

NSF-Simons Research Centers for Mathematics of Complex Biological Systems (MathBioSys)

PROGRAM SOLICITATION

NSF 17-560



National Science Foundation

Directorate for Mathematical & Physical Sciences
Division of Mathematical Sciences

Directorate for Biological Sciences
Division of Integrative Organismal Systems
Division of Molecular and Cellular Biosciences



Simons Foundation

Letter of Intent Due Date(s) (required) (due by 5 p.m. submitter's local time):

August 10, 2017

Full Proposal Deadline(s) (due by 5 p.m. submitter's local time):

September 29, 2017

IMPORTANT INFORMATION AND REVISION NOTES

Any proposal submitted in response to this solicitation should be submitted in accordance with the revised *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) (NSF 17-1), which is effective for proposals submitted, or due, on or after January 30, 2017.

SUMMARY OF PROGRAM REQUIREMENTS

General Information

Program Title:

NSF-Simons Research Centers for Mathematics of Complex Biological Systems (MathBioSys)

Synopsis of Program:

The purpose of the NSF-Simons Research Centers for Mathematics of Complex Biological Systems (MathBioSys) is to enable innovative collaborative research at the intersection of mathematics and molecular, cellular and organismal biology, to establish new connections between these two disciplines, and to promote interdisciplinary education and workforce training. The National Science Foundation Directorates for Mathematical and Physical Sciences (MPS) and for Biological Sciences (BIO) and the Simons Foundation Division of Mathematics and the Physical Sciences (MPS) and Division of Life Sciences shall jointly sponsor up to three new research centers to facilitate collaborations among groups of mathematicians, statisticians, and biologists. Research activities conducted at each center will be focused on a particular set of topics at the interface of the mathematical sciences with molecular, cellular, and organismal biology. Each center will conduct interdisciplinary education and training through research involvement of recent doctoral degree recipients and graduate students from across this multi-disciplinary spectrum. Each center is also expected to conduct convening activities, including short-term and/or long-term visitors programs, workshops, and/or outreach activities. These centers will have annual meetings of the Principal Investigators (PIs) and other principal researchers, held at the Simons Foundation in New York City.

Cognizant Program Officer(s):

Please note that the following information is current at the time of publishing. See program website for any updates to the points of contact.

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- Kathryn Dickson, telephone: (703) 292-7380, email: kdickson@nsf.gov
- Elizabeth Roy, Simons Foundation, telephone: (212) 524-6966, email: eroy@simonsfoundation.org
- Junping Wang, Directorate for Mathematical and Physical Sciences, NSF, telephone: (703) 292-4488, email: jwang@nsf.gov
- Henry A. Warchall, telephone: (703) 292-4861, email: hwarchal@nsf.gov

Applicable Catalog of Federal Domestic Assistance (CFDA) Number(s):

- 47.049 --- Mathematical and Physical Sciences
- 47.074 --- Biological Sciences

Award Information

Anticipated Type of Award: Continuing Grant

Estimated Number of Awards: 3

Anticipated Funding Amount: NSF estimates that \$15,000,000 will be available to support three center awards of five years duration each. The Simons Foundation estimates that \$15,000,000 will be available to support these three center awards over the five-year duration of the awards. NSF and the Simons Foundation expect to co-fund each of the three center awards, and that each center will have an annual budget of \$2,000,000 combined from both sources. The anticipated number of awards is three.

Proposals must be written with a five-year plan for research, teaching and other Broader Impact activities. The plan must reflect a ramp-up of the center's activities during Years 1 and 2, with a full complement of activities implemented no later than the beginning of Year 3. In the third year of the award, NSF and the Simons Foundation will conduct mid-term site visits. The Management Plan, required as a Supplemental Document, should include metrics for performance evaluation of the center.

Anticipated Funding Amount: \$30,000,000

The total amount available for this solicitation is \$30,000,000. Of this amount, NSF anticipates contributing approximately \$15,000,000 and the Simons Foundation anticipates contributing approximately \$15,000,000. This plan is subject to the availability of funds.

This is a partnership between NSF and the Simons Foundation, therefore meritorious proposals will be funded jointly by two organizations. Recommended for Funding proposals will be resubmitted by the PIs to the Simons Foundation, in accordance with instructions given by the cognizant Simons Foundation Program Officer. Subsequent grant administration procedures will be in accordance with the individual policies of the awarding agency.

Eligibility Information

Who May Submit Proposals:

Proposals may only be submitted by the following:

- Universities and Colleges - Universities and two- and four-year colleges (including community colleges) accredited in, and having a campus located in, the US acting on behalf of their faculty members. Such organizations also are referred to as academic institutions.
- 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.

Who May Serve as PI:

There are no restrictions or limits for the allowable organizations listed above. Eligible Federal agencies and federally funded research and development centers (FFRDCs) can only participate as subawardees. FFRDCs and federal agency scientists cannot serve as lead PI. Non-NSF sponsored FFRDCs are required to provide a letter of support from their agency.

Limit on Number of Proposals per Organization:

There are no restrictions or limits on the number of proposals per organization. However, there is a limitation on the number of submissions per scientist as noted below.

Proposals submitted in response to this solicitation cannot be duplicates of proposals to any other Federal agency for simultaneous consideration. The only exceptions to this rule are: (1) when the program officers at the relevant Federal agencies have previously agreed to joint review and possible joint funding of the proposal; or (2) proposals for PIs who are beginning investigators (individuals who have not been a PI or co-PI on a Federally funded award with the exception of doctoral dissertation, postdoctoral fellowship or research planning grants). For proposers who qualify under this latter exception, the box for "Beginning Investigator" must be checked on the Cover Sheet.

Limit on Number of Proposals per PI or Co-PI:

An individual may appear as PI, co-PI, or other senior personnel on no more than two proposals submitted in response to this solicitation. Other senior personnel include lead PIs on subawards and named postdoctoral research associates. There is no limitation on unpaid consultants. Please be advised that if an individual's name appears as PI,

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co-PI or other senior personnel on more than two proposals, all proposals submitted after the first two proposals (based on the time-stamp) will be returned without review.

