Electromagnetic Mixer for Low-Response Paramagnetic Particles

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ABSTRACT

Surface functionalized magnetic particles are used widely in sample processing.[1-3] They provide convenient automation options for removing, adding, and manipulating reagents in a well-controlled manner. However, the mixing is mainly achieved by mechanical agitation, with less effective particle dispersion. Recently, we introduced an electromagnetic sample preparation platform that contains a set of electromagnets with AC frequencies and field strengths tuned for optimal beads trajectories within the sample vial, which worked well for the high-response ferromagnetic particles.[4-5] However, low-response paramagnetic particles are more commonly applied in real assays. In this study, we describe the electromagnetic mixer system that could efficiently process the samples containing low-response paramagnetic beads.

INTRODUCTION

Methods using magnetic beads have been widely used for sample preparations. However, the magnetic property of particles is utilized only during the buffer exchange (supernatant removal) process. The sample mixing with surface-functionalized beads is still achieved by mechanical agitation (e.g. shaking, pipette mixing).[6] With these methods, magnetic particles may aggregate and cluster in discrete areas close to the walls of the container, greatly reducing mixing efficiency. In addition, it is challenging to solve the problems of resuspension of dried particles and the generated bubble during mechanical mixing.

Recently, we introduced the electromagnetic mixer designed for high-response ferromagnetic particles. Oscillating electromagnetic fields (300-350 Hz) were used to fully disaggregate magnetic beads, allowing an optimal exposure and enhanced mixing with surrounding liquid medium. The reaction kinetics can be significantly improved (>10x). Figure 1 shows the system designed for ferromagnetic particles.

