Magnetic Mobile Microrobots for Upstream and Downstream Navigation in Biofluids with Variable Flow Rate

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Magnetic mobile microrobots navigating biofluids with both upstream and downstream locomotion provide a promising solution to targeted drug delivery for precision medicine. However, the biofluid environment in blood vessels is complicated due to variations in flow rate and direction. It is still unknown how to make magnetic microrobots resist the variable flow rate in biofluids with both upstream and downstream locomotion. Herein, magnetic microrobots with various shapes and sizes have been controlled to navigate diverse biofluids under different flow rates and directions. Simulation and experimental studies have been conducted to analyze the influences of microrobot size and shape on translational velocity in confined microchannels filled with biofluids. A strategy is proposed to choose the optimized parameters of rotating magnetic field actuation for precise delivery of microrobots in a microfluidic chip, which contains a complex biofluid environment with variable flow rate and direction. The results are validated using various microrobots navigating the microfluidic chip and the yolks of zebrafish larvae in vivo. This work provides a guideline for selecting desirable microrobot dimensions and magnetic field actuation parameters for controllable navigation of magnetic mobile microrobots in complex biofluid flows.

1. Introduction

The circulatory system provides a natural route for reaching all organs and tissues inside the human body. Untethered micro-robots capable of swimming in circulatory systems provide a promising solution for next-generation minimally invasive cargo delivery to hard-to-reach regions.[1–3] In the literature, various artificial swimming microrobots have been fabricated for active navigation.[4] For instance, bacterial-like micromachines,[5] helical micro-swimmers,[6,7] porous microstructures,[8–10] and many other shapes of mobile microrobots[11–18] powered by external fields, e.g., magnetic, acoustic, thermal, and optical fields, have been reported recently. In particular, magnetic actuation renders microrobot propulsion with advantages in wireless driving, penetration into biological entities, and biocompatibility, and it has been widely adopted for powering microrobots.[19–21] Inspired by leukocytes or neutrophils, which locomote in vascular channels along the vessel walls due to a relatively low flow velocity therein, magnetic surface microrollers have been propelled to navigate blood vessel-mimicking microfluidic channels.[22,23] To name a few, spherical microrollers,[24] cube-shaped microrollers,[22] peanut-like microrollers,[25] and doublet spherical microrollers[26] have been presented for target delivery in confined microchannel environments.

For potential biomedical applications, carrier liquids containing a certain density of magnetic microrobots can be injected into blood vessels, and then the microrobots are steered by applying an external magnetic field gradient or rotating magnetic field.[27,28] Although the investigation of individual or doublet microrobots is beneficial for understanding their swimming behaviors in physiologically relevant flow conditions, single or doublet microrobots are not sufficient for targeted cargo delivery due to their limited payload capability.[19,29] Moreover, it is not easy to obtain single or doublet microrollers due to the aggregation of magnetic microrobots after injection into the biofluids. In contrast, it is more realistic for various microrobots composed of multiple aggregated magnetic particles to emerge.[30] It is desirable to investigate the navigation behavior of microrobots in vascular environments filled with dynamic biofluids. In the literature, a swarm of helical magnetic micropropellers has been injected to penetrate the vitreous body of the eye by overcoming
the adhesion forces under magnetic driving navigation.\textsuperscript{32} Nanoparticle microswarms induced by magnetic fields have been investigated for navigating various stagnant biofluids.\textsuperscript{33} 2D static and dynamic formation of magnetic microrobot swarms with cooperative behavior has been implemented by programming external ferromagnet arrays.\textsuperscript{34} Magnetic microswarms (vortex-like and ribbon-like) have been implemented for passing through tortuous, branched, and confined environments through morphological transformation.\textsuperscript{35, 36}

