Visualization of the Structure and Dynamics of the Human Transcription Initiation Machinery by Cryo-EM

Single-particle cryo-electron microscopy (cryo-EM) has emerged over the last two decades as a technique capable of studying challenging systems that otherwise defy structural characterization. Among its advantages are the fact that crystallization is not required, only small amounts of sample are needed, and, because images can be classified in a computer, the technique has the potential to deal with compositional and conformational mixtures. Therefore, cryo-EM can be used to investigate complete and fully functional macromolecular complexes in different functional states, providing a richness of biological insight. Recent technical advances have resulted in a “quantum leap” in applicability, throughput and achievable resolution that has made this technique gain worldwide attention. We are using cryo-EM in the study of complex gene expression machinery. In the past few years we have visualized the assembly process of the human pre-initiation complex (PIC), as well as its structural reorganization during different stages of the initiation process. A major effort has also been to describe the structure and dynamics of human TFIID, a complex of over 1 MDa that binds to core promoter DNA and recruits the rest of the initiation machinery. I will present our latest results describing the subunit architecture of TFIID and the details of its interaction with core promoter DNA.

Host: Patrick Cramer