

CLAIMS

What is claimed is:

1. An apparatus for automated purification of a target biomolecule, such as a target nucleic acid or a target protein, from a biological sample, the apparatus comprising:
 - an input reservoir for receiving the biological sample;
 - a first bioprocessing assembly in fluid communication with the input reservoir and a lysis buffer reservoir, the first bioprocessing assembly configured to generate a lysate comprising target biomolecule, such as the target nucleic acid or the target protein;
 - a second bioprocessing assembly in fluid communication with the first bioprocessing assembly and a first elution buffer reservoir, the second bioprocessing assembly including a target-biomolecule-binding filter, such as a target-nucleic-acid-binding filter or a target-protein-binding filter, configured to retain the target biomolecule; and
 - a receptacle in fluid communication with the second bioprocessing assembly, the receptacle configured to receive an output container for receiving the target biomolecule, such as the target nucleic acid or the target protein, from the second bioprocessing assembly.
2. The apparatus of claim 1, wherein the apparatus comprises a consumable cartridge.
3. The apparatus of claim 1, wherein the biological sample is a bacterial culture, a cell culture, a prokaryotic cell culture, a eukaryotic cell culture, a clinical sample, an environmental sample, a food sample, or a beverage sample.
4. The apparatus of claim 1, further comprising an optical density detector window disposed between the input reservoir and the first bioprocessing assembly, the optical density detector window being configured to allow detection of an optical density of the biological sample.
5. The apparatus of claim 1, wherein the first bioprocessing assembly comprises a clarification filter.
6. The apparatus of claim 5, wherein the clarification filter is in fluid communication with the input reservoir and the lysis buffer reservoir, the clarification filter being configured to separate a target-nucleic-acid-containing portion of the biological sample from a first waste portion of the biological sample.

7. The apparatus of claim 5, wherein the first bioprocessing assembly comprises a cell capture filter, wherein the cell capture filter is disposed upstream of the clarification filter.
8. The apparatus of claim 7, wherein the cell capture or concentration filter is in fluid communication with the input reservoir and the lysis buffer reservoir, the cell capture or concentration filter being configured to separate a target-nucleic-acid-containing portion of the biological sample from a first waste portion of the biological sample.
9. The apparatus of claim 7, wherein the lysis buffer reservoir is fluidically coupled to the cell capture filter to enable backwashing of the cell capture filter and passage of backwash to the clarification filter.
10. The apparatus of claim 9, further comprising a first mixing chamber disposed between the clarification filter and the cell capture filter, the first mixing chamber configured to receive the backwash.
11. The apparatus of claim 10, further comprising a neutralization buffer reservoir in fluid communication with the first mixing chamber, the first mixing chamber being configured to receive the backwash and a neutralization buffer and to provide mixing of the backwash and the neutralization buffer to form a neutralized lysate.
12. The apparatus of claim 11, wherein the clarification filter is in fluid communication with the first mixing chamber, the clarification filter being configured to separate a second waste portion from the target-nucleic-acid-containing portion of the biological sample.
13. The apparatus of claim 9, wherein the clarification filter comprises the cell capture filter, the cell capture filter being configured to concentrate a cellular component of the biological sample at a first purification step and to clarify the neutralized lysate at a second, later purification step.
14. The apparatus of claim 1, wherein the target-biomolecule-binding filter of the second bioprocessing assembly comprises a silica-based filter or a column of beads having affinity for the target nucleic acid.

