Theoretical Analysis of Magnetically Propelled Microrobots in the Cardiovascular System

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Abstract— **The field of medical microrobotics is rapidly progressing; however, it is particularly challenging to control microrobots inside blood vessels. In this paper, the magnetic propulsion of a microrobot in pulsating flow is investigated. Regarding this task, the advantages of a reduced blood flow velocity are examined. The required magnetic field gradient in relation to the size of the microrobot is theoretically analyzed and compared to that for propulsion during reduced blood flow velocity. Quantitative and qualitative advantages together with the practical challenges are discussed.**

I. Introduction

Many teams around the world are researching on medical microrobotics because it will facilitate the development of many innovative and advantageous treatment approaches [1][2][3]. Medical microrobots for the vascular system are especially attractive for drug delivery and the treatment of cardiovascular diseases, and they offer many possibilities for interaction and a high degree of accessibility. However, there are some challenges to the use of microrobots. In addition to issues with biocompatibility, possible damage of blood vessels, and agglutination due to foreign objects, and control and navigation inside blood vessels and especially against the blood flow is arguably one of the biggest challenges for intravascular microrobots [4]. This is necessary to retrieve the microrobot and as a security measure in case of a failed branch selection.

In the authors' previous paper, a control concept for navigation in blood vessels has been described [5]. The microrobot considered had a cuboid size of 1 mm × 1 mm × 4 mm. Other groups have experimented with larger and more complex devices for the treatment of cardiovascular diseases (e.g., atherosclerotic plaque) [6][7]. The currently followed standard treatment of cardiovascular disease is also enhanced by catheters that can be steered by a magnetic field and advanced or retracted automatically [8]. All these methods are limited to use in relatively large blood vessels owing to the size of the devices. Previously developed microrobots could only be navigated in blood vessels with significantly larger diameters than the devices. An improved treatment of cerebral hemorrhage for example, would require the navigation in blood vessels very different in size and often smaller than 1 mm in diameter. Further, more than two blood vessel branches must frequently be navigated in order to reach the treatment area. This is very challenging and often impossible with a catheter, and thus, it limits the treatment area in the brain. Currently, the alternative treatment used in this case is a highly invasive surgical procedure. Therefore, microrobots that can be navigated in such small branching blood vessels are desirable for expanding the application of minimally invasive cardiovascular treatment.

One of the most common propulsion methods of microrobots is using a magnetic field, which propels the robot by a gradient or torque [9][10][11]. However, this constrains the minimal size of a microrobot operated in the cardiovascular system if it has to be fully controllable. The search for alternative or modified propulsion techniques has been motivated by the work of Nakamura et al. [5] and Pouponneau et al. [12], which only allow limited navigation.

This paper investigates how the blood flow influences the control of the microrobot. . The blood flow velocity changes in a pulsating flow and this should influence the control of the microrobot, but no previous work considered the change. Besides, there is a wide variety of possibilities available with which the blood flow velocity can be reduced (medication, balloon catheter, etc.), and such methods could be available in actual clinical cases. Thus, the required magnetic gradient field is analyzed for regular flow velocities and compared to the results for altered flow velocities.

II. Size of an Intravascular Microrobot

One of the main requirements for intravascular microrobots is small size. The small size aids navigation in blood vessels with small diameters. A smaller sized robot enhances access to the cardiovascular system significantly, thereby enabling treatments that are currently difficult or impossible using catheters.

A. Propulsion by a magnetic gradient field

State of the art research focuses on microrobots propelled by a magnetic gradient field, sometimes utilizing MRI scanners, as described in Folio et al. [13]. As mentioned above, a key requirement is the controllability of the microrobot against the blood flow to retrieve it. Thus, the minimal size of a spherical microrobot can be calculated by considering two major forces: drag force and magnetic force.

