Simplifying Progress

Digital, Automation, and Analytics: Enabling the Future of Intensified Biomanufacturing

September, 2025 | Cyril Mak

Keywords or Phrases:
Process intensification, digital transformation, automation, Biobrain® Control, Supervise, and Operate, Umetrics® Digital Twin AI Ecosystem, SIMCA®, SIMCA®-online

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Introduction

A Robust Digital Infrastructure: The Enabler of End-to-End Intensification

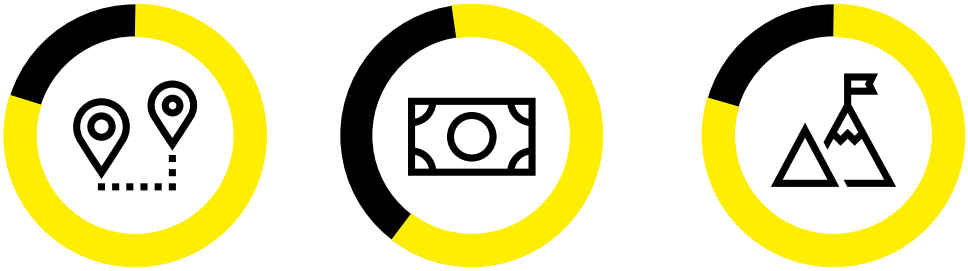
Biopharmaceutical manufacturing is rapidly evolving. The need for faster, more flexible, and more sustainable production is accelerating the adoption of process intensification (PI)—which includes concentrated fed-batch, perfusion, and integrated continuous processing. These intensified strategies offer a clear path toward higher productivity, lower cost of goods, and reduced facility footprints.

While the benefits of PI are clear, its implementation brings significant operational complexity. Continuous or semi-continuous processes require the precise coordination of interdependent unit operations, digital twins used for real-time monitoring of critical variables, and rapid (often automated) decision-making. These requirements push traditional automation and analytics strategies beyond their limits.

To succeed, intensified processes require robust and intelligent digital infrastructure that spans local equipment control, cross-unit orchestration, advanced analytics, and data-driven decision-making. However, integrating these elements remains one of the most overlooked challenges. Industry data reflects this gap: 80% of biopharma companies report being only at the start of their digital transformation, with more than half citing insufficient funding as a barrier (Figure 1).[1]

This white paper outlines how Sartorius enables the transformation to PI through a unified digital platform that integrates equipment control, cross-system orchestration, and predictive analytics—from development to commercial scale.

Figure 1: *Digitization in Biopharma Survey Results (MIT Sloan Management Review | Deloitte Digital Business Global Executive Study)*



80% are at the beginning of their digital transformation journey or are expanding their capabilities

54% said that there is a lack of sufficient funding for the digital transformation

79% expect to realize the value of digital initiatives within the next five years

Why Intensified Bioprocessing Requires Digital Innovation

PI promises significant gains, but it also introduces operational complexity. Ultimately, PI can only deliver on its full promise when supported by a strong digital foundation. Often, companies underestimate the cost, time, and risk involved in connecting equipment, systems, and software. Without the right digital architecture, integration projects can take months, incur significant validation and consulting costs, and introduce operational delays.

In contrast, platforms designed with open standards for connectivity — such as Open Platform Communications Unified Architecture (OPC UA) — and featuring extensive interfaces for manufacturing execution systems (MES) and | or distributed control system (DCS) interfaces, dramatically reduce this burden, accelerating deployment, minimizing errors, and ensuring long-term scalability, providing relevant data for MES and DCS interfaces.

Moreover, as PI evolves, so do logic requirements. Coordinating upstream perfusion, continuous viral inactivation, or multi-column chromatography requires smart orchestration logic, built-in safeguards, and the ability to synchronize dynamic flows. This growing complexity is fueling the demand for ready-to-use, pre-configured digital solutions that embed best practices and accumulated process knowledge from the outset.

Sartorius addresses this gap through a modular digital ecosystem that integrates:
- Equipment-level automation and orchestration logic via Biobrain®
- Predictive analytics and soft sensors via Umetrics® Digital Twin AI Ecosystem
- Integration-ready architecture built on OPC UA and MES | DCS interfaces.

These solutions allow manufacturers to begin with targeted improvements, like automating a perfusion reactor or linking a chromatography train, and scale over time toward fully integrated, adaptive processes, unlocking the full potential of intensified biomanufacturing.

As manufacturers intensify their processes by adopting perfusion bioreactors, continuous purification, or modular single-use facilities, the complexity of operations increases dramatically. These intensified approaches demand not only physical equipment upgrades but also a shift in how processes are monitored, controlled, and synchronized.

This section outlines the core digital challenges that emerge in the context of PI and why digital solutions are essential to addressing them.

Coordinating Multiple Simultaneous Operations

In intensified manufacturing, upstream and downstream operations are often decoupled from the traditional batch rhythm. Continuous perfusion bioreactors may run for weeks, while downstream steps such as viral inactivation or polishing occur on independent timelines.

While control systems regulate individual equipment functions (e.g., maintaining flow rate, temperature, or pH), without centralized orchestration and real-time communication between systems, manual handoffs or poorly synchronized steps can lead to bottlenecks, process drift, or even batch losses. The more continuous the process, the more intelligent the orchestration must be.

