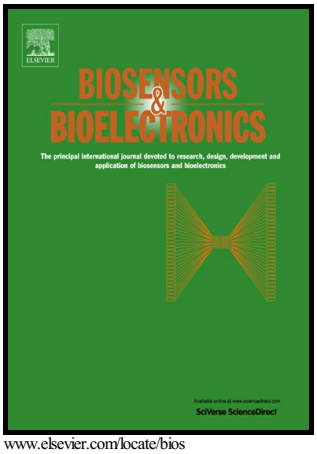

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Ultrasensitive nanostructure sensor arrays on flexible substrates for multiplexed and simultaneous electrochemical detection of a panel of cardiac biomarkers

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Abstract

Multiplexed detection of protein biomarkers offers new opportunities for early diagnosis and efficient treatment of complex diseases. Cardiovascular diseases (CVDs) has the highest mortality risk in USA and Europe with 15-20 million cases being reported annually. Cardiac Troponins (T and I) are well established protein biomarkers associated with heart muscle damage and point-of-care monitoring of both these two biomarkers has significant benefits on patient care. A flexible disposable electrochemical biosensor device comprising of vertically oriented zinc oxide (ZnO) nanostructures was developed for rapid and simultaneous screening of cardiac Troponin-I (cTnI) and cardiac- Troponin-T (cTnT) in a point-of-care sensor format. The biosensors were designed by selective hydrothermal growth of ZnO nanostructures onto the working electrodes of polyimide printed circuit board platforms, resulting in the generation of high density nanostructure ZnO arrays based electrodes. The size, density and surface terminations of the nanostructures were leveraged towards achieving surface confinement of the target cTnT and cTnI molecules on to the electrode surface. Multiplexing and simultaneous detection was achieved through sensor platform design comprising of arrays of Troponin functionalized ZnO nanostructure electrodes. The sensitivity and specificity of the biosensor was characterized using two types of electrochemical techniques; electrochemical impedance spectroscopy (EIS) and Mott-Schottky analysis on the same sensor platform to demonstrate multi-configurable modes. Limit of detection of 1 pg/mL in human serum was achieved for both cTnI and cTnT. Cross reactivity analysis showed the selectivity of detecting cTnT and cTnI in human serum with wide dynamic range.

Keywords: Multiplexed detection, cardiac Troponins, ZnO nanostructures arrays, EIS, Mott-Schottky, point-of-care

1. Introduction

Early detection and reliable diagnosis play a central role in making effective therapeutic decisions for treatment of diseases. Detection involves identification of disease-specific biomarkers (i.e. proteins, DNA or RNA, metabolites, etc.) in human body fluids (i.e. blood, plasma, urine, etc.) that represents the irregularities in cellular regulatory functions, pathological responses or intervention to any therapeutic drugs (Neumann 2015). Quantitative detection of these biomarkers in a simultaneous or multiplexed manner at the early stages of the disease when expressed in very low concentrations has been a technological challenge. Also, accuracy in diagnosis is further enhanced when the quantification of the disease can be done through a panel of biomarkers (Joos et al. 2002). Hence there is immense interest and value in designing ultrasensitive biosensors towards detection of a panel of biomarkers from a single sample of human body fluids.

A number of transduction strategies have been adopted to achieve the goal of ultra-sensitive and multiplexed label-free detection. One leading methodology that is widely implemented by