# Nanobiosensors

Biosensor technology combines the knowledge of biology with advances in microelectronics.

A biosensor usually consists of three parts:

1. **biological element** – cells, enzymes, organelles, DNA or antibodies
2. **interfaces** – polymer thin film, chemically modified surface
3. **converter**

The biological element specifically detects the presence of the detected substance - the analyte. The interface connects the biological element to the transducer. The transducer converts the biochemical signal into other, more easily quantifiable and measurable signal forms (e.g. electrical, thermal or optical).

A biosensor can therefore be defined as a detector that combines a biological and physicochemical element to identify an analyte.

A specific type of biosensors are nanobiosensors with dimensions moving in the nanometric scale. Despite the fact that synthetic nanobiosensors are new to us, they have existed in the biological world for centuries. Plants use them to detect sunlight, fish are able to detect tiny vibrations in the water with them, and many types of insects analyze pheromones with their nanosensors. The potential of man-made nanobiosensors lies in the fact that they could become a tool for investigating biological cellular processes in an organism. Their application in medicine is promising.

Important nanobiosensors from the point of view of use in medicine are: [1]

## Sensors with beam arrangement

These are sensitive mechanical sensors. Absorption of analyte to target molecules on the surface of the beam induces surface tension and subsequent bending of the beam. Bend detection occurs most often with a laser (optical method), which is problematic in opaque liquids, such as blood, because it absorbs the emitted light. For this reason, other "reading" methods, e.g. piezoelectric, are more suitable. The piezoresistor is built into the beam. During detection, there is a change in resistance, which is measured as an electrical signal in micro and nanoelectromechanical systems (MEMS, NEMS).

### Artificial nose

It is a nanotechnological olfactory sensor - NOSE, which is used to identify smells. Compared to a natural olfactory organ, the advantage of an artificial device is that it is tireless, can work in an environment that is harmful to humans, and achieves reproducible results. The device consists of eight silicon beams, their upper surface is coated with a 2 nm layer of titanium, a 20 nm layer of gold and a layer of polymer. The detected gas diffuses into the polymer, which subsequently causes it to bud and bend the beam. Beam deflection is measured by 8 lasers.

### Detection of bacteria, mold and viruses

An example is the detection of Escheria coli bacteria , which is based on the interaction of specific antibodies with antigens on the surface of their cell membranes. The interaction causes an increase in mass, which is detected by the instrument. The immobilized E. coli are placed on the carrier during the analysis. The detection sensitivity is on the order of one bacterium, which corresponds to a mass of approximately 1 pg.

## Nanotube-based sensors

The basic building block of sensors are carbon nanotubes – allotropic modifications of carbon with a cylindrical nanostructure. There are a number of possible applications of nanotube-based sensors in medicine:

- sensors monitoring the level of glucose in blood (fluorescence biosensor) and urine
- sensors for capnography (measurement of the concentration of carbon dioxide in the breath)
- sensors detecting DNA
- biosensors for the detection of the nitric oxide radical NO, which plays an important role in the body (causes smooth muscle vasodilatation, erection of the penis, fulfills the function of a neurotransmitter)
- platforms for biosensing and detection of dopamine and ascorbic acid for the purpose of diagnosing Parkinson's disease

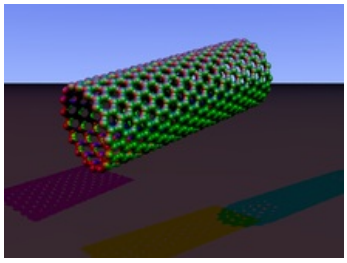
### Fluorescent biosensor

It serves for continuous monitoring of the blood glucose level. It is implanted into the tissue, where it is subsequently excited by a laser. Carbon nanotubes, of which the sensor is composed, are encapsulated in a sensitive protein. Their functionalization occurs with yellow blood salt (K4[Fe(CN)6]), sensitive to hydrogen peroxide. Glucose is converted by the enzyme glucose oxidase into gluconolactone, with hydrogen peroxide being produced as a byproduct. Hydrogen peroxide reacts with the cyanoferrate ion of yellow blood salt. The reaction

results in a change in the electron density of the nanotube, thus also in its optical properties. The higher the concentration of glucose in the blood, the brighter the carbon nanotube will glow. The sensor is not yet used in medical practice, but successful analyzes of blood samples in vitro have been performed . (19,24,25) [1] [2]

### Nanotube-based sensors for capnography

Sensors for chemical gases have a significant application in medicine. One of them is a sensor based on carbon nanotubes coated with polyethyleneimine serving capnographic purposes. Measurement of carbon dioxide concentration in the breath is important because the level of carbon dioxide indicates the condition of the patient during the administration of anesthetic agents .



