Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).
Description

BACKGROUND OF THE INVENTION

[0001] There has been a growing interest in the manufacture and use of microfluidic systems for the acquisition of chemical and biochemical information. Techniques commonly associated with the semiconductor electronics industry, such as photolithography, wet chemical etching, etc., are being used in the fabrication of these microfluidic systems. The term, "microfluidic", refers to a system or device having channels and chambers which are generally fabricated at the micron or sub-micron scale, e.g., having at least one cross-sectional dimension in the range of from about 0.1 μm to about 500 μm. Early discussions of the use of planar chip technology for the fabrication of microfluidic systems are provided in Manz et al., Trends in Anal. Chem. (1990) 10 (5):144-149 and Manz et al., Avd. in Chromatog. (1993) 33:1-66, which describe the fabrication of such fluidic devices and particularly microcapillary devices, in silicon and glass substrates.


[0002] Applications of microfluidic systems are myriad. For example, International Patent Appln. WO 96/04547, published February 15, 1996, describes the use of microfluidic systems for capillary electrophoresis, liquid chromatography, flow injection analysis, and chemical reaction and synthesis. A related patent application, U.S. Appln. No. 671897, entitled "HIGH THROUGHPUT SCREENING ASSAY SYSTEMS IN MICROSCE FLUIDIC DEVICES", filed June 28, 1996 by J. Wallace Parce et al. and assigned to the present assignee, discloses wide ranging applications of microfluidic systems in rapidly assaying compounds for their effects on various chemical, and preferably, biochemical systems. The phrase, "biochemical system" generally refers to a chemical interaction that involves molecules of the type generally found within living organisms. Such interactions include the full range of catabolic and anabolic reactions which occur in living systems including enzymatic, binding, signaling and other reactions. Biochemical systems of particular interest include, e.g., receptor-ligand interactions, enzyme-substrate interactions, cellular signaling pathways, transport reactions involving model barrier systems (e.g., cells or membrane fractions) for bioavailability screening, and a variety of other general systems.

[0003] Many methods have been described for the transport and direction of fluids, e.g., samples, analytes, buffers and reagents, within these microfluidic systems or devices. One method moves fluids within microfabricated devices by mechanical micropumps and valves within the device. See, Published U.K. Patent Application No. 2 248 891 (10/18/90), Published European Patent Application No. 568 902 (5/2/92), U.S. Patent Nos. 5,271,724 (8/21/91) and 5,277,556 (7/3/91). See also, U.S. Patent No. 5,171,132 (12/21/90) to Miyazaki et al. Another method uses acoustic energy to move fluid samples within devices by the effects of acoustic streaming. See, Published PCT Application No. 94/05414 to Northrup and White. A straightforward method applies external pressure to move fluids within the device. See, e.g., the discussion in U.S. Patent No. 5,304,487 to Wilding et al. [0004] Still another method uses electric fields, and the resulting electrokinetic forces, to move fluid materials through the channels of the microfluidic system. See, e.g., Published European Patent Application No 544 969 Published European Patent Application No. 376 611 (12/30/88) to Kovacs. Harrison et al., Anal. Chem. (1992) 64:1926-1932 and Manz et al. J. Chromatog. (1992) 593:253-258, U.S. Patent No. 5,126,022 to Soane. Electrophoretic forces have the advantages of direct control, fast response and simplicity. However, there are still some disadvantages with this method of operating a microfluidic system.

[0005] Present devices use a network of channels in a substrate of electrically insulating material. The channels connect a number of fluid reservoirs in contact with high voltage electrodes. To move fluid materials through the network of channels, specific voltages are simultaneously applied to the various electrodes. The determination of the voltage values for each electrode in a system becomes complex as one attempts to control the material flow in one channel without affecting the flow in another channel. For example, in a relatively simple arrangement of four channels intersecting in a cross with reservoirs and electrodes at the ends of the channels, an independent increase of fluid flow between two reservoirs is not merely a matter of increasing the voltage differences at the two reservoirs. The voltages at the other two reservoirs must also be adjusted if their original flow and direction are to be maintained. Furthermore, as the number of channels, intersections, and reservoirs are increased, the control of fluid through the channels become more and more complex.

