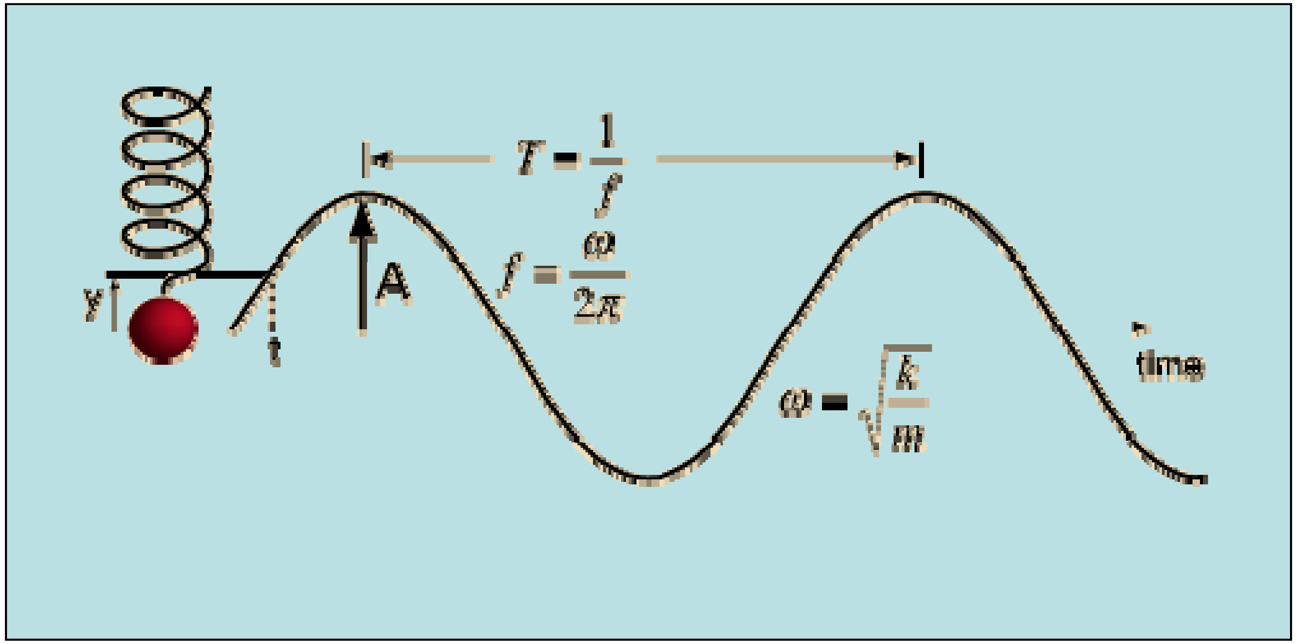
Lecture 5

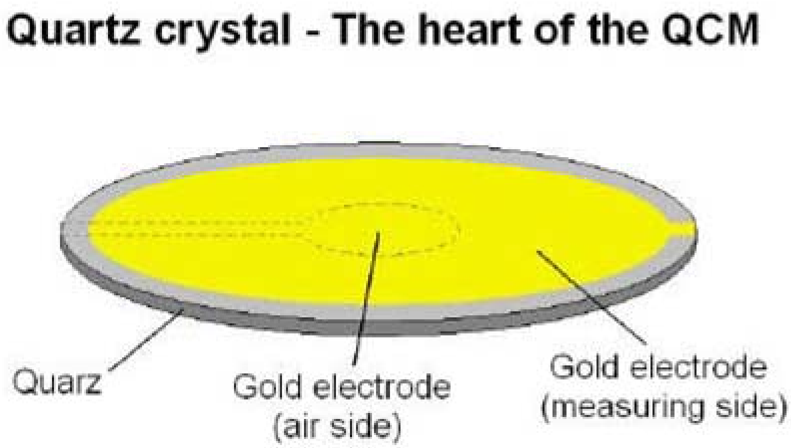
Mechanical biosensors.
Microcantilevers.Thermal sensors.

Mechanical Mass Sensitive Sensors



- Mechanical shift of a resonance can be used for detection of mass change (due to adsorption or chemical reaction)

Mechanical Mass Sensitive Sensors



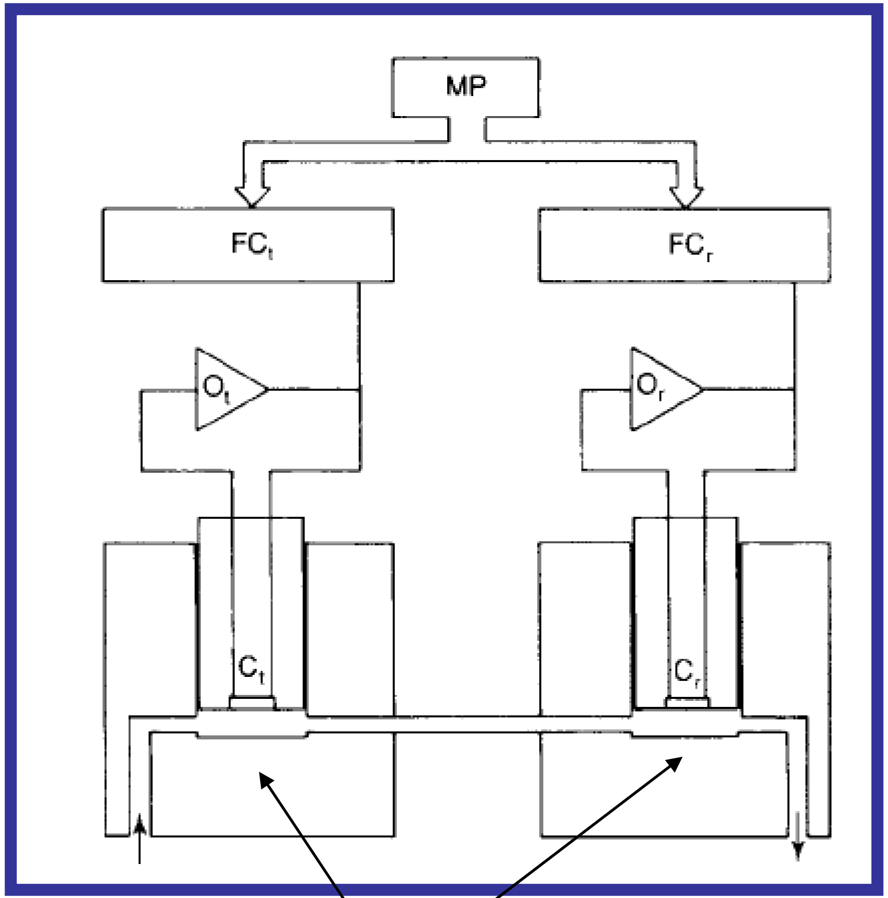
- Sauerbrey equation:

