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Micromachined bubble-jet cell sorter with multiple operation modes

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Abstract

We present a high-speed microfluidic cell sorter employing embedded heaters and nozzles to generate deflecting jets to change the movement of the cells. We simulated the transient flow fields to validate the concept and optimize the sorter design. The simulation demonstrates spatial switching windows corresponding to 1.1, 1.5, and 2.4 times the switching chamber length for push, pull, and combined operation modes, respectively. A single-jet sorter with one actuator and one nozzle is also demonstrated for binary sorting. Experimental verification was obtained using micromachined devices characterized by stroboscopic measurements. With a 4.9 μs working period for the 20 μm × 20 μm heaters that generate the deflecting jets, the sorter can potentially attain a working frequency of 50 kHz or higher. We built a scattered-light based optical system to detect moving particles and successfully performed sorting of 20 μm microspheres. This type of sorter is promising for micromanipulation of a variety of biological cells and inorganic particles.

Keywords: Bubble jet; Cell sorting; Flow cytometry; Microfluidics

1. Introduction

Flow cytometric cell sorting rapidly separates cells one at a time based on optical or other properties [1]. The most widely used method is droplet sorting. Drops containing desired cells are charged and separated at very high speed (tens of thousand cells per second) by electrostatic deflection [2]. The enclosed-type cell sorter (e.g. BD FACSCalibur™) has the advantages of lower cost and aerosol-free environment for enhanced safety when processing biohazardous samples. Large cells and embryos can be sorted by mechanical switches, but this method suffers from slow sorting rates (100 cells/s or less) and large size [3]. Micromachined fluidic channels can replace conventional large flow chambers, and several research groups have reported using electro-osmosis [4], magnetic fields [5] and fluidic-switching [6] to manipulate cells. None of these previous reported micro sorting devices can provide a sorting speed comparable to that of the droplet sorter. In this paper we describe the design, simulation, fabrication and experimental verification of a micromachined thermal bubble-jet sorter capable of high speed cell sorting. Similar bubble actuators have been used to release particles from single-cell capture wells [7].

2. Design and simulation

The schematic drawing of the bubble-jet sorter is shown in Fig. 1. The sorter is comprised of one cell inlet channel and two buffer inlet channels that all open into a switch chamber with two outlet channels. The buffer inlets are connected to a common buffer source. Each buffer channels is terminated in a firing chamber and a nozzle connected to the switch chamber. A micro heater is integrated on the wall of the firing chamber. As a result of applying an electric pulse, one of the micro heaters generates a micro thermal bubble. The volume expansion of the bubble forces the buffer liquid to pass through the nozzle and to form a deflecting jet that pushes the selected cell toward the farther outlet. Compared to other sorting mechanisms, this method has the following advantages:

1. No external electrostatic or magnetic fields are required.
2. No slow pressure valves or switches are required.
3. No moving parts will cause clogging or mechanical failure.

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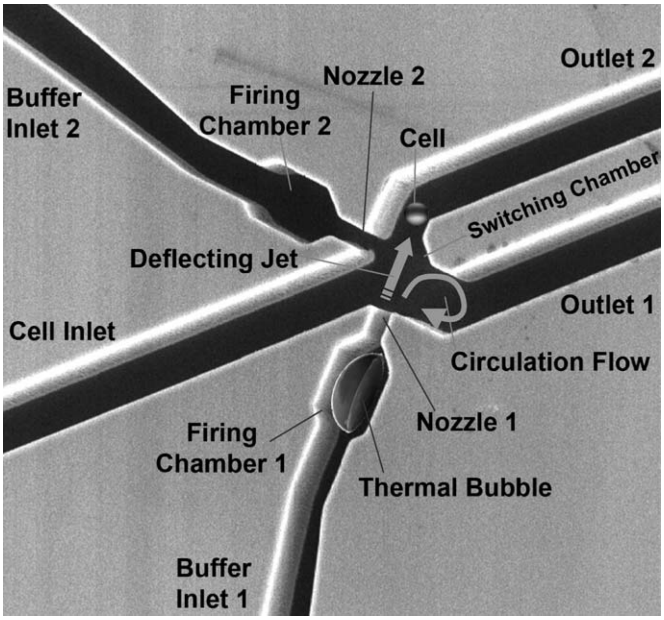

Fig. 1. Design of the high speed bubble-jet cell sorter.

