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*Corresponding author

Solomon W Leung, Department of Civil & Environmental Engineering and ISU Measurement & Control Research Center, Idaho State University, Pocatello, ID 83209, USA

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Metabolites, Diagnosis, Nanoparticles, Biosensor, Environmental Monitoring.

Abbreviations

GCE: Glassy Carbon; GFAP: Glial Fibrillary Acidic Protein; GDH: Glutamate Dehydrogenase; BSA: Bovine Serum Albumen; EA: Ethanolamine; PSA: Prostate-Specific Antigen

Review Article

Comprehensive Review of High Performing Electrochemical Biosensors for Biomedical and Environmental Applications

Solomon W Leung[1*], David Assan[1] and James CK Lai[2]

[1]*Department of Civil & Environmental Engineering and ISU Measurement & Control Research Center, USA*

[2]*Department of Biomedical and Pharmaceutical Sciences, Idaho State University, USA*

Abstract

We have mounted seven different biocatalysts on a sensor platform to examine the performance of this electrochemical sensing system for the detection of different biomolecules/metabolites and environmental important molecules, with such we also compared how this sensing system fares with literature results of similar measurements. The sensor platform constitutes of a layer of bio composite mounted on different electrodes made out of Au, Ag, Pt, and glass carbon; the bio composite is fabricated with polymers and sol-gel Au nanoparticles with or without an extra layer of branching biomolecules. The targeting species for measurements include NH4+, NO3-, CN-, H2O2, and the biomolecules that post specific biomedical functions/identities. In this report, we provide a systematic update of analyses of this sensing system, including the unique identification potentials and sensitivities. This novel sensing system can be a valuable tool in biomedical diagnosis and environmental forensics; in particular the sensor platform used here, any biomedical diagnosis can be conducted with extremely high sensitivity as long as the biomolecules and their antigens are known.

Introduction

For more than two decades, research into the uses, functionality, and fabrication of immunosensors have received considerable interest from the biochemical and biomedical communities. Different methods of fabrication and combination of reagents are being employed to obtain efficient biosensors for a variety of purposes. In particular, focus has been concentrated on biosensors for the early detection of diseases in human body, such as cancers and congenital disorders. With such, the need for a highly sensitive and selective biosensor is therefore the key to unlock this avenue of research. Biosensors are generally composed of immobilized layers of biomolecules such as proteins that are attached to support materials, these biomolecules are selectively coupled with the targeted substrates, thus define the selectivity of the sensors. Sensitivity of the biosensors depends on the efficacy of the availability of the biomolecules that will bind with the targeted substrates, thus modification of how the biomolecules are linked to the supporting materials and their configurations (distribution) can improve sensitivity of the biosensors. For example, implanting of mangold particles between the supporting materials and biomolecules enhances the binding surface availability for the substrates, thus increases the sensitivity of the biosensors [1-5]. In this summary review, we update the results of our findings of several different enzymes that we used for developing an electrochemical sensor platform that can be used for varieties of biomedical applications and environmental monitoring. The resulting biosensors have superior detecting sensitivity and in general are orders of magnitude better than those found in literature reports are are. More importantly, all these sensors were based on one sensor platform that can be used for many applications as long as the enzyme conjugate pairs are known.

Materials and Methods

Materials

The electrodes used in this review were highly modified and the surface of the electrodes were Gold (Au), Platinum (Pt) and Glassy carbon (GCE), they were purchased from Tianjin Aida Heng Sheng Co, Tianjin, China. The electrodes had a diameter of 0.2 cm. The platinum counter electrode had diameter of 0.1 cm and length of 0.5 cm. The biocatalysts LDH (lactate dehydrogenase), GDH (glutamate dehydrogenase), human IgG (human immunoglobulin G), Hb (hemoglobin), glial fibrillary acidic protein (GFAP) and anti-GFAP, and PSA (prostate-specific antigen), S100 calcium-binding protein B (S100B) and S100B protein antibody (anti-S100B), and other chemicals such as cysteamine, melamine, bovine serum albumen (BSA), $AuCl_3HCl{\cdot}4H_2O$ (Au %> 48 %), ethanolamine (EA), and sodium citrate were purchased from Sigma-Aldrich Chemical Co, St. Louis, MO, USA. Potassium cyanide was obtained from Fisher Scientific; all the other chemicals used were of analytical grade. All experiments were carried out in a deoxygenated 0.1 M phosphate buffer solution at pH 7.0.