$\Delta f = -[2 \times f_0^2 \times \Delta m] / [A \times (\rho_q \mu_q)^{1/2}]$, where

Δf = measured frequency shift,
f_0 = resonant frequency of the fundamental mode of the crystal,
Δm = mass change per unit area (g/cm^2),
A = piezo-electrically active area,
ρ_q = density of quartz, 2.648 g/cm^3,
μ_q = shear modulus of quartz, 2.947×10^{11} $g/cm \times s^2$.

$$\Delta f = -2.3 \times 10^6 f^2 \Delta m / A$$

Quartz Crystal Microbalance



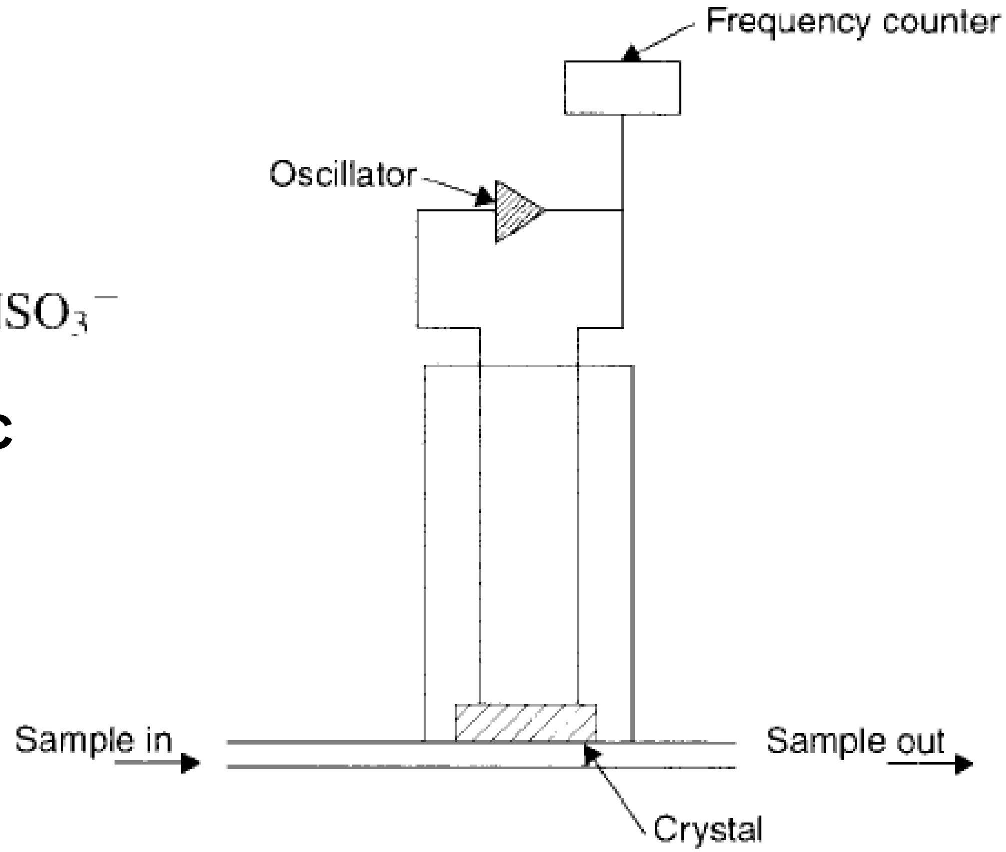
differential signal between two cells is measured

Mechanical Mass Sensitive Sensors

- Gas-Sensor Applications

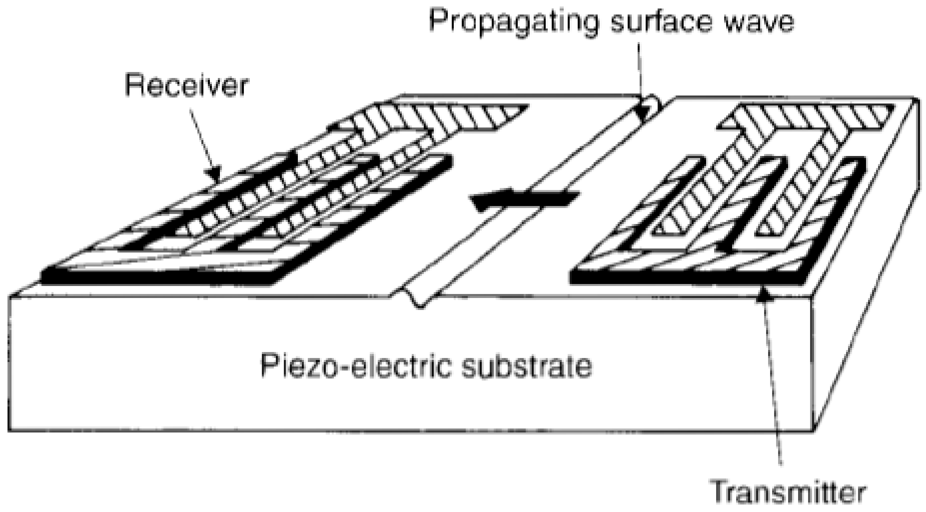
$$R_3N + SO_2 + H_2O \rightleftharpoons R_3NH^+HSO_3^-$$

$$HgO + CO = Hg + CO_2$$ **@210C**



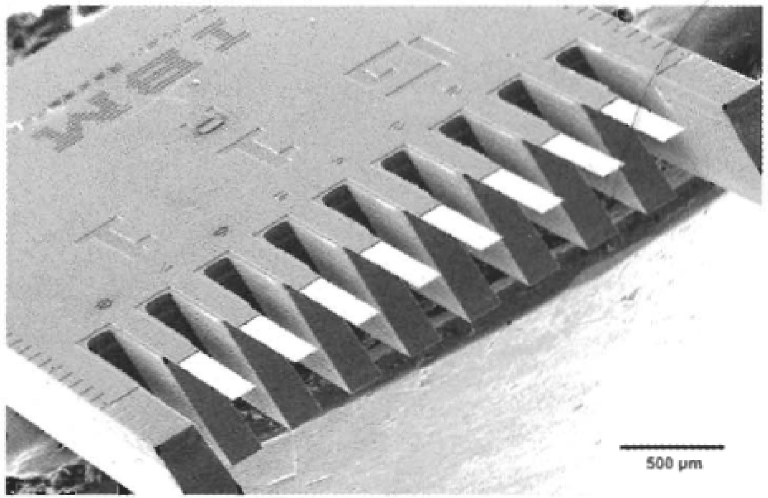
Mechanical Mass Sensitive Sensors

- Surface Acoustic Waves

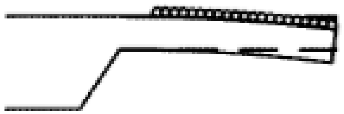


Cantilever-based sensing

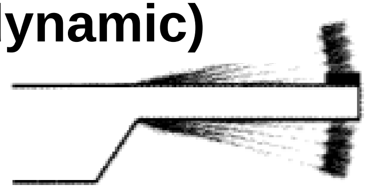
- label-free measurements
- low fabrication costs, mass production possible
- high sensitivity



surface stress sensor

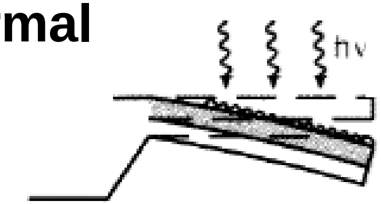


mass sensor (dynamic)



