Lecture 3

Mass sensors
Optical sensors.
SPR Sensors.
– mass sensors (QCM, SAW, u-cantilevers)
– thermal sensors
– optical sensors:
  • adsorption
  • diffractive index change
– SPR
  • history
  • concept
  • performance characteristics
  • SPR instrumentation: examples
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:

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

\( \Delta f \) = measured frequency shift,
\( f_0 \) = resonant frequency of the fundamental mode of the crystal,
\( \Delta m \) = mass change per unit area (g/cm²),
\( A \) = piezo-electrically active area,
\( \rho_q \) = density of quartz, 2.648 g/cm³,
\( \mu_q \) = shear modulus of quartz, 2.947×10¹¹ g/cm×s².

\[ \Delta f = -2.3 \times 10^6 f^2 \Delta m/A \]
Quartz Crystal Microbalance

differential signal between two cells is measured
Mechanical Mass Sensitive Sensors

- Gas-Sensor Applications

\[ \begin{align*}
R_3N + SO_2 + H_2O & \rightleftharpoons R_3NH^+HSO_3^- \\
HgO + CO & = Hg + CO_2 \quad @210^\circ C
\end{align*} \]
Mechanical Mass Sensitive Sensors

- Surface Acoustic Waves
Cantilever-based sensing

- Surface stress sensor
- Mass sensor (dynamic)
- Heat sensor
- Photothermal sensor
- Electrostatic sensor
- Magnetic sensor
Cantilever-based biosensing

- static bending
- frequency change
- reference is required
Functionalization of Microcantilevers

- Challenging!

- Insertion into microfluidic channels
- Insertion into microcapillaries
- Individual coating with inkjet dispenser
Cantilever-based biosensing

• Canteon technology (NanoNord)
  • Static bending is detected
  • Piezoresistive cantilevers
  • Can be used in referenced mode
  • Placed in a fluidic cartridge
Thermal sensors

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

- Enzyme reaction

\[
\text{glucose} + \text{O}_2 + \text{H}_2\text{O} \xrightarrow{\text{GOD}} \text{gluconic acid} + \text{H}_2\text{O}_2
\]
\[
\Delta H = -80 \text{ kJ mol}^{-1}
\]

\[
\text{CO(NH}_2\text{)}_2 + \text{H}_2\text{O} \xrightarrow{\text{urease}} \text{CO}_2 + 2\text{NH}_3
\]
\[
\Delta H = -6.6 \text{ kJ mol}^{-1}
\]

- Catalytic gas sensor

\[
\text{CH}_4 + 2\text{O}_2 \rightarrow \text{CO}_2 + 2\text{H}_2\text{O}
\]
\[
\Delta H = -800 \text{ kJ mol}^{-1}
\]
Thermal sensors

- Thermal conductivity devices (typically gas chromatography)
Optical sensors

What they can be based on:

- Absorption spectroscopy (UV-VIS, IR)
- Fluorescence/phosphorescence spectroscopy
- Bio- and chemiluminescence
- Refractive index sensing
- Laser light scattering
Absorption photometry (UV-VIS)

Beer-Lambert law
$\log(I/I_0) = A = \varepsilon C L$

$I$ – intensity of the transmitted light
$I_0$ – intensity of the incident light
$A$ – adsorbance
$\varepsilon$ – extinction coefficient;
$C$ – concentration of analyte;
$L$ – pathlength

Absorption spectrum of NAD in oxidized and reduced form
Optical Transducers

Design examples:
Detecting Refractive Index Changes

- Grating based biosensors

Axela’s Diffractive Optics “Dot”- technology
Detecting Refractive Index Changes

- **SPR**
  - the most sensitive technique $\Delta n < 10^{-7}$.
  - detect changes in a thin layer adjacent to the sensor surface

**Equipment Images:**
- BIAcore 3000
- IBIS-iSPR
- Reichert SR7000
Brief History of Surface Plasmons

• first observed in 1902 by R. Wood as narrow dark bands in the spectrum of metal gratings
• observed in thin metal films as a drop in reflectivity by Thurbadar in 1958 and explained by Otto, Kretchmann and Raether in 1968.
• 1970s plasmons used to characterize metal films and study processes on the metal surfaces.
• 1990 first commercial SPR (Surface Plasmon Resonance sensor is launched by BIAcore AB.
What is surface plasmon?

