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Book Series: Analytical Techniques in the Sciences About this Book Covering the huge developments in sensor technology and electronic sensing devices that have occurred in the last 10 years, this book uses an open learning format to encourage reader understanding of the subject.

Electrochemical[edit] Electrochemical biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons such enzymes are rightly called redox enzymes. The sensor substrate usually contains three electrodes ; a reference electrode , a working electrode and a counter electrode. The target analyte is involved in the reaction that takes place on the active electrode surface, and the reaction may cause either electron transfer across the double layer producing a current or can contribute to the double layer potential producing a voltage. We can either measure the current rate of flow of electrons is now proportional to the analyte concentration at a fixed potential or the potential can be measured at zero current this gives a logarithmic response. Note that potential of the working or active electrode is space charge sensitive and this is often used. Further, the label-free and direct electrical detection of small peptides and proteins is possible by their intrinsic charges using biofunctionalized ion-sensitive field-effect transistors. Such biosensors are often made by screen printing the electrode patterns on a plastic substrate, coated with a conducting polymer and then some protein enzyme or antibody is attached. They have only two electrodes and are extremely sensitive and robust. All biosensors usually involve minimal sample preparation as the biological sensing component is highly selective for the analyte concerned. The signal is produced by electrochemical and physical changes in the conducting polymer layer due to changes occurring at the surface of the sensor. Such changes can be attributed to ionic strength, pH, hydration and redox reactions, the latter due to the enzyme label turning over a substrate. One such device, based on a 4-electrode electrochemical cell, using a nanoporous alumina membrane, has been shown to detect low concentrations of human alpha thrombin in presence of high background of serum albumin. Capture molecules such as antibodies can be bound to the ion channel so that the binding of the target molecule controls the ion flow through the channel. This results in a measurable change in the electrical conduction which is proportional to the concentration of the target. An ion channel switch ICS biosensor can be created using gramicidin, a dimeric peptide channel, in a tethered bilayer membrane. Breaking the dimer stops the ionic current through the membrane. The magnitude of the change in electrical signal is greatly increased by separating the membrane from the metal surface using a hydrophilic spacer. Quantitative detection of an extensive class of target species, including proteins, bacteria, drug and toxins has been demonstrated using different membrane and capture configurations. Therefore, it can function continuously if immobilized on a solid support. A fluorescent biosensor reacts to the interaction with its target analyte by a change of its fluorescence properties. A Reagentless Fluorescent biosensor RF biosensor can be obtained by integrating a biological receptor, which is directed against the target analyte, and a solvatochromic fluorophore, whose emission properties are sensitive to the nature of its local environment, in a single macromolecule. The fluorophore transduces the recognition event into a measurable optical signal. The use of extrinsic fluorophores, whose emission properties differ widely from those of the intrinsic fluorophores of proteins, tryptophan and tyrosine, enables one to immediately detect and quantify the analyte in complex biological mixtures. The integration of the fluorophore must be done in a site where it is sensitive to the binding of the analyte without perturbing the affinity of the receptor. Antibodies and artificial families of Antigen Binding Proteins AgBP are well suited to provide the recognition module of RF biosensors since they can be directed against any antigen see the paragraph on bioreceptors. A general approach to integrate a solvatochromic fluorophore in an AgBP when the atomic structure of the complex with its antigen is known, and thus transform it into a RF biosensor, has been described. This residue is changed into a cysteine by site-directed mutagenesis. The fluorophore is chemically coupled to the mutant cysteine. When the design is successful, the coupled fluorophore does not prevent the binding of the antigen, this binding shields the

fluorophore from the solvent, and it can be detected by a change of fluorescence. This strategy is also valid for antibody fragments. Antibodies and artificial families of AgBPs are constituted by a set of hypervariable or randomized residue positions, located in a unique sub-region of the protein, and supported by a constant polypeptide scaffold. The residues that form the binding site for a given antigen, are selected among the hypervariable residues. It is possible to transform any AgBP of these families into a RF biosensor, specific of the target antigen, simply by coupling a solvatochromic fluorophore to one of the hypervariable residues that have little or no importance for the interaction with the antigen, after changing this residue into cysteine by mutagenesis. More specifically, the strategy consists in individually changing the residues of the hypervariable positions into cysteine at the genetic level, in chemically coupling a solvatochromic fluorophore with the mutant cysteine, and then in keeping the resulting conjugates that have the highest sensitivity a parameter that involves both affinity and variation of fluorescence signal. An alternating potential A. This frequency is highly dependent on the elastic properties of the crystal, such that if a crystal is coated with a biological recognition element the binding of a large target analyte to a receptor will produce a change in the resonance frequency, which gives a binding signal. In a mode that uses surface acoustic waves SAW , the sensitivity is greatly increased. This is a specialised application of the quartz crystal microbalance as a biosensor Electrochemiluminescence ECL is nowadays a leading technique in biosensors. In particular, coreactant ECL operating in buffered aqueous solution in the region of positive potentials oxidative-reduction mechanism definitively boosted ECL for immunoassay, as confirmed by many research applications and, even more, by the presence of important companies which developed commercial hardware for high throughput immunoassays analysis in a market worth billions of dollars each year. Thermometric and magnetic based biosensors are rare. Placement of biosensors[edit] The appropriate placement of biosensors depends on their field of application, which may roughly be divided into biotechnology , agriculture , food technology and biomedicine. In biotechnology, analysis of the chemical composition of cultivation broth can be conducted in-line, on-line, at-line and off-line. As outlined by the US Food and Drug Administration FDA the sample is not removed from the process stream for in-line sensors, while it is diverted from the manufacturing process for on-line measurements. For at-line sensors the sample may be removed and analyzed in close proximity to the process stream. These techniques are mainly used in agriculture, food technology and biomedicine. In medical applications biosensors are generally categorized as in vitro and in vivo systems. An in vitro, biosensor measurement takes place in a test tube, a culture dish, a microtiter plate or elsewhere outside a living organism. The sensor uses a bioreceptor and transducer as outlined above. An example of an in vitro biosensor is an enzyme-conductimetric biosensor for blood glucose monitoring. There is a challenge to create a biosensor that operates by the principle of point-of-care testing , i. A biosensor can be sent directly to the location and a quick and easy test can be used. Medical biosensor implant for glucose monitoring in subcutaneous tissue 59x45x8 mm. Electronic components like microcontroller, radio chip etc. Of course, biosensor implants have to fulfill the strict regulations on sterilization in order to avoid an initial inflammatory response after implantation. The second concern relates to the long-term biocompatibility , i. If there is failure, the device must be removed and replaced, causing additional surgery. An example for application of an in vivo biosensor would be the insulin monitoring within the body, which is not available yet. Most advanced biosensor implants have been developed for the continuous monitoring of glucose. Biosensors can also be integrated into mobile phone systems, making them user-friendly and accessible to a large amount of users. 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 a suitable biological recognition element, and the potential for disposable portable detection systems to be preferred to sensitive laboratory-based techniques in some situations. Some examples are glucose monitoring in diabetes patients, other medical health related targets, environmental applications e. A common example of a commercial biosensor is the blood glucose biosensor, which uses the enzyme glucose oxidase to break blood glucose down. This in turn is oxidized by the electrode in a number of steps. The resulting current is a measure of the

