

MAST Sample Pilot™ Modules

In Beta Testing

Introduction

Compelling demand exists in the bioprocessing industry for a reliable system that transfers bioprocess samples directly from bioreactors to analytical devices while maintaining process sterility.

Bend Research is developing the Modular Automated Sampling Technology™ (MAST) platform to meet this need and to help scientists sample the right data at the right time. This new technology allows for advances in achieving the bioprocessing industry's goals of advanced real time testing, predictive control, and overall bioprocess guidance.

A critical module within the MAST platform is the Sample Pilot™. As shown in Figure 1, the MAST Platform consists of one or more Sample Pilot™ modules integrated with multiple analytic devices through the MAST Sample

Navigators and Scheduler, which coordinate and control the sampling process.

Benefits include the following.

- More frequent, reproducible sampling from bioreactors
- Hands off, contamination free sampling
- Automated process scheduling
- Minimal operator involvement
- Minimal operator exposure to biohazards
- Customized sample volume for different bioreactor types/sizes
- Enables more sophisticated process control strategies
- Custom engineering, installation, and consulting

As the MAST platform advances toward commercialization, system components are undergoing extensive beta testing by numerous pharmaceutical and biotechnology companies. Test sites include Pfizer and Eli Lilly, which are funding development of the MAST platform.

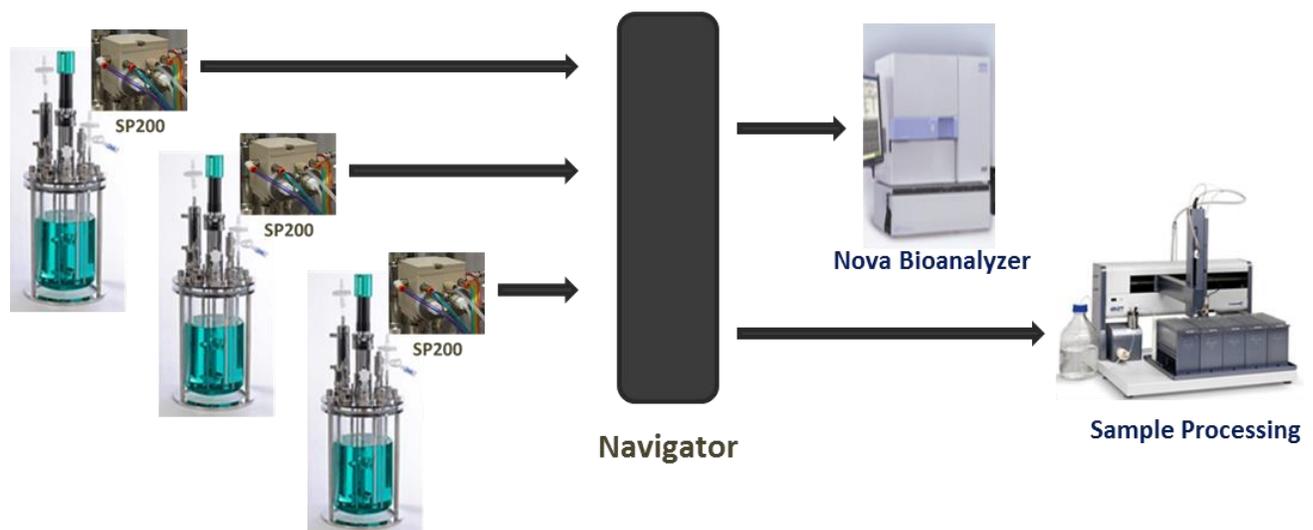


Figure 1. Automated Sample Pilot™ – Modular Automated Sampling Technology™ Platform

MAST Platform Overview

The MAST platform is a collection of unique modules that together facilitate the automatic collection and analysis of samples from bioreactors or other sterile sources.

The modular nature of the platform allows great flexibility. A simple setup can collect samples from a single bioreactor and deliver them to a generic sample collection system. More complex systems can take samples from up to eight bioreactors and direct them to four different analytical instruments.

For more information, please see the MAST Platform Technical Brief.

Click here to view a short video of the MAST Platform <http://youtu.be/Fy93XuOKEyA>

Sample Pilot™ Modules

Sample Pilot™ SP100 Overview

The Sample Pilot SP100 module is designed for fixed bioreactor applications. It can be used at



the development to manufacturing scale, and takes a fixed volume 50 mL sample.

