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**Presidential Early Career Award for Scientists and Engineers
F49620-02-1-0322**

April 1, 2002 to December 31, 2007

**FINAL REPORT for the
Air Force Office of Scientific Research (AFOSR)**

June 2008

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Status of effort

Effort has primarily been directed towards improving the resolution of scanning probe microscopy in order to enhance the imaging quality of nanostructure materials. In particular, disturbance suppression schemes were implemented with the scanning tunneling microscope (Section I) and with conventional tapping mode (Section II). Effort was also directed towards the development of an ultrasensitive mass sensor known as the suspended microchannel resonator. As described in Section III, the Quality factor (and hence mass resolution) was improved by nearly ten-fold with a wafer-scale vacuum packaging technique that was developed at MIT's Microsystems Technology Laboratory.

Accomplishments/New Findings

I. Scanning Probe Microscopy with Inherent Disturbance Suppression Using Micromechanical Devices

Scanning probe microscopes are notoriously susceptible to disturbances, or mechanical noise, from the surrounding environment that couple to the probe-sample interaction. These disturbances include vibrations of mechanical components as well as piezo drift and thermal expansion. Disturbance effects can be substantially reduced by designing a rigid microscope, incorporating effective vibration isolation, and selecting an appropriate measurement bandwidth and image filter. However, it is not always possible to satisfy these requirements sufficiently, and as a result, critical features in an image can be obscured.

The cause of this problem is that the actuator (control) signal is used both to readout topography and correct for disturbances. We have introduced a general approach for inherently suppressing out-of-plane disturbances in scanning probe microscopy. In this approach, two distinct, coherent sensors simultaneously measure the probe-sample separation. One sensor measures a spatial average distributed over a large sample area while the other responds locally to topography underneath the nanometer-scale probe. When the localized sensor is used to control the probe-sample separation in feedback, the distributed sensor signal reveals only topography. This configuration suppresses disturbances normal to the sample. We have applied this approach to scanning tunneling microscopy (STM) with a microcantilever that integrates a tunneling tip and an interferometer (Figure 1) and have shown that it enables Angstrom resolution imaging of nanometer-sized gold grains in a noisy environment (Figure 2). For disturbances applied normal to the sample, we measured disturbance suppression of -50 dB at 1 Hz, compared to 0 dB with conventional imaging.

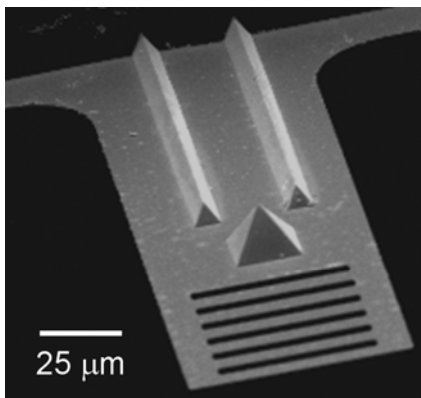


Figure 1: Scanning electron micrograph of the silicon nitride cantilever with integrated tunneling probe and interferometer.

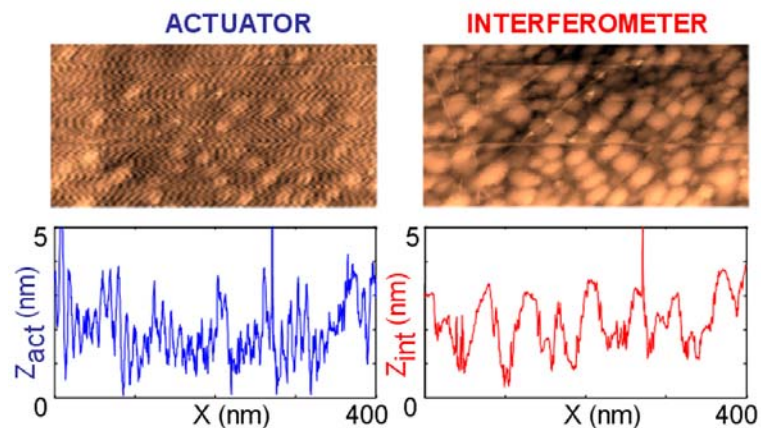


Figure 2: 400 x 200 nm² STM images of Au/Pd/Ti on a silicon substrate, imaged at 0.2 Hz on a mechanically grounded optics table. Cross-sections from each image are shown for the same scan line.

