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### **Single Molecule Manipulation and Analysis in Nanofluidic Systems**

HAROLD CRAIGHEAD, Cornell Univeristy

We have used simple small-scale structures to isolate and manipulate individual biomolecules in order to observe their activity and identity. Nanofluidic devices with dimensions, smaller than a relevant molecular length scale, have been used to sort or control the conformation of long biopolymers such as DNA. Structurally-derived entropic and frictional forces balanced against the forces resulting from applied fields can elongate and controllably move a selected molecule. This can be used for measuring the length of the DNA or presenting it in an oriented manner for analysis. We have also employed metallic apertures a few tens of nanometers in diameter to confine a region of optical excitation to a volume on the order of  $10^{-20}$  liters, which allows the observation of single molecule motion and binding activity at meaningful rates and concentrations. This approach enables measuring the motility of proteins and binding of individual molecules in lipid layers and cell membranes. Small fluid channels have also been used to isolate individual optically detected molecules for evaluation in flowing systems. The measurement of mobility and detection of discrete molecular binding events can be done at the individual molecule level in such fluid systems.