

## **Bayesian inference of three-dimensional chromosomal organization from Hi-C data**

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Knowledge of spatial organization of the genome is critical for the study of transcription regulation and other nuclear processes in the cell. Recently, chromosome conformation capture (3C) based technologies such as Hi-C and TCC have been developed to provide a genome-wide, three-dimensional (3D) view of chromatin organization, but analysis algorithms for inferring chromosomal structures from such experiments are still under-developed. Here we describe a novel Bayesian probabilistic approach and Markov Chain Monte Carlo algorithm, denoted "Bayesian 3D constructor for Hi-C data" (BACH), to infer three-dimensional (3D) chromosomal structures. Applying BACH to a high resolution Hi-C dataset generated from mouse embryonic stem cells led to a model of the spatial arrangement of chromatin that revealed structural properties associated with euchromatic and heterochromatic regions in the genome. We also describe a BACH-MIX algorithm that can model the stability of chromatin structures, and found that variations of chromatin modeling are associated with genomic and epigenetic features. Our results demonstrate that BACH and BACH-MIX have the potential to provide new insights into the chromosomal architecture in mammalian cells.

Based on the joint work with Ming Hu, Steve Z Qin, Ke Deng, Jesse Dixon, and Bing Ren.