CLAIMS

What is claimed is:

1. A bioreactor system, comprising:

a) a bioreactor including an input port and an output port;

b) a feed stream conduit operably connected to the output port and inlet of a Hollow Fiber (HF) filter, the feed stream conduit operable to carry fluid from the bioreactor to the HF filter;

c) a retentate stream conduit operably connected to the input port of the bioreactor and an outlet of the HF filter, the retentate stream conduit operable to carry fluid to the bioreactor from the HF filter; and

d) a multi-purpose assembly operably connected to the HF filter, the multi-purpose assembly including a first flow path and a second flowpath:

wherein the first flowpath includes a first pump operable to draw fluid from the HF filter and a flow meter operable to measure flow rate of fluid in the first flowpath;

wherein the second flowpath includes a second pump operable to draw fluid from the HF filter; and

wherein the first pump and the second pump are configured to have different pump capacities.

2. The bioreactor system of claim 1, wherein the HF filter is operable for tangential flow, optionally wherein the HF filter is a tangential flow depth filtration® (TFDF®) filter.

3. The bioreactor system of claim 1, wherein the first and second pump are configured to have different accuracy ratings.

4. The bioreactor system of claim 1, further including:

one or more clarification filter(s) in the first and/or second flow path.

5. The bioreactor system of claim 1, wherein the first and second pumps are selected from the groups consisting of peristaltic, centrifugal, magnetic drive, positive displacement, membrane, pressure-based, quantex™, gear, diaphragm, syringe, and piston pumps, optionally wherein the first pump and second pumps are peristaltic pumps.

6. The bioreactor system of claim 1, wherein the feed stream conduit comprises a feed stream pump selected from the groups consisting of peristaltic, centrifugal, magnetic drive, positive displacement, membrane, pressure-based, quantex™, gear, diaphragm, syringe, and piston pumps, and is operable to carry unfiltered fluid from the bioreactor to the HF filter.

7. The bioreactor system of claim 1, wherein the retentate stream conduit is operable to carry cell culture fluid to the bioreactor from the HF filter.

8. The bioreactor system of claim 1, wherein the first flowpath including the first pump operable to draw fluid from the HF filter, draws perfusion permeate stream fluid from the HF filter; or wherein the second flowpath including the second pump operable to draw fluid from the HF filter, draws harvest permeate stream fluid from the HF filter.

9. The bioreactor system of claim 1, wherein the first flowpath and the second flowpath have the same or have different internal diameters.

10. The bioreactor system of claim 1, wherein the second flowpath is capable of conducting fluids at a higher flowrate than the first flowpath.

11. The bioreactor system of claim 1, wherein the first pump is operable to draw fluid from the HF filter at a flow rate of between 0.01 liters per min (LPM) and 5 LPM, between 0.01 LPM to 10 LPM, or between 0.01 LPM to 15 LPM.

12. The bioreactor system of claim 1, wherein the first flowpath and pump are operable to draw a feed flow rate from the HF filter of 0.8 to 2.2 liters per fiber per minute (L/fiber/min).

13. The bioreactor system of claim 1, wherein the first pump is:
(i) operable to draw fluid from the HF filter while maintaining a viable cell density (VCD) of greater than 75 x 10^6 cells/mL, greater than 50 x 10^6 cells/mL, or greater than 25 x 10^6 cells/mL;
(ii) operable to draw fluid from the HF filter at a rate of between 0.1 and 5 bioreactor vessel volumes per day (VVD), or between 0.5 and 4.3 bioreactor vessel volumes per day (VVD); or

(iii) operable to draw fluid from the HF filter at a filter flux rate of between 50 and 800 liters per square meter per hour (LMH), or between 100 and 600 LMH;
(iv) operable to draw fluid from the HF filter at a throughput equal to between 10,000 liters per square meter (L/m^2) to 30,000 L/m^2, or equal to between 10,000 liters per square meter (L/m^2) to 70,000 L/m^2; or
(v) operable to draw fluid from the HF filter while maintaining a shear rate (s-1) of less than 5,000 s-1, less than 3,500 s-1, or less than 2,500 s-1.