15. The apparatus of claim 14, wherein the second bioprocessing assembly further comprises a purification reagent reservoir in fluid communication with the target-biomolecule-binding filter, such as the nucleic-acid-binding filter.
16. The apparatus of claim 14, wherein the target-biomolecule-binding filter, such as the nucleic-acid-binding filter, is in fluid communication with the elution buffer reservoir and the output container.
17. The apparatus of claim 16, wherein the second bioprocessing assembly comprises a second mixing chamber disposed between the first bioprocessing assembly and the target-biomolecule-binding filter.
18. The apparatus of claim 17, wherein the second mixing chamber is in fluid communication with an endotoxin removal buffer reservoir.
19. The apparatus of claim 1, wherein the target-biomolecule-binding filter is the nucleic-acid binding filter comprising an anion exchange membrane.
20. The apparatus of claim 19, wherein the second bioprocessing assembly comprises a precipitator membrane disposed downstream of the anion exchange membrane.
21. The apparatus of claim 20, wherein the anion exchange membrane is configured to separate a third waste portion from the target-nucleic-acid-containing portion of the biological sample.
22. The apparatus of claim 20, further comprising a second elution buffer reservoir, the first elution buffer reservoir being fluidically coupled to the anion exchange membrane to enable elution of the target nucleic acid from the anion exchange membrane, and the second elution buffer reservoir being fluidically coupled to the precipitator membrane to enable elution of the target nucleic acid from the precipitator membrane.
23. The apparatus of claim 20, wherein the precipitator membrane is configured to separate a fourth waste portion from the target-nucleic-acid-containing portion of the biological sample.

24. The apparatus of claim 20, wherein the precipitator membrane is in fluid communication with a precipitation reagent reservoir, the precipitation reagent reservoir optionally comprising isopropanol.
25. The apparatus of claim 20, wherein the precipitator membrane is in fluid communication with a wash/desalting solution reservoir, the wash/desalting solution reservoir optionally comprising about 70% ethanol.
26. The apparatus of claim 20, wherein the second bioprocessing assembly comprises a third mixing chamber disposed between and in fluid communication with the anion exchange membrane and the precipitator membrane, wherein the third mixing chamber is fluidically coupled to the precipitation reagent reservoir and/or the desalting solution reservoir and is disposed between the precipitator membrane and the precipitation reagent reservoir and/or the desalting solution reservoir.
27. The apparatus of claim 1, wherein the output container is selectively detachable from the apparatus.
28. The apparatus of claim 1, wherein the input reservoir is sized and shaped to receive at least 5 mL, preferably at least 100 ml, or up to 2 L of biological sample.
29. An apparatus for automated purification of a target nucleic acid from a biological sample, comprising:
- a first bioprocessing assembly configured to receive the biological sample, the first bioprocessing assembly comprising a waste separation filter and a plurality of reservoirs fluidically coupled to the waste-separation filter;
 - a second bioprocessing assembly comprising an anion exchange membrane, a washing solution reservoir fluidically coupled to the anion exchange membrane and a first elution buffer reservoir fluidically coupled to the anion exchange membrane; and
 - a third bioprocessing assembly comprising a precipitation filter and a second elution buffer reservoir fluidically coupled to the precipitation filter.

30. The apparatus of claim 29, wherein the first bioprocessing assembly additionally comprises a cell capture filter, and wherein a first reservoir of the plurality of reservoirs comprises a resuspension buffer reservoir.

31. The apparatus of claim 30, wherein an input reservoir is fluidically coupled to a first side of the cell capture filter and the resuspension buffer reservoir is fluidically coupled to a second side of the cell capture filter.

32. An apparatus for automated purification of a target biomolecule, such as a target nucleic acid or target protein, from a biological sample, comprising:

a casing having an internal compartment configured in size and shape for receiving a purification cartridge;

optionally, a selectively closable access door providing access to the internal compartment; and

a pump assembly disposed within the interior chamber and configured to provide pumping action through peristaltic motion.

33. The apparatus of claim 32, further comprising a clamp mechanism disposed within the internal compartment and configured to move between an open position in which the internal compartment is accessible and a closed position in which the clamp mechanism is clamped against an inserted purification cartridge to enable processing of the biological sample, optionally wherein when in the closed position, the clamp mechanism operates to fluidically seal the biological sample cartridge.

