Performance comparison of batch and multicolumn protein A capture processes

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Summary

▪ Batch, 2C-PCC (CaptureSMB), 3C-PCC and 4C-PCC Protein A capture processes were compared in a numerical optimization study using an experimentally validated shrinking core model for mAb capture

▪ Performance parameters for comparison: Productivity (Throughput) and Capacity Utilization (Resin costs)

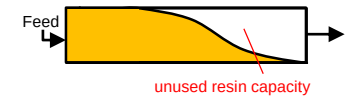
▪ Outcome 1: Multicolumn processes ensure high capacity utilization, low buffer consumption

▪ Outcome 2: 2C-PCC outperforms 3C-PCC and 4C-PCC

▪ Additional advantage of 2C-PCC: Minimal multi-column hardware configuration

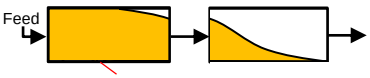
Process Description

➢ Single column Batch Capture: A large fraction of the affinity resin remains unused



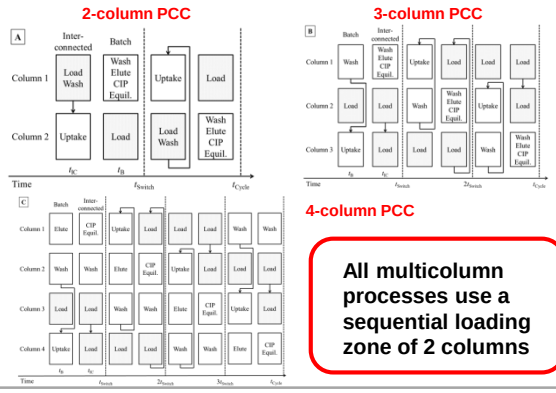
→ Used capacity typically 40-50% of static binding capacity (SBC).

➢ Sequential loading processes: By splitting the bed into two columns, the capacity utilization is maximized.



→ Used capacity typically > 90% of SBC
→ Faster loading flow rates can be used

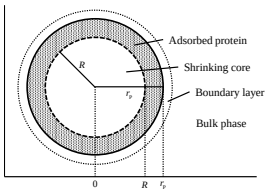
Multicolumn processes complexity



All multicolumn processes use a sequential loading zone of 2 columns

Chromatography model

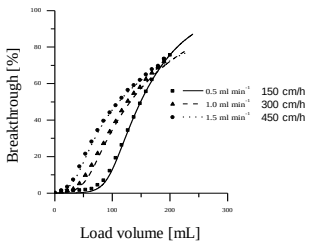
▪ Shrinking core model:



▪ Resin: MabSelect Sure
▪ 10 cm bed height per column
▪ mAb: IgG1
▪ Harvest titer 2.5 g/L // 5.0 g/L
▪ CIP time 30 min

Model calibration

➢ The model was calibrated by fitting experimental breakthrough curves at various flow rates and titers



Performance objectives

▪ The model was used to numerically optimize the 1-4 column processes with respect to the following objectives:
▪ Productivity (Throughput), mAb produced per resin volume and time:

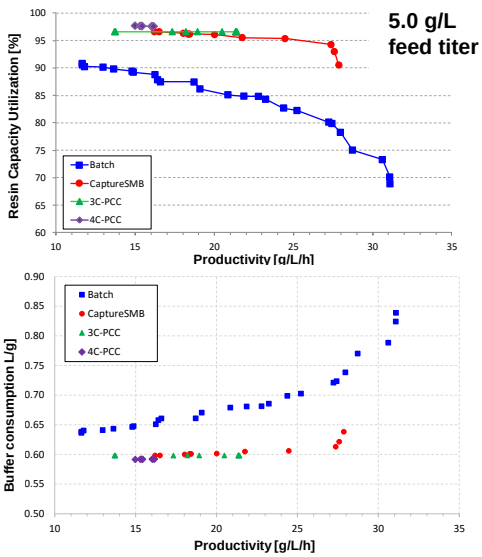
$$Prod = \frac{m_{mAb\,eluate\,cycle}}{n \cdot V_{col} \cdot t_{cycle}}$$

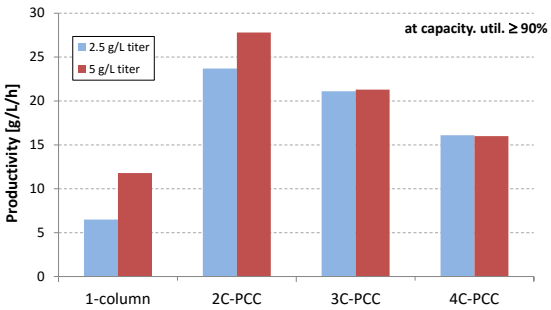
▪ Capacity Utilization (proportional to 1/resin costs): Load divided by static binding capacity. The higher the CU, the lower the resin costs.

$$CU = \frac{\text{Load}}{\text{SBC}} \sim \frac{1}{\text{resin cost}}$$

▪ Optimization variables: Flow rates, switch times

Optimization Results





2C-PCC outperforms other processes:

▪ **Outperforms single column capture because of sequential loading principle, leading to increased capacity utilization (lower resin costs) and lower buffer demand**

▪ **Outperforms 3C-PCC and 4C-PCC in terms of productivity because its sequential loading phase is independent of recovery and regeneration steps running in parallel. Therefore the duration of sequential loading phase of 2C-PCC can be changed as larger titers are used**

Conclusion

✓ **Multicolumn process enable high capacity utilization and high throughput at the same time**

✓ **Multicolumn processes have 40-60% reduced resin costs, decreased buffer consumption and increased product concentration compared to batch chromatography**

✓ **2C-PCC outperforms 3C-PCC and 4C-PCC in terms of productivity, while operating at similar capacity utilization and buffer consumption**

✓ **2C-PCC requires least complex hardware of all multicolumn process, positive impact on equipment costs and risk of failure**

Reference: Baur D et al. 2016. Comparison of batch and continuous multi-column protein A capture processes by optimal design. Biotechnology Journal. 11: 1860-7314