 2024/2025 under one of the following research themes:

Biological Informatics

Proposals should develop informatics approaches and cyberinfrastructure resources to enable novel and more effective use of data in biological research. Proposals should address important current or emerging challenges faced by researchers, supporting the generation of new knowledge from biological data.

Proposals should clearly identify their relevance to one of two biological informatics focus areas, either:

- research to design novel or greatly improved research tools and methods; or
- the implementation of, scaling of, or major improvements to research tools, products, and services for biology applicable to a wide range of researchers.

Proposals can be in any bioinformatics research area within the remit of both NSF/BIO and UKRI/BBSRC, including Artificial Intelligence (AI) or machine learning. Proposals should clearly describe their potential to advance and enable data driven research undertaken by biological research communities primarily supported by both NSF/BIO and UKRI/BBSRC.

Proposals must be within the remit of UKRI/BBSRC and aligned to NSF/BIO's Division of Biological Infrastructure informatics (Innovation) or cyberinfrastructure (Capacity) programs, but not both. Proposers are advised to consult the appropriate program officers of both agencies to ensure that their portion of the project is in alignment.

Depending on the choice of lead agency, full proposals will be submitted to and assessed by either:

- NSF/BIO [Infrastructure Innovation for Biological Research \(Innovation\)](#)
- NSF/BIO [Infrastructure Capacity for Biology Core Program \(Capacity\)](#)
- UKRI/BBSRC [Responsive Mode 25RM2](#)

Understanding host-microbe Interactions

Proposals are invited that address questions relating to infection and infection-like processes. Host-microbe interactions can result in a range of pathogenic and non-pathogenic outcomes for the host. Indeed, some interactions could be beneficial to the host/and other infectious agent. The goal is to identify and understand the fundamental basis of these interactions in plants or animals as the first step towards harnessing infection biology to solve societal problems.

Proposals are welcome on investigations that shape our understanding of infection and infection-like processes in complex multifaceted scenarios such as:

- modulation of host-microbe interactions in response to varied environmental conditions;
- the influence of co-infection and the wider microbiome, both in initial responses and in influencing the dynamics of longer-term interactions;
- how changes to host physiology through the life course may alter susceptibility or resistance to infection; and
- host or microbial factors that contribute towards fundamental shifts in the nature of infections, such as transitions between commensal, mutualistic, and pathogenic outcomes.

Relevant areas of investigation include:

- using genetically similar hosts or microbes that result in different phenotypic outcomes of infection;
- the use of comparative cross-species approaches to develop insights that have broad relevance across biological organisms; and
- studies that pair theory with lab-based experiments and utilize machine learning or AI to model immune systems in silico.

Proposals must aim to progress knowledge of immunology in either non-human, non-mouse animals, or plants through integration of a range of approaches and data across the host-microbe interface to develop new systems-level insights.

Exclusions:

- Proposals that focus solely on human or mouse immune systems will not be accepted.
- Proposals with a focus on human pathogens will not be accepted.
- Proposals that focus on industrial applications and settings (including agriculture) will not be accepted.
- Proposals that are solely data based are outside of the scope of this topic; all projects must include a lab-based element.

Proposals must be within the remit of UKRI/BBSRC and aligned to NSF/BIO's Division of

Integrative Organismal Systems Core Program. Proposers are advised to consult the appropriate program officers of both agencies to ensure that their portion of the project is in alignment

Depending on the choice of lead agency, full proposals will be submitted to and assessed by either:

- NSF/BIO [Division of Integrative Organismal Systems Core Program](#)
- UKRI/BBSRC [Responsive Mode 25RM2](#)

Synthetic Cells and Cellular Systems

Can we design, build, and control a synthetic cell or synthetic cellular system? Natural cells emerge from the coordinated operation of a large number of biomolecules with their environment. One goal of synthetic cell research is to decipher the basic requirements of a living cell by understanding the myriad functions that make it resilient and adaptive. Similarly, synthetic approaches to build multicellular systems may reveal new mechanistic understanding of how both biophysical and biochemical intercellular interactions drive spatial organization and emergent behavior within cell populations.

