CLAIMS

What is claimed is:

1. A system for electroporating a biological cell, the system comprising:

a micro fluidic channel adapted to receive a flow of a plurality of biological cells in a buffer solution, wherein the micro fluidic channel comprises a detection area;

a pair of electrodes adapted to apply an electrical field across the detection area;

a signal generator unit, wherein the signal generator unit is capable of generating a first signal and a second signal through the electrodes, wherein the first signal is a cell detection signal and the second signal is a permeabilization signal;

a sensing unit, wherein the sensing unit is adapted to continuously monitor an impedance value of the detection area; and

a controller unit, wherein the controller unit is adapted to:

determine that a single one of the plurality of biological cells has entered the detection area when the impedance value of the detection area increases over a baseline threshold in the presence of the first signal,

in response to detecting the single one of the plurality of biological cells has entered the detection area, control the signal generator unit to generate the second signal, determine whether the impedance value of the detection area is greater than a permeabilization threshold value,

control the signal generator unit to stop generation of the second signal in response to determining that the impedance value of the detection area is greater than the permeabilization threshold value,

control the signal generator unit to generate a third electrical signal, wherein the third electrical signal is a delivery signal (102) that causes delivery of a molecule into the single one of the plurality of cells within the detection area, and

control the signal generator unit to dynamically adjust at least one parameter of the delivery signal based on the monitored impedance value to allow molecular delivery without reaching excessive changes in impedance indicative of cell death.

2. The system of claim 1, wherein the signal generator unit is capable of generating the cell detection signal and the permeabilization signal simultaneously.

3. The system of claim 1, wherein the sensing unit comprises a lock- in amplifier.

4. The system of claim 3, wherein the sensing unit further comprises an imaging device capable of measuring the fluorescence of a cell within the detection area.

5. The system of claim 1, wherein the microfluidic channel is adapted to hydrodynamically focus the flow of a plurality of biological cells through the detection area.

6. The system of claim 1, wherein the system further comprises a second microfluidic channel adapted to receive a flow of buffer, and wherein the second microfluidic channel comprises a second detection area.

7. The system of claim 6, wherein the sensing unit is adapted to detect the impedance value of the second detection area.

8. The system of claim 1, wherein the controller unit is adapted to control the signal generator unit to stop generation of the third signal in response to at least one of the following:

determining that the monitored impedance value is less than the threshold impedance indicating that the single one of the plurality of biological cells has exited the detection area; or

determining that the monitored impedance value is less than or equal to a viability threshold for over-exposure.

9. The system of claim 1, wherein the controller unit controls the signal generator unit to generate the second signal such that the second signal has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

10. The system of claim 1, wherein the controller unit controls the signal generator unit to generate the third signal that has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

11. A method for sequentially electroporating a plurality of biological cells in continuous flow in a buffer solution through a microfluidic channel, the method comprising:

continuous monitoring each of the plurality of single biological cells before, during and after electroporation within a detection area of the microfluidic channel by monitoring an impedance value of the detection area.

12. The method according to claim 11, further comprising:

generating a first electrical signal to detect a presence of a single one of the plurality of biological cells in the detection area;

determining that the single one of the plurality of biological cells has entered the detection area when the impedance value of the detection area increases over a baseline threshold in the presence of the first signal;

in response to detecting the single one of the plurality of biological cells has entered the detection area, generating a second electrical signal, , wherein the second electrical signal is a permeabilization signal;

determining whether the impedance value of the detection area is greater than a permeabilization threshold value;

stopping generation of the second electrical signal in response to determining that the impedance value of the detection area is greater than the permeabilization threshold value;

generating a third electrical signal, wherein the third electrical signal is a delivery signal that causes delivery of a molecule into the single one of the plurality of cells within the detection area; and

dynamically adjusting at least one parameter of the delivery signal based on the monitored impedance value to allow molecular delivery without reaching excessive changes in impedance indicative of cell death.

