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Selected Publication

Silva DA, Weiss DR, Pardo F, Da, L-T, Levitt M, Wang D, and Huang X. (2013) Millisecond dynamics of RNA polymerase II translocation at atomic resolution. *PNAS* 111:7665-70

Research Aims and Interests

**The Transcription Elongation Cycle of RNA Polymerase Elucidated by Markov State Models**

Functional conformational changes play crucial roles in numerous biological processes. The research of the lab focuses on understanding fundamental mechanisms of conformational changes in complex biological systems especially in the gene transcriptional machinery using simulations and statistical mechanics based algorithms. To bridge the gap between experiments and simulations, we have developed efficient kinetic network models (KNM) for modelling long timescale conformational dynamics. We have used KNM to study the transcription elongation process performed by RNA polymerase. The RNA polymerase processively adds nucleotides to a nascent RNA transcript based on a DNA template during gene transcription. The series of steps required to add a nucleotide are known as the nucleotide addition cycle (NAC). Multiple structural studies have provided static snapshots of the different steps of the NAC, however, the dynamical mechanisms connecting the steps remain elusive or controversial. In particular, we have built KNM for the following processes: Trigger Loop Motion, Backtracking, Translocation and Pyrophosphate Ion release. Our results have allowed us to identify key residues, and their function has been confirmed by experiments. Taken together, all these projects provide a working model of the complete NAC at atomic resolution and at the millisecond timescale.