# A Future-Proof Solution for Bioprocess Applications

The New Eppendorf Flexible Bioreactor Control System
Evolves with the Changing Needs of Modern Biotechnology



**BioProcess International**
SPECIAL REPORT

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# A Future-Proof Solution for Bioprocess Applications

## The New Eppendorf Flexible Bioreactor Control System Evolves with the Changing Needs of Modern Biotechnology

**Stephan Zelle and Berit Cleven**

I n the biopharmaceutical industry's quality-by-design (QbD) era, optimizing tools for process monitoring and control has become a major focus of development and manufacturing. This increased attention brings challenges into upstream and production processes, cell-line development, process optimization, and scale-up. Suppliers of equipment and technologies also focus on helping their customers improve development timelines. With that increased attention to speed, they are offering tools to streamline development and maximize flexibility.

BPI spoke with Dr. Stephan Zelle and Dr. Berit Cleven about Eppendorf's approaches to optimizing process development. Below are their combined comments in response to our questions.

**What was the motivation behind Eppendorf's decision to develop what would become the SciVario twin controller?** Stimulating Growth, Cultivating Solutions: This is the passion we live here at the Eppendorf Bioprocess Center. It is our ambition to support our customers in their daily work of growing cells. We want to work with them together from early discovery over process development until they move into pilot and production scale. With our solutions, we want to live up to Eppendorf's mission of improving human living conditions.

We aimed to develop a bioprocess controller that would enable us to work with our customers together now and in the future. Laboratory digitalization is becoming more and more important. Constant monitoring of a process and/or notifications about updates speed up laboratory processes and reduce the risk of lost experiments. We therefore wanted to develop a solution that evolves together with a laboratory and is flexible to adapt to fast changes.



Dr. Stephan Zelle



Dr. Berit Cleven

**Figure 1:** The SciVario twin controls cell culture as well as microbial fermentation processes in both BioBLU single-use vessels and glass vessels without the need of hardware changes.

Ready for the digital age, we now offer the first bioprocess twin controller, a modular bioprocess controller that can be flexibly adapted to the changing needs of our customers by support of our service technician.

### AGILE DEVELOPMENT

**Can you describe Eppendorf's "agile development" approach and how it helped in realizing the SciVario concept?** Developing a product by following the agile development approach is possible only if an entire company restructures the ways in which every person and each group is working. For agile development, we enforced our crossfunctional collaboration and established a constant working rhythm in which the team works and communicates. *Agile development* means that we gather all the information, feedback, and requirements and collect them in a so-called backlog, which is a kind of a big Christmas wish

> Our customers have a big need for **INTERCONNECTIONS** between analytical devices and the bioreactors themselves, and that became a core function for the SciVario twin.

list. We prioritize the wish list and collect all features and issues with the highest value for a customer. With this selection, we start our working rhythm. The great advantage here is that we don't need to know exactly what will happen in three or five years. We will deliver the features with the highest value first. If something comes up next year, then we can restructure easily and quickly. Especially for development of such a complex

**Figure 2:** Up to ±0.1 K set point accuracy and with nearly no overshot (<0.3); SP = set point, PV = process variable



DR04F (2.5 L, with agitation)
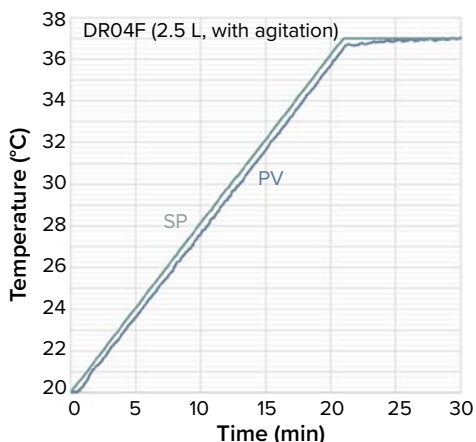
product as the SciVario twin controller, that agile approach is especially helpful. A broad number of prototypes in many iterations have been developed and can be accessed by team members, experts, and stakeholders. This provides constant feedback to allow our product to grow and become more complete and beautiful.

