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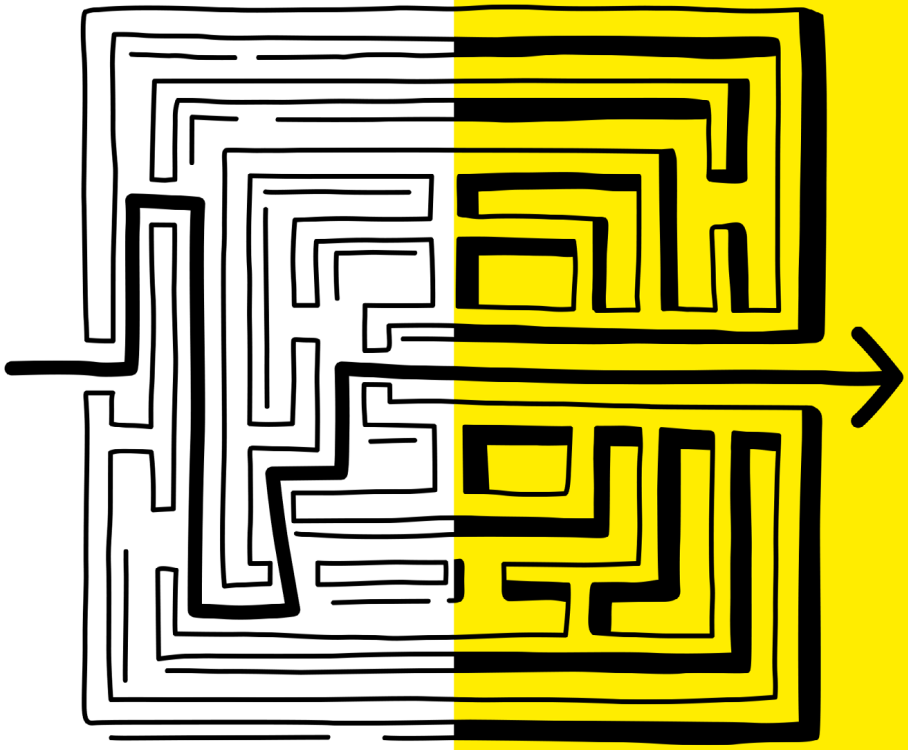
Complexity: Simplified.

The Process Intensification Playbook



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Simplifying Progress

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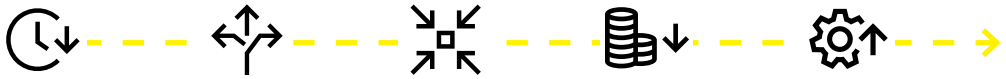

Introduction

Biomanufacturing is entering a new era, driven by urgent demands for lower drug costs, faster development timelines, and more sustainable operations. The traditional batch-based models that once defined monoclonal antibody (mAb) production are no longer sufficient to meet the growing complexity of today's therapeutic pipeline or the global need for affordable access.

Process intensification (PI) is emerging as a transformative response. Rather than viewing PI as a single technology or step, industry leaders are increasingly embracing it as a holistic, stepwise strategy to reimagine the entire biomanufacturing process, from upstream scale-up to downstream purification and beyond. PI enables manufacturers to maximize productivity per square meter, reduce costs of goods to below €50 per gram, accelerate time to clinic, and shrink the environmental footprint of production facilities, all while maintaining product quality.

Yet, implementing PI isn't without challenges. Shifting from conventional to intensified workflows requires rethinking process architecture, redesigning infrastructure, integrating real-time automation, and navigating change within organizations accustomed to batch-based systems. It demands more than the right tools; it demands the right mindset, roadmap, and partnerships.

This eBook explores the key trends and considerations driving PI adoption, and outlines practical solutions across upstream, downstream, and digital domains. It highlights how strategic collaboration, smart technology integration, and data-driven decision-making are enabling organizations of all sizes, from small biotechs to global CDMOs, to intensify with confidence.

You'll discover how stepwise intensification strategies can be tailored to specific process demands, how connected and automated systems reduce complexity while increasing control, and how the shift to continuous manufacturing is already underway. Most importantly, you'll gain insight into how these innovations are being applied today to build more flexible, efficient, and future-ready biomanufacturing facilities.

Whether you're just starting your intensification journey or looking to scale it to the next level, this eBook offers the strategic foundation and operational perspective to help you move forward.

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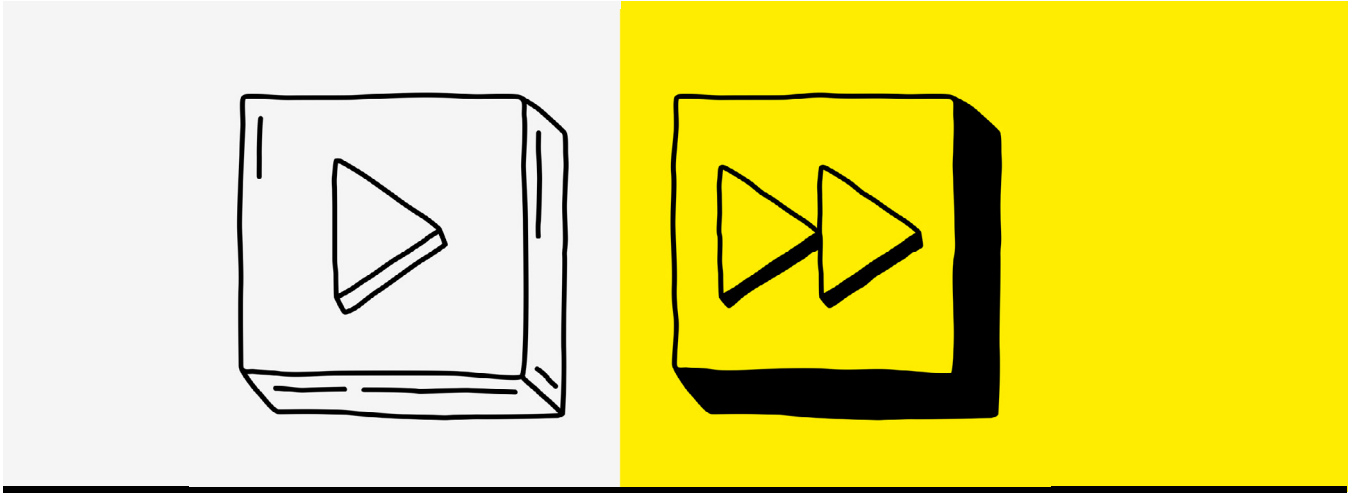
Whitepaper

Time to Intensify:
Taking mAb Manufacturing to the Next Level



Gerben Zijlstra, Jean-Marc Cappia

Keywords or Phrases: Process Intensification, Intensified Bioprocessing, Continuous Biomanufacturing, Connected Bioprocessing, Upstream Intensification, Downstream Intensification, Automated Bioprocess Solution, PI Consultation

Introduction

The mAb Industry is Evolving Towards Intensified Processing

The monoclonal antibody (mAb) industry is evolving towards intensified processing to meet global healthcare needs and address a broad range of indications, including cancers, infectious diseases, cardiovascular conditions, and autoimmune disorders. With mAb demand growing at over 10% CAGR,[1] there is a pressing need to accelerate drug development, reduce costs, improve capacity utilization, and prioritize sustainability.

Process intensification (PI) offers a holistic approach to maximize productivity in biomanufacturing, improving unit operations, manufacturing processes, and facility output.[2,3] Recent advancements, including single-use technologies, perfusion bioreactors, membrane chromatography, data analytics, automation, and continuous processing, have significantly reduced the cost of goods (COGs) for mAbs from over €1,000/g to under €200/g,[2,4,5,6] with aims to further reduce COGs to below €50/g (*Figure 1*).

