Microcantilever Sensors for *in-situ* Sub-surface Characterization

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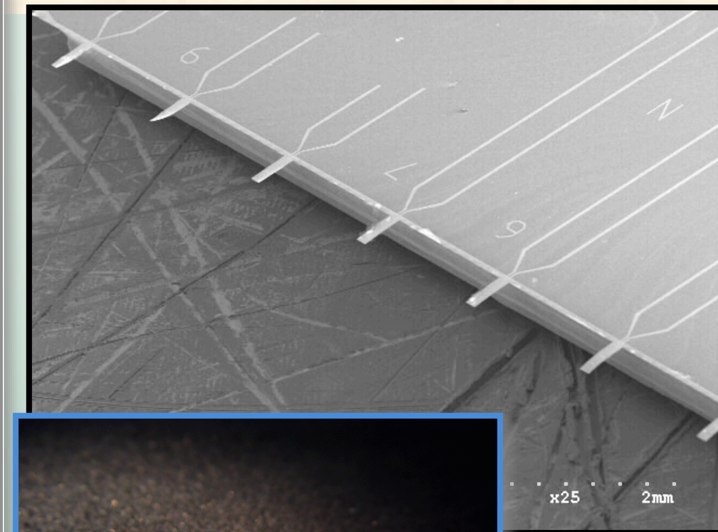
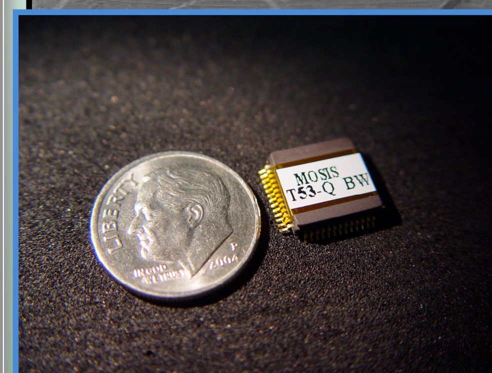
Outline

- Sensor Characteristics
- Nanomechanical Sensors
- Receptor-Based Sensing
- Small Molecule Detection
- Receptor-Free Selectivity
  - Thermal effects
  - Electrochemistry
  - Pre-concentration
- Instrumentation
- Conclusions





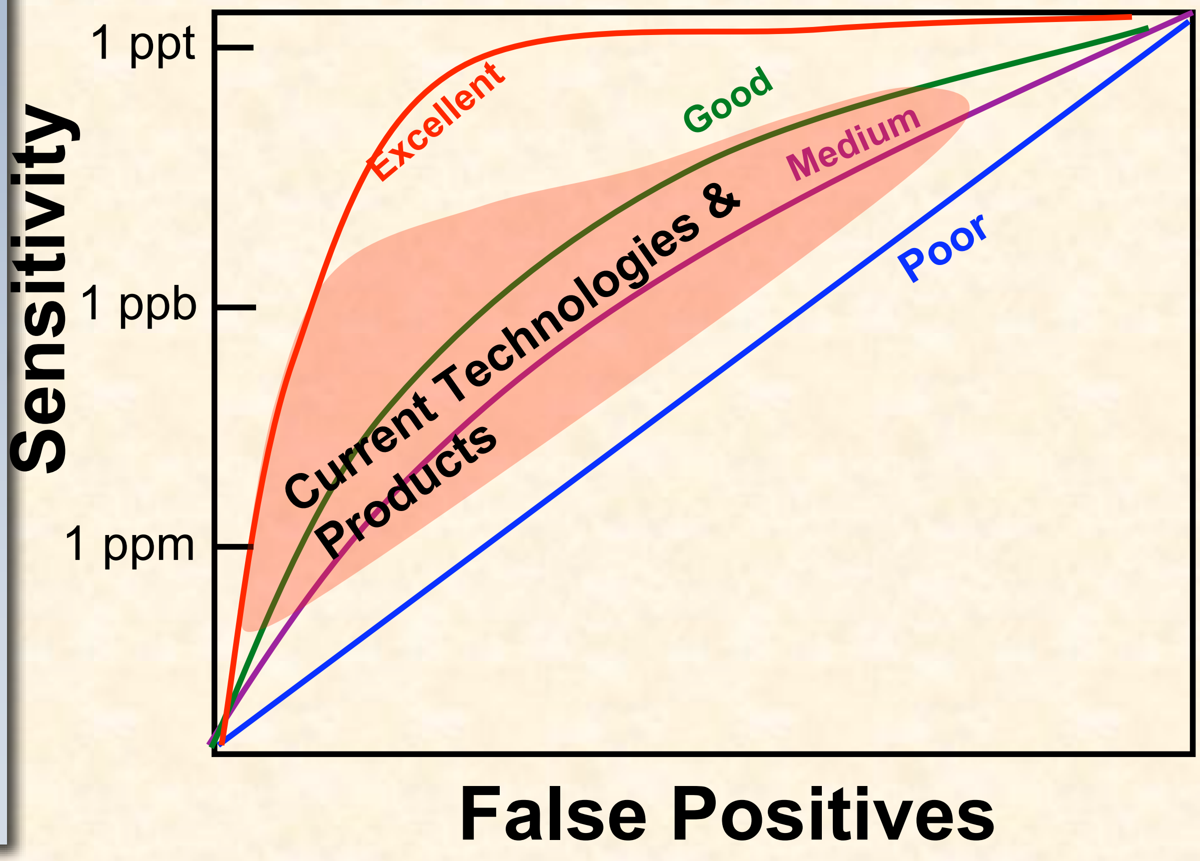
Sensor Performance Characteristics

ERSP
Sensor requirements:
- High sensitivity
- High selectivity
- Fast detection time
- Fast regeneration
- Real-time detection
- Multi-analyte detection

- No consumables
- Mass production
- Low power
- Miniature
- Low cost
- Wireless

Nanomechanical Sensors

- Receiver Operating Characteristic (ROC) Curves

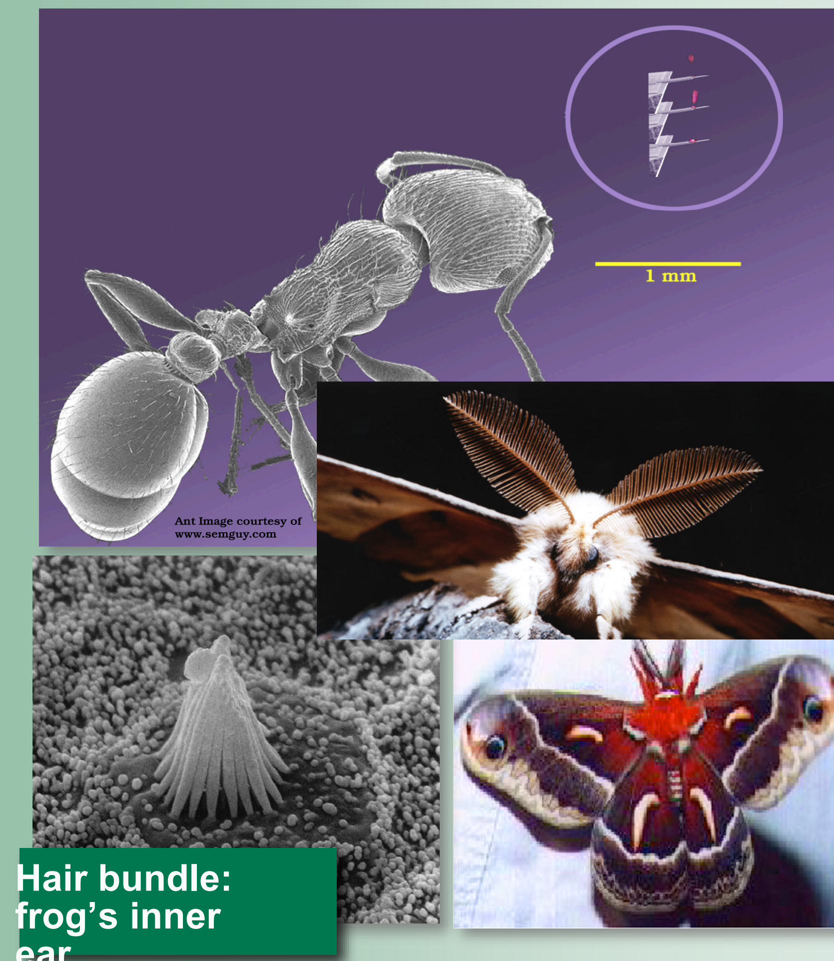


Sensitivity Without Selectivity is Useless for Practical Applications

Nanomechanical Sensors

At the fundamental level, all interactions in biology and chemistry involve nanomechanics

Nanomechanics in nature

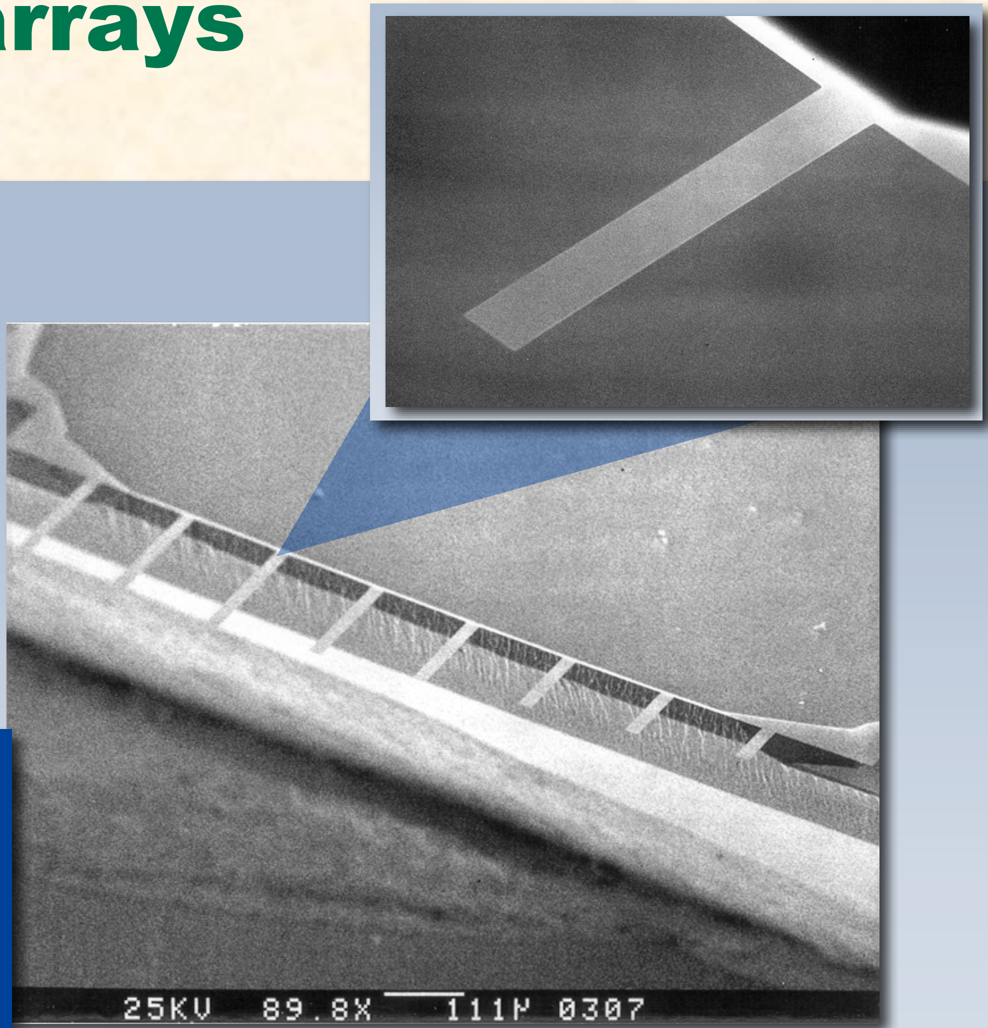


Microcantilever arrays

- Ideal displacement sensor
  - Sub nm sensitivity
- Displacement ~ force
- Surface stress (Bending)
- Frequency (mass loading)
- Temperature (Bi-metallic effect)

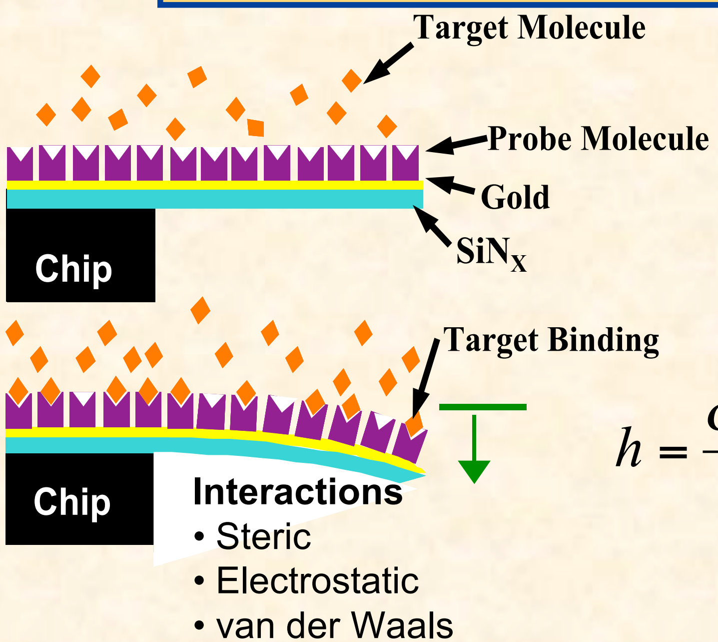
Sensitivity:
 Function of dimensions

Selectivity:
 Function of coatings



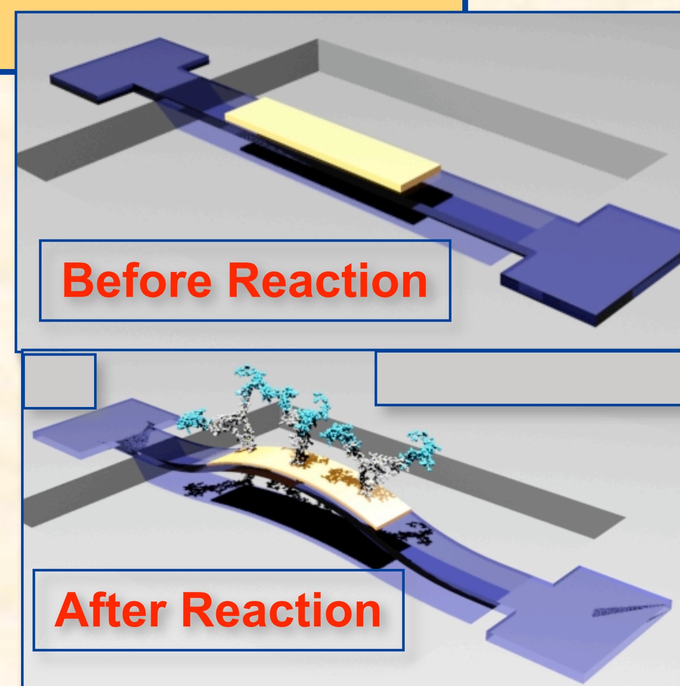
Molecular Adsorption and Nanomechanics

- Adsorption decreases surface free energy
- Surface free energy density (J/m^2) = Surface stress (N/m)
- Cantilever beams with spring constant in the same order of magnitude as the free energy change undergo bending due to adsorption
- Resonance frequency variation - inertial mass loading
- Bending and frequency signals



$$\sigma = \gamma + \left(\frac{\partial \gamma}{\partial \varepsilon}\right)$$

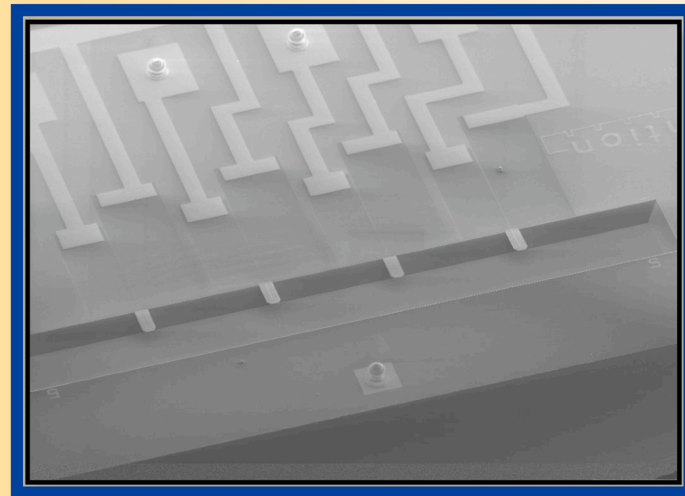
$$h = \frac{\sigma(1-\nu)}{E}\left(\frac{L}{d}\right)^2$$

