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ETH ICB Institute for Chemical and Bioengineering

Contichrom® Twin-column FPLC Chromatography

Comparison of Multicolumn Capture Processes

Process Modeling and Simulation

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a. Adsorption

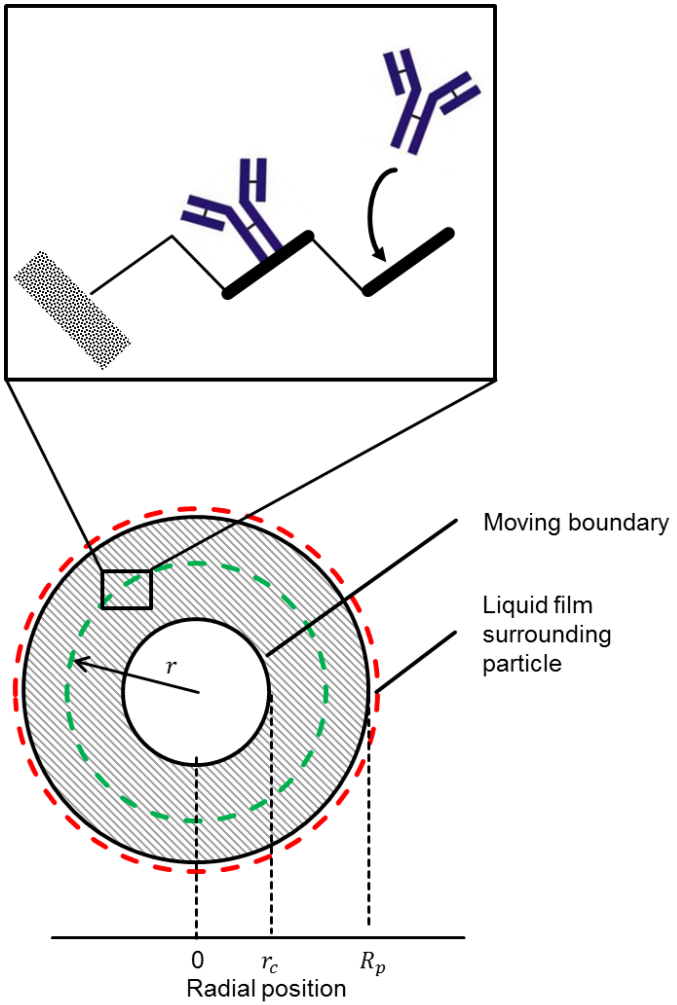
- Molecular level
- 2 Adsorption sides for each Protein A molecule

b. Mass transport

- Resin particle level
- Core shrinkage with moving boundary due to adsorption

c. Mass balance

- Column level
- Integration of mass balance results in breakthrough curve



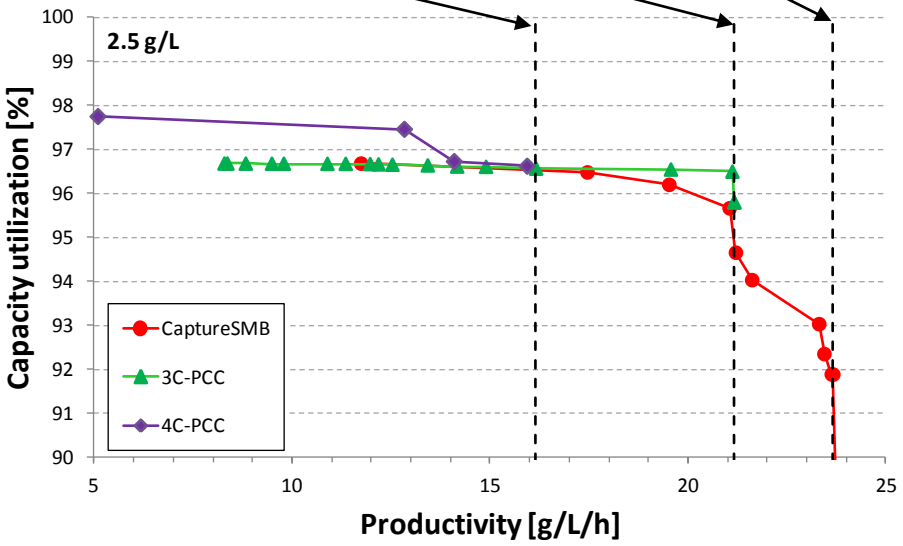
Comparison of Multicolumn Capture Processes

