Maximize efficiency, minimize risks with integrated automation in biomanufacturing

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A highly integrated automation approach is a prerequisite for operational efficiency and comprehensive visibility across the biomanufacturing process. With centralized control and collection of information and data, process efficiency and product consistency can be maximized. When combined with other enabling technologies such as single-use processing equipment, centralized automation can facilitate flexible, efficient multi-product manufacturing.

The bioprocess industry is transitioning from the "islands of automation" paradigm, where individual operation units are automated, to centralized solutions that provide greater control, efficiency and repeatability. This transition to centralized automation on a single-use production line is transforming the bioprocessing industry.

- Process automation provides control and consistency critical in a heavily regulated manufacturing environment.
- Automated control, together with single-use systems, reduces the risks of operator error and bioburden entry.
- Single-use systems and recipe-based automated batch control reduce the time and effort required to implement a new process, enabling flexible capacity with high utilization.
- Data collection via a centralized historian simplifies data aggregation and batch record creation, providing auditable data to reduce compliance burdens.
- Monitoring and control with fail-safe redundant systems reduce the risk of batch failure or loss of data.

The road to centralized automation, and beyond

Centralized automation for biomanufacturing typically utilizes automation software that is widely used in manufacturing across multiple industries. This software will then need to be integrated with the process equipment, either directly with the local instrumentation, or with the proprietary software that runs each process equipment unit. Retrofitting or overlaying centralized automation onto an existing process manufacturing facility is complex and time-consuming, even more so in a strictly regulated environment. Not only would the implementation itself be extremely disruptive, but it would likely necessitate verifying and re-validating the entire process. This re-qualification effort may result in modifying or even re-licensing the process. Therefore, the best time to implement centralized automation in biomanufacturing is when planning for new capacity.

Once the decision is taken to implement centralized automation, this also creates opportunities for further integration into enterprise systems such as manufacturing execution systems (MES), laboratory management systems (LIMS, ELN) and enterprise resource planning systems (ERP) through data integration. Steps should be taken at the planning stage to allow for future enterprise integration activities to leverage the efficiencies that automation enables.

Elements of automation architecture for bioprocessing

All major upstream and downstream bioprocessing unit operations are automated, and each configured unit operation is managed by the centralized automation platform, which includes the following subsystem components

- **Centralized automation IT infrastructure** provides centralized automation platform software, integrated servers, network components, and central user management.
- **Equipment-specific software for unit operations**, e.g. UNICORN™ software is included with some GE Healthcare bioprocessing systems.
- **Programmable logic control (PLC) units** provide the physical interface between the controlling software and the unit operations equipment and perform the actual control logic.
- **Recipe creation, batch creation and scheduling** enable the execution of process batches and the subsequent creation of batch reports.
- **Centralized data acquisition** via an enterprise grade historian server, which provides data management and trending of all configured parameters. The historian server stores large volumes of data for process optimization, regulatory support and future reference.
- **Human-machine interface (HMI)** providing user interface to unit operations for the operator.
- **Reporting capability** to create reports to meet business needs and regulatory requirements.

An automation platform built on an industry open architecture can be designed to enable data integration with applications such as MES, LIMS and ERP systems.

Centralized automation in the GE Healthcare FlexFactory™

GE Healthcare's FlexFactory platform with integrated automation addresses the increasing demand for a connected and flexible manufacturing platform solution for bioproduction. The FlexFactory combines equipment, automation, connectivity solutions and supporting services in a turnkey solution, delivering centralized monitoring and control in a single-use processing environment. The extensive application of single-use automated technology provides the flexibility to modify and scale-out individual processes as production needs change, or to develop and rapidly deploy a completely new production line.

In the FlexFactory solution, all process equipment is run under the automation platform that includes central control, data acquisition, centralized user management and recipe control. The use of centralized automation helps reduce the risk of user error, process variation, and risks associated with manual processing.

