Conformation and dynamics of single molecules of DNA in solution

Adam E. Cohen cohen@chemistry.harvard.edu

Departments of Chemistry and Chemical Biology and Physics, Harvard University

To study a single molecule in solution, one would like to hold the molecule still without perturbing its dynamics along internal degrees of freedom. We have addressed this challenge by building a machine we call an Anti-Brownian Electrokinetic trap (ABEL trap). The ABEL trap consists of a nanofluidic cell mounted in a fluorescence microscope. A real-time tracking system follows the Brownian motion of a single fluorescent molecule, and a feedback system generates a time-dependent electrokinetic drift that cancels this Brownian motion.

We used the ABEL trap to study the conformation and dynamics of single molecules of fluorescently labeled double stranded DNA. Shape fluctuations were observed with high speed fluorescence imaging, leading to an accumulation of nearly 60,000 images. These images were analyzed statistically to extract the density-density correlation functions of a single molecule.³ Principal Components Analysis yields a set of conformational normal modes which are an efficient way to characterize the shape fluctuations of the molecule.⁴ Many aspects of the data await theoretical explanation.

- 1. Cohen, A. E. & Moerner, W. E. Suppressing Brownian motion of individual biomolecules in solution. *Proc. Natl. Acad. Sci. U. S. A.* **103**, 4362-4365 (2006).
- 2. Cohen, A. E. & Moerner, W. E. Controlling Brownian motion of single protein molecules and single fluorophores in aqueous buffer. *Optics Express* **16**, 6941-6956 (2008).
- 3. Cohen, A. E. & Moerner, W. E. Internal mechanical response of a polymer in solution. *Phys. Rev. Lett.* **98**, 116001 (2007).
- 4. Cohen, A. E. & Moerner, W. E. Principal-components analysis of shape fluctuations of single DNA molecules. *Proc. Natl. Acad. Sci. U. S. A.* **104**, 12622 (2007).