

OVERCOMING THE DIFFUSION BARRIER: ULTRA-FAST MICRO-SCALE MIXING VIA FERROFLUIDS

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Abstract: We report on the design, development, fabrication and characterization of a novel, micro-scale mixing device based on stable water suspensions of magnetic nanoparticles (i.e. ferrofluids). The micro-mixer prototypes are built using standard microfabrication and simple soft-lithography, and the design can be incorporated as a sub-system into any chemical micro-reactor or a miniaturized biological sensor. The devices achieve mixing virtually instantaneously and may be used to greatly increase mass transport towards chemically or biologically active sites on lab-on-a-chip devices for rapid incubation and highly improved detection sensitivity.

Keywords: ferrofluid, ferrohydrodynamics, micromixer.

1. INTRODUCTION

On-chip biological and chemical analysis devices, often called micro-total-analysis-systems (μ TAS) or labs-on-a-chip, have received significant attention over the past decade [1]. Miniaturization of analysis systems offers many advantages: small footprints for the devices, low cost, short times for analysis, the ability to use small quantities of samples and reagents, as well as separations and detections with high resolution and sensitivity [2]. A μ TAS device typically incorporates micropumps, micromixers, reaction chambers and detectors. A bottleneck inherent in this miniaturization is that flow regimes are typically laminar, and diffusion processes limit reaction rates, analyte accumulation times and ultimately, detection sensitivities.

Rapid and efficient mixing is critical to most μ TAS systems because many biological processes - such as DNA hybridization, cell activation, enzyme reactions, and protein synthesis - demand rapid reactions which inevitably require efficient mixing of the reagents. Typically, biological reagents have relatively low diffusion coefficients; for a diffusion-based device, the mixing process can take on the order of tens of seconds or minutes. This is particularly true when the solution contains macromolecules (e.g., DNA and proteins) or large particles (e.g. bacteria and blood cells) that have diffusion coefficients orders of magnitude lower than that of most small molecules.

In general, micro-scale mixing methods can be categorized into passive and active schemes. Passive micromixers utilize complex channel geometries to increase the interfacial area between liquid streams, in order to reduce diffusion lengths. They are typically designed for a given flow rate and may require multilayer fabrication processes for their microchannels. Examples of such mixers include parallel [3] and serial [4] lamination micromixers, as well as three-dimensional serpentine channel designs for chaotic advection [5].

Active micromixers, on the other hand, require moving parts or external energy input to enhance mixing. Depending on the application, their faster mixing rates may outweigh the complications of integrating electrodes or actuators in their designs. Among active micromixers, those based on electromagnetic forces directly on the carrier liquid are typically more practical, compact and easier to integrate; classic examples of such mixers rely on dielectrophoretic [6], electrohydrodynamic [7], electrokinetic [8] or magnetohydrodynamic [9] effects.

Here we introduce a new microfluidic mixing concept, one based on ferrohydrodynamic actuation [10], involving the manipulation of an entire ferrofluid stream via local alternating magnetic fields. Water-based ferrofluids can be made bio-compatible with relative ease and may be utilized in highly-sensitive and integrated pathogen detectors (Fig. 1). The rapid mixing within ferrohydrodynamic micromixers may also

be utilized to overcome the diffusion barrier in other integrated biosensors [10].