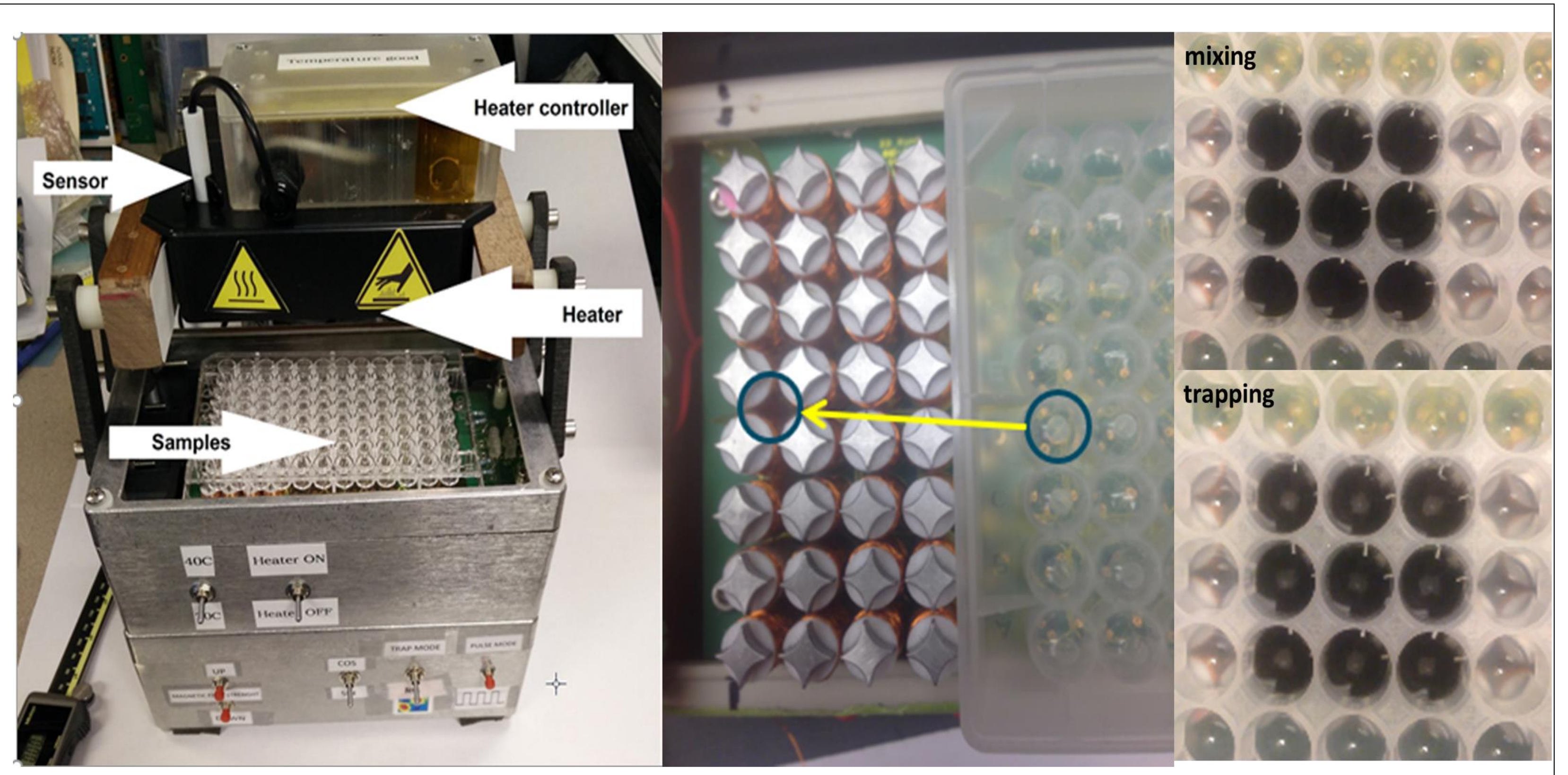


Figure 1. Electromagnetic mixer designed for ferromagnetic particles.

Low-response paramagnetic particles such as Dynal beads and SPRI beads are widely used in beads-based sample preparation assays. In this study, several critical modifications have been made to enable the system work for these beads with much lower magnetic responses.

HARDWARE DESCRIPTION

Orientation of the electromagnets:
In order to increase the localized magnetic field strength, the electromagnetic field orientation (N to S) are modified from vertical (along z-axis) to within the x-y plane, as shown in Figure 2.

Electromagnets for ferromagnetic particles | Electromagnets for paramagnetic particles

Figure 2. Electromagnets orientation for ferromagnetic and paramagnetic particles

AC waveforms:
The square-shaped AC waveform was applied to the electromagnets for the system designed for paramagnetic particles in stead of sin-waveform for high-response ferromagnetic beads, so that the maximized electromagnetic field strength would be applied for longer periods (Figure 3). The phase delay was kept the same, which was 90° for adjacent electromagnets.

Waveform for ferromagnetic particle mixer | Waveform for paramagnetic particles mixer

Red and blue: currents for two adjacent electromagnets

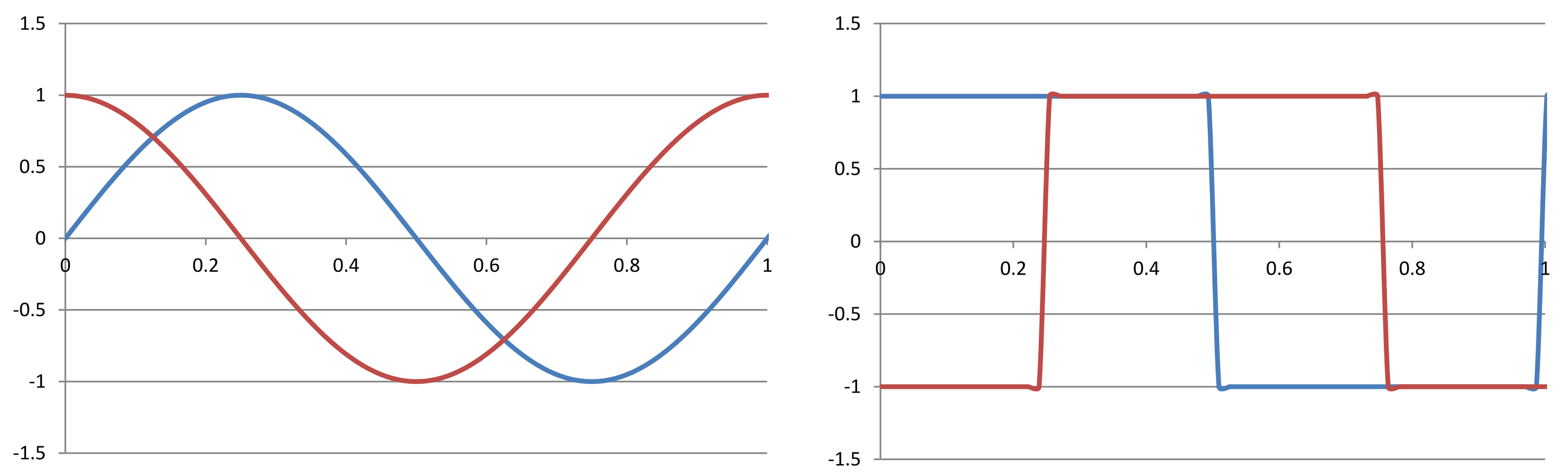
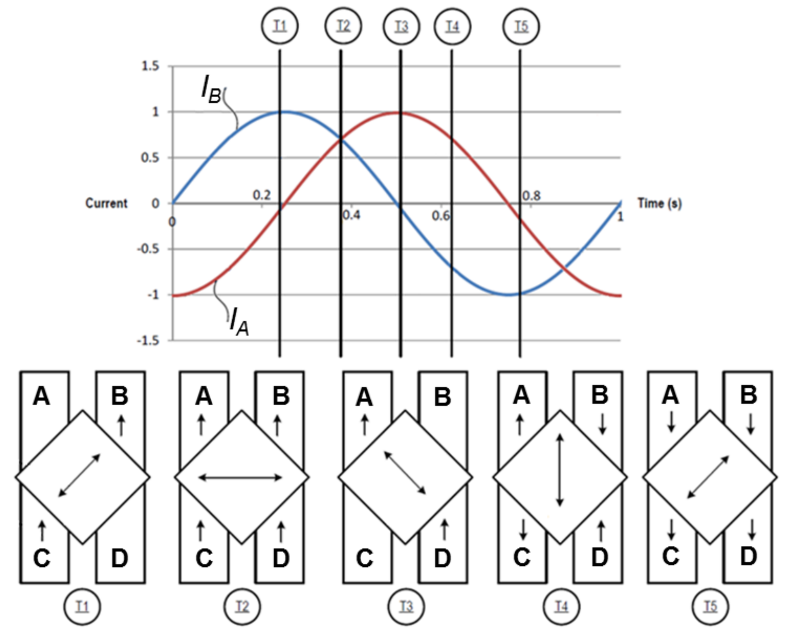


