BIOSENOSRS

BIO 580

Overview, history & types of biosensors

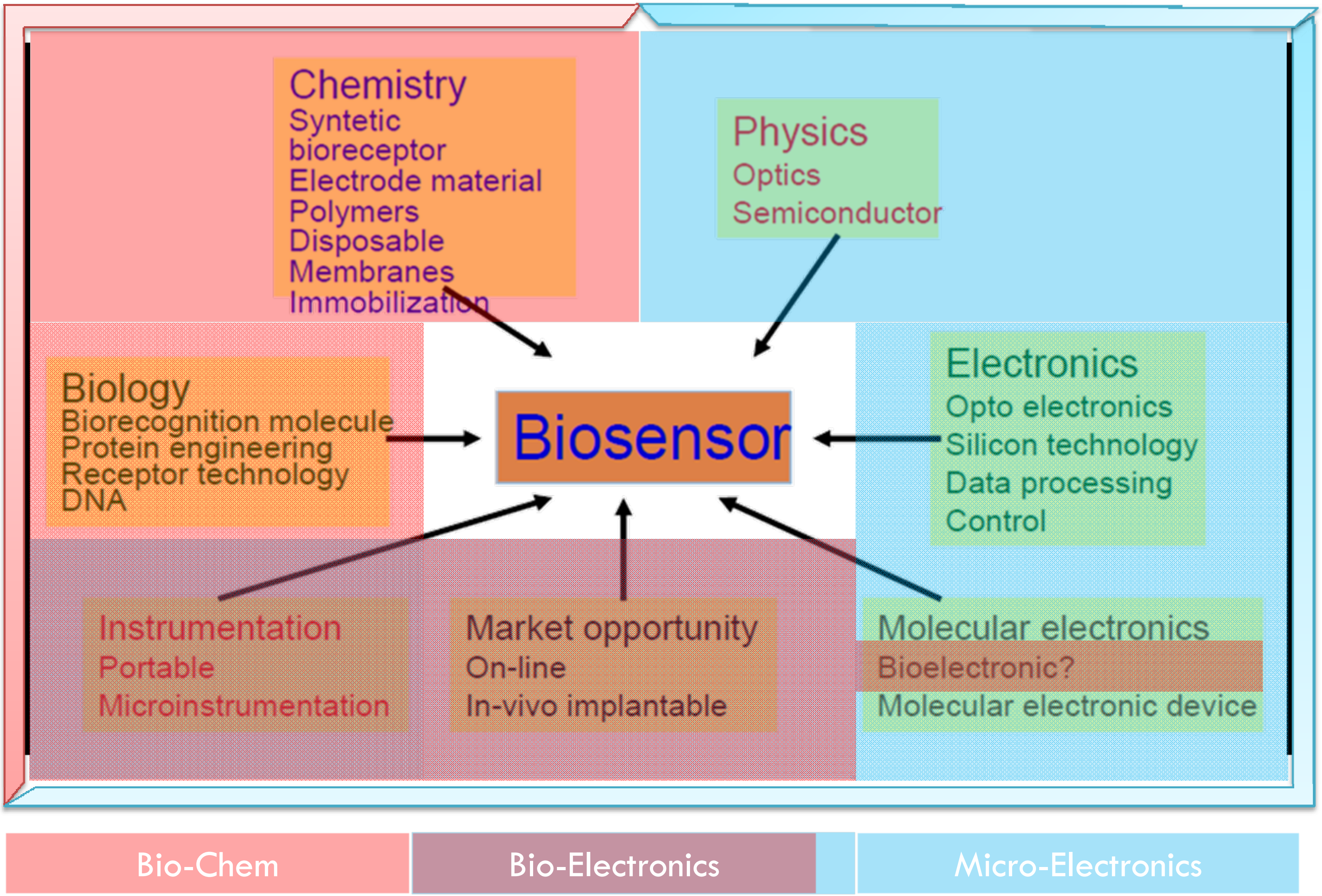
Introductory Week

Faculty: Dr. Javed H. Niazi KM
Faculty of Engineering & Natural Sciences
Sabanci University