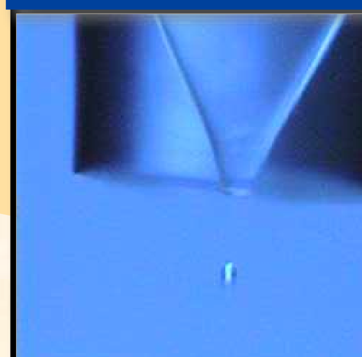


Basis for highly sensitive sensors

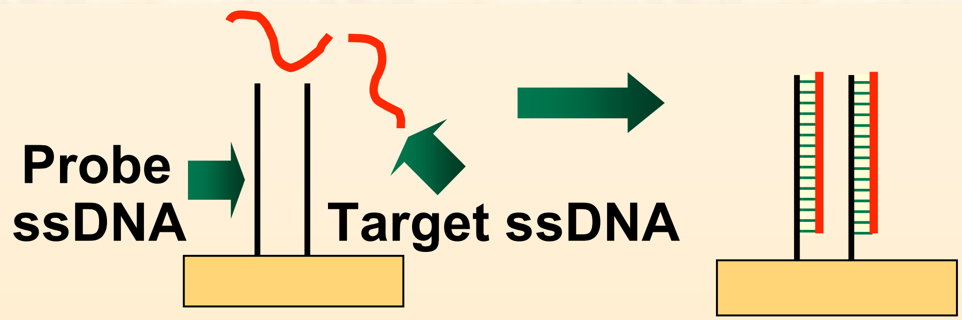
Immobilized Receptors Bring Selectivity

- Receptors (Selective Coatings)
  - Polymers,
  - Self-assembled monolayers (SAM),
  - Nanoparticles,
  - Bio-molecules
- Surface coupling chemistry
  - Linkers For Optimum Stress Transduction
  - Adhesion Layers
  - Nanostructures
- Application techniques
  - Self-Assembly
  - Evaporation/sublimation
  - Matrix assisted laser desorption
  - Ink-jet deposition

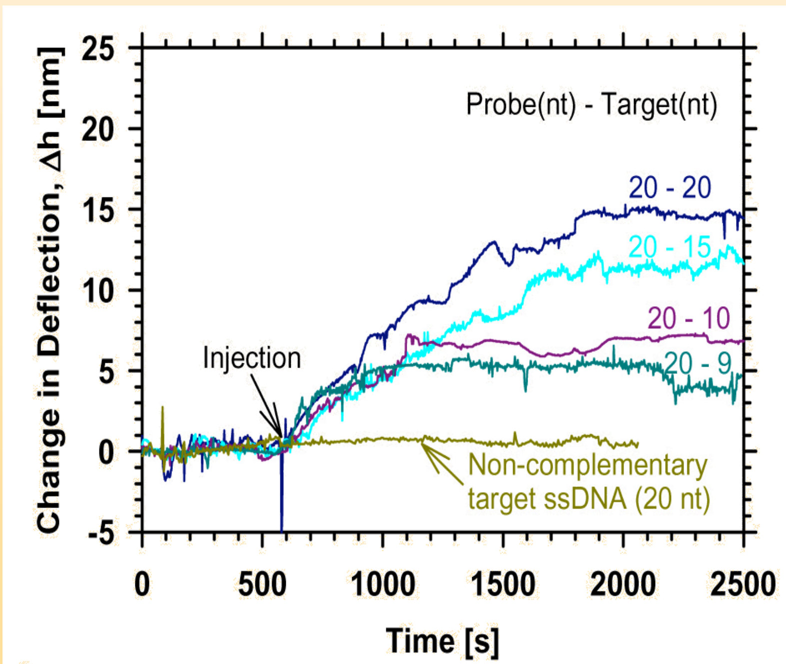


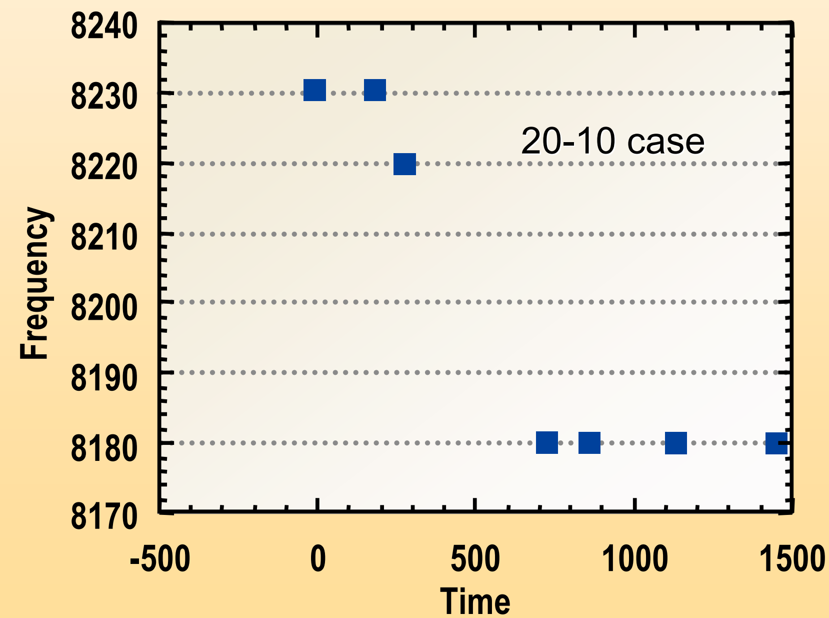


DNA hybridization Detection



Brownian Motion



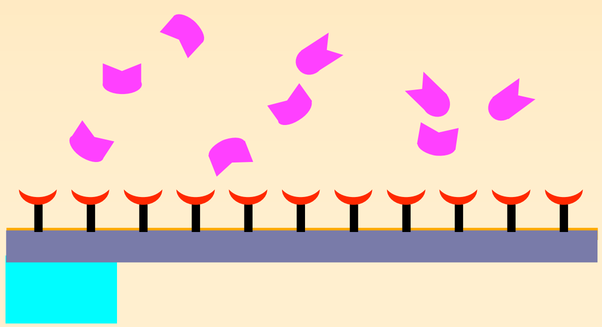


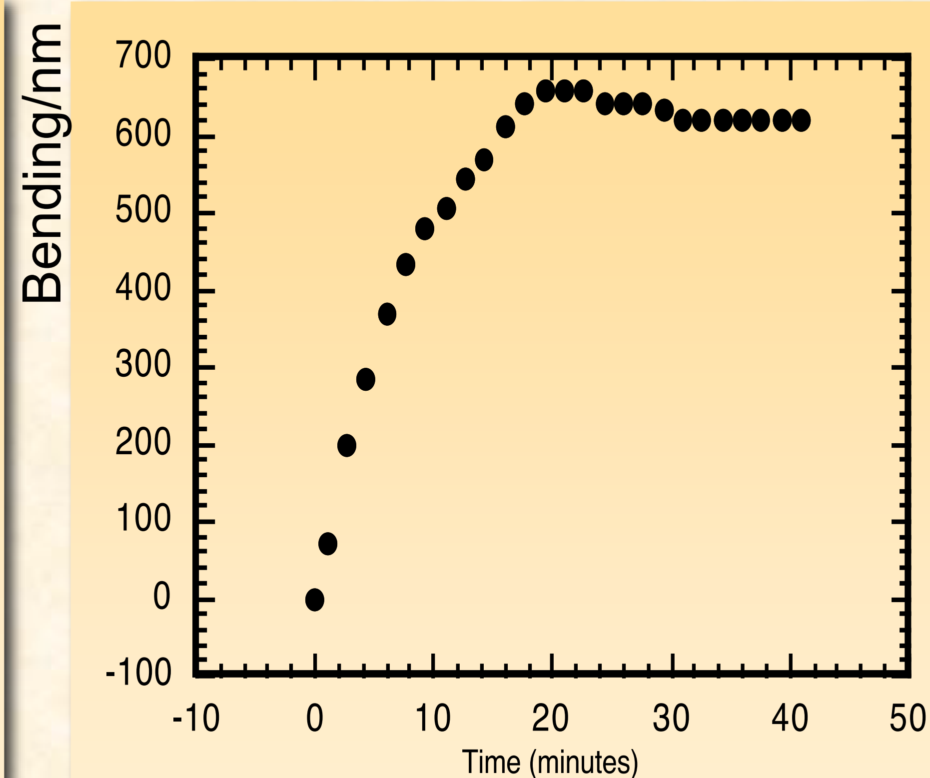
Wu, G. *et al.* "Origin of nanomechanical cantilever motion generated from biomolecular interactions," *PNAS* 98(4), 1560-1564 (2001).

Measured mass is 5-10 times higher

Antibody-antigen interactions: High Selectivity

- Cantilevers with immobilized ricin antibodies undergo bending when exposed to ricin under solution
- Response time can be reduced by using smaller liquid volume
- 40 parts-per-trillion sensitivity





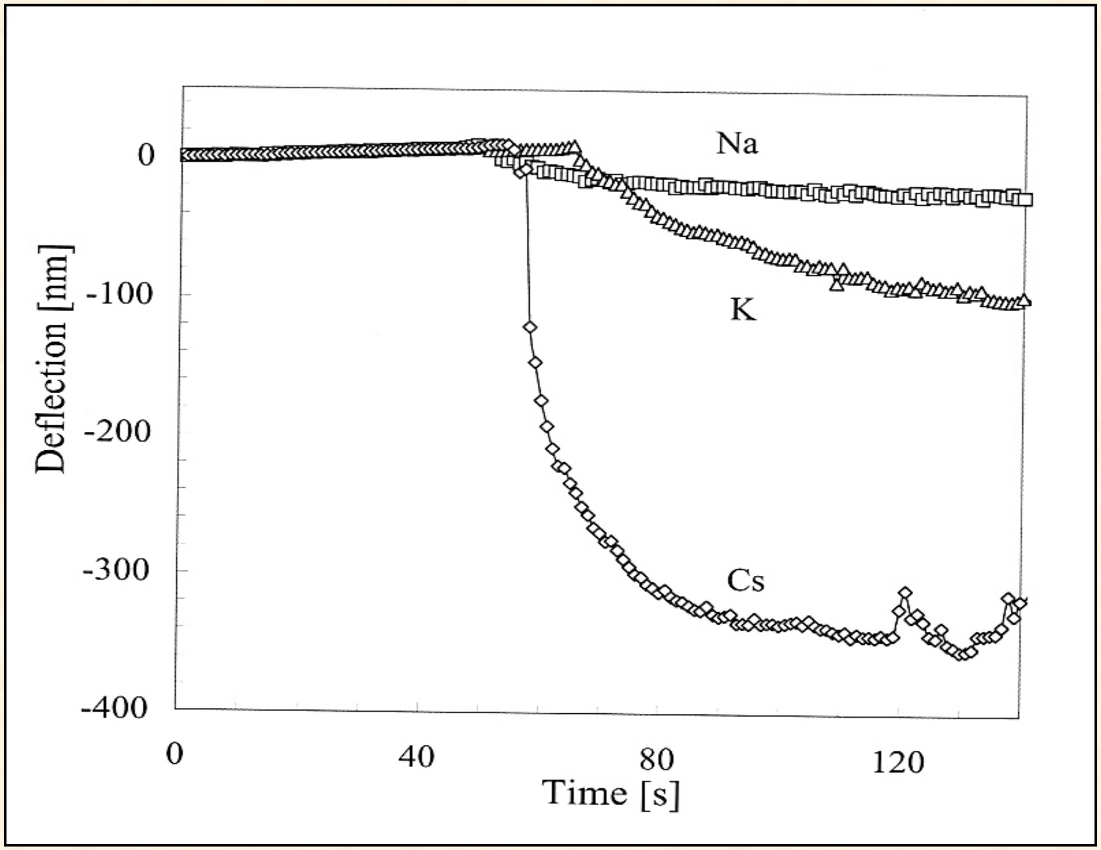
Bio-Receptors Are Highly Selective

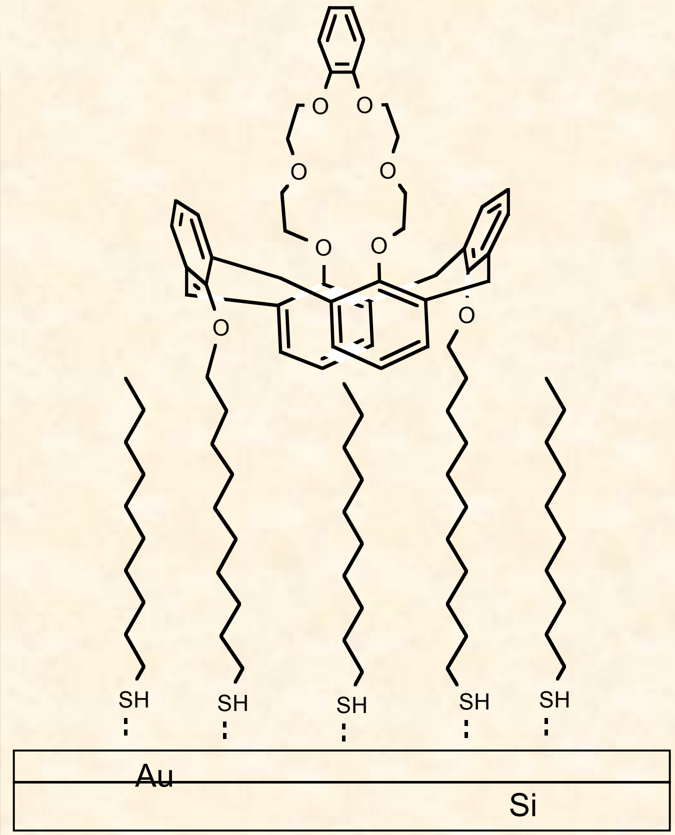
Selectivity Non-Biological Molecules

- Selectivity can be achieved by incorporating a multimodal approach of receptor and receptor-free techniques that can be integrated into the cantilever platform
- Self-Assembled Monolayers
- Receptor-free approaches
  - Electrochemical techniques
  - Nano thermal effects
- MEMS can provide a versatile platform for multi-modal detection

