

described above formed therein. FIG. 14 illustrates a plurality of the channels 202 formed in the microfabricated chip 214 that can be configured for receiving a sample introduced through the inlet 206 and/or filter 208. An analysis region 216 can be provided in proximity to an output channels 218 of the channels 202 to monitor, sort, count, image, or otherwise analyze the focused streams of particles. The output channels 218 can be provided to receive and/or collect one or more focused streams of particles per channel after the streams travel through the analytical region of the chip. One or more output channels 218 can also be provided for separating particles of a predetermined type away from a main stream of particles via a microfluidic valve. A controller 220, which can include any number of hardware, software, and analytical elements can be included to assist in pre-sample processing, pumping, flow rate regulation, valve operation, and any analysis to be performed on focused particles. After focusing, particles can be collected from the output channels into a reservoir or outlet 212 for initial or additional analysis elsewhere, or for disposal.

**[0180]** Referring in more detail now to the system 200 described above, one or more inlets can be provided for introducing samples and/or other substances into the channels within the system. An inlet can generally contain an inlet channel, a well or reservoir, an opening, and any other features which facilitates the entry of particles into the system. The opening in the inlet can be in a floor of the microfabricated chip, to permit entry of the sample into the device. The inlet can also contain a connector adapted to receive a suitable piece of tubing, such as liquid chromatography or HPLC tubing, through which a sample can be supplied from an external reservoir. The inlet is generally in fluid communication with the channels and is generally upstream therefrom. As noted above, a sample can be diluted or concentrated before entering the channels and a separate inlet can be provided for introducing such a diluent or concentrate to mix with the sample to achieve a desired particle to volume ratio. Additional inlets can be provided for other substances having labels or tags as will be described below, to facilitate mixing with the sample before introduction into the channels. Any number and combination of inlets can be provided. In the same way, any number of outlets can be provided for receiving and collecting the sample and focused streams of particles within the sample, as will be described in more detail below.

**[0181]** Various methods can be used for identifying ordered and focused particles of a predetermined type within the channels. Labels or tags for identifying or manipulating particles to be focused within the channels can be introduced into the sample before, during, and/or after introduction of the sample into the system. Labeling or tagging of particles is well known in the art for use, for example, in fluorescence-activated cell sorting (FACS) and magnetic-activated cell sorting (MACS), and any of the various methods of labeling can be used in the systems described herein. In general, any techniques or methods related to the identification and/or manipulation of particles based on their size, weight, density, electrical properties, magnetic properties, dielectric properties, deformable properties, fluorescent properties, surface characteristics, intraparticle characteristics such as interparticle spacing, and/or rotational characteristics such as rotational rate, rotational frequency, and variation in rotational rate over a cycle, can be used, to name a few. In other embodiments, characteristics of a particle can be changed so that the particle can be manipulated and/or identified based on its

changed characteristic. For example, the size of a particle can be changed by adding a bead, particle, or other tag to it such that the particle will be shifted and focused into a particular stream, and perhaps a particular channel branch or outlet, based on its changed size. Exemplary labels can include, but are in no way limited to quantum dots, pentamers, antibodies, nano-beads, magnetic beads, molecules, antimers, affinity label beads, micro-beads, cell/cell signaling, etc. There is no limit to the kind or number of particle characteristics that can be identified or measured using known labeling techniques, provided only that the characteristic or characteristics of interest be sufficiently identifiable. Exemplary labeling methods and techniques are discussed in detail in U.S. Pat. No. 6,540,896 entitled, "Microfabricated Cell Sorter for Chemical and Biological Materials" filed May 21, 1999; U.S. Pat. No. 5,968,820 entitled, "Method for Magnetically Separating Cells into Fractionated Flow Streams" filed Feb. 26, 1997; and U.S. Pat. No. 6,767,706 entitled, "Integrated Active Flux Microfluidic Devices and Methods" filed Jun. 5, 2001; all of which are incorporated by reference in their entireties.

**[0182]** As noted above, particles can be labeled or tagged prior to introduction of the sample into the system. Alternatively or in addition, a secondary inlet can be included in the system to facilitate introduction of labels in parallel with introduction of the sample such that the labels and sample mix while entering the channels. In other embodiments, inlet ports can be included at various locations within the system along channel lengths such that mixing of labels and particles can occur within the channels before, during, and/or after focusing of the particles.

**[0183]** Various techniques exist for moving the sample through the channels described herein and in general, the system can include a pumping mechanism for introducing and moving the sample into and through the channels. The pumping mechanism can also regulate and control a flow rate within the channels as needed. A specific pumping mechanism can be provided in a positive pumping configuration, in a negative pumping configuration, or in some combination of both. In one embodiment, a sample can be introduced into the inlet and can be pulled into the system under negative pressure or vacuum using the negative pumping configuration. A negative pumping configuration can allow for processing of a complete volume of sample, without leaving any sample within the channels. Exemplary negative pumping mechanisms can include, but are not limited to, syringe pumps, peristaltic pumps, aspirators, and/or vacuum pumps. In other embodiments, a positive pumping configuration can also be employed. A sample can be introduced into the inlet and can be injected or pushed into the system under positive pressure. Exemplary positive pumping mechanisms can include, but are not limited to, syringe pumps, peristaltic pumps, pneumatic pumps, displacement pumps, and/or a column of fluid. Oscillations caused by some pumping mechanisms, such as a peristaltic pump, can optionally be damped to allow for proper focusing within the channels. Alternatively, the oscillations can be used to encourage mixing of particles and labels within the channels. As will be appreciated by those skilled in the art, any other pumps configured for pumping fluid can be used depending on the requirements of the system. A single pump can be used for all pumping requirements, including introduction of the sample, adjustment substances, and labels. Alternatively, independent pumping systems can be used to control introduction of independent samples, substances, and labels into the system. Generally, pumps can be