Interdisciplinary Nanomechanics: From Acoustic Holographic Imaging to Microcantilever-based Bio-Chem Sensing

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NUANCE Staff Development

Other Collaborations:
- Center for Nanofabrication & Molecular Self-Assembly (CNAMS)
- Central and Surface Facilities (NUANCE, NIFTI, etc.)
- Institute for BioNanotechnology in Advanced Medicine (Stupp)
- Network for Computational Nanotechnology (CCNC)
- Argonne National Laboratory
- Argonne Center for Nanoscale Materials
- Robert H. Lurie Medical Research Center
- Argonne National Laboratory

International Institute for Nanotechnology (IIN)

Steering Committee

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International Outreach:
- US-Ireland (Chang)
- US-South Africa (Kung)
- US-India (Dravid)
- Ongoing

Networks for Computational Nanotechnology:
- PIs: Miller, A. Siraki (Department of Physics)

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International Outreach:
- U.S.-Israel (Agarwal)
- U.S.-South Africa (Agarwal)
- Ongoing
Collaborations in 18 Countries
Active exchange program with Ajou University
Sponsorship from Saarland, Germany government
MoU with IIT Bombay, India

Outline

• Seeing the Invisible:
  – Scanning Near-Field Ultrasound Holography (SNFUH)
  ➔ Nanomechanical response to acoustics

• MOSFET-embedded microcantilevers:
  – Translating bio-chem binding into nanomechanics
  – Translating nanomechanics to electronic signal
Scanning Near-Field Ultrasound Holography (SNFUH)

Near-Field SPM Platform:
- Excellent Lateral Resolution

Ultrasound source:
- Non-destructive and Depth-Sensitive

Holography Paradigm:
- Sensitive to “Phase” Perturbations

**Detection of Perturbation to the Acoustic Standing Surface Wave via SPM Probe Detector**

**Seeing the Invisible:**
*Scanning Near-Field Ultrasound Holography (SNFUH)*

Implications for Non-Invasive Sub-Surface Imaging

- Quantitative modulus imaging of polymers/soft-structures
- Non-invasive monitoring of molecular markers/tags – signal pathways
- Nanoscale non-invasive 3-D tomography
- Non-destructive 3-D metrology

Science, October 7, 2005

Figure 2: (A) Typical AFM (topography) image shows featureless top polymer surface, while the phase image of SNFUH clearly reveals the buried gold nanoparticles with high definition.

This is schematically explained in (C) and (D). In (C) no sub-surface scattering is present which does not perturb the standing wave while (D) shows perturbation to standing beat frequency due to sub-surface scattering, which is monitored by SPM tip.
Scanning Near-Field Ultrasound Holography (SNFUH)

Advantages over traditional metrology:

- Non-invasive: *based on acoustic waves; no electron beams, no cross-sectioning*
- Sub-surface: *all materials of interest are transparent to acoustic waves*
- Nano-scale resolution: *detection at the scale of defects - nanometers*

*Science, October 7, 2005*

*In-vitro Non-Invasive SNFUH Imaging in Cell Biology*

AFM

<table>
<thead>
<tr>
<th></th>
<th>SNFUH</th>
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<tbody>
<tr>
<td>24 hr incubation</td>
<td>Malaria Parasites inside RBC</td>
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AFM

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<thead>
<tr>
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<th>SNFUH</th>
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<td>4 hr incubation</td>
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</table>
• **Seeing the Invisible:**
  – Scanning Near-Field Ultrasound Holography (SNFUH)
  ➔ *Nanomechanical* response to acoustics

• **MOSFET-embedded microcantilevers:**
  – Translating bio-chem binding into *nanomechanics*
  – Translating *nanomechanics* to electronic signal

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**Systems Approach to Sensing & Diagnostics**

- **Pattern**
  - DNAs, Proteins, Receptors...

- **Binding Event**
  - DNA Hybridization
  - Protein-Protein binding

- **Signal Transduction**
  - High sensitivity & specificity
  - Fast response
  - Fluid compatibility
  - Low cost, reliability, reproducibility..

- **Signal Detection**

**System Packaging:**

- e.g., integration w/CMOS and RF circuits
New All-Electronic Label-Free Transduction via MOSFET-Embedded Microcantilevers

What is New?