Topics that will be covered in the course

- ❑ History of biosensor development, applications and requirements of biosensors and classification
- ❑ Principles of molecular recognition and transduction signal acquisition
  - ✓Sources of Biological Recognition elements – enzymes/proteins, ssDNAs, antibody and Others
  - ✓Design considerations for use of recognition elements in biosensors
  - ✓Modeling of reactions for various biosensor applications- electrochemical, optical, piezoelectric, colorimetric, fluorometric and others.
- ❑ Modification of sensor surfaces and immobilization techniques
  - ✓Covalent modification of surfaces using surface chemistry
  - ✓Self Assembled Monolayers (SAM) and adsorptions
  - ✓Other ways to immobilize biological macromolecules on various solid surfaces
- ❑ Detection methods and Physical Sensors
  - ✓Electrodes/transducers – electrochemical (amperometric, potentiometric, and conductimetric transductions)
  - ✓Other sensors - for e.g., optical sensors (colorimetric/fluorimetric/luminometric sensors), Surface Plasmon Resonance (SPR) sensors, and piezoelectric resonators.
- ❑ Fabrication of biosensors
  - ✓Miniaturization-application of nano-materials, nanoparticles, carbon nanotubes (CNTs) and others
  - ✓Biocompatibility – stability, reproducibility and repeatability of biomolecules on transducer surfaces
- ❑ Data acquisition, statistical and error analysis
  - ✓Inter and Intra-assays and Coefficient of variation (CV)
  - ✓Signal to noise ratio
  - ✓Normalization/optimization and signal retrieval
- ❑ Examples of commercial biosensors

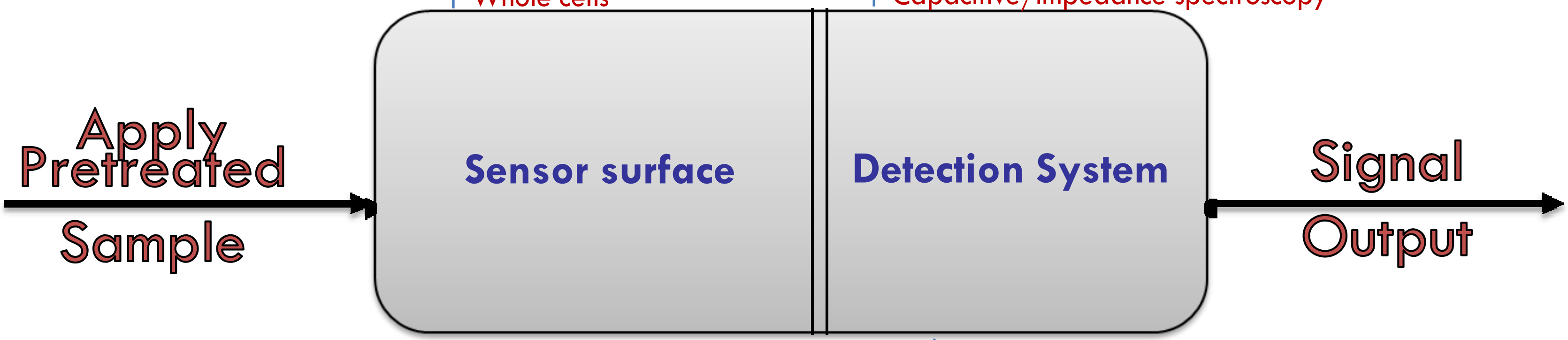
Biosensors - combines multiple disciplines



Biosensensing

- Electrode
- Interdigitated array chip
- Metal sufcace- gold, platinum
- Glass
- Silicon &/or dioxide
- Whole cells

- Electrochemical- amperometric, potentiometric, conductimetric
- Optical- SPR, fibre-optic, interferometric
- Colorimetric/Fluorimetric - Color change, fluorescence, luminos
- Piezoelectric
- Microbalance - QCM, cantelivers
- Capacitive/impedance spectroscopy



- Antibodies/antigens (immunosensors)
- Enzymes/receptors (any other protein)
- Whole microbial/animal cells
- Small organic molecules
- Nanoparticles
- Unlimited types of other molecules

- Electrodes (metal-Au, Ag, Pt, Ni, Cu)
- Device that measure light intensity/RI
- Spectrophotometric
- Digital read out- current change
- Photomultiplier tubes, CMOS, CCDs etc.

