

chemical etching, milling, diamond cutting, Lithographie Galvanoformung and Abformung (LIGA), and electroplating. For example, for glass, traditional silicon fabrication techniques of photolithography followed by wet (KOH) or dry etching (reactive ion etching with fluorine or other reactive gas) can be employed. Techniques such as laser micro-machining can be adopted for plastic materials with high photon absorption efficiency. This technique is suitable for lower throughput fabrication because of the serial nature of the process.

**[0189]** For mass-produced plastic devices, thermoplastic injection molding, and compression molding can be used. Conventional thermoplastic injection molding used for mass-fabrication of compact discs can also be used to fabricate the microfluidic chips described herein. For example, channel features as well as other features required on the chip can be replicated on a glass master by conventional photolithography. The glass master is electroformed to yield a tough, thermal shock resistant, thermally conductive, hard mold. This mold can serve as the master template for injection molding or compression molding the features into a plastic device. Depending on the plastic material used to fabricate the chip and the required throughput of the finished system, compression molding can be chosen as a preferred method of fabrication. Compression molding, also known as hot embossing or relief imprinting, has the advantage of being compatible with high molecular weight polymers, which are excellent for small structures. For high aspect ratio structures, injection molding can be a preferred method of fabrication but is most suitable for low molecular weight structures.

**[0190]** A microfluidic chip such as those described herein can be fabricated in one or more pieces that are then assembled. In one embodiment, separate layers of the chip can contain channels for a single fluid. Layers of the chip can be bonded together by clamps, adhesives, heat, anodic bonding, or reactions between surface groups (wafer bonding). Alternatively, a chip having channels in more than one plane can be fabricated as a single piece, for example using stereolithography or other three-dimensional fabrication technique.

**[0191]** In one particular embodiment, the chip can be formed of PMMA. The features, including channels, can be transferred onto an electroformed mold using standard photolithography followed by electroplating. The mold can be used to hot emboss the features into the PMMA at a temperature near its glass transition temperature (105° C.) under pressure (5 to 20 tons). The mold can then be cooled to enable removal of the PMMA chip. A second piece used to seal the chip, composed of a similar or dissimilar material, can be bonded onto the first piece using vacuum-assisted thermal bonding. The vacuum prevents formation of air gaps in the bonding regions. As will be appreciated by those skilled in the art, the chip can be formed of any material or combination of materials as needed for specific pressure requirements within the channels, as well as specific channel geometries and size requirements.

**[0192]** As illustrated in FIG. 14 and as noted above, the system can optionally include a controller. The controller can include, be operatively connected to, and/or control various analytical equipment or analyzers disposed within the chip and/or around the chip to accommodate processing and analysis of focused particles as the particles enter the analysis region, as well as to control various flow rates, pumping systems, and/or valve systems. An analyzer can include any

sample analyzing device known in the art, such as, for example, a microscope, a microarray, a cell counter, etc. An analyzer can further include one or more computers, databases, memory systems, and system outputs, for example, a computer screen or printer. In some embodiments, an analyzer can include a computer readable medium, for example, floppy diskettes, CD-ROMS, hard drives, flash memory, tape, or other digital storage medium, with a program code having a set of instructions for detection or analysis to be performed on the focused stream or streams of particles. In some embodiments, computer executable logic or program code of an analyzer can be loaded into and/or executed by a computer, or transmitted over some transmission medium, such as over electrical wiring or cabling, through fiber optics, or via electromagnetic radiation. When implemented on a general purpose microprocessor, the computer executable logic configures the microprocessor to create specific logic circuits. In one embodiment, the computer executable logic performs some or all of the tasks described herein including sample preparation, dilution, concentration, pumping, flow rate regulation, detection, and/or analysis. In some embodiments, the controller can be at a location remote from the chip, channels, pumping mechanism, and other components of the system. For example, the chip, channels, and other system components can be located in one room, building, city, or location and the controller can be located in another room, building, city, or location. The controller can be configured to communicate wirelessly with the components from a remote location to configure, control, program, and/or otherwise manage any and all aspects of the procedures and devices related to the focusing of particles and analysis of focused particles as described herein. The controller can communicate with the other components in a system of the invention using any wireless technology known in the art, including but not limited to, Bluetooth, the IEEE 802.11 standard, Wi-Fi, broadband wireless, and/or any wireless communication that can be accomplished using radio frequency communication, microwave communication, and infrared communication. The controller may utilize point-to-point communication, point-to-multipoint communication, broadcasting, cellular networks, and/or wireless networks. The controller may also utilize wired networks such as local area networks, wide area networks, and/or the Internet.

**[0193]** It is contemplated that the system described herein can be packaged together as a kit or singular unit for diagnostics and point-of-care applications. In other embodiments, some, any, and/or all components can be separate to work in individualized locations to maximize size and/or efficiency, for example in industrial applications. In one embodiment, a kit or singular unit for diagnostics and point-of-care applications can include a microfabricated chip having channels formed thereon, a pumping mechanism, valves, filters, controller, and any other components that may be required for a particular application. The components and channel configurations can vary as needed in a particular unit. In some embodiments, the unit can be in the form of an open system in which various components of the system, for example, the chip, can be replaced as needed by a user. In other systems, the unit can be in the form of a closed system in which no components can be replaced by the user. In any of the embodiments and configurations, any and all components of the system can be single use, disposable, time limited, reconditionable, and/or reusable.