

CLAIMS

1. A perfusion manifold assembly, comprising (i) one or more fluid reservoirs, (ii) a fluidic backplane positioned under, and in fluidic communication with, the fluid reservoirs, the fluidic backplane comprising a fluid resistor and fluid channels that terminate at ports.
- 5 2. An assembly according to Claim 1, further comprising (iii) a skirt, the skirt comprising a guide mechanism.
3. An assembly according to Claim 2, in which the guide mechanism comprises one or more side tracks.
4. An assembly according to Claim 3, in which the one or more side tracks are configured
10 for engaging a microfluidic device positioned in a microfluidic device carrier having one or more outer edges configured to slideably engage the one or more side tracks.
5. An assembly according to Claim 4, in which the resistor comprises serpentine channels.
6. An assembly according to Claim 5, in which the fluidic backplane comprises linear fluid channels in fluidic communication with the serpentine channels, the linear channels
15 terminating at one or more ports.
7. An assembly according to Claim 1, further comprising a cover for the fluid reservoirs, in which the cover comprises a plurality of through-hole ports associated with filters, the filters positioned above corresponding holes in a gasket.
8. An assembly according to Claim 4, in which the side track comprises a closed first end
20 proximal to the reservoirs and an opened second end distal to the reservoirs, the opened end comprising an angled slide for engaging the one or more outer edges of the microfluidic device carrier.
9. An assembly according to Claim 8, in which the side track comprises a linear region between the closed first end and the opened second end.
- 25 10. A system, comprising:
 - (a) a perfusion manifold assembly, comprising (i) one or more fluid reservoirs, (ii) a fluidic backplane positioned under, and in fluidic communication with, the fluid

reservoirs, the fluidic backplane comprising fluid channels that terminate at fluid outlet ports, and (iii) a skirt having a guide mechanism; and

(b) a microfluidic device positioned in a carrier, the carrier detachably engaging the guide mechanism of the skirt, the microfluidic device comprising (i) microchannels in fluidic communication with the perfusion manifold assembly via (ii) one or more inlet ports on a (iii) mating surface, in which the one or more fluid inlet ports of the microfluidic device are positioned against the one or more fluid outlet ports of the skirt of the perfusion manifold assembly under conditions such that fluid flows from the fluid reservoirs of the perfusion manifold assembly through the one or more fluid outlet ports into the one or more fluid inlet ports of the microfluidic device.

11. A system according to Claim 10, in which the microfluidic device comprises living cells perfused with fluid from the fluid reservoirs.

12. A system according to Claim 10, in which the microfluidic device comprises at least two different cell types that function together in a manner that mimic one or more functions of cells in an organ in the body.

13. A system according to Claim 12, in which the microfluidic device comprises a membrane having top and bottom surfaces, the top surface comprising a first cell type, the bottom surface comprises a second cell type.

14. A system according to Claim 13, in which the first cell type is epithelial cells and the second cell type is endothelial cells.

15. A system according to Claim 13, in which the membrane is porous.

16. A system according to Claim 10, in which the fluidic backplane comprises a fluid resistor.

17. A system according to Claim 10, in which the guide mechanism comprises one or more side tracks.

18. A system according to Claim 17, in which the carrier comprises one or more outer edges, the outer edges detachably engaging the one or more side tracks of the skirt.

19. A system according to Claim 10, in which the carrier further comprises a locking mechanism for restricting movement of the carrier when the one or more fluid inlet ports of

the microfluidic device are positioned against the one or more fluid outlet ports of the perfusion manifold assembly.

20. A method of perfusing cells, comprising:

(A) providing (a) a perfusion manifold assembly comprising (i) one or more fluid reservoirs, (ii) a fluidic backplane positioned under, and in fluidic communication with, the fluid reservoirs, the fluidic backplane comprising fluid channels that terminate at fluid outlet ports, and (iii) a skirt having a guide mechanism; and (b) a microfluidic device positioned in a carrier, the carrier configured for detachably engaging the guide mechanism of the skirt, the microfluidic device comprising (i) living cells, and (ii) microchannels in fluidic communication with (ii) one or more inlet ports on a (iii) mating surface;

(B) positioning the carrier such that it engages the guide mechanism of the skirt; and

(C) moving the carrier until the one or more fluid inlet ports of the microfluidic device are positioned against the one or more fluid outlet ports of the perfusion manifold assembly under conditions such that the microfluidic device is linked and fluid flows from the fluid reservoirs of the perfusion manifold assembly through the one or more fluid outlet ports into the one or more fluid inlet ports and into the microchannels of the microfluidic device, thereby perfusing the cells.

