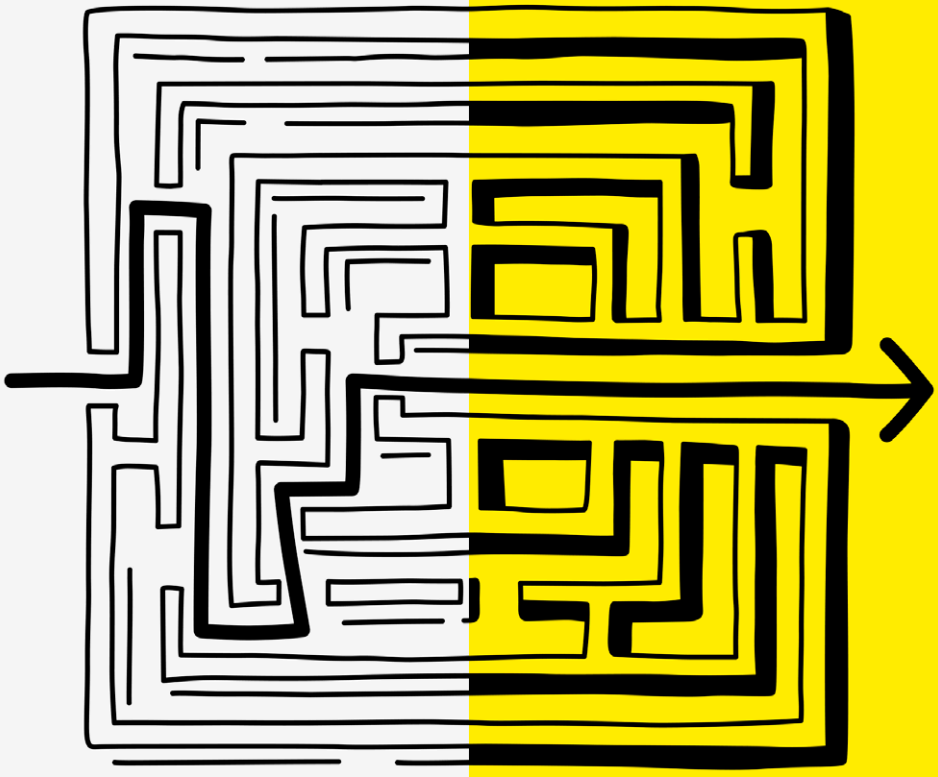


Simplifying Progress

From Capture to Final Polishing:

Chromatography Consultation Tools for Process Intensification

SARTORIUS

Introduction

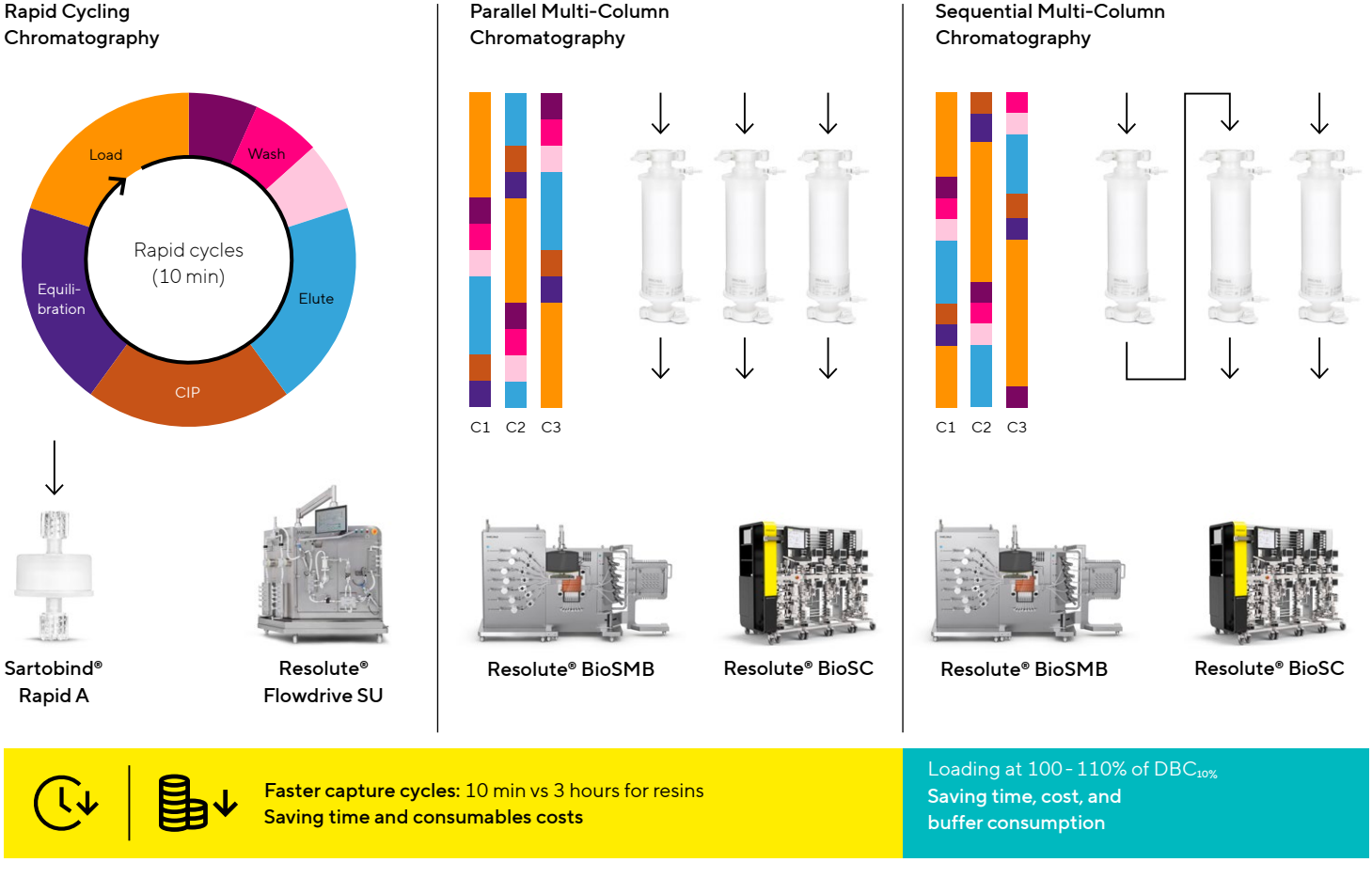
Process intensification (PI) has become a strategic imperative in biomanufacturing, particularly for downstream processing (DSP), where productivity gains are essential to match advancements in upstream productivity and the resulting high titers achieved in recent years. However, transitioning to intensified workflows can be complex, especially for organizations with entrenched batch-based processes or legacy infrastructure.

