

nozzle structures for purposes of illustrating the use of the microfluidic nozzle array device **100** in UV spectrophotometry. In this exemplary arrangement, UV light is emitted from a source **540** and travels toward the microfluidic nozzle array device **100** and is incident on the reservoir side **120**. The UV light travels through the reservoir **160** and continues to travel along the length of the microfluidic channel **140**, both of which hold the sample (e.g., liquid and analytes). The UV light travels through the nozzle opening **144** to a detector **550** that is disposed such that it faces the side of the microfluidic nozzle array device that contains the nozzles **170**. The UV light carries the spectrophotometric information of the analyte is detected by the detector **550** of the UV reader. In this manner, the formation of perpendicular orientated microfluidic channels provides advantageously permits UV spectrophotometry to be carried out in an easy and convenient manner since the microfluidic nozzle array device **100** can easily be disposed between a UV light source and the detector **550** of the UV reader. Likewise, transmission fluorescence spectroscopy can be carried out using the microfluidic nozzle array device **100**.

[**0088**] Unlike conventional microfluidic devices where optical windows formed of an optical material were fabricated in the devices, the substrate body of the present microfluidic nozzle array device does not have to be formed of an optically transparent material. This reduces the complexity of the fabrication process since this requirement is not present in the microfluidic nozzle array device.

[**0089**] The present microfluidic nozzle array devices disclosed herein also can be used in a wide range of other applications in which similar conventional devices have typically been used. For example, the microfluidic nozzle array device can be used for spotting DNA or protein array on a substrate instead of using the conventional capillary wicking methods that are now used with metallic capillaries. Presently, the DNA array spotting is primarily carried out by "wicking" DNA fragments into an open split end of a metallic capillary. To spot in an array format on a glass slide, the split end of the capillary is pressed slightly onto the glass slide by a robotic arm or the like to facilitate the deposition of the DNA fragments. On being lifted from the glass slide, the metallic capillary has a tendency to "spring" off the glass slide. As a result of this phenomena and other factors, it is common that about 20% of spots in the array are deficient in some way, e.g., either the spot is bare or an inadequate amount of material has been deposited. Spotting is typically carried out with a row of eight to twelve capillaries using an expensive machine and the capillaries are rinsed and reused for different DNA samples.

[**0090**] The present microfluidic nozzle array devices disclosed herein have smaller nozzle openings (e.g., 20  $\mu\text{m}$  or less) than conventional nozzle constructions and a number of advantages can be realized using the present microfluidic nozzle array devices in comparison to the conventional metal capillaries. First, the injection-molded microfluidic nozzle array devices can be disposed of after each deposition. Thus, the time consuming rinsing process is eliminated and there is no risk of cross-contamination since the devices are not reused. Second, DNA or protein molecules are not adsorbed on the walls of the polymeric nozzle as they are adsorbed on metallic surfaces. The spotting is therefore more complete when the molecules leave the polymeric nozzle to be deposited on the glass slide. Third, a two

dimensional nozzle spotter can be manufactured inexpensively thereby greatly increasing the speed of the spotting operation. Fourth, the deposition of the DNA or protein molecules from the polymeric nozzle can be assisted by pumping the molecules out of the nozzle with high pressure air using one of the aforementioned devices and/or with an electric field for electrospray.

[**0091**] The microfluidic nozzle array device can also be used for spotting the plate for matrix-assisted laser desorption ionization (MALDI), replacing the pipette and capillary spotting methods. For matrix-assisted laser desorption and ionization mass spectrometry, a dominant analytical technique for protein molecules and fragments of high molecular weight, the molecules to be analyzed are deposited on a layer of matrix material, usually UV-absorbant molecules that can be vaporized by a UV laser. The molecules of interest are thus carried into the gas phase and are ionized alongside the matrix molecules. Traditionally, the metallic (usually aluminum) MALDI plate is spotted manually with the use of micropipettes and more recently with capillaries. The efficiency of the ionization process will be enhanced if the metallized polymeric nozzles are used for spotting. The matrix material is first electrosprayed onto the aluminum MALDI plate which is held at ground potential, whereas the metal coated nozzle is held at high voltage or vice versa. The molecules of interest are then electrosprayed in a new nozzle onto the matrix material. The spraying allows the matrix molecules and the molecules of interest to be more evenly intermingled with one another, thus enhancing the efficiency of laser assisted desorption and ionization. The spotting of the MALDI plate may also be carried out with a two-dimensional array of nozzles for high throughput. Thus, the density of the nozzle array can be greatly increased and this permits the density of the spotting array to be increased. Accordingly, more testing or experimental sites are provided on the substrate as a result on the increased density in the spotting. It will also be appreciated that an electric field can also be used to assist in the spotting process. The electric field can be generated by using the arrangement illustrated in **FIG. 3** or by some other type of suitable arrangement.

[**0092**] One will further appreciate that the manufacturing methods disclosed herein that are based on injection molding techniques can be used to make pipette tips for nano to picoliter dispensing. In other words, a mold can be fabricated and resin can be injected into the mold to form pipette tips that have an elongated body and terminate in a tip section that has a tip opening having an inside diameter of less than about 20  $\mu\text{m}$  (with the tip section having an outside diameter of less than about 50  $\mu\text{m}$ ).

[**0093**] The following examples serve merely to illustrate several embodiments of the present microfluidic array devices and do not limit the scope of the present invention in any way.

#### EXAMPLE 1

[**0094**] A polymeric microfluidic nozzle array device is fabricated using the technology disclosed herein is by first providing a mold designed for an injection mold process. The mold is formed of a metal and a conical surface of the mold that defines the nozzle portion of the microfluidic device is polished with a diamond paste to form a highly polished surface. More specifically, the conical surface is