Please note: All materials should be submitted to NSF. NSF will share all submitted materials with the Simons Foundation.

Proposal Preparation and Submission Instructions

A. Proposal Preparation Instructions

- **Letters of Intent:** Submission of Letters of Intent is required. Please see the full text of this solicitation for further information.
- **Preliminary Proposal Submission:** Not required
- **Full Proposals:**
 - Full Proposals submitted via FastLane: *NSF Proposal and Award Policies and Procedures Guide (PAPPG)* guidelines apply. The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.
 - Full Proposals submitted via Grants.gov: *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov* guidelines apply (Note: The *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide).

B. Budgetary Information

- **Cost Sharing Requirements:**

Inclusion of voluntary committed cost sharing is prohibited.
- **Indirect Cost (F&A) Limitations:**

Awards will be jointly made with the Simons Foundation. Half the budget should be prepared by following the NSF Proposal and Award Policies and Procedures Guide (PAPPG), and the other half of the budget must be prepared by following instructions from the Simons Foundation, included with the announcement of this funding opportunity at the Simons Foundation website (<https://www.simonsfoundation.org>). Note that the Simons Foundation has a specific indirect cost rate policy.
- **Other Budgetary Limitations:**

Not Applicable

C. Due Dates

- **Letter of Intent Due Date(s) (required)** (due by 5 p.m. submitter's local time):

August 10, 2017
- **Full Proposal Deadline(s)** (due by 5 p.m. submitter's local time):

September 29, 2017

Proposal Review Information Criteria

Merit Review Criteria:

National Science Board approved criteria. Additional merit review considerations apply. Please see the full text of this solicitation for further information.

Award Administration Information

Award Conditions:

Additional award conditions apply. Please see the full text of this solicitation for further information.

Reporting Requirements:

Additional reporting requirements apply. Please see the full text of this solicitation for further information.

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I. INTRODUCTION

A predictive understanding of how and why emergent properties arise in living systems remains a significant and compelling challenge. Biological systems are complex, often involving a multitude of non-linear interactions among an enormous number of components at different spatial (molecules, cells, tissues, organs, organ systems, whole organisms) and temporal (molecular interactions at fractions of a second, to developmental and physiological time scales measured in hours to months, to evolutionary time scales measured in generation times that may span many years) scales. Examples of emergent properties include the robustness of developmental processes that produce the same form consistently within any one species. That consistency of form must reflect robustness of cell division, one of the processes involved in development. Robustness of cell division is also an emergent property. Morphological, physiological and behavioral (phenotypic) plasticity of cells and organisms is an emergent property. Understanding how multi-scale, often non-linear interactions give rise to emergent properties of molecular, cellular and organismal systems at different time scales requires the development of new mathematical, statistical, and computational approaches. This solicitation responds directly to the need to facilitate long-term collaborations between the biological and the mathematical sciences communities to leverage their complementary expertise, and to build capacity to address this important challenge over a longer period of time.

Recent research has resulted in progress in many fields in biology through the application of powerful technologies and analytical approaches (e.g., genome sequencing; gene expression measurement and manipulation; epigenetics; metabolomics and proteomics; genome engineering of many different species, etc.). These efforts have resulted also in large amounts of data, which presents new challenges to understanding and has opened up new avenues of inquiry. Approaches such as genome-wide association studies have yielded initial insights about genetic loci associated with traits of varying complexity, from pigmentation patterns to temperature stress resistance. However, biological systems are extremely complex, and have largely resisted efforts to understand causal relationships between genes and phenotypes at the molecular, cellular and organismal levels of biological organization. Phenotypes at any of these levels cannot be predicted from gene sequences alone because phenotypes are the emergent product of interactions between multiple gene sequences (the genome), the state of the internal environment (molecular, cellular and organismal) and the external biotic and abiotic environment. Understanding the causal processes that relate genes to traits, and genomes to phenomes, is one of the Grand Challenges in biology. Mathematical approaches to understanding how and why emergent properties are produced from these multi-scale biological interactions, and more broadly how phenotypes are causally related to genomes, are essential to accelerating progress.

Mathematical scientists search for underlying patterns and laws in order to formulate new conjectures and theories through the use of mathematical modeling, statistical analysis, and computational simulation. Mathematical models that are well verified and validated with experimental data, together with knowledge of the biological systems motivating the work, can be employed to discover testable hypotheses related to multi-scale integration, non-linear interactions and emergent properties in biological systems. Some areas of the biological sciences, such as molecular biophysics, population dynamics, epidemiology, and ecosystem dynamics, have a long history of advances owing to mathematical and statistical approaches. Other biological areas have been less tightly connected with the mathematical sciences, but even so, differential equations, probability, and statistical methods have played important roles for describing interactive biomolecular systems, such as protein-protein interaction networks, gene regulation networks, enzyme kinetics, protein-ligand binding rates, metabolomics, and proteomics. Multi-scale modeling and analysis using quantum mechanics, molecular mechanics, continuum mechanics and electrostatics has recently offered effective approaches in understanding cellular dynamics and function. Techniques using stochastic modeling and uncertainty quantification have been developed for revealing how individual biomolecular system behavior is related to macroscopic measurements. In addition, multiple areas of foundational mathematics, such as topology, geometry, combinatorics, and graph theory have been playing significant roles in biological sciences (e.g. in the understanding of the structure, function, dynamics and evolution of biopolymers and their interacting complexes).

