Article:

Sun, B., Wood, G. and Miyashita, S. orcid.org/0000-0002-9795-9247 (2021) Milestones for autonomous in vivo microrobots in medical applications. Surgery, 169 (4). pp. 755-758. ISSN 0039-6060

https://doi.org/10.1016/j.surg.2020.10.040

Milestones for Autonomous In-Vivo Microrobots in Medical Applications

Bo Sun[1], Georgina Wood[2], and Shuhei Miyashita[1*]

[1]Department of Automatic Control and Systems Engineering, University of Sheffield, Portobello St, Sheffield, S1 3JD, UK.
[2]Department of Bioengineering, University of Sheffield, UK.

*Corresponding author
Email: shuhei.miyashita@sheffield.ac.uk

Abstract

In light of recent developments within both healthcare and robotics, the use of robots within the human body has become attainable. Here we discuss the milestones for the realization of autonomous microrobots in medical applications. The desired tasks were classified by identifying the difficulties and requirements faced by the robot. In addition, we classified the levels of autonomy seen in microrobots for these uses. The aim of this article is to provide readers with a good understanding of the current state and future possibilities in this field.

The standardized information

Topic	Deriving milestones for highly autonomous microrobots in medical fields.
Purpose	This manuscript aims to describe the technical challenges for the realization of in-vivo microrobots for medical applications.
State-of-the-Art	The current state-of-the-art of microrobots is remote control of passive agents supervised by an external operator for simple single-event tasks such as drug delivery or proof-of-concept level biopsies.
Knowledge Gaps	The challenges associated with various medical and surgical procedures broken down to respective microrobotic tasks are not well studied and remain unknown.
Technology Gaps	Microrobot hardware is currently at the level of a simple combination of sensors and actuators with limited single-event task employability and operation time.
Future Directions	Future investigation and applications of autonomous microrobots will likely include more effective and autonomous locomotion, real time environment sensing, and the planning and execution of tasks such as drug delivery and suturing.

Robots have shown great potential in increasing access to remote locations and carrying out procedures in various sectors from the deep ocean to space. When it comes to scales smaller than a centimeter, which is often a requirement for use inside the human body, microrobots[1] are required. Due to their size, microrobots provide the possibility to conduct non-invasive examinations and surgeries inside the body, which has the potential to decrease complications from these procedures due to reduced tissue trauma. However, the development and operation of microrobots faces significant technical challenges mainly due to difficulties in packaging all the components required to achieve the desired performance. The issue of packaging constraints particularly affects a microrobot's degree of autonomy, as the onboard computing hardware must be kept to a minimum. These robots are required to have the intelligence to consider various physiological and pathological factors, and the ability to make decisions in real time in treating patients with a range of diseases. An autonomous microrobot for surgical and medical intervention could ensure that monitoring is carried out in situ at all times during treatment while under the supervision of clinical operators. Such robots could thus move treatments to homes, rather than hospitals. One example of a microrobot currently being developed is an ingestible robot which is deployable in the stomach which is able to patch a wound and remove a foreign object without the need for surgical interventions developed by Miyashita *et al*[1]. In this article, we discuss the challenges for microrobots to become fully autonomous for in-vivo operation, and present a framework for evaluating the degree of microrobot autonomy. First we review the technical difficulties of in-vivo clinical micro-operations referring to the work by Nelson *et al* [2] and others, classifying them into three levels. Then we argue a possible classification of autonomy level for microbots in medical applications, based on the definition of surgical robots in the work of Haidegger [3].