We simulated the flow dynamics with the CFD-ACE+ software to validate the sorter concept and optimize the channel geometries and flow parameters of the microfluidic sorter design. The study employed the volume-of-fluid (VOF) method for free-surface flows with surface tension to model the floating cell motion in the transient incompressible fluid flow. The moving-wall and grid-deformation methods simulate the motion of the thermal bubble actuator and the volume change of the firing chamber. The displacement of the actuator can be specified by an oscillating mathematical expression with sine function. The fluid-flow model solves the coupled time dependent continuity equation, the pressure-based Navier–Stokes equations, and the energy balance equation.

Fig. 2 shows four instances of transient results of the simulated cell sorting. The upper actuator was activated when the cell entered the switch chamber. The actuator displaced and expelled the liquid into the nozzle and formed a jet that pushed the cell, as shown in Fig. 2(a) and (b). The actuator retracted after the cell left the switch chamber. A suction flow was formed to refill the firing chamber. Most of the refilling fluid came from the designated circulation zone as shown in Fig. 2(c). The cell was not pulled back by the suction flow.

We performed a series of simulations to study the switching window of the jet sorter. The actuator was activated when the cell passed different locations. If the actuator was activated too early, the cell entered the switching chamber while the actuator already retreated. The suction effect around the nozzle pulled the cell in the wrong direction. Fig. 3(a) shows an example of failed switching with two overlapping instances (the earlier one in lighter tone). On the other hand, if the jet was activated too late, the cell had already reached the dividing wall. The jet then pushed the cell against the wall, which resulted in marginal sorting. As shown in Fig. 3(b), the cell was deformed (lighter) and split into two parts (darker). The larger part still moved in the right direction. Within the switching window, W_{SW}, the cell can be successfully switched to the correct outlet, as illustrated

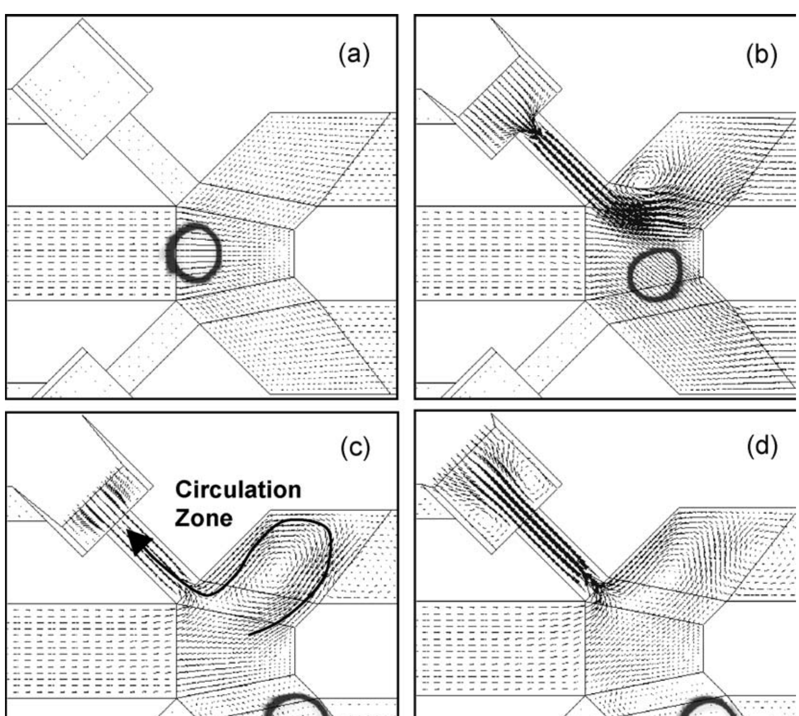

Fig. 2. Four consecutive instances of simulated cell sorting using deflecting jet.