

## INTEGRATED MICROFLUIDICS FOR AT-LINE CULTURE MONITORING OF PROTEINS AND METABOLITES

Inês F. Pinto, Div. of Nanobiotechnology, Dept. of Protein Science, KTH Royal Institute of Technology & Science for Life Laboratory, Sweden  
ines.pinto@scilifelab.se

Leila Josefsson, Kantisto, Netherlands

Saara Mikkonen, Div. of Applied Physical Chemistry, Dept. of Chemistry, KTH, Sweden

Debbie van der Burg, Div. of Applied Physical Chemistry, Dept. of Chemistry, KTH, Sweden

Fabien Abeille, Micronit, Netherlands

Meeri E.-L. Mäkinen, KTH, Sweden

Sebastian Gierhing, PAIA Biotech, Germany

Matthias Stich, Presens Precision Sensing, Germany

Christian Krause, Presens Precision Sensing, Germany

David Sergeant, Ipratech, Belgium

Cari Sängler, Kantisto, Netherlands

Åsa Emmer, Div. of Applied Physical Chemistry, Dept. of Chemistry, KTH, Sweden

Aman Russom, AIMES; Div. of Nanobiotechnology, Dept. of Protein Science, KTH Royal Institute of Technology & Science for Life Laboratory, Sweden

Veronique Chotteau, KTH, Sweden

Miniaturization of analytical instruments is a very appealing avenue for Process Analytical Technology (PAT). Allied with automation, it can offer monitoring of cell culture at lower cost as well as lower requirement for highly qualified personal in comparison with instruments such as LC-MS. Within the EU project iConsensus, a new platform based on microfluidics has been created for at-line monitoring of cell cultures [1], the ALIAS standing for At-Line Integrated Analytical System. For this, several modules have been developed to quantify metabolites and proteins in the culture supernatant. The metabolites are detected by micro-chip capillary electrophoresis or optical sensors, while the proteins are detected in chip-based modules based on affinity. This latter can be multiplexed and versatile for simultaneous quantification of different proteins, such as antibody, host cell protein and lactate hydrogenase, marker of the cell viability. This monitoring has detection limits in the ng/mL range and performance comparable to commercial ELISA's. The method is also amenable to lectin-based detection of IgG main glycans. Thanks to capillary electrophoresis chips, amino acids or sugars can be detected as successfully demonstrated for the detection of 17 amino acids or different sugars, i.e. glucose, mannose, galactose, fucose, and lactose, with performances similar to capillary electrophoresis. Finally optical sensors have been developed for enzymatic-based detection of important metabolites such as glucose, lactate or ammonia. These different modules of affinity-based protein quantification, microchip capillary electrophoresis and optical sensors have been integrated in a proof-of-concept prototype of the ALIAS, to monitor CHO cell cultures.

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### References

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