There is a wide range of potential applications for microbots in surgery and medicine which can be categorized by the difficulty of the task needing to be executed (see Table 1). Task difficulty level 1 (TDL-1) encompasses processes that require a microrobot to act as a sensing device or controllable mechanical structure. Examples of this level include remotely activated stents and scaffolds [4] and capsule endoscopes; which are able to carry out telemetry and send information about the internal environment, such as images, temperature and pH [5] to the user. Task difficulty level 2 (TDL-2) is where the majority of current research effort lies. These robots show basic levels of local environment sensing, motion and simple decision making capabilities which enables them to assist medical professionals with a series of one-time treatments including drug delivery [6]and biopsies [7]. The main challenge faced with the development of these TDL-2 robots is the inability of the microrobot to carry out tasks without operator control, as it is difficult to encompass enough onboard intelligence in a compact body to make the correct decisions. Although human interaction is still required, some exciting steps have been made towards the use of TDL-2 robots in clinical applications. One example has been capsule endoscopes that are capable of taking an intestinal biopsy with an onboard biopsy needle [8]. This has been carried out successfully in porcine small intestines. TDL-3 tasks are classified as being fully autonomous meaning they are able to carry out various diagnostic and treatment processes alone, replacing the role usually carried out by a medical professional. This level includes tasks such as excision or material removal and thermoablation, however, most TDL-3 microrobots are still in the exploration stage and are far from realization. One of the main requirements of robots is the ability to actuate tasks meaning the robots have the ability to start an action. This is a requirement in order for any movement to be started by the robot. As the robot exhibits more control in the decision making process, the tasks can be considered to become more difficult for the robot itself which is an important distinction to be made in this classification process.

---

[1] By convention, the term "microbots" pertains to both milli- and micro-scale robots.

Autonomy and Decision making in Microrobots

To understand and describe autonomy and decision-making in microrobots, we discuss levels of autonomy required for their use in medicine, and the milestones in their performance of tasks traditionally carried out by a human operator. When a low level of autonomy is required, often a single decision needs to be made meaning the autonomous nature of the device is clear to see. This becomes more difficult when the autonomous tasks required become more expansive. In order to design autonomous devices we need to consider surgeons' abilities and the choices they make whilst carrying out these decisions and ensure the robot is too. Haidegger defines level of autonomy (LoA) in robotic surgery in levels from LoA-0 where no autonomy is recognized to LoA-5 with *"complete robotic treatment planning and execution"*. We have adapted these definitions to microrobots which can be seen in Table 2.

When specifying the level of decision making carried out by the robot the degree to which the robot can complete the project autonomously is considered. If the decision is decided through manual intervention and takes into account a low number of external factors it is considered a low-level decision. If the decisions and actions are carried out autonomously and have little to no manual intervention they can be considered high-level. This definition means that robots sit along a scale and their 'level' of decision making can vary depending on the task at hand.According to the Defence Advanced Research Projects Agency (DARPA), Artificial Intelligence can be characterized by the possessions of the following four capabilities: perceiving, reasoning, learning, and abstracting [9]. In microrobotics, perceiving is the use of sensors, reasoning is the choosing of proper actions referring to sensory input and own states (so to speak a lookup decision and solution table), learning is the tuning of control variables such as a motor activation pattern for improved grasping and morphologies to adapt to new situations, and abstraction is the processing of sensory raw data so that the information can be interpreted by humans interfaced with other components in the system and the environment. Decision making for a microrobot can be regarded as a problem-solving activity utilizing the above five capabilities to determine what to do next based on the current state and known conditions during the execution of the task. As operations become more complex, a higher level of decision making is required. Problems need to be identified using onboard sensors which consider the patients safety and possible side effects of their actions. This requires the processing of small and sometimes ambiguous biological signals which further increases the difficulty for the robot.

