be capable of sensing the interactions. Field-effect transistors (FET) have been widely used as biosensors, but are generally used with a large number of molecules to obtain a sufficient signal. The measurements taken with the FET-based biosensors are mostly "on" or "off" measurements, which are determined by the presence or absence of a reaction. A specific type of FET, the p-type metal oxide semiconductor FET (pMOSFET) appears to be a promising biosensor device. The pMOSFET contains holes in the channel, also known as the inversion layer, opposite in carrier type to the substrate. An atomic force microscope (AFM) has shown the ability to measure molecular interactions down to the single molecular level and to control the distance between a ligand and a receptor protein up to subatomic resolution. The integration of AFM and FET technologies has the potential to provide not only valuable information about these biomolecular interactions that has not been accomplished by other methods, but also a much more rapid drug screening technique. The ability to control single molecules will allow for the comprehensive study of biomolecular interactions at the single-molecular level. This presentation will show how the AFM and FET were integrated into one functioning biosensor. The efficiency at detecting single molecular binding and unbinding events will be demonstrated by probing the interactions between avidin-biotin complexes.

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Design and Optimization of a High Force Neodymium Iron Boron based Magnetic Tweezers Device using Finite Element Analysis
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We present the design and characterization of a high force magnetic tweezers device that can apply controlled forces to magnetic beads embedded into soft materials or biological systems, while visualizing the resultant material deformation with microscopy. Using finite element analysis (FEA), we determined the effect of the geometry of the NdFeB magnet array, as well as the geometry of iron yokes designed to focus the magnetic fields. Sixteen shape parameters including the magnet size, positioning and yoke curvature were defined and modeled using open-source magnetic FEA software. Parameter sweeps were performed using custom-written Matlab code. Geometries were optimized for the magnitude of the magnetic field gradient and the length scale over which the magnetic force operated. Once an optimal design was identified, the yoke was fabricated in-house and the FEA validated by mapping the device’s magnetic field. To demonstrate the usefulness of this approach, we produced a magnetic tweezers device designed for use with optical microscopes available in a core imaging facility. The application demanded device portability and the ability to interface with a number of microscopes, thus imposing significant size restrictions on the magnets used. Iterative FEA delivered an optimal magnet-yoke geometry, which could be mounted to a carriage that advances or retracts on command, giving the operator fine control over the applied force. Such automation allows for rapid force switching, and also allows the effects of long periods of cyclical loading to be determined. In future work, such an FEA approach could easily be adapted to a range of design goals/restrictions to create an efficient means of testing possible magnet configurations, while streamlining the design and construction of specialized instrumentation for force-sensitive microscopy.

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smAP: Manipulating DNA by Ultrasound - Single-Molecules Go Acoustic
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The ability to study individual biomolecules in vitro has greatly expanded our knowledge of biological systems. Existing single-molecule techniques, such as optical and magnetic tweezers or atomic force microscopy, allow manipulation of individual biomolecules like DNA. They suffer from either being technically challenging or they offer low experimental throughput. We invented a novel lab-on-a-chip method to exert controllable forces on multiple DNA molecules simultaneously using ultrasound: single molecule Acoustical Pushing (smAP).
smAP consists of a resonator integrated into a micro-fabricated fluidic chip. An acoustical pressure gradient is created homogeneously throughout the sample enabling to exert forces on DNA-tethered beads. By changing the amplitude of the driving voltage the pressure gradient can be altered, allowing sensitive control of the force applied to the DNA molecules.
This approach makes it possible to apply forces up to hundreds of picoNewtons homogeneously over an area of several millimeter squared, allowing multiplexing to an unprecedented level. We validate this novel single-molecule method by recording force-distance curves of DNA molecules, both double- and single-stranded, in the presence of DNA-binding proteins. The simplicity and low cost makes smAP a widely accessible tool for biophysicists.

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An AFM Force Pulling Study of Riboflavin Receptor Targeting Nanoparticles
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Riboflavin ligands present an alternative pathway for targeted drug delivery as riboflavin receptors are over-expressed in breast and prostate cancer cells. We have examined a riboflavin-conjugated PAMAM dendrimer (generation 5) for...