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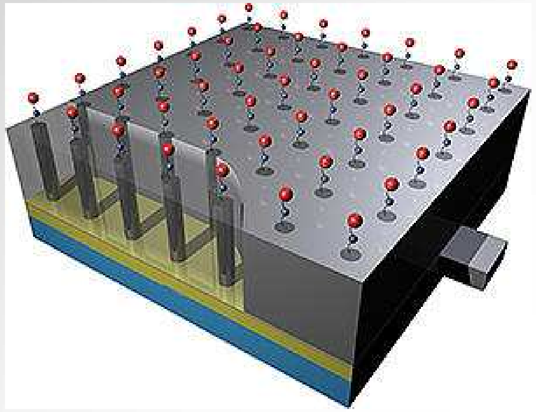
Lecture I



Introduction and Overview of Biosensors .

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Outlines

- Introduction of the course
- Terms and definition
- Rational of a biosensor
- Types of biosensor
- Applications of biosensors
- Electrochemistry and biosensors
- Nanotechnology in biosensor

Course Introduction

What will we learn from the course?

- Principals of biosensors
- Fundamentals of analytical electrochemistry
- Biofunctionalization and surface modification
- Aspects and perspectives of nanobioelectronics
- Nanomaterials and nanoengineering for biosensor development
- DNA, protein based electronics

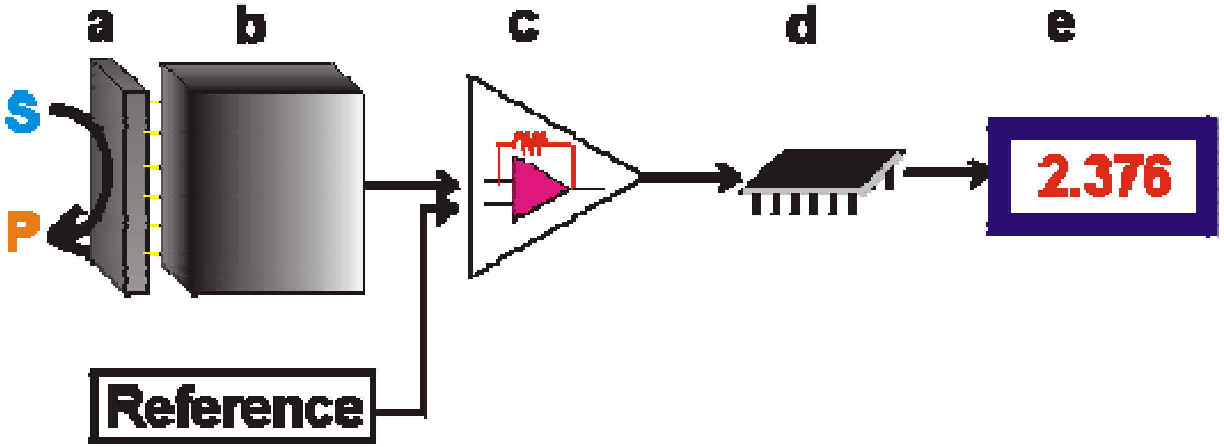
"An important player in 21st century engineering will be the 'biotraditional engineer,' the recipient of a traditional engineer's training and a modicum of exposure to life science." M.H. Friedman, J. Biomechanical Eng, V123, December 2001

What is biosensor?

Chemical Sensors:
"A chemical sensor is a device that transforms chemcial information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal" – IUPAC

Biosensors: are analytical tools for the analysis of bio-material samples to gain an understanding of their bio-composition, structure and function by converting a biological response into an electrical signal. The analytical devices composed of a biological recognition element directly interfaced to a signal transducer which together relate the concentration of an analyte (or group of related analytes) to a measurable response.

Biosensor Components



Schematic diagram showing the main components of a biosensor. The bio-reaction (a) converts the substrate to product. This reaction is determined by the ***transducer*** (b) which converts it to an electrical signal. The output from the transducer is amplified (c), processed (d) and displayed (e).