For practical use, rather than steering in stagnant liquids, it is more desirable to navigate the microrobots in blood vessels with dynamic microfluidic flows.\textsuperscript{37–39} Until recently, active navigation of magnetic microrobots in fluid flow environments has gained extensive attention from researchers. For example, cell-sized spherical microrollers have been presented for upstream propulsion by rolling on 3D surfaces in physiologically relevant blood flow, where the microroller rolling upstream and crossing bifurcating blood flow was demonstrated with a high speed of 600 $\mu$m/s.\textsuperscript{22} Self-assembled microswarms driven by combined external acoustic and magnetic fields have been reported with upstream mobility by rolling-type motion.\textsuperscript{40} In that work, each microswarm was formed by dipole–dipole interactions of individual superparamagnetic particles, and microswarm rheotaxis was studied against the stream as high as 1.2 mm s$^{-1}$. In addition, nanoparticle microswarm swimming in simulated blood flows under permanent magnet actuation and ultrasound Doppler image-guided navigation has been reported.\textsuperscript{41} However, the biofluid environment in blood vessels is rather complicated due to the variations in flow rate and direction. Controlling microrobots to freely navigate upstream and downstream in blood vessels with variable flow rates is a challenging and open issue. Considering a microfluidic channel with a specific magnetic microrobot material, the locomotion of the microrobots is mainly governed by the appearance (e.g., size and shape) of the microrobots and the parameters of the magnetic actuation system. To date, it is still unclear how to make microrobots resist the variable flow rate in biofluid microchannels with both upstream and downstream locomotion. Without overcoming this problem, the microrobots could not pass through the blood vessels in a controllable manner to arrive at the targeted location.

Here, we investigate the influence of the microrobot’s appearance and magnetic field actuation parameters on the locomotion of mobile microrobots, which are translated by surface rolling in biofluids with variable flow rates and directions. Due to the random shapes and sizes of the microrobots formed by the dipole–dipole interaction force of the permanent magnetic nanoparticles, the relationship between the translation velocity and dimensions of the microrobots was examined by conducting a computational fluid dynamics simulation study. Typical microrobots with different sizes and shapes have been adopted for simulation in a confined microchannel filled with a constant flow rate of blood. For each type of microrobot, the simulation results of the microrobot with different sizes have been obtained under upstream, static, and downstream flow navigations. To validate the size effect, the controlled navigations of the magnetic microrobots in glass microchannels have been experimentally tested in physiologically relevant flow conditions (up to 750 $\mu$m s$^{-1}$), including pure water, viscous glycerin (40%), and blood serum. Furthermore, an experimental study of microrobot locomotion has been carried out in microfluidic chip channels with variable flow rates and directions. A strategy is proposed to select the optimized parameters of rotating magnetic field actuation for precise delivery of microrobots in a microfluidic chip. The strategy has been validated by navigating various microrobots in microfluidic chip channels with higher flow rate (up to 1.5 mm s$^{-1}$) and in the yolk of zebrafish larvae in vivo. The results provide a guideline for the selection of the microrobot and its actuation system for precise navigation in complex biofluid flows toward targeted cargo delivery.