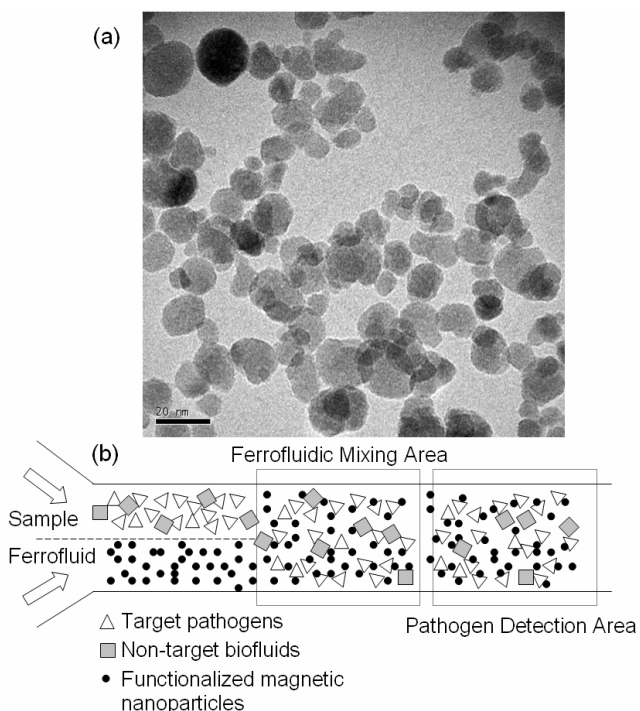


Figure 1: (a) TEM image of magnetic nanoparticles in a commercial ferrofluid (EMG 700, FerroTec, Nashua, NH); the scale bar represents 20 nm. (b) Schematic diagram of the ferrohydrodynamic micromixer concept.

2. EXPERIMENTAL SECTION

The flow channel (103 μm deep, 300 μm wide) of the ferrohydrodynamic micro-mixer (Fig. 2) is defined by soft lithography [11] with poly(dimethylsiloxane) (PDMS). It forms a 45° angle with respect to embedded electrodes carrying traveling magnetic waves, which act on the ferrofluid/analyte interface and create local vortices that accelerate mixing. Copper electrodes (35 μm high and 240 μm wide) are patterned on a metal insulated substrate using standard wet etching of the top copper layer [12]. SU-8 negative photoresist is used as the etching mask. The copper electrodes are connected by wire bonds to form a two-phase traveling magnetic wave, which is generated using a current amplifier driven by two phase-locked function generators. A thin layer of black paint is used over the electrodes to create an optically uniform background for subsequent experiments.

A water-based commercial ferrofluid (Fig. 1) is introduced through one inlet of the micro-mixer. The other inlet carries a pH-matched fluorescein solution, and the mixing process in the main channel is monitored optically (Zeiss Axioplan with a QImaging RETIGA 2000R CCD camera; see Fig. 2c).

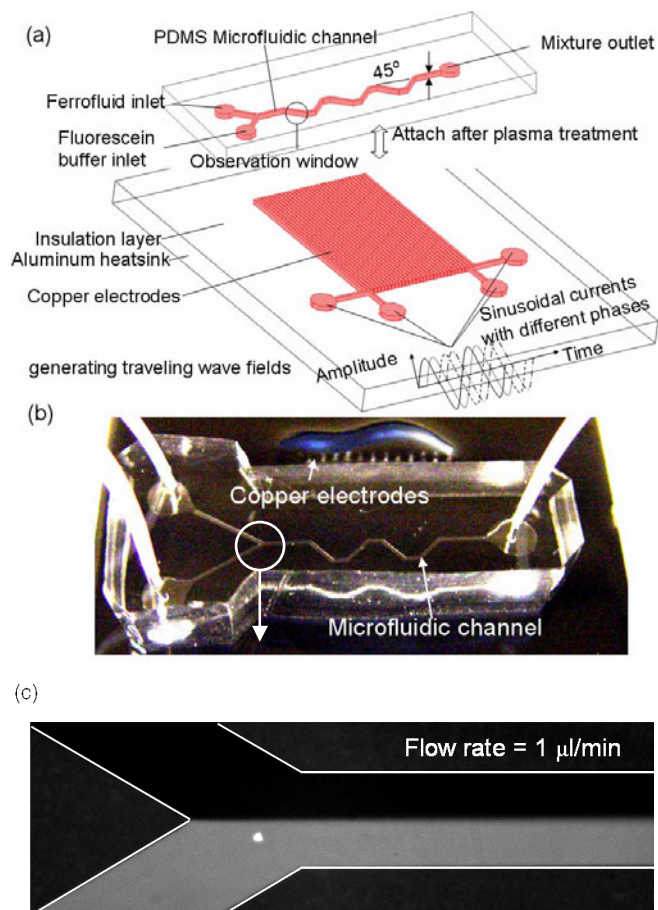


Figure 2. (a) Schematic diagram of the ferrohydrodynamic micromixer; (b) image of the actual device; (c) a fluorescent image depicting the intersection of the ferrofluid (dark) and fluorescein buffer inlets. Gravity-induced fluid reorientation is not obvious at the intersection.

