

1

## THERMAL MICRO-VALVES FOR MICRO-INTEGRATED DEVICES

This is a conversion of the Provisional Application No. 60/423,594 filed on Nov. 4, 2002.

This work was funded in part by NIH grant number R01-HG01406. The government may have certain rights in the invention.

### FIELD OF THE INVENTION

The present invention relates to microfabrication of microscale devices and reactions in microscale devices, and in particular, movement of biological samples in microdroplets through microchannels to initiate biological reactions. More particularly, the present invention relates to phase change latched valves for micro-integrated devices.

### BACKGROUND

Current bioassay technologies are adequate for the detailed analysis of samples that range in number from hundreds to thousands per year. Projects requiring on the order of millions of assays, however, are beyond the capabilities of today's laboratories because of the current inefficiencies in (i) liquid handling of reagent and DNA template solutions, (ii) measurement of solution volumes, (iii) mixing of reagent and template, (iv) controlled thermal reaction of the mixed solutions, (v) sample loading onto an electrophoresis gel, and (vi) DNA product detection on size-separating gels. What is needed is methodology that allows for a high-volume of biological reactions without these existing inefficiencies.

Microfabricated devices are finding application in a wide range of new areas. As the functions performed by a device increases the design becomes more complicated. It then becomes essential to realize complex fluidic manipulation on the microfabricated chip device. Central to this problem, is the need to develop a microfluidic valve which is not only simple to integrate but also has high reliability as failure of one valve would lead to the failure of the entire device. This is one of the main problems hindering the commercialization of microfluidic devices. A lot of work is being done in both academic institutions and industry to solve this problem. However, most of the valves consist of a movable diaphragm, have intricate principles of actuation and elaborate fabrication procedures. This makes them difficult to integrate into a microfabricated device and makes them much more susceptible to failures such as leakage and breakdown. Therefore, what is needed is a reliable, easy to integrate and, preferably, inexpensive valve for use in conjunction with microfabricated microfluidic devices.

### SUMMARY OF THE INVENTION

The present invention relates to an improvement in the design, production and use of valves in microscale devices and, in particular, the movement and control of liquids through microscale devices utilizing the improved valving devices and methodologies of the present invention.

The present invention relates to microfabrication of phase change latched valves for microscale devices and reactions in microscale devices, and in particular, movement and control of biological samples in microdroplets through microchannels via the phase change latched valves of the present invention. In one embodiment, the present invention contemplates microscale devices, comprising microdroplet

2

transport channels, reaction regions (e.g. chambers), electrophoresis modules, radiation detectors and phase change latch valves. In a preferred embodiment, these elements are microfabricated from silicon and glass substrates. In another embodiment, the various components are linked (i.e., in liquid communication) using a surface-tension-gradient mechanism in which discrete droplets are differentially heated and propelled through etched channels. Electronic components are fabricated on the same substrate material, allowing sensors and controlling circuitry to be incorporated in the same device. Since all of the components are made using conventional photolithographic techniques, multi-component devices can be readily assembled into complex, integrated systems.

In one embodiment, the present invention contemplates phase change latched valves. Although the present invention is not limited to any particular theory, the valves of the present invention operate by inducing a phase change in a material whereupon the material may be liquified in order to move it to a predetermined location where it can act to block the flow of substance through a channel. Upon reaching the predetermined location the material is solidified and, thus, blocks the flow of liquids, gases or other substances through the channel. When desired, the material can be reliquified and drawn back out of the channel to allow the flow of material through the channel.

In one embodiment of the present invention, the particular composition of the material used as the valve may be any material that can convert from a liquid to solid or semisolid form as a result of a change in temperature. In another embodiment, the valving material is inert with respect to the substances being conveyed through the microdevice. In the case of biological assays, said substances may be saline solutions, blood, cell extracts, solutions comprising proteins, minerals (e.g., minerals typically found in biological organisms) or other molecules and compositions found in biological systems, solutions of varying pH typically in the range of pH 1 to pH 13, more typically in the range of pH 4 to pH 10 and even more typically in the range of pH 6 to pH 8, solutions of varying salinity and solutions of varying temperature providing that the temperature of the substrate solution is less than the melting point of the valving material.

In one embodiment of the present invention, the valving material comprises wax (e.g., Logitech wax, paraffin wax, M1595 synthetic wax, C105 wax, APS wax or a mixture thereof). In another embodiment, any wax can be chosen that matches the values of temperature required for other operations on the chip and the melting point of the wax. In yet another embodiment of the reaction, the valving material comprises any material that is relatively inert to the substrate moving through the microdevice channel, and has a melting point that allows for rapid liquification and solidification within the microdevice. For example, in addition to the waxes listed above, metal alloys (e.g., solder) and plastics (any plastic known in the art that has the required melting, cooling and biocompatibility properties) are contemplated for use as valving materials.

It is contemplated in one embodiment of the present invention that the fluid wax is move by positive and negative air pressure. Although the present invention is not limited to any particular theory, in one embodiment, the wax (located, for example, in a side channel) is heated to convert it from a solid or semisolid state to a liquid state. Since the volume of wax used is small and the heating device is located in the microfabricated device, the wax can be heated to melting point quickly. Upon melting, the wax is pushed forward by