

REQUEST FOR PROPOSALS

MY BRAIN MAP INITIATIVE

BRINGING A SYSTEMS APPROACH TO PERSONALIZED HEALTH IN EPILEPSY

The Epilepsy Innovation Institute (Ei²) is pleased to announce a Request for Proposals for the My Brain Map initiative to fund pilot studies (up to \$200,000) that would propose novel exploratory ways to model seizure propagation in a personalized brain network model. We are looking for proposals that seek to test novel, unconventional hypotheses or pursue major methodological or technical challenges in network modeling for epilepsy. We are interested in funding innovative multi-scale approaches to brain mapping. Therefore, we encourage proposal submissions that can begin to correlate standard measures of macro-network activity (i.e. EEG and/or fMRI) with microphysiological mechanisms (such as oxygen, microdialysis of extracellular fluids, local field potentials, etc).

Our ultimate end-goal is to create a user-friendly data visualization tool for seizure propagation personalized to the individual's brain network. This request for proposals will be used to fund the preliminary exploratory work needed to develop a prototype visualization tool. The following will be prioritized:

- Investigators who propose employing new technologies and/or new analytical methods on existing data sets already collected.

Successful applicants would be awarded up to a one year 200,000-dollar grant as seed funding to generate preliminary data that could then be used to secure further follow on funding at other funding agencies. Note that if the proof of concept exploratory project is funded and is extremely successful, there may also be opportunities to apply for follow on funding from Ei² to validate the work in the clinic.

Please see [Letter of Intent section under Applicant Instructions](#) for more details. Note that Letter of Intent submissions are due June 21, 2019.

[Full grant applications](#) will be due on November 29, 2019.

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INTRODUCTION

The Epilepsy Innovation Institute (Ei²) is a research program of the Epilepsy Foundation, a 501(c)3 nonprofit whose mission is to lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, fund cures and save lives.

In 2018, Ei² launched the [My Brain Map initiative](#) to better define personalized network modeling of seizure propagation to transform care in epilepsy. Our moonshot goal is to create a Google Map for the brain that highlights one's unique brain traffic pattern over time. With this map, we can better identify the routes an individual's seizure could take, where the potential traffic jams might be, and how activity can get rerouted in the brain during those situations.

In the past decade, there have been advances in complex system network approaches, such as those used in mathematics and computer science to study effective retrieval of web information or impact of failures in airline networks. Our objective with this request for proposals is to encourage the application of complex system network approaches to understanding the underlying neurophysiological mechanisms underlying seizure propagation and termination in epilepsy.

As we are still in early days of understanding how best to model brain networks, the goal of this proposal is to support exploratory analysis in this area by encouraging either:

- the development of new mathematical approaches that utilize multi-scale approaches to constrain and parameterize epilepsy network modeling, or

- the testing of novel noninvasive tools to map the epilepsy network for multi-scale modeling.

Note that if the proof of concept exploratory project is funded and is extremely successful, there may also be opportunities to apply for follow on funding from Ei² to validate the work in the clinic. Our end-goal is to lay the foundation for developing a user-friendly tool for clinicians that could visualize an individual's seizure propagation network throughout the brain.

If successful, this project could be used to:

- Identify key brain regions unique to the individual that could be critical for seizure control
- Improve our abilities to visualize how a seizure spreads, which may improve surgical options and prediction of long-term outcomes
- Optimize neurostimulation therapies to the individual
- Better understand the biological profiles of epilepsy syndromes, which in turn could improve diagnosis and address why seizures occur

Prior to releasing this RFP, Ei² hosted an innovation workshop to assess the current state of the science in brain network mapping in epilepsy. **For more information on the outcomes of the workshop, please [click here](#).**

OBJECTIVES AND STRATEGIC AREAS OF INTEREST

The objective of this RFP is to support pilot studies that encourage new analytical approaches and/or tools to modeling seizure propagation in a brain network. These are seed funding grants for exploratory research that has the potential to transform our understanding of how seizures can propagate throughout the network. The Foundation encourages applications to take multi-scale approaches that could correlate our current standard measures of macro-network mapping such as EEG and/or fMRI with micro-network physiological mechanism. *This is **not** an effort to support the collection and curation of large data sets.* Therefore, those with data sets already available for analysis will be given preference.

