Continuous capture chromatography as part of an integrated downstream purification platform for mAbs

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Abstract

In recent years, continuous capture chromatography has moved from a concept on the benchtop to pilot scale solutions, becoming an option for platform purification of monoclonal antibodies. This presentation focuses on the twin-column approach for the capture step. Through an on-site evaluation using industry relevant feed streams, this approach successfully demonstrated a flexible and easily transferrable process, resulting in up to 50% reduction in required resin and 50% reduction in buffer consumption while maintaining critical product quality attributes (CQAs). The accompanying software was used to quickly and accurately model the breakthrough of 3 different in-house mAbs, facilitating rapid process transfer to the pilot-scale equipment with yields above 90%. This flexible platform was tested using batch, continuous, and integrated modes of operation for the capture and polishing of molecules with reduced cost of goods. Looking forward, new approaches for integrated polishing steps can also be leveraged to further improve downstream process productivity.

Introduction

- Evaluated batch and twin column continuous capture of mAb using YMC EcoPrime Twin 100 LPLC system
- Evaluated sequential polishing capability of YMC EcoPrime Twin 100 and compared to historical product quality parameters of batch-processed mAb
- Compared productivity of continuous capture and sequential polishing process modalities to batch

Methods

Batch and Continuous Capture Comparison

- Single lot of mAb A was processed in both batch and continuous capture mode on YMC EcoPrime Twin 100 LPLC system using 10 cm x 10 cm affinity columns
- Batch capture column was loaded to 40 g/L
- Column load challenge was increased to 60 g/L for continuous capture method based on dynamic breakthrough curve estimate provided from YMC software

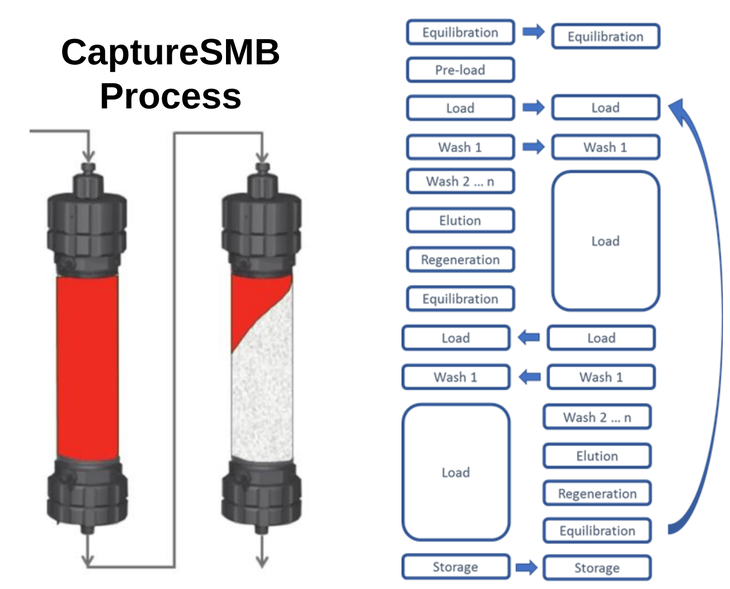

Figure 1. Continuous capture process diagram

Sequential Polishing

- Sequential polishing of mAb A was performed with a mixed mode flowthrough column process and a CEX bind-and-elute column operation
- Mixed mode flowthrough product was loaded directly on to CEX column followed by elution from CEX

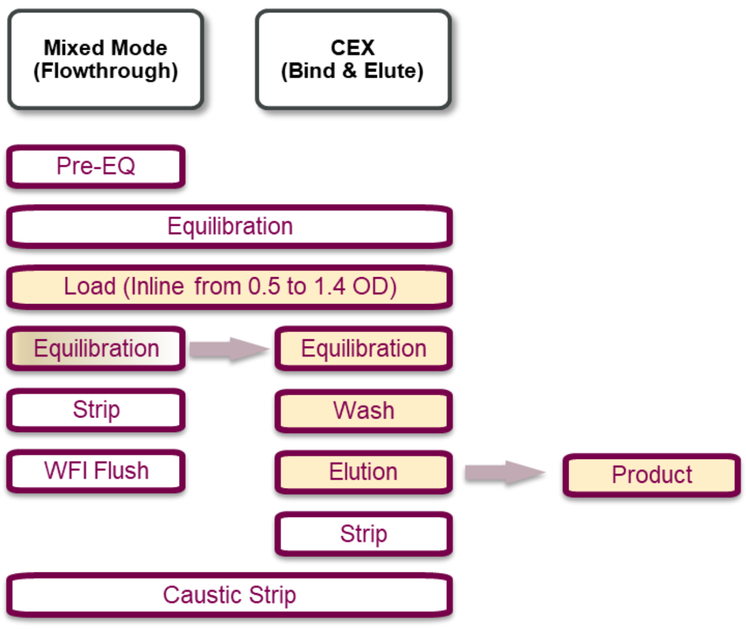

Figure 2. Sequential polishing process diagram. Yellow indicates presence of product.