2. Results and Discussion

2.1. Self-Generation of Magnetic Microrobots in a Rotating Magnetic Field

Under the action of gravity and magnetic force, magnetic microswarms usually exhibit various flat shapes.\textsuperscript{33} Here, the magnetic field-induced microrobots with different stereo shapes and sizes are self-generated mainly by dipole–dipole interactions of permanent magnetic nanoparticles (NdFeB). Moreover, each magnetic field-induced microrobot is composed of a group of least number of permanent magnetic nanoparticles, which cannot be changed and separated anymore under the fluid drag and substrate collision. Thus, in this work, the microrobot shapes cannot be designed and changed during the experiments. Scheme 1 illustrates the schematic of the formation of magnetically controlled microrobots with random shapes and their navigation in blood vessels. The sizes of the adopted magnetic particles range between 30 and 40 $\mu$m. It has been shown that rotating magnetic field actuation is more effective than magnetic field gradient actuation.\textsuperscript{25} For actuation, the rotating magnetic field is produced as $B(t) = B_0 \cos(\omega t) \cos(\alpha) e_x + \cos(\omega t) \sin(\alpha) e_y - \sin(\omega t) e_z$, where $t$ denotes the time variable and $e_x$, $e_y$, and $e_z$ represent the unit vectors of the $x$-, $y$-, and $z$-axes, respectively. $B_0$ is the magnitude, $\omega$ is the angular frequency, and $\alpha$ is the angle between the driving direction and the positive $x$-axis direction, as illustrated in Figure S1b, Supporting Information. Under the actuation of a rotating magnetic field provided by a custom-built five-coil electromagnetic system (see Figure S1a, Supporting Information), spinning microrobots with irregular shapes and sizes ($\approx$100–300 $\mu$m) are randomly formed (see Figure S1b, Supporting Information).

To explore the influences of the shape and size of the microrobot on its propulsion in biofluid flow, simulation studies were first performed with different microrobots by COMSOL software. For investigating the influence of shape on the flow profile, 2D model was adopted in simulation study to reduce the calculation time. Here, the basic circular, triangular, and rectangular shapes of the cross-sectional area for the microrobots were considered, as shown in Figure 1a. Other shapes can be considered as the combination of these basic shapes. The dimension of the height ($h$) is defined as the characteristic length of the cross-sectional area for the microrobot. The simulation study was carried out in a microchannel of 0.53 mm inner diameter filled with blood at a flow rate of 750 $\mu$m s$^{-1}$, which is slightly larger than the blood flow rate (0.3–0.7 mm s$^{-1}$) in the capillary of an
The dynamic viscosity and density of the fluid were set as $4.8 \times 10^{-3}$ Pa s and 1052 kg m$^{-3}$, respectively. For simplicity, the fluid was considered as Newtonian liquid. The distribution of the flow rate is illustrated by the flow profile in Figure 1a. Due to the friction effect, the flow rate near the inner surface of the microchannel is close to zero. In the simulation study, there is a lubrication (separation) distance from the circumscribed circle of the microroller to the nearby wall. The lubrication (separation) distance was set as 5 μm through trial-and-error. It is the minimum gap that is applicable to the mesh partitions and calculations of all the simulation models here. The simulation results in Figure 1b display the pressures generated around the microrobots ($h=200$ μm) with various shapes in the downstream flow at different time instants. This reveals that the pressure near the microrobot with a circular cross-sectional shape (i) remains stable, while the pressures around the microrobots with the other two types of shapes change significantly along with their rotations. The pressure change of the microrobot cross section with a rectangular cross-sectional shape (iii) is larger than that with a triangular cross-sectional shape (ii). The pressure difference surrounding the microrobot induces a torque to prevent the microrobot from rotating. To make the microrobots navigate upstream or downstream liquid flow by surface rolling, the actuation torque should overcome the flow-induced torque. The simulation results of the flow-exerted torques on the microrobots rolling at a frequency of 5 Hz on the inner surface of the microchannel in static, downstream, and upstream blood flows were obtained as shown in Figure S2, Supporting Information. It is found that the upstream flow exerts a larger absolute torque on the microrobot than the downstream flow.

For illustration, concerning the three groups of microrobots with different shapes and sizes steering in the downstream flow of the microchannel, the mean values of the exerted torques were obtained, as shown in Figure 2a. It indicates that the average amplitude of the flow-exerted torques is approximately linearly proportional to the square of characteristic length ($h$) of the cross-sectional area for the microrobot. Moreover, the ratio of the perimeters for the shapes (i), (ii), and (iii) is 1.41:1.18:1, which indicates that the pressure-carrying area and the average length of force arm for the shapes (i) are the largest. As the pressure-carrying area and the average length of force arm are both proportional to the flow-exerted torque, the average amplitude (absolute value) of the flow-exerted torque of the microrobot with circular cross-sectional shape (i) is the largest under the same characteristic length. However, the fluctuation of the flow-exerted torque is correlated with the difference between