34. The apparatus of claim 33, further comprising a controller, wherein the controller routes power to the clamping mechanism only upon determining that the access door is closed.

35. The apparatus of claim 33, further comprising a locking mechanism configured to lock the access door in a closed position when the clamp mechanism is moved to the closed position.

36. The apparatus of claim 33, wherein the clamp mechanism is powered by a motor, optionally wherein the motor is operatively coupled to a worm gear or drive screw which is rotatable to cause movement of the clamping mechanism.

37. The apparatus of claim 33, further comprising a manual release mechanism operatively coupled to the clamp mechanism to enable manual release of the clamp mechanism independent of the motor.

38. The apparatus of claim 33, wherein the casing comprises an open end to which the access door is attached, and a closed end opposite the open end, the open end and closed ends defining a longitudinal direction, wherein the clamp mechanism is configured to move in a direction transverse to the longitudinal direction.

39. The apparatus of claim 32, further comprising: an optical density sensor for measuring optical density of a biological sample received within the biological sample cartridge, an optical density sensor for measuring target biomolecule concentration, such as target nucleic acid concentration or target protein concentration, of a purified product, or both.

40. The apparatus of claim 32, further comprising a user interface for displaying instrument information and for receiving user input, the user interface configured to receive user input related to one or more of a volume of biological sample, a selected purification protocol, operating instructions for the selectively closable door, a desired concentration of target biomolecule, such as target nucleic acid or target protein, or a final volume of eluent comprising the target biomolecule.

41. The apparatus of claim 32, wherein the interior compartment comprises a position sensor for determining that a purification cartridge has been fully inserted within the interior compartment, the limit switch being positioned such that it is actuated upon contact with a leading edge of a purification cartridge when the purification cartridge is fully inserted within the interior compartment.

42. The apparatus of claim 32, further comprising one or more access door sensors configured to determine whether the access door is in an open or closed position, wherein the one or more access door sensors optionally comprise one or more Hall effect sensors and one or more corresponding magnets.

43. The apparatus of claim 32, further comprising an output container sensor configured to detect a presence of an output container at an inserted purification cartridge.

44. The apparatus of claim 32, further comprising one or more rotatable magnets disposed so as to direct an electromagnetic field inward to the interior compartment.

45. The apparatus of claim 32, wherein the pump assembly comprises a camshaft coupled to a motor via a power transmission assembly, a plurality of cam elements being attached to the camshaft and extending transversely therefrom toward the purification cartridge when inserted, the cam elements optionally including beveled tips for engaging the purification cartridge when inserted.

46. The apparatus of claim 45, wherein the cam elements are arranged such that rotation of the camshaft causes linear peristaltic motion of cam element tips.

47. A system comprising the apparatus of any one of claims 32–46 and a purification cartridge, wherein the purification cartridge includes the apparatus according to any one of claims 1–31.

48. A control system for controlling an automated purification apparatus as in any one of claims 32–46, comprising:

- one or more processors; and

- one or more hardware storage devices having stored thereon computer-executable instructions which are executable by the one or more processors to cause the control system to at least:

- receive sensor data from one or more sensors to determine one or more process states of the automated purification apparatus;

- compare the determined process states to a set of different protocols stored within a protocol library;

- select a purification protocol from the protocol library based on the determined process states; and

- carry out the selected purification protocol by causing one or more instrument actuators of the automated purification apparatus to operate according to the selected purification protocol.

49. The control system of claim 48, wherein the one or more sensors include an optical density sensor, an access door sensor, a cartridge proximity or contact sensor, an output container proximity or contact sensor, a cartridge scanner, a timer, a temperature sensor, a weight sensor, a volumetric sensor, or combinations thereof.

50. The control system of claim 48, wherein the determined process states includes at least a determined optical density of an initial input sample, and optionally wherein the selected purification protocol provides a cell capture duration that is based on the determined optical density of the initial input sample.

