

1. Apparatus for manipulating biological cells, the apparatus comprising:

a substrate including a plurality of through holes and having a central region and a peripheral region around the central region, wherein the through holes have a higher density in the peripheral region than in the central region;

one or more soft magnetic layers disposed on the substrate and in proximity to the through holes; and

a magnetic source, wherein the magnetic source is capable of controlling a magnetic field strength and/or a magnetic field gradient provided by the soft magnetic layers.

2. The apparatus of claim 1, wherein a distribution of the through holes is selected such that flow rates through the holes are substantially the same when fluid passes through the substrate via the holes.

3. The apparatus of claim 1, wherein the shapes of the through holes are selected from the group consisting of: square holes, rectangular holes, circular holes, and bow-tie holes.

4. The apparatus of claim 1, further comprising a non-magnetic spacer layer disposed to reduce magnetic leakage flux at the soft magnetic layers when the soft magnetic layers are in a demagnetized state.

5. The apparatus of claim 1, further comprising an anti-fouling layer disposed at the through holes and substrate.

6. The apparatus of claim 1, further comprising a flow cell in which the substrate is disposed, wherein the flow cell includes an optical window in proximity to the through holes.

7. The apparatus of claim 1, wherein the magnetic source comprises an electromagnetic source or a permanent magnet.

8. A method for manipulating biological cells, the method comprising:

providing a substrate including a plurality of through holes and having a central region and a peripheral region around the central region, wherein the through holes have a higher density in the peripheral region than in the central region;

providing one or more soft magnetic layers disposed on the substrate and in proximity to the through holes;

tagging biological cells with one or more magnetic tags to provide tagged cells;

passing a fluid including the tagged cells through the holes of the substrate; and

capturing and/or releasing the tagged cells at the through holes by applying an external magnetic field to control a

magnetic field strength and/or a magnetic field gradient provided by the soft magnetic layers.

9. The method of claim 8, wherein a distribution of the through holes is selected such that flow rates through the holes are substantially the same.

10. The method of claim 8, wherein the releasing tagged cells comprises one or more methods selected from the group consisting of: altering the magnetic field direction at the magnets by about 90 degrees; setting the external magnetic field to about zero; reducing the external magnetic field to about zero in a manner that provides demagnetization of the magnets, and mechanically agitating the substrate and/or fluid passing through the holes.

11. The method of claim 8, further comprising quantifying cells that are captured at the through holes.

12. The method of claim 11, wherein the quantifying cells includes providing one or more fluorescent markers that bind to specific cell types.

13. A method for manipulating biological cells, the method comprising:

first performing the method of claim 8 to provide a processed cell stream;

second performing the method of claim 8 one or more additional times on the processed cell stream.

14. The method of claim 13, wherein the magnetic tags for the first performing differ from the magnetic tags for the second performing.

15. A method for clinical evaluation comprising:

capturing cells from a patient blood sample according to the method of claim 8 to provide captured cells; and quantifying the captured cells.

16. The method of claim 15, wherein the quantifying the captured cells includes providing a first fluorescent marker that binds specifically to a first cell type, a second fluorescent marker that binds specifically to a second cell type, and a third fluorescent marker that binds specifically to both the first cell type and the second cell type.

17. A method for clinical evaluation of cancer comprising clinically evaluating circulating tumor cells according to the method of claim 15.

18. A method for clinical evaluation of disease states comprising clinically evaluating lymphocytes according to the method of claim 15.

* * * * *