Heat sensor

Photothermal sensor

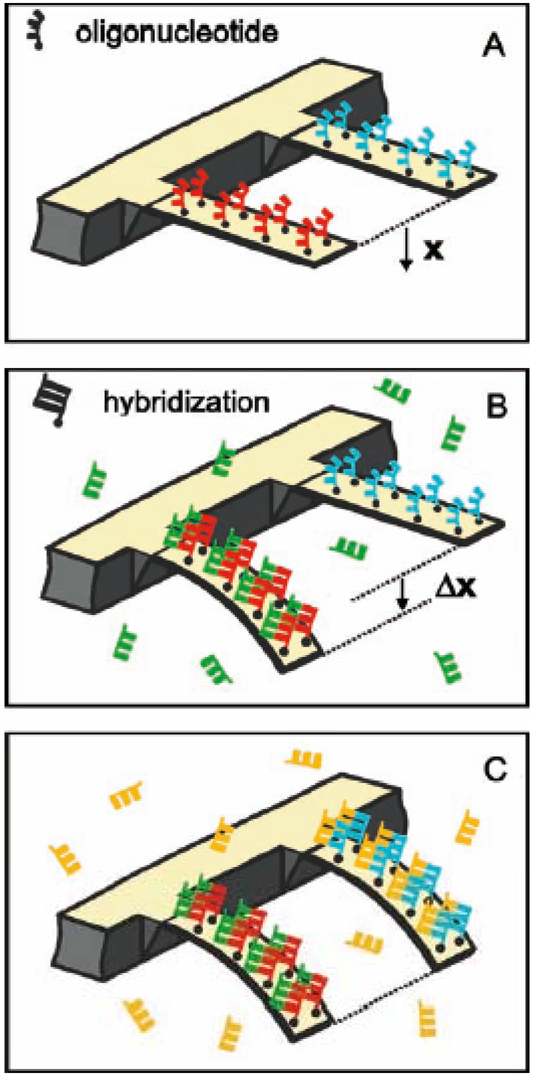


Electrostatic sensor

Magnetic sensor

Cantilever-based biosensing

- static bending
- frequency change
- reference is required



Static mode sensing

- Static mode:
  - essential to functionalize one side of the cantilever **only**.
  - cantilever deformation is related to the interaction forces (binding to the receptor and the surface as well as intermolecular interaction incl.
    - electrostatic,
    - van der Waals,
    - changes in surface hydrophobicity
    - conformational changes of the adsorbed molecules

Stoney formula (1909):

$$\Delta\sigma_1 - \Delta\sigma_2 = \frac{Eh^2}{3L^2(1-\nu)}\Delta z$$

$(\Delta\sigma_1 - \Delta\sigma_2)$ – surface stress change between top and bottom,

E – Young's modulus

L and h - length and thickness of the cantilever

ν – Poissonmodule

Δz – cantilever free end displacement

Dynamic mode sensing

- Measures the total mass adsorbed
- Can be used with both sides functionalization
- Attogram sensitivities can be achieved
- Main difficulties related to the energy dissipation and low Q-factor in fluids

$$\Delta f = \sqrt{3}\,\frac{f_0}{Q}$$

operating frequency (f_0)

quality factor (Q)

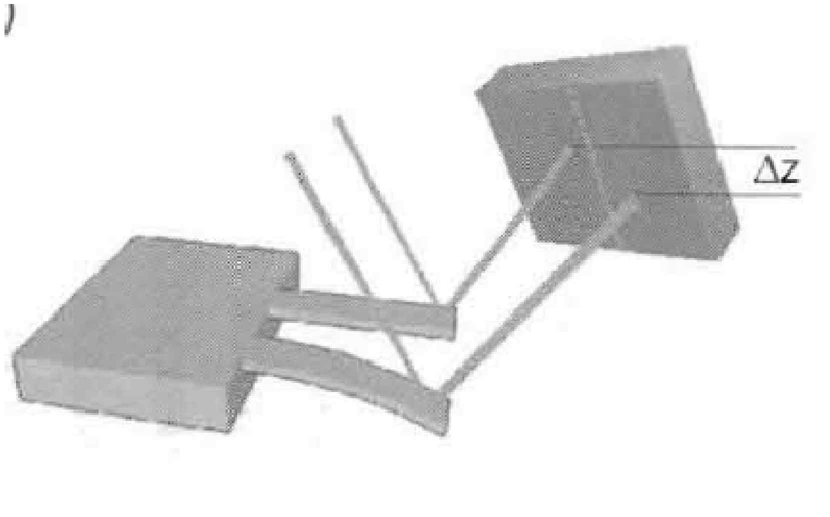
  - using high eigen frequency cantilevers
  - performing measurements in air after functionalization
  - using higher harmonics
  - using external feedback (Q-control)

Detection Techniques

Most used technique!