Digital orchestration tools are required to coordinate these interdependent operations dynamically and in real time, ensuring correct sequencing, flow balancing, and data integrity across the process chain. This ensures that all unit operations and operator actions work together across the process.

Maintaining Real-Time Visibility and Control

Intensified processes operate within narrower control windows. Small variations in feed rate, pH, conductivity, or residence time can significantly impact product quality or downstream performance. The vast number of interrelated variables makes it impossible to rely solely on periodic checks or offline sampling.

Integrated process control systems must provide real-time monitoring of critical process parameters (CPPs) and critical quality attributes (CQAs), with closed-loop feedback where possible. Machine learning, multivariate data analytics and soft sensors are often necessary to detect early signs of deviation not visible through single-point measurements.

Rapid Detection and Response to Deviations

In a conventional batch process, issues can often be identified and corrected between steps; for example, if the yield of a bioreactor increases from one batch to the next in fed-batch processes, there is time to adjust the clarification strategy before starting. In contrast, continuous and intensified processes—with less buffer time, a larger number of variables, and increased sensitivity—require immediate intervention to avoid extended downtime and significant material loss.

Only predictive analytics and data-driven decision-making tools can support the level of responsiveness required in these settings. These tools not only detect problems earlier but also recommend or automate corrective actions in real time.

Scaling From Development to Commercialization

Many development facilities do not have the same automation capabilities as commercial plants, and run non-intensified processes where units are typically not fluidically connected. Developing an intensified process requires similar levels of automation as the clinical or commercial plant. Without a consistent digital foundation, scaling up becomes slow, error-prone, and expensive.

Modular automation platforms and portable control strategies help ensure that digital control, monitoring, and orchestration logic can be reused and adapted across different scales and facilities.

Managing Integration Across Systems and Vendors

In many facilities, upstream and downstream equipment are sourced from multiple vendors, and each system may have its own control platform. As a result, integration becomes a project in itself, involving custom interfaces, bespoke scripting, and costly engineering time. The more complex the process, the more damaging this fragmentation becomes.

Sartorius addresses these challenges through native support for open communication standards (e.g., OPC UA, DCS | MES connectivity) and a digital platform designed for multi-vendor, multi-layer integration. Furthermore, pre-integrated solutions — such as Pionic® — reduce project risk by delivering proven, ready-to-deploy systems that integrate control, logic, process orchestration templates, recipes, and out-of-the-box analytics. This reduces project risk, accelerates deployment, and frees engineering teams from reinventing standard operations.

Maintaining Compliance and Data Integrity

As processes intensify and digital complexity grows, ensuring regulatory compliance becomes more challenging. Data integrity, electronic batch records, and real-time traceability are essential for day-to-day quality assurance and successful audits:

- A digitally integrated system enables automated data capture, electronic record generation, and full traceability, while reducing human error and paperwork.
- Compliance is simplified when the digital infrastructure is designed from the ground up to meet standards such as 21 CFR Part 11, GAMP5, and Annex 11.

Digital Platforms Enabling Process Intensification

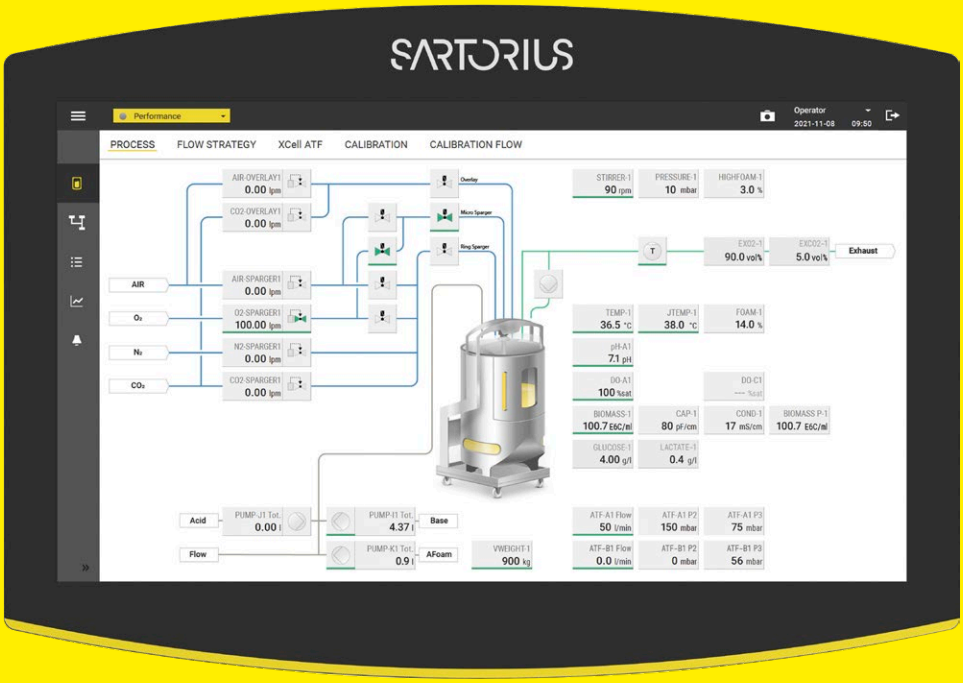
To address the digital challenges of PI, Sartorius has developed a modular, integration-ready digital ecosystem designed specifically for biopharmaceutical manufacturing. This platform combines equipment-level automation, centralized process orchestration, and advanced data analytics to deliver synchronized, high-performance operations from process development to commercial manufacturing.

