STUDY OF ACCURACY AND SELECTIVITY OF A HYDROGEL-BASED SENSOR ARRAY BY DESIGN OF EXPERIMENTS (DOE)

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Reliable continuous sensors are salient to achieving advanced Process Analytical Technologies in the bioproduction industry. Sensors provide information on key parameters in a bioreactor such as physical variables (temperature, pressure, speed of stirrer), chemical variables (pH, pO_2, pCO_2, nutrients, metabolites), and biological variables (biomass, cell metabolism).[1-2] Simultaneously, chemometric analysis using multivariate data analysis, bioprocess modeling, and design of experiments (DOE) have become important in developing advanced biosensors because of the need to clean the complex raw data from biosensors to provide repeatable, robust, and reliable information.[3-4] In this work, the first step of the chemometric analysis process, DOE was performed with a prototype biosensor developed to simultaneously monitor glucose, lactate, pH, and osmolarity to understand the accuracy and selectivity of this sensor.
Sets of experiments for the DOE were designed with 4 factors (glucose, lactate, pH, and osmolarity) and 3 levels of interaction of each factor in the continuous level mode using JMP® (SAS Institute). A total of four sensor probes were tested to confirm reproducibility and repeatability. Other environmental conditions such as temperature, type of media, speed of stirring, and depth of the sensor probe in the bioreactor were controlled. HPLC (Rezex ROA-Organic Acid H+, 150 x 7.8 mm ID, refractive index detector), pH electrode (Mettler Toledo), freezing point osmometer (Precision system, INC.) were used for independent measures for evaluation of the test-sensor data. Key results were: (a) the response trend of the pH hydrogel sensor showed a good correlation with the commercially available pH electrode data (figure 1). The accuracy of pH prediction by the pH hydrogel sensor was 92 % from this study, (b) glucose hydrogel sensor showed a cross-sensitivity to lactate (60% contribution of magnitude changes, figure 2), (c) 70 % of prediction accuracy can be achieved by using data from lactate responsive hydrogel (figure 3). Glucose response data analysis reflects the importance of an experiment set up and chemometric analysis process to obtain meaningful data from newly developed biosensors. The sensitivity of the osmolality sensor was less than expected from the prototype sensor. Since this study, a new osmolarity responsive hydrogel has been formulated that has improved osmolarity sensitivity.

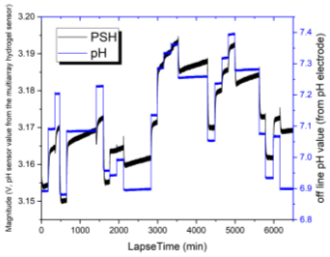

Figure 1. Comparison of pH response from the pH hydrogel sensor and a pH electrode (raw sensor data)

Gl

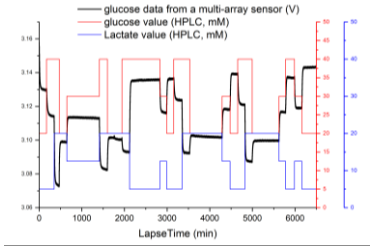

Figure 2. Comparison of continuous hydrogel glucose sensor response to glucose & lactate samples measured by HPLC (raw sensor data)

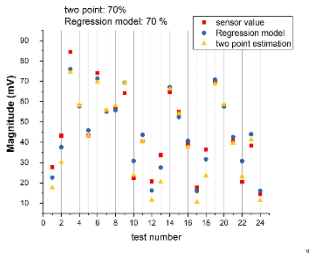

Figure 3. Glucose sensor accuracy based on the DOE data (used regression & two point estimation model to predict sensor magnitude).

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