Even though a number of areas at the interface of biological and mathematical sciences have been relatively better developed, insufficient attention has been directed to mathematical approaches aimed at understanding the complex causal relationships leading to

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emergent properties of molecular, cellular and organismal systems, or to the emergent properties resulting from the complex integration across these levels of organization at different time scales. Accelerating our understanding of biological complexity in these less well-studied areas requires close, sustained collaborations between biologists and mathematical scientists that leverage their complementary expertise. These collaborations would not only advance our understanding about the rules of life, but also lead to new foundational mathematical, statistical, and computational concepts, and the development of new mathematical theories and tools. This activity will support collaborative research between mathematical scientists and biologists to advance our understanding in these areas. The support is enabled by cooperation between a federal funding agency, NSF, and a private funding organization, the Simons Foundation, both of which are focusing on important problems in biology that are expected to challenge mathematical scientists and inspire new mathematics. This partnership allows the two organizations to combine resources to identify and fund the most highly meritorious and highest-impact projects that are consistent with the respective missions of the partners, while eliminating duplication of effort. These centers will build cross-disciplinary capacity, and advance knowledge in the biological and mathematical sciences.

II. PROGRAM DESCRIPTION

The NSF-Simons Research Centers for Mathematics of Complex Biological Systems (MathBioSys) is a new program that expects to fund up to three new center awards of five-years duration from this one-time call for proposals. The MathBioSys Program is responsive to the scientific opportunity to understand emergent properties in biological systems, an area of study that is germane to one of the 10 Big Ideas of the National Science Foundation, i.e., Understanding the Rules of Life (https://www.nsf.gov/about/congress/reports/nsf_big_ideas.pdf), which includes topics that were examined by experts in a recent NSF-sponsored workshop (https://www.nsf.gov/mps/dms/documents/Deciphering_Genome-to-Phenome_Relationships.pdf). The workshop participants identified a lack of focused support for mathematical approaches in this scientific area as a significant impediment to progress. The MathBioSys Program is intended to provide such focused support, and to address the need to build capacity at this topical interface to ensure long-term cross-disciplinary effort in this area.

This program supports basic research in mathematical and biological sciences. Proposals on human health-related research, or clinically motivated projects are not appropriate for this program and will be returned without review.

Proposals to establish centers at which sustained collaborations are facilitated between mathematical scientists and biologists to develop novel mathematical, rigorous computational, and statistical approaches to advance fundamental understanding of how and why emergent properties arise in molecular, cellular and organismal systems are welcomed. The MathBioSys Program strongly encourages proposals aimed at developing predictive frameworks for understanding emergent properties or phenotypes. Successful projects are expected to have a cohesive set of goals, and a convincing plan that substantial progress will be made to establish a predictive and causal understanding of emergent properties during a five-year award period for the proposed center.

Examples of relevant research areas/topics of inquiry about emergent properties include, but are not limited to:

- Improved, vertically integrated (genes-to-phenotype, multi-scale) mathematical description and causal understanding of phenotypic robustness (the mechanisms resulting in stability of phenotype in the face of genetic and/or environmental change)
- Development of mathematical, statistical, and computational approaches to rigorously formalize the set of rules behind representation of biological data as complex networks
- Parameter estimation and inference for multi-scale deterministic and stochastic models for spatiotemporal processes in biology (e.g., phenotypic plasticity; kinetics of molecular and cellular interactions in developing embryos)
- Development of sparse and low-dimensional predictive models for high-dimensional biological data with uncertainty (e.g., heterogeneous molecular interactions of transcripts, proteins, metabolites, etc., and associated kinetics)
- Mathematical and statistical foundations of shape analysis and their application for analysis of biological images; differential geometry approach to synthetic biology
- Mathematical, statistical, and computational approaches to dissect noise, variability, and heterogeneity in biological systems
- Development of hybrid and stochastic approaches connecting discrete and continuum dynamics in complex biological systems

To build capacity in this cross-disciplinary area, substantial training and professional development components are required in successful proposals. Successful proposals are also expected to include plans for a significant effort in cross-disciplinary training of cohorts of future scientists, such as postdoctoral research associates, graduate students, and/or undergraduates from mathematical sciences and the areas of the biological sciences that are the focus of this activity. Each center is envisaged to conduct convening activities, including short-term and/or long-term visitors programs, workshops, and/or outreach activities.

Although the MathBioSys Program focuses on support of mathematical, computational, and statistical approaches to understanding emergent properties in molecular, cellular and organismal systems, the Program recognizes that the most productive cross-disciplinary collaborations in advancing this area will include those in which development of the mathematical, computational, and statistical approaches will be informed by experimentation, and, reciprocally, that experiments will be informed by mathematical models. Therefore, proposers should consider existing or new collaborations that take advantage of ongoing biological research that is relevant to the MathBioSys program, and the associated research facilities and infrastructure that could be important elements in developing productive collaborations. The MathBioSys program particularly encourages development of new cross-disciplinary collaborations as a way to build capacity. To insure a balance of perspectives from mathematics and biology in the research conducted at the Centers for Mathematics of Complex Biological Systems, successful proposals must describe the disciplinary balance of senior personnel and postdocs, as well as a multi-disciplinary balance among graduate student participants.

REVIEW PROCESS OVERVIEW:

Letter of Intent (LOI): All proposers intending to submit a full proposal in response to this activity must submit a LOI, which contains the names of senior personnel, a list of participating organizations, and a synopsis that describes the proposed research of the center in sufficient detail to permit a selection of reviewers with relevant expertise. Letters of intent are not externally evaluated or used in funding decisions.

Full Proposals: MathBioSys full proposals will receive ad hoc and/or panel review at the discretion of the Program, as described in Section VI of this Solicitation. MathBioSys full proposals that are not preceded by a LOI will be returned without review.

III. AWARD INFORMATION

NSF estimates that \$15,000,000 will be available to support three center awards of five years duration each. The Simons Foundation estimates that \$15,000,000 will be available to support these three center awards over the five-year duration of the awards. NSF and the Simons Foundation expect to co-fund each of the three center awards, and that each center will have an annual budget of \$2,000,000 combined from both sources. The anticipated number of awards is three.

