

What is claimed is:

1. A hollow fiber tangential flow filter for bioprocessing applications comprising:
 - (a) a housing having an interior,
 - (b) a fluid inlet,
 - (c) a retentate fluid outlet,
 - (d) a permeate fluid outlet, and
 - (e) at least one hollow fiber comprising a porous wall that is formed from a plurality of extruded polymer filaments, the at least one hollow fiber having an interior surface, an exterior surface, and a wall thickness ranging from 1 mm to 10 mm, the interior surface forming an interior lumen having a width ranging from .75 mm to 13 mm and extending through the at least one hollow fiber,

wherein the at least one hollow fiber is positioned in the housing interior, wherein the fluid inlet and the retentate fluid outlet are in fluid communication with the interior lumen of the at least one hollow fiber and wherein the permeate fluid outlet is in fluid communication with the housing interior and the exterior surface of the porous wall.
2. The hollow fiber tangential flow filter of claim 1, wherein the extruded polymer filaments are mono-component filaments.
3. The hollow fiber tangential flow filter of claim 1, wherein the extruded polymer filaments are bi-component filaments.
4. The hollow fiber tangential flow filter of claim 3, wherein the bi-component filaments comprise a polyolefin and a polyester.

5. The hollow fiber tangential flow filter of claim 3, wherein the bi-component filaments comprise polypropylene and polyethylene terephthalate.
6. The hollow fiber tangential flow filter of any of claims 1-5, wherein the extruded polymer filaments are melt-blown filaments.
7. The hollow fiber tangential flow filter of any of claims 1-6, wherein a plurality of the extruded polymer filaments are bonded to one another at spaced apart points of contact to define the porous wall.
8. The hollow fiber tangential flow filter of any of claims 1-6, wherein a plurality of the extruded polymer filaments are thermally bonded to one another at spaced apart points of contact to define the porous wall.
9. The hollow fiber tangential flow filter of claim 8, wherein the hollow fiber is formed by assembling the extruded polymer filaments into a tubular shape and heating the extruded polymer filaments such that the extruded polymer filaments become bonded to one another.
10. The hollow fiber tangential flow filter of any of claims 1-9, wherein the wall thickness ranges from about 2 mm to about 7 mm.
11. The hollow fiber tangential flow filter of any of claims 1-10, wherein the wall has a mean pore size ranging from 0.2 to 10 microns.
12. The hollow fiber tangential flow filter of any of claims 1-11, wherein the interior lumen has a width ranging from 0.75 mm to 5 mm.

13. The hollow fiber tangential flow filter of any of claims 1-12, comprising a plurality of said hollow fibers.
14. The hollow fiber tangential flow filter of claim 13, further comprising an inlet chamber positioned in an interior of the housing and in fluid communication with the fluid inlet, an outlet chamber positioned in the interior of the housing and in fluid communication with the retentate fluid outlet, wherein the plurality of hollow fibers extend between the inlet chamber and the outlet chamber, and wherein the inlet chamber and the outlet chamber are in fluid communication with the interior lumen.
15. Use of a hollow fiber tangential flow filter of any of claims 1-14 to separate a fluid that comprises large size particles and small size particles into a permeate comprising the small size particles and a retentate comprising the large size particles.
16. The use of claim 15, wherein the fluid further comprises intermediate-sized particles that are trapped in the wall of the at least one hollow fiber.
17. The use of claim 16, wherein the large particles comprise cells, wherein the intermediate-sized particles comprise cell debris, and wherein the small particles comprise one or more of proteins, viruses, virus like particles (VLPs), exosomes, lipids, DNA, and cell metabolites.
18. A filtration method comprising introducing a fluid that comprises large size particles and small size particles into the fluid inlet of a hollow fiber tangential flow filter in accordance with any of claims 1-14, wherein the fluid is separated into a permeate comprising the small particles that exits the hollow fiber tangential flow filter through the permeate fluid outlet and a retentate comprising the large particles that exits the hollow fiber tangential flow filter through the retentate fluid outlet.

