

Towards the Future Development of an Electrochemical Continuous Multimarker Biosensor for Enhanced Glycemic Management

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Keywords

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The enhancement of future glycemic management using electrochemical impedance-based biosensors offers many advantages for detection and management of type 1 and type 2 diabetes. The technique, electrochemical impedance spectroscopy (EIS), is highly regarded as having the potential to become an ideal state-of-the-art detection technique for diabetes management.¹ The various benefits begin with an ultralow detection limit ranging from millimolar for glucose to picomolar for insulin. In addition, EIS offers label-free analyte detection allowing direct measurement of analyte nondestructively. Last, EIS offers the user rapid results; the results are displayed in 90 seconds or less, all while the process stays manufacturer-friendly.² Most important, EIS has demonstrated novel success in multimarker detection on a single electrode surface³ with the potential for continuous monitoring.⁴ Multimarker detection is achieved via optimal binding frequency (OBF) based off the biological specificity from molecular recognition elements (MRE). The OBF is the interaction at which an MRE and analyte can be detected with best responsivity and specificity. With all these benefits EIS-based biosensors are an ideal platform for enhancing and improving glycemic management over the current gold standard platform.

EIS could be extremely useful in enhancing glycemic control for diabetes mellitus as current clinical standards aim for tighter glycemic management. However, given such a complex disease, measuring glucose alone is insufficient and other significant biomarkers, such as insulin and glucagon, should be included in the detection for increased disease management and reduced potential comorbidities.³ Currently, studies have shown that diabetes can be better managed with a multimarker detection model.⁵ Furthermore, the development of a continuous EIS biosensor with multimarker capabilities could answer the need for enhanced detection and tighter glycemic control. Verification and determination of OBFs specific to glycemic management has determined

different OBF values for individual biomarkers. Shown in Figure 1A is the OBF for markers such as insulin at 810.5 Hz,² glucose at 1170 Hz, 1,5-anhydroglucitol 3,710 Hz,⁶ glycated albumin at 1.18 Hz, and glycated hemoglobin of 547 Hz. Knowing the OBF allows for the use of a single electrode with multiple markers as shown in Figure 1B.

Currently, we have successfully shown that it is possible to decouple combined biomarkers OBF into two separate OBFs at which each biomarker can be detected simultaneously.³ The decoupling algorithm is key for detection of multiple immobilized biomarkers on a single electrode. Furthermore, continuous multimarker detection provides optimal comfort and comprehensive results through the detection of multiple targets with potential to achieve close-loop artificial pancreas, offering a carefree and decision-free management of diabetes. Figure 1C shows detection of blood glucose with three different methods: continuous, discrete, and continuous multimarker detection. The continuous multimarker system is proposed to better control glycemic management through enhanced detection of multiple markers and increased disease management. Currently continuous glucose detection and auto insulin injection has been introduced with the Guardian 3 sensor. However, to develop a future biosensor for complex disease management, such as diabetes, qualities such as affordability, specificity, sensitivity, user-friendliness, reliably, equipment free, and deliverability can be achieved with the methods and work of EIS biosensors.

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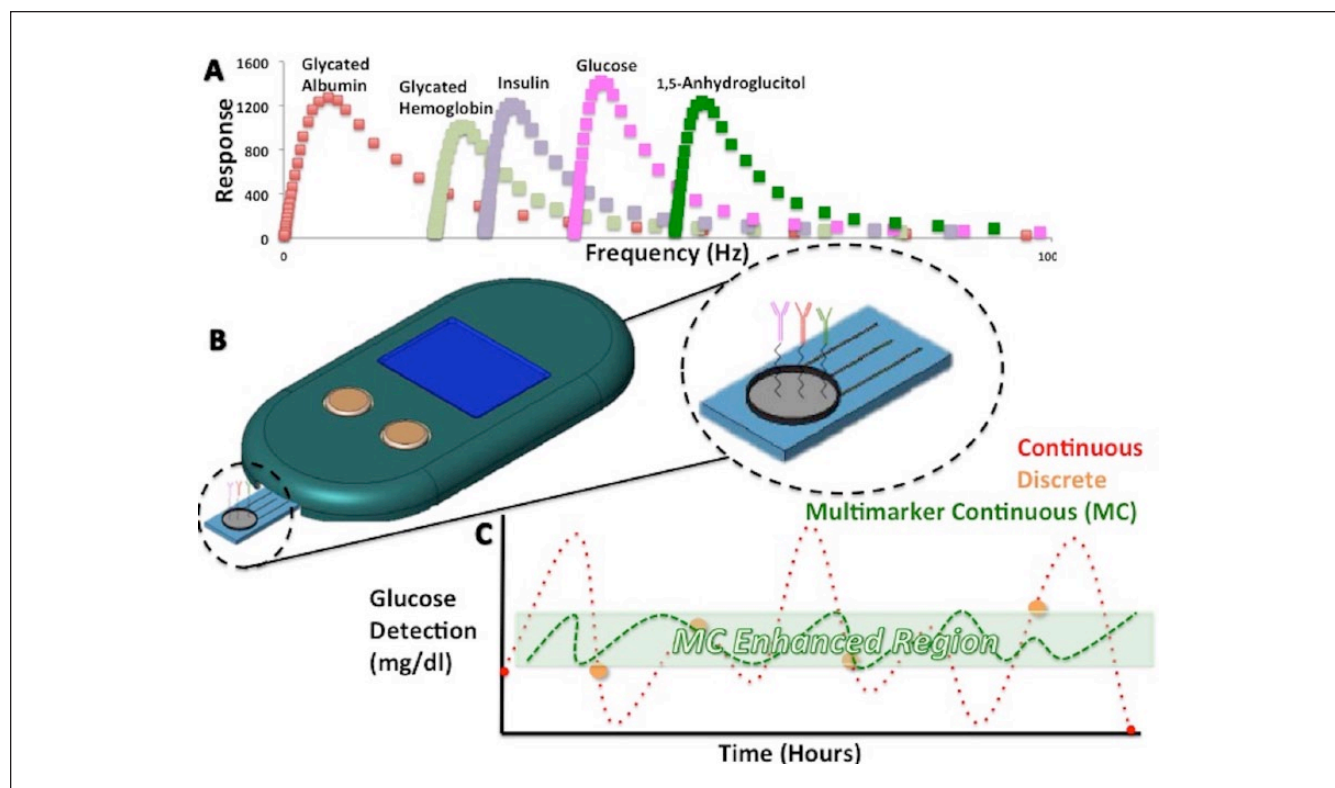


Figure 1. (A) Varying optimal frequency ranges of different glycemic management markers. (B) Multimarker glycemic meter for enhanced glycemic control, showing multiple biomarkers on the sensor surface. (C) Glucose detection using different mechanisms; continuous detection is shown by the red curve, discrete are the yellow dots, and the multimarker continuous system showing detection of the enhanced region.

Abbreviations

EIS, electrochemical impedance spectroscopy; MRE, molecular recognition element; OBF, optimal binding frequency.

Declaration of Conflicting Interests

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