NATIONAL SCIENCE FOUNDATION
2415 Eisenhower Avenue
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NSF 18-031

Dear Colleague Letter: Rules of Life (RoL): Forecasting and Emergence in Living Systems (FELS)

December 11, 2017

Dear Colleagues:

NSF seeks to highlight the importance of research that forecasts the direction and dynamics of change in living systems. The robustness and reproducibility of processes associated with the emergence of complex properties in biological systems suggests the existence of underlying general principles ("rules") across the spectrum of biological phenomena. Identification and application of these fundamental rules would be of high value to both the scientific community and the Nation. This Dear Colleague Letter (DCL) describes an initial opportunity to identify areas where such rules may exist, to catalyze approaches toward their discovery, and to focus efforts on using these rules for prediction and design of useful biological systems. Activities supported via this DCL include Conferences, EArly-concept Grants for Exploratory Research (EAGERs), and Research Advanced by Interdisciplinary Science and Engineering (RAISE) grants to create opportunities for enabling predictive capability

BACKGROUND

The development of new research tools has revolutionized our ability both to investigate and manipulate the genome and to measure multiple aspects of the environment. The current challenge in biological systems is to assimilate new information into causal, predictive relationships. For example, we are on the cusp of solving one of the greatest challenges in understanding the living world – namely, predicting how the set of observable characteristics (phenotype) arises from the genetic makeup of the individual in concert with environmental factors acting at diverse spatial and temporal scales.

The approach to this challenge resonates with NSF's emphasis on convergent research, one of the ten Big Ideas for future investment that the Director announced in May 2016, which emphasizes deep integration across disciplines inspired by powerful scientific questions or pressing societal needs. NSF is interested in submission of proposals to jump-start community thinking about research that considers both genomic and environmental inputs, at all spatial and temporal scales, to identify steps along the critical path to de novo prediction of complex biological systems in a variety of organisms. These steps will take advantage of the increasing conjunction between the biological sciences and research in the computer and information sciences, engineering, geosciences, mathematical and physical sciences, and social, behavioral, and economic sciences. These investments should have the potential to transform our understanding of living systems and benefit the public through addressing societal issues.

SUMMARY OF THE OPPORTUNITY

Proposals funded via this DCL will help refine emerging research areas under the Rules of Life, one of the NSF's ten Big Ideas. In Rules of Life, "rules" are the general principles or theoretical constructs that explain and predict the characteristics of living systems. NSF seeks to identify rules for phenomena that cross spatial or organizational levels (from the molecular and sub-cellular to organisms, populations, communities, clades, and biomes) and/or temporal scales (e.g., from macromolecular folding to development to evolutionary processes across all of life).

Research activities under Rules of Life should lead to new and predictive understanding of how higher-order structures and functions result from the interactions of heterogeneous biological components with the environments in which they are found, and the associated evolutionary changes. These activities should bring together diverse teams of scientists to create novel framings and solutions for research problems. Currently, we are unable to predict the outcomes of many biological processes in spite of the fact that organisms occupy only a small portion of the potential phenotypic landscape. Although we have accumulated massive amounts of genomic and environmental data, we cannot synthesize a cell from its fundamental building blocks. Similarly, we do not understand the basic rules that underlie the emergence of multicellular structures, the regulation of circadian and seasonal rhythms, or how to re-engineer sustainable and resilient biological systems at any scale. Further, there are open scientific questions about the role of social interactions and experiences in reshaping the genome through genetic and epigenetic changes. One long-term outcome of the Rules of Life effort will be a set of comprehensive genome/environment-to-phenome theories with predictive capability. These theories could, for example, enable us to design phenotypes to respond to environmental challenges or lead to new technologies and industries.

We seek to define the key challenges and research imperatives to understand the organizational principles and rules of living systems, encouraging projects that include diverse disciplinary perspectives in addition to the biological sciences, including but not limited to those from: computer and information sciences, engineering, geosciences, mathematical and physical sciences, and social and behavioral sciences. Projects may address linkages between genomic and phenotypic diversity to encompass biological and environmental processes spanning the genome to ecosystem across multiple scales of space and time.

NSF is seeking catalytic activities, such as:

- Conferences that engage the research and research infrastructure communities in identifying and developing potential new areas of research and technology development. This could include tools for manipulation of biological systems, communities or ecosystems; research and infrastructure for collection, management, and analysis of heterogeneous, noisy data; and engagement of methods of machine learning and artificial intelligence as they pertain to biological systems
- EAGER projects to develop and test new concepts as per above.
- RAISE projects that engage multidisciplinary teams in innovative approaches to examine rules of life as per above.