PI is particularly relevant in the protein-based thera-

Figure 1: mAb Process Evolution Towards Intensification and the Impact on Cost of Goods

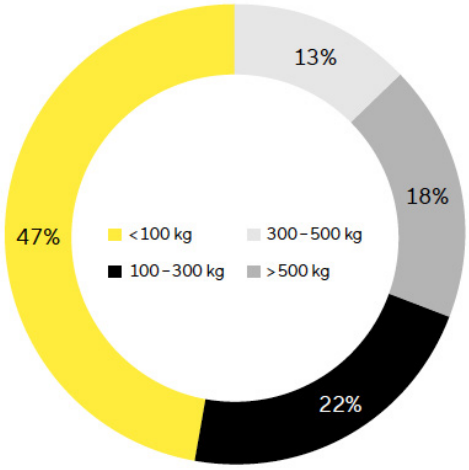
pies market, which is transitioning from conventional mAbs to more complex modalities, such as multi-specifics, antibody drug conjugates (ADCs), Fc-fusion proteins, and personalized molecules with lower demand. PI is also highly applicable to the biosimilars space, where increased competition—driven by more candidates targeting the same indications—is reshaping pipelines and encouraging a shift toward smaller, more regionalized production facilities.[4,7] As shown in *Figure 2*, most commercial drugs today are produced at annual volumes under 500 kg/year.

Fed-batch upstream processing (USP) improvements have increased mAb titers up to 10 g/L,[8–18] highlighting downstream bottlenecks and increasing the need for downstream PI. As well as increasing titers, PI also enables efficient manufacturing with lower COGs, wider drug accessibility, and reduced environmental impact (*Figure 3*). Biopharmaceutical companies typically start exploring PI during the early process development stage as a means to develop and deliver more cost-effective therapeutics faster, supporting more affordable medicine and better health for more people.

In an industry driven by quality and safety, PI progresses incrementally and continually. Over the past decades, efforts have primarily focused on the adoption of single-use technologies and upstream PI, with the development of more efficient cell lines and cell culture media systems, combined with intensified fed-batch and perfusion technologies. mAb titers exceeding 10 g/L in fed-batch mode and productivities beyond 3 g/L/day in perfusion mode, demonstrated at small scale, are expected to be achieved more broadly in future commercial manufacturing.[12,14,15]

As upstream yields improve, downstream efficiencies are the next challenge, paving the way

Figure 2: 2027 Commercial Drug Demand in kg/year



(% of number of commercial drugs in each demand scale)
Note. Source: Mammalian Demand Forecast, BioTrak, BDO 2023.

Note that the calculation only include mAb products approved prior to 2020 to eliminate bias of newly launched products

for end-to-end intensification and sustainable, cost-effective, compact facilities in the coming years. Downstream PI is also critical for companies producing more complex recombinant proteins, such as Fc-fusion proteins or multi-specifics, where titers of 6 g/L in fed-batch and up to 11 g/L with N-1 perfusion and high-inoculation seeding, have been reported.[19]

Several front-runners in the biopharma industry have implemented flexible, single-use PI facilities as part of their commercial manufacturing networks. By leveraging standardized single-use unit operations, they have achieved significantly faster build-out times and reduced capital expenditure.

In this white paper, we outline a practical, stepwise PI approach across the full mAb manufacturing workflow. We explore upstream and downstream PI strategies, innovative enabling technologies, digital solutions, and supporting tools that help simplify the transition to intensified and continuous processing. The goal is to provide actionable insights that help manufacturers accelerate the adoption of PI and maximize its benefits in terms of cost, productivity, and sustainability.

Figure 3: Process Intensification Drivers and Adoption Status

Drivers of Process Intensification: Economics, Timelines, and Sustainability

- Shorten Timelines
  Faster buildout time (< 2 years)
- Increase Flexibility
  Multiple molecules in the same facility
- Reduce Footprint
  Flexible, smaller footprint (50–70% reduction)
- Lower COGs
  >30% reduction in cost of goods
- Increase Productivity and Capacity
  2–3× higher productivity
- Sustainability
  Less plastic waste, reduced water use, lower CO_2 emissions

Adoption Status of Process Intensification Today

- 1 in 3 bioreactors used for process development include perfusion functionality
- > 80 facilities are manufacturing in intensified mode
- 1 in 3 bioreactors sold include perfusion functionality
- >100 customers use our intensified chromatography solutions

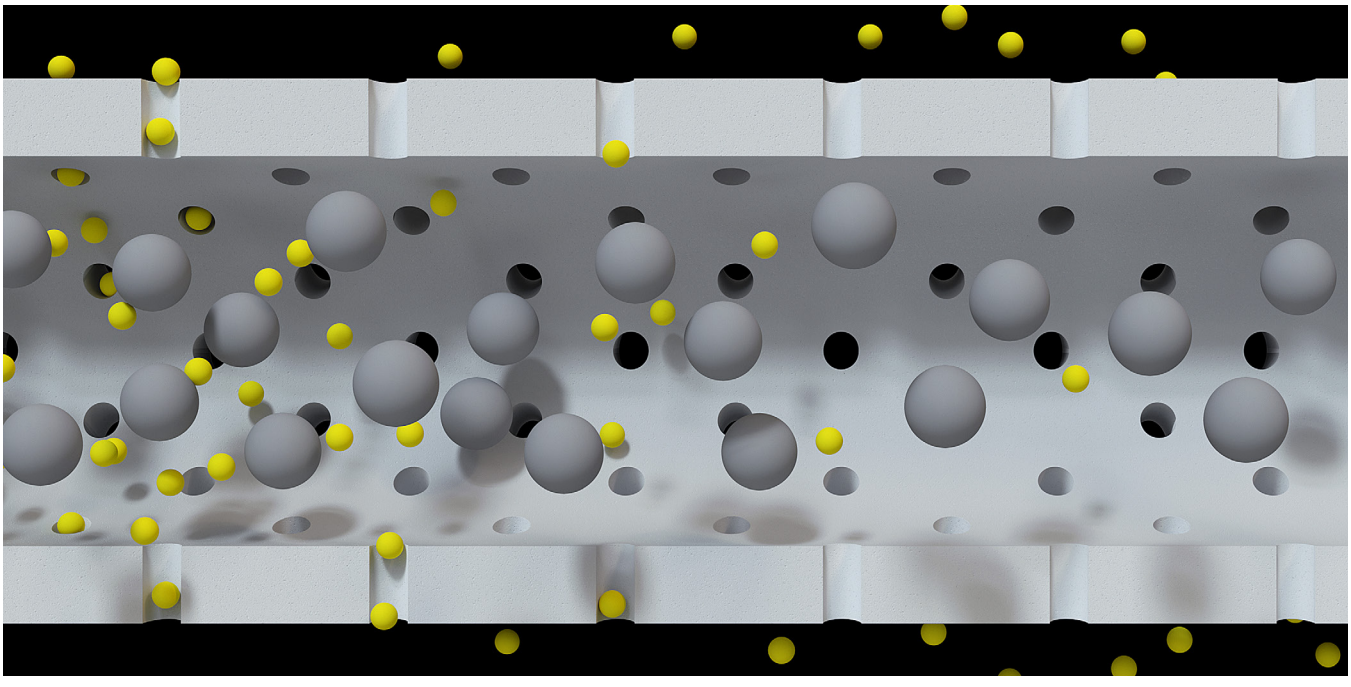
A Stepwise Strategy for USP Intensification

Fed-batch remains the dominant mode of cell culture in conventional mAb manufacturing. PI in fed-batch mode has been driven by continuous improvements in cell line engineering, cell culture media, feeds, and feeding strategies. With the growing understanding of cellular metabolism through omics technologies and the rapid advancement of genetic tools such as CRISPR | Cas technologies, targeted cell line modifications are becoming a viable strategy for large biopharmaceutical companies to optimize their platforms.[20, 21]

These approaches have not only improved cellular protein expression but have also led to increased cell densities and improved cell growth profiles by, for example, the targeted modification of pathways responsible for inhibitor production.

