Keynote Lecture

KN30

The future is bright-- structural biology at FELs

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Protein crystallography using synchrotron radiation sources has had tremendous impact on biology, having yielded the structures of thousands of proteins and given detailed insight into their working mechanisms. However, the technique is limited by the requirement for macroscopic crystals, which can be difficult to obtain, as well as by the often severe radiation damage caused in diffraction experiments, in particular when using tiny crystals. To slow radiation damage, data collection is typically performed at cryogenic temperatures. With the advent of X-ray free-electron lasers (FELs) this situation appears remedied. Theoretical considerations had predicted that with sufficiently short pulses useful diffraction data can be collected before the onset of significant radiation damage that ultimately results in Coulomb explosion of the sample. This has been shown recently at the first hard X-ray FEL, the LCLS at Stanford. High resolution data collected of a stream of microcrystals of the model system lysozyme agree well with conventional data collected of a large macroscopic crystal [1] With the demonstration that de-novo phasing is feasible [2], serial femtosecond crystallography has been established as a useful tool for the analysis of tiny crystals [3] and thus the large group of proteins that resist yielding macroscopic crystals such as membrane proteins. In addition to ensure the required fast exchange of the microcrystals upon exposure, liquid jet delivery has the advantage of allowing data collection at room temperature. As demonstrated recently, this is important since structural dynamics and thus the observed conformation is often temperature dependent. Recent results will be described.

[1] *Boutet,S. et al. High-Resolution Protein Structure Determination by Serial Femtosecond Crystallography. Science 337, 362-364 (2012).,* ***[2]*** *Barends,T.R. et al. De novo protein crystal structure determination from X-ray free-electron laser data. Nature 505, 244-247 (2014).,* ***[3]*** *Redecke,L. et al. Natively inhibited Trypanosoma brucei cathepsin B structure determined by using an X-ray laser. Science 339, 227-230 (2013).*

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