BIOLOGICAL DETECTION BASED ON THE THERMOMECHANICAL NOISE OF A NANOMECHANICAL RESONATOR: ORIGIN OF THE RESPONSE AND DETECTION LIMITS

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The nanometer-scale vibration of flexible microstructures such as microcantilevers can be exquisitely tuned by a number of interactions. Temperature, electrical and magnetic fields, intermolecular forces, molecular adsorption and fluid properties (density and viscosity) can sensitively shift the natural vibration frequencies. This intimate connection between a nanomechanical resonator and its surrounding is the basis of scanning probe microscopes and recently developed nanomechanical sensors for chemical and biological detection. The last application is based on that the resonant properties of nanomechanical resonators are largely affected by the molecules that land on their surface. The change of the natural frequency of the resonator has been widely attributed to the mass of the adsorbed molecules. Nanomechanical resonators have shown their potential for ultrasensitive label-free detection of pathogens, proteins and DNA[1-3].

In common with many emerging nanotechnology-based sensors, nanomechanical sensors still require of a major understanding of the mechanisms responsible for the sensor response. This is necessary to obtain i) a correct quantification of the amount of target in the sample and ii) for obtaining those parameters that allow optimization of the sensor response.

Here, we demonstrate that the resonance frequency can sensitively be measured without need of external excitation by measuring the Brownian motion in air. Then we study the effect of molecular adsorption on the resonance frequency by using two models: bacteria on 400x100x1 μm^3 cantilevers and DNA on 15x6x0.1 μm^3 cantilevers. We found in both cases that the sign and amount of the resonant frequency change is determined by the position and extent of the adsorption on the cantilever with regard to the shape of the vibration mode[4-8]. To explain these results, a theoretical one-dimensional model is proposed. We obtain analytical expressions for the resonant frequency that accurately fits the data obtained by the finite element method. More importantly, the theory data shows a good agreement with the experiments. Our results indicate that there exist three mechanisms that can produce a significant resonant frequency shift: the stiffness, the surface stress gradient and the mass. Based on the thermomechanical noise, we analyze the regions of the cantilever of lowest and highest sensitivity to the attachment of bacteria and DNA as a function of the used vibration mode. The confinement of the adsorption to defined regions of the cantilever allows the detection of single bacterial cells and the hybridization of nucleic acids at the level of few femtograms.

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Figures:

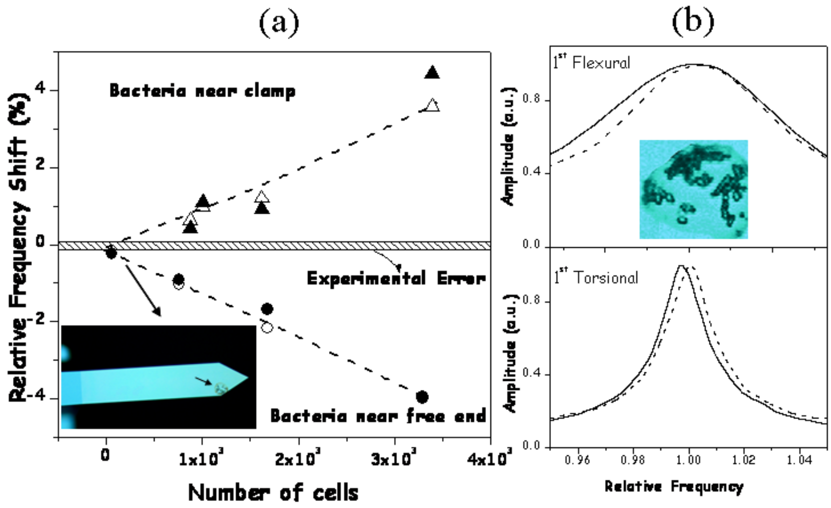

Fig. 1. (a) Relative frequency shift of the fundamental flexural (open symbols) and torsional (solid symbols) vibration modes as a function of the number of adsorbed E. coli cells. The bacteria were deposited near the cantilever base (triangles) and near the cantilever free end (circles). The dashed region represents the experimental error due to the non-specific adsorption of material during the deposition of bacteria. The inset shows an optical picture of a cantilever with approximately fifty bacteria on the tip. **(b)**. Frequency spectra of the fundamental flexural (top) and torsional (bottom) modes of the cantilever with approximately 50 bacteria near the tip (inset in (a)). Inset shows a zoom of the inset in (a).