Development of paper-based lab-on-chip devices based on molecularly imprinted polymers

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In this work a biomimetic sensor based on the heat-transfer method(HTM) and molecularly imprinted polymers(MIPs) has been developed as a paper-based lab-on-chip device. These microfluidic paper-based analytical devices (μPADs) are considerably smaller, faster and cheaper compared to its lab-sized predecessors. They can be used, disposed after usage and easily replaced for a new test without the requirement of expensive equipment. This makes it the ideal sensor for detecting molecules in point-of-care testing.

Introduction

Molecularly imprinted polymers are biomimetic receptors that contain imprints with the exact shape of the analyte i.e. molecules. Purely based on morfology the analyte will bind to the cavities. Molecules with other shapes have poor affinity towards the MIPs and will not bind permenantly to the cavities [1]. MIPs have a long shelf life, are cheap and yet have equaly sensitive and selective properties as their biological counterparts i.e. nanobodies.

The transducer of the biomimetic sensor is based on the heat-transfer method [2]. This label-free, versatile and low-cost transducer turns the heat transfer properties (e.g. the thermal resistance) of the biomimetic receptor into an easy to measure signal. In the case of the paper-based lab-on-chip devices, only an heating element and an electric current source is required. The amount of current sourced is dependent on the heat transfer properties and these properties are in their turn dependent on the amount of target that has bound to the cavities. Finaly the amount of binding is a direct value for the concentration of the sample under test. A schematic representation of the biomimetic sensor is represented in figure 1.

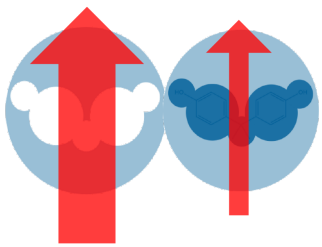

Figure 1: Schematic representation of the heat transfer resistance of a Bisphenol-A MIP with and without bounded Bisphenol-A. The red arrow represents the transfer of heat.

The novelty of this work lies in the use of paper-based microfluidics to administer the sample to the reaction chamber. The capillary force the paper performs on the fluid sample eliminates the need for pumps. Further, the low amount of sample required decreases the stabilization time of the heat-transfer method. In addition the lab-sized sensor requires a long assembling time whereas an old µPAD only needs to be removed and a new one reapplied.

Results and discussion

The µPADs were laser-cut from Whatman nr.1 filter paper and sealed with Kapton Tape to prevent evaporation and to create additional capillary forces. The developed µPADs have been functionalized with molecularly imprinted polymers and non-imprinted polymers (NIPs), hence differential measurements can be performed with only one µPAD. The functionalized areas are placed on top of the HTM transducer. The µPAD design has a pumping capacity of 20 µl. A measurement with this µPAD takes 30 seconds to stabilize. This is a 60-fold decrease in stabilization time. It is possible to increase flow time by enlarging the pump to allow the MIPs to capture more molecules. A schematic representation of the µPAD is represented in figure 2. Preliminary tests with Bisphenol-A

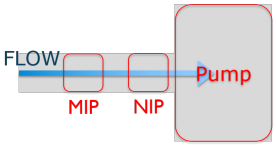

Figure 2: Schematic representation of a functionalized µPAD

show a trend in the response for MIP compared to the NIP of the same µPAD. It seems that there is no clear baseline level. This can be explained by the fact that the amount of MIP and NIP added to the µPADs happens in an uncontrolled way.

Conclusion

Paper-based lab-on-chip devices based on molecularly imprinted polymers and the heat-transfer method have proven to be a promising, fast, disposable and diagnostic point-of-care device. A lot of optimization is still possible and some opportunities of the µPADs still have to be tapped in to.

References

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