Abstract

The three-dimensional structure of the genome plays a crucial role in gene regulation and cellular functions by influencing the spatial organization of chromatin and interactions among genomic elements. Recent advances in the field of 3D genomics have significantly enhanced our understanding of how chromatin structure affects gene expression and biological processes. Chromatin loops facilitate long-range chromatin interactions, mediated by specific protein factors such as cohesin complexes and CTCF.

This work describes the implementation of the ChromoLooping tool (https://github.com/SFGLab/ChromoLooping), designed for modeling the three-dimensional structure of chromatin from super-resolution microscopy data and its use in reconstructing the shape of chromatin loops from iPALM microscopy images. The project achieved a localization precision of up to 2 nm, resulting in a simulated genomic resolution of 10 base pairs. Additionally, the application of ChromoLooping to model the chromatin structure from publicly available multi-domain light microscopy images is presented, as well as the adaptation of ChromoLooping for confocal microscopy images.

The second part of the work details the implementation of the nf-HiChIP tool (https://github.com/SFGLab/hichip-nf-pipeline) for automated analysis of HiChIP data. This tool allows for parallel processing of multiple HiChIP and ChIP-seq data samples and supports automatic analysis of multiple replicates, their merging, and the analysis of the combined sample. Projects utilizing this tool are discussed, along with a proposed comprehensive comparative analysis of multiple 3D genomics data samples derived from next-generation sequencing (NGS).

The thesis presents two approaches to studying three-dimensional structure: one based on microscopy techniques and observation of DNA conformation in single cells, and the other focusing on population-level genomic data. Together, these fields form a comprehensive tool for studying chromatin architecture. This work not only deepens the understanding of the three-dimensional structure of chromatin but also offers innovative methods for investigating dynamic interactions within the genome.

key words: 3D structure, chromatin, image processing, next-generation sequencing