In parallel, omics technologies have enhanced process understanding to the extent that cellular nutrient requirements are characterized across the distinct phases of the fed-batch process. This enables the fine-tuning of basal media and feeds, as well as the development of phase-specific feeding regimes to meet the cellular nutrient needs across different cell culture stages.[22]

Finally, the increasing implementation of real-time process analytical tools (PATs) like capacitance and Raman probes, even at commercial scale, enables the precise monitoring of cell culture phases and nutrient levels. As a result, suitable infrastructure for these advanced process phase-based control strategies is now in place.[23] Together, these innovations have substantially increased mAb titers, with 5 g/L routinely achieved and 10 g/L no longer an exception— particularly among large biopharmaceutical companies.



In cases where the titer or product quality in fed-batch mode is insufficient to support progression into manufacturing, PI using different perfusion strategies can be very effective to boost titer or salvage product quality. Such cases are common and can include, for example, biosimilars developed under time pressure, where strategies like N-1 perfusion and high- intensity fed-batch cultures can be used to boost titers. Other cases include new molecular formats that exhibit low expression levels or structural instability, degrading under standard bioreactor conditions, e.g., bispecific antibodies, and requiring the short residence times provided by perfusion.[24]

While perfusion approaches also benefit from ongoing advances in cell line engineering and media development, they offer the added advantage of actively removing inhibitory and toxic cellular byproducts.[25] This allows cultures to reach much higher densities than in traditional batch processes, enabling 1,000 – 2,000 L single-use bioreactors to match the output of large stainless- steel bioreactors, paving the way for highly productive, flexible single-use facilities. Perfusion processes rely on a cell retention device (CRD) of which various forms exist. For single-use biomanufacturing, hollow-fiber membrane-based CRDs—such as alternating tangential flow (ATF) or tangential flow filtration (TFF) devices—are widely used.[24]

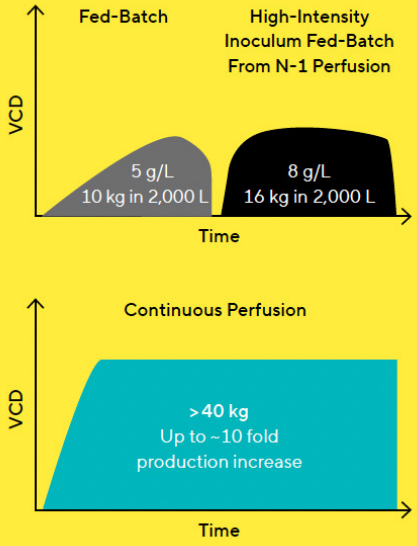
Upstream PI Approaches

N-1 Perfusion Culture

The first perfusion strategy that can be employed to increase the titer is N-1 perfusion followed by high-inoculation fed-batch (*Figure 4*). By inoculating the production bioreactor at a much higher cell density (typically between 5 and 10 million cells/mL rather than the traditional ~0.5 million cells/mL), the length of the unproductive growth phase in the main bioreactor is significantly short-

Figure 4: Different Process Intensification Strategies Using Perfusion Approaches

Level 0	Level 1	Level 2	Level 3
Standard fed-batch	N-1 perfusion or high-intensity fed-batch	Concentrated fed-batch	Dynamic or continuous perfusion
~10 kg	~16 kg	~30 kg	>40 kg
Batch harvest	Batch harvest	Batch harvest	Continuous harvest
0.4 g/L_{BR}/day	0.8 g/L_{BR}/day	1.1 g/L_{BR}/day	>1.1 – 3 g/L_{BR}/day
Baseline productivity (1×)	2× productivity	3× productivity	Required for unstable or low-yielding molecules



ened, reducing the overall run time. With further process optimization, this approach can yield up to a twofold increase in productivity.

N-1 perfusion is widely used in industry and can be performed in existing fed-batch facilities with minimal disruption; it maintains batchwise harvesting, simplifying integration with downstream processing (DSP), and requires only a modest increase in media consumption. Still, factors such as additional media preparation and the effects of higher cell densities on downstream operations must be taken into account.[7, 10, 11, 13–18, 24]

Concentrated Fed-Batch Culture

If further titer increases are needed, and media preparation capacity is not a limiting factor, concentrated fed-batch could be a viable option (*Figure 4*). This approach mimics a fed-batch strategy, but much higher cell densities and productivities can be achieved by continuous removal of inhibitory metabolites using ultrafiltration hollow fiber membranes (typically with a molecular weight cut-off < 200 kDa, depending on the product). These membranes retain both the cells and the product, allowing 3- to 5-fold increases in yield.

Concentrated fed-batch strategies have been implemented in commercial-scale single-use manufacturing facilities, combining the flexibility of single-use solutions with outputs similar to large-scale stainless-steel sites. Because the harvest is still carried out in batch mode, multiple bioreactors can be aligned to feed into a single downstream process, supporting efficient asset utilization. However, the substantially increased media logistics and adapted harvesting strategy should be considered.[8, 26]

Perfusion Culture

Finally, the only technology suitable for unstable molecular formats and capable of delivering the highest volumetric productivity (i.e., grams of product per liter of bioreactor per day) is dynamic or continuous perfusion (*Figure 4*). In perfusion mode, CRDs are used to retain the cells while allowing the passage of metabolites and the product. One variant is dynamic perfusion, which can run for up to three weeks without cell bleed and may employ cell arrest, e.g., using a temperature shift, to boost productivity. The other variant is continuous perfusion, where a controlled cell bleed removes a certain fraction from the cell culture to keep it in a growing state at a constant cell concentration. While continuous perfusion can theoretically run indefinitely, production batches typically last 30 to 40 days.

Perfusion cultures enable very high cell densities of beyond 100 million cells/mL, significantly increasing bioreactor volumetric output. Continuous product harvest, typically with direct capture and (partial) purification, allows unstable molecules to be continuously extracted and transferred to stabilizing conditions. More than 10-fold increases in yield are possible, and perfusion technology has been implemented in commercial-scale flexible single-use facilities. This combines the high output of large stainless-steel facilities with the agility of single-use solutions, while also providing the flexibility to handle a wide range of protein-based modalities. Since the

product from perfusion processes resides in the outgoing perfusion flow—and the concentration can vary between products as well as over the course of a perfusion run, particularly in dynamic perfusion—this presents challenges for connected DSP. Appropriate control strategies are therefore required to manage these variations effectively.[5-9, 12, 24, 25, 27-30]

