

## Encased Cantilevers for Low-Noise Mass and Force Sensing in Liquids

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The smallest detection levels in cantilever based sensing are associated with damping of the resonator. When operating in water viscous damping is dominant. Hence, compared to air the resulting force or mass sensitivities of the same cantilever are decreased by more than one order of magnitude. As a result, atomic force microscopy (AFM) imaging of biological samples is very challenging as they easily deform under the minimum force required. In contrast to previous attempts to lower viscous damping by miniaturization, we present a solution where low damping is achieved by keeping the resonator dry[1]. This is realized by fabricating a hydrophobic encasement around the cantilever, so that surface tension prevents water from entering and only the sensing tip is immersed. A simplified fabrication process is illustrated in figure 1a. A silicon oxide and Parylene layer are uniformly deposited onto commercially available silicon AFM cantilevers. Then, we use focused ion beam to cut open the Parylene layer around the apex. This exposes the sacrificial oxide layer and enables releasing the cantilever by a final hydrofluoric acid etch. Figure 1b shows an electron microscope image of final functional device. The optically transparent encasement allows the devices to be used on any setup using regular beam deflection. The thermal spectra shown in figure 1c demonstrate that a high resonance frequency and quality factor are maintained while submerged in water. The resulting force noise in liquid of  $12\text{fN}/\sqrt{\text{Hz}}$  is more than one order of magnitude lower than for regular cantilevers of similar size ( $150\text{fN}/\sqrt{\text{Hz}}$ ).

Figure 2 shows few liquid AFM images that demonstrate the gentleness of our probes. Figure 2a shows correct height measurements of lipid bilayers, which typically deform under the applied force [3]. Figure 2b shows lattice resolution of mica obtained in liquid. And Figure 2c shows the formation of D-band upon self-assembly of collagen fibrils from loose bundles of tropocollagen. An important application besides imaging is mass sensing in liquids. In encased cantilevers, applied functionalization as well as binding of an analyte only occurs at the tip (figure 3a), this allows quantitative extraction of the added mass from the measured frequency shift. This technique, therefore, surpasses conventional cantilever based mass sensing, where the uncertainty of the location of the added mass, or the indirect measurement over stress induced bending [4] require various assumptions or models in order to extract the exact value of the added mass. Figure 3c shows two jumps in frequency shift resulting from two consecutive attachments of single gold particles with a mass of about 180 fg. Using first flexural eigenmode we achieved a mass sensitivity of 80 attograms/ $\sqrt{\text{Hz}}$ . Improved cantilever geometries and the use of higher eigenmodes, however, have the potential to extend the frontier of measurements in liquids down to the zeptogram range. This corresponds to the mass of single small proteins. The encasement can as well serve as position reference for an interferometric readout. To this end a metal layer is deposited onto the encasement to form a Fabry-Pérot optical cavity. For selected wavelengths or gap sizes, the light reflected from the encasement destructively interferes with light reflected from the cantilever (figure 4a,b). Measuring intensity of the reflected light rather than its position only requires crude alignment and enables high bandwidth position detection by using a single photodiode. Our first prototypes achieve a deflection noise density of  $5.5\text{ fm Hz}/\sqrt{\text{Hz}}$  (figure 4c), which clearly outperforms typical commercial AFM instruments.

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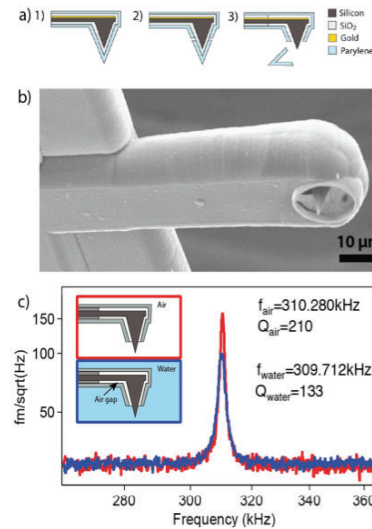


Figure 1 a) Electron microscope image of a final encased cantilever device. b) Thermal noise spectra recorded in air (red curve) and water (blue curve) show that exceptionally high quality factor and resonance frequency are maintained while operating in liquids.

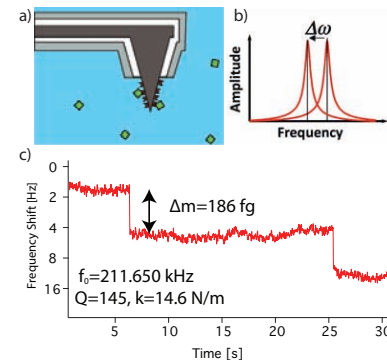


Figure 3 Encased cantilevers for quantitative mass sensing in liquids, a) local binding of the analyte to the tip (b) induce a frequency shift (c) quantitative measurement of the mass of gold beads.

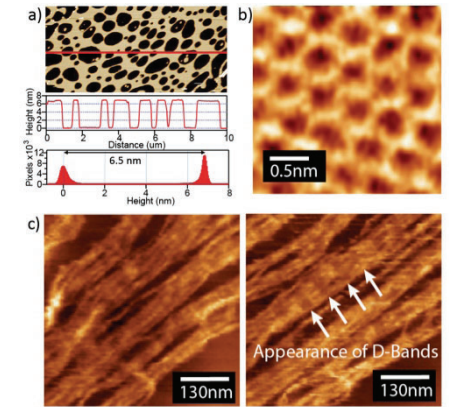


Figure 2 Liquid AFM images using encased cantilevers a) DPPC lipid bilayers supported on mica b) lattice resolution of mica c) Self-assembly of bundles of tropocollagen into collagen fibrils (See D-Bands).

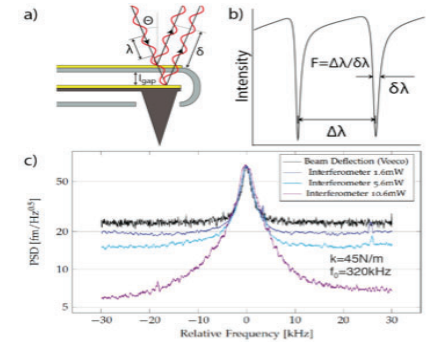


Figure 4 Encased cantilever with integrated Fabry-Pérot optical cavity