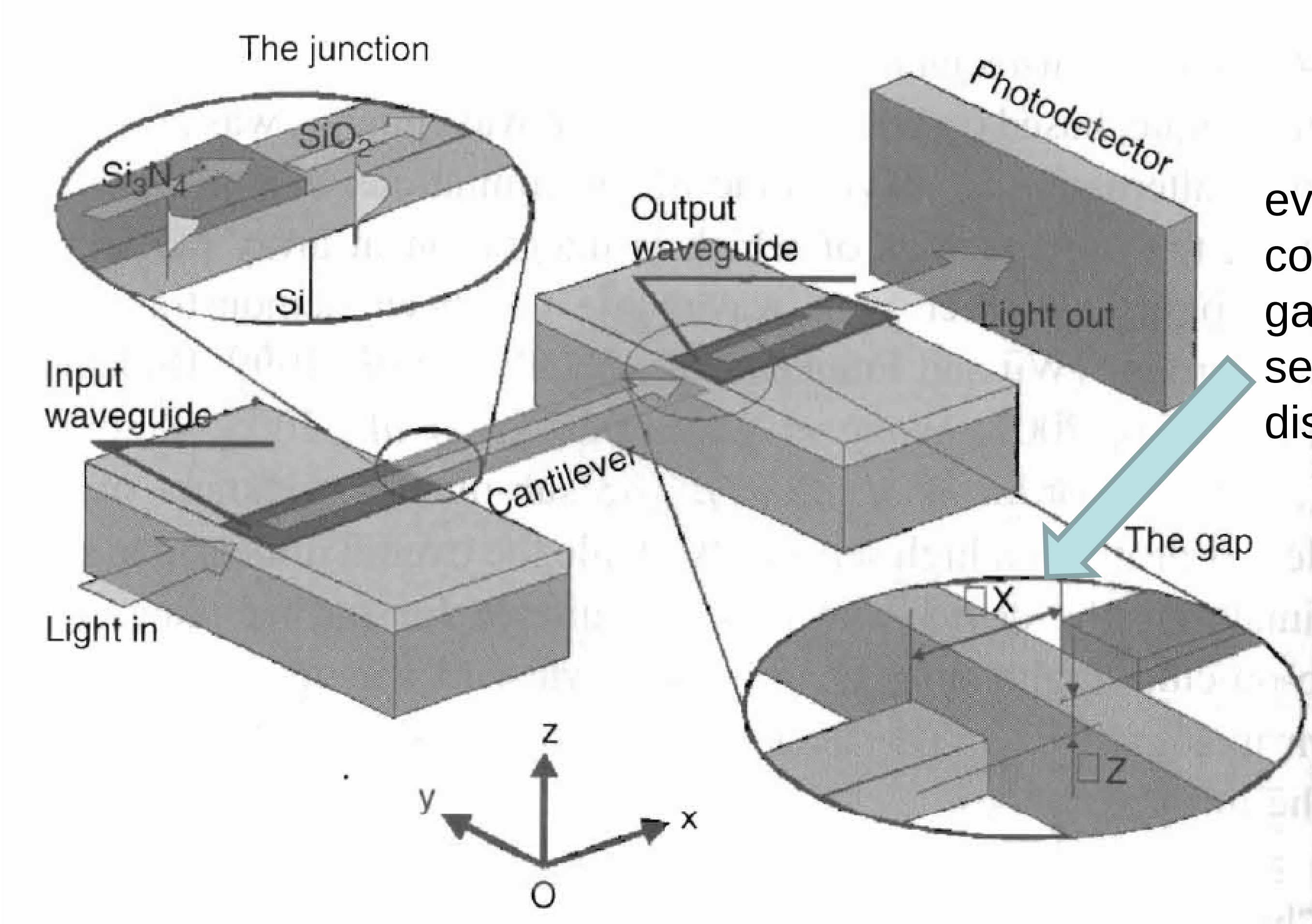
- Optical beam deflection
  - sub-angstrom resolution achievable
  - array measurement (difficult!) achievable using photodetector arrays or scanning laser sources
- Piezoresistivity
- Piezoelectricity
- Interferometry,
- Capacitance

$$\Delta z = \frac{XL}{2D}$$



Detection techniques

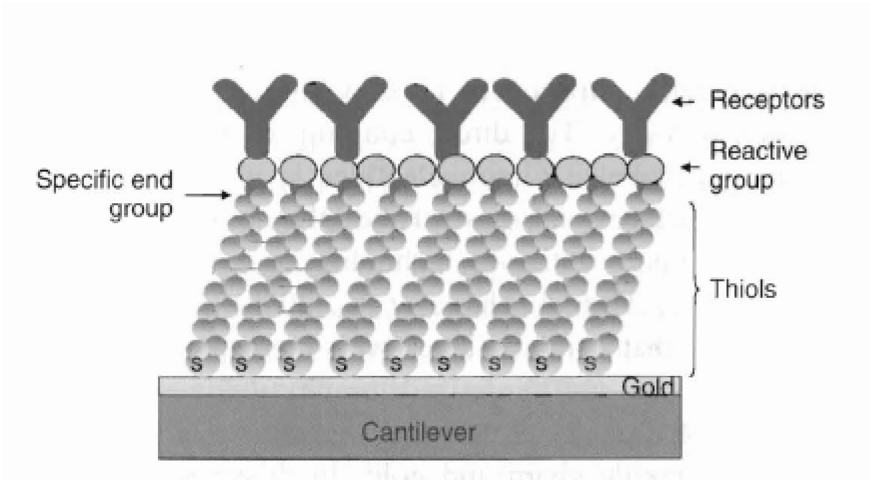
- Detection via waveguide coupling



evanescent field coupling through the gap: exponentially sensitive to the distance!

Functionalization of Microcantilevers

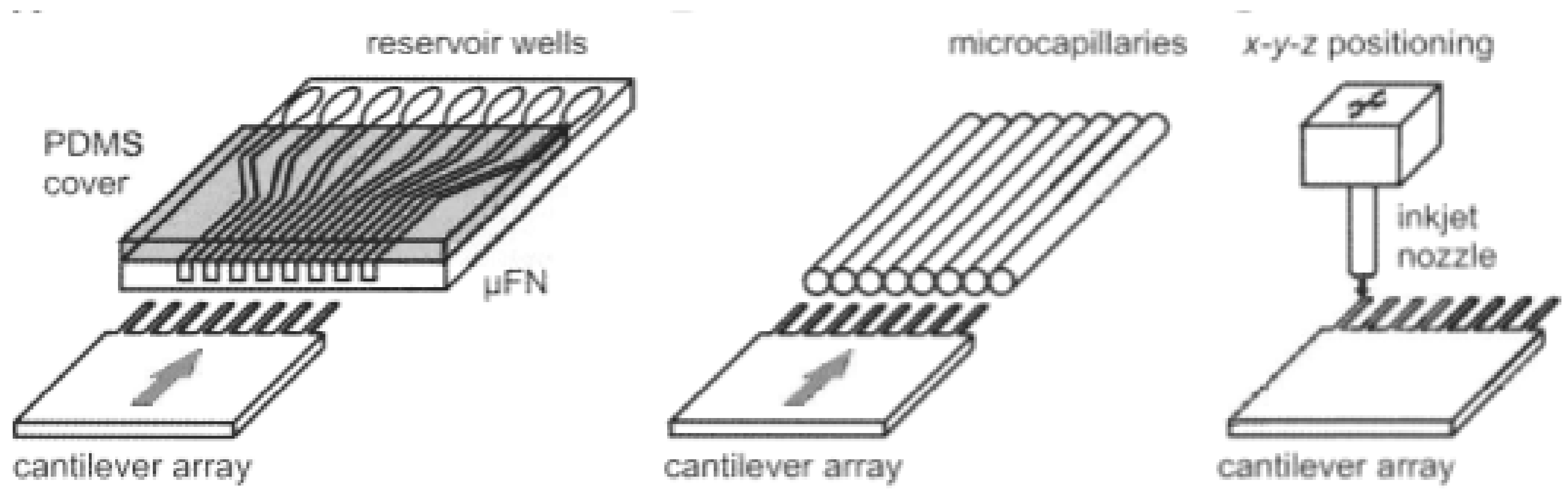
- Mainly based on Au-thiols binding
  - binding of mercapto-acids with subsequent EDC-NHS esterification and binding of a protein via an amino group



  - Direct binding of S-terminated DNA molecules
- Binding to silicon via silane chemistry
- Coating with poly-L-lysine, nitrocellulose etc.

