otide sample under thermal cycling conditions suitable for creating PCR amplicons from the neutralized polynucleotide sample.

[0049] A multi-lane substrate that is heated by a heater unit described herein is configured to accept a number of samples in series or in parallel, in particular embodiments **12** samples, wherein the samples include at least a first sample and a second sample, wherein the first sample and the second sample each contain one or more polynucleotides in a form suitable for amplification. The polynucleotides in question may be the same as, or different from one another, in different samples and hence in different lanes of the substrate. The substrate typically processes each sample by increasing the concentration of a polynucleotide to be determined and/or by reducing the concentration of inhibitors relative to the concentration of polynucleotide to be determined.

[0050] FIG. **1** shows a schematic cross-sectional view of a part of an apparatus as described herein, showing input of sample into a microfluidic cartridge **100** via a pipette **10** (such as a disposable pipette that may be integrated into an automated dispensing hear **110**) and an inlet **102**. Inlet **102** is preferably configured to receive a pipette or the bottom end of a PCR tube and thereby accept sample for analysis with minimum waste, and with minimum introduction of air. Cartridge **100** is disposed on top of and in contact with a heater substrate **140**. Read head **130** is positioned above cartridge **100** and a cover for optics **131** restricts the amount of ambient light that can be detected by the read head. Heater substrate **140** is part of a heater unit (not shown in its entirety in FIG. **1**) that is disposed within an apparatus, as further described herein. Cartridge **120** is situated in a suitably configured receiving bay **112**.

[0051] The contact heat source typically includes a plurality of contact heat sources, each configured at the receiving bay to be independently thermally coupled to a different distinct location in a microfluidic cartridge received therein, whereby the distinct locations are independently heated. The contact heat sources can be configured to be in direct physical contact with one or more distinct locations of a microfluidic cartridge received in the bay. In various embodiments, each contact source heater can be configured to heat a distinct location having an average diameter in 2 dimensions from about 1 millimeter (mm) to about 15 mm (typically about 1 mm to about 10 mm), or a distinct location having a surface area of between about 1 mm^2 about 225 mm^2 (typically between about 1 mm^2 and about 100 mm^2, or in some embodiments between about 5 mm^2 and about 50 mm^2). Various configurations of heat sources are further described in U.S. patent application Ser. No. _____, entitled "Heater Unit for Microfluidic Diagnostic System" and filed on even date herewith.

Heater Unit

[0052] An exemplary heater unit **2020** is shown in FIG. **2**. The unit is configured to deliver localized heat to various selected regions of a cartridge received in a receiving bay **2014**. Heater unit **2020** is configured to be disposed within a diagnostic apparatus during operation, as further described herein, and in certain embodiments is removable from that apparatus, for example to facilitate cleaning, or to permit reconfiguration of the heater circuitry. In various embodiments, heater unit **2020** can be specific to particular designs of microfluidic networks and microfluidic substrate layouts.

[0053] FIG. **3** illustrates heating operation of a heater substrate as further described herein. A schematic of a heater/sensor chip is shown at left. An actual heater/sensor chip bonded to a PCB is in the center of the FIG., A thermal image of the same chip in operation showing highly localized heating (95° C.) in the PCR regions (yellow) is shown at right.

[0054] Shown in FIG. **2** is a heater unit having a recessed surface **2044** that provides a platform for supporting a microfluidic cartridge when in receiving bay **2014**. In one embodiment, the cartridge rests directly on surface **2044**. Surface **2044** is shown as recessed, in FIG. **2**, but need not be so and, for example, may be raised or may be flush with the surrounding area of the heater unit. Surface **2044** is typically a layer of material that overlies a heater chip or board, or a heater substrate, that contains heater micro-circuitry configured to selectively and specifically heat regions of a microfluidic substrate, such as in a cartridge, in the receiving bay **2014**.

[0055] Area **2044** is configured to accept a microfluidic cartridge in a single orientation. Therefore area **2044** can be equipped with a registration member such as a mechanical key that prevents a user from placing a cartridge into receiving bay **2014** in the wrong configuration. Shown in FIG. **2** as an exemplary mechanical key **2045** is a diagonally cutout corner of area **2044** into which a complementarily cutoff corner of a microfluidic cartridge fits. Other registration members are consistent with the heater unit described herein, for example, a feature engineered on one or more edges of a cartridge including but not limited to: several, such as two or more, cut-out corners, one or more notches cut into one or more edges of the cartridge; or one or more protrusions fabricated into one or more edges of the cartridge. Alternative registration members include one or more lugs or bumps engineered into an underside of a cartridge, complementary to one or more recessed sockets or holes in surface **2044** (not shown in the embodiment of FIG. **2**). Alternative registration members include one or more recessed sockets or holes engineered into an underside of a cartridge, complementary to one or more lugs or bumps on surface **2044**. In general, the pattern of features is such that the cartridge possesses at least one element of asymmetry so that it can only be inserted in a single orientation into the receiving bay.

[0056] Also shown in FIG. **2** is a hand-grasp **2042** that facilitates removal and insertion of the heater unit into an apparatus by a user. Cutaway **2048** permits a user to easily remove a cartridge from receiving bay **2014** after a processing run where, e.g., a user's thumb or finger when grabbing the top of the cartridge, is afforded comfort space by cutaway **2048**. Both cutaways **2042** and **2048** are shown as semicircular recesses in the embodiment of FIG. **2**, but it would be understood that they are not so limited in shape. Thus, rectangular, square, triangular, half-oval, contoured, and other shaped recesses are also consistent with a heater unit as described herein.

[0057] In the embodiment of FIG. **2**, which is designed to be compatible with an exemplary apparatus as further described herein, the front of the heater unit is at the left of the figure. At the rear of heater unit **2020** is an electrical connection **2050**, such as an RS-232 connection, that permits electrical signals to be directed to heaters located at specific regions of area **2044** during sample processing and analysis, as further described herein. Thus, underneath area **2044** and not shown in FIG. **2** can be an array of heat sources, such as resistive heaters, that are configured to align with specified locations of a microfluidic cartridge properly inserted into the