

Enhancing Productivity of CHO Cell Lines With DASGIP Parallel Bioreactor Systems

CHO Cells

In industrial cell culture, Chinese Hamster Ovary (CHO) cells are the No. 1 work horse: They have been extensively studied and developed, and today provide a stable platform for producing monoclonal antibodies and recombinant proteins.

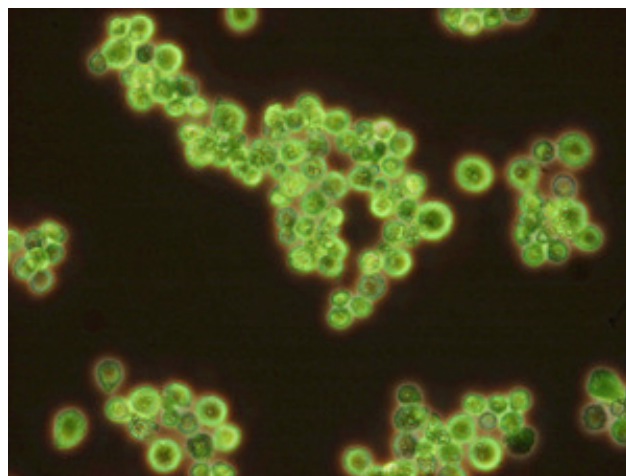
However, each (sub)clone may be different: growth characteristics, nutrition needs, and expression level can vary greatly between clones.

The sole dedication to maximize density can lead to unsuitable conclusions, as density does not necessarily mean higher productivity. One goal therefore can be to distinguish between the fast growers from the more productive variations among the sub clones of the same cell line. Another aspect of interest is the feeding strategy: Apart from glucose and glutamine feeds amino acids are critical to CHO growth and expression. In a nutshell: Enhancing productivity of CHO cell lines requires selecting the right sub-clone as well as the right cultivation parameter.

Parallel Experiments

When considering clone selection; process optimization, parameters, and other variables can at times be overwhelming. To compare subclones and parameters, each experiment requires a set-up allowing reproducible cultivation conditions.

As the investigation of a whole number of critical aspects can easily get extensive, a technology to look into different combinations at the same time, i.e. allowing parallel operations, will help to reduce time and other resources spent on selection and optimization.



DASGIP Applications

And this is exactly what DASGIP has to offer: A parallel small-scale cultivation system providing controlled conditions. Four up to 16 bioreactors with working volumes between 35 mL and 15 L provide users flexibility in experiment size and throughput.

By combining different modules for monitoring, gassing, feeding and data logging, all integrated with each other, the process parameters are controlled within a tight range.

For instance, the mass flow controlling gassing module supplies a precise mix of up to four gases for pH and PO₂ control. Another example is the peristaltic micro-pumps of the feeding module, which have a variable speed drive delivering continuous feeding with each of its eight channels. Samples can be taken from various positions (7 ports) on the reactors' head plates while maintaining sterile conditions. Individual parameters of each reactor can be isolated and optimized.

Application CHO Cells

Quality System certified by DQS ■ DIN EN ISO 9001 ■ Reg.-No. 63431

Enhancing Productivity of CHO Cell Lines With DASGIP Parallel Bioreactor Systems

Sophisticated software combined with integrated control modules for monitoring, gassing and feeding provide precise control of temperature, pH, dissolved oxygen and other critical parameters for optimizing CHO culture. Every DASGIP module serves at least four vessels in parallel.

■ Curagen

The pharmaceutical company CuraGen Corp., Branford, CT, confirmed, that in 2006 it has taken advantage of the DASGIP's cell cultivation system's reproducibility factors.

They aimed at optimizing the monoclonal antibody production in a CHO fed-batch culture. As they could reproduce the same results in every vessel and in every run they could rely on comparable data when studying the impact of pH, dissolved oxygen and temperature. By



using two eight-vessel DASGIP systems they completed 47 experiments with a minimum of twelve days runtime, within a six week time frame.

■ Research Center Jülich, Institute for Biotechnology I

Thomas Noll and his group at the Institute of Biotechnology, Research Center Jülich (Germany), in 2005 chose a CHO cell line secreting the recombinant protein (MUC1-Fc) when studying the impact of the small-scale, stirred cultivation system with oxygen and pH control. They used the DASGIP system, including micro-pumps, gas mixing station and pH- and DO control, all integrated into the DASGIP monitoring, documentation and steering system. The CHO culture was grown in four Mini Spinner flasks with a working volume of 30 mL.

What Noll found out is that the Mini Spinner flasks provided the multi-parallel cultivation in reduced working volumes under controlled conditions (pH and DO). He observed also, that the mixing and oxygen transfer characteristics were similar to standard stirred systems of greater volume resulting in good scalability.

Receiving comparable results when working with a Hybridoma cell line he concluded that the DASGIP system is suitable for different mammalian cell culture applications such as process development, cellular engineering and primary cell application.