How do I get beamtime, and money? Some comments on writing proposals

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Support: Basic Energy Sciences, US Department of Energy; National Institutes of Health

Proposals and peer review

- In an ideal world, all scientists would have full financial and facilities support for their research.
- In the real world, there are finite resources for both funding and access. Fortunately this is allocated by anonymized peer review.

> **Winston Churchill: "It has been said that democracy is the worst form of Government, except for all those other forms that have been tried from time to time…"**

- Hopefully your advisors will give you a chance to contribute to the writing of proposals, and at some point you will be asked to review the proposals of others.

MAX-IV proposals

“Research Area” to be selected in DUO:

- **Structural Biology** for beamtime at the BioMAX beamline.
- **Spectroscopy** for beamtime at the Bloch, FinEstBeAMS, FlexPES, HIPPIE, MAXPEEM, SPECIES and Veritas beamlines.
- **Nano science** for beamtime at the NanoMAX beamline.
- **Chemistry** for beamtime at the Balder.

CET 23:59, Tuesday 17 March 2020	DUO opens 20 February 2020	September 2020 - February 2021 (BAG: September 2020 - August 2021)	General users

Program Advisory Committee

- “Proposals are evaluated by the Program Advisory Committee (PAC) who provide recommendations for the allocation of beamtime. The final decision on beamtime allocation is taken by the MAX IV Laboratory management.
- The scientific merit, the proposal feasibility and the technical safety check of the proposed experiment will be the guiding criteria for awarding beamtime. Previous experimental reports will be of importance in the proposal evaluation process.
- To assist in the allocation of beamtime, a MAX IV Programme Advisory Committee (PAC) is appointed. The committee reviews and evaluates submitted proposals and provides recommendations for the allocation of beamtime, based on the scientific excellence and feasibility of the suggested experiments.”

Who are the PAC members?

- **Do NOT contact them directly**.
- But **DO** look up their research specialties.
- At some facilities, *ad hoc* reviewers might also be consulted regarding specific proposals.

- Margarida Archer Frazao, Instituto de Tecnologia Quimica e Biologia (ITQB), Portugal
- Oliver Bunk, Paul Scherrer Institute (PSI), Switzerland
- Ralf Ficner, Georg-August-Universität Göttingen, Germany
- Wendy Flavell, University of Manchester, UK
- Sine Larsen, University of Copenhagen, Denmark
- David Le Bolloc’h, Université Paris Sud, France
- Gema Martínez Criado, CSIC – Instituto de Ciencia de Materiales de Madrid (ICMM), Spain
- John McGeehan, University of Portsmouth, UK
- David Mueller, Forschungszentrum Jülich, Germany
- Virginia Perez Dieste, ALBA Synchrotron Light Source, Spain
- Ehmke Pohl, Durham University, UK
- Laszlo Vincze, Ghent University, Belgium
- Phil Woodruff, University of Warwick, UK

Steps in writing a beamtime proposal

1. **Contact the beamline staff!**
   A. Is your experiment feasible at the beamline? **They might even be able to run a test specimen for you "squeezed in"!**
   B. Is that beamline the best place to do your experiment?
   C. What hints can they offer you on how the Programme Advisory Committee (PAC) looks at different proposals? What does the PAC "like," and what does it "dislike"?
2. Write a draft of your proposal and circulate it amongst your team.
   A. One approach is to transcribe the web form questions into a Microsoft Word or Google Docs file that all the team can look at, and edit.
3. Submit the proposal no later than a few hours before the deadline
4. When you get your score and reviews back:
   A. The user office might be able to tell you how your score compares with averages; beamline staff might also know this.
   B. Look carefully at the comments the reviewers provide. Sometimes you get some very useful feedback; unfortunately you can also get very unhelpful feedback like "Experiment not deemed compelling."
   C. **Do NOT contact the PAC members directly** to ask them about the review of our proposal, before or after!!!!

Ingredients in a MAX-IV proposal

A) Goal of the experiment

- **Step outside of your speciality.** Can your goal be understood by someone who's *not* a specialist in your area?
- **Your first sentences can color a reviewer's view of your entire proposal!** Make them memorable, with some flair!

