Abstract: Precise control of gene activation lies at the heart of nearly all biological processes. However, despite enormous advances in understanding this process from both experimental and theoretical perspectives, we are still missing a quantitative description of the underlying transcriptional control mechanisms, and the remaining questions, such as how DNA sequence elements ‘compute’ expression from the inputs they receive, are still very basic. In this talk, I will present our progress towards the ultimate goal of developing integrated quantitative models for transcription regulation. I will describe a novel thermodynamic model that computes gene activation patterns as a function of DNA sequence and show that this model accurately predicts gene activation patterns in fly from DNA sequence alone.