Simulation of the particle trajectory under laminar flow for MDDS application

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Abstract：

Magnetic drug delivery systems (MDDS) can gather magnetic drugs to specific areas through an external magnetic field, increase drug concentration and improve efficiency, while reducing side effects on healthy tissues. To understand the motion of the magnetic drugs under magnetic field, this study established a multi-physics simulation model (including: magnetic force, drag force, and buoyancy-gravity), and verified with the trajectory of magnetic particles in the microfluidic channel. Nd-Fe-B permanent magnets and Y-Ba-Cu-O superconductors were placed under the microfluidic channels as magnetic sources, and their maximum magnetic field strengths are 0.247 T and 0.662 T, respectively. In the microfluidic validation experiment, the flow rate (1.5-7.1 cm/sec), channel width (0.8-1.8 mm), and viscosity (3.2 cP) referred to the vein conditions were considered. The results show that in the validation experiment under external magnetic field, the particle trajectory error is less than 1.72 um for every 1mm of flow distance, which means that our model has a high degree of reliability. In addition, we also studied the influence of different magnetic field sources on different particle sizes in the vein environment. The simulation results show that when the magnetic source is placed at z = -11 mm and the flow rate was 1 mm/s, the attracting particle size range of permanent magnets is 1-7 μm, and the attracting size range of Y-Ba-Cu-O superconductors is 0.5-7 μm, showing that the stronger magnetic field strength and gradient can attract smaller magnetic particles.

