Innovations to bring the MFG-100 Magnetic Field Generator to the Mechanobiology market

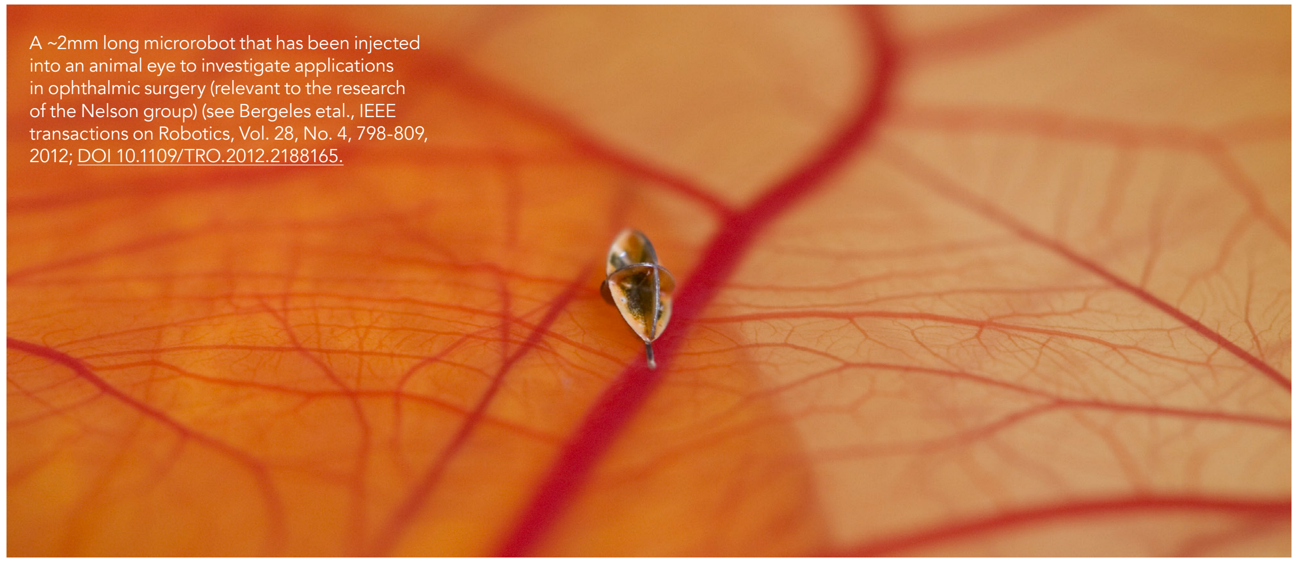
MagnebotiX AG, formed in 2014 as a spin-off company of the Institute of Robotics and Intelligent Systems at the Swiss Federal Institute of Technology in Zürich (ETH Zürich), specialises in developing tools for use in microrobot manipulation in biomedicine and other applications and produces the MFG-100 magnetic field generating system. In a project funded by the Swiss Committee for Technology and Innovation, Magnebotix AG is partnering with the research groups at ETH Zürich to develop new force-centred techniques for the global, small-scale magnetic actuation and manipulation market.

Small-scale robotics is a rapidly growing field of research with numerous potential applications in sensing, environmental remediation and the manipulation of small objects but especially in the biomedical sector. The last ten years has seen a huge increase in research efforts in the field, mainly due to advances in Nanotechnology and in the ability to fabricate as well as manipulate these tiny robots on such a small scale. Microrobotics (tiny robots measuring less than 1mm long) and nanorobotics (microrobots measuring less than 1micrometer), can now be manufactured using processes such as Direct Laser Writing (DLW), a newer technology that involves carving out the desired form from a block of some material such as plastic or resin with a microscopic laser beam. Three-dimensional printing on a micro scale is also being used to manufacture micro and nanorobots with growing success.

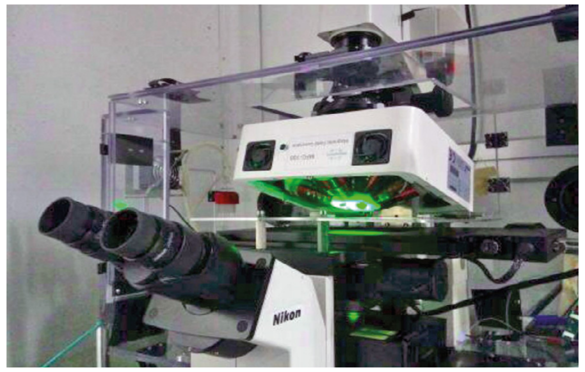
The manipulation of small-scale robots is most commonly done using magnetic fields, which can move the robots and adjust their orientation, direction and speed. These bots commonly have nickel or iron components, creating the magnetic forces needed for propulsion or other movements. Magnetic force is very versatile and can be applied to microbots at different frequencies and in many ways such as varying magnetic fields, magnetic gradients, rotating fields, or combinations of these.

