elsewhere in the microfluidic substrate assembly. Such operational devices, including, for example, devices integrated as an external component-on-board mounted in fluid-tight fashion to any surface of the substrate and/or devices embedded within the body of the substrate, in accordance with preferred embodiments of the microfluidic substrate assembly, are micro-scale devices, as defined above.

[0011] In accordance with another aspect, fluid handling devices are provided comprising a multi-layer laminated substrate defining at least one fluid inlet port and at least one microscale fluid flow channel within the multi-layer laminated substrate in fluid communication with the inlet port for transport of fluid to be tested. At least one operative component is mounted aboard the multi-layer laminated substrate in communication with the microscale fluid flow channel. In certain preferred embodiments the mounted component (referred to here also as a "component-on-board" or by similar term) is in fluid communication with the microchannel(s) in the substrate. The component-on-board can be any of numerous components useful for fluid separation methods or other operations. Exemplary components include heaters, coolers, pumps, fluid reservoirs, mixers, e.g. ultrasonic mixers, sensors, the fluid separation conduit cartridges as disclosed in the commonly assigned U.S. Patent Applications incorporated herein by reference, and other devices discussed here. As discussed further below, any necessary or desired function not performed by a suitable component-on-board can be performed by other equipment associated with the microfluidic substrate assembly. As an example of components of the multi-layer laminated substrates disclosed here, or the microfluidic substrate assembly incorporating or integrating such fluid-handling substrate, in certain embodiments will advantageously comprise a heating/cooling element for controlling the temperature of fluid being tested or measured, e.g., an electrical heating element and/or a refrigeration element. An electrical heating element may be integrated into the substrate, with electrical elements for power mated to matching electrical contacts in a larger associated device which receives the substrate. Alternatively, the larger associated device may include internal or external heating devices, such as a laser or other source of electromagnetic energy. A microprocessor may be used to regulate the heating element and/or control other functions of the microfluidic substrate assembly. A thermocouple may also be provided in the substrate in electrical contact with the associated device to allow such microprocessor or other electronic controller to detect and maintain desired fluid temperatures. A cooling element, such as a miniature thermoelectric heat pump (Materials Electronic Products Corp., Trenton, N.J.), may also be included in the associated device for adjusting the temperature of the amplification chamber

[0012] In accordance with another aspect, fluid handling devices are provided comprising a generally planar multi-layer laminated substrate defining at least one fluid inlet port, at least one microscale fluid flow channel at each of more than one level within the multi-layer laminated substrate for transport of fluid to be tested, and at least one microchannel via extending between levels within the multi-layer laminated substrate for fluid communication between microscale fluid flow. Such channels are referred to in some instances below as interlayer microfluidic channels. In preferred embodiments, the microscale fluid flow channels at each of multiple levels within the substrate are formed at the surface-to-surface interfaces between layers of the substrate. Two levels of microchannels are formed, for example, by a PEEK or other plastic plate or disk having micromachined or micromilled grooves on both an upper and lower surface and sandwiched between two other layers of the substrate. A through-hole micromachined or otherwise formed in the plastic plate passing from an upper surface groove to a lower surface groove provides a fluid communication via, e.g. provides a fluid flow channel. In certain preferred embodiments one or both of the sandwiching layers of the substrate is a flexible sheet or film. As used here, the term "generally planar multi-layer laminated substrate" means card or cartridge-like, optionally being curvo-planar or otherwise irregular, but typically being rectilinear or right-cylindrical, and having a thickness less than about one third, preferably less than one quarter, more preferably less than about one fifth, e.g., about one sixth or less, the largest dimension of the major (i.e., largest) surface of the laminated substrate. The dimensions of the laminated substrate referred to here are measured without including any external components mounted on-board the substrate. Nor do they include electrical leads or connectors or conduits carrying sample fluid to or from the laminated substrate. One or both of the sandwiching layers can be welded or otherwise bonded, selectively or not, to the micromachined layer to provide fluid-tight sealing along the microchannels. Additional levels of microchannels are provided by stacking additional micromachined plates in the substrate. Directional references used here are for convenience only and not intended to limit the orientation in which the multi-layer laminated substrates are used. In general, the multi-layer laminated substrates can be used in any orientation; solely for purposes of discussion here, they are assumed to be in the orientation shown in the drawings appended hereto. One skilled in the art, given the benefit of this disclosure, will recognize that microchannels and vias of the multi-layer laminated substrate can have any suitable configuration including straight, curvo-linear, serpentine or spiral. The cross-sectional configuration of the microchannels can be regular, i.e., uniform, or irregular, to suit the needs of an intended application.

[0013] In accordance with another aspect, fluid handling devices are provided comprising a multi-layer laminated substrate defining at least one fluid inlet port and at least one microscale fluid flow channel within the multi-layer substrate in fluid communication with the inlet port for transport of fluid to be tested, wherein at least one layer of the multi-layer laminated substrate is formed of plastic and the substrate assembly is operative and fluid tight at high fluid pressure in the microscale fluid flow channel. Certain preferred embodiments are fluid tight and operative at fluid pressures in excess of 100 psi, preferably in excess of 200 psi, more preferably in excess of 300 psi, most preferably at pressures greater than 500 psi. As used here psi preferably refers to psi gauge as opposed to psi absolute. Especially preferred embodiments are operative, including being fluid-tight along the periphery of the microchannels within the substrate, even at fluid pressure in the microscale fluid flow channel in excess of 1000 psi. Preferred embodiments employing plastic substrate layers in high pressure embodiments provide significant advantages in manufacturing cost and flexibility. In certain preferred embodiments, the microfluidic substrate assembly employs a multi-layer laminated substrate having rigid plates sandwiching plastic layer between them. The plastic layers optionally are welded one to another and the rigid plates sandwiching the multiple