At the heart of this ecosystem is the Biobrain® architecture, which provides a layered digital framework—Control, Supervise, and Operate—enabling stepwise digital transformation. This is enhanced by the Umetrics® Digital Twin AI Ecosystem, which delivers advanced analytics for building digital twins with experimental design, mechanistic models, and | or machine learning. The analytics suite can be deployed into execution engines, connects to Biobrain®, and can be used with third-party systems and enterprise environments.

Biobrain® Control, Supervise, and Operate Layers

Biobrain® Control Layer
The Biobrain® Control layer delivers real-time, local automation for individual unit operations in both upstream and downstream processing (Figure 2). It can function autonomously or integrate seamlessly with broader control environments (e.g., DCS). Designed for robust process control, it ensures precise regulation of critical parameters and supports both batch and continuous operations.

Figure 2: *Biobrain® Control Layer*

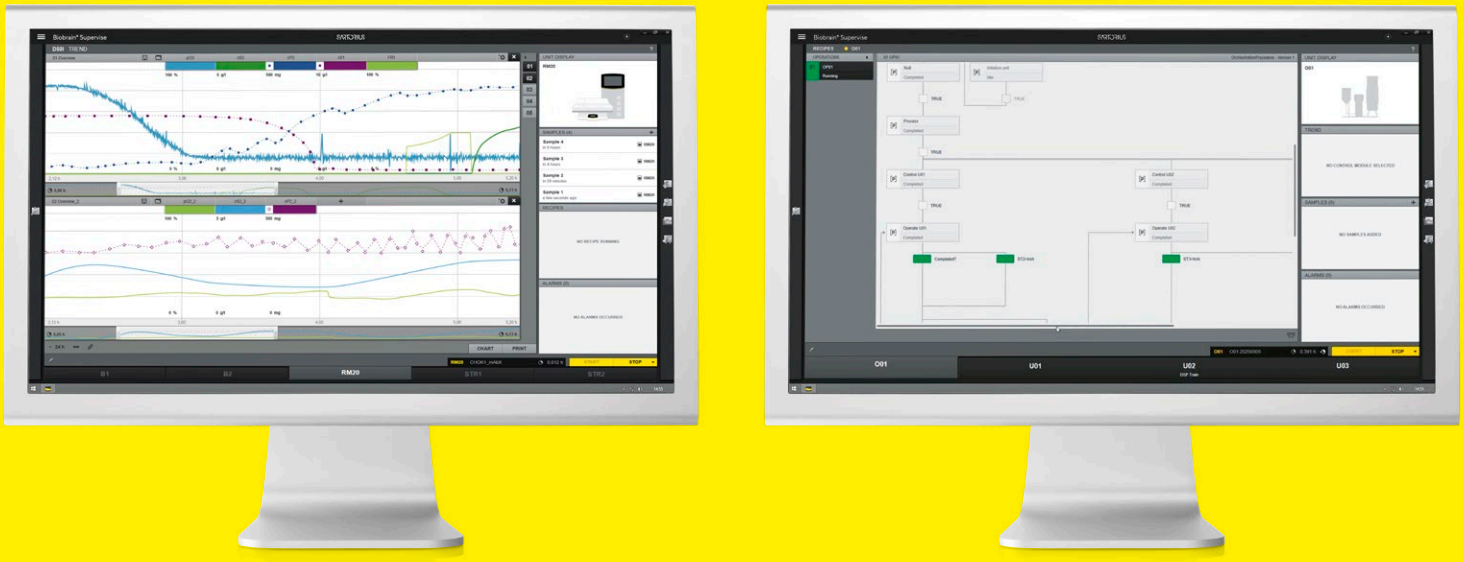


Biobrain® Supervise Layer
The Biobrain® Supervise layer aggregates data across equipment and systems, enabling centralized process monitoring, alarm management, and performance visualization (Figure 3). It serves as an information hub, ensuring traceability, historical data availability, and process transparency across units and runs.

Importantly, Biobrain® Supervise also includes complete process orchestration capabilities designed specifically for intensification processes, providing out-of-the-box rule sets required for the reliable execution of continuous operations. These include decision matrices that define equipment behavior in response to various scenarios, such as flow interruptions, step transitions, buffer delays, or upstream | downstream mismatches, ensuring all connected operations remain synchronized and resilient in dynamic environments. This orchestration logic eliminates the need for custom-coded scripting, reduces engineering effort, and reflects best practices validated across numerous intensified manufacturing setups.

The Biobrain® Supervise layer also enables cross-equipment integration, whether Sartorius or third-party, using standard protocols such as OPC UA, making it a powerful bridge across heterogeneous systems and vendors.

