BIOGRAPHICAL SKETCH

NAME: Michal Hammel

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

POSITION TITLE: Research Scientist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Comenius University, Bratislava, Slovakia	MS	1998	Pharmacy
Karl-Franzens University, Graz, Austria	MS	1998	Pharmacy
Karl-Franzens University, Graz, Austria	Ph.D.	2002	Biophysics
Centre National de la Recherche Scientifique, Marseille, France	PostDoc	2005	Structural Biology
University of Missouri and Kansas City, Kansas City, USA.	PostDoc	2006	Structural Biology

A. Personal Statement

My role within SBDR is to develop user experiment instrumentation and computational tools needed for SIBYLS beamline to explore structures of dynamic macromolecules and macromolecular assemblies. As a research scientist at Lawrence Berkeley National Laboratory (LBNL) I led the development of high throughput -SAXS (HT-SAXS) approach at SIBYLS beamline (1) . I currently leading the design of the SAXS inline with size exclusion chromatography (SEC-SAXS) with the ultimate goal to have a SIBYLS capable of simultaneous HT-SAXS and SEC-SAXS scattering measurements in both small- and wide-angle X-ray scattering range. In addition, I successfully collaborated with other SBDR projects, and produced several peer-reviewed publications from each project (2, 3). To target SBDR needs I developed new structural approaches for investigating flexible and dynamic DNA repair assemblies using a combination of SAXS, macromolecular crystallography (MX) and computational modeling (reviewed in (4)). I have a demonstrated record of successful and productive research projects with outcome of over 60 peer-reviewed scientific publications that have required innovative applications of MX and SAXS.

1. Hura GL, Menon AL, Hammel M, Rambo RP, Poole FL, 2nd, Tsutakawa SE, Jenney FE, Jr., Classen S, Frankel KA, Hopkins RC, Yang SJ, Scott JW, Dillard BD, Adams MW, Tainer JA. Robust, high-throughput solution structural analyses by small angle X-ray scattering (SAXS). Nature methods. 2009;6(8):606-12.

2. Hammel M, Yu Y, Mahaney BL, Cai B, Ye R, Phipps BM, Rambo RP, Hura GL, Pelikan M, So S, Abolfath RM, Chen DJ, Lees-Miller SP, Tainer JA. Ku and DNA-dependent protein kinase dynamic conformations and assembly regulate DNA binding and the initial non-homologous end joining complex. J Biol Chem. 2010;285(2):1414-23..

3. Hammel M, Rey M, Yu Y, Mani RS, Classen S, Liu M, Pique ME, Fang S, Mahaney BL, Weinfeld M, Schriemer DC, Lees-Miller SP, Tainer JA. XRCC4 protein interactions with XRCC4-like factor (XLF) create an extended grooved scaffold for DNA ligation and double strand break repair. The Journal of biological chemistry. 2011;286(37).

4. Hammel M. Validation of macromolecular flexibility in solution by small-angle X-ray scattering (SAXS). Eur Biophys J. 2012;41(10):789-99.

B. Positions and Honors

Positions and Employment

1994-1996 Research Assistant, Institute of Biophysics, Comenius University, Faculty of Pharmacy (FaFUK), Bratislava, Slovakia,

1996-1998 Research Assistant: Institute of Molecular Biology, Biochemistry & Microbiology, Karl-Franzens University (KFUG), Faculty of Pharmacy, Graz, Austria.

2002-2003 Representative of the Directorate-General in the development department. HERMES Pharma GmbH , Austria

2003-2005 Post-doctoral Fellow, Centre National de la Recherche Scientifique (CNRS) in Marseille, France

2005-2006 Post-doctoral Fellow, University of Missouri and Kansas City, Kansas City, USA.

2007- Research Scientist, Physical Biosciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA

Others Experience and Professional Memberships

- Member of American Crystallographic Associationn (ACA)
- Reviewer for NIH P41, R01 and P01 programs; Peer Reviewer for Journal of Biological Chemistry, Structure, Journal of Physical Chemistry, Biophysical Journal, Journal of Molecular Biology, Journal of Physics.
- Organizing Bio-SAXS workshops at Advance Light Source (LBNL), 2011,2012, 2013, 2014, 2015
- Organizing ACA workshop 2013
- Gave numerous plenary speeches and keynotes at international conferences, research institutes, and universities.
- Co-investigator for NIH/NCI Structural Cell Biology of DNA Repair Machines (SBDR) consortium.

Honors

2003 Erwin Schrödinger Fellowship of the FWF Austrian Science Fund

2004 Award, International conference on "Structural Biology at Crossroads: From biological molecules to biological systems" Hamburg, Germany.