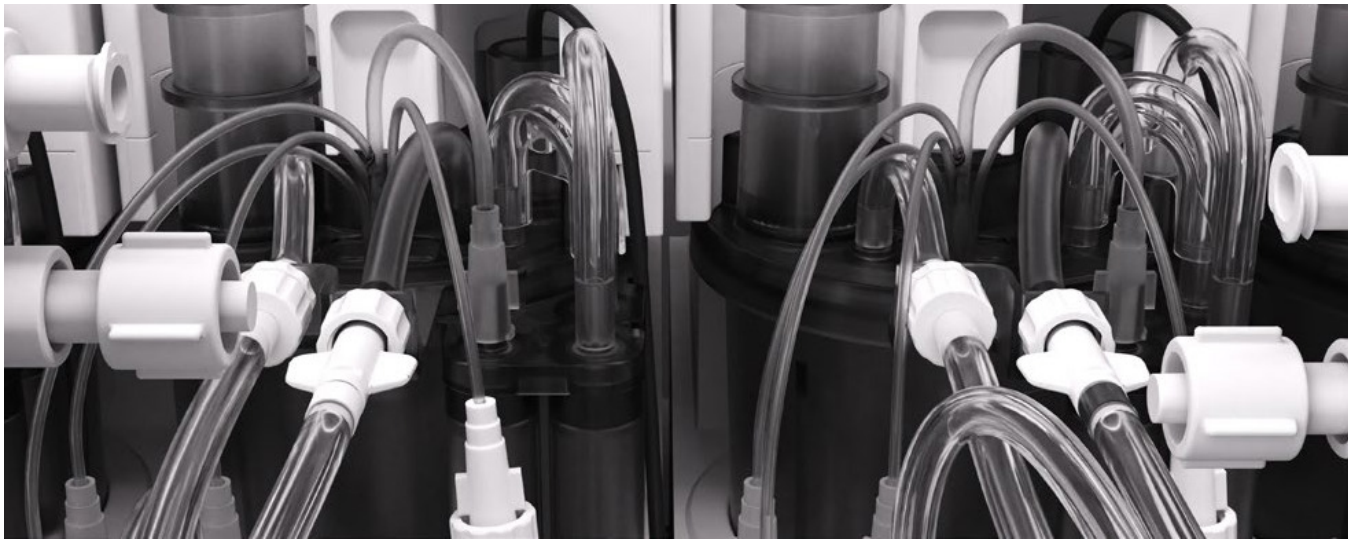
Choosing an Upstream PI Strategy

Several factors must be considered when selecting the appropriate upstream PI strategy. These include the existing product portfolio and pipeline, properties of the molecule at hand, market demand (and its associated uncertainties), existing facility infrastructure or contract development manufacturing organization (CDMO) partner capabilities, and the marketing strategy, i.e., regional or global.

The key challenges when implementing a PI approach include the extensive, costly, and labor-intensive cell line and process development efforts, as well as the need to scale and implement the advanced control strategies that ensure robust and reliable manufacturing in both clinical and commercial manufacturing sites.

Developing an intensified process requires the high-throughput generation and selection of suitable clones under the appropriate process conditions. It also requires cell culture media and feeds that maximize product output, while minimizing media consumption—particularly in perfusion mode—to achieve acceptable COGs. In addition, the process must be optimized using high- throughput, scale-down models. For perfusion processes, careful characterization and optimization of the CRD is critical, as these components can be very costly and prone to sieving and blocking.

When scaling intensified upstream bioprocesses in single-use facilities, it is critical that the bioreactors, as well as the associated CRDs, can handle the increased cell densities. Platforms should also be compatible with the required PATs and automation systems to enable advanced control strategies, such as cell density- based feeding, temperature shifts, and accurate nutrient concentration control.



A Stepwise Strategy for Downstream Process Intensification

A traditional downstream process for mAb production involves a sequence of operations, including capture, viral inactivation, polishing, virus filtration, ultrafiltration | diafiltration (UF | DF), and final filtration—which can be time-consuming and inefficient. DSP typically accounts for over 50% of mAb production costs,[2,6] with unit operations scheduled consecutively over 3–5 days, depending on the mass of the product to be purified.

Downstream PI can be achieved through a stepwise approach, transitioning from staggered batch processes to a concurrent three-level intensification model as described in *Figure 5* and *Figure 6*.

Level 1 focuses on intensifying standalone unit operations using technologies like rapid cycling chroma-tography (RCC) with membranes, multi-column chromatography (MCC) with membranes or resins, and continuous viral inactivation. These innovations can reduce costs by up to 30% and shorten processing times by up to 24 hours. Level 1 intensification is the simplest and fastest strategy to implement, offering immediate time and cost savings during clinical production.

Level 2 connects standard or intensified DSP unit operations to run simultaneously, including buffer preparation, while still operating each

Figure 5: Stepwise Approach From Batch Production to Three Levels of Intensified Processing

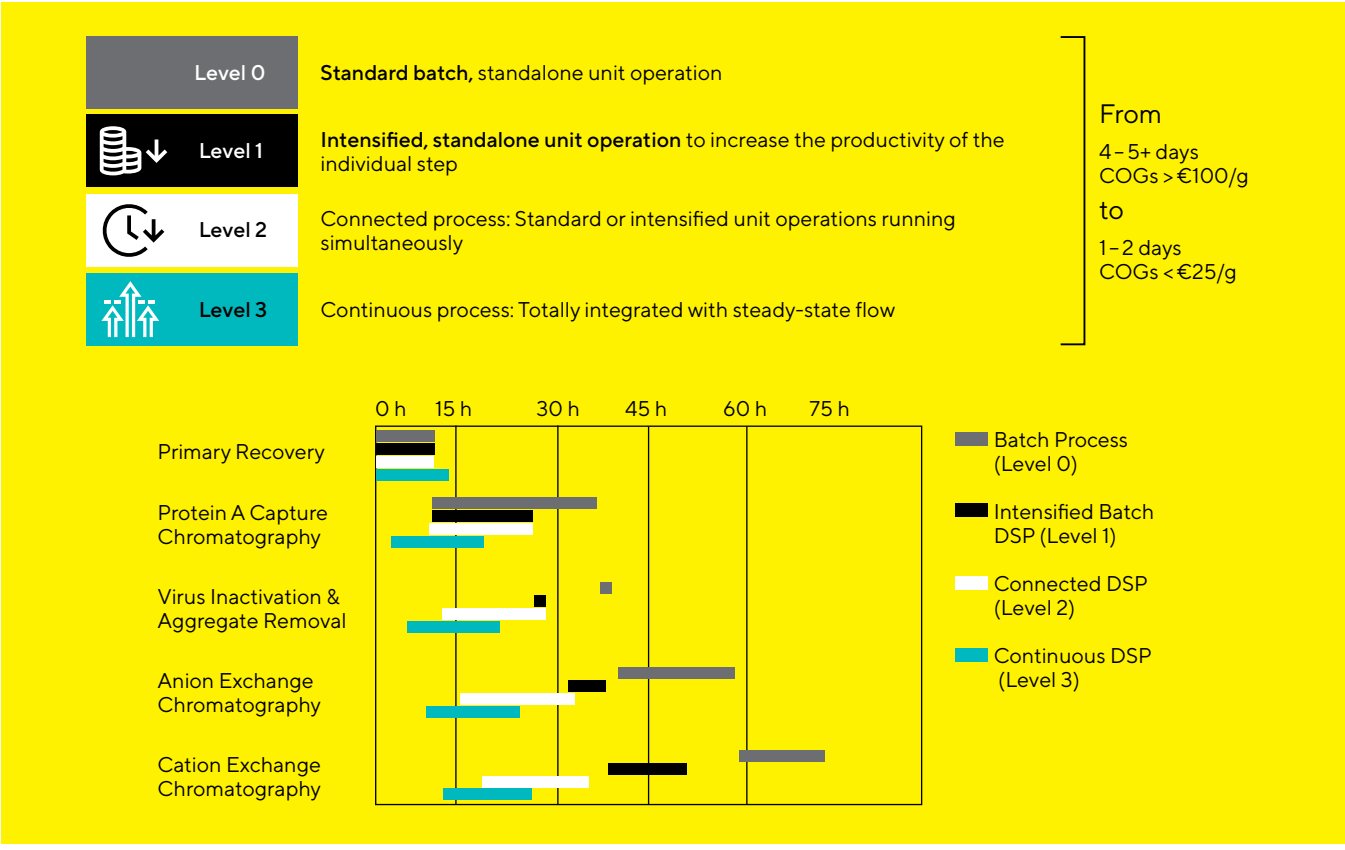
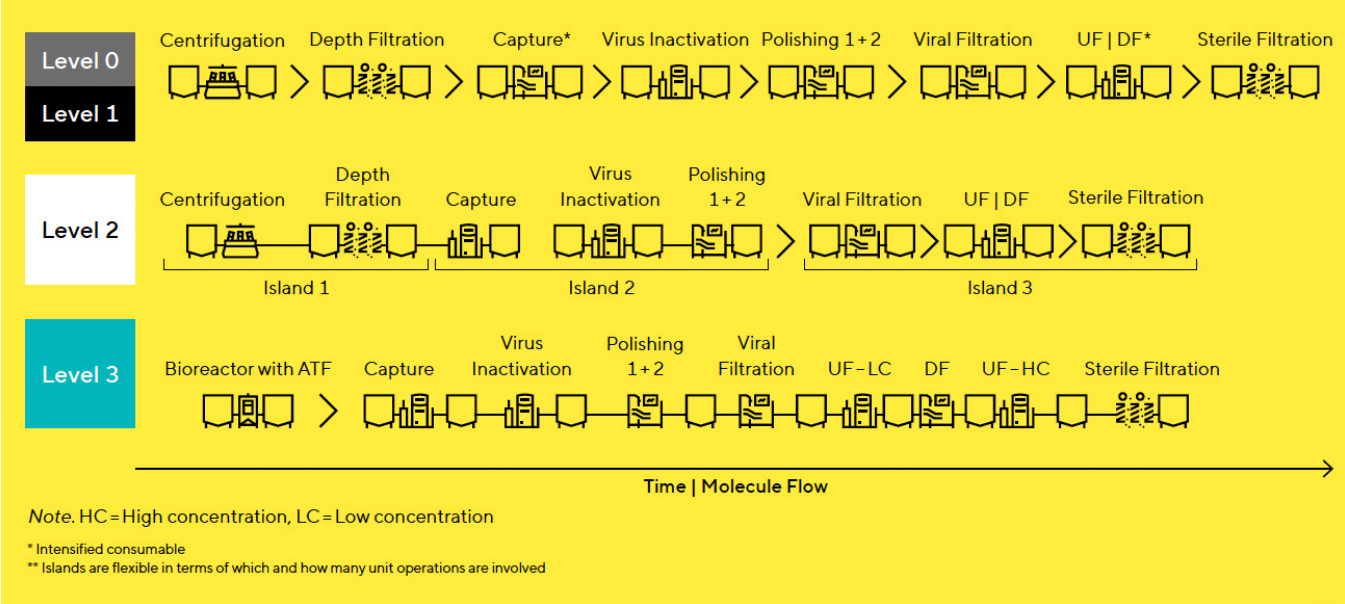


