

Cutting-edge DNA-Biomacromolecule Sensor: Boosting Sensitivity in Clinical Cancer Sample Detection

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Abstract

An ultrasensitive DNA-biomacromolecule system or technology can detect and analyze DNA molecules with exceptional precision. As the fundamental genetic material in living organisms, DNA is crucial for numerous biological processes and has extensive applications in diagnostics and research. These ultrasensitive technologies are designed to identify and quantify tiny amounts of DNA within a sample. Utilizing various detection methodologies such as fluorescence, electrochemical sensing, nanopore sequencing, or amplification techniques like polymerase chain reaction, these technologies allow scientists to achieve highly accurate and sensitive detection of DNA molecules, even at extremely low concentrations.

Keywords: DNA-biomacromolecule • Nanopore • Ultrasensitive DNA

Introduction

Ultrasensitive DNA detection plays a pivotal role in molecular diagnostics, enabling the identification of diseases, genetic disorders, and infectious agents. By pinpointing specific DNA sequences linked to particular conditions, it supports early disease detection and personalized medicine initiatives. Furthermore, DNA analysis is fundamental in forensic investigations, aiding in suspect identification and establishing genetic relationships with exceptional accuracy. These ultrasensitive technologies excel in extracting and analyzing DNA from minimal biological samples, thereby enhancing the precision and reliability of forensic analyses. Additionally, DNA-based monitoring techniques are used to evaluate the presence and abundance of diverse organisms in environmental samples. These technologies empower the detection of rare or low-abundance species, enriching biodiversity studies and ecological research endeavours [1].

Literature Review

Detecting and analyzing DNA mutations or abnormalities associated with cancer is crucial for understanding the disease's molecular mechanisms and developing targeted therapies. Ultrasensitive DNA technologies are vital in identifying rare mutations or circulating tumor DNA, facilitating early cancer diagnosis and monitoring treatment efficacy. DNA analysis is integral to drug development and clinical trials, enabling the quantification of drug target genes, assessment of treatment effectiveness, and monitoring for drug-resistant mutations. In disease detection, particularly cancer, the importance of diagnostic testing of biological macromolecules cannot be overstated. However, achieving sensitive detection of macromolecules through interface-based sensing methods is challenging due to their limited surface area and significant steric hindrance. Introducing the "biphasic replacement" electrochemical aptamer-based sensing technique, this method replaces the

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capture reaction of the biomacromolecule with a small diameter of single-stranded DNA attached to the interface. Demonstrating the ultrasensitive detection of luteinizing hormone with this BRE-AB sensor showcases its promising potential for sensitive molecular detection in clinical settings [2].

Discussion

The aptamer-target LH binding mechanism is investigated using Molecular Dynamics simulations. Additionally, the BRE-AB sensor has demonstrated superior sensing capabilities in both undiluted plasma and whole blood. It successfully quantified LH concentrations in 40 clinical samples, revealing that breast cancer patients have higher LH expression. The sensor's simplicity, low cost, and ease of regeneration and reuse highlight its potential for biological macromolecule diagnostics at the point of care. The BRE-AB system's signaling mechanism involves both solution and interface reactions. In the absence of a target, prehybridized aptamer/signal duplexes remain in the solution phase, with only a few free signal probes with the redox indicator methylene blue able to enter the interface. Meanwhile, the anchored helper probes on the interface maintain a steady state. Upon the addition of target biomacromolecules, more stable aptamer/target complexes form by specifically binding to the aptamer and releasing signal probes from the aptamer/signal duplexes. The helper probes, anchored to the surface of the gold electrode via Au-S chemistry, then hybridize with the released signal probes at the interface. Consequently, the MB indicators are brought close to the gold surface, significantly accelerating electron transfer [3-6].

Conclusion

This study introduces a Biphasic Replacement E-AB sensing platform for highly sensitive detection of biomacromolecules at the picomolar level. The sensor offers several notable advantages, including ultrahigh sensitivity, excellent regenerability, and reusability, all achieved through a straightforward and cost-effective fabrication process. Remarkably, the BRE-AB sensor maintains a low detection limit even in whole blood samples. Molecular Dynamics (MD) simulation findings suggest that electrostatic interaction, hydrogen bonding, and the alkyl hydrophobic effect are the predominant forces driving Luteinizing Hormone (LH) binding to the aptamer. The BRE-AB sensor holds significant promise for analyzing and detecting various target molecules, facilitated by well-designed probe sequences informed by theoretical simulations and free energy predictions. This study highlights the potential of the BRE-AB sensor for early cancer diagnosis, positioning it as a promising candidate for macromolecular detection applications.

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Conflict of Interest

No potential conflict of interest was reported by the authors.

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