ON-LINE CALCULATION OF CTR AND OTR DURING HIGH-CELL DENSITY RECOMBINANT *E. COLI* FED-BATCH FERMENTATION: MS CALIBRATION, ON-LINE DATA ACQUISITION, ANALYSIS AND INTEGRATION

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ABSTRACT

During a high-cell density fed-batch fermentation of recombinant *E. coli*, both oxygen and carbon dioxide transfer rates (OTR and CTR) were calculated on-line from inlet and exhaust gas composition measurements obtained with Mass Spectrometry (MS) and from the culture weight. These rates, together with on-line measurements of acetate concentration by Flow Injection Analysis, were used to implement an adaptive control law in a real fermentation.

For MS calibration, a new method was adapted, where several gas mixtures were used, their composition being chosen from the analysis of the expected experimental space. A calibration factor was then calculated by linear regression that correlated the pressure values obtained in the MS for a given mass to charge ratio with the mixture composition in oxygen, carbon dioxide and nitrogen.

During the fermentation, 12 MS and weight data points (corresponding to approximately 3 minutes) were acquired in a developed LabVIEW subroutine where a C embedded window performed data analysis by statistical significance assessment to exclude potential outliers. Afterwards, the noise was partially eliminated by applying a moving average filter and MS raw data was converted to molar fractions, according to the calculated calibration factors.

CTR and OTR values are then computed from inlet and exhaust gas composition and reactor weight.

This LabVIEW subroutine was then integrated in a supervisory programme, together with the measurements of other equipments, acquired by serial ports or analog input and using string interpretation or the standard Windows Dynamic Data Exchange (DDE) protocol.