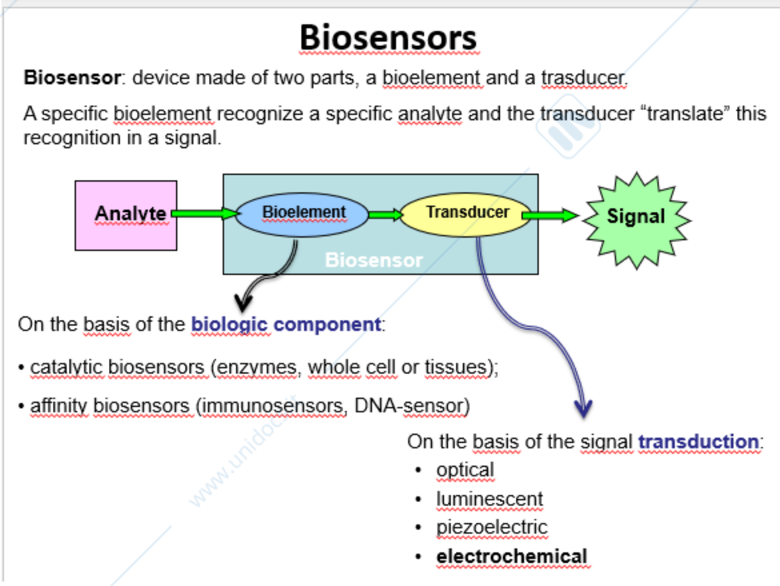
12/10/22 Biosensors Arbizzani

Introduction to electrochemical biosensors

A **biosensor** is a device made of two parts: **a bioelement and a transducer**. A biosensor, to be defined so, need to contain a bioelement inside.

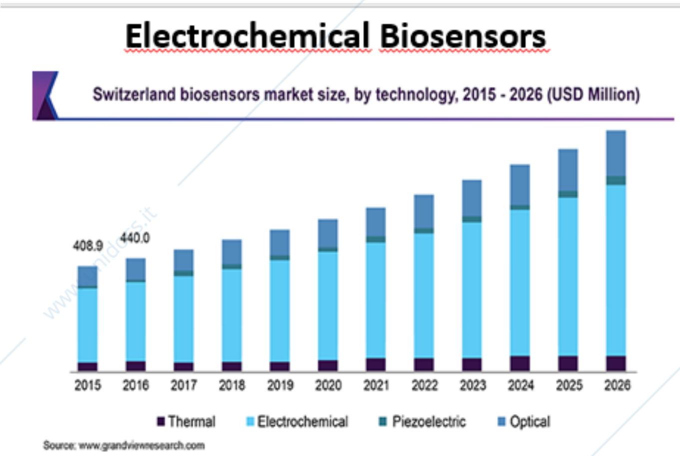
The bioelement is used to recognize the specific analyte present in the sample.

The transducer translate the recognition of the analyte into a signal that can be interpreted in some ways. The bioelement can be something like an enzyme, a DNA chain, an antbody, a cell, a tissue.



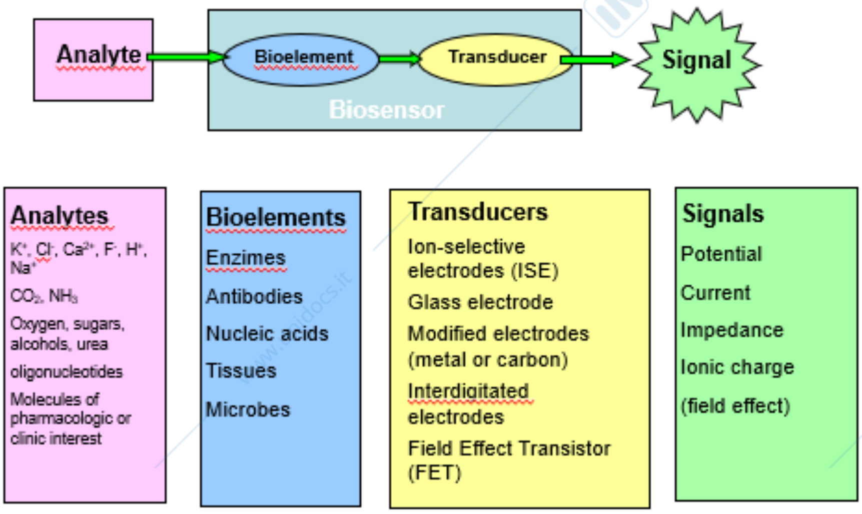
Regarding the transducer we can have different transduction technologies: optical, luminescent, electrochemical, piezoelectric ecc.