This is a partnership between NSF and the Simons Foundation, therefore meritorious proposals will be funded jointly by two organizations. Recommended for Funding proposals will be resubmitted by the PIs to the Simons Foundation, in accordance with instructions given by the cognizant Simons Foundation Program Officer. Subsequent grant administration procedures will be in accordance with the individual policies of the awarding agency.

Estimated program budget, number of awards, and average award size/duration are subject to the availability of funds.

IV. ELIGIBILITY INFORMATION

Who May Submit Proposals:

Proposals may only be submitted by the following:

- Universities and Colleges - Universities and two- and four-year colleges (including community colleges) accredited in, and having a campus located in, the US acting on behalf of their faculty members. Such organizations also are referred to as academic institutions.
- 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.

Who May Serve as PI:

There are no restrictions or limits for the allowable organizations listed above. Eligible Federal agencies and federally funded research and development centers (FFRDCs) can only participate as subawardees. FFRDCs and federal agency scientists cannot serve as lead PI. Non-NSF sponsored FFRDCs are required to provide a letter of support from their agency.

Limit on Number of Proposals per Organization:

There are no restrictions or limits on the number of proposals per organization. However, there is a limitation on the number of submissions per scientist as noted below.

Proposals submitted in response to this solicitation cannot be duplicates of proposals to any other Federal agency for simultaneous consideration. The only exceptions to this rule are: (1) when the program officers at the relevant Federal agencies have previously agreed to joint review and possible joint funding of the proposal; or (2) proposals for PIs who are beginning investigators (individuals who have not been a PI or co-PI on a Federally funded award with the exception of doctoral dissertation, postdoctoral fellowship or research planning grants). For proposers who qualify under this latter exception, the box for "Beginning Investigator" must be checked on the Cover Sheet.

Limit on Number of Proposals per PI or Co-PI:

An individual may appear as PI, co-PI, or other senior personnel on no more than two proposals submitted in response to this solicitation. Other senior personnel include lead PIs on subawards and named postdoctoral research associates. There is no limitation on unpaid consultants. Please be advised that if an individual's name appears as PI, co-PI or other senior personnel on more than two proposals, all proposals submitted after the first two proposals (based on the time-stamp) will be returned without review.

Please note: All materials should be submitted to NSF. NSF will share all submitted materials with the Simons Foundation.

V. PROPOSAL PREPARATION AND SUBMISSION INSTRUCTIONS

A. Proposal Preparation Instructions

Letters of Intent (required):

Submission of a Letter of Intent is required to be eligible to submit a full proposal to this Solicitation. Letters of Intent must be submitted via FastLane by an Authorized Organizational Representative.

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A Letter of Intent must contain the following information under the headings shown below:

- PIs, co-PIs and Other Senior Personnel: List up to 5 Senior Personnel, including the PI.
- Proposed title of proposal.
- Participating Organizations: List confirmed and possible participating organizations, up to a maximum of 5, including the lead organization.
- Synopsis: Describe the research foci, approaches and other center activities. Maximum 2500 characters.
- Training Summary: In the space provided for "Other Comments", describe plans for significant effort directed to training of postdocs, graduate and/or undergraduate students at the center. Maximum 2500 characters.

Letter of Intent Preparation Instructions:

When submitting a Letter of Intent through FastLane in response to this Program Solicitation please note the conditions outlined below:

- Submission by an Authorized Organizational Representative (AOR) is required when submitting Letters of Intent.
- A Minimum of 1 and Maximum of 4 Other Senior Project Personnel are permitted
- A Minimum of 0 and Maximum of 4 Other Participating Organizations are permitted
- Submission of multiple Letters of Intent is permitted

Full Proposal Preparation Instructions: Proposers may opt to submit proposals in response to this Program Solicitation via Grants.gov or via the NSF FastLane system.

- Full proposals submitted via FastLane: Proposals submitted in response to this program solicitation should be prepared and submitted in accordance with the general guidelines contained in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG). The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg. Paper copies of the PAPPG may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-7827 or by e-mail from nsfpubs@nsf.gov. Proposers are reminded to identify this program solicitation number in the program solicitation block on the NSF Cover Sheet For Proposal to the National Science Foundation. Compliance with this requirement is critical to determining the relevant proposal processing guidelines. Failure to submit this information may delay processing.
- Full proposals submitted via Grants.gov: Proposals submitted in response to this program solicitation via Grants.gov should be prepared and submitted in accordance with the *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov*. The complete text of the *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: (https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide). To obtain copies of the Application Guide and Application Forms Package, click on the Apply tab on the Grants.gov site, then click on the Apply Step 1: Download a Grant Application Package and Application Instructions link and enter the funding opportunity number, (the program solicitation number without the NSF prefix) and press the Download Package button. Paper copies of the Grants.gov Application Guide also may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-7827 or by e-mail from nsfpubs@nsf.gov.

In determining which method to utilize in the electronic preparation and submission of the proposal, please note the following:

Collaborative Proposals. All collaborative proposals submitted as separate submissions from multiple organizations must be submitted via the NSF FastLane system. PAPPG Chapter II.D.3 provides additional information on collaborative proposals.

See PAPPG Chapter II.C.2 for guidance on the required sections of a full research proposal submitted to NSF. Please note that the proposal preparation instructions provided in this program solicitation may deviate from the PAPPG instructions.

The Project Summary and Project Description must describe the goals and activities of the Center for the entire five-year award period, including research, teaching and other Broader Impact activities. Proposers may consider a ramp-up of the center's activities in the earlier stages of the award, but a full complement of activities must be implemented no later than the beginning of Year 3. In the third year of the award, NSF and the Simons Foundation will conduct mid-term site visits. In developing the Project Description, proposers should consider the ways in which they will demonstrate progress in achieving goals of the center during the first two years. In the same context, proposers need to consider the metrics they will use to measure performance of the center as they develop their Project Description. The required Management Plan (see Supplemental Documents) must include a description of the metrics that will be used to evaluate the performance of the center. Therefore the Project Description and the Management Plan must be consistent and coherent.