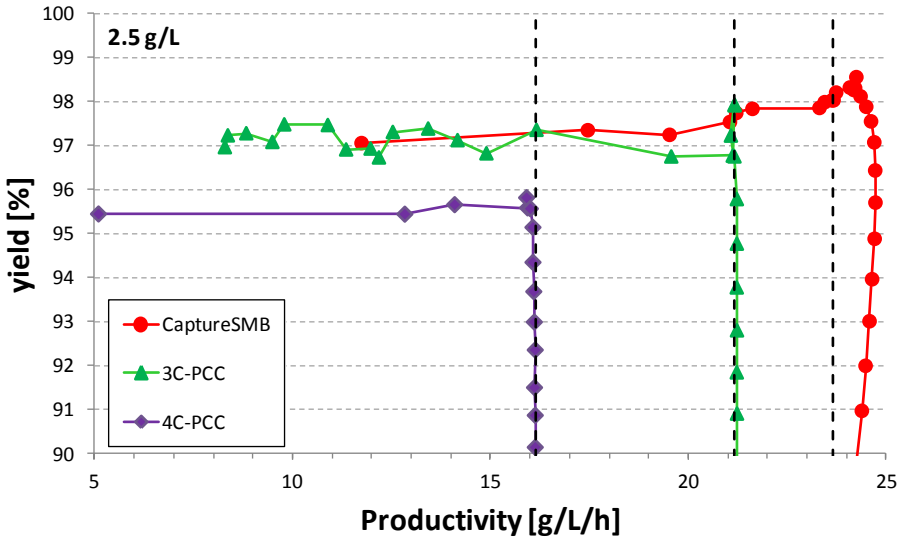
4C-PCC
100%
16 g/L/h

3C-PCC
130%
21 g/L/h

2C-PCC
150% productivity
24 g/L/h

Sudden yield decrease for 4C-PCC (green) and 3C-PCC (violet) at 17 g/L/h and 21 g/L/h when attempting to increase productivity. 2C-PCC (red) retains yield at higher productivity





- All multicolumn processes use a sequential loading zone of 2 columns:
- Same high load and capacity utilization of the different multi-column processes
- Optimized loading phase kinetics with CaptureSMB (2C-PCC) increases productivity
- 3C- and 4C-PCC processes become less productive due to parallel tasks performed on the additional columns
- Attempts to increase productivity beyond their maximum values by increasing the load lead to dramatic losses in yield

→ 2C-PCC Process (CaptureSMB) is superior to 3-or 4-column processes

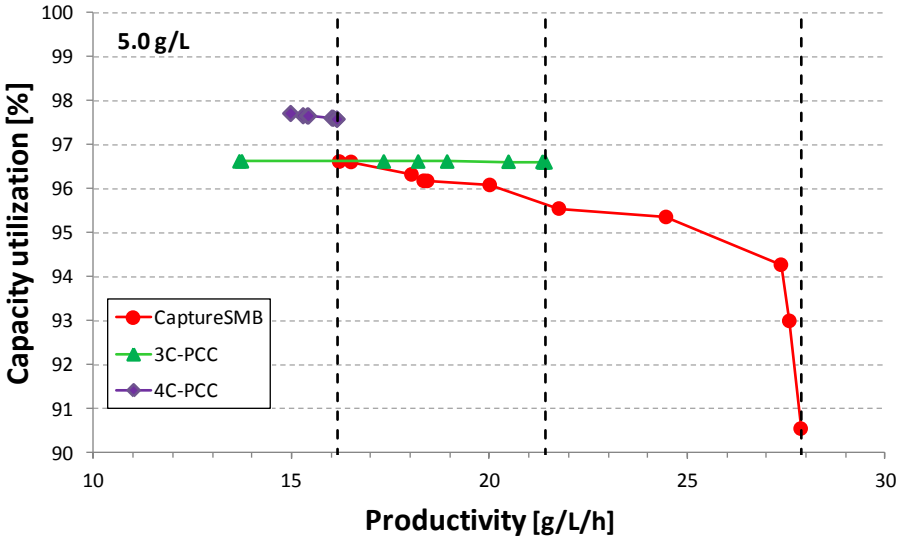
Reference: Baur et al.,
Biotechnology Journal, 2016,
DOI: 10.1002/biot.201500481

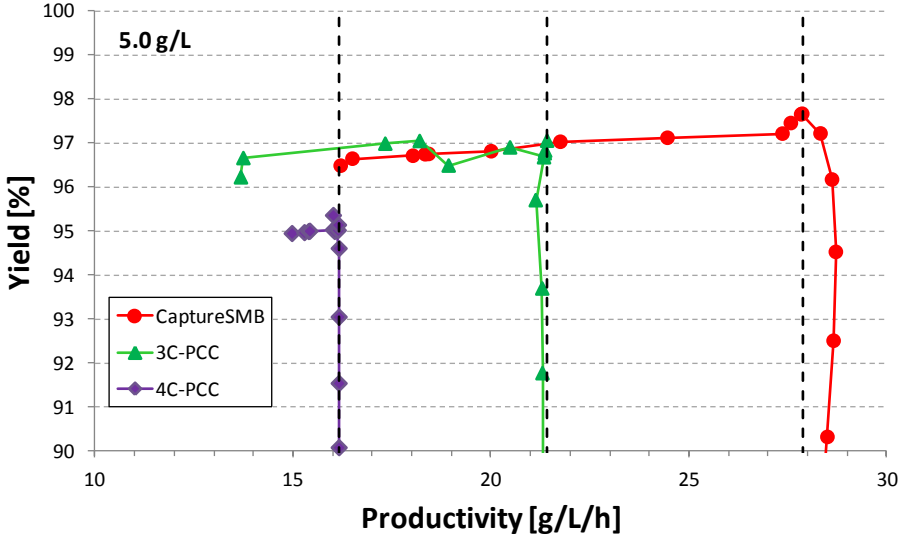
Superior Performance by Twin-column Capture Process

