Application Note

October 23, 2024

Keywords or phrases: Single-use fermenter, single-use foam control, capacitance-based foam control, non-invasive foam detection, Biostat STR® Microbial, Flexsafe STR® Microbial bag

Foam Sensor Performance and Controller Capabilities of the Biostat STR® Microbial Single-Use Fermenter

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Abstract

Microorganisms are frequently used in the production of mature and emerging biotherapeutics. In line with trends across mammalian processes, single-use (SU) technologies are increasingly employed in microbial cultures as a more flexible, robust, and sustainable choice. However, SU solutions must be able to handle high-density and demanding microbial cultures. A critical feature for maintaining process robustness is the supervision and control of foaming through a reliable sensor.

The Biostat STR® Microbial is a high-performing SU solution that can support high-density microbial cultures. This application note shares its foam sensing capabilities, including high foam alarming and interlocking (High Foam function), as well as automated sensor-based foam control (Foam Control function).

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Introduction

Microbial fermentation has broad applications within the biopharmaceutical industry, including plasmid DNA production, vaccine development, and recombinant protein manufacturing. Therefore, ensuring fermentation processes are robust and efficient is important for the successful production of a variety of clinical applications.

Single-use (SU) solutions are commonly employed in mammalian processes owing to their ease of use, flexibility, and consistency, among other benefits. However, microbial processes are more demanding to SU equipment than their mammalian counterparts due to high rates of heat evolution and high oxygen demand,[1] making their transition to SU systems more challenging.

Foam generation is an undesirable phenomenon that occurs due to the high degree of gassing and agitation required to support fermentation, especially at high cell or protein concentrations. In addition, foam properties are highly process-specific. Foam presence increases the risk of exhaust filter clogging, resulting in batch failures and significant financial losses. It also has an adverse effect on oxygen transfer and can reduce cell viability and product yield.

Antifoam detergents can be added to minimize the surface tension of the production fluid and thus help reduce foaming. Reliable sensors and automated foam control eliminate the reliance on manual additions of unnecessary amounts of antifoam, reducing its potential influence on cell growth, saving costs, and simplifying downstream processes.

The goal of this study was to evaluate the reliability and robustness of the foam control function in the Biostat STR® Microbial single-use bioreactor.

Materials and Methods

Equipment Used in This Study

- Biostat STR® Microbial Single-Use Bioreactor
- Flexsafe STR® disposable bioreactor bag (Prototype)
- BioPAT® Foam Sensor

Figure 1: *Equipment Used in This Study*

Note. Left—transmitter with holder for fixation at bag holder systems rail. Right—transmitter with single-use foam patch.

The BioPAT® Foam sensor system can detect foam and trigger actions at Biostat STR® Microbial. It consists of a SU patch and a transmitter. The SU patch is attached to the outside of the Flexsafe STR® bags by the end user.

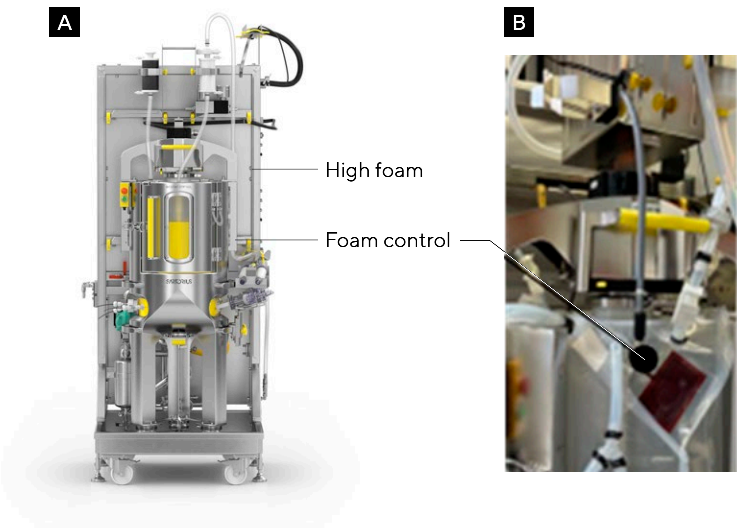
An internal model *E. coli* process was run to push the fermenter to its technical limits, as previously described.[2]

Results and Discussion

Positioning of the Foam Sensor

While the foam sensor patch can theoretically be placed anywhere on the bag, Figure 2 illustrates our suggested positioning for an *Escherichia coli (E. coli)* fed-batch process with a final maximum filling level of 40 L. However, process-specific optimizations may be required. The foam level in relation to the sensor position is documented, and the according sensor values are displayed at the HMI.