(http://www.lsbu.ac.uk/biology/enztech/biosensors.html)

Selective Elements and Transducers

Selective elements	Transducers
synthetic ionophores	electrochemical: (Current, potential, Resistance, impedance)
synthetic carriers	– potentiometric
supramolecular structures, clusters	– amperometric
solid layers: metals	– conductimetric
– metal oxides, crystals	– voltammetric, polarographic
– polymers, conducting polymers	– impedimetric, capacitive
organisms	– piezoelectric
microorganisms	optical: (florescence, light scattering, etc.),
plant and animal tissues	– transmission / absorbance / reflection
cells	– dispersion, interferometric
organelles	– polarimetric
membranes, bilayers and monolayers	– circular dichroism, ellipsometry
enzymes	– scattering
receptors	– emission intensity, photon counting
antibodies	(luminescence) decay time
nucleic acids	calorimetric (Thermal, temperature)
natural organic and inorganic molecules	acoustic / gravimetric: (Mass Sensitive)
micelles, reversed micelles	– surface photo-acoustic wave
	– quartz microbalance

Ref: Spichiger-Keller U.E., "Chemical Sensors and Biosensors for Medical and Biological Applications, Wiley-VCH, 1998

Defining events in the history of biosensor development

1916	First report on the immobilisation of proteins: adsorption of invertase on activated charcoal
1922	First glass pH electrode
1956	Invention of the oxygen electrode (**Clark**)
1962	First description of a biosensor: an amperometric enzyme electrode for glucose **(Clark)**
1969	First potentiometric biosensor: urease immobilised on an ammonia electrode to detect urea
1970	Invention of the Ion-Selective Field-Effect Transistor (ISFET) (**Bergveld)**
1972/5	First commercial biosensor: Yellow Springs Instruments glucose biosensor
1975	First microbe-based biosensor First immunosensor: ovalbumin on a platinum wire Invention of the pO_2 / pCO_2 optode
1976	First bedside artificial pancreas (Miles)

Biosensor History (cont.)

1980	First fibre optic pH sensor for *in vivo* blood gases (**Peterson**)
1982	First fibre optic-based biosensor for glucose
1983	First surface plasmon resonance (SPR) immunosensor
1984	First mediated amperometric biosensor: ferrocene used with glucose oxidase for the detection of glucose
1987	Launch of the MediSense ExacTech™ blood glucose biosensor
1990	Launch of the Pharmacia BIACore SPR-based biosensor system
1992	i-STAT launches hand-held blood analyser
1996	Glucocard launched
1996	Abbott acquires MediSense for $867 million
1998	Launch of LifeScan FastTake blood glucose biosensor
1998	Merger of Roche and Boehringer Mannheim to form Roche Diagnostics
2001	LifeScan purchases Inverness Medical's glucose testing business for $1.3billion

1999-current	BioNMES, Quantum dots, Nanoparticles, Nanocantilever, Nanowire and Nanotube

Type of Biosensors (by analytes)

Types of Biological Recognition Elements	Name of the BIOSENSOR
Enzymes	Enzyme electrode
Proteins	
Antibodies	Immunosensor
DNA	DNA sensor
Organelles	
Microbial cells	Microbial sensor
Plant and animal tissues	

Types of Biosensor (by detection mode)

Types of Transducers	Measured Property
Electrochemical	Potentiometric
	Amperometric
	Voltametric
Electrical	Surface conductivity
	Electrolyte conductivity
Optical	Fluoresence
	Adsorption
	Reflection
Mass sensitive	Rezonans frequency of piezocrytals
Thermal	Heat of reaction
	Heat of adsorpsion