This course is about electrochemical biosensors.



The demand for electrochemical biosensors is expected to increse steadily in he next years.

The main field in which biosensors are requested is the biomedical field, expecially for medical testing, like DNA sequencing, infectious disease diagnostics, cancer diagnostics and genetic testing.

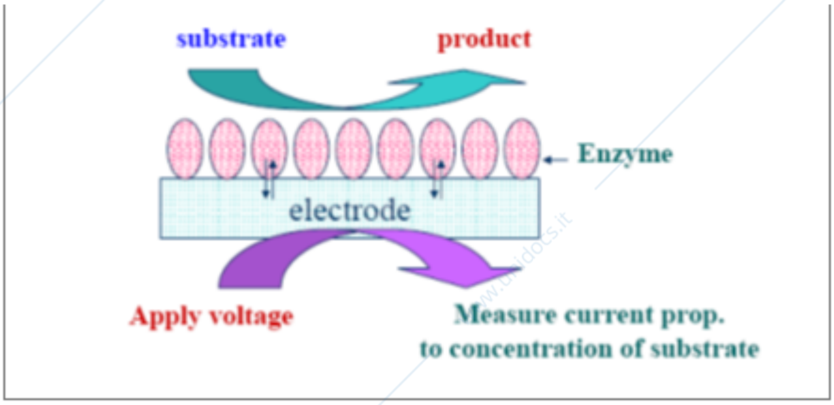


The analyte can be small molecules, but also big molecules like glucose, oligonucleotides or molecules with pharmacologica interest.

As transducer we can use ion-selective electrodes, glass electrodes, modified electrodes, field effect transistors.

The signal that we can produce is related to electrochemistry. It can be:

- Potential
- Current
- Impedance
- ionic charge.



An electrochemical biosensor is a biosensor with an electrochemical transducer (IUPAC, Pure Appl. Chem., Vol. 71, No. 12, pp. 2333-2348, 1999).

A biosensor works in this way:

1. current or a voltage is applied to the electrode
2. the reaction of the analyte with the bioelement cause a variation of the voltage or current.
3. This variation is the signal obtained by the biosensor.

If a voltage is applied, then I will measure the variation of the current. If I apply a current, I will measure a variation of the voltage.

Characteristics of electrochemical biosensors

The electrode has to be a **good electron conductor**. The electrode has also to be **suitable for the immobilization of the bioelement** on the bioelement. Sometimes the surface has to be modified to permit the formation of covalent bonds between the surface and DNA.

Suitable materials for electrodes are **platinum or carbon** as they are **good conductors** and also **tend to not react** with the components of the sample.

Usually in electrochemical biosensors the reaction that occur is a transfer of electrons. So, I need a detection system that can detect the variation in:

- Potential
- Current
- Resistance
- ionic charge.