Self-assembled Monolayers (SAM):

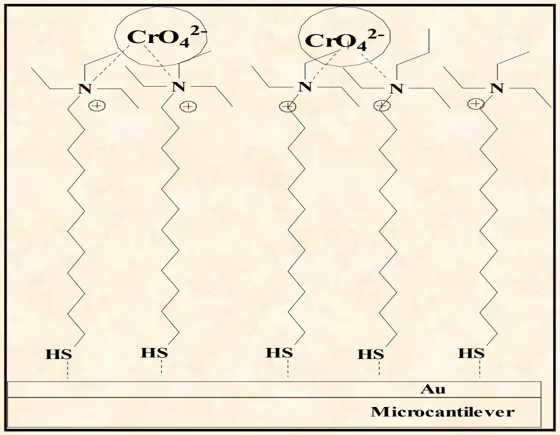
Detection of Cs^+ Ions in Water With High Specificity

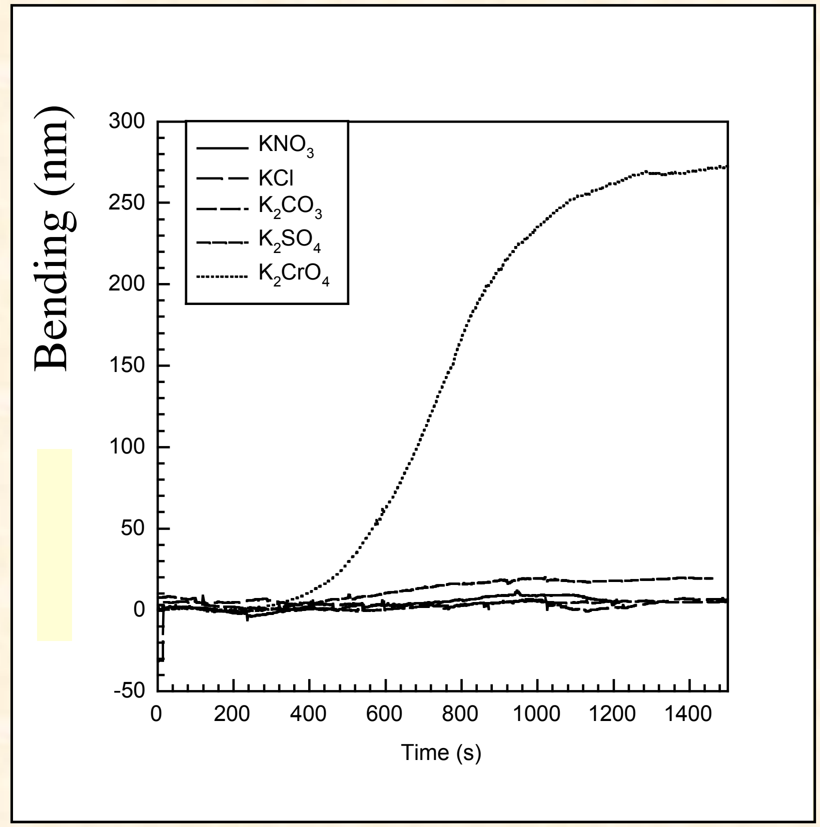




Bending deflection response of the coated microcantilever towards different alkali metal ions (10^{-5} M concentration of Cs^+, K^+, and Na^+).

Detection of CrO_4^{2-} in ground water: Triethyl-12-Mercaptododecyl Ammonium Bromide





SAM is Extremely Selective to CrO_4^{2-} Ion

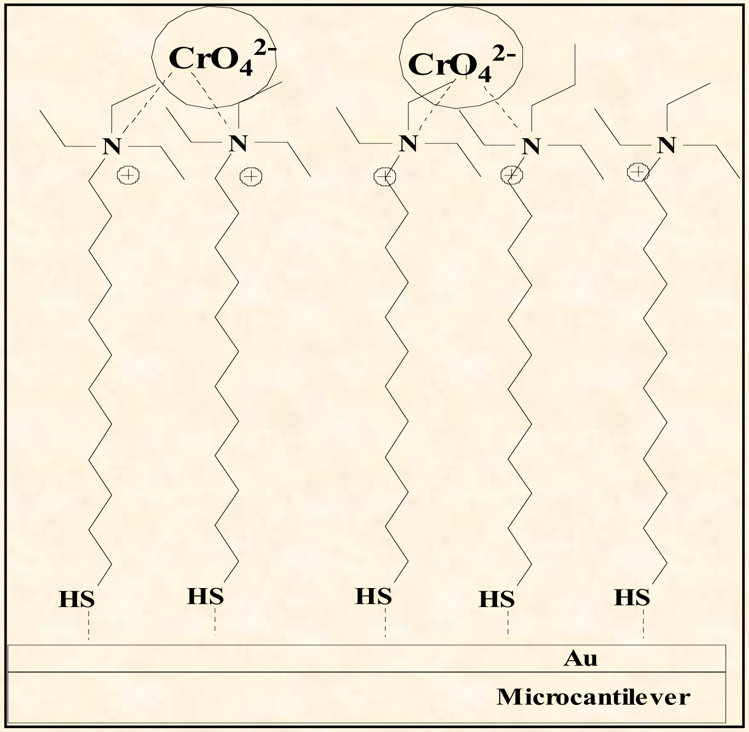
SAM Reduces The Surface Stress

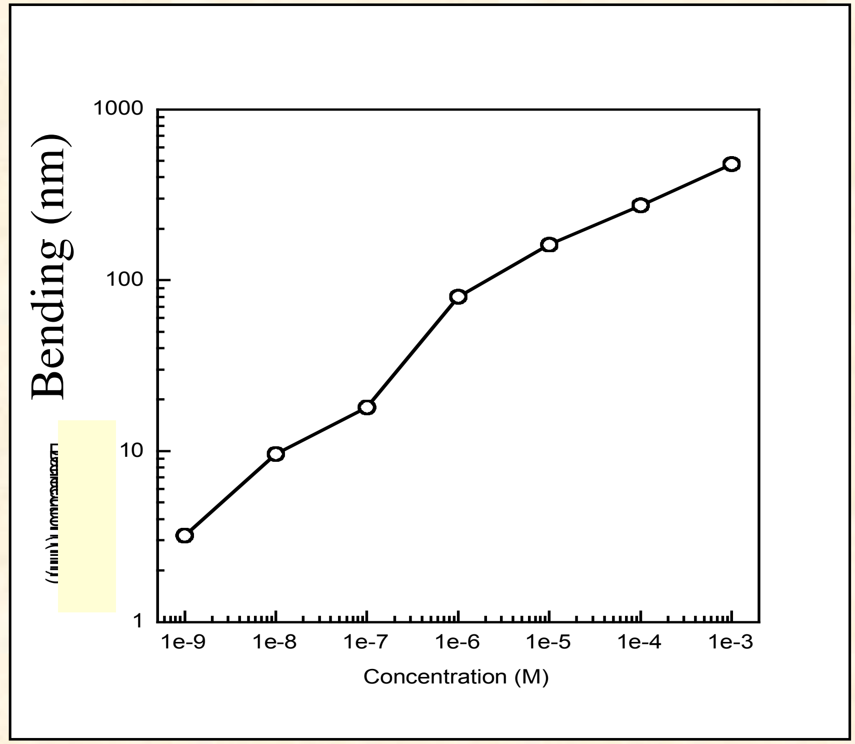
CrO_4^{2-} Forms Ion Pairs And Increases The Surface Stress

Extremely sensitive and highly selective

Specific Ion Detection: CrO_4^{2-}

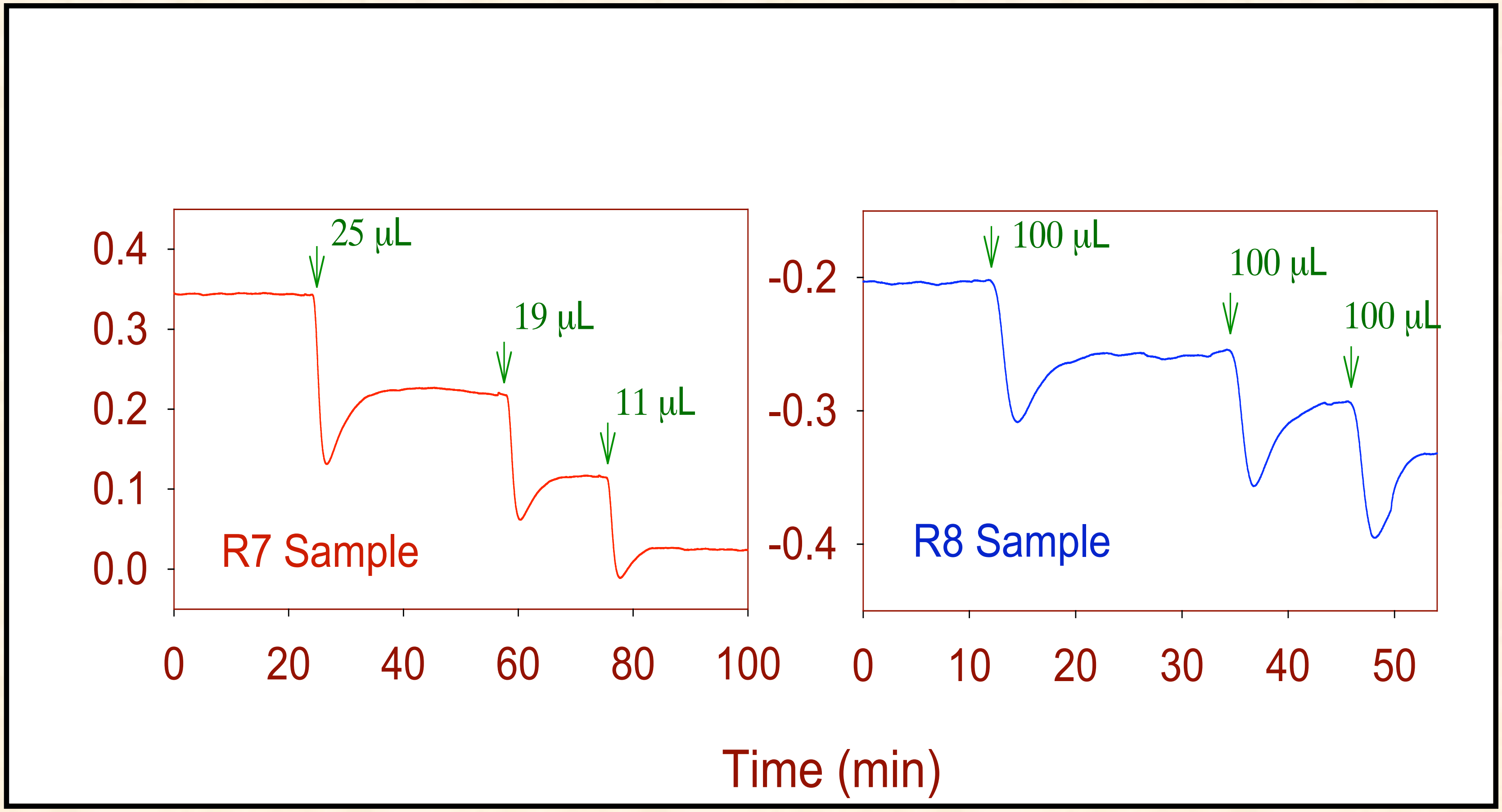
Triethyl-12-Mercaptododecyl Ammonium Bromide SAM And Ion Pair Formation With CrO_4^{2-}





Equilibrium cantilever deflection as a function of CrO_4 ion concentration

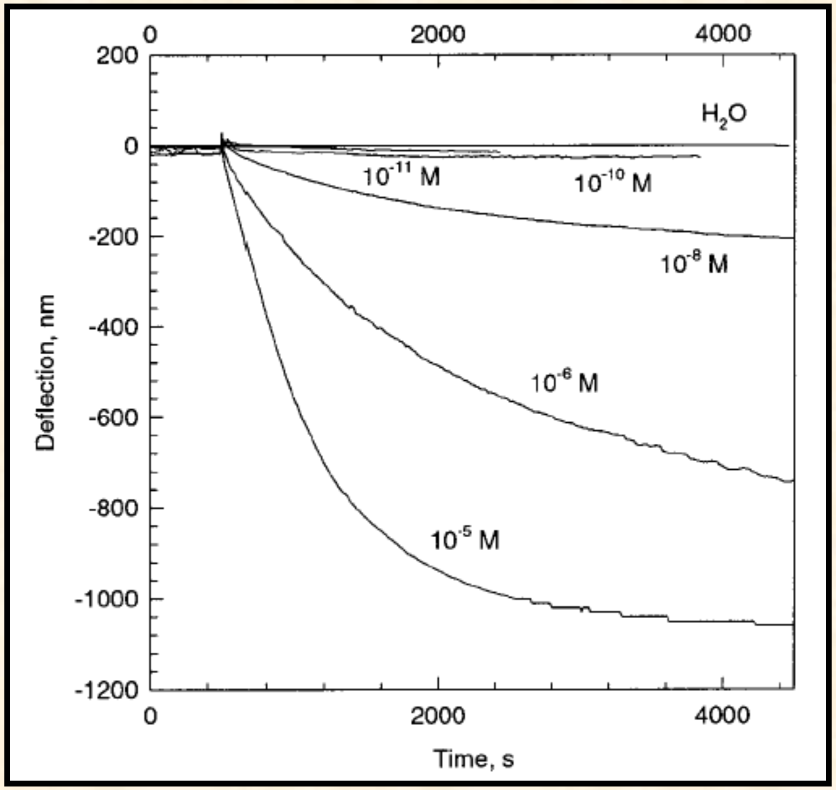
CrO_4^{2-} Detection Using 4-mercaptopyridine SAM:

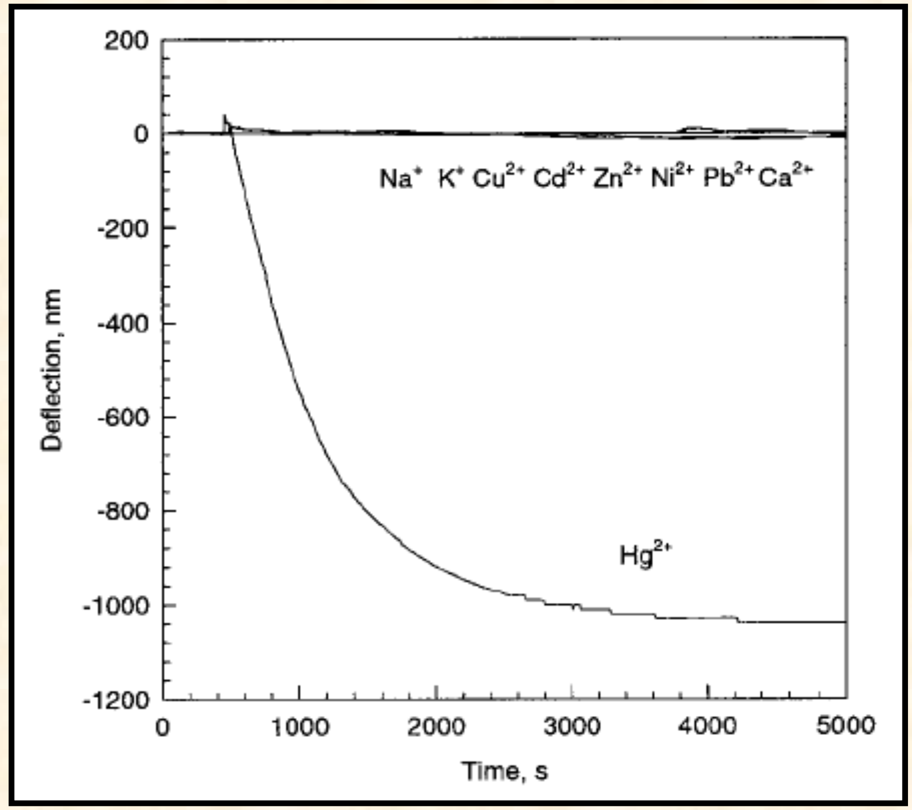


Microcantilever Response to Contaminated Hanford Water

0.1 M H_2SO_4 electrolyte, electrochemically reduce to regenerate

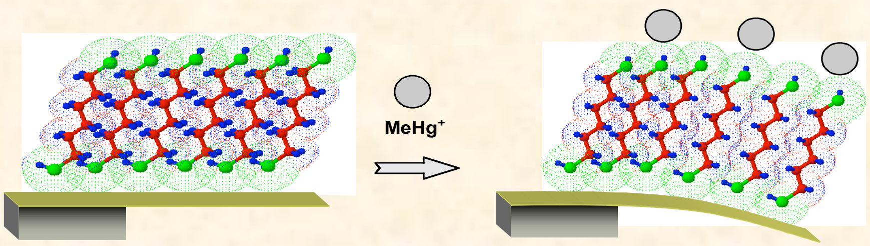
Hg^{2+} Detection: Sensitivity and selectivity of gold-coated cantilever sensors

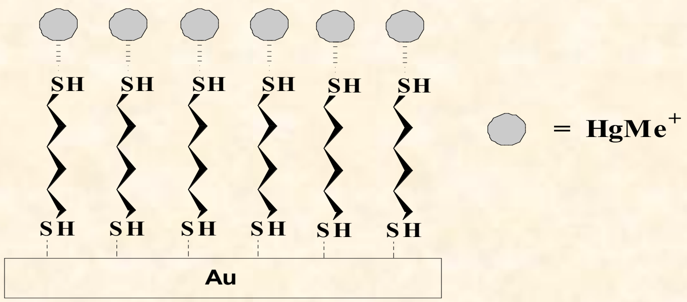


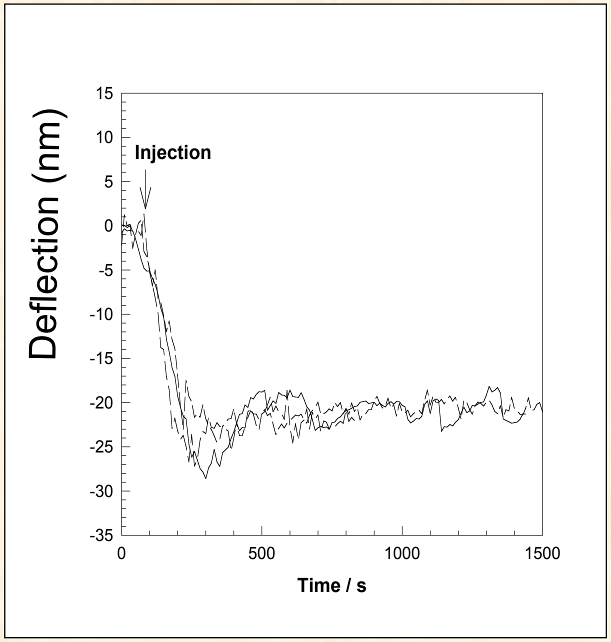


X. Xu et al., Anal. Chem., 74, 3611 (2002)

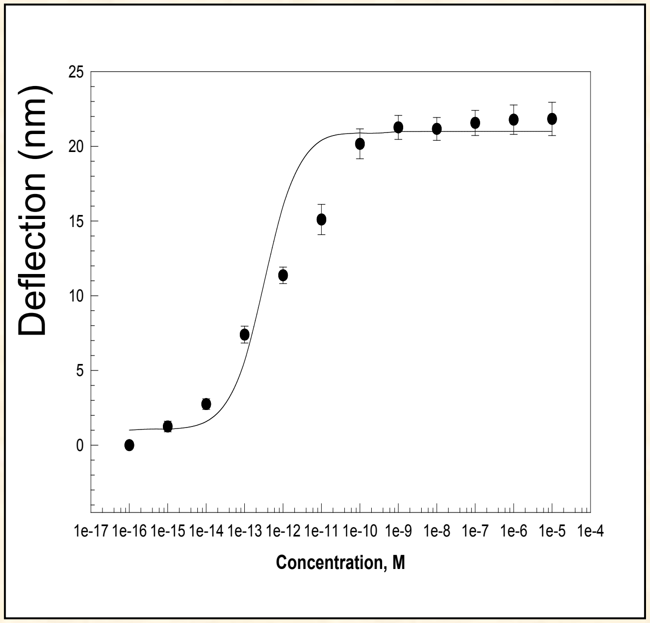
Detection of Methyl Mercury:
1,6-Hexanedithiol monolayers modified cantilevers







Bending of the cantilever to $1x10^{-6}$ M of CH_3Hg^+ in water (three experiments)



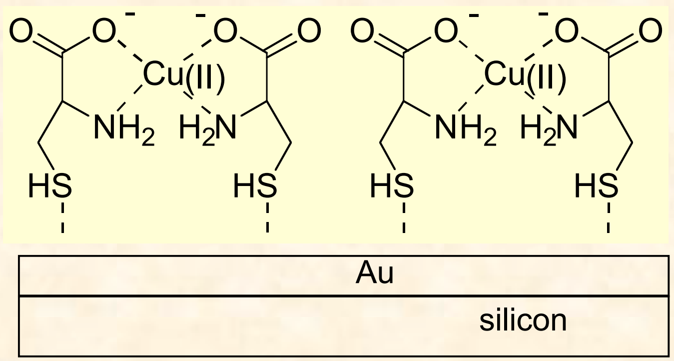
Bending of the cantilever as a function of the concentration of CH_3Hg^+

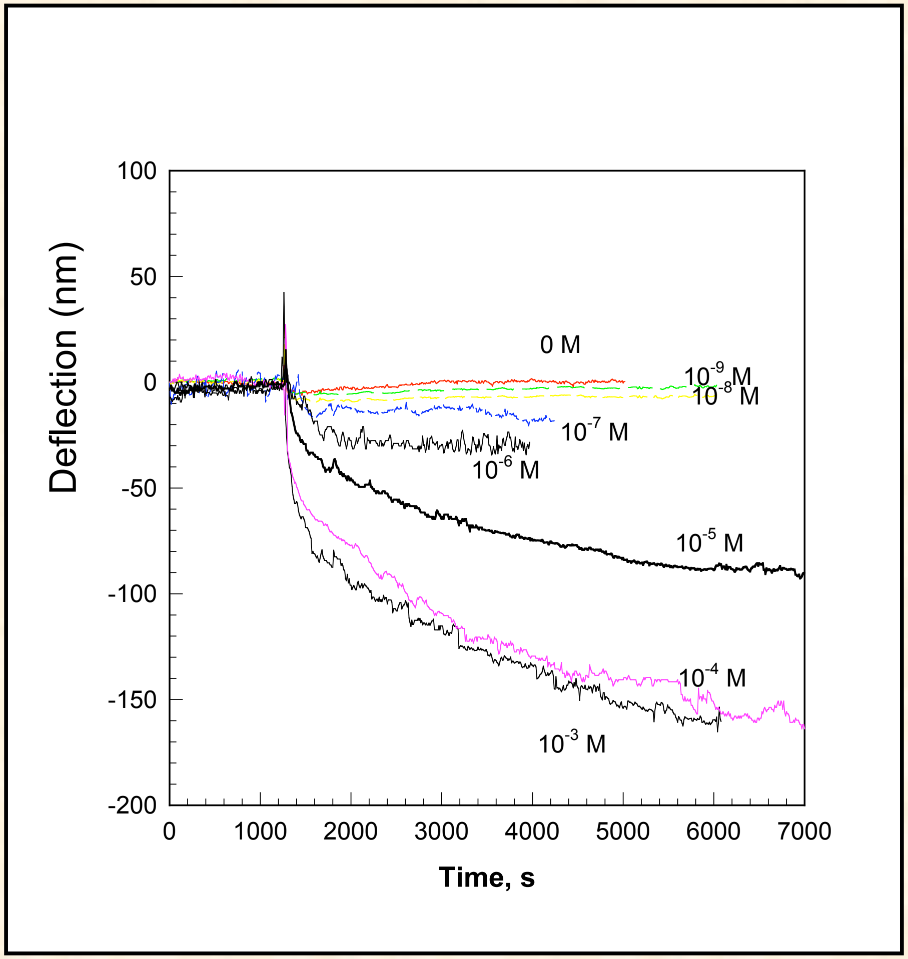
Detection of Cu(II) ions in Solution

Cysteine forms a SAM on gold

Previously reported for electrochemical sensor for copper

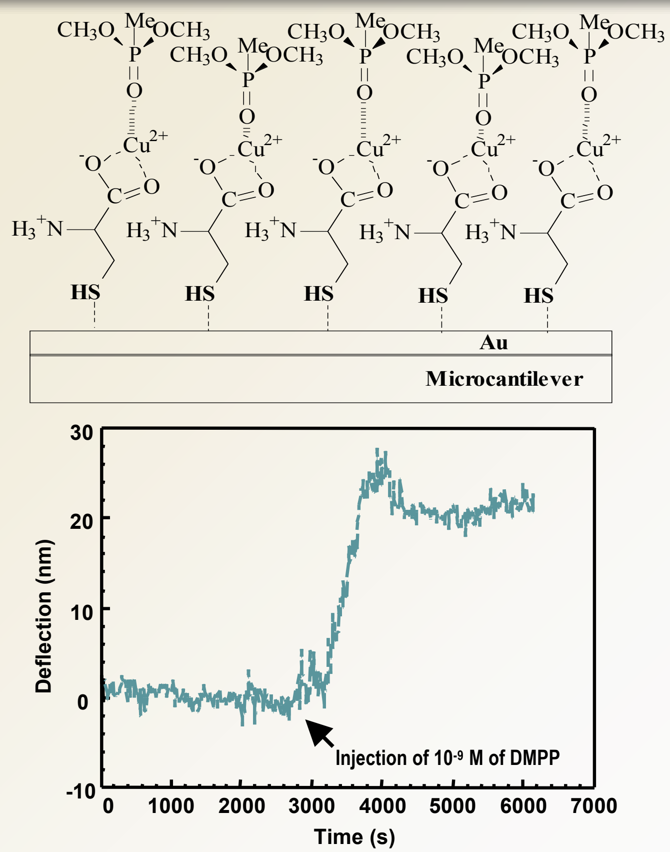
One Cu per two cysteines



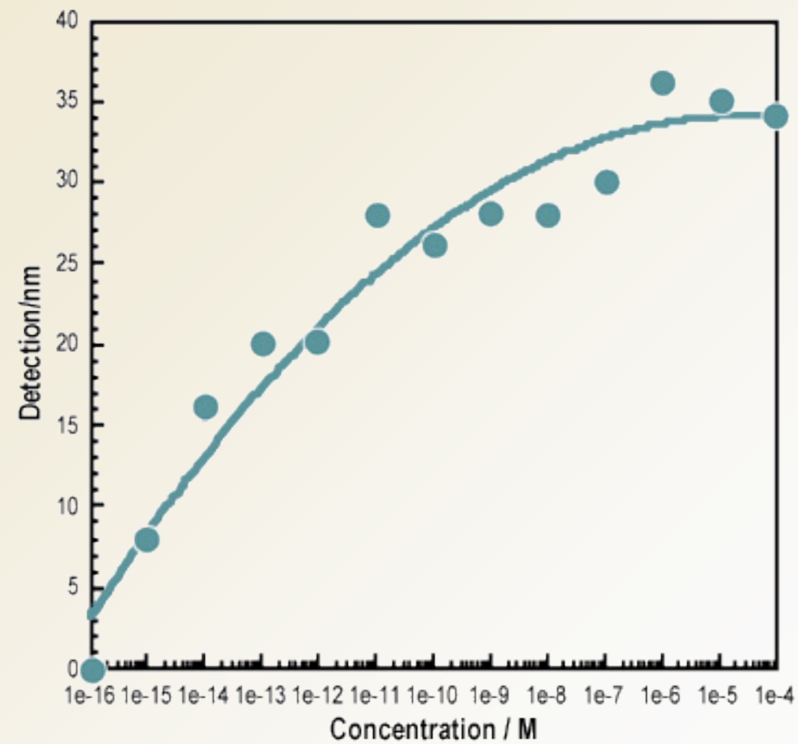


Cu2+/L-cysteine SAMs are highly selective for detecting DMMP

Cu^{2+}/L-cysteine bilayer coated microcantilever



Dimethyl methyl phosphonate (DMMP) used as Sarin nerve gas simulant

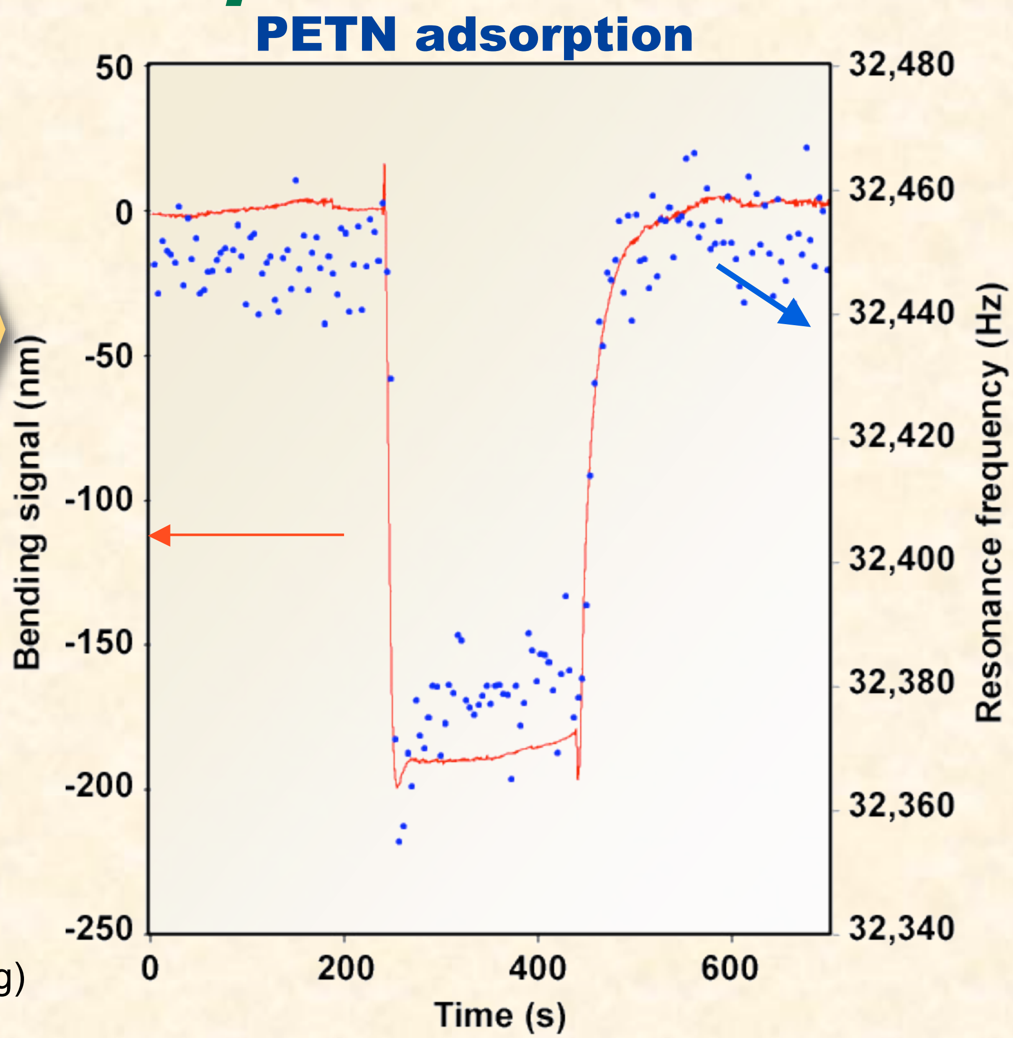


Yang, Ji and Thundat, JACS, 2002

SAM-based Sensing of Vapors

Cantilevers with self-assembled monolayers (SAM)