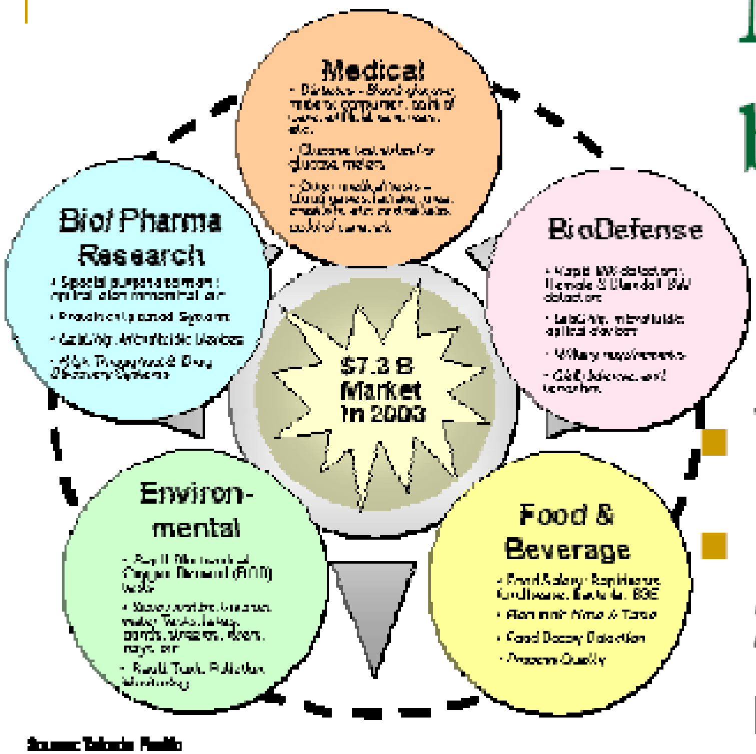
Typical Sensing Techniques for Biosensors

- Fluorescence
- DNA Microarray
- SPR Surface plasmon resonance
- Impedance spectroscopy
- SPM (Scanning probe microscopy, AFM, STM)
- QCM (Quartz crystal microbalance)
- SERS (Surface Enhanced Raman Spectroscopy)
- Electrochemical

Application of Biosensor

- Applications
- • Study of biomolecules and how they interact with
- one another
- - E.g. Biospecific interaction analysis (BIA)
- • Drug Development
- • In- home medical diagnosis
- • Environmental field monitoring
- • Scientific crime detection
- • Quality control in small food factory
- • Food Analysis

Biosensor Market



Market size of biosensor

- 7.3 Billion $ in 2003
- 10.2 Billion $ in 2007 with a growth rate of about 10.4%

Biomedical Diagnostics

- **Doctors increasingly rely on testing**
- **Needs: rapid, cheap, and “low tech”**
- **Done by technicians or patients**
- **Some needs for *in-vivo* operation, with feedback**

Glucose-based on glucose oxidase
Cholesterol - based on cholesterol oxidase
Antigen-antibody sensors - toxic substances, pathogenic bacteria
Small molecules and ions in living things: H^+, K^+, Na^+, NO, CO_2, H_2O_2
DNA hybridization, sequencing, mutants and damage

