Mechanical Methods for Bioreactor Foam Breaking

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Introduction

ThermoFisher Scientific, through the lead of Jason Brown, has commissioned a design team at Utah State University (USU) to create a mechanical foam breaker capable of being used in a single use bioreactor setup. These chemical agents in concentrations higher than 1% total volume, can lead to higher optical densities and lower protein yield [1].

Objectives

- Reduce relative foam height by 60%
- Implement the design in 30 L and 300 L bioreactors
- Must maintain sterility

Methods and Materials

- Bioreactor is filled with water to a predetermined level (testing here reflects 30 L and 24 L volumes)
- 50 mg of F68 pluronic acid is added per liter of water in the bioreactor
- Foam is generated for 5 minutes by turning on an agitator
- Allow approximately 5 minutes for the foam to rise to the top and form a clear foam head
- Measure from the top of the water line to the top of the foam line
- These methods were repeated with the cone, bristle, blade, and wire frame foam breaking designs installed

Figure 1: Image of the baseline foam height in the 30 L bioreactor

Figure 2: Height of the foam reduced after the inverted cone was connected to the inner shaft

Results

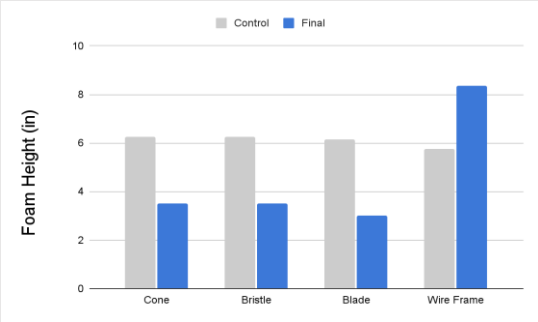

Figure 3: Bar graph showing relative foam heights

Table 1: Data used to generate bar graph. This includes the volume of water used in a given test

	Volume used (L)	Control Foam Height (in)	Final Foam Height (in)
Cone	30	6.25	3.5
Bristle	30	6.25	3.5
Blade	30	6.13	3
Wire Frame	24	5.75	8.375

- The cone, briste, and blade designs were successful at foam breaking while the wire frame design generated foam instead of breaking it
- The cone and bristle designs reduced the measured foam height by 44%
- The blade design reduced the measured foam by 61%
- Surface area seemed to be a determining factor in the success of a given foam breaking design

Conclusion and Future Work

Conclusions:

- Blade design method reduced foam height by 61%
- The wire frame design was the least effective as that generated more foam
- Future design changes and optimization to specific designs will show that some designs are viable in certain conditions, where others may not be

Future Work and Objectives:

- Must be installed in a quick and sterile manner
- The design has the ability to be installed through a 3-inch port at the top of the bag by a technician
- The design has the ability to be integrated as a part of the bioreactor manufacturing process
- Must be shippable for international clients as that would ensure the design can widely used in other bioreactor systems

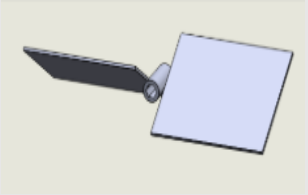

Figure 4: Solidworks drawing of Blade Foam breaker

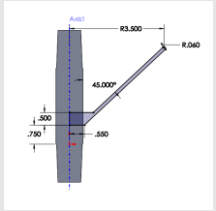

Figure 5: Solidworks design of initial cone concept used for printing

Figure 6: Image of wire frame foam breaker

Figure 7: Image of bristle foam breaker

References:
[1]Holmes, W., Smith, R. & Bill, R. Evaluation of antifoams in the expression of a recombinant FC fusion protein in shake flask cultures of Saccharomyces cerevisiae & Pichia pastoris. Microb Cell Fact 5, P30 (2006). https://doi.org/10.1186/1475-2859-5-S1-P30

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