CLAIMS

What is claimed is:

1. A system for electronically and optically monitoring biological samples, the system comprising:

a multi-well plate having a plurality of wells configured to receive a plurality of biological samples, each of the wells comprising a set of electrodes and a transparent window on a bottom surface of the well that is free of electrodes;

an illumination module configured to illuminate the wells;

a cradle configured to receive the multi-well plate, the cradle having an opening on the bottom that is configured to expose the transparent windows of the wells; ~~and~~

an optical imaging module movable across different wells of a same multi-well plate to capture images through the exposed windows; and

a computer processor for selectively operating each of the sets of electrodes for electronically monitoring cell-substrate impedance within one or more wells; the illumination module for selectively illuminating the one or more wells; and the optical imaging module for its selective movement and capturing and receiving images from the one or more wells;

wherein the computer processor is programmed to capture images from the one or more wells via the optical imaging module in response to the one or more wells reaching or following a set impedance-based value or impedance-based parameter from the electronic monitoring.

2. The system of claim 1, wherein the biological samples comprise cells, optionally cancer cells.

3. The system of claim 1, wherein the illumination module comprises a plurality of lights configured to independently illuminate one or more of the wells.

4. The system of claim 1, wherein the illumination module comprises a light emitting diode (LED) array, each LED arranged to illuminate a single well.

5. The system of claim 1, wherein the illumination module is a bright field illumination module.

6. The system of claim 1, wherein the cradle further comprises a hinged cover, wherein the illumination module is joined to the cover.

7. The system of claim 1, wherein the cradle electrically engages both the multi-well plate for electronic communication with the sets of electrodes and the illumination module for communicating illumination instructions.

8. The system of claim 1, wherein the optical imaging module is configured to capture one or more images from a single well at a time.

9. The system of claim 1, wherein the optical imaging module is underneath the cradle.

10. The system of claim 1, wherein the optical imaging system further comprises an excitation light source configured to excite one or more molecules, the excitation light source optionally comprising one or more lights selected from the group consisting of an ultraviolet light, a violet light, a blue light, a green light, a yellow light, an orange light, and a red light.

11. The system of claim 1, wherein the optical imaging module comprises a camera.

12. The system of claim 1, wherein the optical imaging module comprises a camera, a bandpass filter, a tube lens, and an objective lens.

13. The system of claim 1, further comprising a computer processor communicatively coupled to:

the cradle for selectively operating each of the sets of electrodes for electronically monitoring cell-substrate impedance within one or more wells;

the illumination module for selectively illuminating the one or more wells; and the optical imaging module for its selective movement and capturing and

receiving images from the one or more wells.

14. The system of claim 13, wherein the computer processor is programmed to capture images from the one or more wells via the optical imaging module in response to the one or more wells reaching or following a set impedance-based value or impedance-based

parameter from the electronic monitoring.

15. The system of claim 13, wherein the processor is programmed to electronically monitor cell-substrate impedance and optically monitor a same well and is configured to pair impedance and optical data for a display or analysis.

16. The system of claim 1, further comprising:

two additional multi-well plates, each having a plurality of wells configured to receive a plurality of samples, each of the wells comprising a set of electrodes and a transparent window on a bottom surface of the well that is free of electrodes;

two additional illumination modules configured to illuminate the wells of the two additional multi-well plates; and

two additional cradles configured to receive the two additional multi-well plates, the two additional cradles each having an open bottom that exposes the transparent windows of the wells;

wherein the optical imaging module is movable across all wells to capture images through all windows.

17. The system of claim 1, further comprising a cell or tissue culture vessel that is not configured for electronic monitoring, wherein the optical imaging module is configured to capture images within the cell or tissue culture vessel.

18. A method of monitoring cells, the method comprising:

electronically monitoring cells within wells of a multi-well plate continuously over a time period at a specific time interval between consecutive monitoring, each of the wells comprising a set of cell-substrate impedance monitoring electrodes, and a transparent window on a bottom surface of the well that is free of electrodes; and

capturing images through the transparent window from at least one well that is being electronically monitored, wherein prior to the step of capturing images from the at least one well, the electronic monitoring outputs a result from the at least one well that meets a set value, which instructs the optical imaging module to capture the images from the at least one well.

19. The method of claim 18, wherein the images are captured regularly or irregularly over a time period within the electronic monitoring time period, the method optionally comprising capturing the images at a same time as performing electronic measurement of the cells.

~~20. The method of claim 18, wherein prior to the step of capturing images from the at least one well, the electronic monitoring outputs a result from the at least one well that meets a set value, which instructs the optical imaging module to capture the images from the at least one well.~~

~~21~~ 20. The method of claim 18, wherein the images being captured comprise bright field images of the cells, and the method further comprises determining cell confluence numbers or parameters from the bright field images and optionally counting cells.

~~22~~ 21. The method of claim 18, wherein the captured images comprise fluorescence images of the cells, the method further comprising determining a fluorescence parameter from the images, optionally selected from one or more of the group consisting of total fluorescence counts, total fluorescence intensity, and average fluorescence intensity.

~~23~~ 22. The method of claim 18, wherein the images captured comprise bright field images of the cells and fluorescence images of the cells, the method further comprising:

deriving cell confluence numbers or parameters from the bright field images and optionally counting cells from the bright field images;

determining a fluorescence parameter from the fluorescence images, optionally selected from one or more of the group consisting of total fluorescence counts, total fluorescence intensity, and average fluorescence intensity; and optionally,

superimposing the bright field images and fluorescence images or one or more colors for a same well.