The drag force can be calculated as

$$F_d = \frac{1}{2}\rho_f u_d^{\ 2} A C_d\,, \tag{1}$$

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where ρ_f is the fluid density (in this case, blood), u_d is the relative velocity between the microrobot and blood, and A is the frontal area of the microrobot [14]. The drag coefficient C_d is approximated by

$$C_d \approx \frac{24}{\text{Re}} + \frac{6}{1+\sqrt{\text{Re}}} + 0.4; \quad 0 \le \text{Re} \le 2\times10^5, \quad (2)$$

with the Reynolds number being defined as

$$\text{Re} = \frac{\rho_f u_d d}{\mu}, \quad (3)$$

where d is the microrobot's diameter, and μ is the viscosity of blood. Equation (1) in combination with (2) and (3) shows that the drag force scales proportional to the radius squared or even the radius for Re < 1. This implies that it becomes increasingly difficult to transfer the necessary magnetic force to the microrobot with decreasing size. The transferrable magnetic force is defined by

$$\mathbf{F}_m = V\mathbf{M} \bullet (\nabla \mathbf{B}), \quad (4)$$

where V is the magnetic volume, $\mathbf{M}$ is the magnetization and $\nabla \mathbf{B}$ is the magnetic field gradient. Thus, the magnetic force is proportional to the magnetic volume, which scales with the cube of the radius for a sphere.

For successfully controlling microrobots in the cardiovascular system, the minimum requirement can be assumed to be the counteraction of the average blood flow velocity. This would result in the microrobot being at the same position after one heart beat cycle if the robot is propelled with the maximum magnetic field gradient. A microrobot for clinical utilization should be able to move against the flow or even hold its position during maximum blood flow velocity; however, this simplification is introduced to show the magnitude of forces and sizes necessary for actuation. Assuming blood flow velocities from Berger et al. [15], the necessary magnetic field gradient is calculated and shown in Fig. 1. The magnetization of the microrobot is assumed as 5 * 10^5 A/m. However, an adaptation for different magnetizations is straightforward as the necessary magnetic field strength behaves inversely proportional to the magnetization.

B. Magnetic propulsion with altered blood flow

Clinical usage of intravascular microrobots requires high controllability as well as additional space for tools, sensors, and/or drugs. Thus, a smaller magnetic volume would have a great advantage. The blood flow, particularly in large blood vessels, is highly pulsatile. Thus, the reduction of the blood flow velocity during the intervention with the microrobot would be advantageous. Especially, the minimization of the peak flow would be beneficial to facilitate microrobots more accurately.

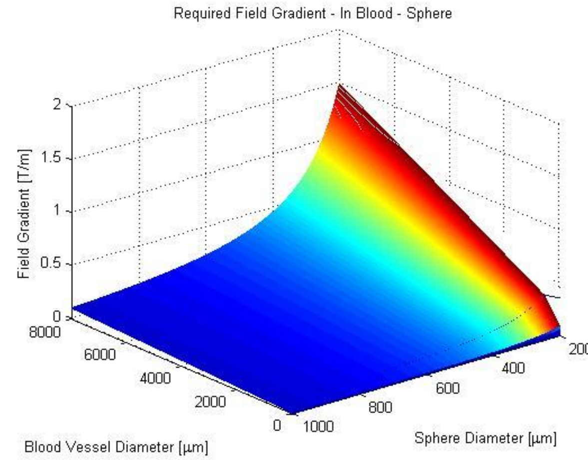

Figure 1. Required magnetic field gradient to hold a sphere at one location for the average flow velocity of different blood vessels sizes

1) Pulsatile Blood Flow

In some clinical applications, a microrobot would be required to be stationary during the treatment. This requires a microrobot to counteract the maximum blood flow velocity with very high accuracy. A blood flow with high peak velocities would result in even more challenging specifications for the controller. Thus, intravascular interventions using microrobots would benefit from a reduction of the blood flow velocity. For ease of visualization, two examples are given. First, the ratio of minimum blood flow velocity to maximum blood flow velocity is assumed 0.6 and 0.8 [16]. This value can be significantly different between individual patients. The correlation of the microrobot's size and necessary magnetic field gradient can be calculated, and is shown in Fig. 2 for a ratio of 0.6, and in Fig. 3 for a ratio of 0.8. For a velocity ratio of 0.6 in an 8 mm blood vessel, the magnetic field gradient for a microrobot during minimum blood flow can be reduced by approximately 50% in comparison to the navigation during maximum blood flow. Another option would be to reduce the magnetic volume of the robot. If a maximum magnetic field gradient of 0.2 T/m is assumed, a magnetic microrobot would need a minimal diameter of 860 µm during maximum blood flow velocity. The minimum diameter can be reduced to 550 µm for the minimum flow velocity as shown in Fig. 2. The magnetic volume of the microrobot during minimum blood flow velocity could be reduced by more than 30% compared to the maximum velocity.