[0006] Also, the voltages applied to the electrodes in the device can be high, i.e., up to a level supportive of thousands of volts/cm. Regulated high voltage supplies are expensive, bulky and are often imprecise and a high voltage supply is required for each electrode. Thus the cost of a microfluidic system of any complexity may become prohibitive.

[0007] The present invention solves or substantially mitigates these problems of electrokinetic transport in a microfluidic system which uses another electrical parameter, rather than voltage, to simplify the control of material flow through the channels of the system. A high throughput microfluidic system having direct, fast and straightforward control over the movement of materials through the channels of the microfluidic system with a wide range of applications, such as in the fields of chemistry, biochemistry, biotechnology and molecular biology and numerous other fields, is possible.

SUMMARY OF THE INVENTION

[0008] The present invention provides for a microflu-
idic system with a plurality of interconnected capillary channels according to claim 15 and a method of using a microfluidic system according to claim 1 and a use of a substrate according to claim 8.

[0009] Furthermore, the present invention provides for time-multiplexing the power supply voltages on the electrodes of the microfluidic system for more precise and efficient control. The voltage to an electrode can be controlled by varying the duty cycle of the connection of the electrode to the power supply, varying the voltage to the electrode during the duty cycle, or a combination of both. In this manner, one power supply can service more than one electrode.

[0010] The present invention also provides for the direct monitoring of the voltages within the channels in the microfluidic system. Conducting leads on the surface of the microfluidic system have widths sufficiently narrow in a channel to prevent electrolysis. The leads are connected to voltage divider circuits also on the surface of the substrate. The divider circuit lowers the read-out voltage of the channel reservoir so that special high-voltage voltmeters are not required. The divider circuits are also designed to draw negligible currents from the channels thereby minimizing unwanted electrochemical effects, e.g., gas generation, reduction/oxidation reactions.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] Figure 1 shows a representative illustration of a microfluidic system;

Figure 2A illustrates an exemplary channel of a microfluidic system, such as that of Figure 1; Figure 2B represents the electrical circuit created along the channel in Figure 2A;

Figure 3A is a graph of output voltage versus time for a prior art power supply; Figure 3B is a graph of output voltage versus time for a time-multiplexed power supply according to the present invention;

Figure 4A is a representative illustration of a microfluidic system operating with time-multiplexed voltages according to the present invention; Figure 4B is a block diagram illustrating the units of a power supply in Figure 4A;

Figure 5A is a representative illustration of a microfluidic system with voltage-monitored nodes according to the present invention; Figure 5B details the voltage divider circuit of Figure 5A; and

Figure 6A is a block diagram of the power supply unit of Figure 4B; Figure 6B is an amplifier block representation of the DC-DC converter block of Figure 6A.

DETAILED DESCRIPTION OF THE INVENTION

[0012] Figure 1 discloses a representative diagram of a portion of an exemplary microfluidic system 100 oper-
techniques that are well known in the art. For example, lithographic techniques may be employed in fabricating glass, quartz or silicon substrates, for example, with methods well known in the semiconductor manufacturing industries. Photolithographic masking, plasma or wet etching and other semiconductor processing technologies define micromask elements in and on substrate surfaces. Alternatively, micromachining methods, such as laser drilling, micromilling and the like, may be employed. Similarly, for polymeric substrates, well known manufacturing techniques may also be used. These techniques include injection molding techniques or stamp molding methods where large numbers of substrates may be produced using, e.g., rolling stamps to produce large sheets of microscale substrates or polymer microcasting techniques wherein the substrate is polymerized within a micromachined mold.

[0016] Besides the substrate 102, the microfluidic system 100 includes an additional planar element (not shown) which overlies the channels 100 to enclose and fluidly seal the various channels to form conduits. The planar cover element may be attached to the substrate by a variety of means, including, e.g., thermal bonding, adhesives or, in the case of certain substrates, e.g., glass, or semi-rigid and non-rigid polymeric substrates, a natural adhesion between the two components. The planar cover element may additionally be provided with access ports and/or reservoirs for introducing the various fluid elements needed for a particular screen.