2007 “A Bacterial Anticomplement” discovery highlighted in SCIENCE 315, 1768

C. Contribution to Science

C.1 I have been developing new analysis methods for X-ray scattering since I was a PhD student at the Graz University. Here I focused on structural changes of LDL upon drug loading which were monitored simultaneously by differential scanning calorimetry (DSC) and small angle X-ray scattering (SAXS) (5). The uniqueness of my approach was evident as early as during PhD research when I used my own blood to purify Lipoproteins and their apo-proteins fractions (apoB and apoH). The year was 2000 and I was one of the first to combine small angle X-ray scattering (SAXS) and ensemble analysis to extract multiple conformers of dynamic proteins from SAXS experiment (6, 7). Based on this work I was awarded the Schroedinger Fellowship and started my first postdoctoral studies at Centre National de la Recherche Scientifique (CNRS) in Marseille. My journey as a bioSAXS expert can be highlighted with my first author review of the joint application of SAXS and MX (8) which is now approaching 600 citations and early predictions of the impact SAXS have largely held true.

5. Hammel M, Laggner P, Prassl R. Structural characterisation of nucleoside loaded low density lipoprotein as a main criterion for the applicability as drug delivery system. Chem Phys Lipids. 2003;123(2):193-207.

6. Hammel M, Kriechbaum M, Gries A, Kostner GM, Laggner P, Prassl R. Solution structure of human and bovine beta(2)-glycoprotein I revealed by small-angle X-ray scattering. Journal of molecular biology. 2002;321(1):85-97. Epub 2002/07/26. doi: S0022283602006216 [pii]. PubMed PMID: 12139935.

7. Hammel M, Walther M, Prassl R, Kuhn H. Structural flexibility of the N-terminal beta-barrel domain of 15-lipoxygenase-1 probed by small angle X-ray scattering. Functional consequences for activity regulation and membrane binding. Journal of molecular biology. 2004;343(4):917-29.

8. Putnam CD, Hammel M, Hura GL, Tainer JA. X-ray solution scattering (SAXS) combined with crystallography and computation: defining accurate macromolecular structures, conformations and assemblies in solution. Quarterly reviews of biophysics. 2007;40(3):191-285.

C.2 As a postdoctoral fellow at Centre National de la Recherche Scientifique (CNRS) in Marseille I focused my research on the structural determination of the megadalton-large Celulosome which required the development of novel computational methods (9, 10). I developed the now frequently used BILBOMD software (11) which combines molecular dynamics, SAXS validation and Minimal Ensemble Search (MES) algorithm (reviewed in (4)). At the University of Missouri and Kansas City, (UMKC) Kansas City, I expanded my research to include molecular biology and crystallography of macromolecules involved in bacterial pathogenicity . These work had a direct impact on medical research defining the mechanism for complement inhibition by the Staphylococcus aureus and was highlighted in the journal SCIENCE.

9. Hammel M, Fierobe HP, Czjzek M, Finet S, Receveur-Brechot V. Structural insights into the mechanism of formation of cellulosomes probed by small angle X-ray scattering. J Biol Chem. 2004;279(53):55985-94. Epub 2004/10/27. doi: M408979200 [pii] 10.1074/jbc.M408979200. PubMed PMID: 15502162.

10. Hammel M, Fierobe HP, Czjzek M, Kurkal V, Smith JC, Bayer EA, Finet S, Receveur-Brechot V. Structural basis of cellulosome efficiency explored by small angle X-ray scattering. J Biol Chem. 2005;280(46):38562-8. Epub 2005/09/15. doi: M503168200 [pii] 10.1074/jbc.M503168200. PubMed PMID: 16157599.

11. Pelikan M, Hura GL, Hammel M. Structure and flexibility within proteins as identified through small angle X-ray scattering. Gen Physiol Biophys. 2009;28(2):174-89.

C.3 During my second postdoctoral studies at the University of Missouri and Kansas City, (UMKC), I expanded my research to include molecular biology and crystallography on large protein complexes from the human complement and pathogen *S. aureus*. *S. aureus* can inactivate the complement cascade through a secreted protein Efb. In combination with crystallography (12, 13), SAXS and HDX (14, 15), I show that bacterial secreted proteins mediate allosteric changes in complement and block the human complement cascade. In additional to the direct medical impact of this study, this research showed that hybrid structural techniques are absolutely necessary to probe general hypothesis that changing macromolecular conformations are critical features of cellular network. These studies were highlighted in journal SCIENCE.

12. Hammel M, Sfyroera G, Pyrpassopoulos S, Ricklin D, Ramyar KX, Pop M, Jin Z, Lambris JD, Geisbrecht BV. Characterization of Ehp, a secreted complement inhibitory protein from Staphylococcus aureus. J Biol Chem. 2007;282(41):30051-61.

13. Hammel M, Sfyroera G, Ricklin D, Magotti P, Lambris JD, Geisbrecht BV. A structural basis for complement inhibition byStaphylococcus aureus. Nat Immunol. 2007;8(4):430-7.

14. Hammel M, Nemecek D, Keightley JA, Thomas GJ, Jr., Geisbrecht BV. The Staphylococcus aureus extracellular adherence protein (Eap) adopts an elongated but structured conformation in solution. Protein Sci. 2007;16(12): 2605-17.

