Transducers

General Definition:

A device that converts variations in a physical quantity, such as pressure, temperature, brightness, etc, into an electrical signal, or vice versa

In a biosensor:

The transducer converts the biochemical interactions into measurable electric signals.

- Thermal : temperature, heat, heat flow, etc
- Mechanical : position, acceleration, force, pressure, etc
- Chemical : concentration, composition, reaction rate, etc
- Optical : intensity, wavelength, polarization, etc
- Magnetic : field intensity, flux, etc.
- Electrical : voltage, current, charge, etc

Transducers

Sensor and actuator are kinds of transducers

Sensors:

- a device that converts a physical parameter to an electrical output.

Actuators :

- a device that converts an electrical signal to a physical output.

Transducers

The transduction efficiency determines many of the analytical characteristics of the biosensors:

- the signal stability,
- reproducibility,
- detection limit,
- in many cases the operational stability and selectivity.

Electrochemical Biosensors

- Electrochemical reactions that take place at electrode-electrolyte interface are detected
- Three types:
  - Potentiometric
  - Amperometric
  - Conductometric

Amperometric transduction

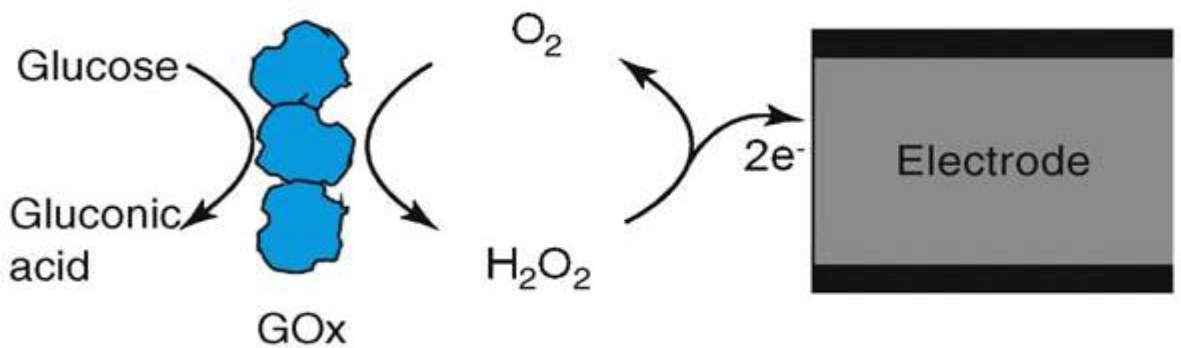
- The electrode potential is maintained at a constant level sufficient for oxidation or reduction of the species of interest
- The current that flows is proportional to the analyte concentration
- Amperometric enzyme electrodes based on oxidases in combination with hydrogen peroxide indicating electrodes have become most common among biosensors

Amperometric transduction

Typical electrochemical oxidase biosensor

- The product, H_2O_2, is oxidised at +650mV vs a Ag/AgCl reference electrode.
- Thus, a potential of + 650mV is applied and the oxidation of H_2O_2 measured.
- This current is directly proportional to the concentration of glucose

☹ They are very prone to interferences from exogenous oxygen.



Amperometric transduction

To increase the selectivity of the detecting electrode:

- Membranes
- Mediators
- Metallised electrodes
- Polymers

Amperometric transduction

Discriminative Membrane. Membranes are one of the essential components of a biosensor. They are used for

(1) preventing fouling;
(2) eliminating interference;
(3) controlling the operating regime of the biosensor.

Examples:

- Cellulose acetate (charge and size),
- Nafion (charge)
- Polycarbonate (size)

The disadvantage of using membranes is, however, their effect on diffusion.

Amperometric transduction

Mediators

- Artificial electron acceptor molecules
- e- transfer shuttle: a low molecular weight redox couple which can transfer electrons from the active site of the enzyme to the surface of the electrode → electrical contact between them

Amperometric transduction

Metallised electrodes

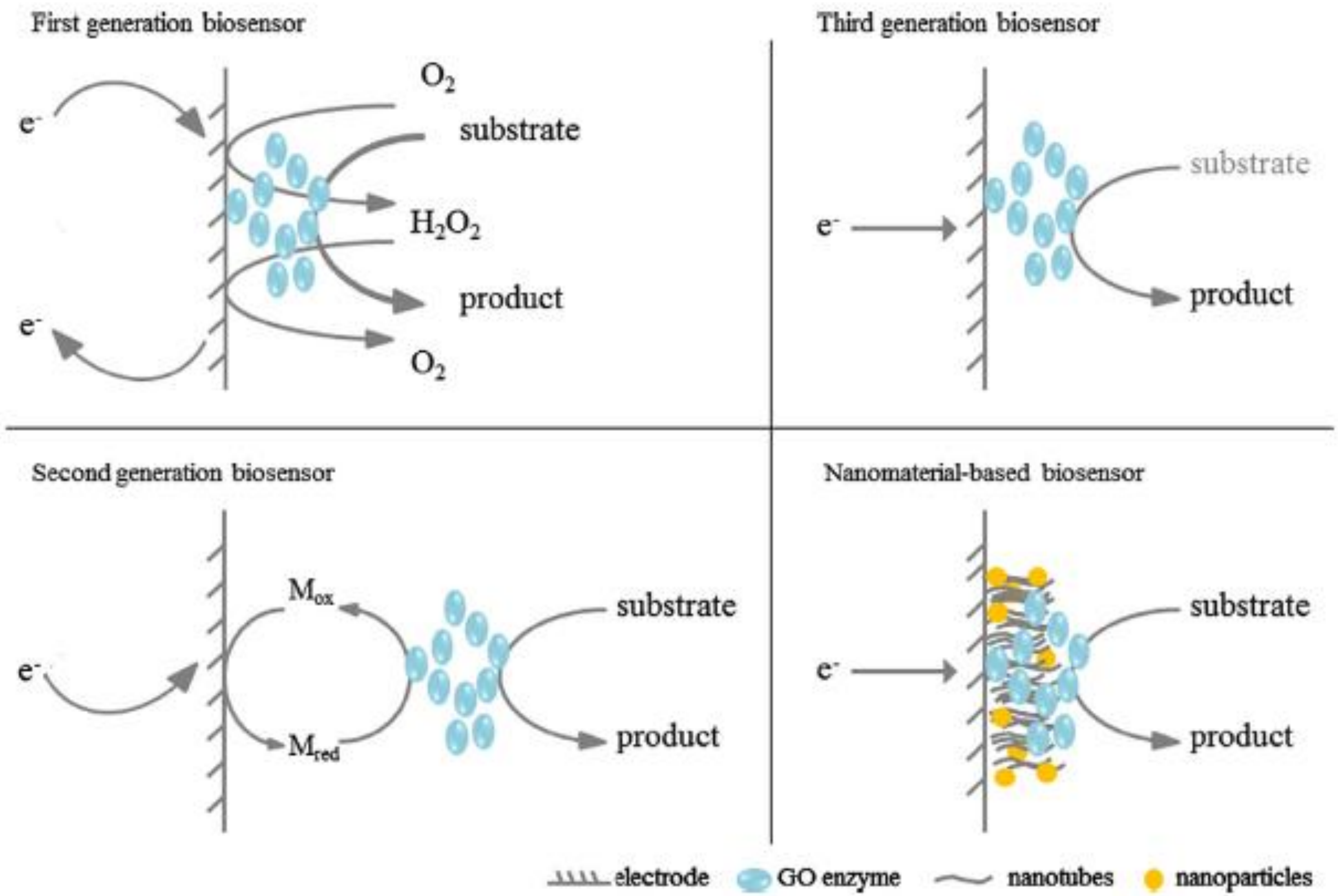
- To create conditions in which the oxidation of enzymatically generated H_2O_2 can be achieved at a lower applied potential, by creating a highly catalytic surface.
- Metallization is achieved by electrodepositing the relevant noble metal on to a glassy carbon electrode using cyclic voltammetry.
- Most promising ones: platinum, palladium, rhodium and ruthenium.

