

Non-Invasive In-Line Raman Spectroscopy – Ready for Flexible Real-Time Bioprocess Monitoring

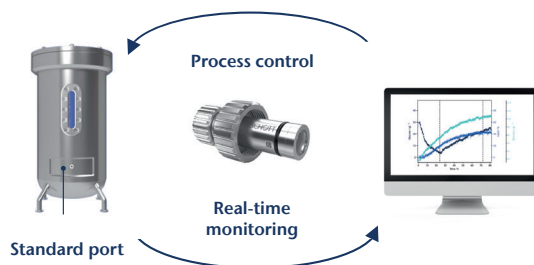
Christian Ott¹, Karin Wieland^{2,3}, Kristina Gruber¹, Thomas Brück⁴, Christoph Haisch²

¹ Schott AG, Christoph-Dorner-Strasse 29, 84028 Landshut, Germany | ² Chair of Analytical Chemistry, Technical University of Munich, Elisabeth-Winterhalter-Weg 6, 81377 Munich, Germany | ³ Competence Center CHASE GmbH, Altenbergerstr. 69, 4040 Linz, Austria | ⁴ Werner Siemens-Chair of Synthetic Biotechnology, Technical University of Munich, Lichtenbergstr. 4, 85748 Garching, Germany

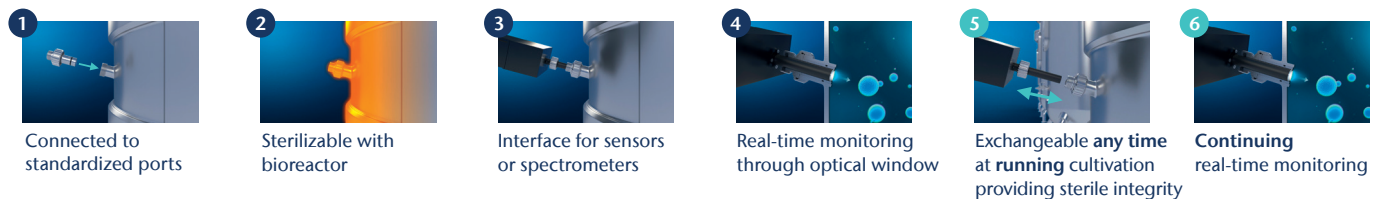
1. | INTRODUCTION

Raman spectroscopy as a direct, label-free, in-line process analytical technology (PAT) tool is used in a pilot-scale environment for lipid fermentation in yeast cells. To help gain more flexibility during a running process and reduce the overall contamination risk, a comprehensive PAT solution in combination with the novel sensor interface is proposed:

It enables enhanced automation and real-time in-line monitoring of bioprocesses without compromising the sterile boundary. The presented use case describes a compatible system of a bioreactor equipped with the sensor interface and a removable spectrometer system, as well as the exemplary results of the chemometric data analysis.

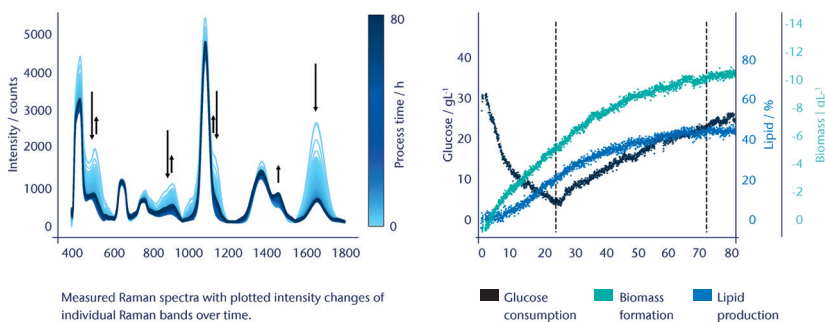


2. | EXPERIMENTAL SETUP and ASSEMBLY



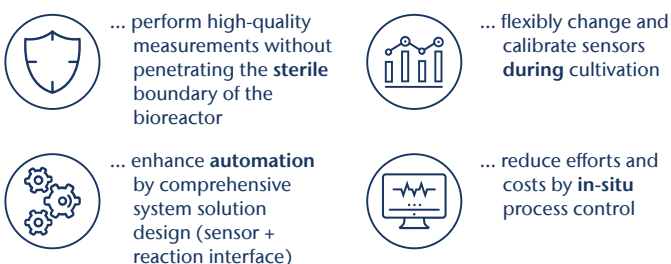
3. | USE CASE – PILOT SCALE

Information derived from the spectra can then be used for direct process control.



- Performance test of an **in-line Raman probe** in a **non-invasive setting** by using the ViewPort® sensor interface on a **yeast cell cultivation** for **intracellular lipid production**
- Use of **glucose** as a **carbon source** in a **bioreactor**, subsequently fed in a **fed-batch cultivation** at two different feed rates
- **In-situ monitoring** of the key process parameters: Set-up of a **data model** to continuously **adjust** the feed rate to the target (prerequisite for optimized yield)

4. | RESULTS



5. | OUTLOOK



Flexible system

- Cost efficient set-up. Change of spectrometer possible at any time during cultivation instead of permanently mounted back-up spectrometer.
- Change of spectrometer after manufacturing approval is possible. The novel sensor interface is in direct contact with the medium and not the spectrometer itself.

