

chamber gas inlet conduit at a rate of equal to or less than about 1 milliliter per second; ~~and a humidifier configured to humidify the gas transported through the reactor chamber gas inlet conduit, the humidifier positioned between the flow control mechanism and the reactor chamber gas inlet; a reactor chamber gas outlet conduit~~
5 ~~configured to transport gas out of the reactor chamber through a reactor chamber gas outlet; and a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.~~

In another aspect, the present invention refers to a reactor system comprising a reactor chamber; ~~a reactor chamber gas inlet conduit configured to transport gas into the reactor chamber through a reactor chamber gas inlet; a reactor chamber gas outlet~~
10 ~~conduit configured to transport gas out of the reactor chamber through a reactor chamber gas outlet; a flow control mechanism configured to regulate the flow of gas through the reactor chamber gas outlet conduit at a rate of equal to or less than about 1 milliliter per second; and a liquid trap configured to remove liquid vapor from the gas within the~~
15 ~~reactor chamber gas outlet conduit, the liquid trap positioned between the flow control mechanism and the reactor chamber gas outlet; and a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.~~

The reactor system comprises, in certain examples, a reactor chamber, comprising a liquid sub-chamber configured to contain a liquid growth medium
20 including at least one biological cell; a gas sub-chamber configured to contain a gaseous headspace above the liquid growth medium; and a gas-permeable flexible membrane separating the liquid sub-chamber from the gas sub-chamber. In certain examples, the reactor system comprises a gas inlet conduit configured to transport gas into the gas sub-chamber; a gas outlet conduit configured to transport gas out of the gas sub-chamber;
25 and a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.

~~In yet another aspect, the present invention refers to a reactor system, comprising: a reactor chamber, comprising: a liquid sub-chamber configured to contain a liquid growth medium including at least one biological cell; a gas sub-chamber configured to~~
30 ~~contain a gaseous headspace above the liquid growth medium; and a gas-permeable flexible membrane separating the liquid sub-chamber from the gas sub-chamber; a gas inlet conduit configured to transport gas into the gas sub-chamber; a gas outlet conduit configured to transport gas out of the gas sub-chamber; and a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.~~

35 In a further aspect, the present invention refers to a method of operating a reactor, comprising:
~~providing a reactor chamber, comprising: a liquid sub-chamber configured to contain a liquid growth medium including at least one biological cell; a gas sub-chamber~~

configured to contain a gaseous headspace above the liquid growth medium; and a flexible membrane separating the liquid sub-chamber from the gas sub-chamber; transporting a gas from a gas source through a gas inlet conduit to the gas sub-chamber to deform the gas-permeable flexible membrane such that liquid is at least partially removed from the liquid sub-chamber; reducing the supply of the gas to the gas sub-chamber such that the flexible membrane returns toward its original position; transporting gas from the gas source through a gas bypass connected to the gas inlet conduit and external to the reactor chamber to remove liquid from the gas inlet conduit; and supplying gas from the gas source to the gas sub-chamber at least a second time to deform the gas-permeable flexible membrane such that liquid is at least partially evacuated from the liquid sub-chamber.

Certain examples relate to methods of operating a reactor. In certain examples, the method comprises providing a reactor chamber, comprising a liquid sub-chamber configured to contain a liquid growth medium including at least one biological cell; a gas sub-chamber configured to contain a gaseous headspace above the liquid growth medium; and a flexible membrane separating the liquid sub-chamber from the gas sub-chamber. In some examples, the method comprises transporting a gas from a gas source through a gas inlet conduit to the gas sub-chamber to deform the gas-permeable flexible membrane such that liquid is at least partially removed from the liquid sub-chamber; reducing the supply of the gas to the gas sub-chamber such that the flexible membrane returns toward its original position; transporting gas from the gas source through a gas bypass connected to the gas inlet conduit and external to the reactor chamber to remove liquid from the gas inlet conduit; and supplying gas from the gas source to the gas sub-chamber at least a second time to deform the gas-permeable