Proposals are expected to focus on building a synthetic cell, or cellular system, to understand biology. Synthetic cells might be protocells containing only the most basic cellular components that allow an understanding of the origin of life, artificial cells that contain both natural and synthetic cellular components, or minimal cells that use natural molecules to build self-replicating cellular entities through 'bottom-up' approaches. Synthetic multi-cellular systems would couple engineering at a cellular level to the development of higher order spatially organized structures, through control of cellular interactions, geometries, movement, and collective behaviors.

Proposals with a focus on synthetic plant cell and cellular systems research are welcome.

Exclusions:

- Proposals focused exclusively on building a synthetic cell as a biomanufacturing platform or as a therapeutic moiety will not be accepted.
- Biomedically-focused proposals such as regenerative medicine and tissue engineering will also not be accepted.

Depending on the choice of lead agency, full proposals will be submitted to and assessed by either:

- NSB/BIO [Division of Molecular and Cellular Biosciences Core Program](#)
- UKRI/BBSRC [Responsive Mode 25RM2](#)

Proposals must be within the remit of UKRI/BBSRC and aligned to NSF/BIO's Division of Molecular and Cellular Biosciences Core Program. Proposers are advised to consult the appropriate program officers of both agencies to ensure that their portion of the project is in alignment.

Synthetic Microbial Communities

Microbial communities contain remarkable genetic, physiological and biochemical diversity, allowing them to flourish in environments all over the planet and in a variety of substrates and hosts. While the means of harnessing individual microbes for biotechnological application are well established, in recent years researchers have begun to explore the wider properties and potential of more complex mixed microbial communities.

The study of natural microbiomes can be hampered by their inherent complexity and an inability to fully map how the functional properties of their constituents combine to deliver a collective phenotype. Advances in synthetic biology and allied fields are enabling researchers to assemble and engineer synthetic microbial communities from a bottom-up perspective that have novel compositions, genetics and phenotypes. This offers an alternative to natural microbiomes, allowing researchers to address more precisely fundamental questions about complex microbial communities while also providing routes towards novel bio-based solutions to societal problems.

Proposals are invited to support research that:

- Examines the underlying mechanisms or rules that can be used to inform the construction, maintenance, and evolution of synthetic microbial communities, considering factors such as cooperative and competitive interactions within communities, as well as emergent properties within these systems;
- Examines how to design and control increasing complexity in microbial composition, behaviors, and the genetic, metabolic, signaling and physical interactions that occur, as well as how these properties may change within differently spatially structured environments or as processes are scaled to enable practical application; and
- Builds complex mixed synthetic communities with novel physiological and metabolic outputs, offering potential bio-based solutions that contribute to tackling global challenges such as production of novel biochemical cycles to enable more circular use of resources in the bioeconomy, biodegradation of recalcitrant or 'forever chemicals', or the development of biorenewable resources that could mitigate our impact on the environment and climate.

All proposals should expand our understanding of biological systems, even if an application is proposed.

Exclusions:

Proposals focused exclusively on biomedical or therapeutic applications will not be accepted

Depending on the choice of lead agency, full proposals will be submitted to and assessed by either:

- NSF/BIO [Division of Molecular and Cellular Biosciences Core Program](#)
- UKRI/BBSRC [Responsive Mode 25RM2](#)

Proposals must be within the remit of UKRI/BBSRC and aligned to NSF/BIO's Division of Molecular and Cellular Biosciences Core Program or to NSF/BIO's Division of Integrative Organismal Systems Core Programs. Proposers are advised to consult the appropriate program officers of both agencies to ensure that their portion of the project is in alignment.

Biosecurity and AI Considerations that Apply to all Proposals

NSF and UKRI acknowledge the rapidly evolving nature of computational biology and the advances in artificial intelligence in biology, and the potential that such technologies can both contribute to the advance of science and the production of dual-use biological knowledge, technology, and products. As such, regardless of whether UKRI or NSF is the lead agency, all proposals that are recommended for funding will be reviewed for compliance with best practices and standards as set out by the [U.S. AI Safety Institute](#) and US government policies and guidelines on biosafety, [biosecurity](#), [dual use research in the life sciences](#), potential enhanced pandemic pathogen research, and [safe and responsible use of AI](#). Proposers for UKRI funding may be asked to further demonstrate how their proposed projects will comply with the UKRI approach and expectation towards [Trusted Research and Innovation](#).

PROPOSAL PREPARATION AND SUBMISSION

There is a **2-stage application process** for this opportunity (see timeline below).

