[005] Therefore, there is a need for apparatuses for and methods of concentrating biomolecule-containing solutions, such as oligonucleotide-containing solutions, to a concentration > 100 mg/mL.

BRIEF SUMMARY

[006] To address this need, the disclosure first describes an apparatus for concentrating biomolecules in a solution such as oligonucleotides for high dose/low volume administration. The apparatus includes:

i. a first reservoir in fluid communication with a first side of a membrane, where the first reservoir is a retentate feed, and where the membrane has a molecular weight cutoff (MWCO) of < about 5 kDa;

ii. a second reservoir in fluid communication with a second opposing side of the membrane, where the second reservoir is a draw solution feed and a permeate collector;

iii. a first feed pump for cycling a retentate past the first side of the membrane;

iv. a second feed pump for cycling the draw solution or draw solution/permeate mixture past the second opposing side of the membrane;

v. a first balance with stir plate, where the first balance with stir plate is for stirring the retentate in the first reservoir and measuring the retentate;

vi. a second balance with stir plate, where the second balance with stir plate is for stirring the draw solution/permeate mixture in the second reservoir and measuring the draw solution/permeate mixture; and

vii. a transmembrane pressure (TMP) controller.

[006a] In a first aspect of the present disclosure, there is provided an apparatus for concentrating biomolecules in a solution, the apparatus comprising:

i. a first reservoir in fluid communication with a first side of a membrane, wherein the first reservoir is a retentate feed, and wherein the membrane has a molecular weight cutoff (MWCO) of < about 5 kDa;

ii. a second reservoir in fluid communication with a second opposing side of the membrane, wherein the second reservoir is a draw solution feed and a permeate collector;

iii. a first feed pump for cycling a retentate past the first side of the membrane;

iv. a second feed pump for cycling a draw solution or draw solution/permeate mixture past the second opposing side of the membrane;

v. a first balance with stir plate, wherein the first balance with stir plate is for stirring the retentate in the first reservoir and for measuring the retentate;

vi. a second balance with stir plate, wherein the second balance with stir plate is for stirring the draw solution or draw solution/permeate mixture in the second reservoir and for measuring the draw solution or draw solution/permeate mixture; and

vii. a transmembrane pressure (TMP) controller.

[007] In some instances, the MWCO is at least about 1 kDa. In other instances, the MWCO is at least about 2 kDa.

[008] In some instances, the membrane further includes a surface area of at least about 0.02 m^2 to about 0.1 m^2.

[009] In some instances, the membrane is a polyethersulfone (PES) membrane or a regenerated cellulose membrane.

[0010] In addition, the disclosure describes a method of concentrating an oligonucleotide-containing solution that includes at least steps of:

a. cycling a first solution past a first side of a membrane, where the first solution is a retentate having a starting oligonucleotide concentration of < about 95 mg/mL

and a pH between about 6 to about 7, and where the membrane has a MWCO of < about 5 kDa;

b. cycling a second solution past a second opposing side of the membrane, where the second solution is a permeate having a pH between about 6 to about 8 and an ionic strength greater that the first solution;

c. maintaining a TMP across the membrane between about 30 psi to about 45 psi; and

d. maintaining the cycling of the retentate and the permeate past the first and second opposing membrane sides, respectively, until the first solution has a final oligonucleotide concentration of at least about 100 mg/mL.

[0010a] In another aspect of the present disclosure, there is provided a method of concentrating oligonucleotides in a solution, the method comprising the steps of:

a. cycling a first solution past a first side of a membrane, wherein the first solution is a retentate having a starting oligonucleotide concentration of < about 95 mg/mL and a pH between about 6 to about 7, and wherein the membrane has a MWCO of < about 5 kDa;

b. cycling a second solution past a second opposing side of the membrane, wherein the second solution is a draw solution having a pH between about 6 to about 8 and an ionic strength greater than the first solution;

c. maintaining a transmembrane pressure (TMP) between about 30 psi to about 45 psi across the membrane; and

d. maintaining the cycling of the retentate and the permeate past the first and second opposing membrane sides, respectively, until the first solution has a final oligonucleotide concentration of at least about 100 mg/mL.

[0011] In some instances, the starting oligonucleotide concentration is at least about 20 mg/mL.

[0012] In some instances, the first solution is water.

[0013] In some instances, the MWCO is at least about 1 kDa. In other instances, the MWCO is at least about 2 kDa.

[0014] In some instances, the membrane further includes a surface area of at least about 0.02 m^2 to about 0.1 m^2.

[0015] In some instances, the membrane is a PES membrane or a regenerated cellulose membrane.

[0016] In some instances, the ionic strength of the second solution is between about 0.01 mol/L to about 2 mol/L.

[0017] In some instances, the second solution includes a NaCl concentration between about 0.01 M to about 2 M.

[0018] In some instances, the second solution comprises a $MgCl_2$ concentration between 0.03 M about to about 2.0 M.

[0019] In some instances, the second solution comprises a dextran sulfate concentration between 100 mg/mL about to about 200 mg/mL.

[0020] In some instances, the ionic strength of the second solution is increased during the cycling. In other instances, the ionic strength of the second solution is maintained during the cycling.

[0021] In some instances, the final oligonucleotide concentration is from about 150 mg/mL to about 200 mg/mL. In other instances, the final oligonucleotide concentration is