Figure 2: *Foam Sensor Positioning*



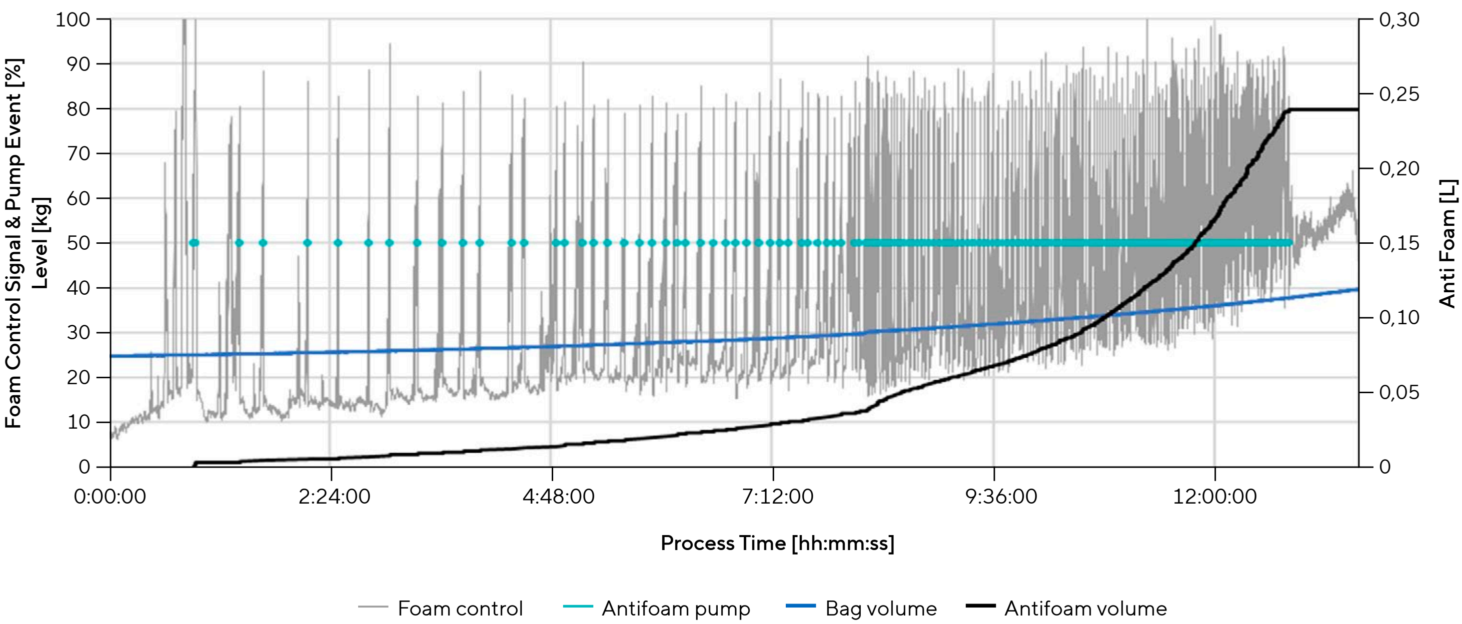
Note. A) Schematic displaying foam control and high foam patch positioning
B) Real-life view of the position of the foam control patch

Foam Sensor Sensitivity

As the media level rises during the fed-batch process, so does the cell density, leading to an increased demand for oxygen. Consequently, gassing should be boosted to enhance aeration and sustain the cells. However, this action also leads to greater foam production. The capabilities of the foam sensor in detecting this increased foaming were evaluated, and the results are shown in Figure 3.

The sensor rapidly detected the presence of foam, initiated the addition of antifoam, and increased stirring to maintain good dispersion (Figure 3). The foam measurements align with the increase in the volume of antifoam, indicating that the sensor provides accurate and reliable insights.

Figure 3: *The Foam Control Sensor Triggers the Addition of the Antifoam Agent With High Frequency in an E. coli Fed-Batch Process. The Graph Shows the Relevant Process Time Only*



The zoomed-in view (Figure 4) shows that every time the sensor threshold of 80% is exceeded, the pump triggers the addition of the antifoam agent. A single foam event is shown in Figure 5, which demonstrates that foaming is immediately reduced after antifoam addition. The effect of the antifoam is also shown visually in Figure 6.

