connected to the cell culture chamber; a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller; and a cellular sample output fluidly connected to the tangential flow filter.

[0005a] In one aspect, the present disclosure refers to a cassette for use in an automated cell engineering system, comprising: (a) a cell culture chamber; (b) a pumping system fluidly connected to the cell culture chamber; (c) a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller; and (d) a cellular sample output fluidly connected to the tangential flow filter, wherein (a)-(d) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector, wherein the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter, and wherein the cassette is configured to be contained within an enclosable housing of the automated cell engineering system.

[0006] In further examples, provided herein is a cassette for use in an automated cell engineering system, comprising: a cell culture chamber; a pumping system fluidly connected to the cell culture chamber; a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller; a satellite volume connected to the tangential flow filter; a fluidics pathway for recirculating the retentate flow back through the tangential flow filter; a fixed volume waste collection chamber fluidly connected to the tangential flow filter; and a cellular sample output fluidly connected to the tangential flow filter.

[0006a] In one aspect, the present disclosure refers to a cassette for use in an automated cell engineering system, comprising: (a) a cell culture chamber; (b) a pumping system fluidly connected to the cell culture chamber; (c) a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller, and the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter; (d) a satellite volume connected to the tangential flow filter; (e) a fluidics pathway for recirculating the retentate flow back through the tangential flow filter; (f) a fixed volume waste collection chamber fluidly connected to the tangential flow filter; and (g) a cellular sample output fluidly connected to the tangential flow filter, wherein (a)-(g) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector.

[0007] In additional examples, provided herein is a method of reducing a volume of a cellular sample during automated processing, the method comprising introducing a cellular sample into a tangential flow filter having a retentate flow and a permeate flow, wherein the permeate flow is controlled by a flow controller, passing the cellular sample through the retentate flow of the tangential flow filter, removing volume from the cellular sample via the permeate flow to a fixed volume waste collection chamber, and collecting the cellular sample having the reduced volume.

[0008] In still further examples, provided herein is an automated cell engineering system, comprising: an enclosable housing; a cassette contained within the enclosable housing, the cassette comprising: i. a cell culture chamber; ii. a pumping system fluidly connected to the cell culture chamber; iii. a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller; and iv. a cellular sample output fluidly connected to the tangential flow filter; and a user interface for receiving input from a user.

[0008a] In one aspect, the present disclosure refers to an automated cell engineering system, comprising: (a) an enclosable housing; (b) a cassette contained within the enclosable housing, the cassette comprising: i. a cell culture chamber; ii. a pumping system fluidly connected to the cell culture chamber; iii. a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller, and the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter; and iv. a cellular sample output fluidly connected to the tangential flow filter, wherein (i)-(iv) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector; and (c) a user interface for receiving input from a user.

Brief Description of the Figures

[0009] FIG. 1 shows various steps that can be performed with a cassette of an automated cell engineering system, as described in embodiments hereof.

[0010] FIG. 2A shows an exemplary cassette in accordance with embodiments hereof.

[0011] FIGS. 2B shows an exemplary tangential flow filter for use in the cassettes, systems and methods described herein.

[0012] FIGS. 2C shows exemplary flow controllers for use with the tangential flow filters as described herein.

[0013] FIGS. 3A and 3B show images of an automated cell engineering system in accordance with embodiments hereof.

[0014] FIG. 4 shows a lab space containing exemplary cell engineering systems as described in embodiments hereof.

[0015] FIG. 5 shows a flowpath for cell concentration in a cassette of an automated cell engineering system as described in embodiments hereof.

[0016] FIG. 6A-6B show the effect of serum on tangential flow filtration, in accordance with embodiments hereof.

[0017] FIGS. 7A-7C show the use of permeate control to reduce the clogging of the tangential flow filter in accordance with embodiments hereof.

[0018] FIGS. 8A-8B show volume reduction of peripheral blood mononuclear cells (PBMC) using tangential flow filtration in accordance with embodiments hereof.