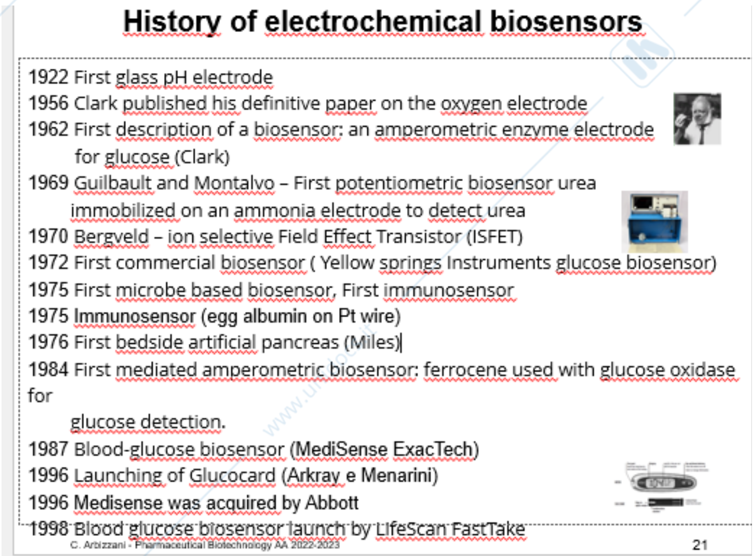
The **advantages** of electrochemical biosensors are:

- the easy incorporation within electronics
- easy to miniaturize
- can be used with solutions that are not transparent (blood for example)
- robustness (depends on the transduction system)
- good limit of detectability (depends on the transduction system)
- high sensitivity (depends on the transduction system)
- low response time (depends on the transduction system)

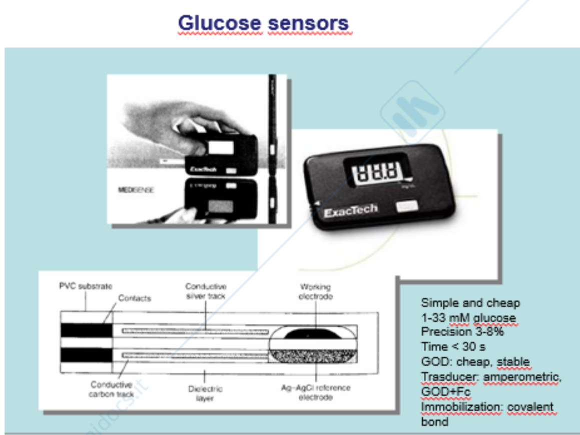
A desirable biosensor is

- independent from pH, T, stirring;
- response free from background noise;
- cheap, small, portable; should be used by not trained personnel.
- biocompatible (to stay in contact with the skin or under the skin

Historical note

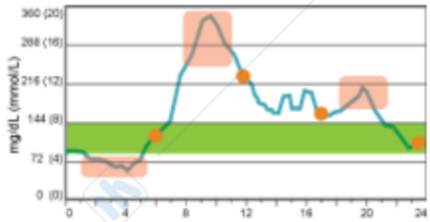


The first blood sugar analyzer is the YSI Blood Glucose Analyzer, Model 230 (1975). It was quite big and not portable. In 2002 the portable blood sugar analyzer Lifescan, One Touch®has been commercialized. Nowadays glucose sensors can be implanted, and the levels of sugar can be received on the smartphone.
In this slide you can see the evolution of electrochemical biosensors.
Modern biosensors are increasingly accurate, sensible e biocompatible.
In the future, the demand for blood sugar analysers will grow because of the increasing numbers of people affected by diabetes. Accurate sensors could help in avoiding the consequences of this disease.



A glucose sensor contains a working electrode and a reference electrode. These devices are usually amperometric, so they measure a current. When the strip with the blood is put inside, a defined potential is applied between the two electrodes. When the potential is applied, a reaction occur and electrons are produced. The intensity of the current is proportional to the concentration of sugar in the blood.

