insights and products ranging from life-saving antibiotics to fertilizers that improve food production and security.

SUMMARY

The present disclosure provides microbiology systems, apparatus, kits, and methods for streamlining the cultivation workflow, supporting high throughput screening, and/or developing new insights and products in accordance with some examples. For example, an apparatus may comprise a microfabricated device for receiving a sample comprising one or more cells. The microfabricated device defines a high density array of microwells for cultivating one or more cells.

In one aspect, the present disclosure refers to a method of transferring material from a first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, the method comprising: loading at least one magnetic bead into at least one microwell of the first array of microwells such that the at least one microwell of the first array of microwells includes at least one cell and at least one magnetic bead; incubating the first microfabricated device to cultivate a plurality of cells in at least one microwell of the first array of microwells; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least one cell from the plurality of cells in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells and wherein the material comprised by the second array represents a copy of the material retained in the first array.

In another aspect, the present disclosure refers to a method of transferring material from a

first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, the method comprising: preparing the first microfabricated device such that at least one microwell of the first array of microwells includes a material of interest and at least one magnetic bead; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

In yet another aspect, the present disclosure refers to a method of transferring material from a first microfabricated device including a first array of microwells, at least one microwell of which comprises at least one magnetic bead, to a second microfabricated device including a second array of microwells, the method comprising: providing a material of interest into the at least one microwell which comprises the at least one magnetic bead; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at

least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

In yet another aspect, the present disclosure refers to a method of transferring material from a first microfabricated device including a first array of microwells, at least one microwell of which comprises at least one magnetic bead and a material of interest, to a second microfabricated device including a second array of microwells, the method comprising: positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

In some examples, a method of transferring material from a first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, is provided. The method includes: loading at least one magnetic bead into at least one microwell of the first array of microwells; incubating the first microfabricated device to cultivate a plurality of cells in at least one microwell of the first array of microwells; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device; and applying a magnetic field (e.g., by using permanent magnet or an electromagnet) so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least one cell from the plurality of cells in the at least one microwell of the

first array of microwells is transferred to the at least one microwell of the second array of microwells.

In some examples, the method further includes: prior to incubating the first microfabricated device, preparing the first microfabricated device such that at least one microwell of the first array of microwells includes at least one cell and at least one magnetic bead, wherein incubating the first microfabricated device comprises cultivating a plurality of cells in the at least one microwell of the first microfabricated device from the at least one cell. In some of these examples, preparing the first microfabricated

device includes loading a magnetic bead solution including a solvent and at least one magnetic bead into the at least one microwell; and loading at least one cell into the at least one microwell. A magnet can be used to draw the at least one magnetic bead to the inside of the at least one microwell, and the solvent can be allowed to evaporate.

Preparing the first microfabricated device can include loading into the at least one microwell a sample solution that includes at least one magnetic bead and at least one cell. A membrane can be further applied to the microfabricated device to seal the at least one microwell after the bead(s) and cell(s) are loaded.

In some examples, each of the first and second microfabricated devices includes an upper surface, and positioning the second microfabricated device relative to the first microfabricated device can be by positioning the upper surface of the second microfabricated device opposing and apart from the upper surface of the first microfabricated device.

In some examples, each of the first and second microfabricated devices comprises an upper surface, and positioning the second microfabricated device relative to the first microfabricated device comprises positioning the upper surface of the second microfabricated device opposing and in contact with the upper surface of the first microfabricated device.

In some examples, prior to applying the magnetic field, a liquid layer is applied on the at least one microwell of the first array of microwells of the first microfabricated device. The liquid layer can be a layer immiscible with water (e.g., an oil layer), an aqueous layer, or other layer.

In some examples, the method further includes obtaining a genomic DNA from the at least one cell which has been transferred into the at least one microwell of the second microfabricated device, and amplifying the genomic DNA sequence using polymerase chain reaction in the at least one microwell of the second microfabricated device in the presence of the transferred at least one magnetic bead.

