MICRO THERMAL CYCLER WITH SELECTIVE HEAT ISOLATION

Field of the Invention

[0001] The present invention generally relates to miniature automation devices, and more particularly to a micro thermal cycler with selective heat isolation.

Background of the Invention

[0002] Microfluidic technology has been applied broadly to chemical and biomedical applications. Microfluidic devices offer distinctive advantages of low manufacturing cost, high throughput, minimal reagent consumption, and high degree of automatability. Another advantage is that multiple operations can be performed simultaneously on a single microfluidic platform. Yet another advantage is that the devices can be automated for chemical and biological assays.

[0003] One of the biological assays being the focus for automation is the polymerase chain reaction (PCR) that artificially amplifies nucleic acids in-vitro. This amplification process is realized by a series of temperature cycles applied to the sample solutions which contain priming molecules for the reaction start, nucleotide triphosphates and the enzyme polymerase. For classical PCR assays, comparatively large sample volumes (about 500 down to 50 μL) are used in conventional thermocyclers. Sample and device size cause maximum heating and cooling rates of about 2-4 K/s and, therefore, periods for each temperature cycle of about 5 minutes. This means that the whole cycling process with up to 40 cycles takes at least 3 hours.

[0004] DNA analysis using PCR can be performed using smaller volumes. These volumes can be handled in miniaturized devices with low parasitic heat capacities. In these devices, high heating and cooling rates up to 50 K/s can be realized. Chip devices on silicon have been developed for a miniaturized thermocycling process. The heat capacity of such devices is minimal, and the power consumption is extremely low. High temperature ramp ups are realized by electrical heating of thin film resistors, cooling proceeds by an

efficient heat transfer to the surroundings supported for example by a small fan or other means.

[0005] Published patents and literature have shown various methods of controlled heating of micro areas on a chip. These publications use various combinations of different geometries and layouts of heating, sensing microelements and die substrates to enhance the performance of the PCR device.

[0006] Microfluidic devices are extensively explored for their applications in biomedical operations, especially in these circumstances where multiple operations are required for performing analysis/processing either sequentially or in parallel. For instance, identifying a target DNA sequence within a biological sample is very crucial in a large number of fields such as clinical diagnostics, forensic investigations, research, military applications, food and water testing, homeland security and drug research and development. With traditional DNA-analysis apparatuses, the identification of a target DNA sequence requires isolation of DNA samples with a DNA isolation kit, amplification of the target DNA sequence by PCR with a bulky PCR machine, and hybridization/sequencing to confirm the identity of the target DNA sequence with a bulky hybridization/sequencing apparatus. It is apparent that these traditional apparatuses are not satisfactory as demand increases for more genetic information to be found and mined at the point-of-care in shorter time and at lower costs.

[0007] Rapid heat transfer is crucial for an efficient polymerase chain reaction (PCR), and this makes temperature control one of the most essential and critical functional features in a micro-PCR system, which may include heaters and sensors composing a closed-loop. Yet, the fabrication of the heater and the sensor often prevented micro-PCR systems from achieving both cost-effectiveness and fabrication-easiness. For most of the researches micromachining techniques are used to enable sensors and heaters be integrated on a silicon or glass chip. However, the inherent high cost prevents them from wide applications and successful commercialization. The work described in this invention disclosure is part of our effort to solve the cost/fabrication dilemma.

[0008] The current ways of solving the problem are as follows:

[0009] Silicon Surface Micromachining as a low cost method of achieving a micro PCR device leveraging on batch fabrication;

[0010] Micromachining of heaters and temperature sensors on glass substrates; and

[0011] Polymer/Plastic fabrication with metallization to create heating elements and thermal sensors.

[0012] Silicon-based micro-PCR devices were facilitated by the micro-fabrication technology. Silicon was preferred because of its high thermal conductivity and controllable etching properties. However, this material is not transparent, and untreated silicon may cause inhibition to PCR.