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**Scheme 1.** Schematic illustration of magnetically controlled microrobot navigation in blood vessels.
the largest rolling length \(l_m\) and smallest rolling length \(l_s\) of the cross-sectional shape for the microrobot. For microrobots with the same characteristic length, different shapes give different length ratios of the largest and smallest rolling lengths \(l_m/l_s\). Figure 2b indicates the relationship between the fluctuation range of flow-exerted torque and length ratio \(l_m/l_s\) of different microrobots with identical \(h = 200 \mu m\). Concerning the circular, triangular, and rectangular cross-sectional shapes considered here, their values of length ratio \(l_m/l_s\) are calculated as 1.0, 1.15, and 8.40, respectively. With \(l_m/l_s = 1.0\), i.e., no area change of the flow impact surface, the circular cross-sectional shape is expected to have no fluctuation of torque. The nonzero fluctuation value of circular cross-sectional shape in Figure 2b is induced by the calculation error of simulation study due to nonideal mesh quality resulted from the arc of the circle. As evidence, the microrobot with a circular cross-sectional shape exhibits a stable flow-exerted torque with almost no change (see Figure 2c). Except for the result of circular cross-sectional shape, the larger the length ratio is, the larger the fluctuation of the torque exerted on the microrobot in either upstream or downstream flows. The characteristic length and rotating frequency have severe influence on the motion capability of the microrobot. Except for the result of circular cross-sectional shape (with nonideal mesh quality), Figure 2c indicates that as the length ratio \(l_m/l_s\) increases, the fluctuation of the flow-exerted torques on the microrobot becomes more severe regardless of its characteristic length. This is mainly caused by the area change of the flow impact surface (heading against the flow direction) because the variation in the flow impact surface area becomes larger as the length ratio \(l_m/l_s\) increases. In addition, the influence of the rotating frequency on the microrobot was also analyzed by a simulation study. Figure 2d reveals that as the frequency increases, both the fluctuation magnitude and mean amplitude of the flow-exerted torque change in approximately linearly proportional to its rotating frequency.

In summary, these simulation results demonstrate that upstream navigation requires a larger actuation torque than downstream navigation. The amplitude of the required actuation
torque is mainly governed by the largest rolling length \((l_m)\) of the microrobot. The variation magnitude of the actuation torque is determined by the length ratio \(l_m/l_s\) of the largest and smallest rolling lengths of the microrobots with different shapes. In addition, the variation magnitude of the actuation torque increases with increasing rotating frequency. Considering that the actuation torque is in proportional to angular velocity, and hence, translational velocity of the rolling microrobot, the simulation results also predict the size influence on the microrobot velocity.

2.2. Driving a Microrobot in Static, Upstream, and Downstream Microchannel Flows

To investigate the influence of flow conditions on the translational velocity of irregular microrobots, various microrobots (with different sizes and shapes) were driven to navigate a straight microchannel filled with static, upstream, and downstream flows of different liquids by experimental study. Similar to the setup in the foregoing simulation study, the flow speed was set as 750 \(\mu\text{m} \text{s}^{-1}\). The flow rate is comparable to the velocity of physiological blood in the adult capillary.\(^{43}\) Microrobots were self-generated by using NdFeB nanoparticles (size \(\approx 30\text{–}40\mu\text{m}\)) through dipole–dipole interactions. Under the actuation of a rotating magnetic field provided by a custom-built electromagnetic system, spinning microrobots were formed due to particle aggregation in a microchannel with an inner diameter of 0.53 mm. To facilitate experimental testing, a rotating magnetic field with an intensity of not higher than 5 mT was adopted to prevent heat generation for long-term (over 30 min) actuation.

