SCALABLE BIOREACTOR SYSTEMS AND METHODS FOR TISSUE ENGINEERING

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/879,773, filed July 29th, 2019, and U.S. Provisional Application No. 62/991,958, filed March 24th, 2020, both of which are incorporated herein by reference.

BACKGROUND

[0002] Current tissue engineering bioreactors were neither intended for nor directly applicable in large scale commercial manufacturing. A scalable bioreactor system as described herein can address the need for large scale commercial manufacturing.

SUMMARY OF THE DISCLOSURE

[0003] Disclosed herein are devices. In a first aspect, the present disclosure provides a tissue culturing device comprising a plurality of trays substantially within a device, wherein each tray can be configured to hold at least one cell culturing container, wherein trays can be stacked within a device, and wherein a device can be configured to repeatedly tilt such that an angle between a bottom of a stack and a base of a device can repeatedly cycle between about 0 and about 360 degrees. In some embodiments, at least one tray can comprise at least one cell culture container that contains a liquid medium and cells. In some embodiments, at least one tray can be approximately rectangular on a side. In some embodiments, a device can comprise a pivot and a lifting mechanism configured to tilt stacked trays by angular raising and lowering. In some embodiments, an angular raising and lowering can create a wave in a wave in a cell culture medium within said cell culturing container. In some embodiments, a lifting mechanism can comprise a hydraulic mechanism, an electric mechanism, a spring mechanism, a piston, or a combination thereof. In some embodiments, a device can be jacketed. In some embodiments, a device can be temperature controlled. In some embodiments, a base of a device can comprise a pallet. In some embodiments, a device can be stacked on a pallet rack. In some embodiments, a pallet can be detachable. In some embodiments, a pallet can be non-detachable. In some embodiments, a pallet can comprise a plastic, a metal, or a combination thereof. In some embodiments, a pallet can comprise flats, grids, has an elevated foundation such that air can move underneath, or any combination thereof. In some embodiments, a base of a device can comprise means for moving said device using a forklift truck. In some embodiments, a length of a cell culturing container ranges from about 1 cm to about 1000 cm. In some embodiments, a width of a cell culturing container ranges from about 1 cm to about 1000 cm.

In some embodiments, a height of a cell culturing container ranges from about 1 cm to about 1000 cm. In some embodiments, a wall thickness of a cell culturing container ranges from about 0.01 cm to about 10 cm. In some embodiments, at least one tray can comprise a handle. In some embodiments, at least one tray can slide in and out of a device. In some embodiments, a device can comprise a monitoring system. In some embodiments, a monitoring system can alert a user that an action must be taken. In some embodiments, a monitoring system comprises, a sensor, a camera, or a combination thereof. In some embodiments, a sensor can comprise a thermistor, a thermometer, a pH sensor, a humidity sensor, a pressure sensor, a smoke detector, or any combination thereof. In some embodiments, a device can be jacketed. In a second aspect, the present disclosure provides a system comprising the device according to the first aspect and a cell culture medium reservoir. In some embodiments, a cell culture medium reservoir can comprise a monitoring system. In some embodiments, a monitoring system can alert a user that an action must be taken. In some embodiments, a monitoring system comprises, a sensor, a camera, or a combination thereof. In some embodiments, a sensor can comprise a thermistor, a thermometer, a pH sensor, a humidity sensor, a pressure sensor, a smoke detector, or any combination thereof. In some embodiments, a cell culture medium reservoir can be jacketed. In some embodiments, a cell culture medium reservoir can be temperature controlled. In some embodiments, a cell culture medium reservoir can be maintained at a lower temperature than a device. In some embodiments, a cell culture medium can be warmed before entering a device. In some embodiments, a gas can be bubbled into a cell culture medium. In some embodiments, a gas can comprise carbon dioxide, nitrogen, oxygen, or a combination thereof. In some embodiments, a cell culture medium reservoir can be connected to an inlet in a device. In some embodiments, an inlet can comprise an inlet manifold. In some embodiments, a device can comprise an outlet for waste cell culture medium. In some embodiments, an outlet can comprise an outlet manifold. In some embodiments, a system can comprise racks. In some embodiments, racks can be stackable vertically. In some embodiments, racks can be from about 1m high to about 200m high. In some embodiments, racks can be arranged from approximately floor to ceiling in a warehouse. In some embodiments, a system can comprise a pallet retrieval system. In some embodiments, a system can be configured to fit on a North American 40” x 48” pallet. In some embodiments, a system can be configured to fit on a conveyer system. In some embodiments, at least one container can comprise a tube operatively connected thereto. In some embodiments, a system can further comprise a temperature control system. A temperature control system can be configured to heat or cool at least a portion of a system to a temperature of from about -200 degrees Celsius to about 200 degrees Celsius. In some embodiments, a system can further comprise an intermediate bulk container heating jacket operatively coupled to a temperature control system. An intermediate bulk container heating jacket can be configured to heat a portion of a system. In some embodiments, a system can further comprise an intermediate bulk container cooling jacket