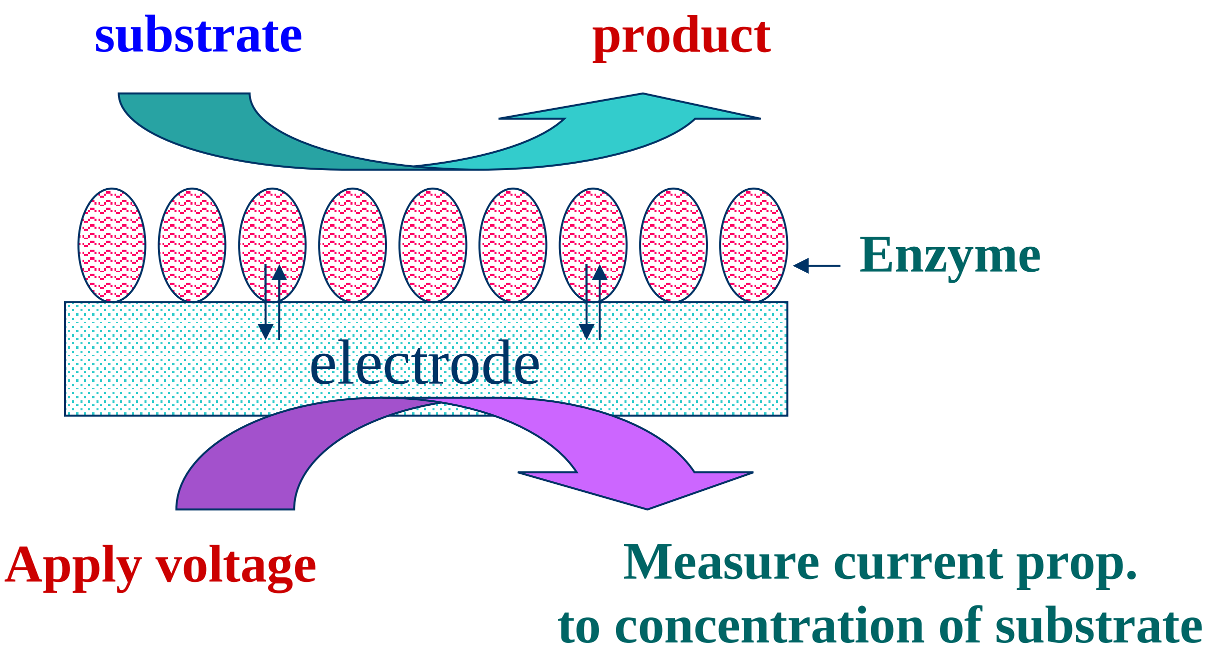
Commercial Glucose Sensors

- Biggest biosensor success story!
- Diabetic patients monitor blood glucose at home
- First made by Clark in 1962, now 5 or more commercial test systems
- Rapid analysis from single drop of blood
- Enzyme-electrochemical device on a slide

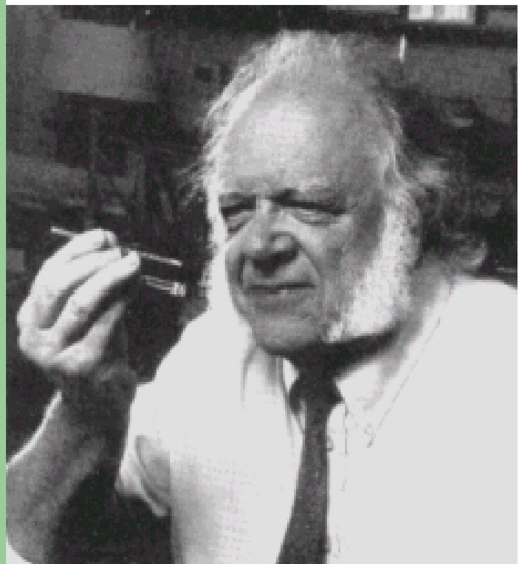
Basic Characteristics of a Biosensor

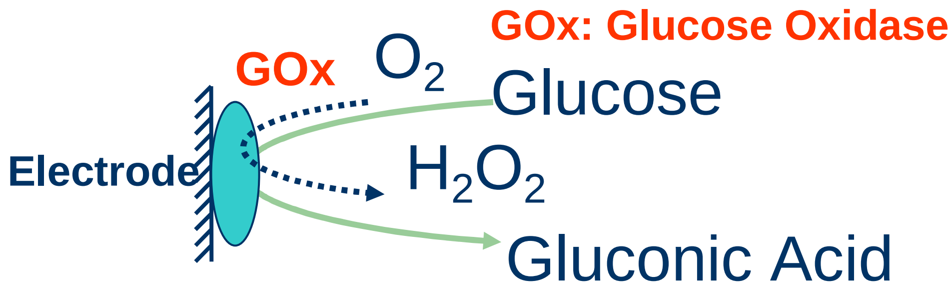
1. **LINEARITY:** Maximum linear value of the sensor calibration curve. Linearity of the sensor must be high for the detection of high substrate concentration.
2. **SENSITIVITY:** The value of the electrode response per substrate concentration.
3. **SELECTIVITY:** Interference of chemicals must be minimised for obtaining the correct result.
4. **RESPONSE TIME:** The necessary time for having 95% of the response.