Challenges

Currently, sensing and operation of the microrobot are the primary areas of research focus in microbotics. Autonomous robots need not only to be equipped with sensors that are able to measure the environmental conditions of interest but also general multimodal sensors which can provide it with more comprehensive information about influencing factors to support its low level decision making. Force, torque production and dexterity will be the principal challenges of microrobot action. Under certain circumstances, a microrobot arm needs a specific degree of freedom to complete a basic manipulation task in a 3D space, which is quite demanding. Robots are programmed to carry out these tasks using two methods, scaled advanced mechanical and electronic components or programmable materials. Component integration requires the utilisation of electronic components on a micro scale using a tiny computer. The size limitations have meant difficulties in control, component integration and power supply but large steps are being made towards overcoming these problems such as wireless control and powering [11]. Programmable materials do not use electronic components and instead combine chemical, biological and smart material technologies which change shape based on the local environment enabling them to carry out specific tasks [1]. Besides high-density power storage and wireless powering, harvesting energy from the environment is another possible solution for microscale power supplies. High-level decisions will need to be assisted by comprehensive understanding of the patient's local physiological and pathological condition and their general health. Such decisions continue to face the classical but fundamental AI problem of how to interpret physics with semantics which is known as the 'Symbol Grounding Problem'. Statistics on many similar patients around the world, involving remotely conducted learning processes may help making those decisions, though the challenge will remain difficult for a microrobot to accurately analyze all available data in real-time. Research is still needed to understand these factors before the data can be applied to and used by microrobots. Through understanding the requirements and developments needed to create microrobots for use in surgery, exciting steps can start to be made towards their use. In the future there are two directions to be taken in microrobot development. One will focus on the development of smart materials, which use their architecture to create robots and the other will focus on the development of mechanical and electrical components enabling the development of smaller scale more 'traditional' robots. These developments will be used to assist and cooperate with doctors to complete medical tasks.

Table 1: Task difficulty level (TDL) for microrobots in medical applications

Task difficulty level and description	Examples of clinical applications	Robot tasks
TDL-1: A robot needing to act as a mechanical or chemical transmitter of the input signal carrying out a simple action and limited local sensing.	- Stent - Scaffold - Telemetry	**Movement and Control** -No self driven locomotion is necessary -Actuation of structure and/or volume change. -Load carriage -Act as a passive agent or externally controlled by an operator. **Sensing:** - On-site sensing of physical environmental values (mechanical stress, pH, temperature, biochemical) - Visual/optical sensing - Detecting objects and communicating positional location
TDL-2: Basic level of local perception, ability of primary action and simple decision making required.	- Targeted therapy - Drug delivery - Marking - Biopsy - Excision - Implant placement - Remote palpation - Laparoscopy	**Movement and Control** -Some but limited motion within the environment. -Material grasping means material manipulation, transportation and removal is possible. -Operator is still involved but is able to carry out simple tasks under supervision such as navigation and simple planning. **Sensing - Better knowledge of the surrounding environment and areas of interest:** - Recording, data storing - Real time detection of own locomotion - Multimodal sensory input integration
TDL-3: High level recognition of the global state, high performance capability and proper execution of tasks required.	- Laser/Ultrasound ablation - Brachytherapy - Chemotherapy - Targeted hyperthermia and thermoablation [2] - Suturing	**Movement and control** -Able to carry out extensive movement within the environment. -Can plan and evaluate tasks with much greater autonomy. **Sensing:** - Visual and higher level information processing - Realtime creation of an environmental map - Object identification

Table 2: Levels of autonomy in microrobots for medicine, adapted from [3]