A wide range of strategies exists to intensify purification workflows, each with different implications for process efficiency, scalability, costs, and facility fit. Selecting the right approach from the outset—along with the appropriate enabling technologies—is critical to realizing the full benefits and return on investment from PI.

Because chromatography is the most expensive technology in DSP, the intensification journey often starts with selecting the appropriate chromatography media from a panel of high-performance resins or membranes. It is important to choose the chromatography method that will best achieve the expected gains for specific process production constraints and yearly output targets. Choosing the right strategy to match facility requirements and production targets relies on process modeling tools and expert support.

Downstream PI methods vary in complexity and outcomes, from a simple rapid cycling chromatography (RCC) with membranes to more complex multi-column chromatography (MCC) processes using either resins or membranes (Figure 1).

Figure 1: *Different Methods for Intensifying a Chromatography Step With Membrane Chromatography*



Note. Methods can be developed stepwise from clinical to commercial production using Resolute® modular systems. CIP = Clean-in-place

Parallel batch-MCC (B-MCC) enables continuous capture and is usually paired with a perfusion bioreactor. Serial-MCC (S-MCC) allows continuous capture and maximizes the binding capacity, resulting in reduced cost and buffer consumption.

The required level of intensification—which could range from intensified standalone unit operations to a fully continuous process—should be defined (Figure 2).

Level 1 consists of intensification of standalone unit operations, which can be achieved using RCC with membranes or MCC with membranes or resins. This is the simplest and fastest to implement, providing immediate cost and time savings, particularly during early clinical production.

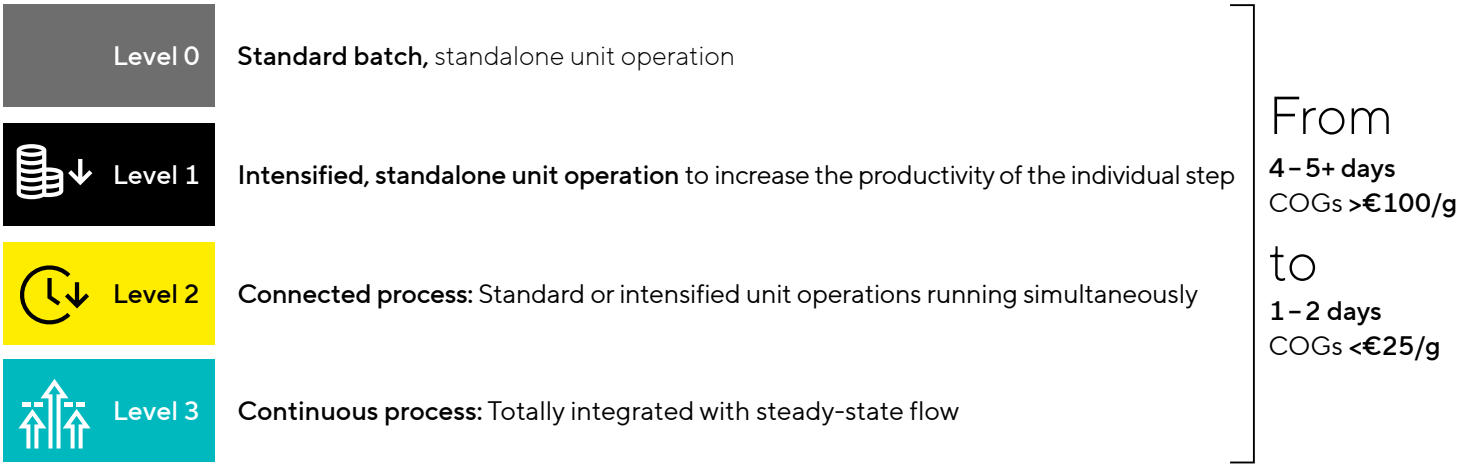
Level 2 connects some unit operations to run simultaneously. Connected DSP can halve process timelines and double the throughput of DSP operations. This level is typically paired with a fed-batch bioreactor.

Level 3 integrates all DSP steps into a continuous flow, orchestrated by software, enabling fully continuous DSP. This can be linked to a fed-batch bioreactor, reducing DSP timelines from more than 5 days to 1-2 days, or coupled with a continuous perfusion bioreactor for end-to-end continuous manufacturing.

The choice of chromatography media, method, and level of intensification is driven by multiple factors such as bioreactor size, culture mode (fed batch or perfusion), titer, production volume, batch frequency, type of chromatography systems (single-use or multi-use flowpath) and the gains expected from intensification.

With multiple strategies available, selecting the right approach and predicting the cost and productivity benefits from the outset ensures the downstream PI journey is worth the effort before committing resources. To help our partners evaluate the relevance and the impact of downstream PI strategies, Sartorius has developed a range of process and cost modeling tools.

Figure 2: *Stepwise Approach From Batch Production to Three Levels of Intensified Processing*



Make the Right PI Choice Faster—With Modeling and Expert Support

Capture Intensifier Application

The first tool is a web-based Capture Intensifier Application that allows end users to predict and evaluate cost savings and productivity gains from intensifying the Protein A capture step under their specific process conditions.

Users can enter the bioreactor size, titer, time targeted for capture, and number of production batches (Figure 3) to immediately generate a tailored report. The report—available in PDF format with a few clicks—compares resins and membranes used in either batch, parallel MCC, or serial MCC modes, and predicts costs, cycle times, buffer volumes, and productivity of the different technologies (Figure 4).

