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Finding the rules of *cis*-regulatory logic: from Drosophilidae to Sepsidae and back again

ABSTRACT:

A developing organism executes an exquisitely precise program of transcriptional control. This accuracy is enforced by natural selection, since failure to generate correct cell types in the right locations is fatal to the organism. This precision is encoded in *cis*-regulatory DNA, but the rules by which gene expression is read out from sequence have remained largely obscure. We are engaged in a long-term effort to understand these rules using a quantitative model of transcriptional control based on thermodynamics and phenomenological laws. Our model has both explanatory and predictive power for understanding the control of transcription at cellular resolution. In this talk I will discuss recent results in this area. These will include an explanation, supported by confirmed predictions, of how enhancer elements conserve function while not conserving sequence. I will also discuss a theory of the intact *Drosophila even-skipped* locus that correctly predicts the location and function of its constituent enhancers.