
TOWARDS A SINGLE CELL LABORATORY ON A CHIP

Alexandra Ros

Department of Chemistry and Biochemistry, Arizona State University, Tempe 85287-1604,
AZ, USA, Alexandra.Ros@asu.edu

Typical bioanalytical cellular assays are carried out in ensembles of roughly one million cells, thus are not capable of resolving biological diversity in small cellular clusters or even single cells. Resolving the biological complexity on the single cell level will allow the investigation of a variety of biological processes and phenomena which would otherwise be averaged in ensemble measurements. It is expected that the investigation of important cellular pathways on the single cell level could lead to significant advances in drug design and development, early disease diagnostics as well as tissue engineering. Clearly, our aim for novel analytical tools on the single cell level confronts us with the challenge of sampling and manipulation of micro- to nanometer sized biological objects as well as separation and quantitative analysis of biomolecules in ultra-small volumes. In this talk, various aspects of these challenges will be addressed and our recent activities of integrating important analytical steps in the microfluidic or lab-on-a-chip format will be presented. I will report on our recently proposed concept for combining single cell navigation, trapping and steering with subsequent on-chip lysis, protein separation and laser induced fluorescence detection in microfluidic systems. The proof of principle of our microfluidic single cell analysis concept was demonstrated with single cell electropherograms of genetically modified *Spodoptera frugiperda* (Sf9) insect cells expressing both GFP- and YFP-mutants [1; 2]. Furthermore, we have exploited migration dynamics giving rise to novel manipulation and separation tools as well as non-intuitive phenomena for microseparations. I will discuss the non-equilibrium migration phenomenon named absolute negative mobility with which particles can be driven into the direction opposite to an averaged driving force and which has high potential for separation of biological entities [3; 4]. Furthermore, I will present how length dependent dielectrophoretic behavior of DNA can be employed for ultra-fast separations in pL volumes [5]. The future investigation and improvement of such novel analytical approaches for a variety of biomolecules and cell types will be of outmost importance for the realization of a single cell laboratory on a chip.

References:

- [1] Hellmich, W., Pelargus, C., Leffhalm, K., Ros, A., and Anselmetti, D., Single cell manipulation, analytics and label-free protein detection in microfluidic devices for systems nanobiology, *Electrophoresis* 2005. 26, 3689
- [2] Ros, A., Hellmich, W., Regtmeier, J., Duong, T. T., and Anselmetti, D., Bioanalysis in structured microfluidic systems, *Electrophoresis* 2006. 27, 2651
- [3] Ros, A., Eichhorn, R., Regtmeier, J., Duong, T. T., Reimann, P., and Anselmetti, D., Brownian Motion: Absolute Negative Particle Mobility, *Nature* 2005. 436, 928
- [4] Regtmeier, J., Grauwin, S., Eichhorn, R., Reimann, P., Anselmetti, D., and Ros, A., Acceleration of Absolute Negative Mobility, *J.Sep.Sci.* 2007. 30, 1461
- [5] Regtmeier, J., Eichhorn, R., Duong, T. T., Anselmetti, D., and Ros, A., Dielectrophoretic Manipulation of DNA: Separation and Polarizability, *Anal.Chem.* 2007. 79, 3925