

Novel paradigms for biological sensing based on nanomechanical systems

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The development of ultrasensitive protein spectrometers and ultrasensitive biological sensors will speed up the identification of disease biomarkers and their rapid detection [1,2]. Nanomechanical resonators have emerged as promising candidates for ultrasensitive mass sensors [3,4]. The continuous advancements in top-down micro- and nanofabrication techniques has made possible increasingly smaller nanomechanical resonators with detection limits in the subattogram range. Moreover, resonant nanowires and nanotubes fabricated by bottom-up methods can weigh masses below a zeptogram (1.66 10^{-21} g). However, the implementation of these devices is hindered by several obstacles such as the need of operation in high vacuum, low specificity and low reproducibility and still little understanding of the effect of biomolecular adsorption on the mechanical properties of nanoresonators.

In this talk, I will present our recent developments oriented to apply nanomechanical systems for biological detection. In particular, I will present two novel paradigms for sensing that opens the door to develop ultrasensitive biological sensors. The first approach is the use of coupled nanomechanical resonators fabricated by standard silicon technology [5,6] (Fig. 1). When the resonators are identical, the vibration of the eigenmodes is delocalized over the array. In a similar way to the Anderson's localization, the addition of the mass on one of the resonators leads to the spatial localization of the eigenmodes. Since vibration localization is insensitive to uniform adsorption, coupled nanomechanical resonators allows decoupling of unspecific and specific molecular adsorption in differentially sensitized resonators. The main advantage of measuring eigenmode localization, is the possibility of tune it sensitivity through the modification of the coupling constant. By decreasing the coupling they become more sensitive, being able even to beat current frequency shift measurements with isolated cantilevers. On this way, we can improve the resonator sensitivity without fall in miniaturation, that could be feasible in some applications. In addition, eigenmode localization is no longer depending on the extreme miniaturization.

The second approach uses resonant nanowires/nanotubes (Fig. 2) and it is based on the fact that if a molecule alights on a perfectly axisymmetric resonant nanobeam, the frequency degeneration of the stochastic two-dimensional orbits is abruptly broken, and the vibration can be described as the superposition of two orthogonal vibrations with different frequency. The tracking of both frequencies and the orientation of the vibrational planes, enables the determination of the adsorbate's mass and stiffness, as well as the azimuthal direction from which the adsorbate arrives [7]. We experimentally demonstrate such sensing paradigm with resonant silicon nanowires, which serves to add kPa resolution in Young's modulus determination to their currently established zeptogram mass sensitivity. The proposed method provides a unique asset for ultrasensitive mass and stiffness spectrometry of biomolecules by using nanowire-like resonant structures.

