WHAT IS CLAIMED IS:

Claim CLAIMS

1:. A perfusion cell culture apparatus comprising:

(a) a bioreactor vessel configured to receive liquid media;

(b) a first filtration assembly in fluid communication with the bioreactor vessel, wherein the first filtration assembly comprises:

(i) a first filtration system;

(ii) a first harvest pump connected in series with the first filtration system, wherein the first harvest pump is configured to pump the liquid media from the bioreactor vessel through the first filtration system; and

(iii) a sensor, wherein the sensor is configured to interact with the liquid media inside the first filtration assembly; and

(c) a second filtration assembly configured to operate in parallel with the first filtration assembly, wherein the second filtration assembly is in fluid communication with the bioreactor vessel, and wherein the second filtration assembly comprises:

(i) a second filtration system; and

(ii) a second harvest pump connected in series with the second filtration system, wherein the second harvest pump is configured to pump the liquid media from the bioreactor vessel through the second filtration system; and

(d) a controller, wherein the controller executes operations comprising:

(i) receiving, from the sensor, information indicative of an operational operable state of the first filtration system;

(ii) determining, based on at least the received information from the sensor, whether the first filtration system is in an operable state; and

(iii) responsive to a determination that the first filtration system is not in an operable state, causing the first harvest pump to stop pumping liquid media through the first filtration system.

Claim 2: The perfusion cell culture apparatus of claim 1, wherein at least one of the first filtration system and the second filtration system comprises an alternating tangential flow filter.

Claim 3: The perfusion2. The cell culture apparatus of claim 1, wherein at least one of the first filtration system and the second filtration system comprises a tangential flow filter. or an alternating tangential flow filter.

Claim 4:3. The perfusion cell culture apparatus of claim 1, wherein each of the first filtration system and the second filtration system comprise a filter membrane having a pore size of about 0.1 micron to about 1 micron.

Claim 5:4. The perfusion cell culture apparatus of claim 1, wherein the sensor comprises a pressure sensor, and wherein determining that the first filtration system is not in an operable state comprises determining that a pressure in the first filtration assembly is greater than a threshold value.

Claim 6:5. The perfusion cell culture apparatus of claim 1, wherein the sensor comprises a capacitance or optical sensor.

Claim 7:6. The perfusion cell culture apparatus of claim 1, wherein the sensor comprises an optical sensoris configured to monitor cell density or flow rate.

Claim 8:

7. The perfusioncell culture apparatus of claim 1, wherein the sensor is a Raman sensor or a Fourier transform infrared (FTIR) sensor.

8. The cell culture apparatus of claim 1, wherein the controller is further configured to:

responsive to the determination that the first filtration system is not in an operable state, cause the second harvest pump to increase a flow rate of liquid media through the second filtration system.

Claim 9: The perfusion cell culture apparatus of claim 8, wherein causing the second harvest pump to increase the flow of liquid media through the second filtration system comprises approximately doubling the flow rate.

Claim 10:. The perfusion cell culture apparatus of claim 1, wherein the controller is further configured to:

responsive to the determination that the first filtration system is not in an operable state, output a notification.

Claim 11:. The perfusion cell culture apparatus of claim 10, wherein the notification comprises a visual alert or an auditory alert.

Claim 12:. The perfusion cell culture apparatus of claim 1, further comprising an isolation valve connected in series with the first filtration assembly, wherein the valve is configured to control the flow of liquid media through the first filtration assembly, and wherein the controller is further configured to:

responsive to the determination that the first filtration system is not in an operable state, close the isolation valve.

Claim 13:. The perfusion cell culture apparatus of claim 1, wherein the first filtration assembly further comprises a guard filter connected in series with the first filtration system, wherein the guard filter is connected downstream of the first filtration system and the sensor.

Claim 14:. The perfusion cell culture apparatus of claim 13, wherein the guard filter comprises has a pore size of about 0.1 micron to about 1 micron.

Claim 15:. The perfusion cell culture apparatus of claim 1, further comprising a capture operation configured to collect product from the liquid media, wherein the capture operation is in fluid communication with the bioreactor vessel by way of at least the first filtration assembly., wherein the capture operation comprises a multi-column chromatography (MCC).

Claim 16: The perfusion cell culture apparatus of claim 15, wherein the capture operation comprises a periodic continuous counter-chromatography skid.

Claim 17: A perfusion cell culture apparatus comprising:

(a) a bioreactor vessel configured to receive liquid media;

(b) a filtration assembly in fluid communication with the bioreactor vessel, wherein the filtration assembly comprises:

(i) a filtration system;

(ii) a harvest pump connected in series with the filtration system, wherein the harvest pump is configured to pump the liquid media from the bioreactor vessel through the filtration system; and

(iii) a sensor, wherein the sensor is configured to interact with the liquid media inside the filtration assembly; and

(c) a controller, wherein the controller executes operations comprising:

(i) receiving, from the sensor, information indicative of an operational state of the filtration system;

(ii) determining, based on at least the received information, whether the filtration system is in an operable state; and

(iii) responsive to a determination that the filtration system is not in an operable state, causing the harvest pump to stop pumping liquid media through the filtration system.