Figure 3 shows the experimental results of driving a microrobot for navigating a microchannel filled with pure water, viscous glycerin (40%), and blood serum. As illustrated in Figure 3b, three microrobots were adopted for steering in each type of liquid flow. The sizes of the formed microrobots (with different shapes) were between 100 and 300 \(\mu\text{m}\) in the experimental test. Time-lapse images of the microrobot steering in viscous glycerin (40%) under downstream, static, and upstream flow states are depicted in Figure 3g. The experimental results of the average velocity \((v_{\text{avg}})\) for three microrobots of different sizes in static flows in blood serum are shown in Figure 3b. Figure 3c depicts the maximum average velocities of the microrobots swimming in three liquid environments with three different flow states. Figure 3c shows that the peak average velocities of the microrobots in various liquid environments are different. Among the three liquids, the peak average velocities in glycerin (40%) under all the flow states are the smallest because glycerin (40%) has the largest viscosity. As a result, the glycerin (40%) liquid imposes the largest fluidic drag on the microrobots, which counteracts the magnetic torque exerted on the microrobots and decreases their translational velocity. Although the viscosity of water is smaller than that of blood serum, the average speed of the microrobot in blood serum is larger than that in water. This may be caused by the surface modification of the magnetic microrobot in blood serum due to chemical reaction, which eases the surface interaction and decreases the fluidic drag on the microrobots.

The propulsion of the microrobot in the liquid flow of a microchannel by surface rolling is further explained below. Without
considering the influence of the magnetic field, the motion of the microrobot can be determined by \( v_{\text{avg}} = \pi f l_{\text{eq}} \) and \( \tau = \tau_f + \tau_d \), where \( v_{\text{avg}} \) denotes the average velocity of the microrobot and \( f \) and \( l_{\text{eq}} \) are the rotating frequency and equipment rolling length of the microrobot, respectively. \( \tau \) is the required actuation torque for the rotation, which is the sum of the spinning friction-induced resistive torque (\( \tau_f \)) and the drag force (\( \tau_d \)) for the microrobot. The magnetic torque (\( \tau_m \)) exerted on the microrobot can be calculated by \( \tau_m = \int (M \times B) \, dV \), where \( M \) and \( V \) represent the magnetization vector and the volume of the microrobot, respectively. \( B \) is the rotating magnetic actuation field of the microrobot. When \( \tau_m \) exceeds the required torque \( \tau \), the microrobot starts to rotate smoothly for surface rolling.

Moreover, the experimental results also confirm the simulation prediction of the size effect on the locomotion of the microrobot. Figure 3b indicates that under the same rotating frequency (5 Hz) below the step-out frequency, the translational velocity of the microrobot is significantly dependent on its largest rolling length (\( l_{\text{m}} \)), which is consistent with the simulation result. The maximum rolling velocity of the microrobot and its corresponding actuation frequency are governed by the magnetization intensity and the shape of the microrobot. Nevertheless, it is difficult to keep the magnetization intensities and shapes of different microrobots consistent in practice. To reduce the influence of the magnetization intensity and equivalent rolling length, the magnitudes of the translational velocity and actuation
frequency of a microrobot are characterized by defining two variables $\nu_{\text{avg}}/l_m$ and $f/\nu_{\text{peak}}$, respectively, where $\nu_{\text{avg}}$ and $f$ denote the average velocity (of at least five tests) and actuation frequency of the microrobot, respectively. $\nu_{\text{peak}}$ is the real actuation frequency at which the microrobot reaches the maximum velocity under static fluid flow in the microchannel. In Figure 3c, the error bar represents the standard deviation of the differences between the mean value and the experimental data for the average velocity. Additionally, $\Delta \nu_{\text{avg}}/l_m$ indicates the difference between the average velocities of the microrobot in the upstream (or downstream) flow state and static state.

