Biosensors in our Daily Life

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Abstract

A biosensor is any piece of hardware that interacts with a biological or physiological system to acquire a signal for either diagnostic or therapeutic purposes. Data gathered using biosensor are then processed using biomedical signal processing techniques as a step toward facilitating human or automated interpretation. Biosensors are used in almost all the fields-engineering, medicine, nanotechnology, science, cancer diagnosis, DNA analysis, food analysis, blood tests and waste water treatment. Biosensors are pollution free, environmental friendly, easily available, inexpensive, reusable, recyclable and reliable. The given paper explores the importance of phone oximeter, FRET- Foster Resonance Energy Transfer, medical telesensors and miniaturized devices.

Keywords - Biosensor, Engineering, FRET, Sensors

Introduction

A biosensor is an analytical device for the detection of an analyte that combines a biological component with a physicochemical detector component (Jusoh and Aziz, 2006; Zhao *et al.,* 2010; Omotaya *et al.,* 2008; Feng *et al.,* 2005; Gleason and Sherrianne, 2008). The body sends out very weak electrical signal, which must somehow be captured and converted into information that can be used by a healthcare worker. With the development of the EKG, for example, engineers managed to isolate a very small and noisy signal polluted by other signal from the body to provide a real-time display of the activity of the heart.

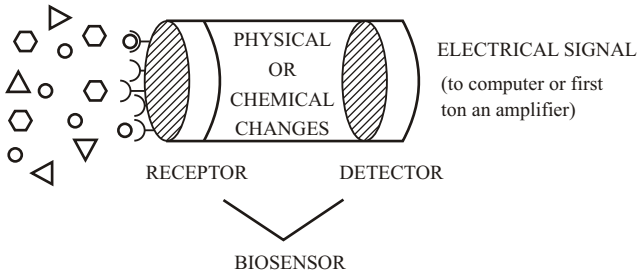

Figure 1: Biosensor (Adriano *et al.,* 2008).

In the area of imaging, the strong magnetic field used by MRIs prohibits the use of anything metal in conjunction with this valuable diagnostic tool. So, biomedical engineers have developed MRI-compatible electrodes and other instrumentation that allows, say, a patient with epilepsy to be monitored for changes in EEG activity during an MRI. A common example of a commercial biosensor is the blood glucose biosensor, which uses the enzyme glucose oxidase to break blood glucose down. In doing so it first oxidizes glucose and uses two electrons to reduce the FAD (a component of the enzyme) to FADH2. This in turn is oxidized by the electrode (accepting two electrons for the electrons from the electrode) in a number of steps. The resulting current is a measure of the concentration of glucose.

Pulse Oximeter

Given the concerns about the costs of healthcare, particularly in developing nations, low-cost alternatives to traditional monitoring equipment and machines are being sought. Rather than purpose-built physical boxes, the power of the cell phone is being used to both monitor and transmit biomedical signals. Pulse oximetry is used to monitor blood oxygen level; particularly in settings where anesthesia is administered. Researchers at the University of British Columbia are taking advantage of the computing power, real-time wireless communication and low cost of smart phones to provide pulse oximetry outside the hospital setting. Biosensor technology incorporates a wide range of devices, from the basic stethoscope, thermometer and blood pressure cuff to sophisticated PET scanners, MRI and ultrasound machine.

Immunosensors

Biosensors may be used in conjunction with enzyme-linked immunosorbent assays (ELISA). ELISA is used to detect and amplify an antigen-antibody reaction; the amount of enzyme-linked antigen bound to the immobilized antibody being determined by the relative concentration of the free and conjugated antigen and quantified by the rate of enzymic reaction. Enzymes with high turnover numbers are used in order to achieve rapid response. The sensitivity of such assays may be further enhanced by utilizing enzyme-catalyzed reactions, which give intrinsically greater response; for instance, those giving rise to highly colored, fluorescent or bioluminescent products. Assay kits using this technique are now available for a vast range of analyses.

