Title

Design of a magnetic manipulation microscope and its application to torsional-dependent DNA binding kinetics

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Abstract

We describe the design of a microscope system in which magnetic micro-manipulation and optical detection are combined for biological applications. Our multiple pole design allows maximum flexibility in 3-D micro-manipulation of biological samples. First, a uniform force field is generated for isotonic 3-D manipulation within the observation volume. Second, our design enables application of time-dependent torsional stress to samples of interest. In our design, attempts were made to maximize the magnitude of force and torque generated by optimizing pole geometry and material to permit usage of a high NA objective for enhanced optical resolution. Constant force in the range of 100 pN can be generated on paramagnetic beads 4.5 pm in size and torque in the range of 106 pN.pm can be produced on microspheres with magnetic moments of 5x10'2 A.m2. A force microscope with such versatility allows us to study a wide range of biological problems from force and torsional response of cells to controlling enzymatic activities of single biological macromolecules by applied stress. In this presentation, we will present a detailed description of our magnetic manipulation microscope. The application example of our instrument will be a study on the effects of torsional stress on association constants of DNA binding ligands. Our study can be a precursor to understand DNA-drug interaction at the single molecular level and can have important pharmaceutical consequences. (This work is supported by NSF MCB-9604382).