

Foreword

Testing of mechanical properties is a crucial aspect of engineering and materials science. Dr. Milad Radiom's thesis describes the development of a new testing device, the correlation force microscope, which measures the mechanical properties of single polymer molecules. Prior work on single molecule properties utilized either a pair of micrometer-scale beads with optical or magnetic tweezers, or an atomic force microscope (AFM). Dr. Radiom took the best of both worlds by developing a two cantilever derivative of the AFM. In this device, a polymer was straddled between the two AFM cantilevers. The advantage of this system is that he could then measure the correlations between the ends of the single molecule. Such measurements have a much lower noise than a single cantilever, so the signal-to-noise ratio is greater. In addition, much greater forces and much shorter polymer chains could be studied than in the two bead apparatus. An additional, unanticipated advantage was that the background damping in the correlation was much lower, leading to the ability to resolve the internal damping (friction) of a single molecule.

Using the new correlation force microscope, Dr. Radiom performed the first measurement of the friction of an individual short DNA molecule as it moves through water. It showed that at the high amplitude/high frequency limit the friction is much greater than predicted by simple models due to the excitation of higher modes. The friction limits the characteristic time of conformational change, and thus the rate at which biochemical changes can occur. The characteristic time for conformational change in DNA, which is necessary for replication and transcription, was determined from the friction. The technique described in this thesis can now be applied to a variety of other polymers and DNA under various solution conditions.

The new correlation force microscope was also used to understand the flow of fluid between two particles. Many materials are composed of small particles (nanoparticles or colloids) dispersed in a fluid. Such a material can have complex properties because of the combination of materials and the importance of thermal energy in deciding the structure and interaction between the particles. Although it is an important area of materials science, the nature of the fluid flow between such particles was not understood when the particles oscillated at high frequency. Using his new correlation force microscope, Dr. Radiom was able to accurately measure the hydrodynamic interaction between the two spheres. He found that, in

fact, the interaction was much simpler than had been thought previously, it could be understood in terms of low frequency number flow, for which analytical equations already existed. This simplifies analysis of high frequency number technologies such as electroacoustic determination of zeta potential.

We anticipate that the procedures developed in the correlation force microscope will be widely adopted for testing both the single molecule properties, and in understanding the properties of fluids.

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Abstract

This thesis addresses the development of a new force spectroscopy tool, correlation force spectroscopy (CFS), for the measurement of the mechanical properties of very small volumes of material (molecular to μm^3) at kHz-MHz timescales. CFS is based on AFM and the principles of CFS resemble those of dual-trap optical tweezers. CFS consists of two closely-spaced micro-cantilevers that undergo thermal fluctuations. Measurement of the correlation in thermal fluctuations of the two cantilevers can be used to determine the mechanical properties of the soft matter, e.g., a polymeric molecule, that connects the gap between the two cantilevers. Modeling of the correlations yields the effective stiffness and damping of the molecule. The resolution in stiffness is limited by the stiffness of the cantilever and the frequency by the natural frequency of the cantilevers, but, importantly, the damping resolution is not limited by the damping of the cantilever, which has enabled high-resolution measurements of the internal friction of a polymer. The concept of CFS was originally presented by Roukes' group in Caltech (Arlett et al., Lecture Notes in Physics, 2007); I developed the first practical versions of CFS for experimentation, and have used it in two applications (1) microrheology of Newtonian fluids and (2) single molecule force spectroscopy. To understand the correlation in thermal fluctuations of two cantilevers, I initially validated the theoretical approach for analyzing correlation in terms of deterministic model using the fluctuation-dissipation theorem (Paul and Cross, PRL, 2004). I have shown that the main advantages of such correlation measurements are a large improvement in the ability to resolve stiffness and damping. Use of CFS as a rheometer was validated by comparison between experimental data and finite element modeling of the deterministic vibrations of the cantilevers using the known viscosity and density of fluids. Work in this thesis shows that the data can also be accurately fitted using a simple harmonic oscillator model, which can be used for rapid rheometric measurements, after calibration. The mechanical properties of biomolecules such as dextran and single stranded DNA (ssDNA) are also described. CFS measurements of single molecule properties of ssDNA reveal the internal friction of the molecule in solution.

Correlation Force Spectroscopy for Single Molecule
Measurements

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