15. Ricklin D, Tzekou A, Garcia BL, Hammel M, McWhorter WJ, Sfyroera G, Wu YQ, Holers VM, Herbert AP, Barlow PN, Geisbrecht BV, Lambris JD. A molecular insight into complement evasion by the staphylococcal complement inhibitor protein family. J Immunol. 2009;183(4):2565-74.

C.4 Besides the development of new structural techniques I'm focusing my research on the characterization of the macromolecular assemblies in the non-homologues end joining (NHEJ) pathway from humans and have become the key person inside the SBDR in the investigation of the molecular mechanism of NHEJ (16, 17). My recent discovery of the grooved scaffold for DNA ligation (3, 18, 19) proved that the hybrid structural techniques will yield dividends in terms of understanding and ultimately rationale drug design for combating human illnesses.

16. Fan L, Fuss JO, Cheng QJ, Arvai AS, Hammel M, Roberts VA, Cooper PK, Tainer JA. XPD helicase structures and activities: insights into the cancer and aging phenotypes from XPD mutations. Cell. 2008;133(5):789-800.

17. Bernstein NK, Hammel M, Mani RS, Weinfeld M, Pelikan M, Tainer JA, Glover JN. Mechanism of DNA substrate recognition by the mammalian DNA repair enzyme, Polynucleotide Kinase. Nucleic acids research. 2009;37(18): 6161-73. Epub 2009/08/13.

18. Hammel M, Yu Y, Fang S, Lees-Miller SP, Tainer JA. XLF regulates filament architecture of the XRCC4.ligase IV complex. Structure. 2010;18(11):1431-42.

19. Williams GJ, Hammel M, Radhakrishnan SK, Ramsden D, Lees-Miller SP, Tainer JA. Structural insights into NHEJ: building up an integrated picture of the dynamic DSB repair super complex, one component and interaction at a time. DNA Repair (Amst). 2014;17:110-20.

C.5 As a research scientist at the LBNL and co-Investigator on the NCI-funded Structural Biology of DNA Repair (SBDR) consortium, I laid the groundwork for my research in developing new technology to examine molecular interaction in solution (20) and to study macromolecular flexibility and conformational changes (11). The characterization of macromolecular flexibility has driven much of my research as laid out in one of my most fruitful collaboration with Andrej Sali group (UCSF). Since starting our collaboration I develop multiple bioSAXS modeling tools to allow visualization of dynamic macromolecules (11, 20) and macromolecular assemblies (21). These tools yielded high impact results in diverse pathways highlighting that flexibility and transient complexation is a key component for biology and requires renewed development beyond what static structures can provide.

20. Schneidman-Duhovny D, Hammel M, Tainer JA, Sali A. Accurate SAXS Profile Computation and its Assessment by Contrast Variation Experiments. Biophys J. 2013;105(4):962-74.

21. Schneidman-Duhovny D, Hammel M, Sali A. Macromolecular docking restrained by a small angle X-ray scattering profile. Journal of structural biology. 2011;173(3):461-71.

22. Schneidman-Duhovny D, Hammel M, Sali A. FoXS: a web server for rapid computation and fitting of SAXS profiles. Nucleic acids research. 2010;38(Web Server issue):W540-4.

Publications (from over 60 peer reviewed publications)

D. Research Support.

ONGOING

Work for Others Agreement No. FP00001511 (Hammel, Michal)
Biogen INC 07/01/2015 - 06/30/2017
Utilization of SAXS capabilities at SIBYLS for interrogating the structures and dynamics of protein biologics and their cognate complexes.
***Role:** PI*

P01 CA092584 (Tainer, John A.) 09/27/2001 - 08/31/2016
NIH/NCI
Structural Cell Biology of DNA Repair Machines
This integrated multi-institutional Program Project in structural biology of DNA repair (SBDR) addresses the challenge of understanding at the molecular level the pathways controlling genetic integrity through integration of five projects and three cores. SBDR will a) produce biologically relevant DNA repair structures; b) identify fundamental structural principles for repair proteins; and c) provide the structural framework for a unified understanding of the molecular choreography of DNA repair processes.
Role: Structural Biologist & Beamline Scientist

DE AC02 05CH11231 (Tainer, John A.)
DOE/BER 10/01/2004 - 9/30/2015
Integrated Diffraction Analysis Technologies
Integrated X-ray crystal and X-ray solution scattering of molecular complexes. General support for SIBYLS beamline efforts including technology development.
Role: Beamline Scientist

R01 GM105404 (Tainer, John A.) 7/01/2012 - 5/31/2016
NIH/MIGMS
Macromolecular INsights Optimized by Scattering
MINOS is a High-Throughput (HT) approach to structurally characterize human and human-related PSI:Biology protein targets. MINOS will provide comprehensive expertise in the areas of developing and employing Small Angle X-ray Scattering (SAXS) in combination with homology modeling and high-resolution macromolecular X-ray crystallography (MX) to define accurate conformations and assemblies in solution.
Role: Project Leader

COMPLETED

None