Stage 1: Expression of Interest (EOI)

1. Prior to submission of a full proposal, proposers will discuss within their research team where they feel the largest proportion of research lies (typically, this means the largest budget request) and agree on a proposed lead agency (either NSF/BIO or UKRI/BBSRC). Where advice is required about lead agency or fit of the proposal to this DCL, the proposer should contact the relevant staff member at the proposed lead agency to discuss the research project. The staff member will then confirm that they will act as lead agency (and subsequently inform the other participating agency) or will consult with the other agency to identify a new lead agency prior to returning a decision to the proposer (generally within 10-15 working days).
2. Proposers will then be required to submit a PDF Expression of Interest (EOI) to the proposed lead agency that outlines the research proposed, research teams involved,

and bottom-line estimates of funding to be requested from the NSF/BIO and UKRI/BBSRC. For NSF, bottom line estimates should include both direct and indirect costs. The EOI should not exceed 2 pages

- a. Where UKRI/BBSRC is the proposed lead agency, the EOI should be submitted by completing the appropriate Funding Service (TFS) application (see further guidance on UKRI/BBSRC [website](#)).
 - b. Where NSF/BIO is the proposed lead agency, the EOI should be submitted via email to NSFBIOBBSRC@nsf.gov. The EOI must identify the participating NSF program to which the EOI is directed.
3. The EOI will be shared with the non-lead agency to check for eligibility (namely whether the proposed research fits within the agency's portfolio, the scope of the proposed research, and whether the proposed researchers and organizations meet the agency's funding eligibility requirements). The EOI will also be used to gauge proposal pressure by program and assist programs with budget planning. The result of this discussion will be relayed to the submitter within 10-15 working days.

Stage 2: Full proposals

1. If the EOI presents an eligible research project based on the eligibility description above, the proposer(s) will be notified by the lead agency and a full proposal may be submitted. The subsequent full proposal must be submitted in accordance with the proposal preparation requirements of the lead agency, i.e., for NSF/BIO, the specific program solicitations, and [NSF Proposal & Award Policies & Procedures Guide](#) (PAPPG), and for UKRI/BBSRC, the [BBSRC Grants Guide](#).
2. The proposal should include a description of the full proposed research program and research team and describe the total resources for the joint project (that is, the funds requested from both the NSF/BIO and UKRI/BBSRC). However, the budgets submitted to the lead agency should only indicate the amount requested from that agency. A copy of the proposed requested budget of the non-lead agency should be included as part of the full proposal (In the case of NSF, this should be added as a "Supplementary Document"; in the case of UKRI/BBSRC, this should be added as an attached document to the grant application).
3. For proposals submitted to NSF, the full names and affiliations of U.K. personnel should be listed in the Overview section of the Project Summary as "non-NSF funded Collaborators." This listing is for administrative purposes and is not intended to characterize the level or value of the contribution of U.K. personnel to the project. Guidance on information to provide for "non-NSF funded Collaborators" is below.
 - Biographical Sketch – Required. The biographical information submitted must be clearly identified as "non-NSF funded Collaborators" biographical information and uploaded as a single PDF file in the **Other Supplementary Documents** section of the proposal. Use of a specific format is not required.

- Collaborators and Other Affiliations (COA) Information – Required – The COA information should be provided through the use of the [COA template](#), identified as "non-NSF funded Collaborators" COA information and uploaded as a PDF file in the **Single Copy Documents** section of the proposal.
 - Current and Pending (Other) Support and Results from Prior NSF Support are not required for U.K. personnel for proposals submitted to NSF.
4. For projects involving human subjects/participants or animals, proposers are advised to check both NSF/BIO and UKRI/BBSRC policies and are advised to consult with appropriate staff at NSF/BIO or UKRI/BBSRC prior to submitting a proposal. Proposers are expected to adhere to the published policies and guidelines concerning research ethics and to have requisite organizational approvals or exemptions in place prior to any potential award.
 5. The proposal should indicate the proposal is to be considered under this Lead Agency Opportunity by prefacing the title with 'NSF/BIO-UKRI/BBSRC'.
 6. The proposal must be submitted by established program deadlines or target dates determined by the lead agency. For NSF/BIO, proposals may be submitted at any time after the EOI is deemed eligible but must be submitted within 6 months of the EOI to be considered for funding during the U.S. 2025 fiscal year.