B) Scientific background

- Don't say bad things about results or approaches used by others! At most say "These interesting previous results worked in the limits of XXX. However, a complete understanding requires one to consider YYY which is central to our proposal."

C) Experimental method; specific requirements

- Will the beamline staff say that your experiment is technically feasible on their beamline?
- Does it have extra requirements that are more costly in terms of non-standard setup that would otherwise eat into beam time?

D) Results expected and their impact

- **If your experiment succeeds, who cares?** What might it lead to? A new understanding, a new process, a new disease cure?

Ingredients in a MAX-IV proposal (continued)

E) Relation to previous experiments
- If you received beamtime before, have you submitted an activity report to the facility?
- Have you published results, and submitted them to the facility's database?

F) Justification of the beamtime and beamline
- Ask the beamline staff for guidance.

G) References relevant to the experiment description
- Don't toss gratuitous citations in there… but are you citing important papers by those who might be reviewers of your proposal?

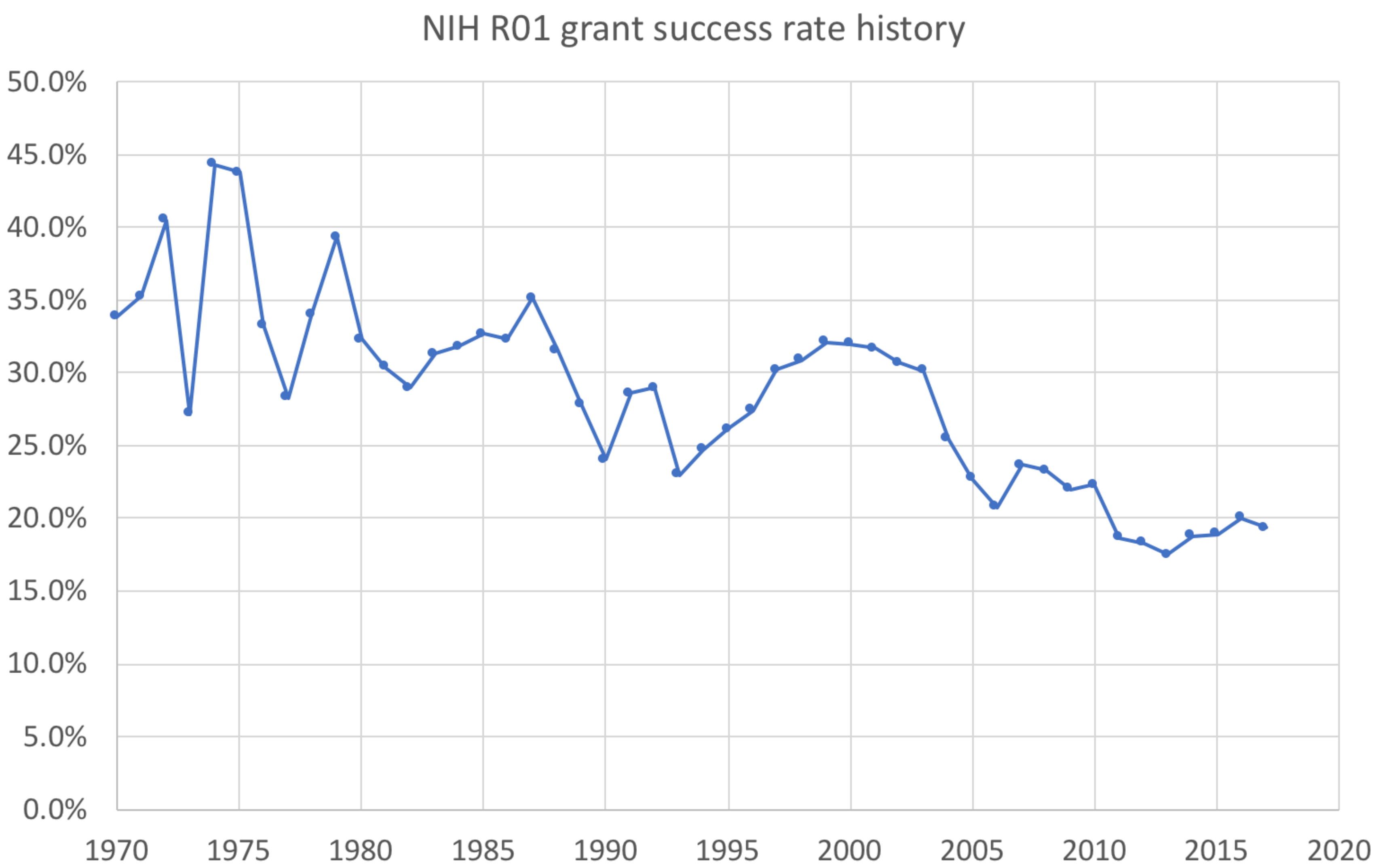
From beamtime proposals to funding proposals