To facilitate the analysis of the experimental results, the fitting curves of the experimental data are generated by using MATLAB software. The fitting model is selected as $f(x) = (ax^b + cx^d) e^{-x}$, which gives root mean squared errors (RMSEs) below 4.41, 1.76, and 6.38 s$^{-1}$ for the liquid flows of pure water, viscous glycerin (40%), and blood plasma, respectively. The coefficients of the fitting models are tabulated in Table S1, Supporting Information. Figure 3d–f shows that regardless of the type of liquid flow, the fitting curves exhibit similar variation tendencies. This validity of the two variables ($\nu_{\text{avg}}/l_m$ and $f/\nu_{\text{peak}}$) defined above. The error bars in Figure 3d–f represent the standard deviation of discrepancies between the fitting value and the experimental data of multiple microrobots. Compared with the static flow state in the microchannel, the average velocities of the microrobots increase and decrease in the downstream and upstream flows, respectively.

In summary, these experimental results demonstrate controllable magnetic microrobots navigating upstream and downstream liquid flows in a confined microchannel with a constant flow rate. As expected, the experimental results reveal that the biofluid with a much large viscosity causes a low translational velocity for the microrobots. The experimental results also indicate that the maximum translational velocity is governed by the largest rolling length of the microrobots, which validates the simulation evaluation of the size effect of microrobot locomotion.

2.3. Microrobot Navigation in a Microfluidic Chip with Variable Flow Rate

To investigate the influence of the rotating magnetic field actuation parameters on the navigation of the microbot in upstream and downstream flows with variable flow rates, experimental studies have been conducted by propelling the magnetic microrobot in a microfluidic chip filled with blood serum under different actuation frequencies and magnitudes. The microfluidic chip contains multiple bifurcation branches, as shown in Figure 4a. To mimic the blood flow rate in the capillary of an adult, the flow rate in two subbranch channels was set as 300–350 μm s$^{-1}$. Due to the identical width (600 μm) of the channels in the microfluidic chip, the flow rate is doubled as 600–700 μm s$^{-1}$ at the bifurcation junction of the two subbranch channels, as depicted in Figure 4a. Microrobots with different sizes around $l_m = 159$ μm and $l_m = 174$ μm were tested.

As illustrated in Figure 4a, the objective was to steer the microrobot to locomote by rolling on the inner surface of the microfluidic channels in a subbranch of upstream flow, attending the junction position of the bifurcations, and then navigating another subbranch of downstream flow. That is, the microrobot should cross the bifurcations successfully with a certain rolling velocity. Figure 4b–e shows that the motion states of the microrobots change as the microbot size, actuation frequency, and magnitude of the rotating magnetic field vary. In each plot, the magenta straight line indicates the boundary between the drivable and undrivable areas. In the controllable area (indicated by yellow) above the magenta straight line, the microrobot can be driven to navigate the entire journey. It is found that with a small magnitude (1 mT), the microrobot cannot be navigated regardless of the frequency. As the magnitude increases, the microrobot is drivable as long as the frequency is high enough. In contrast, with a large magnitude (5 mT), the microrobot can be driven to locomote in the two subbranches at the majority of frequencies. However, if the frequency is too high (50 Hz), the microrobot can only locomote intermittently in the whole journey. The reason is that there is a step-out frequency, i.e., the maximum frequency at which the rolling of the microrobot is synchronized with the actuation. Once passing the step-out frequency, the translational velocity of the microrobot decreases as the frequency increases. This phenomenon is caused by the fluidic drag over the generated maximal magnetic torque, which results in the loss of synchronization between the microrobot and rotating magnetic field and the reduction of translational velocity. By comparing the four cases in Figure 4b–e, it is found that the flow rate increase (600–700 μm s$^{-1}$) does not influence the controllable area of the microrobots. However, the larger the microrobot size is, the smaller the controllable area is. Generally, it is safer to select a larger magnitude and smaller frequency for magnetic field actuation. It is notable that the shape and size of the microrobots (formed by permanent nanoparticles) are not changed by the magnetic actuation system here. The proposed selection strategy provides a guideline for selecting the optimal actuation frequency and magnitude of the rotating magnetic field applied to the microrobot.