SWIMMERS, WALKERS AND MICRODAGGERS

Mechanobiology is an emerging field where biology and engineering intersect, and which requires quantifications on how physical forces acting on cells and tissues regulate cell functions, tissue physiology and if unbalanced cause various diseases. Many researchers in the field of small-scale robotics have been inspired by the way cells or other microorganisms propel themselves in solutions and current nanobot designs are able to move easily through body fluids just as cells do. One such nanobot, known as a helical swimmer, moves through solutions in a rotating, corkscrew-type movement when exposed to a rotating magnetic field. By adjusting the frequency and direction of the magnetic field, these devices can roll, spin, or be propelled forward. Flexible Swimmers are nanorobots with flexible tails or joints that can move through fluid when they are exposed to an oscillating or rotating magnetic field. Surface Walkers can roll or tumble and are able to transport or manipulate small cargos inside cells or tissues. Other nanobots known as Microdaggers, can drill holes in cells and are composed of a non-magnetic body and several magnetic cilia on both sides. All these designs have valuable application in drug delivery.


A ~2mm long microrobot that has been injected into an animal eye to investigate applications in ophthalmic surgery (relevant to the research of the Nelson group) (see Bergeles etal., IEEE transactions on Robotics, Vol. 28, No. 4, 798-809, 2012; DOI 10.1109/TRO.2012.2188165.

The MagnebotiX MFG-100-i magnetic field generator on an inverted microscope for experiments at higher magnification, as used in mechanobiology. Both transmitted light or fluorescent optics can be used. The system shown is in a controlled atmosphere enclosure.



The MagnebotiX MFG-100 magnetic field generator under an upright microscope for micromanipulation tasks at intermediate magnification.

MAGNETICALLY MANIPULATING MICROBOTS

MagnebotiX, a spinoff company of the Multiscale Robotics Laboratory at ETH Zürich, develops and produces machines that generate magnetic fields and tools for the manipulation of micro and nanorobots. The company has developed and produced the MFG-100, a system that generates magnetic fields to manipulate small-scale robots to move in a variety of ways.

MagnebotiX develops and produces machines that generate magnetic fields and tools for the manipulation of micro and nanorobots.

Electromagnets consist of copper wire wound into a coil around an iron core. A current is passed through the wire, generating a magnetic field. The MFG-100 has eight fixed electromagnets which are individually controlled. The magnetic force extends from the ends of the electromagnets into a spherical region with a diameter of approximately 10 mm at the intersection of the axes of the electromagnets. The direction and strength of the resultant field is flexible and can be adjusted easily. This is accomplished through the summed contributions of the electromagnets acting together. The MFG-100-i is a modified version of the MFG-100, which can be easily used with an inverted microscope, allowing the simultaneous observation and manipulation of microbots inside of cells.

MagnebotiX also produces the RodBot, a wireless mobile microbot that can be used to harvest protein crystals from the bottom of small amounts of solution using a rotating magnetic field supplied by the MFG-100. The magnetic field causes movement of the RodBot in solution and creates a vortex, allowing protein crystals to be transferred gently without any resulting damage.

MICROSCOPIC TOOLS FOR INDUSTRY AND MEDICINE

Magnebotix AG CEO Dr David Sargent is now partnering with MagnebotiX cofounders and Professors Bradley Nelson and Simone Schuerle, and Prof Viola Vogel, all of ETH Zürich, in a project funded by the Swiss Committee for Technology and Innovation that focuses on innovations to bring the MFG-100 to the growing mechanobiology market. Each of these researchers brings extensive knowledge and expertise to the ongoing development of nano-scale tools for use with the MFG-100 and the field of mechanobiology.

Prof Brad Nelson has degrees in Mechanical Engineering (U. Illinois and U. Minnesota) and Robotics (Carnegie Mellon), and extensive experience in nanotechnology and biomedicine. Prof Nelson's lab drives robotics research in several areas and develops tools and processes needed to fabricate and assemble micron-sized robots and nanometer scale robotic components. Traditionally robotics has been a discipline to aid other fields, such as manufacturing and space exploration. However biomedical applications that exploit Mechanobiological Principles are growing rapidly, and Brad's lab has worked with the Vogel and Schuerle groups at ETH Zürich to develop tools for use in solving problems in mechanobiology. Other research areas of Brad's lab range from drug delivery inside cells using microscopic-sized magnetic particles, the manipulation of tiny, fragile protein crystals using the RodBot, and magnetically guided catheters for medical interventions.

While medicine has typically looked for the genetic and biochemical basis of disease, recent findings suggest that changes in cell mechanics and of the extracellular matrix that surrounds the cells contribute to the development of many diseases, including fibrosis, asthma, osteoporosis, heart failure, and cancer. Professor Viola Vogel, trained in Physics (Frankfurt Univ.) and founder of the Center for Nanotechnology (UW Seattle), is Head of the Laboratory of Applied Mechanobiology at ETH Zürich. Viola's research group uses nanotechnology to investigate how bacteria and mammalian cells exploit mechanical forces to recognise and respond to both their native and to engineered environments. For example, bacteria sense mechanical

A medium sized magnetic field generator (see hand for scale) used to study magnetically controlled surgical procedures in small animals.

Flexible Swimmers are nanorobots with flexible tails or joints that can move through fluid when they are exposed to an oscillating or rotating magnetic field.

forces and use this to regulate their adhesion to surfaces and tissue fibres.