- Some of you may be leading your own laboratories someday!
- At universities in the USA, your job gives you your salary for 9-12 months (0-6 months at some US medical schools), and often not much else. You have to get funding to actually do any research!
  - New faculty might get startup funds to set up a lab and make an initial start on research - such as for the first three years.
  - Very successful senior faculty might get an “named chair” which provides a modest bit of research funding.
- In the USA system, graduate students are paid for their first year by the university to work as teaching assistants, and then they need to be paid by the professor’s research grants. There are some exceptions, but that’s the usual route.
- Postdocs and Research Professors are usually paid out of grants, too - so-called “soft money” positions, because if the research grant goes away, the job goes away too.
- Getting funding is a key step towards getting tenure at a US university.

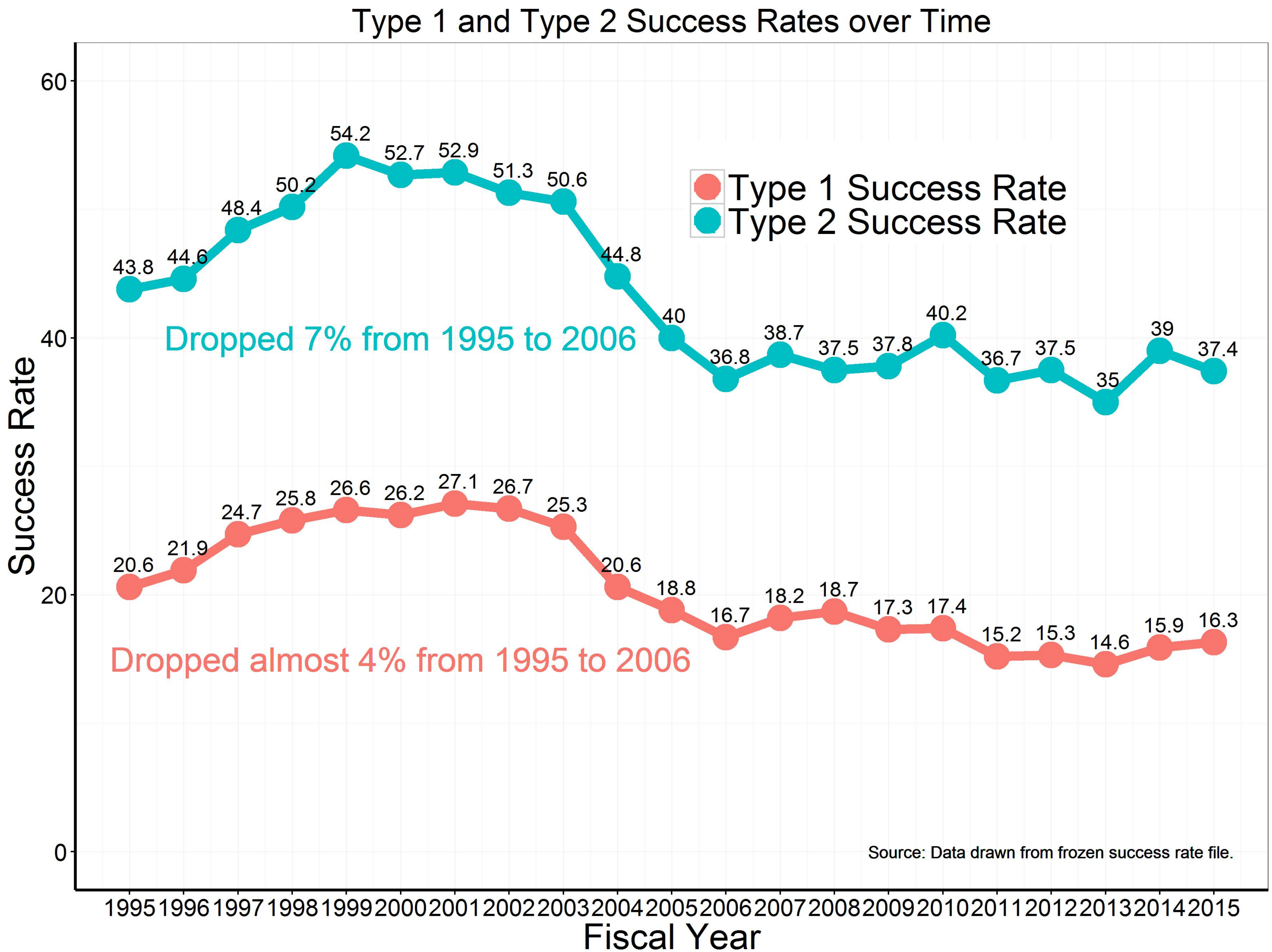
USA science funding agencies

- US Department of Energy (DoE)
  - Mostly supports staff at the basic science National Laboratories (Argonne, Brookhaven, Lawrence Berkeley, Oak Ridge, Pacific Northwest/PNNL, Stanford/SLAC).
  - Or at the National Nuclear Security Agency labs (Los Alamos, Lawrence Livermore, Sandia)
  - Some university support too, but only as targeted by specific program managers.
  - Program managers have long tenures and considerable decision-making power, with less peer review ("dictionary" for program managers to write a summary review).
- National Science Foundation (NSF)
  - Basic research, aimed mainly at University researchers.