Figure 6: Three Levels of DSP Intensification to Minimize Costs, Shorten Timelines, Reduce Footprint, and Maximize Throughput



step in batch mode. Initiating the next step in parallel with the preceding operation can save an additional day, reduce the footprint by half, and double the throughput of the facility. Level 2 strategies are typically paired with a traditional fed-batch bioreactor and are often implemented during larger-scale phase 3 clinical and commercial production.

Level 3 integrates all DSP steps into a continuous flow, using small intermediate tanks orchestrated by software to enable a fully continuous process. Each unit operation is carried out in continuous mode, e.g., through MCC. This setup can be linked to a fed-batch bioreactor, reducing DSP timelines from five days to one to two days, or coupled with a continuous perfusion bioreactor for end-to-end continuous manufacturing.

Both approaches enhance throughput and flexibility while reducing footprint, capital, and resource utilization.

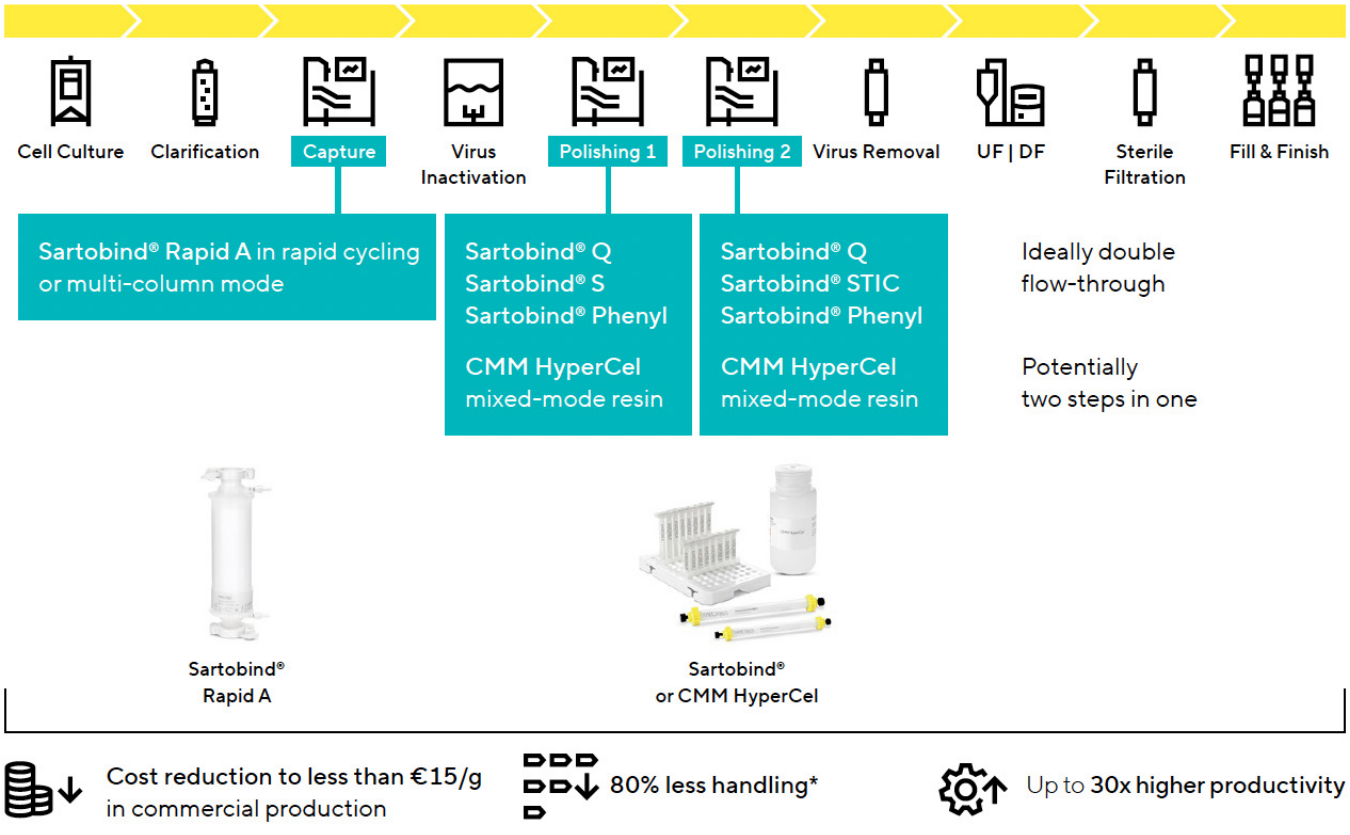
Ideal targets for chromatography are COGs of less than €15/g and a downstream workflow timeline of one to two days. Achieving these goals involves implementing a stepwise intensification strategy, as illustrated in *Figure 6*.

Technologies and Methods for Chromatography Intensification

The chromatography steps required for capturing antibodies and removing fragments, aggregates, host cell protein (HCP), and host cell DNA (hcDNA) are among the most costly and time-consuming operations in DSP, accounting for 25% to 30% of the total COGs in mAb production. Key cost drivers are the high cost of resins—which are often underutilized in clinical or low-demand production—long setup times for column installation, resin packing, height equivalent to a theoretical plate (HETP) testing, and validation studies, as well as the need for dedicated storage. These factors present critical bottlenecks for DSP intensification efforts that can be addressed by chromatography technologies such as membranes and mixed-mode resins (*Figure 7*) and methods such as RCC and MCC (*Figure 8*).

