Introduction

Over the past few decades, researchers have devoted considerable effort to the integration of synthetic receptors into chemical sensing platforms. In general, molecularly imprinted polymers (MIPs) have been developed for targets ranging from small molecules to proteins while surface imprinted polymers (SIPs) are generally used to detect larger entities such as microorganisms or whole cells [1]. These synthetic receptors have been combined with traditional electrochemical, optical or microgravimetric readout approaches to create sensors for various applications including medical diagnostics and environmental screening [2]. In 2012, a surprisingly versatile readout tool for label-free sensing was developed; the so-called heat-transfer method (HTM) [3]. The technique was originally developed for the detection of point mutations in DNA but was soon extended towards chemical sensing by coating the chips with synthetic receptors. In this way, it can be used for a wide variety of applications ranging from *e.g.* bacteria detection in urine samples for UTI diagnosis to cardiac biomarker testing in serum [4-5].
The benefit of these thermal chemical sensing platforms over existing state-of-the-art technology lies in the unique combination of highly selective synthetic receptors and a low-cost, user-friendly readout platform that requires minimal instrumentation. The challenges towards commercial application mainly involve standardizing and upscaling the MIP/SIP synthesis procedure as well as the limited sensitivity of the readout approach. However, progress is being made in both aspects in recent years.
Method

Bacteria imprints were made by spin coating aluminum chips with semi-cured polyurethane layers. Template bacteria are immobilized onto a PDMS stamp and pressed into the polyurethane layer that was cured over-night. Removal of the stamp and template leads to a SIP containing microcavities that are complementary to the template. Thermal resistance over the solid-liquid interface was monitored by sending a thermal wave through the chip with an average temperature of 37.0°C and an amplitude of 0.1 °C. The phase shift of the transmitted thermal wave at 0.03 Hz was analyzed in function of the bacteria concentration in spiked urine samples [4].
MIPs can be made in a more reproducible manner than SIPs, through the so-called solid phase synthesis approach. MIP nanoparticles were obtained by immobilizing selected cardiovascular biomarkers onto glass beads that were packed in a column. Radical polymerization was performed at room temperature and the colum was eluded at different temperatures. The particles that elute at elevated temperatures were retained, as their affinity for the target is the highest. The MIP particles were directly immobilized onto the surface of the thermocouples for thermal resistance measurements.

Results and Conclusions

The results shown in Figure 1a illustrate that the phase shift observed in the transmitted thermal wave will increase when exposing the SIP-coated aluminum chip to the target bacterium, in this case *E. coli*. These findings can be explained by the fact that bacteria binding to the cavities in the SIP layer will displace the urine (water-based so a good thermal conductor) that was previously present, leading to an increase of the thermal-resistance at the solid-liquid interface and a tempered propagation of the thermal wave that was send through the chip.
The experiments using the nano-sized MIP particles for biomarker illustrate that it is possible to multiplex the thermal analysis for the detection of cardiac biomarkers in serum. The data in figure 1b show that the thermal resistance of the MIP particles at the interface only change

when exposed to their target (red, ST2). Exposing the MIPs to a similar cardiac biomarker (blue, H-FABP) results in a response that is similar to the response of the non-imprinted reference channel (black) with no significant change in the phase shift observed.

References

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