**Were any users involved in early development of the SciVario twin controller?** Of course — agility places our customers and all their needs into the center of all our developmental steps. For example, we listened to our customers' increasing needs for new, innovative technologies such as those related to the Internet of Things (IoT) or a digital laboratory. Our customers have an increasing need for interconnections between analytical devices and the bioreactors themselves, and that became a core function for the SciVario twin. Using cloud services such as the VisioNize Cloud platform offers additional values and features.

## TECHNICAL DETAILS

**Does the SciVario twin system work with both single-use and multiuse bioreactors? And what is the size range?** The SciVario twin is one of the most flexible systems we have ever developed. It can control a broad number of vessel types and sizes in any combination at the same time individually or in parallel. As launched, the SciVario twin is compatible with our BioBLU single-use vessels and glass bioreactors and fermentors ranging from 0.7 L to 3.8 L working volumes. With future planned updates, the compatible portfolio will be enlarged to working volumes up to 50 L.

**Will it meet the different needs of bacterial, fungal, plant/algae, and animal cell cultures?** Application flexibility was one vision when we started developing the SciVario twin controller. The new system can cultivate bacteria, yeast, fungi, algae, and plant cells as well as insect, mammalian, animal, and stem cells.
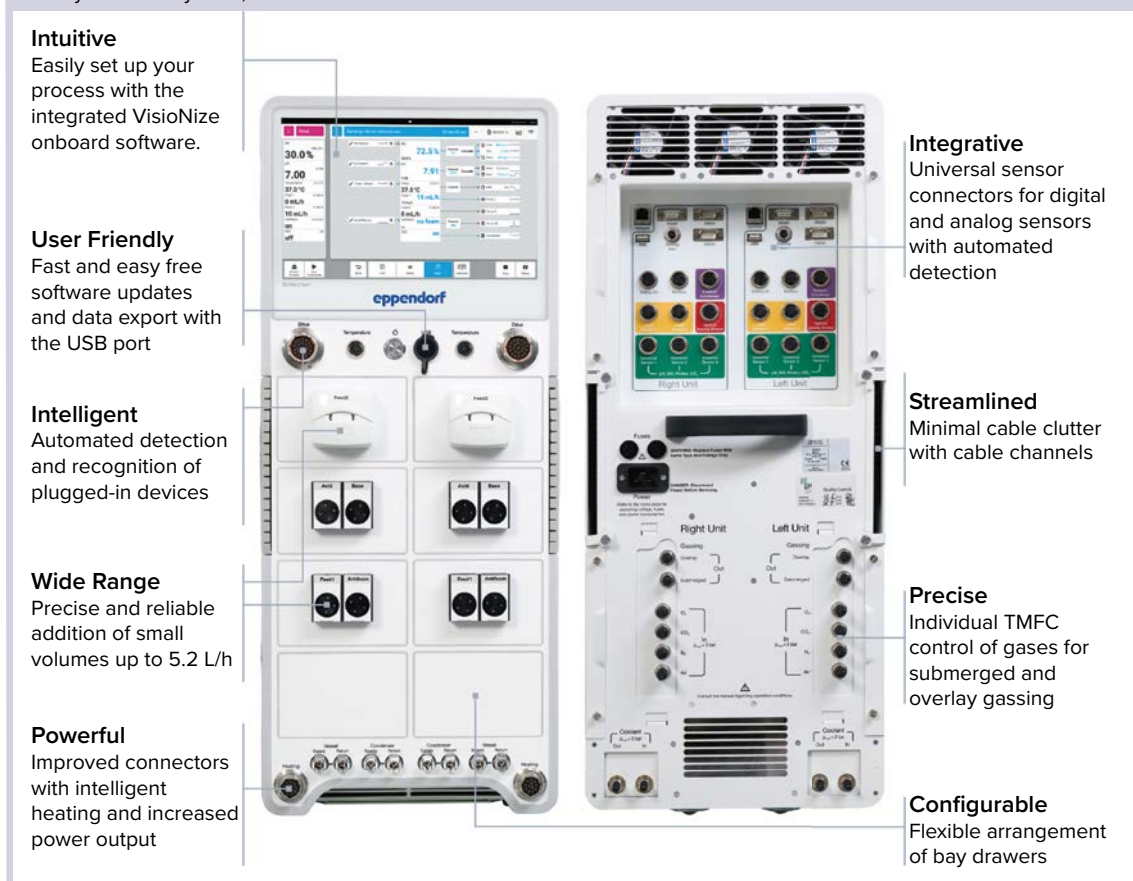
**Can you describe the bay-drawer configuration and what kind of advancement it represents?** A key feature of the controller's flexibility is our new, innovative bay-drawer system that allows for flexible adaptation of configurations controlled by the base unit. The controller can be equipped with eight drawers that allow for the flexible configuration of accessories suited to current requirements. The software update needed for new functional modules will be provided for free and can be installed using the USB port at the front of the controller. The intelligent software automatically recognizes the software update and guides a user step-by-step through the installation process.

