

ing multiple markers. Obviously, the idea can be extended to greater numbers of markers, three, four, etc.

[0112] Sorting Performance

[0113] The CMACS devices of this invention may be characterized by certain performance metrics. As indicated, these include at least (i) purity of the final target, (ii) throughput, and (iii) 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. Throughput refers to the number of analyte species (e.g., cells) that can be processed in a given amount of time. Purification refers to the purity of the purified target analyte collected from the microfluidics device. Obviously, this is strongly dependent upon the initial purity, the number of separation stages employed, etc. Note that in some embodiments, such as the one depicted in FIG. 5A, the multiple separation stages are integrated in a device or system. Each sequential separation stage will further purify the target. Finally, the recovery refers to the percentage of the target that is recovered. Typically, there will be losses but one advantage of the microfluidic devices disclosed herein is their ability to provide high recovery rates for rare species. In some examples, a lossless recovery may occur.

[0114] The values of these various parameters achievable using certain embodiments of the present invention will be presented here. As indicated, a target collected from a sorting device of this invention routinely achieves high purity. In one case, it was found that a CMACS device of this invention was capable of enriching a target by >10,000-fold in a single pass at a high throughput 1,000,000 particles/second/microchannel. Typical device designs sometimes have a throughput of at least about 10 microliters/hour/channel. In certain embodiments, the throughput is at least about 100 ml/hour/channel. Obviously, these throughput rates scale with the number of parallel channels in a device or system. Thus, for example, some five-channel devices may have a throughput of at least about 500 ml/hour.

[0115] The CMACS devices of this invention provide, in certain embodiments, recovery levels of rare components (e.g., rare cells) not previously achievable. In this context, recovery refers to the percentage of the target that is recovered. In some cases, the recovery rate is at least about 50%, even when sorting samples having a very low fraction of target (e.g., the initial concentration of target of about 10^{-5} or less target/total species (target and non-target)) and when operated at commercially reasonable throughput rates. In some embodiments, the recovery level reaches at least about 75% when sorting samples having an initial concentration of target of about 10^{-5} target/total species. It has also been found that sorting modules of this invention can recover at least 90% and even 100% of target in samples having initial concentrations of target of about 10^{-5} target/total species or less. In certain embodiments, these recovery rates can be achieved in samples having initial concentrations of target of about 10^{-6} target/total species or less, and in some cases in samples having initial concentrations of target of about 10^{-7} target/total species or less,

[0116] Methods of Using Magnetophoretic Devices

[0117] As indicated, the CMACS devices of this invention may be used in many different applications. Among these are recovering rare cells, screening molecular libraries, sorting magnetic materials in industrial settings, etc.

[0118] One general approach to using a CMACS device in accordance with an embodiment of the invention is presented in the flow chart of FIGS. 6A and 6B. As shown there, the process can be generally divided into a pre-processing stage, a magnetophoretic sorting stage, and a post-processing stage. Each of these stages may constitute one or more sub-stages. For example, as indicated in the discussion above a sorting device may include multiple magnetophoretic stages. In the example of FIGS. 6A and 6B, operations 605, 607, and 609 fall into the pre-processing stage, operations 611, 613, and 615 constitute the magnetophoretic sorting stage, and operations 617, 619, and 621 constitute the post-processing stage. In some embodiments, all or some of the pre-processing operations are performed on an integrated device or system that also includes the magnetophoretic sorting station(s).

[0119] In the depicted example, a target purification process begins with provision of a sample to be flowed through the CMACS device for sorting. See block 603. The term "sample" as used herein refers to a material or mixture of materials, typically, although not necessarily, in fluid form, containing one or more target species (e.g., biomolecules) of interest. If the sample is not already in liquid form it will be suspended, dissolved or otherwise incorporated in a liquid medium for delivery to a microfluidic sorting device. In certain embodiments, the sample is a physiological sample. The physiological sample may be a fluid or solid, where the solid may or may not be treated to render it fluid. Samples of interest include, but are not limited to: blood, serum, urine, plasma, sputum, as well as cell and tissue homogenates etc, from animal, plant and microbial sources. The sample may be pretreated as is desired and/or convenient, where pretreatment may include removal of particulate matter, viscous material, insoluble material, and the like. Optionally, sample components that bind non-specifically with the magnetic particles are removed in a sample pretreatment operation in which the sample is contacted with a pool of magnetic particles. See block 605. This optional process may be appropriate when, for example, the magnetic particles are coated with streptavidin or other moiety to which some sample components are reasonably likely to bind. After the magnetic particles and sample remain in contact for a period of time, the particles are removed from the sample by, e.g., a negative magnetophoretic operation. At least some of the non-specifically binding sample components will thereby be removed from the sample.

[0120] Next, the target species in the sample are labeled with magnetic particles. See block 607. Typically, this simply involves contacting the sample with magnetic particles that have been coated with an antibody or other capture moiety specific for the target, where the antibody or other capture agent has suitable binding affinity and specificity for the target species. In certain embodiments, the antibody or other capture moiety has an affinity for its target species of at least about 10^{-4} M, such as at least about 10^{-6} M and including at least about 10^{-8} M, where in certain embodiments the antibody or other capture moiety has an affinity for its target species of between about 10^{-9} and 10^{-12} M. In certain embodiments, the antibody or other capture moiety is specific for the target species, in that it does not significantly bind or substantially affect non-target species that may be present in the sample of interest. In some cases, the sample and magnetic particles may be contacted with a bifunctional reagent having one moiety that binds with a target species and another moiety that binds with the surface of magnetic particles. If the