14. The bioreactor system of claim 1, wherein the flow meter operable to measure flow rate of fluid in the first flowpath continuously monitors the VVD rate and is in communication with the first pump to adjust the first pump rate to maintain a desired VVD rate, or wherein the flow meter operable to measure flow rate of fluid in the first flowpath is capable of accurately monitoring a flow rate of 0 to 8 LPM, or 0.5 LPM to 6 LPM.

15. The bioreactor system of claim 1, wherein the bioreactor has:
(i) a volume less than or equal to 15 or 50 liters;
(ii) a volume greater than or equal to 500 liters, greater than or equal to 1,000 liters, greater than or equal to 1,500 liters, equal to between 2,000 liters and 3,500 liters, or equal to between 2,000 liters and 7,000 liters; or
(iii) at least two input ports and at least two output ports, and at least two of b), c), and d).

16. The bioreactor system of claim 1, wherein the bioreactor system is capable of:
(i) operating in a perfusion process;
(ii) operating in a harvest process;
(iii) operating in a perfusion process, an in-between perfusion and harvest process, and a harvest process;
(iv) operating in more than one perfusion process;
(v) operating in more than one perfusion process, an in-between perfusion and harvest process, and a harvest process; or
(vi) operating in a continuous harvest process.

17. The bioreactor system of claim 1, further comprising:

(i) a human machine interface (HMI) control unit, optionally wherein the HMI control unit is programmed and can display perfusion process controls, in-between perfusion and harvest process controls, or harvest process controls;
(ii) one or more sensors;
(iii) one or more of a feed stream or retentate stream fluid pump; or
(iv) at least one component capable of facilitating at least one process intensification parameter, optionally wherein the process intensification parameter is one or more of increased cell number, increased cell density, provision of rich cell culture growth media, rapid cell number expansion, or increased biologic production.

18. The bioreactor system of claim 1, further capable of backflushing the HF filter with permeate fluid, or further comprising a second flow meter operable to measure flow rate of fluid in the second flowpath and accurately monitoring a flow rate of 0 to 10 LPM, or 0.5 LPM to 8 LPM.

19. The bioreactor system of claim 1, wherein the second pump is:
(i) operable to draw fluid from the HF filter at a throughput equal to between 12,000 liters per square meter (L/m^2) to 36,000 L/m^2, equal to between 12,000 liters per square meter (L/m^2) to 60,000 L/m^2, and/or between 10,000 liters per square meter (L/m^2) to 70,000 L/m^2;
(ii) operable to draw fluid from the HF filter at a filter flux rate of between 150 and 900 liters per square meter per hour (LMH), or between 200 and 700 LMH; or
(iii) operable to draw fluid from the HF filter at a flow rate of between 0.01 LPM to 8 LPM, between 0.01 LPM to 13 LPM., or between 0.01 LPM to 18 LPM.

20. The bioreactor system of claim 1, wherein the second flowpath and pump are operable to draw a feed flow rate from the HF filter of 1 to 3 liters per fiber per minute (L/fiber/min).

21. The bioreactor system of claim 1, wherein the first flowpath comprises a connection system with 3/8″ ID tubing or 1/8″ ID tubing, or wherein the second flowpath comprises a connection system with 1/2″ ID tubing or 1/8″ ID tubing.

22. The bioreactor system of claim 1, wherein the first flowpath has an accuracy requirement of about 1%, or wherein the second flowpath has an accuracy requirement of about 3%.

23. A multi-purpose filter assembly, comprising:

a) a Hollow Fiber (HF) filter; and

b) a multi-purpose assembly operably connected to the HF filter, the multi-purpose assembly including a first flow path and a second flowpath:

wherein the first flowpath includes a first pump operable to draw fluids from the HF filter and a flow meter operable to measure flow rate of fluid in the first flowpath;

wherein the second flowpath includes a second pump operable to draw fluid from the HF filter; and

wherein the first pump and the second pump are capable of having different pump capacities and accuracy ratings.

24. The multi-purpose filter assembly of claim 23, wherein the HF filter is operable for tangential flow, optionally wherein the HF filter is a tangential flow depth filtration® (TFDF®) filter.