21. A method according to Claim 20, in which the one or more inlet ports on the mating surface of the microfluidic device comprise droplets protruding above the mating surface and one or more outlet ports comprise protruding droplets, such that the moving of step (C) causes a droplet-to-droplet connection when one or more fluid inlet ports of the microfluidic device are positioned against the one or more fluid outlet ports of the perfusion manifold assembly.

22. A method according to Claim 21, in which the droplet-to-droplet connection does not permit air to enter the one or more fluid inlet ports.

23. A method according to Claim 21, in which the mating surface proximate to the droplets is hydrophobic.

24. A method according to Claim 20, further comprising the step of (D) activating a locking mechanism for restricting movement of the carrier.

25. A method according to Claim 20, in which the fluidic backplane comprises a fluid resistor.
26. A method according to Claim 20, in which the guide mechanism comprises one or more side tracks.
- 5 27. A method according to Claim 26, in which the carrier comprises one or more outer edges, the outer edges configured for detachably engaging the one or more side tracks of the skirt.
28. A method according to Claim 27, in which the moving of step (C) comprises sliding the carrier along the side tracks until the inlet and outlet ports are positioned against each other.
- 10 29. A method according to Claim 20, further comprising the step of placing the perfusion manifold assembly with the linked microfluidic device in an incubator.
30. A method according to Claim 20, further comprising the step of placing the perfusion manifold assembly with the linked microfluidic device in or on a culture module.
31. A method according to Claim 20, in which the fluid reservoirs of the perfusion manifold
15 assembly are covered with a cover assembly comprising a cover having a plurality of ports.
32. A method according to Claim 31, in which the ports are through-hole ports associated with filters and corresponding holes in a gasket, and the culture module comprises a mating surface with pressure points that correspond to the through-hole ports on the cover, such that the step of placing of the perfusion manifold assembly with the linked microfluidic device in
20 or on the culture module results in contact of the through-holes with the pressure points.
33. A method according to Claim 31, in which the ports are through-hole ports associated with filters and corresponding holes in a gasket, and the culture module comprises a mating surface with pressure points that correspond to the through-hole ports on the cover, such that after the step of placing of the perfusion manifold assembly with the linked microfluidic
25 device in or on the culture module, the pressure points of the mating surface of the culture module are brought into contact with the through-holes of the cover assembly.
34. A method according to Claim 30, in which the culture module comprises pressure controllers.

35. A method according to Claim 34, in which the pressure controllers apply pressure to the fluid reservoirs via the pressure points corresponding to the through-hole ports on the cover.
36. A method according to Claim 30, in which the culture module comprises a plurality of perfusion manifold assemblies.
- 5 37. A method according to Claim 30, in which the culture module comprises integrated valves.
38. A method according to Claim 37, in which the valves comprise Schrader valves.
39. A system, comprising (a) device comprising an actuation assembly configured to move a pressure manifold, the pressure manifold comprising integrated valves, the pressure
10 manifold in contact with (b) a plurality of microfluidic devices.
40. A system according to Claim 39, in which the microfluidic devices are perfusion disposables.
41. A system according to Claim 39, in which the valves comprise Schrader valves.
42. A system according to Claim 39, in which each of the microfluidic devices is covered
15 with a cover assembly comprising a cover having a plurality of ports, and the pressure manifold comprising a mating surface with pressure points that correspond to the ports on the cover, in which the pressure points of the mating surface of the pressure manifold are in contact with the ports of the cover assembly.
43. A system according to Claim 42, in which the ports comprise through-hole ports
20 associated with filters and corresponding holes in a gasket.
44. A system according to Claim 39, in which the device further comprises pressure controllers.
45. A system according to Claim 44, in which the pressure controllers are configured to apply pressure via the pressure points.
- 25 46. A system according to Claim 39, in which the actuation assembly comprises a pneumatic cylinder operably linked to the pressure manifold.