Bio-recognition elements

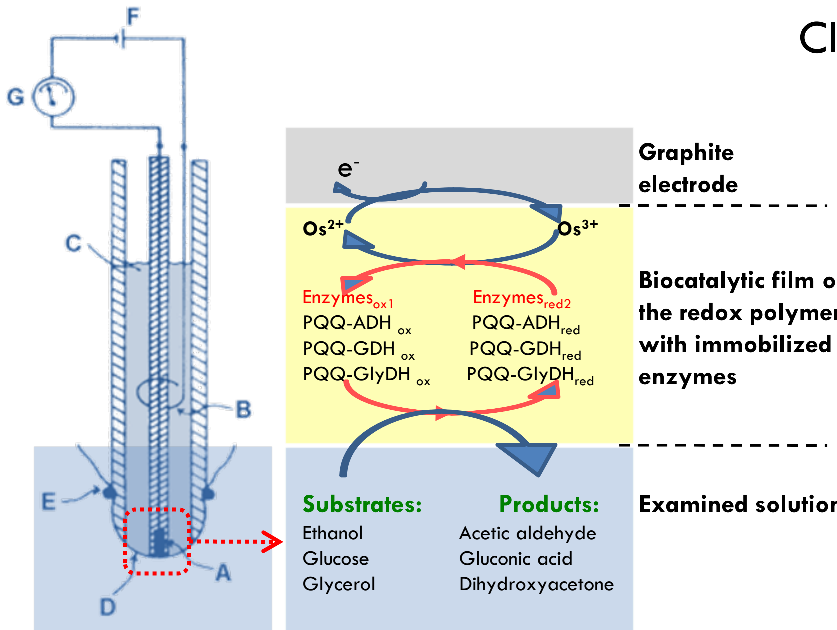
- **Biomolecules on sensor surface**

Transducers

- **Capacitance/Voltage controlled oscillator**

History of biosensors

Leland Clark Jr.

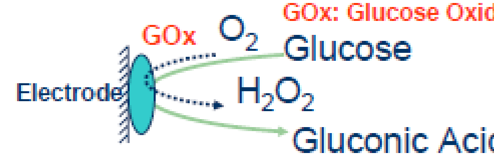


Clark-type electrode: (A) Pt- (B) Ag/AgCl-electrode (C) KCl electrolyte (D) Teflon membrane (E) rubber ring (F) voltage supply (G) galvanometer

Clarks electrode- glucose biosensor

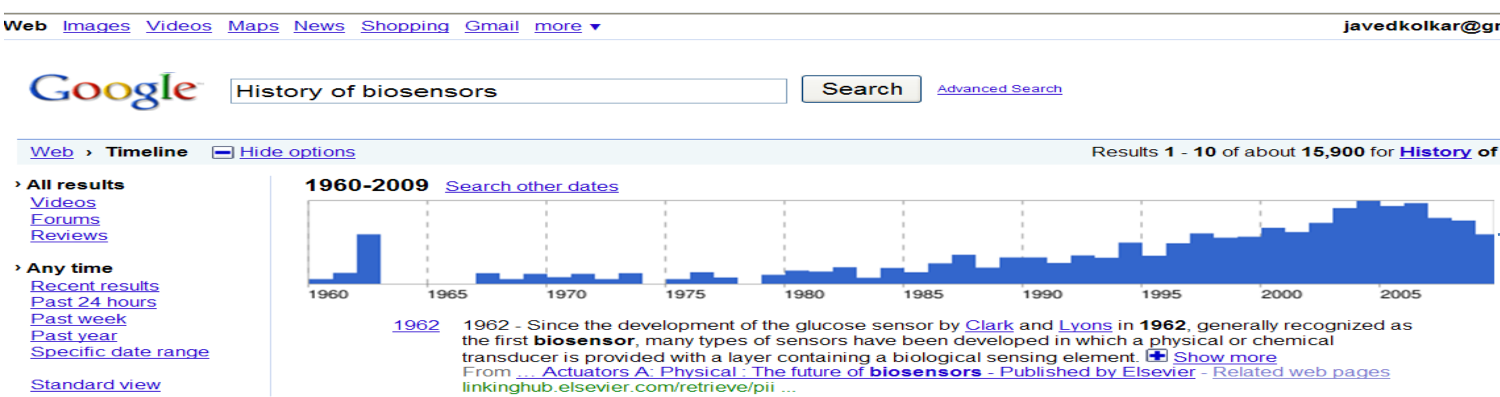
The first and the most widely used commercial biosensor: **the blood glucose biosensor - developed by *Leland C. Clark in* 1962**

