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A next generation of advances in chromosome architecture

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Abstract

New insight into the architecture of chromosomes, their molecular composition, structure and spatial location, and time-resolved features, has grown enormously through developments of a range of pioneering interdisciplinary approaches that lie at the interface of the life and physical sciences. These involve several state-of-the-art 'physics of life' tools that are both experimental and theoretical, used in conjunction with molecular biology methods which enable investigation of chromosome structure and function *in vitro*, *in vivo* and even *in silico*. In particular, a move towards far greater quantitation has enabled transformative leaps in our understanding. These have involved valuable improvements to the spatial and temporal resolution of quantitative measurements, such as *in vivo* super-resolved light microscopy and single-molecule biophysics methods, which facilitate probing of dynamic chromosome processes hitherto impossible. Similarly, there have been important advances in the theoretical biophysics approaches which have enabled advances in predictive modelling of to generate new understanding of the modes of operation of chromosomes across all domains of life. Here, I discuss these advances, and review the current state of our knowledge of chromosome architecture and speculate where future advances may lead.

Key words: Single-molecule biophysics, super-resolution, DNA, nucleus

1. Introduction

This updated edition comprises a collection of truly cutting-edge laboratory protocols, techniques and applications in use today by some of the leading international experts in the broad field of 'Chromosome Architecture'. A key difference in emphasis, compared with previous collections of articles published in this area, is on the emphasis on the development and application of complex techniques and protocols which increase the physiological relevance of chromosome architecture investigation compared to methods utilized previously – these developments are manifest both through application of far more complex bottom-up assays *in vitro*, as well as in striving to maintain the native physiological context through investigation of living, functional cells.***(1)*** In particular, experimental methods which have used advances in optical microscopy, ***(2)*** especially the use of fluorescence microscopy methods to probe functional, living cells.***(3-12)*** The length scale of precision of experimental protocols in this area has improved dramatically over recent years and many cutting-edge methods now utilize state-of-the-art single-molecule approaches,***(13)*** both for imaging the DNA content of chromosome and proteins that bind to DNA, as well as using methods that can controllably manipulate single DNA molecules and can image its structure to a precision better the standard optical resolution limit.***(14,15)*** This volume also includes more complex, physiologically representative methods to investigate chromosome architecture through the use of advanced computational methods and mathematical analysis.

What is clear is that the combination of pioneering molecular biology, biochemistry and genetics methods with emerging, exciting tools from biophysics, bioengineering, computer science and biomathematics are transforming our knowledge of functional chromosome architecture. Improvements in these fields are likely to add yet more insight over the next few years into the complex interactions between multiple key molecular players inside chromosomes.

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