[0013] Glass has the advantage of being electrically nonconductive and optically transparent. Yet, it is not as amenable as silicon in micromachining. Moreover, fabrication of silicon/glass structures usually involves processes such as photolithography, wet etching, electrochemical etching and anodic bonding. The high costs of these processes cannot accommodate the disposability required by PCR reactions to avoid cross-contamination.

[0014] Currently available microfluidic devices have been designed to emphasize on either convenience or cost-efficiency. For example, U.S. 6,830,936 discloses a miniaturized integrated nucleic acid diagnostic device that can integrate several or all of the operations involved in sample acquisition and storage, sample preparation and sample analysis within a single integrated unit. However, the microfluidic chip disclosed therein integrates fluidic channels and chambers, and electronic components such as detection sensors, heaters or voltage sources into one chip unit. It is apparent that this device is very convenient, but not cost effective as a disposable unit.

[0015] On the other end of the integration scale lie devices with no functionality built onto the microfluidic devices, and the microfluidic devices completely depend on externally and commercially available devices and equipment to perform the desired operation. It is apparent that this design offers cost-saving, but is not convenient.

Summary of the Invention

[0016] In one embodiment of the present invention, there is provided a micro thermal cycler. The micro thermal cycler comprises a bulk heating/cooling mechanism that can be controlled to increase/decrease its own temperatures; and a selective heat insulation mechanism being disposed immediately to the bulk heating cooling mechanism, wherein the selective insulation mechanism comprises a plurality of thermal vias and a

plurality of heat conductors that are embedded into the thermal vias, so that, when the bulk heating/cooling mechanism changes its temperatures, the selective heat insulation mechanism can allow the temperature changes pass through the heat conductors embedded in the thermal vias; thereby, when reaction chambers of a microfluidic chip are aligned with the heat conductors, only the temperatures of the reaction chambers are increased/decreased by the control of the bulk heating/cooling mechanism.

[0017] In another embodiment of the micro thermal cycler, it further comprises a heat sink for dissipating the heat generated by the bulk heating/cooling mechanism; wherein the heat sink is disposed onto the bulk heating/cooling mechanism in opposite to the selective heat insulation mechanism. In a further embodiment of the micro thermal cycler, the heat sink is made of metals/ceramics.

[0018] In another embodiment of the micro thermal cycler, the bulk heating/cooling mechanism comprises uniformly spaced heater rods or peltier elements or equivalent for uniform heating/cooling of the block. In a further embodiment of the micro thermal cycler, the heating/cooling element is a Peltier element so that its temperature changes can be controlled by switching the current directions. In yet another further embodiment of the micro thermal cycler, the bulk heating/cooling mechanism further comprises one or more temperature sensors that measure the temperatures of the bulk heating/cooling mechanism.

[0019] In another embodiment of the micro thermal cycler, the selective heat insulation mechanism comprises an insulator block made of plastics/polymers; and wherein the insulator block has the plurality of thermal vias in which heat conductors are embedded. In a further embodiment of the micro thermal cycler, the heat conductors are made of metal. In yet another further embodiment of the micro thermal cycler, the heat conductors are removable from the thermal vias so that the configuration of the heat conductors in the insulator block can be designed according to specific reactions.

[0020] In another embodiment of the present invention, there is provided a microfluidic device for performing chemical and biological reactions. the microfluidic device comprises a microfluidic chip comprising a plurality of reaction chambers in which the chemical and biological reactions can be allowed; and a micro thermal cycler for supporting the microfluidic chip and providing selective controls of temperatures of the reaction chambers; wherein said micro thermal cycler comprises a bulk heating/cooling

mechanism that can be controlled to increase/decrease its own temperatures; and a selective heat insulation mechanism being disposed immediately to the bulk heating cooling mechanism, wherein the selective insulation mechanism comprises a plurality of thermal vias and a plurality of heat conductors that are embedded into the thermal vias, so that, when the bulk heating/cooling mechanism changes its temperatures, the selective heat insulation mechanism can allow the temperature changes pass through the heat conductors embedded in the thermal vias; thereby, when reaction chambers of the microfluidic chip are aligned with the heat conductors, only the temperatures of the reaction chambers are increased/decreased by the control of the bulk heating/cooling mechanism.