  - Grants are often modest (like $150K/year), and have education and training requirements.
  - Strong peer review. Program directors include a mix of permanent staff, and people who come in from universities for 2 year "rotations"
- National Institutes for Health (NIH)
  - Biomedical research, including basic biology or methods that might eventually lead to understanding of and treatments for disease.
  - The core grant is the R01 single investigator grant; often about $250K/year in direct costs. Indirect costs add ~50%, so real award might be for $375K.
  - Two stage process: Center for Scientific Review to assign priority scores, and then permanent program managers to assign funding based on the agendas of various institutes.
- And others… but those are the big 3.

NIH R01 success rate



First-time (type 1) versus renewals (type 2)



NIH R01 success rates

Fiscal Year	Application Type[1] and Submission Number[2]	R01-EQUIVALENT GRANTS[4]			
		Number of Applications Reviewed	Number of Applications Awarded	Success Rate[5]	Total Funding[6]
2016	New First Submission (A0)	18,691	2,248	12.0%	$1,248,669,338
2016	New with Resubmissions (A1)	7,555	2,342	31.0%	$1,128,744,694
2016	Continuations (A0)	2,142	751	35.1%	$369,845,997
2016	Continuations with Resubmissions (A1)	1,643	645	39.3%	$288,385,175
2016	Supplements	75	24	32.0%	$6,762,600
2016	**FY Total**	**30,106**	**6,010**	**20.0%**	**$3,042,407,804**

- If your grant submission doesn't get funded, look *carefully* at the reviewer comments and see if you can address them.
- If they didn't understand your proposal, that's your fault rather than their fault!