19. The filtration method of claim 18, wherein the fluid further comprises intermediate-sized particles and wherein at least a portion of the intermediate-sized particles are trapped in the wall of the hollow fiber tangential flow filter.
20. The filtration method of claim 18, wherein the large particles comprise cells, and wherein the small particles comprise one or more of proteins, viruses, virus like particles (VLPs), exosomes, lipids, DNA, and cell metabolites.
21. The filtration method of claim 18, wherein the large particles and small particles are of the same composition.
22. The filtration method of claim 21, wherein the large and small particles are selected from ceramic particles, metal particles, liposomal structures for drug delivery, biodegradable polymeric particles, and microcapsules.
23. The filtration method of claim 19, wherein the large particles comprise cells, wherein the intermediate-sized particles comprise cell debris, and wherein the small particles comprise one or more of proteins, viruses, virus like particles (VLPs), exosomes, lipids, DNA, and cell metabolites.
24. The filtration method of claim 19, wherein the large particles, the small particles and the intermediate-sized particles are of the same composition.
25. The filtration method of claim 24, wherein the large particles, the small particles and the intermediate-sized particles are selected from ceramic particles, metal particles, liposomal structures for drug delivery, biodegradable polymeric particles, and microcapsules.
26. The filtration method of any of claims 18-25, wherein the fluid is introduced into the fluid inlet in a pulsed fashion.

27. A tangential flow filtering system comprising a pump and a hollow fiber tangential flow filter in accordance with any of claims 1-14.
28. A bioreactor system comprising (a) a bioreactor vessel configured to contain bioreactor fluid, the bioreactor vessel having a bioreactor outlet and a bioreactor inlet, (b) a tangential flow filtering system comprising a pump and a hollow fiber tangential flow filter in accordance with any of claims 1-14, wherein the bioreactor outlet is in fluid communication with the fluid inlet and the bioreactor inlet is in fluid communication with the retentate outlet, and (c) a control system.
29. The bioreactor system of claim 28, wherein the control system is configured to operate the pump such that a first flow of bioreactor fluid is pumped from the bioreactor outlet and into the fluid inlet, thereby separating the first flow of bioreactor fluid into a retentate flow which is re-circulated from the retentate outlet and into the bioreactor inlet and a permeate flow which is collected from the permeate fluid outlet.
30. The bioreactor system of any of claims 28-29, wherein the system is configured to pump the first flow of bioreactor fluid in a pulsed fashion.
31. A hollow fiber tangential flow filtering system comprising:
- (a) a housing having an interior,
 - (b) a fluid inlet,
 - (c) a retentate fluid outlet,
 - (d) a permeate fluid outlet, and
 - (e) at least one hollow fiber comprising a porous wall that has an interior surface, an exterior surface, and a wall thickness ranging from 1 mm to 10 mm, the interior surface forming an

interior lumen having a width ranging from .75 mm to 7.5 mm and extending through the at least one hollow fiber,

wherein the at least one hollow fiber is positioned in the housing interior, wherein the fluid inlet and the retentate fluid outlet are in fluid communication with the interior lumen of the at least one hollow fiber and wherein the permeate fluid outlet is in fluid communication with the housing interior and the exterior surface of the porous wall, and

(f) a pumping system that is configured to provide pulsed flow to the fluid inlet.

32. The hollow fiber tangential flow filtering system of claim 31, wherein the pumping system comprises a pulsatile pump.

33. The hollow fiber tangential flow filtering system of claim 31, wherein the pulsatile pump is a peristaltic pump.

34. The hollow fiber tangential flow filtering system of any of claims 31-33, wherein the pumping system comprises a pump and a flow controller that causes the pump to provide said pulsed flow.

35. The hollow fiber tangential flow filtering system of claim 34, wherein the flow controller comprises an actuator that is configured to periodically restrict flow entering and/or exiting the pump thereby providing pulsed flow to the fluid inlet.

36. The hollow fiber tangential flow filtering system of any of claims 34 and 35, wherein the flow controller is positioned at the pump inlet.

