Introductory Editorial: Special Section on Single-Molecule and Super-Resolution Microscopy of Biopolymers

SINGLE MOLECULES: ALIVE AND WELL RESOLVED

Since taking stock in 2006 of the "Future of Biomedical Sciences: Single Molecule Microscopy" in a *Biopolymers* issue a decade ago, the field has come a long way. The emergence in that same year of multiple "pointillism" based super-resolution tools that image and localize single fluorophores in sequential imaging cycles led—in just 8 years—to the 2014 Nobel Prize in Chemistry to three of the pioneers in the field. A confluence of ever-improving laser, optics and camera equipment, more versatile analysis software, and broadened brainpower of an increasing number of practitioners has led to rapid progress in the applications of single molecule tools to important problems in both biology and materials science. This issue contains a Special Section with a representative current snapshot of five papers on the utility and integration of single molecule tools into the modern biosciences.

First, Chemla and coworkers review how the integration of optical tweezers with fluorescence imaging capabilities has helped maximize the information content extracted from nucleic-acid processing enzymes. Such an expansion of the accessible observables helps correlate mechanical and mechanistic parameters. Next, Lyubchenko and coworkers demonstrate how the assembly of single α-synuclein monomers into aggregates, which may nucleate protein misfolding diseases, can be followed by single molecule fluorescence microscopy. Low pH turns out to stabilize these aggregates, possibly through surface charge neutralization.

Moving to live-cell imaging, Lyu, Xiao and coworkers use super-resolution fluorescence microscopy to investigate the bacterial cytoskeletal Z-ring protein FtsZ that helps carry out cytokinesis, or cell division. They find that prior disparate observations are reconciled by a model in which the Z-ring is composed of only loosely associated, heterogeneously distributed FtsZ clusters.

Next, Luthey-Schulten and coworkers in a tour-de-force integrate fluorescence imaging of live bacterial cells into a spatially resolved whole-cell computational model of ribosome biogenesis to predict the effects of cell growth, DNA replication, and cell division. The authors are able to describe all underlying biological processes in the form of reaction-diffusion master equations that are solved using their Lattice Microbes simulation software. This approach highlights the great potential for future synergies between single molecule tools and whole-cell computational simulations. Finally, Aksimentiev and coworkers showcase the current status of all-atom molecular dynamics (MD) simulations by assessing and improving the performance of models for the divalent cation Ca^{2+} in two common force fields, AMBER and CHARMM. As MD simulations further improve in both accuracy and time domain, the vision of understanding the cellular mechanisms of biopolymers at the single molecule level stands to be realized by an integration of experiment and theory.

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