

WORKSHOP # 7
October 13, 2025
NSLS-II Bldg 745, Room 183

Protein function from protein structures beyond the ground state

Organizers: Martin Fuchs & Jean Jakoncic

The focus of this workshop is to capture future and unmet needs from the structural biology research community making use of new experimental capabilities.

Structural dynamics underly a protein's biological function and structural variations greatly affect it. They are the basis of such diverse processes as enzymatic reactions, molecular transport, signaling, recognition, and targeting. Studying these processes is required to gain a deeper understanding of biological function, under appropriate physiological conditions.

In a five- to ten-year time frame, **the NSLS-II storage ring will undergo a major upgrade** with significant impact on X-ray beam size, brightness and stability. New emerging science cases will harvest these beam properties and deliver insights into fundamental biological processes.

Advances in synchrotron and beamline performance, in data collection methods, in sample handling and in the use of new methods in artificial intelligence now **enable the study of protein structures in much greater detail and beyond their ground state.**

Using enhanced experimental protocols, it will be possible to collect and analyze hundreds to thousands of complete datasets from different crystals of the same sample with ultimate quality. Rarely are such samples truly isomorphous. Ensembles of crystal structures, rather than simple structural snapshots, let one map the conformational space of biological macromolecules and allow access to detailed information on protein dynamics, and a clearer "picture" of the protein. Large scale screening campaigns provide new findings about molecular interactions, and deliver datasets required to train neural networks.

The new beam properties make possible fast, serial room temperature data collection, to enable the study of kinetic intermediates in "time resolved" reaction studies. By creating a common starting point one can create populations in the same state, and follow their chemical kinetics through diffraction collected on a micro-second to second, to minutes time scale, to cover the full range of enzyme reaction rates.

These new emerging science cases can be demonstrated at the NSLS-II MX beamlines, but will truly thrive at the beams expected from a new NSLS-IIU storage ring.

Start Time (ET)	Title	Speaker (Affiliation)
8:00	Breakfast (coffee, tea, pastries) and Check-In NSLS-II Bldg 745, Room 183	
8:30	Introduction	Sean McSweeney, JJ, MF
9:00	X-ray Crystallography and Integrated Structural Biology at St. Jude Children's Research Hospital	Darcie Miller (St Jude)
9:30	TBD	Dale Kreitler (BNL)

10:00	OpenFold 3: On the road to full parity with AlphaFold 3	Mohammed AlQuraishi (Columbia University)
10:30	Group Photo, Discussion Session 1+ coffee, tea, snacks	
11:00	Serial microsecond crystallography to study protein dynamics at the ESRF ID29 beamline	Daniele de Sanctis (ESRF)
11:30	Enzyme activation, substrate entry, and control of product specificity in 5-Lipoxygenase	Marcia Newcomer (Louisiana State University)
12:00	Discussion Session 2	
12:30	Lunch (provided)	
1:30	Using Structural Biology to support a BioEnergy Research Center	Henrique Pereira (Joint BioEnergy Institute)
2:00	Statistical Structural Biology	James Fraser (University of California San Francisco)
2:30	Discussion Session 1 + coffee, tea, snacks	
3:00	Unlocking protein secrets: exploring structures, states, and dynamics	Qun Liu (BNL, Stony Brook University)
3:30	Time-Resolved Crystallography of Iron-Dependent Enzymes: Toward Phototriggered, Anaerobic, and Multi-Modal Approaches	Katherine M. Davis (Emory University)
4:00	Visualizing and controlling how cells and proteins (in crystals) respond to external stimuli: beyond ground state structures	Soichi Wakatsuki (Stanford University)
4:30	Discussion Session 2 + coffee, tea, snacks	
5:00	Joint Discussion + Closing Remarks	
5:30	NSLS-II Tour (optional)	
6:00 – 7:30	Dinner (provided)	

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