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: Scott Lovell

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

POSITION TITLE: Director, Protein Structure Laboratory

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
University of Nebraska at Omaha, Omaha, NE	BS	05/1994	Chemistry
Purdue University, West Lafayette, IN	PhD	05/2000	Organic Chemistry/Solid State Chemistry
University of Wisconsin, Madison, WI	Postdoctoral	06/2002	Protein Crystallography

A. Personal Statement

I currently serve as the Director of the Protein Structure Core Laboratory (PSL) at the University of Kansas which was originally established through an NIH COBRE grant. The main objective as Director of the PSL is to provide assistance to principal investigators, and other researchers throughout Kansas and surrounding regions, to obtain structural information for their proteins of interest using X-ray crystallography. Projects carried out by the PSL include: 1) crystallization-to-structure; the PI supplies the protein samples for crystallization and 2) gene-to-structure; the PSL Director designs the expression constructs for crystallization and manages all stages of protein preparation to obtain samples for crystallization. For the latter type of project, we utilize the KU Protein Production Group (PPG) laboratories which are located adjacent to the PSL. The PSL collaborates on average with approximately 15 investigators, from diverse scientific backgrounds and institutions, and currently maintains a 70% success rate at obtaining protein crystals for various projects. By employing efficient methods to move projects from crystallization to final structure, typically in 1-3 months, dozens of crystal structures are completed by the PSL annually. As the PSL Director, I am also routinely involved in the training of undergraduate/graduate students and post-docs in all aspects of protein crystallography. Depending on a particular student's interest, this training can involve single techniques such as crystallization methods where students learn to screen their own protein samples for crystallization. However, other students wish to be involved in a more comprehensive program in which they learn the theory and methods utilized in all aspects of protein crystallography and ultimately become proficient at solving/refining their own structures. As such I have instructed over 30 graduate students and post-docs in various areas of protein crystallography.

Prior joining the University of Kansas, I managed a structural biology group in industry (deCODE biostructures, aka Emerald Biostructures) and was responsible for overseeing all aspects of gene-to-structure projects for external commercial clients and internal projects, focused on drug discovery and development. My laboratory was responsible for initial construct design, protein expression, protein purification, crystallization, X-ray data collection, structure solution, structure refinement and analysis of the final protein:inhibitor complex structures in support of drug development. Additionally, my laboratory was involved in the development and execution of Fragment Based Drug Design (FBDD) projects to identify initial compound hits for early stage drug discovery. During this time, my laboratory maintained an overall success rate of 95% at obtaining inhibitor bound crystal structures for the projects under my supervision.

In order to provide the best chance of success for a protein structure determination project, it is beneficial to create a series of rationally designed constructs at the beginning of a project which can be utilized downstream for crystallization screening. This is particularly important for proteins that may be more challenging to crystallize since the "right" construct can be essential to enable crystallization. Modern construct design methods that

incorporate techniques such as bioinformatics computations to predict structure and potentially disordered regions, identifying stable protein fragments via limited proteolysis and mutating surface residues to facilitate crystal contact formation are useful tools to guide construct design and may be critical to obtaining a new crystal structure for a protein. These simple yet effective techniques were crucial to the high rate of success in my previous industrial position and have been incorporated as part of our standard procedure for gene-to-structure projects conducted in the PSL.

1. Auld DS, Lovell S, Thorne N, Lea WA, Maloney DJ, Shen M, Rai G, Battaile KP, Thomas CJ, Simeonov A, Hanzlik RP, Inglese J. (**2010**) "Molecular basis for the high-affinity binding and stabilization of firefly luciferase by PTC124." ***Proc Natl Acad Sci U S A***. *107*(11):4878-83. PMID: 20194791; PMCID: PMC2841876.
2. Park KT, Wu W, Battaile KP, Lovell S, Holyoak T, Lutkenhaus J. (**2011**) "The min oscillator uses mind-dependent conformational changes in mine to spatially regulate cytokinesis." ***Cell***. *146*(3):396-407. PMID: 21816275; PMCID: PMC3155264.
3. Yao H, Wang Y, Lovell S, Kumar R, Ruvinsky AM, Battaile KP, Vakser IA, Rivera M. (**2012**) "The structure of the BfrB-Bfd complex reveals protein-protein interactions enabling iron release from bacterioferritin." ***J Am Chem Soc.*** *134*(32):13470-81. PMID: 22812654; PMCID: PMC3428730.
4. Park S, Li X, Kim HM, Singh CR, Tian G, Hoyt MA, Lovell S, Battaile KP, Zolkiewski M, Coffino P, Roelofs J, Cheng Y, Finley D. (**2013**) "Reconfiguration of the proteasome during chaperone-mediated assembly." ***Nature***. *497*(7450):512-6. PMID: 23644457; PMCID: PMC3687086.

