

other preferred embodiments, heat source 46 rests on a PC board 47. Thus, together, elements 46 and 47 are but exemplary ways to heat a cartridge.

[0050] In another preferred embodiment, a protective barrier 48 shields a user of system 10 from various internal workings and internal components thereof.

[0051] FIGS. 2C and 2D show a cross-sectional view of exemplary cartridge receiving element 12, showing various components that facilitate delivery of reagents and heat to cartridge 18. In particular, in order to maintain a good thermal contact between heat source 46 and cartridge 18, one method is to incorporate a user-actuated handle 51 that can apply pressure to cartridge 18. In the embodiment shown in FIG. 2C, handle 51 is attached to a cam-shaft 52 that, when pivoting against fixed ledge 53, causes a plunger 54 to be depressed and platform 55 attached to the plunger to press down against cartridge 18. Platform 55, in the embodiment shown, has a contact heat source that can cause heat to be applied to liquid sample in a lysis chamber of cartridge 18, as further described herein. The pressure exerted on platform 55 not only makes good contact between a heat source in platform 55 and upper surface of cartridge 18, but also causes a good thermal contact between heat source 46 and the microfluidic component on the underside of cartridge 18. Action of cam and plunger 54 also serves to ensure that the position of cartridge 18 is stable during processing. In preferred embodiments, a sensor in communication with platform 55 causes microadjustments of plunger 54 so that undue pressure, such as pressure that would cause undue strain, stress, or damage, is not applied to cartridge 18. One of ordinary skill in the art would understand that a cam and plunger assembly is not the only mechanical arrangement that can apply pressure to cartridge 18 for the purpose of making good thermal contact. For example, a press can be envisaged that utilizes an adjustable screw for changing the height of the press above the cartridge, as can other arrangements that comprise levers and similar mechanisms.

[0052] In preferred embodiments, each cartridge receiving area in system 10 has its own independently controllable mechanism for applying pressure to areas of the microfluidic cartridge that are contact heated. Thus, in FIG. 1, each handle above each cartridge receiving area can be depressed by a user independently of the others. Other aspects of the cartridge receiving area not apparent from FIGS. 2A-2C include the use of a platform underneath the cartridge to keep it rigid while pressure is applied.

[0053] As would be understood by one of ordinary skill in the art, many mechanisms exist for repetitively delivering precise volumes of liquid reagents to a fixed sample. In one embodiment, the mechanism is purely manual and involves a user actively raising and lowering a dispensing head. In preferred embodiments, the dispensing head is under robotic control. In still other embodiments, the dispensing head uses hydraulics.

[0054] FIG. 2D shows an exemplary mechanism for delivering reagents to the microfluidic cartridge. A dispensing head 61, under robotic control, and receiving control signals, e.g., from a microprocessor configured to operate the head, under a user's instructions, is in communication with one or more reagent sources. One or more capillaries 62 feed one or more nozzles 63 with, respectively, one or more reagents such as release buffer, wash buffer, and neutralization buff-

ers, where the one or more reagents are preferably stored on the exterior housing of the system 10, as shown in FIG. 1. Dispensing head 61 has a vertical degree of freedom, as indicated by the arrow in FIG. 2D, that permits it to penetrate and withdraw from the cartridge respectively prior to and after delivering reagent. The two panels of FIG. 2D show the nozzle in a position away from the cartridge, and when delivering reagent. Additionally, and preferably, dispensing head 61 has a degree of freedom sideways—perpendicular to the plane of the paper in FIG. 2D—so that the dispensing head can, e.g., deliver reagent to more than one lane or more than one cartridge of a multi-sample cartridge. Additionally, sideways motion may be for the purpose of permitting the dispensing head to visit more than one cartridge location, such as more than one cartridge receiving element.

[0055] A reagent dispenser preferably and optionally has a sensing mechanism that prevents it from going down too far and damaging either a nozzle 63 or the cartridge, or both. Many sensing mechanisms are consistent with the practice of the invention and may use, e.g., contact sensing (e.g., by detecting onset of or disruption of an electrical current), magnetic sensing, optical sensing, or by use of a mechanical spacer that stops the dispensing head from travelling too far. As further shown in FIG. 2E, an exemplary sensing mechanism uses an optical interrupter. Such a mechanism is effective at ensuring that a good seal is obtained between the dispensing head and the cartridge, without resulting in damage to either. In this embodiment, a screw 66, flag 65 and optical interrupter 64 mounted on a fixed assembly work in cooperation with the dispensing head. Once the dispenser abuts the microfluidic cartridge, the screw pushes the flag up into the sensing position of the optical interrupter, which provides feedback to the motor that controls the dispensing head, causing it to cease the motion of the head.

[0056] As previously described, it is preferable that a nozzle of the dispensing head makes a good contact with a reagent inlet on the microfluidic cartridge. This can be achieved with a number of different approaches known in the art. An exemplary embodiment is shown in FIG. 2F, which can be viewed in conjunction with FIG. 2E. In the left hand panel of FIG. 2F, gasket 67 is shown poised above a pair of adjacent reagent inlets (such as on adjacent lanes) of a microfluidic cartridge 18. Sighting element 68 may facilitate automatic positioning of the gasket. The right hand panel of FIG. 2F shows a cut-away view of gasket 67, in contact with a pair of adjacent reagent inlets of a microfluidic cartridge. The horizontal separation between the reagent inlets may be 1-2 mm. Notches 69 in the underside of the cartridge exemplify a mechanical key used by the cartridge for positioning in the cartridge receiving element. Reagent dispenser tubes, such as capillaries, are shown in cutaway view also, with tips 63 sunk into respective reagent inlets. The configuration shown in the right hand panel of FIG. 2F exemplifies a good seal between dispenser and cartridge, and is desirable for the purpose of avoiding leaks of reagent sample. Leaks are undesirable, because repetitive leaking of reagents within the interior of system 10 can lead to rapid degradation of components through rust, accumulation of mould, and other sources of water-based damage. Leaks are also undesirable because an incorrect (insufficient) quantity of reagent may ultimately be deployed in the microfluidic device, leading to poor sample preparation quality.