

Absolute Configuration Determination of Small Molecules with Microed

Bo Wang¹

¹Biogen

bo.wang2@biogen.com

Microcrystal electron diffraction (MicroED) has shown its complementary role, with X-ray diffraction, in crystal structure elucidation. The minimal specimen preparation in MicroED is very attractive for the pharmaceutical industry, especially in early drug development when the quantity of test substances is limited. Absolute configuration determination of an active pharmaceutical ingredient (API) is a crucial task in drug development. Without extensive crystal growth effort and material quantity limitation, this approach offers a readily route to obtain reliable absolute configuration early in the drug development process.

In this talk, we showcase two real-world examples where MicroED data was utilized to determine the absolute configuration of pharmaceuticals. In the first example, we present the feasibility of absolute structure determination via MicroED by using chiral salt formation. In the second example, we conducted dynamical refinement on the kinematically refined crystal structures of APIs. The two examples showcase the utility of the latest advance in the field of electron diffraction to not only enable, but also unambiguously assign absolute configuration for hard-to-crystallize, complex, and quantity-limited pharmaceuticals.

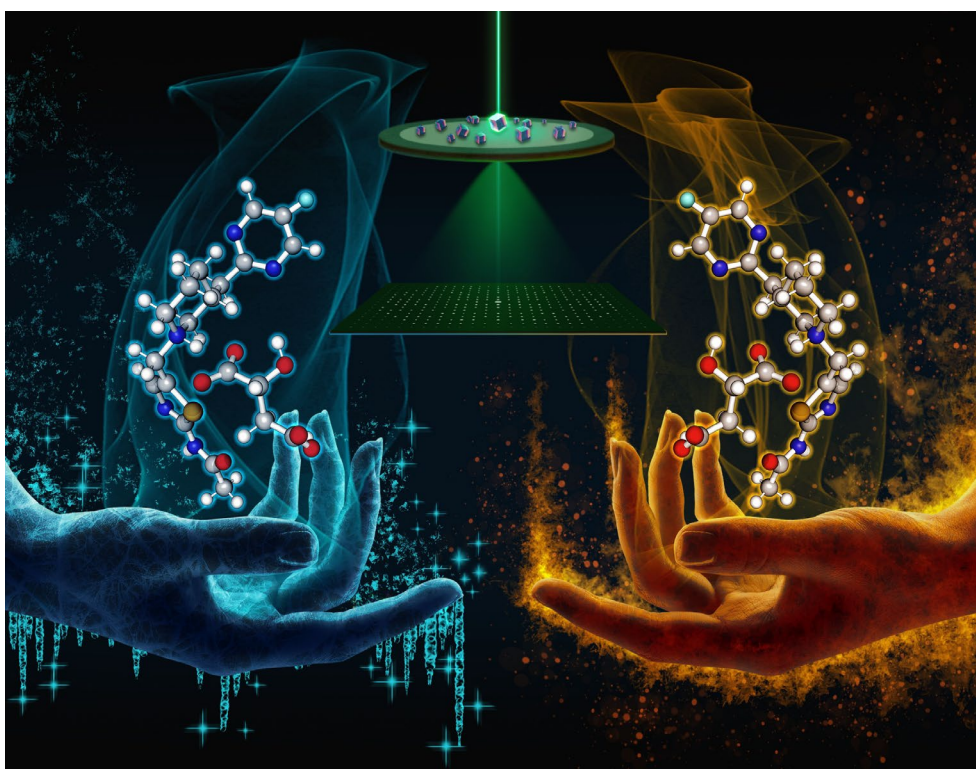


Figure 1