Biosensors

• DNA Microarrays (for chemical analysis)

• Protein Sensors (for identifying viruses)
DNA Microarrays

40,000 detectors in parallel, each detecting a specific DNA sequence.

“Combinatorial Chemistry”
Operation of a DNA Microarray

- Fixed probes
- Different features (e.g., bind different genes)
- Fully complementary strands bind strongly
- Partially complementary strands bind weakly
- Labelled target (sample)
Orientation of DNA from X-ray Absorption Spectroscopy

Single-stranded DNA of the microarray needs to be accessible to the complementary target DNA.

The polarization dependence of the $\pi^*$ peaks tells whether DNA stands up or lies flat (Lect. 10, Slides 14, 15).

Petrovykh et al., JACS 128, 2 (2006)
One interface layer aligns 100μm of liquid crystal, i.e. 50,000 molecular layers: Amplification by $10^4$-$10^5$

Sensor for proteins / viruses: Attach antibodies to a surface which is made bio-compatible. When a protein in a virus locks onto its specific antibody, the orientation of the liquid crystal is lost. This change is detected by a change of the transmission between crossed polarizers, like in a liquid crystal display.

Tagging Specific Proteins by Antibodies Containing a Fluorescent Dye

Immunofluorescence image of a cell. Actin filaments are shown in red, microtubules in green, and the nuclei in blue.
Green Fluorescent Protein (GFP)

Isolated from a jellyfish

2008 Nobel Prize in Chemistry
Green Fluorescent Protein (GFP)
Can be introduced into the genome.
Biomolecules at Surfaces

Biosensor

• Binding of biomolecules ⇒ Change of the surface roughness
• Orientation of liquid crystals ⇒ Amplification factor 10^5

Photosynthesis

• Reaction Center (RC) performs photoinduced charge separation.
• Cytochrome C reduces oxidized donor in the RC.
• Reaction sites of the RC need to face outward.


Immobilization Strategies

Thiol (for gold) and silane (for SiO₂) chemistry

Biotin-Streptavidin binding

Dextran gel

Lipid bilayer

Passivating

Chemical bond

H₂O
Common Detection Methods

Evanescent mode (e.g. SPR or TIRF)

Reflection mode (e.g. Ellipsometry or SFG)

Polarisation

Δd (optical thickness)

Δn (refractive index)

Σ-f-gen

Piezoelectric techniques (e.g. QCM or SAW)

Δf ∝ Δm

ΔD ∝ stiffness

Impedance spectroscopy

ΔR & CΔ

Scanning probe microscopy

Deflection

X-y-Z
Biological Machines

Biomotors

Ion Channels
Molecular Motors

Linear: Contract a muscle, carry cargo

Rotary: Drive flagella for propelling bacteria
         Operate as generator producing ATP
A Muscle
A Muscle Fiber

Myosin molecules (bottom) walk along the surrounding actin filaments and thereby contract the muscle.
Molecular Motor

Walker = Myosin, Kinesin

Rail = Actin, Tubulin

Driven by ATP → ADP + energy

Two Walking Molecules
Motor Parts

Myosin and other walking molecules.

They are powered by ATP (adenosine triphosphate), the fuel of biochemistry. It releases energy by converting into ADP (adenosine diphosphate) and releasing a phosphate group which phosphorylates proteins.

Figure 1 Representative cytoskeletal motors. a, Myosin II; b, conventional kinesin; c, ciliary dynein. The top row shows high-resolution electron micrographs of quick-frozen, rotary-shadowed individual molecules (images courtesy of J. Heuser).

The walking kinesin molecule is attached to a bead, which is held by optical tweezers* (pink laser beam). The position of kinesin stepping along a microtubule is detected by constant force feedback, where the laser focus follows the bead. Steps of 8 nm can be seen.

* Optical tweezers use the attraction of an electric dipole to the high electric field produced at the focus of a laser. Here the electric dipole is the bead, which becomes polarized in the electric field of the laser.

Visscher, Schnitzer, and Block, Nature 400, 6740 (1999)
Schematic of a rotary motor driving a flagellum (filament).
A depiction of $F_0F_1$-ATP Synthase. The free energy of high proton concentration inside the cell is used to generate ATP from ADP. The outflow of protons drives a rotary motion which is used to make conformational changes in the protein and convert ADP into ATP. An efficiency of 80% is achieved.
F₀F₁-ATP Synthase:

Cell Membrane
A Rotary Stepping Motor

Top: Dark field images of gold beads attached to the rotor of $F_1$-ATPase. Centroid positions are shown above the images at 3x magnification. The interval between images is 0.5 ms.

Bottom: Rotation versus time. The three-fold symmetry of the $F_1$ complex produces $120^0$ steps.

An Idea: Lifelike Structures at a Surface

Bacteriorhodopsin: Light-driven proton pump

Rotary generator
Converts ADP to ATP
Powered by proton pump

Electrolyte
Artificial Membrane
Water
Solid substrate

Top view of an ion channel (ion in purple)

2003 Nobel Prize in Chemistry

Peter Agre
Roderick MacKinnon
Side View of an Ion Channel

Cell Membrane

Closed

Open
Detailed Side View of an Ion Channel

The ion is guided by oxygen atoms (red) attached to the protein backbone.
Selectivity of the Potassium Ion Channel

The potassium channel allows only one sodium to pass for every 10,000 potassium ions, even though sodium is smaller than potassium.

The pore is lined with oxygen atoms (red). They mimic the shell of 8 water molecules that surround a potassium ion (bottom). The pore is so wide that a sodium ion cannot bind to the oxygen atoms in the pore wall. Consequently, the sodium ion stays outside to keep its water shell.