To validate the proposed selection approach, an experimental study was also conducted in microfluidic chip channels filled with blood serum under a larger flow rate and variation (see Figure 5a). In particular, the flow rate in the two subbranches was set as 750 μm s$^{-1}$, and the velocity at the junction of the bifurcations was up to 1.5 mm s$^{-1}$. Based on the proposed strategy, the optimized parameters of the rotating magnetic field actuation system were generated. For illustration, using two sets of optimized parameters—(2.0 Hz, 4.5 mT) and (7.5 Hz, 4.5 mT)—which produced fine performance according to real observation by a microscope, the time-lapse images of the microrobots navigating upstream and downstream flows of blood serum are shown in Figure 5c,d, respectively.

Under the actuation frequency of 2.0 Hz, the average velocities of the microrobot in the upstream and downstream flows were calculated as 1.39 and 1.45 mm s$^{-1}$, respectively. With the actuation frequency of 7.5 Hz, the average velocities of the microrobots in the upstream and downstream flows reached 5.19 and 7.39 mm s$^{-1}$, respectively. The velocity variation ranges in the two cases are compared, as shown in Figure 5b. Under the lower actuation frequency of 2.0 Hz, the velocity difference of the microrobot between the upstream and downstream flows was
only 0.06 mm s\(^{-1}\), which is much smaller than the velocity difference of 2.20 mm s\(^{-1}\) obtained under the higher actuation frequency of 7.5 Hz. The experimental results reveal that the variation in the translational velocity for the microrobot in the upstream and downstream microchannel flows (with flow rate up to 750 \(\mu\)m s\(^{-1}\)) is much smaller under a lower driving frequency. This phenomenon is consistent with that generated by driving the microrobots in the straight microchannel flows. In summary, the selected actuation parameters enable controllable upstream and downstream locomotion of the microrobot in bifurcation blood serum flow with large variation in flow rate (750–1500 \(\mu\)m s\(^{-1}\)), validating the effectiveness of the proposed selection strategy for the magnetic field actuation parameters.

2.4. In Vivo Navigation of Microrobots in the Yolk of Zebrafish Larva

To further validate the feasibility of the proposed selection strategy, in vivo navigation of the microrobot was performed.
in the yolk of zebrafish larvae 2 days postfertilization (dpf). Zebrafish have a similar genetic structure to humans and provide an excellent model for human health research, such as drug screening and drug development.\cite{44,45} Compared with other biofluids, the fluid in the yolk of zebrafish larvae exhibits higher viscosity with a nonuniform distribution of the components, which poses greater viscous resistance to the microrobot. It has been reported\cite{46} that the flow velocity in zebrafish embryos is $\approx 80 \mu m \cdot s^{-1}$.

To facilitate the microinjection of zebrafish larvae, as shown in Figure 6a, microrobots were self-generated using smaller NdFeB nanoparticles (below 6.5 $\mu m$) through dipole–dipole interactions. The optimized parameters of magnitude and frequency for the rotating magnetic field were determined to be 4.5 mT and 1 Hz, respectively. Figure 6b shows the planned navigation motion trajectory of the microrobot inside the yolk of zebrafish larvae. The microrobot has the largest rolling length of $l_r = 15 \mu m$. The unevenly distributed biofluids impose a viscous resistance on the rolling microrobot. The time-lapse images of the microrobot locomotion are illustrated in Figure 6d. The selected actuation parameters enable smooth in vivo navigation of the microrobot in the yolk of the zebrafish larva. The average velocities at different segments of the trajectory are depicted in Figure 6c. The experimental results demonstrate controllable locomotion in upstream and downstream flow in the yolk of zebrafish larvae. Additionally, the zebrafish larvae had heartbeats during and after the navigation of the microrobot, which indicates that the zebrafish lived during the in vivo experiment. In summary, the in vivo experimental results further validate the feasibility of the proposed selection strategy and its scalability.

