

Microfluidic mixer using magnetic beads

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Abstract. In this paper, we present a novel, simple and low-cost micromixer that is based on the manipulation of self-assembled structures by an alternating magnetic field of magnetic microbeads over the section of a microfluidic channel. The principle is demonstrated using a microfluidic chip of polymethylmetacrylate (PMMA) that contains a 200 μm wide Y-shaped microchannel and is integrated with soft ferromagnetic plate structures. The latter are part of an electromagnetic circuit and serve to locally apply a magnetic field over the section of the microchannel. The mixing efficiency depends on the fluid perfusion through the magnetic structure. Starting from a laminar flow pattern of parallel fluorescent and non-fluorescent liquid streams, we demonstrate a 95 % mixing efficiency using a mixing length of only 200 μm and at liquid flows of the order of 0.5 cm/s.

Introduction. In the field of miniaturized microfluidic devices for analytical chemistry and biotechnology applications, a rapid and efficient mixing is one of the most important challenges. In fact, the absence of turbulence at small scale restricts the mixing mechanism to that of molecular diffusion, which is a slow process [1]. Various approaches based on different physical mechanisms have been proposed to enhance the mixing efficiency (see [2] and the references therein). One of these approaches consists in placing obstacles in the microchannel in order to create stirring (convective) effects by forcing one fluid stream into another. In this paper, we demonstrate a new microfluidic-mixing concept, which is based on the manipulation by a local alternating magnetic field of self-assembled structures of magnetic microbeads that are placed over the section of a microfluidic channel. These objects, also known as magnetorheological structures (MRS), are formed by the particle magnetic dipole interaction and/or by the presence of a magnetic field. Such structure usually is composed of a very rich and complicated network of magnetic chains, and its size is determined by several competing magnetic forces [3]. Recently, the regular network of paramagnetic chains, formed under the action of a uniform magnetic field, has been demonstrated to be a new type of electrophoresis separation column for DNA analysis on-chip [4]. In our device, the mixing is the result of the chaotic convection generated by the MRS network. Another important factor is the possibility to induce a rotational motion of the magnetic microbeads by using an

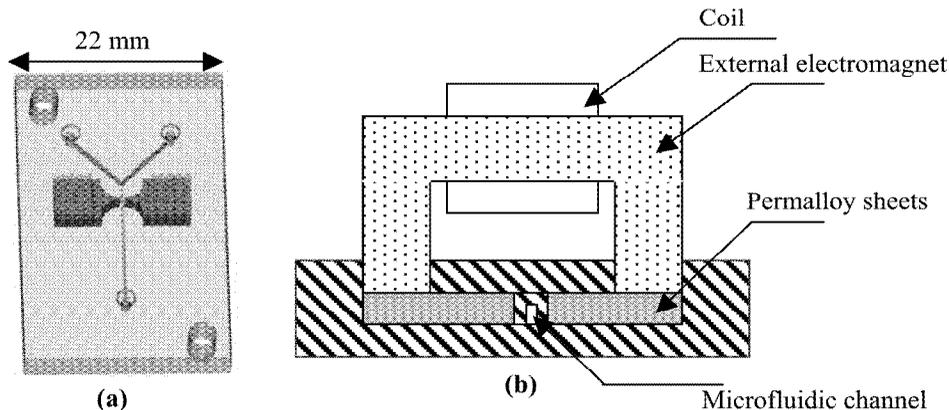


Figure 1: (a) Schematic diagram of the PMMA mixer chip with integrated Permalloy parts. (b) Schematic side view of the mixer chip combined with the external electromagnet.

alternating magnetic field [5]. This rotational motion will offer an additional active contribution to the mixing.

Microchip fabrication. Retention and manipulation of magnetic particles in a flow-through channel necessitates a very localized and large magnetic field. Therefore, we have integrated microstructured soft ferromagnetic permalloy sheets are integrated in a plastic chip near to the microchannel; these serve to transport and focus the magnetic flux generated by an external electromagnet. Figure 1(a) is a schematic diagram of the realised three-dimensional and monolithic microfluidic PMMA chip (22 mm × 32 mm) with embedded permalloy parts. This chip consists of a of 200 μm × 200 μm section Y-shaped microchannel that is composed of mechanically etched PMMA layers assembled with a MMA monomer solution. The hole structures at two opposite corners are used for pin alignment of the PMMA structured layers during the bonding process. Two openings (5 mm × 7 mm) adjacent to the microchannel serve to integrate the ferromagnetic permalloy parts. These parts are structured using laser cutting and end in a wide tip (typically 150 μm wide); the inner distance between the two tips (magnetic air gap), sandwiching the microchannel, is 0.5 mm. The tip width is a critical parameter, since it determines the localization of the generated magnetic field. This magnetic field is generated by an external electromagnet, brought in mechanical contact with the permalloy parts, as schematically shown in figure 1(b). The electromagnet, placed on top of the microchip, consists of an U-shaped pure iron core wired with 1500 Cu windings (wire diameter 0.12 mm).

