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(72) Inventor: **Clemens, Thomas**
97082 Würzburg (DE)

(74) Representative: **Heunemann, Dieter**
Vossius & Partner
Siebertstrasse 4
81675 München (DE)

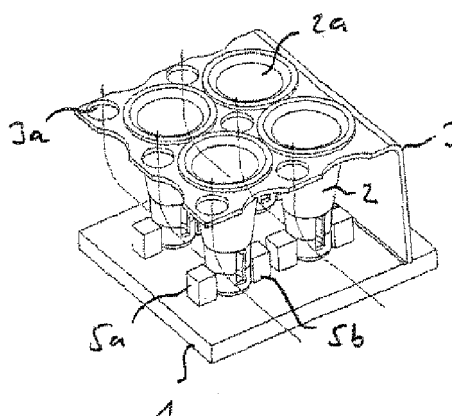
(71) Applicant: **PEQLAB Biotechnologie GmbH**
91052 Erlangen (DE)

(54) **Thermal plate**

(57) The present invention relates to a thermal plate for heating and/or cooling several caps comprising a base plate of thermally conducting material; several receptacles for caps being in thermal contact with the base plate; a support structure for supporting the receptacles

being in thermal contact with the base plate; and means for heating and/or cooling the base plate, wherein the support structure together with the base plate provides a substantially closed hollow space surrounding the receptacles.

Fig. 3



Description

[0001] The present invention is directed to a thermal plate for heating and/or cooling several caps. The thermal plate according to the present invention may in particular be utilized in an apparatus for performing PCR analysis.

[0002] PCR (polymerase chain reaction) is commonly carried out in a thermal cycler. The thermal cycler heats and cools the reaction tubes or caps to achieve the temperatures required at each step of the reaction. A PCR usually consists of a series of 20-40 repeated temperature changes called cycles (each of which typically consists of 2-3 discrete temperature steps). The thermal cycler typically has a thermal block with holes where tubes or caps holding the PCR reaction mixtures can be inserted. The thermal cycler then raises and lowers the temperature of the block in discrete, pre-programmed steps. The temperature is typically controlled by use of peltier elements. Some thermal cyclers contain silver blocks to achieve fast temperature changes and uniform temperature throughout the block. Some thermal cyclers are equipped with multiple blocks along several different PCR reactions to be carried out simultaneously. It is furthermore known to provide a temperature gradient function, which allows different temperatures in different parts of the block.

[0003] Typically, the thermal block or thermal plate of such a thermal cycler comprises a plate made of a thermally conducting material, one or more heating and/or cooling elements arranged at the bottom side of the plate, whose purpose it is to heat and/or cool several tubes or caps arranged in reservoirs or receptacles on the top side of said plate. Furthermore, one or more temperature sensors are provided and thermally coupled to the plate of the thermal block or plate in order to allow for the calculation or estimation of the temperature in the tubes or caps.

[0004] WO 2008/002991 A2 relates to a low-mass sample block. This application describes to reduce the mass of a the sample block by a series of hollows in the block arranged around sample wells for accommodation of samples. In some embodiments, the hollows form parallel non-intersecting channels that run parallel to the top and bottom surfaces of the sample block, while in other embodiments, the hollows form a network of intersecting passages. The sample block is of unitary construction, i.e. the block is formed as a single piece by machining or molding.

[0005] Manufacturing such a sample block is rather elaborate and costly. Molding a single piece with several hollows requires complex and expensive casting molds. In case of the intersecting passages molding may even be impossible. Machining the structure out of a single block of material, however, causes a tremendous amount of waste. Thus, machining the low-mass sample block of WO 2008/002991 A2 is not only time consuming but also rather costly. In addition, these manufacturing processes cause problems with respect to the requirements

regarding tolerances, in particular in case of rather small and detailed structures. It is furthermore difficult to provide for an homogeneous active cooling and/or heating of the samples within the sample block by means of a fluid stream, since the structure is entirely open.

[0006] It is therefore an object of the present invention to provide an improved thermal plate for heating and/or cooling several tubes or caps which takes the above-mentioned problems and disadvantages into account. It is in particular an object of the present invention to provide a thermal plate which can be easily and cost effective manufactured and which may be easily adapted to specific needs and requirements. It is a further object of the present invention to provide a thermal plate which may be easily equipped with additional electronic and/or optical components.

