

Utilization of the DASGIP Mini Bioreactor System as a Tool for Cell Line Evaluation and Selection



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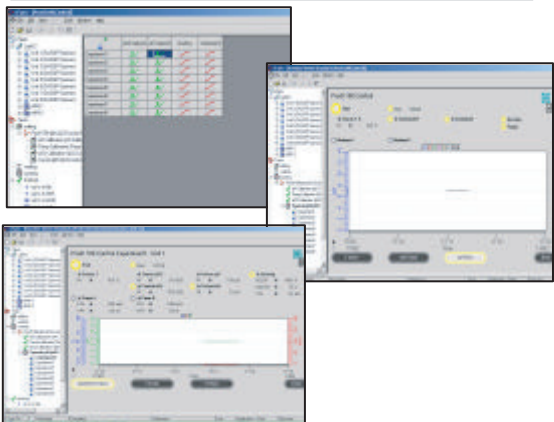
Abstract

The Dasgip Cellferm -pro Bioreactor System is a quick and efficient way to evaluate various antibody producing cell lines for growth, viability, and expression. The Cellferm -pro system consists of eight independently controlled one-liter bioreactors inside of an incubator. Each bioreactor has its own pH and dissolved oxygen control (DO) as well as a unique gas mixture. Using the Cellferm -pro software, experiments can be specifically designed to run up to eight parallel cultures, or to evaluate a range of parameter values. We used this tool to evaluate the performance of three antibody producing cell lines and to select one line as part of a process for therapeutic antibody product development. The bioreactors were inoculated and then sampled daily for cell density, viability, and antibody titer analysis. The selected cell lines were used in high density bioreactors and the results from Dasgip were confirmed. From our experiments, we have seen that the Dasgip is a quick, effective tool for cell line evaluation.

Dasgip System Applications

- Clone Line Selection and Evaluation
- Determining the effects of temperature and pH on the various growth conditions
- Chemostat evaluation of cell lines

Cellferm -pro Eight Bioreactor System



Experimental Design

Objective: To confirm that the results of the Dasgip clone evaluation studies are comparable to those of the 3L perfusion bioreactor clone evaluation studies and qualify the Dasgip as a clone selection tool.

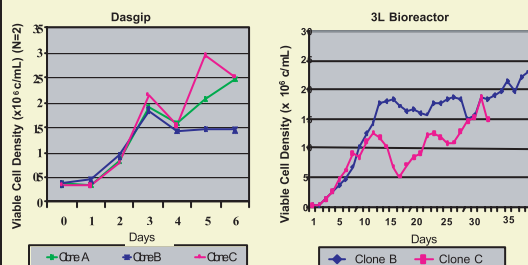
Dasgip Experiment Design:

- Three Clones of Cell Line 1
- The same pH and DO set points as the 3L bioreactors
- Batch mode until <20% viable
- 500 mL working volume Dasgip bioreactors

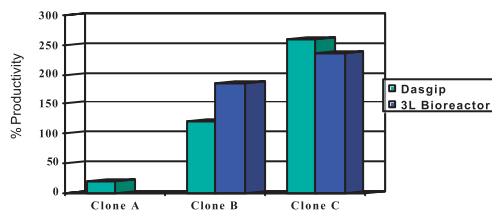
3 L Bioreactor Experiment Design:

- Two clones evaluated in duplicate
- 3 L (wv) perfusion bioreactors
- Runs lasted for 22 to 54 days, depending on viability of culture
- Same media as the 3L bioreactors

Viable Cell Density in the 3L and Dasgip Bioreactors



Specific Productivity Comparison in the Dasgip and 3L Bioreactors

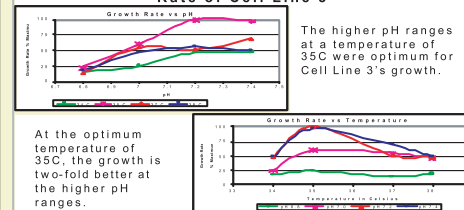


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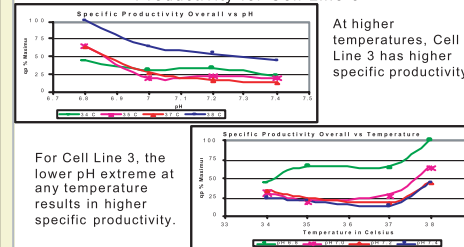
Determine the effects of pH and temperature on various growth parameters of the bioreactor culture

Four Dasgip runs, each using eight bioreactors were performed. The incubator was manually set to the desired temperature for each run and the individual bioreactor profiles were designed to test the various pH set points. The results of these experiments are summarized in the following graphs.

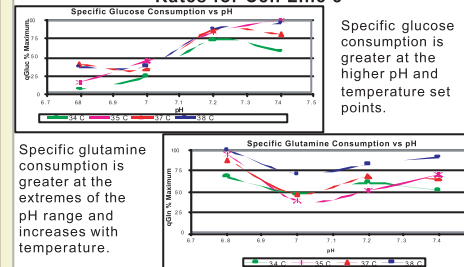
The Effects of pH and Temperature on Growth Rate of Cell Line 3



The Effects of pH and Temperature on Specific Productivity for Cell Line 3



Specific Glucose and Glutamine Consumption Rates for Cell Line 3



Conclusions:

- The Dasgip system is proven to be an effective tool for clone selection and evaluation.
- The Dasgip system can be used for evaluation of the effects that various process parameters have on the cell lines growth and productivity.