2) Increased Robot Size due to Payload

The required magnetic field gradient may be calculated for a magnetic core with a non-magnetic surface around it. This space could be used for designated payload.

As an example, the payload is assumed to account for 40% of the microrobot's volume. All other assumptions are as before with a blood velocity ratio of 0.6. The results are shown in Fig. 4. A microrobot at minimum blood flow rate with 40% of its volume being payload would require a lower magnetic gradient field than a purely magnetic microrobot at maximum

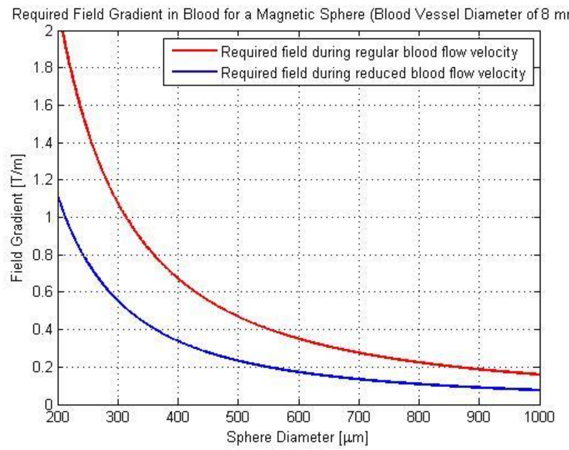

Figure 2. Comparison of required magnetic field gradient for a spherical microrobot to counteract the flow in a 8 mm blood vessel during regular and reduced blood flow velocity (ratio of 0.6)

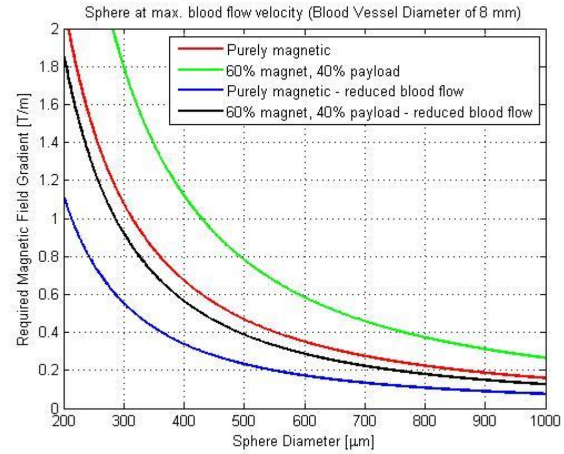

Figure 4. Comparison of required magnetic field gradient of microrobots with and without payload (blood vessel diameter of 8 mm)

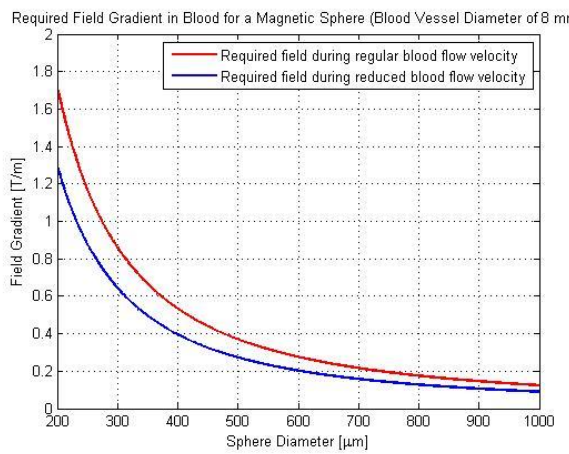

Figure 3. Comparison of required magnetic field gradient for a spherical microrobot to counteract the flow in a 8 mm blood vessel during regular and reduced blood flow velocity (ratio of 0.8)