II. Atomic force microscopy with inherent disturbance suppression for nanostructure imaging

We demonstrate on a modified commercial atomic force microscope that adding an interferometer as a secondary sensor to measure the separation between the base of the cantilever and the sample during conventional feedback scanning can result in real-time images with inherently suppressed out-of-plane disturbances (Figure 3). The modified microscope has the ability to resolve nanometer-scale features in situations where out-of-plane disturbances are comparable to or even several orders of magnitude greater than the scale of the topography. We present images of DNA in air from this microscope in tapping mode without vibration isolation, and show improved clarity using the interferometer as the imaging signal (Figure 4). The inherent disturbance suppression approach is applicable to all scanning probe imaging techniques.

We do not claim that image improvement will be comparable to these results on all SPMs and in all imaging environments. At present, this technique will be most effective in very noisy environments, such as a microfabrication facility, where Z disturbances overwhelm sample topography. However, there are two significant implications of this work: 1) vibration isolation, which is costly and consumes space, can be rendered unnecessary for noisy environments; and 2) this technique can potentially outperform vibration isolation in any environment with further reduction of the interferometer noise floor.

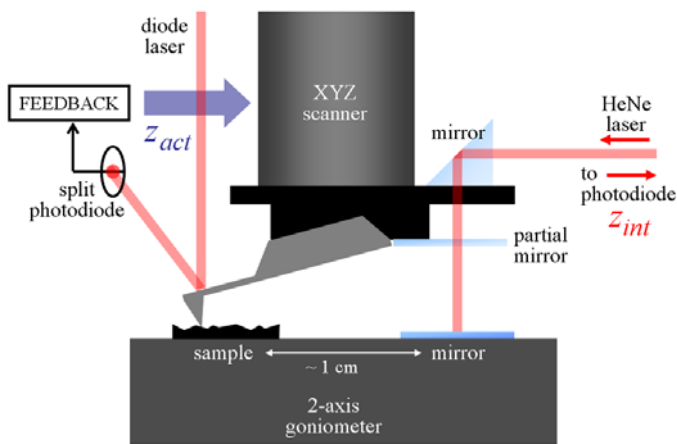


Figure 3: Experimental schematic. Z_{act} (actuator) is the signal that is used for conventional scanning probe microscopy and includes a superposition of topography and mechanical disturbances. However, Z_{int} (interferometer) reveals only topography and suppresses the mechanical disturbances.

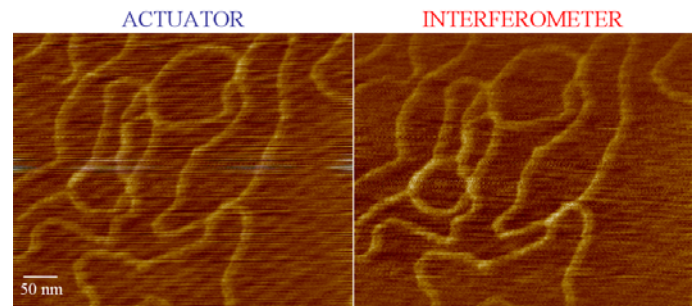


Figure 4: Due to Z disturbance effects, the actuator image appears streaked, and diagonal background stripes are present which are likely due to a resonance of the microscope. The interferometer image does not exhibit streaking and shows suppressed background noise.

III. Vacuum-Packaged Suspended Microchannel Resonant Mass Sensor for Biomolecular Detection

Microfabricated transducers enable the detection of biomolecules in microfluidic systems with nanoliter size sample volumes. Their integration with microfluidic sample preparation into lab-on-a-chip devices can greatly leverage experimental efforts in systems biology and pharmaceutical research by increasing analysis throughput while dramatically reducing reagent cost. Microdevices can also lead to robust and miniaturized detection systems with real-time monitoring capabilities for point-of-use applications.

We have recently fabricated, packaged, and tested a resonant mass sensor for the detection of biomolecules in a microfluidic format. The transducer employs a suspended microchannel as the resonating element, thereby avoiding the problems of damping and viscous drag that normally degrade the sensitivity of resonant sensors in liquid (Figure 5). Our device differs from a vibrating tube densitometer in that the channel is very thin, which

enables the detection of molecules that bind to the channel walls; this provides a path to specificity via molecular recognition by immobilized receptors. The fabrication is based on a sacrificial polysilicon process with low-stress LPCVD silicon nitride as the structural material, and the resonator is vacuum packaged on the wafer scale using glass frit bonding (Figure 6). Packaged resonators exhibit a sensitivity of $0.8 \text{ ppm}/(\text{ng}\cdot\text{cm}^2)$ and a mechanical quality factor of up to 700, which represents a nearly 10-fold improvement over previous devices. To the best of our knowledge, this quality factor is among the highest so far reported for resonant sensors with comparable surface mass sensitivity in liquid at that time. In a separate project, we have recently improved the Q by an additional 10-fold.

