BIOGRAPHICAL SKETCH

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NAME: Bohon, Jen

eRA COMMONS USER NAME (agency login): JBOHON

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Johns Hopkins University, Baltimore, MD	BA	05/1996	Biology
Stony Brook University, Stony Brook, NY	PHD	08/2004	Physiology & Biophysics
Case Western Reserve U., Cleveland, OH	Postdoctoral Fellow	12/2006	Biophysics
Case Western Reserve U., Cleveland, OH	Postdoctoral Fellow	05/2009	Biophysics

A. Personal Statement

I am the lead beamline scientist for the NSLS-II XFP (X-ray Footprinting for *In Vitro* and *In Vivo* Structural Studies of Biological Macromolecules) beamline, being constructed and operated by the Center for Synchrotron Biosciences (CSB) of Case Western Reserve University in partnership with NSLS-II at Brookhaven National Laboratory (BNL). The CSB is dedicated to providing world-class facilities and support for a broad base of highly productive researchers in biological sciences. I have been with the Center since 2005, providing user support and conducting my own research in structural biology, emphasizing synchrotron x-ray footprinting (x-ray radiolysis for hydroxyl-radical-mediated footprinting) and associated technology development. I began as a post-doctoral fellow, winning two NIH fellowships for footprinting research, then joined the faculty at Case Western Reserve University. As an Assistant Professor and beamline scientist, I have organized and maintained all usage pertaining to the NSLS X28C x-ray footprinting beamline, including contacting the users, reviewing proposals, scheduling beamtime for users, training users in beamline usage and data analysis, assisting users with designing and conducting experiments, assessing user productivity and satisfaction with our facilities, and interacting with our technical staff for beamline upgrades and maintenance. I will be responsible for these same activities when the XFP beamline comes online later this year. I have a broad background in biophysics, with experience and expertise in a variety of structural biology techniques, including NMR, IR microspectroscopy, x-ray absorption spectroscopy, cryo-electron microscopy, and x-ray footprinting/mass spectrometry, and am well positioned to help users take advantage of multi-technique capabilities at the CSB. I collaborate closely with x-ray footprinting users to ensure that world-class science is produced at our facility. I also actively work in technology and instrumentation development to improve the tools for performing biophysics research, with support from NSF. I am highly engaged with the user community, and have been elected to several offices to represent the needs of the users to BNL facility management as well as directly to the Department of Energy. I have also worked with other synchrotron facilities around the US to disseminate x-ray footprinting technology and guarantee availability of resources for x-ray footprinting research in the transition period as the new XFP beamline is constructed. In summary, I have a demonstrated record of user support, structural biology research, technology development, organizational capabilities, and community leadership which well prepare me to assist new footprinting users to succeed in producing high-impact science.

1. Bohon J, D'Mello R, Ralston C, Gupta S, Chance MR. Synchrotron X-ray footprinting on tour. J Synchrotron Radiat. 2014 Jan;21(Pt 1):24-31. PubMed PMID: 24365913; PubMed Central PMCID: PMC3874017.
2. Wang L, Qin Y, Ilchenko S, Bohon J, Shi W, Cho MW, Takamoto K, Chance MR. Structural analysis of a highly glycosylated and unliganded gp120-based antigen using mass spectrometry. Biochemistry. 2010 Oct 26;49(42):9032-45. PubMed PMID: 20825246; PubMed Central PMCID: PMC2957511.

3. Shi W, Bohon J, Han DP, Habte H, Qin Y, Cho MW, Chance MR. Structural characterization of HIV gp41 with the membrane-proximal external region. J Biol Chem. 2010 Jul 30;285(31):24290-8. PubMed PMID: 20525690; PubMed Central PMCID: PMC2911339.
4. Bohon J, Jennings LD, Phillips CM, Licht S, Chance MR. Synchrotron protein footprinting supports substrate translocation by ClpA via ATP-induced movements of the D2 loop. Structure. 2008 Aug 6;16(8):1157-65. PubMed PMID: 18682217; PubMed Central PMCID: PMC2929679.