The output includes:

- Comparison of batch, parallel MCC, and serial MCC modes
- Side-by-side assessment of resin vs. membrane technologies
- Quantification of costs, productivity, buffer volumes, and cycle time

This simple, accessible tool helps users establish which Protein A strategy best suits their process needs and intensification objectives—before any lab work begins.

For more information about the Capture Intensifier Application tool, visit capture-intensifier.app.sartorius.com

Figure 3: *Capture Intensifier Application Inputs*

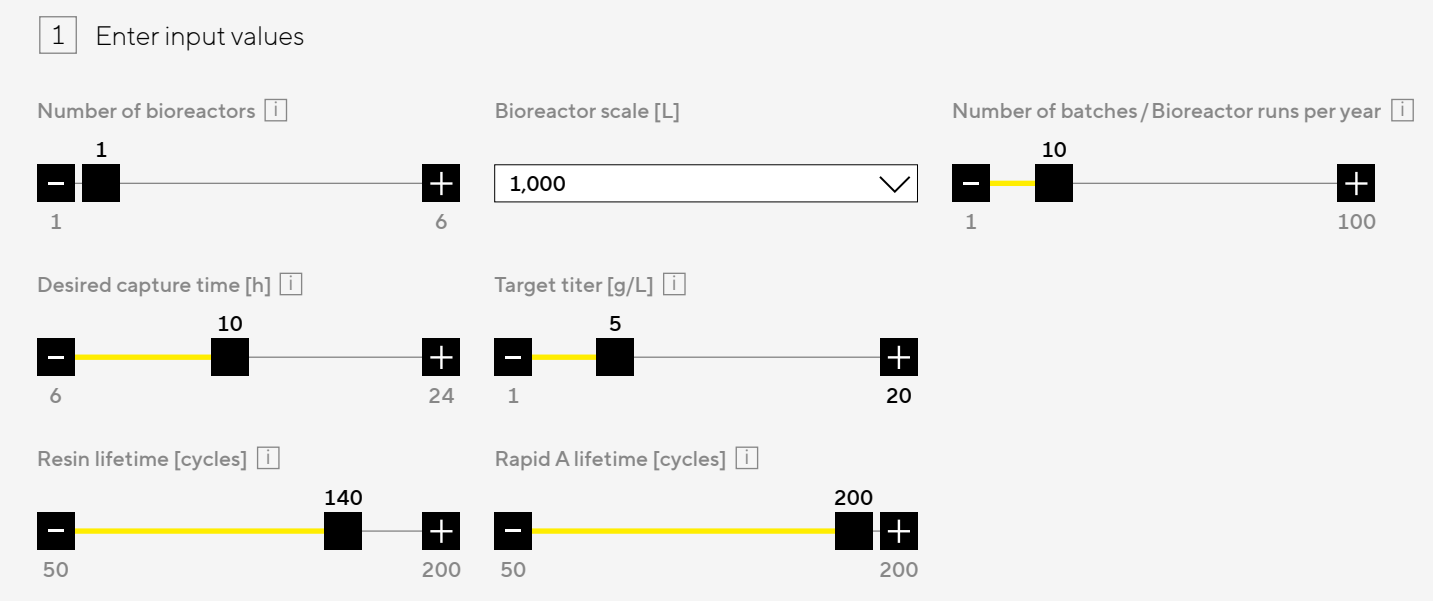


Figure 4: *Capture Intensifier Application Report*

Capture Intesifier Report

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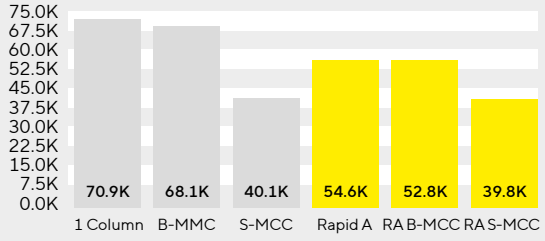
Input Values

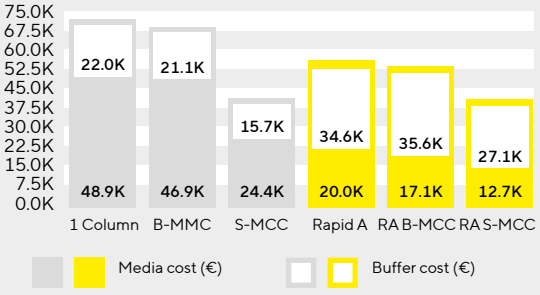
Number of bioreactors	1	Target titer (g/L)	5
Bioreactors scale (L)	1,000	Resin lifetime (Cycles)	140
Number of batches / BR runs per year	10	Rapid A lifetime (Cycles)	200
Desired capture time (h)	10		

Primary Calculation Results

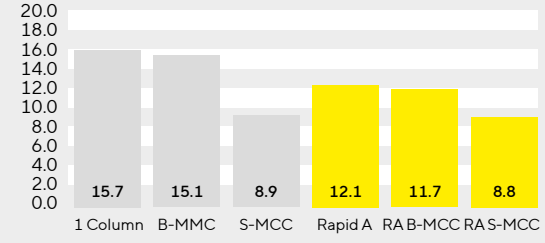
Cost per batch (€)



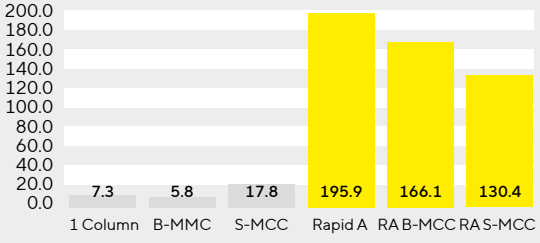
Media & buffer cost per batch (€)



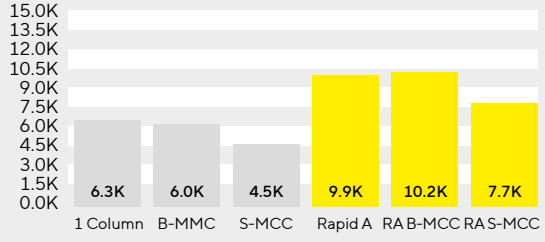
Cost per gram of mAb (€/g)



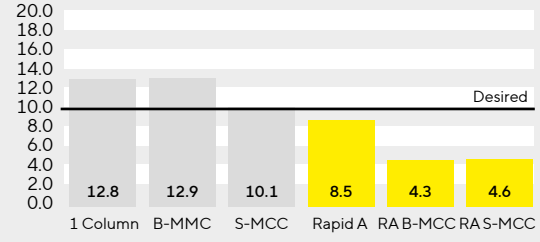
Productivity (g/L/h)



Buffer volume per batch (L)



Capture time (h)



Expert Chromatography Intensifier Tool (ExCIT)

The second tool is the Expert Chromatography Intensifier Tool (ExCIT), a Sartorius-developed modeling and decision-support platform that helps biopharmaceutical companies optimize all key parameters across capture, intermediate purification, and final polishing chromatography.