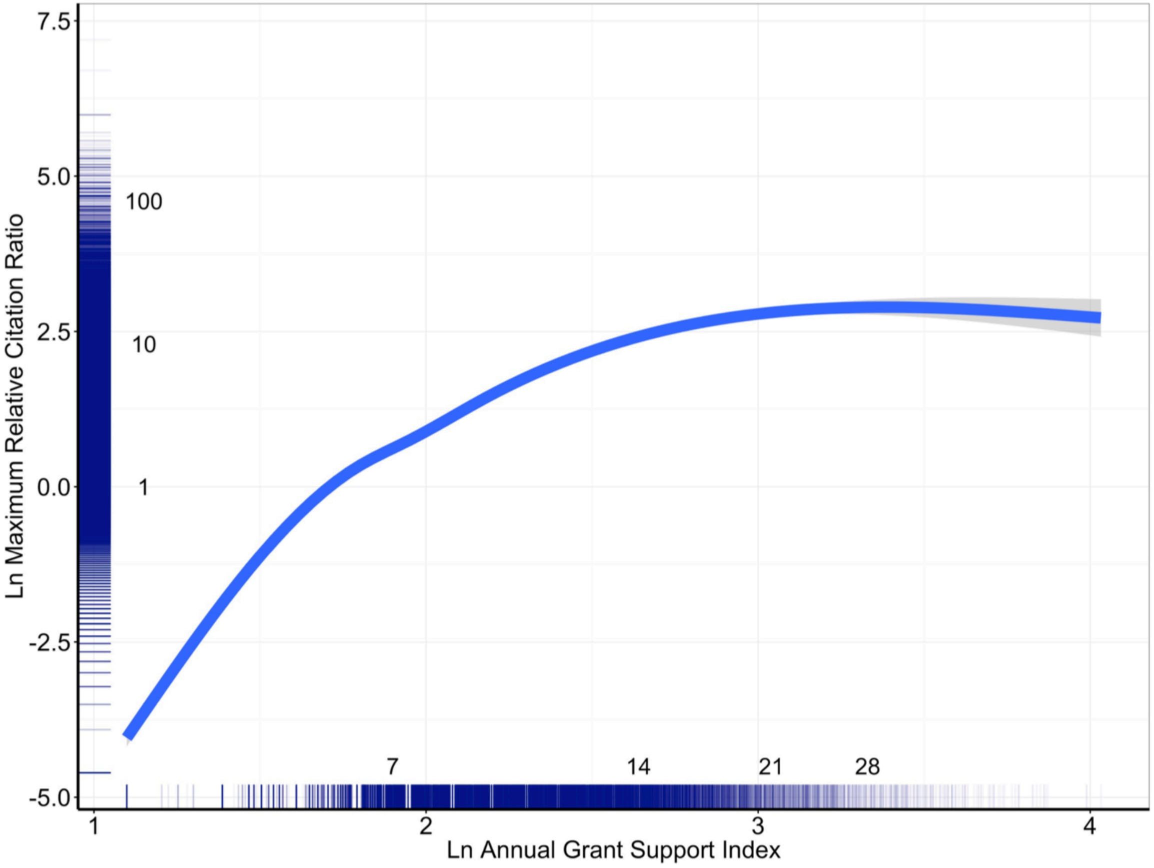
bioRχiv
THE PREPRINT SERVER FOR BIOLOGY

Marginal Returns And Levels Of Research Grant Support Among Scientists Supported By The National Institutes Of Health

Michael S. Lauer, Deepshikha Roychowdhury, Katie Patel, Rachael Walsh, Katrina Pearson

doi: https://doi.org/10.1101/142554

There's lots of discussion on this paper!



Argonne NATIONAL LABORATORY

Ingredients in a NIH R01 proposal

- Cover letter: what review committee? What program officer? Any reviewers to exclude? (1 or 2 are OK to exclude - excluding 10 sends a very bad signal!)
- Curriculum vitae of the investigators in a specific format.
- Budget request and justification.
- List of available equipment and facilities (does the investigator have adequate lab space and instruments, or does the institution have core facilities with equipment that will be required?)
- Project summary: your whole proposal in one paragraph. **Very important!** This initiates the mindset of the reviewer towards your proposal.
- Specific aims: one page, where you might list three distinct goals that you hope to achieve. **Also very important!**
- Research strategy: 12 pagers of text to explain Significance, Innovation, and Approach. The meat of the proposal.

