Summary of Invention

In one aspect, the present invention provides a method of transferring a sample from at least one selected microwell of a microfabricated chip containing a plurality of microwells to a predetermined location in a destination sample holder using a picking instrument. The picking instrument comprises a picking pin, which has a distal tip, and has 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 includes: calibrating the position of the microfabricated chip relative to the position of the picking pin ; determining the coordinates of the at least one selected microwell of the microfabricated chip for picking on the x-y plane relative to a position of the picking pin based on the calibration; based on a current position of the 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 selected microwell; and moving the picking pin and transferring the sample to a predetermined location in the destination sample holder.

In some embodiments of the method, 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 calculating the coordinates of the at least one selected microwell based on the recorded coordinates of the first and second positions of the distal tip of the picking pin. Positioning the picking pin to the first and the second positions can be performed under surveillance of an image capture device and with aid of a digital display, where the image capture device provides images of the picking pin at the first and the second positions to the digital display.

In some embodiments, the calibration comprises calibrating the coordinates of one or more marks created by the picking pin during calibration. The calibration

In some embodiments of the method, after transferring the sample to a predetermined location in the destination sample holder, the picking pin is moved away from the destination sample holder and sterilized with a sterilization device.

In another aspect, the present invention provides a picking instrument, which includes 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 a computer operably connected to the picking pin, the computer having a data memory and a processor, and including a computer program product that enables the determination of the 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 the position of the microfabricated chip relative to a 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 selected microwell; move to a predetermined location at the destination sample holder; and transfer the picked sample to the predetermined location at the destination sample holder.

In some embodiments, the second area of the picking instrument is configured to secure a destination sample holder having a plurality of wells that have greater dimensions than the microwells of the microfabricated chip. In alternative embodiments, the second area is configured to secure another microfabricated chip having a plurality of microwells.

In some embodiments of the picking instrument, 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.

In some embodiments of the picking instrument, the picking pin is mounted on a spring.

In some embodiments of the picking instrument, a pressure sensor is coupled with the picking pin, where the pressure sensor is configured to sense an opposition force experienced by the picking pin when the distal tip of the picking pin contacts an object.

In some embodiments, the picking instrument further includes a camera configured to capture at least a portion of the microfabricated chip when it is loaded onto the loading platform. The camera can be in a fixed spaced relationship with the loading platform.

In some embodiments, the loading platform is movably mounted on a rail structure.

In some embodiments, the picking instrument further includes an optical aligner configured to determine the coordinates of the picking pin. In certain of these embodiments, the optical aligner can include 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.

In some embodiments, the picking instrument further includes a sterilization device that is capable of sterilizing the distal tip of the picking pin.

In some embodiments, a method of operating a picking instrument as described herein is provided. The picking instrument includes 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; and 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. The picking pin is operably connected to a computer, the computer including a computer program product that enables the determination of the 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 the position of the microfabricated chip relative to a position of the picking pin. The first area of the loading platform is loaded with a first microfabricated chip having a top surface defining a plurality of microwells, and the second area of the loading platform is loaded with a destination sample holder. In the method, the position of the