

MAR08-2007-007093

Abstract for an Invited Paper
for the MAR08 Meeting of
the American Physical Society

Max Delbruck Biological Physics Prize Talk: The Biophysics of Gene Regulation, Studied One Molecule at a Time¹
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Advances have led to a new field, dubbed single molecule biophysics. Prominent among the new technologies is the optical trap, or ‘optical tweezers.’ Sensitive systems for measuring force and displacement in optical traps permit the nanomechanical properties of individual macromolecules to be explored with unprecedented precision, revealing behaviors heretofore obscured by ensemble-based approaches. This talk will focus on some of our current work with single-molecule systems, including transcription by RNA polymerase and structural transitions in nucleic acids. We developed high-resolution instrumentation that has broken the nanometer barrier and is thereby able to detect displacements down to the atomic level, in aqueous buffer at room temperature. Consequently, we can monitor the motions of RNA polymerase molecules in real time as these step from base to base along DNA. On the practical side, base-pair resolution makes it possible to sequence DNA in a new way, based on enzyme motions, and points to new directions in nanoscience. The improved stability afforded by the current generation of optical trapping apparatus has allowed us to reconstruct the complete energy landscapes for folding transitions in nucleic-acid hairpins. Recently, we have turned our attention to the problem of co-transcriptional folding, aptamers, and riboswitches formed in nascent mRNAs, and to the DNA or RNA sequence elements that regulate expression.

¹research supported by the NIGMS

²Delbruck Prize Lecture