[0021] In another embodiment of the microfluidic device, the microfluidic chip further comprises at least one calibration port for calibration of the reactions. In yet another embodiment of the microfluidic device, the microfluidic chip is made of one or two polymers selected from the group consisting of Polymethylmethacrylate (PMMA), Polydimethylsiloxane (PDMS), Polycarbonate (PC), Polypropylene (PP), Polytetrafluoroethylene (PTFE) or their derivatives.

[0022] In another embodiment of the microfluidic device, the reaction chambers do not have a floor member so that the reaction materials in the reaction chambers are directly in contact with the heat conductors. In yet another embodiment of the microfluidic device, the reaction chambers have a floor member at the bottom of the chip, so that the reaction samples within the reaction chambers will be separated from the micro thermal cycler by the floor member. In a further embodiment of the microfluidic device, the floor member is designed to be a thin polymeric membrane with thickness ranging from 10 – 50 micrometers, allowing the heat to transfer to the reaction chambers with minimum resistance.

[0023] In another embodiment of the microfluidic device, a dual side adhesion thermal tape is disposed between the microfluidic chip and the micro thermal cycler so as to provide support for the reaction samples within the reaction chambers. In yet another embodiment of the microfluidic device, the micro thermal cycler further comprises a heat sink for dissipating the heat generated by the bulk heating/cooling mechanism; wherein the heat sink is disposed onto the bulk heating/cooling mechanism in opposite to the selective heat insulation mechanism. In a further embodiment of the microfluidic device, the heat sink is made of metals/ceramics.

[0024] In another embodiment of the microfluidic device, the bulk heating/cooling mechanism comprises uniformly spaced heater rods or peltier elements or equivalent for uniform heating/cooling of the block. In a further embodiment of the microfluidic device, the heating/cooling element is a Peltier element so that its temperature changes can be controlled by switching the current directions. In another further embodiment of the microfluidic device, the bulk heating/cooling mechanism further comprises one or more temperature sensors that measure the temperatures of the bulk heating/cooling mechanism.

[0025] In another embodiment of the microfluidic device, the selective heat insulation mechanism comprises an insulator block made of plastics/polymers; and wherein the insulator block has the plurality of thermal vias in which heat conductors are embedded. In a further embodiment of the microfluidic device, the heat conductors are made of metal. In yet another further embodiment of the microfluidic device, the heat conductors are removable from the thermal vias so that the configuration of the heat conductors in the insulator block can be designed according to specific reactions.

[0026] In another embodiment of the microfluidic device, the chemical and biological reaction is a PCR reaction; and wherein the temperature ramp up and ramp down of the PCR reaction are more than 10^{o}C per second.

[0027] The objectives and advantages of the invention will become apparent from the following detailed description of preferred embodiments thereof in connection with the accompanying drawings.

Brief Description of the Drawings

[0028] Preferred embodiments according to the present invention will now be described with reference to the Figures, in which like reference numerals denote like elements.

[0029] FIG 1A is a top view of a microfluidic chip that can be used with the micro thermal cycler of the present invention in accordance with one embodiment of the present invention.

[0030] FIG 1B is a cross-sectional view along the A-A' line of FIG 1A of the microfluidic chip.

[0031] FIG 2 is an isometric and exploded view of the micro thermal cycler in accordance with one embodiment of the present invention.

[0032] FIG 3 is an isometric and exploded view of the insulator block in an upside down orientation in accordance with one embodiment of the present invention.

[0033] FIG 4 shows an isometric view of the assembly of the insulator block **11** and the heating/cooling block **14**.

[0034] FIGS 5A-5C are cross-sectional views of the insulator block, heating/cooling block, and the heat sink in accordance with one embodiment of the present invention.

[0035] FIG 6A shows a rear view of one actual sample of the heating/cooling block used by the inventors for performing PCR reactions.

