論文 / 著書情報
Article / Book Information

題目(和文)	生物活性分子の安定した計測に向けた電気化学アプタマーセンサーの設計と最適化
Title(English)	Design and Optimization of Electrochemical Aptamer-Based Sensor for Stable Monitoring of Bio-Active Molecules
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種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
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論 文 要 旨

THESIS SUMMARY

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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words）

Biosensors have come a long way in taking the essence from technologies in biology, chemistry and materials science to detect specific molecules, markers and organisms with good accuracy in relatively short period of time. Biosensors have emerged as a game changing tool to meet our needs in several fields including healthcare, environmental monitoring and food safety. In general, the biosensor includes the receptor or the moiety, and recognizes the target and transduces the binding event to a signal which can be read out through signal amplification. The recognition moiety of the biosensor can be antibodies, enzymes, nucleic acids or cavities which specifically binds with the target. When the target lands on the recognition moiety, the transduction process is initiated which converts the binding event to optical, electrochemical, mechanical, biological or a mixture of the signals. Upon data collection, there is a data processing portion which takes the recorded signal to visualize and further validate the obtained data. Thus far, continuous monitoring of biomolecules in real-time has been a feat to improve precision and quality of the currently available therapeutics and diagnostics.

To this end, electrochemical aptamer-based (EAB) sensors have demonstrated their ability to recognize a variety of targets including vancomycin, cocaine, phenylalanine, tryptophan, procaine and methotrexate in seconds-resolved, real-time without chemical or enzymatic reactivity with the target molecule in various settings including *in situ* in the vein, subcutaneous space and brain tissue of animal models. EAB sensors are composed of molecular recognition component which are referred to as aptamers. Aptamers are specific strands of oligonucleotide or peptide sequences which have been selected to bind to a specific target. Unlike antibodies for example, aptamers have a reversible binding nature to targets, which allow them to be employed as molecular recognition moieties for continuous monitoring systems.

For use in EAB systems, aptamers are modified with methylene blue (MB) as a redox reporter. When a target analyte binds to the aptamer, the aptamer goes under a structural change causing the physical displacement of the MB on the aptamer to be distanced either close or away from the electrode surface. When MB is distanced closer, electron transfer rate between the gold electrode and redox reporter is sped up causing an increase in the current of redox reporter in a manner that is dose-dependent to the target concentration at present. By employing aptamers in electrochemical systems, target analytes can be measured as change in the interrogating current on the electrode over time. This concept is a key for the EAB sensors since conformational change of the aptamer is what allows electron transfer kinetics to be detected as a signal. In other words, population of aptamers that undergo structural change physically displaces position of redox reporter, relative to the gold working electrode to approximate arbitrary target

concentration in the real-time monitoring.

While EAB sensors provide robust response to targets in various bodily fluids, they would experience biofouling, drift and compatibility issues when measurement is performed in realistic biological environment with varying pH, temperature and buffer media, causing the secondary structure of aptamers to greatly change leading to noticeable difference in the binding affinity and selectivity. Hence, in this thesis, I explore several studies with a common goal of reconsidering each component of an EAB sensor for its further optimization and improvement.

The first chapter covers the purpose and background of the studies to be addressed. Chapter 2 explores properties of the self-assembled monolayer (SAM) of the EAB sensor to assess how anti-fouling self-assembled molecules such as oligoethylene glycol molecules can impact the obtained signal strength, stability and drift in comparison to the conventional SAM employed for EAB sensors, such as mercaptohexanol. Chapter 3 covers displaying EAB sensors on different gold electrode platforms to determine what type of surfaces are ideal for realizing EABs on thin-film electrodes for future use in wearable devices. This chapter particularly focuses on exploring different types of thin-film gold electrode platform commonly employed in flexible electronics to determine what type of topographical and chemical properties are required in gold electrodes for EAB sensors to expand the use of EABs beyond the standard gold wire platform. Chapter 4 aims to introduce an aptamer sensor for monitoring dopamine levels in the brain through exploring challenges observed in measurement differences between *in vitro* and *in vivo* settings. The final chapter concludes the thesis and provides highlights and future prospective on the prospects of EABs in realizing a system to actively monitor biomolecules in concert with other biometrics.