EXPERIMENTAL METHODS IN MODERN BIOTECHNOLOGY

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CHAPTER 11

Response Surface Methodology (RSM) Design for Bioreactor Operation

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1. Introduction

1.1 Design of Experiment

Design of experiments (DOE) approach is considered to be most effective and efficient as it is one of the most powerful and flexible tools available for continuous improvement. The effect of each parameter and also the effects of the possible interactions of the parameters can be estimated effectively and efficiently using the smallest number of experiments. Besides, it can be used to improve both production processes and the products (ReVelle and Margetts, 2010). Consequently, the main advantage of using experimental design is the reduced number of experiments that have to be accomplished with the best choice of experimental points to get maximum production (Ergun and Mutlu, 2000).

1.2 Response Surface Methodology

Response surface methodology (RSM) is a detailed statistical analysis tool that can be used to study the complex relationship of the input parameters to the response (Stamatis, 2003; Myers *et al.*, 2009). It is a modeling method to demonstrate the effects of parameters on response surfaces for the reason of locating the optimum point. Hence, the RSM comprises of the techniques for experimental design, regression analysis, and computation of the optimum (Nakai *et al.*, 2007). It also has significant applications in the design, development, and formulation of new products, as well as in the improvement of existing product designs (Myers *et al.*, 2009; ReVelle and Margetts, 2010).

RSM is widely applied in the industrial world, particularly when several input variables potentially affect some quality characteristic or performance measure of the product or process. The input variables are sometimes called independent variables and they are manipulated by the engineer or scientist, at least for purpose of a test or an experiment, while the quality characteristic or performance measure is called response. Most of real-world RSM applications will involve more than one response (Myers *et al.*, 2009).

1.3 Central Composite Design

Central composite design (CCD) was introduced by Box and Wilson (1951) and it is widely used for fitting a second-order response surface (Nakai *et al.*, 2007; Myers *et al.*, 2009). CCD is the most popular second-order design in use by practitioners (Myers *et al.*, 2009). The testing of three levels and above provides an indication of non-linearity (i.e., the response may be a polynomial or exponential form) of the response across the levels investigated. This non-linearity can be applied in determining specification limits to optimize the response (ReVelle, 2002; Stamatis, 2003).

There are five levels in CCD that involves three components. They are a "composite" of a star design (with axial points at $\pm\alpha$), a two-level factorial design (with design points at ± 1), and a common centre point of the two designs (at zero) (Nakai *et al.*, 2007; Myers *et al.*, 2009).

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