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All-polymer chip with integrated sample handling for molecular diagnostics

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We present an all-polymer chip with passive liquid handling for the automated on-chip molecular amplification and optomagnetic (OM) readout of amplification products from a synthetic type-B influenza target. This demonstrates the feasibility of integration of the OM readout with a multichamber chip with temperature control and presents significant a step towards a complete assay on a low-cost chip.

The bioassay is divided into three steps corresponding to three chambers on the chip (**Fig. 1a**): **(1)** Annealing and enzymatic ligation of padlock probe (PLP) on DNA targets attached to magnetic microbeads (MMBs) to form circular, joined PLP on matching targets (58°C, 20 min); **(2)** enzymatic rolling circle amplification (RCA) of targets on circles to form a long single-stranded concatemer of copies of the sequence complementary to the PLP (38°C, 45 min); **(3)** optomagnetic detection of the binding (depletion) of functionalized magnetic nanoparticles (MNPs) to the RCA product (54°C, 40 min) [1]. The target is attached to MMBs throughout the reaction and the MMBs are transported between the three chambers using an external magnet. The entire assay procedure was automated in LabView and took about 2 hours from chip loading to result.

The chip design has been developed and tested using three layers of PMMA (**Fig. 1b**), which were ablated using CO₂ laser cutting and bonded using pressure sensitive adhesive. The central part consists of three connected chambers of different sizes that contain the liquids for the reactions. The top part contains inlet holes and phaseguides [2] (ridges protruding from top to control filling) and the bottom part is a flat PMMA surface. The chambers in the central part are connected to different waste engraved channels, which are then connected to outlets. The phaseguides combined with capillary stop structures enable well-controlled passive filling of liquids without air bubbles.

The automated measurement setup consists of sandwiched resistive heaters heating the reaction and analysis chambers, plus a dual xz-motorized stage moving the magnet to transport MMBs between the chambers. The optomagnetic measurements, performed in the third chamber, monitor the modulation of intensity of transmitted light ($\lambda = 405 \text{ nm}$) in response to an applied oscillating magnetic field [3]. The modulation arises from the rotation of MNPs to align along the field. When these bind to the RCA products, their rotation is essentially frozen and a turn-off of the signal from free MNPs is observed. We present results of our ongoing work on the detection of influenza virus DNA.

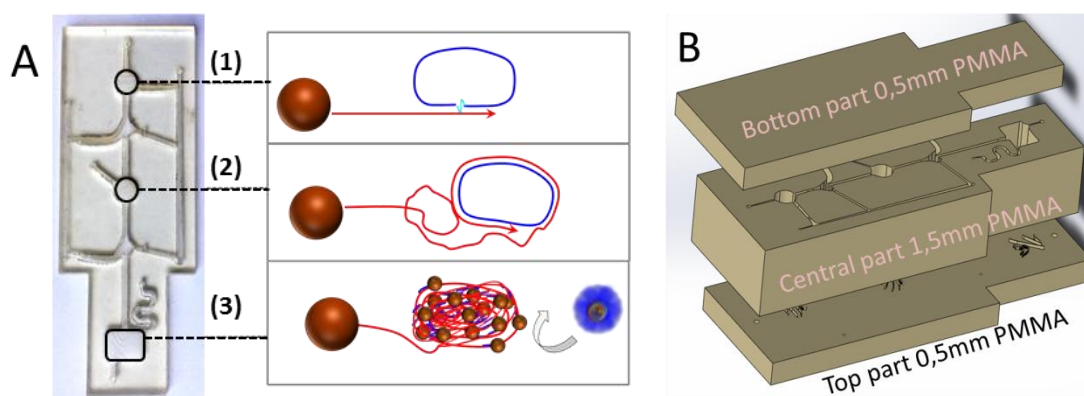


Figure 1: A) Schematic representation of the bioassay with different steps explained in the text. B) CAD representation of the three layers of PMMA chip and its features.

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