Introduction：

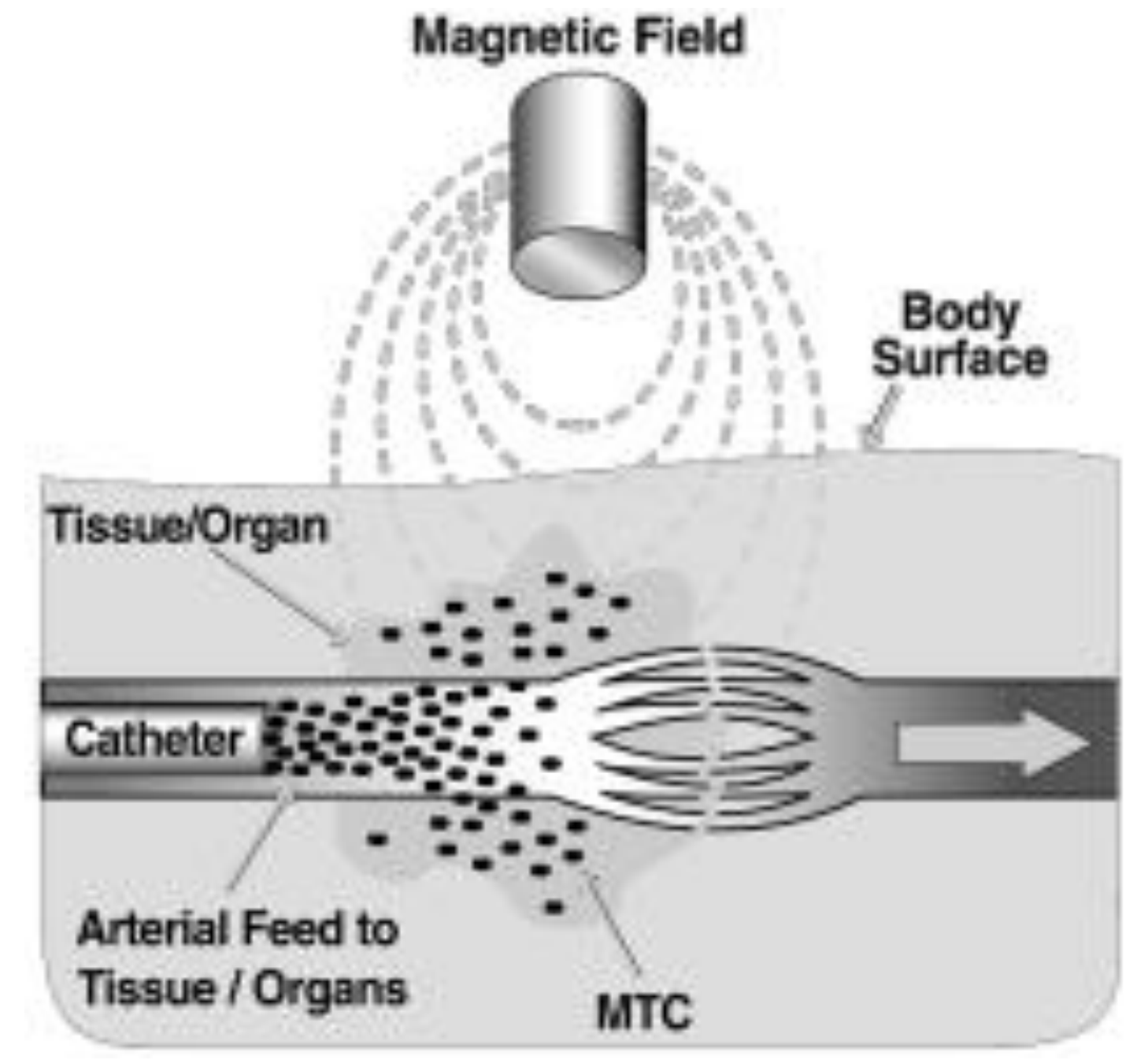


Fig. 1. diagram depicts the mode of action of Magnetic drug delivery system [1].

The Magnetic Drug Delivery System (MDDS) has been proposed in cancer and gene therapy since its development in 1980. The main mechanism is to attract magnetic drugs (carriers) injected into the human body through an external magnetic field. Compared with traditional treatment, MDDS can concentrates the drug to the target affected area, minimize the side effects on other tissues, and increased the dose concentration in the target area. Thereby, the dosage of the drug can be reduced, and better therapeutic effect can be obtained with the traditional method.