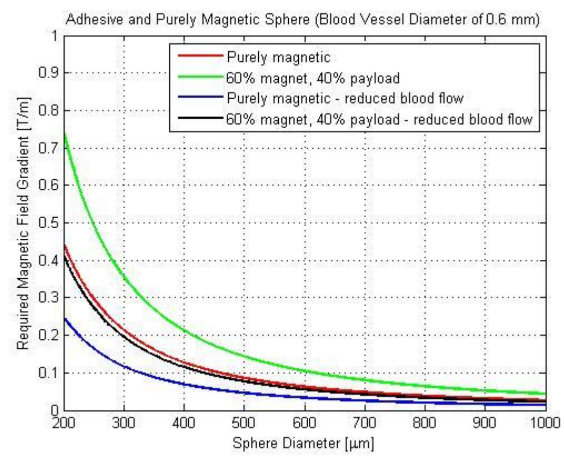

Figure 5. Comparison of required magnetic field gradient of microrobots with and without payload (blood vessel diameter of 0.6 mm)

flow rate. The required field gradients for all specified results in Fig. 4 are considerably high and it is questionable if these can be achieved conveniently and securely in a clinical environment [17]. The calculations assume a blood vessel diameter of 8 mm, in which considerably small microrobots would probably not be used. Thus, the assumption of a smaller blood vessel seems realistic. Further, the microrobot could be introduced by a catheter or injected from the outside into a considerably smaller blood vessel. This would result in a significant reduction of the necessary magnetic field gradient. Fig. 5 shows the results of the calculations for a blood vessel diameter of 0.6 mm. For example, a purely magnetic microrobot with a sphere diameter of 300 µm would require a magnetic field gradient of 200 mT/m. This would increase to approximately 350 mT/m if 40% of the volume were used for payload. The continuous reduction to the minimum blood flow rate would reduce the necessary field gradient of the microrobot including payload to approximately 200 mT/m.

III. Future Work

The presented results are simulations, and thus their accuracy has to be tested in experiments. Further, more analysis have to be made regarding the magnetic field gradient necessary for practical and safe navigation in realistic environments.

Medically available methods to reduce the peak and average blood flow velocity during the intervention with the microrobot should be investigated. Besides, the optimal shape and size of the microrobot has to be determined, depending on the specified task. The pulsating blood flow has to be taken into account. One possibility would be the stabilization of the stationary robot during high blood flow velocities and moving the robot during slow blood flow velocities.

The successful real-time navigation of the microrobot is highly dependent on the accuracy and frequency at which the microrobot is tracked. This requires a medical imaging modality with high resolution, and in particular, observation inside the skull is required for tracking in the cerebral circulation system. The most promising method might be computer tomography. A higher autonomous navigation would be preferable to reduce the radiation exposure of the patient.

The materials of the microrobot need to be biocompatible even for temporal use. Durable coatings are required to guarantee patient safety. Further, the system should fail safe, and the attachment of a safety tether to the microrobot would be an option.

IV. Conclusion

The cardiovascular system offers many opportunities to improve upon current treatments with microrobots. The requirements for a magnetic field gradient propulsion have been analyzed theoretically, identifying the main possibilities and challenges. The propulsion of microrobots in the cardiovascular system seems generally feasible but challenging. Gradient fields around 200 - 400 mT/m could allow the navigation in small blood vessels with a wide range of possible interventions. The reduction of the average and peak blood flow velocity are key variables for a practical use in a clinical environment. This has to be achieved while ensuring the safe operations of the microrobot at all times.

References

[1] J. Rosen, B. Hannaford, and R. M. Satava, *Surgical Robotics.* New York: Springer-Verlag, 2011, ch. 13.

[2] J. N. Weaver, J. C. Alspaugh, and B. Behkam, "Toward a Minimally Invasive Bladder Pressure Monitoring System: Model Bladder for In Vitro Testing," in *Proc. of the 3rd IEEE RAS/EMBS International Conf. on Biomedical Robotics and Biomechatronics*, Tokyo, 2010, pp. 638–643.