CLAIMS

1. A reactor system, comprising:

a reactor chamber;

5 a reactor chamber gas inlet conduit configured to transport gas into the reactor chamber through a reactor chamber gas inlet;

a flow control mechanism configured to regulate the flow of gas through the reactor chamber gas inlet conduit at a rate of equal to or less than about 1 milliliter per second;

10 a humidifier configured to humidify the gas transported through the reactor chamber gas inlet conduit, the humidifier positioned between the flow control mechanism and the reactor chamber gas inlet;

a reactor chamber gas outlet conduit configured to transport gas out of the reactor chamber through a reactor chamber gas outlet; and

15 a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.

2. A reactor system, comprising:

a reactor chamber;

20 a reactor chamber gas inlet conduit configured to transport gas into the reactor chamber through a reactor chamber gas inlet;

a reactor chamber gas outlet conduit configured to transport gas out of the reactor chamber through a reactor chamber gas outlet;

a flow control mechanism configured to regulate the flow of gas through the reactor chamber gas outlet conduit at a rate of equal to or less than about 1 milliliter per second;

25 a liquid trap configured to remove liquid vapor from the gas within the reactor chamber gas outlet conduit, the liquid trap positioned between the flow control mechanism and the reactor chamber gas outlet; and

a gas bypass conduit external to the reactor chamber, connecting the gas inlet conduit to the gas outlet conduit.

30 3. The reactor system of claim 2, comprising:

a humidifier configured to humidify the gas transported through the reactor chamber gas inlet conduit.

4. The reactor system of claim 3, comprising an inlet flow control mechanism
5 configured to regulate the flow of gas through the reactor chamber gas inlet conduit at a rate of equal to or less than about 1 milliliter per second.

5. The reactor system of claim 4, wherein the humidifier is positioned between the inlet flow control mechanism and the reactor chamber gas inlet.

10 6. The reactor system of any one of claims 1-5, wherein the reactor chamber contains a liquid and at least one biological cell.

7. The reactor system of claim 6, wherein the biological cell is a eukaryotic cell.

15 8. The reactor system of claim 7, wherein the biological cell is a mammalian cell.

9. The reactor system of claim 8, wherein the mammalian cell is selected from the group consisting of primate cells, bovine cells, horse cells, porcine cells, goat cells, dog cells, cat
20 cells, rodent cells, human cells, and a hamster cells.

10. The reactor system of claim 9, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

25 11. The reactor system of any one of claims 7-9, wherein the biological cell is a cardiac cell, a fibroblast, a keratinocyte, a hepatocyte, a chondrocyte, a neural cell, a osteocyte, a muscle cell, a blood cell, an endothelial cell, an immune cell, or a stem cell.

12. The reactor system of any one of claims 1-11, wherein the reactor chamber has a
30 volume of less than or equal to about 50 milliliters.

13. The reactor system of any one of claims 1-12, wherein the gas comprises carbon dioxide and/or oxygen.

14. The reactor system of any one of claims 1 and 3-13, wherein the humidifier
5 comprises a vessel including a first liquid having a temperature at least about 1°C higher than the temperature of the liquid phase.

15. The reactor system of any one of claims 2-14, wherein the liquid trap comprises a
10 vessel including a second liquid having a temperature at least about 1°C lower than the temperature of the liquid phase.

16. The reactor system of any one of claims 1-15, wherein the flow control mechanism comprises a gas supply conduit comprising a constriction.

17. The reactor system of claim 16, wherein a cross-sectional dimension of the gas supply
15 conduit within the constriction is at least about 10% smaller than cross-sectional dimensions of the gas supply conduit at locations upstream and downstream of the constriction.

18. The reactor system of any one of claims 1-17, wherein the flow control mechanism
20 comprises a pressure regulator.

19. The reactor system of any one of claims 1-18, wherein the reactor chamber is configured to contain a volume of the liquid medium that is equal to or less than about 50 milliliters and equal to or greater than 10 microliters.