[0017] The system 100 shown in Figure 1 also includes reservoirs 104, 106 and 108, which are disposed and fluidly connected at the ends of the channels 114, 116 and 110 respectively. As shown, the channel 112 is used to introduce a plurality of different subject materials into the device. As such, the channel 112 is fluidly connected to a source of large numbers of separate subject materials which are individually introduced into the channel 112 and subsequently into another channel 110 for electrophoretic analysis, for example. The subject materials are transported in fluid slug regions 120 of predetermined ionic concentrations. The regions are separated by buffer regions 121 in Figure 1. Related patent applications, U.S. Appln. No. 08/671,986, filed June 28, 1996, and U.S. Appln. No. 08/760,446, filed December 6, 1996, both entitled "ELECTROPINETTOR AND COMPENSATION MEANS FOR ELECTROPHORETIC BIAS," by J. Wallace Parce and Michael R. Knapp, and assigned to the present assignee, explain various arrangements of slugs, and buffer regions of high and low ionic concentrations in transporting subject materials with electokinetic forces.

[0018] To move materials through the channels 110, 112, 114 and 116, a voltage controller which is capable of simultaneously applying selectable voltage levels, including ground, to each of the reservoirs, may be used. Such a voltage controller may be implemented using multiple voltage dividers and relays to obtain the selectable voltage levels. Alternatively, multiple independent voltage sources may be used. The voltage controller is electrically connected to each of the reservoirs via an electrode positioned or fabricated within each of the reservoirs 104, 106 and 108. See, for example, international Patent Application No. WO 96/04547 to Ramsey.

[0019] Besides complexity, there are other problems with voltage control in a microfluidic system. Figure 2A illustrates an exemplary channel 130 between two reservoirs 132 and 134, each respectively in contact with electrodes 133 and 135, connected to electrical leads are shown leading off the substrate 128. To make the example more realistic, the channel 130 is shown as being connected to two other channels 136 and 138. Operationally, the reservoir 132 is a source for slugs 120 containing the subject material. The slugs 120 are moved toward the reservoir 134, which acts as a sink. The channels 136 and 138 provide buffer regions 121 to separate the slugs 120 in the channel 130.

[0020] The different resistances of the slugs 120 and buffer regions 121 in the channel 130 create an electrical circuit which is symbolically indicated in this simple example. The voltage V applied between the two electrodes 133 and 135 is:

\[
V = I \sum_{i=0}^{n} R_i
\]

where I is the current between the two electrodes 133, 135 (assuming no current flow into 136, 138) and R the resistance of the different slugs 120 and buffer regions 121.

[0021] A voltage control system is subject to many factors which can interfere with the operation of the system. For example, the contact at the interface between an electrode and fluid may be a source of problems. When the effective resistance of the electrode-to-fluid contact varies due to contaminants, bubbles, oxidation, for example, the voltage applied to the fluid varies. With V set at the electrodes, a decrease in electrode surface area contacting the solution due to bubble formation on the electrode causes an increase in resistance from the electrode to the solution. This reduces the current between electrodes, which in turn reduces the induced electromotive and electrophoretic forces in the channel 130.

[0022] Other problems may affect the channel current flow. Undesirable particulates may affect the channel resistance by effectively modifying the cross-sectional area of the channel. Again, with a change of channel resistance, the physical current flow is changed.

[0023] With other channels, such as channels 136 and 138, connected to the exemplary channel 130, dimensional variations in the geometry of the channels in the substrate 102 can seriously affect the operation of a voltage control system. For example, the intersection node
for the channels 130, 136 and 138 might be X distance from the electrode for the reservoir at the terminus of the channel 136 (not shown) and Y distance from the electrode for the reservoir at the terminus of the channel 138 (not shown). With a slight lateral misalignment in the photolithographic process, the distances X and Y are no longer the same for the microfluidic system on another substrate. The voltage control must be recalibrated from substrate to substrate, a time-consuming and expensive process, so that the fluid movement at the intersection node can be properly controlled.