References

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Figures

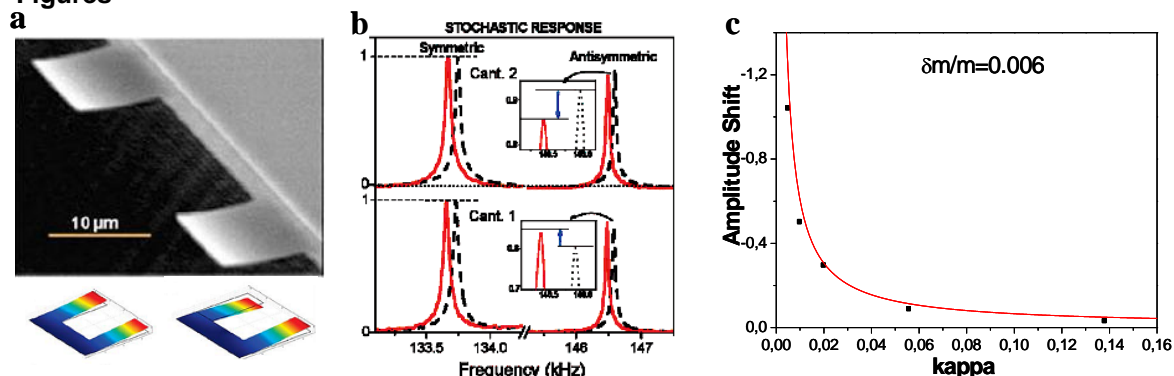


Figure 1. (a)Top. Scanning electron micrograph of a system of coupled cantilevers. The cantilevers were fabricated in low stress silicon nitride. The length, width, and thickness of the cantilevers were 25, 10, and 0.1 μm , respectively. The gap between the cantilevers is 20 μm . The structural coupling between the cantilevers arises from the overhang connecting the cantilevers at the base, L_0 , which is about 8 μm long. Bottom. FEM simulation of symmetric and antisymmetric mode of vibration of this coupled array modes (b) Stochastic response driven by ambient thermal excitation, of a two couple resonators before (black, broken line) and after (red, solid line) the deposition of 170 fg of mass on cantilever 2. All the spectra have been normalized such that the height of the symmetric peak equals 1. The insets show a zoom of the relative change in the amplitude of the antisymmetric mode. Ratio between the relative changes of the antisymmetric/symmetric amplitude ratio and resonance frequency shift versus the coupling constant. The symbols are experimental data and the dashed red line is a theoretical prediction based on coupled harmonic oscillator theory and the fluctuation-dissipation. (c) Relative changes of the antisymmetric/symmetric amplitude ratio produced by the deposition of 100 fg on cantilever 2, versus the coupling constant. The coupling constant is decreased by increasing the pitch between cantilevers. Pitch range from 2- 100 μm . The symbols are experimental data and the dashed red line is a theoretical prediction based on coupled harmonic oscillator theory and the fluctuation-dissipation.

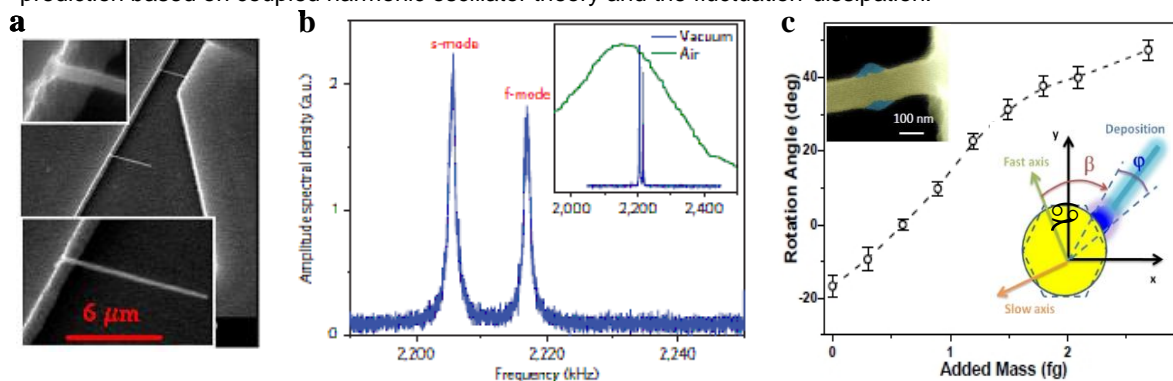


Figure 2.(a) Scanning electron micrograph (SEM) of a typical nanowire used in this work. Nanowires anchored normal to the trench wall were selected, with lengths and diameters of 5–10 μm and 100–300 nm, respectively. (b) A fast Fourier transform of the signal from the photodetector is dominated by the displacement thermal fluctuation of the nanowires. Only a single resonant peak can be seen in air (green line in inset), but two resonant peaks can be clearly seen in vacuum (blue lines). Depending on the nanowire dimensions, the resonance frequencies range from 2 to 6 MHz. s-mode and f-mode refers to the splitting of the resonance frequency into slower and faster vibration modes vibrating at orthogonal directions. (c) Evolution of the angle between the fast vibration axis and the optical axis (a) versus mass added to the clamped end of the nanowire after successive depositions of ~ 0.6 fg. Deposition was performed at an angle of $\sim 45^\circ$ to the optical axis (inset). Each deposition rotates the fast vibration plane through 7–12 $^\circ$ towards the deposition direction, as indicated by the green arrows.