

## **A NOVEL ACOUSTIC CELL PROCESSING PLATFORM FOR CELL CONCENTRATION AND WASHING.**

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Acoustofluidics involves the interaction of ultrasonic standing waves with particle suspension flows. The field has seen considerable growth in the last decade, particularly for diagnostic MEMS scale applications but also in biological applications. Typically, an ultrasonic standing wave is generated across a fluid flow by a piezoelectric transducer and an opposite acoustic reflector. The scattering of the ultrasound field by the suspended particle results in an acoustic radiation force acting on the suspended particle. The strength of the acoustic radiation force is a function of fluid and particle density and compressibility and particle size. The dynamics of the particle are then controlled by a number of forces, such as the fluid drag force, gravity/buoyancy force, acoustic radiation force, and inter-particle forces.

FloDesign Sonics has developed a novel acoustic cell processing platform based on multi-dimensional standing waves. The platform has broad applications in biopharmaceutical, e.g., cell clarification, continuous manufacturing, and cell processing within cellular therapy applications, e.g., cell concentration and wash, cell culturing, and microcarrier/cell separation. In fed batch cell clarification, e.g., CHO cells for mAb production, the multi-dimensional standing wave is designed to trap the cells in the acoustic field. The three-dimensional acoustic radiation forces cause the trapped cells to form tightly packed cylindrical shaped clusters of cells, which continuously settle out due to enhanced gravitational separation. This technology is single use, continuous, and scalable. A small scale clarification product operating at 4 L/hr was launched in April of 2016. Scaling of the technology has been successfully shown with larger units operating at flow rates of 10 and 50 L/hr, providing cell clarification efficiencies of 90% across a wide range of feed stream cell densities up to 80 M cells/ml.

The same platform technology has been modified to enable a single use (gamma irradiated) continuous cell concentration and wash application for manufacturing of cell based therapies. The device has been designed to be able to process several liters of a suspended cell culture, e.g., T-cells, at concentrations of 1 to 10 M cells/ml. The cell suspension flows through the device. The acoustic radiation force field is used to trap and hold the cells in the acoustic field. After concentrating the cells, one or multiple washing steps are accomplished by flowing the washing fluid through the device, using the acoustic field to trap the cells while displacing the original cell culture fluid. The holdup volume of the device is about 30 ml. Depending on cell concentration and initial volume of the cell suspension, measured cell recoveries of 90% have been achieved with concentration factors of 20 to 50 for Jurkat T-cell suspensions. Scaling strategies used previously for cell clarification will be used to scale up the current cell concentration device to accommodate large volumes.