B. Positions and Honors

Positions and Employment

2004 - 2005 Research Associate, BROOKHAVEN SCIENCE ASSOC-BROOKHAVEN LAB
2005 - 2009 Postdoctoral Fellow, CASE WESTERN RESERVE UNIVERSITY
2009 - 2010 Senior Research Associate, CASE WESTERN RESERVE UNIVERSITY
2010 - 2014 Instructor, CASE WESTERN RESERVE UNIVERSITY
2014 - Assistant Professor, CASE WESTERN RESERVE UNIVERSITY
2014 - XFP Lead Beamline Scientist, NSLS-II, BROOKHAVEN SCIENCE ASSOC-BROOKHAVEN LAB

Other Experience and Professional Memberships

2008 - Member, Biophysical Society
2009 - 2012 Elected Member, NSLS Users' Executive Committee
2012 - 2013 Chair, NSLS Users' Executive Committee
2013 - 2016 Outreach Officer, NSLS-II Users' Executive Committee
2016 - Elected Member, NSLS-II Users' Executive Committee
2013 - Elected Member, National User Facilities Organization Steering Committee
2015 - Member (alternate), Brookhaven Community Advisory Council
2015 - Review Panelist, Instrument Development for Biological Research, National Science Foundation Division of Biological Infrastructure

C. Contribution to Science

1. My early work focused on the anti-cancer agent 6-thioguanine (also known as 2-amino-6-mercaptopurine, or TabloidR), and its effects on DNA. This antimetabolite has been utilized to combat acute myelogenous and acute lymphoblastic leukemia for decades, but the precise mechanism of action was poorly understood. Specifically, the replacement of a single oxygen by a sulfur seemed unlikely to make a significant difference in the structure of the DNA. My doctoral work, using NMR, showed that the structural differences were, in fact small, however, the structural DYNAMICS were strongly effected, with base pairs opening out into the solvent much more rapidly when the thioguanine was present. Further studies with polymerases also showed that this caused some stalling of the elongation of the DNA. These factors indicated that dynamics - and likely interactions with other cellular factors, rather than structural disruptions, were important for the activity of 6-thioguanine. I was the primary investigator throughout these studies.

    a. Bohon J, de los Santos CR. Effect of 6-thioguanine on the stability of duplex DNA. Nucleic Acids Res. 2005;33(9):2880-6. PubMed PMID: 15905476; PubMed Central PMCID: PMC1131932.
    b. Bohon J, de los Santos CR. Structural effect of the anticancer agent 6-thioguanine on duplex DNA. Nucleic Acids Res. 2003 Feb 15;31(4):1331-8. PubMed PMID: 12582253; PubMed Central PMCID: PMC150222.

2. My postdoctoral studies enabled me to branch out into additional structural biology techniques. A significant contribution to the understanding of the mechanism of action of the ClpAP molecular machine was enabled by synchrotron footprinting, in a project that was a collaboration with the Massachusetts Institute of Technology. During this program, we studied the formation of the ClpA chaperone hexameric structure, and using a non-hydrolyzable nucleotide analog, we were able to observe structural changes in

the substrate-interacting loop. These conformational changes indicated a pathway for substrate translocation upon ATP-hydrolysis associated with the movement of this loop with substrate bound down into the ClpA pore to facilitate unfolding and delivery to the ClpP protease. Within this project, we were also able to investigate the full ClpAP protease complex, and showed via x-ray footprinting, enzymatic kinetics, and mutational studies that the N-terminus of ClpP serves as a gateway, removed upon binding to the ClpA chaperone to allow access to the ClpP pore and active sites for subsequent proteolysis.

a. Jennings LD, Bohon J, Chance MR, Licht S. The ClpP N-terminus coordinates substrate access with protease active site reactivity. Biochemistry. 2008 Oct 21;47(42):11031-40. PubMed PMID: 18816064; PubMed Central PMCID: PMC2920337.
b. Bohon J, Jennings LD, Phillips CM, Licht S, Chance MR. Synchrotron protein footprinting supports substrate translocation by ClpA via ATP-induced movements of the D2 loop. Structure. 2008 Aug 6;16(8):1157-65. PubMed PMID: 18682217; PubMed Central PMCID: PMC2929679.

3. Building on the successful use of synchrotron footprinting, additional contributions were made in the study of HIV proteins with this technique. In conjunction with X-ray crystallography, we were able to elucidate structures of the gp41 membrane-proximal external region, and also the fully glycosylated gp120 outerdomain with the V3 loop intact, performing the first x-ray footprinting experiment with a fully glycosylated protein. I was a co-investigator on these projects.

a. Wang L, Qin Y, Ilchenko S, Bohon J, Shi W, Cho MW, Takamoto K, Chance MR. Structural analysis of a highly glycosylated and unliganded gp120-based antigen using mass spectrometry. Biochemistry. 2010 Oct 26;49(42):9032-45. PubMed PMID: 20825246; PubMed Central PMCID: PMC2957511.
b. Shi W, Bohon J, Han DP, Habte H, Qin Y, Cho MW, Chance MR. Structural characterization of HIV gp41 with the membrane-proximal external region. J Biol Chem. 2010 Jul 30;285(31):24290-8. PubMed PMID: 20525690; PubMed Central PMCID: PMC2911339.