The SP100 is constructed of PEEK (polyether ether ketone), a robust organic polymer thermoplastic known for its thermal stability. It is sterilized by Steam In Place (SIP) in an automated process. (i.e., after each sample is taken, the sample lines are flushed with sterile steam condensate and then an SIP cycle is performed automatically).

There are no disposable components or ancillary supplies required for standard operation. The module is mounted to the bioreactor using an industry standard 25 mm Ingold port and requires an approximate 3 inch radius of space.

Sample Pilot™ SP200 Overview

The Sample Pilot™ SP200 is designed for bench scale or disposable applications and allows custom sample sizes in 5 mL increments.

The module is compact, requiring little space on a bioreactor (~2 inch radius). Installation is straightforward, with multiple port connection options that allow integration directly into a bag, insertion through a Pall Kleenpak connector, or insertion through a dip tube into a bench top development bioreactor. The SP200 can be used on bioreactors of all scales and can be adapted to all ports and fitting types.



The modules are constructed of materials suitable for autoclave sterilization and, after taking a sample, the module is sanitized using a liquid sanitant.

Results

In recent tests, use of the SP100 module has been successfully demonstrated on 130 L and 500 L (pilot scale) bioreactors that were being used to produce regulatory toxicology supplies. The SP100 module has also successfully completed initial sterility challenges, taking more than 200 samples with no bioreactor contamination. As shown in Figure 2, during recent development runs on Pfizer's pilot scale bioreactors, the MAST platform and SP100 successfully delivered more than 300 samples without contamination. This includes more than 152 days of successful operation at the 30L, 130 L, and 500 L scales. The SP100 module has also demonstrated effectiveness when used in microbial cultures.

The SP200 module has been tested in a broad range of applications. Multiple tests at the

Development scale and pilot scale (using single use bioreactors) have been completed. To date, more than 19 cell culture or media challenge runs have been performed with an accumulated duration of more than 240 days and 1,900 samples without contamination. The SP200 has also been deployed in a downstream application.

In a development scale run, manual and MAST samples were compared head-to-head. Using the Nova BioProfile Flex, samples manually collected and introduced to the Nova manually were indistinguishable from automated SP200 samples that were automatically analyzed by the Nova system using the Direct Delivery system developed at Bend Research (Figure 3).

The Future of Innovation

At Bend Research, we constantly strive to remove the “black box” around the cell providing the ultimate guidance to understand how bioprocess variables affect overall product quality. Bend Research believes that its clients deserve better technologies to meet their product quality goals. The MAST platform opens the door to improved fundamental understanding of the true cell environment. Coupling the right tools, the MAST platform provides in-depth guidance to optimize the environment to meet cell needs.

With meaningful real time analytics, process measurements, and novel data management techniques, we can use existing technology to provide state based predictive control models driving increased product consistency and batch-to-batch reproducibility.

Ultimately, we seek to use these tools and advanced control methods to provide guidance on the state of the manufacturing process and fundamental knowledge of the cell state.

About Bend Research

For more than 35 years, Bend Research has worked with clients to solve their most difficult scientific and technical problems, advancing new medicines that improve human health. This success is based on a solid understanding of scientific and engineering fundamentals, enabling Bend Research to develop, progress, and commercialize pharmaceutical technologies. The firm’s innovative drug delivery solutions grow from a solid base of scientific and engineering fundamental understanding.

Bend Research provides formulation and dosage form support, assists in process development and optimization, manufactures clinical trial quantities of drug candidates in its cGMP facilities, advancing promising drug candidates from conception through commercialization. It is a leader in novel formulations, including solubilization technologies such as spray dried dispersions and hot melt extrusion formulations, as well as controlled release, inhalation, and biotherapeutics.

