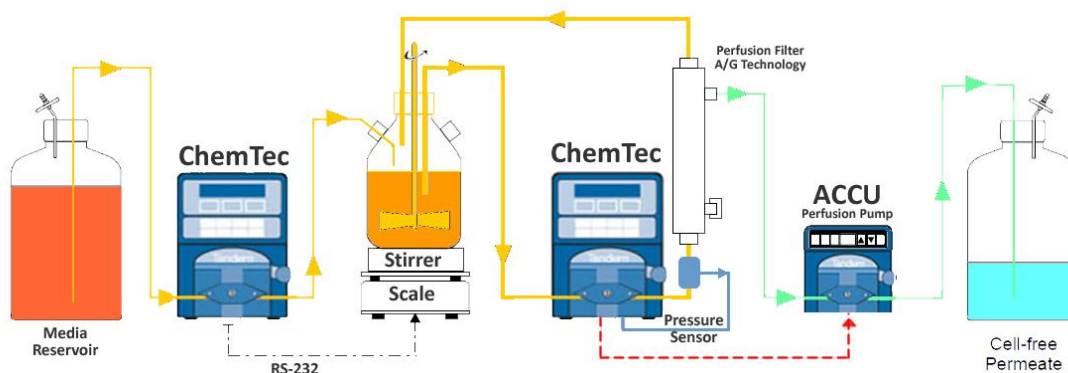


Continuous Harvesting of Extra-Cellular Proteins from Mammalian Cell Cultures Utilizing Small-Scale Perfusion

Summary:

The use of a small-scale cell culture system not only maximizes the production of valuable protein but also avoids the high capital cost associated with system scale-up. Continuous harvesting can provide significant improvements in protein yields when compared to those of typical batch operations. For example, Brennan et al¹ reported a 27-fold higher level of monoclonal antibody in a 48-day perfusion culture of hybridoma cells (800µg/ml versus 30µg/ml in a 7-day batch culture).



Features:

Reactor level problems typically associated with level probes and sensors are avoided by scale feedback to the ChemTec. In the small-scale continuous perfusion system shown above, a ChemTec smart pump maintains the media level (constant weight) of a Bellco Spinner Flask during perfusion. An autoclavable hollow fiber filtration cartridge (*A/G Technology, 800-248-2535*) was used to generate cell-free permeate.

The ChemTec automatically meters fresh media into the bioreactor in response to the continuous removal of cell-free permeate containing the expressed protein. The ChemTec maintains a constant bioreactor weight over many days and weeks of continuous perfusion. The ChemTec displays and documents the reactor weight as well as the volume of media added to the reactor. Three (3) different alarms can be activated. For example, the reactor weight alarm is turned on when the set-point weight cannot be maintained (i.e. the media reservoir has run empty).

- (1) Brennan, A.J., J. Shevitz and J.D. MacMillan. 1987. A perfusion system for antibody production by shear sensitive hybridoma cells in a stirred reactor. New Brunswick Scientific. Edison, NJ
- (2) Kieron Walsh, *Private communication*, A/G Technology Corporation.

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Additional Features:

In the Perfusion System, the ChemTec system functions as an automated re-circulation pump that also controls the operation of the ACCU perfusion pump. The UltraTec senses a filter plug-up condition by continuously monitoring the filter back- pressure. The UltraTec will stop and alarm as soon as a user-definable pressure limit is exceeded, simultaneously, the UltraTec will stop the ACCU perfusion pump.

A ChemTec pump delivers the suspended cells at a low shear rate, typically $1000-2000 \text{ sec}^{-1}$, through a hollow fiber microfiltration cartridge (*A/G Technology, Tel: 800-248-2535*) and returns the cells back to the Spinner Flask. The cell-free permeate, containing the expressed protein, is perfused with an ACCU pump at a rate that is measured in bioreactor volumes per day (BVD). The BVD should be optimal for cell viability, cell density and / or production of protein (i.e. 0.5 – 2.0 BVD).

In a typical application, the required microfilter surface area is one (1) square foot for every 50 liters of perfused media (2). For example, in a 3-liter bioreactor, perfusion volumes may range from 1.5 –6.0 liters per day over the course of 30 days or a total 45 -180 liters. Thus the perfused volume requires a filter surface area ranging from 0.9 sq. ft. to 3.6 sq. ft.. A/G Technology offers microfiltration cartridges with surface areas of 0.5 sq. ft. (P/N: CFP-6-D-4A), 1.7 sq. ft. (P/N: CFP-6-D-5A), and 4.0 sq. ft. (P/N: CFP-6-D-6A).

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ORDERING INFORMATION: SciLog Customer Service: 1-800-955-1993

Catalog #	Description
100-138MASS	ChemTec, CP-120, Media Addition Pump with TANDEM peristaltic pump head; 160 RPM motor; 30 psi max, pump rate from 0.3 to 500 ml/min., <i>includes factory installed perfusion metering software.</i>
100-018	ACCU CP-10, Perfusion Pump with TANDEM peristaltic pump head, 160 RPM motor; 30 psi max, pump rate from 0.3 to 500ml/min. Includes RUN / STOP control cable. When connected, RUN/STOP functions of ACCU are remotely controlled by UltraTec.
100-SPE060	Mettler “SpeedWeigh” Scale, programmable weight capacity (60kg max), readability: 10 grams at 60kg capacity. Connects to “Balance” Serial Port of the ChemTec for maintaining constant bioreactor weight
080-095A	Printer Kit, interfaces with ChemTec or UltraTec, documents your process.

***Note:** All pump and communication parameters of both the ChemTec smart pump and Panther scale have been entered and factory tested for easy system setup.*