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An integrated lab-on-a-disc approach to detect inflammatory biomarkers from whole blood

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We demonstrate a novel integrated assay from a whole blood (WB) sample to detect the two most common inflammation biomarkers, C-reactive protein (CRP) and white blood cell (WBC) count on a low-cost centrifugal microfluidic disc. CRP detection is performed using a magnetic nanobead (MNB)-based agglutination assay and a Blu-ray based optomagnetic reader unit [1], whereas the WBC count is obtained using an optical imaging unit (oCelloScope). Both detection units are integrated with the centrifugal microfluidics platform and are performed on a single disc ensuring automation and reliability of the assay (Fig. 1a). In-house fabricated microfluidic discs (Fig. 1b) were used for sample processing and detection using both readout methods. First, 35 μl of PBS-diluted human WB (EDTA-treated) was loaded into the disc. High speed centrifugation (45 Hz) with a low acceleration (2.5 Hz) first caused the blood to overlay on a pre-loaded density gradient medium (DGM) followed by stratification into plasma, WBC layer and red blood cells. The blood plasma and the WBC were then transferred to different microfluidic chambers using centrifugo-pneumatic valving [3]. CRP antibody-functionalized MNBs were mixed on-disc with different amounts of plasma resulting in MNB agglutination as detected optomagnetically in the 2nd harmonic component of the transmitted light as function of an applied oscillating magnetic field at low frequency (Fig. 1d) [2]. The WBCs were counted on-disc by scanning the WBC chamber using the oCelloScope followed by quantification using the instrumental software Uniexplorer 8.0 [4] (Fig. 1c). Current work aims to test the efficacy of the method with blood samples from multiple subjects and compare the efficiency of the WBC count with that of a hemocytometer.

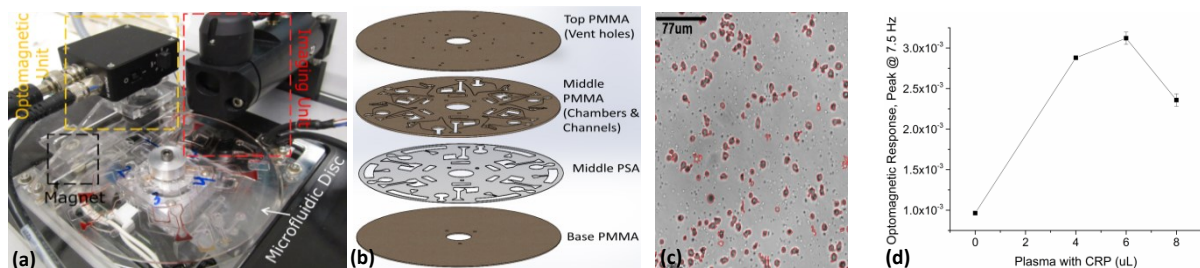


Fig 1.(a) Setup with integrated detection units and a pair of permanent magnets to perform magnetic incubation for enhancing agglutination [2,4].(b) Microfluidic discs fabricated by thermal bonding from three layers of PMMA and one layer of PSA. (c) On-disc automated quantification of WBC ($2245 \pm 322/\mu\text{l}$ blood, $n=3$) using the oCelloScope software.(d) Normalized optomagnetic signal peak for different volumes of plasma with CRP ($n=3$) showing higher peak value for higher CRP level until MNPs are saturated with CRP (6 μl) above which a hook-effect is observed [2].

References

- [1] M. Donolato et al., *Biosens. Bioelectron.* **67**, 649 (2015); [2] J. Fock et. al, *Biosens. Bioelectron.* **88**, 94 (2017)
- [3] R. Burger et al., *J. Micromech. Microeng.* **23**, 035035 (2013); [4] R. Uddin et al., *Biosens. Bioelectron.* **85**, 351 (2016).