sions, applied voltages, and time provide a precise and reproducible method of sample apportionment or deposition from an array of nozzles, such as for the generation of sample plates for molecular weight determinations by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry ("MALDI-TOFMS"). The capability of transferring analytes from a mother plate to daughter plates may also be utilized to make other daughter plates for other types of assays, such as proteomic screening. The fluid to substrate potential voltage ratio can be chosen for formation of an electrospray or droplet mode based on a particular application.

[**0164**] The electrospray device of the present invention can be integrated with miniaturized liquid sample handling devices for efficient electrospray of the liquid samples for detection using a mass spectrometer. The electrospray device may also be used to distribute and apportion fluid samples for use with high-throughput screen technology. The electrospray device may incorporate polymer monolith for producing a liquid separation stationary phase. The electrospray device may be chip-to-chip or wafer-to-wafer bonded to plastic, glass, or silicon microchip-based liquid separation devices capable of, for example, capillary electrophoresis, capillary electrochromatography, affinity chromatography, liquid chromatography ("LC"), or any other condensed-phase separation technique.

[**0165**] An array or matrix of multiple electrospray devices of the present invention may be manufactured on a single microchip as silicon fabrication using standard, well-controlled thin-film processes. This not only eliminates handling of such micro components but also allows for rapid parallel processing of functionally similar elements. The low cost of these electrospray devices allows for one-time use such that cross-contamination from different liquid samples may be eliminated.

[**0166**] A multi-system chip thus provides a rapid sequential chemical analysis system fabricated using Micro-ElectroMechanical System ("MEMS") technology. For example, the multi-system chip enables automated, sequential separation and injection of a multiplicity of samples, resulting in significantly greater analysis throughput and utilization of the mass spectrometer instrument for, for example, high-throughput detection of compounds for drug discovery.

[**0167**] Another aspect of the present invention provides a silicon microchip-based electrospray device for producing electrospray of a liquid sample. The electrospray device may be interfaced downstream to an atmospheric pressure ionization mass spectrometer ("API-MS") for analysis of the electrosprayed fluid. Another aspect of the invention is an integrated miniaturized liquid phase separation device, which may have, for example, glass, plastic or silicon substrates integral with the electrospray device.

[**0168**] Electrospray Device Fabrication Procedure

[**0169**] The polymer monolith/multiple-electrospray device **250** is preferably fabricated as a monolithic silicon substrate utilizing well-established, controlled thin-film silicon processing techniques such as thermal oxidation, photolithography, reactive-ion etching (RIE), chemical vapor deposition, ion implantation, and metal deposition. Fabrication using such silicon processing techniques facilitates massively parallel processing of similar devices, is time- and cost-efficient, allows for tighter control of critical dimensions, is easily reproducible, and results in a wholly integral device, thereby eliminating any assembly requirements. Further, the fabrication sequence may be easily extended to create physical aspects or features on the injection surface and/or ejection surface of the electrospray device to facilitate interfacing and connection to a fluid delivery system or to facilitate integration with a fluid delivery sub-system to create a single integrated system.

[**0170**] Ejection or Nozzle Surface Processing

[**0171**] FIGS. **13A-13E** illustrate the processing steps for the ejection or nozzle side of the substrate in fabricating the electrospray device of the present invention. Referring to the plan view of **FIG. 13A, a** mask is used to pattern **202** that will form the nozzle shape in the completed electrospray device **250**. The patterns in the form of circles **204** forms through-substrate channels and **206** forms a recessed annular space around nozzles of a completed electrospray device. **FIG. 13B** is the cross-sectional view taken along line **13**B-**13**B of **FIG. 13A**. A double-side polished silicon wafer **200** is subjected to an elevated temperature in an oxidizing environment to grow a layer or film of silicon dioxide **210** on the nozzle side and a layer or film of silicon dioxide **212** on the reservoir side of the substrate **200**. Each of the resulting silicon dioxide layers **210, 212** has a thickness of approximately 1-3 μm. The silicon dioxide layers **210, 212** serve as masks for subsequent selective etching of certain areas of the silicon substrate **200**.

[**0172**] A film of positive-working photoresist **208** is deposited on the silicon dioxide layer **210** on the nozzle side of the substrate **200**. Referring to **FIG. 13**C, an area of the photoresist **204** corresponding to the entrance to through-wafer channels and an area of photoresist corresponding to the recessed annular region **206** which will be subsequently etched is selectively exposed through a mask (**FIG. 13A**) by an optical lithographic exposure tool passing short-wavelength light, such as blue or near-ultraviolet at wavelengths of 365, 405, or 436 nanometers.

[**0173**] As shown in the cross-sectional view of **FIG. 13**C, after development of the photoresist **208**, the exposed area **204** of the photoresist is removed and open to the underlying silicon dioxide layer **214** and the exposed area **206** of the photoresist is removed and open to the underlying silicon dioxide layer **216**, while the unexposed areas remain protected by photoresist **208**. Referring to **FIG. 13**D, the exposed areas **214, 216** of the silicon dioxide layer **210** is then etched by a fluorine-based plasma with a high degree of anisotropy and selectivity to the protective photoresist **208** until the silicon substrate **218, 220** are reached. As shown in the cross-sectional view of **FIG. 13**E, the remaining photoresist **208** is removed from the silicon substrate **200**.

[**0174**] Injection or Reservoir Surface Processing

[**0175**] Referring to the plan view of **FIG. 14A, a** mask is used to pattern **224** in the form of a circle on the injection surface. **FIG. 14B** is the cross-sectional view taken along line **14**B-**14**B of **FIG. 14A**. A film of positive-working photoresist **226** is deposited on the silicon dioxide layer **212** on the reservoir side of the substrate **200**. Referring to **FIG. 14**C, an area of the photoresist **224** corresponding to the reservoir placement is selectively exposed through a mask (**FIG. 14A**) by an optical lithographic exposure tool passing