[0024] To avoid these problems, the present invention uses electric current control in the microfluidic system 100. The electrical current flow at a given electrode is directly related to the ionic flow along the channel(s) connecting the reservoir in which the electrode is placed. This is in contrast to the requirement of determining voltages at various nodes along the channel in a voltage control system. Thus the voltages at the electrodes of the microfluidic system 100 are set responsive to the electric currents flowing through the various electrodes of the system 100. Current control is less susceptible to dimensional variations in the process of creating the microfluidic system on the substrate 102. Current control permits far easier operations for pumping, valving, dispensing, mixing and concentrating subject materials and buffer fluids in a complex microfluidic system. Current control is also preferred for moderating undesired temperature effects within the channels.

[0025] Of course, besides electric current which provides a direct measure of ionic flow between electrodes, other electrical parameters related to current, such as power, may be used as a control for the microfluidic system 100. Power gives an indirect measurement of the electric current through an electrode. Hence the physical current between electrodes (and the ionic flow) can be monitored by the power through the electrodes.

[0026] Even with a current control system described above, high voltages must still be applied to the electrodes of the microfluidic system. To eliminate the need for expensive power supplies which are capable of generating continuous and precise high voltages, the present invention provides for power supplies which are time-multiplexed. These time-multiplexed power supplies also reduce the number of power supplies required for the system 100, since more than one electrode can be serviced by a time-multiplexed power supply.

[0027] Figure 3A illustrates the exemplary output of a high power supply presently used in an electrokinetic system. The output is constant at 250 volts between two electrodes over time. In contrast, Figure 3B illustrates the output of a power supply operating according to the present invention. To maintain a constant voltage of 250 volts, the output voltage is time-multiplexed with a one-quarter duty cycle at 1000 volts. Averaged in time, the output of the time-multiplexed voltage supply is 250 volts, as illustrated by the horizontal dotted line across the graph. Note that if the voltage must change, say, in response to current control, as discussed above, the output voltage of the time-multiplexed power supply can also change by a change in the applied voltage, or by a change in the duty cycle, or a combination of both.

[0028] Electroosmotic fluid flow can be started and stopped on the microsecond time scale in channels of the dimensions described here. Therefore, voltage modulation frequencies which are lower than one Megahertz result in choppy movement of the fluids. This should have no adverse effects on fluid manipulation due to the plug flow nature of electroosmotic fluid. Because most chemical mixing, incubating and separating events occur on the 0.1 to 100 second time scale, the much lower frequencies for voltage manipulation may be acceptable. As a rule of thumb, the modulation period should be less than 1% of the shortest switching event (e.g., switching flow from one channel to another) to keep mixing or pipetting errors below 1%. For a switching event of 0.1 seconds, the voltage modulation frequency should be 1 KHz or higher.

[0029] Figure 4A is a block diagram of a multiplexed power supply system with two power supplies 200 and 202 and controller block 204 for an exemplary and simple microfluidic system having a channel 180 which intersects channels 182, 184, 186 and 188. The channel 180 terminates in reservoirs 179 and 181 with electrodes 190 and 191 respectively. The channel 182 ends with a reservoir 183 having an electrode 193; the channel 184 ends with a reservoir 185 having an electrode 195; the channel 186 with reservoir 187 having an electrode 197; and the channel 188 with reservoir 189 having an electrode 199.

[0030] The power supplies 200 and 202 are connected to the different electrodes 190, 191, 193, 195, 197 and 199 of the microfluidic system. The power supply 200 is connected to three electrodes 190, 193 and 195, and the power supply 202 is connected to the remaining three electrodes 191, 197 and 199. The controller block 204 is connected to each of the power supplies 200 and 202 to coordinate their operations. For instance, to control the movements of fluids through the channels 182, 184, 186 and 188, the voltages on the electrodes 190, 191, 193, 195, 197 and 199 must be properly timed. The voltages on the electrodes change in response to electric current flow, as described above, for example, as the controller block 204 directs the power supplies 200 and 202.

