

Ready-to-Use Devices for Optimizing Bioprocesses with Integrated Sensors

Real-Time Bioprocess Monitoring in Shake Flasks, Spinner Flasks and Microtiter Plates

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Bioprocess fermentors are typically equipped with real-time monitoring devices such as temperature, pH, oxygen, or even viable cell density. The advantages of on-line over off-line measurements are easiness of use, timely results, and the possibility of immediate responses to the measured value.

By contrast with the well-equipped fermentors used for production, the disposables used in bioprocess development have lacked such on-line measurement devices so far. Cultivation conditions could be monitored only by means of off-line sampling, typically performed at a predefined point in time. These predefined measurement times do not take into account the metabolism of a cultivated biological system.

This situation has changed. PreSens Precision Sensing is offering noninvasive sensors for the on-line measurement of oxygen, pH, and even CO₂ in small devices such as shake flasks, spinner flasks, and microplates.

PreSens offers ready-to-use disposables with integrated sensors and the appropriate measurement devices.

PRESENS pH MONITORING FOR MEDIA OPTIMIZATION (1)

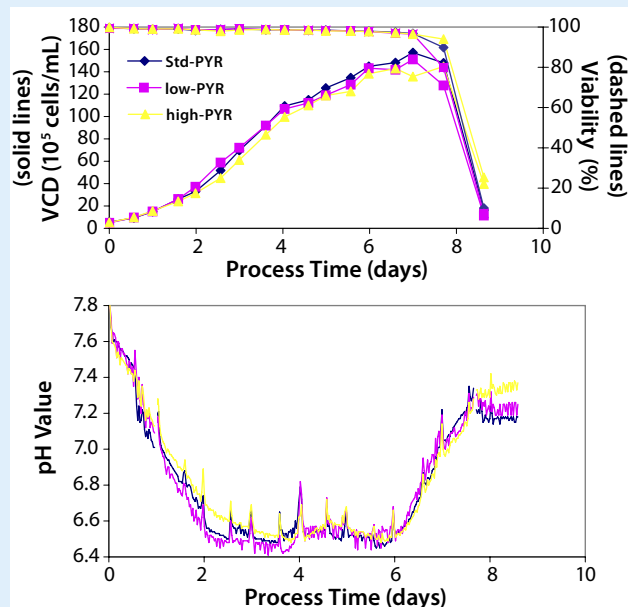
Substrate composition and concentration effect metabolism and therefore pH. The SFR Shake Flask Reader (2) (www.presens.de/SFR) monitors pH in shake flasks. As shown in Figure 1, even small differences in pH of an industrial CHO cell line can be detected. High pyruvate levels result in reduced glycolytic activity, less lactate accumulation, and therefore higher pH in the cultivation.

PRESENS OXYGEN MONITORING AT DIFFERENT CULTIVATION VOLUMES (2)

Growth kinetics of baculovirus-infected insect cells Sf21 were examined at different cultivation volumes in shake flasks. Under oxygen limited conditions Sf21 cell growth is just slightly reduced. As expected, L-lactate production is increased significantly and recombinant protein production is substantially reduced. At the same time, cell viability is maintained better under oxygen-limited conditions suggesting an inhibition of the viral replication cycle. The on-line measured oxygen efficiently allows identification of the current phase of baculovirus infection and reveals possible process limitations.



Figure 1: Cell density, cell viability, and pH of an industrial CHO cell line measured in real time in 250-mL shake flasks



PRESENS CO₂ SENSOR AS AN ALTERNATIVE TO OFF-LINE SAMPLING (3)

The latest development is a CO₂ sensor (www.presens.de/CO2) that monitors the cultivation of cells in glass and disposable reactors. As shown in Figure 3, these sensors show excellent long-term stability over a period of 10 days during growth of CHO cells with an initial seed density of 0.4 × 10⁶ cells/ml.

Figure 2: Oxygen concentration of insect cells Sf21 at different filling volumes, measured in real time in 1,000-mL shake flasks

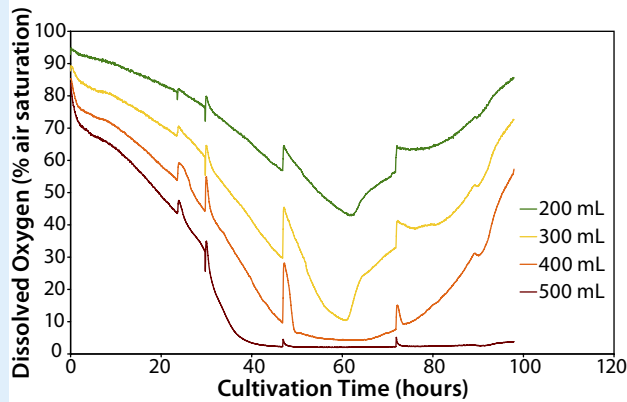
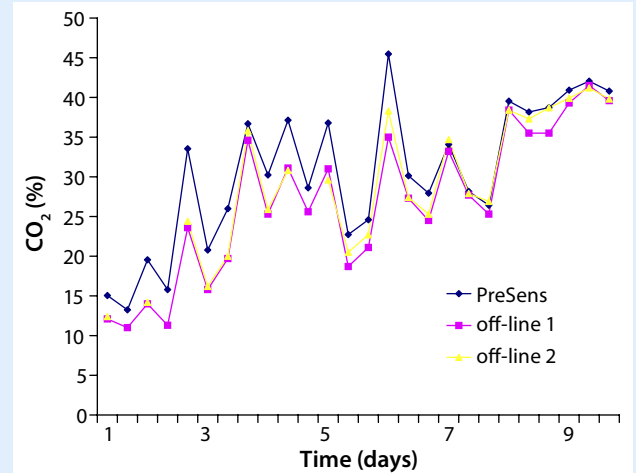



Figure 3: Comparison on-line and off-line measurement of CO₂ in a 3-L bioreactor



REFERENCES

- 1 Heinrich, et al. New Application for an Established Luminescence Based Sensor System: Monitoring pO₂ and pH in Shaker Flasks. *ESACT 2009*, Dublin, Ireland.
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3 Baggio, et al. Physical-Chemical Sensors: Application to Bioreactor Monitoring and Control. *ESACT 2009*, Dublin, Ireland. 

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