The rationale for this program was modeled after the EUREKA initiatives of the National Institutes of Health. We believe that for epilepsy research to move forward, investigators must have opportunities to test unconventional, potentially paradigm-shifting hypotheses, and to attempt to use novel, innovative approaches to solve difficult technical and conceptual problems that severely impede progress in the field. Conventional grant applications often emphasize the feasibility of the proposed research rather than the novelty. Therefore, it is difficult to secure funding for intriguing projects that do not yet have sufficient preliminary data. The goal of this RFP is to allow investigators to have access to pilot seed funds that could assess the feasibility of their proposed bright idea for network modeling and generate preliminary data that would assist in securing future follow on funding from other sources.

For this effort, we want to:

- Support interdisciplinary approaches involving clinicians, neuroscientists, computer scientists, and mathematicians to facilitate different perspectives in these early days of multi-scale network modeling of seizure propagation, and
- Support the development of preliminary data visualization tools for clinicians to better understand different types of seizure propagation networks that could in future better tailor care to the individual.

TEAM SCIENCE AWARD

This award is designed to foster collaborative research amongst researchers with complementary expertise and capabilities, who will work together to advance our understanding on seizure propagation in personalized brain network models. Ei² expects to provide up to \$200,000 per multidisciplinary teams of two or more established Principal Investigators (PIs). Our goal is to support interdisciplinary approaches involving clinicians, neuroscientists, computer scientists, and mathematicians to facilitate different perspectives in these early days of network modeling.

Teams may consist of investigators from the same institution, different institutions, may be public/private partnerships and may be international. A designated Administrative PI is responsible for administrative leadership in ensuring all documents are submitted (see Application instructions). All PIs on the team share authority for scientific leadership. A representative of Ei² will also be part of the selected winning team.

This award has a collaborative and multidisciplinary emphasis, involving meaningful collaboration between participants. **Applications therefore must include a description of the nature of and rationale for the proposed collaboration, the specific role of all PIs, and synergistic opportunities.**

Note that a successful full grant application will need a team with expertise and capacity to address the following:

- Epilepsy expertise to understand the multi-modal data set being analyzed and validation of the network assignment upon which the modeling will be applied
- Mathematical capabilities to test out novel network modeling approaches
- Computer software development expertise to develop prototype data visualization tools

APPLICANT ELIGIBILITY

PIs must hold a full-time faculty or industry appointment at the level of Assistant Professor (or equivalent) or above at an academic, non-profit research institution, or industry organization whose primary mission includes medical research within or outside the United States. PIs must be able to show clear evidence of an independent research program. Fellows or those in other training or research support positions are encouraged to be part of the team. Investigators need not be specifically trained

in the field of epilepsy or have any documented experience with epilepsy research. However, researchers who are new to epilepsy will need to ensure that there is an epilepsy research expert on their team during the formative stages of the research plan. If there are any questions about eligibility, please contact Ei² before submitting an application. Contact information appears at the end of this RFP. Applications from PIs who do not meet the eligibility criteria will not be reviewed.

APPLICATION INSTRUCTIONS:

There will be a two-stage peer-review application process:

1. Letters of Intent (LOIs) are due by 5:00 PM Eastern Time on June 21, 2019.
2. For those that are selected to move forward, Full grant applications are due by 5:00 PM Eastern Time on November 29, 2019.

LOIs and proposals received after the applicable deadline will not be considered.

The Epilepsy Foundation utilizes the [proposalCENTRAL](#) online application tool and the document templates and requirements therein. Please carefully follow the instructions in proposalCENTRAL and below. Applications include the following steps and components.

LETTER OF INTENT

All applicants must submit a LOI to the Epilepsy Foundation prior to submission of a full proposal. Please carefully follow the instructions in [proposalCENTRAL](#). The LOI application consists of the following components:

1. **Title Page:** Enter the project title. (Title length cannot exceed 75 characters)
2. **Applicant/PI Information:** For Team applications, identify one PI for administrative purposes of grant submission. This is the Applicant.
3. **Organization/Institution Information:** This is the Administrative PI's institution.
4. **Key Personnel Information:** Identify other PIs on the team. All PIs share authority for project leadership.
5. **LOI:** 4-page maximum that must be formatted in Arial 11 point or Times New Roman 12-point font with no less than ½ inch margins. Components of the LOI include:

- (a) Description of how the team/individual/organization can contribute to the project, outlining the specific role of each participant, and synergistic opportunities
- (b) Description of the unmet need that the proposal is addressing for network modeling of seizure propagation. If you are testing an unconventional, exceptionally novel hypothesis, how does it challenge the standard paradigm for network modeling of seizure propagation? If you are addressing a technological or methodological problem, what makes the problem especially challenging?
- (c) Description of the data sets being used for the network modeling exploratory analysis and the capacity of the team to either use this existing data or obtain this data with novel technologies to do pilot work during the term of the proposal.
- (d) Description of the network assignment (i.e. nodes and edges of the connectome) upon which the dynamic mathematical modeling or tool development will be based.
- (e) Discussion of how this proposal is unique from already ongoing initiatives in brain mapping.