[0036] FIG 6B shows a cross-sectional view along the B-B' line of FIG 6A of the heating/cooling block.

[0037] FIG 7A shows a top view of one actual sample of the insulator block with embedded heat conductors used by the inventors of the present invention for performing PCR reactions.

[0038] FIG 7B shows a cross-sectional view along the C-C' line of FIG 7A of the insulator block.

[0039] FIG 8 shows one microfluidic chip with PCR reaction chambers that match the heat conductors of the insulator block shown in FIG 7.

[0040] FIG 9A shows a top view of an insulator block with removable heat conductors in accordance with another embodiment of the present invention.

[0041] FIG 9B shows a cross-sectional view along the D-D' line of FIG 9A of the insulator block.

Detailed Description of the Invention

[0042] The present invention may be understood more readily with reference to the following detailed description of certain embodiments of the invention.

[0043] Throughout this application, where publications are referenced, the disclosures of these publications are hereby incorporated by reference, in their entireties,

into this application in order to more fully describe the state of art to which this invention pertains.

[0044] In the following detailed description, specific details are set forth in order to provide a thorough understanding of the invention. However, it will be understood by those skilled in the relevant art that the present invention may be practiced without these specific details. In other instances, well-known methods, procedures, components, and materials have not been described in detail so as not to obscure the present invention.

[0045] The present invention provides a micro thermal cycler that is compatible with microfluidic chips for automation of chemical and biological reactions. Briefly, the micro thermal cycler of the present invention employs a selective heat insulation mechanism and a bulk heating/cooling mechanism. In one embodiment, the selective heat insulation mechanism comprises an insulator block with a plurality of vias in which metallic heat conductors can be embedded; wherein when the vias with the metallic heat conductors are aligned with reactions chambers of a microfluidic chip, the reaction chambers are heated/cooled directly through the vias while the remaining of the microfluidic chip is insulated from the heating/cooling cycles. In one embodiment, the bulk heating/cooling mechanism is a heating/cooling block that is entirely heated/cooled (e.g., using peltier elements) and controlled through a thermocouple-sensed feedback. Thus it completely eliminates the need to microfabricate heating and temperature sensing elements, thereby resulting in significantly lower development and manufacturing costs.

[0046] Prior to more detailed description of the micro thermal cycler, there is provided a brief description of the microfluidic chip that is suitable for being used with the micro thermal cycler.

[0047] Referring to FIG 1A, there is provided a top view of a microfluidic chip that can be used with the micro thermal cycler of the present invention in accordance with one embodiment of the present invention. The microfluidic chip **1** comprises a plurality of reaction chambers **2** and a calibration port **3**. While four reaction chambers with a square configuration and one calibration port are shown in FIG 1A, it is to be appreciated that the number and configuration of the reaction chambers and calibration port can vary according to any design. More on these will be provided hereinafter in reference to FIG 8.

[0048] The microfluidic chip can be made of any suitable materials. In one embodiment, the microfluidic chip can be made of polymers including but not limited to

Polymethylmethacrylate (PMMA), Polydimethylsiloxane (PDMS), Polycarbonate (PC), Polypropylene (PP) and Polytetrafluoroethylene (PTFE) or their derivatives.

[0049] Now referring to FIG 1B, there is provided a cross-sectional view along the A-A' line of FIG 1A of the microfluidic chip. The microfluidic chip **1** comprises the reaction chambers **2** that have a chip cover **4** on the top of the chip and a floor member **5** at the bottom of the chip. The microfluidic chip **1** will be disposed upon the top of the micro thermal cycler (described in detail hereinafter) for carrying out desired reactions within the reaction chambers. In this embodiment, the reaction samples within the reaction chambers will be separated from the micro thermal cycler by the floor member **5**. The chip cover **4** can be made of any transparent materials so that a user can see through the chip cover or measure any signals such as fluorescence directly. The floor member **5** can be fabricated together with the microfluidic chip when the polymer is used for making of the microfluidic chip. In other embodiments, the floor member **5** can be made of other materials that can be attached to the bottom of the microfluidic chip. The floor member **5** may be designed to be a thin polymeric membrane with thickness ranging from 10 – 50 micrometers, allowing the heat to transfer to the reaction chambers with minimum resistance.