Figure 3: *Biobrain® Supervise Layer*



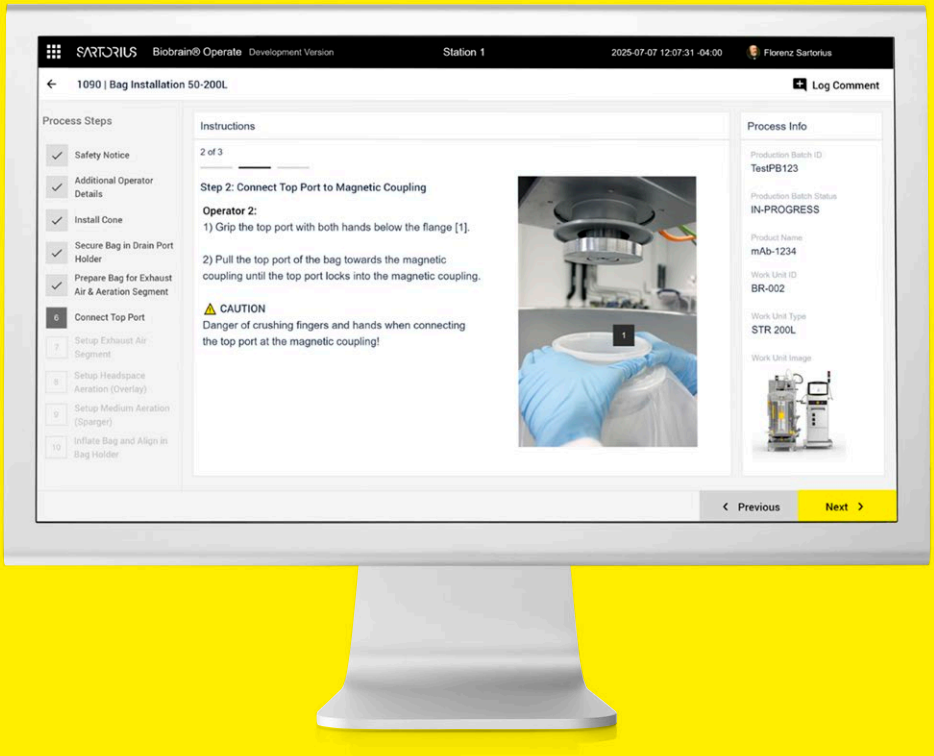
Biobrain® Operate Layer
While Biobrain® Supervise handles system-level orchestration, Biobrain® Operate complements it by orchestrating human activity across the process. The Biobrain® Operate layer manages the workflow across process areas, coordinating all activities involved in manufacturing execution, regardless of whether they are automated, manual, or hybrid in nature (Figure 4).

This layer includes:
- Electronic batch records (EBR) generation and review
- Operator task tracking and execution support
- Logbook and equipment management features
- Audit-ready compliance documentation

In intensified environments, even small manual errors, like a delayed buffer switch or incorrect tubing connection, can have major downstream impacts. Biobrain® Operate addresses this by providing dynamic, step-by-step operator guidance tailored to each role and process area. Out-of-the-box digital workflows for all Sartorius instruments (e.g., bioreactors, tangential flow filtration skids, and chromatography systems) simplify integration.

By orchestrating full production workflows, spanning human and system actions, Biobrain® Operate ensures that process execution remains accurate, traceable, and compliant, even as operational complexity increases.

Figure 4: *Biobrain® Operate Layer*



Umetrics® Digital Twin AI Ecosystem: Enabling Predictive Control

PI increases the throughput, flexibility, and efficiency of biomanufacturing, but these benefits also compress timelines, tighten process tolerances, and raise the stakes for deviations. More steps running in parallel and fewer buffers between them means that the margin for error is significantly smaller.

In this environment, reactive process control is no longer sufficient. Manufacturers must detect deviations before they occur, adapt in real time, and continuously optimize operations to maintain yield, quality, and compliance. As such, predictive control is a core enabler of intensified and continuous bioprocessing.

Umetrics® Digital Twin AI Ecosystem is Sartorius' advanced analytics suite developed specifically for the needs of the life science industry. It brings together advanced tools, providing the data intelligence required for predictive control, process optimization, and early deviation detection.

Through multivariate data analysis (MVDA), machine learning models, and soft sensors, Umetrics® Digital Twin AI Ecosystem allows users to:

- Build predictive digital twin models (of, for example, titer, pH, and viability) based on real-process dynamics
- Optimize the process in real-time, either with open- or closed-loop optimization
- Detect early deviations through pattern recognition, enabling corrective action even before thresholds are crossed
- Monitor product quality trends across batches or campaigns
- Execute real-time release strategies by increasing process understanding and control

With faster cycles, narrower limits, and higher variability risks, Umetrics® Digital Twin AI Ecosystem helps teams anticipate deviations and operate intensified processes with efficiency, building toward real-time release. These capabilities are essential for future-proofing intensified operations and meeting the expectations of global regulators who increasingly encourage data-driven process control.

In practice, process systems are subject to real-world disturbances: sensors may malfunction, drift, or require replacement; data networks may fail; and databases can experience errors or inconsistencies. These events must be managed effectively to maintain the digital twin reliability and accuracy — capabilities that the Umetrics® Digital Twin AI Ecosystem is specifically designed to provide.