[0007] These and other objects are achieved by a thermal plate according to claim 1. Preferred embodiments are claimed in the dependent claims.

[0008] Accordingly, the present invention provides a thermal plate for heating and/or cooling several tubes or caps. The thermal plate comprises a base plate of thermally conducting material, several receptacles for tubes or caps being in thermal contact with the base plate, a separate support structure for supporting the receptacles being in thermal contact with the base plate and means for heating and/or cooling the base plate, wherein the support structure together with the base plate provides a substantially closed hollow space surrounding the receptacles. Preferably, the receptacles are adapted to receive tubes or caps in such a manner that the tubes or caps are in thermal contact with the base plate.

[0009] The present invention is based on the idea to replace the solid thermal block known from the prior art by a honeycomb-like or porous structure, which effectively reduces the thermal mass. Thus, the thermal plate according to the present invention may much faster adapt to or reach the temperature steps of the typical PCR cycles. While the heat capacity of the thermal plate according to the present invention is reduced compared to the prior art, the thermal conductivity is nevertheless large enough to provide for fast temperature cycles. In contrast to the series of open hollows describes in WO 2008/002991 A2, the present invention aims at a single, substantially closed hollow space surrounding the receptacles. This hollow space allows for a good heat transfer throughout the structure, e.g. by convection or a directed fluid stream through the hollow space. In addition, the thermal plate according to the present invention comprises a base plate, several receptacles and a separate support structure. By contrast, the sample block known from WO 2008/002991 A2 is of unitary construction. While a unitary construction is disadvantageous as outlined above, the thermal plate of the present invention can be easily and cost-effectively manufactured by mounting the single components. E.g., the receptacles may be brazed or soldered to the support structure. Furthermore, the support structure being a separate piece allows the use

of different materials for, e.g., receptacles and support structure. Thus, an optimum but more costly material may be used for the receptacles.

[0010] According to a preferred embodiment of the present invention the thickness of the walls of the receptacles along their circumference is substantially constant. This allows for a homogeneous heat transfer to the samples placed in the receptacles. As can be seen, e.g., in Figure 3 of WO 2008/002991 A2, the thickness of the wall of each sample well varies along its circumference, i.e. the thickness of the walls of the receptacles is not concentrically constant. This can be rather problematic, since this causes a difference in heat transfer from the hollows to the sample depending on the wall thickness. If the thickness of the walls of the receptacles along their circumference is substantially constant, homogenous constant heat transfer from the substantially closed hollow space to the samples in the receptacles is improved tremendously.

[0011] It is further preferred that the thickness of the walls of the receptacles is in general (i.e. along their circumference and their height) substantially constant. Preferably, the thickness of the walls of the receptacles is between about 0,2 mm and about 1,0 mm, more preferably between about 0,3 mm and about 0,5 mm. It is preferred that the thickness of the walls of the receptacles varies less than about 20%, preferably less than about 10%.

[0012] According to a preferred embodiment of the present invention the support structure for supporting the receptacles comprises vent holes. These vent holes are arranged at specific positions only in order to provide for a predetermined fluid stream. Thus, a fluid stream may be utilized to additionally heat and/or cool the thermal plate. For example, the vent holes are only arranged at the top surface of the thermal plate. For this purpose, it is further preferred that the thermal plate comprises a fan.

[0013] According to a further preferred embodiment the support structure comprises an inlet and an outlet for a cooling and/or heating fluid. The fluid may be ambient air or another gas, water, oil or another fluid which is suitable for cooling and/or heating. Preferably, the thermal plate further comprises means for pumping the cooling fluid through the support structure. Thus, a large transfer of heat from the support structure to the cooling fluid or from a heating fluid to the support structure can be achieved.

[0014] It is further preferred that the support structure accommodates one or more temperature sensors. The one or more temperature sensors should be in thermal contact with the receptacles for the tubes or caps, either in direct contact or in indirect contact via, e.g., the base plate. Preferably, the one or more temperature sensors are located close to or adjacent the receptacles for the tubes or caps. It is in particular preferred that the temperature sensors are arranged within the substantially closed hollow space. Thus, a more precise temperature measurement may be performed. This is a further advantage of the structure according to the present invention,

since the substantially closed hollow space provides enough space for such sensors on the one hand and is in thermal equilibrium with the samples on the other hand.

