LAB-ON-A-CHIP: FROM MICRO/NANOFLUIDIC RESEARCH-PLATFORM TO BIOMEDICAL APPLICATIONS

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Over the past 15 years, the concept of Lab on a Chip (LOC) has been developed to a great level of maturity. These microfluidics systems are nowadays employed both for research purposes as for a variety of applications in physics, analytical chemistry and biomedical applications. The first example is the use of a nanofluidic channel to separate DNA. It is found that the movement of DNA fragments is 20 nm high nanoslits in a strong electrical field is not continuous, but in a so-called "stop-and-go" manner. DNA fragments are in the stop-phase for up to 90% of the time, and in the go-phase for only 10% of the time.

Moreover, even in the go-phase, the calculated electrophoretic mobility is 10-100 times smaller than that of DNA in microchannels. We suggest two possible explanations for this effect, di-electrophoretic trapping (DEP) or mechanical trapping, both induced by surface roughness effects [1]. (see fig 1). In a second example, the development of a chip for monitoring lithium medication levels in manic-depressive patients.

This chip consists of a separation microchannel with integrated conductivity detection electrodes [2]. (see fig 2). Moving towards cell-manipulation and analysis, the fabrication of a million-well petri-dish will be presented, for very high throughput cell-experiments [3]. More focused on the single cell-level, we developed a chip for electroporation and gene transfection of single cells. First, we show that single cells can efficiently be electroporated as indicated by the translocation of dye's into the cell. Then, it is found that using a microfluidic chip we can electroporate and transfect C2C12 cells and human mesenchymal stem cells with high yield (>75%). It is found that GFP-ERK1 constructs transfected in HMSC's translocate form cytosol to nucleus upon stimulus with growth factor bFGF [4]. In a final example, the use of a simple microfluidics chip for evaluation of the efficiency of cancer-drugs is shown. It is found that the efficiency of drugs can be measured by determining the cell-covered surface after drug treatment. Application of different drugs lead to either apoptosis or necrosis of cancerous cells [5]. From these experiments future possibilities for a "Lab-in-a-Cell" will be discussed.

References

[1] G.B. Salieb-Beugelaar, J. Teapal, J.W. van Nieuwkasteele, D. Wijnperlé, J.O. Tegenfeldt, F. Lisdat, A. van den Berg and J.C.T. Eijkel (2008), "Field-dependent DNA mobility in 20 nm high nanoslits", *Nano Letters*, **8** (7), 1785-1790.

[2] E.X. Vrouwe, R. Luttge & A. van den Berg (2004), "Direct measurement of lithium in whole blood using microchip capillary electrophoresis with integrated conductivity detection", *Electrophoresis*, , **25**(10-11), 1660-1667.

[3] C.J. Ingham, S.J. Sprenkels, J.G. Bomer, D. Molenaar, A. van den Berg J.E.T. van Hylckama Vlieg and W.M. de Vos (2007), "The micro-Petri dish, a million-well growth chip for the culture and high-throughput screening of microorganisms", *Proceedings of the National Academy of Sciences of the United States of America* **104** (**46**), 18217-18222.

[4] A. Valero, J.N. Post, J.W. van Nieuwkasteele, P.M. ter Braak, W. Kruijer and A. van den Berg (2008), "Gene transfer and protein dynamics in stem cells using single cell electroporation in a microfluidic device", *Lab on a Chip* **8** (1), 62-67

[5] J. Komen, F. wolbers, H.R. Franke, H. Andersson, I. Vermes and A. van den Berg (2008), "Viability analysis and apoptosis induction of breast cancer cells in a microfluidic device: effect of cytostatic drugs", *Biomedical microdevices*, **10** (**5**), 727-737.







Fig. 2 Lithium chip for blood analysis