The standardized bays allow for the future exchange with upcoming new drawers to support different needs. The controller itself already controls all important process parameters for cell culture and fermentation applications. The drawers enable the
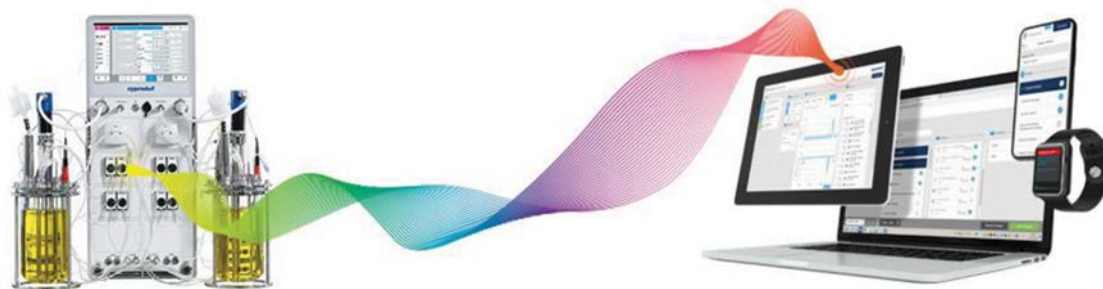


**VisioNize Cloud services enable users to manage their laboratories from any location and have more time for their research.**

**Figure 3:** The intuitive VisioNize-onboard software enables all process parameters to be adapted and monitored directly with the system; TMFC = thermal-mass flow control.

**Intuitive**
Easily set up your process with the integrated VisioNize onboard software.

**User Friendly**
Fast and easy free software updates and data export with the USB port

**Intelligent**
Automated detection and recognition of plugged-in devices

**Wide Range**
Precise and reliable addition of small volumes up to 5.2 L/h

**Powerful**
Improved connectors with intelligent heating and increased power output

**Integrative**
Universal sensor connectors for digital and analog sensors with automated detection

**Streamlined**
Minimal cable clutter with cable channels

**Precise**
Individual TMFC control of gases for submerged and overlay gassing

**Configurable**
Flexible arrangement of bay drawers

flexible customization of the controller according to the current, and also future needs of the experiments.

**What types of sensors, pumps, cabling, and tubing are compatible with this system? Does it have integrated digital/analog sensors and pumps?** The system is initially delivered with six drawers containing two big pumps and eight small pumps that cover a liquid/media addition range from 0.005 mL/h to 5.2 L/h. Several RS232, RS485, ethernet, and universal connectors allow for connection of a number of digital and analog sensors. Users can choose from different manufacturers for, e.g., monitoring pH and DO in digital and analog configurations.

