fluid mixture flow through the column by provision of an acoustic standing wave at one end of the column that can prevent the support structures from passing.

An aspect of the present disclosure provides a separation system, comprising a vertically oriented column with an opening on each end to permit a fluid flow therethrough, the column being configured as a fluidized bed to permit introduction and containment of a plurality of support structures, an acoustic transducer on one end of the column for generating an acoustic wave in the column. The acoustic transducer is configured to generate the acoustic wave across a direction of fluid flow through the column to form an edge effect to block and retain the plurality of support structures in the column against the fluid flow.

Another aspect of the present disclosure provides a method for separating materials, comprising providing support structures in a vertically oriented column configured as a fluidized bed for binding with a first material; flowing a fluid mixture that includes the first material into the column; and generating an acoustic wave by vibrating an acoustic transducer near an end of the column to form an edge effect that generates a pressure rise on an upstream side of the acoustic wave to block the support structures from leaving the column with the fluid flow.

Another aspect of the present disclosure provides an acoustic affinity separation method, comprising: providing affinity beads in a fluid to a vertically oriented column configured as a fluidized bed; generating an acoustic wave with an acoustic transducer near an end of the column; flowing a cellular material fluid mixture in the column and through the acoustic wave; configuring the acoustic wave to form an edge effect that generates a pressure rise on an upstream side of the acoustic wave to prevent the affinity beads from passing through the acoustic wave.

In some examples, methods, systems, and apparatuses are disclosed for separation of biomaterials accomplished by functionalized material distributed in a fluid chamber that bind the specific target materials. The specific target materials can be particles, including cells, recombinant proteins and/or monoclonal antibodies. The

functionalized material, which may be beads and/or microcarrier structures are coated or otherwise provided with an affinity material for attracting and binding the specific target materials. The affinity material may be a protein, ligand or other material that can form a bond with the target material.

In some example implementations, the affinity material and the target material can form antigen-antibody interactions with binding sites on the functionalized material. In some instances, the target material become bound to the functionalized material when a ligand of the target material or the functionalized material is conjugated to a matrix on the complementary material. The functionalized material includes functionalized microbeads. The functionalized microbeads include a particular antigen ligand that has affinity for a corresponding antibody.

In some examples, material adhered to the support structures with the functionalized material remains in the column, while other free material in the fluid may pass through the acoustic standing wave to provide separation of materials. The support structures may be implemented to have a certain acoustic contrast factor based on their density, compressibility, size or other characteristics that permits the support structures to react more strongly to the acoustic standing wave than other materials in the fluid mixture.

The support structures may be agitated in the column to enhance the affinity process. In different modes, the column fluid mixture that passes through the acoustic standing wave can be recirculated to the column or not. The fluid flow in the column can be controlled to flow or not, and when flowing, the rate of flow can be controlled. The fluid may be stationary in the column and may have other processes applied thereto, such as temperature adjustment, agitation, incubation, and/or any other useful process. The volume of the column can be effectively modified, such as with the provision of a plunger or piston in the column. Heating or cooling can be applied to the column or the contents of the column, internally or externally to the column.

CLAIMS

What is claimed is:

1. A separation system, comprising:

a vertically oriented column with an opening on each end to permit a fluid flow therethrough, the column being configured as a fluidized bed to permit introduction and containment of a plurality of support structures;

an acoustic transducer on one end of the column for generating an acoustic wave in the column; and

the acoustic transducer being configured to generate the acoustic wave across a direction of fluid flow through the column to form an edge effect to block and retain the plurality of support structures in the column against the fluid flow.

2. The system of claim 1, further comprising an agitator coupled to the column for agitating the fluid.

3. The system of claim 1, wherein the acoustic transducer is configured to operate in a plurality of modes.

4. The system of claim 3, wherein the plurality of modes comprise a clustering mode and an edge effect mode.

5. The system of claim 1, wherein the acoustic transducer is configured to generate a multi-dimensional acoustic wave in the column.

6. The system of claim 1, further comprising mobile support structures for cellular material in the column that are responsive to the acoustic wave.

7. The system of claim 6, wherein the support structures comprise affinity beads.

8. The system of claim 7, wherein the affinity beads comprise column packing in a range of from 10% to 30%.

9. The system of claim 7, wherein the affinity beads are configured with one or more of anti-TCR or anti-CD52 capturing antibodies.

10. The system of claim 7, wherein the affinity beads are configured as avidin-conjugated methacrylate beads.

11. A method for separating materials, comprising:

providing support structures in a vertically oriented column configured as a fluidized bed for binding with a first material;

flowing a fluid mixture that includes the first material into the column; and

generating an acoustic wave by vibrating an acoustic transducer near an end of the column to form an edge effect that generates a pressure rise on an upstream side of the acoustic wave to block the support structures from leaving the column with the fluid flow.

12. The method of claim 11, further comprising agitating the fluid mixture in the column.

13. The method of claim 11, further comprising generating the acoustic wave in a plurality of modes.

14. The method of claim 13, wherein the plurality of modes comprise a clustering mode and an edge effect mode.

15. The method of claim 11, further comprising generating a multi-dimensional acoustic wave in the column.

16. The method of claim 11, wherein the support structures comprise affinity beads.

17. The method of claim 16, further comprising packing the column in a range of from 10% to 30% with the affinity beads.

18. The method of claim 16, wherein the affinity beads are configured with one or more of anti-TCR or anti-CD52 capturing antibodies.

19. The method of claim 16, wherein the affinity beads are configured as avidin-conjugated methacrylate beads.

20. An acoustic affinity separation method, comprising:

providing affinity beads in a fluid to a vertically oriented column configured as a fluidized bed;

generating an acoustic wave with an acoustic transducer near an end of the column;

flowing a cellular material fluid mixture in the column and through the acoustic wave;

configuring the acoustic wave to form an edge effect that generates a pressure rise on an upstream side of the acoustic wave to prevent the affinity beads from passing through the acoustic wave.