CLAIMS

WHAT IS CLAIMED IS:

1. A tissue culturing device comprising a plurality of trays substantially within the device, wherein each tray is configured to hold at least one cell culturing container, wherein the trays are stacked within the device, and wherein the device is configured to repeatedly tilt such that the angle between the bottom of the stack and the base of the device can repeatedly cycle between about 0 and about 360 degrees.
2. The device of claim 1, wherein the plurality of trays comprises at least one cell culture container that contains a liquid medium and cells.
3. The device of claim 1, wherein the plurality of trays is approximately rectangular on a side.
4. The device of claim 1, wherein the device comprises a pivot and a lifting mechanism configured to tilt the stacked trays by angular raising and lowering.
5. The device of claim 4, wherein the angular raising and lowering creates a wave in a wave in a cell culture medium within said cell culturing container.
6. The device of claim 1, wherein the lifting mechanism comprises a hydraulic mechanism, an electric mechanism, a spring mechanism, a piston, or a combination thereof.
7. The device of claim 1, wherein the device is jacketed.
8. The device of claim 1, wherein the device is temperature controlled.
9. The device of claim 1, wherein the base of the device can comprise a pallet.
10. The device of claim 9, wherein the device can be stacked on a pallet rack.
11. The device of claim 9, wherein the pallet is detachable.
12. The device of claim 9, wherein the pallet is not detachable.
13. The device of claim 9, wherein the pallet comprises a plastic, a metal, or a combination thereof.
14. The device of claim 9, wherein the pallet comprises flats, grids, has an elevated foundation such that air can move underneath, or any combination thereof.
15. The device of claim 1, wherein the base of the device can comprise means for moving said device using a forklift truck.
16. The device of claim 1, wherein a length of the trays is from about 1 cm to about 1000 cm.
17. The device of claim 1, wherein a width of the trays is from about 1 cm to about 1000 cm.
18. The device of claim 1, wherein a height of the trays is from about 1 cm to about 1000 cm.
19. The device of claim 1, wherein a wall thickness of the trays is from about 0.01 cm to about 10 cm.
20. The device of claim 1, wherein a length of the cell culturing container ranges from about 1 cm to about 1000 cm.

21. The device of claim 1, wherein a width of the cell culturing container ranges from about 1 cm to about 1000 cm.

22. The device of claim 1, wherein a height of the cell culturing container ranges from about 1 cm to about 1000 cm.

23. The device of claim 1, wherein a wall thickness of the cell culturing container ranges from about 0.01 cm to about 10 cm.

24. The device of claim 1, wherein at least one of the trays comprises a handle.

25. The device of claim 1, wherein at least one of the trays can slide in and out of the device.

26. The device of claim 1, comprising a monitoring system.

27. The device of claim 26, wherein the monitoring system can alert a user that an action must be taken.

28. The device of claim 26, wherein the monitoring system comprises, a sensor, a camera, or a combination thereof.

29. The device of claim 26, wherein the sensor comprises a thermistor, a thermometer, a pH sensor, a humidity sensor, a pressure sensor, a smoke detector, or any combination thereof.

30. The device of claim 1, wherein the device is jacketed.

31. A system comprising the device of claim 1 and a cell culture medium reservoir.

32. The system of claim 31, wherein the cell culture medium reservoir comprises a monitoring system.

33. The system of claim 32, wherein the monitoring system can alert a user that an action must be taken.

34. The system of claim 32, wherein the monitoring system comprises, a sensor, a camera, or a combination thereof.

35. The system of claim 34, wherein the sensor comprises a thermistor, a thermometer, a pH sensor, a humidity sensor, a pressure sensor, a gas sensor, a CO_2 sensor, an O_2 a smoke detector, or any combination thereof.

36. The system of claim 31, wherein the cell culture medium reservoir is jacketed.

37. The system of claim 31, wherein the cell culture medium reservoir is temperature controlled.

38. The system of claim 31, wherein the cell culture medium reservoir is maintained at a lower temperature than the device.

39. The system of claim 38, wherein the cell culture medium is warmed before entering the device.

40. The system of claim 31, wherein a gas is bubbled into the cell culture medium.

41. The system of claim 40, wherein the gas comprises carbon dioxide, nitrogen, oxygen, or a combination thereof.

42. The system of claim 31, wherein the cell culture medium reservoir is connected to an inlet in the device.

43. The system of claim 42, wherein the inlet comprises an inlet manifold.

44. The system of claim 31, wherein the device comprises an outlet for waste cell culture medium.

45. The system of claim 44, wherein the outlet comprises an outlet manifold.

46. The system of claim 31, wherein the system comprises racks.

47. The system of claim 46, wherein the racks are stackable vertically.

48. The system of claim 47, wherein the racks are from about 1m high to about 200m high.

49. The system of claim 48, wherein the racks can be arranged from approximately floor to ceiling in a warehouse.

50. The system of claim 31, wherein the system comprises a pallet retrieval system.