Modeling the effects of capsule formation on glucose transport to subcutaneously implanted sensors

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Introduction: The biofouling and the formation of a foreign body capsule around implanted sensors are purported to be key contributors to sensor failure [1]. A 1D partial differential equation model was constructed to examine glucose transport through the interstitium and assess the effects that the wound healing process would have on glucose transport to the sensor surface. By including the effects of biofouling, macrophage adhesion, and fibrous encapsulation, subcutaneous glucose traces with attenuated signals and delayed responses were generated that mimic those reported experimentally. This method allows the characteristic traits of the foreign body capsule (avascularity, dense fibrous matrix, inflammatory cell presence, etc.) to be probed to gain a better understanding of what aspects of the wound healing process contribute most to sensor failure.

Methods: Post-implantation tissue was modeled as a two compartment system. The first compartment, the foreign body capsule (FBC) compartment, was represented by 1D diffusion of glucose with a consumption sink, meant to represent consumption of glucose by inflammatory cells in the capsule. In this case, uptake of the analyte was described by Michaelis-Menten kinetics.

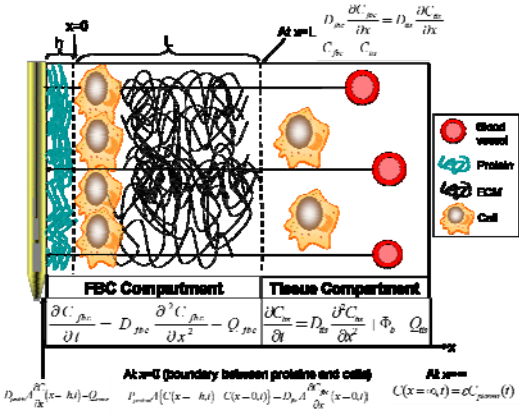

Figure 1: Physical schematic of model space.

The second compartment, the tissue compartment, was modeled by 1D diffusion with the addition of two different terms. The first term, Φ_b, represents a source of glucose from vasculature in the native tissue and is described by simplified Kedem-Katchalsky equations. Such a term was not contained in the FBC because it was assumed to be avascular. The term, Q_{tis}, is similar to the consumption term of the FBC, but with different representative constants for different cell types.

Blood glucose data from Armour et al were taken and fit to a sum of Gaussian curves to provide an expression for blood glucose response after an intravascular infusion of glucose [2]. All physiologically relevant values for the model were gathered from existing literature. Governing equations were discretized using finite difference methods and solved in MATLAB (The Mathworks, Natick, MA).

To examine the effects of different physiological parameters upon glucose transport to the sensor, simulations were run on a range of different values for each parameter. Parameters examined in this study include vessel density proximal to the sensor, metabolic activity, and thickness of the capsule.

Results/Discussion: When varied in the simulations, all of the parameters listed above had visible effects on glucose transport, inducing both an attenuation of amount that reached the sensor and a lag time between peak blood glucose levels and sensor glucose levels. Since a decrease in vessel density is a hallmark of the native tissue surrounding the sensor and its foreign body capsule, we believe it may have a considerable impact on reducing glucose transport [3]. When vessel density was decreased from its pre-implantation tissue value of 166.3 cm^2/cm^3 to the 3 week post-implantation value of 15.4 cm^2/cm^3, the peak amount of glucose delivered decreased ~70% (Figure 2a). Additionally, lag time was lengthened by a factor of 2.7 when the vessel density was decreased to 15.4 cm^2/cm^3 (Figure 2b). Such values could be anticipated as an increased vessel density correlates to an increased source of glucose in the system.

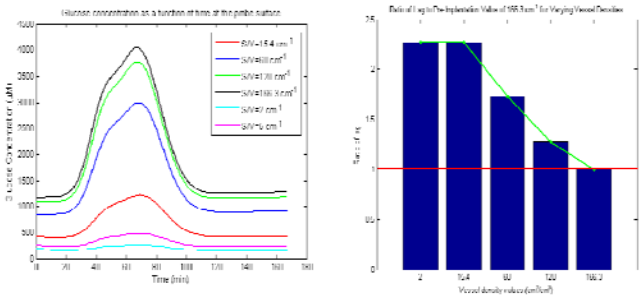

Figure 2: (a) Glucose surface concentrations for varying vessel densities. (b) Ratio of lag times for different vessel densities. Relative to value at 166.3 cm^{-1}.

With a combination of lower glucose levels and increased time for delivery, the decline in vessel density has a considerable impact on the transport of glucose to sensors, with the potential to affect sensor performance.

Summary: By understanding the implications that observed post-implantation occurrences such as decreased vessel density have on the transport of glucose, we can more completely explain both how and why functional sensors fail. A comparison of a range of vessel density values demonstrated an increased time lag and attenuated transport when densities decreased as they would post-implantation. Such a comparison will demonstrate how different parameters contribute to sensor failure.

References:

[1]. Wisniewski, N. Colloids and Surfaces B. Biointerfaces 2000 18: 197-219.
[2] Armour, JC. Diabetes. 1990 39 (12):1519-1526.
[3] Koschwanez, HE. J. Biomed. Mat. Res. 2008 87A(3):792-807.