Sensitivity
10 parts-per-trillion



Frequency - Brownian motion - Adsorbed Mass

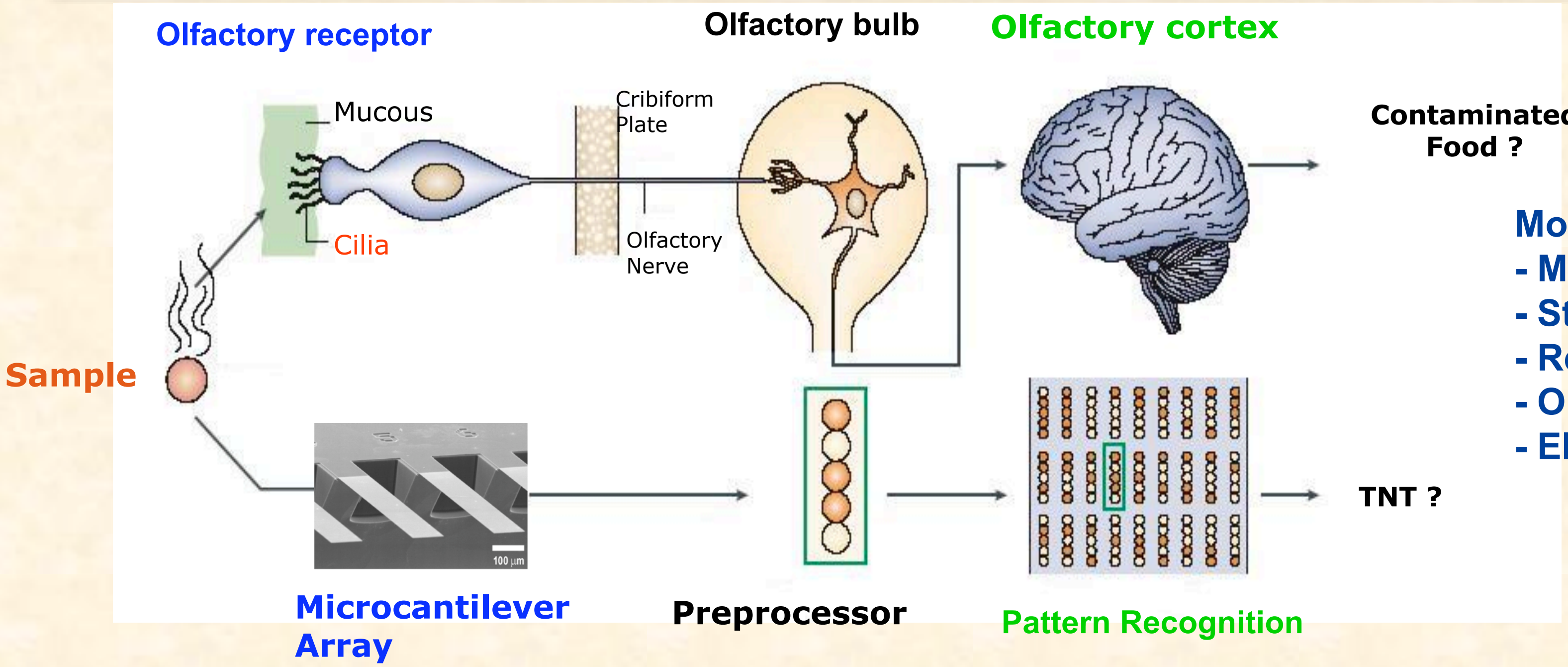
Bending - Adsorption Energy

(Pinnaduwage et al., **App. Phys. Lett**. 2003)

Two Orthogonal Signals (frequency and bending) collected simultaneously

Increasing Selectivity Using Cantilever Array: Pattern Recognition

Small molecule detection requires pattern recognition since there are only limited number of interactions that we can use for receptor-based detection

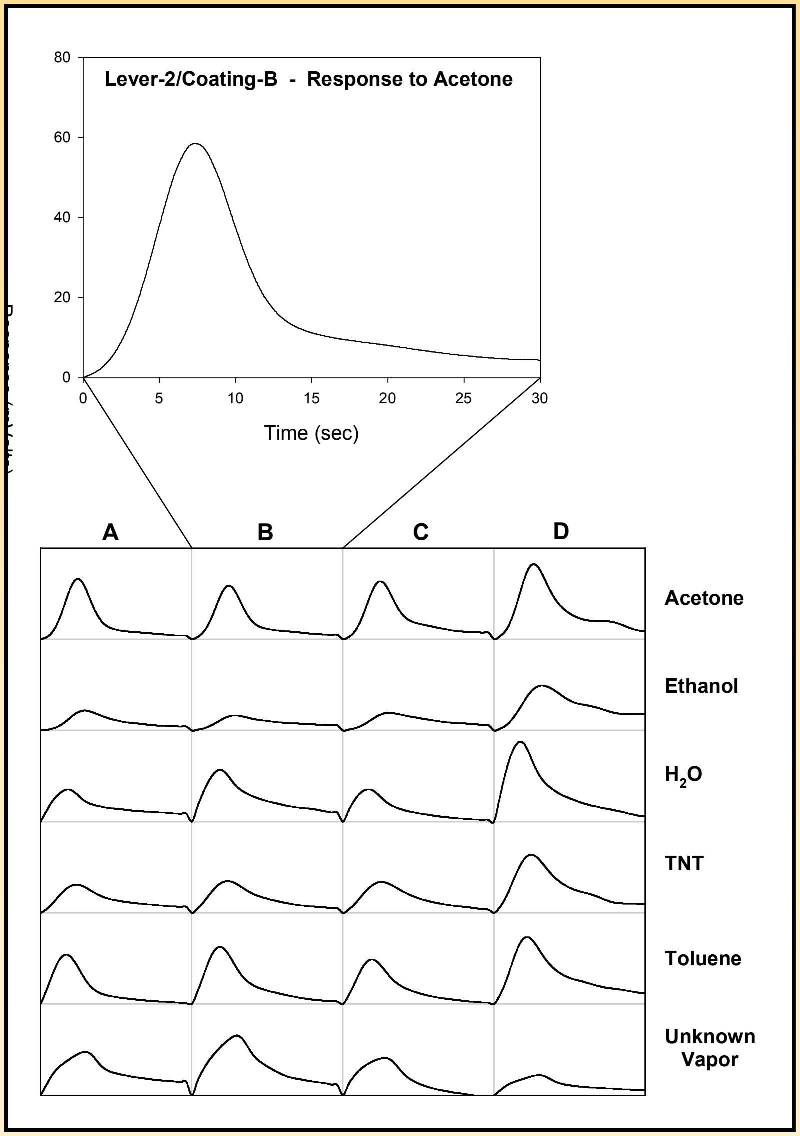


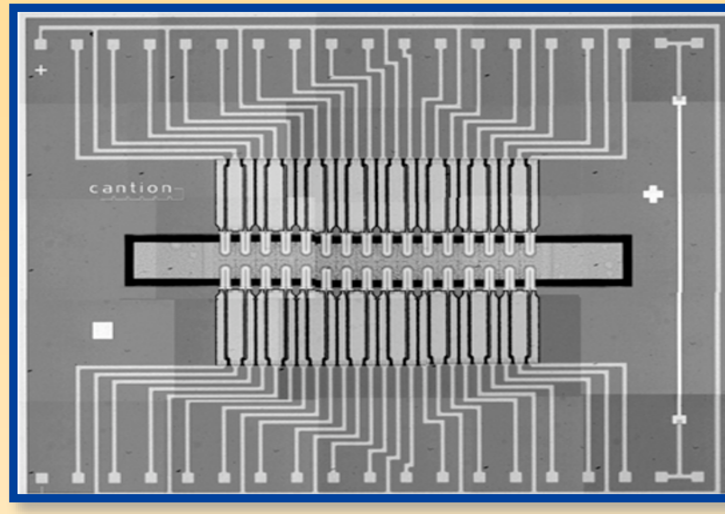
More than one signal
- Mass
- Stress
- Relaxation Time
- Optical
- Electrical

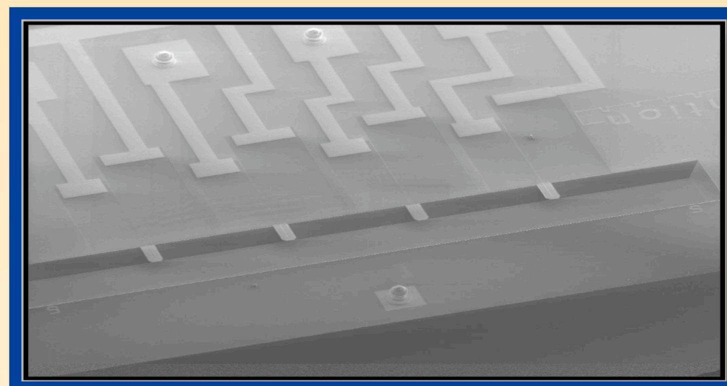
Covalent Bonds	Antibody-Antigen	Hydrogen Bond	Dipole-Dipole	London Forces
100	>25	2-16	0.5 -2	<1

Reversibility at k_BT

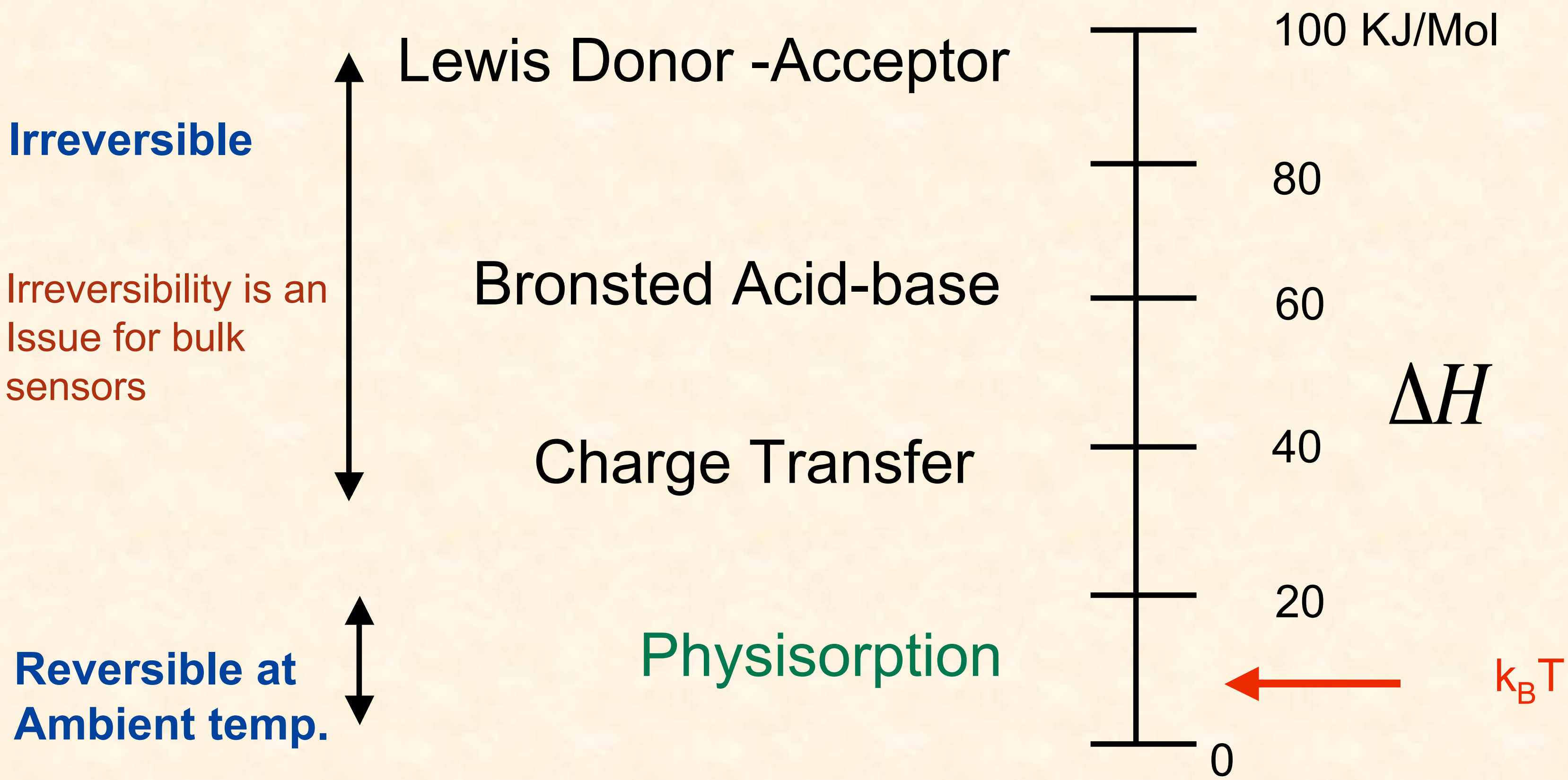
Array-Based Selectivity of Small Molecules