Supplementary Documents:

Appendix 1, Simons Foundation Budget: Awards will be jointly made with the Simons Foundation. Half the budget should be prepared by following the NSF Proposal and Award Policies and Procedures Guide (PAPPG), and the other half of the budget must be prepared by following instructions from the Simons Foundation, included with the announcement of this funding opportunity at the Simons Foundation website (<https://www.simonsfoundation.org>). Note that the Simons Foundation has a specific indirect cost rate policy.

Appendix 2, Other Senior Personnel and Center Leadership (maximum 5 pages): Describe the roles of Other Senior Personnel, including lead investigators on sub-awards, in the activities of the proposed center. Provide a list of key leadership personnel, and a brief description of what each person brings to the leadership team of the center.

Appendix 3, Management Plan (maximum 5 pages): Provide a detailed management plan describing key leadership positions, reporting relationships, means of communication and interaction among the members of the group and with the community, oversight and accountability mechanisms, metrics to evaluate the performance of the Center, external advisory committees (optional), etc. If an external advisory committee is to be utilized, do not list individual names, but list the number of members and describe the range of expertise needed to constitute an efficient and functional committee.

Appendix 4, Institutional Capabilities (maximum 2 pages): Describe how the current capabilities and resources of the lead and participating institutions will facilitate the proposed center activities. Include information on organizational leadership, technical expertise, general support, and maintenance as well as space, infrastructure, and technologies for collaborations of mathematical

scientists and biologists.

B. Budgetary Information

Cost Sharing:

Inclusion of voluntary committed cost sharing is prohibited.

Indirect Cost (F&A) Limitations:

Awards will be jointly made with the Simons Foundation. Half the budget should be prepared by following the NSF Proposal and Award Policies and Procedures Guide (PAPPG), and the other half of the budget must be prepared by following instructions from the Simons Foundation, included with the announcement of this funding opportunity at the Simons Foundation website (<https://www.simonsfoundation.org>). Note that the Simons Foundation has a specific indirect cost rate policy.

C. Due Dates

- **Letter of Intent Due Date(s) (required)** (due by 5 p.m. submitter's local time):
August 10, 2017
- **Full Proposal Deadline(s)** (due by 5 p.m. submitter's local time):
September 29, 2017

D. FastLane/Grants.gov Requirements

For Proposals Submitted Via FastLane:

To prepare and submit a proposal via FastLane, see detailed technical instructions available at: <https://www.fastlane.nsf.gov/a1/newstan.htm>. For FastLane user support, call the FastLane Help Desk at 1-800-673-6188 or e-mail fastlane@nsf.gov. The FastLane Help Desk answers general technical questions related to the use of the FastLane system. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this funding opportunity.

For Proposals Submitted Via Grants.gov:

Before using Grants.gov for the first time, each organization must register to create an institutional profile. Once registered, the applicant's organization can then apply for any federal grant on the Grants.gov website. Comprehensive information about using Grants.gov is available on the Grants.gov Applicant Resources webpage: <http://www.grants.gov/web/grants/applicants.html>. In addition, the NSF Grants.gov Application Guide (see link in Section V.A) provides instructions regarding the technical preparation of proposals via Grants.gov. For Grants.gov user support, contact the Grants.gov Contact Center at 1-800-518-4726 or by email: support@grants.gov. The Grants.gov Contact Center answers general technical questions related to the use of Grants.gov. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this solicitation.

Submitting the Proposal: Once all documents have been completed, the Authorized Organizational Representative (AOR) must submit the application to Grants.gov and verify the desired funding opportunity and agency to which the application is submitted. The AOR must then sign and submit the application to Grants.gov. The completed application will be transferred to the NSF FastLane system for further processing.

Proposers that submitted via FastLane are strongly encouraged to use FastLane to verify the status of their submission to NSF. For proposers that submitted via Grants.gov, until an application has been received and validated by NSF, the Authorized Organizational Representative may check the status of an application on Grants.gov. After proposers have received an e-mail notification from NSF, Research.gov should be used to check the status of an application.

VI. NSF PROPOSAL PROCESSING AND REVIEW PROCEDURES

Proposals received by NSF are assigned to the appropriate NSF program for acknowledgement and, if they meet NSF requirements, for review. All proposals are carefully reviewed by a scientist, engineer, or educator serving as an NSF Program Officer, and usually by three to ten other persons outside NSF either as *ad hoc* reviewers, panelists, or both, who are experts in the particular fields represented by the proposal. These reviewers are selected by Program Officers charged with oversight of the review process. Proposers are invited to suggest names of persons they believe are especially well qualified to review the proposal and/or persons they would prefer not review the proposal. These suggestions may serve as one source in the reviewer selection process at the Program Officer's discretion. Submission of such names, however, is optional. Care is taken to ensure that reviewers have no conflicts of interest with the proposal. In addition, Program Officers may obtain comments from site visits before recommending final action on proposals. Senior NSF staff further review recommendations for awards. A flowchart that depicts the entire NSF proposal and award process (and associated timeline) is included in PAPPG Exhibit III-1.

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A comprehensive description of the Foundation's merit review process is available on the NSF website at: https://www.nsf.gov/bfa/dias/policy/merit_review/.

Proposers should also be aware of core strategies that are essential to the fulfillment of NSF's mission, as articulated in *Investing in Science, Engineering, and Education for the Nation's Future: NSF Strategic Plan for 2014-2018*. These strategies are integrated in the program planning and implementation process, of which proposal review is one part. NSF's mission is particularly well-implemented through the integration of research and education and broadening participation in NSF programs, projects, and activities.

One of the strategic objectives in support of NSF's mission is to foster integration of research and education through the programs, projects, and activities it supports at academic and research institutions. These institutions must recruit, train, and prepare a diverse STEM workforce to advance the frontiers of science and participate in the U.S. technology-based economy. NSF's contribution to the national innovation ecosystem is to provide cutting-edge research under the guidance of the Nation's most creative scientists and engineers. NSF also supports development of a strong science, technology, engineering, and mathematics (STEM) workforce by investing in building the knowledge that informs improvements in STEM teaching and learning.