GOx: Glucose Oxidase



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

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

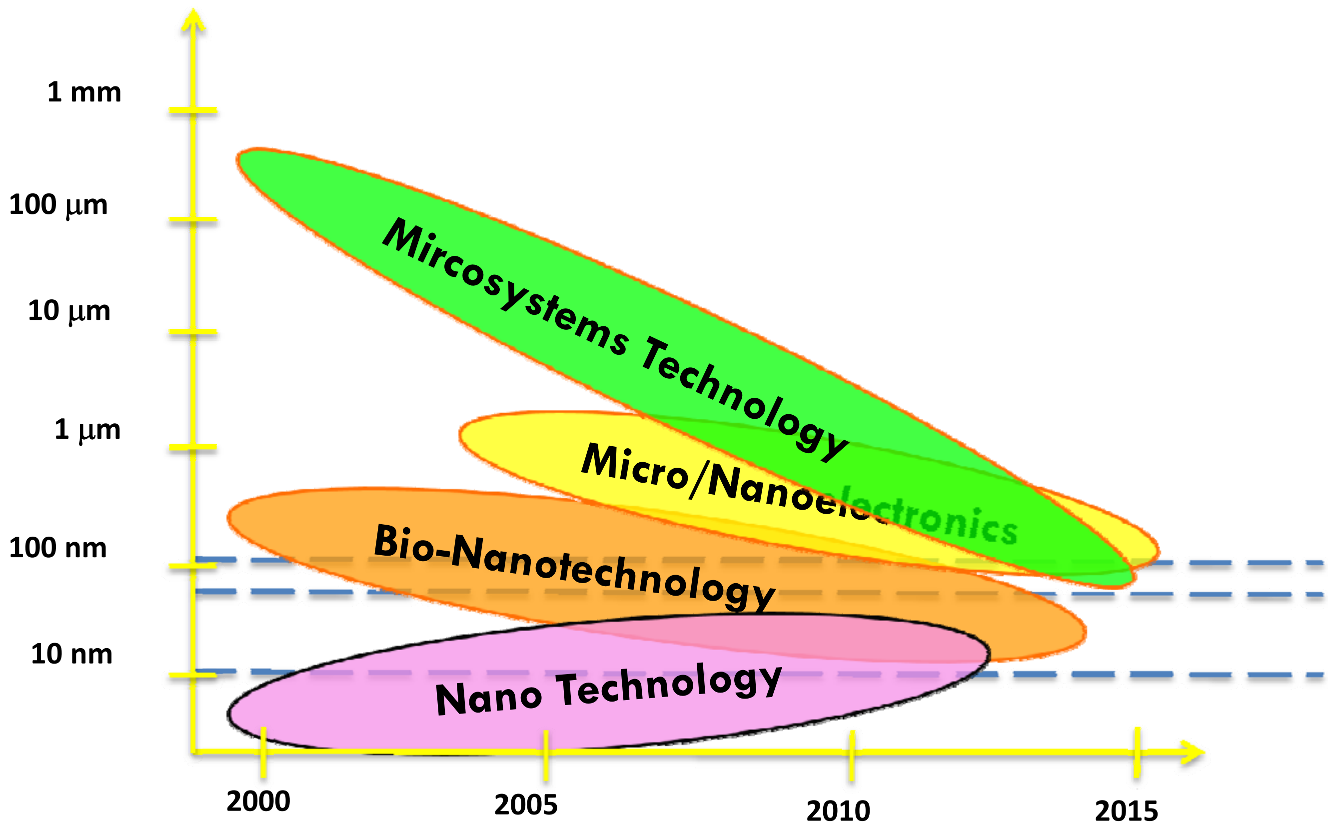


→ Number of articles published

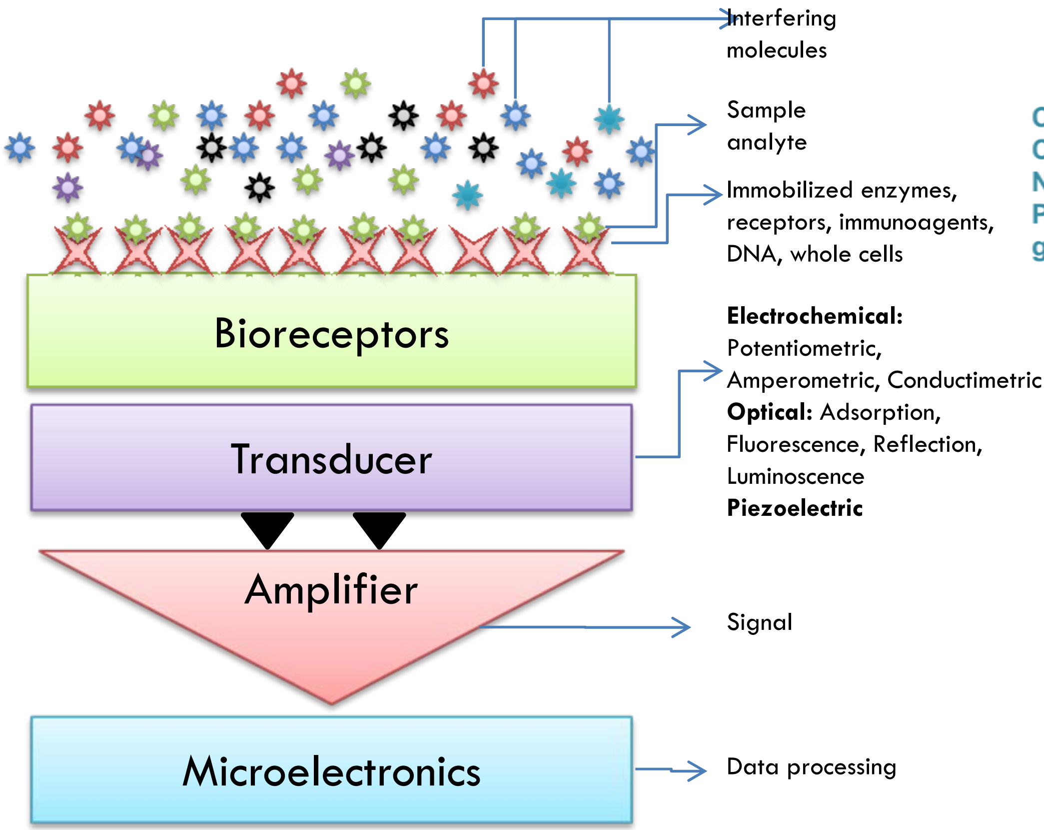
History of biosensors

Sl. No.	Year	Events
1	1916	First report on the immobilization of proteins: adsorption of invertase on activated charcoal -Nelson and Griffin
2	1922	First glass pH electrode
3	1956	Invention of the oxygen electrode (Clark)
4	1962	First description of a biosensor: an amperometric enzyme electrode for glucose (Clark)
5	1969	First potentiometric biosensor: urease immobilized on an ammonia electrode to detect urea
6	1970	Invention of the Ion-Selective Field-Effect Transistor (ISFET) (Bergveld)
7	1972/5	First commercial biosensor: Yellow Springs Instruments glucose biosensor (pen shaped single use electrode)
8	1975	First microbe-based biosensor First immunosensor: ovalbumin on a platinum wire Invention of the pO_2/pCO_2 optode (fluorescence signal & gas permeable membrane usage)
