CHAOTIC FLUID MIXING BY ALTERNATING MICRO-PARTICLE TOPOLOGIES TO ENHANCE BIOCHEMICAL REACTIONS

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ABSTRACT

We report experimental results on chaotic mass transport induced by alternating topological changes of magnetic particle chains actuated by a rotating magnetic field. We show the induced fluid flows and the level of fluid mixing for (1) the regime of rigid chain rotation and (2) the regime in which the chains periodically fragment and reform. The effects of the different actuation regimes on a biological binding reaction in the solution are also reported. We conclude that the alternating topological change of microparticle chains is an effective mechanism to achieve chaotic mixing and thereby promote and homogenize reactions in lab-on-a-chip systems.

KEYWORDS

Microfluidic flow, Microfluidic mixing, Magnetic particles, Particle dynamics, Affinity assay.

INTRODUCTION

Magnetic micro- and nanoparticles are being applied in lab on chip systems as labels, sorters, capture particles, transporters and mixers. In such applications, external magnetic fields are used to manipulate the particles and thereby the fluid and the biochemical materials. Specifically, there is an interest to achieve effective mixing by chaotic fluid transport [1] in order to promote reactions and homogenize the biochemical processes.

A recent approach is to apply rotating magnetic fields in order to generate chaotic fluid transport. Numerically and experimentally, rotating magnetic particle chains have been observed to induce enhanced mixing [2-4]. Under certain circumstances, the formed bead chains begin to periodically break-up and reform. Kang et al. [4] concluded from numerical simulations that this repeating topological change of the particle chains should be the most efficient way to induce chaotic mixing. In this paper, we show experimental proof of chaotic fluid mixing. We report experimental results on the fluid flows induced by rotating magnetic particle chains, for (i) the regime of rigid chain rotation and (ii) the regime wherein chains periodically fragment and reform.

EXPERIMENTAL SYSTEM

An octopolar electromagnetic system has been designed for full three-dimensional control of the magnetic fields over a wide range of frequencies (Fig. 1). The setup consists of 8 individually controlled copper coils (brown) together with 8 soft-iron (ARMCO®) poles (grey) connected by soft-iron frames. Magnetic fields are produced by the flow of electrical currents through the coils and the fields are guided to the fluid cell by the soft-iron frames. At the center of the sample area, a closed fluid cell is placed which contains a suspension of particles

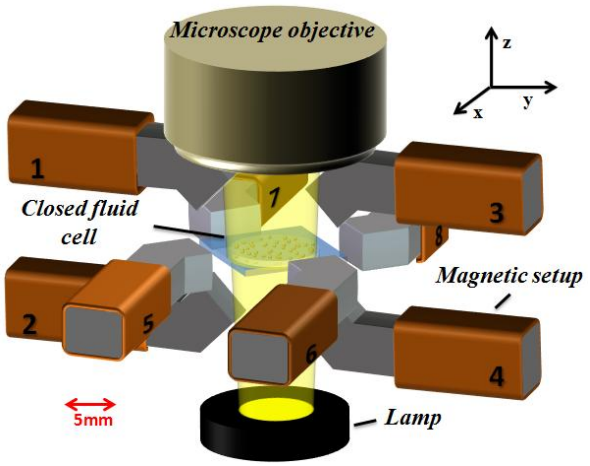

Fig. 1 The octopolar electromagnetic system.

Flow analysis experiments were conducted with superparamagnetic microparticles (3 μm) and fluorescent tracer particles (0.5-0.2 μm). The corresponding bulk solution was a high viscosity fluid (~6 mPa·s) used to limit the diffusive mass-transport of the fluorescent tracer particles and the sedimentation of the magnetic particles. Incubation experiments were conducted utilizing streptavidin-coated magnetic capture particles (3 μm, $4 \cdot 10^6$/ml) and biotin-coated fluorescent target particles (200 nm, $2 \cdot 10^6$/ml). A buffer solution (PBS with 10 mg/ml BSA) was used to suppress nonspecific interactions.

RESULTS AND DISCUSSSION

Particle tracking experiments were conducted with isolated rotating magnetic particle chains, for (1) the regime of rigid chain rotation and (2) the regime wherein chains periodically fragment and reform. To quantify the fluid flow induced by the rotating magnetic particle chains, we followed the small tracer particles in close proximity to the rotating magnetic particle chains using an in-house built particle tracking software with a resolution of 2 pixels per μm.

In the case of rigid rotating chains, the overall trajectories of the tracer particles are steady slightly modulated circles around the center of the microparticle chains (Fig. 2A). In the regime wherein chains break and reform, the tracer-particle trajectories indeed become chaotic (Fig. 2B).

