Engineering Conferences International
ECI Digital Archives

Cell Culture Engineering XV | Proceedings

Spring 5-9-2016

Cell-controlled high-intensity perfusion and hybrid fed-batch systems that drastically reduce perfusion rates and harmonize with continuous downstream processing

Gregory Hiller
Pfizer, gregory.hiller@pfizer.com

Matthew Gagnon
Pfizer

Ana Maria Ovalle
Pfizer

Bhanu Chandra
Pfizer

Wenge Wang
Pfizer

See next page for additional authors

Follow this and additional works at: http://dc.engconfintl.org/cellculture_xv

Part of the Biomedical Engineering and Bioengineering Commons

Recommended Citation

Gregory Hiller, Matthew Gagnon, Ana Maria Ovalle, Bhanu Chandra, Wenge Wang, and Elizabeth Eydelman, "Cell-controlled high-intensity perfusion and hybrid fed-batch systems that drastically reduce perfusion rates and harmonize with continuous downstream processing" in "Cell Culture Engineering XV", Robert Kiss, Genentech Sarah Harcum, Clemson University Jeff Chalmers, Ohio State University Eds, ECI Symposium Series, (2016). http://dc.engconfintl.org/cellculture_xv/17

This Abstract is brought to you for free and open access by the Proceedings at ECI Digital Archives. It has been accepted for inclusion in Cell Culture Engineering XV by an authorized administrator of ECI Digital Archives. For more information, please contact franco@bepress.com.

Authors
Gregory Hiller, Matthew Gagnon, Ana Maria Ovalle, Bhanu Chandra, Wenge Wang, and Elizabeth Eydelman

This abstract is available at ECI Digital Archives: http://dc.engconfintl.org/cellculture_xv/17

CELL-CONTROLLED HIGH-INTENSITY PERFUSION AND HYBRID FED-BATCH SYSTEMS THAT DRASTICALLY REDUCE PERFUSION RATES AND HARMONIZE WITH CONTINUOUS DOWNSTREAM PROCESSING

Gregory Hiller, Pfizer, Inc.
gregory.hiller@pfizer.com
Matthew P. Gagnon, Pfizer, Inc.
Ana Maria Ovalle, Pfizer, Inc.
Bhanu Chandra Mulukutla, Pfizer, Inc.
Wenge Wang, Pfizer, Inc.
Elizabeth Eydelman, Pfizer, Inc.

Key Words: Perfusion, hybrid process, continuous culture.

Peak cell densities in fed-batch cultures of mammalian cells can be limited by the depletion of nutrients or accumulation of inhibitors. Since addition of nutrients is relatively straight forward, inevitably it is growth inhibitor buildup, combined with the practical limits of feed volume addition and the problem of amino acid counter ion and miscellaneous osmolyte accumulation, that serve to limit productivity in the industry standard fed-batch bioreactor. To break these barriers we have begun to investigate mixed modes of bioreactor operation, some using novel methods for cell-controlled perfusion, which can substantially reduce the volumes of perfusion medium required, suppress lactic acid formation, shorten the time to reach peak cell densities, and reduce the complications associated with cell retention devices. Our methods of high-intensity perfusion and mixed mode bioreactor operation are also more compatible with the move to continuous downstream processing as the stream delivered is more concentrated and provides a more continuous daily mass of product to allow for reduced affinity chromatography scale.

The techniques we will describe significantly increase viable cell densities and have achieved volumetric productivities of 1.0-1.5 grams/L/day (nearly 4X the optimized fed-batch culture in one case) for several moderate specific productivity cell lines, while using very modest medium volumes, highly concentrated perfusion media, comparatively simple bioreactor operations, and a batch length that fits in a standard fed-batch window. Methods of operation and experimental results obtained at the pilot (100 liter) scale when coordinating these hybrid continuous cultures with a continuous downstream process will also be discussed.