The Fundamental Limit of Implantable Electrochemical Glucose Sensors

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Summary: The fundamental lifetime limit of a glucose oxidase based electrochemical sensor has been characterized by modeling the deactivation of glucose oxidase over time. With an understanding of the sensor’s degradation the requirements of the sensing electronics to acquire the sensor's signal can be determined.

Electrochemical sensors operate by allowing an immobilized enzyme (glucose oxidase in our study) to chemically react with the molecule being sensed (glucose in our study). The chemical reaction, a reduction and oxidation reaction (or redox reaction), generates a current that is a function of the glucose concentration around the sensor. The redox reaction also produces H$_2$O$_2$ as a byproduct. The H$_2$O$_2$ causes the glucose oxidase to deactivate over time decreasing the sensitivity of the sensor. In this study we simulated the effect H$_2$O$_2$ will have on the sensor over time. The results of this simulation are shown in Fig. 1. It is important to note that there are other means of sensor degradation, but the deactivation of glucose oxidase creates an unavoidable limit that is fundamental to the electrochemical sensor.

![Fig. 1. Sensor output current density [nA/mm$^2$] per unit concentration of glucose [mM] over time. Glucose oxidase inactivation decreases the sensor output to less than 1% of original value after 60 months of implantation.](image)

To acquire useful information from the ECS, the signal must first be amplified. The output of the ECS is a current, but it is desirable to perform signal processing with a voltage mode signal with a transimpedance amplifier (TIA). The two TIA techniques most commonly used in glucose sensors were studied and their noise performance was analyzed and compared to that of the ECS as a function of time. This allows us to determine if the noise floor of the amplifier will be low enough to detect the signal as it decreases in strength over time. The circuit topologies of the amplifiers include an op amp with shunt feedback (Fig. 2a), and a topology where the bias circuit for the sensor is integrated with the amplifier to lower power consumption (Fig. 2b).

![Fig. 2. Two TIA topologies studied as sensing amplifiers to acquire sensor output. Three terminal device labeled W, R, and C represents the electrochemical sensor with output $I_{ox}$. a) op amp with shunt feedback, and b) bias circuit integrated with TIA.](image)