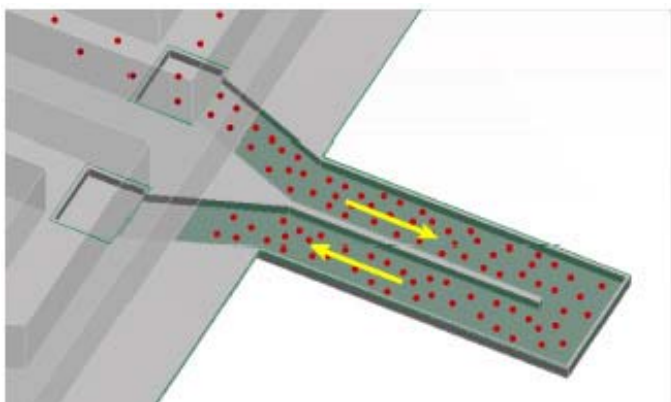


Figure 5: Suspended microchannel resonator (SMR). In SMR detection, target molecules flow through a vibrating suspended microchannel and are captured by receptor molecules attached to the interior channel walls. What separates the SMR from existing resonant mass sensors is that the receptors, targets, and their aqueous environment are confined inside the resonator, while the resonator itself can oscillate at high Q in an external vacuum environment, thus yielding extraordinarily high sensitivity.

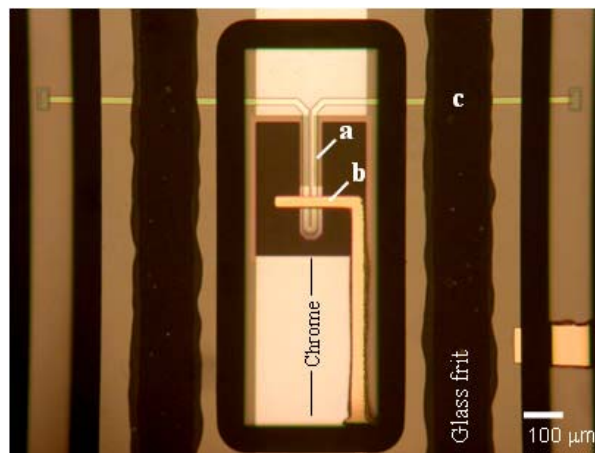


Figure 6: Optical micrograph of a packaged cantilever resonator. The $300 \mu\text{m}$ long beam contains a $1 \times 20 \mu\text{m}$ microfluidic channel (a). An electrode on the glass surface above the cantilever enables electrostatic actuation (b). Glass frit conforms to the surface topography and does not collapse the thin channel in location (c) during bonding.

Personnel Supported

Scott Manalis (PI-summer)
Andrew Sparks (RA & Postdoc)
Marie-Eve Aubin (RA)
Thomas Burg (RA)

Publications

J. Fritz, E.B. Cooper, S. Gaudet, P.K. Sorger, and S.R. Manalis. Electronic detection of DNA by its intrinsic molecular charge. *Proceedings of the National Academy of Sciences*, 99 14142 (2002).

A.W. Sparks and S.R. Manalis. Scanning probe microcopy with inherent disturbance suppression. *Applied Physics Letters*, 85 3929 (2004).

A.W. Sparks and S.R. Manalis. Atomic force microscopy with inherent disturbance suppression for nanostructure imaging. *Nanotechnology*, 17 1574 (2006).

T.P. Burg, A.R. Mirza, N. Milovic, C.H. Tsau, G.A. Popescu, J.S. Foster, S.R. Manalis. Vacuum-Packaged Suspended Microchannel Resonant Mass Sensor for Biomolecular Detection. IEEE Journal of Microelectromechanical Systems, online (2006).

S. Son, W.H. Grover, T.P. Burg, S.R. Manalis. Suspended microchannel resonators for ultra-low volume universal detection. Analytical Chemistry (2008).

Interactions/Transitions:

Participation/presentations at meetings, conferences, seminars, etc.

10th International Conference on Miniaturized Systems for Chemistry and Life Sciences (μ TAS2006)

IEEE Sensors

APS

MRS

CHI

National Academy of Engineering (NAE)

BioDetection

SPIE

BMES

Stanford Optical MEMS

Cornell, seminar

Harvard, seminar

Hewlett Packard Corvallis, seminar

Princeton, seminar

Consultative and advisory functions to other laboratories and agencies

None

Transitions

A company called Affinity Biosensors was started in order to commercialize the suspended microchannel resonator (described in Section III) for the direct sizing of nanoparticles. Affinity Biosensors recently received a Phase II award from the NSF.

Patent disclosures

Suspended microchannel detectors (patent issued, 7,282,329)

Measurement of concentrations and binding energetics (patent issued, number TBA)

Honors/Awards

None.