[0031] Each of the power supplies 200 and 202 are organized into units illustrated in Figure 4B. A control unit 212 receives control signals from the controller block 204 and directs the operation of a switching unit 214: The switching unit 214, connected to a power supply unit 216, makes or breaks connections of the power supply unit 216 to the connected electrodes. In other words, the switching unit 214 time-multiplexes the power from the power supply unit 216 among its connected electrodes. The power supply unit 216 is also connected to the control unit 212 which directs the variation of output from the power supply unit 216 to the switching unit 214. In an alternate arrangement, this connection to the control unit...
The node between the two resistances 221 and 223 which form a voltage divider connected to ground through two series-resistors 221 and 223. The second output terminal of the converter 231 is grounded to the power supply output terminal 241. The voltage amplifier is connected to ground through the resistors 221-223 and operational amplifier 230. The switch 234 connects its output terminal to either the output terminal 241, the voltage at the terminal 241 is high, the feedback voltage is fed directly back to the mixing block and is connected to the second input terminal of the mixing block, as described previously.

The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.

The power supply output terminal 241 is also connected to ground through two series-connected resistances 221 and 223 which form a voltage divider circuit. The node between the two resistances 221 and 223 is connected to one input terminal of a current/voltage mode switch 234. The node is also connected to the negative input terminal of a feedback operational amplifier 232 through a resistance 225. The negative input terminal is also connected to the output terminal of the converter 231 through a resistor 224 and to the output terminal of the amplifier 232 through a feedback resistor 226. The output terminal of the amplifier 232 is also connected to a second input terminal of the switch 234, which has its output terminal connected to the negative input terminal of the input operational amplifier 230 through a resistor 229.

The switch 234 is responsive to a signal on the control terminal 242. As shown in Figure 6A, the switch 234 connects its output terminal to either the output terminal of the feedback operational amplifier 232, or the voltage divider node between the two resistors 221 and 223. The connection determines whether the power supply circuit operates in the voltage mode (connection to the voltage divider node) or in the current mode (connection to the output of the feedback operational amplifier 232). Note that the resistor 221 is very large, approximately 15 MΩ, so that the voltage on the output terminal 241 can be easily fed back when the power supply is operated.

The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.

The power supply output terminal 241 is also connected to ground through two series-connected resistances 221 and 223 which form a voltage divider circuit. The node between the two resistances 221 and 223 is connected to one input terminal of a current/voltage mode switch 234. The node is also connected to the negative input terminal of a feedback operational amplifier 232 through a resistance 225. The negative input terminal is also connected to the output terminal of the converter 231 through a resistor 224 and to the output terminal of the amplifier 232 through a feedback resistor 226. The output terminal of the amplifier 232 is also connected to a second input terminal of the switch 234, which has its output terminal connected to the negative input terminal of the input operational amplifier 230 through a resistor 229.

The switch 234 is responsive to a signal on the control terminal 242. As shown in Figure 6A, the switch 234 connects its output terminal to either the output terminal of the feedback operational amplifier 232, or the voltage divider node between the two resistors 221 and 223. The connection determines whether the power supply circuit operates in the voltage mode (connection to the voltage divider node) or in the current mode (connection to the output of the feedback operational amplifier 232). Note that the resistor 221 is very large, approximately 15 MΩ, so that the voltage on the output terminal 241 can be easily fed back when the power supply is operated.

The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.

The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.

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The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.

