MANIPULATION OF MAGNETIC PARTICLES IN μ-FLUIDIC VOLUMES

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ABSTRACT

This paper reports various ways of field-based manipulation of magnetic colloidal particles to enhance biochemical reactions in lab-on-chip systems [1]. For one (I), we show the possibility to assemble the suspended magnetic micro-particles as tunable re-formable micro-stirrers capable of performing enhanced micro-scale mixing and biochemical-assays. Secondly, we show that (II) magnetically-induced clusters and aggregates of magnetic micro-particles can be dis-assembled (within 1 minute) into individual entities using time-varying magnetic fields. Lastly, we show (III) that very strong vortical fluid flows (1 mm/s) can be induced by a so-called swarm of magnetic particle chains, resulting in an en-hancement of biochemical capture kinetics.

KEYWORDS: Magnetic micro-particles, Mixing, Biochemical assays

INTRODUCTION

Magnetic colloidal particles as field-responsive micro-structures have many applications in micro-scale systems, for example as actuators to generate fluid flows, as stirrers to mix laminar fluid streams and, when functionalized with bio-specific surface coatings, as mobile binding sites for biochemical assays. Here, we report various ways of field-based ma-nipulation of magnetic colloidal particles to enhance biochemical reactions in lab-on-chip systems.

RE-FORMABLE MICRO-STIRRES

One of the most well-known strategies for micro-scale mixing is the stirrer strategy. We have implemented this strate-gy by exposing a suspension of magnetic particles (Figure 1) to a horizontal rotating magnetic field, thereby creating ro-tating chains of magnetic particles.

Within a specific range of field magnitude, field frequency and fluid and particle properties, chains of magnetic parti-cles periodically self-assemble and thereby induce chaotic fluid flow. When compared to rigid rotating particle chains, the breakup and reform of particle chains (Figure 2) gives a significant enhancement in both mixing (5x) as well as particle-based target capture (3x), utilizing an assay with streptavidin coated magnetic capture particles (MC, 3 μm, $4 \cdot 10^6$/mL) and biotinylated target particles (FT, 200 nm, $2 \cdot 10^6$/mL) [2].

When compared to a purely diffusional process, i.e. a collection of static magnetic capture particles, rotating chains of magnetic particles that break and reform show a 10x enhancement of the reaction rate constant.

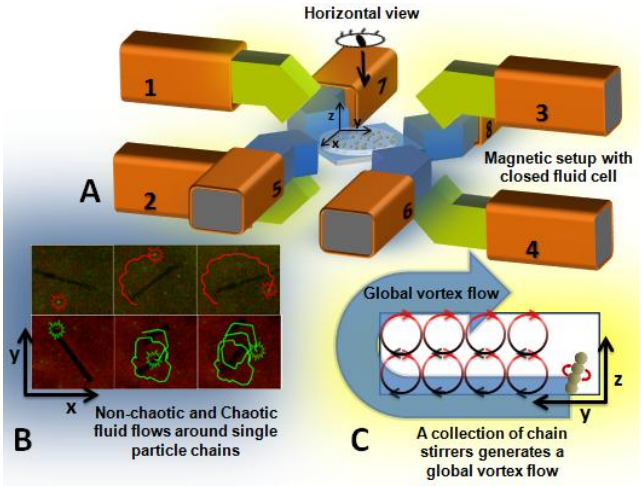

Figure 1: (A) A suspension of magnetic particles is placed in a closed fluid cell at the center of a magnetic setup capable of generating horizontal (blue) and vertical (yellow) rotating magnetic fields and field gradients. (B) Rotating particle chains are formed that either rotate rigidly (red) or they breakup and reform while rotating (green). We follow the motion of a tracer particle in order to record the induced fluid flow near the rotating chains at different time steps. (C) Rotating particle chains act as stirrers and the stirring of fluid by the magnetic micro-stirrers induces a global vortex flow of fluid and particles, as shown in Figure 4.

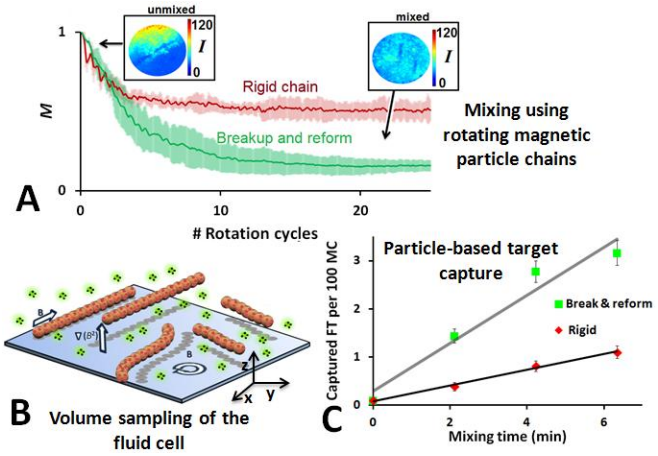

Figure 2: (A) We compare the mixing efficiencies between rigid and re-formable rotating magnetic particle chains, utilizing a mixing index M, i.e. in a unmixed state M=1 while in a mixed state M=0. When chains breakup and reform, M decreases to a value of 0.1, indicating good mixing. (B) The magnetic capture (MC) particles are functionalized with streptavidin and are used to capture biotinylated fluorescent targets (FT). Utilizing fields and field gradients, we are able to move the rotating particle chains through the entire cell volume. (C) Magnetic particle chains that periodically breakup and reform result in a higher target capture, i.e. 3 FT per 100 MC.