There are various strategies for intensifying chromatography, including RCC, MCC, mixed-

Figure 7: Chromatography Solutions for DSP Intensification

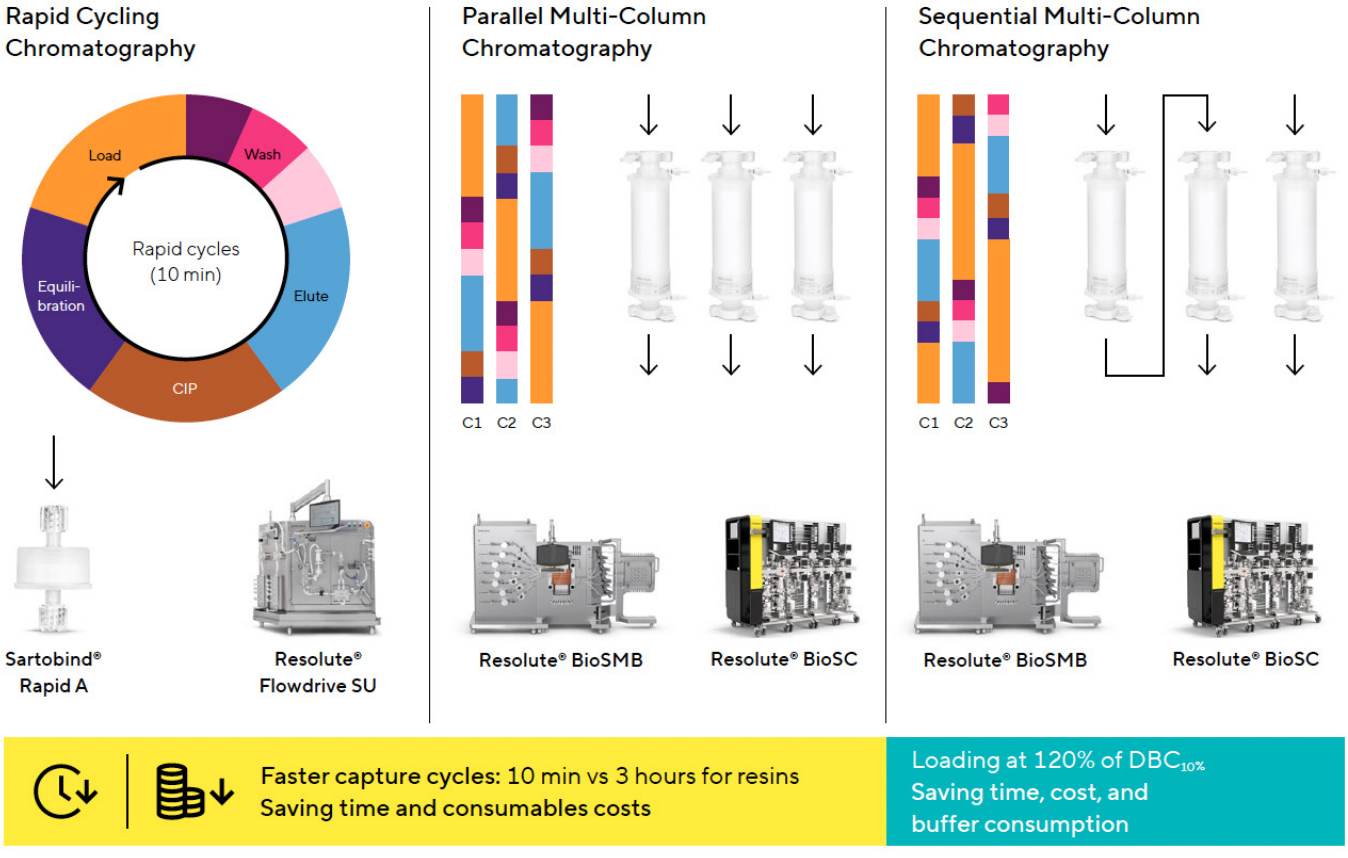


* Compared to classical resins

mode chromatography, and continuous chromatography, either in bind-elute or flow-through modes. While RCC using a single Protein A membrane device is the simplest way to intensify the capture step, applying MCC to membrane adsorbers offers additional benefits. Parallel MCC is a straightforward intensification method in which chromatography devices are installed in parallel to enable continuous capture, particularly beneficial in processes using perfusion bioreactors. For resins, MCC reduces column size and enables the use of smaller, prepacked columns.

Sequential MCC (S-MCC) is the most effective intensification method, reducing costs, time, and buffer consumption while enabling continuous capture. S-MCC maximizes binding capacity by overloading the first membrane or resin and capturing the breakthrough in the second, resulting in a 50% increase in binding capacity and equivalent decreases in costs and buffer consumption.[3]

Figure 8: Multi-Column Chromatography With Membranes Reduces Costs and Buffer Consumption



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

Digital Solutions: The Backbone of PI and Continuous Manufacturing

As demonstrated throughout this white paper, PI and continuous manufacturing fundamentally transform bioproduction. However, they also introduce greater complexity. Tighter process windows, simultaneous upstream and downstream operations, and real-time quality requirements mean that traditional automation strategies are insufficient.

Predictive control will no longer be optional in continuous and intensified manufacturing. Anticipating process trends, detecting deviations before they occur, and dynamically optimizing operations are essential to maintaining product quality, improving yields, and ensuring uninterrupted production flows.

Integration: A Critical Success Factor for PI

Integration across systems and equipment is often one of the most significant barriers to successful PI. In intensified and continuous processes, poor integration can result in:

- **Loss of synchronization between process steps**
- **Delays and extended downtime**
- **Increased risk of batch failures**
- **Missing information | gaps in data integrity**
- **Higher validation, operational, and lifecycle costs**

Modern biomanufacturing environments require digital systems that can integrate reliably and flexibly across multiple layers of operation. Key features of a well-integrated setup include:

- **Seamless connectivity across layers:** Control and operation layers that integrate seamlessly into external DCS and manufacturing execution systems (MES).
- **Cross-platform interoperability:** Interoperability with third-party equipment through open protocols such as Open Platform Communications Unified Architecture (OPC UA), ensuring efficient cross-platform communication.
- **Standardized and validated interfaces:** Interfaces that follow industry standards help

Without advanced control, monitoring, and analytics, intensified and continuous manufacturing processes face higher operational costs, longer time to market, and greater regulatory challenges.

In this new environment, digital solutions are essential. They enable manufacturers to:

Synchronize multiple unit operations dynamically and reliably

Monitor critical process and product parameters continuously (e.g., titers, flow rates, pH, and conductivity)

Detect deviations early and apply immediate corrective actions, including predictive control and advanced process orchestration

Shorten batch release timelines through integrated data management

Reduce failure rates and increase overall process robustness

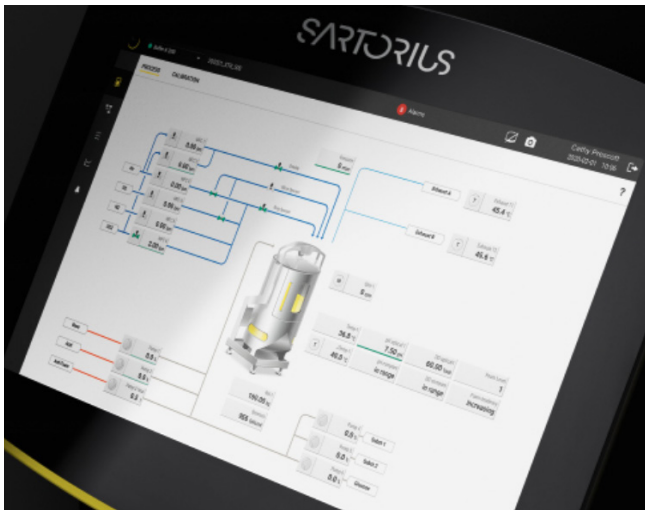
Scale processes flexibly from laboratory to commercial production while maintaining full control

reduce project risks, shorten implementation timelines, and lower complexity across operations.