Results and discussion. Figure 2 shows a typical finite element simulation of the magnetic induction over the channel length. A magnetic induction of 0.6 Tesla is calculated in the middle of the two tips, by just applying a current of 0.1 A in the coil.

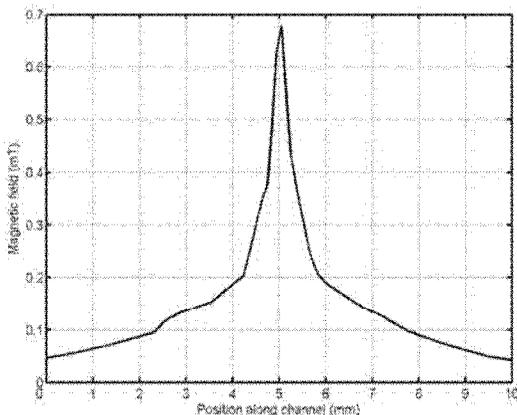


Figure 2: Typical finite element simulation of the magnetic induction over the channel length

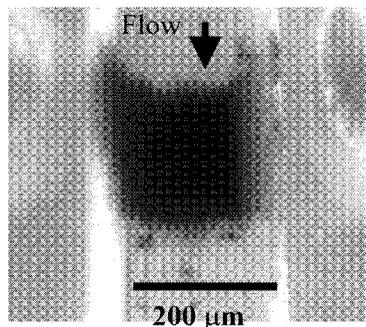


Figure 3: Magnetorheological structure in a microfluidic channel

The resulting magnetic induction gradient along the microchannel is strictly localized over a distance of the order the pole tip width. Figure 3 is a photograph of a MRS, composed of magnetic beads of few microns, retained by the magnetic field and placed in a water flow of 0.5 cm/s. The mixing efficiency is defined as [2]

$$E = \left(1 - \frac{\int_0^l |I_{am} - I_{\infty}| dx}{\int_0^l |I_{bm} - I_{\infty}| dx} \right) \times 100\%$$

where $I_{am}(x)$ is the fluorescent intensity distribution over the channel width l after the mixing area, I_{∞} is the fluorescent intensity at perfect mixing and $I_{bm}(x)$ is the fluorescent intensity distribution before the mixing area. We have quantified the mixing efficiency by monitoring the fluorescent intensity profile over the channel width. Fluorescent and non-fluorescent fluid streams are combined and mixing is said to be perfect when uniform fluorescent intensity is obtained over the channel. Figure 4(a) is a fluorescent intensity photograph of the two fluids forming the typical laminar flow pattern before the mixing region. When passing through the MRS region, the steady laminar flow will be strongly stirred. In this context, one can imagine that the mixing is the result of the chaotic splitting of the fluid streams through the MRS network. Another important factor is the collective dynamical behaviour of the MRS in an alternating magnetic field at low frequencies ($5 \text{ Hz} < f < 100 \text{ Hz}$). Briefly, this dynamics is the result of the rotation of the magnetic dipoles induced by the changing magnetic field polarity [4]. We can easily use in our set-up time-dependent magnetic fields to induce such motion of the MRS. Figure 4(b)-(c)

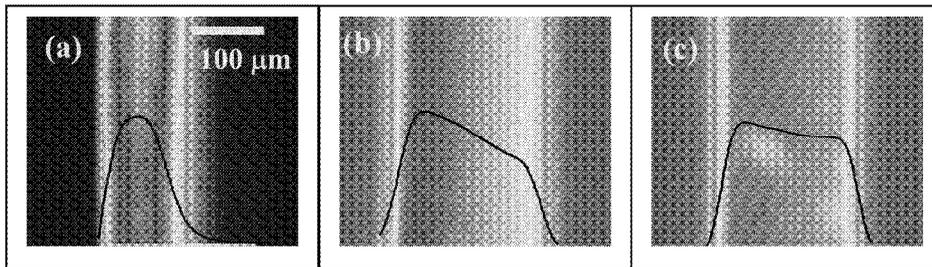


Figure 4: Mixing efficiency using parallel fluorescent and non-fluorescent streams monitored before (a) and after (b, c) the active MRS region; (b) is obtained using a static and (c) using a dynamic magnetic field. For each case, the profile of the fluorescent intensity over the channel cross-section is indicated.

show the fluorescent intensity of the flow after passing through the MRS at a flow rate of 0.5 cm/s. When a static field is used (figure 4(b)) about 70 % mixing efficiency is obtained, while we reach a nearly perfect mixing of 95 % using an alternating magnetic field.

Conclusion. We have developed a new mixing concept, which is based on the retention and manipulation of magnetic microbead structures held in place in a microchannel under a flow by a magnetic field. The mixing efficiency directly depends on the fluid perfusion through the magnetic structure, which in turn depends on the magnetic field. We demonstrate this concept using a plastic microchip with integrated soft ferromagnetic plate structures, which are part of an external electromagnetic circuit and which focus a magnetic field over the section of the microchannel. The results show the possibility to reach a nearly perfect mixing when a sinusoidal magnetic field is applied. These results are obtained by using an active MRS mixing area of only 150 μm long and at a flow rate of 0.5 cm/s, which is one of the best mixing performances reported yet.

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