When a deviation occurs, identifying the root cause is critical. Multivariate machine learning methods consistently outperform conventional machine learning approaches in diagnosing such issues, as they account for the complex, multivariable relationships inherent to bioprocesses. Importantly, this approach can be applied across the entire PI line, enabling a comprehensive view of system performance and revealing the full potential of the Umetrics® Digital Twin AI Ecosystem.

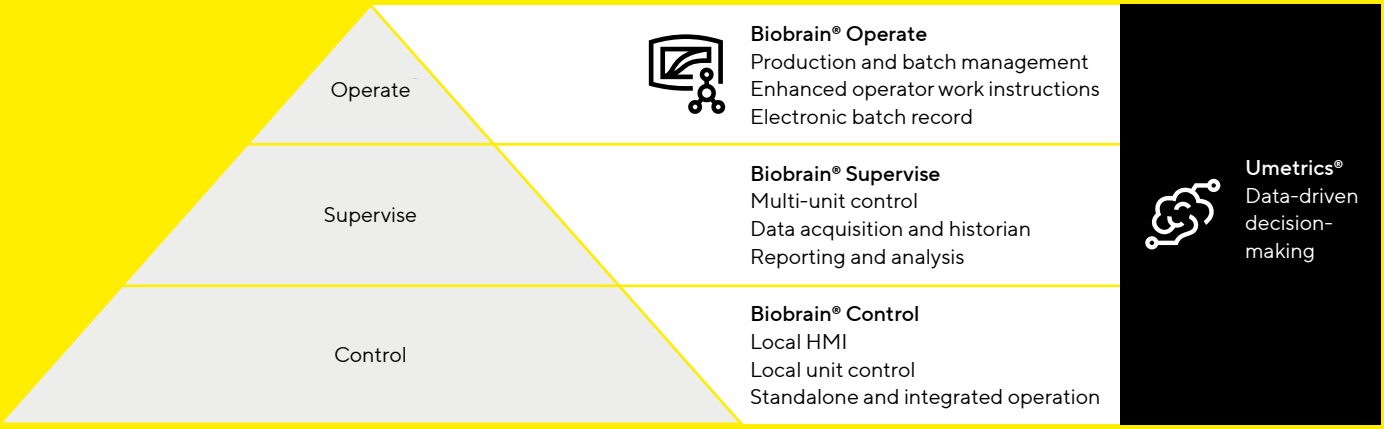
Table 1 outlines real-world examples where predictive analytics deliver concrete benefits.

Table 1: *Umetrics® Digital Twin AI Ecosystem Use Case Examples*

Use-Case	Value Delivered
Perfusion titer prediction	Helps operators adjust feed strategy before productivity drops
pH drift modeling	Identifies upcoming instability in cell culture, allowing preventive action
Cycle end prediction in chromatography	Enables precise control of elution to maximize yield and reduce impurities
Early fouling detection in filters	Reduces the risk of unexpected downtime and product loss
Real-time monitoring dashboards	Provide QA | QC with visibility into batch health as it runs, whether it is a steady state process, a batch process, or a combination of the two

Figure 5 summarizes the relationship between the Biobrain® Control, Supervision, and Operation layers, and how they connect with Umetrics® Digital Twin AI Ecosystem to enable data-driven decision-making.

Figure 5: *Automation and Analytics Platforms From Sartorius*



A Digital Infrastructure With Integration by Design

Integration is often the silent bottleneck in digital transformation, and PI makes this challenge impossible to ignore. As systems grow more interconnected and as logic spans multiple operations and vendors, the burden of integration can quickly escalate into one of the most expensive, risky, and time-consuming elements of implementing intensified processes.

Manufacturers that overlook integration in the early design phase often face extended timelines, inflated validation costs, and inflexible architectures that are difficult to scale or adapt. In contrast, those who adopt integration-ready digital infrastructure with standardized interfaces, modular logic, and native compatibility across systems can reduce time-to-value dramatically and future-proof their operations.

