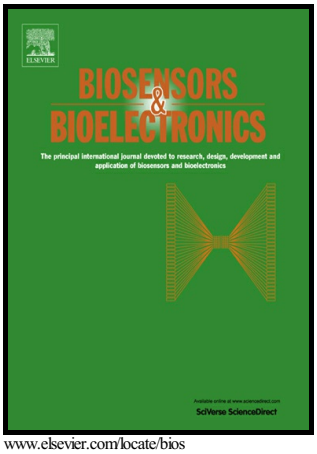

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Real-time Monitoring of Macromolecular Biosensing Probe Self-assembly and On-chip ELISA using Impedimetric Microsensors[1]

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Abstract

This paper presents a comprehensive study of the self-assembly dynamics and the biosensing efficacy of *Tobacco mosaic* virus-like particle (TMV VLP) sensing probes using an impedimetric microsensor platform. TMV VLPs are high surface area macromolecules with nanorod structures constructed from helical arrangements of thousands of identical coat proteins. Genetically modified VLPs express both surface attachment-promoting cysteine residues and FLAG-tag antibody binding peptides on their coat protein outer surfaces, making them selective biosensing probes with self-assembly capability on sensors. The VLP self-assembly dynamics were studied by the continuous monitoring of impedance changes at 100 Hz using interdigitated impedimetric microsensors. Electrical impedance spectroscopy revealed VLP saturation on impedance sensor surface in 8 hours with surface coverage of 68% in self-assembly process. The VLP-functionalized impedance sensors responded to 12 ng/ml - 1.2 μg/ml of target anti-FLAG IgG antibodies in the subsequent enzyme-linked immunosorbent assays (ELISA), and yielded 18% - 35% total impedance increases, respectively. The detection limit of the target antibody is 9.1 ng/ml using the VLP-based impedimetric microsensor. These results highlight the significant potential of genetically modified VLPs as selective nanostructured probes for autonomous sensor functionalization and enhanced biosensing.

Keywords

Virus-like particle, impedance sensor, microfabrication, macromolecule, bioreceptor

1. Introduction

Selective and sensitive detection of pathogens are crucial steps in identifying sources of disease outbreaks and forming effective strategies to ensure public health and food safety (Mandal et al. 2011; Yang and Bashir 2008). Among the current most effective and widely used biosensing methods, immunoassays, such as enzyme-linked immunosorbent assays (ELISA), are implemented to sense specific types of pathogens based on receptor-target interactions. Researchers have integrated the conventional lab-scale immunoassays with microfabrication technologies, and developed micro biosensors based on signal changes from bioluminescence, impedance or piezoelectric responses during the target-receptor interactions (Babacan et al. 2000; Katz and Willner 2003; Narsaiah et al. 2012; Roda and Guardigli 2012; Roda et al. 2004). In these microfabricated biosensors, receptor molecules with high affinity to target molecules are used to functionalize the transducer surfaces to achieve high selectivity. The efficacy of sensitive and selective biosensing is therefore largely determined by the density and binding affinity of the functional receptor layer. Currently, antibodies are the most commonly used receptors due to their versatility, convenience in handling and selectivity to targets (Mandal et al. 2011). However, a major problem associated with antibody sensing probes in

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