37. The hollow fiber tangential flow filtering system of 35, wherein the actuator is selected from an electrically controlled actuator, a pneumatically controlled actuator, or a hydraulically controlled actuator.
38. The hollow fiber tangential flow filtering system of any of claims 34-37, wherein the flow controller comprises a servo valve or a solenoid valve.
39. The hollow fiber tangential flow filtering system of any of claims 34-37, wherein the flow controller is configured to provide a pulsed flow having a flow rate that is pulsed at a rate ranging from 1 cycle per minute to 1000 cycles per minute.
40. The hollow fiber tangential flow filtering system of any of claims 31-39, wherein the at least one hollow fiber comprises a porous wall that is formed from a plurality of particles and/or filaments that are bonded together.
41. The hollow fiber tangential flow filtering system of any of claims 31-39, wherein the at least one hollow fiber comprises a porous wall that is formed from a plurality of particles and/or filaments that are thermally bonded together.
42. A bioreactor system comprising (a) a bioreactor vessel configured to contain bioreactor fluid, the bioreactor vessel having a bioreactor outlet and a bioreactor inlet, (b) a hollow fiber tangential flow filtering system in accordance with any of claims 31-41, wherein the bioreactor outlet is in fluid communication with the fluid inlet and the bioreactor inlet is in fluid communication with the retentate outlet.
43. The bioreactor system of claim 42 wherein the pumping system is configured to provide pulsed flow of bioreactor fluid into the fluid inlet, thereby separating the pulsed flow of bioreactor

fluid into a retentate flow which is re-circulated from the retentate outlet and into the bioreactor inlet and a permeate flow which is collected from the permeate fluid outlet.

44. A method of filtering a fluid comprising large size particles and small size particles using a hollow fiber tangential flow filter that comprises (a) a housing having an interior, (b) a fluid inlet, (c) a retentate fluid outlet, (d) a permeate fluid outlet, and (e) at least one hollow fiber comprising a porous wall that has an interior surface, an exterior surface, and a wall thickness ranging from 1 to 10 mm, the interior surface forming an interior lumen having a width ranging from .75 mm to 7.5 mm and extending through the at least one hollow fiber, wherein the at least one hollow fiber is positioned in the housing interior, wherein the fluid inlet and the retentate fluid outlet are in fluid communication with the interior lumen of the at least one hollow fiber, and wherein the permeate fluid outlet is in fluid communication with the housing interior and the exterior surface of the porous wall, the method comprising: pumping a pulsed flow of the fluid into the fluid inlet thereby separating the fluid into a retentate flow comprising the large particles and a permeate flow comprising the small particles.
45. The method of claim 44, wherein the pulsed flow has a flow rate that is pulsed at a rate ranging from 1 cycle per minute to 1000 cycles per minute.
46. The method of any of claims 44-45, wherein the at least one hollow fiber comprises a porous wall that is formed from a plurality of particles and/or filaments that are bonded together.
47. The method of any of claims 44-45, wherein the at least one hollow fiber comprises a porous wall that is formed from a plurality of particles and/or filaments that are thermally bonded together.

48. The method of any of claims 44-47, wherein the fluid further comprises intermediate-sized particles that are trapped in the wall of the at least one hollow fiber.
49. The method of claim 48, wherein the large particles comprise cells, wherein the intermediate-sized particles comprise cell debris, and wherein the small particles comprise one or more of proteins, viruses, virus like particles (VLPs), exosomes, lipids, DNA, and cell metabolites.
50. The method of any of claims 44-49, wherein the fluid is fluid from a bioreactor and wherein the retentate flow is circulated back into the bioreactor.
51. A hollow fiber tangential flow filter for bioprocessing comprising:
- a housing having an interior, a fluid inlet, a retentate fluid outlet, and a permeate fluid outlet; and
 - at least one thick-walled hollow fiber comprising a porous wall formed from at least one polymer, the thick-walled hollow fiber having an average pore size and a density, the wall defining a lumen, and the at least one hollow fiber being disposed in the interior such that the fluid inlet and the retentate fluid outlet are in fluid communication with the lumen and the permeate fluid outlet is in fluid communication with the interior and the porous wall;
- wherein the density is between 51% and 56% of the density of an equivalent solid volume of the polymer.
52. The hollow fiber tangential flow filter for bioprocessing of claim 51, wherein the density is about 53%.
53. The hollow fiber tangential flow filter for bioprocessing of any of claims 51 and 52, wherein the average pore size is about 2 μm with a 90% nominal retention.
54. The hollow fiber tangential flow filter for bioprocessing of any of claims 51-53, wherein the at least one polymer is melt-blown.

