Additionally, many currently available SPTFF solutions aim for a high volumetric concentration factor, often greater than 5.0, and the resulting membrane area and membrane configurations required for the target concentration factor (typically at least 3-4 filter stages) results in high pressure drop across the filter membranes (e.g., greater than 30psi). The volumetric concentration factor, as discussed throughout, is a function of the feed flow rate and the retentate flow rate.

[0006] Further, the magnitude of the pressure drop across the system under these operating conditions often prevents direct connection to a prior process step (e.g. chromatography column) to enable continuous processing. As such, the high target concentration factors and resulting high pressure drops across existing SPTFF solutions make connected and continuous processing difficult.

SUMMARY

[0007] As such, a need exists for SPTFF systems and methods that can serve as modular ("plug and play") systems to alleviate the manufacturing bottlenecks described above. The SPTFF systems and methods described herein are configured to increase protein solution concentration of a fluid by receiving a feed flow at one or more feed flow inlets/ports and directing the feed flow to one or more filter membranes configured to remove buffering solution as the fluid flows across the one or more semipermeable filter membranes while retaining product. The removed buffering solution is described throughout as the "permeate" and the product is described throughout as the "retentate." As described, SPTFF systems are typically designed to achieve volumetric concentration factors, which is the ratio of retentate protein concentration to feed protein concentration, but which can be approximated by the retentate and feed flow rates, of greater than 5.0, and to achieve these high volumetric concentration factors, at least 3-4 filtration stages are typically required. In contrast, the systems and methods disclosed herein are designed for lower concentration factors (e.g., between 1.0 and 5.0), and thus require only one or two filtration stages. In some examples, SPTFF systems disclosed herein may include a 3:2 filter membrane configuration (i.e., the system may include two filtration stages, the first having three membranes and the second having two membranes), a 3:1 filter membrane configuration, or a 4:1 filter membrane configuration.

[0008] The one- or two-stage configuration can provide a reduced pressure drop across the system (from the feed flow inlet to the retentate outlet or retentate port) relative to a three to four stage configuration, providing for a modular SPTFF system that can be connected to various preceding and subsequent processes as required without the need for a feed pump or pool tank at the outlet of a preceding process. In other words, whereas existing SPTFF solutions are commonly configured as an independent operation with pool tanks on the inlet and outlet (rather than connected processes), a feed pump on the inlet of the SPTFF to control flow, and no pump on the permeate line, the SPTFF systems and methods disclosed herein may be configured such that the system can be readily inserted in-line with an existing purification system, such as a chromatography unit with no feed pump or pool tank provided therebetween. The systems disclosed herein may further be provided on a mobile cart, with minimum space requirements, such that the system can be readily transported to various connection points on an as-needed basis.

[0009] The SPTFF systems disclosed herein may include a tangential flow filtration device holder and corresponding membrane devices assembled into a one- or two-stage SPTFF configuration. The system may further include a variety of sensors, including pressure sensors, flow meters, temperature sensors, and so on, placed on one or more feed lines, permeate lines, and/or retentate lines. A feed line may be configured to transmit a feed stream from preceding system to a feed inlet on the SPTFF system, and the retentate lines may be respectively configured to receive the retentate from respective retentate outlets and transmit the retentate to various subsequent systems. Additionally, the SPTFF system may, in some examples, include various other components, including valves, clamps, or pumps provided on any of the feed, retentate, or permeate lines.

[0010] According to an example, a single pass tangential flow filtration system comprises: a single pass tangential flow filtration unit configured to be fluidly connected to one or more preceding systems and one or more subsequent systems, wherein: the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one- or two-stage configuration, and a pressure drop across the one or more membranes or membrane devices is less than or equal to 30psi. In one aspect, the disclosure provides a single pass tangential flow filtration system, the system comprising: a single pass tangential flow filtration unit configured to be fluidly connected to one or more preceding systems and one or more subsequent systems, wherein: the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one- or two-stage configuration, and a pressure drop across the one or more membranes or membrane devices is less than or equal to 30psi.

[0011] In some examples, the pressure drop across the one or more membranes or membrane devices is less than 20psi.

[0012] In some examples, the single pass tangential flow filtration unit is configured to be connected to the one or more preceding systems by a feed flow inlet configured to receive a feed stream. In some examples, no pump is provided between the single pass tangential flow filtration unit and the one or more preceding systems.

