A SINGLE-MICROBEAD-BASED MICROFLUIDIC DIODE FOR ULTRA-LOW REYNOLDS NUMBER APPLICATIONS
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ABSTRACT
Passive fluidic components that are capable of rectifying fluid flow at ultra-low Reynolds Number are critical to the advancement of micro/nanofluidic circuitry for diverse chemical and biological applications, such as sample preparation on chip, molecular diagnostics, point-of-care (POC) testing, and quantitative cell biology platforms. Previously, a wide range of diodic components have been developed to rectify flow in fluidic systems; however, engineering microfluidic diodes that function at the ultra-low Reynolds Number flows (i.e., Re < 0.25) of emerging micro/nanofluidic platforms has remained a considerable challenge. Here we present a microfluidic single-microbead-based diode (SMD) that uses a single suspended microbead as a dynamic resistive element to rectify fluid flow under Re ≤ 0.25 conditions. Simulations of the SMD yielded a theoretical diodicity (Di) of 1.4. Experiments for Re varying from 0.05 to 0.25 revealed average Di’s ranging from 1.14±0.01 to 2.51±0.03.

INTRODUCTION
Next-Generation Integrated Microfluidic Circuitry
Similar to the way in which integrated circuits (ICs) revolutionized electronics, the advent of integrated microfluidic circuitry could significantly impact the field of biology [1]. Microfluidics offers a variety of benefits for biochemical applications, including low reagent volumes and rapid reaction times. The introduction of an externally-controlled, multi-layer elastomeric microfluidic valve – often referred to as the Quake valve – provided the foundation for microfluidic circuitry research [2]. The first generation of integrated microfluidic circuits utilized high numbers of these valves to create large-scale integrated microfluidic processors (e.g., microfluidic memory arrays) [3-5]. In contrast to the aforementioned systems that are controlled externally (e.g., via computer-controlled flow pumps), recently, research has shifted toward the development of microfluidic chips capable of autonomous self-regulation, including flow oscillators, pressure-gain valves, and fluidic logic gates [6-8]. To fully realize the promise of the next generation of microfluidic circuitry for accomplishing functional biological and biomedical microprocessors, researchers will need to create robust microfluidic components that are analogous to those of electrical circuits.

Passive Microfluidic Diodic Components
For low Re flow associated with microfluidic systems, the contribution of the non-linear inertial term of the Navier-Stokes equation is minimal, thereby rendering “fixed geometry” valves (e.g., diffusers and Tesla valves) ineffective [9, 10]. To bypass this issue, researchers have primarily used double-layer “flap-type” check valves to achieve Di’s of 1.1 to 4.6 (i.e., for Re ≈ 1 to 35); however, prior reports have found that flap valves fail at Re < ~0.3 [10, 11]. Additionally, flap valves are constructed by means of multi-layer microfabrication processes, which are limited by increased costs, time, and labor versus single-layer photolithography and soft lithography processes. To bypass such limitations, Ou et al. presented a bead-based diode that employed up to 700 suspended microbeads to rectify flow at Re < 1 [12]. Although millimeter-scale ball valves have been successfully demonstrated in prior reports [13, 14], developing check valves that utilize a single microbead has remained a significant challenge. To achieve this goal, here we present a SMD to determine the potential resistive contribution of one suspended microbead in a rectangular channel, thereby providing a necessary foundation for future microbead-based fluidic diodes.

CONCEPT
Figure 1 shows illustrations of the SMD concept. Previously, microbeads have been effectively employed

![Figure 1. Conceptual illustrations of the microfluidic single-microbead-based diode (SMD). (a) Under forward flow, the microbead is released from the entrance of the trapping channel to promote fluid flow, and remains within the diode chamber. (b) Under reverse flow, the microbead is immobilized at the entrance of the trapping channel, which obstructs fluid flow through the SMD. This process can be repeated continuously by switching the flow polarity. (c) Initially, a single polystyrene microbead is pre-loaded under reverse flow via our micropost array railing (μPAR) technique [18].](image)
as a dynamic and versatile resistive element in a variety of microfluidic platforms, such as bead-based arraying systems [15-17]. In this work, a single suspended microbead is used to passively regulate fluid flow depending on the flow polarity. Similar to a “ball check valve,” the diode chamber of the SMD includes a trapping channel (5 μm in width; 18 μm in height) for microbead docking or releasing – to limit or promote fluid flow, respectively (Fig. 1a, b). The diode also includes our previously presented micropost array railing (μPAR) technique [18], which serves as a one-way track to ensure that after a suspended polystyrene microbead (15 μm in diameter) enters the diode chamber, the microbead is maintained within the chamber (regardless of the flow polarity) because the microposts (15×15 μm²) act as a physical barrier (Fig. 1a). During operation, a single microbead is pre-loaded into the diode chamber (Fig. 1c). Thereafter, both the microbead loading inlet and the microbead loading outlet are sealed (Fig. 2a). For forward flow, the microbead is released from the diode trapping position to facilitate fluid flow through the trapping channel (Fig. 1a). When the flow polarity is reversed, the microbead is re-immobilized at the entrance of the trapping channel, which obstructs fluid flow through the SMD (Fig. 1b). This process can be repeated continuously by switching the flow polarity as desired.