B. Positions and Honors

Positions and Employment

1997-2000	Staff X-ray Crystallographer, Department of Chemistry, University of Washington, Seattle, WA
2000-2002	Post-doctoral Research Associate and Staff Scientist, University of Wisconsin, Madison, WI
2002-2003	Crystallographer, Advanced X-ray Analytical Services, COM-CAT Sector 32 Advanced Photon Source, Argonne National Laboratories, Argonne, IL
2002-2008	Senior Research Scientist/Group Leader, deCODE biostructures (aka Emerald Biostructures), Woodridge, IL
2008-present	Director (Protein Structure Laboratory), University of Kansas, Lawrence, KS
2012-present	Research Associate, Department of Molecular Biosciences, University of Kansas, Lawrence, KS

Other Experience and Professional Memberships

Professional Memberships:
American Crystallographic Association (ACA)
International Chemical Biology Society (ICBS)

Study sections and grant review:

2012	National Science Centre, Polish Narodowe Centrum Nauki, grant reviewer
2013	National Science Centre, Polish Narodowe Centrum Nauki, grant reviewer
2013	Biotechnology and Biological Sciences Research Council, grant reviewer
2014	NIAID Special Emphasis Panel on Partnerships for Biodefense
2014	NIAID Special Emphasis Panel for Investigator Initiated Program Project Applications
2015	NIAID Special Emphasis Panel for Development of Novel Therapeutics for Select Anaerobic Protozoa
2015	NIH Macromolecular Structure and Function B (MSFB) study section, *ad hoc* reviewer
2016	NIH Macromolecular Structure and Function B (MSFB) study section, *ad hoc* reviewer

Consulting and advisory boards: Scientific Advisory Board, MicroProtein Technologies Inc., 2013-present

C. Contribution to Science

1. My scientific career has been devoted to the study of molecular structure using mainly X-ray crystallography. This began as a graduate student where my research focused on the examining the orientation of guest chromophores in organic crystal matrices. Many of these host:guest solid solutions were reported by investigators in the late 19th century but their research had been abandoned. Using "modern" instrumental methods, we were able to determine how the guest molecules (chromophores) are oriented during crystallization onto specific growth sectors of the host crystal and explained their observed linear dichroism relative to the host crystal structure. We were able to further expand the incorporation of guest molecules from small chromophores to biomolecules such as whole proteins or nucleic acids and demonstrated that macromolecules can be specifically oriented within organic crystal matrices.
   a) Lovell S, Subramony P, Kahr B. (**1999**) "Poppy Acid: Total Synthesis and Crystal Chemistry." ***Journal of the American Chemical Society***. *121*(30):7020-5.
   b) Lovell S, Marquardt BJ, Kahr B. (**1999**) "Crystal violet's shoulder." ***Journal of the Chemical Society, Perkin Transactions 2***. (11):2241-7.
   c) Kurimoto M, Subramony P, Gurney RW, Lovell S, Chmielewski J, Kahr B. (**1999**) "Kinetic Stabilization of Biopolymers in Single-Crystal Hosts: Green Fluorescent Protein in α-Lactose Monohydrate." ***J Am Chem Soc***. *121*(29):6952-3.
   d) Chmielewski J, Lewis JJ, Lovell S, Zutshi R, Savickas P, Mitchell CA, Subramony JA, Kahr B. (**1997**) "Single-Crystal Matrix Isolation of Biopolymers." ***J Am Chem Soc***. *119*(43):10565-6.