Letters exceeding the 4-page limit will not be considered. References are not included in the page limit amount.

FULL-LENGTH APPLICATION

Full-length applications will be invited from meritorious LOIs selected by the Epilepsy Foundation Ei² review committee.

Please carefully follow the instructions in proposalCENTRAL and below. Applications include the following steps and components. [For more detailed description of the proposal narrative, please download Proposal Narrative in templates section of ProposalCentral.](#)

1. **Title Page:** Enter the project title. (*Length cannot exceed 75 characters*)
2. **Templates and Instructions:** Download RFP and templates.
3. **Enable Other Users to Access this Proposal:** Allow others (e.g., institutional administrators or collaborators) to view, edit, or submit your proposal.
4. **Applicant/PI:** Key information about the applicant PI. This must be the Administrative PI on team science applications.
5. **Organization/Institution:** Key information about the Applicant/PI's institution, including name and email address of the signing official who, in addition to the PI, will be contacted if the award is selected for funding.

6. **Key Personnel:** List and provide contact information for key persons. Include all PIs on the proposal as well as any additional key personnel.

7. **Abstracts and Keywords:** Provide a lay audience friendly abstract and a technical abstract (2,000 characters maximum each) and key words. Please note: the lay abstract will become public if the award is selected for funding; therefore, it should not contain any proprietary information.

8. **Budget Period Detail:** Enter budget detail for each award period requested. For proposals involving multiple institutions, please include a total amount requested for each institution in the budget justification section. Epilepsy Foundation will not support indirect costs, overhead costs, or other similar institutional levies in excess of 10% of the total award amount. Fringe benefits for personnel salaries are allowable.

9. **Budget Summary and Justification:** A description of why the attached budget is appropriate for the proposed work. Be sure to include personnel responsibilities and effort commitments.

10. **Other Support:** Please provide the title, role in grant, percent effort, amount of funding and years of current and pending support for each grant (including SBIR, STTR, RAID). Include all non-governmental funding (e.g. CURE, Epilepsy Foundation, American Epilepsy Society, other foundations) for work related to this proposal (past, present, pending). Information should be provided in the format shown in the Other Support template. No page limit applies for Support information. Note that support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Please specify who the Primary Investigator is for all support listed.

- The Epilepsy Foundation will not award funds to duplicate any work that is being supported by other funding agencies.** Budgetary overlap is not permitted; however, scientific overlap will be evaluated on an individual basis. In cases of significant scientific overlap, a successful applicant will have the option to choose between the Epilepsy Foundation award and that of the other organization

11. **Organizational Assurances:** Ensure Compliance with Human Subjects and Animal Care Assurance as applicable.

12. **Upload Attachments:** Upload the following:
 - a. **Curriculum vitae for PIs and other key personnel:** Applicants may use the template provided or the NIH biosketch format.

- b. **Other Support (see above):** Use the template provided in proposalCENTRAL, which includes a statement of overlap. Any overlap of current or pending support with the Epilepsy Foundation proposal must be described and explained.
- c. **Project description:** Must be formatted in Arial 11 point or Times New Roman 12 point font with no less than ½ inch margins. 15 pages maximum, inclusive of the following:
 - i. **Abstract**
 - ii. **Proposed Solution** – Provide a description of the unmet need that this project plan will address. If you are testing an unconventional, exceptionally novel hypothesis, how does it challenge the standard paradigm for network modeling of seizure propagation? If you are addressing a technological or methodological problem, what makes the problem especially challenging?
 - iii. **Work Plan and Aims** – As this is exploratory work, a detailed experimental plan is not required. But reviewers need to have enough information to understand the methodology, rationale, and logic of the proposed research plan. Be sure to:
 - a. provide an explanation for how approach is exceptionally novel or important to test, and how it differs from approaches that have already been tried.
 - b. outline the network assignment (i.e. nodes and edges of the connectome) will be assessed and characterized.
 - c. Explain which data sets are being used for the network modeling exploratory analysis and the capacity of the team to either use this existing data or obtain this data with novel technologies to do pilot work during the term of the proposal.
 - d. describe the quality assurance testing and validation steps that the team will use when developing the seizure map.
 - e. provide a plan for how a user-friendly visualization tool could be utilized in the clinic based on the mapping proposed.
 - iv. **Potential for Impact** – Provide an overview of how this pilot project on network modeling could set the stage for transforming the epilepsy field? Please indicate what type of results you anticipate generating by the end of the funding period and how this would be sufficient for preliminary data in a larger grant application to secure funds elsewhere. Indicate how the proposed activities differ from your current ongoing efforts.
 - v. **Team** – Describe the makeup of the team, how it is composed of the needed strengths and expertise to accomplish the work plan and aims, and how this will be a productive collaboration rather than a “drive-by” working relationship.
 - vi. **Managing Challenges** – Briefly describe the past achievements that best illustrate your ability to make paradigm-shifting discoveries or solve very difficult problems. The achievements that you highlight need not be

