Molecules and Cells

Editorial

Emerging Biophysics Tools for Biologists

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Through evolution, molecular machines employed by biological systems have achieved a remarkable level of complexity and versatility, which is not adequately described by the physical and chemical methods originally developed for abiotic materials and processes. For example, the x-ray crystallography method had to be further improved for more than 30 years with the tenacious efforts by Drs. Max F. Perutz and John C. Kendrew before application to protein structures, which laid a foundation for what we know as the current structural biology (NobelPrize.org, 2022). Such efforts are still actively ongoing, and this special issue is intended to introduce the recent efforts in development of novel biophysics tools that may afford to reveal otherwise hidden complexity and details of the biology. It is thrilling to see that the efforts are being made on various fronts covering virtually all length scales relevant to molecular and cellular biology (i.e., sub-nanometer to micrometer scales).

For example, the article by Dr. Nam-Ki Lee and co-worker summarizes a collection of biophysical tools that study bending of the double-stranded DNA structures at the single-molecule level, trying to fill a knowledge gap that how the stiff double-stranded DNAs with a persistence length of more than 40 nm can be steeply bent and wound around nucleosomes to create chromatin structures (Yeou and Lee, 2022). Dr. Min-Ju Shon and co-workers describe another roster of single-molecule tools called force spectroscopy, which tracks extension of single biological molecules while applying different levels of mechanical tension (Yang et al., 2022). The authors discuss how mechanobiology processes, where mechanical tension is converted to a cellular biochemical signal or vice versa, can be understood with recent single-molecule force spectroscopy data, as well as an intriguing hypothesis that neurotransmitter release from a presynapse might be understood as a tension-regulated process. The article by Dr. Hye Ran Koh and co-workers introduces a collection of tools complementary to the single-molecule force spectroscopy, where a mechanical tension applied to single protein complexes (e.g., integrin signaling complexes) is measured in situ in live cells (Baek et al., 2022).

In addition to these ultra-molecular details revealed by the single-molecule methods, the biophysics tools find their use at the other end of the spectrum by providing collective insights that emerge from intricate interplays between numerous cellular components. Dr. Yongdae Shin discusses the theoretical frames describing biological phase separation, where proteins, RNAs and/or genomic DNAs coalesce into membraneless condensates, a process forming remarkably diverse cellular objects including stress granules, immune synapses on membranes, and Cajal bodies in nucleus (Shin, 2022). Finally, in the cover article of this issue, Dr. Doory Kim and co-authors introduce an ambitious project where super-resolution fluorescence microscopy is combined with electron microscopy (Jeong and Kim, 2022). With perfect alignment of these two imaging apparatuses, the rich topographical information generated by the electron microscopy (or tomography) could be overlaid with molecular identities afforded by the super-resolution fluorescence microscopes. Considering these two types of information are highly complementary, this correlative super-resolution and electron microscopy —albeit still in an infant stage of development—could be a platform for revealing both mesoscale organization of cellular components and their molecular identities.

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Most biological processes, if not all, depend on extremely rugged free energy landscapes with energy scales only barely larger than thermal fluctuations (Dill and Bromberg, 2010). This remarkable energetics makes biological structures and interactions between them largely labile and transient, endowing an astonishing adaptability to biological systems. Even seemingly distant parts in single molecules are intricately intertwined through allostery, and the individual molecules and complexes in turn cooperate with one another, defining higher levels of complexity. It would thus be preposterous to expect a single method fits all purposes. With continuous development of novel tools and potential mix-and-match of these tools, however, the biologists will be increasingly ready and armed in their efforts to reveal the true complexity of biological processes.

CONFLICT OF INTEREST

The author has no potential conflicts of interest to disclose.

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