Example TP1 review for reference

Training Proposals
These proposals are a different category than instrumentation access. We can take on a limited number of people who want to shadow our staff as they operate a national facility and center to learn best practices and our workflow. The proposal below probably should be treated more like a TP1 (embedded training) rather than a TP2 (facility manager training)

1) Project ID: NCCAT-TP2-GJ181106 (*submitted as TP2 re-categorized as TP1*)
Project Name: Embedded User Training to Establish Cryo-EM at Brown University
Primary User Name: Gerwald Jogl
eRA Commons User Name: G_JOGL
Institution: Brown University, RI
Submission Date: November 06, 2018 8:41 pm

Averaged URC scores:
(i) training goals: **1.5**
(ii) training plan: **3**
(iii) resources requested: **4**
(iv) user EM background and history: **2**
(v) geographical demographics or need: **1**
Raw average score: 2.3

Comments:
Reviewer 1:
This is a request of training on sample preparation, EM operation, and data processing. Vitrobot training can be achieved in 1/2 a day from a qualified staff member, but the request for both EM training and data processing seems to be ambiguous. The user also proposed to use their own sample for the training but failed to provide information on sample quality or prescreening results. Suggest to revise to a request for EM training only, and to either provide sample quality data, or to use a well characterized sample from the center.
This proposal demonstrates the need to obtain cryo-EM expertise by the applicant. It lays out objectives & milestones, but does not indicate the specific steps for each objective, number of staff, or access to computing needed to reach these goals. As such, the applicant should be more explicit in their expectation of oversight from NCCAT staff.

Reviewer 2:
For objectives 2 & 3 the user will collect high-resolution cryo-EM data on their sample. Based on the biosketch, I assume this is a ribosome sample? The applicant does not explain the sample, nor how they will go from purified sample to cryo-EM grids that will be screened. For instance, how much screening time is needed ahead of objective 2 high-resolution data collection? Then, once data is collected, where the data be processed? Finally, the application plans 2 or 3 day-long visits to learn the entire cryo-EM process, and this appears to be not enough time to go from novice to independent.

Reviewer 3:
N/A

Project ID: NCCAT-TP2-GJ180611
Primary User Name: Gerwald Jogl
eRA Commons User Name: G_JOGL
Project Name: Embedded User Training to Establish Cryo-EM at Brown University

Summary statement:
The overall goal of this proposal is to train a scientist to become an independent cryo-EM researcher.

Training Goals:
Training goal: Gain sufficient experience to carry out independent cryo-EM structure determinations.
Areas: cryo-EM grid preparation, data collection and data processing.
Scope of training: all practical aspects related to instrument usage and being able to efficiently interface with staff at the NCCAT.

Training Plan:
Specific objective 1: learn to prepare cryo-EM grids
Milestone: successful evaluation of grids on a screening microscope
Current proficiency: I have observed grid preparation using a vitrobot.
Specific objective 2: learn how to collect cryo-EM data
Milestone: collection of high-resolution data from our sample
Current proficiency: I have observed grid evaluation on a screening scope.
Specific objective 3: learn how to process cryo-EM data
Milestone: calculation of a final map from own data and write-up of experimental methods for a publication
Current proficiency: None. I worked through the Relion tutorial.

Resources requested:
I envision two- or three-day visits throughout spring 2019 to cover the three objectives separately until all milestones have been achieved. Required time and resources will be determined following advice from trainers. Samples from our ribosome research will be used to drive the training program.

Background and history:
Current expertise: I am a faculty at Brown University in Providence, RI. My lab studies ribosome structure and function of the ribosome with a focus on antibiotic resistance mutations. We primarily use X-ray crystallography. Since about 2 years, I am collaborating with Reza Khayat at the City College to use cryo-EM for our projects. On several visits to his lab, I have observed grid preparation using the Vitrobot and preliminary grid evaluation on a screening microscope. I have watched the online cryo-EM course by Grant Jensen as well as the MRC Cryo-EM17 lecture series to familiarize myself with the method.
Instrumentation at Brown University: We recently obtained funding to purchase a Vitrobot. There is currently no screening microscope available at Brown. We envision applying for an instrumentation grant to purchase an instrument that will then be housed in the Brown Microscopy facility. Facility manager Geoff Williams has substantial EM expertise, which will help with this effort.