~~24~~ 23. A method of monitoring cells, the method comprising:

electronically monitoring cells within wells of a multi-well plate over a time period, each of the wells comprising a set of cell-substrate impedance monitoring electrodes, and a transparent window on a bottom surface of the well that is free of electrodes; ~~and~~

capturing images through the transparent window from at least one well of the multi-well plate over a time period that is within or outside the time period for electronic monitoring;

wherein the step of electrically monitoring cells and the step of capturing images are coupled according to one or more of the following:

i) electronically monitor cell-substrate impedance and capture an image of the same well and pairing impedance and optical data for display or analysis;

ii) capturing images from the at least one well in response to one or more wells reaching or following a set impedance-based value or parameter from the electronic monitoring; and

iii) electronically monitor cell-substrate impedance over a time period including a specific time interval between two consecutive electronic impedance monitoring; and capture images of the same well over a period that is within the time period for electronic monitoring or over a different time period from electronic monitoring.

~~25. The method of claim 24, wherein:~~

~~the images being captured are bright field images of the cells, the method optionally comprising counting cells or determining cell confluence numbers or parameters from the bright field images; or~~

~~the images being captured are fluorescence images of the cells, the method optionally comprising determining a fluorescence parameter from the images, optionally selected from one or more of the group consisting of total fluorescence counts, total fluorescence intensity, and average fluorescence intensity; or~~

~~the image being captured comprise bright field images of the cells and fluorescence images of the cells, the method further comprising:~~

~~counting cells from the bright field images and optionally deriving cell confluence numbers or parameters from the bright field images;~~

~~determining a fluorescence parameter from the fluorescence images, optionally selected from one or more of the group consisting of total fluorescencecounts, total fluorescence intensity, and average fluorescence intensity; and~~

~~optionally, superimposing the bright field images and fluorescence images of one or more colors for one or more of the wells.~~

24. The method of claim 23, wherein:

the images being captured are bright field images of the cells, the method optionally comprising counting cells or determining cell confluence numbers or parameters from the bright field images; or

the images being captured are fluorescence images of the cells, the method optionally comprising determining a fluorescence parameter from the images, optionally selected from one or more of the group consisting of total fluorescence counts, total fluorescence intensity, and average fluorescence intensity; or

the images being captured comprise bright field images of the cells and fluorescence images of the cells, the method further comprising:

counting cells from the bright field images and optionally deriving cell confluence numbers or parameters from the bright field images;

determining a fluorescence parameter from the fluorescence images, optionally selected from one or more of the group consisting of total fluorescence counts, total fluorescence intensity, and average fluorescence intensity; and

optionally, superimposing the bright field images and fluorescence images of one or more colors for one or more of the wells.

25. The method of claim 23, comprising the step of item ii), wherein the value or parameter is indicative of an established cell monolayer or established cell population.

26. The method of claim 23, comprising counting cells or determining cell confluence numbers of parameters to ensure cells are properly settled against the bottom of the well prior to electronic monitoring.

27. The method of claim 23, wherein the step of capturing images comprises illuminating one or more light sources in response to results from electronic monitoring of the biological sample.

28. The method of claim 23, wherein the step of capturing images comprises illuminating in response to changes in cell-substrate impedance monitoring for cell imaging to confirm a change in population of cells, preferably a reduced population of cells.

29. The method of claim 27, wherein the one or more light sources are diodes.

30. A system for electronically and optically monitoring biological samples, the system comprising:

a multi-well plate having a plurality of wells configured to receive a plurality of biological samples, each of the wells comprising a set of electrodes and a transparent window on a bottom surface of the well that is free of electrodes;

an optical imaging module configured to image the wells;

an illumination module configured to illuminate the wells; and

a computer processor that is programmed to electronically monitor cell-substrate impedance and optically monitor a same well and is configured to couple impedance and optical data coupled according to one or more of the following:

i) electronically monitor cell-substrate impedance and capture an image of the same well and pairing impedance and optical data for display or analysis;

ii) capturing images from the at least one well in response to one or more wells reaching or following a set impedance-based value or parameter from the electronic monitoring; and

iii) electronically monitor cell-substrate impedance over a time period

including a specific time interval between two consecutive electronic impedance monitoring; and capture images of the same well over a period that is within the time period for electronic monitoring or over a different time period from electronic monitoring.

31. The system of claim 30, wherein the optical imaging module movable across different wells of a same multi-well plate to capture images through the exposed windows; and

wherein the computer processor is communicatively coupled to the optical imaging module and illumination module to:

selectively operate each of the sets of electrodes for electronically monitoring cell-substrate impedance within one or more wells;

selectively illuminating the one or more wells; and

selectively operating the optical imaging module for capturing and receiving images from the one or more wells.

32. The system of claim 30, wherein the computer processor is programmed to capture images from the one or more wells via the optical imaging module in response to the one or more wells reaching or following a set impedance-based value or impedance-based parameter from the electronic monitoring, and wherein the value or parameter preferably is indicative of an established cell monolayer or established cell population.

33. The system of claim 30, wherein the illumination module comprises a plurality of lights configured to independently illuminate one or more of the wells.

34. The system of claim 30, further comprising a cradle that electrically engages both the multi-well plate for electronic communication with the sets of electrodes and the illumination module for communicating illumination instructions.

35. The system of claim 30, wherein the optical imaging module further comprises an excitation light source configured to excite one or more molecules, the excitation light source optionally comprising one or more lights selected from the group consisting of an ultraviolet light, a violet light, a blue light, a green light, a

yellow light, an orange light, and a red light.