

Unraveling Genome Biophysics

While digitizing the human genome has been one of the major recent scientific achievements, unraveling genome structure and, more importantly, structure/function relationships has been a major preoccupation for many scientific teams worldwide. Indeed, the understanding of structure from the DNA level to nucleosomes, chromatin fibers, genes, and chromosomes holds the key to interpreting many of the associated genome functions, from DNA repair and duplication to gene transcription.

Recognizing the central role of biophysics in meeting this scientific challenge, we launched a new section in *Biophysical Journal*, “Nucleic Acids and Genome Biophysics” (Section I), in January 2016.

To celebrate the anniversary of this successful new Section, we are pleased to present this Special Issue of the journal devoted to Genome Biophysics. These are exciting times for the field because many techniques are, as never before, being developed and applied by both experimentalists and modelers to decipher aspects of the genome puzzle (as emphasized on the cover). These include x-ray crystallography, Cryo-electron microscopy, in vitro and in situ biochemistry, single-nucleosome resolution nanoscopy, genome-wide high throughput measurements, and a large range of computational approaches on various spatial and temporal scales, from histone tails to entire chromosomes.

The contributions in this volume reflect this exciting range of topics, as well as the breadth and depth of our fascinating subject.

Three perspectives discuss fundamental aspects of genome structure, such as nucleosome positioning, chromosomal domains, and looping networks.

Specifically, these articles focus on chromatin looping as a function of nucleosome positioning (W. Olson and colleagues); the application of energy landscape theory to the study of chromosome architecture (P. Wolynes and B. Zhang); and the role of hierarchical looping in chromatin fibers and genes (T. Schlick and G. Bascom).

Two noteworthy contributions are accompanied by New and Notable articles.

D. Discher and colleagues visualize chromatin deformations under nuclear movements (see the accompanying New & Notable overview by D. Thirumalai). A. Spakowitz and colleagues analyze the diffusion dynamics of RNA-protein particles in yeast cells (see the New & Notable article by R. Metzler).

Among the other exciting contributions in this volume, M. Betterton and colleagues present a biophysical model of chromosome segregation during cell division, focusing on the dynamics of microtubules in this process. M. Sasai and N. Tokuda study the relationship between the spatial distribution of genes and their transcriptional level in yeast. C. Sing and K. Dahlke focus on the dissociation dependence of nucleoid-associated proteins on the freely diffusing proteins and DNA in the cellular environment. N. Kellermayer and colleagues study the nanomechanical properties of hypermethylated DNA. A. Onufriev and colleagues highlight the importance of partially assembled nucleosome states for genome regulation by both modeling and atomic force microscopy. J. Langowski and colleagues simulate a common epigenetic mark to understand the structural and energetic aspects of the associated mechanism. S. Harris and co-workers examine the influence of the DNA supercoiling dynamics in minicircles on the binding of other biomolecules. M. Tompitak and colleagues employ an organism-wide analysis of nucleosome positioning signals in promoter regions to show a correlation between nucleosome positioning and organism complexity. Finally, K. Rippe and colleagues introduce multi-scale correlation models to relate genome sequencing data to patterns of chromatin domain networks on multiple length scales.

It is difficult to predict how the field of genome biophysics will develop in the coming decade, but it is likely that both high-resolution visualization of genome processes and multi-scale modeling on many genome levels will intensify and illuminate our understanding of genome structure and function. In particular, the increased usage of modeling by experimentalists, and of experiments by modelers in this area, holds great promise for fruitful collaborations and discoveries. Together, all basic science advances in genome architecture and processes, as reflected

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by the contributions in this volume, are of fundamental importance to practical applications in medicine and technology.

In particular, the application of CRISPR-like gene editing techniques opens unprecedented opportunities for engineering optimal chromatin folding conditions for design of epigenome-based therapies.

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