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Simplifying Progress

Intensification of mAb Processes Leveraging Sartobind® Rapid A and Full Connected Membrane-Based DSP

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Introduction

In the field of mAb purification, high performances chromatography membranes that are ready-to-use, for "one-batch-one device" manufacturing strategy, take off. The newly Protein A capture technology "Sartobind® Rapid A", used in rapid cycling conditions, brings a 10-fold higher productivity (203 g/L vs 14 g/L with traditional resins), has similar performances for DBC, yield and HCP | hcDNA removal. This allows new-generation full membrane-based purification platforms.

Protein A › IEX › Polishing

The first milestones to fully membrane-based process is achieved by implementing a competitive double-flowthrough polishing process with connected Sartobind® Q and Sartobind® S. Comparable purity and yield are obtained (>98% for each flowthrough steps) with a strong footprint reduction of the purification process. The second step to a full membrane process is combining the Resolute® MCC multicolumn technology with protein A, AEX and CEX membranes in parallel batch mode. This results in increasing even more the productivity (>400 g/L/h) compared to a resin-based multi-column chromatography process (<200 g/L/h).

This innovative Sartobind® Rapid A combined with process intensification solutions demonstrates that alternative mAb purification platforms are safer and highly competitive against classic resin-based approaches.

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Sartobind® Rapid A as Convecdiff Membrane vs Purely Convective | Diffusive Materials

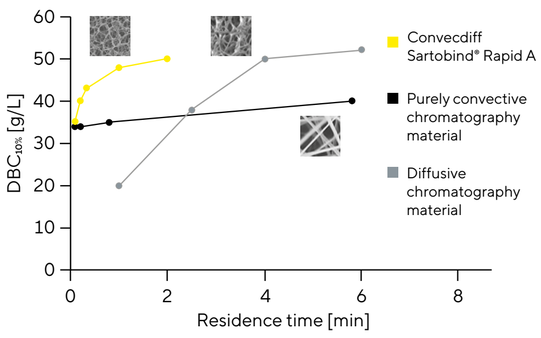
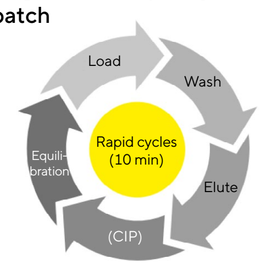


Figure 1: *$SDBC_{10\%}$ As a Function of Residence Time for Commercially Available Materials and the Convecdiff Sartobind® Rapid A.*

Convecdiff materials ally high DBC & high flowrate to enable short cycle time

Sartobind® Rapid A enabling lifetime capacity utilization in one single-batch

- Fast cycles: 10 – 15 min
- ~30 – 150 cycles/batch



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CPP and CQA of IgG Purified With Sartobind® Rapid A and Standard Resin[1]

In this comparison, we show how Sartobind® Rapid A compares to standard protein A resin. Both materials were tested with the same feed material. The analyzed data show a very good comparability of Sartobind® Rapid A with the protein A resin. The membrane showed superior performance in DNA reduction and protein A leaching, with a 14.5-fold increase in productivity.

	Sartobind® Rapid A	Protein A Resin
DBC10% [g/L]	42.9 ± 0.8	30.4 ± 0.5
Residence time [min]	0.2	4.0
Yield [%]	94.7 ± 0.2	96.4 ± 0.4
HCP reduction [LRV]	2.2 ± 0.2	2.3 ± 0.1
hcDNA reduction [LRV]	2.9 ± 0.2	2.3 ± 0.1
Protein A leached [ppm]	2.7 ± 0.7	6.7 ± 0.3
av. Productivity [g/L*h]	203.6	14.1

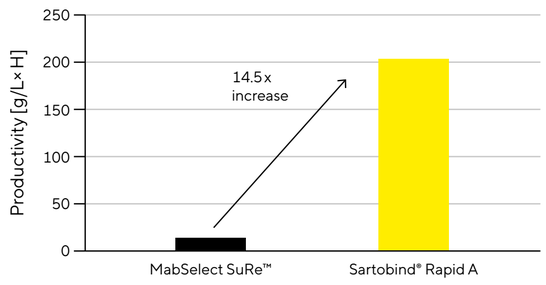

Figure 2: *Productivity Comparison of HiTrap® MabSelect SuRe™ to Sartobind® Rapid A*

