240w Development of a Feasibility Index for Bioprocess under Uncertainty

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A robust bioprocess is crucial to ensure the consistent process performance and provide the product high quality for drug manufacturing in biopharmaceutical industries.

Mechanisms to achieve the desirable robust bioprocess operation have not been established in the existing methodologies hence the bioprocesses designs have low capacity in handling the inherent uncertainty in manufacturing. Despite its importance, the robustness of a bioprocess has not been properly defined and studies carried out in statistic sense are often retrospective. To successfully achieve a robust process design, the process feasibility under uncertainty needs to be understood. Such issue for continuous chemical processes has been studied and the problem is generally presented as a min-max optimization problem. The computational cost is expensive due not only to the complexity of the problem but also to using a line search algorithm to approximate optimal operating solutions through partial differential or differential equations. Examples shown in these works only dealt with limited variables. It is likely to have potential scale-up problems which will make them difficult to apply whole bioprocess.

This paper attempts to define rigorously a measure for process feasibility under uncertainty and presents a new methodology to evaluate bioprocess operations and their performance under uncertainty with respect to process feasibility. The methodology is based on the concept of ‘windows of operation' which shows the whole range of possible operating alternatives. The feasibility space obtained from the possible operating regions is discretised into finite points and simply represented by a point set. By doing so, the min-max optimization problem for process feasibility study can be solved much more easily. The methodology establishes a lower bound and an upper bound for the largest variation of a design variable to ensure a certain level of process performance. These bounds are achieved by a min-max optimization technique. A direct search algorithm has been developed and its computational cost is much lower than that of the line search algorithm. Results include visualization of robust operating regions and a set of indices which compare the performance of different operating strategies. The capabilities and efficiency of this methodology are illustrated by applying it to the centrifuge selection for the clarification of high solids density cell broths. This case study illustrates how the methodology may be successfully used to select the most suitable equipment for robust bioprocess operation.