Figure 3. Shapes of waveforms applied for ferromagnetic and paramagnetic particle mixer.

Frequencies:
The frequency of 300-350 Hz was used in the electromagnetic mixer for ferromagnetic particles. For the system designed for low-response paramagnetic particles, a much lower frequency was used (below 30 Hz). The low frequency allows the longer time for the electromagnetic field to be applied for particles, before the field direction was changes.

Mixing directions:
Each sample vial is surrounded by four electromagnets, and each pair of electromagnets facing to each other always generate the magnetic field in parallel with the same strength. Figure 4 shows the samples of the configuration in the ferromagnetic particle mixer. T1, T2,…T5 are five time points within a cycle, and particles align through different directions at the respective time point. Thus, a general clockwise rotation direction can be observed.



(1) $I_A = I_0 \sin(ft)$

(2) $I_B = I_0 \sin(ft + \frac{\pi}{2})$

(3) $I_C = I_0 \sin(ft + \pi)$

(4) $I_D = I_0 \sin(ft + \frac{3\pi}{2})$

Figure 4. One example of the control of four electromagnets surrounding one sample well in ferromagnetic mixer.

By changing the phase delay of the currents applying on each electromagnets, a reversed mixing direction (counter clockwise) mixing direction can be observed, as described in Figure 5.

(1) $I_A = I_0 \sin(ft)$

(2) $I_B = I_0 \sin(ft + \frac{3\pi}{2})$

(3) $I_C = I_0 \sin(ft + \pi)$

(4) $I_D = I_0 \sin(ft + \frac{\pi}{2})$

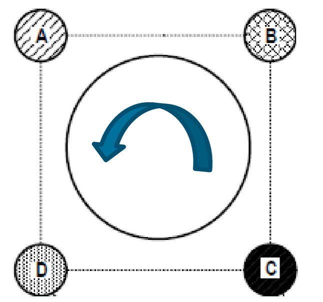


Figure 5. Another example of the control of four electromagnets surrounding one sample well in ferromagnetic mixer.

Similarly, both mixing directions can be achieved in the electromagnetic mixer for paramagnetic particles. The alternative mixing directions could be used to enhanced the mixing efficiency.

RESULTS

With the electromagnetic mixer designed for low-response parametric particles, various samples can be mixed with high efficiency. Figure 6 shows some examples of Dynal beads and SPRI beads.