- Microcantilever Deflection Stresses MOSFET Channel
- MOSFET Drain Current Changes with Microcantilever Bending

Selectivity: Probe/receptor molecule selection
Sensitivity: Extent of bending and its detection

Science, March 17, 2006

NU patent: 2005
MOSFET-embedded microcantilever sensors

- Microcantilever bending induced stress
- Change in channel resistance
- Modulation of carrier mobility
- Change in the drain current

MOSFET-embedded Microcantilevers

- MOSFETs embedded at the high stress region of a microcantilever
- Microcantilever arrays
- A microcantilever pair composed of a gold-coated and a SiNx cantilever
- MOSFET terminals

Bashir et al., J Micromech Microeng. 2000

NU patent: 2004
Science, March 17, 2006
Detection of Antibody-Antigen binding

- Negligible change in ID for the gold coated cantilever with rabbit IgG
- A change in ID of almost two orders of magnitude with target binding
- No change in the SiNx reference cantilever
- Change in ID with time reaches a steady-state

Detection of Streptavidin-Biotin binding

- Streptavidin (10 μg/ml) – Biotin (100 fg/ml to 100 ng/ml)
- Negligible change in $i_d$ of the streptavidin coated cantilever without target molecules
- $i_d$ decreases (bending increases) with increasing target concentration
- No change in the SiNx reference cantilever

- Increase in the surface stress with increasing target concentration
- Surface stress sensitivity is of the same order as that of optical detection
### Comparison with current major biosensors

<table>
<thead>
<tr>
<th>Surface Plasmon Resonance (SPR)</th>
<th>Enzyme-Linked Immunosorbent Assay (ELISA)</th>
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</thead>
<tbody>
<tr>
<td>• High initial and operational costs</td>
<td>• Ag-Ab reactions detected by indicator enzyme activity</td>
</tr>
<tr>
<td>• No reference to compensate for the background</td>
<td>• Require labeling</td>
</tr>
<tr>
<td>• Label-free</td>
<td>• Time-consuming sample preparation and detection procedure</td>
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<tr>
<td>• Real-time detection &amp; monitoring</td>
<td>• Versatility</td>
</tr>
<tr>
<td>• Versatility</td>
<td>- Measure binding kinetics, affinity of the interaction, analyte concentration, etc.</td>
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**MOSFET-embedded microcantilever sensors**

• Label- and optics-free, all electronic
• Direct integration with application-specific microelectronics
• Miniaturization of the device → Portable, wider-deployment
• Low-cost by mass-production

### Highlights of MOSFET-embedded microcantilever sensors

- **High sensitivity**
  - Detection of ~5 nm deflection by analyte concentration in ppt range
- **Simple direct current measurement** with large signal-to-noise ratio
  - Label- and optics-free
  - Massively parallel signal sensing
  - Enable creating a portable device
  - Differential signal minimizes noise
  - Mass-production at low-cost
- **Direct integration with application-specific microelectronics**

**MOSFET-embedded microcantilevers may overcome the limitations imposed by currently available signal transduction and detection mechanisms**
MOSFET-Embedded Microcantilever System: Vision for Wider Deployment for Remote-addressing and Networking

MOSFET-embedded microcantilevers: A new electronic transduction paradigm comprising two-dimensional microcantilever arrays with embedded MOSFETs. An adsorption-induced surface stress at the functionalized cantilevers leads to precise, measurable and reproducible change in the MOSFET drain current. It can be readily integrated with application-specific on-chip microelectronics platform.
Combining MOSFET-Cantilevers and SNFUH:

**Summary and Vision**

- Non-destructive
- Nanoscale resolution
- Sensitive to embedded/sub-surface structures/features
- 3-D nanoscale tomography

- Fast scanning with multiple SPM probes
- Integrated turn-key system with embedded software architecture

Further (Collaborative) Opportunities

**Non-invasive sub-surface imaging with SNFUH:**

- 1-D and 2-D parallel multi-probe SNFUH array
- Higher frequency piezo’s
- Fundamentals of ultrasound-scattering in near-field regime: *modeling, simulation and 3-D tomography*

**MOSFET-embedded microcantilevers for bio-chem sensing:**

- MOSFET-embedded parallel/multiplexed 1-D and 2-D array
- On-chip lock-in, read-out and RF circuit for remote-sensing
- Back-end microfluidics, sampling and integration

Applications to hard, soft (biological/polymer) and hybrid structures