SEMINARIO

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Sala Consiglio di Facoltà

Michael Roukes
Frank J. Roshek Professor of Physics, Applied Physics, and Bioengineering
California Institute of Technology, Pasadena, CA

SINGLE-MOLECULE ANALYSIS WITH NANOMECHANICAL SYSTEMS

***Abstract*:**
Nanoelectromechanical systems (NEMS) offer exciting prospects for research in the life sciences and medicine. Throughout this talk, while presenting the technological underpinnings of our efforts, I will focus on new applications that become possible – including the analysis of intact protein complexes (such as membrane proteins, antibody isoforms, organelles, and viruses) and the unprecedented potential for deep proteomic profiling of individual cells.
NEMS uniquely enable ultrasensitive measurement of the inertial mass of individual atoms and molecules [1] and, thereby, permit realization of a new form of mass spectrometry (MS) with single-molecule resolution. We have used this to analyze individual large-mass biomolecular complexes, one-by-one, in real-time [2]. More recently, we've developed an approach that permits resolving the spatial mass distribution of the individual analytes – in real time, with molecular-scale resolution [3]. We term this approach inertial imaging; it employs the discrete time-correlated perturbations to multiple vibrational modes – resulting from each individual molecular adsorption event – to yield the spatial moments of the mass distribution for each analyte in real time. The lowest moment yields the analyte's total mass; higher moments reveal its center-of-mass position of adsorption, the analyte's average diameter, and its spatial skew and kurtosis, etc. Once acquired, these moments permit reconstruction of each analyte's image. However, unlike conventional imaging, precision here is not set by wavelength-dependent diffraction phenomena; instead frequency fluctuation processes determine the ultimate spatial resolution limits. Today's advanced NEMS devices are already capable of resolving molecular-scale analytes. In our current efforts, we are both upscaling measurement throughput [4] and harnessing cavity optomechanics to multiplex arrays of NEMS sensors to superconducting microwave resonators. I will provide a description of these advances, and then outline the potential mass sensitivity down at the quantum limit, why they are special in enabling ultrasensitive measurements with minimal backaction, and how such a "quantum" approach could ultimately be transformational for molecular analysis.

[1] Naik, A. K., Hanay, M. S., Hiebert, W. K., Feng, X. L. & Roukes, M. L., Towards Single-molecule Nanomechanical Mass Spectrometry. Nature Nanotechnology 4, 445–450 (2009).
[2] Hanay, M. S., Kelber, S. I., Naik, A. K., Chi, D., Hentz, S., Bullard, E. C., Colinet, E., Duraffoug, L. & Roukes, M. L., Single-protein Nanomechanical Mass Spectrometry in Real Time. Nature Nanotechnology, 7, 602-608 (2012).
[3] Hanay, M. S., Kelber, S. I., O'Connell, C. D., Mulvaney, P., Sader, J. E. & Roukes, M. L., Inertial Imaging with Nanomechanical Systems. Nature Nanotechnology 10, 339-344 (2015).
[4] Eric Sage, et al., Single-particle mass spectrometry with arrays of frequency-addressed nanomechanical resonators. Nature Communications 9, 3283 (2018).

Michael Roukes is the Frank J. Roshek Professor of Physics, Applied Physics, and Bioengineering at the California Institute of Technology. His scientific interests range from quantum measurement to applied biotechnology with a unifying theme of the development, very-large-scale integration and application of complex nanosystems to precision measurements in physics, the life sciences and medicine. Roukes was the founding Director of Caltech's Kavli Nanoscience Institute (KNI) from 2003-2006. In 2007, he co-founded the Alliance for Nanosystems VLSI (very-large-scale integration) with scientists and engineers at CEA/LETI in Grenoble, which maintains a $B-scale microelectronics research foundry. He then continued as co-director of Caltech's KNI from 2008 until 2013. Since then he has returned to full-time pursuit of research efforts with his group and collaborators. Concurrent with his Caltech appointment, held a Chaire d'Excellence in nanoscience in Grenoble, France from 2008-2016. Among his honors, Roukes is a recipient of the NIH Director's Pioneer Award and has been awarded Chevalier (Knight) dans l'Ordre des Palmes Academiques by the Republic of France. (roukes@caltech.edu)