[0050] In another embodiment of the present invention, the microfluidic chip may be designed in such a way that the reaction chambers have no floor. The samples within the reaction chambers are exposed directly to the top of the conductors of the micro thermal cycler. In another embodiment of the present invention, a dual side adhesion thermal tape with a wide ranging thickness and good electrical resistivity may be disposed between the microfluidic chip and the micro thermal cycler so as to provide support for the reaction samples within the reaction chambers. In this configuration, the reaction sample is not in direct contact with the conductor but the heat is transferred via the thermal tape. This solution can be adopted to minimize the formation of air bubbles during temperature cycling.

[0051] Now there are provided more details of the micro thermal cycler of the present invention.

[0052] Referring to FIG 2, there is provided an isometric and exploded view of the micro thermal cycler in accordance with one embodiment of the present invention. The micro thermal cycler **10** comprises an insulator block **11**, a plurality of metallic heat

conductors **12**, a plurality of aligning and locking means **13,** a heating/cooling block **14**, and a heat sink **15**. The insulator block **11** also serves as a base for supporting the microfluidic chip. The plurality of metallic heat conductors **12** are inserted into the vias pre-formed on the insulator block **11**. While there are four vias/metallic heat conductors shown in FIG 2, it is to be appreciated that the numbers and configurations of the vias/metallic heat conductors are not so limited. The plurality of aligning and locking means **13** can be any suitable ones known to those skilled in the art. As shown in FIGS 5B and 6B in more details, the heating/cooling block **14** may be made of Peltier elements so that the heating/cooling cycles can be easily controlled by switching of the current directions. The heat sink **15** can be any suitable materials that have good heat dissipation characteristics.

[0053] Many different materials are suitable for making each component of the micro thermal cycler of the present invention. Preferably, the microfluidic chip **1** is made of polymer; the insulator block **11** of plastic/polymers; the heat sink/cooling fins **15** of metals/ceramics; and the thermal conductors **12** of metal (Copper, Aluminum, etc).

[0054] Referring now to FIG 3, there is provided an isometric and exploded view of the insulator block in an upside down orientation in accordance with one embodiment of the present invention. In the central part of the insulator block **11**, there is one recession with a plurality of islands forming the thermal vias **16** for inserting the metallic heat conductors **12**. The remaining of the recession forms the air pockets **17**. The recession receives the heating/cooling block **14**. FIG 4 shows an isometric view of the assembly of the insulator block **11** and the heating/cooling block **14**.

[0055] Referring to FIG 5A, there is provided a cross-sectional view of the insulator block in accordance with one embodiment of the present invention. The insulator block **11** comprises a plurality of metallic heat conductors **12** embedded in the thermal vias **16**, and air pockets **17.** FIG 5B shows a cross-sectional view of the heating/cooling block in accordance with one embodiment of the present invention. The heating/cooling block **14** comprises a peltier element with the hot side **21** and a cold side **22** under reversible conditions as per the voltage bias applied. FIG 5C shows a cross-sectional view of the heat sink/cooling fins **15** in accordance with one embodiment of the present invention.

[0056] Referring to FIG 6A, there is provided a rear view of one actual sample of the heating/cooling block used by the inventors for performing PCR reactions. The

heating/cooling block **14** is of dimensions chosen as appropriate for specific applications with one central and four corner thermocouples **20** or similar temperature measurement device positioned in suitable areas for uniform and accurate temperature measurement. FIG 6B shows a cross-sectional view along the B-B' line of FIG 6A of the heating/cooling block. The heating/cooling block **14** comprises uniformly spaced heater rods or peltier elements or equivalent for uniform heating/cooling of the block. In one embodiment, when the heating/cooling block **14** is a peltier element, it has the hot side **21** and a cold side **22** under reversible conditions as per the voltage bias applied, where the thermocouples **20** are disposed onto the cold side. The heater rods or peltier elements are controlled by the controller **23** (not shown in detail).