Amperometric transduction

Polymers

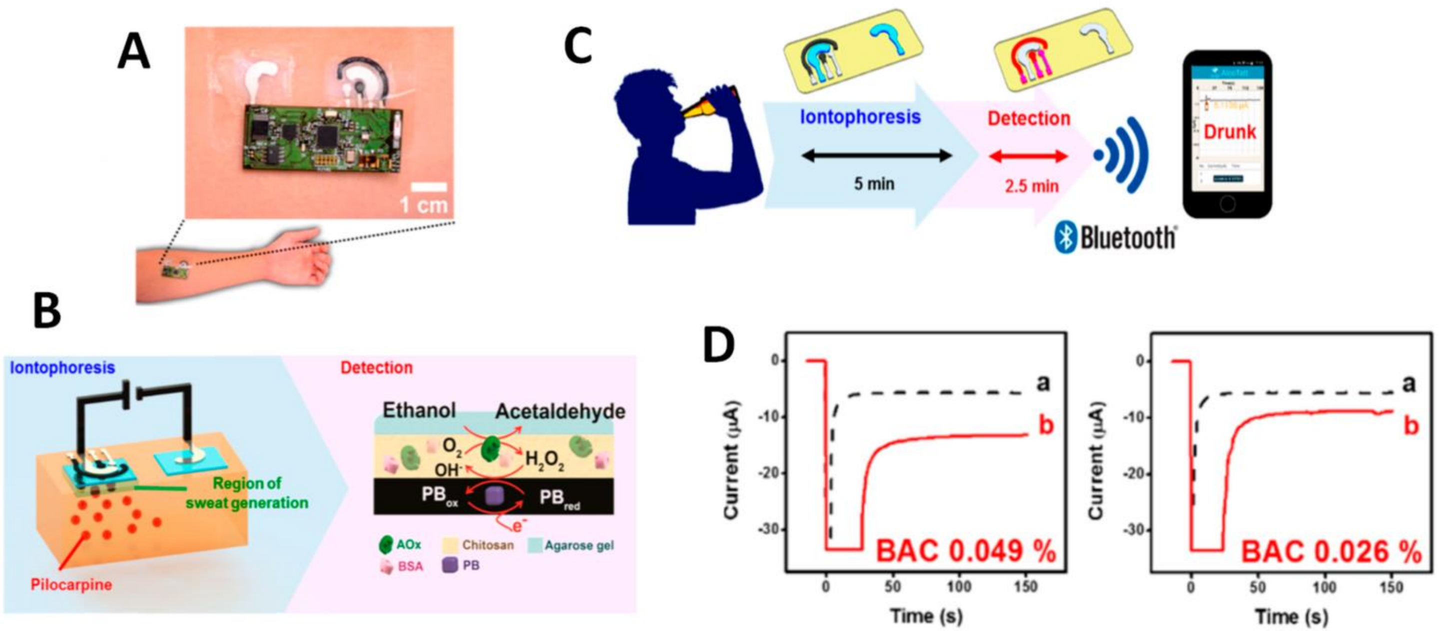
- polymers could be used to prevent interfering species from reaching the electrode surface.
- Ex: polypyrrole. A polypyrrole film has to be in the reduced state to become permeable for anions. If the film is oxidised, no anion can permeate.

Amperometric sensors



Noninvasive Alcohol Monitoring Using a Wearable Tattoo-Based Iontophoretic-Biosensing System, *ACS Sens.* 2016, 1, 8, 1011–1019

- wearable tattoo-based alcohol biosensing system for noninvasive alcohol monitoring in induced sweat.
- The wearable prototype enables the transdermal delivery of the pilocarpine drug to induce sweat via iontophoresis and amperometric detection of ethanol in the generated sweat using the alcohol-oxidase enzyme and the Prussian Blue electrode transducer.
- The new skin-compliant biosensor displays a highly selective and sensitive response to ethanol.



Alcohol iontophoretic-sensing tattoo device with integrated flexible electronics applied to a human patient (**A**); schematic diagram of constituents in the iontophoretic system (left) and processes involved in the amperometric sensing of ethanol (right) (**B**); scheme of the wireless operation for transdermal alcohol sensing (**C**); amperograms recorded before (a) and after (b) drinking alcohol beverage (**D**). BAC (blood alcohol concentration) recorded by a breath analyzer. Potential step to −0.2 V vs. Ag/AgCl.

Potentiometric transduction

- A potentiometric biosensor monitors the potential (relative to a reference) under zero current conditions.
- The potential generated is directly proportional to the logarithm of the analyte concentration ($E = Eo + RT/nF \ln[\text{analyte}]$).
- Ion-selective electrodes are used to determine changes in concentration of chosen ions, e.g., hydrogen ions → pH electrode

Potentiometric transduction

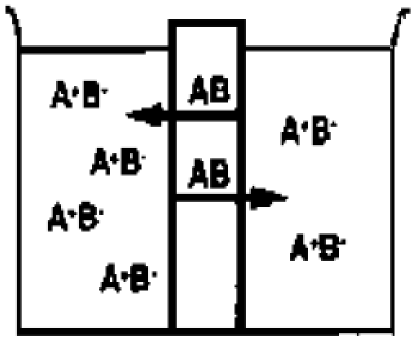
Ion Selective Electrode (ISE)

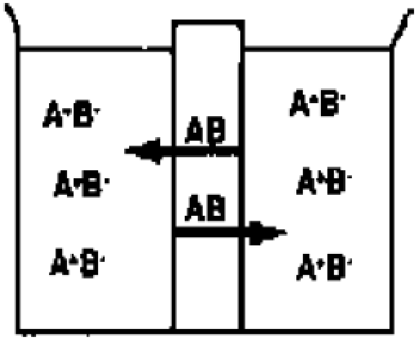
- Polymeric membrane electrodes are commercially available and routinely used for the selective detection of several ions such as K^+, Na^+, Ca^{2+}, NH_4^+, H^+, CO_3^{2-} in complex biological matrices.

