

device **100**. Alternatively, other types of bonding, for example, using a reversible sealant, using physical clamping and holding under pressure, and the like, can be used. In some implementations, the substrates can be securely bonded together through chemical bonds, and can subsequently be separated by breaking the bonds under the application of mechanical forces.

FIGS. **4A-4C** illustrate the formation of a microfluidic device **100** including an upper substrate **405** manufactured using PDMS and a lower substrate **410** manufactured using glass. The upper substrate **405** including the upper and side walls of the microchannel **415** can be formed using previously described techniques. Alternatively, or in addition, the upper wall can include multiple grooves **440**, each formed in an asymmetric “V” shape. In some implementations, symmetric grooves **440** and asymmetric grooves **445** can be interspersed in the herringbone pattern. Each groove further includes an apex **445** and two ends **450** and **455**. In addition, the micro-channel **415** includes two side walls **420** and **425**.

To configure the microfluidic device **400** to capture the biological analyte of interest, an adherent **460** is disposed on the inner surfaces of the micro-channel **115**. Specifically, surface modification is performed on the inner surfaces. In some implementations, as shown in FIG. **4B**, the adherent **460** can be mixed in a solution and flowed through the micro-channel **415**. As the solution flows through the micro-channel **415**, the adherent **460** binds to, and is thereby disposed in the inner surfaces of the channel **415**.

Techniques other than flowing the adherent through the micro-channel **115** can also be used to dispose the adherent. For example, in implementations in which plastic substrates are employed, the adherent can be disposed on the substrate, for example, by ultra-violet (UV) radiation treatment to alter the surface properties such that analytes bind to the altered surface prior to bonding the upper and lower substrates. In implementations in which the lower substrate is glass, the glass can be functionalized, for example, by sputtering, by gas phase deposition, by building up layers of nanoparticle monolayers, and the like prior to bonding the glass substrate to the upper substrate.

As shown in FIG. **4C**, the adherent **460** can be disposed throughout the inner surfaces of the micro-channel **415**. Alternatively, the adherent **460** can be disposed in one or more walls of the micro-channel **415**, for example, in the wall in which the grooves **445** are formed. In some embodiments, the adherent **460** can be disposed only on a lower substrate **410** manufactured from glass. In such embodiments, the lower substrate **410** can be bonded to the upper substrate **405** after the adherent is disposed on the lower substrate. In such implementations, the flow rate of the fluid is selected such that the microvortices established by the grooves **440** drive the cells in the fluid toward the lower substrate **410** increasing a number of cell-lower substrate **410** interactions. Subsequently, the lower substrate **410** can be separated from the upper substrate **405** and the captured cells can be cultured.

In some implementations, the adherent **460** can be selected such that the micro-channel **415** can be used for affinity-based cell capture utilizing wet chemistry techniques. In such implementations, the adherent **460** can be an antibody, for example, antibody for EpCAM, or an aptamer, for example, aptamer for surface proteins, with which the inner surfaces of the micro-channel **415** are functionalized. Additional examples of adherent **460** include avidin coated surfaces to capture amplified target cells that express biotin through the biotin-avidin linkage. Further examples of adherents corresponding to cells that can be captured are shown in Table 1 below.

TABLE 1

Cell-type	Adherent
Neutrophil	Anti-CD66
Monocyte	Anti-CD14
Lymphocyte	Anti-CD4; Anti-CD8
Circulating tumor cells	Anti-EpCAM
Neutrophils	E, P Selectins
HIV-specific T cell	HAL A2-SL9
Any disease specific T cell	Pentamer

Once functionalized, the inner surfaces function as capture devices that can bind the analytes of interest. Capture efficiencies of exemplary microfluidic devices are described with reference to FIG. **5**.

## EXAMPLE 1

## Capture Efficiency

FIG. **5** shows capture efficiencies of example microfluidic devices for different flow rates. As described previously, the inner surfaces on which the adherent **460** are disposed bind cells that interact with the surfaces. To study the capture efficiency of microfluidic devices, a buffer solution spiked with cancer cells (lung cancer cells—H1650 line) was flowed through a microfluidic device **400** having herringbone patterns in the upper wall and microfluidic device **200** having flat wall surfaces. The microfluidic device **400** used in this example is a small footprint design having a width of 2 mm and a length of 2 cm. The fluids were flowed through the micro-channel **415** of the device **400** at flow rates of 0.12 ml/hr, 0.24 ml/hr, 0.36 ml/hr, and 0.48 ml/hr. All fluids that traveled through the microfluidic devices **200** and **400** were collected into a specially designed, serpentine waste chamber. Cell capture efficiency was determined by counting the number of cells captured in the devices (flat **200** or herringbone **400**) and dividing that number by the total number of cells put through the device (counting the cells in the waste chamber and adding that to the number of cells captured in the device).

For these experiments, three different flow rates were studied, with four data points taken for each condition. It is desirable that a device provide a high capture efficiency at high flow rates. This can reduce the time and sample size required to capture a desired number of cells of interest. As shown in FIG. **5**, the microfluidic device **400**, that included the herringbone pattern, outperformed the microfluidic device **200**, that has only flat surfaces, in cell capture efficiency for all flow rates. As flow rates increase, the advantage of the device **400** with the herringbone pattern increased. Even at very high flow rates, the capture efficiency for the device **400** with the herringbone patterns was ~50%, whereas for the device **200** without the grooves, it dropped to ~30%.

## EXAMPLE 2

## Capture Efficiency

FIG. **6** shows capture efficiencies for example microfluidic devices with and without grooves. Similar to the previously described experiments, the microfluidic device **200** having flat surfaces and the device **400** having the herringbone pattern were compared by determining the capture efficiency of cancer cells spiked into whole blood (5,000 cells/ml). The microfluidic device **400** used in this example was the small footprint design described with reference to FIG. **5**. Four different flow rates, similar to the flow rates described with