**Can you describe the supported methods of temperature control, gas/sparging, and mixing?** With 14 integrated thermal-mass flow control (TMFC) modules (seven per unit), the system is equipped for submerged and overlay gassing of $CO_2$, $O_2$, $N_2$, and air. For submerged gassing, all gasses are mixed in parallel by six MFCs, whereas for overlay gassing, the gasses are mixed sequentially by one TMFC

All process parameters can be adapted and monitored directly with the system. The 12.1-inch touchscreen shows all **IMPORTANT** parameters of a run, including agitation, DO concentration, temperature, and pH.

subunit. The temperature is controlled either by our advanced temperature control blocks or with heat blankets and cooling fingers, depending on the bioreactor size, with a ±0.1 K accuracy. The intelligent temperature control loop chooses the optimal parameter automatically for all different vessel sizes and vessel materials.

**What process control software does the system use? What process parameters can be measured and controlled?** The system comes with the new, intuitive VisioNize-onboard software that enables the system to

**Figure 4:** VisioNize-onboard comes with a structured user interface that shows all important process parameters at a glance. Small sparkline and event logs help to keep track of process performance.
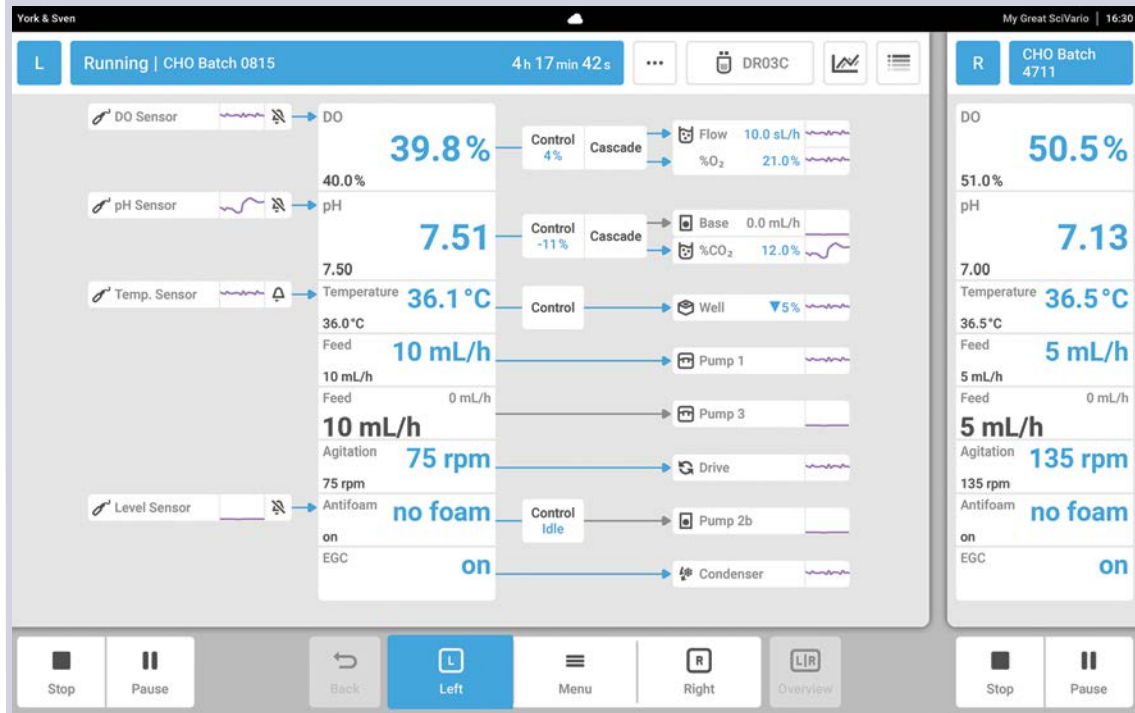
The software recognizes the intelligent accessories and **WARNS A USER** when, for example, a vessel is selected that cannot be used with the connected drive.