One technique for studying such phenomena involves highly specialised microscopic magnetic tweezers to manipulate micro-objects. Developed with the research groups of Professors Nelson and Schuerle, the tweezers can remotely measure and apply minute mechanical forces using magnetic particles inside of cells and tissues to unravel complex processes that occur at the microscopic scale. Such work has enormous potential for use in investigating how cells move or adhere to surfaces or other cells to fight disease, or in medicine to reveal how nutrition, ageing or disease affect the structure or properties of cells or tissues of the body.

Professor Simone Schuerle has degrees in Industrial Engineering and Management (Karlsruhe Inst. Technology) and Microrobotics (ETH Zürich). She is Professor in the Department of Health Science and Technology at ETH, leading their Responsive Biomedical Systems Laboratory. Simone is a co-founder of MagnebotiX AG and serves as Global Future Council for the World Economic Forum. With extensive expertise in the use of magnetic manipulation techniques for biomedical applications, her group develops microtools to study disease at the nano- and microscale level, including cancer and musculoskeletal diseases. This knowledge is then used to guide the design and fabrication of novel nanosystems that are used in diagnostics and therapy for next-generation healthcare.

THE FUTURE OF THE MFG-100 AND NANOROBOTICS

The manipulation of nano and microrobots, especially in viscous complex fluids is still a developing area of research. Fabrication of small-scale robots remains challenging; however, their small size means that when manufactured in bulk they have the potential for low cost. The next decade will see a continuing exponential increase in the use of micro and nanorobots in biomedicine, and the development of the MFG-100 for the market will be the first step in defining its potential applications and future contributions to the field of mechanobiology.

Behind the Bench

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Bio

The partners in this project combine extensive experience in physics, robotics, bioengineering, nanotechnology and mechanobiology. Viola Vogel and Simone Schuerle are Professors in the Department of Health Sciences and Technology, and Brad Nelson is Professor of Robotics and Intelligent Systems, all ETH Zürich. David Sargent is CEO of MagnebotiX AG.

Research Objectives

The aim of this project is to allow the MagnebotiX magnetic field generator MFG-100 to access a broad, new market. They are currently developing i) a calibration module to enable assured, quantitative application in mechanobiology research, ii) calibration procedures for magnetic particles, iii) algorithms for standard procedures, and iv) carry out proof of concept studies to show that experiments performed with the improved MFG-100 are consistent with and also extend the range of present-day studies in this field.

Funding

Swiss Federation

Collaborators

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References

Simone Schuerle, Ima Avalos Vizcarra, Jens Moeller, Mahmut Selman Sakar, Berna Öz kale, Andre Machado Lindo, Fajer Mushtaq, Ingmar Schoen, Salvador Pane, Viola Vogel and Bradley J. Nelson. 2017. Robotically controlled micro prey to resolve initial attack modes preceding phagocytosis. Science Robotics, Volume 2, Issue 2: eaah6094, DOI: 10.1126/scirobotics.aah6094.

Xiang-Zhong Chen, Marcus Hoop Fajer Mushtaq Erdem Siringil Chengzhi Hu, Bradley J.Nelson and Salvador Pané. 2017. Recent developments in magnetically driven micro- and nanorobots. Applied Materials Today. Volume 9: 37-48. https://doi.org/10.1016/j.apmt.2017.04.006.

Tung, Hsi-Wen, David F. Sargent and Bradley J. Nelson. 2014. Protein crystal harvesting using the RodBot: A wireless mobile microrobot. Journal of Applied Crystallography. 47: 692-700 (2014). https://doi.org/10.1107/S1600576714004403.

Jens Möller, Tessa Lühmann, Mamta Chabria, Heike Hall and Viola Vogel. 2013. Macrophages lift off surface-bound bacteria using a filopodium-lamellipodium hook-and-shovel mechanism. Scientific Reports 3:2884 DOI:10.1038/srep02884.

Personal Response

What are the next steps for MagnebotiX AG?

In addition to the CTI project described in this article, MagnebotiX AG is also involved in an M-ERA.NET project with partners from Taiwan, Israel, Hungary, Austria, Luxemburg and Switzerland. Due to start in June this year, this project will work on the development of a novel organs-on-a-chip platform for nano drug delivery and functionality testing. Aiming at a treatment for Parkinson's disease, the project will use novel magnetoacoustic guidance for nano-drug carriers to achieve targeted drug delivery. With the developments from these two collaborations, MagnebotiX AG sees itself in an excellent position to both stimulate and capture a significant share of the magnetically guided microrobot manipulation and manufacturing markets. This includes engineering studies in robotics as well as applications in biological and medical research, as described here. With the ability to remotely control magnetic microprobes in 3D, our equipment will allow researchers to apply mechanical stimuli with well-controlled forces, loading rates and torques. These unparalleled capabilities will make the system a top contender in the mechanobiology community. Starting with market entry within 12 months, we expect to achieve sales of €8m and create new 15 positions within five years. Ultimately, we aim to capture 30% of a market valued at €85m annually.