MERIT REVIEW

1. Proposals will be reviewed in competition with other unsolicited proposals or with proposals received in response to a specific call by the lead agency (that is, proposals submitted to the Lead Agency Opportunity will not undergo a special review process).
2. Proposals will be reviewed in accordance with the lead agency's review criteria. While not identical, the NSF/BIO and UKRI/BBSRC ask reviewers to evaluate the proposed project on both its scientific or intellectual merit as well as its broader or societal impacts. A description of the NSF merit review process is provided on the [NSF merit review website](#). A description of the [UKRI/BBSRC assessment process](#) is provided on the UKRI/BBSRC website.
3. The lead agency may share proposal documents and reviews with the non-lead agency via secure file transfer, according to the lead agency's confidentiality regulations. In the case of NSF/BIO, only unattributed reviews and panel summaries will be shared. BBSRC will share only unattributed reviews.

FUNDING DECISION

1. After the reviews are received, program officers from the lead and non-lead agencies will share the potential outcomes. Afterwards, the lead agency will use its usual internal procedures to determine whether a proposal will be awarded or declined. In the case of NSF, an award requires a formal recommendation by the cognizant program officer and

then concurrence by the cognizant Division Director. NSF's Division of Grants and Agreements will review the proposal from a business and financial perspective. NSF funding decisions are subject to the availability of funds. Only the NSF Grants and Agreements Officer can make commitments on behalf of the Foundation or authorize the expenditure of funds. In the case of the UKRI/BBSRC, funding recommendations from Panels are received by Research Council Officers who, considering the availability of funds, will fund those proposals recommended for funding in the order identified by the Panel.

2. Proposers will be advised whether their proposal has been recommended for funding or will be declined by the lead agency. Proposers will receive copies of the unattributed reviewers' comments and, where applicable, a panel summary.
3. Once a proposer has been notified of a pending award, the non-lead researcher(s) associated with the project must submit a copy of the proposal to the non-lead agency so that each agency has complete documentation of the overall proposed research project. Further guidance will be provided to successful proposers at this stage.
4. If a proposal is recommended for funding, the U.S. organization(s) will be supported by NSF/BIO and the U.K. organization(s) will be supported by UKRI/BBSRC. NSF/BIO and UKRI/BBSRC staff will review budgets to ensure that there are no duplications in funding.
5. NSF/BIO and UKRI/BBSRC will coordinate award timing as much as possible, but because of different funding cycles, it is possible that some projects will have delayed start dates to wait until funds become available or until all pre-award requirements are met. Wherever possible, NSF and UKRI/BBSRC will endeavor to hold standard turnaround times for each participating agency. In exceptional circumstances outcomes could be delayed.

AWARD CONDITIONS AND REPORTING REQUIREMENTS

1. NSF/BIO and UKRI/BBSRC will clearly state in award notices and any related documents that awards resulting from this activity were made possible by the NSF/BIO-UKRI/BBSRC Lead Agency Opportunity.
2. Recipients will be expected to comply with the award conditions and reporting requirements of the agencies from which they receive funding.
3. All NSF and UKRI/BBSRC requirements for data storage are applicable to investigators funded by their respective agencies.
4. Researchers will be required to acknowledge both NSF and UKRI/BBSRC in any reports or publications arising from the award.
5. Requests for extensions will be considered by the lead agency using standard procedures and discussed with the non-lead agency prior to decision. Requests for changes to awards will be discussed with the non-lead agency before a mutual decision is reached.

TIMELINE FOR SUBMISSIONS

Deadline for EOI (UKRI/BBSRC and NSF/BIO): **October 31, 2024**

Feedback on EOI will generally be provided within 10-15 working days from the submission deadline.

FULL PROPOSALS

BBSRC Responsive Mode 25RM2 application deadline: Expected to be **April 2025** (date TBD)

NSF/BIO: Full proposals accepted anytime but should be received by **February 28, 2025**, to ensure timely review for U.S. FY2025 funding.

CONTACTS

UKRI/BBSRC International Collaborative Agreements
Email: inca@bbsrc.ac.uk

NSF/BIO UKRI/BBSRC Working Group
Email: NSFBIOBBSRC@nsf.gov

Sincerely,

Susan Marqusee, Assistant Director
Directorate for Biological Sciences