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Analysis of Single Molecules and Particles by Active Control in Nanofluidic Devices

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Nanofluidics involves flow of ions, molecules, and fluids in channels with dimensions approaching molecular length scales. In particular, nanofluidic devices offer the capability of single molecule detection by monitoring change in ionic current through nanopores or nanochannels during translocation (passage) of a molecule through the pore. This current signal can yield information about the size, charge, conformation, and molecular interactions within the pore. However, nanopore sensors can typically perform only a single measurement on a molecule, precluding observation of dynamic events and also limiting the ability of the pore to sensitively distinguish between different molecules. To enhance the discrimination ability of nanopore sensors, we are developing methods for active manipulation of single molecules in nanofluidic devices. As a first step, we have demonstrated multiple measurements on the same DNA molecule by active feedback control: upon detection of a translocation signal the voltage bias was reversed, which allowed for hundreds of measurements on the same molecule. Multiple measurements allowed for statistical averaging of the translocation signal, which increased the ability of the pore to distinguish between DNA molecules of different lengths. This approach may lead to rapid single molecule and single particle assays including DNA fragment sizing and enzymatic digestion assays, analysis of colloidal or polymer suspensions, and sizing of biomolecules.