47. A system according to Claim 42, in which the mating surface further comprises alignment features configured to align a microfluidic device when the microfluidic device engages the mating surface.
48. A system according to Claim 39, in which the device further comprises elastomeric membranes and the elastomeric membranes are in contact with the microfluidic devices.
49. A system according to Claim 39, in which the device is a culture module for perfusing cells.
50. A system according to Claim 49, in which the culture module is configured to accept one or more trays, each tray comprising a plurality of microfluidic devices.
51. A system according to Claim 49, in which the culture module further comprising a user interface to control the culture module.
52. A method of perfusing cells, comprising:
- (A) providing (a) a culture module, the culture module comprising (i) an actuation assembly configured to move (ii) a pressure manifold, the pressure manifold comprising a mating surface with pressure points; and (b) a plurality of microfluidic devices, each of the microfluidic devices comprising (i) one or more microchannels comprising living cells, (ii) one or more reservoirs comprising culture media, and (iii) a cover assembly above the one or more reservoirs, the cover assembly comprising a cover with ports that correspond to the pressure points on the pressure manifold mating surface;
- (B) placing the plurality of microfluidic devices on or in the culture module; and
- (C) simultaneously contacting the ports on the cover of each microfluidic device of the plurality of microfluidic devices with the mating surface of the pressure manifold, such that the ports are in contact with the pressure points, under conditions such that culture media flows from the reservoirs into the microchannels of the microfluidic devices, thereby perfusing the cells.
53. A method according to Claim 52, in which the plurality of microfluidic devices are positioned on one or more trays prior to step (B) and the placing of step (B) comprising moving at least a subset of the plurality of microfluidic devices simultaneously into the culture module.

54. A method according to Claim 52, in which the simultaneous contacting of step (C) is achieved by moving, via the actuation assembly, the mating surface of the pressure manifold down onto the cover assemblies of the plurality of microfluidic devices.

55. A method of controlling pressure while perfusing cells, comprising:

- 5 (A) providing (a) a culture module, the culture module comprising (i) an actuation assembly configured to move (ii) a pressure manifold, the pressure manifold comprising a mating surface with pressure points, and (iii) one or more pressure controllers to provide pressure to the pressure points; and (b) a plurality of microfluidic devices, each of the microfluidic devices comprising (i) one or more microchannels comprising living
10 cells, (ii) one or more reservoirs comprising culture media, and (iii) a cover assembly above the one or more reservoirs, the cover assembly comprising a cover with ports that correspond to the pressure points on the pressure manifold mating surface;
- (B) placing the plurality of microfluidic devices on or in the culture module;
- (C) simultaneously contacting the ports on the cover of each microfluidic device of the
15 plurality of microfluidic devices with the mating surface of the pressure manifold, such that the ports are in contact with the pressure points, under conditions such that culture media flows from the reservoirs into the microchannels of the microfluidic devices, thereby perfusing the cells; and
- (D) turning the one or more pressure controllers off and on, thereby controlling pressure
20 while perfusing the cells.

56. A method according to Claim 55, in which the pressure controllers are turned off and on in a switching pattern.

57. A method according to Claim 56, in which the switching pattern is selected such that the average value of pressure acting liquid in the one or more reservoirs corresponds to a desired
25 value.

58. A method according to Claim 56, in which the switching pattern is selected such that the average gas pressure is maintained below 1 kPa.

59. A system comprising: (a) instrument for interfacing with (b) a microfluidic device, the microfluidic device comprising (i) one or more fluid reservoirs and (ii) a pressure lid
30 comprising one or more instrument-interface ports and one or more reservoir-interface ports,

in which the pressure lid is adapted to convey pressure between at least one of the instrument-facing ports and at least one of the reservoir-facing ports.

60. A system according to Claim 59, in which the instrument comprises a pressure manifold.

5 61. A system according to Claim 59, in which one or more fluid reservoirs are disposed in a cartridge, the cartridge in fluidic communication with the microfluidic device.

62. A system according to Claim 59, in which one or more fluidic reservoirs are disposed in the microfluidic device.