The diafiltration buffer is supplied at the final diafiltration stage. Permeate from the final stage then serves as the diafilterant for the preceding stage, resulting in a flow "counter-current" to the feed stream. However, CCBE-TFF processes come with their own set of challenges, including complex process control, an increased number of necessary pumps and other instrumentation, and a greater requirement for surface area relative to traditional bTFF systems. Further, the requirement of serial stages presents process control challenges, including, but not limited to, unstable flow rates, system over-pressure, undesired mixing, tightly coupled flow control loops between stages, and complex start-up and shut down procedures, which further complicates situations requiring a disturbance response, where restart of the system is necessary, resulting in further inefficiencies.

SUMMARY

[0004] The present disclosure relates to tangential flow filtration systems and, more specifically, to continuous tangential flow filtration ("cTFF") systems comprised of single-pass modules configured to transition from a first process configuration to a second process configuration and/or operate under both the first process configuration and the second process configuration for customization of the cTFF system. Each of the modules has at least one break tank for regulation of flow and pressure throughout the module and, on a larger scale, the cTFF system.

[0005] In a first example of the disclosure, a tangential flow filtration module is described. The module comprises a flow supply comprising a module exchange buffer supply and a module feed supply; a feed break tank positioned downstream of the flow supply, the feed break tank including a powered agitator; and a first filter positioned downstream of the feed break tank.

[0005a] In an aspect, the disclosure provides a tangential flow filtration module, the module comprising: a flow supply comprising a module exchange buffer supply and a module feed supply; a feed break tank positioned downstream of the flow supply, the feed break tank including a powered agitator; and a first filter positioned downstream of the feed break tank.

[0006] In another example of the disclosure, a tangential flow filtration module is described. The module comprises a flow supply comprising a module exchange buffer supply and a module feed supply; a filter positioned downstream of the flow supply and having two outputs, including a permeate output and a retentate output; and a permeate

break tank positioned downstream of the filter and supplied by the permeate output of the filter.

[0006a] In another aspect, the disclosure provides a tangential flow filtration module, the module comprising: a flow supply comprising a module exchange buffer supply and a module feed supply; a filter positioned downstream of the flow supply and having two outputs, including a permeate output and a retentate output; and a permeate break tank positioned downstream of the filter and supplied by the permeate output of the filter.

[0007] In yet another example of the disclosure, a tangential flow filtration system is described. The tangential flow filtration system comprises a plurality of individual modules, each of said individual modules configured to perform a process associated with tangential flow filtration, wherein each individual module includes a plurality of valves and a control system. Actuation of the plurality of valves is configured to alter a flow path of the corresponding individual module. The control system is configured to calculate a current stage removal factor for the individual module and automatically operate the plurality of valves to alter the flow path so that the current stage removal factor for the individual module approaches a target stage removal factor. The current stage removal factor is a ratio between any two of a permeate flow rate, a feed flow rate, and a retentate flow rate for the individual module.

[0007a] In another aspect, the disclosure provides a tangential flow filtration system, the tangential flow filtration system comprising: a plurality of individual modules, each of said individual modules configured to perform a process associated with tangential flow filtration, wherein each individual module includes: a plurality of valves, wherein actuation of the plurality of valves is configured to alter a flow path of the corresponding individual module; and a control system configured to: calculate a current stage removal factor for the individual module, the current stage removal factor being a ratio between any two of a permeate flow rate, a feed flow rate, and a retentate flow rate for the individual module; and automatically operate the plurality of valves to alter the flow path so that the current stage removal factor for the individual module approaches a target stage removal factor.

[0008] In another example of the disclosure, a tangential flow filtration system is described. The system comprises a plurality of modules, each module comprising a module flow supply; a filter positioned downstream of the module flow supply; and at least one of a feed break tank positioned between the module flow supply and the filter and a permeate break tank positioned downstream of the filter.

[0008a] In another aspect, the disclosure provides a tangential flow filtration system, the system comprising: a plurality of modules, each module comprising: a module flow supply; a filter positioned downstream of the module flow supply; and at least one of: a feed break tank positioned between the module flow supply and the filter; and a permeate break tank positioned downstream of the filter.

[0009] In various examples of the disclosure, the module may further comprise a feed pump positioned between the feed break tank and the first filter. The feed pump may be configured to control a flow rate of a flow between the feed break tank and the first filter.

[0010] In various examples of the disclosure, operation of the powered agitator is configured to create a homogenous solution.

[0011] In various examples of the disclosure, the feed break tank may define an air gap.

[0012] In various examples of the disclosure, the feed break tank may define a vent in fluid communication with ambient pressure.

[0013] In various examples of the disclosure, a permeate break tank may be positioned downstream of the first filter.