[3] W. Wang, S. Li, L. Mair, S. Ahmed, T. J. Huang, and T. E. Mallouk, "Acoustic Propulsion of Nanorod Motors Inside Living Cells," *J. Angew. Chem. Int. Ed.*, vol. 53(12), pp. 3201-3204 2014.

[4] S. Martel, "Microrobotics in the vascular network: present status and next challenges," *J. Micro-Bio Robot*, vol. 8, no. 1, pp. 41–52, Feb. 2013.

[5] S. Nakamura, K. Harada, N. Sugita, M. Mitsuishi, and M. Kaneko, "Electromagnetic Drive of Microrobot Geometrically Constrained in Blood Vessel," in *Proc. 33rd Annual International Conference of the IEEE EMBS*, Boston, 2011, pp. 6664–6667.

[6] M. Mura, G. Ciuti, P. Dario, and A. Menciassi, "An Ultrasound-based Methodology for Endoluminal Robot Tracking in Cardiovascular Procedures," in *Proc. The Hamlyn Symposium on Medical Robotics*, London, 2013, pp. 39–40.

[7] P. Miloro, M. Khorami Llewellyn, S. Tognarelli, G. Ciuti, E. Sinibaldi, P. Dario, and A. Menciassi, "An innovative platform for treatment of vascular obstructions: system design and preliminary results," in *Proc. The Fourth IEEE RAS/EMBS International Conf. on Biomedical Robotics and Biomechatronics*, Roma, 2012, pp. 731–736.

[8] J. Bradfield, R. Tung, R. Mandapati, N. G. Boyle, and K. Shivkumar, "Catheter Ablation Utilizing Remote Magnetic Navigation: A Review of Applications and Outcomes," *J. PACE*, vol. 35, pp. 1021–1034, Aug. 2012.

[9] B. J. Nelson, I. K. Kaliakatsos, and J. J. Abbott, "Microrobots for Minimally Invasive Medicine," *Annu. Rev. Biomed. Eng.*, vol. 12, pp. 55–85, Apr. 2010.

[10] K. E. Peyer, L. Zhangb, and B. J. Nelson, "Bio-inspired magnetic swimming microrobots for biomedical applications," *Nanoscale*, vol. 5, pp. 1259–1272, 2013.

[11] P. Vartholomeos, C. Bergeles, L. Qin, and P. E. Dupont, "An MRI-powered and controlled actuator technology for tetherless robotic interventions," *Int. J. Robot. Res.*, vol. 32, pp. 1536–1552, 2013.

[12] P. Pouponneau, J. Leroux, G. Soulez, L. Gaboury, and S. Martel, "Co-encapsulation of magnetic nanoparticles and doxorubicin into biodegradable microcarriers for deep tissue targeting by vascular MRI navigation," *Biomaterials*, vol. 32, pp. 3481–3486, 2011.

[13] D. Folio, C. Dahmen, T. Wortmann, M. A. Zeeshan, K. Shou, S. Pané, B. J. Nelson, A. Ferreira, and S. Fatikow, "MRI Magnetic Signature Imaging, Tracking and Navigation for Targeted Micro/Nano-capsule Therapeutics," in *Proc. IEEE/RSJ International Conf. on Intelligent Robots and Systems*, San Francisco, 2011, pp. 1297–1303.

[14] F. M. White, *Viscous Fluid Flow*, ser. Mechanical Engineering. New York: McGraw Hill, 1991.

[15] S. A. Berger, W. Goldsmith, and E. R. Lewis, *Introduction to Bioengineering*, Oxford: Oxford Univ. Press, 1996.

[16] S. Hajsadeghi, S. Fereshtehnejad, S. Gholami, M. Chitsazan, and M. R. Keramati, "Pulsatility Index in Aortic Coarctation: A Possible Way to Evaluate Factors Affecting Stenting Outcome," *J. Tehran University Heart Center*, vol. 7(1), pp. 19–24, 2012.

[17] A. Kangarlu and P. L. Robitaille, "Biological Effects and Health Implications in Magnetic Resonance Imaging," *Concept. Magnetic Res.*, vol. 12(5), pp. 321–359, 2000.