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Dynamical Chromatin Chains Facilitate Enhancer-promoter Communication Through Transcription Factor Clustering

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Enhancers are key regulators of gene expression, activating transcription by forming physical contacts with promoters, often across significant genomic distances. Effective enhancer-promoter (E-P) communication can be challenging due to these distances. Recent studies highlight the role of biomolecular condensates, formed via liquid-liquid phase separation, in facilitating E-P interactions and enhancing transcriptional activity. While much focus has been on transcription factors (TFs) driving phase separation, the role of the chromatin chain remains unclear. Here, we employed polymer physics models to construct two chromatin chain models with "stable" and "dynamic" properties. Despite similar ensemble-average Hi-C-like contact maps, the models exhibited distinct structural and dynamic characteristics. Consistent with recent experiments, our findings reveal a multi-step process in E-P interactions. The dynamic chromatin model enhances E-P spatial proximity by promoting TF cluster formation and mobility, driven by chromatin chain flexibility. This suggests chromatin dynamics are crucial for TF condensate formation, facilitating E-P communication through spatial and interactional optimization.