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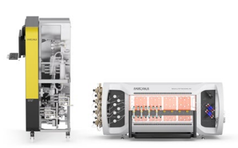
Levels of Intensification for Downstream Processing

Level 0	Level 1	Level 2	Level 3	Level 3.1
Standard batch, standalone UO	**Intensified, standalone** UO increases the individual step productivity; higher cycling (RCC or MCC), improved buffer management (ILD, ILC), high DBC resins; pooling tanks	**Connected process:** at least 2 UO; subsequent steps started before first step is finished; could be staggered batch; may have pooling tanks; **software orchestration** is beneficial; might be called clustered or linked process	**Continuous process:** more integrated case of a connected process; **steady state flow;** only small intermediate (surge) tanks; software orchestration is a must have; **long run times; closed processing;**	**Flow-through continuous process:** further integrated case with complete steady state flow. **All bind and elute steps are replaced with flow through mode.** Molecule does not stop – ideally no intermediate (surge) tanks



Resolute® RCC MU

Resolute® BioSMB PD

Resolute® BioSC Pilot

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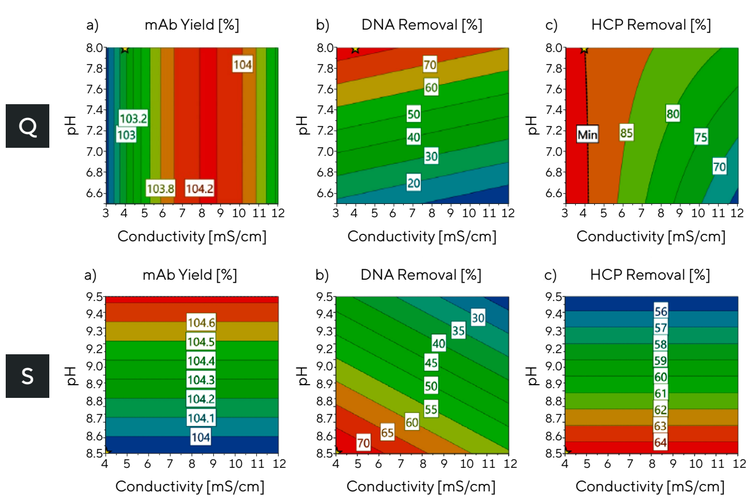
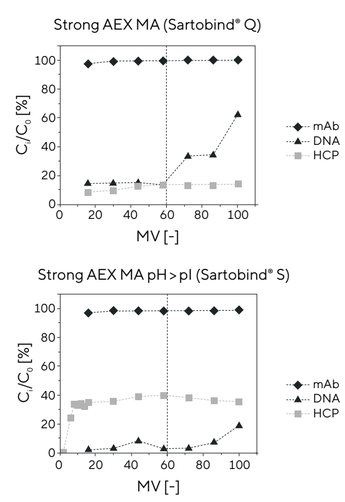
Double Flow-Through With Membrane Adsorbers[2]