Based on real customer workflows and used by more than 50 biotechs, CDMOs, and biosimilar manufacturers, ExCIT allows technical teams to simulate and evaluate intensification strategies in silico — before lab work begins. The tool defines the optimum number and size of columns and membranes, flow rates, and buffer consumption.

It then calculates the costs, productivity, and capacity utilization of the chromatography media for the entire chromatography workflow (Figure 5).

PI introduces choices that impact cost, scalability, productivity, and facility fit. ExCIT enables:

- Case-by-case comparison of resin vs. membrane chromatography
- Evaluation of bind-elute vs. flow-through modes
- Modeling of batch vs. connected or continuous workflows
- Quantification of cost, time, buffer use, and throughput across all chromatography unit operations

After selecting a process intensification strategy and evaluating it in the laboratory, ExCIT allows the scale-up process to be modeled using R&D data such as capacity, buffer sequence, and residence times. This approach not only provides a more accurate assessment but also accounts for system capabilities at large scale.

This modeling capability provides a data-driven foundation for downstream PI decisions and investment justification.

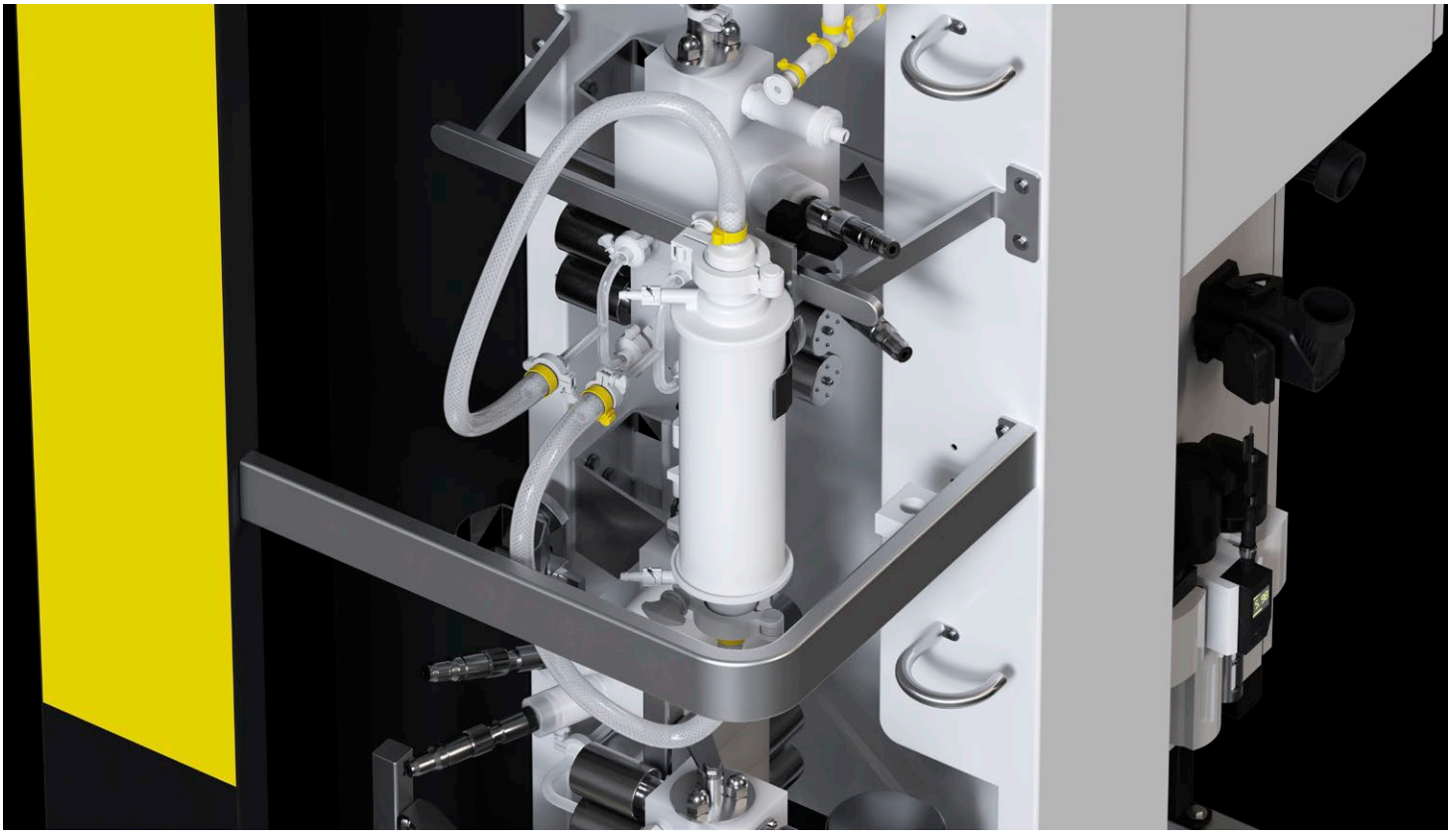
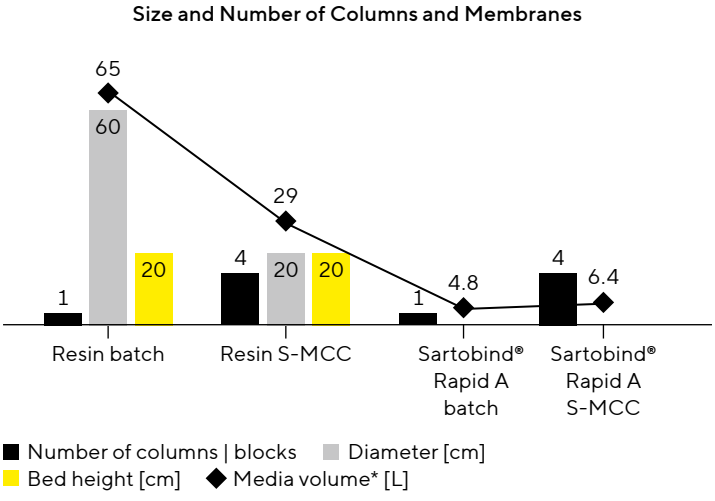
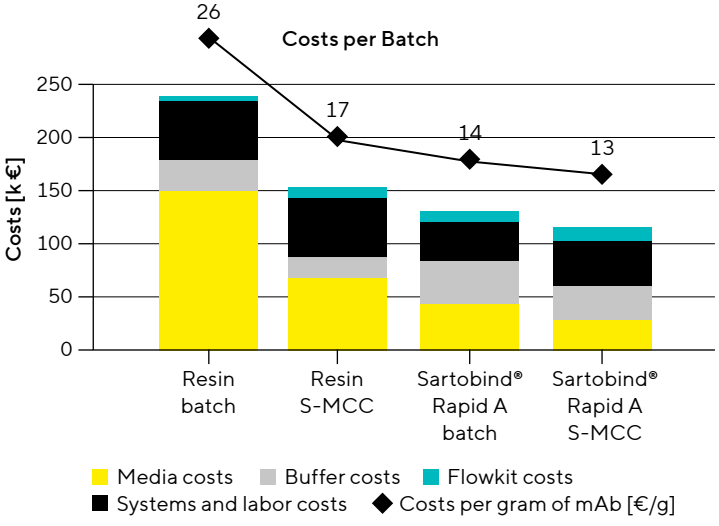
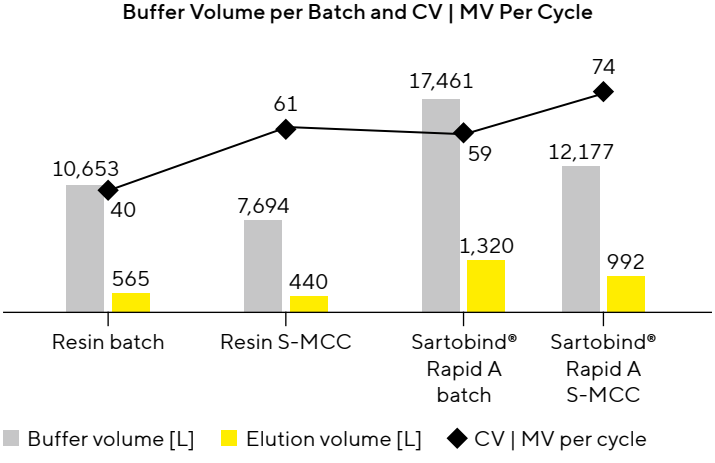
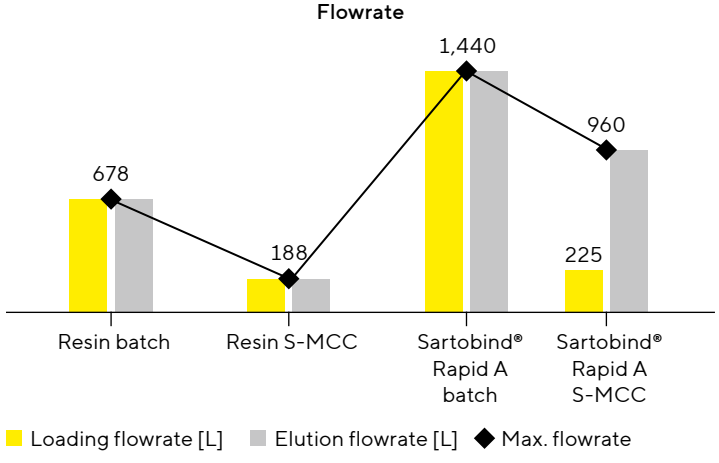