Potentiometric transduction

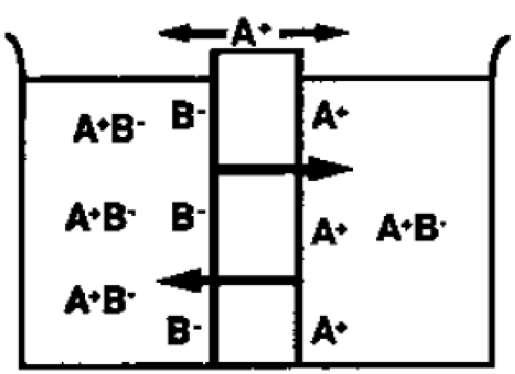
Ion Selective Electrode (ISE)

- If two solutions are separated by an ion-permeable membrane, they will equilibrate:





- If the membrane is permeable to only one species, a charge quickly develops which opposes further movement
- The charge is proportional to the difference in concentration on the two sides
- The total number of ions that diffuse is very small



Potentiometric transduction

Ion Selective Electrode (ISE)

☺Responsive over a wide concentration range

☺Not affected by color or turbidity of sample

☺Durable

☺Rapid response time

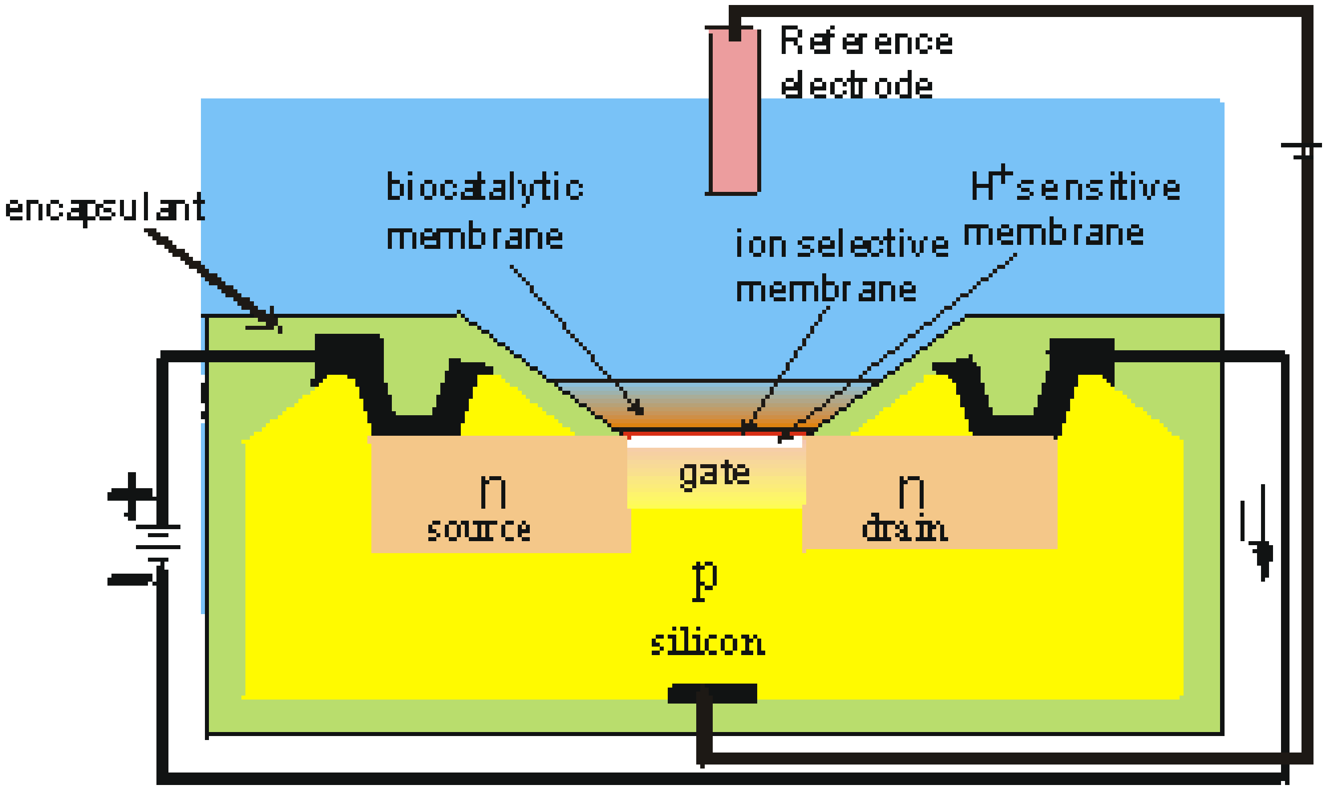
☺Real time measurements

☺Low cost to purchase and operate

☺Easy to use

Potentiometric transduction

Ion Selective Field Effect Transistors (ISFETs): miniature ISEs
CMOS (Complementary metal–oxide–semiconductor) technology to fabricate integrated circuits, is generally used
☺Miniaturized, solid state