9	1976	First bedside artificial pancreas (Miles)
10	1980	First fibre optic pH sensor for in vivo blood gases (Peterson)
11	1982	First fibre optic-based biosensor for glucose
12	1983	First surface plasmon resonance (SPR) immunosensor
13	1984	First mediated amperometric biosensor: ferrocene used with glucose oxidase for the detection of glucose
14	1987	Launch of the MediSense ExacTech™ blood glucose biosensor (strips/pen model and disposable)
15	1990	Launch of the Pharmacia BIACore SPR-based biosensor system
16	1992	i-STAT launches hand-held blood analyser
17	1996	Glucocard launched
18	1996	Abbott acquires MediSense for $867 million
19	1998	Launch of LifeScan FastTake blood glucose biosensor
20	1998	Merger of Roche and Boehringer Mannheim to form Roche Diagnostics
21	2001	LifeScan purchases Inverness Medical's glucose testing business for $1.3billion
22	1999 to now	BioNMES, Quantum dots, Nanoparticles, Nanocantilever, Nanowire and Nanotube

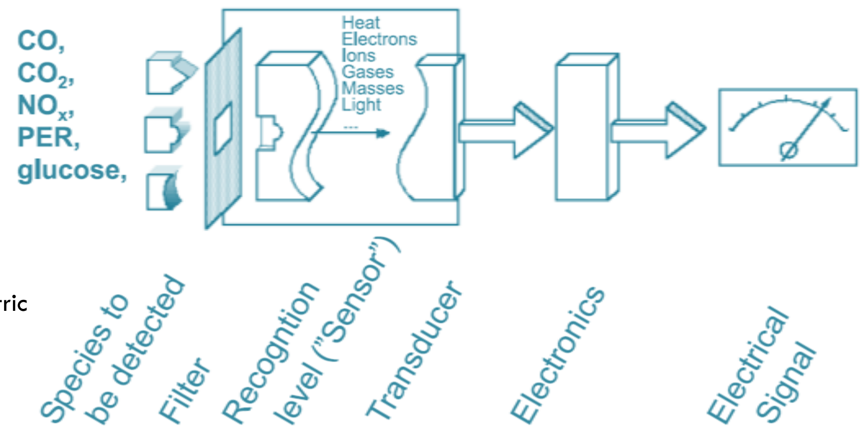
Status of merging interdisciplinary areas toward miniaturization



