CLAIMS

1. A method of transferring a sample from at least one selected microwell of a microfabricated chip including a plurality of microwells to a predetermined location in a destination sample holder using a picking instrument comprising a picking pin having a distal tip, the picking pin having three degrees-of-freedom and configured to move in x, y, and z directions, the x, y directions constituting an x-y plane, the method comprising:

calibrating a position of the microfabricated chip relative to a position of the picking pin;

determining coordinates of the at least one selected microwell of the microfabricated chip for picking on the x-y plane relative to the position of the picking pin based on the calibration;

based on a current position of picking pin and the determined coordinates of the at least one selected microwell, moving the picking pin to a position above the location of the at least one selected microwell;

dipping at least a portion of the distal tip of the picking pin into the at least one selected microwell to pick up a sample contained in the at least one selected microwell; and

moving the picking pin and transferring the sample to a predetermined location in the destination sample holder.

2. The method of claim 1, wherein the calibration comprises:

positioning the picking pin to a first position such that its distal tip is above a first reference microwell or a first fiducial mark, and recording the coordinates of the first position in a data memory;

positioning the picking pin to a second position such that its distal tip is above a second reference microwell or a second fiducial mark, and recording the coordinates of the second position in the data memory; and

determining the coordinates of the at least one selected microwell relative to the position of the picking pin based on the recorded coordinates of the first and second positions of the distal tip of the picking pin.

3. The method of claim 2, wherein positioning the picking pin to the first and the second positions are performed under surveillance of an image capture device and with aid of a digital display, the image capture device providing images of the picking pin at the first and the second positions to the digital display.

4. The method of claim 1, wherein the calibration comprises calibrating the coordinates of one or more microwells of the microfabricated chip.

5. The method of claim 1, wherein the calibration comprises calibrating the coordinates of one or more fiducial marks pre-existing on the microfabricated chip.

6. The method of claim 1, wherein the calibration comprises:

positioning the picking pin above the microfabricated device at provided coordinates of at least one target microwell of a microfabricated chip,

lowering the picking pin such that the distal tip of the picking pin contacts the microfabricated device and creates at least one mark;

retracting the picking pin;

determining the displacement of the coordinates of the at least one mark from the provided coordinates of the at least one target microwell; and

calibrating the position of the microfabricated chip relative to the position of the picking pin based on the determined displacement.

7. The method of claim 6, wherein the microfabricated chip used in the calibration is the same microfabricated chip where the at least one selected microwell for picking is located.

8. The method of claim 6, wherein the microfabricated chip used in the calibration is a microfabricated chip different from the microfabricated chip that comprises the at least one selected microwell for picking.

9. The method of claim 6, wherein determining the displacement of the coordinates of the at least one mark from the provided coordinates of the target microwell comprising examining the position of the at least one mark relative to the position of the at least one target microwell under a microscope.

10. The method of claim 1, wherein the calibration comprises:

(a) using an image capture device to capture one or more images of at least a portion of the microfabricated chip, and determining the coordinates of the at least one selected microwell based on an analysis of the one or more captured images; and

(b) using an optical aligner to determine the coordinates of the position of the picking pin.

11. The method of claim 10, wherein the optical aligner comprises a first light source, a first light detector, a second light source, and a second light detector, where the first light source and the first light detector are arranged such that a first light beam emitted from the first light source and received by the first light detector is along the y direction, and the second light source and the second light detector are arranged such a second light beam emitted from the second light source and received by the second light detector is along the x direction, and wherein using the optical aligner to determine the coordinates of the position of the picking pin comprises:

translating the picking pin along the x direction and detecting the x coordinate of the picking pin when the first light beam along the y direction is blocked by the picking pin, x0;

translating the picking pin along the y direction and detecting the y coordinate of the picking pin when the second light beam along the x direction is blocked by the picking pin, y0; and

determining the coordinates of the position of the picking pin based on its offset in the x direction relative to x0, and its offset in the y direction relative to y0.

12. The method of claim 1, wherein the calibration comprises:

(a) using an image capture device to capture one or more images of at least a portion of the microfabricated chip, and determining the coordinates of the at least one selected microwell based on an analysis of the one or more captured images; and

(b) using a digital touchscreen to determine the coordinates of the position of the picking pin.

13. The method of claim 1, wherein dipping the picking pin comprises:

inserting the distal tip of the picking pin into the at least one selected microwell such that the distal tip of the picking pin has traveled a predetermined distance into the microwell; and

retracting the distal tip of the picking pin out of the at least one selected microwell.

14. The method of claim 1, wherein dipping the picking pin comprises:

inserting the distal tip of the picking pin into the at least one selected microwell;

determining whether the distal tip of the picking pin has contacted the bottom of the at least one selected microwell; and

upon confirmation that the distal tip has contacted the bottom of the at least one selected microwell, retracting the distal tip out of the at least one selected microwell.

15. The method of claim 14, wherein determining whether distal tip of the picking pin has contacted the bottom of the at least one selected microwell is based on a distance in the z direction traveled by the picking pin.

16. The method of claim 15, wherein the picking instrument further comprises a pressure sensor operably coupled with the picking pin for sensing an opposition force experienced by the picking pin when the distal tip of the picking pin contacts an object, and wherein determining whether the distal tip of the picking pin has contacted the bottom of the at least one selected microwell is based on a detected opposition force when the distal tip of the picking pin contacts the bottom of the at least one selected well.