Piezo-Electric Biosensor

Piezo-electric crystals (e.g. quartz) vibrate under the influence of an electric field. The frequency of this oscillation (f) depends on their thickness and cut, each crystal having a characteristic resonant frequency. A simple use of such a transducer is a formaldehyde biosensor utilizing a formaldehyde dehydrogenase coating immobilized to a quartz crystal and sensitive to gaseous formaldehyde. The major drawback of these devices is the interference from atmospheric humidity and the difficulty in using them for the determination of material in solution. They are however inexpensive, small and robust, and capable of giving a rapid response.

Theory of Fluorescence

Fluorescence is a property present in certain molecules, called fluorescence, in which they emit a photon shortly after absorbing one with a higher energy wavelength. To be specific, in order for an electron in the outer orbital of a molecule to jump from a ground-state orbital to an exited state orbital, it requires a fixed amount of energy, which, in the case of chromophores (molecules that absorb light), can be acquired by absorbing a photon with an energy equal or slightly higher. This state is short-lived, and the electron returns to the ground-level orbital, losing the energy either as heat or in the case of fluorescence by emitting a photon, which, due to the loss of the difference between the energy of the absorbed photon and the excitation energy required, will have a lower energy than the adsorbed photon, or, expressed in terms of wavelength, the emitted photon will have a longer wavelength. The difference between the two wavelengths is called Stokes' shift. This property can be found in quantum dots, certain lanthanides and certain organic molecules with delocalized electrons (Grattarola and Massabrio, 1998).

Forster Resonsance Energy Transfer

Over the years, using a combination of rational design and screening procedures, many possible topologies of fluorescent sensors for glucose have been created with varying degrees of success. In general, these sensors rely either on FRET or on sensitivity to polarity changes to translate the glucose concentration into fluorescent intensity. These sensors contain, in addition to the fluorophore(s). A molecule that confers glucose specificity, in general is a protein. A variety of proteins have been used for this purpose, often with different labs concentrating on one particular protein. Apoenzymes can still bind

glucose but, due to the lack of cofactors (in vitro), cannot catalyze their reaction so are less likely to get damaged. Sensors have been made using JD as FRET donors and a small molecule or gold nanoparticle (dark quenched) as acceptor. An example of the former is Loebe's sensil, an optic fibre system in which the quantum dot is attached to ConA whilst tetramethylrhodiamine is attached to cyclodextran, which in turn is attached to the PEG diacrylate scaffold. An example of the letter is Tang with QDs-ConA-beta-CDs-AuNPs.

Fluorescent protein can be made into a fusion protein with a desired protein, circumventing the labelling steps. Shultz made a GGBP molecule with two GFP at each end. In theory, it is possible to improve this by doing a directed in vitro evolution using FACS, but it has not reported in the literature, which is not easily doe by labeling although a screening has been attempted by Pitner. Fluorescence is not the only type of luminescence achievable in biological systems: Chemiluminescence, the generation of light by means of chemical reactions, is produced by some protein, such as Aqueorin form symbiont in jellyfish and luciferase from symbiont in fireflies (Bradford *et al.,* 1962). These been used to make glucose sensors: Daunert makes a GGBP-split Aqueorin sensor and Koji Soda in 2009 made GGBP-luciferase with Asp459Asn (Glc not Gal).In addition to small-molecule dyes, fluorescent proteins have been used. In addition to protein as the glucose-binding moiety, boronic acid functionalized molecules have been used: Boronic acid in fact binds to vicinal groups, preferably hydroxyl; therefore, it has a high affinity for carbohydrates. One approach is by FRET quenching, in which the system can work through the modulation of the quenching of a dye by a boronic acid functionalized viologen. An alternative approach is by photo-induced electron transfer (PET), a mechanism of fluorescence quenching due to the electron-rich tertiary amino group near the fluorophore, which is affected by the change in charge of the nearby boronate group when glucose is bound. This has been used in combination with lifetime by one group. Not only in fluorescence but as NMR agent for imaging with a Europium (3+) boronic acid dye (Grattarola and Massabrio, 1998).