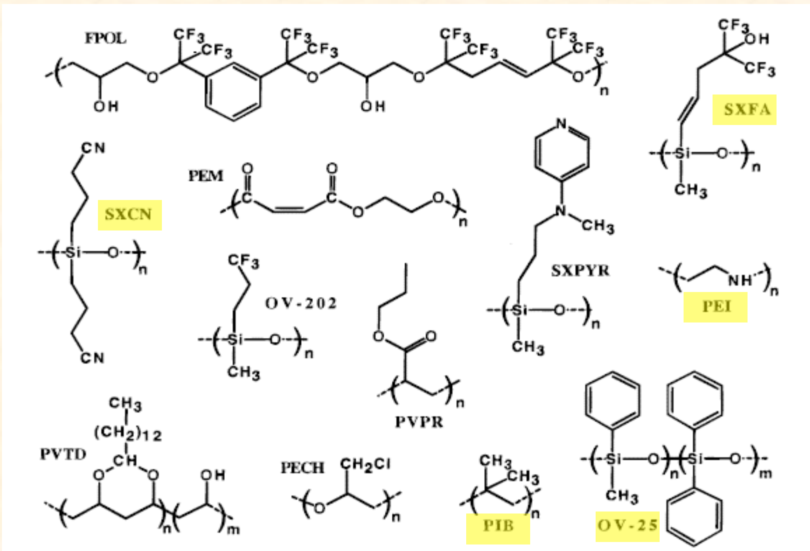
Receptor-Based Chemical Sensing Involves Molecular Interactions



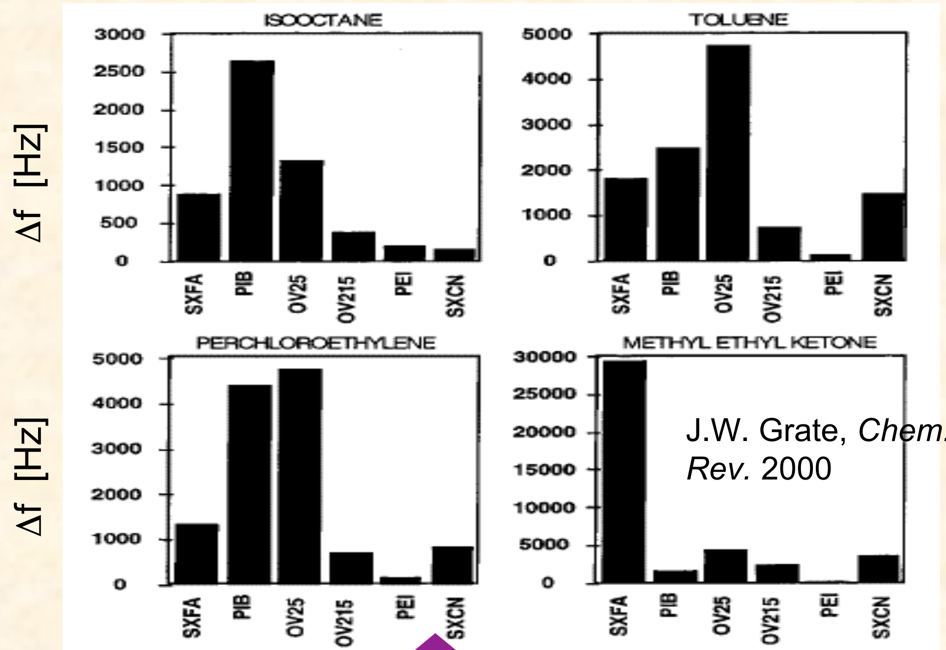
- Cantilevers can be heated to higher temperatures in milliseconds
- Higher binding energy interactions can be used

Selectivity Challenge: *Lessons from the nature*

Polymers Currently Used



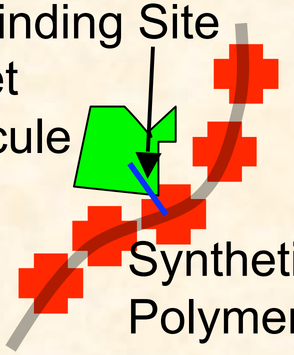
Poor Selectivity



J.W. Grate, *Chem. Rev.* 2000

Single Binding Site

Target Molecule

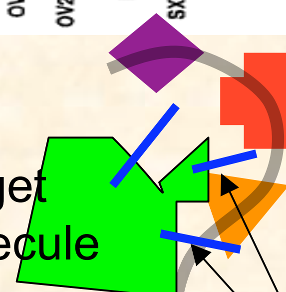


Synthetic Polymer

ΔG_1

How do biomolecules recognize each other?

Selectivity ~ $\exp(\Delta G/k_B T)$



Target Molecule

Sequence-specific biopolymer

Multiple Binding Sites

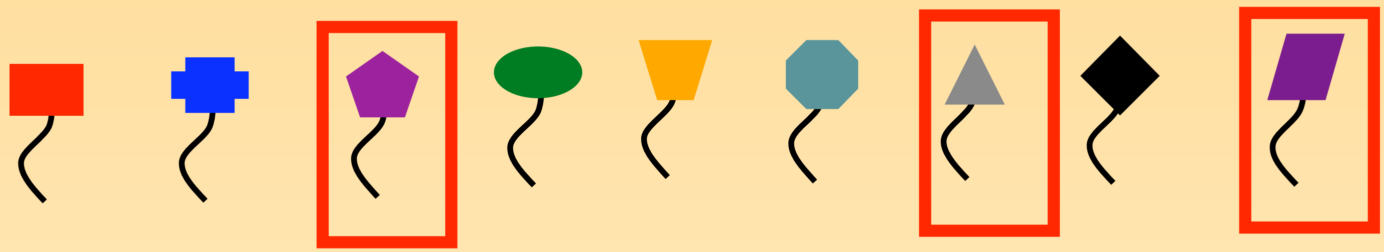
$\Delta G_2 = n\Delta G_1$
$n > 1$

Combinatorial Screening of Sequence-Specific Polymer

Analyte or Target Molecule

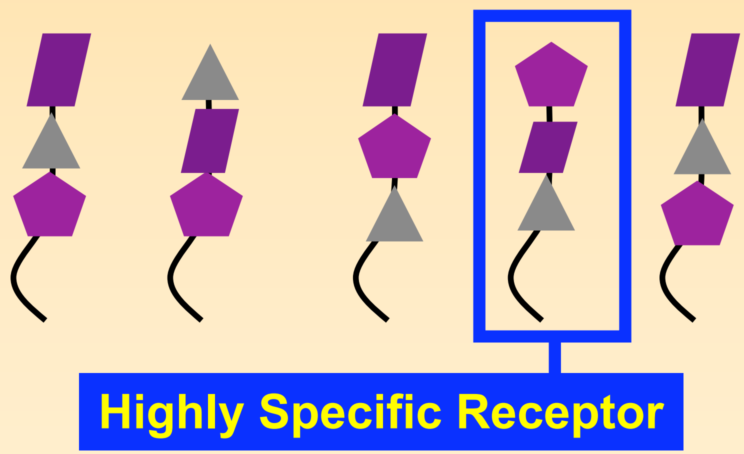
Step 1

Select Top 3 Monomers for Binding Affinity



Step 2

Select Sequence with Highest Binding Affinity



For 3 top monomers
-27 different trimers
-729 different hexamers

Screening for multiple target molecules can be done simultaneously

Time consuming process

Electrochemical Speciation -
Electrochemistry on a cantilever

- **Boltzmann distribution**

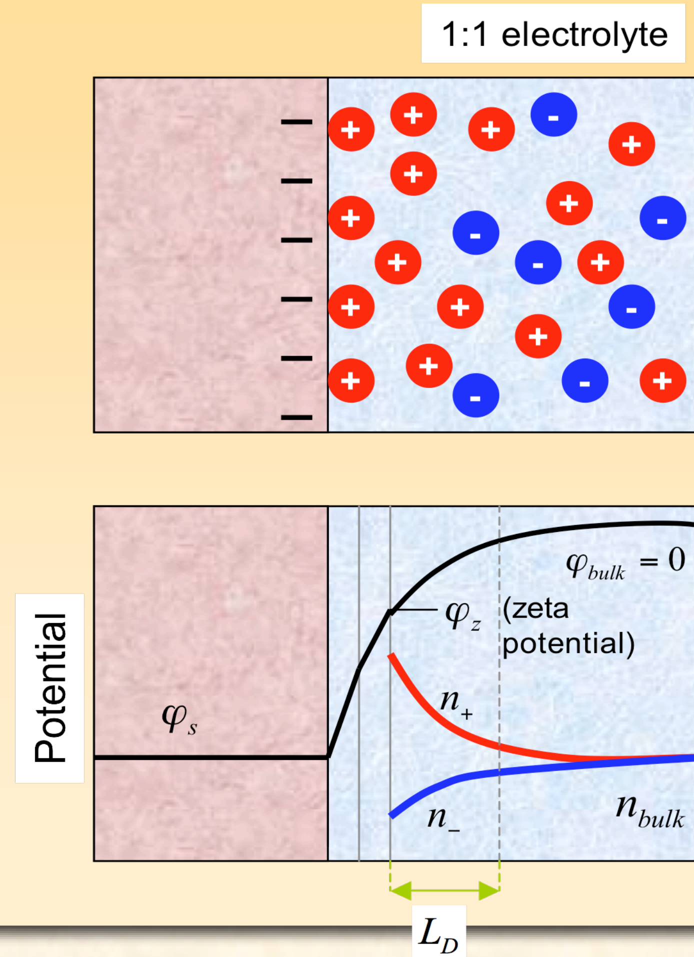
$$n_{\pm} = n_{bulk} \exp\left(\frac{\mp e\varphi}{kT}\right)$$

- **Poisson equation**

$$\nabla^2\varphi = \frac{-\rho}{\varepsilon} = -\frac{e(n_+ - n_-)}{\varepsilon}$$

- **Debye length**

$$L_D = \sqrt{\frac{\varepsilon kT}{2n_{bulk}e^2}} \quad (1\text{-}100\ \text{nm})$$



Electrolyte window
Detection of limited analytes

Mechanical Electrochemistry: Charge Transfer

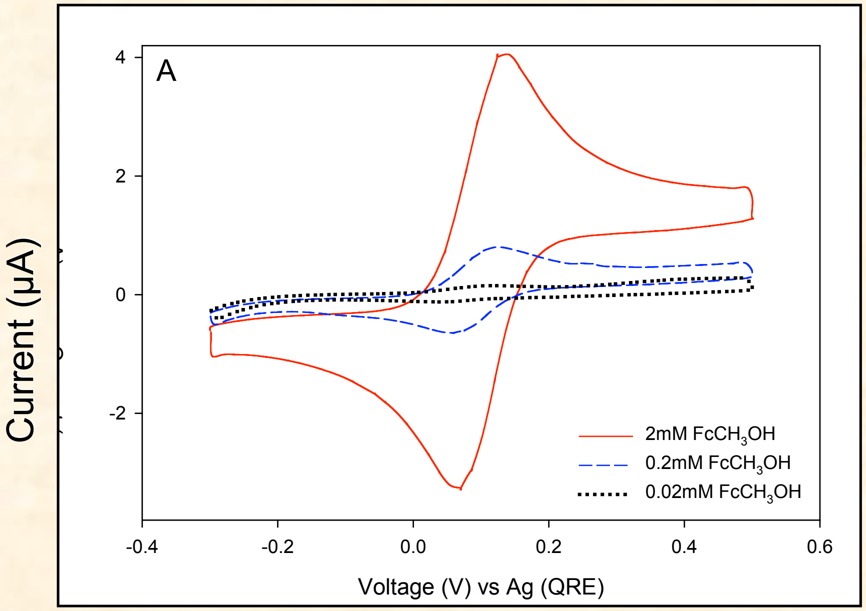
gold-coated cantilever electrode (0.1 M PB solution in presence of $FcCH_2OH$)

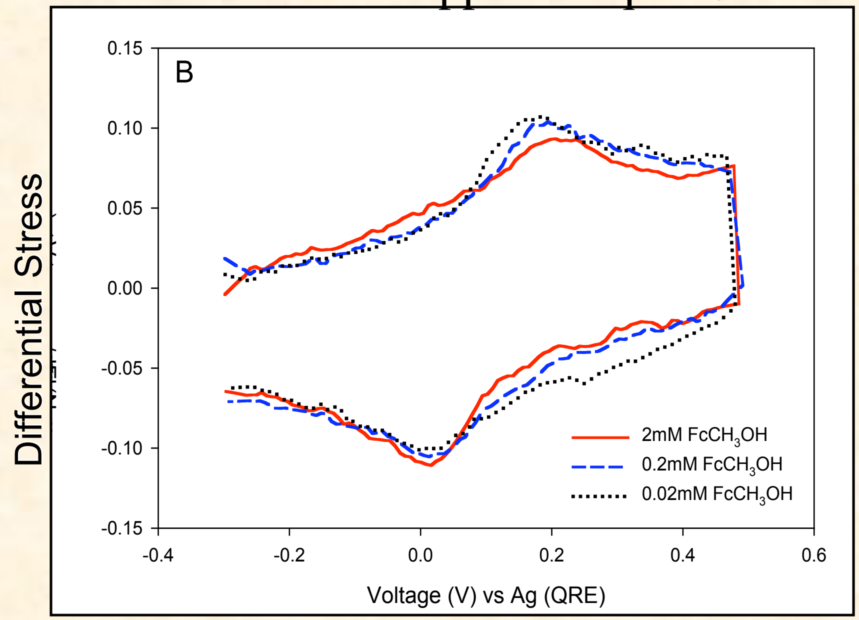
$$d\gamma = -q dE - \sum_i F_i d\mu_i + 2(\sigma - \gamma) d\varepsilon$$

Gibbs-Duhem Equation

$$-\left(\frac{\partial \gamma}{\partial E}\right)_{T,P,\mu} = q + 2(\sigma - \gamma)\left(\frac{\partial \varepsilon}{\partial E}\right)_{T,P,\mu}$$

Lippman Equation





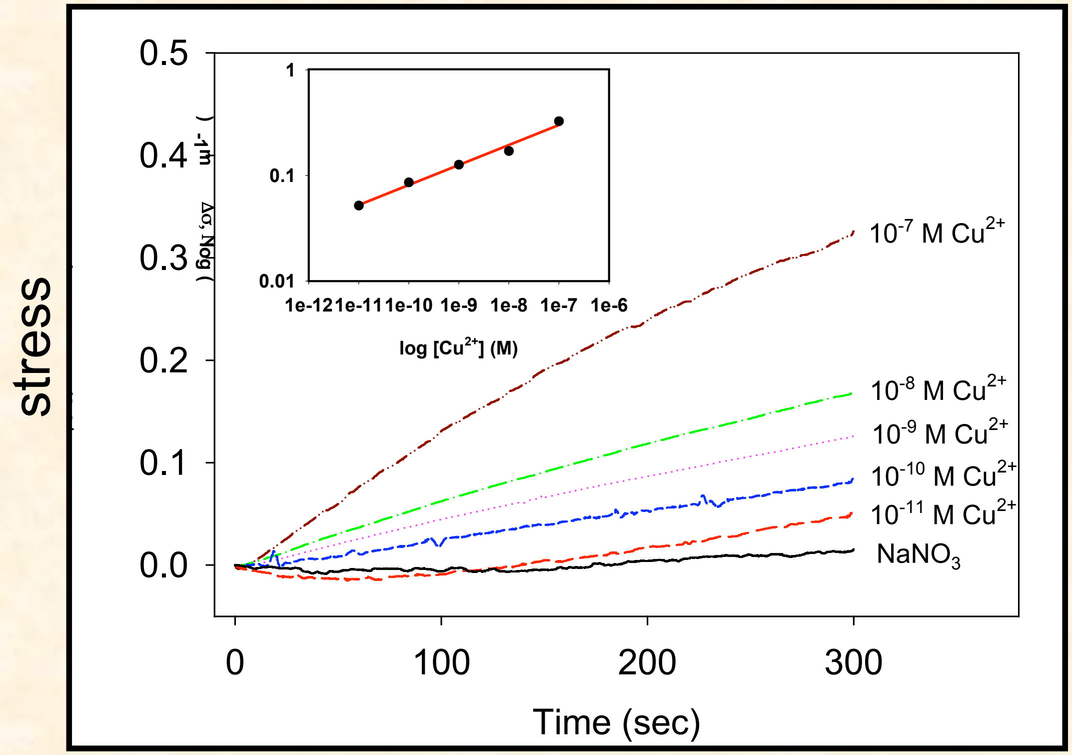
A. Voltammogram: concentration dependent