conceptually related to the hypothesis or problem that you are addressing in this application. If your previous research was not unusually innovative, and you have not yet made a paradigm-shifting discovery or solved a very difficult problem, which aspect of the logic of the experimental approach suggests that there is some probability that the proposed research will be successful, or that the approach should be tried in spite of the risks?

- vii. **Implementation Pathway** – If the exploratory analysis is highly successful, what would be the anticipated next steps for validation to get this in human trials?

Descriptions exceeding the 15-page limit will not be considered. [For more detailed description of the proposal narrative, please download Proposal narrative in templates section of ProposalCentral.](#)

d. **Cited references:** A list of up to 20 references (maximum) supporting the project description is allowed.

e. **If appropriate - IRB protocol (or international equivalent):** We recognize that the IRB approval (or international equivalent) may not have been granted by the time of the grant submission, however we request that a proposal be submitted for review by the time of the full grant application, and that this protocol is uploaded to the grant review. If the IRB application (or international equivalent) is approved, please list the number.

f. **For multi-institutional proposals:** Attach a letter from the Administrative PI's institution confirming that if the award is made, the institution will execute the necessary sub-award agreements within 30 days of execution of the award agreement between Epilepsy Foundation and the applicant institution and will transfer funds from their institution to the collaborating institution(s).

13. **Validate:** Check for any missing required information.

14. **Signature pages:** Print the signature page, which must be signed by the PI and the institution's signing official, and uploaded as part of the application package.

15. **Submit:** Please note that no proposals will be able to be submitted past the deadline. Technical support for the on-line application system is not available after 5:00 PM Eastern Time.

TIMELINE

- **March 15, 2019:** Submissions open
- **June 21, 2019:** Letters of Intent are due by 5:00 pm Eastern Time.

- **August 5, 2019:** Applicants are notified of their status.
- **November 29, 2019:** Full-length proposals are due by 5:00 PM Eastern Time
- **January 6, 2020:** peer and organizational review
- **January 20, 2020:** Awardees notified (Epilepsy Foundation may adjust date without notice to applicants)
- **February 2020:** Projects commence

REVIEW MECHANISM

All proposals will undergo rigorous peer review by the Epilepsy Foundation, comprised of experts in Epilepsy and diverse areas of data science, mathematics, and precision medicine. Applications will be scored based on Significance, Investigator, Innovation, Approach, and Environment. Specifically, the quality of the science, strength of the team, uniqueness and thoroughness of the approach and value relative to the budget will be considered. Applications that are utilizing existing data sets and/or are attempting to correlate macro-network recordings (such as EEG and fMRI) with physiological mechanisms on the microscale are strongly encouraged.

The Epilepsy Foundation will provide reviewer evaluations to applicants through proposalCENTRAL. Depending on peer review and Ei² program priorities, the Epilepsy Foundation may work with applicants to modify the submitted work plan and/or budget.

AWARD ADMINISTRATION

AWARD LETTER

Upon acceptance of an award, the PI and his/her employing Institution will be required to sign an Award Letter indicating acceptance of Epilepsy Foundation Award Terms and Conditions within 30 days. The Epilepsy Foundation must be notified in advance and approve of any significant changes in research objectives, key personnel, or budget both at the time of the award and throughout the term of the award. This includes moves of key personnel between institutions.

APPROVALS

The Epilepsy Foundation requires certification through proposalCENTRAL of compliance with Human Subjects and Animal Care Assurance as applicable. In cases where ethical/regulatory approval is required to perform the work, such approvals will be required before initial payments are made.