Applications of Biosensors

There are many potential of biosensors of very types. The main requirements for a biosensor approach to be valuable in terms of research and commercial applications are the identification of a target molecule, availability of suitable biological recognition element, and the potential for disposable portable detection systems to be preferred to sensitive laboratory - based techniques in some situations (Deepika, 2009).

In Engineering

Label-free biosensors with high sensitivity and high specificity have shown tremendous potential in medical diagnostics environmental monitoring, and food safety evaluation (Park, 2005; Chung, 2007). Optional microcavities, such as the microsphere and microtoroid, have very low optional loss, and are therefore uniquely suited to sensing application that require high sensitivity, particularly when paired with a biochemical recognition element that grants high specificity. The primary limitation of these biosensors, however, is that they are generally single-use systems. This limitation is due to the nature of the target-recognition moiety interaction, where binding events are difficult to reverse without degrading the optional performance of the sensor. However, this type of one-use, disposable system may be cost-prohibitive for extension into commercial application, especially considering that it is only the recognition moiety, and not the optical transducer, that must be regenerated for biosensor re-use. Typically, the regeneration of recognition moieties is carried out via strong acid or base treatments, which can unbind the target-probe pair, usually result in damage to the recognition and transducer elements, thus diminishing the biosensor sensitivity and specificity. Therefore, an alternative approach to traditional wet-chemistry regeneration techniques, which allows maintenance of the sensor performance, refreshing of the recognition moiety, and potential recycling of the device to lower the overall cost, would provide a critical step forward in the extension of optical biosensors to commercial applications (Joshi, 2006).

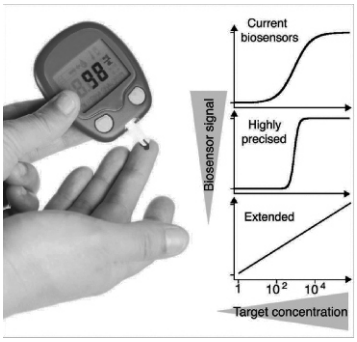

Figure 2: Biosensors in Glucose Monitoring.

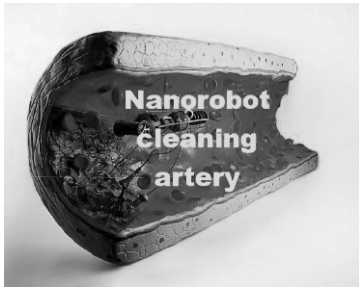

Figure 3: Biosensors in Nano-robotics.

Biosensors in medicine

The size of a small band-aid, it is designed to be worn anywhere on the body, where the biosensor samples tiny amounts of fluids that lie just beneath the skin. The device is small and convenient, and makes measuring glucose levels pain free and noninvasive. The new bio-sensor, however, makes possible a different, painless approach. Instead of puncturing a "big" hole into the skin, the bio-sensor works by making tiny pores in the skin, through which the interstitial fluid can rise. This would be similar to melting a very small region in the ice to access the water below.

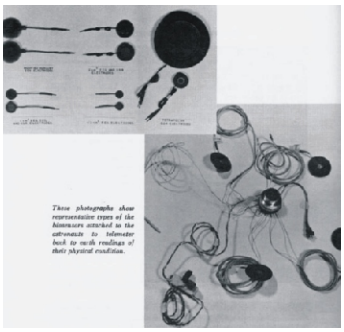

Figure 4: Biosensors in medicine.

The biosensor device works to painlessly remove this outer-dermis, or dead- sin layer, by using a "micro - hotplate" (or micro-heater), which measures about 50 microns square and is carefully controlled to apply a small amount of power. (To imagine how small this area is, note that the period at the end of this sentence is about 10 times larger than hotplate). For 30 milliseconds (that's 30 one-thousandths of a second) the "hotplate" is turned on to a temperature of 130^{O}C. Sounds hot, but in such a small spot, and for such a short time, a person cannot even detect the heat, or feel, as it is applied to the outer layers of skin. This hotplate causes a tiny micro-pore to form through which a little bubble of fluid passively emerges.