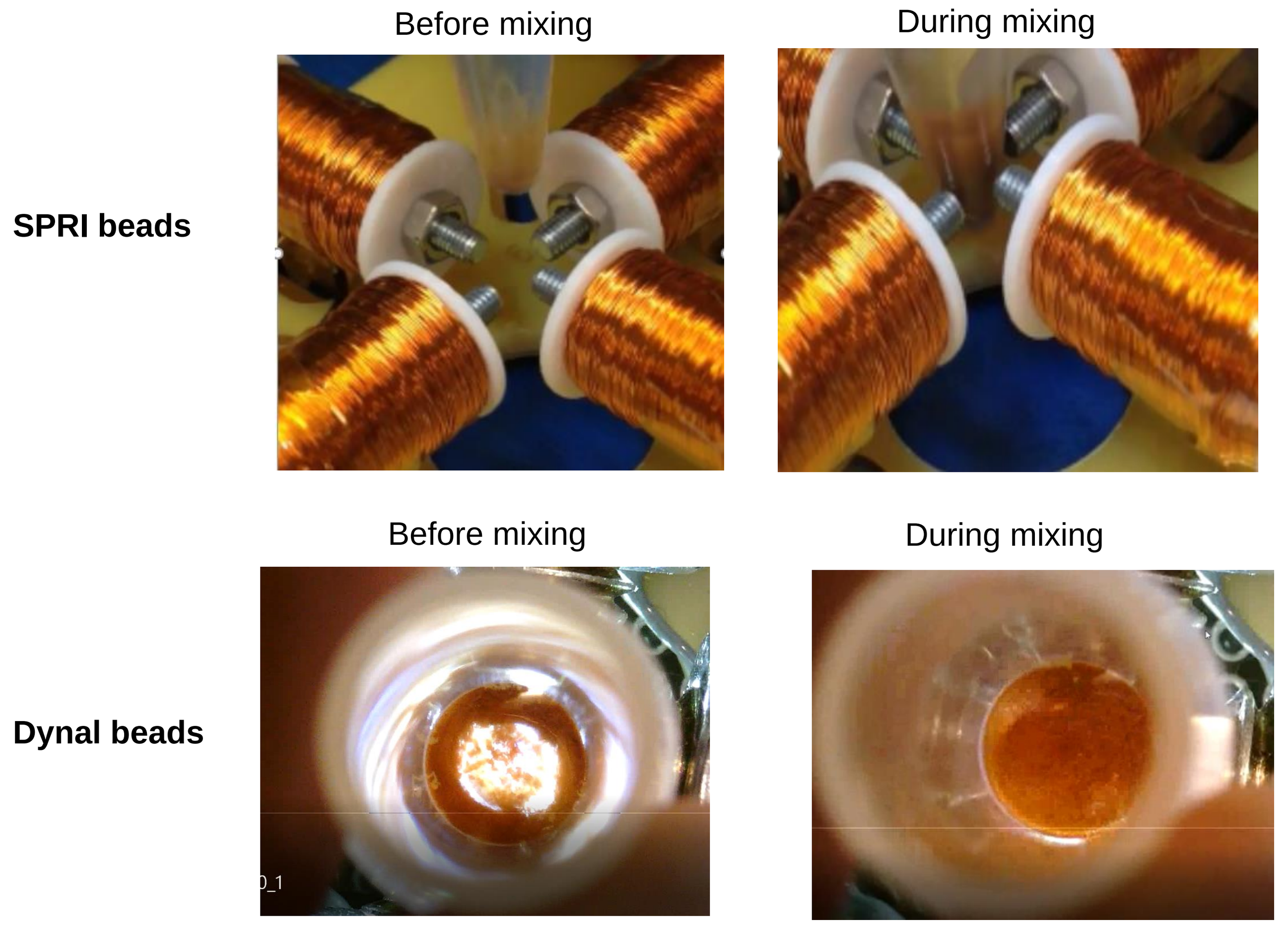


Figure 6. The electro-magnetic mixing of low-response paramagnetic particles

CONCLUSIONS

A electromagnetic mixer has been introduced in this study low-response paramagnetic particles. The use of square-wave AC driven oscillating magnetic fields could form a homogenous "dynamic fog" suspension of magnetic beads, allowing an optimal exposure and enhanced mixing with surrounding liquid medium. This platform could be potentially used as an ultra-fast sample preparation device for the high-throughput analysis.

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TRADEMARKS/LICENSING

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