

Mechanism of pioneer transcription factor binding to the DNA

The mechanistic details of how pioneer transcription factors exert their functions over a range of specific targets in a timely and coordinated way during early development remains in its infancy. For instance, zygotic genome activation (ZGA) in fruit fly *Drosophila melanogaster*, is largely controlled by a protein called Zelda, a pioneer factor, binds at the vicinity of multiple developmental and constitutive genes and drives their activation during ZGA. Uncovering the mechanisms through which Zelda binds to its binding sites on the DNA and exerts its effects has been a challenge. In vitro experiments that observe the binding of Zelda to the DNA show that Zelda form spherical 'drop-like' structures at the specific binding sites on the DNA at low concentrations of the proteins in the bulk. As the bulk concentration of the protein is increased, they wet the whole DNA. To understand these observations, we have developed a simple model of 'Pre-wetting transition' following Cahn-Landau formalism. This model can explain the key features observed in the experiments such as the stationary size of Zelda drops on the DNA which remains mostly unaltered irrespective of the bulk concentration. Overall, our experimental framework sheds light onto the binding of pioneer transcription factor to the DNA, and offer experimentally testable predictions.

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