The gold standard for the control of diabetes should be the continuous monitoring of glucose. Some sensors of this kind exist and are linked to small pumps that inject small quantities of insulin and glucagon, acting like an artificial pancreas.



http://www.dexcom.com/seven-plus

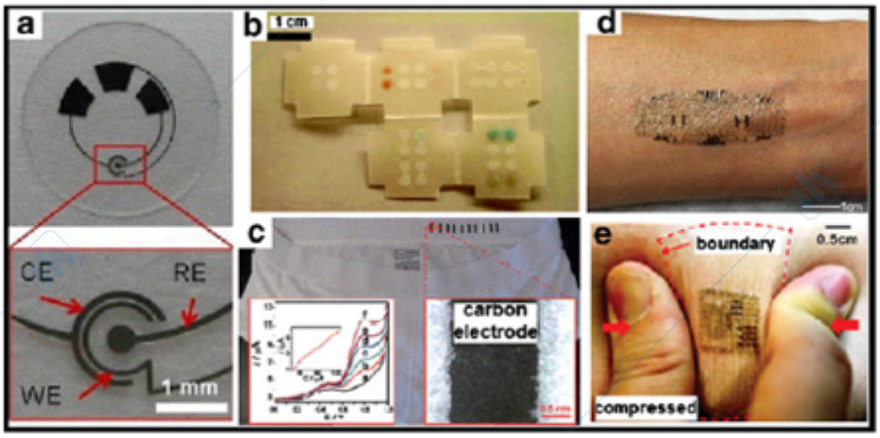
Lactate sensors

Lactate sensors also exist. They are used in the field of sport but also on patients because lactate can be used to monitor the state of health of people in with hearth failure or shock.

This kind of sensors can be attached to the skin or inserted in contact lenses.

They are used on people that have to face intense activities wearing heavy clothes like soldiers, astronauts, people that have to work underwater.

Lactic acid / lactate



This is another portable analyser that can do many different analysis of blood simply by using different cartridges. This is an example of point-of-care. It can measure:

- lactate
- haematology parameters
- electrolytes
- cardiac markers
- coagulation factors
- blood gases
- hormone

The *i-STAT*® *System*: Advanced Handheld and Test Cartridge Blood Analysis System that Delivers Lab-quality Results
i-STAT System enables patient-side blood testing, so that health care professionals can access real-time, lab-quality results within minutes, rather than hours. https://www.pointofcare.abbott/int/en/offerings/istat

i-STAT System provides information needed to make treatment decisions sooner, which may lead to enhanced quality of care and improved system efficiency.

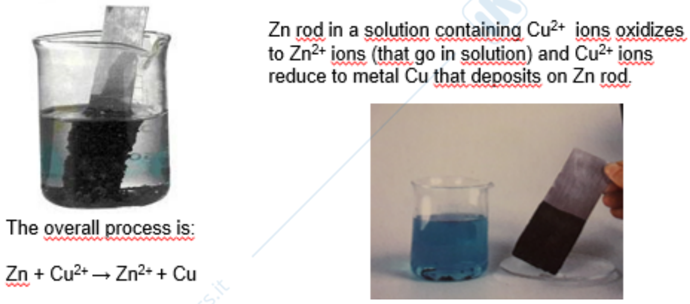
Small volumes of blood (17-95 μL) are needed.

Basics of electrochemistry

What is an electrochemical cell?

An electrochemical cell is a cell where there is a circulation of electrons. The circulation of electrons produces some energy. Batteries contains electrochemical cells that produce the energy used by the devices.

Redox reactions always happen in electrochemical cells. A redox reaction is a chemical reaction where a species is oxidized and another one is reduced. Not every redox reaction produce energy. For example, the reaction



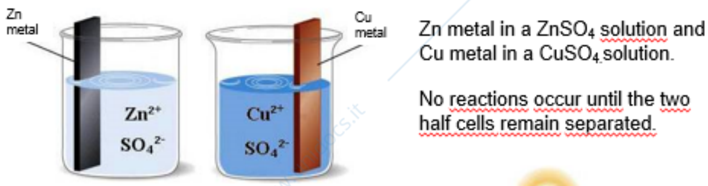
$Zn + Cu^{2+} \rightarrow Zn^{2+} + Cu$, if it takes place in a single container, does not produce energy as there is no flow of electrons.