MULTI-INSTITUTIONAL PROJECTS

For projects including key personnel at other institutions, the PI must verify in advance that funds can be transferred from his/her institution to the collaborating institution. This requirement can be met by

attaching a letter from the PI's sponsored programs office stating a commitment to comply with this requirement. Sub-award agreements between collaborating institutions must be executed within 30 days of the Epilepsy Foundation's execution of the award agreement with the applicant institution, and will be subject to the Epilepsy Foundation Award Terms and Conditions.

FUNDING

For all proposals, the level and duration of funding may be adjusted by the Epilepsy Foundation as appropriate for the scope of the proposal and the funds available. Partial funding will also be considered to obtain proof-of-principle data in support of innovative ideas with transformative potential. The Epilepsy Foundation will not provide more than 10% of the total award amount for indirect costs, overhead costs, or other similar institutional charges. Full-term funding will be contingent upon review of annual progress reports and other oversight activities conducted by the Epilepsy Foundation. Multi-year support is not automatic for any Epilepsy Foundation award and is conditioned on submission of complete and accurate progress reports and demonstrated progress on the funded proposal.

ANNUAL MEETING

PIs whose projects are selected for funding are expected to attend the annual Ei² meeting, at which they will present research findings made under their awards to an advisory group. The Epilepsy Foundation will cover reasonable travel costs related to participation in these meetings.

FREQUENTLY ASKED QUESTIONS

ELIGIBILITY

Q: Must PIs have an academic faculty appointment? Is this a hard-and-fast rule?

A: PIs must have a full-time appointment at an academic, non-profit research institution or biomedical-focused industry organization at the level of Assistant Professor (or equivalent) or above; however, while a tenure-track is preferred, it is not required. Evidence of independent investigator status and an environment conducive and supportive of translational research is required. If there is any doubt or question about a PI's eligibility, please contact Ei² (contacts provided below) before an application is submitted. Applications from PIs who do not fit the eligibility criteria will not be reviewed.

Q: Does Ei² fund investigators and institutions outside of the United States?

A: Yes, investigators at institutions outside of the United States are eligible. PIs must be at the level of Assistant Professor or equivalent. Academic appointments of institutions outside of the US can differ from those traditionally found in the US. Contact Ei² if there are any questions about eligibility prior to submitting a proposal.

Q: If I am awarded the grant, and my proposal is successful, will there be potential to request additional follow-up funds to validate the tool that was developed?

A: Yes. If the proof of concept exploratory project is funded and is extremely successful, there may also be opportunities to apply for follow on funding from Ei² to validate the work in the clinic. More details to follow for those who are successful in their grant application.

APPLICATION COMPONENTS

Q: How are LOIs submitted? Do I need to send a hard copy?

A: All LOIs must be submitted electronically via proposalCENTRAL. Hard copies will not be accepted.

Q: How are full proposals submitted? Do I need to send a hard copy?

A: All proposals must be submitted electronically via proposalCENTRAL. The signature page should be signed and a scanned PDF copy be uploaded as part of the application in proposalCENTRAL. Hard copies will not be accepted.

Q: Does the Epilepsy Foundation require the NIH salary cap to be used when calculating salary and fringe benefit requests for the budget?

A: Yes.

Q: What needs to be included in the “other support” section?

A: Please submit a listing of all sponsored research support for the effort of the PI that is active or pending (submitted or awarded by a research sponsor but not yet started). Include the title of the project, research sponsor, total annual funding, start and end dates, and percent of committed time. For each project, you must include a statement of overlap or non-overlap with the Ei² My Brain Map proposal. A template is provided in proposalCENTRAL.

Q: Is the NIH biosketch CV format acceptable for submission?

A: Yes, you may use your NIH biosketch or the template provided in proposalCENTRAL.

Q: Could the team be composed of a public/private partnership?

A: Yes, the team can be a mix of industry and academic partners.

ADDITIONAL INFORMATION AND CONTACTS

Technical questions about the proposalCENTRAL submission system should be directed to their customer support at 800-875-2562 (Toll-free US and Canada), +1 703-964-5840 (Direct Dial International), or by email at pcsupport@altum.com.

For administrative questions regarding this RFP and eligibility, please email Liz Schreiber, Grants and Fellowships Program Manager, at lschreiber@efa.org.

For other questions regarding the My Brain Map initiative, please contact Sonya Dumanis, Senior Director of Innovation, at sdumanis@efa.org.