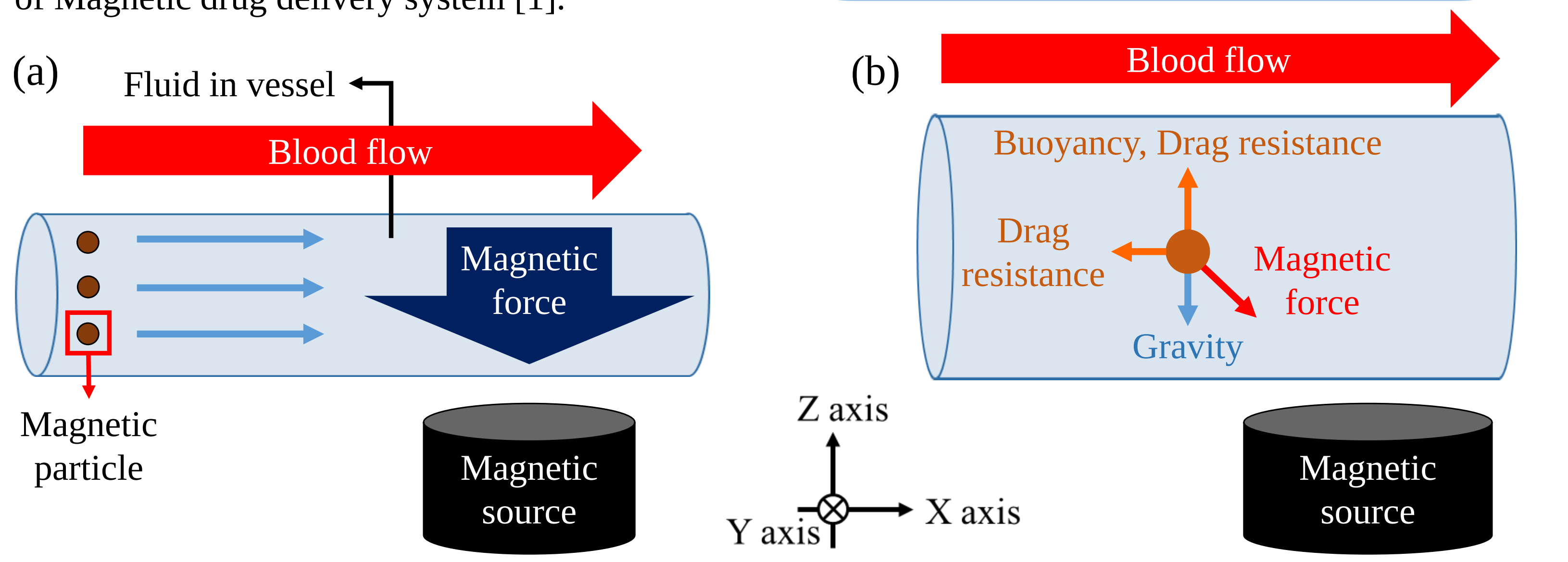


Fig. 2. Schematic diagram of the force of magnetic particles attracted by the magnet in the fluid [2]. (a) three sets of parameters (magnetic particle, fluid in vessel, magnetic source) were mainly concerned to describe the motion behavior of magnetic particle. (b) The force acting on magnetic particles can be divided into two direction (X and Z axis) in the mathematical model.

This study explore the influence of the magnetic field on the motion of magnetic particles in the fluid at laminar state. To be noticed, the boundary condition and parameter using in this study referred to the real situation of magnetic particles in a vein, e.g. the blood flow rate (1.5-7.1 cm/sec), the vein diameter (0.8-1.8 mm), and the blood viscosity (3.2 cP) [3].

