Macromolecular Powder Diffraction: Ready for Genuine Biological Problems

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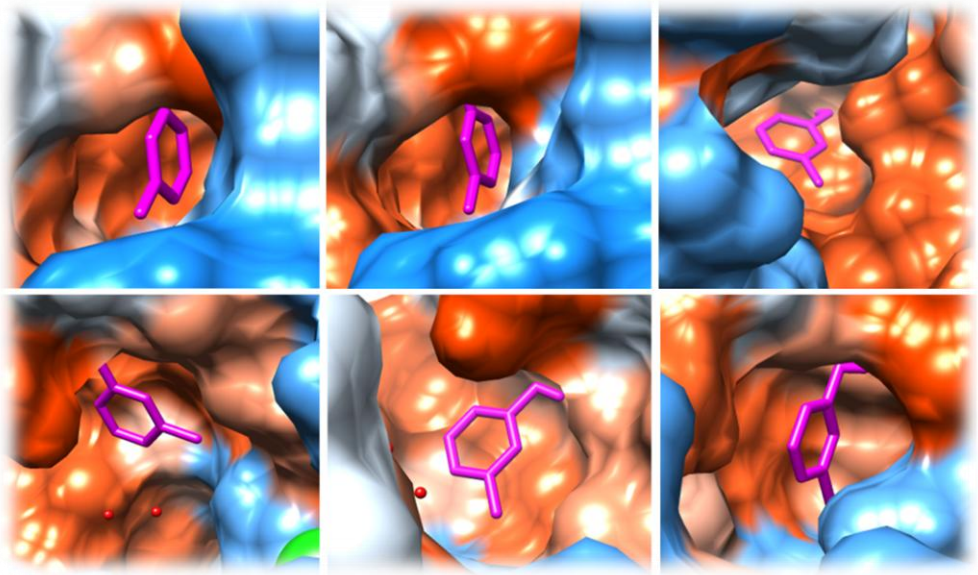

Ligand identification in protein structures via XRPD.

Identification of 6 m-cresol hydrophobic binding sites in a new monoclinic form of Human Insulin. (Valmas et al., 2015; ESRFNews 2015; Karavassili et al., 2017).

Knowledge of 3D structures of biological molecules plays a major role in both understanding important processes of life and developing pharmaceuticals. Among several methods available for structure determination, macromolecular X-ray powder diffraction (XRPD) has transformed over the past decade from an impossible dream to a respectable method. XRPD can be employed in biosciences for various purposes such as observing phase transitions, characterizing bulk pharmaceuticals, determining structures via the molecular replacement method, detecting ligands in protein–ligand complexes (Karavassili et al., in preparation), as well as in situ detection of novel protein crystal forms upon controlled relative humidity variation using laboratory XRPD. This presentation aims to provide necessary elements of theory and current methods, along with practical explanations, available software packages and highlighted case studies. We will demonstrate the value of in-house and synchrotron XRPD as an analysis tool in industrial protein-based drug screening, and its potential to help troubleshooting the production process and to provide information for further refining the manufacturing of pharmaceuticals. Selected examples will be presented regarding studies of pharmaceutical proteins and their complexes with organic ligands including Human Insulin, Urate Oxidase as well as peptide drugs (Fili et al., Acta Cryst. B, in press).