Modeling Whole Genome of Budding Yeast throughout the Cell Cycle

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The three-dimensional organization of the genome plays a critical role in regulating cellular processes such as transcription, replication, and DNA repair. In yeast (Saccharomyces cerevisiae), genome architecture undergoes substantial reorganization throughout the cell cycle, including changes in chromatin compaction, formation of chromosomal territories, alterations in centromere clustering, and telomere positioning. These structural rearrangements significantly influence gene expression patterns and ensure accurate chromosome segregation during cell division. Here, we present a polymer-based model of the yeast genome at a 5 kb resolution, employing a maximum entropy approach to infer effective potentials from chromosome conformation capture (Hi-C) datasets obtained at various stages of the cell cycle. Our simulations accurately reproduce experimental Hi-C contact frequencies, capturing essential structural features such as centromere-centromere and telomere-telomere interactions, as well as correctly recapitulating the polymer scaling. Examination of the resulting 3D structures reveals dynamic genomic rearrangements across the cell cycle: centromere clustering intensifies from G1 to G2 phases, consistent with experimental observations, while telomere interactions become prominent predominantly in later stages. The radius of gyration increases from G1 to Anaphase, likely reflecting chromosome duplication events and microtubule-mediated chromosome stretching. This computational approach provides a versatile framework for understanding the physical mechanisms underlying genome organization and its dynamic changes during the yeast cell cycle.