Levels of autonomy in microrobots for medicine	**LoA-0** **No autonomy (e.g., medication).** Purely passive and no communication outside of the body.	**LoA-1 and LoA-2** **Externally controlled device and task-level autonomy.** Microrobots perform low-level, single event operations guided by an operator.	**LoA-3 and LoA-4** **Supervised autonomy and high autonomy.** Microrobots can reflect sensory information in low-level actions choosing from a list, while some critical decisions are made by an operator.	**LoA-5** **Full autonomy.** Microrobots can access fertile sensory information, understand the situation from various viewpoints, develop elaborate task execution methods, and carry out a series of actions of their own.
Existence of operator	No communication with the outside of the body needed hence no operator involved.	Professional monitors the operating environment.	Microrobot monitors the operating environment, but leaves room for a human operator to control in an emergency.	Microrobot monitors the operating environment.
Sensing	No sensing	Yes Onboard sensors or smart materials to measure or respond to various physical, chemical and physiological input		
Actuation and Motion-The ability of the robot to start and continue an action. This is a requirement in order for any movement to be carried out by the robot.	No Actuation. (eg.Intelligence pills rely on gastrointestinal motility to move)	Low power in action and simple dexterity in monitors. Such as Electromagnetic control (e.g.Capsule endoscopes)	High power in action and dexterity in monitors. - Electromagnetic actuation - Magneto-mechanical actuation - Opto-thermal actuation - Ultrasonic actuation	
Power supply- It is desirable for the power to be autonomous meaning it is able to carry or produce its own power negating the need for wires.	- No battery	- Onboard battery - Wireless power transfer	- Onboard battery - Wireless power transfer - Energy harvesting from environment (e.g., microbial fuel cell [10])	
Programmability	No		Yes	
Self-diagnosis and fault tolerance	No			Yes System can self-diagnose its state with sensors that monitor its own state and can recover from error with fault tolerance ability.
Decision making control	Decisions completely made by an operator.	Decisions mainly made by an operator.	Microrobot makes the decisions, but is overseen by an operator.	Decisions completely made by the microrobot.

COI/Disclosure: There is no conflict of interest to declare.

Funding/Support: Authors thank the Department of Automatic Control and Systems Engineering at the University of Sheffield for their financial support.

References

[1] Miyashita, S., Guitron, S., Yoshida, K., Li, S., Damian, D. and Rus, D., 2016. Ingestible, controllable, and degradable origami robot for patching stomach wounds. *IEEE International Conference on Robotics and Automation (ICRA)*, pp.909-916.

[2] Nelson, B., Kaliakatsos, I. and Abbott, J., 2010. Microrobots for Minimally Invasive Medicine. *Annual Review of Biomedical Engineering*, 12(1), pp.55-85.

[3] Haidegger, T., 2019. Autonomy for Surgical Robots: Concepts and Paradigms. IEEE *Transactions on Medical Robotics and Bionics*, 1(2), pp.65-76.

[4] Zhang, H., Hutmacher, D., Chollet, F., Poo, A. and Burdet, E., 2005. Microrobotics and MEMS-Based Fabrication Techniques for Scaffold-Based Tissue Engineering. *Macromolecular Bioscience*, 5(6), pp.477-489.

[5] Biao, H., Guozheng, Y. and Peng, Z., 2009. Multi-sensor radiotelemetry system for intestinal motility measurement. *Journal of Medical Engineering & Technology*, 33(1), pp.66-71.

[6] Mandsberg, N., Christfort, J., Kamguyan, K., Boisen, A. and Srivastava, S., 2020. Orally ingestible medical devices for gut engineering. *Advanced Drug Delivery Reviews*, doi:10.1016/j.addr.2020.05.004.

[7] Kong, K., Yim, S., Choi, S. and Jeon, D., 2012. A Robotic Biopsy Device for Capsule Endoscopy. *Journal of Medical Devices*, 6(3), pp.1-9.

[8] Hoang, M., Le, V., Nguyen, K., Nguyen, V., Kim, J., Choi, E., Bang, S., Kang, B., Park, J. and Kim, C., 2020. A Robotic Biopsy Endoscope with Magnetic 5-DOF Locomotion and a Retractable Biopsy Punch. *Micromachines*, 11(1), p.98.

[9] Launchbury, J., 2017. A DARPA Perspective On Artificial Intelligence. Available at: https://www.darpa.mil/about-us/darpa-perspective-on-ai.

[10] Li, H., Liao, B., Xiong, J., Zhou, X., Zhi, H., Liu, X., Li, X. and Li, W., 2018. Power output of microbial fuel cell emphasizing interaction of anodic binder with bacteria. *Journal of Power Sources*, 379, pp.115-122.

[11] Basset, P., Kaiser, A., Legrand, B., Collard, D. and Buchaillot, L., 2007. Complete System for Wireless Powering and Remote Control of Electrostatic Actuators by Inductive Coupling. *IEEE/ASME Transactions on Mechatronics,* 12(1), pp.23-31.