

Title

Investigating human chromosome organization by whole-genome simulations

Authors

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Abstract

Both theoreticians and experimentalists have been dedicating significant effort to studying chromosome organization. Many experimental procedures were designed, such as Hi-C or ChIA-PET, to capture structural information of chromosomes. Based on the observations from Hi-C data, our group has previously proposed the Minimal Chromatin Model (MiChroM), aiming to understand the principles underlying chromosome compartmentalization. MiChroM is a model that describes the compartmentalization behavior of interphase chromosomes. Compared to experimental data, the agreement of the *in silico* contact maps suggested that phase separation of A/B compartments is a key feature determining the structure of individual chromosomes. In this work, we use the Open-MiChroM software to simulate the 46 chromosomes of a GM12878 human cell at 50 kb resolution, seeking to understand whether the nuclear organization of the whole genome would rely on the same principles observed for the organization of a single chromosome. The ensemble of structures generated by our simulations captures chromosome organization within territories and phase separation of chromatin compartments. The intra-chromosomal contact maps of each territory are consistent with experimental data, and phase separation is also observed in the interface between chromosomes. The resulting genome architecture resembles the inverted nucleus configuration, with aggregation of dense heterochromatin in the center, which drives heterochromatin-abundant chromosomes inwards. These results suggest that heterochromatin plays a central role in determining the nuclear architecture. We also see that MiChroM's assumptions seem to capture chromatin-chromatin interactions in the whole nucleus, whereas the overall nuclear structure is also influenced by interactions between chromatin and other nuclear bodies.