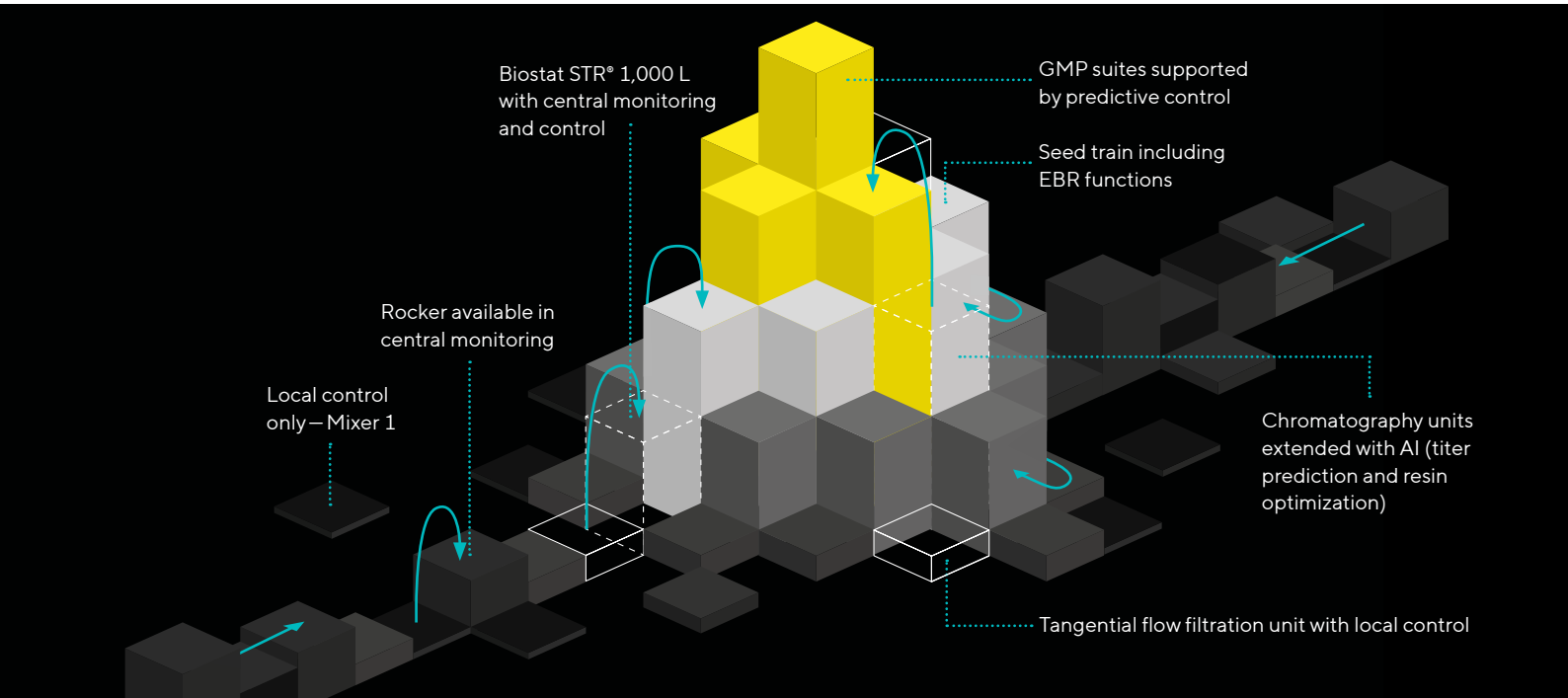
To leverage the full benefits of PI, advanced tools must be paired with robust, reliable integration. Sartorius' platform is designed from the ground up to integrate with:

- External DCS and MES
- Third-party equipment across unit operations
- Data historians, SCADA systems, and cloud infrastructure

This integration is enabled via standard protocols like OPC UA, without the need for complex custom development.

This architecture allows for stepwise deployment: manufacturers can begin by automating a single step, then add orchestration, analytics, or MES integration as needs evolve (Figure 6). Furthermore, Sartorius provides validated process templates and automation libraries, enabling customers to adopt pre-configured logic based on real-world best practices, dramatically reducing commissioning time, engineering effort, and project risk.

Figure 6: *Examples of Automation and Digitalization Use Cases Across a Facility*



The Role of Integration in Process Synchronization

In intensified manufacturing, the role of integration goes beyond communication between systems and becomes critical in synchronizing connected operations, which must be adjusted in real time based on the status of upstream and downstream processes. Key adjustments could include:

- Flow rates adapting to buffer tank levels
- Filtration steps pausing or resuming automatically based on upstream continuity
- Alarms and state changes cascading through the process chain with traceability

This level of synchronization is only achievable when systems are integrated digitally, logically, and operationally. It is also critical for manual activities, such as ensuring logbooks, audit trails, and deviation tracking are up-to-date and accurate for full GMP compliance, and that review and approval workflows are ready for QA sign-off.

In intensified operations, both automated systems and manual activities must be coordinated seamlessly. Sartorius' combined Biobrain® Supervise and Operate platform harmonizes these within a unified digital ecosystem

Scaling Logic and Workflow Across Facilities

One of the major advantages of digital orchestration is its scalability. With Sartorius' modular architecture, manufacturers can start by orchestrating a single step (e.g., chromatography and buffer prep), before gradually expanding orchestration of a full work center (e.g., downstream processing). They can then replicate validated logic and workflows across facilities, and standardize execution across Contract development and manufacturing organizations (CDMOs) and global sites, reducing tech transfer efforts.

In summary, orchestration bridges the gap between control and operations, enabling consistent, resilient, and compliant execution of intensified processes — without the complexity of disconnected systems and manual workarounds.

Built for Compliance and Future-Readiness

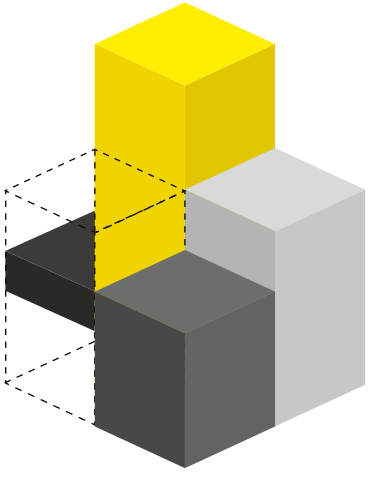
All layers of the Sartorius digital stack are built to meet the highest standards of compliance, including FR Part 11 (electronic records & signatures), EU Annex 11 (GMP-compliant computerized systems), and GAMP5 (risk-based validation methodology).