CLAIMS

1. A reactor system, comprising:
a reactor chamber;
5 a reactor chamber gas inlet conduit configured to transport gas into the reactor chamber through a reactor chamber gas inlet;
a flow control mechanism configured to regulate the flow of gas through the reactor chamber gas inlet conduit at a rate of equal to or less than about 1 milliliter per second; and
10 a humidifier configured to humidify the gas transported through the reactor chamber gas inlet conduit, the humidifier positioned between the flow control mechanism and the reactor chamber gas inlet.
2. A reactor system, comprising:
15 a reactor chamber;
a reactor chamber gas outlet conduit configured to transport gas out of the reactor chamber through a reactor chamber gas outlet;
a flow control mechanism configured to regulate the flow of gas through the reactor chamber gas outlet conduit at a rate of equal to or less than about 1 milliliter per
20 second; and
a liquid trap configured to remove liquid vapor from the gas within the reactor chamber gas outlet conduit, the liquid trap positioned between the flow control mechanism and the reactor chamber gas outlet.
- 25 3. The reactor system of claim 2, comprising:
a reactor chamber gas inlet conduit configured to transport gas into the reactor chamber, and
a humidifier configured to humidify the gas transported through the reactor chamber gas inlet conduit.
- 30 4. The reactor system of claim 3, comprising an inlet flow control mechanism configured to regulate the flow of gas through the reactor chamber gas inlet conduit at a rate of equal to or less than about 1 milliliter per second.

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5. The reactor system of claim 4, wherein the humidifier is positioned between the inlet flow control mechanism and the reactor chamber gas inlet.
- 5 6. The reactor system of any one of claims 1-5, wherein the reactor chamber contains a liquid and at least one biological cell.
7. The reactor system of claim 6, wherein the biological cell is a eukaryotic cell.
- 10 8. The reactor system of claim 7, wherein the biological cell is a mammalian cell.
9. The reactor system of claim 8, wherein the mammalian cell is selected from the group consisting of primate cells, bovine cells, horse cells, porcine cells, goat cells, dog cells, cat cells, rodent cells, human cells, and a hamster cells.
- 15 10. The reactor system of claim 9, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.
11. The reactor system of any one of claims 7-9, wherein the biological cell is a
20 cardiac cell, a fibroblast, a keratinocyte, a hepatocyte, a chondrocyte, a neural cell, a osteocyte, a muscle cell, a blood cell, an endothelial cell, an immune cell, or a stem cell.
12. The reactor system of any one of claims 1-11, wherein the reactor chamber has a volume of less than or equal to about 50 milliliters.
- 25 13. The reactor system of any one of claims 1-12, wherein the gas comprises carbon dioxide and/or oxygen.
14. The reactor system of any one of claims 1 and 3-13, wherein the humidifier
30 comprises a vessel including a first liquid having a temperature at least about 1°C higher than the temperature of the liquid phase.

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15. The reactor system of any one of claims 2-14, wherein the liquid trap comprises a vessel including a second liquid having a temperature at least about 1°C lower than the temperature of the liquid phase.

5 16. The reactor system of any one of claims 1-15, wherein the flow control mechanism comprises a gas supply conduit comprising a constriction.

17. The reactor system of claim 16, wherein a cross-sectional dimension of the gas supply conduit within the constriction is at least about 10% smaller than cross-sectional
10 dimensions of the gas supply conduit at locations upstream and downstream of the constriction.

18. The reactor system of any one of claims 1-17, wherein the flow control
15 mechanism comprises a pressure regulator.

19. The reactor system of any one of claims 1, 3-4, and 6-18, wherein the humidifier is positioned upstream of the flow control mechanism.

20. The reactor system of any one of claims 2-19, wherein the liquid trap is
20 positioned upstream of the flow control mechanism.

21. The reactor system of any one of claims 1-20, wherein the reactor chamber is configured to contain a volume of the liquid medium that is equal to or less than about 50 milliliters and equal to or greater than 10 microliters.

