

Development of a MEMS-Based Electrochemical Platform for Label-Free Viral Antibody Sensing

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Summary:

Monitoring of antibody levels plays a critical role in evaluating immune response and disease control. In this work, a MEMS-based electrochemical sensing platform is developed for label-free viral antibody sensing using impedance measurements. The platform exhibits a concentration-dependent impedance response at the picogram (pg) level, while at higher concentrations (nanogram, ng) it shows a nonlinear response, suggesting surface-related limitations in binding. Selective detection is achieved with minimal non-specific interference, demonstrating a compact and scalable sensing approach.

Keywords: MEMS, electrochemical biosensor, impedance spectroscopy, label-free detection, antibody sensing

Background, Motivation and Objective

Protection against infectious diseases is largely based on humoral immunity, making antibody monitoring essential for evaluating immune response, vaccine efficacy, and population-level protection [1]. Conventional serological methods, including ELISA and lateral flow immunoassays, remain limited in terms of protocol complexity, reproducibility, and applicability for on-site testing. These limitations highlight the need for reliable antibody detection platforms. Electrochemical biosensors offer advantages due to their sensitivity and suitability for label-free measurements [2]. In particular, MEMS-based electrochemical platforms enable precise electrode structuring, reduced sample volumes, and scalable device architectures, providing a promising route for high-performance antibody sensing. In this context, a MEMS-based electrochemical sensing platform is developed for label-free viral antibody detection using impedance measurements. Antibody recognition is achieved through binding to a bioengineered protein expressed in a recombinant system, enabling a miniaturized and scalable sensing approach [3].

Sensor Design and Experimental Methods

MEMS-based electrochemical sensors were fabricated in the cleanroom facilities of METU MEMS Center (Ankara, Turkey). The platform is based on a planar three-electrode configuration

with a gold (Au) working electrode (WE), a platinum (Pt) counter electrode (CE), and a silver (Ag) reference electrode (RE) on a glass substrate, as shown in Fig. 1. Thin-film metal layers (Ti/Au, Ti/Pt, Ti/Ag; ~50/500 nm) were patterned using standard photolithography and lift-off processes [4]. The working electrode was designed as a circular structure (~1000 μm in diameter) surrounded by concentric counter and reference electrodes. For surface functionalization, a self-assembled monolayer (SAM) was formed on the gold electrode using 5 mM 11-mercaptopundecanoic acid (11-MUA) in ethanol, followed by EDC/NHS activation for antigen immobilization. After rinsing, the antigen was introduced, and non-specific sites were blocked using bovine serum albumin (BSA). Subsequently, target and non-target antibody solutions were applied, and interfacial changes were monitored via impedance measurements, enabling label-free sensing.

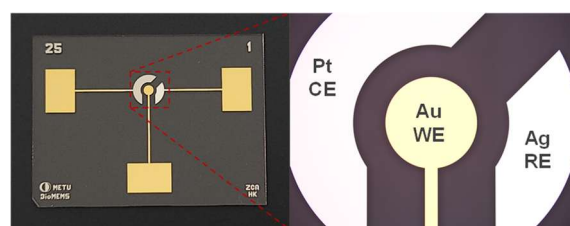


Fig. 1. Photograph of the fabricated MEMS-based sensor with a magnified view of the electrode region.

Electrochemical impedance spectroscopy (EIS) measurements were performed in a 5 mM ferri-cyanide/ferrocyanide solution using an Autolab PGSTAT128N system with a frequency response analyzer (FRA) module (Metrohm, Switzerland). Measurements were carried out from 0.1 Hz to 50 kHz using a 10 mV sinusoidal perturbation. The impedance spectra were analyzed with a Randles-type equivalent circuit, and charge transfer resistance (R_{ct}) was used as the sensing parameter. The sensing performance was evaluated over a concentration range from 10 pg to 5 ng, and responses were normalized with respect to the lowest concentration condition (10 pg).

Results

The sensing performance of the platform was evaluated by monitoring the impedance response as a function of antibody concentration (Fig. 2). The normalized R_{ct} was plotted against the logarithm of concentration, exhibiting a clear concentration-dependent behavior over a wide range. A progressive decrease in normalized R_{ct} was observed with increasing antibody concentration, indicating enhanced interaction at the electrode interface. At lower concentrations in the pg range, the response is gradual and well-resolved. In contrast, at higher concentrations (ng range), the response becomes nonlinear with reduced incremental signal change, suggesting surface-related limitations in binding and partial saturation of available sites. This behavior is highlighted in the inset of Fig. 2.

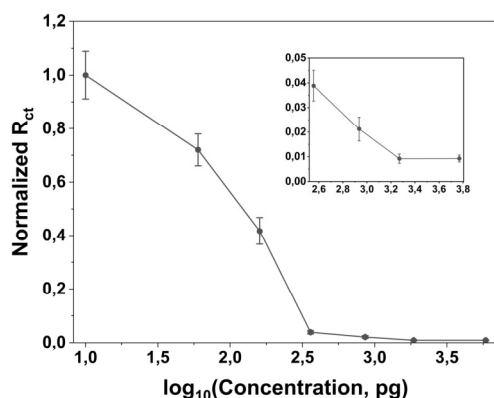


Fig. 2. Normalized R_{ct} versus logarithmic antibody concentration (picogram, pg). Inset shows the high-concentration regime.

The selectivity of the platform was evaluated at a representative concentration of 200 pg/mL by comparing the response of the target antibody with non-target species, including a model protein (BSA) and a non-target bacterial antibody (Fig. 3). The target analyte exhibited a pronounced decrease in normalized R_{ct} , whereas non-specific species showed significantly higher R_{ct} values. In particular, the responses for BSA and the bacterial antibody were approximately

10-fold and 30-fold higher than that of the target, respectively. These results indicate that target binding reduces interfacial resistance, while non-specific interactions do not produce a comparable effect, confirming minimal cross-reactivity and high selectivity of the sensing interface.

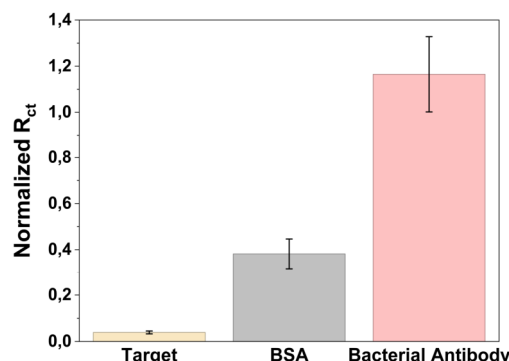


Fig. 3. Normalized R_{ct} for the target antibody, BSA, and a non-target bacterial antibody at 200 pg.

Conclusion

In this study, a MEMS-based electrochemical sensing platform for label-free viral antibody sensing was demonstrated. The system exhibited a concentration-dependent impedance response, with nonlinear behavior at higher concentrations, suggesting surface-related limitations in binding. Selective sensing of the target antibody was achieved with minimal interference from non-specific species, confirming the specificity of the sensing interface. The integration of a microfabricated electrode architecture with impedance-based readout enables a compact, label-free, and scalable sensing approach. These results highlight the potential of the platform for reliable and miniaturized antibody sensing.

References

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