Results

Table 1:
Scale-down process configuration and productivity analysis

YMC EcoPrime Twin 100: 100L of 3 g/L Product

	Batch	Twin Column
# of Columns	1	2
Column Diameter (cm)	20	10
Column Bed Height (cm)	20	10
Total Resin Volume (L_{resin})	6.3	1.6
Binding Capacity (g/L_{resin})	40	60
	Batch	**Twin Column**
Cycles	2	3
Process Time (hr)	6	9
Buffer Requirement (L)	300	150
Resin Cost ($16k/$L_{resin}$)	$100,800	$25,600
Productivity (g/ L_{resin} -hr)	10	20

Table 2:
Production-scale process configuration and productivity case study analysis

YMC EcoPrime Twin 1000 : 2000L of 5 g/L Product

	Batch	Twin Column
# of Columns	1	2
Column Diameter (cm)	60	45
Column Bed Height (cm)	20	10
Total Resin Volume (L_{resin})	56	28
Binding Capacity (g/L_{resin})	35	65
	Batch	**Twin Column**
Cycles	6	5
Process Time (hr)	18	11
Buffer Requirement (L)	7100	3900
Resin Cost ($16k/$L_{resin}$)	$896,000	$448,000
Productivity (g/ L_{resin} -hr)	22	40

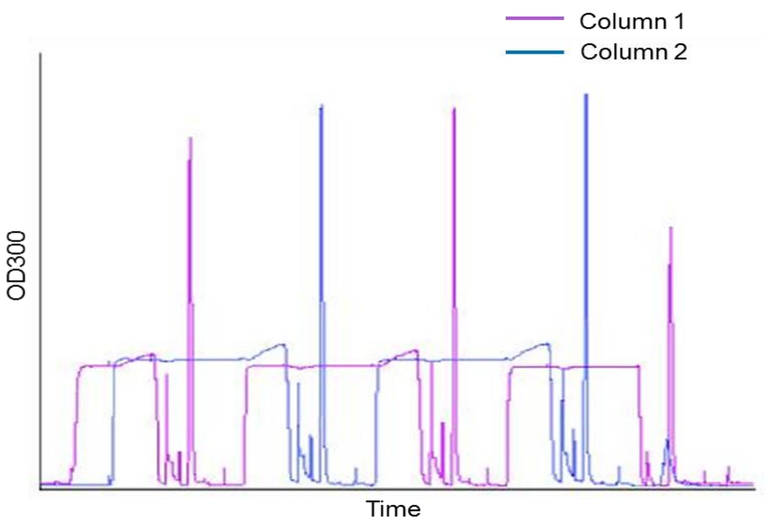

Figure 3. Continuous capture UV traces at 300 nm for 2 cycles of operation.

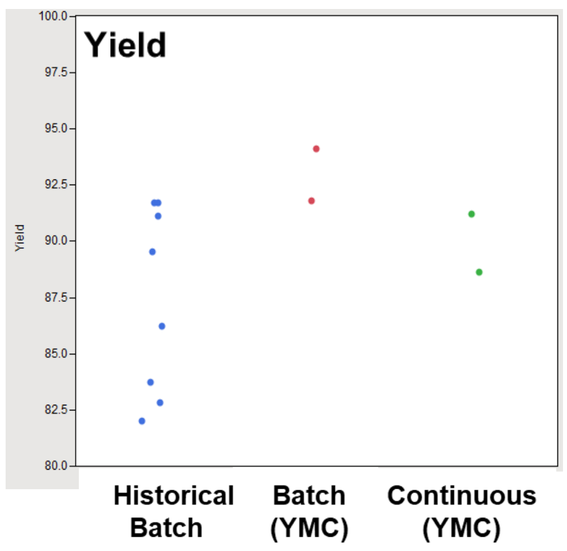

Figure 4. Continuous capture yield data comparison to historical batch runs, a batch run with the YMC system, and a continuous capture run with the YMC system.