Functionalization of Microcantilevers

- Challenging!



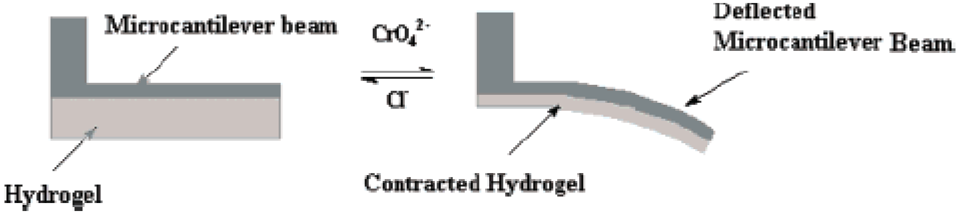
insertion into microfluidic channels

insertion into microcapillaries

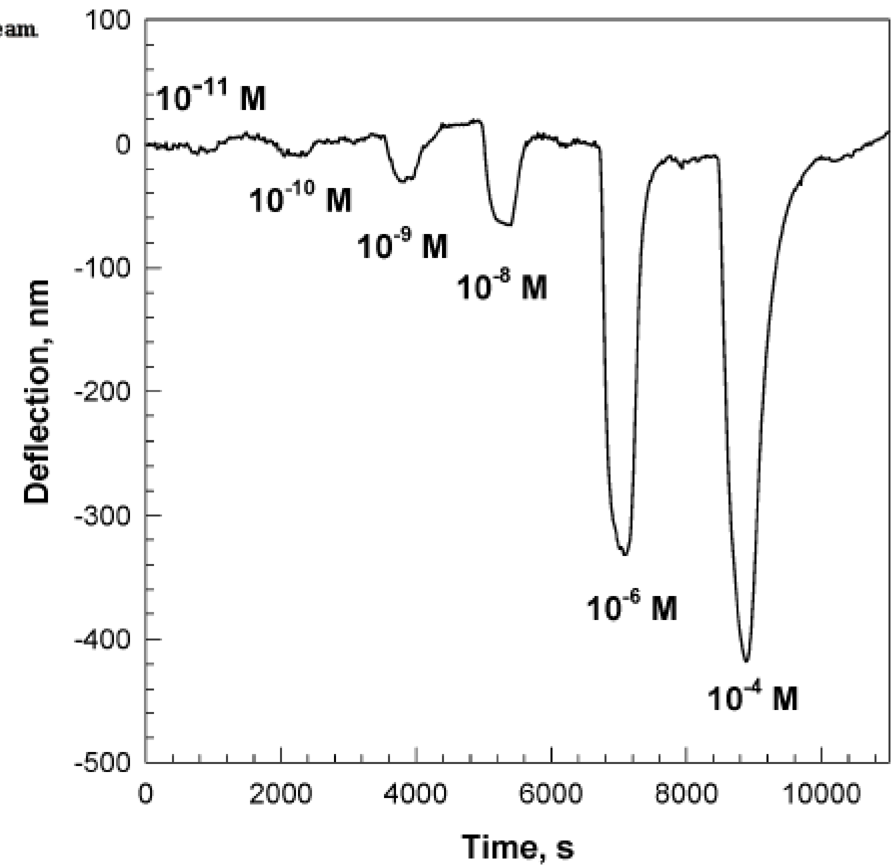
individual coating with inkjet dispenser

Sensing with cantilevers

- static bending detection is very sensitive to the environment (pH, ionic strength). Functionalization allows to detect specific ions