NSF's mission calls for the broadening of opportunities and expanding participation of groups, institutions, and geographic regions that are underrepresented in STEM disciplines, which is essential to the health and vitality of science and engineering. NSF is committed to this principle of diversity and deems it central to the programs, projects, and activities it considers and supports.

A. Merit Review Principles and Criteria

The National Science Foundation strives to invest in a robust and diverse portfolio of projects that creates new knowledge and enables breakthroughs in understanding across all areas of science and engineering research and education. To identify which projects to support, NSF relies on a merit review process that incorporates consideration of both the technical aspects of a proposed project and its potential to contribute more broadly to advancing NSF's mission "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense; and for other purposes." NSF makes every effort to conduct a fair, competitive, transparent merit review process for the selection of projects.

1. Merit Review Principles

These principles are to be given due diligence by PIs and organizations when preparing proposals and managing projects, by reviewers when reading and evaluating proposals, and by NSF program staff when determining whether or not to recommend proposals for funding and while overseeing awards. Given that NSF is the primary federal agency charged with nurturing and supporting excellence in basic research and education, the following three principles apply:

- All NSF projects should be of the highest quality and have the potential to advance, if not transform, the frontiers of knowledge.
- NSF projects, in the aggregate, should contribute more broadly to achieving societal goals. These "Broader Impacts" may be accomplished through the research itself, through activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. The project activities may be based on previously established and/or innovative methods and approaches, but in either case must be well justified.
- Meaningful assessment and evaluation of NSF funded projects should be based on appropriate metrics, keeping in mind the likely correlation between the effect of broader impacts and the resources provided to implement projects. If the size of the activity is limited, evaluation of that activity in isolation is not likely to be meaningful. Thus, assessing the effectiveness of these activities may best be done at a higher, more aggregated, level than the individual project.

With respect to the third principle, even if assessment of Broader Impacts outcomes for particular projects is done at an aggregated level, PIs are expected to be accountable for carrying out the activities described in the funded project. Thus, individual projects should include clearly stated goals, specific descriptions of the activities that the PI intends to do, and a plan in place to document the outputs of those activities.

These three merit review principles provide the basis for the merit review criteria, as well as a context within which the users of the criteria can better understand their intent.

2. Merit Review Criteria

All NSF proposals are evaluated through use of the two National Science Board approved merit review criteria. In some instances, however, NSF will employ additional criteria as required to highlight the specific objectives of certain programs and activities.

The two merit review criteria are listed below. **Both** criteria are to be given **full consideration** during the review and decision-making processes; each criterion is necessary but neither, by itself, is sufficient. Therefore, proposers must fully address both criteria. (PAPPG Chapter II.C.2.d(i), contains additional information for use by proposers in development of the Project Description section of the proposal). Reviewers are strongly encouraged to review the criteria, including PAPPG Chapter II.C.2.d(i), prior to the review of a proposal.

When evaluating NSF proposals, reviewers will be asked to consider what the proposers want to do, why they want to do it, how they plan to do it, how they will know if they succeed, and what benefits could accrue if the project is successful. These issues apply both to the technical aspects of the proposal and the way in which the project may make broader contributions. To that end, reviewers will be asked to evaluate all proposals against two criteria:

- **Intellectual Merit:** The Intellectual Merit criterion encompasses the potential to advance knowledge; and
- **Broader Impacts:** The Broader Impacts criterion encompasses the potential to benefit society and contribute to the achievement of specific, desired societal outcomes.

The following elements should be considered in the review for both criteria:

1. What is the potential for the proposed activity to
 - a. Advance knowledge and understanding within its own field or across different fields (Intellectual Merit); and

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- b. Benefit society or advance desired societal outcomes (Broader Impacts)?
2. To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts?
3. Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success?
4. How well qualified is the individual, team, or organization to conduct the proposed activities?
5. Are there adequate resources available to the PI (either at the home organization or through collaborations) to carry out the proposed activities?

Broader impacts may be accomplished through the research itself, through the activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. NSF values the advancement of scientific knowledge and activities that contribute to achievement of societally relevant outcomes. Such outcomes include, but are not limited to: full participation of women, persons with disabilities, and underrepresented minorities in science, technology, engineering, and mathematics (STEM); improved STEM education and educator development at any level; increased public scientific literacy and public engagement with science and technology; improved well-being of individuals in society; development of a diverse, globally competitive STEM workforce; increased partnerships between academia, industry, and others; improved national security; increased economic competitiveness of the United States; and enhanced infrastructure for research and education.

Proposers are reminded that reviewers will also be asked to review the Data Management Plan and the Postdoctoral Researcher Mentoring Plan, as appropriate.

Additional Solicitation Specific Review Criteria

In addition to the National Science Board merit review criteria, reviewers will be asked to use the following program-specific criteria when reviewing MathBioSys proposals.

1. The quality of the stated mission and goals of the center, and its likely effectiveness in meeting the mission and goals;
2. The potential and commitment of the center leadership and the key personnel to effectively lead and manage the proposed center;
3. The proposed structure and management of the center, including the quality and effectiveness of the Management Plan, and its likely effectiveness in fostering new teams that will build cross-disciplinary capacity in areas relevant to MathBioSys;
4. The potential for the Institutional Capabilities to contribute to a successful cross-disciplinary center in areas relevant to MathBioSys;
5. The quality, likely effectiveness, and accountability of the proposed outreach activities and proposed strategies for dissemination of results;
6. The extent to which the proposed center will take advantage of co-located, ongoing biological research that is relevant to the MathBioSys Program to foster the development of productive, cross-disciplinary research collaborations.

B. Review and Selection Process

Proposals submitted in response to this program solicitation will be reviewed by Ad hoc Review and/or Panel Review, Site Visit Review, or Reverse Site Review.