Geographical Demographics:
The impact of this training for the local EM community will be substantial. The only faculty on campus with cryo-EM experience is my colleague Alexandra Deaconescu who trained with Niko Grigorieff. With a second active user on campus, we will be able to apply for internal and external funding to purchase a screening microscope and enable more efficient use of high-resolution instrumentation at nearby cryo-EM centers. In addition, there are several groups on campus who would be highly interested in collaborating with a local cryo-EM group. Their research programs would benefit significantly by having active EM users on campus.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: JOGL, GERWALD

eRA COMMONS USER NAME (credential, e.g., agency login): G_JOGL

POSITION TITLE: Associate Professor of Biology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Karl Franzens Universität Graz, Austria	Mag. rer. nat.	05/1994	Chemistry/Crystallography
Karl Franzens Universität Graz, Austria	Dr. rer. nat.	12/1999	Chemistry/Protein Cryst.
Columbia University, New York	Post-Doc	08/2004	Structural Biology

A. Personal Statement

The course of my professional training reflects my overall goal to contribute to the development of new drugs for the treatment of human disease. My undergraduate research in chemistry and small molecule crystallography focused on the structure of cob(II)alamin, the radical species of coenzyme B12. My graduate research extended this work to structure-function studies of coenzyme B12 binding enzymes. During my postdoctoral training, I contributed to the structural biology of enzymes in central metabolic pathways (eg. triose phosphate isomerase) as well as enzymes in fatty acid metabolism that are potential drug targets for the treatment of obesity (eg. carnitine acetyl transferase, acetyl Co-A synthetase, carnitine palmitoyl transferase). Overall, I acquired substantial expertise in X-ray crystallography and neutron crystallography that provides a strong foundation for our current work. After I moved to Brown University, I began a collaboration with Dr. Steven Gregory. Our long-term vision from the very beginning was to build a collaborative research team to leverage our combined expertise in genetics and structural biology to study ribosome structure and function. In the past years, we succeeded in independently reproducing well-diffracting crystals of *Thermus thermophilus* 70S ribosomes carrying base substitutions in ribosomal RNA or even deletions of ribosomal proteins. Recently, we began using cryo-EM in collaboration with Dr. Reza Khayat to study antibiotic-dependent mutant ribosomes. Insights from this work will contribute to the molecular understanding of decoding by the ribosome.

1. Demirci H., Murphy IV F.V., Murphy E., Gregory S.T., Dahlberg A.E., Jogl G. (2013). A structural basis for streptomycin-induced misreading of the genetic code. Nature Comms. 4, 1355. PMCID: PMC3552334
2. Demirci H., Wang L., Murphy IV F.V., Murphy E.L., Carr J.F., Blanchard S.C., Jogl G., Dahlberg A.E., Gregory S.T. (2013). The central role of protein S12 in organizing the structure of the decoding site of the ribosome. RNA 19(12), 1791-801. PMCID: PMC3884664
3. Demirci, H., Murphy IV F.V., Murphy E.L., Connetti J.L., Dahlberg A.E., Jogl G., Gregory S.T. (2014). Structural analysis of base substitutions in *Thermus thermophilus* 16S ribosomal RNA conferring streptomycin resistance. Antimicr. Agents Chemotherapy 58(8), 4308-17. PMC: PMC4136021.
4. Gregory S.T., Connetti J.L., Carr J.F., Jogl G., Dahlberg A.E. (2014). Phenotypic interactions among mutations in a Thermus thermophilus 16S rRNA gene detected with genetic selections and experimental evolution. J. Bact. 196(21), 3776-83. PMC: PMC4248807.

B. Positions and Honors

Positions and Employment

2011 – present	Associate Professor of Biology, Brown University
2004 – 2011	Assistant Professor of Biology, Brown University.