3. RESULTS AND DISCUSSION

Time-stamped fluorescent images (Fig. 3) obtained using the ferrohydrodynamic micromixer reveal the effectiveness of the mixing scheme. Within the first second of the excitation signal, the flow becomes unstable and vortices in the flow quickly mix the ferrofluid with the fluorescein

buffer. This phenomenon occurs throughout the microfluidic channel. Pressure-driven bulk flow rate in the channel is $1 \mu\text{l}/\text{min}$, and the observation window is only 5 mm downstream from the intersection of the inlets.

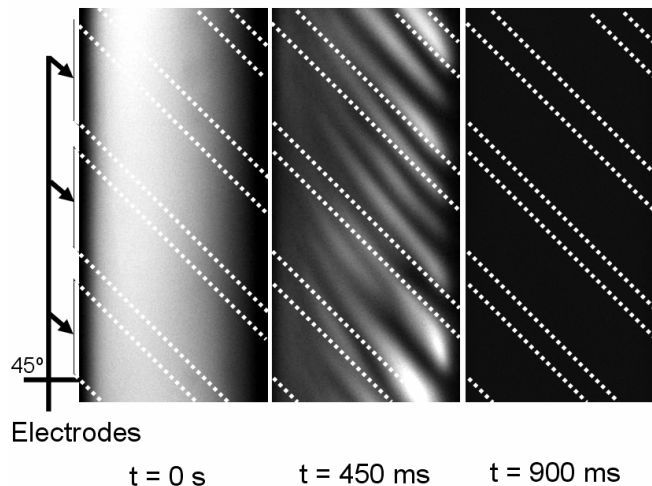


Figure 3. Time-stamped fluorescent images obtained using the ferrohydrodynamic micromixer (at the observation window shown in Fig. 2a) depict an initially laminar profile mixing via diffusion alone and the development of flow instabilities after the onset of the magnetic traveling wave excitation (10A current peak-peak, 1 kHz excitation). Bulk flow rate is $1 \mu\text{l}/\text{min}$

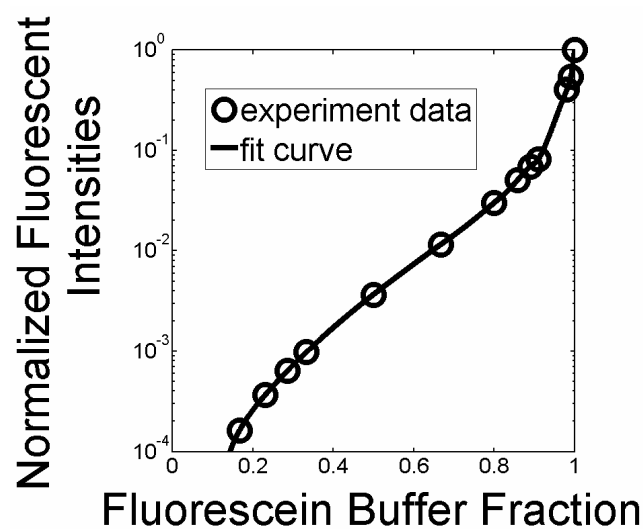


Figure 4. Fluorescence intensity calibration curve (as a function of relative fluorescein fraction within the ferrofluid) for the camera used in this experiment. The nonlinearity stems from the low transparency of the ferrofluid.