Opportunities for participation by graduate students and postdoctoral fellows in conference, EAGER and RAISE proposals are encouraged. Additionally, proposals that include efforts to broaden participation and, as appropriate, education and outreach, regarding Rules of Life.

To be considered, each conference or EAGER proposal must explicitly address all four points below:

1. Propose strategies to discover, elucidate, or apply a fundamental rule that, when more fully understood, could be used to predict a specific complex aspect of biological systems;
2. Target a specific emergent property, which by definition spans biological scales (spatial and/or temporal scales; levels of biological organization);
3. Generate tools or theory and results that will be broadly generalizable beyond the system under investigation; and
4. Be a project that crosses Divisional boundaries in the Directorate for Biological Sciences (BIO), i.e., a project that requires review by two or more of the four Divisions in BIO (Biological Infrastructure, Environmental Biology, Integrative Organismal Systems, Molecular and Cellular Biosciences). A project may involve other Directorates (e.g., GEO, CISE, MPS, etc.) but for consideration as a conference (workshop) or EAGER, it must still involve two or more Divisions in BIO. These proposals will be reviewed by Divisional and Directorate Program Directors as appropriate to the intellectual foci of the proposal.

To be considered for a RAISE award, projects must address the first three criteria listed above for EAGER and Conference requests, but they are required to include only one BIO Division (although they may include more). In addition, RAISE proposals must address the fifth point below:

5. Would not normally be funded by only the BIO Directorate; proposed research must also cross the disciplinary boundary represented by at least one of these directorates: Computer and Information Science and Engineering (CISE); Education and Human Resources (EHR); Engineering (ENG); Geosciences (GEO); Mathematical and Physical Sciences (MPS); and Social, Behavioral, and Economic Sciences (SBE).

PREPARATION INSTRUCTIONS

Each proposal submitted in response to this DCL should be grounded in a compelling research challenge. The proposal should address the current state of the research challenge and describe an integrated strategy for addressing the challenge. Proposals submitted in response to this DCL should be prepared and submitted in accordance with the guidelines contained in the NSF Proposal & Award Policies & Procedures Guide (PAPPG) and the instructions provided below.

RoL:FELS EAGERs: For a project to be considered for EAGER funding through this opportunity, a 2-page prospectus of the proposed research must be submitted to the RoL:FELS mailbox (RoLBIO@nsf.gov) by February 20, 2018. The 2-page summary must be a PDF file that clearly lays out the idea of the EAGER and illustrates how the project would address the 4 eligibility criteria. Based on those summaries, EAGER proposals will be invited; full proposals must be received by May 15, 2018. EAGER proposals submitted in response to this DCL must be submitted to the most relevant program within the BIO Directorate and include the prefix 'RoL:FELS' in front of the title. RoL:FELS EAGER proposals should follow normal PAPPG guidance.

Any RoL:FELS EAGER received without discussion with, and subsequently followed by an written invitation from a Program Director, will be returned without review.

RoL:FELS conference: These awards will provide up to one year of support for projects that do not exceed $100,000. PIs are encouraged to contact any relevant Program Director in a participating Directorate about suitability of the proposed conference prior to submission. RoL:FELS conference proposals may be submitted to any relevant program in a participating Directorate, but must include the prefix 'RoL:FELS' in front of the title. The deadline for submission of these proposals is June 1, 2018. received. RoL:FELS conference proposals should follow normal PAPPG guidance.

RoL:FELS RAISE: For a project to be considered for RAISE funding through this opportunity, a 2-page prospectus of the proposed research must be submitted to the RoL:FELS mailbox (RoLBIO@nsf.gov) by February 20, 2018. The 2-page summary must be a PAPPG-compliant PDF file and clearly lay out the idea of the RAISE and illustrate how the project would address the 4 criteria noted above. In addition, RAISE submissions must clearly explain the interdisciplinary nature of the project and indicate the relevant NSF directorate(s) in addition to BIO that would need to be involved in considering the merits of the project. Invited RAISE proposals must follow the guidelines contained in the PAPPG. Directorates participating with BIO include CISE, EHR, ENG, GEO, MPS, and SBE.

POINTS OF CONTACT

Inquiries about the Dear Colleague Letter and questions about submission of EAGER and RAISE proposals should be directed to RoLBIO@nsf.gov.

Sincerely,

James L. Olds, Assistant Director, BIO
Jim Kurose, Assistant Director, CISE
William Lewis, Assistant Director (Acting), EHR
Dawn M. Tilbury, Assistant Director, ENG
William E. Easterling, Assistant Director, GEO
James S. Ulvestad, Assistant Director (Acting), MPS
Fay Lomax Cook, Assistant Director, SBE