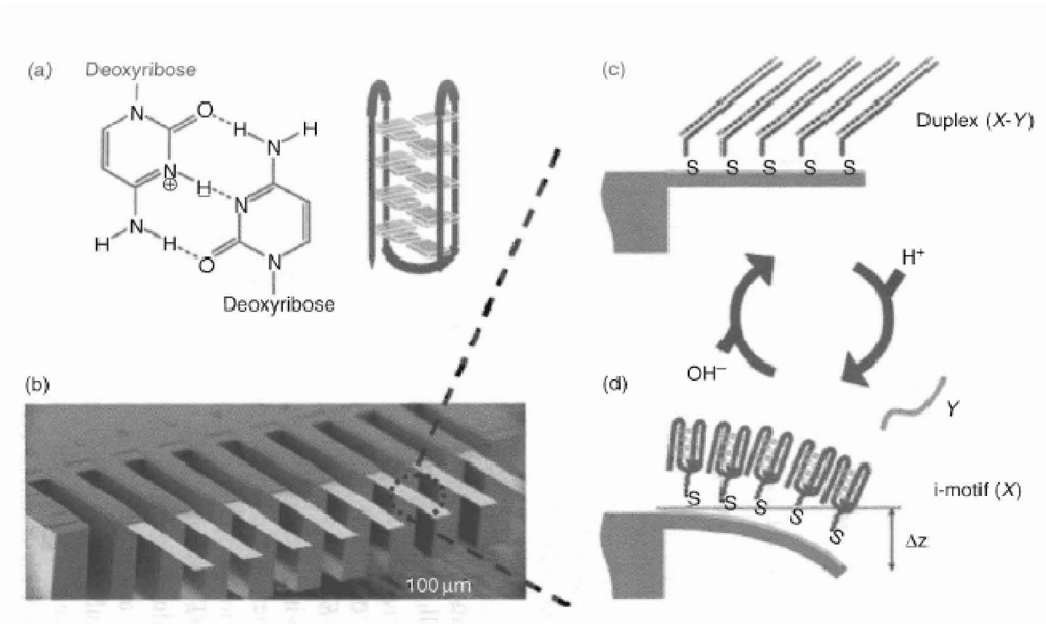


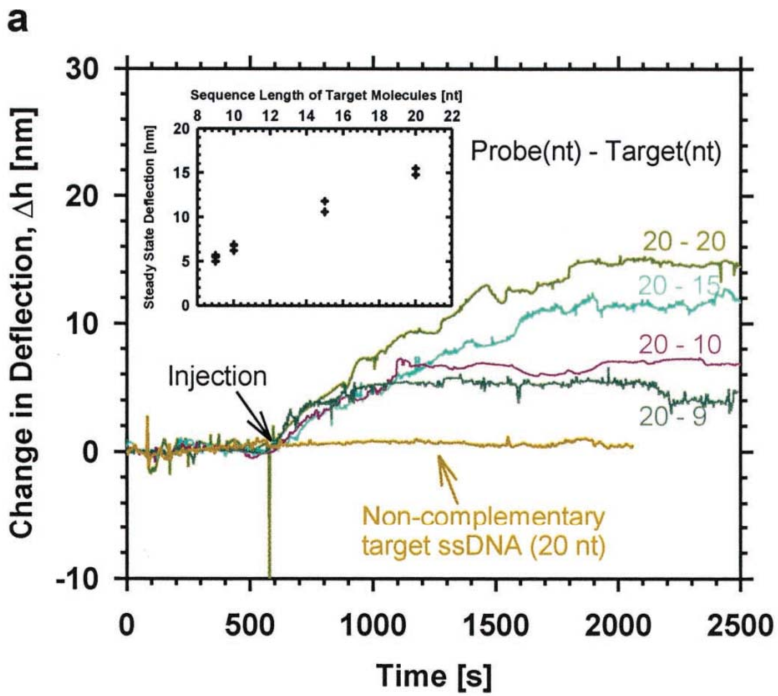
Detection of CrO4 ions using ATAC ((3-Acrylamidopropyl)-trimethylammonium chloride) hydrogel coated cantilevers



Sensing with cantilevers

- Genomics:
  - hybridization of DNA (1bp mismatch can be detected)
  - melting temperature
  - conformational changes in DNA

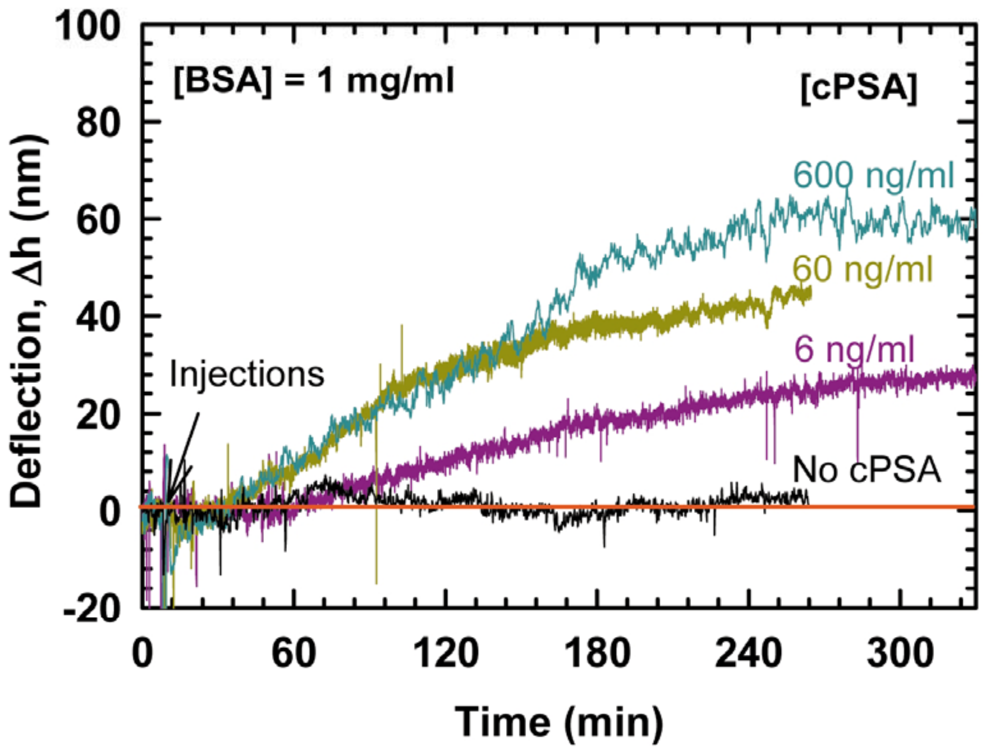


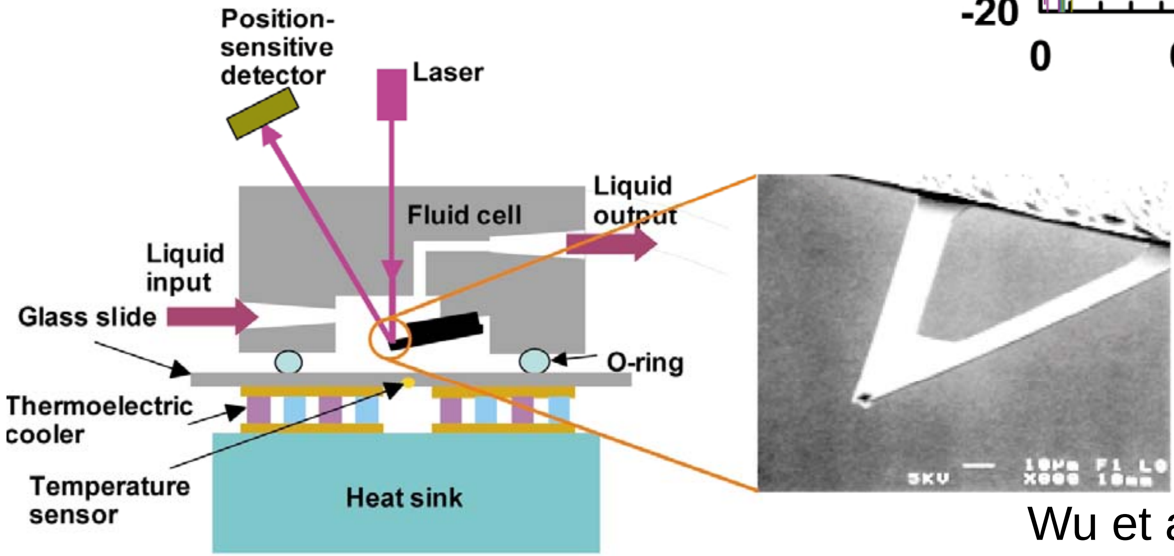


Sensing with cantilevers

- Immunosensing (incl. detecting bacteria and spores)