NIH Center for Scientific Review

- Review panel with ~25 scientists. Mostly university researchers, but some national lab and even biotech industry reviewers - all PhDs. Broad expertise.
- One panel might have ~50 proposals assigned to it for a one-day meeting.
- Each reviewer might have 6-8 proposals to review: 2-3 primary, and 4-5 secondary.
- Online submission of preliminary score, to "triage" the best 40% of proposals. You get to read the reviews of others only **after** you have submitted your own reviews - that's good!
- In-person meeting:
  - Three reviewers give their scores (1=best, 7=worst).
  - Lead reviewer summarizes proposal, and then gives his or her reaction to it.
  - Secondary reviewer might say "I agree," or "I agree except for," or "I disagree because of." Tertiary reviewer also comments. Sometimes one reviewer may say "I had missed that in the proposal; I'm glad you brought that out!"
  - Panel can ask questions and discuss.
  - Three reviewers re-visit their numerical scores. Panelists have the option of giving a score outside of the range of the three reviewers, but then they need to provide a written explanation.
  - Three reviewers have the chance to modify their written reviews.
- You get to learn who's on the panel, but not which individuals wrote your three reviews.

A recent panel on neuroscience imaging technologies

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Reviewer reports

- You get what you pay for!
- Mail-in reviews tend to be less thorough, and can veer off in different directions.
- Beamtime proposal reviews often produce only a few sentences, where it is hard to know why you received the score you did. This is unfortunate.
- In-person review panel meetings are more expensive (travel etc.) but offer several powerful advantages.
  - It is easy to have one's bias be hidden behind a score number, and a 2-3 sentence review. One is forced to be more open-minded and objective when verbalizing and defending one's reaction to a proposal to a group of your peers, and following it up with a 2-3 page written review.
  - The discussion often leads to consensus regarding a proposal, though sometimes an agreement to disagree.
  - NIH program officers attend the reviews, but cannot offer opinions; at most, they might ask one or two questions. This really is **peer group** review, rather than gut feelings by program officers who are no longer active researchers and who may (like anyone else) be affected by personal likes and dislikes.

Reviews of a recent NIH R01

SUMMARY STATEMENT

(Privileged Communication)

PROGRAM CONTACT:
Fred Friedman
301-443-4058
ffriedma@mail.nih.gov

Release Date: 06/21/2017
Revised Date:

Application Number: 1 R01 MH115265-01

Principal Investigator

JACOBSEN, CHRIS JOHNSON

Applicant Organization: NORTHWESTERN UNIVERSITY

Review Group: NOIT
Neuroscience and Ophthalmic Imaging Technologies Study Section

Meeting Date: 06/08/2017
Council: OCT 2017
Requested Start: 10/01/2017

RFA/PA: PA16-160
PCC: 1H-TDB1
Dual IC(s): EB

Project Title: Development of Sub 100 nm Resolution X-ray Nanotomography of Centimeter-Sized Tissues
SRG Action: Impact Score:23 Percentile:11
Next Steps: Visit https://grants.nih.gov/grants/next_steps.htm
Human Subjects: 10-No human subjects involved
Animal Subjects: 30-Vertebrate animals involved - no SRG concerns noted

Project Year	Direct Costs Requested	Estimated Total Cost
1	250,000	358,799
2	250,000	358,799
3	250,000	358,799
4	250,000	358,799
TOTAL	1,000,000	1,435,195

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

Panel summary (written by chair)

RESUME AND SUMMARY OF DISCUSSION: This is an application from an investigator who plans to develop sub 100 nanometer (nm) resolution x-ray nanotomography of centimeter-sized tissues. It is significant because if successful it will utilize cryogenic dissection and x-ray techniques to produce whole brain images. The premise is sound and the work viewed as exciting, and could lead to new insights into brain anatomy. The investigator is a physicist with a track record of accomplishment in similar technology development with information extraction in x-ray microscopy, and the team is outstanding. The level of innovation is considered very strong with the use of point-projection x-ray focusing to obtain sub-micron level information from x-ray beam microscopy; it was noted that the image reconstruction techniques were fairly standard. The approach is well developed, generally very rigorous, and is mainly technology development. Some reviewers wanted to see what new anatomical information would be obtained. The team will be able to process very large sets of brain imaging data of the whole mouse brain. Sex as a biological variable was not considered in the approach. The environment is strong with unique facilities for execution of the plan; access was a minor concern. Overall reviewers thought this was an extremely strong application.

