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Glucose Biosensing Applications of Carbon Nanotubes

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For diabetic individuals, the monitoring of blood glucose levels is currently performed by pricking the finger and drawing a small sample of blood (Canadian Diabetes, 2013). Although traditional glucose sensors are improving and causing less discomfort to patients, alternative, non-invasive methods such as sensing glucose in other bodily fluids including saliva, tears, sweat, and urine are possible substitutions. Very low molar concentrations make providing accurate measurements more complex, however a promising area for glucose biosensing appears in the technology surrounding carbon nanotubes (CNT). This paper focuses on the different methods of using CNTs as electrochemical sensors in this regard.

CNT's As Electrochemical Sensors

Electrochemical sensors in general are small devices that can be used to detect a specified compound within a larger sample. They are designed so that they do not alter the makeup of the sample, but still provide continuing and reversible results (Mazloum-Ardakani et al., 2011). Sensors contain two main parts; a transducer and a recognition component. The recognition component reacts chemically with the desired compound, which is then translated by the transducer into an electrical signal. By measuring the quantity and alteration of electric signals, the number and frequency of reactions can be monitored and the concentration of the desired compound can be determined (Grieshaber et al., 2008). CNTs have great potential as being transducers because they are semiconductors and can act as small electrodes, carrying an electric signal. The surface area to volume ratio of CNTs along with their rapid electron transport properties make them particularly effective in this regard. They are capable of sensitive detection at low concentrations with fast response time. The inert nature of CNTs and their large surface area also makes for smaller, longer-lasting sensors (Mazloum-Ardakani et al., 2011).

In a sensor, CNTs are placed onto a main electrode. This is because they are so small and a sufficient electrical reading cannot be obtained otherwise (Wang et al., 2007). Electrodes are generally made of conductive metals, glassy carbons, or carbon pastes. Immobilization of CNTs on these electrodes comes in two forms; non-aligned and aligned. Non-aligned CNTs are randomly placed on the substrate and attach via physical absorption or with a solubilising agent. (Grieshaber et al., 2008). Aligned CNTs attach perpendicular to the electrode and are usually grown directly onto the surface through catalysed chemical vapour deposition (Li et al., 1996). Once the CNTs are present on an electrode they are still not usable. In order to properly utilize CNTs in a sensor, an appropriate recognition component must be applied Currently, the protein enzyme glucose oxidase (GOx) is the main recognition component used for the biosensing of glucose (Wang et al., 2007). GOx catalyses the redox reaction of glucose into hydrogen peroxide and D-glucono-δ-

Figure 1: A glucose molecule (a) is oxidized with O_2 (b) by the protein enzyme glucose oxidaze (GOx) creating D-glucone-δ–lactone (c) and hydrogen peroxide (d).

lactone (Li et al., 1996). Multiple methods of binding GOx to CNTs are used, depending on design of the sensor.

Several types of glucose sensors

Lin and coworkers have produced a CNT nanoelectrode ensemble that can be utilized as a glucose sensor. This is an aligned form of CNT immobilization (Lin et al., 2004). CNTs can be grown on a silicon substrate through chemical vapour deposition by depositing a catalyst, such as iron nanoparticles, at regular intervals on its surface (Li et al., 1996). This creates a patterned array of CNTs, the density of which can be regulated by the spacing of the catalyst (Lin et al., 2006). Carboxylic acid groups that are bound to the end of the CNTs form amide bridges with nitrogen found in a given protein; in this case, glucose oxidase (GOx). When GOx catalyses glucose the redox reaction that occurs transfers electrons to the CNT, which carries the charge to the main electrode. Because the CNTs are spaced evenly at a distance larger than their diameter, there is negligible overlap, making readings quicker and more accurate (Lin et al., 2004).

GOx can also be bound to CNTs using a layer by layer (LBL) technique. This technique works on the basis of attaching a layer of positive cationic polymers such as poly(diallyldimethylammonium) (PDDA)on to the negatively charged surface of a CNT. Negative regions of GOx then bind to the positive PDDA layer. This multilayer format does not interfere with the uptake and conduction of electrons by the CNT (Lin et al., 2006). By functionalizing CNTs along their surface rather than only at the exposed end, more GOx molecules are able to bind and, in comparison to other sensors, fewer individual CNT electrodes are needed for an equivalent amount of redox reactions (Wang et al., 2007).

The insolubility of CNTs is a recurring obstacle in the development of electrochemical CNT sensors (Wang et al., 2007). By utilising the perfluorinated polymer Nafion as a solubilising agent, CNTs become soluble in water.[8] The non-aligned dispersion of the resulting solution onto a glassy carbon electrode creates an effective sensor with high signal strength at low potentials. Experimentation has shown that Nafion does not interfere with the electrochemical properties of GOx functionalized CNTs (Wang et al., 2003), giving this method of deposition great potential in the production of glucose sensors.