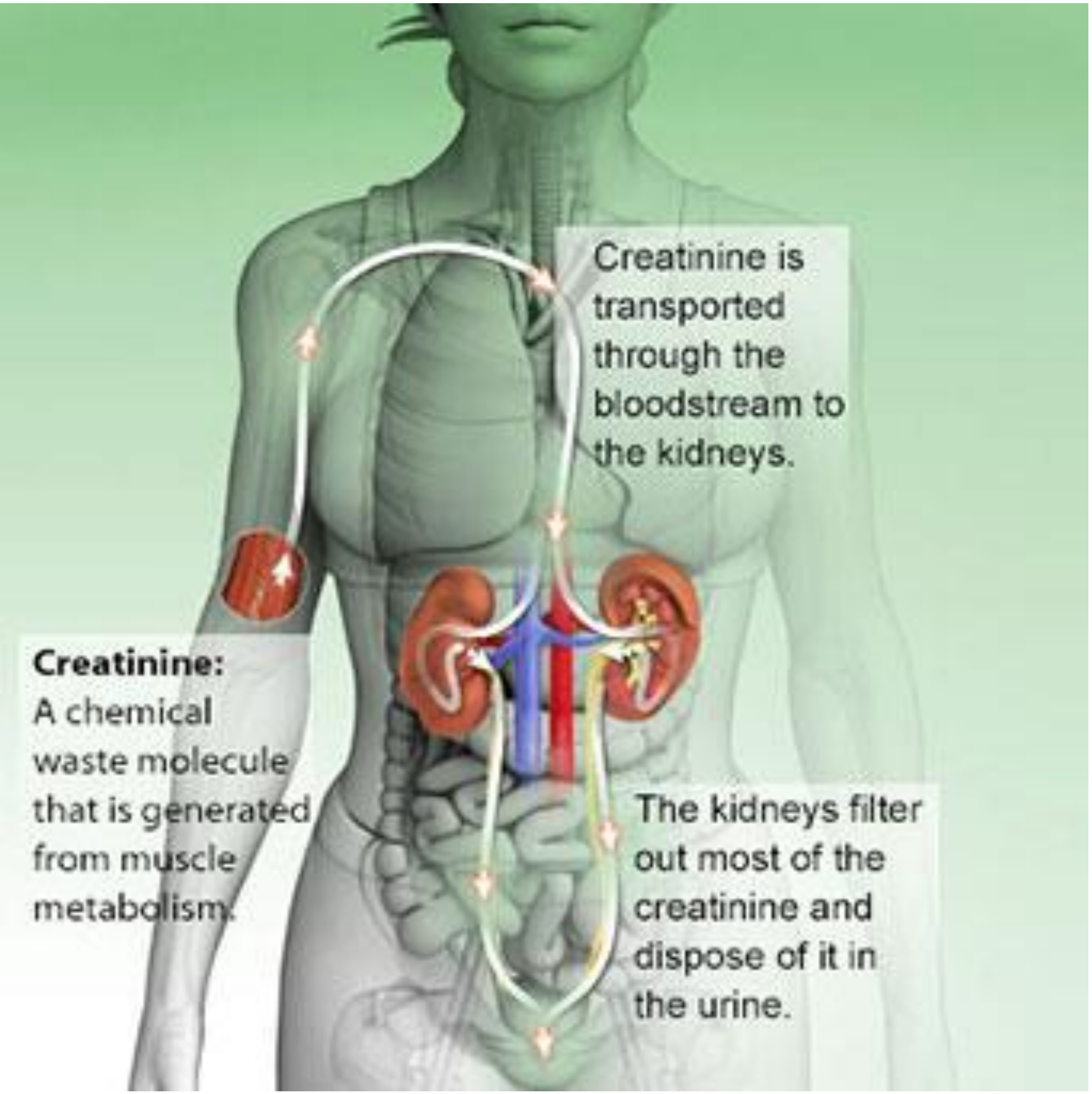


Potentiometric transduction

ISE-based biosensors

- The two main ones are for urea and creatinine.
- These potentiometric enzyme electrodes are produced by entrapment of the enzymes urease and creatinase, on the surface of a cation sensitive (NH_4^+) ISE

$$CO\left(NH_2\right)_2 + 3H_2O \xrightarrow{\text{urease}} CO_2 + 2NH_4^{\ +} + 2OH^-$$



- The kidneys maintain the blood creatinine in a normal range. Creatinine has been found to be a fairly reliable indicator of kidney function. Elevated creatinine level signifies impaired kidney function or kidney disease.

Amplified potentiometric transduction of DNA hybridization using ion-loaded liposomes

DOI: 10.1039/c0an00198h

- Amplified potentiometric transduction of DNA hybridization based on using liposome 'nanocarriers' loaded with the signaling ions is reported.
- The liposome-amplified potentiometric bioassay involved the duplex formation, followed by the capture of calcium-loaded liposomes, a surfactant-induced release and highly-sensitive measurements of the calcium signaling ions using a Ca2+ ion-selective electrode (ISE).
- The high loading yield of nearly one million signaling ions per liposome leads to sub-fmol DNA detection limits.

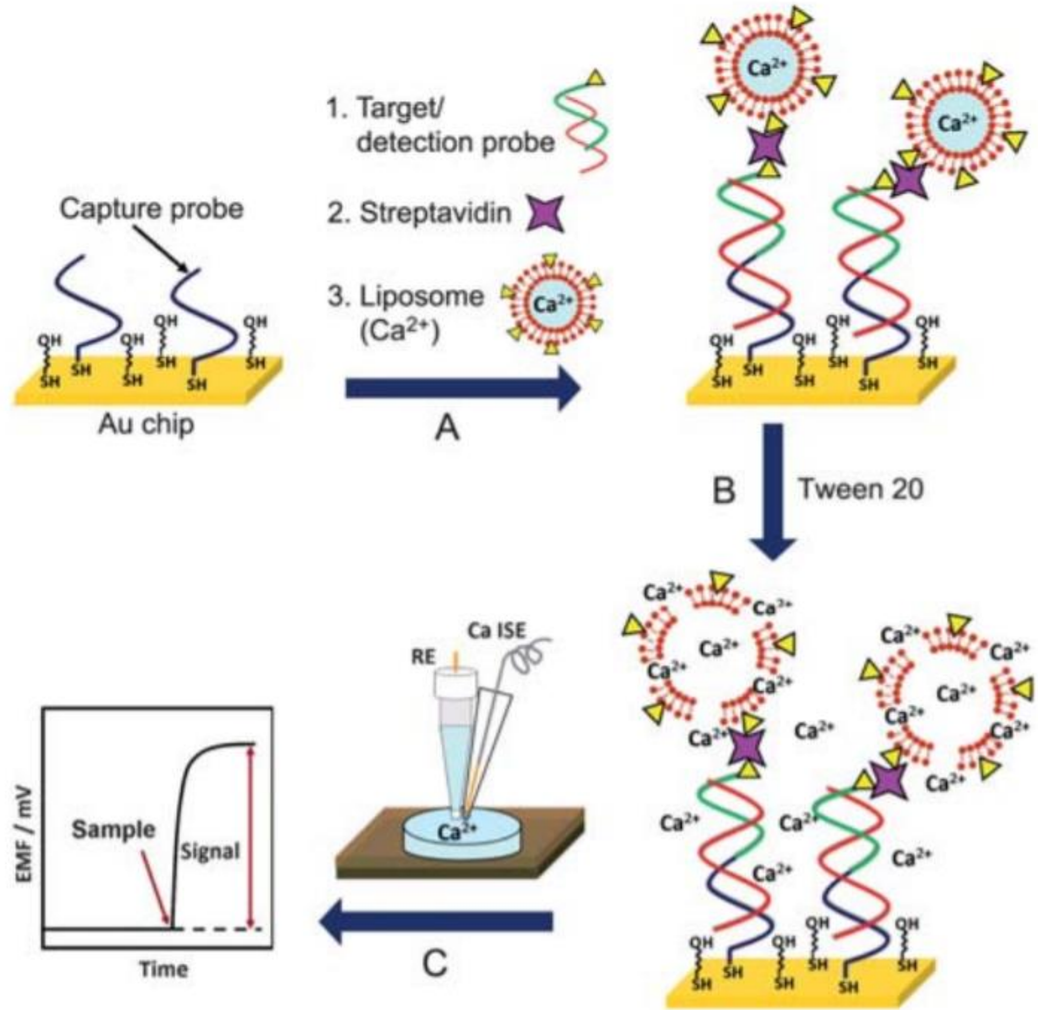


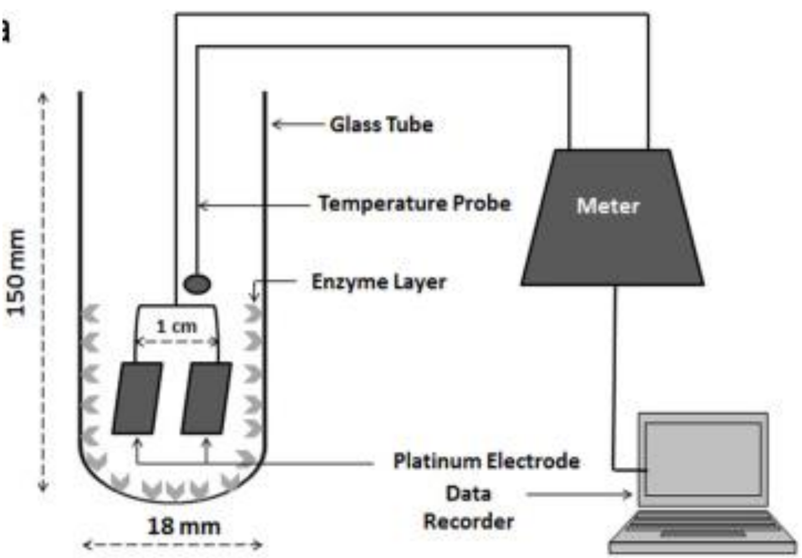
Fig. 1 Representation of the potentiometric detection of DNA hybridization based on ion-loaded liposomes and Ca^{2+}-ISE.

