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Thermodynamic Modeling of Genome-wide Nucleosome Depleted Regions in Yeast

LU BAI, Pennsylvania State University

Nucleosome positioning in the genome is essential for the regulation of many nuclear processes. We currently have limited capability to predict nucleosome positioning in vivo , especially the locations and sizes of nucleosome depleted regions (NDRs). Here, we present a thermodynamic model that incorporates the intrinsic affinity of histones, competitive binding of sequence-specific factors, and nucleosome remodeling to predict nucleosome positioning in budding yeast. The model shows that the intrinsic affinity of histones, at near-saturating histone concentration, is not sufficient in generating NDRs in the genome. However, the binding of a few factors, especially RSC towards GC-rich and poly(A/T) sequences, allows us to predict ˜66% of genome-wide NDRs. The model also shows that nucleosome remodeling activity is required to predict the correct NDR sizes. The validity of the model was further supported by the agreement between the predicted and the measured nucleosome positioning upon factor deletion or on exogenous sequences introduced into yeast. Overall, our model quantitatively evaluated the impact of different genetic components on NDR formation and illustrated the vital roles of sequence-specific factors and nucleosome remodeling in this process.