

New Tools for Studying Protein Dynamics by X-ray crystallography

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Abstract

Protein dynamics is now studied at synchrotron sources for time-scales ranging from microseconds to minutes on proteins in the crystalline state by time-resolved room temperature crystallography. Complementary approaches such in crystallo optical spectroscopy can be used in addition to X-ray crystallography experiments to optimize the experimental conditions, to identify potential artefacts resulting from the crystalline state and to sample the most relevant time points. At the ESRF, a dedicated laboratory, the icOS lab,⁽¹⁾ has been developed to record optical spectroscopy data from protein crystals in a static or time-resolved manner.⁽²⁾ In addition, X-ray diffraction data can be recorded in parallel to UV-Vis absorption spectra on the beamline BM07-FIP2. One of the main limitations in studying protein dynamics through crystallography can be the tightness of the crystalline architectures which is influenced by crystal contacts. Molecular glues,^(3,4) a class of ligands with properties that can modify protein-protein interactions in crystals, offer a promising solution to this issue. In this presentation, I will describe our latest spectroscopic instruments and demonstrate how we have used them in combination with X-ray crystallography. Additionally, I will discuss the application of molecular glues in crystal engineering.

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⁽⁴⁾ Ramberg KO *et al.* Facile Fabrication of Protein-Macrocycle Frameworks. *J Am Chem Soc.* **2021**, (4), 1896-1907.