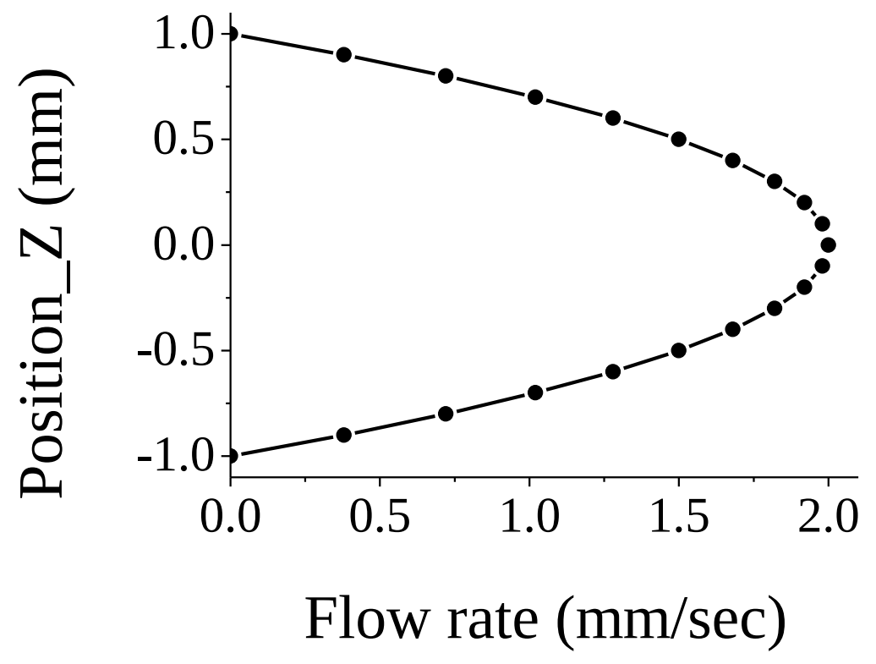
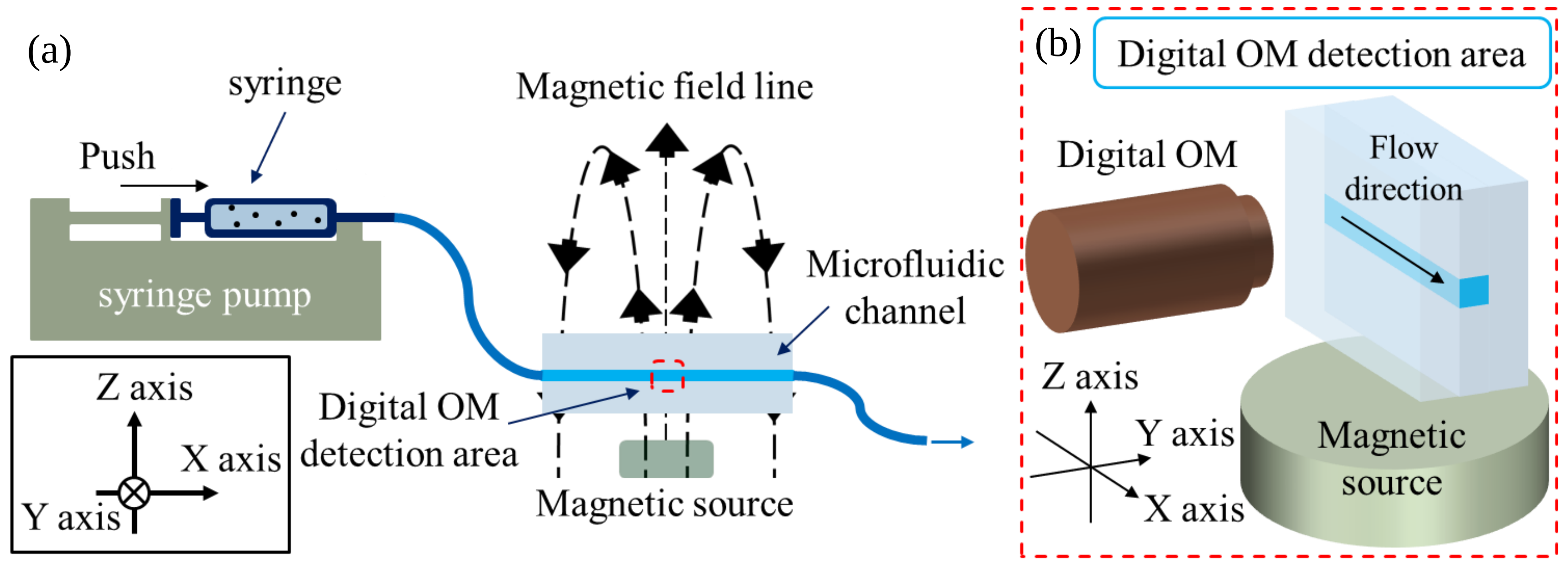


Fig. 3. Laminar flow velocity distribution diagram shows that the farther away from the center, the lower the velocity will be. The flow rate of the laminar flow in the cylindrical channel is given by:

$$v_f = 2v_A\left(1-\left(\frac{Py}{L}\right)^2-\left(\frac{Pz}{L}\right)^2\right)$$

Where v_f is the flow rate of laminar flow, v_A is the average flow rate, Py and Pz are distances between particle and center of channel on the y and z axis.

