

causing the particles to more frequently interact with and bind to the walls. In comparison to microfluidic devices having micro-channels without the grooves, cell-substrate interactions can be increased when cells suspended in a buffer solution are flowed through the micro-channel that includes the grooves. This, in turn, can increase the capture efficiency of the device. Further, passive microfluidic fluid manipulation techniques described here can negate the need for external sources of energy, and can consequently decrease energy consumption and cost of manufacture, particularly when the microfluidic device is scaled up to highly parallel μ TAS or LOC systems or both. The devices can be transparent based on the choice of materials for manufacturing. The volumes of samples and reagents consumed can be decreased due to the micrometer-range dimensions through which the volumes are flowed. Consequently, cost of samples and reagents can also be decreased. The techniques described are applicable to capture and culture live cells.

The details of one or more implementations of the specification are set forth in the accompanying drawings and the description below. Other features, aspects, and advantages of the specification will become apparent from the description, the drawings, and the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows an embodiment of a microfluidic device having grooves.

FIGS. 2A-2D illustrate particle flow paths in a micro-channel having flat walls and another micro-channel having grooves formed in a wall.

FIGS. 3A-3C illustrate exemplary grooves.

FIGS. 4A-4C illustrate an exemplary method of forming the microfluidic device of FIG. 1.

FIG. 5 shows capture efficiencies of example microfluidic devices for different flow rates.

FIG. 6 shows capture efficiencies of cancer cells spiked in whole blood.

FIG. 7 shows an embodiment of a high throughput microfluidic device having columns of herringbone patterns.

FIG. 8 shows an embodiment of a microfluidic device for culturing captured cells.

FIGS. 9A-9C are micrographs showing the growth of captured cells on a glass substrate.

FIG. 10 shows an analysis of EpCAM expression on the cells captured with the microfluidic device having grooves and control cells.

FIGS. 11A-11E show a circulating tumor cell captured from a prostate cancer patient using the microfluidic device.

FIG. 12 show healthy donor controls.

FIG. 13 shows CTC capture from patient samples using the microfluidic device having grooves.

FIGS. 14A-14D shows Wright-Giemsa staining of CTCs in the microfluidic device having grooves.

FIG. 15 shows a comparison of two microfluidic devices having different groove dimensions.

Like reference numbers and designations in the various drawings indicate like elements.

DETAILED DESCRIPTION

Methods, apparatuses, and systems for affinity-based particle capture in microfluidic devices having grooves are described. A micro-channel formed in a microfluidic device can be treated to capture particles suspended in a fluid flowing through the channel. A particle capture efficiency of the microfluidic device can be defined as a ratio of a number of

particles captured in the channel and a total number of particles flowed through the channel. As described below, grooves are formed extending into the walls of the micro-channel to create flow patterns in the fluid that promote an interaction between the particles suspended in the fluid and inner surfaces of the walls of the channel. The increased interaction can lead to an increase in a number of particles captured in the channel, and consequently, in the particle capture efficiency of the microfluidic device. The efficiency can further be increased by tailoring structural features of the microfluidic device including, for example, device substrate material, channel and groove dimensions, and the like, as well as fluid flow parameters such as flow rates based on types of particles and the types of fluids in which the particles are suspended. An example of such a microfluidic device manufactured using soft lithography techniques is described with respect to FIG. 1. As described later, particles are captured in the micro-channel of the microfluidic device by forming grooves in a wall of the micro-channel, coating an adherent on the inner surfaces of the walls of the micro-channel, and flowing particles suspended in the fluid through the micro-channel.

FIG. 1 illustrates a microfluidic device **100** having grooves **135**, **140** extending into one of the walls defining a channel **115** of the device **100**. In some embodiments, microfluidic devices include protrusions extending outward from the wall (e.g., V-shaped protrusions) rather than grooves extending into a wall of the channel **115**. In some implementations, a microfluidic device **100** can include an upper substrate **105** bonded to a lower substrate **110**, each of which can be fabricated using an appropriate material. For example, the upper substrate **105** can be fabricated using an elastomer such as, for example, polydimethylsiloxane (PDMS), and the lower substrate can be fabricated using glass, PDMS, or another elastomer. Alternatively, or in addition, the substrates can be manufactured using plastics such as, for example, polymethylmethacrylate (PMMA), polycarbonate, cyclic olefin copolymer (COC), and the like. In general, the materials selected to fabricate the upper and lower substrates can be easy to manufacture, for example, easy to etch, and can offer optical properties that facilitate ease of testing, for example, can be optically clear, and can be non-toxic so as to not negatively affect the cells attached to the substrate. In addition, the materials are preferred to exhibit no or limited autofluorescence. Further, the materials can be easy to functionalize so that analytes can be attached to the substrate. Furthermore, the materials can be mechanically strong to provide strength to the microfluidic device **100**. The upper substrate **105** can be securely fastened to the lower substrate **110**, with a micro-channel formed between them, as described below.

In some implementations, the micro-channel **115** can have a rectangular cross-section including two side walls **120** and **125**, and an upper wall **130** formed in the upper substrate **105**. Terms of relative location such as, for example, "upper" and "lower" are used for ease of description and denote location in the figures rather than necessary relative positions of the features. For example, the device can be oriented such that the grooves are on a bottom surface of the channel or such that a central axis of the channel extends vertically. Alternatively, the cross-section of the micro-channel **115** can be one of several shapes including but not limited to triangle, trapezoid, half-moon, and the like. The lower substrate **110** can form the lower wall of the micro-channel **115** once bonded to the upper substrate **105**. In some implementations, the micro-channel **115** includes multiple grooves **135** formed in the upper wall **130** of the micro-channel **115**. Alternatively, the grooves **135**