The bio-sensor then reads the glucose levels in the sample fluid through tiny electrodes coated with a substance that reacts specifically to the glucose. The bio-sensor project initially began with the intention of developing a miniature device to remotely monitor the health status of soldiers in a battlefield, This tiny prototype chip, which acts as a patch on the skin and is called the B-FIT (Bio-Flips Integrable Transdermal Micro System), can obtain samples of fluids from under the skin one time every hour for a 24-hour period. In this application, troops being sent onto a battlefield could be fitted with biosensors. A medic in a central location could be removed from the field for medical care (Grattarola and Massabrio, 1998).

In cancer treatment: The earlier cancer can be detected, the better the chance of a cure. Currently, many cancers are diagnosed only after they have metastasized throughout the body. Effective, accurate methods of cancer detection and clinical diagnosis are urgently needed. Biosensors are devices that are designed to detect a specific biological analyte by essentially converting a biological entity (ie, protein, DNA, RNA) into an electrical signal that can be detected and analyzed. The use of biosensors in cancer detection and monitoring holds vast potential. Biosensors can be designed to detect emerging cancer biomarkers and to determine drug effectiveness at various target sites. Biosensor technology has the potential to provide fast and accurate detection, reliable imaging of cancer cells, and monitoring of angiogenesis and cancer metastasis, and the ability to determine the effectiveness at various target sites. Biosensor technology has the potential to provide fast and accurate detection, reliable imaging of cancer cells, and monitoring of angiogenesis ad cancer metastasis, and the ability to determine the effectiveness of anticancer chemotherapy agents. This review will briefly summarize the current obstacles to early detection of cancer and the expanding use of biosensors as a diagnostic tool, as well as some future applications of biosensor technology.

Medical Tele-Sensors

This biosensor consists of an optical fiber to which is attached a synthesized hybrid molecule. One half of the hybrid molecule binds calcium ions are bound to the molecule. Blood pressure and pulse rate may be measured by chips designed to detect pressure change. Unlike a glass fiber, a silicone fiber is flexible-it can be squeezed or stretched, and the amount of compression or expansion can be measured by changes in light transmission through the fiber. Thus, silicone fibers embedded in roads can be used to weigh trucks. If a silicone fiber on a chip can sense pressure at various positions in the body, it may be used for monitoring blood pressure, pulse rate, breathing (chest expansion), knee bending during physical rehabilitation, and foot pressure distribution.

Aging, diseases such as diabetes and Alzheimer's and chemical warfare agents cause changes in metal ion concentrations in the body. If these changes could be detected and measured, the information could provide clues about changes in disease states and exposure to toxins. Tuan Vo-Dinh and his coworkers have developed a biosensor using a glass optical fiber and a hybrid molecule he synthesized. One half of the hybrid molecule bind calcium ions and the other half fluoresces when calcium ions are bound to the molecule. By attaching this molecule to the end of a very small diameter optical fiber, Vo-Dinh measured the concentration of calcium ions in a solution. He plans to make a similar measurement within a single living cell.

Miniaturized Devices

Another class of biosensors uses various techniques to turn a biological system into a tiny electronic device, to analyze or physiological processes, or to detect and identify bacteria. Some of these techniques produce or are carried out in miniaturized devices. The site for photosynthesis in a green leaf contains a complex set of enzymes and proteins that capture light energy and convert carbon dioxide into compounds that help the plants grow. If a platinum salt in a certain oxidation state is supplied to one of two photosynthetic systems in plant chloroplasts, one photosynthetic reaction system will use light energy to provide electrons that will reduce platinum to the metal form.

The metal is deposited on the photosystem complex to form a tiny platinum center that can be employed in sophisticated diode-based microelectronics for measurements at extremely high sensitivity, resolution, and speed. The infrared micro-spectrometer developed at ORNL can be used for blood chemistry analysis, gasoline octane analysis, environmental monitoring, industrial process control, aircraft corrosion monitoring, and detection of chemical warfare agents.

