Title:
PHASE SEPARATION OF AB COMPARTMENTS MODULATED BY LAMINA-CHROMATIN INTERACTION

Abstract:

Recent experiments reveal that chromatin is able to bind to nuclear lamina proteins such as lamin A/C and lamin B1. Loci with high binding affinity to the lamina are called Lamin Associated Domains (LADs), primarily made up of inactive chromatin. This connection between heterochromatin and the nuclear envelope points to the possibility of further chromatin organization based on nucleus placement. Here we explore such a phenomenon by simulating five different human chromosomes in close proximity to a spherical confinement, which is attractive only to loci marked as LADs. Utilizing the chromatin types taken from the cell line GM12878, the chromosomes were modeled using the Minimal Chromatin Model (MiChroM) at 50Kbp resolution. This model ensures that the main fold of the chromatin is due to compartmentalization, while the lamina interaction falls into the perturbative regime. According to the simulations, introducing lamina interaction alone can drive the chromatin conformation from the inverted nucleus to the conventional nucleus, and vice versa. Also, the presence of lamina interaction enhances the compartmentalization at the intrachromosomal level. Further, depleted lamina simulations show that only chromatin-chromatin interactions are not enough to reproduce the experimental interchromosomal Hi-C maps, while the addition of nuclear lamina-chromatin interaction increases the frequency of the interchromosomal euchromatin interactions. This indicates that the nuclear lamina plays an important role in chromatin folding and dynamics.