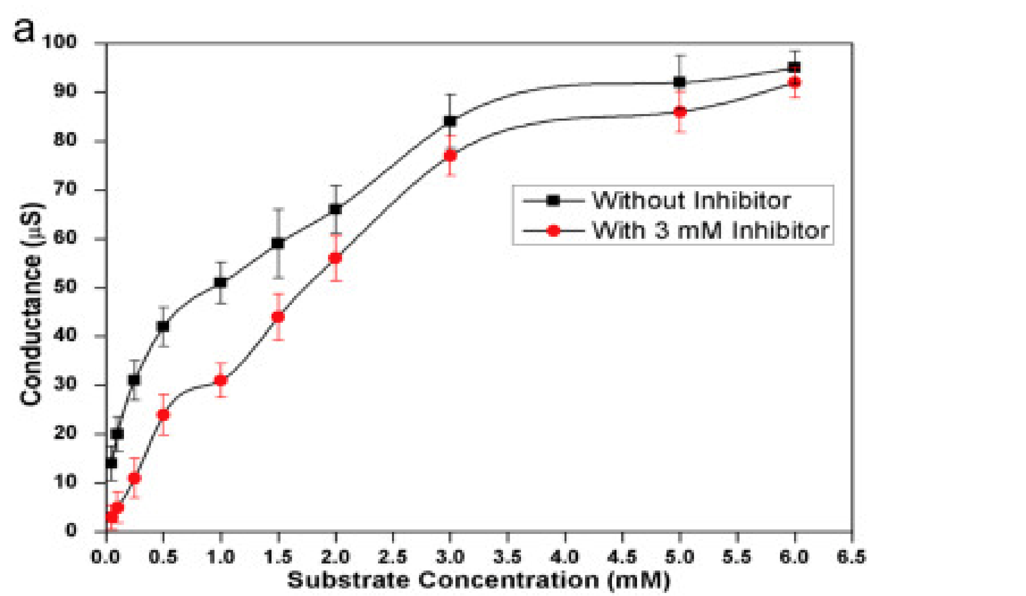
Conductometric transduction

- Conductivity is a measurement of the ability of a solution to conduct an electric current.
- Instruments measure conductivity by placing two plates of conductive material with known area and distance apart in a sample.
- Then a voltage potential is applied and the resulting current is measured.
- This is a technique where the changes in ionic concentrations are measured.
- If the biocatalyst produces ionic products, or consumes ions, this is often a convenient and simple technique.

- **Example: Alkaline phosphatase inhibition based conductometric biosensor for phosphate estimation in biological fluids**

In this study, a simple, novel, and cost-effective conductometric biosensor for the indirect determination of phosphate ions in aqueous solution has been demonstrated. The developed biosensor is based on the inhibition of the activity of alkaline phosphatase, immobilized on the glass internal surface.