[0013] In some examples, the single pass tangential flow filtration unit is configured to be connected to the one or more subsequent systems by one or more retentate flow outlets each configured to output a retentate stream.

[0014] In some examples, the system is positioned on a mobile platform.

[0015] In some examples, the system further comprises a controller in electrical communication with one or more sensors, the one or more sensors provided on a feed line in fluid communication with the feed flow inlet, one or more permeate lines in fluid communication with the one or more permeate outlets, and one or more retentate lines in fluid communication with the one or more retentate outlets.

[0016] In some examples, the controller is configured to control a volumetric concentration factor based on a determined volumetric concentration factor.

[0017] In some examples, the volumetric concentration factor is determined based on a reading from a first sensor and a second sensor of the one or more sensors.

[0018] In some examples, the first sensor is a flow meter provided on the feed line in fluid communication with the feed flow inlet and the second sensor is a flow meter provided a retentate flow line of one or more retentate flow lines in fluid communication with one or more of the retentate outlets.

[0019] In some examples, the volumetric concentration factor is determined based upon a ratio of a measured flow rate of the feed stream to a measured flow rate of the retentate stream, wherein the respective flow rates are measured by the first and second sensors.

[0020] In some examples, the first sensor is a protein concentration sensor provided on the feed line in fluid communication with the feed flow inlet and the second sensor is a

protein concentration sensor provided a retentate flow line of one or more retentate flow lines in fluid communication with one or more of the retentate outlets, and wherein the volumetric concentration factor is determined based upon a ratio of a measured protein concentration of the retentate stream to a measured protein concentration of the feed stream, wherein the respective protein concentrations are measured by the first and second sensors.

[0021] In some examples, controlling the volumetric concentration factor comprises: in accordance with determining that the volumetric concentration factor is outside of a threshold range based on the determined volumetric concentration factor, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range. In some examples, adjusting a flow rate of the permeate stream can achieve a VCF and a resulting protein concentration which is desired for protein stability and/or downstream purification step performance.

[0022] In some examples, the threshold range is between 1.0 and 3.0, including 1.0 and 3.0.

[0023] In some examples, the threshold range is between 1.5 and 2.5, including 1.5 and 2.5.

[0024] In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises: activating or deactivating one or more permeate control pumps provided on one or more of the one or more permeate lines downstream of the one or more permeate outlets.

[0025] In some examples, one or more of the permeate control pumps include one or more variable displacement pumps.

[0026] In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises increasing a displacement of a variable displacement pump of the one or more variable displacement pumps.

[0027] In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises decreasing a

displacement of a variable displacement pump of the one or more variable displacement pumps.

[0028] In some examples, one or more of the permeate control pumps include one or more fixed displacement pumps.

[0029] In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises: adjusting a valve provided on one or more permeate lines downstream of the one or more permeate outlets.

[0030] In some examples, adjusting the valve comprises opening the valve.

[0031] In some examples, adjusting the valve comprises closing the valve.

[0032] In some examples, the one or more sensors comprise a flow meter, a pressure sensor, a temperature sensor, and a protein concentration sensor.

[0033] In some examples, the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one stage configuration.

[0034] In some examples, the one stage configuration is configured to receive a feed stream from the feed flow inlet and separate the feed stream into a retentate stream and a permeate stream by allowing a portion of the feed stream to pass through one or more membranes or membrane devices, the portion passing through the one or more membranes or membrane devices forming the permeate stream.

[0035] In some examples, the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a two-stage configuration.

[0036] In some examples, the two-stage configuration is configured to receive a feed stream from the feed flow inlet and separate the feed stream into a retentate stream and a permeate stream by allowing a portion of the feed stream to pass through one or more membranes or membrane devices of a first stage and one or more membranes or membrane devices of a second filtration stage, the portion passing through the one or more membranes of the first and second stage forming the permeate stream.

[0037] In some examples, the operating temperature of the feed stream is between 2 degrees Celsius and 30 degrees Celsius, including 2 degrees Celsius and 30 degrees Celsius.

[0038] In some examples, the operating temperature of the feed stream is less than or equal to 20 degrees Celsius.