2. During my time as a post-doc and staff scientist at the University of Wisconsin in Madison, I learned the techniques utilized in the protein crystallography field. The main area of focus involved the structural studies of Tn5 transposase:DNA complexes aimed at gaining mechanistic insight regarding DNA transposition. From this work, we were able to demonstrate how metal ions facilitate DNA processing and further understand how specific transposase:DNA interactions guide transposition.

   a) Klenchin VA, Czyz A, Goryshin IY, Gradman R, Lovell S, Rayment I, Reznikoff WS. (**2008**) "Phosphate coordination and movement of DNA in the Tn5 synaptic complex: role of the (R)YREK motif." ***Nucleic Acids Res***. *36*(18):5855-62. PMID: 18790806; PMCID: PMC2566895.
   b) Lovell S, Goryshin IY, Reznikoff WR, Rayment I. (**2002**) "Two-metal active site binding of a Tn5 transposase synaptic complex." ***Nat Struct Biol***. *9*(4):278-81. PMID: 11896402.
   c) Steiniger-White M, Bhasin A, Lovell S, Rayment I, Reznikoff WS. (**2002**) "Evidence for "unseen" transposase--DNA contacts." ***J Mol Biol***. *322*(5):971-82. PMID: 12367522.

3. As a structural biologist for the past 15 years, I have dedicated my efforts to working in a team setting with other scientists in order to solve a particular problem. While working in industry (deCODE biostructures), I was tasked with: 1) assisting in the operation of a synchrotron beamline, that was maintained by deCODE, at the Advanced Photon Source at Argonne National Laboratory (COM-CAT, sector 32) and 2) establishing and managing a biostructures group at the company's chemistry site in Illinois. During this time, my group carried out structural biology projects (gene-to-structure) for external industrial clients and internal drug development projects and solved over 150 protein:inhibitor crystal structures. Apart from standard structure determination efforts, my group assisted with the development and validation of internal libraries for fragment based drug design projects. In addition, my laboratory worked closely with the company's product development group to advance methods for protein construct design and microfluidic protein crystallization.

   a) Raymond A, Lovell S, Lorimer D, Walchli J, Mixon M, Wallace E, Thompkins K, Archer K, Burgin A, Stewart L. (**2009**) "Combined protein construct and synthetic gene engineering for heterologous protein expression and crystallization using Gene Composer." ***BMC Biotechnol***. *9*:37. PMID: 19383143; PMCID: PMC2680836.
   b) Gerdts CJ, Elliott M, Lovell S, Mixon MB, Napuli AJ, Staker BL, Nollert P, Stewart L. (**2008**) "The plug-based nanovolume Microcapillary Protein Crystallization System (MPCS)." ***Acta Crystallogr D Biol Crystallogr***. *64*(Pt 11):1116-22. PMID: 19020349; PMCID: PMC2585160.

c) Braselmann S, Taylor V, Zhao H, Wang S, Sylvain C, Baluom M, Qu K, Herlaar E, Lau A, Young C, Wong BR, Lovell S, Sun T, Park G, Argade A, Jurcevic S, Pine P, Singh R, Grossbard EB, Payan DG, Masuda ES. (**2006**) "R406, an orally available spleen tyrosine kinase inhibitor blocks fc receptor signaling and reduces immune complex-mediated inflammation." ***J Pharmacol Exp Ther***. *319*(3):998-1008. PMID: 16946104.

4. My experience in collaborative research and structural biology service facilitated the transition from industry to academia to serve as the Director of the Protein Structure Laboratory (PSL) at the University of Kansas (KU). Since X-ray crystallography is a somewhat specialized field, most non-crystallographer investigators who study proteins need assistance for the structure determination of their proteins of interest. Therefore, it is highly beneficial for these investigators to have access to a core laboratory to advance their research. However, it is crucial to the success of a project that the core laboratory is not seen as a "hired hand" but is rather viewed as a collaborator who is extensively involved in the investigator's research. This is accomplished in the PSL by conducting thorough literature research prior to initiating a particular project and providing a detailed project plan to each investigator. Using this approach, my laboratory at KU has collaborated with over 47 PI's and worked with 335 unique protein constructs since 2009. By employing efficient methods for protein structure determination, the PSL maintains a high rate of success at obtaining crystal structures and deposits approximately 20 structures to the Protein Databank (PDB) annually. Collaborations between the PSL and investigators have resulted in 47 publications since 2009 in which the PSL staff are listed as co-authors.

