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Molecular Tweezers: Using the Electric Field in a Synthetic Nanopore to Disrupt Biomolecular Binding Forces[1]

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The forces binding proteins to DNA in an aqueous solution are vital to biology, but inadequately understood. In particular, restriction enzymes like EcoRI are extraordinarily sequence-specific and yet the complex with DNA is very stable. To stringently test these forces, we use the electric field inside a synthetic nanometer-diameter pore in a thin membrane to pull on double-stranded DNA bound to EcoRI and BamHI, introducing a shear between the enzyme and their respective cognate sites in DNA. We observe a sharp threshold near 1nN in the force required to disrupt the binding in the complex, which is in stark contrast with previous measurements of the force (10pN) accomplished by unzipping the DNA molecule at a constant loading rates (1nN/sec). This force, acting over a distance corresponding to the separation between bases, coincidentally corresponds to the free energy of formation for the EcoRI-DNA complex. Using molecular dynamics, we interpret the measurements and elucidate the binding with atomic precision.

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