CRITIQUE 2

Significance: 2
Investigator(s): 2
Innovation: 3
Approach: 3
Environment: 2

Overall Impact: To further enhance resolution capabilities of x-ray tomography, the PI proposes to develop; a) methods to obtain sub-100 nm resolution tomographic images of thick specimens using point projection x-ray microscopy, b) cryogenic sample preparation and imaging capabilities to mitigate radiation damage effects; and c) validate image reconstruction methods and cryogenic preparations for neuroanatomic studies. While the strength of the proposal lies in high significance, strong scientific premise, track record of the principle investigator, innovation, significant scientifically robust pilot data on feasibility of proposed studies, and institutional infrastructure, there are also minor concerns associated on comparative analysis of proposed methodology with existing state of the art techniques and lack of discussion on alternative strategies and remedial measures, if the proposed design does not deliver desired resolution. Overall, the level of enthusiasm on successful realization of proposed aims of this well-conceived proposal is extremely high.

1. Significance:

Strengths

- Over the last 2-decades, high resolution imaging has revolutionized biomedical research. Among various techniques, x-ray tomography (using parallel beam methods) provides an important complementary capability of imaging whole and intact mouse brains with isotopic resolution (1 μm) without distortions from sectioning. Extending resolution capabilities below sub 100nm range will allow better understanding of pathophysiology of neurodegenerative diseases thus aiding design of new molecular imaging probes and therapeutic interventions to treat those conditions.
- The proposed methodology is highly significant, and is based upon previous seminal contributions to the field thus based upon a strong scientific premise.

2. Investigator(s):

Strengths

- The PI is Professor in the department of Physics & Astronomy and a distinguished fellow, within Argonne National Laboratory.
- The PI has pioneered first 100 nm resolution 3D image of a frozen hydrated mammalian cell, using a soft x-ray cryogenic microscope and sub-micrometer resolution x-ray fluorescence tomography for obtaining 3D views of trace elements in cancer cells
- He is a highly accomplished principal investigator and fully-equipped to design the methodology.

3. Innovation:

Strengths

- Development of point projection x-ray microscopy, using cryogenic sample preparation for imaging is an innovative initiative.
- Improvement of spatial resolution could enable advancement from cell identification to cell classification and subcellular structure identification thus facilitating studies within intracellular compartments of studied tissues.

4. Approach:

Strengths

- The PI proposes to develop; a) methods to obtain sub-100 nm resolution tomographic images of thick specimens using point projection x-ray microscopy, b) cryogenic sample preparation and imaging capabilities to mitigate radiation damage effects; and c) validate image reconstruction methods and cryogenic preparations for neuroanatomic studies.
- This is a well-written and -argued proposal for discovering new methodologies to perform X-ray tomography at high resolution.
- Provocative pilot data on feasibility of the approach using x-ray microtomography data from a cubic millimeter brain sample imaged at the APS.
- Well-conceived alternative strategies to overcome unanticipated difficulties at various stages of the project.

Weaknesses

- Minor weakness continues to be on consideration of alternative strategies and remedial measures, if the proposed design does not deliver desired resolution.

5. Environment:

Strengths

- All infrastructure and instruments either available or the PI have access to these resources via institutional arrangements. Therefore, the environment for the project is outstanding.

