

microfluidic sorting device; (b) providing a buffer stream to the microfluidic sorting device; (c) magnetizing a magnetic field gradient generator to divert at least some of the magnetic species from the sample to the buffer stream; and (d) collecting at least a portion of the buffer stream comprising purified magnetic species at a collection outlet channel. In some embodiments, the collected magnetic species includes target species associated with magnetic particles.

[0013] The magnetic field gradient generator and the flow channel configuration may have various configurations as mentioned above. For example, providing the sample may involve providing two sample streams on opposite sides of the buffer stream in the microfluidic sorting device. Also, magnetizing the magnetic field gradient generator may involve applying an external magnetic field from a permanent magnet or an electromagnet to the magnetic field gradient generator.

[0014] The methods may include additional operations such as, but not limited to, detecting the purified target species in the collected buffer stream, amplifying a component, e.g., nucleic acid, of the target species in the microfluidic sorting device, lysing cells in the microfluidic sorting device, and separating components of the sorted target species, e.g., separating genetic material from target viruses, in the microfluidic sorting device.

[0015] Other methods involve (a) flowing a sample into a microfluidic sorting device having a magnetic field gradient generator to thereby capture at least some the magnetic particles; (b) removing or reducing a magnetic field applied to the magnetic field generator to thereby release captured magnetic particles; and (c) collecting purified target species with at least some of the magnetic particles at a collection outlet channel. In this method, the sample includes a target species and magnetic particles having an affinity for the target species.

[0016] Yet another aspect of the invention pertains to integrated microfluidic devices or systems. In some embodiments, an integrated microfluidic sorting device includes the following elements: (a) a magnetic field gradient generator for exerting a magnetic force on a sample to divert magnetic particles in the sample to a collection channel; (b) an amplification station for amplifying nucleic acid of a target species associated with the magnetic particles in the collection channel; and (c) a detection station for detecting amplified nucleic acid. The microfluidic sorting device may also include a cell lysis station, a labeling station for labeling target species with magnetic particles, etc.

[0017] In certain embodiments, an integrated microfluidic sorting device includes the following elements: (a) a labeling station for labeling target species in a sample with magnetic particles having an affinity for the target species; (b) a magnetic field gradient generator for exerting a magnetic force on the sample to divert magnetic particles in the sample to a collection channel; and (c) a detection station for detecting the target species. In some cases, the device may also include a second labeling station for labeling diverted target species with a fluorophore having an affinity for the target species or for the magnetic particles. In some cases, the device may include a sample reservoir disposed upstream from the magnetic field gradient generator.

[0018] In still other embodiments, an integrated microfluidic sorting device may include the following elements: (a) a magnetic field gradient generator for exerting a magnetic force on a sample to divert magnetic labeled target species, e.g., cells or viruses, in the sample to a collection channel; (b)

a first detection station for detecting magnetic labeled target species, e.g., cells or viruses, diverted to the collection channel; (c) a component release station for releasing components from the magnetic labeled target species, e.g., cells or viruses; and (d) a second detection station for detecting released components of the magnetic labeled target species, e.g., cells or viruses. Such a device may also include a component manipulation station for modifying released components to facilitate their detection in the second detection station. As an example, the component manipulation station may include an amplification station for amplifying nucleic acid of the magnetic labeled target species, e.g., cells or viruses. The device may optionally include a labeling station for labeling target species, e.g., cells or viruses, in the sample with magnetic particles having an affinity for a target species on surfaces of target cells or viruses.

[0019] These and other features and advantages of the invention will be presented in further detail below with reference to the associate drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] FIGS. 1A and 1B provide a top view of the channels and magnetic field gradient generating structures in one example of a microfluidics device.

[0021] FIG. 2 is a cross sectional diagram of a magnetic field generating element showing contours of a simulated magnetic field distribution near the MFG element that is 20 μm in width and 0.2 μm in thickness, with the assumption that the external magnet magnetized the MFG element to saturation (6,000 Gauss) along the horizontal direction.

[0022] FIGS. 3A-3E are diagrams of various arrangements of peg or pin-type as well as strip and chevron-type magnetic field generating elements in accordance with various embodiments.

[0023] FIGS. 4A-4G are diagrams of various inlet and outlet channel configurations for buffer switching structures in accordance with certain embodiments.

[0024] FIG. 5A is a schematic diagram of a multistage sorting structure in accordance with certain embodiments.

[0025] FIG. 5B is a schematic diagram of a fractionating sorting station.

[0026] FIG. 5C is a flow chart of operations associated with a cell fractionating sorting device having an integrated cell detector.

[0027] FIGS. 6A and 6B together constitute a process flow diagram showing a method of using a CMACS device in accordance with an embodiment of the invention.

[0028] FIG. 7A is a generic depiction of a multi-module integrated microfluidics device or system in accordance with certain embodiments.

[0029] FIGS. 7B, 7C and 7D are block diagrams showing integrated devices or systems in accordance with various embodiments.

[0030] FIG. 8 is a schematic diagram of a peptide library screening and epitope mapping example using a microfluidic sorting device. Bacterial cells displaying peptides complementary to the antibody-binding region are captured on superparamagnetic beads, allowing continuous-flow separation by magnetophoresis. The binding population is then either amplified by growth for a further round of labeling and sorting, or plated on solid media to isolate single clones for sequence determination.

[0031] FIG. 9 is a series of three graphs showing results of flow cytometric analysis of the CMACS selection: A peptide