- Multicolumn processes for > 90% Capacity utilization, 5.0 g/L titer:

4C-PCC	3C-PCC	2-col CSMB
100%	130%	175% productivity
16 g/L/h	21 g/L/h	28 g/L/h

Sudden yield decrease for 3C-PCC and 4C-PCC when attempting to increase productivity. CSMB yield remains stable





Productivity advantage of CaptureSMB (2C-PCC) is more pronounced for higher titers

At 2.5 g/L: 50% increase compared to 4C-PCC, 15% increase compared to 3C-PCC

At 5.0 g/L: 75% increase compared to 4C-PCC, 35% increase compared to 3C-PCC

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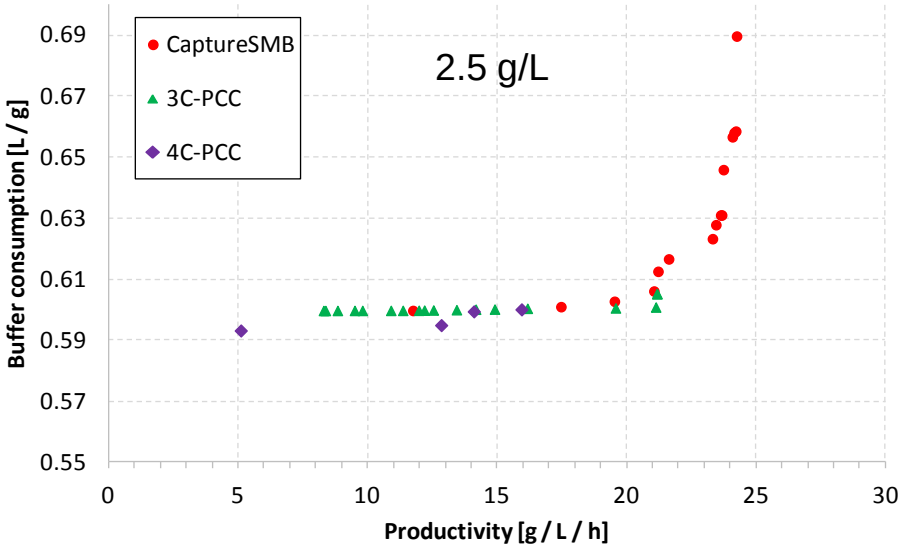
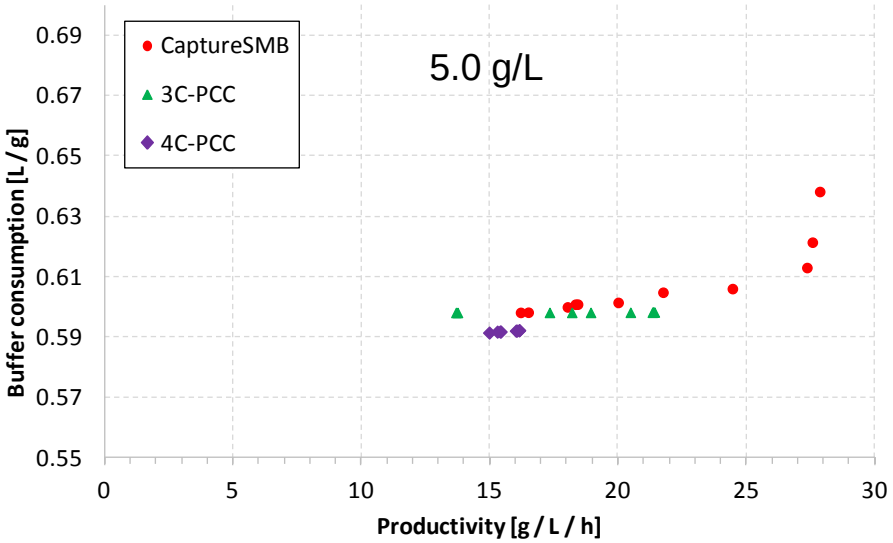
Results: Protein A Capture Optimization

- Process comparison buffer demand





All multicolumn processes have similar buffer consumption

Summary on comparison of multicolumn processes

✓ 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

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

✓ CaptureSMB (2C-PCC) requires least complex hardware of all multicolumn processes, positive impact on equipment costs and risk of failure

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ICB Institute for Chemical and Bioengineering ETH

Contact Info

ChromaCon

www.chromacon.com

+41-(0)-44 445 2010

info@chromacon.com