Modeling chromosomes using the full-inversion method

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The human genome is organized within a nucleus where chromosomes fold into an ensemble of different conformations. Chromosome conformation capture techniques such as Hi-C provide information about the genome architecture by creating a 2D proximity. Initially, Hi-C experiments were performed in human interphase cell lines. Recently, measuring efforts were expanded to several organisms, cell lines, tissues, and cell cycle phases, where obtaining high-quality maps is challenging. In addition, some organisms, such as Bacterial samples, do not have compartments or any organization feature when analyzing the Hi-C experiments, making the modeling challenging. Aided by the developed chromatin folding and structure model, we develop a framework for training interactions based on each pair of loci separately. To enhance the training, we included a first-order minimization in combination with the maximum entropy approach that allows us to speed up the modeling, even for large chromosomes. We use the Open-MiChroM platform to perform the simulations assisted by first-order minimization procedure. The models generated are precise compared to the experimental Hi-Cs, and the 3D structures ensemble is consistent with the crystal liquid theory for chromosomes. This novel modeling allows the exploration of a broad spectrum of 3D genome organizations on different organisms, cell lines, and cell phases.