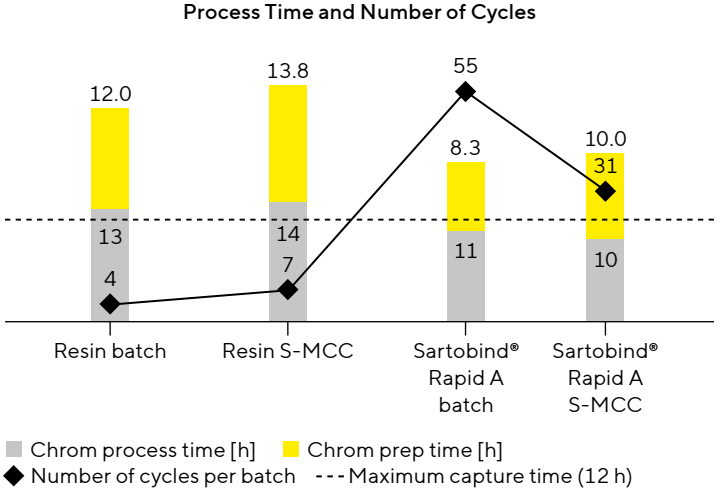
Figure 5: *Example Outputs From ExCIT*

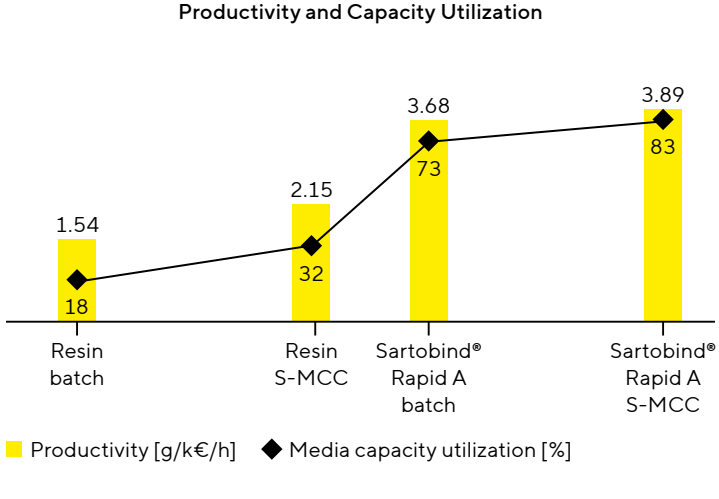












*Resin volumes include the extra media required for packing

Workflow Modeling

Clinical-Scale Modeling Example

Early- and Late-Stage Clinical Production: Strategy Comparison

Using a conventional resin workflow as a benchmark—with Protein A capture, bind-elute ion exchange (IEX) polishing, and a final IEX flow-through step—ExCIT was used to evaluate two intensification strategies for a 500 L bioreactor titer at 5 g/L, running three batches per clinical campaign (Figure 6).

Intensified Resin Process: The first PI option employed a serial MCC with a Protein A resin for the capture step, and IEX resins in a double flow-through mode for the polishing steps.

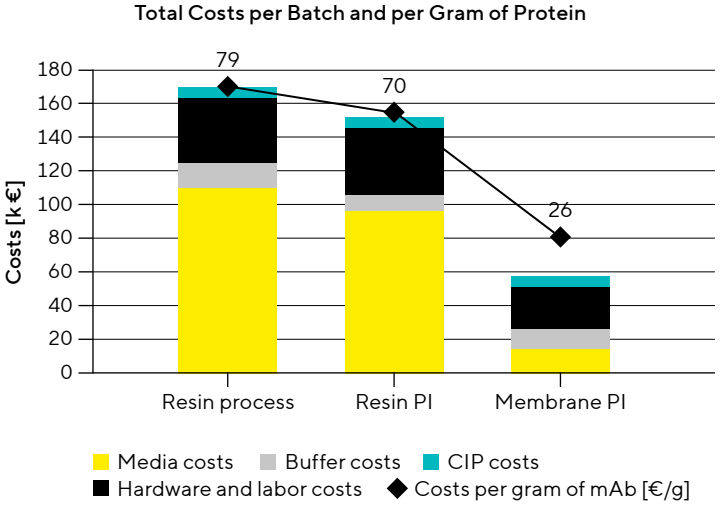
Intensified Membrane Process: The second PI option used a single Sartobind® Protein A membrane in batch RCC mode for the capture step, followed by double flow-through polishing steps with Sartobind® Q (anion exchange; AEX) and Sartobind® S (cation exchange; CEX).

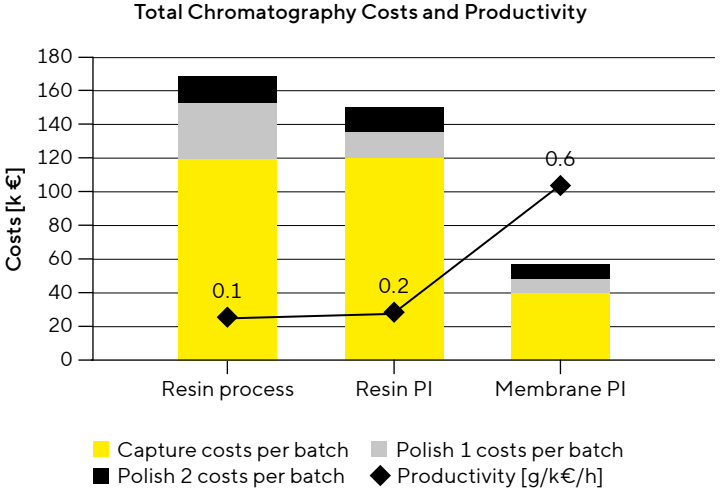
Figure 6: *ExCIT Cost Modeling For a Chromatography Workflow at Clinical Scale*

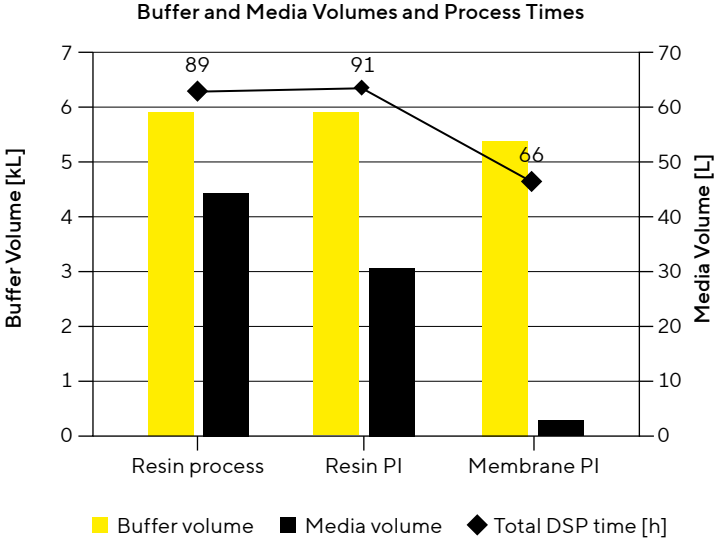
Strategy	Cost Savings [%]
MCC Resin Capture and Double Flow-Through	11
Full Sartobind® Membrane Workflow	67

PI Outcomes	Resin Process Intensification	Membrane Process Intensification
Cost difference	-11%	-67%
Time difference	+2%	-26%
Productivity difference	+10%	+305%
Buffer Use difference	+0%	-8%
Cost savings per campaign	€-92,144	€-566,012
Time savings per campaign	+9 h	-115 h

Membrane Chromatography drives fast setup and change-over, making it ideal for variable campaigns. It ensures efficient membrane utilization, achieving full lifetime value within just a few runs. In addition, its simplified validation approach supports the flexibility requirements of clinical-stage development.