[0015] Preferably, the support structure accommodates one or more optical sensors for analyzing light originating from the receptacles. For this purpose it is also preferred that the support structure accommodates one or more light sources. The term "light source" in the context of the present application is to be understood as any source of electromagnetic radiation including inter alia UV-light, infrared light and light from the optically visible spectrum. The one or more optical sensors and the one or more light sources are preferably arranged in such a manner that light emitted from the light sources is directed into the receptacles for the tubes or caps, i.e. illuminating the samples within the tubes or caps, and that the light emitted from the samples within the receptacles (by transmission, scattering or reflection) is detected by the one or more optical sensors. Depending on the specific purpose of the optical measurement the light source and the sensor may be located on the same side of a receptacle or on opposite sides. For the purpose of the optical measurements it is further preferred that the receptacles are optically transparent and/or comprise optically transparent windows with respect to the light emitted by the light sources. If optically transparent windows are provided, the receptacle may comprise only one window (reflective mode) or two or more windows (for measuring transmission and/or scattered light).

[0016] Even though the heat capacity of the thermal plate according to the present invention is rather small, a large thermal conductivity is nevertheless advantageous. It is therefore preferred that the support structure and the receptacles have a thermal conductivity of at least 0.02 W/K per receptacle, preferably of at least 0.2 W/K per receptacle. For this purpose, it is preferable that the base plate and/or the support structure is made of one or a combination of the following materials : Cu, Al, Ag, Sn, Fe, C, Ceramics.

[0017] Preferably, the receptacles have a volume between 50 μ l and 300 μ l, more preferably between 100 μ l and 250 μ l.

[0018] According to a preferred embodiment of the present invention, the heat capacity of the thermal plate divided by the number of receptacles is smaller than 1.6 J/K, more preferably smaller than 1.2 J/K.

[0019] According to another aspect of the present invention an apparatus performing PCR analysis is provided, the apparatus comprising a thermal plate as described above.

[0020] In the following, preferred embodiments of the present invention are described with respect to the following Figures:

Figure 1 shows a cross-section of a preferred embodiment of a thermal plate according to the present invention.

Figure 2a shows a perspective view of a receptacle together with a sensor according to the present invention.

Figure 2b shows a perspective view of a receptacle together with a light source and a sensor according to the present invention.

Figure 3 shows a perspective sectional view of another preferred embodiment of a thermal plate according to the present invention.

[0021] Figure 1 shows a cross-section of a preferred embodiment of the thermal plate according to the present invention. The thermal plate comprises a base plate 1 of thermally conducting material, several receptacles 2 for tubes or caps and a support structure 3 for supporting the receptacles. Both the receptacles and the support structure are in thermal contact with the base plate. Furthermore, means for heating and/or cooling the base plate are provided, which are not shown in Figure 1. Preferably, the means for heating and/or cooling the base plate comprises one or more peltier elements. As can be seen in Figure 1, the support structure 3 together with the base plate 1 provide a substantially closed hollow space surrounding the receptacles 2. The receptacles are adapted to receive tubes or caps, which preferably accurately fit into the receptacles. Thus, good heat transfer from the receptacles to the tubes or caps can be guaranteed.

[0022] The thermal plate is made out of several separate components which are mounted together. The single components may be cut, bent, and deep drawn and, e.g., soldered together. Thus, for each component a preferred material may be chosen. While the purpose of the support structure is mostly to stabilize the thermal plate, the receptacles are specifically meant to transfer heat from and to the sample. Accordingly, the receptacles are preferably made from a material having excellent heat transfer properties, such as silver, copper or aluminium.

[0023] Figure 3 shows another preferred embodiment of the thermal plate according to the present invention in a perspective sectional view. This embodiment also comprises a base plate 1 of thermally connecting material, several receptacles 2 for caps being in thermal contact with the base plate and support structure 3 for supporting the receptacles 2. In this Figure the substantially closed hollow space surrounding the receptacles provided by the support structure 3 and the base plate 1 is more clearly visible. Even though the embodiment shown in Figure 3 additionally comprises several vent holes 3 a, the support structure and the base plate of said embodiment are considered to provide a substantially closed hollow space surrounding the receptacles. The purpose of the vent holes 3a is to provide a stream of cooling fluid (indicated by the arrows) which promotes a fast cooling rate. Preferably, a fan is provided (not shown in Figure 3) which increases the velocity of the fluid flow through the support structure during cooling phases.