Zig-zag structure

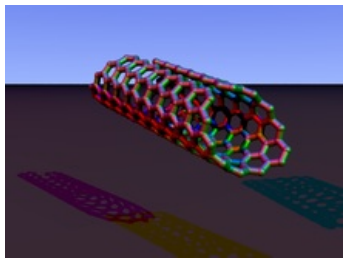
## Nanowire-based sensors

These are sensitive sensors controlled by an electric field. The nanowires making up the sensors are functionalized with specific surface receptors that allow them to work in solution. Use in medical and biological fields:

### Electrical detection of viruses

The semiconductor silicon nanowires forming the nanosensor are assembled as transistors controlled by an electric field (FET transistors). The sensor on the surface carries antibodies against the virus in question. After the detected virus binds to the antibody, the conductivity of the semiconductor nanowire changes from basic to a certain value. After the virus is released, the conductivity will return to its original value. By monitoring changes in conductivity, the virus can be identified.

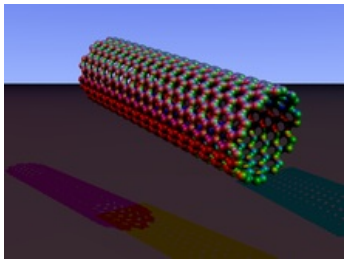
[1] [3]



Chiral structure

## Bio-bar code assay

Among the main problems of classical methods of protein or antigen detection is their relative insensitivity to target molecules. Therefore, they do not allow establishing a diagnosis in the early phase of the disease. Therefore, highly sensitive tests have been developed that are able to detect very low concentrations of pathogenic biomarkers. In a simplified way, the accuracy of detection can be imagined as being able to analyze a grain of salt in a swimming pool. An important highly sensitive test developed by Mirkin's group is the so-called "bio-bar code assay". The method makes it possible to analyze attomolar concentrations of the determined substances (antigens, antibodies, DNA of target molecules - targets).



Armchair structure

The test uses two types of probes:

1. gold nanoparticle probes – functionalized with hundreds of identical hybridized DNA oligonucleotides (also called "barcoded DNA" because they represent an identification tag)
2. probes of polyclonal antibodies and magnetic microparticles - functionalized with monoclonal antibodies

Polyclonal and monoclonal antibodies bind to the same target protein. By binding, they squeeze the protein between the gold nanoparticle and the magnetic microparticle, creating a so-called "sandwich" structure. After removing the "sandwich" from the solution by applying a magnetic field , the DNA chains with the barcode will be released and subsequently detected. The test can be used to detect free prostate-specific antigens (PSA), the presence of which indicates prostate cancer. The method makes it possible to identify the disease in the embryo before its symptoms appear. Early diagnosis leads to effective treatment. The test can also be used to examine blood for the presence of HIV and prions (Creuzfeldt-Jakob disease).

## Links

### References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- PATOLSKY, Fernando – LIEBER, Charles M. *Nanowire nanosensors* [online]. [cit. 2015-11-04]. <http://www.sciencedirect.com/science/article/pii/S1369702105007911>.

1. PRNKA, Tasilo – ŠPERLINK, Karel. *BIONANOTECHNOLOGIE NANOBIOTECHNOLOGIE NANOMEDICÍNA* [online]. [cit. 2013-02-07]. <http://www.nanotechnologie.cz/storage/nanotechnologie200610.pdf>.
2. PICKUP, John C – HUSSAIN, Faeiza – BIRCH, David J.S, et al. *Fluorescence-based glucose sensors* [online]. [cit. 2013-02-07]. <https://sensor.phys.strath.ac.uk/pdf-library/Fluorescence-based%20glucose%20sensors.pdf>.

3. PATOLSKY, Fernando – LIEBER, Charles M. *Nanowire nanosensors* [online]. [cit. 2013-02-07]. <http://www.sciencedirect.com/science/article/pii/S1369702105007911>.