[0039] In some examples, the operating temperature of the feed stream is less than or equal to 15 degrees Celsius.

[0040] In some examples, the operating temperature of the feed stream is less than or equal to 10 degrees Celsius.

[0041] In some examples, the operating temperature of the feed stream is less than or equal to 5 degrees Celsius.

[0042] In some examples, the operating temperature of the feed stream is between 1 degree Celsius and 3 degrees Celsius, including 1 degree Celsius and 3 degrees Celsius.

[0043] In some examples, the one or more preceding systems comprise a purification system or a harvest system.

[0044] In some examples, the purification system comprises a viral filtration system.

[0045] In some examples, the purification system comprises a chromatography system.

[0046] In some examples, the purification system comprises a diafiltration system.

[0047] In some examples, the purification system comprises an ultrafiltration system.

[0048] In some examples, the one or more subsequent systems comprise a purification system.

[0049] In some examples, the one or more subsequent systems comprise a viral filtration system.

[0050] In some examples, the one or more subsequent systems comprise a chromatography system.

[0051] In some examples, the one or more subsequent systems comprise a diafiltration system.

[0052] In some examples, the one or more subsequent systems comprise an ultrafiltration system.

[0053] In some examples, the feed flow comprises a polypeptide preparation.

[0054] In some examples, the polypeptide preparation comprises a polypeptide and one or more impurities.

[0055] In some examples, an exemplary single pass tangential flow filtration method comprises: receiving a feed flow at a feed flow inlet of a single pass tangential flow filtration unit, wherein the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one- or two-stage configuration, and wherein a pressure drop across the one or more membranes or membrane devices is less than or equal to 30psi; separating, using the one or more membranes or membrane devices, the feed stream into a permeate stream and a retentate stream; and outputting the permeate stream through one or more permeate outlets and the retentate stream through one or more retentate outlets. In one aspect, the disclosure provides a single pass tangential flow filtration method, the method comprising: receiving a feed flow at a feed flow inlet of a single pass tangential flow filtration unit, wherein the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one- or two-stage configuration, and wherein a pressure drop across the one or more membranes or membrane devices is less than or equal to 30psi; separating, using the one or more membranes or membrane devices, the feed stream into a permeate stream and a retentate stream; and outputting the permeate stream through one or more permeate outlets and the retentate stream through one or more retentate outlets.

[0056] In some examples, the pressure drop across the one or more membranes or membrane devices is less than 20psi.

[0057] In some examples, the single pass tangential flow filtration unit is configured to be connected to the one or more preceding systems by a feed flow inlet configured to receive a feed stream. In some examples, no pump is provided between the single pass tangential flow filtration unit and the one or more preceding systems.

[0058] In some examples, the single pass tangential flow filtration unit is configured to be connected to the one or more subsequent systems by one or more retentate flow outlets each configured to output a retentate stream.

[0059] In some examples, the single pass tangential flow filtration unit is positioned on a mobile platform.

[0060] In some examples, an exemplary system performing the method comprises a controller in electrical communication with one or more sensors, the one or more sensors provided on a feed line in fluid communication with the feed flow inlet, one or more permeate lines in fluid communication with the one or more permeate outlets, and one or more retentate lines in fluid communication with the one or more retentate outlets.

[0061] In some examples, the method further comprises controlling a volumetric concentration factor based on a determined volumetric concentration factor. In some

examples, the volumetric concentration factor is determined based on a reading from a first sensor and a second sensor. In some examples, the first sensor is a flow meter provided on the feed line in fluid communication with the feed flow inlet and the second sensor is a flow meter provided a retentate flow line of one or more retentate flow lines in fluid communication with one or more of the retentate outlets. In some examples, the volumetric concentration factor is determined based upon a ratio of a measured flow rate of the feed stream to a measured flow rate of the retentate stream, wherein the respective flow rates are measured by the first and second sensors. In some examples, the first sensor is a protein concentration sensor provided on the feed line in fluid communication with the feed flow inlet and the second sensor is a protein concentration sensor provided a retentate flow line of one or more retentate flow lines in fluid communication with one or more of the retentate outlets, and wherein the volumetric concentration factor is determined based upon a ratio of a measured protein concentration of the retentate stream to a measured protein concentration of the feed stream, wherein the respective protein concentrations are measured by the first and second sensors.