25 22. A reactor system, comprising:
a reactor chamber, comprising:
a liquid sub-chamber configured to contain a liquid growth medium
including at least one biological cell;
30 a gas sub-chamber configured to contain a gaseous headspace above the liquid growth medium; and
a gas-permeable flexible membrane separating the liquid sub-chamber from the gas sub-chamber;

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a gas inlet conduit configured to transport gas into the gas sub-chamber;
a gas outlet conduit configured to transport gas out of the gas sub-chamber; and
a gas bypass conduit external to the reactor chamber, connecting the gas inlet
conduit to the gas outlet conduit.

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23. The reactor system of claim 22, comprising a humidifier configured to humidify
the gas transported through a reactor chamber gas inlet conduit configured to transport
gas into the reactor chamber through a reactor chamber gas inlet.

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24. The reactor system of claim 23, comprising an inlet flow control mechanism
configured to regulate the flow of gas through the reactor chamber gas inlet conduit at a
rate of equal to or less than about 1 milliliter per second.

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25. The reactor system of claim 24, wherein the humidifier is positioned between the
inlet flow control mechanism and the reactor chamber gas inlet.

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26. The reactor system of any one of claims 22-25, comprising a liquid trap
configured to remove liquid vapor from the gas within a reactor chamber gas outlet
conduit configured to transport gas out of the reactor chamber through a reactor chamber
gas outlet.

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27. The reactor system of claim 26, comprising an outlet flow control mechanism
configured to regulate the flow of gas through the reactor chamber gas outlet conduit at a
rate of equal to or less than about 1 milliliter per second.

28. The reactor system of claim 27, wherein the liquid trap is positioned between the
flow control mechanism and the reactor chamber gas outlet.

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29. The reactor system of any one of claims 22-28, wherein the reactor chamber has a
volume of less than or equal to about 50 milliliters.

30. The reactor system of any one of claims 22-29, wherein the gas-permeable
flexible membrane is permeable to carbon dioxide and/or oxygen gas.

31. The reactor system of any one of claims 22-30, wherein the reactor chamber is configured to contain a volume of the liquid medium that is equal to or less than about 50 milliliters and equal to or greater than 10 microliters.

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32. The reactor system of any one of claims 22-31, wherein the cell is a eukaryotic cell.

33. The reactor system of claim 32, wherein the eukaryotic cell is an animal cell.

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34. The reactor system of claim 33, wherein the animal cell is a mammalian cell.

35. The reactor system of claim 34, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

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36. A method of operating a reactor, comprising:

providing a reactor chamber, comprising:

a liquid sub-chamber configured to contain a liquid growth medium

including at least one biological cell;

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a gas sub-chamber configured to contain a gaseous headspace above the liquid growth medium; and

a flexible membrane separating the liquid sub-chamber from the gas sub-chamber;

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transporting a gas from a gas source through a gas inlet conduit to the gas sub-chamber to deform the gas-permeable flexible membrane such that liquid is at least partially removed from the liquid sub-chamber;

reducing the supply of the gas to the gas sub-chamber such that the flexible membrane returns toward its original position;

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transporting gas from the gas source through a gas bypass connected to the gas inlet conduit and external to the reactor chamber to remove liquid from the gas inlet conduit; and

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supplying gas from the gas source to the gas sub-chamber at least a second time to deform the gas-permeable flexible membrane such that liquid is at least partially evacuated from the liquid sub-chamber.

- 5 37. The method of claim 36, wherein the reactor chamber contains a volume of the liquid medium that is equal to or less than about 50 milliliters and equal to or greater than 10 microliters.
38. The method of any one of claims 36-37, wherein the cell is a eukaryotic cell.
- 10 39. The method of claim 38, wherein the eukaryotic cell is an animal cell.
40. The method of claim 39, wherein the animal cell is a mammalian cell.
- 15 41. The method of claim 40, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.