Contact

Bend Research is looking for partners to collaborate in the development of the Sample Pilot modules toward commercialization. Units are available for beta testing. Engineering support is available for assessment, implementation, and exploitation of the data management system. To discuss potential application of the MAST platform to your bioreactor or other unit operation, please contact:

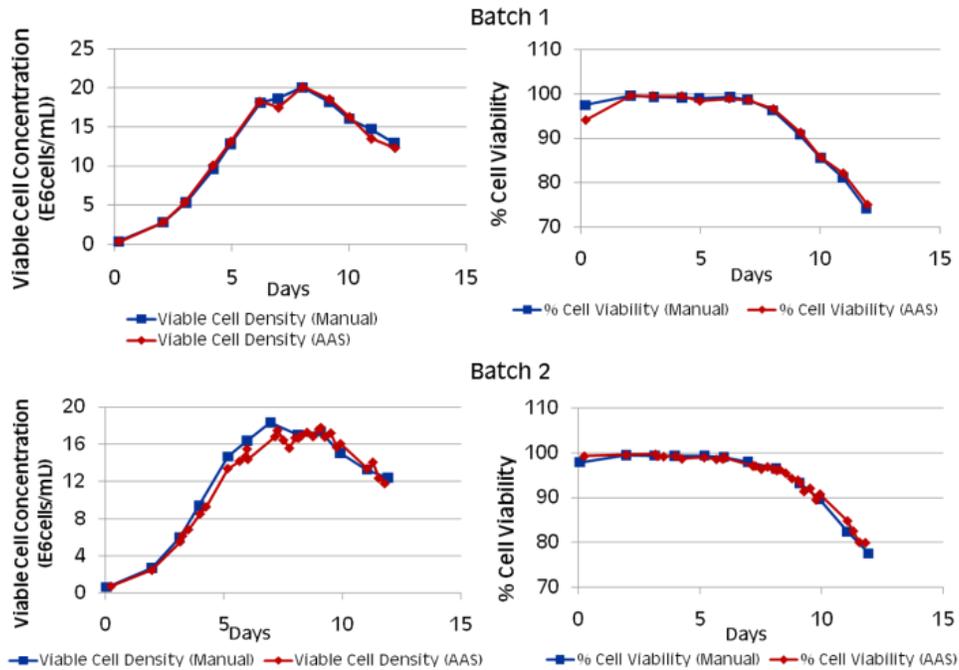
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Viable Cell Density and Cell Viability (%)



Other Variables of Interest

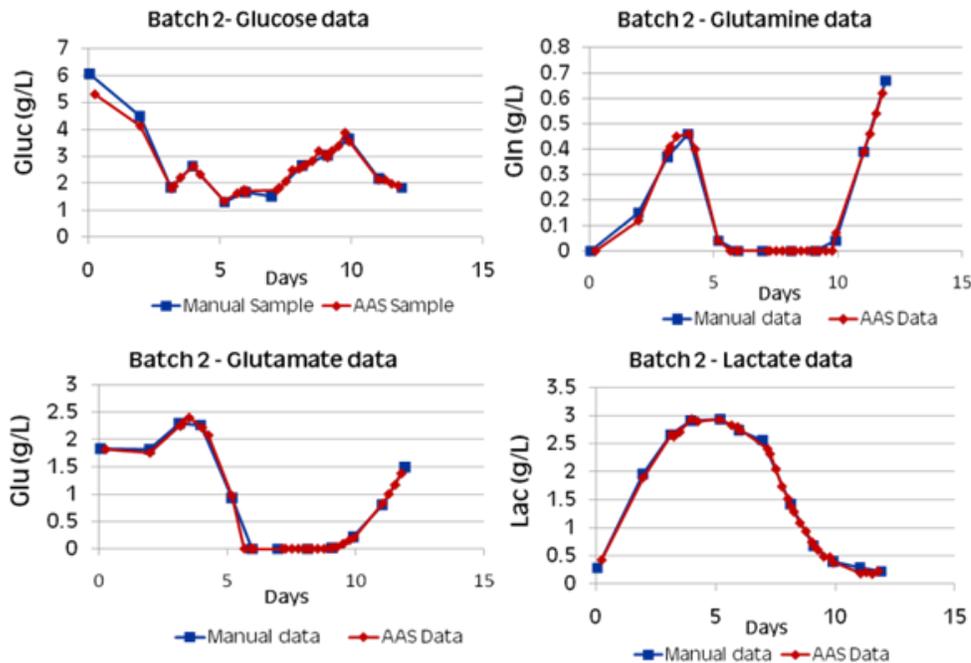


Figure 2. Comparison Of Manual And Automated SP100 Samples On A 500 L Bioreactor Producing Regulatory Toxicology Supplies, Showing Viable Cell Density, Cell Viability, and Other Process Variables.

