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MUC1 impedimetric aptasensing based on interdigitated array electrode chip using a novel diffusion element

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poster pitch video

INTRODUCTION

The miniaturized size and coplanar two electrode configuration make IDA electrode ideal for developing on-site immunosensing. It's a reliable way to immobilize aptamer on the IDA electrode and perform EIS spectrum analysis to investigate the aptamer-protein interaction. As IDA-based aptasensor possesses several advantages, such as robust, high thermo-stability, and ease of fabrication, it becomes a promising device to put into practical applications. Nevertheless, due to finite diffusion of IDA electrode, the Nyquist plot of it in low frequency region is different from standard planar electrode. It lacks an appropriate circuit element to explain this phenomenon. In this work, an IDA-based MUC1 impedimetric aptasensor using a novel K2 aptamer selected by our team is developed. We apply a diffusion element proposed by our team [1] to interpret the EIS data in low frequency region and analyze impedimetric sensing data using IDA electrode. This helps us explore the applicability of using IDA diffusion element in biosensing, and specificity and affinity of this sensor is also verified.

EXPERIMENTS

The IDA electrode chip was composed of a 3D-printed PLA clipper, a 3.5-mm-thick PDMS micro-well, and an IDA gold electrode with band/gap width 100/25 μm fabricated by photolithography and e-beam vapor deposition on a glass slide (Fig.1a).

Fig. 1d displays the fabrication and repeatedly sensing process of IDA-based MUC1 impedimetric aptasensor, Thiolated K2 aptamer, which is a ssDNA specific to the SEA domain of MUC1, is the sensing probe. For electrochemical analysis, $Fe(CN)_6^{3-/4-}$ was used as redox mediators, and EIS was performed using CHI614b electrochemical analyzer. The protein samples were prepared in binding buffer.

An equivalent circuit fitting program was developed by our team [1]. By analyzing the data in each step with the proposed IDA diffusion element in each binding and regeneration process, the dose-response of charge transfer resistance (R_{ct}) relationship was determined.

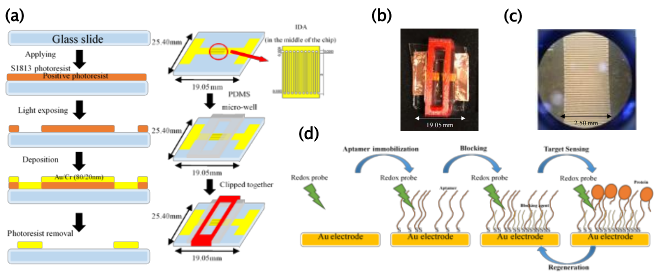


Figure 1. IDA chip (a)device setup, (b)top-view, and (c)under microscope. (d)Scheme of fabrication and detection on aptasensor

RESULTS AND DISCUSSIONS

All of the IDA chip sensing data was calculated by the fitting program. A comparison of data analysis using different diffusion impedance is shown in Fig. 2, which suggested that IDA diffusion element accurately explained the EIS data in low frequency region on Nyquist plot. This IDA-based impedimetric aptasensor is regenerable. Line chart in Fig. 3 displays R_{ct} change in each procedure. To evaluate impedimetric response of the binding event, relative change in R_{ct} ($\Delta R_{ct}/B_{ss}$) was calculated by Eqn. (1)~(4). To prove feasibility of applying a novel K2 aptamer for MUC1 impedimetric sensing on the IDA electrode chip, we built a thrombin aptasensor using HTDQ29 aptamer and a MUC1 aptasensor using K2 aptamer in order. Specificity of these two aptasesnor was verified. In Fig. 4a-b, relative change in R_{ct} of target analyte is significantly larger than non-target analyte even if the concentration of it is much higher than target analyte. The binding curve was also verified in Fig 4c-d.

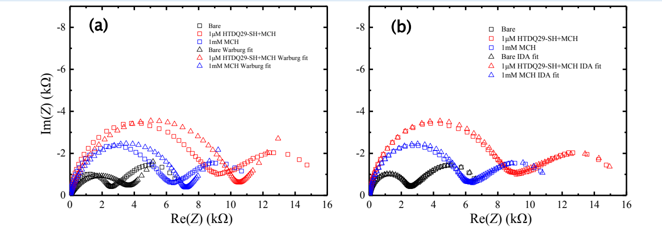
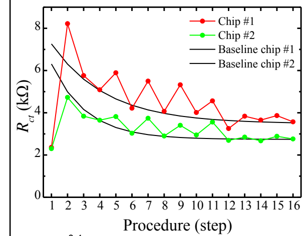


Figure 2. Nyquist plot of IDA electrode EIS raw data fitted with (a) Warburg element (b) IDA element in Randles equivalent circuit.



$$R_{ct,baseline}(k) = B_{ss} + R_{ct,transient}(k) \quad \text{......(1)}$$

$$R_{ct,transient}(k) = B_t e^{-\frac{k}{k_0}} \quad \text{......(2)}$$

$$\Delta R_{ct}(k) = R_{ct}(k) - R_{ct,baseline}(k) \quad \text{......(3)}$$

$$R_{ct,ratio} = \Delta R_{ct} \div B_{ss} \quad \text{......(4)}$$

Figure 3. R_{ct} line chart in each procedure, binding event can be evaluated through finding relative change in R_{ct} by baseline.

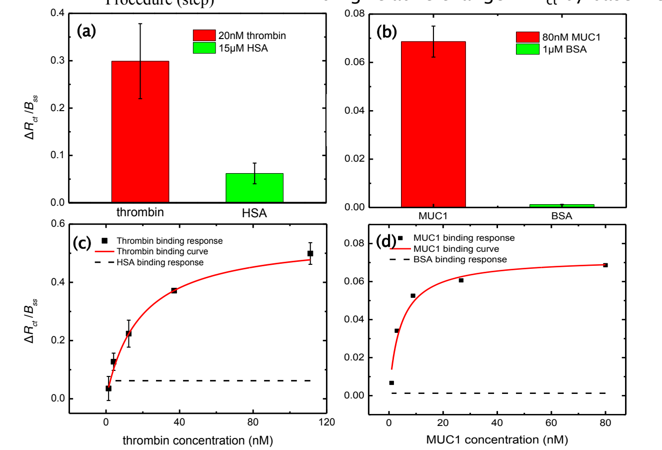


Figure 4. Specificity validation of (a)thrombin (b)MUC1 aptasensor, and binding curve of (c)thrombin (d)MUC1 aptasensor.

CONCLUSIONS

In conclusion, the IDA diffusion element was successfully applied for EIS data fitting. A selective and regenerable MUC1 aptasensor using a novel K2 aptamer was constructed, with K_d = 4.25 nM. It helps us investigate the potential of putting this sensing device into medical use and commercialization.