The power supply has an input terminal 240 which is supplied with a controllable reference voltage from -5 to +5 volts, which is stepped up in magnitude to hundreds of volts at an output terminal 241. The input terminal is connected to the negative input terminal of an input operational amplifier 230 through an resistance 227. The positive input terminal of an operational amplifier 230 is grounded and its output terminal is connected back to the negative input terminal through a feedback resistor 226. The resistors 221-223 may be considered as part of a feedback block which also has resistors 222-226 and operational amplifier 232. The switch 234 is also part of the feedback block and is connected to the second input terminal of the mixing block, as described previously.
[0040] The feedback block also has the operational amplifier 232 and the resistances 224-226 which are connected to configure the operational amplifier 232 as a summing amplifier. One input to the summing amplifier is connected to the node between the resistors 221 and 223. The second input is connected to the node between the resistor 222 connected to ground and the second output terminal of the DC-DC converter 231. The summing amplifier measures the difference between the amount of current through the series-connected resistors 221 and 223 and through the converter 231 (the total current through the resistors 222 and 224). In effect, the summing amplifier measures the amount of current being delivered through the output terminal 241. Thus when the switch 234 is set in the current feedback mode, the output from the operational amplifier 232 acting as a summing amplifier is sent to the mixing block and the power supply circuit is stabilized about the amount of current being delivered through the power supply terminal 241 to a connected electrode of a microfluidic system.

[0041] The output of the summing amplifier is also connected to an operational amplifier 250, configured as a simple buffer, to send the output voltage to the monitoring circuit (not shown). From the outputs of the operational amplifiers 250 and 251, the monitoring circuit has a measure of the voltage at the output terminal 241 and of the current through the terminal. This also allows the monitoring circuit to determine, and to regulate, the amount of power being supplied by the power supply circuit.

[0042] The ability of the described power supply to act as a variable source allows the direction of fluid flow through the microchannels of a microfluidic system to be changed electronically. If all of the electrodes are connected to one or more of the power supplies described above, operation of the microfluidic system is greatly enhanced and the desired movements of fluids through the network of channels in the system are much more flexible.

[0043] Despite operation as a current control system, there is often still a need to determine the voltage at a node in a microfluidic system. The present invention also provides a means for such voltage monitoring. As shown in Figure 5A, an electrical lead 160 is formed on the surface of a substrate 178 near a desired node 173 in the microfluidic system. The node 173 is at the intersection of channel 170 having reservoirs 169 and 171 at each end and channels 172 and 174. The terminus of the channel 174 has a reservoir 175, while the terminus of the channel 172 (and a reservoir) is not shown.

[0044] The lead 160 is preferably formed by the deposition of a conductive metal, or metal alloy, preferably a noble metal, such as gold on chrome or platinum on titanium, used in integrated circuits. With semiconductor photolithography techniques, the lead 160 may be defined with widths of less than 1 μm. To prevent electrolysis, the width of the lead 160 in the channel 170 is narrow enough such that the voltage across the lead in the channel 170 should be less than 1 volt, preferably less 0.1 volt, at all times.

[0045] The voltages used in the microfluidic system are high. A voltmeter directly measuring the voltage at the channel node 173 through the lead 160 must have a very high input impedance to be capable of measuring such high voltages. Such voltmeters are expensive. Furthermore, handling of the substrate of the microfluidic systems increases the possibility of contamination. Such contamination can seriously affect the voltages (and electric fields) required for proper operation of electokinetic forces in the channels of the microfluidic system.

[0046] To avoid these problems and costs, the lead 160 is connected to a voltage divider circuit 163, which is also formed on the surface of the substrate 178. The output of the voltage divider circuit 163 is carried by a conductive output lead 161. The circuit 163 is also connected by a conductive lead 162 to a voltage reference.

[0047] The voltage divider circuit 163, shown in greater detail in Figure 5B, is formed with standard semiconductor manufacturing technology with resistors 165 and 166 connected as a voltage divider circuit. The lead 160 is connected to the input terminal of the circuit 163, which is one end of a linear pattern of high-resistance material, such as undoped or lightly doped polysilicon or alumina. The other end of the linear pattern is connected to a reference lead 162, which is also formed on the substrate 168 and leads to an external reference voltage, presumably ground. As shown for explanatory purposes, the voltage of the lead 160 is divided in a 10-to-1 ratio. The linear pattern is divided into a resistor 165 and a resistor 166. The resistor 165 has nine times more loops than the resistor 166, i.e., the resistance of the resistor 165 is nine times greater than the resistance of the resistor 166. Of course, other ratios may be used and a 1000:1 ratio is typical. The output lead 161, connected between the two resistors 165 and 166, leads to an external connection for a low-voltage reading by a voltmeter. The cover plate then protects the leads 160-162, the voltage divider circuit 163 and the surface of the substrate from contamination.

