Zurich University of Applied Sciences

[H S W] HOCHSCHULE WÄDENSWIL

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Continuous in-line monitoring of ammonium in mammalian cell cultures

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Three ion selective electrodes (ISE's) for the determination of ammonium were sterilised and used for the continuous in-line monitoring of mammalian cell cultures (see figure 1). Because a pH electrode is used anyway, its reference electrode could additionally be used for the three ammonium sensors.

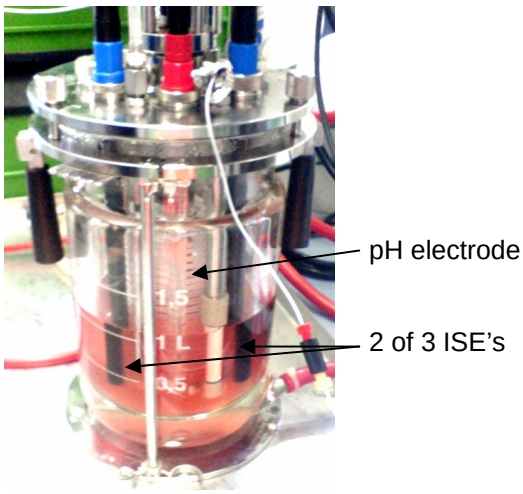

Figure 1: Bioreactor with a pH and two of three ammonium ISE's.

The sensors were calibrated between the sterility test and the inoculation of the reactor, and as a control again after the process.
Samples were taken to do on- and off-line analyses. An overview of the experimental set-up is shown in figure 2.

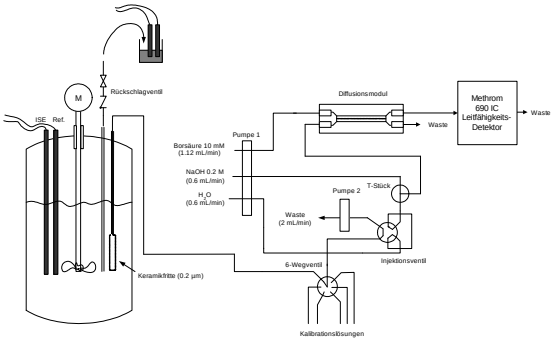

Figure 2: Scheme of the whole set-up.

The three ammonium electrodes showed good reproducibility and operational stability during the whole cultivation period, which took five days (see figure 3). The spikes in figure 3 originate from the feeding with fresh cell culture medium.

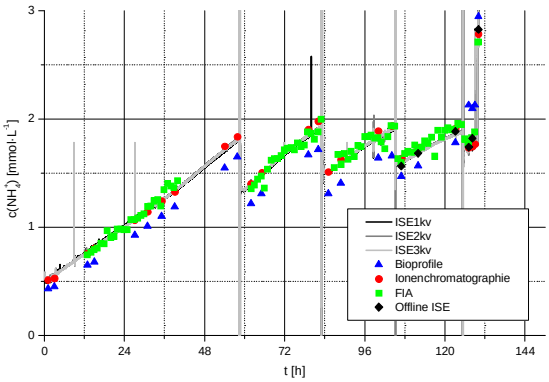

Figure 3: Results of the continuous in-line monitoring and the comparison to on-line and three different off-line analyses.

The off-line analyses were conducted using ISE's, the analyser BioProfile 100® and ion chromatography, respectively. All results are in good correlation with the continuous signals of the in-line analyses. The results of the Bio-Profile 100® are lower than the others. This is probably because of the different calibration solutions which had to be used for the Bio-Profile 100®.

Conclusion

Ion selective electrodes can be sterilised and used for continuous in-line monitoring of ammonium in cell cultures.