Principle of Electrochemical Biosensors



Electrochemical Glucose Biosensor

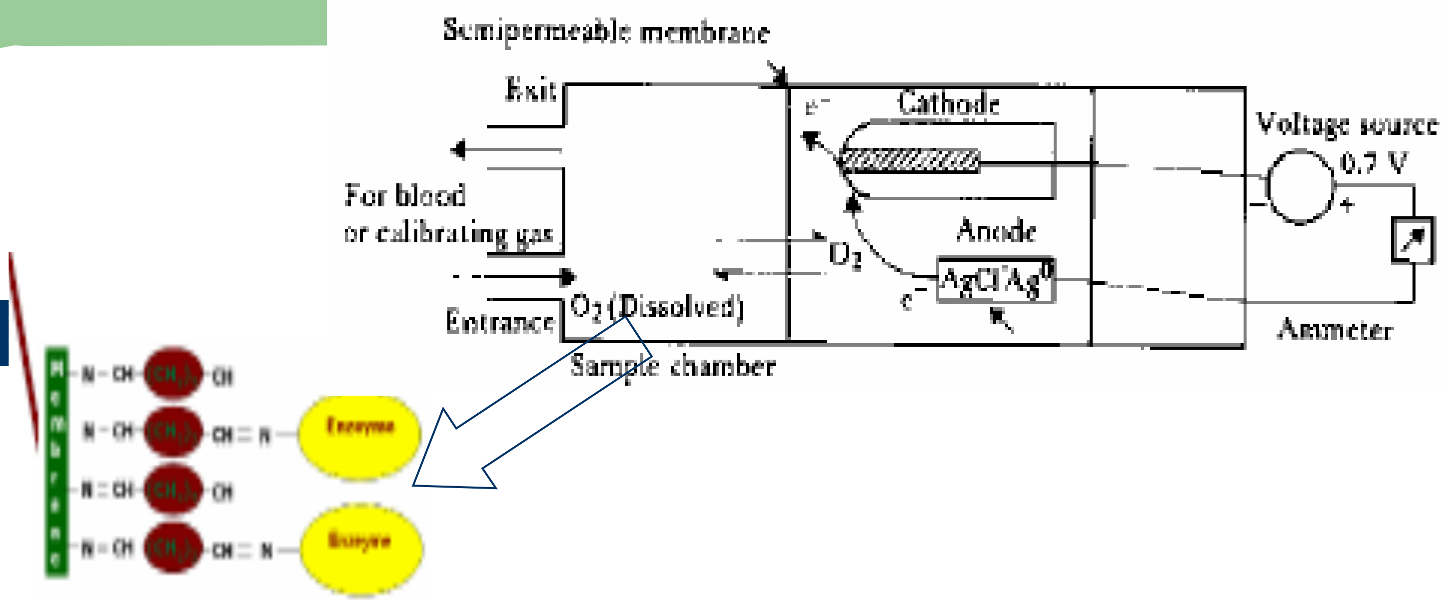


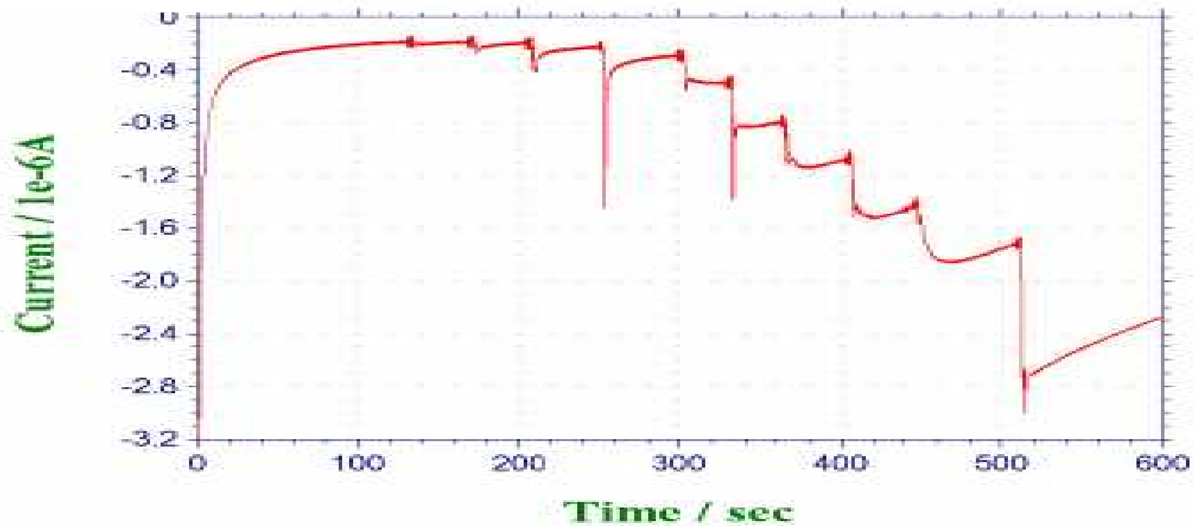


$$\text{Glucose} + O_2 \xrightarrow{\text{GOx}} \text{Gluconic Acid} + H_2O_2$$

$$H_2O_2 \xrightarrow[\text{0.6 V vs. SHE}]{\text{Pt}} 2H^+ + O_2 + 2e^-$$

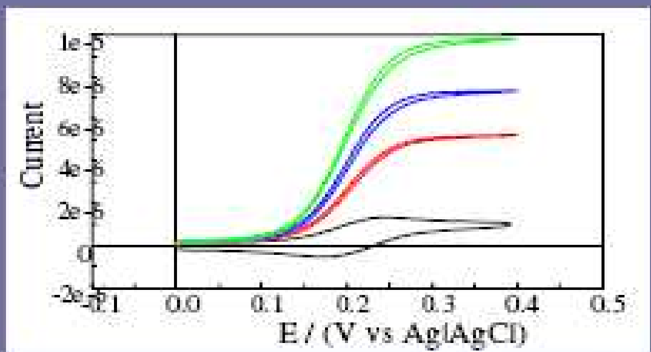
The first and the most widespreadly used commercial biosensor: the blood glucose biosensor – **developed by** ***Leland C. Clark in*** **1962**