[0024] Figure 2a shows a perspective view of the receptacle 2 for a tube or cap having an opening 2a for inserting the tube or cap therethrough. The receptacle 2 is provided with a sensor 4 which is in direct contact with the receptacle 2. The sensor may be a temperature sensor, an optical sensor or another sensor for measuring parameters which are of interest when performing a PCR.

[0025] Figure 2b shows a perspective view of another receptacle 2 with a light source 5a and an optical sensor 5b. The light source 5a may be adapted to emit electromagnetic radiation such as UV-light, infrared light or light in the visible spectrum. The light source 5a may, e.g., comprise a laser diode.

[0026] The light emitted from the light source 5a is transmitted through the receptacle 2 and received by an optical sensor or detector 5b. While in this arrangement transmitted light is detected by the detector 5b, other arrangements of the light source 5a and the detector 5b are also possible. For example, the detector 5b may be located at a position to detect light scattered from the sample in the tube or cap received by the receptacle 2 in a certain angle. Alternatively, the light source 5a and the light detector 5b may be arranged on the same side of the receptacle such as to measure reflected light. It should be evident that once a tube or cap comprising a sample is located within the receptacle 2, the light emitted from the light source 5a is directed into the sample. For this purpose, it is preferred that the receptacles 2 are optically transparent in the light spectrum of the light source 5a or that the receptacles 2 comprise one or more optically transparent windows.

[0027] The receptacles 2 as shown in Figures 2a and 2b are arranged in the thermal plate according to the present invention as shown in Figure 3. The receptacles shown in Figures 2a and 2b can be provided as alternatives or combined in a thermal plate of the invention. Thus, a receptacle 2 may have a temperature sensor 4, a light source 5a and an optical detector 5b. According to another embodiment, every receptacle is provided with a light source 5a and a detector 5b, while only some of the receptacles 2 are provided with a temperature sensor 4. In still another embodiment, every receptacle is provided with an optical detector 5b, while the light for all or some of the receptacles 2 is emitted from one and the same light source and directed into the samples by means of a light guide.

[0028] The thermal plate according to the present invention provides several advantages in view of the prior art. The different components of the thermal plate according to the present invention may be simply and cost efficient manufactured. For example, the single components may be cut, bent, and deep drawn and, e.g., soldered together. In addition, it is easy to add several electrical and/or optical components to the thermal plate as discussed above. The substantially closed hollow space surrounding the receptacles may be easily cooled and/or heated by means of a cooling and/or heating fluid. Thus, the velocity of performing temperature cycles may be in-

creased. Finally, the thermal plate according to the present invention provides a large thermal conductivity while having at the same time a small heat capacity. This also decreases the time between different temperature cycles.

Claims

1. Thermal plate for heating and/or cooling several caps comprising a base plate (1) of thermally conducting material; several receptacles (2) for caps being in thermal contact with the base plate; a separate support structure (3) for supporting the receptacles being in thermal contact with the base plate; and means for heating and/or cooling the base plate, wherein the support structure (3) together with the base plate (1) provides a substantially closed hollow space surrounding the receptacles (2). 10
2. Thermal plate according to claim 1, wherein the receptacles (2) are adapted to receive caps in such a manner that the caps are in thermal contact with the base plate (1). 15
3. Thermal plate according to any of the previous claims, wherein the thickness of the walls of the receptacles along their circumference is substantially constant. 20
4. Thermal plate according to any of the previous claims, wherein the thickness of the walls of the receptacles is between about 0,2 mm and about 1,0 mm, preferably between about 0,3 mm and about 0.5 mm. 25
5. Thermal plate according to any of the previous claims, wherein the thickness of the walls of the receptacles varies less than about 20%, preferably less than about 10%. 30
6. Thermal plate according to any of the previous claims, wherein the support structure (3) comprises vent holes (3a). 35
7. Thermal plate according to any of the previous claims, further comprising a fan. 40
8. Thermal plate according to any of the previous claims, wherein the support structure (3) comprises an inlet and an outlet for a cooling fluid. 45
9. Thermal plate according to claim 8, further comprising means for pumping the cooling fluid through the support structure. 50
10. Thermal plate according to any of the previous claims, wherein the support structure (3) accommo-

dates one or more temperature sensor(s) (4).