55. The hollow fiber tangential flow filter for bioprocessing of any of claims 51-53, wherein the least one polymer is sintered.
56. The hollow fiber tangential flow filter for bioprocessing of any of claims 51-55, wherein the least one polymer is selected from the group consisting of polyolefin, a polyester, and a combination thereof.
57. A bioprocessing system comprising:
- a bioreactor;
 - a tangential flow depth filtration (TFDF) unit comprising a thick-walled hollow fiber formed from at least one polymer and comprising a porous wall having a pore size and a density, the porous wall defining a lumen that is in fluid communication with the bioreactor;
 - a permeate fluid outlet in fluid communication with the porous wall; and
 - a pump in fluid communication with the lumen;
- wherein the density is between 51% and 56% of the density of an equivalent solid volume of the least one polymer.
58. The bioprocessing system of claim 57, wherein the average pore size is about 2 μm with a 90% nominal retention.
59. The bioprocessing system of any of claims 57 and 58, wherein the density is about 53%.
60. The bioprocessing system of any of claims 57-59, wherein the least one polymer is melt-blown.
61. The bioprocessing system of any of claims 57-59, wherein the least one polymer is sintered.
62. The bioprocessing system of any of claims 57-61, wherein the pump is configured to provide a pulsed flow of fluid through the lumen.
63. A method of culturing cells in a perfusion bioreactor system comprising a culture vessel fluidly connected to a tangential flow depth filtration (TFDF) unit having a retentate channel and a filtrate channel, comprising the steps of:
- flowing a culture medium from the culture vessel through the retentate channel of the TFDF unit, whereby a fraction of the culture medium passes into the filtrate channel; and

returning fluid from the retentate channel to the culture vessel;

wherein (a) the culture medium comprises at least 60×10^6 cells/mL and (b) the method is performed for at least 8 consecutive days.

64. The method of claim 63, wherein at least 80% of the cells are viable throughout the 8 consecutive days.
65. The method of any of claims 63 and 64, further comprising a step of adding to the system a volume of fresh culture medium equal to a permeate volume.
66. The method of claim 65, wherein the step of adding the volume of fresh culture medium comprises adding at least 2 times a volume of the culture vessel to the system per day.
67. The method of any of claims 63-66, wherein the culture medium comprises a bioproduct of interest, and a rate of sieving of the bioproduct of interest is at least 99% throughout the 8 consecutive days.
68. The method of any of claims 63-67, wherein the TFDF unit comprises a thick-walled hollow fiber comprising least one polymer, wherein a density of the thick-walled hollow fiber is between 51% and 56% of the density of an equivalent solid volume of the least one polymer.
69. The method of claim 68, wherein the density is about 53%.
70. The method of any of claims 63-69, wherein the least one polymer is selected from the group consisting of polyolefin, a polyester, and a combination thereof.
71. A method of processing a fluid comprising a bioproduct, comprising the steps of:
- flowing a culture medium from a process vessel through a retentate channel of a TFDF unit, whereby a fraction of the culture medium passes into a filtrate channel; and
- returning fluid from the retentate channel to the process vessel;
- wherein the filtrate channel comprises a filter having a 2 mm internal diameter lumen therethrough; and
- wherein the filter has an average pore size of about 2 μm .

