Although the use of magnetic technologies in biology dates to 1949, they have been applied by relatively few groups in basic biological or biomedical research. Technologies for precision studies of forces in biological systems include Atomic Force Microscopy, optical tweezers, MicroElectroMechanical Systems (MEMS), and magnetic forces. Magnetics has the benefits of combining a freely moving probe, as in laser tweezers, with the relatively high forces of an AFM—without damaging the sample. The goal is a 3D Force Microscope (3DFM) with a magnetic bead probe that can be pulled in any direction under user control with the position of the bead tracked dynamically at the nanometer scale. The 3DFM will be able to be used on single molecules, in cells and cell cultures, and in biomaterial studies.

The Challenge
Developing the 3DFM presents challenges in magnetics design, in making the mechanical system suitable for use with high numerical aperture commercial light microscopes, the tracking and control systems, and the user interface.

The goal has been to be able to apply forces in any arbitrary 3D direction. Our novel hexapole design meets this criterion and its geometry allows the pole plates to be microfabricated from permalloy materials onto the specimen cover slips. In use, the pole plate cover slips are positioned between the upper and lower coils visible in the open stage assembly. They are easily removable and so the magnetic field geometry can be redesigned and changed at will.

Highlights
- Magnetic beads apply forces to probe biological systems in 3D
- Nanometer tracking combined with nanoNewton forces

Simulated view of magnetic bead attached to a cilium being pulled by 3DFM
Designing the control system for the 3D force microscope is major activity of this project. Critical areas are tracking the bead with high accuracy, controlling the motion of the stage based on bead position, and calibrating the instrument in real time. High spatial resolution and high bandwidth tracking is achieved with a combination of coarse video tracking and fine-level tracking with a laser trap. Finally, the control system manages the magnetics, including control of the current levels that generate forces and calibration for the particular pole geometries of an experiment.

The bead position/displacement provides information on the bead’s environment. This data is measured in real time and is displayed through the user interface to help the user guide the experiment. The user interface provides a haptic-feedback device so that the user has a sense of actually tugging on the bead to move it through the specimen. As the bead’s motion is within a 3D volume, the visualizations are of necessity in 3D. Among the views that the user can choose are a trace of the bead in 3D, the volume swept by the bead, the image from the video camera (part of the video tracking system), and a vector representing current force direction.
Use with force-feedback interface to 3DFM.

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Variety of visualizations the user can opt to see.