[0014] In various examples of the disclosure, the module exchange buffer supply may be comprised of permeate of a second filter positioned downstream of the first filter, a feed supply of the second filter comprising retentate of the first filter.

[0015] In various examples of the disclosure, the module feed supply is comprised of retentate of a third filter positioned upstream of the first filter.

[0016] In various examples of the disclosure, a feed break tank may be positioned between the flow supply and the filter.

[0017] In various examples of the disclosure, an interior of the permeate break tank may define an air gap.

[0018] In various examples of the disclosure, the permeate break tank may include a vent in fluid communication with ambient pressure.

[0019] In various examples of the disclosure, a valve may be positioned between the first filter and the permeate break tank. The valve may be configured to control permeate pressure on the permeate side of the first filter.

[0020] In various examples of the disclosure, the permeate break tank may supply a second filter positioned upstream of the feed supply. The feed supply may be comprised of retentate of the second filter.

[0021] In various examples of the disclosure, the module exchange buffer supply may be comprised of permeate of a third filter positioned downstream of the first filter, a feed supply of the third filter comprising retentate of the first filter.

[0022] In various examples of the disclosure, the module may comprise at least one valve, wherein operation of the valve is configured to change a configuration of the tangential flow filtration module from a first flow path configuration to a second flow path configuration or a configuration of the tangential flow filtration module from the second flow path configuration to a first flow path configuration. The first flow configuration may be a counter-current buffer exchange flow path configuration. The second flow configuration may be a single-pass tangential flow filtration flow path configuration.

[0023] In various examples of the disclosure, the plurality of individual modules may include at least five modules.

[0024] In various examples of the disclosure, a last individual module of the plurality of individual modules may have a different target stage removal factor than at least one other individual module of the plurality of individual modules.

[0025] In various examples of the disclosure, the control system may be configured to maintain the tangential flow filtration system in a steady state in which the current stage removal factor approaches the target stage removal factor. The system may be configured to allow a user to adjust, when the tangential flow filtration system is in the steady state, at least one valve of the plurality of valves in a way that causes the current stage removal factor to diverge from the target stage removal factor. The control system may be configured to automatically operate remaining valves of the plurality of valves to compensate for the user's adjustment such that the current stage removal factor again approaches the target stage removal factor after the user's adjustment. Each of the plurality of individual modules may comprise a feed break tank positioned downstream of a flow supply and upstream of the filter for the individual module and a permeate break tank positioned downstream of the filter. The flow supply may comprise a module feed supply and a module exchange buffer supply. A first flow rate output of the feed break tank and a second flow rate output of the permeate break tank may be individually adjustable during operation of the tangential flow filtration system. The control system may be configured to maintain the tangential flow filtration system in a steady state by automatically maintaining a substantially constant stage removal factor during adjustment of either of the first flow rate output or the second flow rate output. The control system may be further configured to maintain a constant level within the feed break tank and a constant level within the permeate break tank.

[0026] In various examples of the disclosure, each module may have at least one of a first configuration corresponding to a single-pass tangential flow filtration ("spTFF") process, a second configuration corresponding to a counter-current buffer exchange tangential flow filtration ("CCBE-TFF") process, and a third configuration corresponding to a combined spTFF and CCBE-TFF process. Each module of the plurality of modules may include a plurality of valves so that each module of the plurality of modules is

capable of selectively switching form the first configuration to at least one of the second configuration and the third configuration, selectively switching from the second configuration to at least one of the first configuration and the third configuration, and selectively switching form the third configuration to at least one of the first configuration and the second configuration. A first module of the plurality of modules may be in the first configuration and a second module of the plurality of modules may be in the second configuration. A first plurality of modules including the first module may be in the first configuration and a second plurality of modules including the second module may be in the second configuration. A last module of the plurality of modules may be operated in the third configuration. At least some permeate from the last module may be supplied to a module exchange buffer supply for another module upstream to the last module, and at least some permeate from the last module may be sent to waste.

[0027] In various examples of the disclosure, each module of the plurality of modules may include a retentate flow path and a permeate flow path. The permeate break tank may be positioned along the permeate flow path.

[0028] In various examples of the disclosure, the system may comprise at least five modules.

[0029] In various examples of the disclosure, a first module of the plurality of modules includes a system feed supply. A last module of the plurality of modules includes a system buffer exchange supply.

[0030] In various examples of the disclosure, the system may be configured to operate as a diafiltration system that transfers a solute of interest from within a feed supply from a starting solution matrix into an exchange buffer. The system may be configured to flush the filter of each module with the exchange buffer before starting to filter the feed supply.

[0031] In various examples of the disclosure, the system may be configured to compensate for outputting product during system start-up with a concentration that is lower than process requirements by outputting product during steady-state with a concentration that is higher than process requirements, such that a mixture of product