

ticles **103**, however, experience an effective force that is a vector sum of F_{drag} and $F_{magnetic}$, which is the force exerted on them by the magnetic field gradient as they pass over MFG elements in the sorting region. As can be seen in the figure, the resulting force vector “guides” magnetic particles **103** along the magnetic strips and across a laminar stream boundary into the buffer stream (i.e., toward the center of sorting region **111**). This process is sometimes referred to as “buffer switching.” As a consequence of buffer switching, magnetic particles **103** are directed toward collection channel **115** in a buffer stream, while non-magnetic components **105** are directed toward waste outlet channels **113a** and **113b**. The output of collection channel **115** contains a significantly enriched composition of the target component, as carried by the magnetic particles. As indicated, the magnetic particles are typically coated with a target capture moiety.

[0041] A different embodiment is shown in FIG. 1B. As shown in this figure, the locations of the sample and buffer streams are reversed such that sample (including magnetic particles **103** and non-magnetic particles **105**) flows in a central stream of the sorting device and buffer flows in two outer streams straddling the sample stream. In this example, the MFGs again comprise a series of strips at the interfaces of the sample and buffer streams. However, the strips in this example are angled in the opposite direction (compared with the strips in the embodiment of FIG. 1A) to thereby guide the magnetic particles out of the sample stream and into the peripheral buffer streams. In certain embodiments, the strips are configured so as to impart little if any influence on bulk fluid flow through the sorting region.

[0042] As shown in FIG. 1B, buffer enters the sorting station via inlet channels **121a** and **121b**. Sample enters via a central inlet channel **123** and flows as a stream along side the buffer streams in a sorting region **125**. There, the sample stream encounters magnetic strips **127** which guide the magnetic particles **103** outward and into the buffer streams. The magnetic particles in the buffer streams exit collection channels **129a** and **129b**. Waste, including non-magnetic particles, exits a waste channel **131**. This approach can provide an advantage of providing a sample stream that need not change direction upon entry into the sorting region. As a consequence, it is unlikely that cells or other analyte component will become attached the channel walls.

[0043] As can be seen from the relative dimensions of the inlet and outlet channels of the sorting stations of FIGS. 1A and 1B, some buffer streams “bleedout” and flows out the waste channel. This reduces the likelihood that components from the sample stream will pass through the collection channel. As a result, the high purity of target in the collection stream will not be compromised.

[0044] The relative dimensions of the channels together with the size and arrangement of the MFG structures are chosen to balance and optimize the desired throughput, purity, and recovery of the target from the sample stream. In addition, it is usually important to ensure that there will be no backflow in the channels. Some examples of MFG and hydrodynamic design parameters and appropriate value ranges for these parameters will be presented below.

[0045] Various computational tools are available for modeling the fluid flow and magnetic field gradients to ensure that the hydrodynamics and field gradient of a given design meet the necessary performance criteria. Examples of such tools include PSpice from Cadence Design Systems, San Jose,

Calif., FemLab from Consol Ltd., Los Angeles, Calif., and Mathematica from Wolfram Research, Champaign, Ill.

[0046] In certain embodiments, the device performance is characterized in terms of one or more of the following metrics: throughput, purification, and recovery. Obviously, the actual values and balance of these performance metrics depend on the goals of the application and the unique set of technical constraints imposed by the application. Still it is worth considering these parameters for comparison to other devices. Example ranges that can be realized using embodiments of this invention will be presented below.

[0047] Magnetic Field Gradient Generating Structures

[0048] The magnetic field gradient is responsible for the magnetic force exerted on magnetic particles in microfluidic devices. In weakly diamagnetic media such as most buffer solutions, the magnetophoretic force on a paramagnetic particle can be approximated as $\vec{F}_{magnetic} = V_m \Delta\chi \cdot \nabla(B^2/2\mu_0)$,

where (μ_0) is the permeability of free space, B is the magnetic flux density, $\Delta\chi = \chi_{particle} - \chi_{medium}$ is the differential magnetic susceptibility of the particle relative to its suspension medium, and V_m is volume of the paramagnetic particle. Thus, the force depends on the gradient of the square of the flux density B. For many applications such as those described below, where superparamagnetic particles are in the saturation regime, the total volume magnetization ($\vec{m}_p = V_m \Delta\chi \cdot \vec{H}$) is constant and the equation for the magnetophoretic force on a superparamagnetic particle can be simplified to $\vec{F}_{magnetic} = \vec{m}_{sat} \nabla(|\vec{B}|)$, where m_{sat} is the saturated magnetization of the particle. Since the direction and magnitude of the force on a superparamagnetic particle are governed by the gradient of the applied field, magnetophoretic separation devices may be designed to accurately control this parameter.

[0049] The size and direction of the magnetic field gradient produced via an MFG depends on the applied magnetic field (typically provided by an external magnet proximate the sorting region) as well as the construction of the MFG. Pertinent parameters of MFG construction include the MFG material (s), the size and geometry of the MFG, and the orientation of the MFG with respect to the fluid flow and external magnetic field.

[0050] Of particular importance, the shape and arrangement or pattern of the elements making up an MFG should account for the hydrodynamics of the microfluidic device in the sorting channel. See for example the vector combination shown in FIG. 1. In certain embodiments, the direction of the gradient generated by an MFG be in a direction that promotes buffer switching toward a target collection region. In certain embodiments, the magnetic force exerted in this direction is greater than the component of drag force exerted in the opposite direction. Thus, in some embodiments, $F_d \sin \theta < F_m$, where θ is the angle between the direction of flow and the magnetic field gradient generating structures (for linear strips of these elements). An example of gradient magnitude and direction calculated with Mathematica™ is presented in the examples below.

[0051] The material from which an MFG element is made should have a permeability that is significantly different from that of the fluid medium in the device (e.g., the buffer). In certain cases, the MFG element will be made from a ferromagnetic material. Thus, the MFG element may include at least one of iron, cobalt, nickel samarium, dysprosium, gadolinium, or an alloy of other elements that together form a