PREFACE

Biological cells are active mechanical systems sensing local microenvironments using specialized cell-surface receptors. Physicochemical signals from the extracellular matrix impinge on cellular geometry resulting in altered functional nuclear landscapes and gene function. These alterations regulate diverse biological processes including stem-cell differentiation, developmental genetic programs, and cellular homeostatic control systems. Although the cytoskeleton is a well-appreciated critical component of cellular morphology, emerging evidence suggests that it may also have important consequences for maintenance of nuclear architecture; its mechanical properties and genome function. Regulation of genetic programs in response to cellular geometric cues requires mechanisms that act at a distance. A number of signaling pathways are activated in response to mechanical signals converging on regulatory factors, which translocate to the nucleus via diffusive processes. Recent evidence also highlights the physical transmission of active stresses via cytoplasmic-nucleus connections to remodel chromatin assembly. The physicochemical signals that arrive at the nucleus have to be further sorted to appropriate regulatory sequences within the 3D architecture of the cell nucleus to effect changes in genome function. Although the location of regulatory sequences on the 1D DNA polymer is known from genome sequencing, its 3D location when folded into chromatin via histone and nonhistone proteins within the nucleus is largely unknown. In addition, a number of essential posttranslational modifications of histone proteins determine both specificity and accessibility to regulatory sequences on the genome.

We are just beginning to appreciate the impact of cellular geometry on nuclear mechanics and genome regulation. In addition, the mechanical integrity of the cell nucleus and nuclear mechanical signaling are found to profoundly influence cellular homeostatic controls: driving cells toward differentiation, proliferation, or apoptosis. Further, diseases such as cancer are conjectured to originate at a single-cell level in its local mechanical environment, within tissue contexts. The chapters in this book describe both methods and *advances* in our understanding of the spatio-temporal organization of genome assembly, its integration to mechanical properties of the cell nucleus and how mechanoregulation of gene function may be defined in interphase cells and during their differentiation and development. The last section discusses the growing number of diseases associated with altered nuclear organization. Clearly, understanding the mechanical aspects of the cell nucleus and how it impinges on genome function in living cells has become a central theme in modern cell and developmental biology and biophysics. With the advent of new methods and approaches, some of which are described in this book, there exists now a promising future in this emerging research frontier.

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