Experiment：



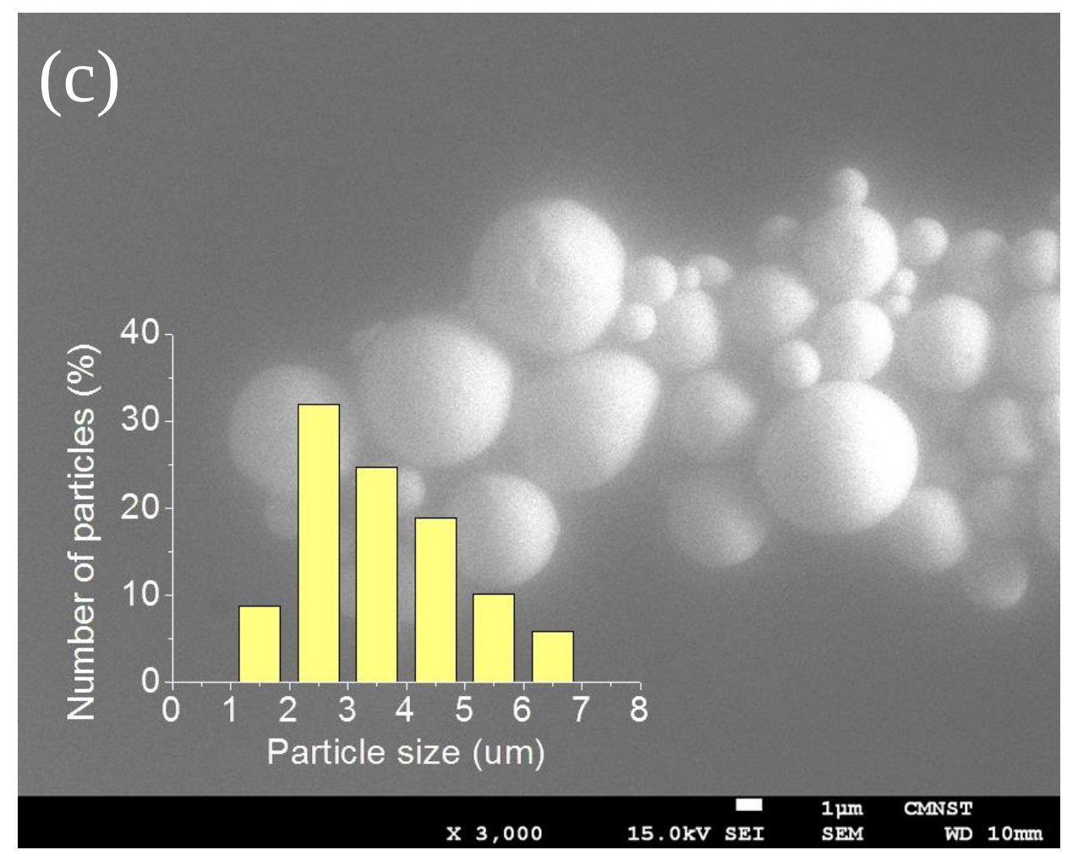


Fig. 4. (a) The schematic diagram of the validation experiment includes a syringe pump, the microfluidic channel, and a digital microscope. The solution is extruded from the syringe through the syringe pump, flows through the catheter to the microfluidic channel on top of a magnetic source. (b) A digital microscope is used to record images on the specific XZ plane from the Y-axis. (c) The SEM image of the magnetic particles (iron particles with size range from 1-7 μm) used in the validation experiment.

TABLE I. parameters used in this article. (PM = Permanent Magnet, HTS = High Temperature Superconductor)

Magnetic Source							
No.	Type	Diameter (m)	Thickness (m)	Temperature (K)	Magnetic field (T)	Surface current density (A/m)	Volume current density (A/m^2)
PM	$Nd_2Fe_{14}B$	0.25	0.5	298	0.247	$1.00*10^6$	0
HTS	YBCO	0.462	0.1461	77	0.662	$3.54*10^4$	$1.73*10^8$

Magnetic Particle				Fluid				
Material	Diameter (μm)	Density (kg/m^3)	Saturation Magnetic Strength (A/m)	liquid	Density (kg/m^3)	Viscosity (g/m*sec)	Flow rate (mm/s)	Channel width (mm)
Iron	<10	7450	$1.34*10^6$	Glucose Solution	1223.5	8.75	0.5, 1, 2	1.8
				Blood	1000	3.2	1	2

