A DISRUPTIVE ALTERNATIVE TO SEMI-CONTINUOUS MULTI-COLUMN CHROMATOGRAPHY PROCESSES

Michael Rose, UCB
Michael.rose@ucb.com
Chris Le Page, UCB
Mark Pearce Higgins, UCB

Key Words: DSP, Continuous, Multi-column, Chromatography, Affinity

Protein purification to date is still dominated by expensive chromatography operations. Within the bioprocessing segment of the biopharmaceutical industry, enormous advances in upstream processing performance have moved the cost-reduction bottleneck to downstream processing (DSP). In an effort to reduce DSP costs, the industry is progressively turning to multi-column semi-continuous manufacturing techniques, adapted from neighbouring chemical processing industries. In the case of Affinity Chromatography, the primary theoretical advantage lies in alleviating particularly expensive bind/elute capture steps by allowing saturation of any given unit of resin with product feed while routing the partially depleted effluent flow-through material to follow-on unsaturated resin through the use of multiple columns in a sequence. The saturation better utilises the resin in each of its cycles allowing a reduction in per gram cost and improved time usage, and since saturation can achieve the full static binding capacity without being limited by a dynamic flow, this allows the system to flow faster, saving even more time.

However, industrial adoption of these new techniques has been slow, owing to their significant increase in developmental and operational complexity and the capital expense of additional hardware requirements.

In this presentation we will reveal and discuss processing factors that may significantly impact the true benefits in speed for multi-column processes, particularly relating to the necessary scheduling effects of aligning multiple synchronous columns, and to back pressure and column height effects that both slow the achievable productivity and mask true comparisons with traditional batch chromatography. We have found scenarios where these factors can combine to make semi-continuous multi-column processes significantly slower than equivalent batch processes, and the loss in productivity can, in some circumstances, cancel much of the cost savings on resin consumption.

In an effort to understand, improve and simplify these semi-continuous processes, we internally developed a novel and potentially disruptive operational method that matches or exceeds the benefits of a semi-continuous process, without the complexity. Data from a prototype un-optimised version tested at pilot scale will show that significant performance gains can be achieved on standard chromatography equipment with minimal modification.