Claim 18: The perfusion cell culture apparatus of claim 17, wherein the filtration system comprises an alternating tangential flow filter.

Claim 19: The perfusion cell culture apparatus of claim 17, wherein the filtration system comprises a tangential flow filter.

Claim 20: The perfusion cell culture apparatus of claim 17, wherein the filtration system comprises a pore size of about 0.1 micron to about 1 micron.

Claim 21: The perfusion cell culture apparatus of claim 17, wherein the sensor comprises a pressure sensor, and wherein determining that the filtration system is not in an operable state comprises determining that a pressure in the filtration assembly is greater than a threshold value.

Claim 22: The perfusion cell culture apparatus of claim 17, wherein the sensor comprises a capacitance sensor.

Claim 23: The perfusion cell culture apparatus of claim 17, wherein the sensor comprises an optical sensor.

Claim 24: The perfusion cell culture apparatus of claim 17, wherein the controller is further configured to:

responsive to the determination that the filtration system is not in an operable state, output a notification.

Claim 25: The perfusion cell culture apparatus of claim 24, wherein the notification comprises a visual alert or an auditory alert.

Claim 26: The perfusion cell culture apparatus of claim 17, further comprising an isolation valve connected in series with the filtration system, wherein the isolation valve configured to control the flow of liquid media through the filtration assembly, and wherein the controller is further configured to:

responsive to the determination that the filtration system is not in an operable state, close the isolation valve.

Claim 27: The perfusion cell culture apparatus of claim 17, further comprising a guard filter connected in series with the first filtration assembly, wherein the guard filter is connected downstream of the first filtration assembly.

Claim 28: The perfusion cell culture apparatus of claim 27, wherein the guard filter comprises a pore size of about 0.1 micron to about 1 micron.

Claim 29: The perfusion cell culture apparatus of claim 17, further comprising a capture operation configured to collect product from the liquid media, wherein the capture operation is in fluid communication with the bioreactor vessel by way of at least the filtration assembly such that the harvest pump is configured to pump the liquid media through the filtration system and into the capture operation.

Claim 30: The perfusion cell culture apparatus of claim 29, wherein the capture operation comprises a periodic continuous counter-chromatography skid.

Claim 31: The perfusion cell culture apparatus of claim 29, wherein the controller is further configured to:

responsive to the determination that the filtration system is not in an operable state, cause the capture operation to stop collecting product from the liquid media.

Claim 32: The perfusion cell culture apparatus of claim 17, wherein the filtration assembly further comprises a waste valve connected in series with the filtration system, wherein the waste valve is configured to divert the liquid media into a waste collection system, and wherein controller is further configured to:

responsive to the determination that the filtration system is not in an operable state, open the waste valve.

Claim 33:. A method of culturing cells, the method comprising:

(a) at least partially filling a bioreactor vessel with cells and liquid media, wherein the bioreactor vessel is in fluid communication with a first filtration system and a second filtration system connected in parallel with the first filtration system;

(b) pumping liquid media from the bioreactor vessel through the first filtration system using a first harvest pump, wherein the first harvest pump is connected in series with the first filtration system;

(c) pumping liquid media from the bioreactor vessel through the second filtration system using a second harvest pump, wherein the second harvest pump is connected in series with the second filtration system;

(d) receiving, from a sensor configured to interact with the liquid media, information indicative of an operational state of the first filtration system;

(e) determining, based on at least the received information from the sensor, whether the first filtration system is in an operable state; and

(f) responsive to a determination that the first filtration system is not in an operable state, causing the first harvest pump to stop pumping liquid media through the first filtration system.

Claim 34: 17. The method of claim 3316, wherein at least one of the first filtration system and the second filtration system comprises an alternating tangential flow filter.

Claim 35:18. The method of claim 3316, wherein the sensor comprises a pressure sensor.

~~Claim 36:~~19. The method of claim ~~35~~18, wherein the received information comprises information relating to a pressure of liquid media downstream of the first filtration system.

~~Claim 37:~~20. The method of claim ~~35~~18, wherein the received information comprises information relating to a transmembrane pressure across the first filtration system.

~~Claim 38:~~21. The method of claim ~~35~~18, wherein determining whether the first filtration system is in an operable state comprises determining that a pressure of the liquid media is above a predetermined threshold value.

~~Claim 39:~~22. The method of claim ~~33~~16, wherein pumping liquid media from the bioreactor vessel through the first filtration system comprises pumping liquid media at a first flow rate, wherein pumping liquid media from the bioreactor vessel through the second filtration system comprises pumping liquid media at a second flow rate, and wherein the first flow rate is approximately equal to the second flow rate.

~~Claim 40:~~23. The method of claim ~~33~~16, further comprising:

responsive to the determination that the first filtration system is not in an operable state, causing the second harvest pump to increase a flow rate of liquid media through the second filtration system.

~~Claim 41:~~24. The method of claim ~~40~~23, wherein causing the second harvest pump to increase a flow rate of liquid media through the second filtration system comprises approximately doubling the flow rate of liquid media through the second filtration system.

~~Claim 42:~~25. The method of claim ~~33~~16, further comprising:

responsive to a determination that the first filtration system is not in an operable state, outputting a notification.