

throughput concentrated target solution (sample components attached to the magnetic particles) through a buffer/target outlet channel 469. The depleted sample streams exit via waste outlet channels 471 and 473.

[0083] In some examples, the buffer and sample streams may be stacked vertically within a channel or sorting region. Obviously, devices such as those depicted in FIGS. 4A-4E, which are normally operated in horizontal arrangement can be turned by 90 degrees to a vertical orientation. However, a device may also be designed such that when the substrate lies flat on a surface, the buffer and sample streams flow within the sorting region on top of one another. One example of such device is depicted in FIGS. 4F (cross sectional view) and 4G (top view).

[0084] As shown in FIGS. 4F and 4G, a vertical sorting station 477 includes vertically stacked sample and buffer streams (479 and 481, respectively) flowing left to right, with the buffer stream flowing over top the sample stream in this example. Magnetic and non-magnetic particles (487 and 489, respectively) enter with the sample stream. A vertical separator 483 at the inlet side of station 477 defines the terminus of separate conduits for sample and buffer streams 479 and 481. Flowing past separator 483 the two streams are in contact and exposed to a magnetic field gradient produced using a series of parallel MFG strips 485 oriented in the direction of flow. As shown in FIG. 4F, magnetic particles are attracted toward the MFG strips and deflect upward into the buffer stream 481. They flow out of the sorting station in the buffer stream through a conduit defined by a separator 487. As shown in FIG. 4F, the interface between streams 479 and 481 is depicted as a dotted line. The relative positions of separators 483 and 487 allow bleedout of the buffer solution into the lower outlet—which is a waste channel.

[0085] Many other buffer switching structures are within the scope of the invention. In an example presented below, for instance, a multi-layer network or flow channels is provided with the buffer channels being provided at one layer of a device and the sample channels being provided at a different layer of the device. In this manner, the paths of the various flow lines can cross over one another without actually intersecting (analogous to multiple layers of metallization in an integrated circuit design). In some embodiments, the buffer and sample lines come together on the same level only as necessary to implement sorting modules. Such designs permit single entry ports for sample and buffer (as well as single outlet ports for waste and target collection) while providing parallel processing for high throughput.

[0086] The above embodiments contemplate that magnetic particles (e.g., magnetically labeled target species) move through the sorting station during a sorting process. While this movement is typically envisioned to be continuous, that is not necessarily the case. In some cases, during their transport the magnetic species may become temporarily suspended against the flow of sample and/or buffer mediums. This situation becomes increasingly likely as the force exerted on the magnetic particles by the MFGs increases relative to the force exerted by the flow field.

[0087] In some embodiments, a sorting device is designed to temporarily hold magnetic particles in place within the sorting station. Later, they are released and collected. In such embodiments, the magnetic particles stop moving through the sorting station while the other sample components (non-magnetic) flow through and out of the station, thereby purifying the magnetic particles. Only after the non-magnetic sample

components have flowed out of the sorting chamber are the magnetic components released and separately collected at an outlet of the sorting station. The design of the sorting station may be relatively simple such as the designs shown in FIGS. 1A, 1B, 4A, 4C, 4F, etc.

[0088] In a typical example, the sample flows into the sorting station, with or without concurrently buffer flowing. The MFG is controlled to provide a field gradient that is sufficiently strong to hold most magnetic particles in place against the hydrodynamic drag force exerted by the flowing fluid. After most or all of the sample has flowed clear of the sorting station, the magnetic components may be released by modifying the magnetic field gradient and/or increasing the hydrodynamic force. Concurrently, buffer may be introduced into the sorting station so that the previously suspended magnetic components (now purified) flow out of the chamber in a buffer solution. In certain embodiments, the magnetic field of an MFG is controlled using an electromagnet so that a strong field gradient is produced early in the process (during capture of the magnetic particles) and then reduced or removed later in the process (during release of the particles). In other embodiments, permanent magnets may be used, which are mechanically movable into and out of proximity with the MFG elements (e.g., strips, pins, etc.), such that the magnetic field gradient in the sorting region can be increased and decreased to effect capture and release of the magnetic particles.

[0089] A capture and release protocol such as this is particularly advantageous when using relatively small target species such as viruses which have a tendency to become entrained in a boundary layer of a flow field within a microfluidic device. In certain embodiments, the following sequence of operations is employed. First, a sample such as a nasal swab potentially containing viral or components expressing a target moiety is mixed with small magnetic nanoparticles coated with a capture moiety (e.g., an antibody) specific for the target moiety. This mixing may take place on or off the microfluidic sorting device. After this labeling, the sample is then and flowed into a sorting station having an MFG which can have its magnetic field temporarily removed or reduced as described. If the sorting chamber has multiple inlets, buffer may be delivered through one or more of these inlets and sample through one or more others. After flowing a defined quantity of sample through the sorting chamber (e.g., all of the sample), the magnetic field to the MFG is reduced or removed and concurrently the sample inlet flow is replaced with buffer flow such that only buffer flows through the sorting station. The purified sample component presenting the target moiety is then collected at an outlet of the sorting chamber, which may be located directly downstream from MFG elements that held the magnetic particles.

[0090] Generally, the buffer entering the sorting region should contain little if any sample. It should provide a medium for collecting relatively pure target material from the sample, as carried by the magnetic particles. Therefore it preferably should contain relatively little sample material that might interfere with subsequent detection and/or treatment of the target material. Further, the buffer should be compatible with both the target and the magnetic particles that carry the target. Thus, the buffer may aqueous or non-aqueous depending on the sample being analyzed. For some applications, the buffer should have a density and composition that maintains