Force sensing with nanoscale DNA tethers

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Force measurement at the single-molecule level provides insight into intra-molecular dynamics and inter-molecular interactions. Traditionally, researchers used atomic force microscopy and magnetic or optical tweezers to investigate the force-dependent biological interactions and mechanical properties of biomolecules. The popularity of these techniques, however, suffers from drawbacks including slow image acquisition rate and/or low data throughput, as well as connections to macro-beads that introduce drift and prevent the investigation of minor conformational changes. Here, we present a force sensor consisting of a single nanoparticle tethered to double stranded DNA (dsDNA) on an ultrasensitive dark-field microscope, enabling the simultaneous characterisation of multiple tethers. We show that upon application of an electric field, the charged nanoparticles are driven from their equilibrium positions, and the stretched dsDNA acts as a polymer nanospring, exerting a restoring force on the piconewton scale. We monitor the nanoparticle displacement by tracking the scattering signal with a micromirror total internal reflection dark-field microscope with angstrom precision. As a result, we can quantify the charge depend displacement of the tether, and how it depends on surface charge and applied potential. Our approach opens up new avenues to study force- and charge-relevant dynamics and the interactions of biological macromolecules.