

Chromatin structure:

One Chromatin, Many Structures: Ensemble Versus Single-Cell Perspectives

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Resumen

Chromatin architecture underlies genome function, yet our understanding of how structural domains emerge from physical constraints and biochemical inputs remains incomplete. Experimental techniques—such as ensemble-averaged and single-cell Hi-C, ChromEMT, and multiplexed FISH—capture aspects of chromatin structure as reduced-dimensional projections, offering indirect views of its full three-dimensional organization. Here we advance the Self-Returning Excluded Volume (SR-EV) model—a computationally efficient framework that generates large-scale 3D chromatin configurations using stochastic rules and steric constraints. We show that ensembles of SR-EV conformations naturally reproduce a range of experimental observables, including slab-wise density heterogeneity, sparse single-cell and ensemble contact maps with topologically associating domains, and one-dimensional genomic profiles of chromatin compaction. By leveraging a post-selection strategy, the model flexibly incorporates the effects of architectural proteins and enables control over the genomic positioning of compacted or accessible regions. This unified framework bridges stochastic 3D organization with 1D and 2D chromatin data, offering a tractable platform to explore genome structure at scale.