The velocities of the magnetic particles in a fluid along the flow direction can be described by the BBO equation, which can be simplified as follows:

$$m\frac{d(u-v_f)}{dt} = mg\left(1-\frac{\rho}{\rho_s}\right)-\frac{1}{8}\pi(2R)^2\rho C_D\left(u-v_f\right)^2-\frac{1}{12}\pi(2R)^3\rho\frac{d(u-v_f)}{dt}$$

Where u is velocity of particles (m/s), m is mass of particle (kg), m is the mass of particle, g is acceleration of gravity, t is time, R is the radius of the particle, C_D is a constant.

Result and discussion：

A. Validation of particle trajectory under magnetic field

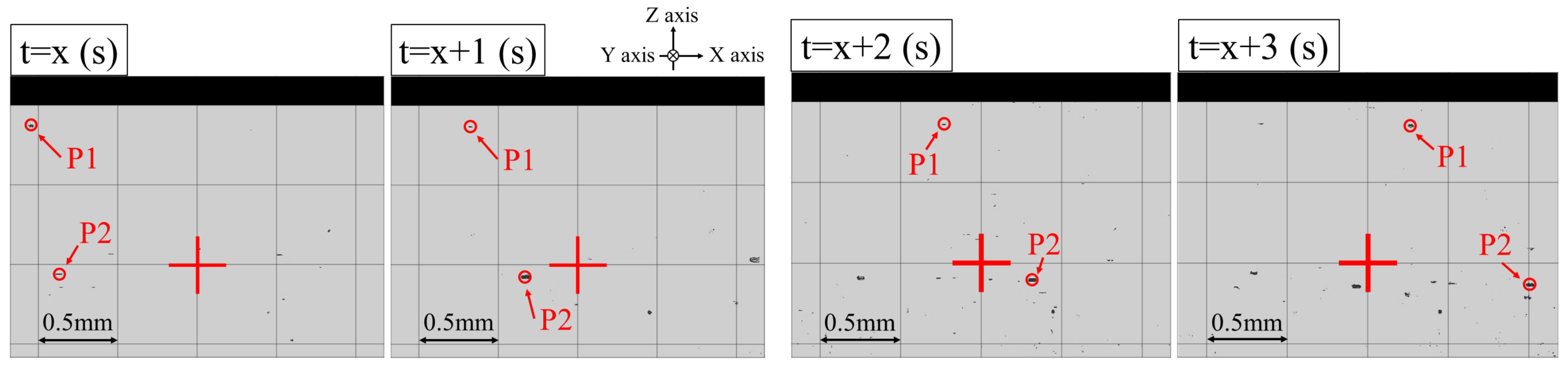


Fig. 5. A set of laminar flow experiment photos modified by the trainable Weka Segmentation processing of image J, showing the trajectory of magnetic particles on the XZ plane observed with a digital microscope. The center of the microfluidic channel (red cross) is the origin of this research. And information such as particle velocity can be obtained from the trajectories corresponding to different times. The width of a single grid is 0.5 mm.