However, Sartorius goes beyond simply meeting these requirements. Our digital solutions to actively reduce the compliance burden for our customers by providing:

- GAMP5 Category 4 software, significantly decreasing the validation effort compared to fully customized or Category 5 systems.
- Comprehensive documentation packages to support customer qualification and validation activities, including user requirement specifications (URS), functional specifications, design specifications, and traceability matrices.
- Pre-developed and validated test scripts, along with clear test guidance for upgrades and feature updates, further reduce engineering and QA effort.
- Detailed compliance response documentation for 21 CFR Part 11, simplifying audit preparation and customer validation file building.

In practice, the qualification effort for Sartorius' Biobrain® standard instruments has been shown to be five times lower than for equivalent customized internal platforms, dramatically reducing project timelines and validation costs.

With this foundation, manufacturers can confidently deploy digital solutions that support regulatory audits, ensure data integrity, and reduce the burden of manual documentation while accelerating the path to compliant, intensified operations.



Outlook – From Digital Support to Autonomous Operations

Across multiple Sartorius collaborations, a consistent pattern has emerged. Digital infrastructure supports biopharma companies beyond PI: it also de-risks scaling, accelerates tech transfer, and enables cross-site standardization.

Customers implementing Sartorius' platform have reported:
- Up to 60% reduction in integration time
- Faster qualification and validation cycles due to pre-validated logic
- Easier cross-site deployment using consistent templates and libraries
- Stronger process robustness through real-time analytics and data transparency

As biomanufacturing continues to evolve, digital solutions will move from supporting PI to driving autonomous and self-optimizing operations. This transformation will drive biopharmaceutical manufacturers toward a connected, orchestrated, and predictive manufacturing environment, where processes adjust themselves in real time and compliance is built into execution.

Real-Time Release and Continuous Quality Assurance

One of the most transformative applications of advanced analytics and orchestration is real-time release testing. By enabling real-time monitoring of CQAs and the process parameters that impact them, Sartorius' digital platform lays the foundation for in-process control, shorter batch release timelines, and enhanced regulatory confidence. As regulators increasingly support data- and risk-based approaches to control strategy, platforms like Umetrics® Digital Twin AI Ecosystem will be key in implementing continuous quality assurance.

From Predictive to Prescriptive and Adaptive Operations

Beyond predictive control lies the next phase of digital maturity: prescriptive analytics. These emerging capabilities include digital twins to simulate multiple process scenarios before changes are implemented, adaptive setpoint control, and autonomous fault detection and mitigation, powered by historical and real-time learning.

Umetrics® Digital Twin AI Ecosystem already supports functionalities in this direction. It includes a Control Advisor module, advising the operator on setpoint changes and automatically applying them. In continuous and intensified processes, this evolution will be essential to managing complexity and ensuring consistent, high-quality outcomes.

Standardized, Modular Deployment Across Networks

As multi-site manufacturing becomes more common—across CDMOs, global networks, or decentralized production networks—a scalable digital infrastructure will become a strategic advantage. With Sartorius' modular architecture, manufacturers can standardize orchestration logic across sites, share analytics models, process templates, and best practices, ensure consistent execution and documentation, and accelerate tech transfer and drug lifecycle management.

A major enabler of this shift is the arrival of the module type package (MTP) standard, which aims to define a common interface for plug-and-play communication between process modules and higher-level systems. Expected to reach maturity in the near future, MTP will further simplify the integration of modular equipment into plant-wide orchestration platforms, reducing the need for custom engineering and enabling faster deployment. Sartorius has aligned its infrastructure with these principles, providing native support for open, standardized communication protocols and a modular digital stack.

Roadmap Toward Biomanufacturing 4.0

Looking ahead, Sartorius continues to invest in the next generation of digital capabilities under the banner of Biomanufacturing 4.0. Development efforts are focused on enabling:

- Integrated edge-cloud environments for hybrid control and analysis
- Expanded tools within Umetrics® Digital Twin AI Ecosystem for adaptive modeling
- Cross-system orchestration frameworks for entire production suites
- Interoperable automation platforms that connect upstream, downstream, and analytical technologies in real time

This roadmap reflects Sartorius' commitment to shaping the path toward intensified, autonomous biomanufacturing.

Expert Guidance and Digital Services

Successful implementation of PI and a supporting digital infrastructure requires expert guidance and practical support throughout the journey. Our comprehensive team of experts supports biomanufacturers with tailored consulting, services, and engineering capabilities to help them realize the full value of PI.