Pyrene boronic acid, an alternative to GOx

There are downfalls to using GOx as the recognition component of a glucose biosensor. As an enzyme, GOx is susceptible to denaturing. Temperature and pH can alter the effectiveness of GOx's

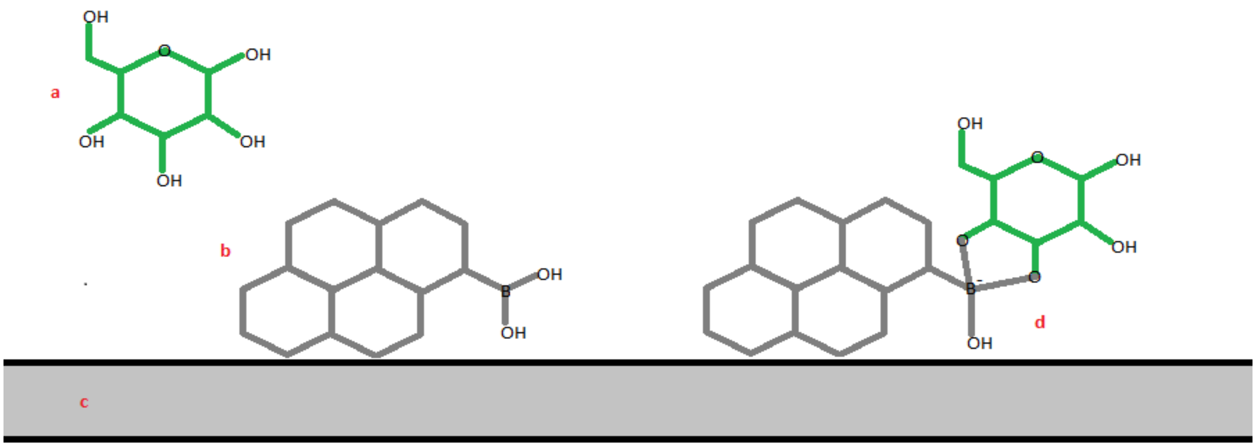

Figure 2: A glucose molecule (a) in solution will bind to pyrene-1-boronic acid (b) that has adhered to a CNT electrode (c). The result is a negative boronate ion complex (d).

catalytic capabilities. Glucose is also consumed when it is catalyzed, meaning the concentration is altered in the biosensing process (Nanotechweb 2013). Although alteration is minimal, sensors are intended to have no influence on the sample they are testing. Additionally, GOx adds a level of complexity to producing electrochemical sensors because it cannot directly bond to a CNT; an intermediate compound such as carboxylic acid or PDDA is required (Wang et al., 2007). For these reasons, other, alternative compounds are being explored such as pyrene-1-boronic acid. This compound is able to link with CNTs while also bonding with glucose, producing a detectable electrical effect (Nanotechweb 2013). Pyrene boronic acid binds selectively with glucose over other organic molecules making it an effective sensor in bodily fluids like saliva, and urine (Lerner et al., 2013).

A research group from the University of Pennsylvania produced a CNT transistor using pyrene boronic acid (Nanotechweb 2013). A silicon wafer was used as a base with a deposited monolayer of aminopropyltriethoxysilane for non-aligned CNT adhesion. Drops of CNT solution were then placed on the wafer and various processes involving incubation, washing and drying were performed. Titanium electrodes were then deposited on the substrate at 10µm intervals (Lerner et al., 2013). The thousands of transistors created by these deposited electrodes and the resulting semiconductive CNT bridges were all nearly identical in nature (Nanotechweb 2013). The CNTs were then functionalized with pyrene-1-boronic acid. The pyrene end of the molecule readily attaches to the CNTs, while the boronic acid end covalently bonds to glucose (Lerner et al., 2013). When the wafer is placed in a glucose solution, boronate ion complexes are produced in close proximity to the CNT (Nanotechweb 2013). In a phenomenon called carrier scattering, the presence of these negative complexes effects the electrostatic environment of the transistor and reduces the current passed through the CNT (Lerner et al., 2013). By measuring the percentage drop in current, the concentration of glucose can be calculated (Nanotechweb 2013). A value of 76 ± 8.2 µM of glucose was recorded to be the optimum functional level for the transistor, with a minimum detection value of 300 nM. This coincides with the concentration of glucose in the saliva of diabetic individuals, found to be

78.7 ± 9.2 μM (Lerner et al., 2013). This association, along with the accuracy, durability, and longevity of the device and straightforward nature of its fabrication, gives this device real, marketable potential (Nanotechweb 2013).

Conclusion

As shown, CNTs have been the subject of extensive research, particularly for their application in electrochemical sensors. Their distinct physical, mechanical and electrical properties can be utilised in various ways to produce highly accurate, highly sensitive sensors (Mazloum-Ardakani et al., 2011). These heightened capabilities are promising for those looking to improve upon traditional biosensing techniques, especially in glucose sensing (Wang et al., 2007). Testing for low concentrations of glucose in saliva and other body fluids is now feasible, meaning that blood glucose testing may soon become obsolete (Nanotechweb 2013). By developing more efficient methods of fabrication, CNT glucose sensors could be produced in bulk, creating easily usable devices that would replace present technology. These developments could increase the quality of life for the millions of individuals living with bodily glucose level disorders, including recurrent ketoacidosis, hypoglycemia, and hyperglycemia (Canadian Diabetes, 2013).

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