CLAIMS

1. A method for purifying a polypeptide from a polypeptide preparation, comprising the following steps in order:

a) subjecting the polypeptide preparation to one or more purification processes and recovering a first resulting pool having a viscosity of about 5-40 cP; and

b) subjecting the pool recovered from step a) to a single pass tangential flow filtration (SPTFF) operation and recovering a second resulting pool having an operating viscosity of about 41-400 cP,

wherein,

i) the operating temperature is about 15-55°C, and

ii) the feed flux is about 5-50 $L/m^2/hr$ (LMH).

2. The method of claim 1, wherein in step a) the viscosity of the first recovered pool is 10-35 cP,

optionally wherein in step b) the STPFF operation comprises use of a serial membrane configuration, a parallel membrane configuration, or both a serial membrane configuration and a parallel membrane configuration,

optionally wherein in step b) the membrane configuration is any of 1:1:1, 1:1:1:1, 2:1:1, or 2:2:1:1,

optionally wherein in step b) the membrane configuration comprises at least one of 10 kD membranes and 30 kD membrane,

optionally wherein in step b) the membrane configuration comprises at least one of narrow channel membranes and wide channel membranes,

optionally wherein in step a) the polypeptide preparation is formulated in a viscosity-reducing excipient,

optionally wherein in step b) the operating temperature is about 15-50°C or about 30-50°C,

optionally wherein in step b) the feed flux is about 5-25 LMH or about 25-50 LMH,

optionally wherein the operating viscosity in step b) is about 200-400 cP or about 200-300cP,

optionally wherein in step b) the retentate pressure is about 5-20 psi.

3. The method of claim 1 or 2, wherein the one or more purification processes of step a) comprises an ultrafiltration,

optionally wherein the one or more purification processes of step a) comprises at least two ultrafiltration operations,

optionally wherein the one or more purification processes of step a) comprises a diafiltration.

4. The method of any one of claims 1-3, wherein step a) comprises

i) subjecting the polypeptide preparation to an ultrafiltration operation to a first target concentration,

ii) subjecting the polypeptide preparation to a diafiltration operation for buffer exchange, and

iii) subjecting the polypeptide preparation to a second ultrafiltration operation to a second target concentration and recovering the first resulting pool having a viscosity of 5-40cP,

optionally wherein the first target concentration is 5-80 g/L, optionally wherein the buffer exchange is a 6-12x exchange, optionally wherein the second target concentration is 100-150 g/L or 100-200 g/L.

5. The method of any one of claims 1-4, wherein the polypeptide preparation comprises the polypeptide and one or more impurities.

6. The method of any one of claims 1-5, wherein the one or more purification processes of step a) comprise at least one of: a harvest step, a sample conditioning step, a viral filtration step, a viral inactivation step, a chromatography polishing step, a chromatography capture step, a dilution step, a tangential flow depth filtration step, a depth filtration step, a diafiltration step, an ultrafiltration step, a guard filtration step, a precipitation step, and a flocculation step.

7. The method of any one of claims 1-6, further comprising: subjecting the second resulting pool to one or more subsequent purification processes, wherein the one or more subsequent purification processes comprise at least one of: a viral filtration step, a viral inactivation step, a chromatography polishing step, a chromatography capture step, a dilution step, a sample

conditioning step, a diafiltration step, a tangential flow depth filtration step, a depth filtration step, a sterile filtration step, and a guard filtration step.

8. A system for purifying a polypeptide from a polypeptide preparation, the system configured to perform the following steps in order:

a) subject the polypeptide preparation to one or more purification processes and recover a first resulting pool having a viscosity of about 5-40 cP; and

b) subject the pool recovered from step a) to a single pass tangential flow filtration (SPTFF) operation and recover a second resulting pool having an operating viscosity of about 41-400 cP,

wherein,

i) the operating temperature is about 15-55°C, and

ii) the feed flux is about 5-50 L/m^2/hr (LMH).

9. The system of claim 8, wherein in step a) the viscosity of the first recovered pool is 10-35 cP,

optionally wherein in step b) the STPFF operation comprises use of a serial membrane configuration,

optionally wherein in step b) the STPFF operation comprises use of a parallel membrane configuration,

optionally wherein in step b) the SPTFF operation comprises use of both a serial membrane configuration and a parallel membrane configuration,

optionally wherein in step b) the membrane configuration is any of 1:1:1, 1:1:1:1, 2:1:1, or 2:2:1:1,

optionally wherein in step b) the membrane configuration comprises at least one of 10 kD membranes and 30 kD membrane,

optionally wherein in step b) the membrane configuration comprises at least one of narrow channel membranes and wide channel membranes,

optionally wherein in step a) the polypeptide preparation is formulated in a viscosity-reducing excipient,

optionally wherein in step b) the operating temperature is about 15-50°C or about 30-50°C,

optionally wherein in step b) the feed flux is about 5-25 LMH or about 25-50 LMH,

optionally wherein the operating viscosity in step b) is about 200-400 cP or about 200-300cP,

optionally wherein in step b) the retentate pressure is about 5-20 psi.

10. The system of claim 8 or 9, wherein the one or more purification processes of step a) comprises an ultrafiltration, optionally wherein the one or more purification processes of step a) comprises at least two ultrafiltration operations, optionally wherein the one or more purification processes of step a) comprises a diafiltration.

11. The system of any one of claims 8-10, wherein in step a) the system is configured to:

i) subject the polypeptide preparation to an ultrafiltration operation to a first target concentration,

ii) subject the polypeptide preparation to a diafiltration operation for buffer exchange, and

iii) subject the polypeptide preparation to a second ultrafiltration operation to a second target concentration and recover the first resulting pool having a viscosity of 5-40cP,

optionally wherein the first target concentration is 5-80 g/L,

optionally wherein the buffer exchange is a 6-12x exchange,

optionally wherein the second target concentration is 100-150 g/L or 100-200 g/L.

12. The system of any one of claims 8-11, wherein the polypeptide preparation comprises the polypeptide and one or more impurities.

13. The system of any one of claims 8-12, wherein the one or more purification processes of step a) comprise at least one of: a harvest step, a sample conditioning step, a viral filtration step, a viral inactivation step, a chromatography polishing step, a chromatography capture step, a dilution step, a tangential flow depth filtration step, a depth filtration step, a diafiltration step, an ultrafiltration step, a guard filtration step, a precipitation step, and a flocculation step.

14. The system of any one of claims 8-13, wherein the system is further configured to: subject the second resulting pool to one or more subsequent purification processes, wherein the

one or more subsequent purification processes comprise at least one of: a viral filtration step, a viral inactivation step, a chromatography polishing step, a chromatography capture step, a dilution step, a sample conditioning step, a diafiltration step, a tangential flow depth filtration step, a depth filtration step, a sterile filtration step, and a guard filtration step.