Where John Spence's Legacy Leads Us To: From Static Pictures To Dynamics Of Biomolecules In Action

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X-ray Free Electron Lasers (XFELs) have opened a new avenue for structural discovery of the function and dynamics of biomolecules. Processes in biology are highly dynamic and the study of their dynamics is one of the grand challenges of Structural Biology as most structures determined so far only provide a static picture of the molecule. Serial Femtosecond Crystallography (SFX),which was pioneered by John Spence, provides a novel concept for structure determination, where X-ray diffraction "snapshots" are collected from a fully hydrated stream of nanocrystals, using femtosecond pulses from high energy X-ray free-electron lasers (XFELs) [1-4]. The XFEL pulses are so strong that they destroy any solid material, but a femtosecond is so short (1 fs =10 -15 s) that X-ray damage is diminished and diffraction from the crystals is observed before destruction takes effect [3]. Structural Biology with X-ray Free electron lasers allows data collection at near physiological conditions at room temperature thereby opening new avenues for the study of medical important proteins that could enhance structure-based drug design with SFX studies of medical important proteins, including the first XFEL studies on an important enzyme from SARS-CoV2 and reveal the "secrets" of energy conversion in Photosynthesis. XFELs also open new avenues to determine molecular snapshots of biomolecules "in action" [6-10]. including studies to reveal the "secrets" of energy conversion in Photosynthesis. In this talk results are presented from recent experiments to study the dynamic processes in light-driven systems that includes photoreceptors as well as the key proteins in oxygenic photosynthesis Photosystem I and II. The talk will also include a discussion on new avenues to study the dynamics of enzymes and receptors, which may play an important role in development of new antibiotics. The talk will close with a prospective of the development of compact femto and attosecond X-ray Sources at ASU (CXLS and CXFEL) [11] and at DESY (AXSIS) [12], which are highly synergistic to large XFELs and will in the future provide new opportunities to study the ultrafast dynamics of reactions with a combination of X-ray diffraction, X-ray spectroscopy and ultrafast optical spectroscopy.

References:

[1] Chapman,HN et al 2011, Nature, 470, 73-77 ; [2] Fromme P and Spence JC 2011 Curr Opin Struct Biol 2011, 21: 509-516; [3] Barty,A et al. 2012 Nature Photonics 6, 35–40; [4] Boutet S et al 2012, Science, 337: 362-364; [5] Liu W et al 20, Science 342: 1521-1524; [6] Aquila,A et al 2012, Optics Express, 20 (3), 2706-16; [7] Kupitz C et al 2014, Nature 5, 261-5; [8] Young ID et al. 2016, Nature 543, 1-5 ; [9], Suga M et al.2017, Nature 543, 1-5 ; [10] Ayyer, K. et al. Nature 2016, 530, 202-206

[11] Zhang, C et al, 9th International Particle Accelerator Conference IPAC2018, Vancouver, BC, Canada JACoW Publishing ISBN: 978-3-95450-184-7, [12] Kartner, F.X. et al. 2016, Nuclear Instruments & Methods in Physics Research Section A - Accelerators Spectrometers Detectors and Associated Equipment, 829, 24-29.

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