13. The method according to claim 12, wherein generating the second electrical signal comprises generating the second electrical signal that has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

14. The method according to claim 12, wherein generating the third electrical signal comprises generating the third electrical signal that has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

15. The method according to claim 12, further comprising stopping generation of the third electrical signal in response to determining that the monitored impedance value is less than or equal to a viability threshold for over-exposure.

16. The method according to claim 12, further comprising stopping generation of the third electrical signal in response to determining that the monitored impedance value of the detection area is equal to the baseline threshold indicating that the single one of the plurality of biological cells has exited the detection area.

17. The method according to claim 12, wherein the baseline threshold is determined by continuously monitoring the impedance value of a second detection area through which only a buffer solution is flowing.

18. The method according to claim 13, wherein at least one of the plurality of pulse parameters of the second electrical signal is selected from the group of: electric field amplitude, pulse duration, pulse train frequency, duty cycle, and number of cycles.

19. The method according to claim 14, wherein at least one of the plurality of pulse parameters of the third electrical signal is selected from the group of: electric field amplitude, pulse duration, pulse train frequency, duty cycle, and number of cycles.

20. The method according to claim 12, wherein the permeabilization threshold value is determined experimentally.

21. The method according to claim 12, wherein the permeabilization threshold value is determined using a mathematical model.

22. The method according to claim 12, wherein the permeabilization threshold value corresponds to an optimal cell permeabilization that does not cause cell death.

23. A method for electroporating a plurality of biological cells, the method comprising:

hydrodynamically focusing a continuous flow of a plurality of biological cells into a single- file flow, wherein the single-file flow passes each of the plurality of biological cells through a detection area;

generating a first electrical signal to detect a presence of a single one of the plurality of biological cells in the detection area;

determining that the single one of the plurality of biological cells has entered the detection area when the impedance value of the detection area increases over a baseline threshold in the presence of the first signal;

in response to detecting the single one of the plurality of biological cells has entered the detection area, generating a second electrical signal, , wherein the second electrical signal is a permeabilization signal;

determining whether the impedance value of the detection area is greater than a permeabilization threshold value;

stopping generation of the second electrical signal in response to determining that the impedance value of the detection area is greater than the permeabilization threshold value;

generating a third electrical signal, wherein the third electrical signal is a delivery signal that causes delivery of a molecule into the single one of the plurality of cells within the detection area; and

dynamically adjusting at least one parameter of the delivery signal based on the monitored impedance value to allow molecular delivery without reaching excessive changes in impedance indicative of cell death.

24. The method according to claim 23, wherein generating the second electrical signal comprises generating the second electrical signal that has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

25. The method according to claim 23, wherein generating the third electrical signal comprises generating the third electrical signal that has a plurality of pulse parameters selected based on the monitored impedance value of the detection area and associated data from a trapped cell experiment or a mathematical model.

26. The method according to claim 23, further comprising:

stopping the third electrical signal in response to determining the impedance value of the detection area is one of: less than or equal to a viability threshold, or equal to the baseline threshold.

27. The method according to claim 23, wherein the baseline threshold is determined by continuously monitoring the impedance value of a second detection area through which only a buffer solution is flowing.

28. The method according to claim 24, wherein at least one of the plurality of pulse parameters of the second electrical signal is selected from the group of: electric field amplitude, pulse duration, pulse train frequency, duty cycle, and number of cycles.

29. The method according to claim 25, wherein at least one of the plurality of pulse parameters of the third electrical signal is selected from the group of: electric field amplitude, pulse duration, pulse train frequency, duty cycle, and number of cycles.

30. The method according to claim 23, wherein the permeabilization threshold value is determined experimentally.

31. The method according to claim 23, wherein the permeabilization threshold value is determined using a mathematical model.

32. The method according to claim 23, wherein the permeabilization threshold value corresponds to an optimal cell permeabilization that does not cause cell death.