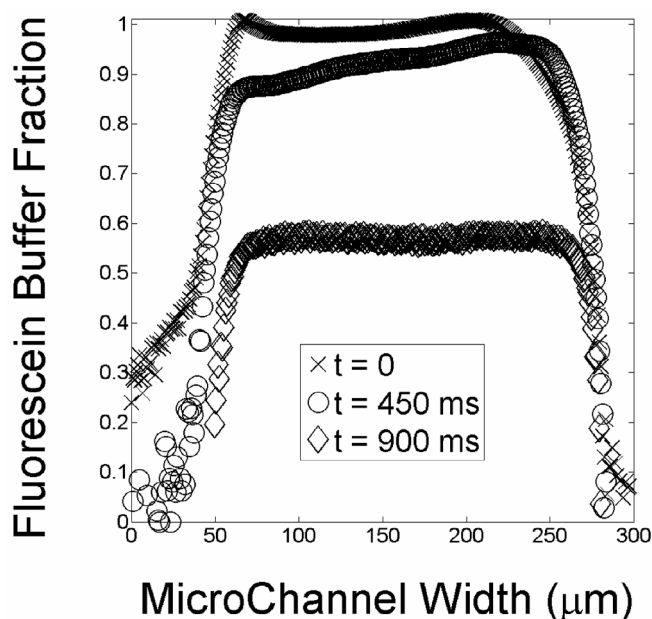


Figure 5. The evolution of fluorescein buffer fraction profile in the microchannel (cross-section intensities are averaged from Fig. 4). The microchannel upper section is initially fluorescein dominated, but quickly tends to a 56% uniform distribution upon application of the traveling wave magnetic field.

Since the ferrofluid used is nearly opaque, an optical calibration is performed to translate the concentration of the fluorescein buffer to a normalized fluorescence intensity, as shown in Fig. 4. With this nonlinear intensity dependence curve, the evolution of fluorescein buffer concentration profile in the microchannel is plotted in Fig. 5. Because the density of the ferrofluid ($1.35 \text{ g}/\text{ml}$) is higher than that of the fluorescein buffer ($1 \text{ g}/\text{ml}$), a gravity-induced pressure mismatch at the interface of the two fluids gradually drives the less dense fluorescein buffer to occupy the upper portion of the microchannel [13]. Therefore, the initial fluorescein buffer concentration depicted in Fig. 5 is close to 100 % at $t = 0$. Once the excitation is turned on, the fluorescein concentration quickly (within 0.9s) tends to a uniform distribution centered on a steady-state value (56 %).

Fig. 6 depicts the effectiveness of ferrohydrodynamic mixing as a function of different excitation frequencies. It is determined that the optimal mixing frequency is about 1 kHz.

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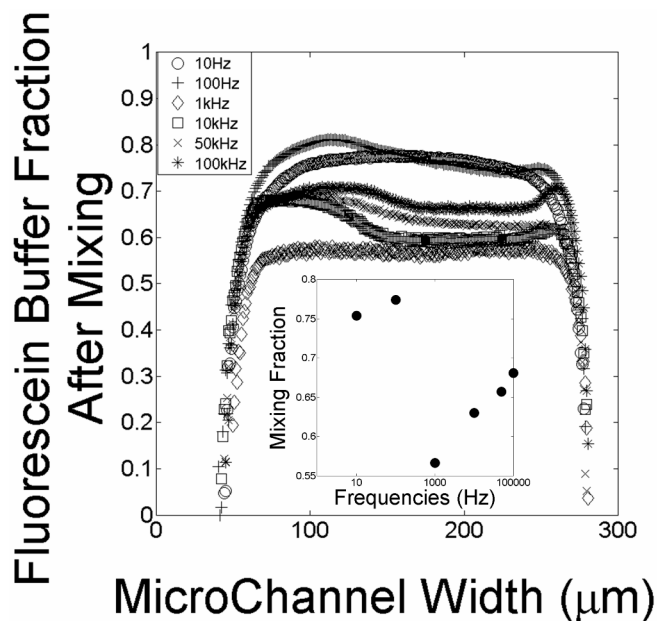


Figure 6. Variation of fluorescein buffer fraction after mixing as a function of applied magnetic field frequencies (10A current peak-peak, flow rate 1 μ l/min). The insert figure shows the averaged fluorescein buffer fraction across the channel.

4. CONCLUSIONS

A novel micro-scale mixing scheme based on ferrohydrodynamics has been introduced and demonstrated. A prototype micromixer has been fabricated and characterized for mixing water-based ferrofluids with a fluorescein buffer solution. Compared with passive mixing methods that rely on diffusion directly, ferrohydrodynamic mixing requires a relatively short microfluidic channel segment to achieve nearly complete mixing. Moreover, unlike other active mixing methods that rely on electromagnetic body forces acting directly on a liquid, this micromixer requires a very low-voltage excitation, and therefore is relatively insensitive to fluid properties, such as density, viscosity, dielectric constant, breakdown voltage, charge density, etc. Ferrohydrodynamic mixing is a robust, flexible and widely usable technology; with the advent of bio-compatible ferrofluids, it offers a viable and practical alternative for micro-scale mixing.

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