DISAGGREGATION OF PARTICLE CLUSTERS

The formation of well-defined particle chains is not obvious. When the particles (3 µm, 10^8/mL) are exposed to a magnetic field, there is a natural tendency of the particles to form multi-particle clusters or aggregates. The clustering reduces the access of target to the particles and thereby reduces the effectiveness and reproducibility of the biochemical assays. Furthermore, the clustering is often not easily reversed, because diffusive particle motion is slow and weak non-specific interactions can keep the particles together.

We show the possibility to disaggregate large clusters of tens of particles within one minute (Figure 3) [3]. After the disaggregation process, the magnetic particles are uniformly distributed over the surface and ready for further lab-on-chip processing.

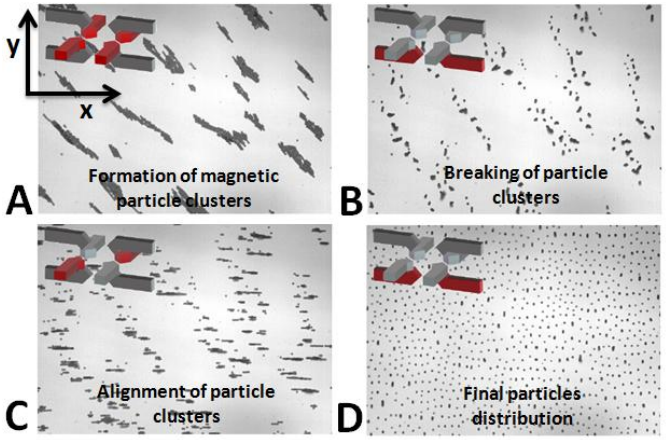

Figure 3: (A) Utilizing horizontal rotating magnetic fields, large chain-like aggregates of magnetic particles are formed at the cell floor. In (B), a vertical magnetic field is applied, orthogonal to the cell floor, to generate magnetic dipole-dipole repulsions which break the particle aggregates into smaller entities. In (C), a horizontal field is applied to realign the broken clusters with the cell floor. The protocols (B) and (C) are performed repeatedly, in sequence, to break the remaining aggregates. (D) The final particle distribution consists of individual small entities distributed uniformly over the cell floor.

VORTICAL FLOWS DUE PARTICLE SWARMING

Lastly, we show the generation of very strong fluid flows induced by a swarm of actuated magnetic particles (10 µm) (Figure 4) [4]. We demonstrate a stable and global vortex flow of fluid and particles stretched along the entire width of the fluid cell (9 mm), with many eddy-type substructures that fluctuate continuously in time, resembling turbulent flow, even though inertial effects are absent due to the low Reynolds number. We have applied the phenomenon of swarming particles to a biochemical assay with magnetic capture particles (4000/µL) and fluorescently labelled IgG targets (500

pM). When compared to a purely diffusion-based capture process, magnetic actuation leads to a ~9 times enhancement of the binding kinetics of the assay.

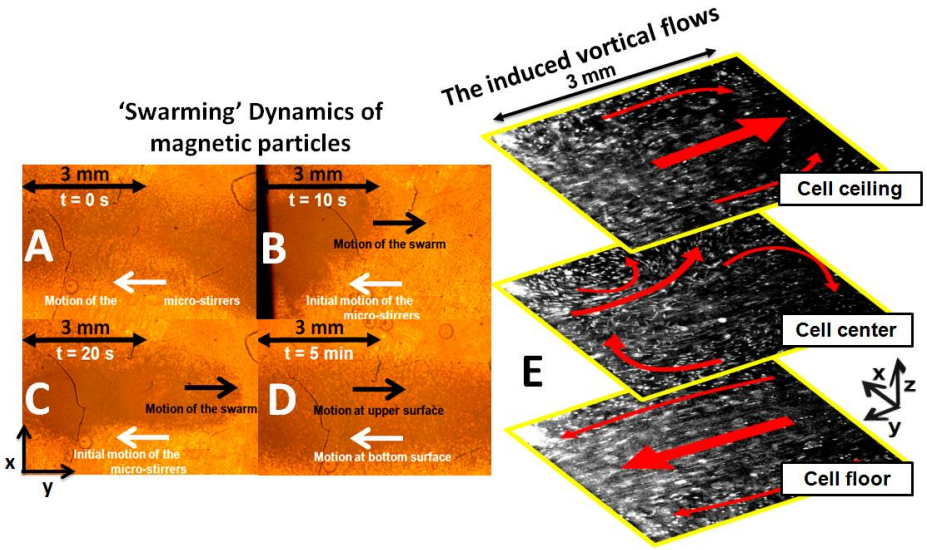

Figure 4: The formation of a global vortex flow of fluid and particles generated by the local stirring of many individual magnetic micro-stirrers as shown in Figure 1(C). (A) The motion of the particle chains at the cell floor is towards the left. (B and C) After reaching the cell left-end, a swarm of magnetic particles is formed that translates to the right at the cell ceiling. (D) A global vortex flow of magnetic particles is formed with particle chains moving to right at the cell ceiling and particle chains moving to the left at the cell floor. (E) We visualize the corresponding induced vortex fluid flow using fluorescent tracer particles (white spots) at different heights in the fluid cell. At the cell surfaces, the fluid flow is unidirectional while the fluid flow at the center is characterized by many eddy-type substructures

CONCLUSION

Actuation of the magnetic micro-particles can create enhanced mixing and enhanced biochemical reactions in lab-on-chip systems. The alternating topological change of the micro-particle chains – with repetitive chain breakup and chain reformation – is a key mechanism to achieve chaotic mixing and enhanced homogenizations of reactions in microfluidic systems. A swarm of magnetic micro-particle chains, on the other hand, can generate very strong and global fluid flows embedded with many eddy-type substructures throughout a whole liquid volume. Chains and clusters of magnetic micro-particle can also be broken up using time-varying magnetic fields.

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