25. The multi-purpose filter assembly of claim 23, further including:

one or more clarification filter(s) in the first and/or second flow path.

26. The multi-purpose filter assembly of claim 23, wherein the first and second pumps are selected from the groups consisting of peristaltic, centrifugal, magnetic drive, positive displacement, membrane, pressure-based, quantex™, gear, diaphragm, syringe, and piston pumps, optionally wherein the first pump and second pumps are peristaltic pumps.

27. The multi-purpose filter assembly of claim 23, wherein the first flowpath and pump are:

(i) operable to draw fluids from the HF filter at a throughput greater than or equal to 10,000 liters per square meter (L/m^2) to 30,000 L/m^2, or greater than or equal to 10,000 liters per square meter (L/m^2) to 70,000 L/m^2;

(ii) operable to draw a feed flow rate from the HF filter of 0.8 to 2.2 liters per fiber per minute (L/fiber/min), 0.8 to 2.0 L/fiber/min, or 1 to 1.8 L/fiber/min;
(iii) operable to draw fluids from the HF filter at a filter flux of 50 to 800 LMH, or 100 to 600 LMH;
(iv) operable to maintain a packed cell volume (PCV) of 2 to 40, 8 to 40, or 12 to 35%;
(v) operable to draw fluid from the HF filter while maintaining a VCD of greater than 25 x 10^6 cells/mL, greater than 50 x 10^6 cells/mL, greater than 75 x 10^6 cells/mL, greater than 100 x 10^6 cells/mL, or greater than 25 x 10^7 cells/mL;
(vi) operable to draw fluid from the HF filter at a shear rate of less than 5,000 s-1, less than 3,500 s-1, or less than 2,500 s-1; or
(vii) operable to draw fluid from the HF filter at a flow rate of between 0.01 LPM to 5 LPM, between 0.01 LPM to 10 LPM, or between 0.01 LPM to 15 LPM.

28. The multi-purpose filter assembly of claim 23, wherein the flow meter operable to measure flow rate of fluid in the first flowpath continuously monitors the LPM rate and is in communication with the first pump to adjust the first pump rate to maintain a desired LPM rate, or wherein the flow meter operable to measure flow rate of fluid in the first flowpath is capable of accurately monitoring a flow rate of 0 to 8 LPM, or 0.01 LPM to 6 LPM.

29. The multi-purpose filter assembly of claim 23, wherein the first flowpath has an accuracy requirement of about 1%, or wherein the second flowpath has an accuracy requirement of about 3%.

30. The multi-purpose filter assembly of claim 23, wherein the first flowpath and the second flowpath have the same or have different internal diameters.

31. The multi-purpose filter assembly of claim 23, wherein the second flowpath and pump are operable to draw fluid from the HF filter at a higher flowrate than the first flowpath and first pump, or draw fluid from the HF filter as a continuous harvest process.

32. The multi-purpose filter assembly of claim 23, wherein the HF filter is not replaced when the multi-purpose assembly directs fluids through one flowpath and pump and then directs fluid through the other flowpath and pump, or when the multi-purpose assembly

directs fluids first through the first flowpath and pump, and subsequently through the second flowpath and pump.

33. The multi-purpose filter assembly of claim 23, wherein the first flowpath and second flowpath of the multi-purpose assembly are connected by a T connector, a Y connector, or a valve.

34. The multi-purpose filter assembly of claim 23, further comprising a second flow meter operable to measure flow rate of fluid in the second flowpath and accurately monitoring a flow rate of 0 to 10 LPM, or 0.5 LPM to 8 LPM.

35. The multi-purpose filter assembly of claim 23, wherein the second pump is:
(i) operable to draw fluid from the HF filter at a throughput equal to between 12,000 liters per square meter (L/m^2) to 36,000 L/m^2, equal to between 12,000 liters per square meter (L/m^2) 60,000 L/m^2, and/or between 10,000 liters per square meter (L/m^2) to 70,000 L/m^2;
(ii) operable to draw fluid from the HF filter at a filter flux rate of between 150 and 900 liters per square meter per hour (LMH), or between 200 and 700 LMH; or
(iii) operable to draw fluid from the HF filter at a flow rate of between 0.01 LPM to 8 LPM, between 0.01 LPM to 13 LPM, or between 0.01 LPM to 18 LPM.