be ready for the digital age and the digital laboratory of tomorrow (Figure 3). All process parameters can be adapted and monitored directly. The 12.1-inch touchscreen shows all important parameters of a run, including agitation, DO concentration, and pH. Comprehensive information is displayed in small sparkline diagrams that enable an operator to keep track of process performance and display the current process parameter(s) (Figure 4). The software keeps track of all events, data, and metadata produced during a run. With VisioNize, Eppendorf's digital platform, the SciVario twin is transformed into a smart bioprocessing control system, able to connect to the digital laboratory VisioNize Cloud. This new service enables remote monitoring of your processes and the receipt of personalized notifications — for example, of current process status.

## USER EXPERIENCE

**What are some key characteristics of the SciVario design and the VisioNize user interface?** We aimed to offer an ease-of-use control station that saves time and reduces the risk for any standard operation. Setting up a process, calibrating a sensor, or switching a vessel has never before been so fast and easy.

From the beginning of development, we closely worked together with our design and user-experience experts. Each design concept did start with an in-depth understanding of user needs in the context of their work and what they want to achieve. We put our users in the center of our development, not only when it comes to the functions of the SciVario, but also in terms of design. With the support of our designers, we wanted to translate the language of technology into the language of our users. Knowing that our customers are experts and conduct difficult and complex bioprocesses, this does not necessarily mean that working with it needs to be complicated.

A key feature of VisioNize-onboard devices is the intuitive, structured, and consistent user interface among all VisioNize-onboard-enabled devices. It doesn't matter whether you are using a freezer, shaker, or centrifuge. The user experience among other Eppendorf products with VisioNize-onboard is

**Figure 5:** Select a vessel while keeping track of the currently running process. Grayed-out vessels will be supported after future updates.
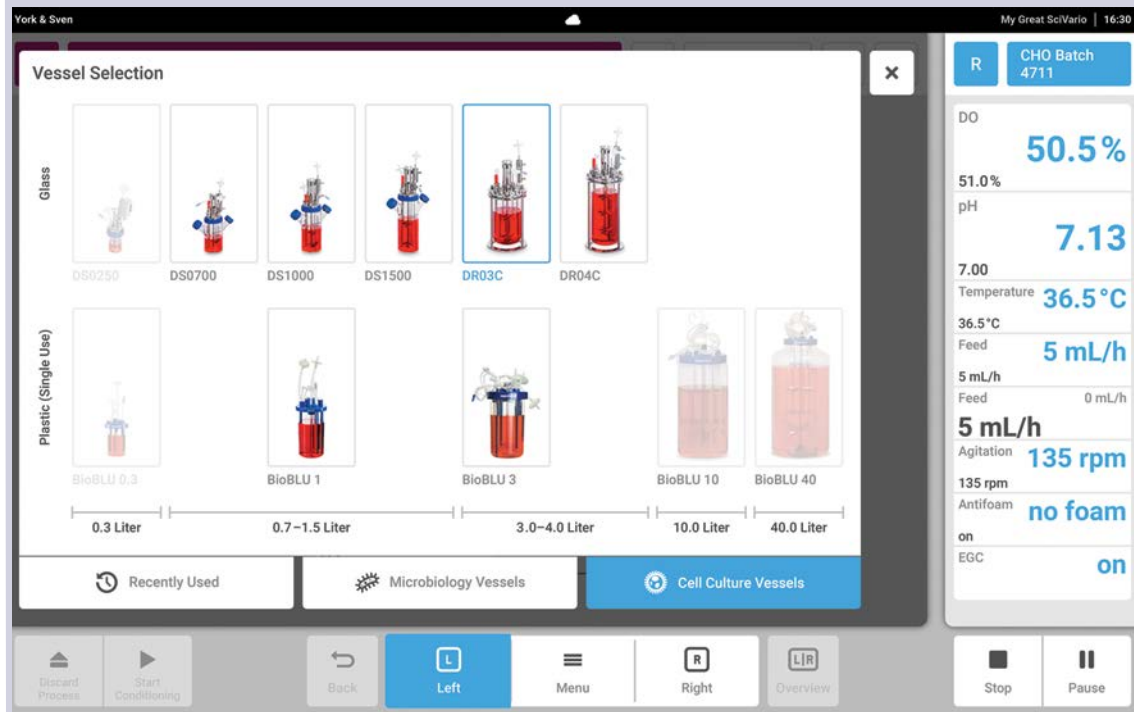
always similar, thus making it easy to learn and to train new users.