Biosensors in Water Treatment

The disturbance the sludge is subjected to is most often in the form of a substrate addition (organic carbon, nitrogen, mixtures, wastewater, etc.). The measurement typically takes place in a small reactor filled with activated sludge that was previously sampled form a treatment plant. The measurement device within this reactor vessel can be a simple probe, for example a dissolved oxygen or PH electrode, but it can also be a more complicated flow injection analysis system. Processing and interpreting the recorded response, in several implementations already done automatically, can be based on a simple regression analysis or a more advanced model based data interpretation procedure.

COD and N Removal Processes

The introduction of combined COD, N and P removal in wastewater treatment significantly increased the complexity of the biological interactions. This created a need for a better understanding of the performance of the biological processes. For COD and N removal processes the "biosensor" development has gone in two directions. First, on-line sensors were developed to obtain information about wastewater and sludge characteristics. These data can be important to control the wastewater treatment plant. Secondly, the introduction of more advanced dynamic models to simulate COD and N removal in activated sludge plant created a need for adequate tests to characterize wastewater and activated sludge. Respirometry, the measurement and interpretation of the activated sludge oxygen uptake rate (OUR), is one of the most popular techniques to study the characteristics of wastewater and activated sludge biodegradation kinetics. The RODTOX respirometer (which is built around a continuously aerated batch reactor) was operated on-line at a full-scale industrial wastewater treatment plant (COD removal, no nitrification) to monitor the readily biodegradable organic substrate. Each of the wastewater oxygen profiles contains three sharp "shoulders", indicating that the wastewater contains three main biodegradable fractions.

For nitrogen removal processes measurements of Ammonium Uptake Rate (AUR) or Nitrate Uptake Rate (NUR) have been applied. However, online application of AUR and NUR is more problematic since ammonium and nitrate sensors are not as robust as for example a dissolved oxygen probe. Recently, a titrimetric method, where the proton consumption or production rate is monitored in a reactor vessel, has been successfully applied for the characterization of nitrification and is currently under development for other processes. This method has proven to be rather simple and robust, and prototypes are tested for on-line measurement of the nitrification capacity. A combined respirometric-titrimetric method mentioned above. The respirometer consists of an aerated vessel with an oxygen probe, and a closed respiration chamber equipped with a second oxygen probe. The activated sludge is continuously pumped around form aeration vessel to respiration chamber and vice versa.

Detection of toxic wastewater

Toxic wastewater can be an important and unexpected source of problems at activated sludge plants. The presence to toxic wastewaters is generally related to industrial activity. In the most optimal situation toxic wastewater is treated at the source. However, this is often not case. Therefore, rapid and simple on-line test methods are useful to detect increased acute toxicity of the wastewater. Several standardized toxicity test methods are available on the market, e.g. with luminescent or immobilized bacteria. The disadvantage of these methods however is that the bacteria used may not be representative for the specific situation of a wastewater treatment plant (Farooqui and Maryam, 2004; Niini, 2002; Chakrabarty and Rameswar, 1989; Khoshmanesh, 2006).

Conclusion

A biosensor is therefore an analytical device for the detection of an analyte that combines a biological component with a physicochemical detector component. Biosensor technology incorporates a wide range of devices, from the basic stethoscope, thermometer and blood pressure cuff to sophisticated PET scanners, MRI and ultrasound machine. It is used in wide variety of applications (Bronwyn, 2004; Booch, 1994; Youngseok, 2008; Kinny *et al.,* 1996). The main requirements for a biosensor approach to be valuable in terms of research and commercial applications are the identification of a target molecule, availability of suitable biological recognition element, and the potential for disposable portable detection systems to be preferred to sensitive laboratory - based techniques in some situations (Deepika, 2009). It is also used as a nano-sensor. Nano-sensors are any biological, chemical or surgical sensory points used to convey information about nanoparticles to the macroscopic world. Their uses mainly include various medicinal purposes and as gateways to building other nano-products, such as computer chips that work at the nano-scale and nano-robots (Farooqui and Maryam, 2004).

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