Toward Single Virus Detection: Nanolithography-free Electrochemical Sensors based on Redox Cycling for Ultrasensitive Particle Detection

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Abstract: Redox cycling (RC) is a powerful method for amplification of electrochemical signals and can significantly enhance the sensitivity of electrochemical biosensors.[1] In this amplification method, the electrons generated as a result of a redox reaction are cycled repeatedly in between two closely spaced electrodes, called the generator and collector. The RC amplification factor increases as the distance between the electrodes is reduced, with the majority of the reported devices demonstrating several-fold signal amplification by including electrodes with a sub-micrometer gap. However, despite achieving high sensitivity, fabrication of devices with sub-micrometer features often requires nanofabrication methods, which are expensive and have limitations in terms of the attainable electrode thickness.[2,3] In this work, we developed a novel nanolithography-free method to robustly fabricate electrochemical sensors with a controllable sub-micrometer gap between the generator and collector interdigitated electrodes (IDTs) using a combination of photolithography and template-driven electrodeposition. Different electrode design parameters (such as the length, width, and number of digits of the IDTs) are investigated to identify the critical parameters affecting the RC amplification factor and collection efficiency. To demonstrate the application of the developed sensors, we performed proof of concept measurements for quantifying polymer particles with similar size (100 nm) and charge of SARS-CoV-2 viral particles (confirmed using Zeta potential measurements). The electric field between the collector and generator electrodes applies electrophoretic force on the charged particles, facilitating particle collision/capture on the electrodes. The signal amplification based on redox cycling and electrophoretic entrapment enables the detection of 1 particle/μL using only 20 μL sample volumes. Future work involves analysis of the sensor performance with viral samples and determining the analytical performance (limit of detection, sensitivity, and specificity). The developed nanolithography-free method for fabricating RC-based electrochemical sensors can offer new low-cost alternatives for detecting charged particles, with applications ranging from direct detection of virions to bio barcode assays.

References

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