The SciVario twin is the first bioprocess controller working with VisioNize-onboard, and that aspect of its development was quite challenging in many ways. The user interface delivers features that previously were delivered only at a desktop workstation. Additionally, it controls two processes at the same time, and both processes can look completely different (Figure 4). The controller supports a wide range of vessel variants already at this stage of its launch, with more vessels to come with future updates. The smart software automatically identifies the intelligent accessories and warns a user when, for example, a vessel is selected that cannot be used with the connected drive. We ensured that each individual step and each feature is easy and intuitive. The software guides a user step-by-step through the workflow and reminds of important steps like calibrations. By this, we aimed to mitigate the risk of failures.

We also put great effort into the physical layout of the connections. The position of all plugs and ports were carefully evaluated to be placed where users need them to be. Frequently used elements are located at the front of the controller, whereas elements used less often are located at the back. Cables and tubes can be tucked into the canal at both

> Our goal is **CONTINUOUS IMPROVEMENT** of the laboratory experience through increasing efficiency, convenience, and peace of mind.

sides of the unit, which keeps the laboratory space clean and organized.

**The control software includes preset "wizards." Does it also offer users the ability to customize?** The whole system was designed to be fully flexible and adaptable for user customization. Not only is the hardware flexible, but users also can set up and tune their control parameters to optimize their processes.

**Can you describe the VisioNize Cloud — and how that works for laboratories in regulated industry?** VisioNize is Eppendorf's digital platform that delivers valuable services in and around our Eppendorf devices. Our goal is continuous improvement of the laboratory experience through increasing efficiency, convenience, and peace of mind. With the VisioNize Cloud services, users can manage a laboratory from any location and have more time for research. Customizable alarm and

> With the system's flexibility to support a process just by changing a drawer, the SciVario twin will be a **ONE-TIME INVESTMENT** for long-term use in a laboratory, even if completely new sensors will be developed.

event notifications can help prevent downtime of laboratory equipment and enable quick responses, thus increasing productivity.

### FUTURE PLANS

**Do you have plans for perfusion operation capability in the future?** Especially thanks to our experienced service and product support team, we are strong in the integration of third-party equipment. The possibility to operate the SciVario twin in perfusion mode will be available after future updates.

**What about software updates and long-term use in R&D laboratories (e.g., compatibility with sensors that have yet to be developed)?** The system was designed to be a future-proof bioprocess control station. The software updates for the controller and new functional modules will be available for free and can

be installed without a service technician. With the system's flexibility to support a process just by changing a drawer, the SciVario twin will be a one-time investment for long-term use in a laboratory, even if completely new sensors will be developed. With future updates, the SciVario twin will be able to support even more vessel types and sizes. New drawer options will be available, and the software is continuously developing and will have more functionalities.

**The SciVario Platform:** The SciVario twin is the first implementation of our new bioprocess controller platform SciVario for small- and bench- scale instruments. The SciVario platform was especially designed for our VisioNize ecosystem and combines the best elements from our long years of expertise and experience in bioprocess controller design and biotech applications. All devices within the platform will provide a consistent user experience and be equipped with highly innovative hardware and software. The platform will enable future-proof functionality extensions and is ready for the digital age. For more information visit us at www.eppendorf.com/scivario.

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