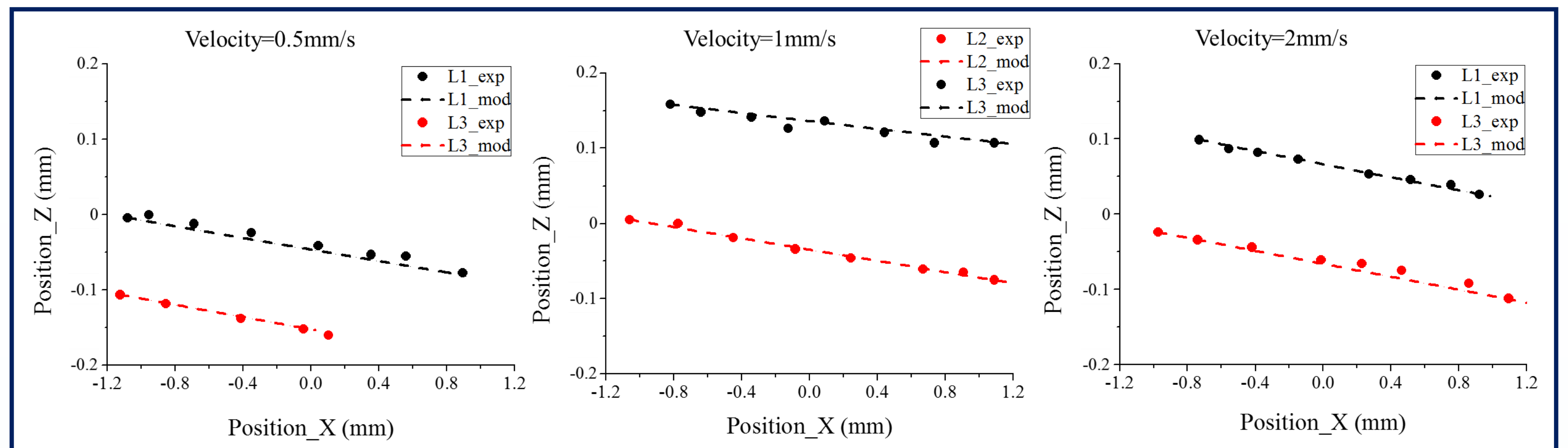


Fig. 6. The trajectories of particles under different flow rate and permanent magnet. The particle size is fitted by the BBO equation, and the calculated particle size is consistent with the size observed by SEM in Fig. 4c. Comparing with experiment data and simulation result, the average error is 1.72 μm (z axis)/mm (x axis). The parameters: magnetic source (PM), iron particles (size is less than 10 μm), liquid (glucose Solution), and channel width (1.8 mm).