51. The control system of claim 48, wherein the selected purification protocol defines: whether cell capture and/or cell lysis is utilized, the duration of cell capture and/or cell lysis, which reagents to utilize, volumes of reagents to utilize, whether and/or when to perform mixing at one or more purification steps, duration and/or speed of one or more mixing steps, duration and/or speed of pumping between one or more purification steps, whether and/or when to open and close one or more valves within the cartridge, whether and/or when to puncture one or more seals within the cartridge to allow corresponding release of fluid or venting of gas, a type of target biomolecule capture involved, a duration of the target biomolecule capture, or a combination thereof.

52. A fluid release system for holding and selectively releasing a fluid, comprising:
a flexible gasket;
a reservoir disposed on a first side of the flexible gasket, the reservoir being configured to hold the fluid;
a frangible seal disposed between the flexible gasket and the fluid reservoir; and
an actuator disposed on a second side of the flexible gasket, wherein the actuator is operable to deflect the flexible gasket to cause the frangible seal to breach and selectively release the fluid from the reservoir.

53. The system as in claim 52, wherein the flexible gasket is an elastomer.

54. The system as in claim 52, wherein the flexible gasket is part of an intermediate layer disposed between two external layers, the reservoir optionally being at least partially defined by the flexible gasket and one of the two external layers.

55. The system as in claim 52, wherein the frangible seal comprises a chemically inert material, the frangible seal also optionally comprising a reinforcing layer, wherein the chemically inert material is associated with or fused to a face of the reinforcing layer such that the chemically inert material is disposed towards and/or forms a sidewall defining the reservoir.

56. The system as in claim 52, wherein the frangible seal comprises a pierceable material configured to catastrophically fail in response to application of a mechanical force exerted by the actuator.

57. The system as in claim 52, wherein the fluid comprises a nucleic acid purification reagent, protein purification reagent, input sample, resuspension buffer, RNase A, DNase, proteinase K, lysis buffer, neutralization buffer, chaotropic salt buffer, non-chaotropic salt buffers, binding buffer, endotoxin removal buffer, wash buffer, elution buffer, isopropanol, ethanol, water, or TE buffer.

58. The system as in claim 52, further comprising a fluid channel in fluid communication with the reservoir, the fluid channel being configured to receive the fluid upon release of the fluid from the reservoir.

59. The system as in claim 52, further comprising a flexible air vent, a frangible air seal disposed on a first side of the flexible air vent, and a venting actuator disposed on a second side of the flexible air vent, optionally wherein the venting actuator is operable to selectively deflect the flexible air vent toward the frangible air seal and thereby breach the frangible air seal to vent air into the reservoir.

60. An automated system for selectively releasing a fluid, comprising:
the fluid release system as in any one of claims 52–59; and
a biological sample cartridge for use with the automated target biomolecule purification system, the biological sample cartridge comprising the apparatus as in any one of claims 1–31, the automated system also optionally comprising the automated purification apparatus or system as in any one of claims 32–46.

61. An apparatus for controlled movement of fluids, comprising:

a first external layer comprising a first side and a second side, the first side comprising a series of channels;

a second external layer disposed opposite the first side of the first external layer; and

an elastomer layer disposed between the first and second external layers, the elastomer layer comprising an arrangement of sealing ribs that corresponds to the series of channels and is configured to fluidically separate the channels when the elastomer layer is compressed between the first and second external layers.

62. The apparatus of claim 61, wherein a first channel of the series of channels comprises a reservoir, and optionally wherein one or more of the first external layer or the second external layer is a thermoform polymer.

63. The apparatus of claim 61, further comprising a nominal gap between the elastomer layer and one or both of the first external layer or the second external layer such that when the elastomer layer is compressed between the first and second external layers, a compressed portion of the sealing ribs is displaced within the nominal gap.

64. The apparatus of claim 61, further comprising a valve associated with the series of channels, the valve being selectively moveable between a closed position and an open position to respectively restrict or allow fluid flow across the valve.

