

Nanomechanical Detection of Biomolecular Interactions

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Sensitive detection of specific biomolecular interactions is essential for elucidating the basic mechanisms of physiological processes as well as for diagnosis and therapy of pathological states. Recent advances in genomics research include the use of microarray chips upon which hundreds if not thousands of specific DNA sequences can be discerned. Detection employs fluorescent probes, which requires laser and imaging optics and either on-chip or external electronics. This paper reports a novel approach for biomolecular detection based on the observation that when one surface of a microcantilever beam is coated with a self-assembled monolayer of receptor molecules, biomolecular binding of ligand on the monolayer produces a differential surface stress that is sufficiently large to bend the cantilever. Such bending can be detected optically, obviating the need for extrinsic labeling.

Silicon atomic force microscopy microcantilevers were coated on one side with gold to create a bimetallic cantilever beam. Thiol-modified single stranded DNA of known sequence was immobilized on the gold side, and deflection was determined using a laser beam reflected off the cantilever and focused onto a position-sensitive detector. Exposure to complementary DNA resulted in upward deflection of the cantilever, the magnitude of which is dependent upon the length of the complementary DNA strand (Figure 1). We can clearly discriminate a one nucleotide difference in sequence length.

We propose that this optical deflection technique is sufficiently general and could potentially be used for specific recognition of other important biomolecular

binding reactions, for example antigen-antibody interactions. A key feature of this approach is that the cantilever deflection signal can be converted to an optical one through ray, interferometric, or diffractive optics, allowing one to detect biomolecules without the use of extrinsic labeling. Manufacture of microcantilevers in array format is underway and such high-density arrays will facilitate genomics and proteomics profiling analyses, with potential applications in assessment of human disease.

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Figure 1. Bending responses of 4 identical microcantilevers modified with 20 nucleotide single-stranded DNA probes as a function of *in situ* hybridization with 20, 15, 10, and 9 nucleotide complementary sequence single-stranded DNA probes.



