CELL CULTURE OXYGEN UTILIZATION AS ORTHOGONAL MEASURE OF BIOMASS FOR FEED CONTROL

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Biocapacitance probes in cell culture processes provide online measurements of biomass for enabling automated feeding and process control, but a back-up biomass measurement is preferred to resolve instances of deviation between redundant probes. A back-up measurement that integrates multiple online process trends to model biomass would provide several advantages over the current secondary method of manually sampling the bioreactor at discrete times and performing an offline particle count of viable cells. We hypothesized that consistency of cell-specific oxygen uptake rates would enable the volumetric oxygen transfer rate (OTR) to be a reliable orthogonal measurement of biomass. An automated data analysis tool was built to rapidly assess the relationship between biocapacitance and OTR for 15,000L bioprocesses in a GMP manufacturing facility, using empirically determined mass transfer coefficients and a data historian of online process trends. A linear correlation existed for multiple processes with a strong relationship between biocapacitance and OTR (R^2 = 0.9173 for 41 batches of Product A, R^2 = 0.9403 for 13 batches of Product B, R^2 = 0.8781 for 7 batches of Product C, R^2 = 0.9583 for 4 batches of Product D, see Figure 1). Batch automation modules are being updated to enable real-time calculation of OTR and transformation to OTR-predicted biocapacitance during GMP processing, which can inform the selection of the correct biocapacitance probe for the purposes of determining feed mass. Successful implementation of this strategy will result in a more sustainable and automated approach to process control with reduced dependency on manual sample analysis.

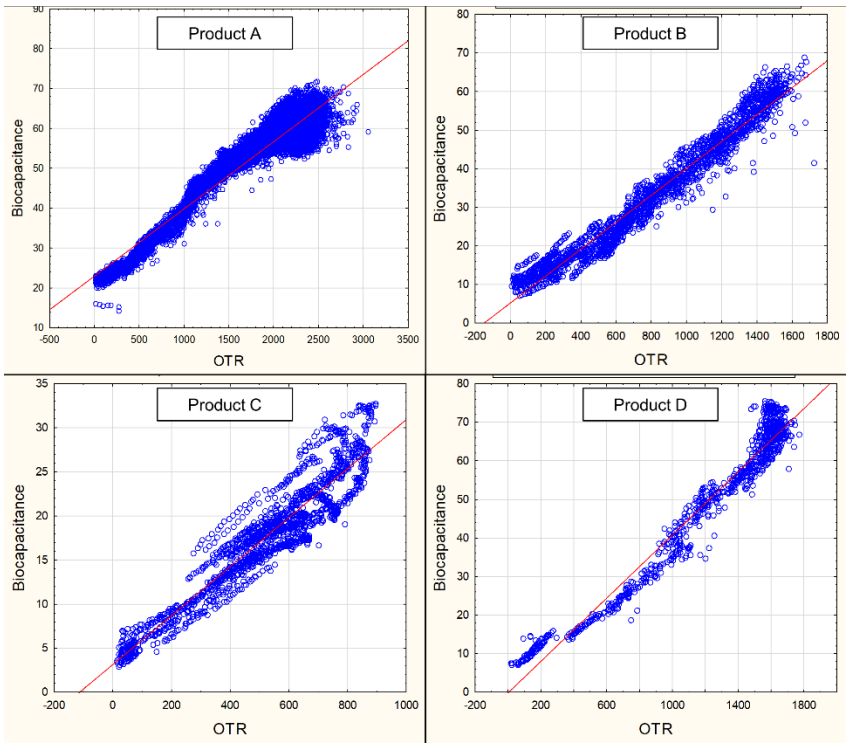

Figure 1 – Scatter plots of hourly biocapacitance measurements (pF/cm) vs. calculated oxygen transfer rate (OTR, %AirSaturation/hour) for four cell culture processes (Products A, B, C, and D) in 15,000L production bioreactors in a GMP facility. Red line shows linear fit.