CLAIMS

What is claimed is:

1. A method for maintaining an electrospray ionization (ESI) tip at a constant voltage relative to ground while performing a separation reaction, the method comprising:

a) applying a first voltage to a proximal end of a separation channel, wherein a distal end of the separation channel is in fluid and electrical communication with the ESI tip;

b) applying a second voltage to a proximal end of an auxiliary fluid channel, wherein a distal end of the auxiliary fluid channel is in fluid and electrical communication with the distal end of the separation channel;

c) performing the separation reaction to separate a mixture of analytes, wherein the separation reaction takes place within the separation channel; and

d) monitoring a change in resistance of the separation channel or a change in voltage at the ESI tip in a feedback loop that adjusts the first and second voltages to maintain a constant voltage drop across the separation channel and a constant voltage at the ESI tip.

2. The method of claim 1, wherein the separation channel is a lumen of a capillary.

3. The method of claim 2, wherein the capillary comprises a microvial spray tip.

4. The method of claim 1, wherein the separation channel is a fluid channel within a microfluidic device.

5. The method of claim 1, wherein the separation reaction comprises an isoelectric focusing reaction.

6. The method of claim 1, wherein the separation reaction comprises an electrophoretic separation reaction.

7. The method of claim 1, wherein the first voltage is applied at a cathode and the second voltage is applied at an anode.

8. The method of claim 1, wherein the voltage at the ESI tip is held at ground.

9. The method of claim 1, wherein the voltage at the ESI tip is held at the second voltage.

10. The method of claim 1, wherein the adjustment to the first and second voltages comprises subtracting a transient voltage change measured at the ESI tip from the first voltage and second voltage.

11. The method of claim 1, wherein the voltage at the ESI tip is measured using a power supply that provides the first or second voltage.

12. The method of claim 1, wherein the feedback loop operates at a frequency of at least 0.1 Hz.

13. The method of claim 1, wherein the feedback loop operates at a frequency of at least 10 Hz.

14. The method of claim 1, wherein the feedback loop maintains the voltage at the ESI tip to within ±10% of a pre-set value.

15. The method of claim 1, wherein the feedback loop maintains the voltage at the ESI tip to within ±1% of a pre-set value.

16. The method of claim 1, wherein the feedback loop maintains the voltage drop across the separation channel to within ±10% of a pre-set value.

17. The method of claim 1, wherein the feedback loop maintains the voltage drop across the separation channel to within ±1% of a pre-set value.

18. A computer-implemented method for maintaining an electrospray ionization (ESI) tip at a constant voltage relative to ground while performing a separation reaction, the method comprising:

a) receiving, using a processor, a first measurement of a voltage at the ESI tip, wherein a distal end of the separation channel is in fluid and electrical communication with the ESI tip;

b) receiving, using the processor, a second measurement of the voltage at the ESI tip;

c) comparing the second measurement to the first measurement using the processor, wherein if the second measurement differs from the first measurement, the processor causes a voltage at a proximal end of the separation channel and a voltage at a proximal end of an auxiliary fluid channel comprising a distal end that is in fluid and electrical communication with the distal end of the separation channel, to be adjusted such that the voltage at the ESI tip is returned to the first measurement value; and

d) repeating steps (a) through (c) at a specified frequency.

19. The computer-implemented method of claim 18, wherein the separation channel comprises a lumen of a capillary or a fluid channel within a microfluidic device.

20. The computer-implemented method of claim 18, wherein the separation reaction comprises an isoelectric focusing reaction.

21. The computer-implemented method of claim 18, wherein the separation reaction comprises an electrophoretic separation reaction.

22. The computer-implemented method of claim 18, wherein the voltage at the ESI tip is held at ground.

23. The computer-implemented method of claim 18, wherein the specified frequency is at least 1 Hz.

24. The computer-implemented method of claim 18, wherein the voltage at the ESI tip is maintained to within ±5% of a specified value.