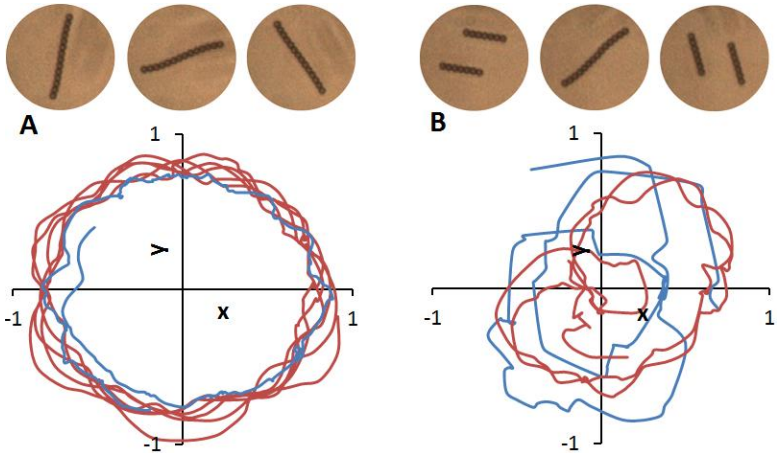

Fig. 2 Experimental rotating magnetic particle chains and the induced tracer particle trajectories. The plotted trajectories are scaled to unit length. (A) Rigid rotating chain behavior. The overall trajectories of the tracer particles are steady slightly modulated circles around the center of the rotating chain. (B) Alternating fragmentation and reformation of a rotating chain. The induced tracer particle trajectories become chaotic.

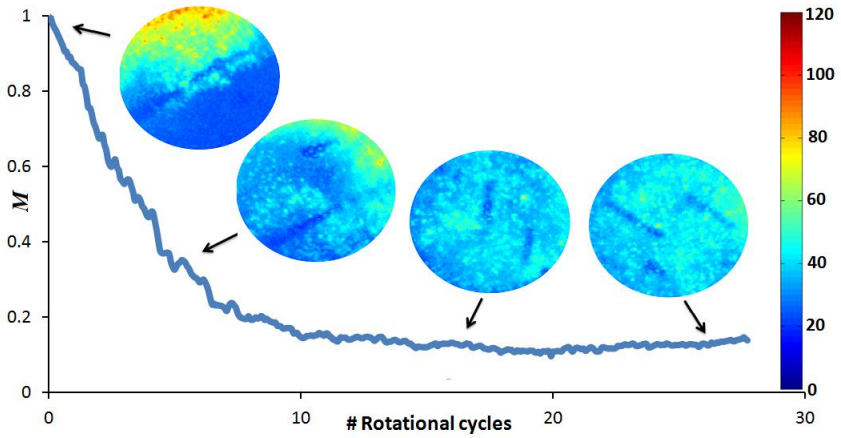

Fig. 3 Chaotic fluid mixing induced by the alternating topological change of a rotating magnetic particle chain. Intensity of segregation (M) is plotted with respect to the amount (#) of rotational cycles. The color bar indicates the intensity of the fluorescent mixing dye. In the unmixed state: M=1 and a clear interface can be seen between the dye and the uncolored water. After 15 rotational cycles, the two fluids are mixed and M drops to 0.1 and remains constant.

Mixing was evaluated by introducing a concentrated drop of fluorescent dye-particles into the fluid cell and visualizing the spatial-temporal variation of the (fluorescent) dye-water interface using in-house built image analysis software; the resolution was 2 pixels per µm. The software is capable of extracting the fluorescent intensity (I) of fluid in a defined area. In this study, we were interested in the local fluid mixing occurring within the rotational range of a magnetic particle chain.

We characterized the mixing using a modified version of the intensity of segregation (M) [3], i.e. in a perfectly mixed system M=0 while in an unmixed system M=1. When particle chains periodically break and reform, we observe that M decreases from 1 to 0.1 within 15 rotational cycles, and then remains constant (Fig. 3), which constitutes an experimental proof of the occurrence of chaotic fluid mixing.

We also characterized the effects of the different mixing regimes on a biochemical binding reaction in the solution, and indeed found that the kinetics are significantly enhanced by the chaotic mixing regime as compared to the non-chaotic regime (Fig. 4). Specifically, rotating streptavidin-coated magnetic particle chains were employed and the fluid was seeded with biotin-coated fluorescent target particles.

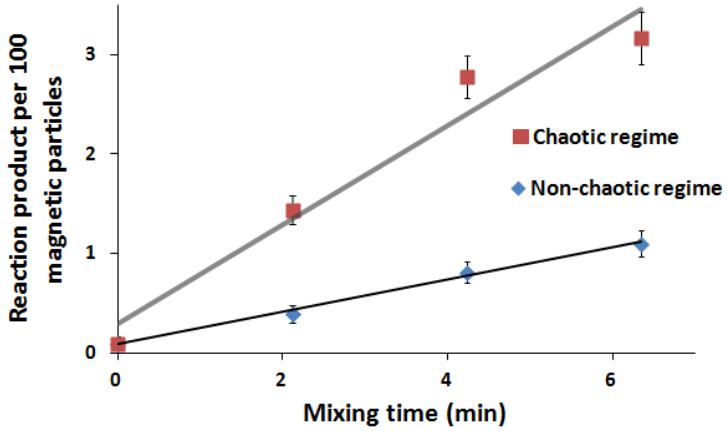

Fig. 4 Reaction product as a function of the mixing time. The chaotic regime corresponds to the chain dynamics of fragmentation and reformation. The non-chaotic regime corresponds to rigid rotating chain behavior. An enhancement of the reaction kinetics can be clearly seen for the chaotic regime when compared to non-chaotic regime.

CONCLUSION

We conclude that the alternating topological change of the microparticle chains – with repetitive chain breakup and chain reformation – is a key mechanism to achieve chaotic mixing and thereby promote and homogenize reactions in lab-on-a-chip systems.

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