[0057] Referring to FIG 7A, there is provided a top view of one actual sample of the insulator block with embedded heat conductors used by the inventors of the present invention for performing PCR reactions. The insulator block **11** has dimensions chosen as appropriate for specific applications with a plurality of metallic heat conductors **12** embedded within the thermal vias **16**. FIG 7B shows a cross-sectional view along the C-C' line of FIG 7A of the insulator block. The thickness of the insulator block **11** is to be chosen as appropriate. The air pockets **17** are shown.

[0058] Referring to FIG 8, there is provided one microfluidic chip with PCR reaction chambers that match the heat conductors of the insulator block shown in FIG 7A. The microfluidic chip **80** shown in FIG 8 comprises a sample inlet **81,** a positive control PCR site **82**, a negative control PCR site **83**, a plurality of sample PCR sites **84**, and a plurality of PCR product outlets **85**. The actual PCR reactions and operations are well known to those skilled in the art.

[0059] Referring to FIG 9A, there is provided a top view of an insulator block with removable heat conductors in accordance with another embodiment of the present invention. The insulator block **14** is very similar to the one shown in FIG 7A except that the metallic heat conductors **12'** inside the thermal vias can be manufactured as separate entities. This allows the conductors and the insulator block to be assembled in a plug-and-play manner so as to have a flexible and generic design of the insulator block. FIG 9B shows a cross-sectional view along the D-D' line of FIG 9A of the insulator block. One of the removable metallic heat conductors **12'** has been shown separately.

[0060] This selective heat insulation mechanism is able to execute PCR thermal cycles without the need to use microheaters and micro thermal sensors. The temperature ramp up and ramp down are in the range of 10-20°C or more per second. The effective heating/cooling volume per reaction well on the MTC is in the range of 5 to 25 ul.

[0061] While the present invention has been described with reference to particular embodiments, it is understood that the embodiments are illustrative and that the invention scope is not so limited as such. Alternative embodiments of the present invention will become apparent to those having ordinary skill in the art to which the present invention pertains. Such alternate embodiments are considered to be encompassed within the spirit and scope of the present invention. Accordingly, the scope of the present invention is described by the appended claims and is supported by the foregoing description.

CLAIMS

What is claimed is:

1. A micro thermal cycler, comprising:

a bulk heating/cooling mechanism that can be controlled to increase/decrease its own temperatures; and

a selective heat insulation mechanism being disposed immediately to the bulk heating cooling mechanism, wherein the selective insulation mechanism comprises a plurality of thermal vias and a plurality of heat conductors that are embedded into the thermal vias, so that, when the bulk heating/cooling mechanism changes its temperatures, the selective heat insulation mechanism can allow the temperature changes pass through the heat conductors embedded in the thermal vias;

thereby, when reaction chambers of a microfluidic chip are aligned with the heat conductors, only the temperatures of the reaction chambers are increased/decreased by the control of the bulk heating/cooling mechanism.

2. The micro thermal cycler of claim 1, further comprising a heat sink for dissipating the heat generated by the bulk heating/cooling mechanism; wherein the heat sink is disposed onto the bulk heating/cooling mechanism in opposite to the selective heat insulation mechanism.

3. The micro thermal cycler of claim 2, wherein the heat sink is made of metals/ceramics.

4. The micro thermal cycler of claim 1, wherein the bulk heating/cooling mechanism comprises uniformly spaced heater rods or peltier elements or equivalent for uniform heating/cooling of the block.

5. The micro thermal cycler of claim 4, wherein the heating/cooling element is a Peltier element with the hot side and a cold side under reversible conditions as per the voltage bias applied.

6. The micro thermal cycler of claim 4, wherein the bulk heating/cooling mechanism further comprises one or more temperature sensors that measure the temperatures of the bulk heating/cooling mechanism.