The program will be managed by program directors from NSF and the Simons Foundation. NSF will take the lead in managing, organizing, and conducting the review process of all proposals. The Simons Foundation program directors will make recommendations for reviewers and will attend NSF review panels as observers. Copies of proposals and unattributed reviews will be shared with the Simons Foundation, as appropriate.

Reviewers will be asked to evaluate proposals using two National Science Board approved merit review criteria and, if applicable, additional program specific criteria. A summary rating and accompanying narrative will generally be completed and submitted by each reviewer and/or panel. The Program Officer assigned to manage the proposal's review will consider the advice of reviewers and will formulate a recommendation.

NSF Process: After scientific, technical and programmatic review and consideration of appropriate factors, the NSF Program Officer recommends to the cognizant Division Director whether the proposal should be declined or recommended for award. NSF strives to be able to tell applicants whether their proposals have been declined or recommended for funding within six months. Large or particularly complex proposals or proposals from new awardees may require additional review and processing time. The time interval begins on the deadline or target date, or receipt date, whichever is later. The interval ends when the Division Director acts upon the Program Officer's recommendation.

After programmatic approval has been obtained, the proposals recommended for funding will be forwarded to the Division of Grants and Agreements for review of business, financial, and policy implications. After an administrative review has occurred, Grants and Agreements Officers perform the processing and issuance of a grant or other agreement. Proposers are cautioned that only a Grants and Agreements Officer may make commitments, obligations or awards on behalf of NSF or authorize the expenditure of funds. No commitment on the part of NSF should be inferred from technical or budgetary discussions with a NSF Program Officer. A Principal Investigator or organization that makes financial or personnel commitments in the absence of a grant or cooperative agreement signed by the NSF Grants and Agreements Officer does so at their own risk.

Once an award or declination decision has been made, Principal Investigators are provided feedback about their proposals. In all cases, reviews are treated as confidential documents. Verbatim copies of reviews, excluding the names of the reviewers or any reviewer-identifying information, are sent to the Principal Investigator/Project Director by the Program Officer. In addition, the proposer will receive an explanation of the decision to award or decline funding.

VII. AWARD ADMINISTRATION INFORMATION

A. Notification of the Award

Notification of the award is made to *the submitting organization* by a Grants Officer in the Division of Grants and Agreements. Organizations whose proposals are declined will be advised as promptly as possible by the cognizant NSF Program administering the program. Verbatim copies of reviews, not including the identity of the reviewer, will be provided automatically to the Principal Investigator. (See Section VI.B. for additional information on the review process.)

B. Award Conditions

An NSF award consists of: (1) the award notice, which includes any special provisions applicable to the award and any numbered amendments thereto; (2) the budget, which indicates the amounts, by categories of expense, on which NSF has based its support (or otherwise communicates any specific approvals or disapprovals of proposed expenditures); (3) the proposal referenced in the award notice; (4) the applicable award conditions, such as Grant General Conditions (GC-1)*; or Research Terms and Conditions* and (5) any announcement or other NSF issuance that may be incorporated by reference in the award notice. Cooperative agreements also are administered in accordance with NSF Cooperative Agreement Financial and Administrative Terms and Conditions (CA-FATC) and the applicable Programmatic Terms and Conditions. NSF awards are electronically signed by an NSF Grants and Agreements Officer and transmitted electronically to the organization via e-mail.

*These documents may be accessed electronically on NSF's Website at https://www.nsf.gov/awards/managing/award_conditions.jsp?org=NSF. Paper copies may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-7827 or by e-mail from nsfpubs@nsf.gov.

More comprehensive information on NSF Award Conditions and other important information on the administration of NSF awards is contained in the NSF *Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

Special Award Conditions:

Proposals selected for funding will be subject to each Foundation's respective award policies and practices. Each center funded by this program will receive two separate awards of equal size in terms of totals costs, one from NSF and one from the Simons Foundation (SF). For NSF, standard NSF award conditions apply. SF awards will use standard SF award terms, conditions and reporting requirements. Award notification and administration will be carried out by NSF with respect to each of its awards, in consultation with SF. Award notification and administration will be carried out by SF with respect to each of its awards, in consultation with NSF.

C. Reporting Requirements

For all multi-year grants (including both standard and continuing grants), the Principal Investigator must submit an annual project report to the cognizant Program Officer no later than 90 days prior to the end of the current budget period. (Some programs or awards require submission of more frequent project reports). No later than 120 days following expiration of a grant, the PI also is required to submit a final project report, and a project outcomes report for the general public.

Failure to provide the required annual or final project reports, or the project outcomes report, will delay NSF review and processing of any future funding increments as well as any pending proposals for all identified PIs and co-PIs on a given award. PIs should examine the formats of the required reports in advance to assure availability of required data.

PIs are required to use NSF's electronic project-reporting system, available through Research.gov, for preparation and submission of annual and final project reports. Such reports provide information on accomplishments, project participants (individual and organizational), publications, and other specific products and impacts of the project. Submission of the report via Research.gov constitutes certification by the PI that the contents of the report are accurate and complete. The project outcomes report also must be prepared and submitted using Research.gov. This report serves as a brief summary, prepared specifically for the public, of the nature and outcomes of the project. This report will be posted on the NSF website exactly as it is submitted by the PI.

More comprehensive information on NSF Reporting Requirements and other important information on the administration of NSF awards is contained in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

For NSF, standard NSF reporting requirements apply.

For the Simons Foundation awards, reports shall be submitted in the form and in the manner set forth in the Simons Foundation grant agreement.

VIII. AGENCY CONTACTS

Please note that the program contact information is current at the time of publishing. See program website for any updates to the points of contact.

