BIOGRAPHICAL SKETCH

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NAME: Scott Lovell

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

POSITION TITLE: Director, Protein Structure and X-Ray Crystallography 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	Postdoctoral	06/2002	Protein Crystallography

A. Personal Statement

I currently serve as the Director of the Protein Structure and X-ray Crystallography Core Laboratory (PSXL) 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 PSXL include: 1) crystallization-to-structure; the PI supplies the protein samples for crystallization and 2) gene-to-structure; the PSXL Director designs the expression constructs for crystallization and manages all stages of protein preparation to obtain samples for crystallization. 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 PSXL 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 PSXL Director, I have instructed over 70 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 and often takes on projects that one could characterize as "routine" structure determination aimed at supporting a particular experiment over a short time period. However, I have also been involved in several longer-term projects and currently serve as a co-investigator and manage the structural biology efforts for NIH funded projects particularly aimed at inhibitor development. Additionally, I am a team member of the Seattle Structural Genomics Center for Infectious Diseases (SSGCID) and my laboratory manages the majority of the high throughput X-ray crystallography tasks for the center.

Highlighted ongoing and completed research projects:

Ongoing

1) R01AI130092 (NCE)
   PI: Chang, Kyeong-Ok, Role: Co-Investigator
   05/15/2018 – 04/30/2023
   Small Molecule Protease Inhibitors Against MERS-CoV

2) R01AI161085
   PI: Chang, Kyeong-Ok, Role: Co-Investigator
   08/06/2021 – 07/31/2026
   Small Molecule Inhibitors Against 3C-Like Protease of SARS-CoV-2

3) R01AI169344
   PI: Rivera, Mario, Role: Co-Investigator
   02/15/2022 – 01/31/2027
   Small molecules for perturbing iron homeostasis in bacterial biofilms

4) HHSN272201700059C
   PI: Myler, Peter, Role: Co-Investigator
   09/01/2022 – 08/31/2027
   Seattle Structural Genomics Center for Infectious Disease

Completed

1) R01AI125529
   PI: Rivera, Mario, Role: Co-Investigator
   07/01/2016 – 06/30/2020
   Chemical tools for perturbing iron homeostasis in *P. aeruginosa*

2) R01GM112736
   PI: Karanicolas, John, Role: Co-Investigator
   09/26/2016 – 08/31/2020
   Identifying stabilizers of p53 using pocket complementarity

3) R01AI109039
   PI: Chang, Kyeong-Ok, Role: Co-Investigator
   02/01/2014 – 01/31/2020
   Norovirus 3CL Protease-Based Anti-norovirus Therapeutics

References:

1) Soldano A, Yao H, Punchi Hewage AND, Meraz K, Annor-Gyamfi JK, Bunce RA, Battaile KP, Lovell S, Rivera M. (**2021**) "Small Molecule Inhibitors of the Bacterioferritin (BfrB)-Ferredoxin (Bfd) Complex Kill Biofilm-Embedded Pseudomonas aeruginosa Cells." ***ACS Infectious Diseases***. *7*(1):123-40. PMID: 33269912.
2) Dampalla C, Zhang J, Perera K, Wong LY, Meyerholz D, Nguyen H, Kashipathy M, Battaile KP, Lovell S, Kim Y, Perlman S, Groutas WC, Chang K-O. (**2021**) "Post-infection treatment with a protease inhibitor increases survival of mice with a fatal SARS-CoV-2 infection." ***Proceedings of the National Academy of Sciences***, PMID: 34210738.
3) Dampalla CS, Rathnayake AD, Galasiti Kankanamalage AC, Kim Y, Perera KD, Nguyen HN, Miller MJ, Madden TK, Picard HR, Thurman HA, Kashipathy MM, Liu L, Battaile KP, Lovell S, Chang K-O, Groutas WC. (**2022**) "Structure-Guided Design of Potent Spirocyclic Inhibitors of Severe Acute Respiratory Syndrome Coronavirus-2 3C-like Protease." ***Journal of Medicinal Chemistry***. *65*(11):7818-32. PMID: 35638577.
4) Yao H, Soldano A, Fontenot L, Donnarumma F, Lovell S, Chandler JR, Rivera M. (**2022**) "Pseudomonas aeruginosa Bacterioferritin Is Assembled from FtnA and BfrB Subunits with the Relative Proportions Dependent on the Environmental Oxygen Availability." ***Biomolecules***. *12*(3). PMID: 35327558.

B. Positions, Scientific Appointments, and Honors

1) Positions and Scientific Appointments

2021-present	Director (X-ray Crystallography Laboratory), University of Kansas, Lawrence, KS
2008-present	Director (Protein Structure Laboratory), University of Kansas, Lawrence, KS
2002-2008	Senior Research Scientist/Group Leader, deCODE biostructures (aka Emerald Biostructures), Woodridge, IL
2002-2003	Crystallographer, Advanced X-ray Analytical Services (deCODE biostructures), COM-CAT Sector 32 Advanced Photon Source, Argonne National Laboratories, Argonne, IL
2000-2002	Post-doctoral Research Associate and Staff Scientist, University of Wisconsin, Madison, WI
1997-2000	Staff X-ray Crystallographer, Department of Chemistry, University of Washington, Seattle, WA

2) Other Experience and Professional Memberships

2022-2023	NIAID Microbiology and Infectious Diseases Research Study Section, *ad hoc* reviewer
2018	NIH Center for Scientific Review (CSR) Anonymization Study (BCMB IRG), grant reviewer
2017	NIH Pioneer Award Program (DP1), phase 1 reviewer
2017	The Netherlands Organisation for Scientific Research (NWO), grant reviewer
2016	NIAID Structural Genomics Centers for Infectious Diseases, panel member
2015-2016	NIH Macromolecular Structure and Function B (MSFB) study section, *ad hoc* reviewer
2015	NIAID Special Emphasis Panel for Development of Novel Therapeutics for Select Anaerobic Protozoa
2014	NIAID Special Emphasis Panel on Partnerships for Biodefense
2014	NIAID Special Emphasis Panel for Investigator Initiated Program Project Applications
2013-present	Scientific Advisory Board, MicroProtein Technologies Inc.
2012-2013	National Science Centre, Polish Narodowe Centrum Nauki, grant reviewer
2011-present	International Chemical Biology Society (ICBS), member
1997-present	American Crystallographic Association (ACA), member

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." ***Journal of the American Chemical Society*****.** *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." ***Journal of the American Chemical Society*****.** *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 Research***. *36*(18):5855-62. PMID: 18790806.
b) Lovell S, Goryshin IY, Reznikoff WR, Rayment I. (**2002**) "Two-metal active site binding of a Tn5 transposase synaptic complex." ***Nature Structal Biology***. *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." ***Journal of Molecular Biology***. *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 Biotechnolgy***. *9* (37). PMID: 19383143.
   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 Crystallographica Section D***. *64* (Pt 11):1116-22. PMID: 19020349.
   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." ***Journal of Pharmacology and Experimental Therapeutics***. *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 and X-ray Crystallography Laboratory (PSXL) 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 that has the expertise to advance their research. However, it is crucial to the success of a project that the core laboratory staff are not seen as a "hired hand" but are rather viewed as a collaborators who are extensively involved in the investigator's research. This is accomplished in the PSXL by conducting thorough literature research prior to initiating a particular project, providing a detailed project plan and a publication quality report for each structure delivered to an 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 PSXL 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 85 publications since 2009 with various investigators that have collaborated with the PSXL.

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