Complete List of Published Work
http://www.ncbi.nlm.nih.gov/sites/myncbi/scott.lovell.1/bibliography/47311330/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

▪1P30GM110761 (PI: Hanzlik, Robert P.) 08/01/14 - 06/30/19
National Institutes of Health COBRE
Protein Structure and Function
Core C: Protein Structure Laboratory

This phase of the COBRE-PSF is designed to 1) continue growth of new and continuing investigators focused on the very broad theme of protein structure and function; 2) support COBRE pilot project grants that utilize the Core Labs; 3) strengthen the existing Core Labs by expanding their capabilities and their user base to position them for long-term sustainability. The mission of the Protein Structure Laboratory (PSL) is to provide investigators with state-of-the-art instrumentation, facilities, and expertise for all aspects of protein crystallography.
Role: Core Lab Director

▪ 1R01AI109039 (PI: Chang, Kyeong-Ok) 02/01/14 – 01/31/19
National Institute of Allergy and Infectious Diseases (NIAID)
Norovirus 3CL Protease-Based Anti-norovirus Therapeutics

The goal of this project is to develop and characterize inhibitors that target the 3CL protease of Norovirus.
Role: Co-Investigator

▪ R01CA191785-01 (PI: Xu, Liang and Aube, Jeff) 04/01/15 – 03/31/20
National Institutes of Health (NCI)
Molecular cancer therapy targeting HuR-ARE interaction

The major goal of this proposal is to obtain small molecule inhibitors as chemical probes that potently bind to HuR and modulate its functions, and ultimately select 1-2 most drug-like lead compounds for further development as a new class of molecular cancer therapy that inhibit cancer with HuR overexpression.
Role: Co-Investigator

■ R01 (PI: Rivera, Mario) 07/01/16– 06/30/21
National Institutes of Health
Chemical tools for perturbing iron homeostasis in P. aeruginosa

The goal of this project is to identify lead compounds hits that bind to BfrB and disrupt its interaction with Bfd which is required for iron mobilization.
Role: Co-Investigator

Completed

■A-4209 (PI: Lovell, Scott) 08/01/11 - 01/31/14
CHDI Foundation, Inc.
Structural Studies of HDAC4:MEF2 for Lead Identification of Protein-Protein Interaction Inhibitors

The goals of this project are to determine the structure of the histone deacetylase HDAC4 in complex with the transcription factor MEF2 and identify lead compounds that may serve as protein:protein interaction inhibitors in the treatment of Huntington's disease.
Role: Principal Investigator

■8P20GM103420 (PI: Hanzlik, Robert P.) 04/01/08 - 03/31/13
National Institutes of Health COBRE
Protein Structure and Function
Core C: Protein Structure Laboratory

This COBRE is designed to mentor junior faculty as they develop a quality, externally funded research program. The major goal of the Protein Structure Laboratory is to provide assistance to COBRE faculty and other researchers throughout Kansas and the surrounding regions in performing structural studies using X-ray crystallography.
Role: Core Lab Director

■1R01AI0958421 (PI: Michel, Kristin) 05/01/11 - 04/30/15
National Institute of Allergy and Infectious Diseases (NIAID)
The function(s) of serpin-2 in mosquito immunity and physiology

The goals of this project are to identify targets for the protease inhibitor SRPN2 from *Anopholes gambiae* using biochemical and genetic methods and to structurally characterize these SRPN2-protease complexes in an effort to develop potential anti-malarial inhibitors.
Role: Co-investigator

■MCB1158469 (PI: Rivera, Mario) 06/01/12 – 05/31/15
National Science Foundation
Protein Interactions in the Utilization of Iron by Bacteria

The goal of these studies is to study the effect of protein dynamics and protein-protein interactions on the regulation of cytosolic iron in the opportunistic pathogen *Pseudomonas aeruginosa*.
Role: Co-Investigator