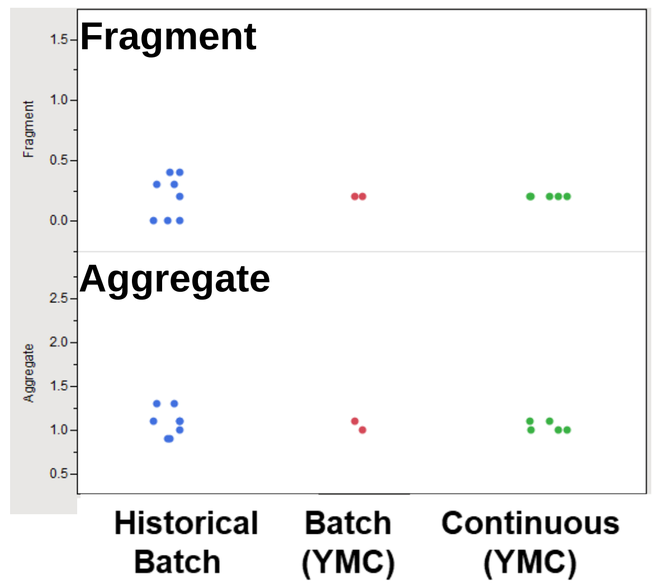

Figure 5. Continuous capture product quality data comparison

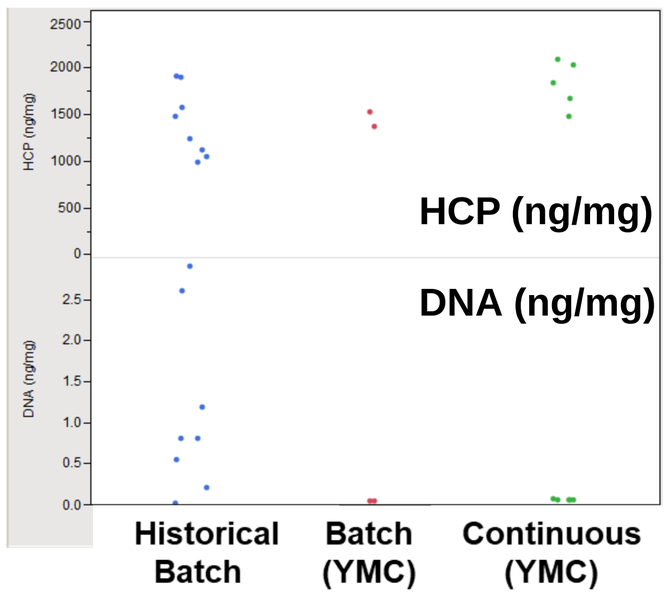

Figure 6. Continuous capture host cell protein (HCP) and DNA clearance data comparison

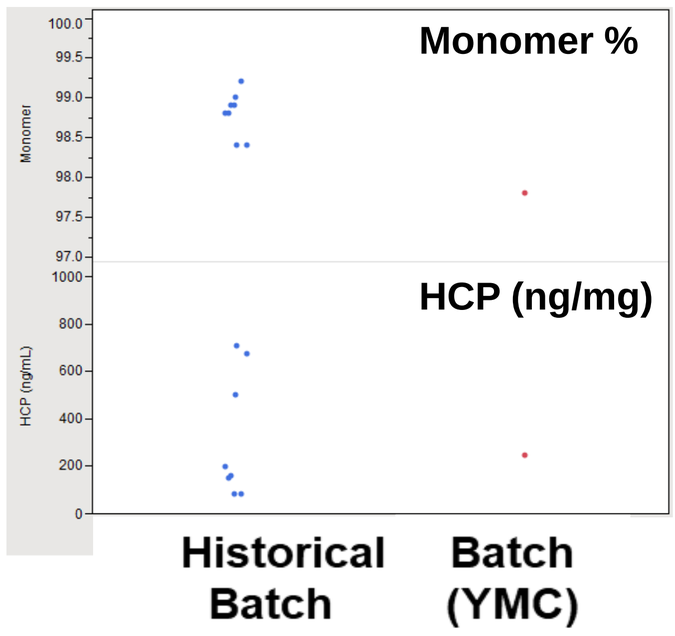

Figure 7. Sequential polishing quality and impurity comparison

Conclusions and Future Work

Conclusions

- Continuous capture processing with the YMC system can reduce resin cost and buffer volumes by 50% while maintaining historical yields and product quality attributes of batch-processed material
- Sequential polishing processing with the YMC system can condense multiple days of processing into a single day

Future Work

- Test inline buffer dilution capabilities and inline adjustment of sequentially processed material
- Explore ways to improve HCP clearance efficiency and process yield

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