Probing drug-protein interactions with MicroED

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Microcrystal electron diffraction (MicroED) permits structure determination from nano/microcrystals using a cryo-electron microscope, bypassing the need for large crystals that are especially challenging to obtain for many samples. Furthermore, microcrystals improve the efficiency of ligand soaking, allowing for rapid structure determination of multiple drug-protein complexes using the same crystalline sample. As such, MicroED is a valuable technique for drug discovery. Here, we summarize the process of protein-ligand structure determination by MicroED. We also present several structures solved by our lab, which showcase the versatility of MicroED and its potential for structure-based drug design targeting both soluble and membrane proteins.

No special data collection procedure is needed for the application of dynamical refinement, and it can be applied to all types of 3D ED data. However, special data processing is required. Such data processing is available in the software PETS2 [7]. The dynamical refinement method is available in the crystallographic computing system Jana2006 [8] and its successor Jana2020.