[0048] While the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be clear to one skilled in the art from a reading of this disclosure that various changes in form and detail can be made without departing from the true scope of the invention.

Claims

1. A method of using a microfluidic system (100) having a plurality of interconnected capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) and a plurality of electrodes (133, 135, 188, 190, 191, 193, 195, 199), each of said plurality of electrodes being disposed respectively at different reservoirs of said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188), and wherein the voltage divider circuit comprises a series of resistors (165, 166) connected in a 1000:1 ratio.
182, 184, 186, 188) for creating electric fields in said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) to electrokinetically move materials (120, 121) in a fluid through said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188), the method characterised by:

simultaneously applying potentials to at least three of said electrodes (133, 135, 188, 190, 191, 193, 195, 199), said potentials being responsive to changes in a current through said at least three electrodes to move said materials (120, 123) into and through one or more intersections of said plurality of channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) of said system (100).

2. The method of claim 1, wherein said microfluidic system (100) has three electrodes.

3. The method of claim 2, wherein said voltage applying step comprises controlling said voltages so that said current is substantially constant.

4. The method of claim 1, wherein the materials (120, 121) to be moved are charged, the charged materials (120, 121) moving to and from said channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) of the system (100) by electrophoresis.

5. The method of claim 1, wherein the voltages are applied at said at least three electrodes to move said materials (120, 121) into and through said system (100) for creating electric fields in said channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) and a plurality of electrodes (133, 135, 188, 190, 191, 193, 195, 199), each of the plurality of electrodes being respectively disposed at different reservoirs of said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) for creating electric fields in said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) to electrokinetically move materials (120, 121) in a fluid through said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188), the use being characterised by simultaneously applying potentials to at least three of said electrodes (133, 135, 188, 190, 191, 193, 195, 199), said potentials being responsive to changes in a current through said at least three electrodes to move said materials (120, 121) into and through one or more intersections of said plurality of channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) of said system (100).

6. The method of claim 1, wherein the plurality of interconnected capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) includes at least one channel intersection, and the voltages applied at the at least three electrodes move material (120, 121) into the intersection from channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) connected to the at least three electrodes.

7. The method of claim 1, wherein the applying step further comprises controlling the voltages applied to the at least three electrodes, such that a current between one of the at least three electrodes and another of the at least three electrodes is maintained substantially constant.

8. The use of a substrate (102, 128, 178) having a plurality of interconnected capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) and a plurality of electrodes (133, 135, 188, 190, 191, 193, 195, 199), each of the plurality of electrodes being respectively disposed at different reservoirs of said capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188).
15. A microfluidic system (100) comprising a substrate having a plurality of interconnected capillary channels (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) and a plurality of electrodes (133, 135, 188, 190, 191, 193, 195, 199), each of said plurality of electrodes (133, 135, 188, 190, 191, 193, 195, 199) being respectively disposed at different reservoirs of said capillary channels (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) for creating electric fields in said capillary channels (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) to electrokinetically move materials (120, 121) in a fluid through said capillary channels (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) and means for simultaneously applying potentials to at least three of said electrodes (133, 135, 188, 190, 191, 193, 195, 199), each of said electrodes being responsive to changes in a current through said at least three electrodes to move said materials (120, 121) into and through one or more intersections of said plurality of channels (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) of said system (100).

Revendications


2. Procédé selon la revendication 1, dans lequel ledit système micro-fluidique (100) a trois électrodes.

3. Procédé selon la revendication 2, dans lequel ladite étape d’application de tension comprend la commande desdites tensions de telle sorte que ledit courant soit essentiellement constant.

