New advances in chromosome architecture

Mark C. Leake[1]

[1] Biological Physical Sciences Institute (BPSI)

University of York

York

YO10 5DD

United Kingdom

[1] Corresponding author

e–mail: mark.leake@york.ac.uk

Tel: +44 (0)1904 322697

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Abstract

Our knowledge of the 'architecture' of chromosomes has grown enormously in the past decade. This new insight has been enabled largely through advances in interdisciplinary research methods at the cutting-edge interface of the life and physical sciences. Importantly this has involved several state-of-the-art biophysical tools used in conjunction with molecular biology approaches which enable investigation of chromosome structure and function in living cells. Also, there are new and emerging interfacial science tools which enable significant improvements to the spatial and temporal resolution of quantitative measurements, such as *in vivo* super-resolution and powerful new single-molecule biophysics methods, which facilitate probing of dynamic chromosome processes hitherto impossible. And there are also important advances in the methods of theoretical biophysics which have enabled advances in predictive modelling of this high quality experimental data from molecular and physical biology to generate new understanding of the modes of operation of chromosomes, both in eukaryotic and prokaryotic cells. Here, I discuss these advances, and take stock on 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 volume of Springer's Methods in Molecular Biology series consists of 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 review articles published in

this area over the past 5 years, 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 light microscopy, ***(2)*** especially the use of fluorescence microscopy methods to probe functional, living cells, especially so using prokaryotic systems as model organisms.***(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)*** 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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