17. The method of claim 1, wherein the at least one selected microwell includes an oil layer covering the sample, and wherein dipping the picking pin comprises passing at least a portion of the distal tip of the picking pin through the oil layer.

18. The method of claim 1, wherein the predetermined location in the destination sample holder is a well containing a culture media, and wherein transferring the sample to the predetermined location in the destination sample holder comprises at least one of: (A) advancing and retracting the picking pin through at least a portion of the culture media repeatedly, and (B) dithering the distal tip of the picking laterally in the culture media.

19. The method of claim 1, further comprising:

after transferring the sample to a predetermined location in the destination sample holder, moving the picking pin and sterilizing the picking pin with a sterilization device.

20. A picking instrument, comprising:

a picking pin having a distal tip and three degrees-of-freedom and configured to move in x, y, and z directions, the x, y directions constituting an x-y plane;

a loading platform comprising a first area, the first area configured to accommodate and secure a microfabricated chip including a plurality of microwells;

wherein the picking pin is operably connected to a computer, the computer including a computer program product that enables determination of coordinates of at least one selected microwell of the microfabricated chip on the x-y plane relative to a position of the picking pin based on a calibration of a position of the microfabricated chip relative to the position of the picking pin, and enables the picking pin to:

move to a position above the at least one selected microwell in the plurality of the microwells of the microfabricated chip;

pick a sample contained in the at least one selected microwell;

move to a predetermined location at a destination sample holder; and

transfer the picked sample to the predetermined location at the destination sample holder.

21. The picking instrument of claim 20, wherein the loading platform further comprises a second area configured to secure a destination sample holder having a plurality of wells that have greater dimensions than the microwells of the microfabricated chip.

22. The picking instrument of claim 20, wherein the loading platform further comprises a second area configured to secure another microfabricated chip having a plurality of microwells.

23. The picking instrument of claim 20, wherein the movement of the picking pin is driven by three programmatically controlled motors, each motor configured to move the picking pin in the x, y, and z direction independently, respectively.

24. The picking instrument of claim 23, wherein the picking pin is mounted on a spring.

25. The picking instrument of claim 20, further comprising a pressure sensor coupled with the picking pin, the pressure sensor being configured to sense an opposition force experienced by the picking pin when the distal tip of the picking pin contacts an object.

26. The picking instrument of claim 20, further comprising a camera configured to capture at least a portion of the microfabricated chip when it is loaded onto the loading platform.

27. The picking instrument of claim 26, wherein the camera is in a fixed spaced relationship with the loading platform.

28. The picking instrument of claim 20, further comprising an optical aligner configured to determine the coordinates of the picking pin.

29. The picking instrument of claim 28, wherein the optical aligner comprises a first light source, a first light detector, a second light source, and a second light detector, where the first light source and the first light detector are arranged such that a first light beam emitted from the first light source and received by the first light detector is along the y direction, and the second light source and the second light detector are arranged such a second light beam emitted from the second light source and received by the second light detector is along the x direction.

30. The picking instrument of claim 20, further comprising a sterilization device that is capable of sterilizing the distal tip of the picking pin.

31. The picking instrument of claim 20, further comprising a touchscreen for locating the coordinates of the picking pin.

32. The picking instrument of claim 20, wherein the loading platform is movably mounted on a rail structure.

33. A method of operating a picking instrument, comprising:

providing a picking instrument comprising:

a picking pin having a distal tip and three degrees-of-freedom and configured to move in x, y, and z directions, the x, y directions constituting an x-y plane;

a loading platform comprising a first area and a second area, the first area configured to accommodate and secure a microfabricated chip including a plurality of microwells, and the second area configured to accommodate and secure a destination sample holder;

wherein the picking pin is operably connected to a computer, the computer including a computer program product that enables the determination of coordinates of at least one selected microwell of the microfabricated chip on the x-y plane relative to a position of the picking pin based on a calibration of a position of the microfabricated chip relative to the position of the picking pin;

wherein the first area of the loading platform is loaded with a first microfabricated chip having a top surface defining a plurality of microwells, and wherein the second area of the loading platform is loaded with a destination sample holder;

calibrating the position of the first microfabricated chip relative to the position of the picking pin;

determine the coordinates of the at least one selected microwell of the first microfabricated chip on the x-y plane relative to the position of the picking pin based on the calibration;

based on the determined coordinates of the at least one selected microwell of the first microfabricated chip, moving the picking pin to a position above the location of the at least one selected microwell of the first microfabricated chip;

dipping at least a portion of the distal tip of the picking pin into the at least one selected microwell of the first microfabricated chip to pick up a sample contained in the at least one selected microwell of the first microfabricated chip; and

moving the picking pin and transferring the sample to a predetermined location in the destination sample holder.

34. The method of claim 33, further comprising:

removing the first microfabricated chip from the first area of the loading platform;

loading a second microfabricated chip into the first area of the loading platform;

without performing further calibration, determining the coordinates of at least one selected microwell of the second microfabricated chip on the x-y plane relative to the position of the picking pin;

based on the determined coordinates of the at least one selected microwell of the second microfabricated chip, moving the picking pin to a position above the location of the at least one selected microwell of the second microfabricated chip; and

dipping at least a portion of the distal tip of the picking pin into the at least one selected microwell of the second microfabricated chip to pick up a sample contained in the at least one selected microwell of the second microfabricated chip.