Detection of PSA

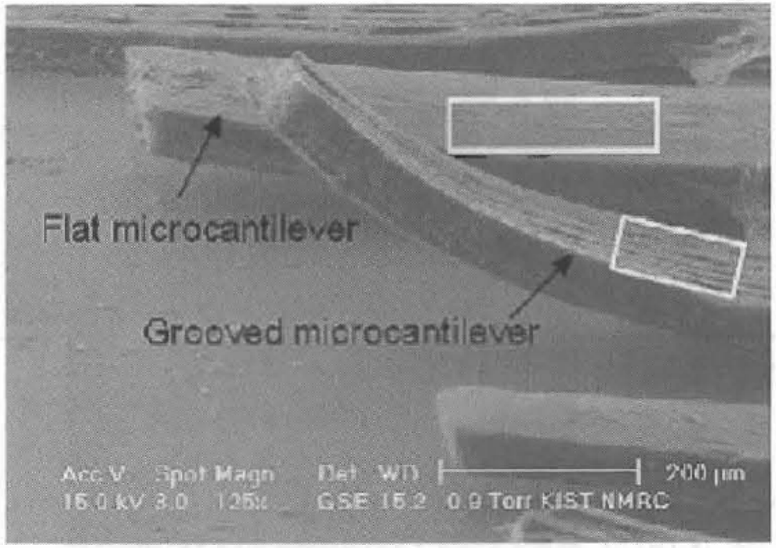


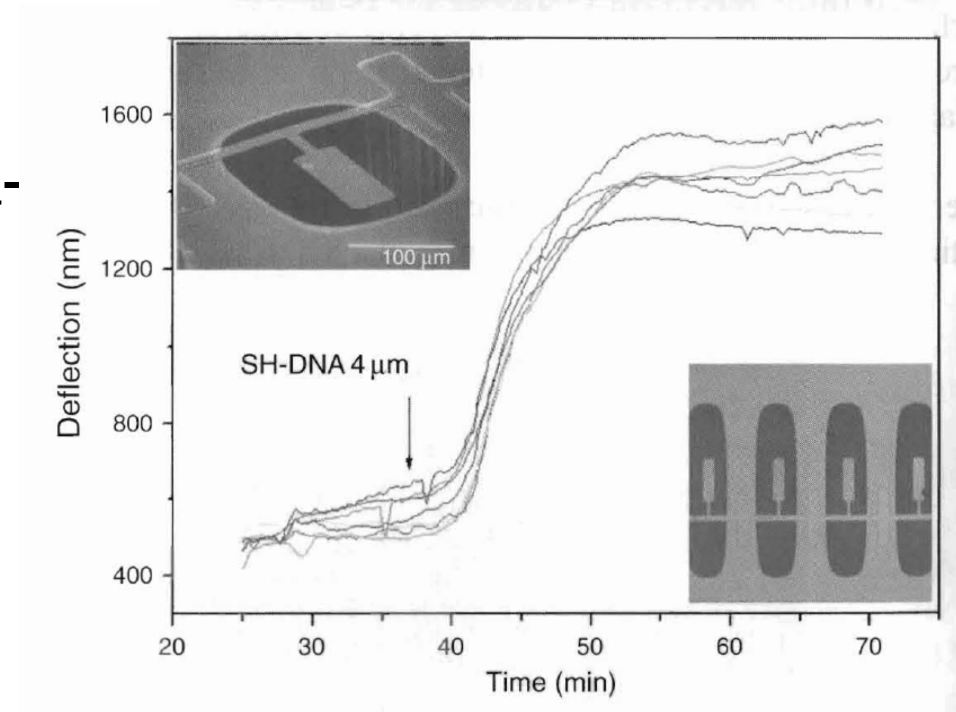


Wu et al, Nature Biotech. 19, 856 (2001)

Further development

- Cantilevers with surface nanostructures show better sensitivity
- cantilevers of different geometry
- polymer cantilevers (SU8, PDMS)
- cantilever arrays (lab-on-a-chip)
- cantilever integrated in microfluidic sysems

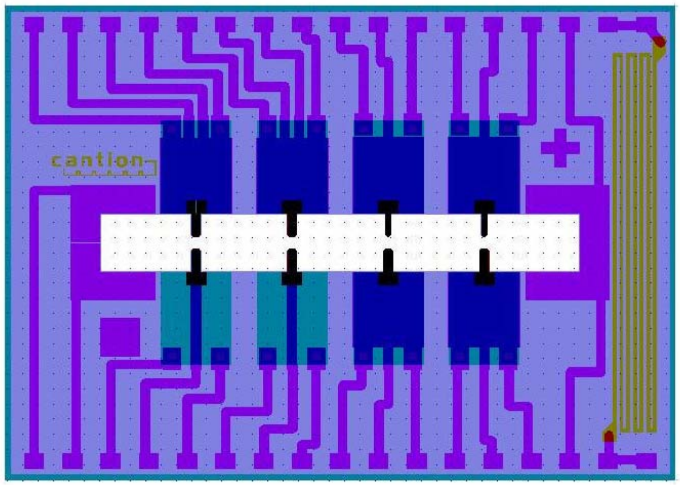


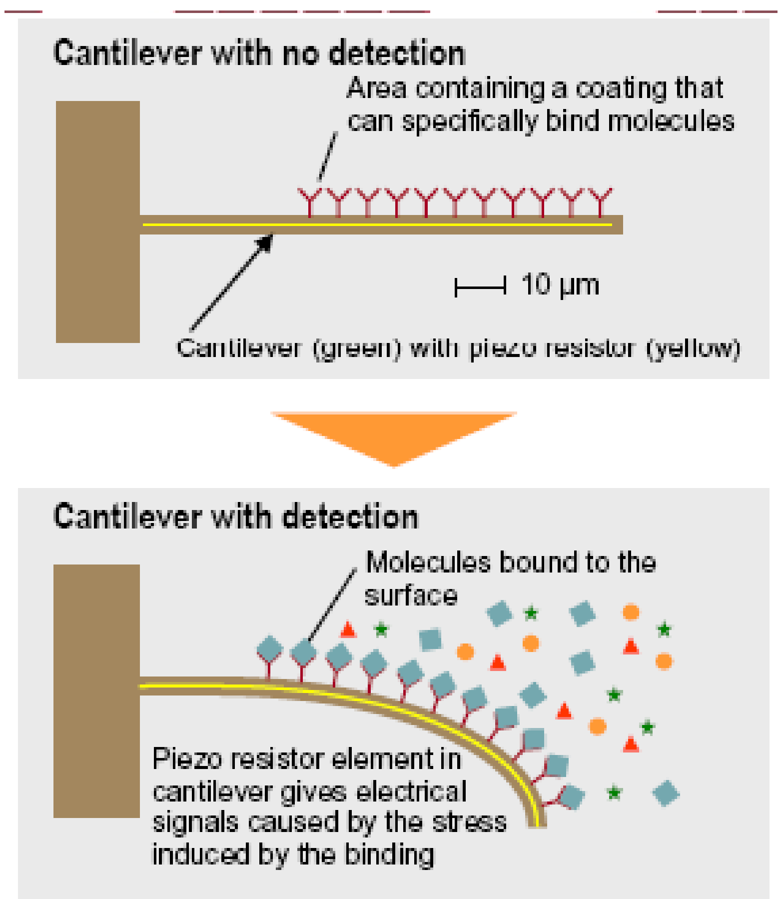


Cantilever-based biosensing

- Canteon technology (NanoNord)

