

## **Abstract:**

### **Space is the Place: Using DOE and Microscale Techniques to Define Process Boundaries**

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Development of protein purification processes is a multivariate challenge to select a winning combination of unit operations and operating parameters that maximize purity, recovery, and process robustness while minimizing cost. For the development of *de novo* processes, this is a time-consuming and assay-intensive exercise. Consequently, platform purification processes have emerged as a means of streamlining process development for proteins having similar physicochemical properties. However, despite having fixed unit operations, platform purifications still require some optimization to adjust for differences in molecular properties between proteins. Techniques for miniaturizing protein purification processes at the microliter scale (microscale) can accelerate process development and reduce resources by enabling parallel experimentation and automation. Design of experiment (DOE) methodologies provide an additional tool for examining multiple variables simultaneously, and when combined with microscale techniques, enable purification processes to be rapidly and efficiently optimized. Two examples will be shown in which DOE in combination with microscale methods was used to optimize process conditions and define operating boundaries. In the first example, factorial and response surface designs were used to screen and optimize the parameters for a small-scale disruption of yeast cells. In the second example, the operating space for two ion-exchange chromatographic steps in a platform purification were defined for a monoclonal antibody, resulting in improved process performance and robustness.

*Well Characterized Biotechnology Pharmaceutical Symposium*

*California Separation Science Society*

*January 27-30, 2008*

*Washington DC*