The LabDisk – A Fully Automated Centrifugal Lab-on-a-Chip System for the Detection of Biological Threats

Thomas van Oordt[1], Oliver Strohmeier[1], Daniel Mark[1], Roland Zengerle[1,2,3], Michael Eberhard[4], Josef Drexler[4], Pranav Patel[5], Manfred Weidmann[6], Andrea Zgaga-Griesz[7], Wolfgang G. Bessler[7], and Felix von Stetten[1,2]

[1] HSG-IMIT - Institut für Mikro- und Informationstechnik, Villingen-Schwenningen, Germany
[2] Laboratory for MEMS Applications, Department of Microsystems Engineering - IMTEK, University of Freiburg, Freiburg, Germany
[3] BIOSS-Centre for Biological Signalling Studies, Universiy of Freiburg, Freiburg, Germany
[4] QIAGEN Lake Constance GmbH, Stockach, Germany
[5] Robert Koch Institut, Berlin Germany
[6] Department of Virology, University Medical Center Göttingen, Göttingen, Germany
[7] Institute for Molecular Medicine and Cell Research, University Medical Center Freiburg, Freiburg, Germany

Abstract. The world's growing mobility, mass tourism and the threat of terrorism increase the risk of a fast spread of infectious microorganisms and toxins. Therefore, there is a growing demand for small, mobile, easy to use diagnostic systems for automated detection of those agents directly at the point of need. However, the state of the art for pathogen detection requires complex stationary devices and trained personal limiting the capability for a rapid and effective response. We present an alternative solution to this demand: the LabDisk platform, a portable fully automated Lab-on-a-Chip system which performs complex biochemical analyses at the point of need. We applied the LabDisk platform to an automated nucleic acid analysis for the detection of *Bacillus anthracis* and *Francisella tularensis* and to an immunoassay for the detection of ricin.

Keywords: Lab-on-a-chip, immunoassay, nucleic acid assay, portable point-of-care devce, LabDisk.

1 The LabDisk Platform

The platform consists of a disposable centrifugal-microfluidic cartridge, the "LabDisk", in which completely integrated biochemical protocols for nucleic acid or protein analyses can be performed. For cartridge processing, a portable device, the "LabDisk Player" was developed. This device automatically controls fluid processing, heating and signal acquisition via fluorescence or luminescence. Due to the size and weight of the processing device (178 x 283 x 150 mm^3; 2 kg), the system is suitable for use at the point-of-need.

N. Aschenbruck et al. (Eds.): Future Security 2012, CCIS 318, pp. 220–223, 2012.

1.1 LabDisk Player

The LabDisk Player is able to run a fully automated and defined rotation- and temperature protocol to control the complete analysis. The processing device incorporates a heater for isothermal incubation or nucleic acid amplification at up to 60 °C and two detection units for either fluorescence or chemiluminescence readout (Figure 1).

Fig. 1. The portable LabDisk Player. Integrated magnets can be used for the automated control and manipulation of magnetic beads e.g. for nucleic acid purification or bead based immunoassays

1.2 LabDisk

Disposable micro-thermoformed polymer films, the LabDisks [1] were used to implement a nucleic acid analysis and an immunoassay. For both assays, the complete microfluidic structures have been integrated into the foil-based cartridges and all the microfluidic unit operations required to perform the assays have been verified.

Nucleic Acid Analysis
The LabDisk for nucleic acid analysis includes blood plasma sample preparation featuring initial pathogen lysis and subsequent DNA extraction according to a standard bench top bind-wash-elute protocol (Figure 2, left). As a solid phase, silica coated magnetic particles are applied that can be manipulated by the magnets that are integrated into the processing device [2]. After DNA extraction the sample solution is aliquoted in up to 11 cavities with 10 µL volume each. In each cavity, a set of pathogen specific primers and probes is prestored and enables specific amplification and detection via isothermal real time recombinase polymerase amplification (RPA). The systems functionality was demonstrated by automated detection of *Bacillus anthracis* and *Francisella tularensis* from blood plasma samples in less than 45 minutes (Figure 2, right).

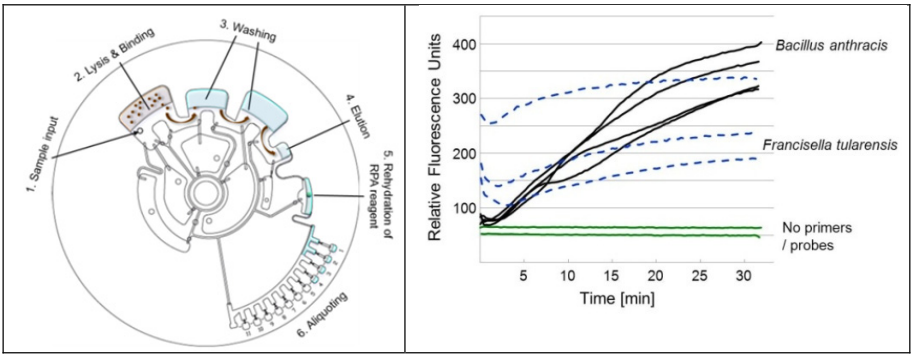

Fig. 2. The nucleic acid analysis. Left: Fluidic design of the disposable LabDisk. Right: On-disk detection of *Bacillus anthracis* and *Francisella tularensis*.

Immunoassay

The immunoassay is based on a sandwich ELISA where one anti-ricin antibody is covalently linked to magnetic beads as solid phase. It will allow the detection of ricin from blood plasma samples. Figure 3 shows a LabDisk with the microfluidic design for the immunoassay with integrated aluminum pouches for reagent pre-storage. Primary tests show the successful detection of 10 ng/ml ricin from a citrated blood plasma sample in 45 minutes of which 30 minutes are needed for incubation. For the primary tests reagents were stored in cavities on the cartridge without the aluminum pouches. In the current stage, the readout is performed by absorption measurements. For that, the LabDisk is taken out of the processing device and readout in an external photometer. Completely automated testing and chemiluminescence detection in the LabDisk player is currently under validation.

Fig. 3. Disposable LabDisk for immunoassay: reagents are stored in aluminium pouches

2 Conclusion and Outlook

A fully integrated system that provides rapid detection of pathogens is being developed. The LabDisk platform is able to perform a wide range of analyses such as immunoassays and nucleic acid detection. Fabrication of the microstructured disposable LabDisks and the detection of different pathogens have been successfully demonstrated. Currently the performance of the assays is under validation. The fabrication of a pilot series of cartridges in a prototyping line will enable us to perform field tests with the LabDisk platform.

Acknowledgement. We acknowledge funding by German Federal Ministry of Education and Research (BMBF), grant number 13N10116.

References

1. Focke, M., Kosse, D., Al-Bamerni, D., Lutz, S., Müller, C., Reinecke, H., Zengerle, R., von Stetten, F.: J. Micromech. Microeng. 21(115002), 11 (2011)
2. Strohmeier, O., Emperle, A., Focke, M., Roth, G., Mark, D., Zengerle, R., von Stetten, F.: The 14th Int. Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS), Groningen, The Netherlands, October 3-10, pp. 402–404 (2010)