[0007] It would be desirable to provide means that can reduce the cost and effort of using bioreactors and separating the desired products from the cells that make them.

BRIEF DESCRIPTION

[0008] The present disclosure relates, in various embodiments, to systems for producing biomolecules such as recombinant proteins or monoclonal antibodies, and to processes for separating these desirable products from a cell culture in a disposable or non-disposable bioreactor system. Generally, the bioreactor includes an acoustophoretic device for producing multi-dimensional acoustic standing waves, which is located near an outlet port for the bioreactor. Such standing waves are produced by an ultrasonic transducer and a reflector. In the present disclosure, the reflector is formed from a thin material that is essentially acoustically transparent, such as certain plastic films, rather than a solid metal. The thin material provides a constant pressure boundary, also known as a free surface. In essence, these embodiments are examples of providing a pressure release surface, such as from a transparent layer of a plastic film.

[0009] Disclosed in various embodiments are apparatuses that include a flow chamber having at least one inlet and at least one outlet. At least one ultrasonic transducer is located on a wall of the flow chamber. The transducer includes a piezoelectric material driven by a voltage signal to create a multi-dimensional acoustic standing wave in the flow chamber. A thin structure is located on the wall on the opposite side of the flow chamber from the at least one ultrasonic transducer. The thin structure provides a pressure release boundary that acts as a reflector.

[009a] In one aspect, there is provided an apparatus, comprising: a flow chamber having at least one inlet and at least one outlet; at least one ultrasonic transducer located on a wall of the flow chamber, the transducer including a piezoelectric material driven by a voltage signal to create a multi-dimensional acoustic standing wave in the flow chamber; and a thin structure located on a wall opposite the at least one ultrasonic transducer, the thin structure providing a pressure release boundary that acts as a reflector.

[0010] In particular embodiments, the thin structure is a plastic film. The plastic film can be made from a material selected from the group consisting of olefins, polyurethanes, polyureas, polyesters, polystyrenes, polyamides, cellulosics, ionomers, polyvinyl chloride, polyvinyl butyral, polyvinylidene fluoride, polyvinylidene chloride, ethylene vinyl acetate, ethylene tetrafluoroethylene, polytetrafluoroethylene, and combinations thereof. More specifically, the plastic film can be a polypropylene.

[0011] The thin structure can be optically transparent. The thin structure may be substantially flat. The thin structure may have a thickness that is 1/2 or less of the

secondary fluid or particles cluster or coalesce at specific points such that gravity separation eventually and continuously occurs. In other words, once the clustering, coalescing or clumping occurs, continuous gravity separation happens. A pulsed voltage signal drives ~~the~~ the at least one ultrasonic transducer.

[0017a] In one aspect, there is provided a method of separating a second fluid or a particulate from a host fluid, comprising:

flowing a mixture of the host fluid and the second fluid or particulate through an apparatus, the apparatus comprising:

a flow chamber having at least one inlet and at least one outlet;

an ultrasonic transducer located on a wall of the flow chamber, the transducer including a piezoelectric material driven by a voltage signal to create a multi-dimensional acoustic standing wave in the flow chamber; and

a thin structure located on a wall opposite the at least one ultrasonic transducer, the thin structure providing a pressure release boundary that acts as a reflector; and

capturing smaller particles of the second fluid or particulate in the multi-dimensional acoustic standing wave to clump, aggregate, and coalesce and continuously gravity separate the second fluid or particulate from the host fluid.

[0018] The particulate may be Chinese hamster ovary (CHO) cells, NS0 hybridoma cells, baby hamster kidney (BHK) cells, insect cells or human cells such as stem cells and T-cells. The mixture may be continuously flowed through the flow chamber. The standing wave may have an axial force and a lateral force, the lateral force being at least the same order of magnitude as the axial force.

[0019] Also disclosed in various embodiments are apparatuses that include a flow chamber having at least one inlet and at least one outlet. At least one ultrasonic transducer is located on a wall of the flow chamber. The transducer includes a piezoelectric material driven by a voltage signal to create a multi-dimensional acoustic standing wave in the flow chamber. A thin structure is located on the wall on the opposite side of the flow chamber from the at least one ultrasonic transducer. The thin structure provides a pressure release boundary that acts as a reflector. The apparatus has an acoustic reflection coefficient of -0.1 to -1.0.

[0019a] In one aspect, there is provided an apparatus, comprising:

a flow chamber having at least one inlet and at least one outlet;

at least one ultrasonic transducer located on a wall of the flow chamber, the transducer including a piezoelectric material driven by a voltage signal to create a multi-dimensional acoustic standing wave in the flow chamber; and

a thin structure located on a wall opposite the at least one ultrasonic transducer, the thin structure providing a pressure release boundary that acts as a reflector, wherein the apparatus has an acoustic reflection coefficient from -0.1 to -1.0.

[0020] These and other non-limiting characteristics are more particularly described below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] The following is a brief description of the drawings, which are presented for the purposes of illustrating the exemplary embodiments disclosed herein and not for the purposes of limiting the same.

[0022] **Figure 1** is a schematic plan view of a flow chamber, illustrating the thin structure / reflector of the present disclosure.

[0023] **Figure 2** is a schematic showing how the acoustic reflection coefficient is calculated for the device of **Figure 1**.

[0024] **Figure 3A** is a picture of an acoustophoretic separator having one ultrasonic transducer and a transparent thin plastic film acting as the reflector.

[0025] **Figure 3B** is a picture showing the thin plastic film reflector.