[0019] FIGS. 9A-9D show permeate pump optimization during tangential flow volume reduction of PMBCs in accordance with embodiments hereof.

[0020] FIG. 10A shows cell recovery post tangential flow filtration, in accordance with embodiments hereof.

CLAIMS

1. A cassette for use in an automated cell engineering system, comprising:

(a) a cell culture chamber;

(b) a pumping system fluidly connected to the cell culture chamber;

(c) a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller; and

(d) a cellular sample output fluidly connected to the tangential flow filter, wherein

(a)-(d) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector,

wherein the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter, and

wherein the cassette is configured to be contained within an enclosable housing of the automated cell engineering system.

2. The cassette of claim 1, wherein the tangential flow filter has a pore size of about 0.40 μm to about 0.80 μm and a fiber diameter of about 0.5 mm to about 0.9 mm.

3. The cassette of claim 2, wherein the tangential flow filter has a pore size of about 0.60 μm to about 0.70 μm and a fiber diameter of about 0.70 mm to about 0.80 mm.

4. The cassette of any one of claims 1-3, wherein the tangential flow filter comprises a polymer selected from the group consisting of poly(ether sulfone), poly(acrylonitrile) and poly(vinylidene difluoride).

5. A cassette for use in an automated cell engineering system, comprising:

(a) a cell culture chamber;

(b) a pumping system fluidly connected to the cell culture chamber;

(c) a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller, and the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter;

(d) a satellite volume connected to the tangential flow filter;

(e) a fluidics pathway for recirculating the retentate flow back through the tangential flow filter;

(f) a fixed volume waste collection chamber fluidly connected to the tangential flow filter; and

(g) a cellular sample output fluidly connected to the tangential flow filter,

wherein (a)-(g) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector.

6. The cassette of claim 5, wherein the tangential flow filter has a pore size of about 0.40 μm to about 0.80 μm and a fiber diameter of about 0.5 mm to about 0.9 mm.

7. The cassette of claim 6, wherein the tangential flow filter has a pore size of about 0.60 μm to about 0.70 μm and a fiber diameter of about 0.70 mm to about 0.80 mm.

8. The cassette of any one of claims 5-7, wherein the tangential flow filter comprises a polymer selected from the group consisting of poly(ether sulfone), poly(acrylonitrile) and poly(vinylidene difluoride).

9. An automated cell engineering system, comprising:

(a) an enclosable housing;

(b) a cassette contained within the enclosable housing, the cassette comprising:

i. a cell culture chamber;

ii. a pumping system fluidly connected to the cell culture chamber;

iii. a tangential flow filter fluidly connected to the pumping system, wherein the pumping system provides a retentate flow to the tangential flow filter and wherein a permeate flow of the tangential flow filter is controlled by a flow controller, and the tangential flow filter is at an angle of about 3º to about 20º relative to horizontal such that an exit end of the tangential flow filter is disposed vertically above an input end of the tangential flow filter; and

iv. a cellular sample output fluidly connected to the tangential flow filter,

v. wherein (i)-(iv) are self-contained and removable, and the cassette comprises a cell culture, a culture media, a cell wash media, an activation reagent, and/or a vector; and

(c) a user interface for receiving input from a user.

10. The automated cell engineering system of claim 9, wherein the tangential flow filter has a pore size of about 0.40 μm to about 0.80 μm and a fiber diameter of about 0.5 mm to about 0.9 mm.

11. The automated cell engineering system of claim 10, wherein the tangential flow filter has a pore size of about 0.60 μm to about 0.70 μm and a fiber diameter of about 0.70 mm to about 0.80 mm.

12. The automated cell engineering system of any one of claims 9-11, wherein the tangential flow filter comprises a polymer selected from the group consisting of poly(ether sulfone), poly(acrylonitrile) and poly(vinylidene difluoride).