

An Electrochemical Aptasensor for Continuous Biomarker Monitoring

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Summary:

This study presents a self-regenerating electrochemical aptamer biosensor for continuous biomarker sensing under controlled buffer conditions. Sensor renewal is achieved by modulating buffer flow, avoiding chemical stripping and enabling repeated measurement cycles. Gold nanorod modified electrodes enhance interfacial electron transfer and improve analytical sensitivity, yielding a concentration dependent response across three orders of magnitude with a subnanomolar detection limit. The platform also exhibits reversible operation, with faster baseline restoration at higher wash flow. Overall, these findings establish hydrodynamic control as a practical strategy for continuous affinity biosensing and a strong basis for future diagnostic systems including but not limited to wearable, implantable, and microfluidic devices for diagnostics in sweat, interstitial fluid, tears, urine, saliva and other human specimens.

Keywords: biosensors, bioelectronics, continuous monitoring, hormone monitoring, 17 β -Estradiol.

Background and Motivation

Continuous hormone monitoring is crucial because endocrine signals evolve over time, and single blood draws often miss physiologically meaningful fluctuations linked to fertility, pregnancy, and women's health. Continuous affinity biosensing offers a path to time-resolved molecular readout, and electrochemical aptamer sensors are especially attractive because they support reagent-free transduction, miniaturization, and direct electronic measurement [1]. For continuous operation, however, affinity biosensors must reversibly track concentration changes without cumulative saturation, memory effects, or signal drift [2-3]. A remaining bottleneck, however, is regeneration. Once affinity sites are occupied, signal recovery often depends on chemical stripping or added reset hardware, which complicates wearable integration and sustained operation [4]. Here, we address this limitation with a flow-triggered self-regenerative electrochemical aptamer sensor for 17 β -Estradiol (E2) sensing. By using buffer-flow modulation alone to restore the sensing interface, the platform enables repeated measurement-regeneration cycles, stable dynamic operation, and selective detection toward practical continuous use.

Description of the New Method

We report a flow-programmed electrochemical aptamer platform for continuous biomarker sensing, combining a methylene blue tagged recognition layer with square-wave voltammetric

(SWV) transduction. The working electrode was nanostructured with AuNRs to enlarge electroactive area, improve electron-transfer efficiency, and increase sensitivity. Regeneration was achieved exclusively through modulation of buffer flow, which accelerated target dissociation and restored the baseline without chemical stripping. To the best of our knowledge, this is one of the first applications of flow-mediated regeneration in an electrochemical biosensor. The method was validated in E2 sensing in buffer to establish reversible operation and repeatable sensing-regeneration cycles.

Results

Figure 1A presents the time-resolved dose response of the E2 electrochemical aptasensor under continuous flow at 3 $\mu\text{L min}^{-1}$, where E2 solutions prepared in binding buffer with different concentrations were sequentially delivered into the sensing chamber. The sensor displayed well-defined, concentration-dependent current transitions, evidencing rapid target binding under dynamic conditions. The corresponding calibration plot in Figure 1B revealed an excellent quasi-linear dependence on the logarithm of concentration over three orders of magnitude, defining a dynamic range from 10 pM to 10 nM, an R^2 of 0.9982, and a limit of detection of 190 pM. Above 1 nM, the response approached saturation, consistent with progressive occupation of the available surface-confined aptamer binding sites.

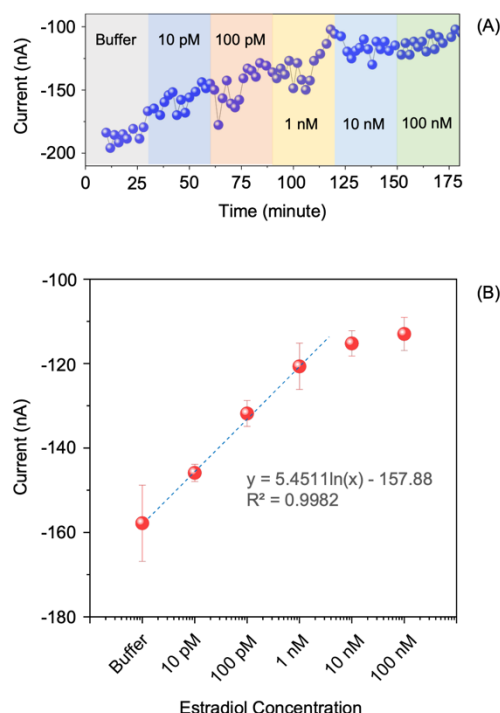


Fig. 1. Sensor characterization. (A) Dynamic dose-response, and (B) calibration curve of the sensor.

Figure 2 demonstrates that the E2 aptasensor preserves dynamic and reversible operation under continuous perfusion, with the measured current reflecting the coupled effects of target binding, fluid exchange, and interfacial re-equilibration. In Figure 2A, exposure to 100 nM E2 at $3 \mu\text{L min}^{-1}$ produces a clear time-dependent signal shift, indicating progressive occupation of the surface-confined aptamer layer and establishment of a new quasi-steady electrochemical state under flow. The non-instantaneous transition shows that the response is not governed solely by equilibrium binding, but also by analyte transport through the chamber and conformational switching of the redox-tagged probe layer. When the inlet is switched to blank buffer at the same flow rate, recovery is markedly slower and proceeds over a longer transition window, revealing incomplete washout of residual analyte and continued rebinding near the electrode surface. Figure 2B further confirms this mechanism. When E2 is introduced at $3 \mu\text{L min}^{-1}$ but the buffer flow is increased to $8 \mu\text{L min}^{-1}$, the sensor undergoes faster and more reproducible regeneration between consecutive cycles. The shortened transition time at higher buffer flow indicates that signal reset is strongly mass-transport limited, with enhanced convection accelerating analyte clearance, thinning the diffusion layer, and reducing memory effects. Collectively, these results establish flow programming as an effective and non-chemical route for regeneration of the E2 biosensor.

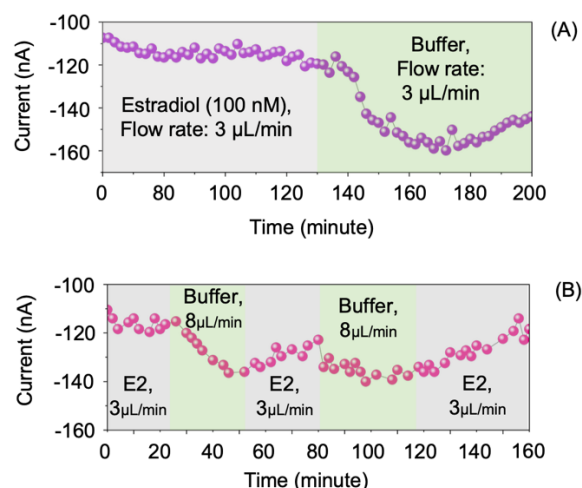


Fig. 2. Flow-induced regeneration. (A) Regeneration at buffer flow rate of $3 \mu\text{L/min}$, and (B) $8 \mu\text{L/min}$.

Conclusion and Outlook

This study establishes an electrochemical aptamer strategy for continuous biomarker monitoring in which sensitivity and reversibility are engineered together. AuNR nanostructuring strengthened SWV transduction and enabled dose-resolved E2 quantification over a broad log-linear range, while flow-programmed washing regenerated the interface without chemical stripping. The dependence of reset kinetics on buffer flow shows that recovery is governed by both aptamer dissociation and convective mass transport. These findings identify hydrodynamics as a controllable design variable for continuous affinity biosensors.

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