Nanomechanical spectrometry of *E. coli* by multifrequency tracking

A. Sanz-Jiménez[1], *O. Malvar*[1], *J. J. Ruz*[1], *S. García-López*[1], *P. M. Kosaka*[1], *I. Panagiotopoulos*[2], *D. Kounadis*[2], *D. Papanastasiou*[2], *M. Calleja*[1] & *J. Tamayo*[1]
Instituto de Micro y Nanotecnología, Calle Isaac Newton 8, 28760 Tres Cantos, Madrid.
adrian.sanz@csic.es

Nanomechanical spectrometry can identify species by measuring the relative frequency shift of nanoelectromechanical resonators (NEMS) when an analyte lands on its surface. This approach was first exploited to measure the mass of IgM antibodies [1]. Furthermore, not only the mass of the analyte but also its stiffness was measured [2]. Recently, the mass of the bacteriophage T5 has been determined making use of the same technique [3]. The latter works tracked several resonance modes of a NEMS by a phase-locked loop (PLL) system. In the present work, we developed a method that eludes the use of PLL systems and still accomplishes the same precision in mass and stiffness than previous work [2]. The method is based in the continuous fitting of the resonance peak and the phase (Fig. 1(a)). Our nanomechanical mass and stiffness spectrometer mounts a µ-electrospray ionization system to nebulize the analytes. The laser beam deflection technique is used to measure up to four resonance frequencies of NEMS. Between them, a heated capillary ensures the desolvation and an aerolens decelerates the adsorbates.

The mass of *Escherichia coli* bacteria has been measured by tracking the first four vibration modes of two NEMS: a commercial rectangular cantilever (Bruker MLCT-O10) and a commercial silicon nitride membrane (Norcada Inc) with size 250x250x0.05 µm. The square membrane provides a very high sensing area so that the efficiency is largely increased. Fig. 1(b) shows the real-time relative frequency shift of the first four flexural modes of the cantilever during *E. coli* adsorption. As shown in Fig. 1(c), the calculated mass for *E. coli* is identical for the two NEMS under a ~<10% of tolerance. The figure also shows the underestimation of the mass when stiffness is not considered.

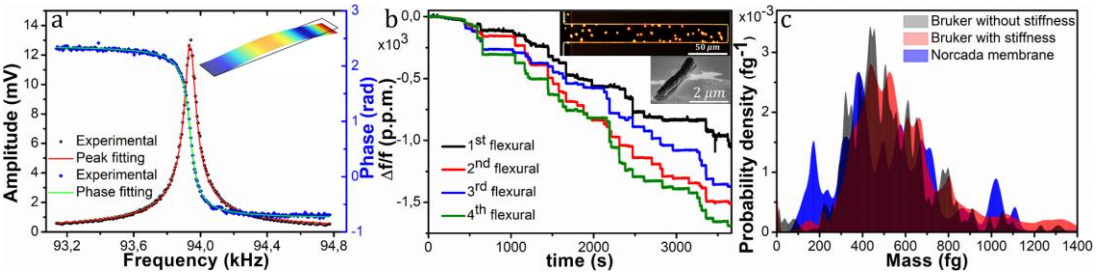

Fig. 1. (a) Fitting of the peak resonance and the phase of the second flexural mode (inset: FEM simulation) of the rectangular cantilever. (b) Relative frequency shift of the first four flexural modes of a microcantilever during the deposition of *E. coli* bacterial cells (inset: dark-field optical microscope image of the cantilever after the experiment with *E. coli* (top) and SEM image of a single bacterium (bottom)). (c) Probability density function of the *E. coli* mass for the NEMS used in this work.

This work was supported by Horizon 2020 FET project, No. 731868 VIRUSCAN.

[1] M. S. Hanay et al., Nature Nanotechnology **7**, 602-608 (2012)
[2] O. Malvar et al., Nature Communications **7**, 13452 (2016)
[3] Dominguez-Medina et al., Science **362**, 918-922 (2018)