Step 1: DOE to Define Buffer Conditions



Step 2: Breakthrough Curves



Note. Sartobind Rapid A - Beta Test Opportunity. DOE done with MODDE® 13

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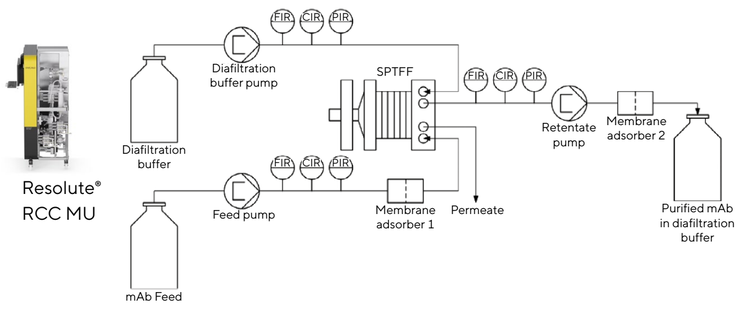
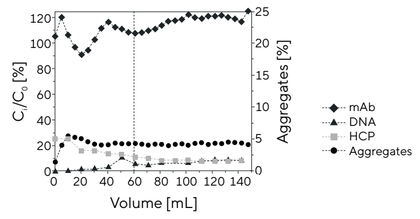
Chromatography Membrane – Towards Connected Process[2]

Step 3: Connected Processing



- Yield > 98% (per step)
- Productivity: 240 $g_{(mAb)} \times L^{-1}_{(membrane)} \times h^{-1}$
- DNA: 2 ppm
- HCP: 29 ppm



- Comparable purity with classical process
- No column packing
- Rapid Cycling Chromatography (RCC) enables strong footprint reduction
- Full single batch use

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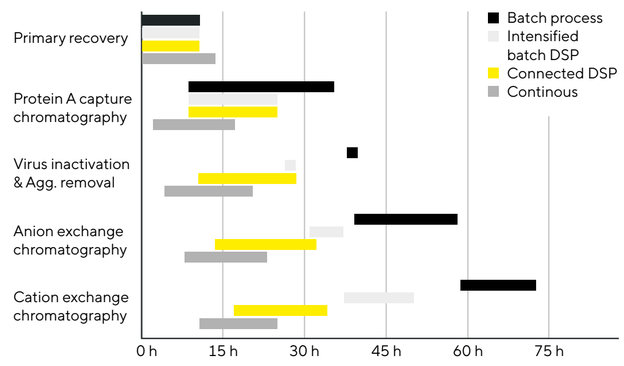
Downstream Intensification Reduces Processing Times

- Each step starts before the previous one ends
- This enables processing the sub-batches from protein A elution
- Reduction of intermediate tanks and chromatography columns' size
- Lower footprint
- Lower OPEX



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The Power of Connected Membrane Processes

Cascade	Resin (MCC Connected Process)	Sartobind®
Number of steps	3	3
Final yield [%]	83	86
DNA [ppb]	<3	<3
HCP [ppm]	3	30
HMW [%]	0.2	0.3
Total process time [h]	10.4	4.0
Av. Productivity [g/h]	179	465

- Connecting the process and using MCC or parallel batch multiplies productivity or drops costs
- Comparable purity and yield
- Lower footprint

Resolute® BioSC Pilot

Clarified harvest

Sartobind® Rapid A (9.6 L @ 45 g/L)
3 × 3.2 L membrane

Sartobind® Q (1.6 L @ 500 g/L)

Sartobind® S (1.6 L @ 500 g/L)

Conclusion

Due to inherent structural characteristics, Sartobind® Rapid A offers unique possibilities in the area of full membrane-based ultra fast mAb purification process

- Ready-to-use and One batch – One device manufacturing strategy enabled thanks to Sartobind®
- DBC highly competitive
- Short cycle time (<30 min)
- High number of cycles per batch (up to 150)
- Double Flow-Through polishing with Sartobind® Q | S
- Full membrane process with ultra high productivity – 3x compared to connected resin-based process
- Innovative agarose platform, scalable, robust for a wide variety of mAbs with limited back-pressure at large scale
- Availability of modular cassette format enables scaling to large production processes

Abbreviations:
ASAP: Accelerated Seamless Antibodies Purification, EASY: Full flow-through process, ILC: Inline Conditioning, ILD: Inline dilution, MoBiDiK: Modular Bioproduction, disposable and continuous, MCC: Multi column chromatography, RCC: Rapid cycling Chromatography

1 Grünberg et al. (2022). Membranes.
2 F. Schmitz et al. (2023). Integrated double flow-through purification of monoclonal antibodies using membrane adsorbers and single-pass TFF. Biochemical Engineering Journal 195.