BIOGRAPHICAL SKETCH

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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
University of Wisconsin, Madison, WI	Post-Doc	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 (KU) where our main objective is to provide assistance to principal investigators at KU, 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. The PSL collaborates on average with approximately 15 investigators, from diverse scientific backgrounds and institutions, and currently maintains a success rate of approximately 70% at obtaining protein crystals. By employing efficient methods to move projects from crystallization to final structure, typically in 1-3 months, dozens of crystal structures are completed annually. As the PSL Director, I am also involved in the training of undergraduate/graduate students and post-docs in all aspects of protein crystallography. Depending on the student's interest, this training can involve single techniques such as crystallization where students learn to screen their own protein samples for crystallization or a more comprehensive program aimed at learning all aspects of protein crystallography and becoming proficient at solving/refining structures. During my time as the PSL Director, I have instructed over 60 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. During this time, my laboratory maintained an overall success rate of 95% at obtaining inhibitor bound crystal structures for the projects under my supervision.

As noted, my current laboratory collaborates consistently with investigators from various scientific disciplines. Therefore, the PSL often takes on projects that one could characterize as "routine" structure determination aimed at supporting a particular experiment over a short time period. Additionally, I am often approached by investigators to collaborate on longer term projects that may span several months or years and currently serve as a co-investigator on NIH funded R01 grants aimed at inhibitor development.

a) Punchi Hewage A, Yao H, Nammalwar B, Gnanasekaran KK, Lovell S, Bunce RA, Eshelman K, Phaniraj S, Lee M, Peterson BR, Battaile KP, Reitz AB, Rivera M. (**2019**) "Small molecule inhibitors of the BfrB-Bfd interaction decrease Pseudomonas aeruginosa fitness and potentiate fluoroquinolone activity." ***Journal of the American Chemical Society***. *141*(20):8171-84. PMID: 31038945.

b) Lan L, Xing M, Kashipathy M, Douglas J, Gao P, Battaile K, Hanzlik R, Lovell S, Xu L. (**2020**) "Crystal and solution structures of human oncoprotein Musashi-2 N-terminal RNA recognition motif 1." ***Proteins***. *88*(4):573-83. PMID: 31603583.

c) Rathnayake AD, Kim Y, Dampalla CS, Nguyen HN, Jesri A-RM, Kashipathy MM, Lushington GH, Battaile KP, Lovell S, Chang K-O, Groutas WC. (**2020**) "Structure-Guided Optimization of Dipeptidyl Inhibitors of Norovirus 3CL Protease." ***Journal of Medicinal Chemistry***. PMID: 32945669. In Press

d) Rathnayake AD, Zheng J, Kim Y, Perera KD, Mackin S, Meyerholz DK, Kashipathy MM, Battaile KP, Lovell S, Perlman S, Groutas WC, Chang K-O. (**2020**) "3C-like protease inhibitors block coronavirus replication in vitro and improve survival in MERS-CoV-infected mice." ***Science Translational Medicine***. *12*(557). PMID: 32747425.

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 (deCODE biostructures), 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

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
2016 NIAID Structural Genomics Centers for Infectious Diseases, panel member
2017 NIH Pioneer Award Program (DP1), phase 1 reviewer
2017 The Netherlands Organisation for Scientific Research (NWO), grant reviewer
2018 NIH Center for Scientific Review (CSR) Anonymization Study (BCMB IRG), grant reviewer

Other Experience and Professional Membership

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

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 20 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 70 PI's and worked on hundreds of unique protein constructs since 2009. By employing efficient methods that enable 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. As a result, I have co-authored 67 publications since 2009 with various investigators that have collaborated with the PSL.

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

Acitve

■ 1R01AI130092 (PI: Chang, Kyeong-Ok) 05/15/18 – 04/30/23
National Institutes of Health (NIAID)
Small Molecule Protease Inhibitors against MERS-CoV

The aim of this project is to conduct a lead optimization campaign aimed at advancing the series of protease inhibitors, against the MERS-CoV viral protease, to a preclinical drug candidate.
Role: Co-Investigator

■ 1R01CA191785-NCE (PI: Xu, Liang and Aube, Jeff) 04/01/15 – 03/31/21
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

Completed

■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 Institutes of Health (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

■ 1R01AI125529 (PI: Rivera, Mario) 07/01/16 – 06/30/20
National Institutes of Health (NIAID)
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

■ 1R01GM112736 (PI: Karanicolas, John) 09/30/16 – 08/31/20
National Institutes of Health (NIGMS)
Identifying stabilizers of p53 using pocket complementarity

The goal of this proposal is to identify compounds that potently bind and stabilize correctly folded p53
Role: Co-Investigator