Modeling an Enzyme Based Electrochemical Blood Glucose Sensor

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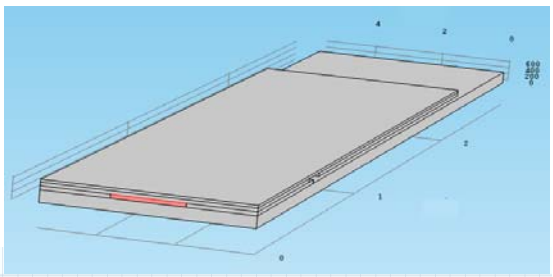
Introduction: Self monitoring blood glucose (SMBG) test systems are essential in the management and control of diabetes[1]. This paper describes the modeling of the glucose dependent, signal-generating, reactions that occur within the blood-filled reaction chamber of an example SMBG test strip during a blood glucose concentration measurement.

This model has built upon legacy work at Lifescan Scotland initially based around analytical solutions to partial differential equations on simplified domains and boundary conditions. Later work extended these models to include multiple species, chemical interactions and full electrochemistry. This COMSOL based model has allowed additional flexibility in rapid model based prototyping, involving alternative chamber dimensions and/or reagent compositions.

Figure 1. Blood Glucose Measurement using SMBG strip and meter

Geometry & Reagents: The geometry comprises two electrodes, overcoated with a thin deposited reagent layer composed of an oxidoreductase enzyme and a redox active electrochemical mediator, all located within a sample capillary volume, which is filled with a blood sample.

Figure 2a. Test strip with capillary volume highlighted in red



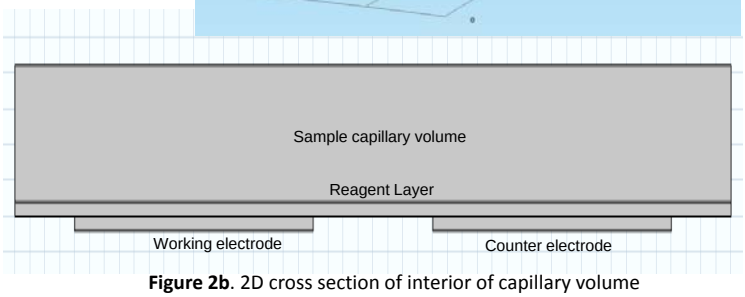


Figure 2b. 2D cross section of interior of capillary volume comprising electrodes (working and counter)reagent layer and sample void

Amperometric Reactions: The glucose analyte within blood is enzymatically oxidised to gluconolactone, with oxidised electrochemical mediator (potassium ferricyanide) being consumed, and reduced mediator (potassium ferrocyanide) being generated. This reduced ferrocyanide subsequently diffuses toward the polarized working electrode where it is electrochemically re-oxidised to ferricyanide, while an equivalent amount of the excess ferricyanide is simultaneously reduced at the counter electrode, completing the circuit and producing an electrochemical current signal[2,3].

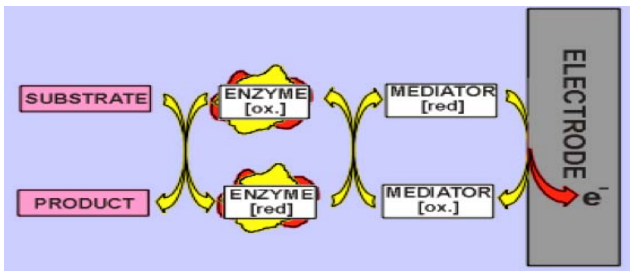


Figure 3. Mediated enzymatic electrochemical reaction

Theory: The physics used to build the model included Fick's diffusion law[4] coupled with Michaelis-Menton based chemical interactions[5]. A Bultler-Volhmer expression was used to provide concentration dependent changes to the base driving potential of the system[6]. Conservation of mass was implicit in the system with ferrocyanide and ferricyanise ions exchanging electrons and driving the base amperometric response.

$$\frac{\partial S}{\partial t} = \frac{\partial}{\partial x}\left(D_S(x).\frac{\partial S}{\partial x}\right) \quad [4]$$

$$v = \frac{d[P]}{dt} = \frac{V_{\max}[S]}{K_m + [S]} \quad [5]$$

$$i_{loc} = i_0\left(C_R \exp\left(\frac{\alpha_a F\eta}{RT}\right) - C_O \exp\left(\frac{-\alpha_c F\eta}{RT}\right)\right) \quad [6]$$

Comsol Methods: Concentration of diluted species, secondary current distribution (battery and fuel cells), chemical reactions, and other boundary conditions using the custom mathematical equation editor were employed. Meshes were physics controlled with extra refinement near each electrode-electrolyte boundary.

Results: The model has been used to characterise existing and new biosensor geometries. Outputs such as the correlation between analyte concentration and current signal at different time periods, and using alternate layouts, has aided with cost effective optimisation of device chemistry and geometry. The detailed concentration gradients produced have increased understanding of signal features and the impact of design changes thereupon.

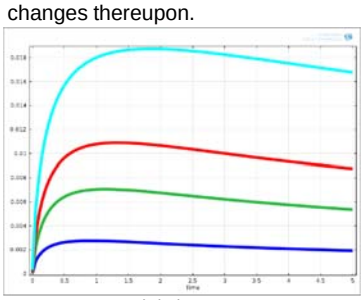


Figure 4. Model chronoamperometric response current at concentrations of 50, 150, 250 and 500mg/dL glucose

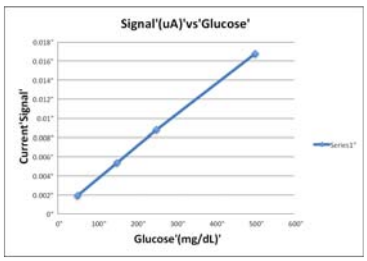


Figure 5. Linearity plot showing sensor response against glucose

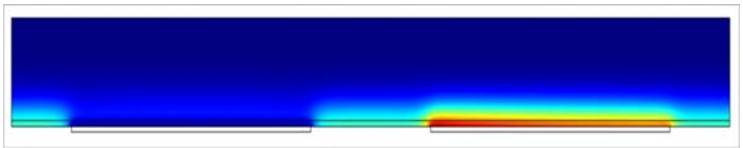


Figure 6. Concentration profile showing the distribution of Ferrocyanide in the cell at a given time point. Local deficiency of Ferrocyanide over the working electrode and its regeneration next to the counter electrode is clearly evident.

Conclusions: Results achieved in this simulation were in general agreement with experimental work using existing systems and prototypes. Whilst such models can never be used to facilitate decisions on the safety or efficacy of medical devices released to the public, they are expected to prove a useful tool in the design and optimisation of such devices in the future.

References:

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