This modular capability enables efficient integration into existing or new manufacturing environments, accelerating deployment, improving synchronization, and minimizing overall project costs and risks. A prime example of this philosophy is Pionic®, a platform fully based on the Biobrain® control automation architecture, offering native, multi-layer integration and orchestration capabilities specifically tailored for the demands of PI.

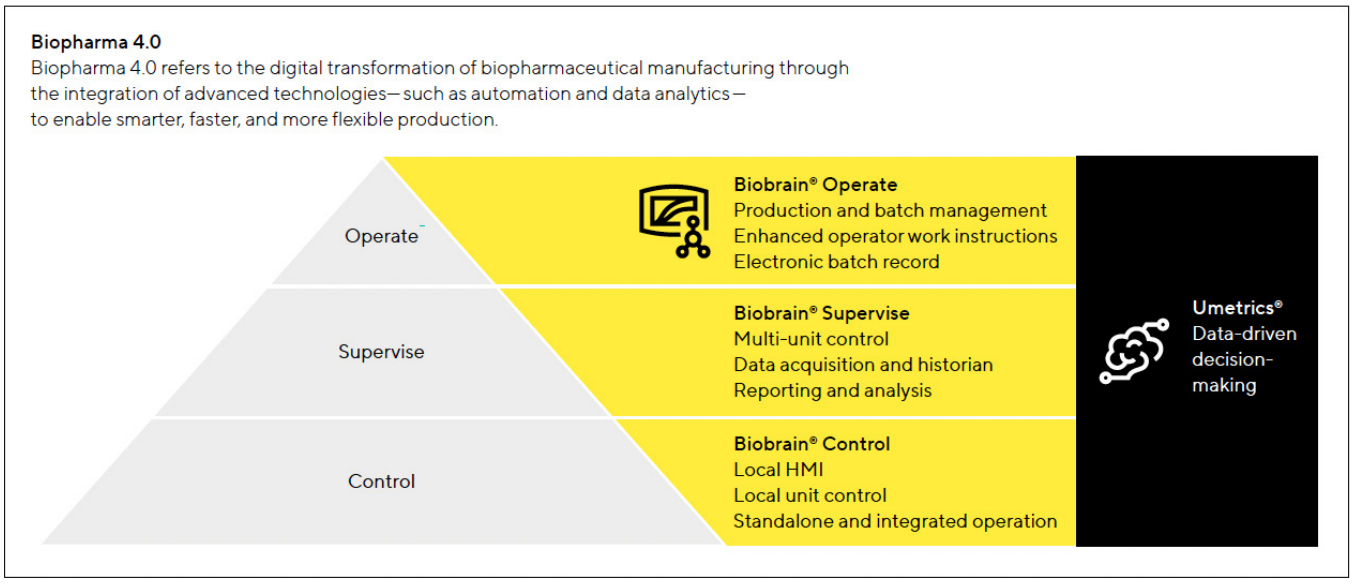
By embedding modular, interoperable digital solutions from the outset, biopharmaceutical manufacturers can transform PI from a technical challenge into a competitive advantage—achieving faster, more reliable, and more flexible production.

Figure 9 illustrates the digital solution platform designed to simplify Biopharma 4.0. Predictive



data analytical tools, PATs, automation software, and services are key enablers for PI. They help lower costs, shorten timelines, reduce the risk of lost batches, improve productivity, and ensure product quality during both process development and manufacturing. Together, these solutions form a robust, integrated, and scalable digital ecosystem, specifically designed to simplify and accelerate the digital transformation journey in biopharma.

Figure 9: Digital Solution Platform to Simplify Biopharma 4.0



Bioprocess Consulting and Technical Services for PI

Implementing PI is often complex and resource-intensive, requiring the appropriate expert tools, knowledge, technical support, and consultancy services from USP and DSP and from conceptual design to facility build-outs.

PI is a stepwise journey beginning with initial process optimization, application development, process modeling, and conceptual design. It progresses through detailed engineering, validation, and regulatory support, culminating in final project execution (*Figure 10*).

Validation and Regulatory Support Services

Working in collaboration with suppliers allows users to obtain the required validation services for all process components essential for PI, including bioreactors, bags, container closure systems, mixing systems, sterile filters, transfer systems, membrane adsorbers, virus filters, and more. Leveraging Sartorius' Confidence® Validation Services, our deep understanding of the regulatory landscape, and extensive experience in PI and continuous manufacturing, we can assist in designing the appropriate validation master plan and ensuring compliance with the latest regulatory requirements.

Figure 10: Technical, Consultancy, and Validation Services to Simplify PI

PI Strategy and Technology Choice		PI Design and Establishment of Process Performances		Scale-Up, Validation, and Project Execution	
Process Optimization	Process Design and Cost Modeling	Process Consulting and Conceptual Design	Process Engineering and Cost Calculation	Validation, Regulatory Support, and Training	System Installation, Factory Acceptance Testing, Site Acceptance Testing, and Installation Qualification and Operational Qualification
Application Specialist • Optimize process • Generate data for process and cost modelling • Base for scale up	**Process Consulting** • PI design • Technology choice • Impact on COGs, timelines, footprint, throughput, buffers	**Integrated Solution Engineer** • Mass balance • COGs modeling • Process flow diagram and layout • Automation	**Process Engineer** • Technical user requirements specification • Piping and instrumentation diagrams and process flow diagrams • 2D and 3D CAD design drawings • Detailed COGs	**Validation Experts** • Virus clearance • Extractables and leachables • Filtration and single-use systems' validation • Particle validation	**Service & Manufacturing Engineers** • Assembly • Commissioning • Factory acceptance testing and site acceptance testing • Training • Post-sales services

Note. Process modelling tools support the selection of the optimal overall PI strategy (USP batch vs. perfusion, DSP batch vs. continuous, single-use vs. multi-use). ExCIT supports the selection of the right chromatography workflow (membrane adsorbers vs. resins, batch vs. connected or continuous, bind and elute vs. flow-through).

Conclusion

PI is essential for addressing the growing demand for mAb therapies, aiming to reduce costs, increase throughput, and minimize environmental impact. While advancements in upstream processes have boosted mAb titers and productivity, they have also shifted bottlenecks to DSP, necessitating comprehensive intensification across the entire manufacturing process.

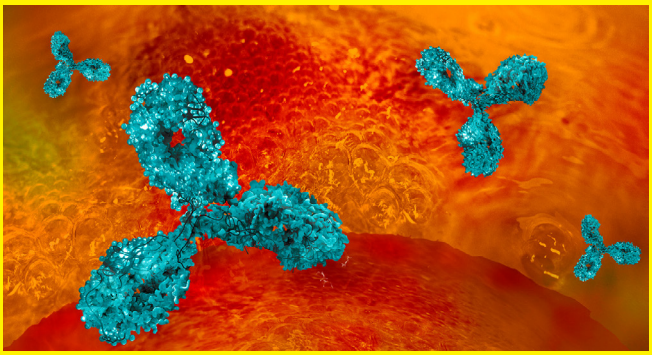
This white paper demonstrates that intensifying upstream processes through intensified fed-batch or dynamic | continuous perfusion bioreactors, coupled with a fully integrated membrane chromatography workflow for downstream purification, offers a cost-effective alternative to traditional platforms. Membrane chromatography, particularly with Sartobind® Rapid A, enables faster purification cycles and efficiently purifies large quantities of antibodies using smaller consumables, significantly reducing overall downstream costs and process footprint. This approach benefits both low-demand and large-scale production, maintaining yield, purity, and product quality attributes.

As a partner in biopharmaceutical development, Sartorius supports the transition to intensified processing. Our suite of process and cost modeling tools, process technologies, digital solutions, and services to facilitate PI, ensure efficient, cost-effective, and sustainable mAb production, enabling the development of new and better therapies and more affordable medicine. It's time to intensify.