B: Stress: concentration independent

Tian et al., Ultramicroscopy (2005)

Electrochemical Deposition of Cu(II)

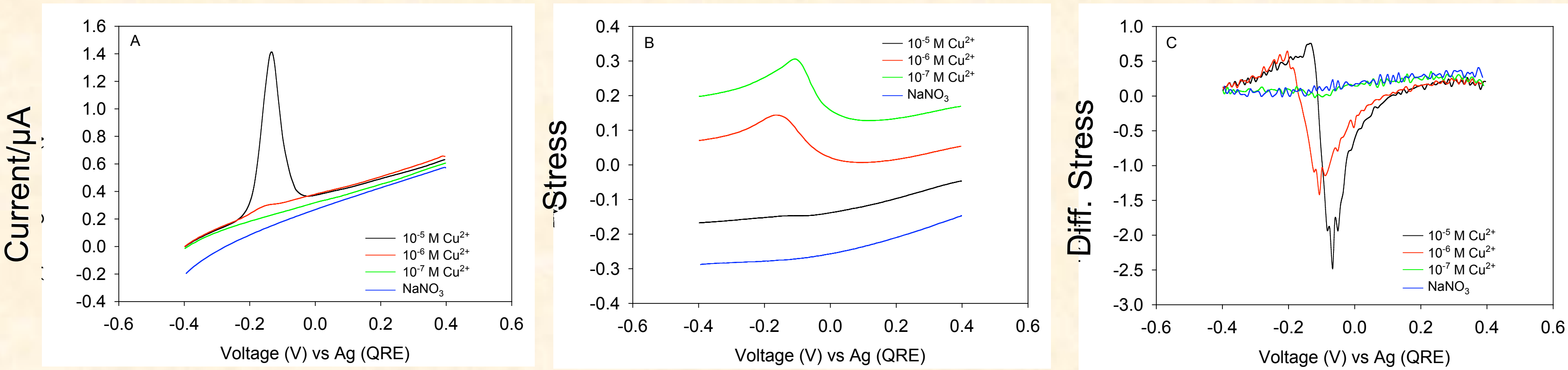
300 sec deposition at -0.4 V



0.1M $NaNO_3$

Potential-controlled microcantilever can be used to detect Cu(II) at a threshold concentration of 10^{-11} M

Stripping Analysis: Voltammogram and Differential Stress in $NaNO_3$ during first anodic sweep at 40 mV/sec after 30 min deposition in $NaNO_3$ solution with and without Cu(II) at –0.4 V

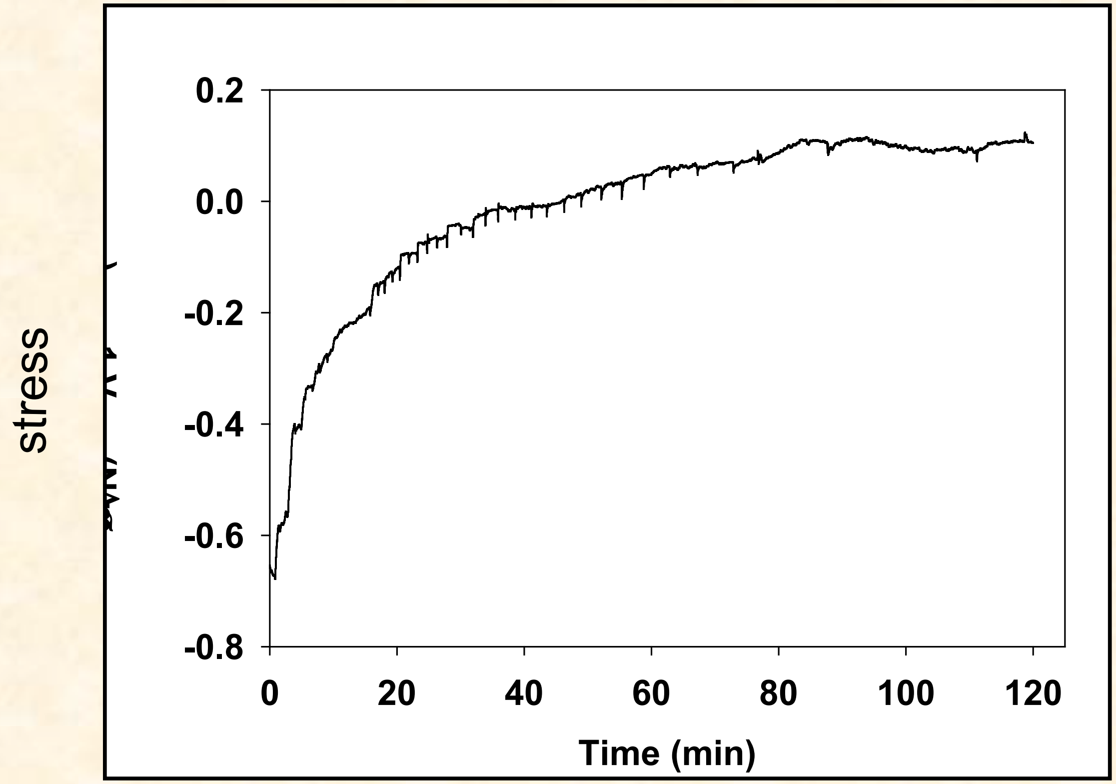


voltammogram

10^{-5} M Cu^{2+}: Γ_o*=1×10^{-9} mol/cm^2
10^{-6} M Cu^{2+}: Γ_o*=6×10^{-10} mol/cm^2
10^{-7} M Cu^{2+}: Γ_o*=0.6×10^{-10} mol/cm^2

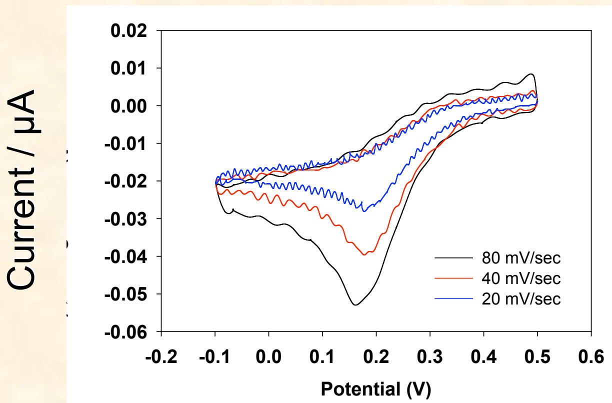
The redox active species on microcantilever electrode during the stripping is approximately the concentration of a MONOLAYER

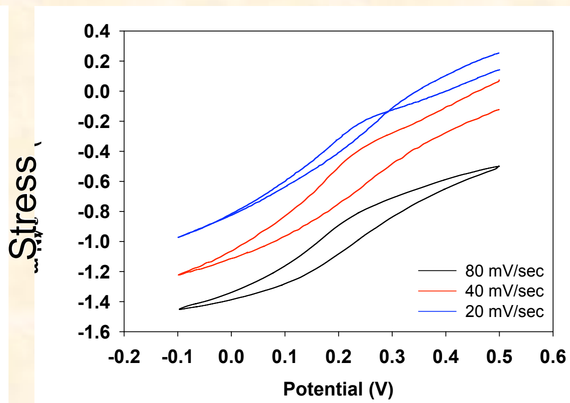
Surface stress of 4-mPy coated microcantilever as function of time in 10^{-4} M $Cr(VI)/H_2SO_4$ solution

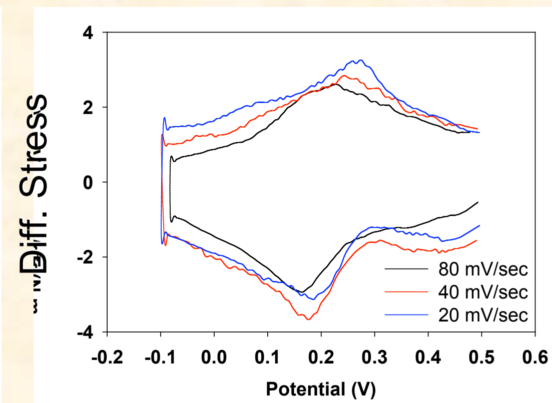


The time dependence of the change in surface stress shows that the adsorption of Cr(VI) on a 4-mPy monolayer approaches equilibrium during 30 min.

Voltammogram and Differential Stress in 10^{-4} M $Cr(VI)/H_2SO_4$ solution as function of sweep rate







Voltammogram: dependent on the potential sweep rate

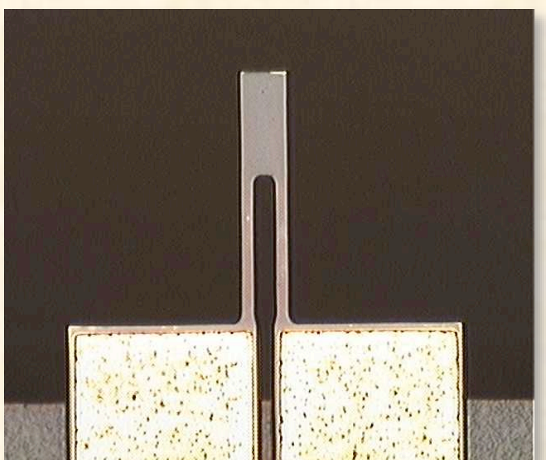
Diffusion-controlled electro-reaction: dissolved Cr(VI) and Cr(III)

Stress: independent of the potential sweep rate

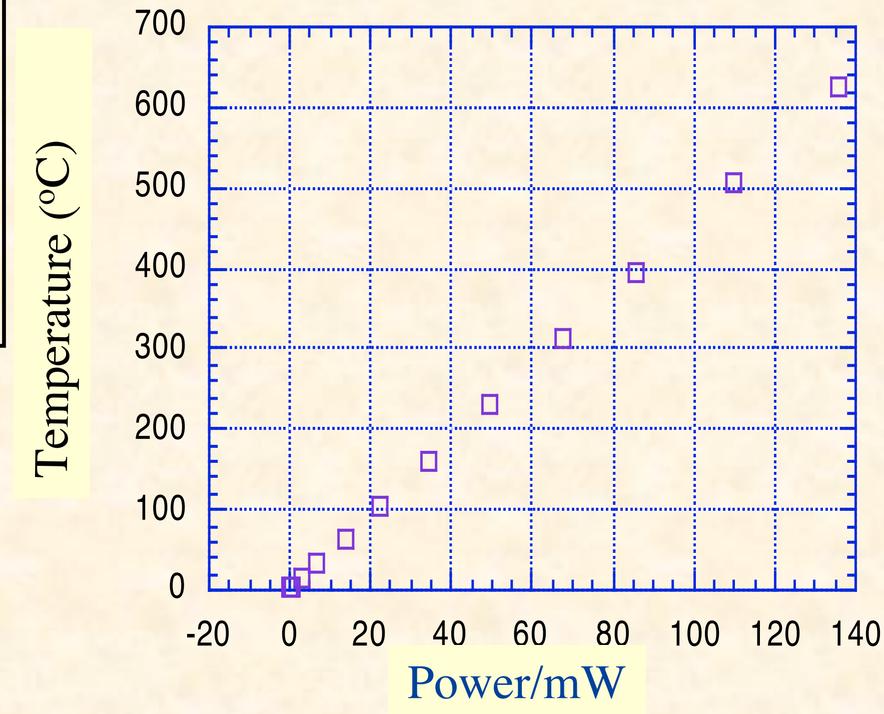
Adsorption-controlled electro-reaction: adsorbed Cr(VI) and Cr(III)

Thermal Characteristics of Cantilevers

- Cantilevers can Be Heated To 600°C in ms
- Temp.-Time Gradient (10^6 - 10^8 °C/s)
- Bending Due To Bimaterial Effect
- Low Thermal Mass
- Low Power Consumption
- Rapid Heating Causes Deflagration



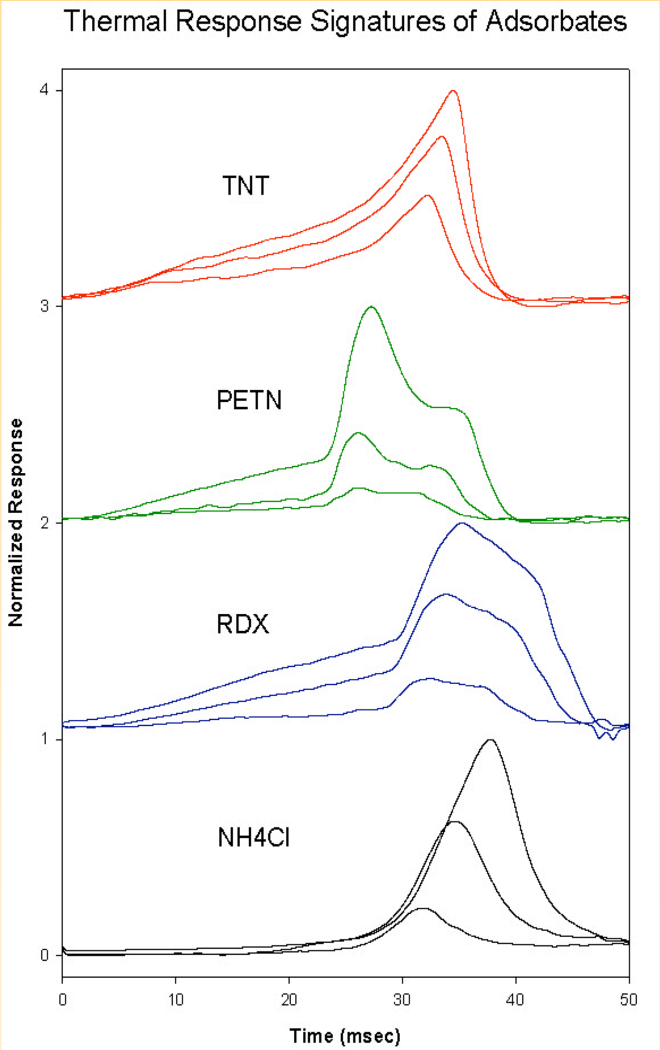
Heating Characteristics of a Cantilevers