- collective excitation of the electrons at the interface between metal and dielectric
- transverse magnetic in character, electric field is perpendicular to the interface
- localized at the interface, evanescent in perpendicular direction
- experience higher (and non-linear) refractive index, cannot be directly coupled to free radiation
Excitation of Surface Plasmons

- Kretschmann geometry (ATR)

For the surface plasmon wave:

\[ \beta^{SP} = \frac{\omega}{c} \sqrt{\frac{\varepsilon_d \varepsilon_m}{\varepsilon_d + \varepsilon_m}} + \Delta \beta \]

correction for prism and finite metal thickness

For the evanescent field:

\[ \beta^{EW} = \frac{\omega}{c} n_p \sin \theta \]

Matching the momentum:

\[ n_p \sin \theta = \text{Re} \left\{ \sqrt{\frac{\varepsilon_d \varepsilon_m}{\varepsilon_d + \varepsilon_m}} \right\} + \Delta n^{SP} \]
Excitation of Surface Plasmons

- effective index is a monotonous function of the wavelength, so there is a matching condition for the angle at the fixed wavelength or for the wavelength at fixed angle
Excitation of surface plasmons

- **Example**: gold on BK7 glass

- fixed wavelength (800nm), angle varied
- fixed angle (66 deg), wavelength varied
Excitation of surface plasmons

- grating coupling

\[ \tilde{k}_m = \tilde{k} + m\tilde{G} \quad \tilde{G} = \frac{2\pi}{\Lambda} \frac{\lambda}{z} \]

\[ n_d \sin \theta + m \frac{\lambda}{\Lambda} = \pm \left( \text{Re} \left\{ \sqrt{\frac{\varepsilon_d \varepsilon_m}{\varepsilon_d + \varepsilon_m}} \right\} + \Delta n^{SP} \right) \]

- waveguide coupling

\[ \beta_M = \text{Re} \{ \beta_{SP} \} \]
Surface plasmon sensor

- The concept

![Diagram showing the relationship between refractive index distribution, surface plasmon characteristics, and light wave characteristics.]
Surface plasmon sensor

- Principle of affinity SP biosensor
Performance characteristics of SPR

- **sensitivity** — slope of the calibration curve
- **linearity** — maximum deviation from linear transfer function within the dynamic range
- **resolution** — smallest change in refractive index that produces detectable output change
- **accuracy** — agreement between the measured value and the actual value
- **reproducibility** — ability to produce the same output over a period of time
- **dynamic range** — range of analyte concentrations that can be measured with a given accuracy
- **limit of detection** — concentration at which one can decide if the analyte is present
Sensitivity of SPR biosensor

\[ S = S_{RI} \frac{dn_b(c)}{dc} \]
measured: fibrinogen, g-immunoglobulin, albumin, and lysozyme on hydrophilic and hydrophobic surfaces

Sensitivity of SPR biosensor

\[ S = S_{RI} \frac{dn_b(c)}{dc} = S_{RI} \cdot \gamma \cdot [C] \]

- for given folding state of the protein (fixed density) the refractive index is proportional to the amount of proteins absorbed (g/cm²)
- Rule of thumb: change of 10^{-6} RI = approx. 1 pg/mm² of adsorption.

- \( S_{RI} \) – sensitivity to refractive index change, includes:
  - modulation method (angle scan, wavelength scan, etc.)
  - hardware
  - software (e.g. method of locating the minimum)
• Scheme of an SPR biosensor
SPR Instrumentation

- Optical modulation schemes
1. Signal normalization
   • subtracting dark signal
   • normalizing intensity to TE or air scan

2. Finding minimum position
   • direct measurement
   • polynomial extrapolation
   • centroid position

   sub-pixel precision!
SPR Instrumentation

- Optical coupling schemes

![Diagram of SPR Instrumentation]

- Light beam
- Coupling prism
- SPR layer
- Sample
- Metallic grating
- Sample
- Attenuated guided mode
- Input light
- Waveguide with SPR layer
SPR sensor based on Prism Coupler and Angular modulation

- Sensor schematics

A

- Light source (Laser or LED)
- Prism
- Fluidic cell
- Polarizer
- CCD sensor
- Optics

B

- Outlet
- Inlet
SPR sensor based on Prism Coupler and Angular modulation

- Reichert SR7000

Specifications:
- sensitivity $2 \times 10^{-7}$ RU
- dynamic range 1.3 – 1.6
 SPR sensor based on Prism Coupler and Angular modulation

- Texas Instr. SPREETA
• Schematics of a 4 channel sensor with wavelength modulation
SPR sensor based on Grating Coupler and Intensity modulation

FLEX chip, HTC Biosystems (acquired by BIAcore)
Integrated Optical SPR sensor

- SPR probe using a side polished optical fiber

- sensitivity (w. wavelength modulation) <10^{-6};
- sensitivity (w. intensity modulation) 5*10^{-5};
Problem

• Calculate position of the SPR minimum for a prism-based setup involving
  – a light source at 780nm,
  – BK7 optical prism (refractive index 1.511 @780nm),
  – gold film (refractive index 0.1420+i*4.7571 @780nm)
  – a water-based buffer on the sensor side (n=1.33).

What change in the absorption minimum we expect when the refractive index of buffer changes by 10^{-4}?