Webinar

Time to Intensify: Taking Process Intensification of mAb Manufacturing to the Next Level

Watch the webinar



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Gerben Zijlstra is a leading expert in process intensification, integration, and continuous biomanufacturing, with over 25 years in the biopharma industry. He holds a Ph.D. from the University of Wageningen, focusing on process integration in animal cell culture. At Patheon, he developed commercial biotherapeutics and advanced process intensification projects with single-use bioreactors. Zijlstra invented the XD® Concentrated Fed-Batch technology, boosting productivity fivefold, and facilitated its scale-up to the Brisbane site, recognized by ISPE for process innovations. At Xendo, he worked on single-use continuous biomanufacturing and gene therapy.

JEAN-MARC CAPPIA
Head of Market Development for Intensified Chromatography, Sartorius

Jean-Marc Cappia is Head of Market Development Intensified Chromatography at Sartorius, based in Aubagne, France. With a biotechnology engineering degree from the INSA of Toulouse and more than 35 years of experience, Mr. Cappia supports the global biopharmaceutical industry, particularly with process design, process intensification, validation, training, and the implementation of single-use filtration, purification, and fluid management technologies.

Since joining Sartorius in 2006, he has been responsible for marketing, product management, and business development for emerging single-use technologies. In his current position he supports customers with their downstream process intensification, with a focus on chromatography and with the objective to produce safer and cheaper biologics in more sustainable manufacturing facilities.

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News

Sartorius Collaborates with Sanofi on Downstream Process Intensification

Sartorius

Sartorius is collaborating with Sanofi to develop an end-to-end platform for integrated and continuous downstream bioprocessing (ICB). Sartorius will contribute its engineering and manufacturing expertise to commercialize ICB platforms based on prototypes developed by Sanofi. In return, Sanofi will grant Sartorius exclusive access to its know-how and patents related to the ICB platform.

"Technological innovation is crucial for biopharmaceutical companies to significantly reduce the cost of drug manufacturing, while improving the environmental footprint of their operations, and ultimately getting life-saving drugs to patients faster," said Jan Schäfer head of separation systems at Sartorius. "As the biologics landscape becomes more diverse, teaming up with Sanofi is an excellent basis for developing a unique modular platform that combines flexibility with the advantages of intensified bioprocessing.

Integrated continuous biomanufacturing is an advanced approach to the production of biopharmaceuticals. The concept aims to maximize efficiency by enabling uninterrupted and

steady materials flow, as opposed to traditional batch methods, and by integrating multiple unit operations into a lean process setup. ICB reduces the overall process footprint, leading to lower raw material and energy consumption, higher productivity, and less waste.

This work is the result of a Collaboration & License Agreement between Sanofi and Sartorius.

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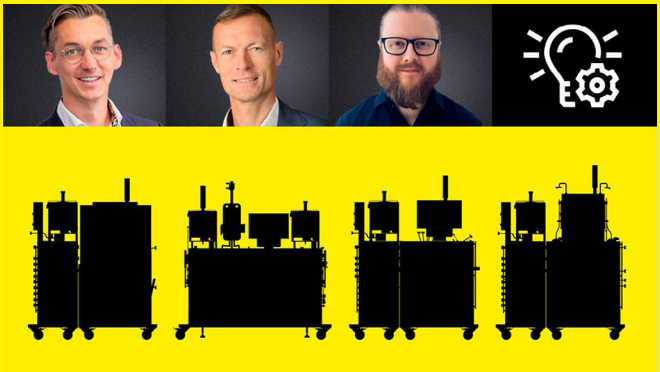
Shaping the Future of Biomanufacturing: Inside Pionic® Platform



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News

Sartorius and Repligen Launch Integrated Bioreactor System

Sartorius

Sartorius and Repligen launched an integrated bioreactor system that incorporates Repligen XCell® ATF upstream intensification technology into Sartorius' Biostat STR® bioreactor. The goal is to simplify intensified seed train and N perfusion implementation for biopharmaceutical manufacturers, according to both companies.

The Biostat STR now contains a fully compatible embedded XCell ATF hardware and software module offering predefined advanced control recipes with integrated Process Analytical Technology (PAT), noted Mario Becker, head of product group bioreactor technologies, Sartorius, adding that this system gives users a streamlined way to control cell growth and improve cell retention in perfusion processes without using a separate cell retention control tower.

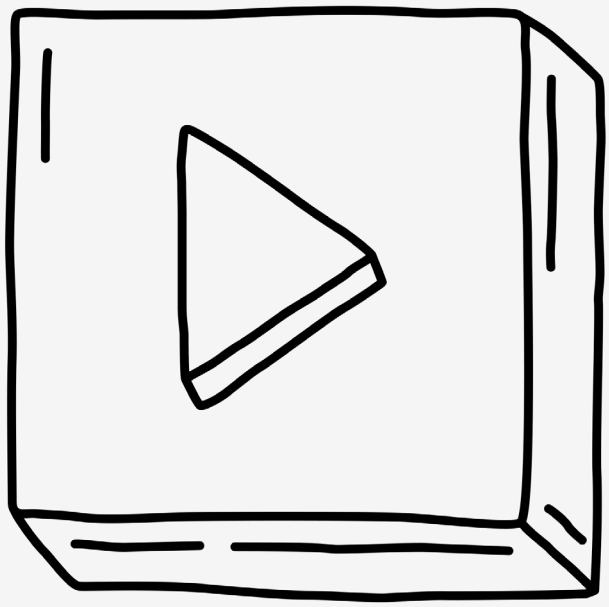
In addition, customers can better utilize facility space with a reduced equipment footprint from the incorporation of the XCell Controller hardware and software in the Biobrain® automation platform, creating a single point of control for 50 L–2000 L upstream intensification processes, pointed out Christine Gebski, senior VP filtration & chromatography at Repligen. The single, integrated controller also reportedly provides integration into Supervisory Control and Data Acquisition (SCADA) and Distributed Control Systems (DCS).

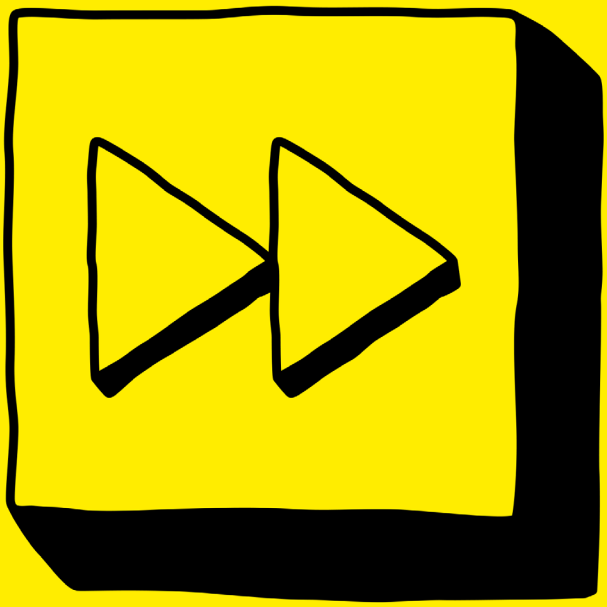
"The market introduction of this integrated bioreactor—intensification system created in partnership with Repligen further reinforces Sartorius' commitment to being an innovator in process intensification and demonstrates our expertise in upstream processing technologies," said Becker. "Ultimately, our goal is to help customers bring more therapeutics to patients faster, and this launch advances our journey along that path to enable continuous manufacturing."

Customers are now able to purchase the integrated system from Sartorius, with available pretested and predefined configurations, he explained.

"The successful pairing of our XCell ATF intensification control technology with Sartorius' single-use bioreactors provides end users with a simplified, easy-to-implement perfusion-enabled bioreactor solution for more efficient, higher density cell culture processes," said Gebski.

The new integrated bioreactor system.





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