Chromatin Accessibility Methods

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Preface

The genomic distribution patterns of chromatin accessibility and its dynamics are key features of the regulation of gene expression and many other aspects of chromatin biology. The genomes of eukaryotes are usually packaged by nucleosomal particles, which have a generally strongly inhibitory effect on transcription and on the occupancy of DNA by regulatory proteins. It is typically active *cis*-regulatory regions (cREs) in the genome that are characterized by depleted nucleosomal occupancy and increased chromatin accessibility, which has in turn proven to be a highly useful property enabling the identification of candidate cREs as well as the tracking of their activity across cell types and conditions as accessible DNA can be preferentially enzymatically or chemically labeled in numerous ways.

Technological advances in the labeling and readout of accessible DNA have played a major role in driving forward our understanding of chromatin and regulatory biology over the last few decades. The last fifteen years have seen a particularly dramatic explosion in the variety and power of approaches for studying chromatin accessibility, driven by two sequential technological revolutions – first the development of high-throughput sequencing in the mid-2000s and then the advent of single-cell genomics in the 2010s. The current book aims to provide a comprehensive resource covering the existing and state-of-the-art tools in the field.

We have divided the protocols in the book in several sections, depending on the different aspects of chromatin accessibility that they measure and/or approaches that they take. In the first section, bulk-cell methods for profiling chromatin accessibility and nucleosome positioning that rely on enzymatic cleavage of accessible DNA and produce information about relative accessibility are covered. The second section is dedicated to methods that use single-molecule and enzymatic approaches to solving the problem of mapping absolute occupancy/accessibility. The third section covers the wide array of emerging tools for mapping DNA accessibility and nucleosome positioning in single cells, as well as a number of single-cell multiomics methods that simultaneously measure chromatin accessibility and other features of the cell, such as the transcriptome, the methylome, and protein markers. More recently, imaging-based methods for visualizing accessible chromatin in its nuclear context have emerged; these are included in the fourth section. The last section features computational methods for the processing and analysis of chromatin accessibility datasets. This book will serve as an extensive and useful reference for researchers studying different facets of chromatin accessibility in a wide variety of biological contexts.

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V. Computational analysis of chromatin accessibility datasets