

MAR13-2013-020898

Abstract for an Invited Paper  
for the MAR13 Meeting of  
the American Physical Society

**Frontiers of Biophysics: Single Molecule and Single Cell Sensing with Nanomechanical Systems**

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Nanoelectromechanical systems (NEMS) resonators can detect inertial mass with exceptional sensitivity. We have used NEMS devices to realize a new method for single-molecule mass spectrometry. In our first-generation approach, mass spectra from several hundred adsorption events were assembled into mass spectra using statistical analysis. Our second-generation approach now enables NEMS-based mass spectrometry (MS) in real time: as each molecule in the sample adsorbs upon the NEMS resonator, its mass and position-of-adsorption are determined by continuously tracking two driven vibrational modes of the device. We demonstrate the potential of this method by analyzing individual IgM antibody complexes and other biological analytes in real-time. NEMS-MS is a unique and promising new form of mass spectrometry: it can resolve neutral species, provides resolving power that increases markedly for very large masses, is readily scalable to millions of channels, and is and producible *en masse* by methods from the semiconductor industry for very-large-scale integration.