Transcription Initiation of Eukaryotic mRNA Coding Genes

The [illegible] laying signals from the environment and during development into the gene expression program of a cell. During transcription initiation, a large, multi-molecular machinery assembles on the promoter of a gene, to enable proper positioning of the RNA Polymerase enzyme and commence accurate mRNA synthesis. The rate of initiation is further controlled by transcriptional activators that recognize cis-regulatory DNA elements, proximal and distant to promoters, to direct remodeling of the local chromatin state and recruitment of the core machinery, often through interactions mediated by separate, large co-activator complexes.

Tremendous amount of work has identified the key molecular players and has revealed high-resolution snapshots of many intermediates in this pathway, however a complete, detailed mechanistic understanding of activator-dependent transcription initiation is still lacking. We are focusing on dissecting the assembly pathway and the structural organization of the transcription pre-initiation complex (comprised of the general transcription factors TFIIA,TFIIB,TFIID,TFIIF,TFIIE,TFIIH and RNA Polymerase II), and how it is regulated by the action of transcription activators.

We are applying single-molecule detection techniques to overcome some of the challenges associated with traditional, ensemble biochemical methods and probe this complex, multi-step process. Our goal is to obtain a high-resolution structural view of transcription initiation, in real-time and ultimately as is occurs in the physiological context of the sub-nuclear chromatin organization.