4μm Thick Cantilever
Present design thickness less than 1 μm

Thermal Speciation of Adsorbed Molecules

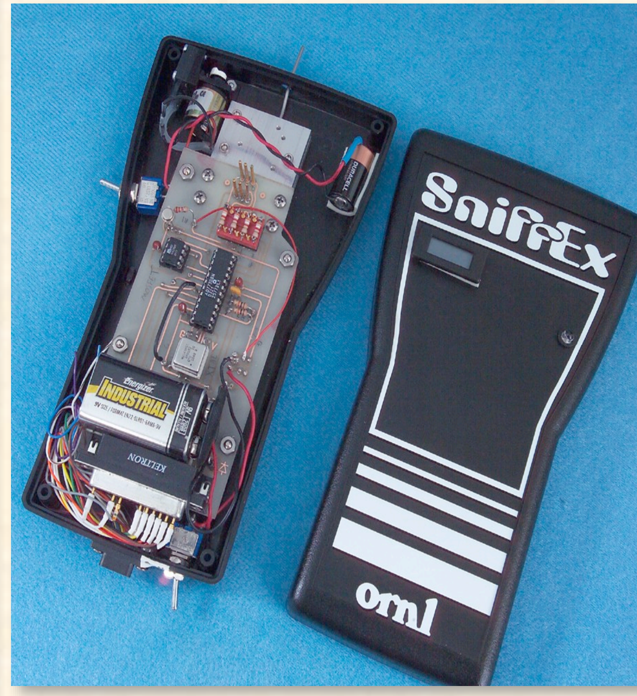
Differential Cantilever Response

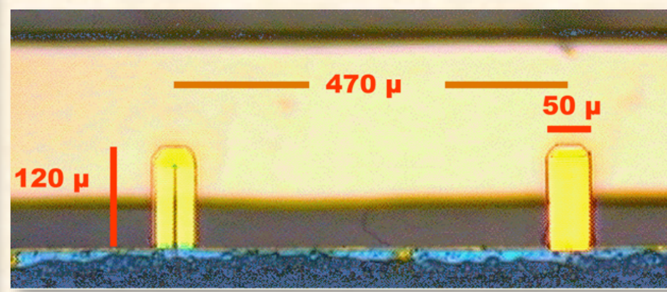


Time milliseconds

- Unique thermal signatures
- Very reproducible
- Detection is done in less than 0.05s
- Pre-concentrator is necessary

Handheld Device

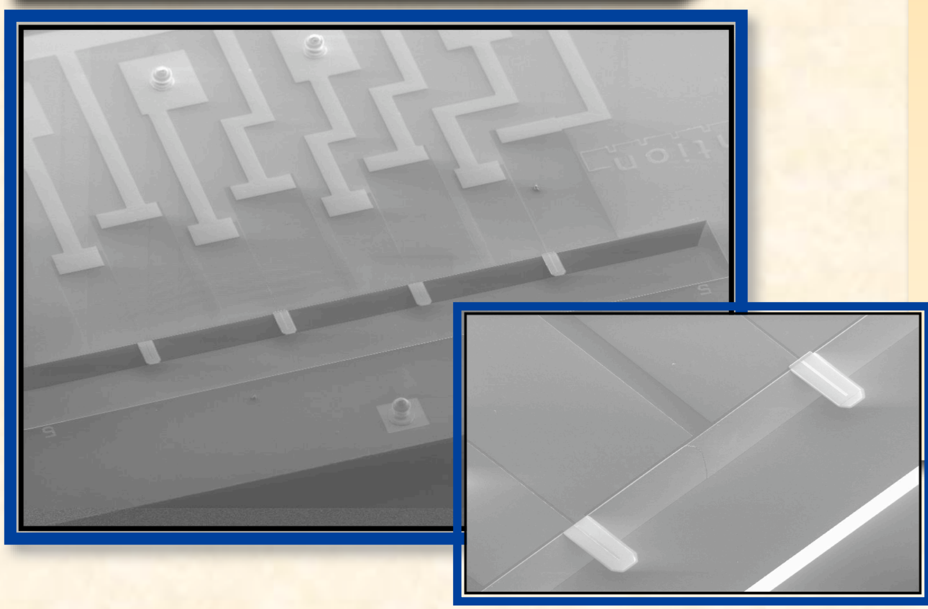


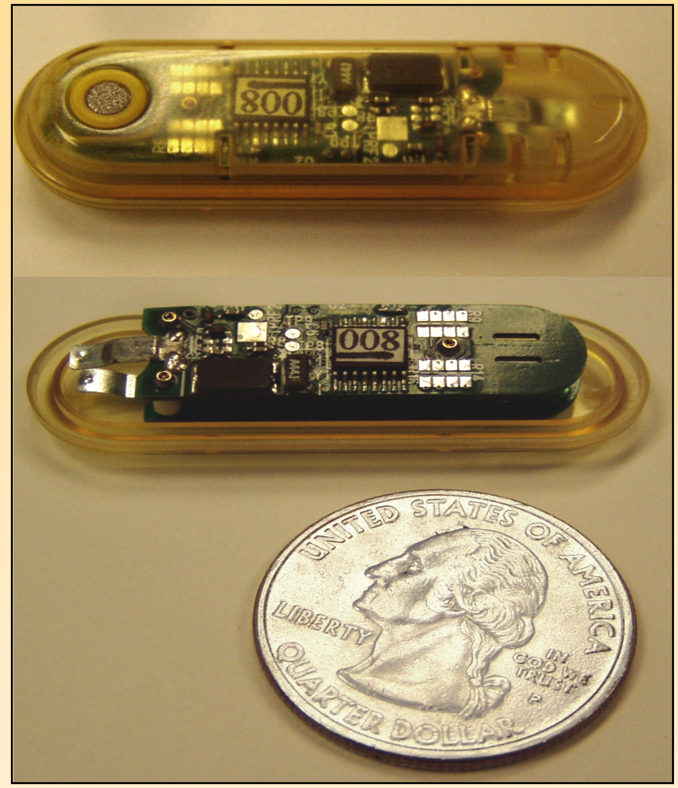


SniffEx Name is no more used

Miniature Sensors With Telemetry: *Batteries Included*

- 8 Piezoresistive cantilevers
- Integrated electronic readout
- Telemetry
- Low power consumption
- 3 cm X 1 cm (diameter)
- No pump

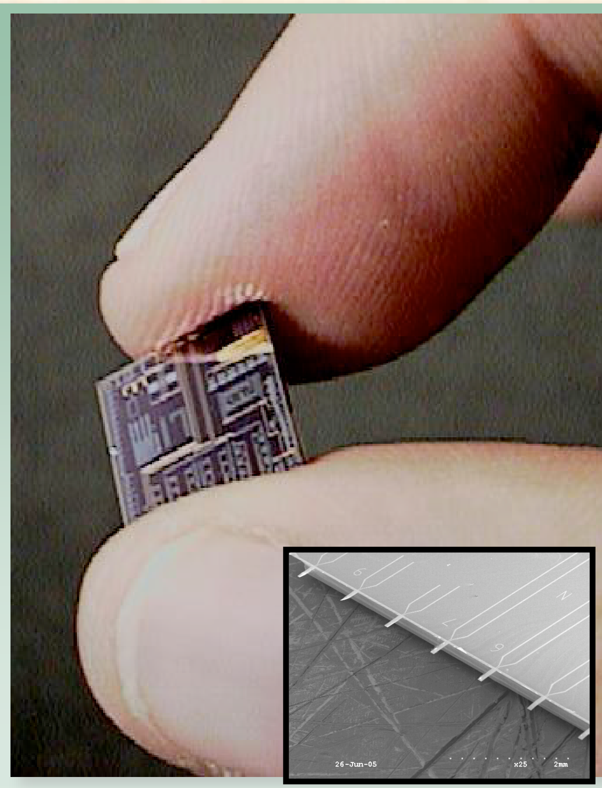




In Collaboration with T. Ferrell (UT)

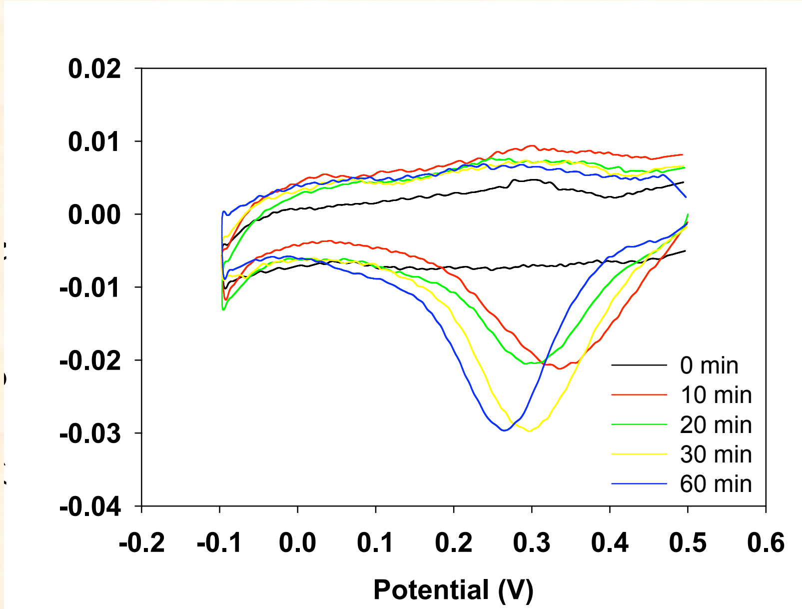
Advantages

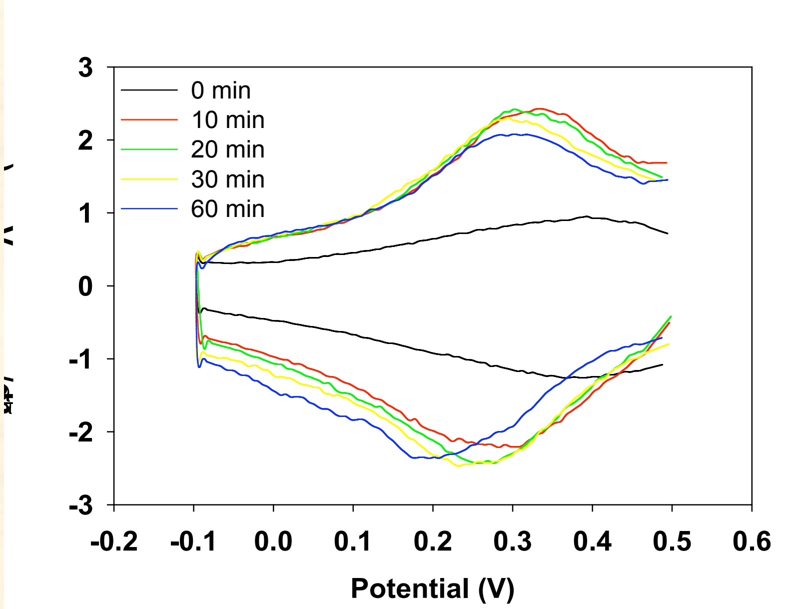
- Arraying
- Size, power
- Sensitivity
- Low cost
  - Integrated processing, intelligence,
  - Wireless
  - Silicon mass-manufacture



- Nanomechanical platform is ideal for sensors
- Chemical, physical, and bio sensing
- Multiple analyte detection
- Many modes of operation
- Two independent signals-Bending&Frequency

Voltammogram and Differential Stress in 0.1 N H_2SO_4 solution during 1st first cyclic voltammetry as function of immersing time in 10^{-4} M Cr(VI)/H_2SO_4

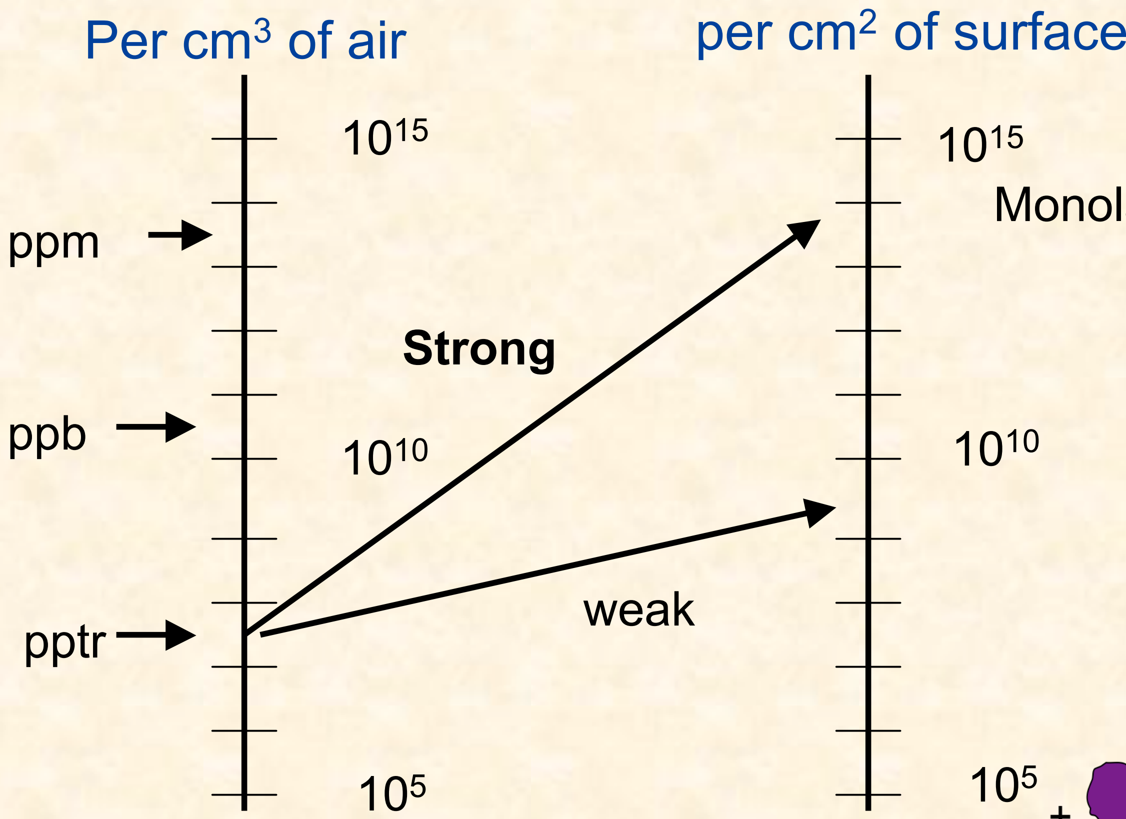




$\Gamma^*=7.40\times10^{-10}$ mol/cm^2

- The adsorption of Cr(VI) on a 4-mPy monolayer approaches the formation of approximately one monolayer after 30 min.
- The contribution of the charge transfer process at the microcantilever-electrolyte interface to the surface stress is limited to that of about one monolayer.

Partition Coefficients:
Surface Concentrations of Analytes

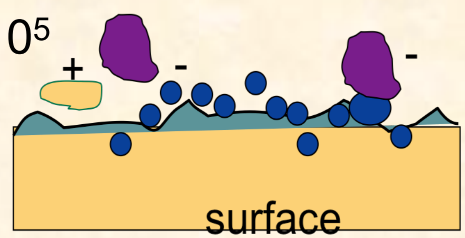


Residence time

$$\tau = \frac{s}{\nu} = \frac{s}{k_o} e^{\Delta H / kT}$$

NANOMECHANICS

Air + contaminant



Oxide + water

Surface charge

Strong interactions lead to high partition coefficients