National Society of Black Engineers Region 1 Regional Conference
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DRAPER LABORATORY

TECHNICAL CHALLENGE COMPETITION

for

NSBE STUDENTS

CHALLENGE

Implantable Device Biocompatibility:

Biocompatibility and the option of implantable is an important factor in the design of new medical devices. While much of the device is often of an electrical nature, concerns governing the biocompatibility are generally of a mechanical and/or chemical nature. Technologies that enable the advancement and miniaturization of implantable medical devices (e.g., neural recording and stimulation) are in need in order to complement advances in sensing, stimulation, and repair technologies. Design an implantable device that addresses a major health issue (e.g. Bloods clots, returned cancer cells, etc.). Potential topics include in-vivo degradation and accelerated lifetime testing, hermetic electronics micro-packaging, biocompatibility enhancements, energy efficient bio-telemetry circuits, neural stimulator circuits, and optical fiber sensors. Your approach can focus on a specific discipline (e.g. electrical, mechanical, biological, chemical).

Introduction

Diabetes mellitus is a metabolic disease that affects as many as 387 million people worldwide[1]. If left untreated, diabetes can lead to long term complications such as stroke, chronic kidney failure, and damage to the eyes[2]. Diabetes arises as a result of the pancreas either not producing a sufficient amount of insulin (Type I diabetes) or the cells inability to properly respond to presence of insulin (Type II diabetes). About 90% of all diabetic cases arise as a result of type II diabetes[3]. Living with diabetes mellitus is achievable through the constant monitoring of one's blood sugar in addition to the use of drugs or insulin therapy. The most prevalent method used for measuring blood glucose levels involve drawing blood from the finger multiple times a day. Due to current system's dependence on fresh blood, many are taking fewer readings than the optimal amount. The creation of a non-invasive procedure would benefit the majority of people suffering from diabetes as well as allow them enhanced monitoring of their sugar levels. With the recent breakthroughs within nanoparticles, the process of passively monitoring one's glucose may be as simple as shining an infrared light on an area of the skin that contains nanoparticles embedded within the dermal tissue. The possibility of utilizing fluorescent detection in monitoring blood glucose levels will be explored below.

Main Body

A basic bio-molecular sensor consists of two parts. A detection component which recognizes and binds the target molecule of interest, and a signaling component which produces a recognizable effect once binding of the target molecule has occurred[4]. The protein glucose oxidase is the ideal detection component for the target as it selectively binds glucose, when it is present. There are several studies on the localization of glucose oxidase and leveraging its properties for the use within biological and chemical systems. One study of interest performed by Huiguang Zhu and his lab used alginate microspheres to encapsulate the protein through a combination of emulsion and chemical conjugation which allow them to survive within the body[5].

The signaling component for an ideal biosensor needs to induce a change in the emission intensity of light at a specific wavelength. In the lab of D'Auria, they enhanced fluoresce of a glucose binding event by using a resonance energy transfer sugar whose emission was quenched

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[1] "Key Findings 2014." *International Diabetes Federation*. Web.

[2] "Diabetes." *World Health Orgnanization*. Web. 14 Oct. 2015.

[3] Shi, Y., & Hu, F. B. (2014). The global implications of diabetes and cancer. The Lancet, 383(9933), 1947–1948. http://doi.org/10.1016/S0140-6736(14)60886-2

[4] De, M., Ghosh, P. S., & Rotello, V. M. (2008). Applications of Nanoparticles in Biology, 01003, 4225–4241. http://doi.org/10.1002/adma.200703183

[5] Zhu, H., Srivastava, R., Brown, J. Q., & McShane, M. J. (2005). Combined physical and chemical immobilization of glucose oxidase in alginate microspheres improves stability of encapsulation and activity. Bioconjugate Chemistry, 16(6), 1451–8. http://doi.org/10.1021/bc050171z

when glucose was not present[6]. The use of the glucose specific protein, concanavalin A, bound to dextran, a glucose analog, caused a decrease in the emission intensity due to the occurrence of resonance energy transfer, which describes the energy transfer between two light sensitive molecules[7]. Glucose, when present competitively competes with dextran in binding to concanavalin A. When the concentration of glucose is high enough, glucose binds to concanavalin A increasing the intensity of emission within the 675 nm wavelength.

Some of the problems that arise when using the sensors is the gradual degradation of the detection component protein and the loss of sensitivity to glucose within the signaling component. A sensor designed using glucose oxidase as the detection component and Pt(II) octaethylporphine as the signaling component has enhanced the stability of both of these components[8]. Glucose oxidase cause the reaction shown in Figure 1 to occur.

$$\text{Glucose} + O_2 + H_2O \rightarrow \text{Gluconic Acid} + H_2O_2$$

Figure 1. Reaction catalyzed by glucose oxidase.

As a result, the sensor indirectly measure glucose though monitoring glucose limited oxygen consumption and producing increased fluorescence.

Conclusion

The development of non-invasive methods to measure biochemical reactions within the body is of great medical significance as it stands to benefit an overwhelming majority of the population. A potential negative of the biosensor described above is the delay in response time to glucose concentration as well the glucose range of detection. While the sensor is still in need of some tweaks for it to be widely applicable, the strategies used above to designing this potential implantable biosensor for the detection of glucose monitoring is not limited strictly to glucose. These methodologies can also be manipulated and applied to other target molecules of interests within the body and potentially provide early notification and mitigation of potential adverse symptoms.

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[6] D'Auria, S., DiCesare, N., Staiano, M., Gryczynski, Z., Rossi, M., & Lakowicz, J. R. (2002). A Novel Fluorescence Competitive Assay for Glucose Determinations by Using a Thermostable Glucokinase from the Thermophilic Microorganism Bacillus stearothermophilus. Analytical Biochemistry, 303(2), 138–144. http://doi.org/10.1006/abio.2001.5544

[7] Ballerstadt, R., Evans, C., Gowda, A., & McNichols, R. (2007). Fiber-coupled fluorescence affinity sensor for 3-day in vivo glucose sensing. Journal of Diabetes Science and Technology (Online), 1(3), 384–393.

[8] Stein, E. W., Grant, P. S., Zhu, H., & McShane, M. J. (2007). Microscale enzymatic optical biosensors using mass transport limiting nanofilms. 1. Fabrication and characterization using glucose as a model analyte. Anal.Chem, 79(4), 1339–1348. http://doi.org/10.1021/ac061414z

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2. D'Auria, S., DiCesare, N., Staiano, M., Gryczynski, Z., Rossi, M., & Lakowicz, J. R. (2002). A Novel Fluorescence Competitive Assay for Glucose Determinations by Using a Thermostable Glucokinase from the Thermophilic Microorganism Bacillus stearothermophilus. *Analytical Biochemistry*, *303*(2), 138–144. http://doi.org/10.1006/abio.2001.5544
3. De, M., Ghosh, P. S., & Rotello, V. M. (2008). Applications of Nanoparticles in Biology, *01003*, 4225–4241. http://doi.org/10.1002/adma.200703183
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8. Zhu, H., Srivastava, R., Brown, J. Q., & McShane, M. J. (2005). Combined physical and chemical immobilization of glucose oxidase in alginate microspheres improves stability of encapsulation and activity. *Bioconjugate Chemistry*, *16*(6), 1451–8. http://doi.org/10.1021/bc050171z