Note. 500 L, 5 g/L feed titer, running for 3 batches per campaign

Commercial-Scale Modeling Example

Evaluating Full-Scale Production: 2,000 L, 40 Batches/Year

ExCIT simulated a traditional three-step resin-based chromatography process at commercial scale and compared two PI strategies for 2,000 L bioreactors operating at a titer of 5 g/L, 40 batches/year (Figure 7).

Intensified Resin Process: The first PI option employed a serial MCC with a Protein A resin for the capture step, and IEX resins in a double flow-through mode for the polishing steps.

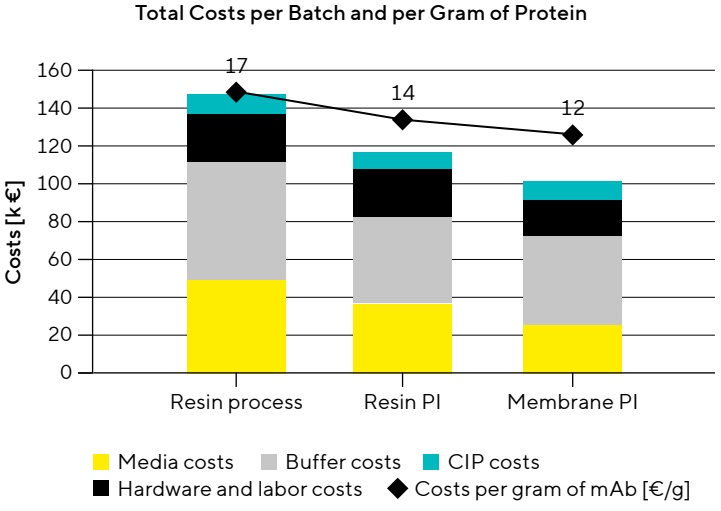
Intensified Membrane Process: The second PI option employed Sartobind® Protein A membranes in a S-MCC mode for the capture step, followed by double flow-through polishing steps with Sartobind® Q (AEX) and Sartobind® S (CEX).

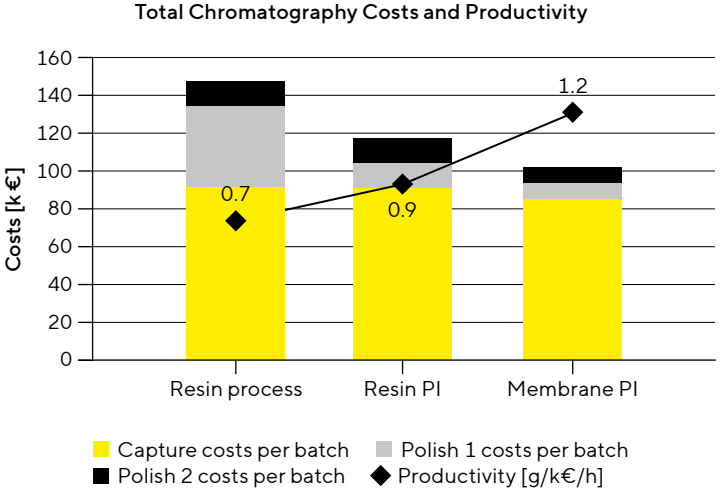
Despite Protein A membranes typically consuming more buffer during capture, the multi-column approach combined with replacing resins with membrane-based polishing ultimately reduced overall buffer consumption compared to a traditional resin-based process.

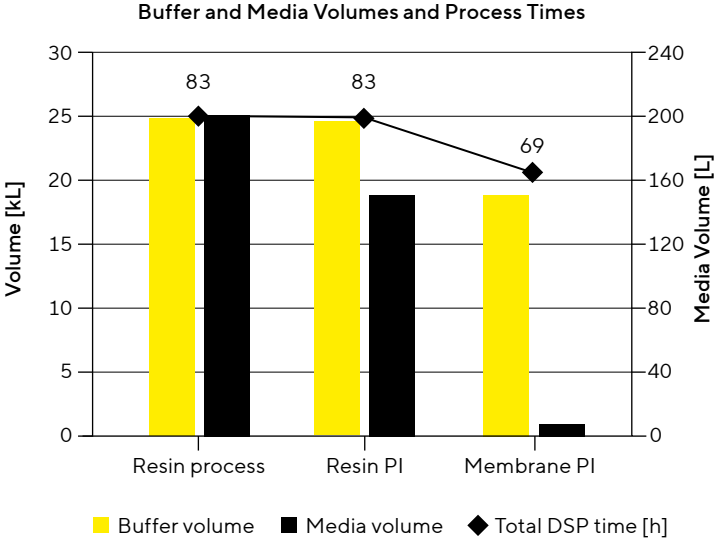
Figure 7: *ExCIT Cost Modeling for a Chromatography Workflow at Commercial Scale*

Strategy	COGS Reduction [%]	Bufffer Volume [%]
MCC Resin Capture and Double Flow-Through	21	0
Sartobind® Full Membrane (Protein A + AEX + CEX)	32	24

PI Outcomes	Resin Process Intensification	Membrane Process Intensification
Cost difference	-21%	-32%
Time difference	0%	-17%
Productivity difference	+26%	+76%
Buffer use difference	0%	-24%
Cost savings per year	€-1,214,214	€-1,865,583
Time savings per year	-15 h	-573 h (8 additional batches)







Note. 2,000 L, 5 g/L feed titer, running for 40 batches per campaign

Connected DSP Modeling Example

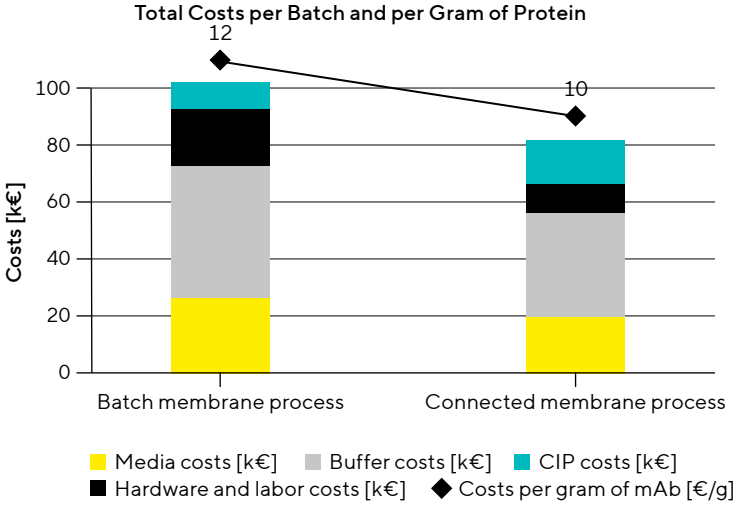
When the full-membrane workflow was further intensified by connecting the three chromatography steps (capture + polishing 1 + polishing 2; Figure 8). The results were:

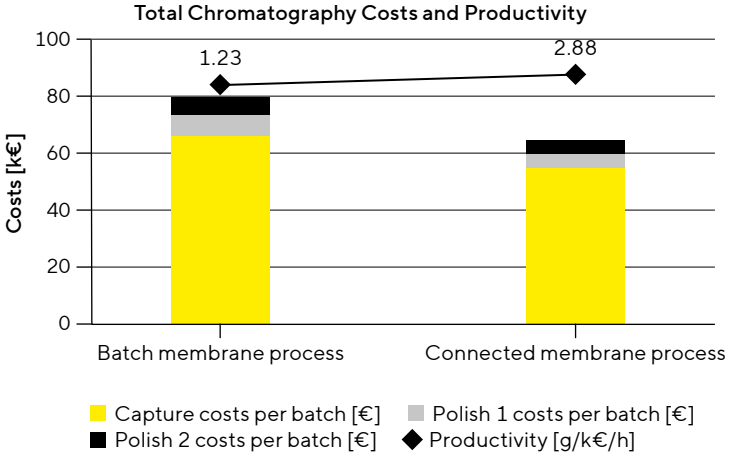
- €12 → €10 per gram of mAb
- €2.6 million in annual cost savings
- 1,882 fewer hours/year, enabling ~52 additional DSP runs

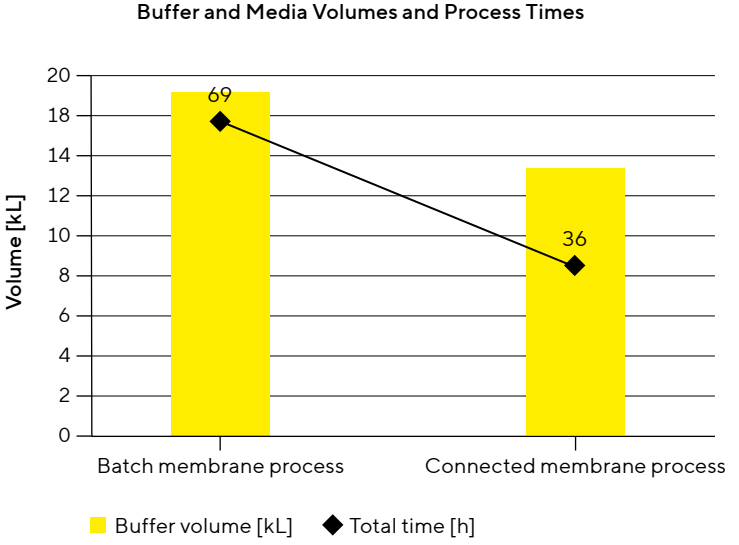
ExCIT demonstrates how connected DSP enables dramatic gains in productivity and cost-efficiency, without requiring a facility rebuild .

Figure 8: *ExCIT Cost Modeling for a Connected Chromatography Workflow at Commercial Scale*

PI Outcomes	Batch Membrane Process	Connected Membrane Process
Cost difference	-32%	-45%
Time difference	-17%	-56%
Productivity difference	+76%	+314%
Buffer use difference	-24%	-41%
Cost savings per year	€-1,865,583	€-2,636,922
Time savings per year	-573 h	-1,882 h (52 additional batches)







Note. 2,000 L, 5 g/L feed titer, running for 40 batches per campaign

Stepwise Strategy Selection & Expert Consultation

Start With the Capture Intensifier Application – Then Model Your Full Strategy With ExCIT

Getting the first step right is essential to the successful intensification of DSP. Sartorius offers a structured, supported approach that starts with self-guided discovery and progresses into expert-led consultation.

1. **Evaluate Your Capture Step Using the Capture Intensifier Application**
   Quickly assess the benefits of intensifying your Protein A capture step under specific process conditions with this fast, web-based tool for instant PI insights. The Capture Intensifier Application lets you input key process variables, like bioreactor size, titer, process time, and number of runs, to generate a custom report.

2. **Find Your Best Chromatography Workflow with an ExCIT Consultation**
   Deep dive into capture, intermediate purification, and final polishing steps with expert modeling. Sartorius experts guide you through a personalized intensification consultation using ExCIT.

ExCIT helps predict process performance, select the right technology, and design lab-scale experiments.

How the Consultation Works:

1. **Define Your Baseline**
   Provide details of your molecule, facility scale, process mode, and current DSP strategy.

2. **Scenario Modeling**
   Sartorius experts use ExCIT to simulate PI strategies – from hybrid to full membrane and batch to connected – and predict technical and financial outcomes.

3. **Interpretation & Roadmap**
   Results are reviewed collaboratively to align with your process goals, timelines, and regulatory context.

Our experts can further support you after the lab experiments, using real-life data to establish your specific costs, processing times, buffer usage, productivity, and throughput for your entire chromatography workflow when scaling up to commercial production.

Why Partner with Sartorius

- 50+ customer projects modeled using ExCIT
- Models based on validated experimental data from real-world workflows
- Tools are integrated into a broader PI offering: Ambr®, Resolute® BioSMB, Resolute® BioSC, Sartobind®, Pionic®, and digital automation tools
- Access to global field application specialists and validation experts

Next Steps

To request a modeling consultation using ExCIT or to explore downstream PI strategies tailored to your molecule and facility constraints, contact your Sartorius representative or visit:

sartorius.com/process-intensification

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