Methods

Preparation of electrodes were the same as previously reported [2,3], except that the bio composite layers were comprised of the said enzymes as mentioned previously depending on applications. To enhance the performance of the sensors, BSA or EA was coated as a final surface layer to eliminate all the possible sites that might be competitive with the reactive bindings of the enzymes. The electrochemical measurements were carried out on a Gamry 600 potentiostat.

Results and Discussion

(Table 1) summarize the results of the 7 enzymes that we used for the analyzes of different metabolites and environmental pollutants. The lowest detection limits for the sensors are in general lower than 1x10-18 M which allowed these sensors to be used for many applications that were not considered in biomedical diagnosis and environmental monitoring, as well as homeland security and early cancer screening diagnosis. Thus far, the best anchoring material for

the electrode sensor is Pt, however, GCE may be preferred in certain applications. The most significant development within our research group recently was the development of GFAP and S100B sensor that are directly related to head trauma. GFAP has been commonly recognized recently to be a significant brain injury biomarker [6,7]. As shown in (Figure 1), the sensor was able to detect the release of GFAP at extremely low concentrations beyond 1x10-18 M, that has the likely potential to develop into a fast responding medical instrument for head trauma detection.

Table 1: Performance summary of Au, GCE, and Pt electrode and the associated enzymes.

Anchoring Material	Target Species	Enzyme	Characteristic Peak (V)	Other Peaks (V)	Current Magnitude*, µA
Platinum	α-ketoglutarate/ NH_4^+	GDH	0.75 (O)	0 (R)	12.6 (O)
Gold			0.75 (O)	-	7.27 (O)
Glassy Carbon			0.75 (O)	-	3.0(O)
Platinum	Lactate	LDH	0(R)	0.6 (O)	0.4 (R)
Gold			0.6 (O)	0.5 (R)	0.15 (O)
Glassy Carbon			0.5 (R)	0.6 (O)	0.37 (R)
Platinum	H_2O_2	Hemoglobin	0 (R)	0.75 (0)	4.33 (R)
Gold			0.485 (R)	1.1 (O)	2.04 (O)
Glassy Carbon			0.45 (R)	0.6 (O), 1.1 (O)	5.5 (O)
Platinum	NO_2^-	Hemoglobin	0 (R)	0.8 (O), 0.5 (R)	3.71 (O)
Gold			0.5 (R)	0.8 (O)	4.20 (O)
Glassy Carbon			0.45 (R)	0.8 (O)	2.24 (O)
Platinum	HigG	Anti-HigG	0.04 (R)	0.6 (O)	4.55 (R)
Gold			0.5 (R)	0.3 (O)	0.073 (R)
Glassy Carbon			1.1 (O)	0.4 (R)	1.95 (O)
Platinum	PSA	Anti-PSA	0.04 (R)	-	2.05 (R)
Gold			-0.2 (R)	-	0.032 (R)
Glassy Carbon			0.5 (R)	-	0.17 (R)
Platinum	CN^-	Anti-HigG	0.025	-	4.8 (R)
Gold			0.025	-	2.6 (R)
Gold	GFAP	Anti-GFAP	0.46	-	6.0 (R)
Platinum	S100B	Anti-S100B	0.3		3.3 (R)

(O): Oxidative peak
(R): Reductive peak
*Concentration dependent of enzymes used

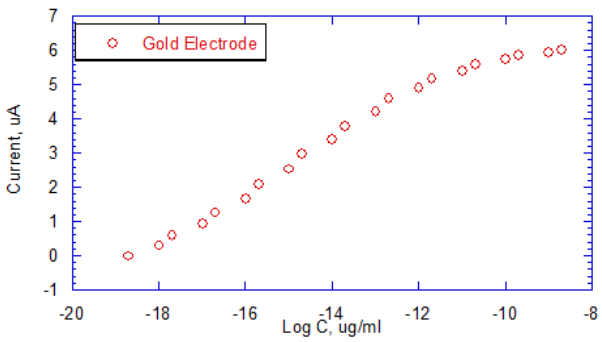

Figure 1: Measurements of GFAP with an Au electrode coated with bio composite. The measurement takes less than 5 minutes.

Conclusion

Our research group has developed some of the most sensitive biosensors ever reported. These biosensors are selective and durable, that allow researchers and practitioners to explore applications in medical diagnosis and monitoring that were not possible in the past. All the measurements were based on one sensor platform with different conjugate enzyme pairs as shown in (Table 1) above; applications for these biosensors are yet to be explored. Some of the likely developments would be head trauma detection, viruses and their antibodies diagnosis, and future diseases detection with known DNAs. For example, the recent COVID 19 virus and its antigen can be detected in less than 5 minutes, with less than a drop of blood, by using this electrochemical sensor platform.

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