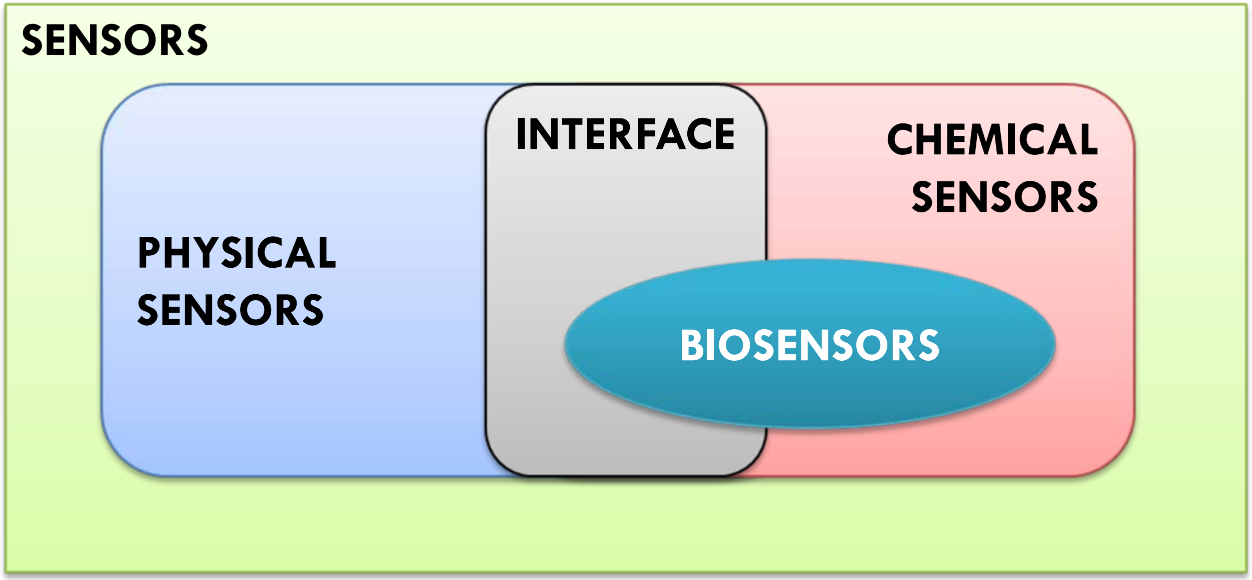
Working principle of biosensors



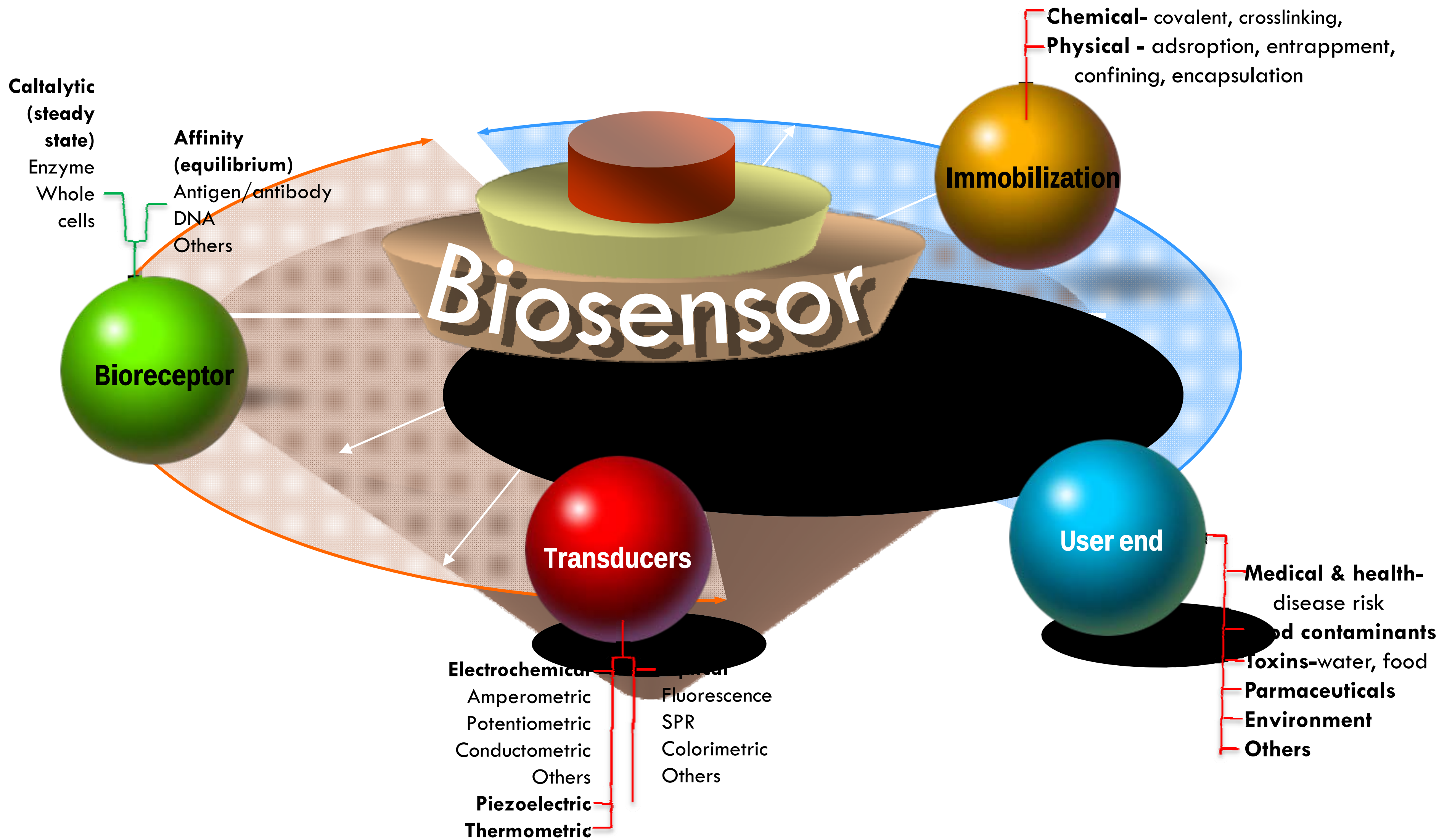
Generalized scheme of biosensors



Classification scheme for different types of sensors



An overview of a biosensor components

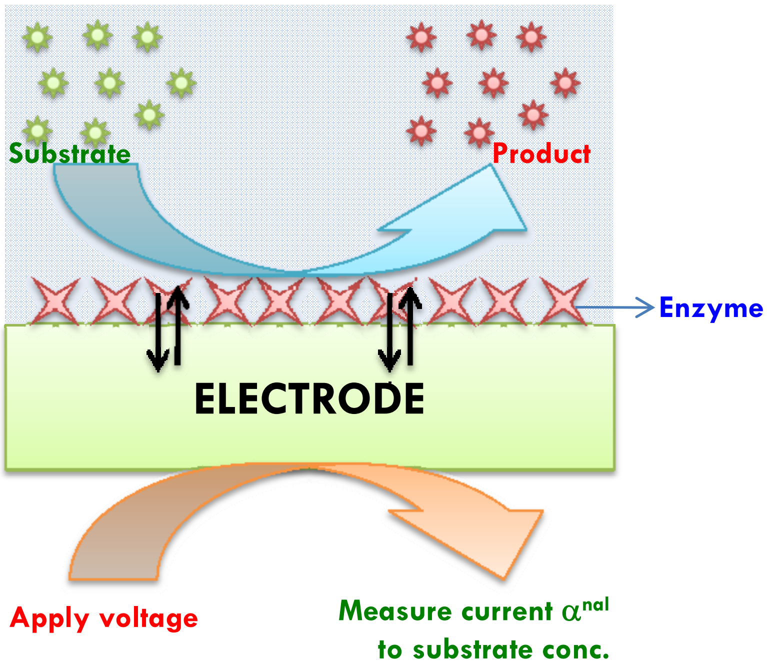


Classification

Biosensors

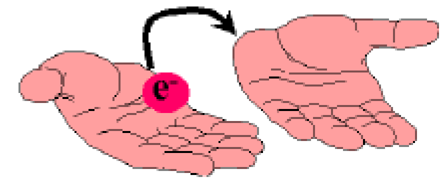
- **Receptor based**
  - Biocatalytic - enzyme, cells, tissuses
  - Biocomplexing - Ag/Ab -immunosensor
  - Receptor/antagonist
- **Based on mode/transducers**
  - **Electrochemical**
    - Amperometry
    - Potentiometry
    - Voltammetry
    - Conductometry
    - Field-effect transistors (surface charge)
  - **Optical**
    - Colorimetric- (NP, QDs)
    - Fluorimetric (fluorescent chemicals)
    - Luminometric (chemo/bio)
    - RI (SPR, interferometer, resonant mirror)
    - fibre-optic
  - **Piezoelectric**
    - QCM
    - Cantilever
    - Ultrasonic
    - Acoustic emission
    - Other actuators