Digital Integration Services

Integrating equipment and software into a broader DCS or MES ecosystem can be complex and resource-intensive. Sartorius offers specialized integration support, helping customers reduce risk, accelerate implementation, and ensure long-term scalability. Our experts provide:

- Integration services for leading platforms including Emerson DeltaV and Siemens PCS 7
- Pre-configured automation libraries and control function blocks
- Support in designing orchestration logic across multiple units
- Field-tested implementation templates that reduce commissioning time and validation effort

Process Recipe Consulting

The transition to intensified or continuous processing often requires rethinking how processes are digitally modeled and executed. Our team offers:

- Expert process engineers to support the creation and optimization of digital recipes
- Consulting on logic flow and state transitions for continuous unit operations
- Guidance on MTP-based modular automation structures
- Process mapping aligned with GMP and data integrity principles

Data Science & Analytics Services

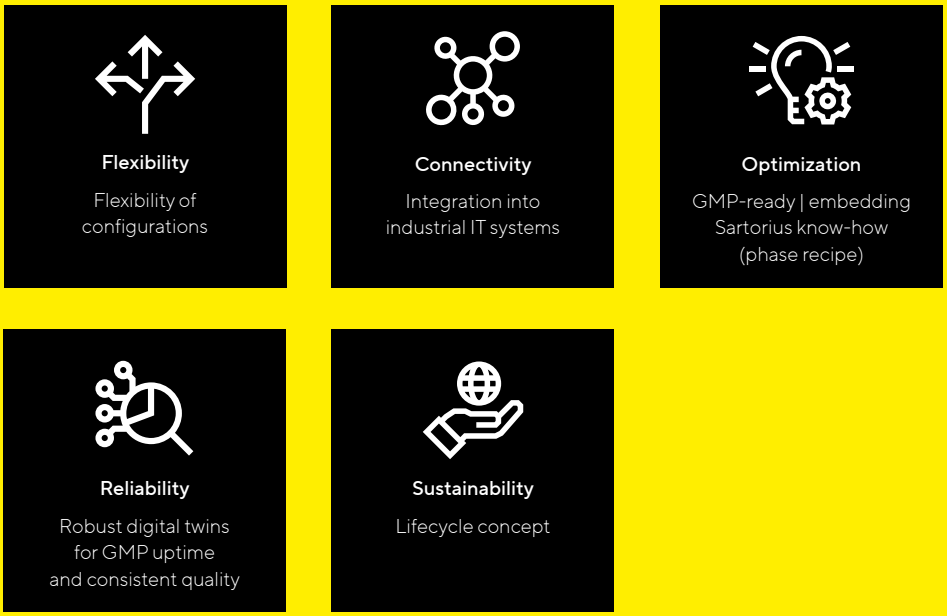
Predictive control and multivariate analytics require deep expertise in data modeling, statistical analysis, and regulatory-compliant deployment. Sartorius offers advanced analytics services through a team of dedicated data scientists and Umetrics® Digital Twin AI Ecosystem experts. We provide assistance by:

- Building and validating custom predictive models
- Supporting model transfer and lifecycle management across development and commercial sites
- Training internal teams on multivariate analysis, soft sensors, and real-time dashboards
- Advising on real-time release strategy and analytics-based control

Enabling the Digital Foundation for Process Intensification

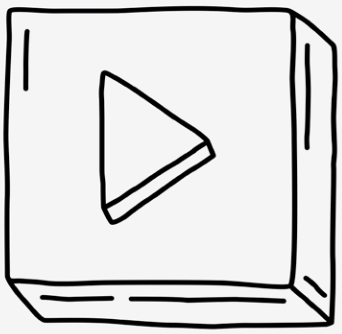
To meet the growing demands for speed, flexibility, sustainability, and quality in biomanufacturing, companies must fundamentally transform how they operate. This transformation relies on the digital infrastructure that connects, controls, and optimizes entire processes and facilities (Figure 7).

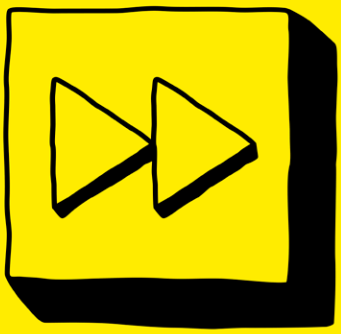
Figure 7: *The Role of a Robust Digital Foundation in Next-Generation Facilities*



At Sartorius, we believe that PI cannot succeed without a strong digital backbone. Our complete, modular, and interoperable platform—spanning real-time control, centralized orchestration, operator workflow guidance, predictive analytics, and system integration—was designed to empower empowers biomanufacturers to implement, scale, and sustain intensified and continuous processes—while shortening timelines and reducing risk.

From development labs to commercial suites, our technologies deliver the digital foundation for the next generation of biomanufacturing, making intensified production robust and accessible.





It’s time to intensify.

For more information, visit
sartorius.com/process-intensification

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Cyril Mak is the Solution Product Manager for Automation and Software at Sartorius. With a strong background in SCADA, DCS, and MES implementation within the life sciences industry, Cyril also brings extensive experience in Business Development for Automation.

Cyril holds a master's degree in bio-chemical engineering and an advanced master's degree in engineering and international affairs. Cyril began his career in MES and EBR implementation (ELAN Software) in the pharmaceutical industry. Subsequently, he served as a Life-Sciences Business Development Manager at Wonderware, focusing on MES, historian, and SCADA solutions.

In 2019, Cyril joined Sartorius as a Product Manager for Automation and Software. He later advanced to the role of Head of Product Management for Standalone Software and Embedded Solutions. Currently, Cyril is dedicated to enhancing Sartorius' automation solution portfolio, encompassing embedded automation, MES layers, and SCADA functionalities.

Acknowledgement
We thank Jonas Elfving, Product Manager Data Analytics at Sartorius, for contributing his expertise in analytics and digital transformation to the development of this whitepaper.

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Last modified: 10 | 2025