65. The apparatus of claim 61, wherein the valve comprises an aperture in the second external layer.

66. The apparatus of claim 65, wherein the aperture provides access to a deflectable portion of the elastomer layer, the deflectable portion comprising a valve sealing rib extending from the elastomer layer toward the first external layer.

67. The apparatus of claim 66, wherein the valve sealing rib contacts the first external layer when the valve is in the closed position and is separated from the first external layer when the valve is in the open position.

68. The apparatus of claim 66, further comprising a plunger in contact with the deflectable portion of the valve, the plunger being configured in size and shape to be passable into the aperture to deflect the deflectable portion and move the valve toward the closed position.

69. The apparatus of claim 66, wherein the valve further comprises a berm formed in the first external layer and extending toward the aperture, optionally wherein the berm contacts the valve sealing rib when the valve is in the closed position.

70. The apparatus of claim 66, wherein the deflectable portion extends out of and beyond the aperture when the valve is fully moved to the open position.

71. The apparatus of claim 61, wherein the second external layer comprises a second series of channels disposed on a first side of the second external layer, the first side of the second external layer facing the first side of the first external layer.

72. The apparatus of claim 71, wherein the arrangement of sealing ribs comprises a first set of sealing ribs that extend toward the first external layer and a second set of sealing ribs that extend toward the second external layer.

73. The apparatus of claim 61, wherein the arrangement of sealing ribs is disposed so as to follow a contour of the series of channels.

74. The apparatus of claim 73, wherein each channel comprises a nadir and forms a surface that rises from the nadir to inflection points disposed on opposite sides of the nadir, and optionally wherein the sealing ribs include an apex, the sealing ribs being arranged such that the apex is disposed at the inflection points of the channels or beyond the inflection points relative to the respective channel nadir.

75. A biological sample cartridge comprising at least two of: the apparatus of any one of claims 1–31; the apparatus of any one of claims 32–46; the fluid release system of any one of claims 52–59; and the apparatus of any one of claims 62–74.

76. An apparatus for automated purification of a target protein from a biological sample, comprising:

an input reservoir for receiving the biological sample;

a first bioprocessing assembly in fluid communication with the input reservoir and a lysis buffer reservoir, the first bioprocessing assembly configured to generate a lysate comprising a target protein;

a second bioprocessing assembly in fluid communication with the first bioprocessing assembly and a first elution buffer reservoir, the second bioprocessing assembly including a protein-binding support configured to retain the target protein; and

a receptacle in fluid communication with the second bioprocessing assembly, the receptacle configured to receive an output container for receiving the target protein.

77. The apparatus of claim 76, wherein the apparatus comprises a consumable cartridge.

78. The apparatus of claim 76, wherein the first bioprocessing assembly comprises a clarification filter.

79. The apparatus of claim 78, wherein the clarification filter is in fluid communication with the input reservoir and the lysis buffer reservoir, the clarification filter being configured to separate a target-protein-containing portion of the biological sample from a first waste portion of the biological sample.

80. The apparatus of claim 76, wherein the first bioprocessing assembly comprises a cell capture or concentration filter, optionally wherein the cell capture or concentration filter is disposed upstream of a clarification filter.

81. The apparatus of claim 80, wherein the cell capture or concentration filter is in fluid communication with the input reservoir and the lysis buffer reservoir, the cell capture or concentration filter being configured to separate a target-protein-containing portion of the biological sample from a first waste portion of the biological sample.

82. The apparatus of claim 76, further comprising one or more additional bioprocessing chambers having reagents for protein purification.

83. The apparatus of claim 76, further comprising one or more filters within the apparatus, wherein the one or more filters comprises a hollow fiber filter.

84. A biological sample cartridge comprising at least two of: the apparatus of any one of claims 76–83; the apparatus of any one of claims 32–46; the fluid release system of any one of claims 52–59; and the apparatus of any one of claims 62–74.