4. Procédé selon la revendication 1, dans lequel les matières (120, 121) à déplacer sont chargées, les matières chargées (120, 121) se déplaçant vers et depuis lesdits canaux (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) du système (100) par électrophorèse.

5. Procédé selon la revendication 1, dans lequel les matières (120, 121) à déplacer se trouvent dans un fluide, et l’étape d’application génère un déplacement électro-osmotique du fluide contenant les matières (120, 121) vers et depuis les canaux (110, 112, 114, 130, 136, 170, 172, 174, 180, 182, 184, 186, 188) du système (100).

6. Procédé selon la revendication 1, dans lequel la pluralité de canaux capillaires interconnectés (110, 112, 114, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) comprend au moins une intersection de canal, et les tensions appliquées aux au moins trois électrodes déplacent la matière (120, 121) dans l’intersection depuis les canaux (110, 112, 114, 130, 136, 170, 172, 174, 180, 182, 184, 186, 188) connectés aux au moins trois électrodes.

7. Procédé selon la revendication 1, dans lequel l’étape d’application comprend en outre la commande des tensions appliquées aux au moins trois électrodes, de telle sorte qu’un courant entre une première des au moins trois électrodes et une autre des au moins trois électrodes soit maintenu essentiellement constant.

9. Utilisation selon la revendication 8, dans laquelle les dites tensions sont appliquées simultanément à plus de trois desdites électrodes associées.

10. Utilisation selon la revendication 9, dans laquelle les dites tensions sont commandées de telle sorte que ledit courant soit essentiellement constant.

11. Utilisation selon la revendication 8, dans laquelle les dites matières (120, 121) sont chargées, et lesdites matières (120, 121) se déplacent vers et depuis lesdits canaux (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) par électrophorèse.


14. Utilisation selon la revendication 8, dans laquelle l’étape d’application de tension comprend la commande desdites tensions auxdite au moins trois électrodes, de telle sorte qu’un courant entre une première desdites au moins trois électrodes et une autre desdites au moins trois électrodes soit maintenu essentiellement constant.


Patentansprüche


2. Verfahren nach Anspruch 1, wobei das Mikrofluidsystem (100) drei Elektroden aufweist.

gen umfasst, so dass der Strom im Wesentlichen konstant ist.

4. Verfahren nach Anspruch 1, wobei die zu bewegenden Materialien (120, 121) geladen sind und sich die geladenen Materialien (120, 121) zu und von den Kanälen (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) des Systems (100) mittels Elektrophorese bewegen.

5. Verfahren nach Anspruch 1, wobei sich die zu bewegenden Materialien (120, 121) in einem Fluid befinden, und wobei der Schritt des Anlegens zu einer elektroosmotischen Bewegung des die Materialien (120, 121) enthaltenden Fluids zu und von den Kanälen (110, 112, 114, 116, 130, 136, 138, 170, 172, 174, 180, 182, 184, 186, 188) des Systems (100) führt.


7. Verfahren nach Anspruch 1, wobei der Schritt des Anlegens weiter Steuern der an die wenigstens drei Elektroden angelegten Spannungen umfasst, so dass ein Strom zwischen einer der wenigstens drei Elektroden und einer anderen der wenigstens drei Elektroden im Wesentlichen konstant gehalten wird.


9. Verwendung nach Anspruch 8, wobei die Spannungen simultan an mehr als drei zugehörigen Elektroden angelegt wird.

10. Verwendung nach Anspruch 9, wobei die Spannungen so gesteuert werden, dass der Strom im Wesentlichen konstant ist.


14. Verwendung nach Anspruch 8, wobei der Schritt des Anlegens von Spannung weiter ein Steuern der an die wenigstens drei Elektroden angelegten Spannungen umfasst, so dass ein Strom zwischen einer der wenigstens drei Elektroden und einer anderen der wenigstens drei Elektroden im Wesentlichen konstant gehalten wird.

FIG. 3A (PRIOR ART)

FIG. 3B
FIG. 4A

FIG. 4B