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Establishment and Validation of Correlation Equations to Estimate Volumetric Oxygen Mass Transfer Coefficient (KLa) from Process Parameters in Stirred-Tank Bioreactors Using Response Surface Methodology

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Abstract : Process scale-up is essential for the biological process to increase production capacity from bench-scale bioreactors to either pilot or commercial production. Scale-up based on constant volumetric oxygen mass transfer coefficient (KLa) is mostly used as a scale-up factor since oxygen supply is one of the key limiting factors for cell growth. However, to estimate KLa of culture vessels operated with different conditions are time-consuming since it is considerably influenced by a lot of factors. To overcome the issue, this study aimed to establish correlation equations of KLa and operating parameters in 0.5 L and 5 L bioreactor employed with pitched-blade impeller and gas sparger. Temperature, gas flow rate, agitation speed, and impeller position were selected as process parameters and equations were created using response surface methodology (RSM) based on central composite design (CCD). In addition, the effects of these parameters on KLa were also investigated. Based on RSM, second-order polynomial models for 0.5 L and 5 L bioreactor were obtained with an acceptable determination coefficient (R^2) as 0.9736 and 0.9190, respectively. These models were validated, and experimental values showed differences less than 10% from the predicted values. Moreover, RSM revealed that gas flow rate is the most significant parameter while temperature and agitation speed were also found to greatly affect the KLa in both bioreactors. Nevertheless, impeller position was shown to influence KLa in only 5L system. To sum up, these modeled correlations can be used to accurately predict KLa within the specified range of process parameters of two different sizes of bioreactors for further scale-up application.

Keywords : response surface methodology, scale-up, stirred-tank bioreactor, volumetric oxygen mass transfer coefficient
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