

[0031] FIG. 19 depicts fluidics layers of a microfluidic chip with a reagent and bead rail.

[0032] FIG. 20 shows four stages (A, B, C, D) of a pumping cycle.

[0033] FIG. 21 shows a photograph of a system without pipette tips or TEC-tip manifold.

[0034] FIG. 22 shows a pneumatic manifold with cutouts for magnet cradles.

[0035] FIG. 23 shows pneumatic routing control of valves and pumps.

[0036] FIG. 24 shows a reaction scheme for preparing and analyzing an mRNA sample.

[0037] FIG. 25 depicts a reaction scheme for amplifying mRNA.

[0038] FIG. 26 shows a script for performing mRNA amplification.

[0039] FIG. 27 shows a script for performing the Eberwine process.

[0040] FIG. 28 shows experimental results for RNA purification using 0.125 uL SpeedBeads.

[0041] FIG. 29 shows experimental results for RNA purification using 0.125/4 uL SpeedBeads.

[0042] FIG. 30 shows experimental results for RNA purification using 0.125/40 uL SpeedBeads.

[0043] FIG. 31 shows experimental results for determining bead mixing accuracy.

[0044] FIG. 32 shows the results of three purification experiments with approximately 1.5 ug total RNA in a microfluidic chip.

[0045] FIG. 33 shows bus channel cutoff.

[0046] FIG. 34 shows the distribution of beads as a function of amount of RNA bound to them.

[0047] FIG. 35 shows the distribution of beads as a function of bead quantity.

[0048] FIG. 36 shows a table of how various experiments were configured.

[0049] FIG. 37 shows results from Experiment 1 and Experiment 2.

[0050] FIG. 38 shows results from Experiment 1 and Experiment 3.

[0051] FIG. 39 shows tables that summarize yield and amplification factors.

[0052] FIG. 40 shows results from Experiment 1 and Experiment 4.

[0053] FIG. 41 shows results from Experiment 1 and Experiment 5.

[0054] FIG. 42 shows the experimental design for a microarray analysis experiment.

[0055] FIG. 43 shows tables of aRNA yields for bench and chip generated samples

[0056] FIG. 44 shows graphs bBioanalyzer electropherograms of the samples before and after fragmentation.

[0057] FIG. 45 shows results of the experiments in a 4x4 comparison matrix.

[0058] FIG. 46 shows a comparison of chip results to bench results.

[0059] FIG. 47 shows that chip and bench fragmentation are indistinguishable.

separating, heating, cooling, and analyzing. The devices can include multiple components, such as a cartridge, a microfluidic chip, and a pneumatic manifold. FIG. 1 shows an exemplary device having a cartridge (101), microfluidic chip (103), and pneumatic manifold (113). These devices can be used to prepare samples for analysis by gene expression microarrays and to perform biochemical and enzymatic reactions for other purposes.

I. Device Components

A. Cartridges

[0061] A cartridge, also referred to as a fluidic manifold herein, can be used for a number of purposes. In general, a cartridge can have ports that are sized to interface with large scale devices as well as microfluidic devices. Cartridges or fluidic manifolds have been described in U.S. Patent Application No. 61/022,722, which is hereby incorporated by reference in its entirety. The cartridge can be used to receive materials, such as samples, reagents, or solid particles, from a source and deliver them to the microfluidic chip. The materials can be transferred between the cartridge and the microfluidic chip through mated openings of the cartridge and the microfluidic chip. For example, a pipette can be used to transfer materials to the cartridge, which in turn, can then deliver the materials to the microfluidic device. In another embodiment, tubing can transfer the materials to the cartridge. In addition, a cartridge can have reservoirs with volumes capable of holding nanoliters, microliters, milliliters, or liters of fluid. The reservoirs can be used as holding chambers, reaction chambers (e.g., that comprise reagents for carrying out a reaction), chambers for providing heating or cooling (e.g., that contain thermal control elements or that are thermally connected to thermal control devices), or separation chambers (e.g. paramagnetic bead separations, affinity capture matrices, or chromatography). Any type of chamber can be used in the devices described herein, e.g. those described in U.S. Patent Publication Number 2007/0248958, which is hereby incorporated by reference. A reservoir can be used to provide heating or cooling by having inlets and outlets for the movement of temperature controlled fluids in and out of the cartridge, which then can provide temperature control to the microfluidic chip. Alternatively, a reservoir can house Peltier elements, or any other heating or cooling elements known to those skilled in the art, that provide a heat sink or heat source. A cartridge reservoir can have a volume of at least about 0.1, 0.5, 1, 5, 10, 50, 100, 150, 200, 250, 300, 400, 500, 750, 1000, 2000, 3000, 4000, 5000 or more μL .

[0062] For example, FIG. 1 shows cartridge (101) with a reservoir with a port (115) opening to a side of the cartridge that can be used to receive materials from a pipette or any other large scale device. The port can also be adapted with fitting to receive tubing or a capillary to connect the cartridge to upstream fluidics. The reservoir can taper down to form a cartridge reservoir opening (117) that interfaces or aligns with an opening 105 in the fluidics layer of the microfluidic chip. The cartridge can have a reservoir that is sized to be larger than a pipette tip, such that a material can be pipetted directly into the microfluidic chip.

[0063] Each chip can be attached to the bottom surface of a Fluidic Manifold with silicone pressure sensitive adhesive (laser cut PSA, not shown). As noted above, a Fluidic Manifold can be designed to use pipette tips both as fluid input/output ports, and as incubation reservoirs. The tips can be

DETAILED DESCRIPTION OF THE INVENTION

[0060] The invention provides devices for fluid and analyte processing and methods of use thereof. The devices of the invention can be used to perform a variety of actions on the fluid and analyte. These actions can include moving, mixing,