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Development of 3D navigation system for micro-nano robot based on a Magnetic Particle Imaging system

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Abstract

The 3D navigation system of micro-nano robot based on Magnetic Particle Imaging (MPI) is a promising technique to be used for targeted drug delivery. Using the magnetic actuator by manipulating field free point (FFP) and non-invasive molecular imaging method such magnetic particle imaging (MPI), the device can reduce the harm in treatment. In this paper, we used closed-loop control to steer a micro robot to a desired position by a 3D FFP magnetic force based system. A custom-built MPI system with a bore size of 90 mm that can generate a gradient as high as 4T/m/µ0 was used to verify the control system in three dimensions

I. Introduction

Target drug delivery using an external magnetic field is of great potential for medical applications [1]. To realize targeted drug delivery, imaging method for particle localization is always required in any control system; it will be used to evaluate the performance of open-loop control [2], or especially for monitoring the important sensor components in closed-loop control systems [3]. There are many imaging methods that can be used for targeted drug delivery, among which magnetic particle imaging (MPI) has several outstanding advantages such as being non-invasive real time, radiation free, and having high resolution and high sensitivity [4]. MPI can image the concentration and position of superparamagnetic iron oxide nanoparticles (SPIO) and also used in steering SPIO [5]. In addition, since MPI works based on magnetic field control, therefore, the magnetic particle control steering system using MPI imaging hardware can be a high potential candidate for this purpose. In such system, there would not be much changes compared to the combination of magnetic particle control system with other imaging modalities in principle of operation. The commercial MPI systems such as Bruker's, Magnetic Insight's systems are developed for high image quality and large FOVs and it will be difficult in terms of hardware design for combining them with targeted drug delivery systems. It is a big challenge to extend the actuator functionality or change firmware to manipulate the field free point (FFP) or field free line (FFL) of system by the user. Here, we used custom-built MPI system with a bore size of 90 mm [6] to develop a 3D FFP navigation platform by adding extra 3D FFP magnetic force function to the system. To test the platform, we utilized a micro-sized magnetic bead injected to a phantom mimicking the blood vessel of human body. The user could control the external electromagnetic field to steer the magnetic bead with intuitive manipulation method by using virtual FFP [1] to the desired destination inside blood vessel. Here, the MPI is only used to trace the bead and there was no back-

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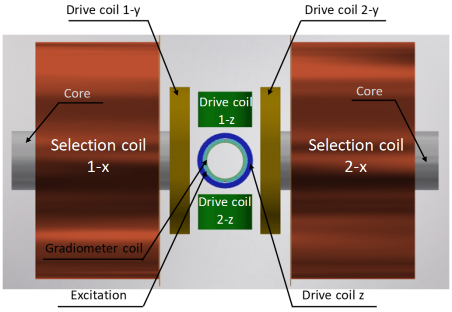

Figure 1: Coils of the proposed 3D FFP navigation system.

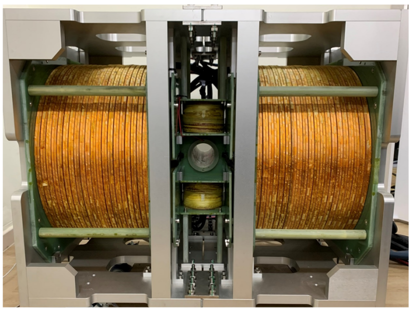

Figure 2: The system of 3D FFP navigation system.

ground information. Therefore, in order to apply this platform in real situation, another imaging modality, for example magnetic resonance imaging (MRI), should be used to capture the background [7]. In present study, the MPI system could achieve a temporal resolution of 2 frames/second with amplitude modulation MPI (AM-MPI) with bore size 90 mm and FOVs (56 × 56 × 56 mm at 4 T/m/µ0 and 89.6 × 89.6 × 89.6 mm at 2.5T/m/µ0) [6]. The system requires a 200-ampere current using a soft magnetic core which is optimized to generate a high gradient field of 4 T/m/µ0. Due to high current, the MPI system requires a special water cooling system inside the coils and a 10 kW cooling machine should be used to keep the system at an operated temperature.