7. The micro thermal cycler of claim 1, wherein the selective heat insulation mechanism comprises an insulator block made of plastics/polymers; and wherein the insulator block has the plurality of thermal vias in which heat conductors are embedded.

8. The micro thermal cycler of claim 7, wherein the heat conductors are made of metal.

9. The micro thermal cycler of claim 7, wherein the heat conductors are removable from the thermal vias so that the configuration of the heat conductors in the insulator block can be designed according to specific reactions.

10. A microfluidic device for performing chemical and biological reactions, said microfluidic device comprising:

a microfluidic chip comprising a plurality of reaction chambers in which the chemical and biological reactions can be allowed; and

a micro thermal cycler for supporting the microfluidic chip and providing selective controls of temperatures of the reaction chambers;

wherein said micro thermal cycler comprises:

a bulk heating/cooling mechanism that can be controlled to increase/decrease its own temperatures; and

a selective heat insulation mechanism being disposed immediately to the bulk heating cooling mechanism, wherein the selective insulation mechanism comprises a plurality of thermal vias and a plurality of heat conductors that are embedded into the thermal vias, so that, when the bulk heating/cooling mechanism changes its temperatures,

the selective heat insulation mechanism can allow the temperature changes pass through the heat conductors embedded in the thermal vias;

thereby, when reaction chambers of the microfluidic chip are aligned with the heat conductors, only the temperatures of the reaction chambers are increased/decreased by the control of the bulk heating/cooling mechanism.

11. The microfluidic device of claim 10, wherein the microfluidic chip further comprises at least one calibration port for calibration of the reactions.

12. The microfluidic device of claim 10, wherein the microfluidic chip is made of one or two polymers selected from the group consisting of PMMA, PDMS, PC, PP, PTFE or their derivatives.

13. The microfluidic device of claim 10, wherein the reaction chambers do not have a floor member so that the reaction materials in the reaction chambers are directly in contact with the heat conductors.

14. The microfluidic device of claim 10, wherein the reaction chambers have a floor member at the bottom of the chip, so that the reaction samples within the reaction chambers will be separated from the micro thermal cycler by the floor member.

15. The microfluidic device of claim 14, wherein the floor member is designed to be a thin polymeric membrane with thickness ranging from 10 – 50 micrometers, allowing the heat to transfer to the reaction chambers with minimum resistance.

16. The microfluidic device of claim 10, wherein a dual side adhesion thermal tape is disposed between the microfluidic chip and the micro thermal cycler so as to provide support for the reaction samples within the reaction chambers.

17. The microfluidic device of claim 10, wherein the micro thermal cycler further comprises a heat sink for dissipating the heat generated by the bulk heating/cooling

mechanism; wherein the heat sink is disposed onto the bulk heating/cooling mechanism in opposite to the selective heat insulation mechanism.

18. The microfluidic device of claim 17, wherein the heat sink is made of metals/ceramics.

19. The microfluidic device of claim 10, wherein the bulk heating/cooling mechanism comprises uniformly spaced heater rods or peltier elements or equivalent for uniform heating/cooling of the block.

20. The microfluidic device of claim 19, wherein the heating/cooling element is a Peltier element with the hot side and a cold side under reversible conditions as per the voltage bias applied.

21. The microfluidic device of claim 19, wherein the bulk heating/cooling mechanism further comprises one or more temperature sensors that measure the temperatures of the bulk heating/cooling mechanism.

22. The microfluidic device of claim 10, wherein the selective heat insulation mechanism comprises an insulator block made of plastics/polymers; and wherein the insulator block has the plurality of thermal vias in which heat conductors are embedded.

23. The microfluidic device of claim 22, wherein the heat conductors are made of metal.

24. The microfluidic device of claim 22, wherein the heat conductors are removable from the thermal vias so that the configuration of the heat conductors in the insulator block can be designed according to specific reactions.

25. The microfluidic device of claim 10, wherein the chemical and biological reaction is a PCR reaction; and wherein the temperature ramp up and ramp down of the PCR reaction are more than 10°C per second.