36. The multi-purpose filter assembly of claim 23, wherein the second flowpath and pump are operable to draw a feed flow rate from the HF filter of 1 to 3 liters per fiber per minute (L/fiber/min).

37. The bioreactor system of claim 1 or the multi-purpose filter assembly of claim 23, wherein the HF filter is constructed of and/or comprises polypropylene, and/or polyethylene terephthalate; or wherein the HF filter comprises isotropic pore structures and/or pores with an average lumen diameter of 0.65 µm to 8 µm.

38. The bioreactor system of claim 1 or the multi-purpose filter assembly of claim 23, operable for use with shear sensitive cells, animal cells, mammalian cells, Chinese Ovarian Hamster (CHO) cells, human embryonic kidney 293 (HEK293) cells, or with cells for the

production of a biologic, optionally wherein the biologic comprises an antibody, peptide, and/or virus.

39. A method of producing biologics from cells, comprising:

a) expanding cells in a cell culture fluid in a bioreactor,

b) during cell expansion, perfusing cell culture fluid through a Hollow Fiber (HF) filter to remove spent cell culture media while retaining the expanding cells, and adding an appropriate replacement volume of cell culture media to the bioreactor to maintain a desired cell culture fluid level in the bioreactor, wherein the spent cell culture media is perfused through the HF filter at a first flow rate to enter a first flowpath, and

c) following cell expansion, harvesting cell culture fluid through a HF filter to obtain the biologics, and adding an appropriate replacement volume of cell culture media to the bioreactor to maintain a desired cell culture fluid level in the bioreactor during different phases of harvest, wherein the cell culture media is harvested through the HF filter at a second flow rate to enter a second flowpath, wherein the second flow rate is greater than the first flow rate.

40. The method of claim 39, wherein the HF filter is operable for tangential flow, optionally wherein the HF filter is a tangential flow depth filtration® (TFDF®) filter.

41. The method of claim 39, wherein replacement volume of cell culture media in b) and/or c) is about the same amount of spent cell culture media as is removed, greater than the amount of spent cell culture media removed, or less than the amount of spent cell culture media removed.

42. The method of claim 39, wherein the replacement volume of cell culture media is fresh cell culture media.

43. The method of claim 39, wherein the perfusion process comprises more than one perfusion stage, optionally wherein the HF filter is used for more than one perfusion stage, an in-between perfusion and harvest process, and a harvest process.

44. The method of claim 39, wherein the first flow rate is less than or equal to 5 LPM, and a second flow rate is greater than 5 LPM.

45. The method of claim 39, wherein the HF filter is constructed of and/or comprises polypropylene, and/or polyethylene terephthalate; or wherein the HF filter comprises isotropic pore structures and/or pores with an average lumen diameter of 0.65 µm to 8 µm.

46. The method of claim 39, wherein the cells are shear sensitive cells, animal cells, mammalian cells, CHO cells, or HEK293 cells.

47. The method of claim 39, wherein the biologic comprises an antibody, peptide, and/or virus.

48. A method of producing biologics from cells, comprising use of a bioreactor system or multi-purpose filter assembly according to any one of claims 1-38.

49. Use of a multi-purpose filter assembly of any one of claims 23-38 in a bioreactor system.

50. The use of claim 49, wherein the bioreactor system comprises the features of any of claims 1 to 22.

51. Use of a bioreactor system of any one of claims 1 to 22 for the culturing of cells.

52. The use of claim 51, wherein the cells produce biologics and the use further comprises harvesting cell culture fluid through the HF filter to obtain the biologics.

53. The system, assembly, method or use of any one of claims 1-52, wherein the system, assembly, method or use results in one or more of improved productivity, improved performance, improved efficiency, reduced contamination rates, reduced capital investment,

reduced physical footprint, reduced consumables attrition, and/or reduced operation costs for a facility comprising a biologics production process.