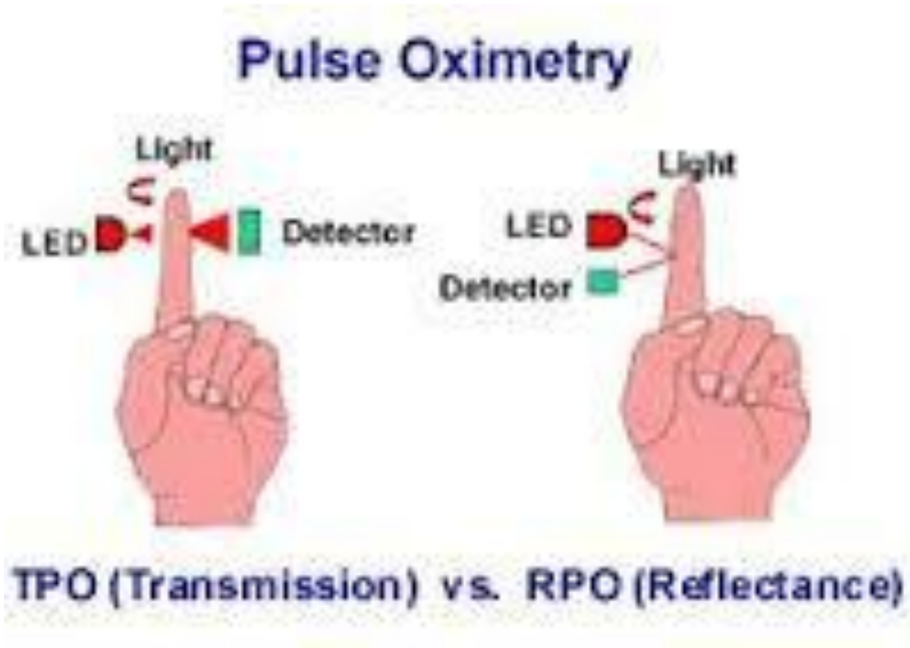




DOI: 10.1016/j.bios.2015.01.064

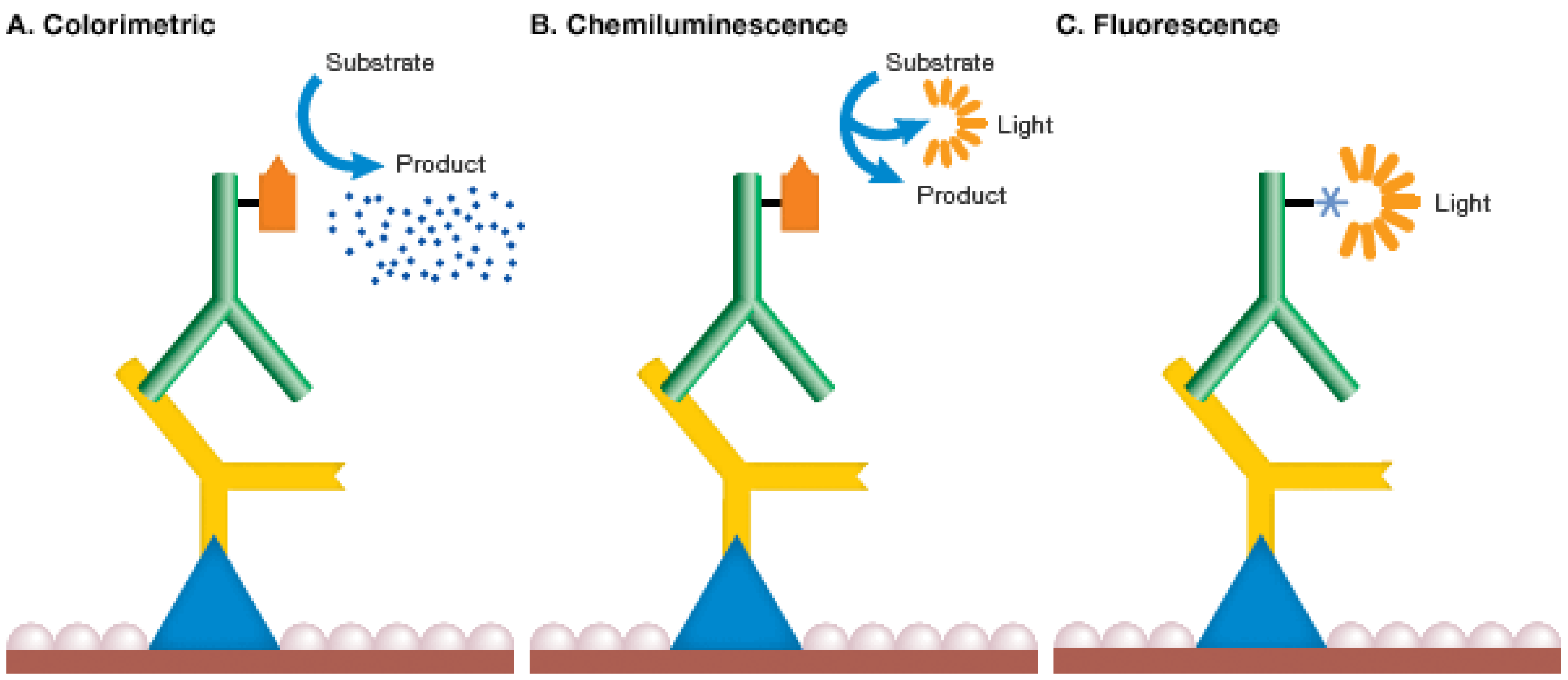
Optical Transducers

- Optical sensors rely on the optical transduction of the signal and comprise ultraviolet, visible and infrared spectrophotometry in transmission or reflectance modes.



- Absorption, refractive indices, fluorescence, phosphorescence, chemiluminescence, etc., can be used in monitoring
- Can be miniaturized by using different systems like optical fibres

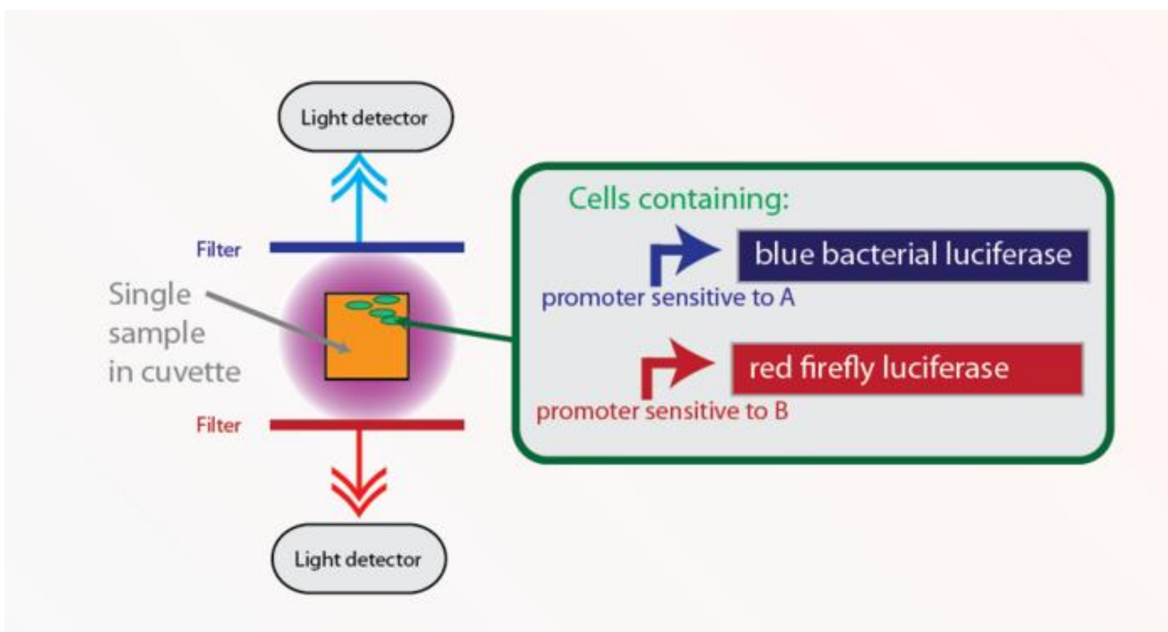
Protein detection- Western Blot (http://www.bio-rad.com/en-tr/applications-technologies/detection-methods)



Mechanism of detection chemistries. In each method of western blot detection, a detectable signal is generated following binding of an antibody specific for the protein of interest. In colorimetric detection (A), the signal is a colored precipitate. In chemiluminescence (B), the reaction itself emits light. In fluorescence detection (C), the antibody is labeled with a fluorophore

Optical Transducers

a mass produced
bioluminescent biosensor



Optical Transducers

☺miniaturization is possible

☺*in vivo* measurements are possible

☺diode arrays allow for multi-analyte detection

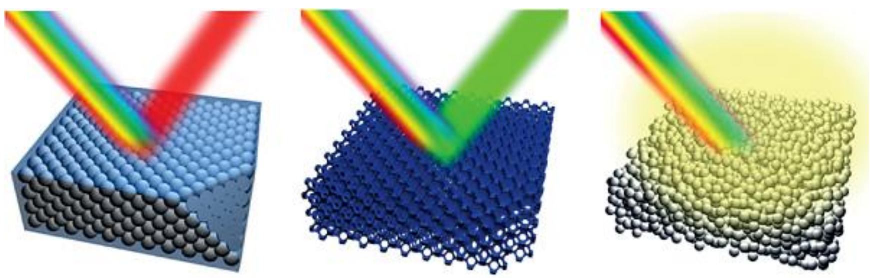
☺signal is not prone to electromagnetic interference