11. Thermal plate according to any of the previous claims, wherein the support structure (3) accommodates one or more optical sensor(s) (5b). 5
12. Thermal plate according to claim 11, wherein the support structure (3) accommodates one or more light source(s) (5a). 10
13. Thermal plate according to claim 11 or 12, wherein the receptacles (2) are optically transparent and/or comprise optically transparent windows with respect to the light emitted by the light source(s). 15
14. Thermal plate according to any of the previous claims, wherein the base plate (1), the support structure (3) and the receptacles (2) have a thermal conductivity of at least 0.02 W/K per receptacle, preferably of at least 0.2 W/K per receptacle. 20
15. Thermal plate according to any of the previous claims, wherein the base plate (1) is made of one or a combination of the following materials: Cu, Al, Ag, Sn, Fe, C, Ceramics. 25
16. Thermal plate according to any of the previous claims, wherein the receptacles (2) have a volume between 50 μ l and 300 μ l, preferably between 100 μ l and 250 μ l. 30
17. Thermal plate according to any of the previous claims, wherein the heat capacity of the thermal plate divided by the number of receptacles is smaller than 1.6 J/K, preferably smaller than 1.2 J/K. 35
18. Apparatus for performing PCR analysis, the apparatus comprising a thermal plate according to any of the previous claims. 40

Fig. 1

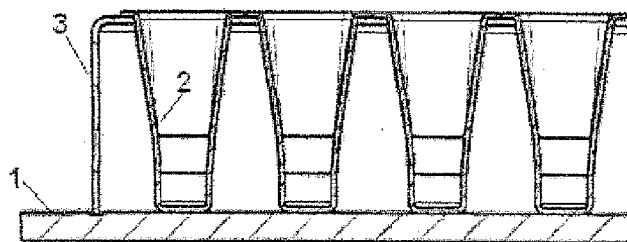


Fig. 2a

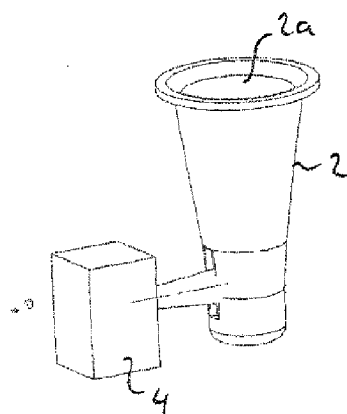


Fig. 2b

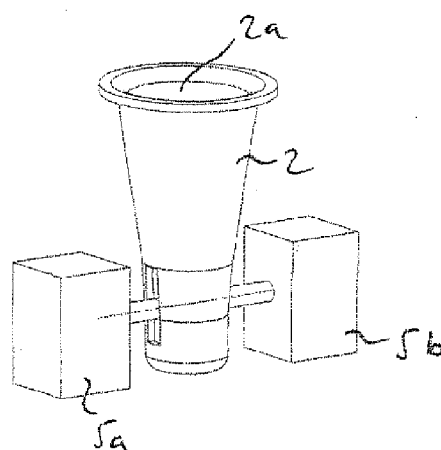
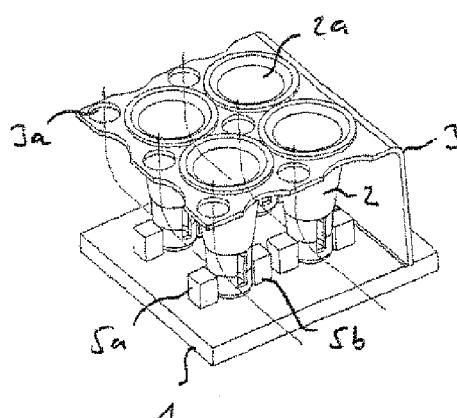


Fig. 3





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Application Number
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Place of search The Hague		Date of completion of the search 18 June 2010	Examiner Sinn, Cornelia
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**ANNEX TO THE EUROPEAN SEARCH REPORT
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