

the single use perfusion device 36 and the stainless steel large scale bioreactor 12 and provides an ability to resteam on subsequent perfusion devices during a single run of the bioreactor 12. Said another way, with this configuration, the perfusion device 36 and/or a new perfusion device may be installed while the stainless steel large scale bioreactor 12 is running a cell culture, by repeating the steam-in-place or by using the aseptic connector assembly 26, for example.

[0031] Referring now to FIG. 6, another large scale bioreactor system 100 is depicted. Like the large scale bioreactor system 10 of FIGs. 1-5, the large scale bioreactor system also includes a stainless steel large scale bioreactor 112 having a side 113 and a first valve assembly 114, such as an autoclaved valve assembly 114, coupled to the side 113 of the stainless steel large scale bioreactor 112. The autoclaved valve assembly 114 includes a first valve 116, a second valve 118 downstream from the first valve 116, a third valve 120 downstream from both the first and second valves 116, 118, and a fourth valve 121 downstream from the third valve 120. Again like the valve assembly 14 of the system 10 of FIGs. 1-5, steam, such as clean steam CS, flows into the third valve 120, upwardly to the first and second valves 116, 118 and to the port 124. Additionally, after flowing into the third valve 120, steam flows downwardly through the fourth valve 121 and through a steam trap 122 to sterilize the bioreactor 112 and create a steam-in-place process of sterilization before further use, for example. In this large scale bioreactor system 100, however, there is only at least one aseptic connector 134 coupled to the autoclaved valve assembly 114, such as the first valve 116 of the autoclaved valve assembly 114, and not a second valve assembly, like the aseptic connector assembly 26 of the system 10 of FIGs. 1-5. This same autoclaved valve assembly 114 enables connection via the at least one aseptic connector 134 of the autoclaved valve assembly 114 to a factory assembled and irradiated perfusion device 136, which may be a single use perfusion device or a reusable perfusion device, for example. More specifically, the irradiated perfusion device 136 includes a first aseptic connector 138 that is coupled to the at least one aseptic connector 134, as depicted in FIG. 6. The irradiated perfusion device 136 also includes a second aseptic connector 140 that is configured to be coupled to a second autoclaved valve assembly (not shown), such as a second valve assembly, which is also configured to be directly coupled to the side 113 of the large scale stainless steel bioreactor 112 on a different valve assembly analogous to the valve assembly 114. As a result, multiple perfusion devices are able to be aseptically coupled to the large scale stainless steel bioreactor 112 without additional steam sterilization.

[0032] Referring now to FIG. 7, a schematic view of another large scale bioreactor system 200 of the present disclosure is depicted. Like the large scale bioreactor system 10 of FIG. 4, for example, the large scale bioreactor system 200 includes a stainless steel large scale bioreactor 212 having a side wall 213 and at least one valve assembly 214 disposed on the side wall 213. Again like the large scale bioreactor system 10 of FIG. 4, the same valve assembly 214 of the large scale bioreactor 200 of FIG. 7 enables connection of an autoclaved perfusion device and cleaning-in-place of the valve assembly 214, but without the use of an aseptic connector, such as the aseptic connector 34 of FIG. 4. Instead, a hose assembly is used as an alternate connector to couple the stainless steel large scale bioreactor 212 to the autoclaved perfusion device, as explained more below.

[0033] More specifically, and as depicted in FIG. 7, the stainless steel large scale bioreactor 212 of the large scale bioreactor system 200 is also a steam-in-place bioreactor with large scale capacity. For example, the large scale bioreactor 212 is configured to hold a volume of fluid of up to or greater than 10,000L in one example. The at least one valve assembly 214 of the steam-in-place large scale bioreactor 212 enables the steam-in-place, stainless steel large scale bioreactor 212 to be completely sterilized when perfusion begins. Specifically, and like the at least one valve assembly 14 of the bioreactor system 10 of FIG. 4, the at least one valve assembly 214 includes a first valve 216, a second valve 218, and a third valve 220 disposed downstream from each of the first and second valves 216, 218. A fourth valve 221 may also be disposed downstream from the third valve 220, as depicted. Steam, such as clean steam CS, again flows into the third valve 220, upwardly to the first and second valves 116, 118 and to a port 224. Additionally, after flowing into the third valve 220, steam also flows downwardly into the fourth valve

What is claimed is:

1. A large scale bioreactor system comprising:
a stainless steel large scale bioreactor having at least one valve assembly;
an aseptic connector assembly coupled to the least one valve assembly of the bioreactor; and
a perfusion device or reusable Alternating Tangential Filtration (ATF) assembly with an autoclaved valve assembly coupled to the aseptic connector assembly, the aseptic connector assembly including one of a triclamp aseptic connector or a hose assembly.
2. The bioreactor system of claim 1, wherein the perfusion device is a single use perfusion device, the single use perfusion device further comprising at least one pressure sensor, and the bioreactor system further comprises a control system coupled to the single use perfusion device for monitoring pressure of the single use perfusion device via the at least one pressure sensor.
3. The bioreactor system of claim 1, wherein the perfusion device or reusable ATF assembly is a single use perfusion device or reusable ATF assembly further comprising at least one pressure sensor, and the bioreactor system further comprises a control system coupled to the single use perfusion device or the reusable ATF assembly for monitoring pressure of the single use perfusion device or the reusable ATF assembly via the at least one pressure sensor.
4. The bioreactor system of claim 2 or claim 3, wherein the control system further comprises an alarm, the alarm configured to be activated when the control system detects a pressure greater than a safe pressure limit, the control system configured to automatically reduce one or more of a flow rate or a pressure in the single use perfusion device or the reusable ATF assembly in response to detection of the pressure greater than the safe pressure limit.
5. The bioreactor system of any one of claims 1-3, wherein the bioreactor has a body with a side having a top end, wherein one or more of the at least one valve assembly of the bioreactor and the autoclaved valve assembly is coupled to the side of the bioreactor near the top portion of the bioreactor.
6. The bioreactor system of any one of claims 1-5, the bioreactor having a body and a bottom portion, wherein the bioreactor is configured to be at least partially disposed in a pit and one or more of the at least one valve assembly of the stainless steel large scale bioreactor and the autoclaved valve assembly is coupled against a bottom weld seam of the bottom portion of the bioreactor.
7. The bioreactor system of any one of claims 1-6, wherein the aseptic connector assembly is an aseptic connector valve assembly having a triclamp aseptic connector, enabling a new perfusion device or ATF assembly to be coupled to the stainless steel large scale bioreactor while the bioreactor is running a cell culture by repeating a steam-in-place of the aseptic connector assembly.
8. The bioreactor system of any one of claims 1-7, wherein the aseptic connector assembly is a hose assembly, the hose assembly coupling the at least one valve assembly of the bioreactor to the perfusion device or ATF assembly, wherein the hose assembly comprises a hose body having a first end and a second end, the first end operatively coupled to the at least one valve assembly and the second end operatively coupled to the perfusion device or ATF assembly.

9. The bioreactor system of any one of claims 1-8, wherein the stainless steel large scale bioreactor has a volume of greater than 2,000 L.
10. The bioreactor system of any one of claims 1-9, wherein the stainless steel large scale bioreactor has a volume in the range of greater than 2,000 L to 20,000 L.
11. A method of integrating at least one perfusion device with a stainless steel large scale bioreactor, the method comprising:
coupling one of: (1) a connector assembly to at least one valve assembly of a stainless steel large scale bioreactor; or
(2) an autoclaved valve assembly to a side of the stainless steel large scale bioreactor;
coupling an autoclaved valve assembly of an Alternating Tangential Filtration (ATF) assembly of a perfusion device to the connector assembly; and
managing pressure of the perfusion device via at least one pressure sensor of the perfusion device and automatically reducing one or more of a flow rate or a pressure in the perfusion device upon detecting a pressure greater than a safe limit pressure by a control system.
12. The method of claim 11, wherein coupling one of: (1) a connector assembly to at least one valve assembly of a stainless steel large scale bioreactor; or (2) an autoclaved valve assembly to a side of the stainless steel large scale bioreactor; comprises coupling an aseptic connector valve assembly to the at least one valve assembly of the stainless steel large scale bioreactor.
13. The method of claim 12, wherein coupling an autoclaved valve assembly of an ATF assembly of a perfusion device to the connector assembly comprises coupling the autoclaved valve assembly of the perfusion device to the connector assembly, the connector assembly comprising one of a triclamp connector assembly or a hose assembly.
14. The method of claim 13, wherein coupling one of: (1) a connector assembly to at least one valve assembly of a stainless steel large scale bioreactor; or (2) an autoclaved valve assembly to a side of the stainless steel large scale bioreactor comprises coupling an autoclaved assembly to the side of the stainless steel large scale bioreactor.
15. The method of claim 11, wherein coupling one of: (1) a connector assembly to at least one valve assembly of a stainless steel large scale bioreactor; or (2) an autoclaved valve assembly to a side of the stainless steel large scale bioreactor comprises coupling a connector assembly to at least one valve assembly of a stainless steel large scale bioreactor, the connector assembly including a wye connector assembly.
16. The method of claim 15, wherein coupling an autoclaved valve assembly of an ATF assembly of at least one perfusion device to the connector assembly comprises coupling the autoclaved valve assembly of an ATF assembly of at least one perfusion device to the connector assembly, wherein the at least one perfusion device comprises a plurality of perfusion devices connected to the wye connector assembly, enabling multiple perfusion devices to be coupled to the bioreactor without having to steam-in-place the bioreactor upon coupling multiple perfusion devices.

17. The method of any one of claims 11-16, further comprising coupling at least one stainless steel transfer panel having a plurality of inputs to the stainless steel large scale bioreactor.
18. The method of any one of claims 11-17, further comprising coupling one or more of the at least one valve assembly of the stainless steel large scale bioreactor and the autoclaved valve assembly to a side of the stainless steel large scale bioreactor.
19. The method of any one of claims 11-18, wherein the stainless steel large scale bioreactor has a volume of greater than 2,000 L.
20. The method of any one of claims 11-19, wherein the stainless steel large scale bioreactor has a volume in the range of greater than 2,000 L to 20,000 L.