4. Through my experience at the synchrotron with using the x-ray footprinting technique (and other techniques as well), I began to contribute to instrumentation development to improve the techniques that I was using and to disseminate the technology. I have participated, and continue to participate (under M. Chance) in construction and upgrades of world-leading x-ray footprinting beamlines (NSLS X28C and now NSLS-II XFP, a program that I lead). However, most of my independent efforts (and my independent funding) in this area have been specifically in improving beam diagnostics - finding a way to characterize and measure the beam to understand and control the dose of x-rays delivered to the sample. X-ray footprinting is a flux-density driven experiment, thus measurement of the beam can be very difficult, and until now, was impossible to do in-line with the experiment. With my collaborators at BNL and StonyBrook University, I have developed a transmission-mode "pixelated" (kilopixel) x-ray detector that we are integrating into a vacuum flange to serve as the beamline exit window. This has taken a significant materials science characterization effort, electronics and software development effort, as well as testing and calibration efforts at biological beamlines. The program has enabled the cross-training of several graduate students and postdoctoral scholars in both instrument development (materials science, electrical engineering) and the needs of biological researchers, helping to develop understanding and dialog between these typically rather separated disciplines. Commercialization of a subset of these devices developed along the pathway to the instrumented window has already occurred. This technology has many potential applications, and we are currently pursuing funding for moving these instruments into use for medical diagnostics.

a. Zhou T, Ding W, Gaowei M, De Geronimo G, Bohon J, Smedley J, Muller E. Pixelated transmission-mode diamond X-ray detector. J Synchrotron Radiat. 2015 Nov;22(Pt 6):1396-1402. PubMed PMID: 26524304; PubMed Central PMCID: PMC4629867.
b. Bohon J, D'Mello R, Ralston C, Gupta S, Chance MR. Synchrotron X-ray footprinting on tour. J Synchrotron Radiat. 2014 Jan;21(Pt 1):24-31. PubMed PMID: 24365913; PubMed Central PMCID: PMC3874017.
c. Muller EM, Smedley J, Bohon J, Yang X, Gaowei M, Skinner J, De Geronimo G, Sullivan M, Allaire M, Keister JW, Berman L, Héroux A. Transmission-mode diamond white-beam position monitor at NSLS.

J Synchrotron Radiat. 2012 May;19(Pt 3):381-7. PubMed PMID: 22514173; PubMed Central PMCID: PMC3329958.

d. Bohon J, Muller E, Smedley J. Development of diamond-based X-ray detection for high-flux beamline diagnostics. J Synchrotron Radiat. 2010 Nov;17(6):711-8. PubMed PMID: 20975215; PubMed Central PMCID: PMC3089012.

D. Research Support

Ongoing Research Support

P30-EB-009998, NIH
Chance (PI)
09/14-08/19
Case Center for Synchrotron Biosciences
This center assists NIH funded users in accessing structural biology beamlines for their research in crystallography, nucleic acid and protein footprinting, and x-ray spectroscopy.

DBI-1228549, NSF
Chance (PI)
08/01/12-07/01/17
MRI Consortium: Development of a Damping Wiggler Beamline for X-Ray Footprinting at NSLS II
This project drives the development of the XFP beamline at NSLS-II - the next generation of beamline for this technology that will replace the previous X28C beamline at NSLS as the world-leading source for in vitro and in vivo synchrotron footprinting of biological macromolecules.
Role: KP

DBI-1255340, NSF
Bohon (PI)
09/01/13-09/01/16
Collaborative Research: IDBR: Instrumented Diamond Window for Synchrotron Beamlines
This project drives the development of diamond-based pixelated transmission detectors integrated into vacuum windows for in-line measurement of beam position, flux, and morphology at synchrotron beamlines, with a focus on the needs of biological beamline users.
Role: PI

Completed Research Support

T32 HL007887-09
SCHILLING, WILLIAM P (PI)
07/01/99-06/30/09
Heart-Lung Physiology: Molecular-Systemic Integration
Role: TA

T32 DK007678-15
Hopfer, Ulrich (PI)
09/20/91-08/31/07
CELL PHYSIOLOGY TRAINING PROGRAM
Role: TA