- **Nanobiosensors**
  - QD's
  - Nanoparticles
  - Nanotubes (CNTs)
  - Nanowires
  - Porous silicon

Electrochemical Biosensor



Electrochemistry

Where there is oxidation, there is reduction

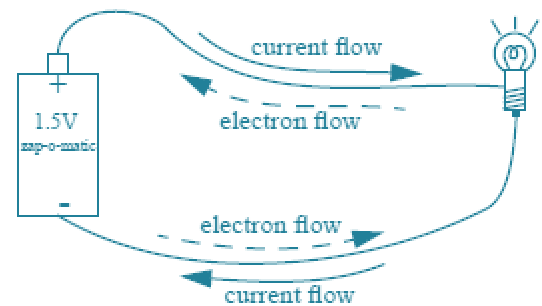


Substance oxidized loses electron(s)

Substance reduced gains electron(s)

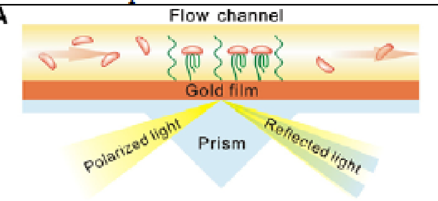
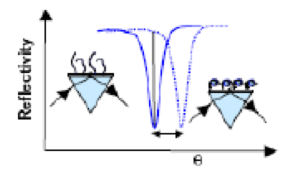
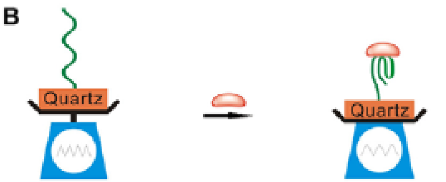
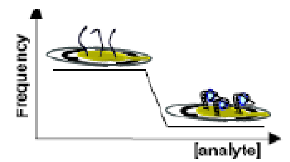
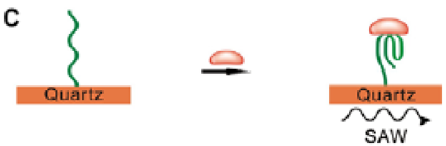
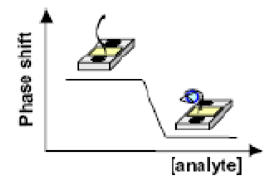
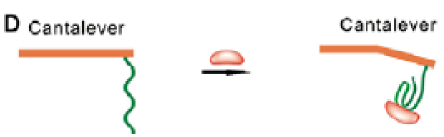
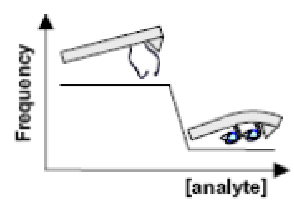
Conventional current flow is opposite to electron flow

eecs.oregonstate.edu/~traylor/ece112/.../elect_flow_vs_conv_I.pdf



To be continued…

Table 2. Mass sensitive sensor formats

Method	Schematic representation	Signal output	Principle
Mass sensitive aptasensors	A 		A: Surface Plasmon Resonance based aptasensors – capable of registering mass changes by the associated change in refractive index at the surface[14].
	B 		B: Quartz crystal microbalance (QCM)-based aptasensors – The frequency of the quartz crystal is controlled by changes in the mass associated with the crystal, thus the association of a target onto aptamer-modified crystals increases the mass on the transducer, resulting in a decrease in the resonance frequency of the crystal[15].
	C 		C: Surface acoustic wave (SAW)-based aptasensors – When mass is loaded onto the surface of these sensors, the propagation velocity of acoustic waves decreases, resulting in a reduction of resonance frequency or in alteration of the phase shift between output and input signal[16].
	D 		D: Micromechanical cantilever-based aptasensors – binding of target to aptamer immobilized cantilever induces a change in surface stress that causes a differential cantilever bending in the range 3–32 nm, depending on aptamer concentration[17].