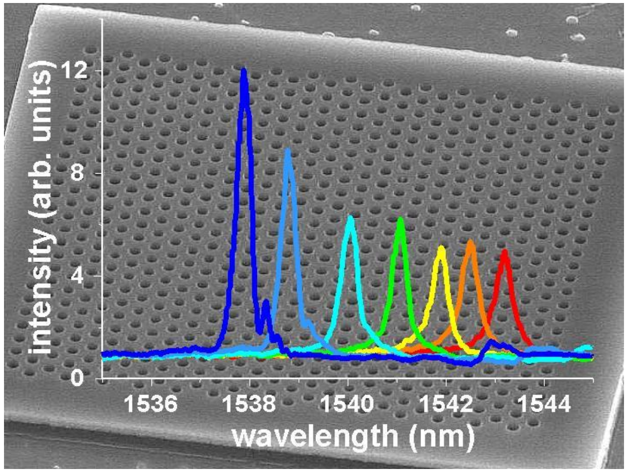
☹Ambient light is a strong interferent

☹Fibres are expensive

Optical Transducers

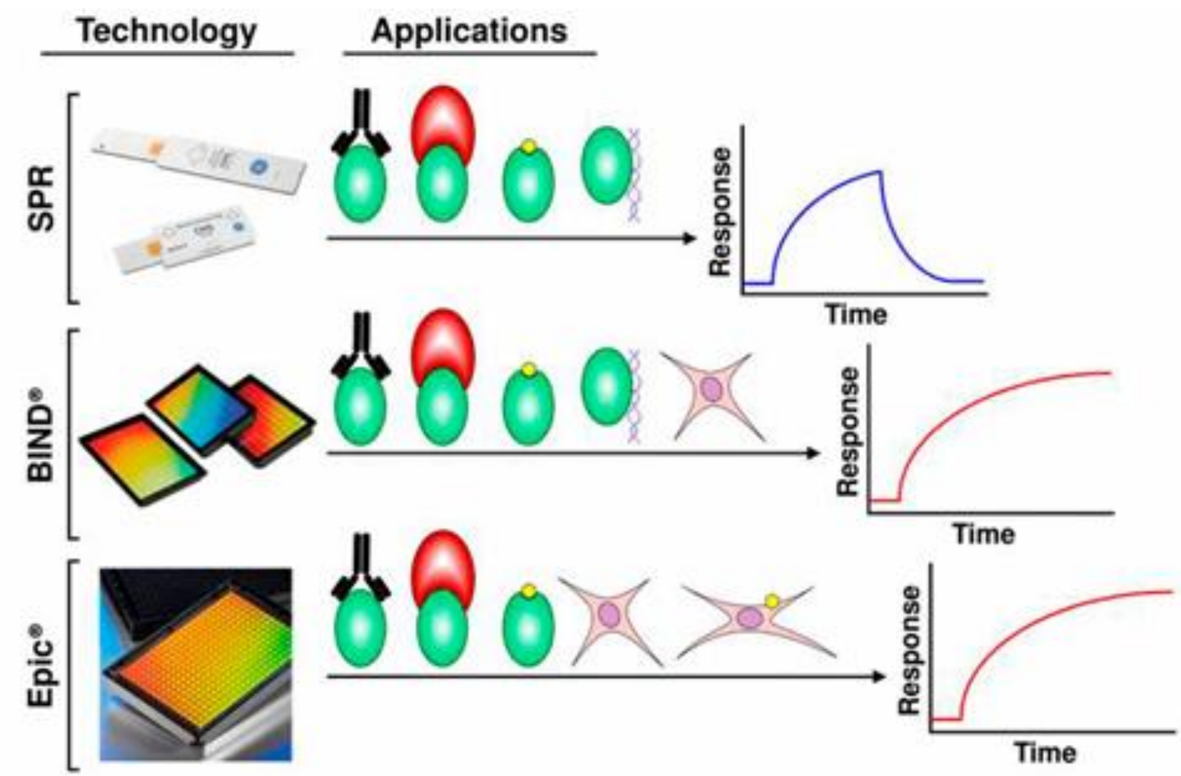
- **Photonic crystals (PC)** are periodic optical nanostructures that affect the motion of photons in much the same way that ionic lattices affect electrons in solids
- If the periodicity and symmetry of the crystal and the dielectric constants of the materials used are chosen appropriately, the Photonic Crystal will selectively couple energy at particular wavelengths, while excluding others
- They can be fabricated for one, two, or three-D.





Optical Transducers-PC

PC biosensors have been applied to the detection of antibody–antigen and small molecule–protein interactions, as well as cell-based assays

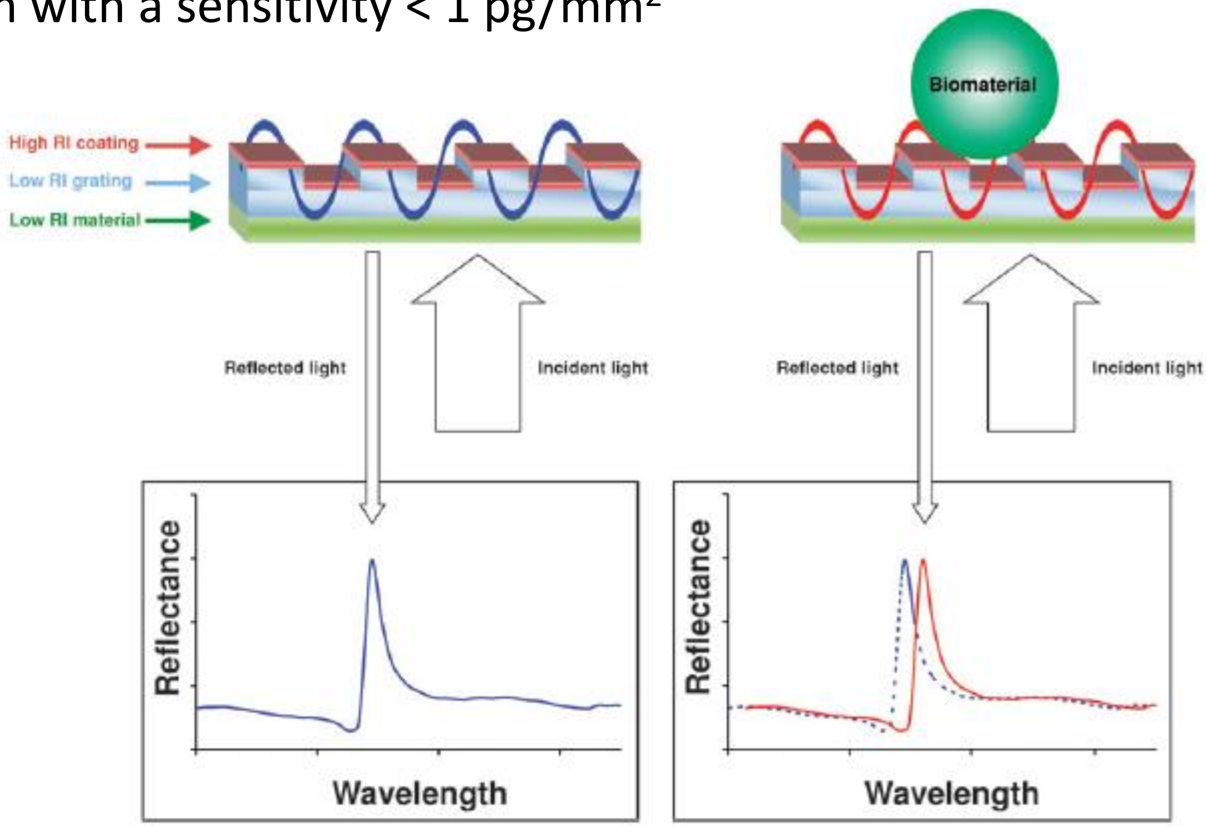


Heeresa and Hergenrother; 2011

Optical Transducers-PC

Ex: Biomolecular interaction detection system (BIND^{TM})