[0062] In some examples, controlling the volumetric concentration factor comprises: in accordance with determining that the volumetric concentration factor is outside of a threshold range based on the determined volumetric concentration factor, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range. In some examples, the threshold range is between 1.0 and 3.0, including 1.0 and 3.0. In some examples, the threshold range is between 1.5 and 2.5, including 1.5 and 2.5. In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises: activating or deactivating one or more permeate control pumps provided on one or more of the one or more permeate lines downstream of the one or more permeate outlets. In some examples, one or more of the permeate control pumps include one or more variable displacement pumps. In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises increasing a displacement of a variable displacement pump of the one or more variable displacement pumps. In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises decreasing a displacement of a

variable displacement pump of the one or more variable displacement pumps. In some examples, one or more of the permeate control pumps include one or more fixed displacement pumps. In some examples, adjusting a flow rate of the permeate stream to bring the volumetric concentration factor within the threshold range comprises: adjusting a valve provided on one or more permeate lines downstream of the one or more permeate outlets. In some examples, adjusting the valve comprises opening the valve. In some examples, adjusting the valve comprises closing the valve. In some examples, the one or more sensors comprise a flow meter, a pressure sensor, a temperature sensor, and a protein concentration sensor. In some examples, adjusting a flow rate of the permeate stream can achieve a VCF and a resulting protein concentration which is desired for protein stability and/or downstream purification step performance.

[0063] In some examples, the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a one stage configuration. In some examples, the method further comprises receiving, by the one stage configuration, a feed stream from the feed flow inlet and separating the feed stream into a retentate stream and a permeate stream by allowing a portion of the feed stream to pass through one or more membranes or membrane devices, the portion passing through the one or more membranes or membrane devices forming the permeate stream.

[0064] In some examples, the single pass tangential flow filtration unit comprises one or more membranes or membrane devices in a two-stage configuration. In some examples, the method further comprises receiving by the two-stage configuration, a feed stream from the feed flow inlet and separating the feed stream into a retentate stream and a permeate stream by allowing a portion of the feed stream to pass through one or more membranes or membrane devices of a first stage and one or more membranes or membrane devices of a second filtration stage, the portion passing through the one or more membranes of the first and second stage forming the permeate stream.

[0065] In some examples, the operating temperature of the feed stream is between 2 degrees Celsius and 30 degrees Celsius, including 2 degrees Celsius and 30 degrees Celsius. In some examples, the operating temperature of the feed stream is less than or equal to 20 degrees Celsius. In some examples, the operating temperature of the feed stream is less

than or equal to 15 degrees Celsius. In some examples, the operating temperature of the feed stream is less than or equal to 10 degrees Celsius. In some examples, the operating temperature of the feed stream is less than or equal to 5 degrees Celsius. In some examples, the operating temperature of the feed stream is between 1 degree Celsius and 3 degrees Celsius, including 1 degree Celsius and 3 degrees Celsius.

[0066] In some examples, the one or more preceding systems comprise a purification system or a harvest system. In some examples, the purification system comprises a viral filtration system. In some examples, the purification system comprises a chromatography system. In some examples, the purification system comprises a diafiltration system. In some examples, the purification system comprises an ultrafiltration system.

[0067] In some examples, the one or more subsequent systems comprise a purification system. In some examples, the one or more subsequent systems comprise a viral filtration system. In some examples, the one or more subsequent systems comprise a chromatography system. In some examples, the one or more subsequent systems comprise a diafiltration system. In some examples, the one or more subsequent systems comprise an ultrafiltration system.

[0068] In some examples, the feed flow comprises a polypeptide preparation. In some examples, the polypeptide preparation comprises a polypeptide and one or more impurities.

[0069] In some examples, any one or more of the characteristics of any one or more of the systems and methods recited above may be combined, in whole or in part, with one another and/or with any other features or characteristics described elsewhere herein.

BRIEF DESCRIPTION OF THE FIGURES

[0070] FIG. 1 illustrates an exemplary single pass tangential flow filtration system, in accordance with some embodiments.

[0071] FIG. 2 illustrates an exemplary single pass tangential flow filtration system, in accordance with some embodiments.

[0072] FIG. 3 illustrates an exemplary single pass tangential flow filtration method, in accordance with some embodiments.