Figure 5. Experimental results of driving a microrobot in microfluidic flows with bifurcations. a) The planned motion trajectory in the microfluidic channel. Scale bar: 1 mm. b) Velocity range of upstream and downstream navigation of the microrobot under different actuation frequencies. Time-lapse images of microrobot navigation in a microfluidic channel driven by an actuation frequency of c) 2.0 Hz and d) 7.5 Hz. Scale bar: 1 mm.
to microrobots with smaller dimensions and biofluids with lower flow rates.

In future work, magnetic microrobots with surface functionalization or surface deposition of the titanium layer can be adopted to enable biocompatibility.[47,48] Microrobots can also be surface-coated with drugs for targeted delivery.

### 3. Conclusion

In summary, in this work we reported the navigation of magnetic mobile microrobot propelled by surface rolling in upstream and downstream biofluids with variable flow rates. The influence of the size and shape of the microrobot on its locomotion has been explored by both simulation and experimental studies. Computational fluid dynamics simulation was carried out to explain the interaction of the microrobot in biofluid conditions. The simulation results reveal the effects of the cross-sectional size and shape of the microrobots on the driving torque and navigation velocity under upstream, static, and downstream flows. The results suggest that the variation in the flow-induced torque is governed by the ratio between the largest and smallest rolling lengths of the microrobot. Experimental studies have been conducted by steering microrobots of different sizes and shapes in a microchannel filled with static, upstream, and downstream flows in pure water, viscous glycerin (40%), and blood serum. The results indicate that the translation velocity of the microrobot is dependent on the viscosity of the liquid and the largest rolling length of the microrobot. Moreover, the controllable navigation of microrobots in upstream and downstream flows of blood serum with variable flow rates has been investigated by carrying out experimental studies using a microfluidic chip. For the first time, a selection strategy has been proposed to choose the optimized parameters for the rotating magnetic field actuation system to navigate the microrobot in both upstream and downstream flows with large flow rate variation. Using the selected parameters, the microrobot was successfully steered to cross the bifurcation blood serum flow with upstream and downstream locomotion at variable flow rates. The selection strategy was validated by both in vitro navigation of the microrobot in a microfluidic chip with a larger flow rate variation (750–1500 μm s⁻¹) and in vivo navigation of a smaller microrobot robot in the yolk of zebrafish larvae (80 μm s⁻¹). This work provides a guideline for the selection of microrobot dimensions and magnetic field actuation parameters for locomoting microrobots in biofluids with variable flow rates and directions. In future work, functional microrobots will be fabricated by coating cargo on surfaces for targeted delivery in various biofluid environments.

### 4. Experimental Section

**Magnetic Manipulation System**: The magnetic coil system was composed of five electromagnetic coils. Each coil was fabricated using copper wires of 1 mm diameter. Two coils were used for the X-axis drive,
two coils were adopted for Y-axis actuation, and another coil was employed for Z-axis control. The three groups of coils were driven by three servo amplifiers (model: ESCON 70/10, from Maxon Motor AG). Each servo amplifier was powered by a current power supply (model: KXN-6020D, from Shenzhen Zhaoxin Electronic Instrument and Equipment Co., Ltd.). The control signal was provided by a personal computer (model: OptiPlex 9020, from Dell Technologies Inc.) equipped with a driving board (model: PCI-6259, from National Instruments Corp.) with analog input and analog output channels. The program was written in LabVIEW software. The images of the microrobot were obtained by an industrial camera (model: 0745-0.5X, from Hangzhou Always Technology Co., Ltd.) with analog output. The images were recorded in the LabVIEW software for analysis.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the supplementary material of this article.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords

downstream motion, flow rate variation, magnetic actuation, microfluidics, microrobots, upstream motion

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.
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