DEVICE FABRICATION

The SMD system can be manufactured using a variety of high-aspect ratio microfabrication techniques to fabricate devices with materials as desired (e.g., glass, polymers, etc.). For this study, the SMD system was fabricated via standard photolithography and soft lithography methods. Briefly, an 18 μm-high layer of SU-8 negative photosist was spin-coated onto a clean Si wafer. Using a photomask, the SMD patterns were UV exposed onto the layer of photosirest via contact photolithography. The wafer was then developed to become a positive master for the micromolding process. Next, the silicone elastomer, polydimethylsiloxane (PDMS), was mixed at a 10:1 ratio and poured onto the master. After curing of the PDMS at 55 °C, the elastomer was removed from the master. Individual devices were cut and then punched with holes at inlet and outlet locations. Glass slides were washed in successive dishes of Acetone, Isopropanol, and DI water, while the PDMS devices were washed in successive dishes of Isopropanol and DI water. The glass slides and PDMS devices were dried with a N₂ gun, and then exposed to UV ozone for 5 minutes. Lastly, the PDMS devices were thermally bonded to the glass slides at 55 °C. The final devices included arrays of rectangular microposts (15×15 μm²), with an interpost spacing of 5 μm. The trapping channel included a width of 5 μm. Figure 2 shows SEM micrographs of fabrication results for the SMD device.

RESULTS

COMSOL Multiphysics Fluid Dynamics Simulations

Three-dimensional fluid pressure field simulations were performed using COMSOL Multiphysics fluid modeling software for the two critical diodic states: (i) the forward flow case, where flow through the trapping channel is not obstructed by the microbead (Fig. 3a), and (ii) the reverse flow case, where flow through the trapping channel is obstructed by the microbead (Fig. 3b). Simulation results showed that the pressure drop across the trapping channel increases significantly from the forward flow case to the reverse flow case after a microbead is trapped (i.e., from approximately 80 Pa to 110 Pa) (Fig. 3). Quantified pressure drop results from pressure field simulations for Re varying from 0.05 to 0.25 revealed a theoretical Di of approximately 1.4.

Figure 2. Fabrication results for the SMD. SEM micrographs at magnifications of: (a) 100X, and (b) 1,000X. Scale Bars = (a) 100 μm; (b) 50 μm

Figure 3. Three-dimensional COMSOL Multiphysics pressure field simulation results for the SMD. (a) Forward flow case. Flow through the trapping channel is unobstructed by the microbead under forward flow. (b) Reverse flow case. Flow through the trapping channel is obstructed by the microbead under reverse flow.
Microbead Dynamics

Sequential micrographs of experimental results for microbead dynamics within the SMD are shown in Figure 4. For pre-loading of a suspended polystyrene microbead, the μPAR system successfully guided the microbead from the initial flow stream into the diode chamber during reverse flow (Fig. 4a). After reversing the flow polarity to achieve forward flow, the microbead was released from the diode trapping position and maintained within the diode chamber (Fig. 4b). By reversing the flow polarity again to achieve reverse flow, the microbead was transported to the entrance of the trapping channel and subsequently immobilized (Fig. 4c). Experimental device runs revealed this process to be repeatable through external switches of the flow polarity.

Diodicity (Di) Quantification

Values of Di for the SMD were quantified via Equation 1:

\[ Di = \frac{\Delta P_{\text{reverse}}}{\Delta P_{\text{forward}}} \]

where \( \Delta P_{\text{reverse}} \) and \( \Delta P_{\text{forward}} \) are the pressure drops measured from the inlet pressure to the outlet pressure of the SMD for the reverse flow and forward flow cases, respectively. Quantified Di results are presented in Figure 5. Experimental results for Re varying from 0.05 to 0.25 revealed average Di’s ranging from 1.14±0.01 to 2.51±0.03. Di was found to increase with increasing Re (Fig. 5a). For Re > 0.15, the experimental results were larger than the theoretical prediction. For example, the average Di’s from Re = 0.15 to 0.2 and 0.2 to 0.25 were 1.93±0.03 and 2.51±0.03, respectively (Fig. 5b). One potential basis for this behavior is the difference in the trapping channel geometry for the simulations versus the fabricated device. Specifically, the device design for the COMSOL simulations included ideal rectangular corners at the trapping channel (Fig. 3); however, the fabricated devices included a slightly rounded trap geometry (Fig. 2b). Higher fluid flow could force an immobilized microbead farther into the trapping channel, which would enhance the resistive contribution of a trapped microbead. This phenomenon could account for the comparatively higher Di’s observed during experimental device runs.

CONCLUSIONS

Micro/nanofluidic circuits offer the potential to revolutionize high-speed and high-content analysis for biological and chemical applications, as well as molecular diagnostics for low-cost healthcare systems. Thus, robust and passive on-chip fluidic components that function autonomously at ultra-low Re are in critical demand. In this work, we presented a single-layer bead-based diode that utilized a single suspended microbead as a dynamic resistive element. Through the use of suspended microbeads rather than elastomeric valve components,
limitations associated with multi-layer fabrication processes (e.g., increased costs, time, and labor) were bypassed. Both COMSOL fluid dynamics simulations and experimental device runs revealed Dir’s within the range of 1.14±0.01 to 2.51±0.03, corresponding to Re varying from 0.05 to 0.25. These results provide a baseline for future bead-based diodic components, such as potential extensions of this work where numerous single-microbead-based diodes are employed in series or in parallel. Although this method used spherical microbeads and rectangular channel geometries, it is expected that the use of circular microfluidic channels could greatly improve upon the diode performance reported in this work. Here, an asymmetric implementation of the μPAR technique was used to direct and then maintain suspended microbeads within the diode chamber; however, adaptations of the presented system can be developed to reduce device area requirements. For chemical and biological applications where microfluidic ICs are advantageous, such as POC molecular diagnostics and on-site chemical detection, the presented bead-based diode offers a simple, yet powerful single-layer methodology for rectifying fluid flow in microfluidic systems.

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