Semipermeable membrane
Exit
For blood
or calibrating gas
Entrance
O_2 (Dissolved)
Sample chamber
Cathode
Anode
O_2
AgCl/Ag
Voltage source
0.7 V
Ammeter


Current / 1e-6A
Time / sec
0
-0.4
-0.8
-1.2
-1.6
-2.0
-2.4
-2.8
-3.2
0
100
200
300
400
500
600

The Glucose Biosensor

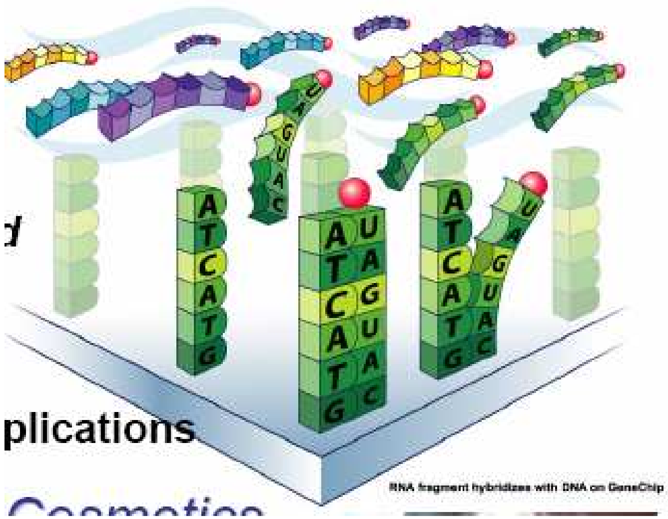
- Coupling of glucose oxidase (via a mediator) to an electrode



