

# **Incorporating Nucleosomes into Thermodynamic Models of Transcription Regulation**

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Transcriptional control is central to many cellular processes and consequently, much effort has been devoted to understanding its underlying mechanisms. Recently, it has become evident that the organization of nucleosomes along promoter regions has an important role in transcriptional control, since most transcription factors cannot bind to sequences bound by nucleosomes, and thus compete with nucleosomes for DNA access. This competition is governed by the relative concentrations of nucleosomes and transcription factors and by their respective sequence binding preferences. Even though competition of nucleosomes and transcription factors may have significant effects on transcription, a mechanistic understanding of its quantitative consequences for gene expression is still missing. Here we employ a thermodynamic framework based on fundamental principles of statistical mechanics to theoretically explore the effect that different nucleosome organizations along promoters have on the activation dynamics of promoters in response to varying concentrations of the regulating transcription factors. We show that even simple landscapes of nucleosome organization reproduce experimental results regarding the effect of nucleosomes as general repressors and as generators of obligate binding cooperativity between transcription factors. Our modeling framework also allows us to characterize the effects that various sequence elements of promoters will have on the induction threshold and on the shape of the promoter activation curves.

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