Disposable Sensors for On-line Monitoring in Disposable Bioreactors

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The pharmaceutical industry produces high-value drugs with the help of bioreactors. To control the production and insure the quality of the biomolecules, some parameters in the cell cultures such as pH, glucose and lactate concentrations, dissolved oxygen are monitored. To lower the price and avoid risks of contamination, disposable bioreactors are gaining popularity. The present work goes in the direction of a complete disposable system, by developing single-use sensors.

Disposable cell culture systems for biotechnology applications are gaining in popularity, and are being introduced in production lines in pharmaceutical companies. However, the monitoring of control parameters in these bioreactors is still being performed with the same methods used in non-disposable bioreactors: using traditional sensors which need to be sterilized and calibrated before each batch, or by sampling of the medium.

The company C-CIT AG entered the market of bioreactor monitoring in 2010, with the launch of the "CITSens Bio" lactate, glucose and glutamate sensors (see Figure 1). The ready to use, pre-calibrated, pre-sterilized plastic-based sensors are disposable, plug and play, and do not require any preparation. As they are single-use, the risks due to batch-to-batch contamination are avoided, as well as the time consuming preparation and re-calibration between runs. The data acquisition system is connected wirelessly to a server for data storage and on-line remote monitoring for up to 2 weeks. The system provides an alarm when the parameters exceed a threshold value, or alternatively the sensed values are injected in a feedback loop to adjust the cell culture conditions and keep the parameters within the optimal values.

Figure 1: The CITSens Bio online cell culture monitoring system; (left) the sensor is introduced in cell culture systems caps; (right) the sensors in a suspended culture flask, and connected to the wireless data transmission system [1]

Since the market launch, users of the CITSens Bio system expressed a strong demand for a multi-parameter system. To respond to this need, combined sensors for glutamate/lactate and pH/ammonium are being developed (Figure 2). All-solid-state pH sensors are being developed and characterized in both calibration solutions and in cell culture. The sensors functional lifetime in cell culture conditions (T=37°C, 100% humidity, 5% CO_2) has been verified for up to 2 weeks.

Figure 2: Screen-printed dual electrode sensors for multiple parameter monitoring

Sensors, gamma-sterilized before usage, are linear in the pH range from 3 to 9 for up to 16 days (see Figure 3), with a reproducible Nernstian sensitivity of 60 mV/pH unit.

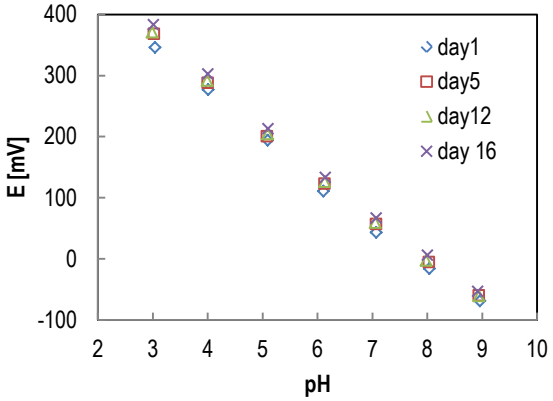

Figure 3: Calibrations for an all-solid-state pH sensor recorded between day1 and day16 of the monitoring of the sensor

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[1] Adapted from www.c-cit.ch