[0154] Preferably, the nozzle, channel and recess are etched from the silicon substrate by reactive-ion etching and other standard semiconductor processing techniques. The nozzle side features, through-substrate fluid channel, reservoir side features, and controlling electrodes are preferably formed monolithically from a monocrystalline silicon substrate—i.e., they are formed during the course of and as a result of a fabrication sequence that requires no manipulation or assembly of separate components.

[0155] Because the electrospray device is manufactured using reactive-ion etching and other standard semiconductor processing techniques, the dimensions of such a device can be very small, for example, as small as 2 μm inner diameter and 5 μm outer diameter. Thus, a through-substrate fluid channel having, for example, 5 μm inner diameter and a substrate thickness of 250 μm only has a volume of 4.9 pL. The micrometer-scale dimensions of the electrospray device minimize the dead volume and thereby increase efficiency and analysis sensitivity when combined with a separation device.

[0156] The electrospray device of the present invention provides for the efficient and effective formation of an electrospray. By providing an electrospray surface from which the fluid is ejected with dimensions on the order of micrometers, the electrospray device limits the voltage required to generate a Taylor cone as the voltage is dependent upon the nozzle diameter, the surface tension of the fluid, and the distance of the nozzle from an extracting electrode. The nozzle of the electrospray device provides the physical asperity on the order of micrometers on which a large electric field is concentrated. Further, the electrospray device may provide additional electrode(s) on the ejecting surface to which electric potential(s) may be applied and controlled independent of the electric potentials of the fluid and the extracting electrode in order to advantageously modify and optimize the electric field in order to focus the gas phase ions resulting from electrospray of fluids. The combination of the nozzle and the additional electrode(s) thus enhance the electric field between the nozzle, the substrate and the extracting electrode. The electrodes are preferable positioned within about 500 microns, and more preferably within about 200 microns from the exit orifice.

[0157] The microchip-based electrospray device of the present invention provides minimal extra-column dispersion as a result of a reduction in the extra-column volume and provides efficient, reproducible, reliable and rugged formation of an electrospray. This electrospray device is perfectly suited for the electrospray of fluids from microchip-based separation devices. The design of this electrospray device is also robust such that the device can be readily mass-produced in a cost-effective, high-yielding process.

[0158] In operation, a conductive or partly conductive liquid sample is introduced into the through-substrate channel entrance orifice on the injection surface. The liquid is held at a potential voltage, either by means of a conductive fluid delivery device to the electrospray device or by means of an electrode formed on the injection surface isolated from the surrounding surface region and from the substrate. The electric field strength at the tip of the nozzle is enhanced by the application of a voltage to the substrate and/or the ejection surface, preferably zero volts up to approximately less than one-half of the voltage applied to the fluid. Thus, by the independent control of the fluid/nozzle and substrate/ejection surface voltages, the electrospray device of the present invention allows the optimization of the electric field emanating from the nozzle. The electrospray device of the present invention may be placed 1-2 mm or up to 10 mm from the orifice of an atmospheric pressure ionization ("API") mass spectrometer to establish a stable nanoelectrospray at flow rates in the range of a few nanoliters per minute.

[0159] The electrospray device may be interfaced or integrated downstream to a sampling device, depending on the particular application. For example, the analyte may be electrosprayed onto a surface to coat that surface or into another device for purposes of conveyance, analysis, and/or synthesis. As described above, highly charged droplets are formed at atmospheric pressure by the electrospray device from nanoliter-scale volumes of an analyte. The highly charged droplets produce gas-phase ions upon sufficient evaporation of solvent molecules which may be sampled, for example, through an ion-sampling orifice of an atmospheric pressure ionization mass spectrometer ("API-MS") for analysis of the electrosprayed fluid.

[0160] One embodiment of the present invention includes an array of multiple electrospray devices which allows for extensive parallel processing. The multiple electrospray devices or systems fabricated by an extensive amount of parallel processing on a single wafer may then be cut or otherwise separated into multiple devices or systems.

[0161] The polymer monolith/electrospray device may also serve to reproducibly distribute and deposit a sample from a mother plate to daughter plate(s) by nanoelectrospray deposition or by the droplet method. A chip-based combinatorial chemistry system including a reaction well block may define an array of reservoirs for containing the reaction products from a combinatorially synthesized compound. The reaction well block further defines channels, nozzles and recessed portions such that the fluid in each reservoir may flow through a corresponding channel and exit through a corresponding nozzle in the form of droplets. The reaction well block may define any number of reservoir(s) in any desirable configuration, each reservoir being of a suitable dimension and shape. The volume of a reservoir may range from a few picoliters up to several microliters.

[0162] The reaction well block may serve as a mother plate to interface to a microchip-based chemical synthesis apparatus such that the droplet method of the electrospray device may be utilized to reproducibly distribute discreet quantities of the product solutions to a receiving or daughter plate. The daughter plate defines receiving wells that correspond to each of the reservoirs. The distributed product solutions in the daughter plate may then be utilized to screen the combinatorial chemical library against biological targets.

[0163] The polymer monolith/electrospray device may also serve to reproducibly distribute and deposit an array of samples from a mother plate to daughter plates, for example, for proteomic screening of new drug candidates. This may be by either droplet formation or electrospray modes of operation. Electrospray device(s) may be etched into a microdevice capable of synthesizing combinatorial chemical libraries. At a desired time, a nozzle(s) may apportion a desired amount of a sample(s) or reagent(s) from a mother plate to a daughter plate(s). Control of the nozzle dimen-