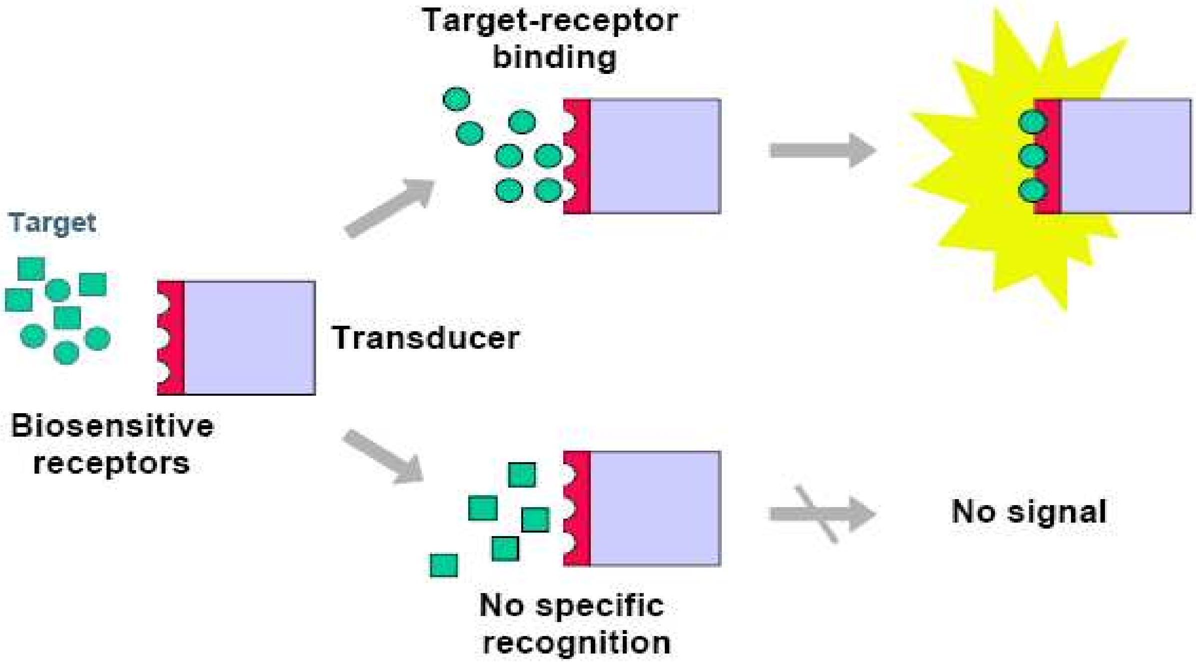
- Increasing concentration of glucose
- Current proportional to glucose concentration
- Randles-Sevcik equation