Figure 4: *Zoomed-In View Displaying Single Foam Events and Antifoam Addition*

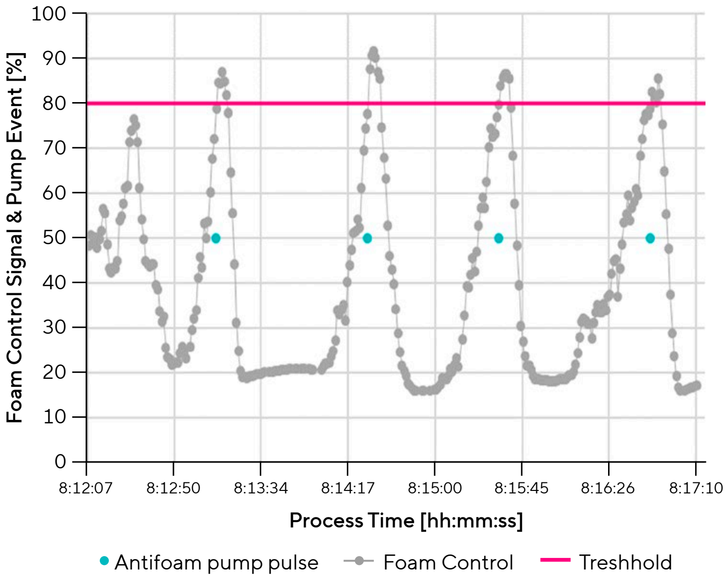


Figure 5: *A Single Foam Event*

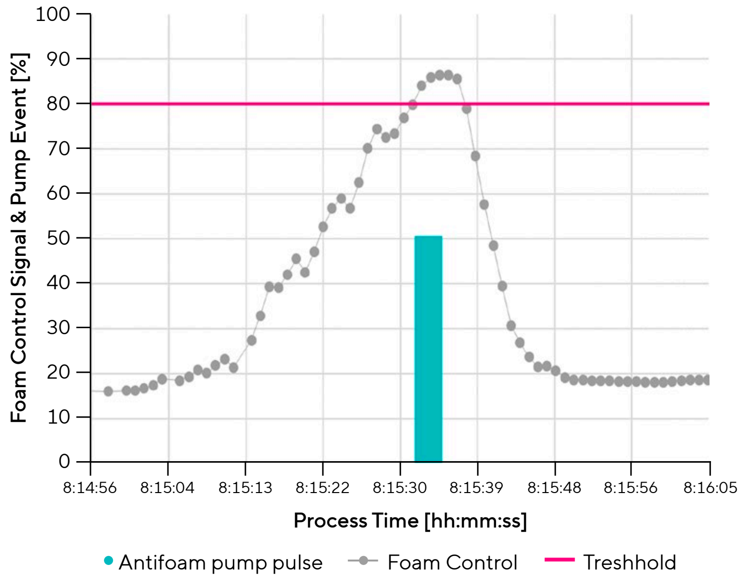
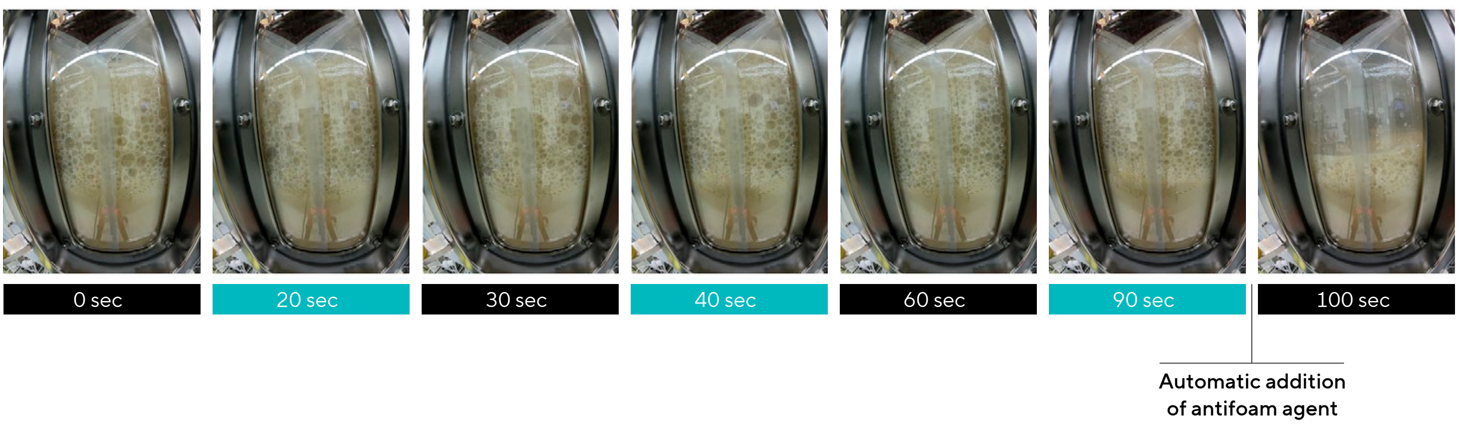


Figure 6: *Photographs Showing Foam Generation and Depletion Following the Addition of Antifoam*



Conclusion

Foam generation in a bioreactor can cause lower oxygen transfer rates by reducing surface area contacts between the cells and the media, leading to cell growth limitations. Reliable foam sensing and control are critical to efficient microbial culture technologies.

The BioPAT® Foam Sensor facilitates automated foam control that performs as well as a manual, continuously supervised process (24 hours). As such, significant labor hours are freed up. Additionally, the tight process control limits fluctuations and minimizes the volume of antifoam added, promoting process consistency.

The results presented in this application note demonstrate that the Biostat STR® Microbial is a high-performing SU solution that can sustain high-density microbial cultures. Supported by robust SU containers and reliable PAT sensors, the Biostat STR® Microbial enables close monitoring throughout the fermentation process. Thus, it supports safer and more robust cultivation of even sensitive microbial cultures.

References

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Last modified: 10 | 2025