II. Materials and Methods

The structure of the navigation system consists of a pair of selection coils with Maxwell coil configuration to generate the FFP. This pair of coils generated a gradient of 2T/m in MPI mode and 2.5T/m to 4T/m in magnetic actuator mode. The axis of the selection coil pair was considered as the x-direction. To move the FFP in two directions, x and z in space, two pairs of drive coils were placed perpendicular to each other. One of these pairs was in x-direction and coaxial with the pair of selection coil and the other in z-direction. These pairs of drive coils were set up as Helmholtz coil configuration. In order to have enough space to place the sample, y-drive coil was designed differently as a cylindrical coil that generates a uniform magnetic field to move the FFP along the y-axis. This structure is illustrated in Fig. 1. The user can control drive coils x, y and z so the FFP is manipulated by the user and movement direction of the bead will be controlled by the user through the manipulated FFP. The closed-loop control requires a feedback signal, in this case, the feedback is the bead position estimated from MPI. In the user's observation, the user can determine the microrobot position, then the user places the virtual FFP to generate magnetic force to the bead of MNPs. In order to place virtual FFP, the user can use a mouse or joystick to place virtual FFP on the panel control. In our case, the virtual FFP is used to support to the user in easier manipulation of the beads since the movement direction of the bead and direction of virtual FFP to the bead is linear. The bead will move with direction from virtual FFP to the bead, the user can control this movement direction to follow the desired direction. After that, the bead moves to the new position, the MPI will update the bead position, and the user will continue to place virtual FFP to control the movement direction of the bead toward the target

The magnetic particle imaging (MPI) is realized continuously in real-time to make sure the closed-loop control works. In the short time when the user places virtual FFP, the MPI mode will be interrupted, and the electric magnetic actuator (EMA) will work. After a short generated force time, the MPI mode is enabled again to capture the bead position. The multiplex control is used to exchange continuously between MPI mode and EMA mode to be compatible with closed-loop control. In order to implement this multiplex control, the pulse width modulation (PWM) technique is used to change the gradient field in MPI mode to the gradient field in EMA mode alternately so the navigation and imaging work simultaneously in the multiplex control.

The bead was fabricated by using 0.8 µL of resovist magnetic particles (55 mg_{Fe}/mL) and covered by artificial-liposome. The bead was a sphere with the final volume of about 1 µL. Such magnetic bead of this size and shape can be considered as a micro robot [8]. To steer the micro bead in condition close to the dynamic blood environment to desired destination by magnetic force, we used a mixture of water and glycerol and used a syringe pump. According the calculation for the viscosity of mixture of glycerol and water in [9], the fluid was a mixture consisted of 33% glycerol and 67% water, such that its viscosity was similar to the viscosity of blood ∼ 3.5 mPa.s. In addition, blood flow was also generated using a syringe pump at the inlet of the vascular model. The pump was set to a flow rate between 0.25 and 1 mm/s [10].

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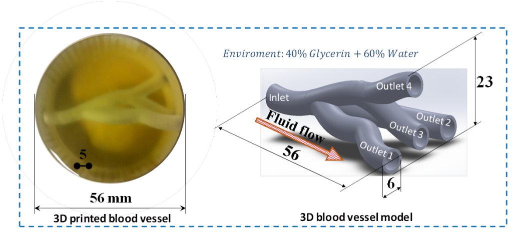

Figure 3: The micro-robot can be steered from Inlet to desired destination outlet which the user control by manipulating virtual FFP.

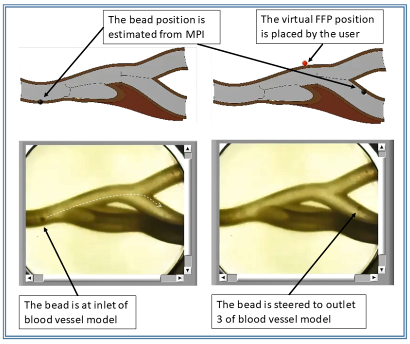

Figure 4: The micro-robot can be steered from Inlet to desired destination outlet 3, the bead position is determined by MPI.

III. Results

The photograph of the final proposed 3D FFP navigation system is shown in Fig 2 [6]. The system achieved a high gradient field of up to 4 $\mathrm{T/m/\mu_0}$ with a bore size of 90 mm. The workspace for magnetic force is 60 x 60 x 60 mm^3, and the system could generate the enough force to steer the micro robot from inlet to the desired outlet as showed in Fig. 3.

To the performance of the 3D navigation platform was tested for all four outlets and the micro robot was steered successfully to the desired one each time.

IV. Conclusion

Development of a 3D FFP magnetic force based platform using a custom-built MPI to control a micro robot movement in blood vessel phantom was demonstrated. By using the MPI system, it was possible to acquire 3D image of magnetic nanoparticles fast enough to use it as feedback signal in closed loop control. The intuitive manipulation of micro robot through placing virtual FFP in 3D space guaranteed high efficiency in controlling the movement direction of the micro robot as we demonstrated that it can reach to any target in the blood vessel phantom, the Fig.4 shows the result of steering the bead to the outlet 3. Such system has the potential to be used for targeted drug delivery for in-vivo application.

Author's statement

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