concentration of glucose. In this case, the electrode is the transducer and the enzyme is the biologically active component. A canary in a cage , as used by miners to warn of gas, could be considered a biosensor. Such devices can be used in environmental monitoring, [57] trace gas detection and in water treatment facilities. Many optical biosensors are based on the phenomenon of surface plasmon resonance SPR techniques. This occurs only at a specific angle and wavelength of incident light and is highly dependent on the surface of the gold, such that binding of a target analyte to a receptor on the gold surface produces a measurable signal. Surface plasmon resonance sensors operate using a sensor chip consisting of a plastic cassette supporting a glass plate, one side of which is coated with a microscopic layer of gold. This side contacts the optical detection apparatus of the instrument. The opposite side is then contacted with a microfluidic flow system. The contact with the flow system creates channels across which reagents can be passed in solution. This side of the glass sensor chip can be modified in a number of ways, to allow easy attachment of molecules of interest. Normally it is coated in carboxymethyl dextran or similar compound. The refractive index at the flow side of the chip surface has a direct influence on the behavior of the light reflected off the gold side. Binding to the flow side of the chip has an effect on the refractive index and in this way biological interactions can be measured to a high degree of sensitivity with some sort of energy. The refractive index of the medium near the surface changes when biomolecules attach to the surface, and the SPR angle varies as a function of this change. Light of a fixed wavelength is reflected off the gold side of the chip at the angle of total internal reflection, and detected inside the instrument. The angle of incident light is varied in order to match the evanescent wave propagation rate with the propagation rate of the surface plasmon plaritons. Other optical biosensors are mainly based on changes in absorbance or fluorescence of an appropriate indicator compound and do not need a total internal reflection geometry. For example, a fully operational prototype device detecting casein in milk has been fabricated. The device is based on detecting changes in absorption of a gold layer. Biological biosensors often incorporate a genetically modified form of a native protein or enzyme. The protein is configured to detect a specific analyte and the ensuing signal is read by a detection instrument such as a fluorometer or luminometer. An example of a recently developed biosensor is one for detecting cytosolic concentration of the analyte cAMP cyclic adenosine monophosphate , a second messenger involved in cellular signaling triggered by ligands interacting with receptors on the cell membrane. Such "assays" are commonly used in drug discovery development by pharmaceutical and biotechnology companies. A live-cell biosensor for cAMP can be used in non-lysed cells with the additional advantage of multiple reads to study the kinetics of receptor response. Nanobiosensors use an immobilized bioreceptor probe that is selective for target analyte molecules. Nanomaterials are exquisitely sensitive chemical and biological sensors. Nanoscale materials demonstrate unique properties. Their large surface area to volume ratio can achieve rapid and low cost reactions, using a variety of designs. One such example, dual polarisation interferometry uses a buried waveguide as a reference against which the change in propagation constant is measured. Other configurations such as the Machâ€”Zehnder have reference arms lithographically defined on a substrate. Higher levels of integration can be achieved using resonator geometries where the resonant frequency of a ring resonator changes when molecules are absorbed. Blood glucose monitoring Commercially available glucose monitors rely on amperometric sensing of glucose by means of glucose oxidase , which oxidises glucose producing hydrogen peroxide which is detected by the electrode. To overcome the limitation of amperometric sensors, a flurry of research is present into novel sensing methods, such as fluorescent glucose biosensors. When light is illuminated through a low magnification objective onto the layered silicon-silicon oxide substrate, an interferometric signature is produced. As biomass, which has a similar index of refraction as silicon oxide, accumulates on the substrate surface, a change in the interferometric signature occurs and the change can be correlated to a quantifiable mass.

Chapter 2 : Chemical Sensors and Biosensors : Brian R. Eggins :

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Chemical sensors and biosensors are among the fastest growing of analytical techniques. This text provides an up-to-the-minute overview of a wide range of sensing systems, discussing the elements of different transducers used in sensors and the selective elements that are employed.

Chapter 3 : Biosensor - Wikipedia

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