

“Active or Passive? Disentangling Mechanisms of Chromatin Compartmentalization”

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Modern measurements show that transcriptionally active euchromatin and transcriptionally silenced heterochromatin are spatially segregated in the cell. These “A/B” compartments are thought to form via equilibrium phase separation due to biochemical affinities between distinct chromatin types. However, different chromatin types also have different levels of active processes, including transcription, motor activity, and nonequilibrium reactions, which enhance the subdiffusion of chromosomal loci. We therefore study a model of an active polymer subject to random forces which vary in magnitude along the chain. Our analysis shows that active regions of the polymer bend and expand, while inactive regions straighten out and condense, resembling the morphology of heterochromatin (B) and euchromatin (A). Using polymer simulations, we predict that two to ten-fold activity differences are sufficient to recapitulate the degree of A/B compartmentalization observed in data. How does *active* folding compare to a passive model with short-ranged attraction between B regions, which can also reproduce the checkerboard pattern in Hi-C data? We find that the active model shows additional “jet”-like features due to spontaneous looping in active regions, slower folding kinetics, and higher cell-to-cell variability. These differences point towards experimental avenues for disentangling active and passive mechanisms of chromatin folding.