  - Static bending is detected
  - Piezoresistive cantilvers
  - Can be used in referenced mode
  - Placed in a fluidic catridge





Thermal sensors

- Thermistors – based on strong change of resistance with temperature – can be used to measure heat production in chemical reactions

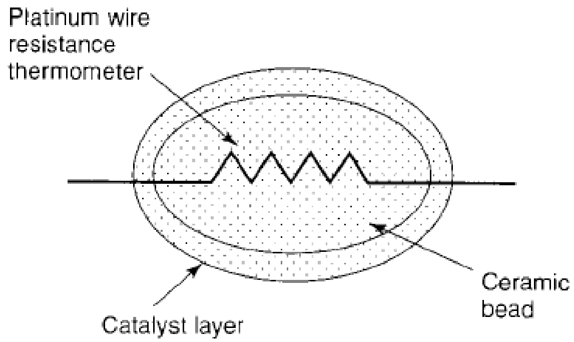
$$\text{glucose} + O_2 + H_2O \xrightarrow[\Delta H = -80\ \text{kJ mol}^{-1}]{\text{GOD}} \text{gluconic acid} + H_2O_2$$

$$CO(NH_2)_2 + H_2O \xrightarrow[\Delta H = -6.6\ \text{kJ mol}^{-1}]{\text{urease}} CO_2 + 2NH_3$$

Enzyme reaction

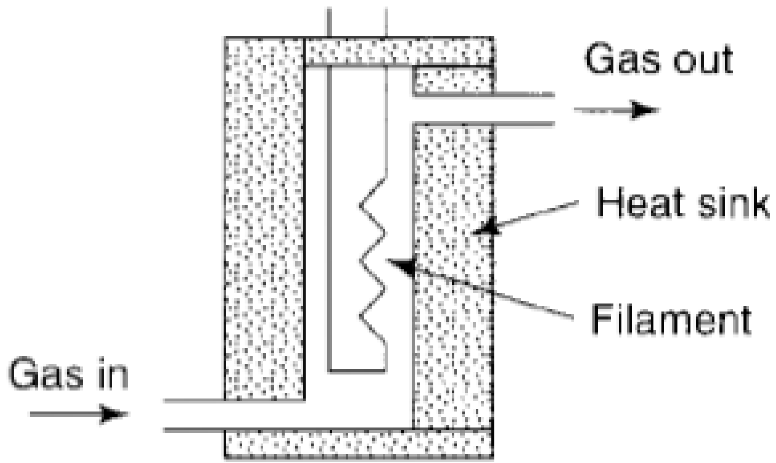
$$CH_4 + 2O_2 \xrightarrow[\Delta H = -800\ \text{kJ mol}^{-1}]{} CO_2 + 2H_2O$$

Catalytic gas sensor



Thermal sensors

- Thermal conductivity devices (typically gas chromatography)



Laboratory exercise

Cyclic voltammetry study of ferrocyanide redox reaction.

- Aims:
  - experimentally find electrochemical potential for ferrcyanide redox reaction
  - check peak current dependence on concentration and voltage scan rate
  - observe transition from reversible to irreversible behaviour, find α for the reaction (if possible ☺)

Laboratory exercise

- Theory

reversible limit

$$\Delta E_{pp} = 2.218\frac{RT}{F} \approx 57mV(at\,298K)$$

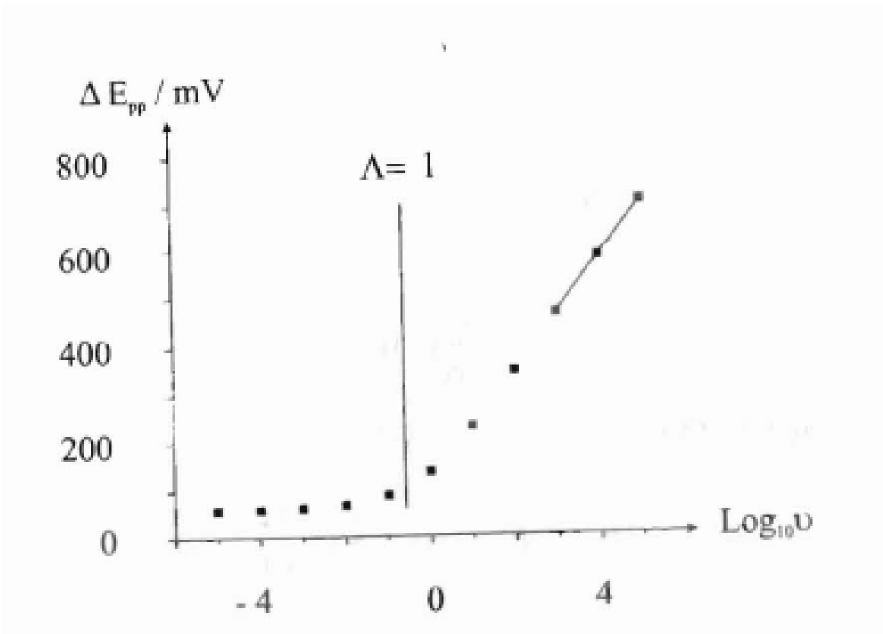
$$I_p = 0.446FA[C_0]\sqrt{\frac{FDv}{RT}}$$

irreversible limit

$$\Delta E_{pp} \propto \frac{RT}{\alpha F}\ln v; \Delta E_{pp} = \frac{59.4mV}{\alpha F}\log_{10} v + const\,(at\,298K)$$

$$I_p = 0.496\sqrt{\alpha}FA[C_0]\sqrt{\frac{FDv}{RT}}$$

peak-peak distance



reversible limit irreversible limit

Laboratory exercise

Experiment

- prepare solutions
  - 100mM KCl
  - 100mM $K_3Fe(CN)_6$ (stock) and 100mM $K_4Fe(CN)_6$ (stock)
- Measurements:
  - Pt film working and counter electrodes, Ag/AgCl reference
  - working concentrations 2mM, 5mM, 10mM, 20mM (at 100 mV/s)
  - scan rates 50mV/s, 100mV/s, 200mV/s, 500mV/s, 1V/s, 2V/s, 5V/s, 10V/s (at 5mM)
- Processing:
  - use diffusion coefficient from Roffel and Graaf article.