In some examples, a method of transferring material from a first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, is provided. The method includes: preparing the first microfabricated device such that at least one microwell of the first array of microwells

includes a material of interest and at least one magnetic bead; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells. The material of interest can be a biological entity, e.g., it can include a plurality of cells. Preparing the first microfabricated device can include: providing the at least one microwell of the first array of microwells with at least one cell and at least one magnetic bead; and prior to applying the magnetic field, incubating the first microfabricated device to grow a plurality of cells from the provided at least one cell in the at least one microwell of the first microfabricated device. Providing the at least one microwell of the first array of microwells with at least one cell and at least one magnetic bead can include: loading a magnetic bead solution including a solvent and at least one magnetic bead into the at least one microwell; and loading at least one cell into the at least one microwell. The at least one magnetic bead can be loaded into the microwell with a sample solution which also includes at least one cell.

In some examples, a method of transferring material from a first microfabricated device to a second microfabricated device. The first microfabricated device includes a first array of microwells and the second microfabricated device includes a second array of microwells. At least one microwell of the first array of microwells of the first fabricated device includes at least one magnetic bead. The method includes: providing a material of interest into the at least one microwell which comprises the at least one magnetic bead; positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one

microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells.

In some examples, a method of transferring material from a first microfabricated device to a second microfabricated device. The first microfabricated device includes a first array of microwells and the second microfabricated device includes a second array of microwells. At least one microwell of the first array of microwells of the first fabricated device includes at least one magnetic bead and at least one cell. The method includes positioning the second microfabricated device relative to the first microfabricate chip such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device; and applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells.

In some examples, a kit is provided, which includes a first microfabricated device including a first array of microwells, at least one microwell of which includes at least one magnetic bead. The kit can further include a membrane suitable for applying on the first microfabricated device to seal the at least one microwell. The kit can further include a second microfabricated device including a second array of microwells, wherein each microwell of the first array of microwells can be aligned with a microwell of the second array of microwells.

In some examples, a kit is provided, which includes a microfabricated device including a high density array of microwells, and a solution including a solvent and a plurality of magnetic beads. The kit can further include a membrane suitable for applying on the first microfabricated device to seal the at least one microwell. The kit can also include a magnet.

In the above methods of transfer of material between chips using magnetic

CLAIMS

What is claimed is:

1. A method of transferring material from a first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, the method comprising:

loading at least one magnetic bead into at least one microwell of the first array of microwells such that the at least one microwell of the first array of microwells includes at least one cell and at least one magnetic bead;

incubating the first microfabricated device to cultivate a plurality of cells in at least one microwell of the first array of microwells;

positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and

applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least one cell from the plurality of cells in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells and wherein the material comprised by the second array represents a copy of the material retained in the first array.

2. The method of claim 1, wherein applying the magnetic field comprises using a permanent magnet.

3. The method of claim 1, wherein applying the magnetic field comprises using an electromagnet.

4. The method of claim 1, further comprising:

prior to incubating the first microfabricated device, preparing the first

microfabricated device such that at least one microwell of the first array of microwells includes at least one cell and at least one magnetic bead, wherein incubating the first microfabricated device comprises cultivating a plurality of cells in the at least one microwell of the first microfabricated device from the at least one cell.

5. The method of claim 4, wherein preparing the first microfabricated device comprises:

loading a magnetic bead solution including a solvent and at least one magnetic bead into the at least one microwell; and

loading at least one cell into the at least one microwell.

6. The method of claim 5, further comprising:

applying a magnet to the first microfabricated device so that the at least one magnetic bead is drawn to the inside of the at least one microwell; and

allowing evaporation of the solvent.

7. The method of claim 4, wherein preparing the first microfabricated device comprises:

loading into the at least one microwell a sample solution including at least one magnetic bead and at least one cell.

8. The method of claim 4, wherein preparing the first microfabricated device comprises:

applying a membrane to seal the at least one microwell.

