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## **Combination of On-line pH and Oxygen Transfer Rate Measurement in Shake Flasks by Fiber Optical Technique and Respiration Activity Monitoring System (RAMOS)**

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### **Abstract:**

Shake flasks are commonly used for process development in biotechnology industry. For this purpose a lot of information is required from the growth conditions during the fermentation experiments. Therefore, Anderlei et al. developed the RAMOS technology [1, 2], which provides on-line oxygen and carbon dioxide transfer rates in shake flasks. Besides oxygen consumption, the pH in the medium also plays an important role for the successful cultivation of micro-organisms and for process development. For online pH measurement fiber optical methods based on fluorophores are available. Here a combination of the on-line Oxygen Transfer Rate (OTR) measurements in the RAMOS device with an on-line, fiber optical pH measurement is presented. To demonstrate the application of the combined measurement techniques, *Escherichia coli* cultivations were performed and online pH measurements were compared with off-line samples. The combination of on-line OTR and pH measurements gives a lot of information about the cultivation and, therefore, it is a powerful technique for monitoring shake flask experiments as well as for process development.

Key-words: Fiber optical pH measurement, shaking flask, oxygen transfer rate, RAMOS, *E. coli*, process development