> *Centralized automation is the core that enables optimization of the end-to-end process, as well as optimization of unit operations.*

FlexFactory can utilize Wonderware™ with Rockwell, DeltaV™, or other automation software as the central automation platform, to meet a range of customer requirements. This discussion will focus on the FlexFactory implementation with the Wonderware/Rockwell automation platform. The unit-level automation software is seamlessly integrated and controlled by the centralized automation platform.

The FlexFactory platform is pre-configured with standardized automation hardware and software system components, reducing the engineering design, integration and validation effort. Installation and initial verified configuration are provided with the FlexFactory automation package, along with supporting documentation meeting the GAMP5 (Good Automated Manufacturing Processes, version 5) guidelines. Pre-configuration of the automation system saves time and reduces costs when adding capacity. Verification and documentation of the automation platform reduce time and effort needed for regulatory compliance.

Server architecture

The FlexFactory automation solution provides the complete server infrastructure required to run the plant. It includes physical and/or virtual servers and controllers to assure the necessary level of redundancy to meet the high availability demands and data integrity requirements of biological manufacturing. Supplied equipment typically includes the domain controllers, application object servers, batch servers, a historian and information server(s). The redundant server architecture mitigates the risk of losing the process or batch data in case of a server failure. The servers are housed in a server rack which includes a built-in KVM (keyboard, video, mouse) that allows direct user communication to all the servers, as well as redundant network switches and power supplies.

Automation architecture in a single-use bioproduction line

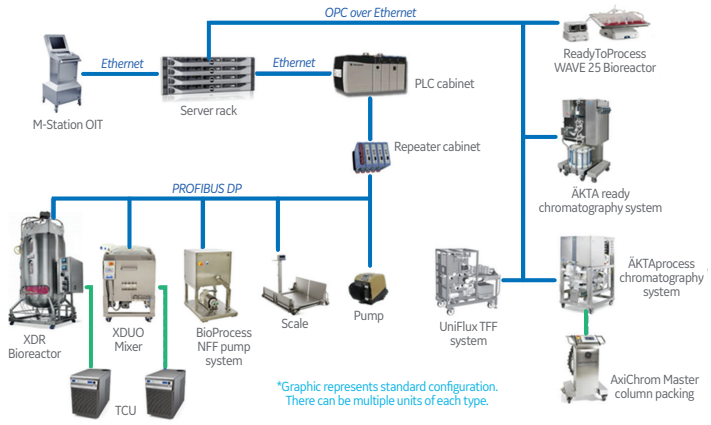

Fig 1. Typical automation architecture in a FlexFactory with a PLC solution.

Human-machine interface

The human-machine interface is the central point of control for the overall FlexFactory. Each HMI allows an operator to monitor and control all the individual unit operations by providing a window into the process through a common user interface. Operators can access all features of the FlexFactory automation, including unit operations systems and historical data in the form of trends and reports. The level and type of access for individual operators is secured through role-based user accounts.

Batch controls and recipes

The FlexFactory automation solution implements batch control based on control recipes for the key unit operations. A recipe, also referred to as a method, is a set of instructions, phases, parameters and transitions, that describe how a product is produced.

- Transitions are a set of conditions that must be true in order to progress to the next step within a sequence. Example transitions include conditions such as: Weight ≤ 50 kgs, Time > 30 seconds, etc.
- Phases are process- or equipment-specific sequences of control commands.
- Parameters are attributes of the process and process stream that are monitored or controlled by the automation system.

Batch control is critical to realizing the value of automation in bioprocessing. Through batch control, biomanufacturers can gain a greater level of consistency in process operation. Automated controls can run the same process consistently with close adherence to process parameters defined in the recipe, greatly reducing the risks of operator error.

With the Wonderware central automation platform, FlexFactory automation utilizes both Wonderware InBatch and UNICORN to create and manage recipes and batches, for the control of unit operations. Both InBatch and UNICORN functions are accessed seamlessly through the HMI. The features include:

- Create, edit, modify or delete a recipe or method
- Schedule, initialize and execute a batch, operation or methodHistorian server

FlexFactory automation utilizes the historian server software that is integral to the centralized automation platform. Data flows from all units and operations to the historian, where it is stored, providing an auditable record of all batches. The FlexFactory implementation provides the necessary data flows and integration, while implementing safeguards to ensure the security of the data. The data is accessed by the reporting software for the report generation.