General inquiries regarding this program should be made to:

- Kathryn Dickson, telephone: (703) 292-7380, email: kdickson@nsf.gov

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- Elizabeth Roy, Simons Foundation, telephone: (212) 524-6966, email: eroy@simonsfoundation.org
- Junping Wang, Directorate for Mathematical and Physical Sciences, NSF, telephone: (703) 292-4488, email: jwang@nsf.gov
- Henry A. Warchal, telephone: (703) 292-4861, email: hwarchal@nsf.gov

For questions related to the use of FastLane, contact:

- FastLane Help Desk, telephone: 1-800-673-6188; e-mail: fastlane@nsf.gov.

For questions relating to Grants.gov contact:

- Grants.gov Contact Center: If the Authorized Organizational Representatives (AOR) has not received a confirmation message from Grants.gov within 48 hours of submission of application, please contact via telephone: 1-800-518-4726; e-mail: support@grants.gov.

Important Note: For timely responses to your questions, please direct your email messages to the Program Directors on the MathBioSys Working Group at mathbiosys@nsf.gov

IX. OTHER INFORMATION

The NSF website provides the most comprehensive source of information on NSF Directorates (including contact information), programs and funding opportunities. Use of this website by potential proposers is strongly encouraged. In addition, "NSF Update" is an information-delivery system designed to keep potential proposers and other interested parties apprised of new NSF funding opportunities and publications, important changes in proposal and award policies and procedures, and upcoming NSF [Grants Conferences](#). Subscribers are informed through e-mail or the user's Web browser each time new publications are issued that match their identified interests. "NSF Update" also is available on [NSF's website](#).

Grants.gov provides an additional electronic capability to search for Federal government-wide grant opportunities. NSF funding opportunities may be accessed via this mechanism. Further information on Grants.gov may be obtained at <http://www.grants.gov>.

ABOUT THE NATIONAL SCIENCE FOUNDATION

The National Science Foundation (NSF) is an independent Federal agency created by the National Science Foundation Act of 1950, as amended (42 USC 1861-75). The Act states the purpose of the NSF is "to promote the progress of science; [and] to advance the national health, prosperity, and welfare by supporting research and education in all fields of science and engineering."

NSF funds research and education in most fields of science and engineering. It does this through grants and cooperative agreements to more than 2,000 colleges, universities, K-12 school systems, businesses, informal science organizations and other research organizations throughout the US. The Foundation accounts for about one-fourth of Federal support to academic institutions for basic research.

NSF receives approximately 55,000 proposals each year for research, education and training projects, of which approximately 11,000 are funded. In addition, the Foundation receives several thousand applications for graduate and postdoctoral fellowships. The agency operates no laboratories itself but does support National Research Centers, user facilities, certain oceanographic vessels and Arctic and Antarctic research stations. The Foundation also supports cooperative research between universities and industry, US participation in international scientific and engineering efforts, and educational activities at every academic level.

Facilitation Awards for Scientists and Engineers with Disabilities (FASSED) provide funding for special assistance or equipment to enable persons with disabilities to work on NSF-supported projects. See the *NSF Proposal & Award Policies & Procedures Guide* Chapter II.E.6 for instructions regarding preparation of these types of proposals.

The National Science Foundation has Telephonic Device for the Deaf (TDD) and Federal Information Relay Service (FIRS) capabilities that enable individuals with hearing impairments to communicate with the Foundation about NSF programs, employment or general information. TDD may be accessed at (703) 292-5090 and (800) 281-8749, FIRS at (800) 877-8339.

The National Science Foundation Information Center may be reached at (703) 292-5111.

The National Science Foundation promotes and advances scientific progress in the United States by competitively awarding grants and cooperative agreements for research and education in the sciences, mathematics, and engineering.

To get the latest information about program deadlines, to download copies of NSF publications, and to access abstracts of awards, visit the NSF Website at <https://www.nsf.gov>

- **Location:** 2415 Eisenhower Avenue, Alexandria, VA 22314
- **For General Information** (NSF Information Center): (703) 292-5111

- **TDD (for the hearing-impaired):** (703) 292-5090
- **To Order Publications or Forms:**
 - Send an e-mail to: nspubs@nsf.gov
 - or telephone: (703) 292-7827
- **To Locate NSF Employees:** (703) 292-5111

PRIVACY ACT AND PUBLIC BURDEN STATEMENTS

The information requested on proposal forms and project reports is solicited under the authority of the National Science Foundation Act of 1950, as amended. The information on proposal forms will be used in connection with the selection of qualified proposals; and project reports submitted by awardees will be used for program evaluation and reporting within the Executive Branch and to Congress. The information requested may be disclosed to qualified reviewers and staff assistants as part of the proposal review process; to proposer institutions/grantees to provide or obtain data regarding the proposal review process, award decisions, or the administration of awards; to government contractors, experts, volunteers and researchers and educators as necessary to complete assigned work; to other government agencies or other entities needing information regarding applicants or nominees as part of a joint application review process, or in order to coordinate programs or policy; and to another Federal agency, court, or party in a court or Federal administrative proceeding if the government is a party. Information about Principal Investigators may be added to the Reviewer file and used to select potential candidates to serve as peer reviewers or advisory committee members. See Systems of Records, [NSF-50](#), "Principal Investigator/Proposal File and Associated Records," 69 Federal Register 26410 (May 12, 2004), and [NSF-51](#), "Reviewer/Proposal File and Associated Records," 69 Federal Register 26410 (May 12, 2004). Submission of the information is voluntary. Failure to provide full and complete information, however, may reduce the possibility of receiving an award.

An agency may not conduct or sponsor, and a person is not required to respond to, an information collection unless it displays a valid Office of Management and Budget (OMB) control number. The OMB control number for this collection is 3145-0058. Public reporting burden for this collection of information is estimated to average 120 hours per response, including the time for reviewing instructions. Send comments regarding the burden estimate and any other aspect of this collection of information, including suggestions for reducing this burden, to:

Suzanne H. Plimpton
Reports Clearance Officer
Policy Office, Division of Institution and Award Support
Office of Budget, Finance, and Award Management
National Science Foundation
Alexandria, VA 22314

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