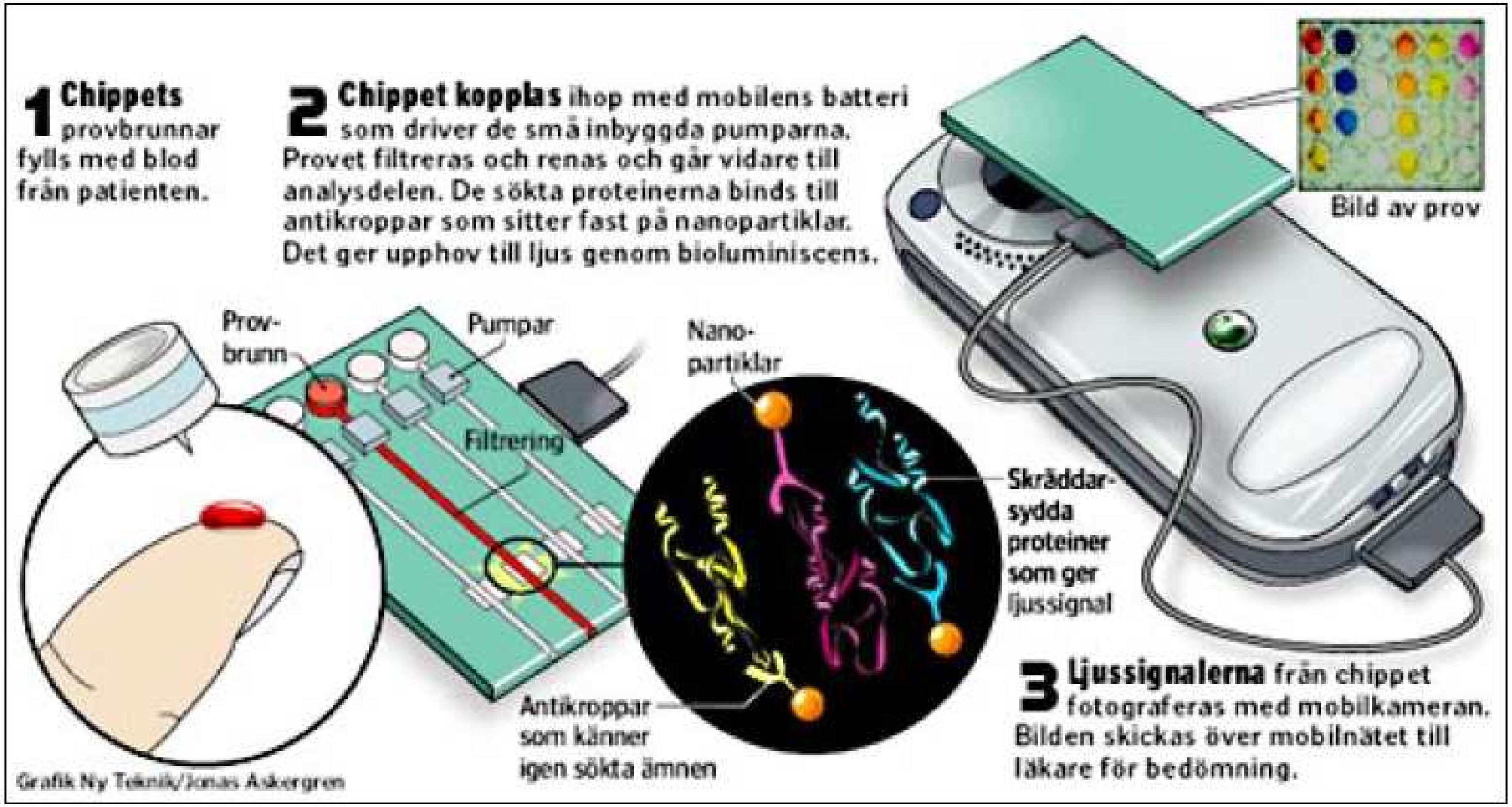
$I_p = (2.687 \times 10^5)\, n^{3/2}\, v^{1/2}\, D^{1/2}\, A\, C$

© J. Lamb



plications
RNA fragment hybridizes with DNA on GeneChip


Target-receptor
binding
Target
Transducer
Biosensitive
receptors
No specific
recognition
No signal


1 Chippets provbrunnar fylls med blod från patienten.
2 Chippet kopplas ihop med mobilens batteri som driver de små inbyggda pumparna. Provet filtreras och renas och går vidare till analysdelen. De sökta proteinerna binds till antikroppar som sitter fast på nanopartiklar. Det ger upphov till ljus genom bioluminiscens.
Bild av prov
Prov-brunn
Pumpar
Nano-partiklar
Filtrering
Skräddar-sydda proteiner som ger ljussignal
Antikroppar som känner igen sökta ämnen
3 Ljussignalerna från chippet fotograferas med mobilkameran. Bilden skickas över mobilnätet till läkare för bedömning.
Grafik Ny Teknik/Jonas Askergren