B. Simulation of particle trajectory under different condition

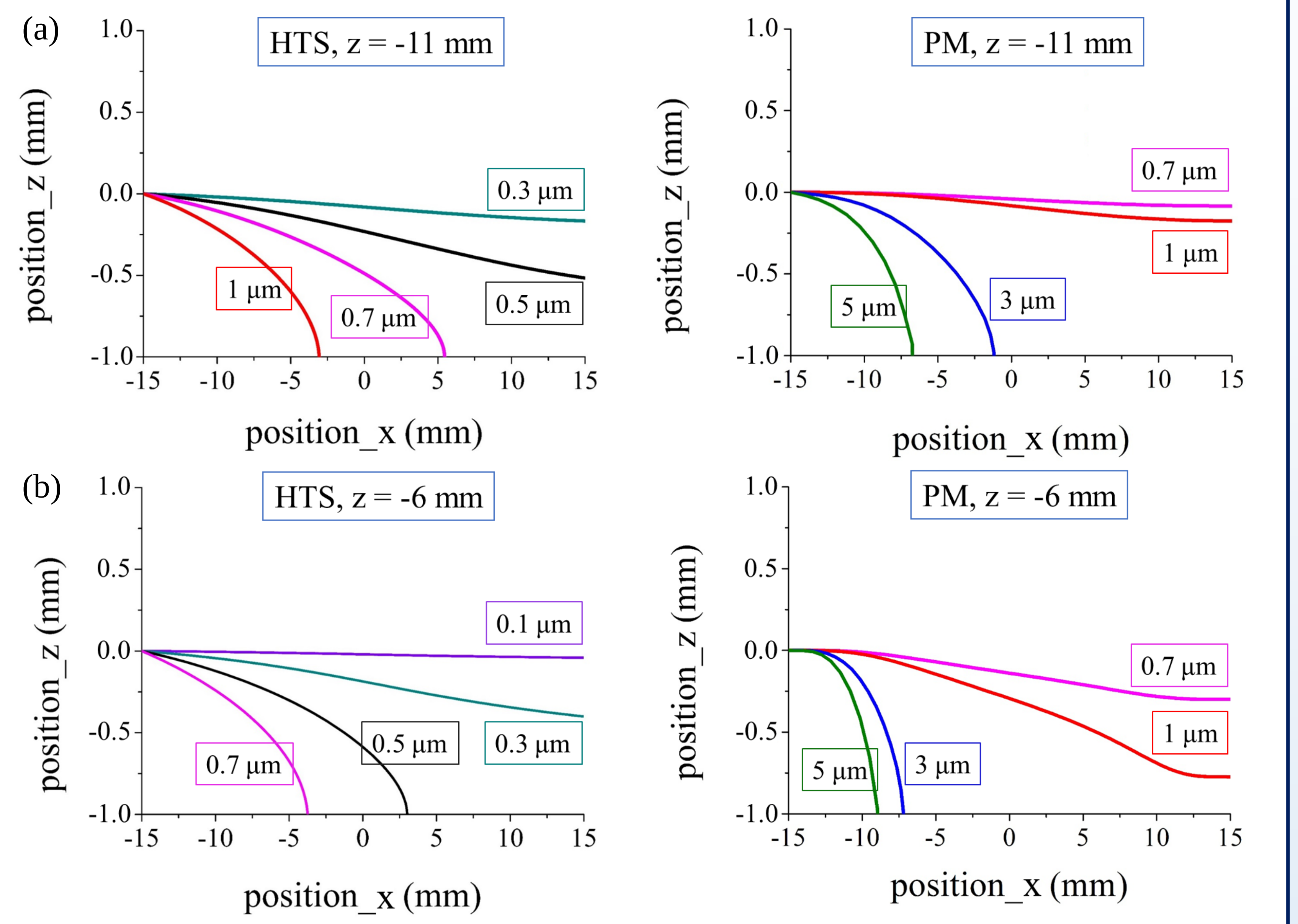


Fig. 7. The simulation results of different magnetic sources attracting particles of different sizes. (a) When the magnetic source at the position z = -11 mm, the attracting particle size of Y-Ba-Cu-O superconductor and permanent magnet is larger than 0.5 μm and 1 μm, respectively. (b) When the magnetic source at the position z = -6 mm. The particle size attracted by the superconductor and permanent magnet is larger than 0.3 μm and 1 μm, respectively. The parameters: magnetic source (HTS), liquid (blood), flow rate (1 mm/s), and channel width (2 mm).

Conclusion：

- In validation experiment under external magnetic field, the theoretical particle size of 1-2 μm can be obtained by model fitting and the average error is 1.72 μm (z axis)/mm (x axis).
  - ➢ Show good agreement with the calculated results, which means that our model is trustworthy.
- Calculate the trajectory of different particle diameters in the vein environment under different magnetic field sources to estimate the limiting sizes of attracting magnetic particles. When the magnetic source at the position z = -11 mm, permanent magnets can attract particles larger than 1 um, while superconductors can attract particles larger than 0.5 um. When the magnetic source at the position z = -6 mm, the permanent magnet can attract particles larger than 1 um, while the superconductor can attract particles larger than 0.3 um.
- Due to the strong magnetic field strength and gradient at the center of the superconductor, the particles can be captured more effectively near the center. The upper limit of the magnetic field strength of a superconductor is several times that of a permanent magnet, so it can capture smaller particles (such as nanoparticles).
- To sum up, the potential of superconductors using in MDDS applications is much higher than that of permanent magnets.

Reference：

[1] Wilson, M. W. et al., 2004. Radiology. 230(1), 287-293
[2] Yang, C. M. et al., (2021). IEEE Transactions on Applied Superconductivity. 31(5), 6800304.
[3] Klarhöfer, M. et al., 2001. Magnetic Resonance in Medicine. 45(4), 716-719.