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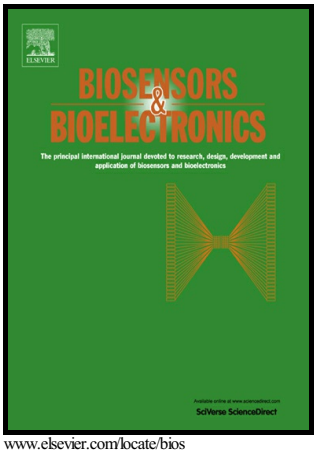

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Quantitative Differentiation of Multiple Virus in Blood using Nanoporous Silicon Oxide Immunosensor and Artificial Neural Network

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Abstract:

In spite of the rapid developments in various nanosensor technologies, it still remains challenging to realize a reliable ultrasensitive electrical biosensing platform which will be able to detect multiple viruses in blood simultaneously with a fairly high reproducibility without using secondary labels. In this paper, we have reported quantitative differentiation of Hep-B and Hep-C viruses in blood using nanoporous silicon oxide immunosensor array and artificial neural network (ANN). The peak frequency output (f_p) from the steady state sensitivity characteristics and the first cut off frequency (f_c) from the transient characteristics have been considered as inputs to the multilayer ANN. Implementation of several classifier blocks in the ANN architecture and coupling them with both the sensor chips, functionalized with Hep-B and Hep-C antibodies have enabled the quantification of the viruses with an accuracy of around 95% in the range of 0.04 fM to 1 pM and with an accuracy of around 90% beyond 1 pM and within 25 nM in blood serum. This is the most sensitive report on multiple virus quantification using label free method.

Keywords: multiple virus, differentiation, nanoporous silicon oxide immunosensor, artificial neural network

1. Introduction

Estimation of trace quantities of virus such as Hepatitis B and C, influenza, HIV in whole blood is of critical importance in clinical diagnostics (Rica et. al., 2012) .Viral infections is considered to be a serious threat to human health and is related to severe illnesses such as high fever, diarrhoea, metabolic imbalance and others. Most of the commercially existing assays suffer from low sensitivity and hence can detect only when the organism has significantly multiplied itself. Initiating treatment at this stage also becomes expensive. Thus, it will be of utmost benefit to mankind, if sub-femtomolar virus detection can be achieved. Therefore, extensive research has been focused towards electronic detection of biomolecules by conductance, impedance or amperometric measurements based on various nanostructured substrates like nanowires (Li et.al., 2014), nanoribbons (Aroonyadet et.al., 2015), ordered and random nanopores (Li et.al., 2015), nanotubes (Martinez-Cisneros et.al., 2014), nanorods (Han et.al., 2016) and nanoparticles (Wu et.al., 2005). The materials deployed for such structures range from silicon and its oxide, indium oxide, graphene, carbon nanotubes, anodized alumina, zinc oxide to various polymers (Aroonyadet et. al., 2015; Li et. al., 2015; Martinez et.al., 2014; Han et.al., 2016; Wu et.al., 2005; Bertok et.al., 2014). Nanostructured substrate not only improves the binding efficiency of the analyte due to large surface area to volume ratio but also shows a possible catalytic effect in the diffusion of the analyte molecules within the nanopores (Bertok et.al., 2014). Further, the 3D configurations of the nanostructures have been reported to be significantly more sensitive than their 2D counterparts owing to larger surface area to volume ratio and increased diffusion flux [Basu et.al., 2016). In particular, 3D graphene in the form of nanogrids, sol-gel silica nanoparticles, carbon nanostructures, suspended nanowires and silicon oxide/nitride nanopores have been widely explored (Liang