But if you separate the two reactions you can force the electrons to circulate and to produce energy. This is what happen in an electrochemical cell.

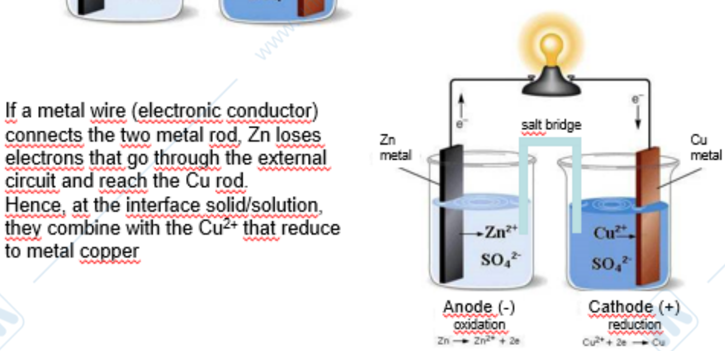
In an electrochemical cell the two semi-reactions are separated. In one container the copper is reduced and in the other the zinc is oxidised.

$$Cu^{2+} + 2e^{-} \longrightarrow Cu \qquad\qquad Zn \longrightarrow Zn^{2+} + 2e^{-}$$

One container has to contain zinc metal in a solution of zinc sulphate, the other contains copper metal in a solution of copper sulphate.



Both zinc sulphate and copper sulphate dissociate in solution giving zinc and copper ions.



In order to let the reaction happen, an **electrical connection** is needed between the two electrodes. The electrical connection needs some kind of resistance otherwise I will have a short circuit.

The **salt bridge** is needed to avoid the formation of a different in charge between the two containers. In fact, in one container Zn+ is forming and in the other Cu2+ is removed. To balance the charge, a tube containing a hight concentration of salts is connected to both the containers.

A **primary cell (or galvanic cell)** is a cell where the reagents are transformed and cannot be recharged. In a primary cell the reaction of discharging is spontaneous.

Batteries are cell that produce electricity from the reagents and that can be recharged using electrical energy. When the cell is recharging it can be defined as electrolytic cell.

A cell is composed of two electrodes with a solution of electrolytes in the middle. The electrodes are electronic conductors whereas the solution is an ionic conductor.

A battery can be composed of more than one cell.

Electrochemical sensors usually contain two electrodes so they can be referred as electrochemical cells,

First Ohm's law **I=E/R**

I = current (in ampere, A); E = voltage (or potential) applied (in volt, V); R = resistance (in ohm, W)

Definition of current: I (A) = Q (Coulomb) / t (s)

Faraday constant (F): $1{,}60 \cdot 10^{-19}$ C x $6{,}023 \cdot 10^{23}$ mol^{-1} = **96485 C/mol e^-**

2nd Ohm's Law: **R= ρ x l /A**

ρ = specific resistance or resistivity (in Ω cm)

l = length of the conductor (cm)

A = section area of the conductor (cm2)

Conductance: **Λ = 1/R** (used for ionic conductors)

Λ = conductance (in siemens, S o W^{-1}) is the reciprocal of the resistance

Specific conductivity: **σ = 1/ ρ**

(Used for ionic conductors, depends on the ionic concentrations, the ions species and the temperature)

Anode: is the electron where the oxidation occurs

Cathode: is the electrode where the reduction occurs

$$Zn_{(s)} \longrightarrow Zn_{(aq)}^{2+} + 2e^-$$

$$Cu_{(aq)}^{2+} + 2e^- \longrightarrow Cu_{(s)}$$

Each half-reaction take place at a well-defined potential measured versus a reference electrode **(standard hydrogen electrode, SHE).**

Each half reaction of reduction can be classified based on the potential it occurs using as a reference the standard hydrogen electrode.

Strong oxidants have high V° values

High reductants have low V° values