A Cell Separation Device for the Biopharmaceutical Industry

Inclined Gravity Settler for Cell Retention

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Inventors
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Field
Production of therapeutic and diagnostic agents

Technology
Inclined gravity settler

Key Features
Disposable
Simple to operate

Key Benefits
Low manufacturing cost
Reduced footprint and residence time
Optimized performance

Stage of Development
Prototype has been developed

Status
Seeking licensing partner

Patent Status
US Patent filed

Background
Traditionally the production of therapeutic and diagnostic agents secreted from cells, whether bacteria, yeast, or mammalian cells, has been done in stirred-tank systems in batch mode. As the number and size of these biotechnology processes increase, manufacturers are more often turning towards continuous perfusion systems to improve the economics of the process. When the product is secreted by the cell, the system productivity is significantly improved by separating viable cells from the perfusion fluid and returning them to the bioreactor, while the fluid and nonviable cells are pumped to the harvest tank for downstream processing and product recovery. One of the major challenges with implementing continuous systems is the existence of a reliable, low-cost, and easy to operate method for retaining the cells within the bioreactor. Furthermore, biopharmaceutical companies using mammalian cell processes are increasingly turning towards single-use bioreactors to reduce costs of sterilization, turn-around time, and process validation.

Inclined Gravity Settler for Cell Retention
The inventors have developed a novel design of an inclined gravity settler that can be used to return a concentrated cell stream to the bioreactor when operated in perfusion mode. This device can be constructed of inexpensive polymeric materials using inexpensive manufacturing methods. These properties allow it to be made as a single-use, pre-sterilized device, to work with existing single-use bioreactors. It has 1/3 the surface area of commercially-available gravity-based devices, which results in lower footprint and lower residence time of the cells in an unfavorable growth environment. The device operates effectively with a recirculation rate that is ¼ that of comparable devices, for the same harvest rate. A lower recirculation rate reduces exposure of the cells to potentially harmful shear stress as well as maximizes cell residence time in the bioreactor.

The prototype can handle 17 L/day flow rate with over 90% viable cell retention efficiency. It has supported non-stop perfusion culture for two months at perfusion rates of 0.5 to 1.6 L/day. This device can be scaled up to support over 1000 L/day perfusion culture systems by increasing the number of channels and by stacking multiple units.

Settling Velocity Measurement Device
Performance of this gravity settler can be optimized by regular measurement of cell settling velocity, which is cell-specific and can change during processing conditions. We have developed a unique device and process for easily measuring the cell settling velocity (patent pending). By means of this device and process, the average settling velocity of both the viable and nonviable cell populations can be determined quickly and inexpensively. The device can be constructed of plastic and is reusable. The only other equipment needed is a microscope and hemocytometer for obtaining a cell count. The device was used to determine the settling velocity of standard polystyrene particles, resulting in excellent agreement with the settling velocity calculated from Stoke's Law

Opportunity
CSU is looking for a commercial partner for licensing and development.

Inventors

Mr. Zhaowei Wang is completing the doctoral program in Applied Biomedical Engineering at Cleveland State University. He has published one paper and has two additional papers undergoing revision. He has one patent approved, one patent filed, and two provisional patents filed.

Joanne M. Belovich, Ph.D., is Professor of Chemical and Biomedical Engineering at Cleveland State University. Dr. Belovich has extensive research experience in biochemical engineering, including mammalian cell separation processes, wastewater treatment using microbial biofilms, lactic acid fermentation and purification, transport in biomaterials and bioreactors, and modeling and simulation of biological systems. She has published 19 papers, and with Mr. Wang, she has one patent filed and two provisional patents filed. She has obtained $2M in research and educational grants.