Vertebrate Animals:

Acceptable

Budget and Period of Support:

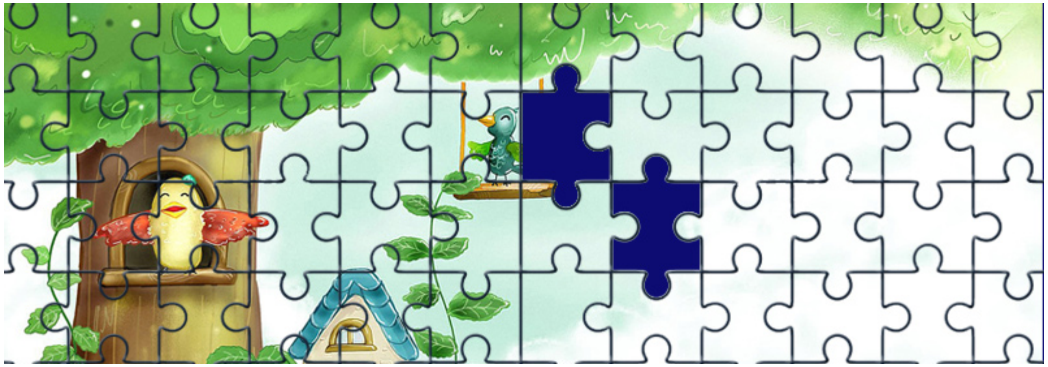
Recommend as Requested

The job of a reviewer

- Take a broad view. Encourage diversity of investigators, and topics, without surrendering quality. Science is filled with advances coming out of surprising areas; be humble on how certain you are that **this** is important today and **that** is not.
  - As a side note, a lot of important papers appeared in “routine” journals, rather than in *Nature.* Consider 2017 Nobel Prize for single particle imaging:
    - Dubochet: key early papers were in *Journal of Microscopy* and *Ultramicroscopy*.
    - Frank: key early papers were in *Trends in Biochemical Sciences* and *Ultramicroscopy.*
    - Henderson: key paper was in *Nature*, but other important papers in *Quarterly Review of Biophysics* and *Journal of Molecular Biology*.
- But also ask this question: if the proposed work is fully successful, what follows afterwards? Might it lead to important new insights, or important new capabilities? Or just an incremental advance along well-trodden paths?

Phrases that really irk me as a reviewer

- "Understanding XXX is crucial for forming a full picture of YYY."



- "The role of XXX in the YYY process is unclear."
  - Do you have a testable hypothesis? Is your experiment likely to lead to a fundamental understanding, or just more phenomenology?
- "There is a clear need for the ability to do XXX."
  - Have you made this clear to me as a literate scientist who is, however, not an expert in your specialty?
  - Are you aware of competing approaches? Can you describe why they do not provide all the information required, yet without bad-mouthing the existing approaches?

Some actual review comments

- As the proposal points out, life on earth involves a selected chirality for biomolecules, affecting things like the chirality required in organic synthesis of some drugs. However, it would have been nice to see just a bit more about what the ultimate implications of this work would be. As is pointed out in the proposal, this will be one of the first studies of ultrafast dynamics in chiral systems at FELs. But beyond being one of the first, why is this experiment important to do?
- A very minor point regarding the introductory statement "**The strong-field laser interaction… has been at the forefront of scientific exploration during the last years and decades**": this seems a bit overdone. There have been certain topics that have been at the forefront of ALL of science at certain times; these are often reflected in Nobel Prizes for certain specific advances, such as for the the discovery of gravitational waves, or the Higgs boson and the origin of mass, etc. Perhaps a more honest statement is to say that "the strong-field laser interaction has been the subject of ongoing study for decades, with new insights emerging continuously."

Some final comments

- Step outside of yourself when you write a proposal. Realize that your reviewers will be competent scientists, but often not from within your exact detailed specialty.
- You have to do many things:
  - Explain why your work is important, in terms a **non-expert** can understand.
  - Provide enough detail of your approach, and alternative strategies, to convince an **expert** that you have a plausible plan.
  - Show that you are aware and appreciative of prior work.
  - Make it clear what you will actually do if you get the requested beamtime, or money. A strong research topic but a poor mapping onto requested beamtime and/or funding weakens a proposal.
    - Beamtime: first record data on X, then on Y, then if time permits on Z.
    - Funding: hire person A to do task B, person C to do task D, etc.
  - Find the right mix of making your competence clear while also not coming off as superior to your reviewers.