Professional Memberships and Other Experience

2004 – present	Member, American Crystallographic Association
2006 – present	Member, American Society for Biochemistry and Molecular Biology
2008 – present	Member, RNA Society
2010	National Science Foundation major research instrumentation review panelist
2012 - present	Ad hoc referee for Acta Crystallographica, Biochemical Journal, Biochemistry, Biomed Central Structural Biology, Biomed Central Microbiology, FEBS Journal, Journal of Bacteriology, Journal of Molecular Biology, Nucleic Acids Research, PLoS One, RNA
2012 - present	Ad hoc grant proposal reviewer for the Biotechnology and Biological Sciences Research Council, UK, the Czech Science Foundation, the Universities of Vienna and of Graz, Austria
2012 - 2015	Lecturer for the RapiData data collection and structure solving course at the NSLS I.
2014	NIH ad hoc reviewer study section ZRG1 IDM S02.
2015	NIH ad-hoc reviewer study section Macromolecular Structure and Function C.
2016	NIH ad-hoc reviewer study section Macromolecular Structure and Function B.
2017	NIH ad-hoc reviewer study section Macromolecular Structure and Function B.

Honors

1992	Erasmus, EU Student Research Scholarship with Glaxo-Wellcome Protein Structure Group, London, UK
1994	M.Sc. Thesis Award, Austrian Chemical Society.
2018	Brown University Elizabeth Leduc Award of Excellence in Teaching in the Life Sciences

C. Contributions to Science

1. Coenzyme B12. My early work in this field focused on the significance of corrin ring flexing motions for the reactivity of coenzyme B12 in enzyme catalyzed reactions. To address this question, we determined neutron crystal structures of the radical coenzyme B12 species cob(II)alamin with a vacant sixth coordination site at the central cobalt atom. Neutron crystallography required the synthesis of this radical B12 coenzyme and the production of up to 5mm long crystals in an oxygen-free environment. This work was complemented by structural studies of two coenzyme B12-dependent enzymes using X-ray crystallography and EXAFS. Our data showed that corrin ring dynamics contribute less to enzyme catalysis than had been anticipated in the field.

1. Langan P., Lehmann M., Wilkinson C., Jogl G., Kratky C. (1998). Neutron Laue diffraction studies of coenzyme cob(II)alamin. Acta Cryst. D 55, 51-59. PMID: 10089394
2. Reitzer R., Gruber K., Jogl G., Wagner U.G., Bothe H., Buckel W., Kratky C. (1999). Glutamate mutase from *Clostridium cochlearium*: the structure of a coenzyme B_{12}-dependent enzyme provides new mechanistic insights. Structure 7, 891-902. PMID: 10467146
3. Champloy F., Jogl G., Reitzer R., Buckel W., Bothe H., Michalowicz A., Meyer-Klaucke W., Kratky C. (1999). EXAFS data support a short axial cobalt-nitrogen bond of the B_{12} cofactor in the two coenzyme B_{12}-dependent enzymes glutamate mutase and 2-methyleneglutarate mutase. J. Amer. Chem. Soc. 121, 11780-11789. DOI: 10.1021/ja990349q.
4. Jogl G., Wang X., Mason S.A., Kovalevsky A., Mustyakimov M., Fisher Z., Hoffman C., Kratky C., Langan P. (2011). High-resolution neutron crystallographic studies of the hydration of the coenzyme cob(II)alamin. Acta Cryst. D 67, 584-591. PMC: PMCID 3107055.

2. Fatty Acid metabolism. My work in this field defined for the first time the structural biology of fatty acid transfer onto carnitine, a fundamental step in fatty acid catabolism. Structural and biochemical studies of four carnitine acyltransferases, crucial enzymes in fatty acid metabolism, explored the potential of these enzymes as drug targets for the treatment of obesity.

1. Jogl G. & L. Tong. (2003) Crystal structure of carnitine acetyltransferase and implications for the catalytic mechanism and fatty acid transport. Cell 112, 113-122. PMID: 12526798.
2. Jogl G. & L. Tong. (2004) Crystal structure of yeast acetyl-coenzyme A synthetase in complex with AMP. Biochemistry 43, 1425-1431. PMID: 14769018.
3. Hsiao Y., Jogl G., Tong L. (2004). Structural and biochemical studies of the substrate selectivity of carnitine acetyltransferase. J. Biol. Chem. 279, 31584-31589 (2004). PMID: 15155726.
4. Jogl G., Hsiao Y., Tong L. (2005). Crystal structure of mouse carnitine octanoyltransferase and molecular determinants of substrate selectivity. J. Biol. Chem. 280, 738-744. PMID: 15492013.