72. The method of claim 71, wherein flowing the culture medium is performed at a shear rate of about 8000 s^{-1} .
73. The method of any of claims 71 and 72, wherein the filter has a flux above about $40 \text{ L} \cdot \text{m}^{-2} \cdot \text{hr}^{-1}$.
74. The method of any of claims 71-73, wherein the filter has a flux of about $2300 \text{ L} \cdot \text{m}^{-2} \cdot \text{hr}^{-1}$.
75. The method of any of claims 71-74, wherein the flowing step further comprises the use of a pump selected from the group consisting of a centrifugal levitating magnetic pump, a positive displacement pump, a peristaltic, a membrane pump, and an ATF pump.
76. A method of harvesting a biomaterial from a bioreactor system comprising a process vessel fluidly connected to a tangential flow depth filtration (TFDF) unit having a feed/retentate channel and a filtrate channel, comprising the steps of:
- pumping a culture medium comprising the biomaterial from the process vessel through the feed/retentate channel of the TFDF unit, whereby a fraction of the culture medium passes into the filtrate channel;
 - returning fluid from the feed/retentate channel to the process vessel; and
 - collecting fluid from the filtrate channel;
- wherein the TFDF unit comprises a thick-walled hollow fiber formed from a polymer and comprising a porous wall, the thick-walled hollow fiber having a density of about 53% of the density of an equivalent solid volume of the polymer, the porous wall defining a lumen of 3 mm to 7 mm that is in fluid communication with the feed/retentate channel, the porous wall having a thickness of about 5 mm;
- wherein the TFDF unit has a flux above about $400 \text{ L} \cdot \text{m}^{-2} \cdot \text{hr}^{-1}$;
 - wherein the TFDF unit has a peak cell passage of under 5%;
 - wherein a rate of sieving of the bioproduct is at least 99%.

77. The method of claim 76, wherein the flowing step further comprises the use of a pump selected from the group consisting of a centrifugal levitating magnetic pump, a positive displacement pump, a peristaltic, a membrane pump, and an ATF pump.
78. A method of harvesting a biomaterial from a bioreactor system comprising a process vessel fluidly connected to a tangential flow depth filtration (TFDF) unit having a feed/retentate channel and a filtrate channel, comprising the steps of:
- flowing a culture medium via a pump from the process vessel through the feed/retentate channel of the TFDF unit, whereby a fraction of the culture medium passes into the filtrate channel;
 - returning fluid from the feed/retentate channel to the process vessel; and
 - collecting fluid from the filtrate channel;
- wherein the TFDF unit comprises a thick-walled hollow fiber formed from at least one polymer and comprising a porous wall, the thick-walled hollow fiber having a density of about 53% of the density of an equivalent solid volume of the at least one polymer, the porous wall defining a lumen that is in fluid communication with the feed/retentate channel;
- wherein the TFDF unit has a flux above about $400 \text{ L} \cdot \text{m}^{-2} \cdot \text{hr}^{-1}$;
 - wherein the TFDF unit has a peak cell passage of under 5%;
 - wherein the culture medium comprises a bioproduct of interest, and a rate of sieving of the bioproduct of interest is at least 99%.
79. A method of harvesting a biomaterial from a bioreactor system comprising a process vessel fluidly connected to a tangential flow depth filtration (TFDF) unit having a feed/retentate channel and a filtrate channel, comprising the steps of:
- flowing a culture medium through the feed/retentate channel of the TFDF unit, whereby a fraction of the culture medium passes into the filtrate channel;
 - returning fluid from the feed/retentate channel to the process vessel; and

collecting fluid from the filtrate channel;

wherein the TFDF unit comprises a thick-walled hollow fiber formed from at least one polymer and comprising a porous wall, the thick-walled hollow fiber having a density of about 53% of the density of an equivalent solid volume of the at least one polymer, the porous wall defining a lumen that is in fluid communication with the feed/retentate channel.

80. The method of claim 79, wherein a pore size of the porous wall is about 2 μm with a 90% nominal retention.
81. The method of any of claims 79 and 80, wherein the flowing step further comprises the use of a pump selected from the group consisting of a centrifugal levitating magnetic pump, a positive displacement pump, a peristaltic, a membrane pump, and an ATF pump.