9. The method of claim 1, wherein each of the first and second microfabricated devices comprises an upper surface, and wherein positioning the second microfabricated device relative to the first microfabricated device comprises positioning the upper surface of the second microfabricated device opposing and apart from the upper surface of the first microfabricated device.

10. The method of claim 1, wherein each of the first and second microfabricated devices comprises an upper surface, and wherein positioning the second microfabricated device relative to the first microfabricated device comprises positioning the upper surface of the

second microfabricated device opposing and in contact with the upper surface of the first microfabricated device.

11. The method of claim 1, further comprising:

prior to applying the magnetic field, applying a liquid layer on the at least one microwell of the first array of microwells of the first microfabricated device

12. The method of claim 11, wherein the liquid layer is an oil layer.

13. The method of claim 11, wherein the liquid layer is an aqueous layer.

14. A method of transferring material from a first microfabricated device including a first array of microwells to a second microfabricated device including a second array of microwells, the method comprising:

preparing the first microfabricated device such that at least one microwell of the first array of microwells includes a material of interest and at least one magnetic bead;

positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and

applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

15. The method of claim 14, wherein the material of interest is a biological entity.

16. The method of claim 14, wherein the material of interest comprises a plurality of cells.

17. The method of claim 14, wherein preparing the first microfabricated device comprises:

providing the at least one microwell of the first array of microwells with at least one cell and at least one magnetic bead; and

prior to applying the magnetic field, incubating the first microfabricated device to grow a plurality of cells from the provided at least one cell in the at least one microwell of the first microfabricated device.

18. The method of claim 17, wherein providing the at least one microwell of the first array of microwells with at least one cell and at least one magnetic bead comprises:

loading a magnetic bead solution including a solvent and at least one magnetic bead into the at least one microwell; and

loading at least one cell into the at least one microwell.

19. The method of claim 17, wherein providing the at least one microwell of the first array of microwells with at least one cell and at least one magnetic bead comprises:

loading into the at least one microwell a sample solution including at least one magnetic bead and at least one cell.

20. A method of transferring material from a first microfabricated device including a first array of microwells, at least one microwell of which comprises at least one magnetic bead, to a second microfabricated device including a second array of microwells, the method comprising:

providing a material of interest into the at least one microwell which comprises the at least one magnetic bead;

positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first

microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells; and

applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

21. A method of transferring material from a first microfabricated device including a first array of microwells, at least one microwell of which comprises at least one magnetic bead and a material of interest, to a second microfabricated device including a second array of microwells, the method comprising:

positioning the second microfabricated device relative to the first microfabricated device such that the at least one microwell of the first array of microwells of the first microfabricated device is aligned with at least one microwell of the second array of microwells of the second microfabricated device, and that the plurality of cells in the at least one microwell is completely accommodated within the at least one microwell and kept apart from the at least one microwell of the second array of microwells;

applying a magnetic field so as to move the at least one magnetic bead contained in the at least one microwell of the first array of microwells into the at least one microwell of the second array of microwells, whereby at least a portion of the material of interest in the at least one microwell of the first array of microwells is transferred to the at least one microwell of the second array of microwells, wherein the material comprised by the second array represents a copy of the material retained in the first array.

22. The method of any of claims 1-21, wherein the surface density of the first array of microwells is at least 150 microwells per cm^2, at least 250 microwells per cm^2, at least

400 microwells per cm^2, at least 500 microwells per cm^2, at least 750 microwells per cm^2, at least 1,000 microwells per cm^2, at least 2,500 microwells per cm^2, at least 5,000 microwells per cm^2, at least 7,500 microwells per cm^2, at least 10,000 microwells per cm^2, at least 50,000 microwells per cm^2, at least 100,000 microwells per cm^2, or at least 160,000 per cm^2.

23. The method of any of claims 1-22, wherein each microwell of the first array of microwells of the first microfabricated device has a diameter of from 5 μm to 500 μm, from 10 μm to 300 μm, or from 20 μm to 200 μm.