Blue = Manual Samples; Red = Sample Pilot™ SP100 Module Samples

Nova BioProfile FLEX Results from Samples Collected and Analyzed Manually versus Results from Samples Collected and Analyzed Automatically

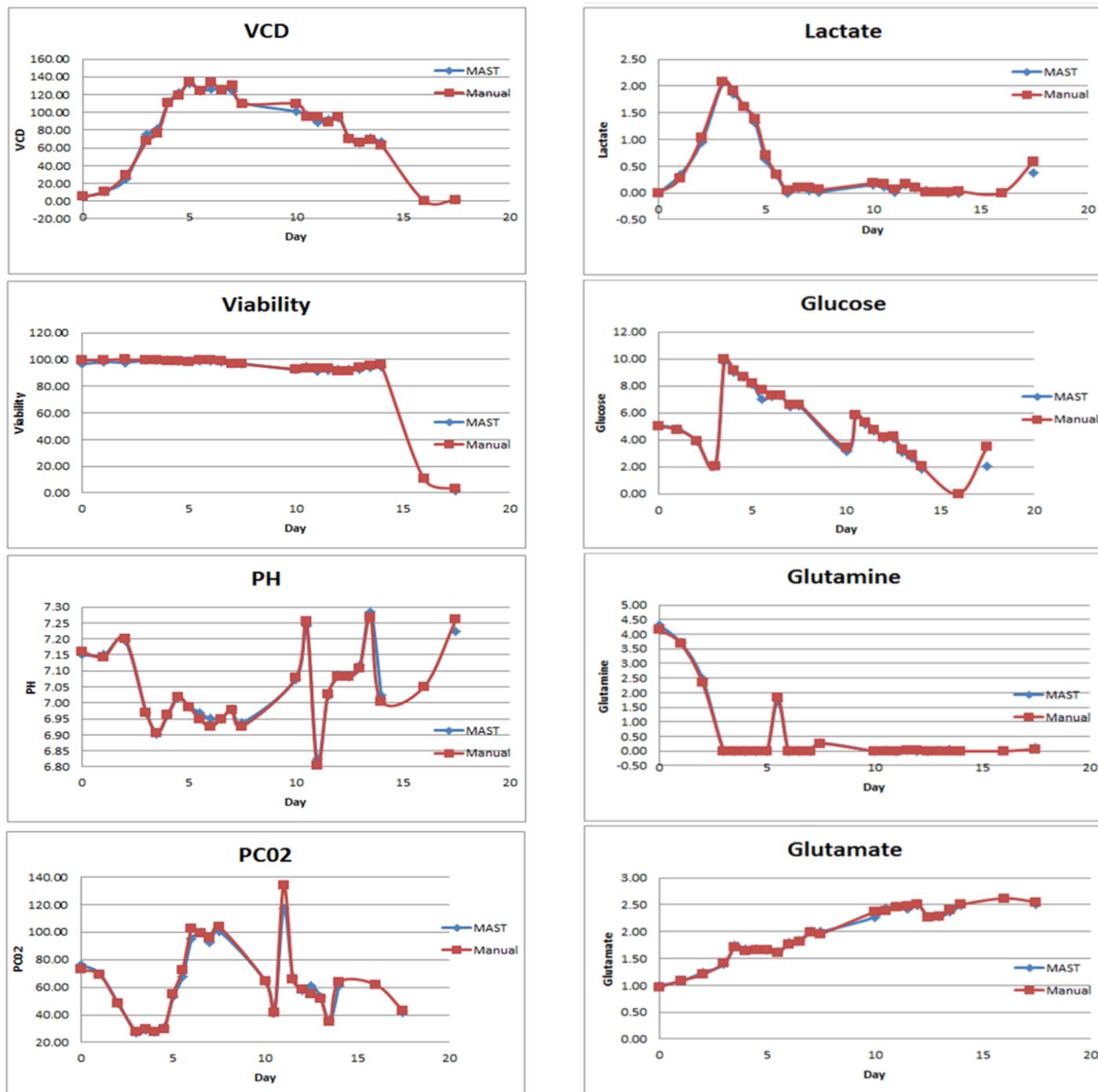


Figure 3. Comparison Of Manual And Automated SP200 Samples From A 2 L Bioreactor With The MAST Samples Automatically Collected And Analyzed By Nova BioProfile FLEX. Blue = Manual Samples; Red = Sample Pilot™ SP200 Module Samples