Dream Report™ reporting software

The FlexFactory platform includes Dream Report, a powerful, flexible reporting package widely used in industrial automation. Dream Report connects directly to the historian server, which gathers and archives process data from all areas within the FlexFactory. Dream Report can be easily configured to create reports to meet specific requirements. Reports can be configured for different types of users, allowing operators, supervisors and managers to access the information that is relevant to their roles.

The reports generated by Dream Report (see Figure 2) support manufacturing in a regulated environment, providing a validated audit trail for each batch and process. Integration and verification of the reporting software with the automation platform reduces the opportunity for user errors in data handling.

Fig 2. Dream Report provides powerful, proven reporting technology with distribution options including print, email and web.

For users knowledgeable in batch reporting software, Dream Report can be utilized to create reports across other systems that the user may have access to, including but not limited to LIMS or MES systems.

Cybersecurity assessment

With the growth of connectivity in industrial settings, operations are increasingly vulnerable to cyber threats. GE Healthcare utilizes an industry standard assessment approach to answering the risks of cyberattacks within GE Healthcare products.

It is typically recommended that centralized automation for a biomanufacturing facility be a completely isolated system, thus avoiding cyber risk. However, external connections will often be used to meet practical operational needs:

- System alerts
- Remote management
- Integration or data export to enterprise systems
- Reporting within the organization
- Backup, archiving and data restoration

All these activities require connections to the corporate network, thus rendering the bioprocess automation platform only as secure–or insecure–as the corporate networks. Maintaining a robust cybersecurity posture at the corporate level is an essential practice.

GE Digital can perform or assist with customer infrastructure assessments. The maturity assessment audits the customer's security practices and technologies to uncover vulnerabilities across the system and provide actionable next steps for ways to strengthen the overall IT security posture.

GE cyber risk benchmark assessment includes:

- Cyber maturity baseline: A rapid, inexpensive survey and analysis of the customer's security strategy, providing benchmarking to industry expectations and sector peers.
- Cyber technology baseline: OpShield™ provides visibility into authorized and unauthorized traffic currently in the customer's systems.

Design for GMP, GAMP5 and regulatory compliance

Automation is at the core of the FlexFactory, and automation adheres to the principles and guidelines of GAMP5. Each version of the FlexFactory platform with Wonderware has been independently audited by recognized industry experts to ensure compliance and suitability for use in a good manufacturing practice (GMP) environment.

FlexFactory provides a verified, turnkey solution with integrated automation and documentation. Compliance support is designed-in at every stage of planning, integration and deployment. Each FlexFactory platform is configured for the customer's specific bioprocess. All systems, including the automation system, are verified, and documentation is provided to support regulatory requirements.

FlexFactory delivers a turnkey solution

The FlexFactory platform delivers an integrated and flexible manufacturing platform for bioprocessing and cellular production. Centralized automation of the FlexFactory provides both efficiency and consistency in biomanufacturing and enhances the flexibility inherent in the single-use model for bioprocessing. The automation software integration is pre-engineered and verified, reducing both the cost and time required to implement the FlexFactory, enabling biomanufacturers to reduce time-to-market when implementing new capacity.

GE Healthcare has implemented automation in biomanufacturing, from unit operations through centralized automation. GE automation project managers draw on deep experience in both automation and bioprocessing. The FlexFactory offers a turnkey solution, combining equipment, automation, connectivity solutions and supporting services. The delivered FlexFactory is production-ready, set up and qualified (installation qualification and operational qualification) on the customer's site.

The FlexFactory concept allows the rapid deployment of automated GMP manufacturing capacity with the flexibility needed to produce therapeutics in a standardized end-to-end single-use system, while meeting evolving production needs for high-quality biologics.

Learn more

For more information about GE Healthcare FlexFactory, contact your GE Healthcare sales representative, or visit gelifesciences.com/FlexFactory

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