- PCs utilized in this system are composed of an epoxy-cured polycarbonate diffraction grating that is coated with a thin layer of TiO_2.
- Binding of macromolecules is monitored by shifts of nanometres in wavelength with a sensitivity < 1 pg/mm^2

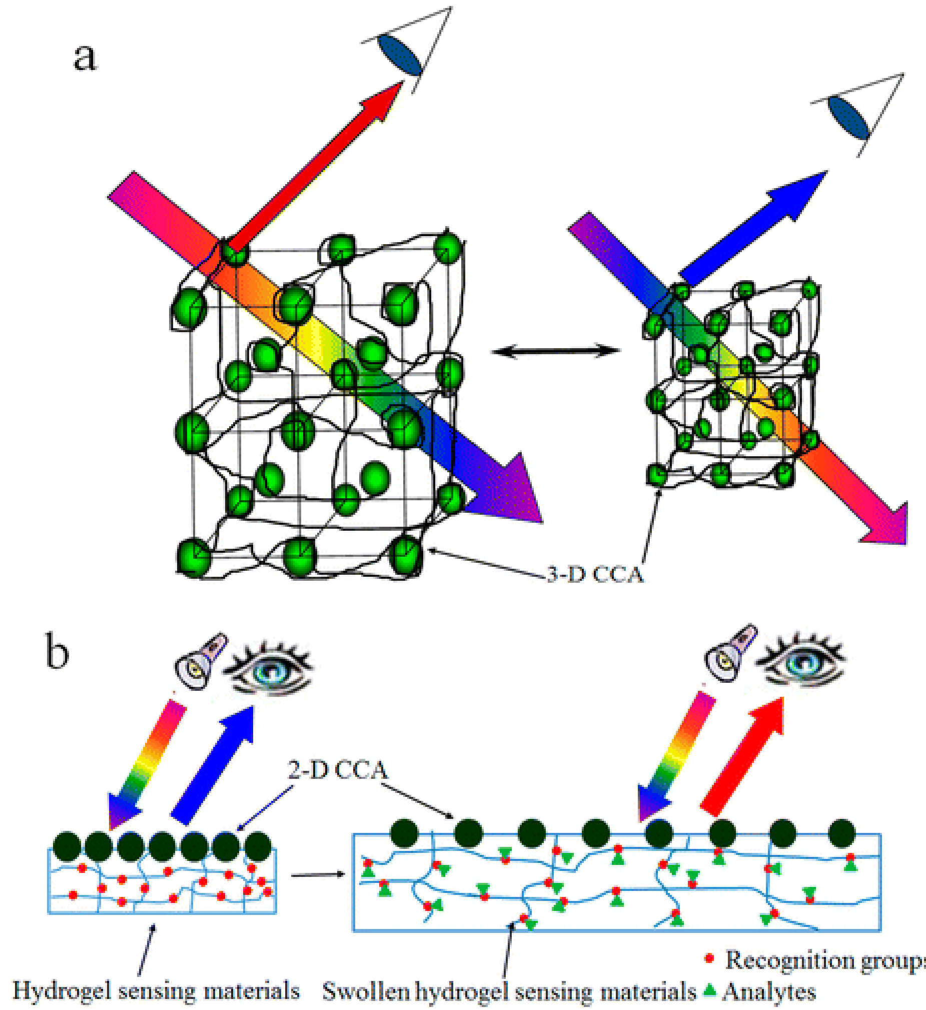


2-PC

Zhongyu Cai et al, Anal. Chem. 2015

Shrinking or swelling:

This alters the CCA (crystalline colloidal array) spacing, which shifts the diffracted wavelength and changes the diffracted color



(a) 3-D crystalline colloidal arrays (CCA) self-assembled because of electrostatic repulsion between particles. The spacings are ~200 nm, such that they diffract visible light. Polymerized CCA (PCCA) are formed by polymerizing a cross-linked hydrogel networks around CCA. The hydrogel is functionalized with a molecular recognition agent, which interacts with the analyte to actuate either shrinking or swelling. This alters the CCA spacing, which shifts the diffracted wavelength and changes the diffracted color. (b) 2-D CCA sensing materials are formed by attaching a 2-D CCA onto a hydrogel containing functionalized recognition groups

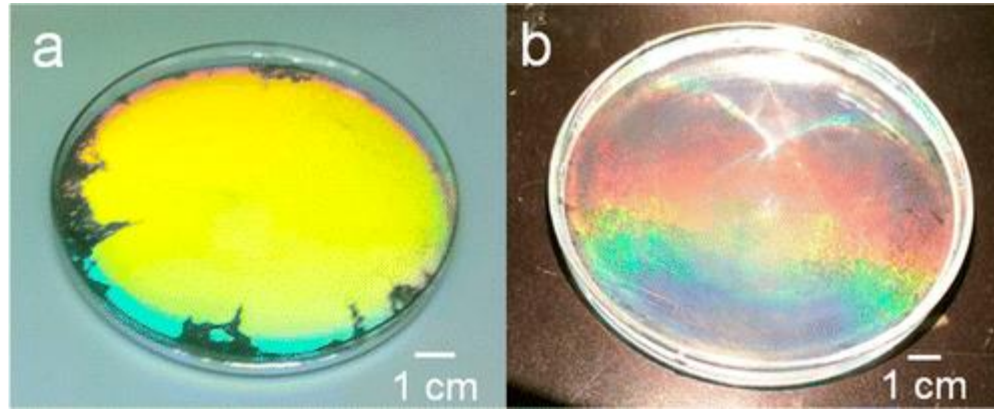
2-PC

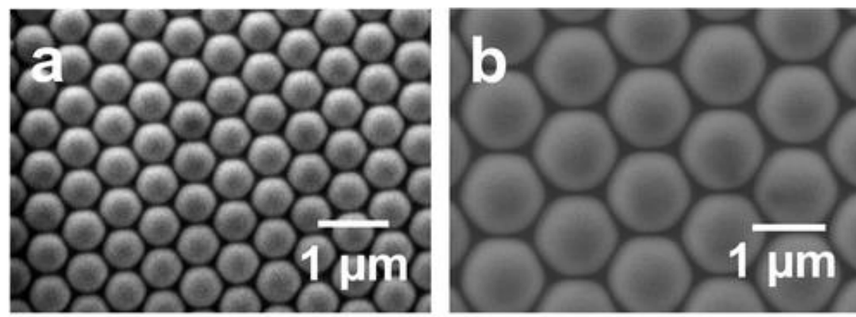
Zhongyu Cai et al, Anal. Chem. 2015

Diffraction colors of a 2-D CCA

(a) of ~580 nm diameter PS colloidal particles on a mercury surface

(b) of 650 nm diameter PS colloidal particles on a water surface





2-PC

Zhongyu Cai et al, Anal. Chem. 2015

(a) Complex formation between glucose (in furanose form) and two boronates

(b) Digital photograph of glucose sensing photonic crystal at different [glucose]