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Molecularly Imprinted Polymers for Diagnostics: Sensing High Density Lipoprotein and Dengue Virus

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Abstract

Molecularly imprinted polymers (MIP) have been an attractive area of research for the past couple decades. Even though they constitute a well-established field of functional materials MIPs still have to make their way into commercial applications. The lack thereof may be explained in part by the absence of MIP systems aimed at analytes that are of relevance in everyday life. In this article two different sensing applications are presented each targeting a clinically relevant analyte. These include the first-ever MIP of high density lipoprotein (HDL), which is exploited as a cardiovascular biomarker, as well as a MIP targeting Dengue virus particles. In both cases the data presented suggests that MIPs targeting these two particular analytes show characteristic behavior that makes them potentially suitable for diagnostic purposes.

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Keywords: molecularly imprinted polymers (MIP), quartz crystal micorbalance (QCM), high density lipoprotein, Dengue virus

1. Introduction

Molecularly imprinted polymers [1] constitute a class of biomimetic receptor materials for sensors [2] whose synthesis is based on self-organizing a highly cross-linked polymer around the target species of interest. This leads to cavities that are both functionally and structurally adapted to re-incorporate said analyte. Although already successful in a wide range of research, real-life applications are infrequent, especially when aiming at bioanalytes in real-life matrices. One recent exception is detecting E. coli directly in a bioreactor [3]. Within this paper, we

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introduce MIP-based QCM sensors for two analytes of substantial potential in diagnostics, namely HDL – a lipoprotein and interesting biomarker – and the Dengue virus.

2. High Density Lipoprotein MIP Sensor Development

LDL and HDL are two out of several classes of lipoproteins which perform a vital role in the metabolism by transporting water-insoluble components such as cholesterol. Their names historically derive from their varying densities and resulting fractionation in a centrifuge. Through epidemiological studies it has been proven that there is a correlation between cholesterol, HDL & LDL blood levels and the onset of arteriosclerosis as well as coronary heart diseases [4]. Therefore HDL and LDL both serve as critical biomarkers in medicine.

While an LDL-targeted MIP sensor operating in the clinically relevant range has already been reported [5], no such sensor currently exists in case of HDL. This is in part due to the much lower physiological concentration of HDL and the resulting problems in regards to concentration assessment. By optimizing a copolymer of methacrylic acid (MAA) and vinyl pyrrolidone (NVP) cross-linked with ethylene glycol dimethacrylate (EGDMA) it has been possible however to overcome the associated issues.

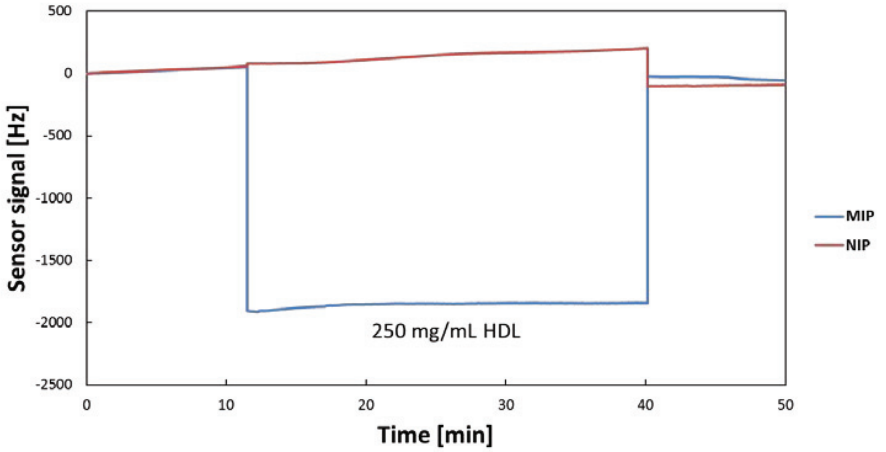

Fig. 1. Sensor signal of a dual-electrode MIP/NIP coated QCM sensor towards a concentration of HDL.

Fig. 1 shows a preliminary sensor effect acquired during measurement of a dual-electrode QCM. In this type of experiment one electrode is coated with the MIP, while the second one is coated with the non-imprinted version of the polymer (NIP) thereby acting as an internal reference excluding influences of temperature, density & ionic strength. As can be seen from the graph, the MIP exhibits a considerable sensor effect in the range of 1750-2000Hz while the NIP shows little to no reaction to injection of the analyte at all. The result strongly suggests that imprinting was indeed successful and that HDL is reversibly bound to the cavities formed on the polymer surface during imprinting. Cross-selectivity measurements of an HDL imprinted MIP using solutions of both HDL and LDL have shown good sensor selectivity with selectivity factors in the order of one magnitude. The data gathered during these investigations is graphically summarized in Fig. 2 and normalized in regards to concentration. Based on the results shown it can be said that MIP based sensors are indeed on a good way to see application in the clinical diagnosis of both HDL and LDL.