THE SIMPLEX ALGORITHM IN AN AUTOMATED HIGH-THROUGHPUT APPROACH FOR THE RAPID SCREENING OF OPERATING CONDITIONS DURING PROCESS UNDERSTANDING AND DEVELOPMENT

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The screening of a large number of conditions to find a suitable window of operation may not be economically feasible at laboratory scale due to the large amount of feedstream and resources required for each experiment (10-100 mL). To overcome this issue, techniques that can generate data with minimal resource expenditure can be invaluable in early bioprocess development. Microscale platforms offer a change in bioprocess development by accelerating process development due to the flexibility for parallel experimentation and automation while requiring microscale quantities of material (20-2000 □L). Critical bioprocess information can be obtained earlier in development providing a better opportunity to understand process parameters and for improved understanding of the robustness of each processing step.

This study utilises the Simplex algorithm combined with an automated high throughput buffer preparation technique as an alternative to conventional experimental approaches for identifying viable operating conditions during early bioprocess development. In general, conventional experimental methods involve performing a large number of experiments in a given design space. This can be undesirable if a significant percentage of the conditions tested are unfavourable when feedstock and analytical resources are limited.

The Simplex algorithm directs each experimental condition towards feasible regions by using the knowledge gained from each condition to direct the choice of subsequent test locations. This study describes the application of the Simplex algorithm for AEX studies performed in a 96 well membrane plate format. The effect of pH and salt concentration on clearing Host Cell Proteins (HCP) from partially purified IgG feedstream was investigated.

The Simplex algorithm results were compared to conventional screening studies with response surface modelling. These models suggested that additional experimentation was required to confirm the robust regions of the initial design space. By comparison, the Simplex algorithm identified a good operating point using 70% fewer conditions for HCP clearance. Therefore, this approach can be a viable and valuable alternative route for identifying sweet spots during screening studies in bioprocess development.