3. Structural enzymology. A number of studies reflect my keen interest in understanding enzymatic function on a molecular and structural level. These publications characterize the structure and function of enzymes either important in eukaryotic cell function or involved in biosynthesis of antibiotic compounds.

1. Jogl G., Rozovsky S., McDermott A.E., Tong L. (2003) Optimal alignment for enzymatic proton transfer: Structure of the Michaelis complex of triosephosphate isomerase at 1.2 Å resolution. Proc. Natl. Acad. Sci. USA 100, 1, 50-55. PMCID: PMC140880.
2. Holmes W. & G. Jogl (2006). Crystal structure of inositol phosphate multikinase 2 and implications for substrate specificity. J. Biol. Chem. 281, 38109-38116. PMID: 17050532.
3. You Z., Omura S., Ikeda H., Cane D.E., Jogl G. (2007). Crystal structure of the non-heme iron dioxygenase PtlH in pentalenolactone biosynthesis. J. Biol. Chem. 282, 36552-36560. PMCID: PMC3010413.
4. Li H. & G. Jogl (2009). Structural and biochemical studies of TIGAR (*TP53*-Induced Glycolysis and Apoptosis Regulator). J. Biol. Chem. 284, 1748-1754. PMCID: PMC2615519.

4. Post-synthesis ribosome modification. Both ribosomal RNA and ribosomal proteins are post-transcriptionally and post-translationally modified on sites that are conserved from bacteria to humans. In contrast to tRNA modifications, the function of ribosomal modifications remains poorly understood. In collaboration with Steven Gregory, we studied a considerable number of ribosome methyltransferases. This work defined substrate recognition mechanisms of bacterial methyltransferases and contributed to understanding the significance of these modifications for ribosome function.

1. Demirci H., Gregory S.T., Dahlberg A.E., Jogl G. (2007). Recognition of ribosomal protein L11 by the protein trimethyltransferase PrmA. EMBO J. 26, 567-577. PMCID: PMC1783454
2. Demirci H., Belardinelli R., Seri E., Gregory S.T., Gualerzi C., Dahlberg A.E., Jogl G. (2009). Structural rearrangements in the active site of the *Thermus thermophilus* 16S rRNA methyltransferase KsgA in a binary complex with 5'-methylthioadenosine. J. Mol. Biol. 388, 271-282. PMCID: PMC2679894
3. Demirci H., Larsen H.G.L., Hansen T., Rasmussen A., Cadambi A., Gregory S.T., Kirpekar F., Jogl G. (2010). Multi-site specific 16S rRNA methyltransferase RsmF from *Thermus thermophilus*. RNA 16, 1584-1596. PMCID: PMC2905757.
4. Demirci H., Murphy IV F.V., Belardinelli R., Kelley A.C., Ramakrishnan V., Gregory S.T., Dahlberg A.E., Jogl G. (2010). Modification of 16S ribosomal RNA by the KsgA methyltransferase restructures the 30S subunit to optimize ribosome function. RNA 16, 2319-2324. PMCID: PMC2995393.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/gerwald.jogl.1/bibliograpahy/44156019/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH 1R01GM094157 (MPI: Jogl G and Gregory ST) 09/01/10 – 04/30/20
NIH/NIGMS
Structural robustness of ribosome functional centers.

Role: Co-PI (contact author).
This project seeks to define the limits of structural variability (introduced by eg. antibiotic resistance mutations) of the major functional centers of the bacterial ribosome. Results from these studies will provide important insights into molecular mechanisms of antibiotic resistance and will further our understanding of ribosome function in general.

Brown University Seed Award (MPI: Deaconescu A and Jogl G) 5/1/18 – 4/30/19
Instrumentation for specimen vitrification for cryo-electron microscopy at Brown University

Completed Research Support (past three years)

Brown University Seed Award (MPI: Jogl G and Gregory ST) 5/1/15 – 4/30/17
Engineering orthogonal ribosomes to study ribosome function