THE CHINESE UNIVERSITY OF HONG KONG
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Chromatin Dynamics and Transcription Factor Condensation as Tunable Rheostats in Enhancer-Promoter Communication

by

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ALL INTERESTED ARE WELCOME
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Abstract

Enhancer-promoter (E-P) interactions are crucial for precise gene activation, particularly across large genomic distances, and are facilitated by phase-separated condensates formed by transcription factors (TFs) and co-factors. Leveraging polymer physics and coarse-grained chromatin modeling, we explored how structural dynamics of chromatin and TF condensation modulate E-P communication. By constructing models exhibiting either stable or dynamic chromatin characteristics, yielding similar ensemble-averaged Hi-C maps, we uncovered a multi-step mechanism governing E-P interactions. The dynamic chromatin model specifically promotes transient TF clustering to enhance E-P proximity and subsequently destabilizes clusters via chromatin chain flexibility, facilitating direct E-P contacts. Moreover, systematic variations of TF condensation strength and genomic distance revealed a “golden mean” of TF condensation that maximizes E-P contact efficiency, balancing cluster size for optimal TF bridging without competitive TF interference. Our findings suggest that TF condensates function as tunable “rheostats”, buffering E-P interactions against genomic separation and ensuring robust, precise transcriptional regulation. This integrated view enhances our physical understanding of chromatin dynamics and TF-mediated gene control mechanisms.

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