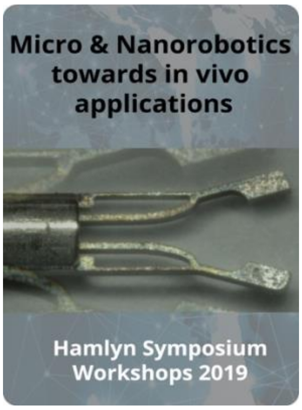

Workshop: Micro and Nanorobotics towards in vivo applications

Code: WPM08 | Wednesday, 26th June

Royal Geographical Society

Co-Chairs and Organisers:

Veronica Iacovacci, The BioRobotics Institute, Scuola Superiore Sant'Anna, Pisa, Italy

Bradley Nelson, Multi-Scale Robotics Lab, ETH Zurich, Switzerland

Salvador Pané, Multi-Scale Robotics Lab, ETH Zurich, Switzerland

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	Lunch
13:40	**Opening: Welcome & Introduction**
13:50	**Enzyme-powered Nanorobots Towards their Applications in vivo: Enhanced Delivery, Sensing and Imaging** *Samuel Sanchez, Barcelona Institute of Science and Technology (BIST), Barcelona, Spain*
14:10	**Wireless Actuation of Micro and Nanorobotic Systems in Real Organs** *Peer Fischer, Max Planck Institute for Intelligent Systems, Stuttgard, Germany*
14:30	**Microrobots for Cell Transplantation** *Hongsoo Choi, DGIST, Daegu, Korea*
14:50	**Sperm Microrobots and its Potential to Improve Reproductive Health** *Mariana Medina-Sanchez, Leibniz-Institut fur Festkorper- und Werkstoffforschung Dresden, Germany*
15:10	**Magnetoelectric Stimulation of Cells with Small-scale Robots** *Salvador Pané, ETHZ Zurich, Zurich, Switzerland*
15:30-15:45	**Coffee Break**
15:45	**SPECT-based Imaging of Soft Magnetic Microrobots** *Veronica Iacovacci, Scuola Superiore Sant'Anna, Pisa, Italy*
16:05	**Magnetic Microrobots for Cell Delivery** *(Keynote) Dong Sun, City University of Hong Kong, Hong Kong, China*

16:25 **Magnetic-based Targeted Therapy: from Accumulation to Retrieval**
Arianna Menciassi, Scuola Superiore Sant'Anna, Pisa, Italy

16:45 **Microrobots: From the Bench, to in vivo, to the Clinic**
Bradley Nelson, ETHZ Zurich, Zurich, Switzerland

17:05 **Closing Remarks**

Keynote Speaker:

Dong Sun, City University of Hong Kong, Hong Kong, China

Title:

Magnetic Microrobots for Cell Delivery

Abstract:

The precise delivery of targeted cells through magnetic-field-driven microrobots is a promising technique for targeted therapy and tissue regeneration. This talk will introduce our recent development of microrobot design and driven technologies for carrying and delivering targeted cells in vivo under a magnetic gradient field-driven mechanism. We have conducted this research in three perspectives of microrobot design, microrobot actuation and imaging, and pre-clinical applications for cancer therapy. The precise delivery of targeted cells offers various applications in precision medicine in the future.

Biography:

Dong Sun (F'15) received the bachelor's and master's degrees from Tsinghua University, Beijing, China, in 1990 and 1994, respectively, and the Ph.D. degree from the Chinese University of Hong Kong, Hong Kong, in 1997.,He is currently a Chair Professor and the Head of the Department of Mechanical and Biomedical Engineering, City University of Hong Kong. After performing his Post-Doctoral research with the University of Toronto, Toronto, ON, Canada, he joined the City University of Hong Kong, as an Assistant Professor, in 2000. His current research interests include robotics and the related biomedical engineering particularly for cellular engineering applications.,Dr. Sun was a recipient of the numerous best paper awards from the international journal and conferences, as well as industrial awards, such as Hong Kong Awards for Industry. He served on editorial boards for several prestigious international journals, such as the IEEE Transactions on Robotics and the IEEE/ASME Transactions on Mechatronics. He organized several international conferences as the general or program chairs.


최홍수 교수

Speaker:

Hongsoo Choi, DGIST, Daegu, Korea

Title:

Microrobots for Cell Transplantation

Abstract:

Magnetically actuated microrobots have been developed for three-dimensional cell culture and precise delivery of stem cells in vitro, ex vivo, and in vivo. Spherical and helical scaffold microrobots have been developed and controlled by rolling and corkscrew motions using a rotating magnetic field for efficient propulsion to overcome resistive forces, such as drag or friction. Hippocampal neural stem cells attached to the microrobots were proliferated and selectively differentiated into astrocytes,

oligodendrocytes, and neurons. The microrobots were also used to transport colorectal cancer cells to a tumor microtissue in a body-on-a-chip system containing an in vitro environment with liver and tumor micro-tissues. For the ex vivo test, the microrobots were manipulated in a mouse–brain slice and rat-brain blood vessel after being made transparent by the CLARITY technique. Finally, microrobots with mesenchymal stem cells derived from the human nose were controlled in the intraperitoneal cavity of a nude mouse for in vivo use. The results demonstrate the potential of microrobots for culture, stem cell delivery and transplantation in vitro, ex vivo, and in vivo.

Biography:

Prof. Hongsoo Choi received Ph.D. in the department of Mechanical Engineering from Washington State University, USA (2007). He is currently a professor in the department of Robotics Engineering at Dague Gyeongbuk Institute of Science and Technology (DGIST) in South Korea. He is also a co-director of DGIST-ETH Microrobotics Research Center (DEMRC). His research areas are biomedical microrobots for targeted therapeutics, MEMS based devices for biomedical applications, especially, piezoelectric devices such as piezoelectric micromachined ultrasound transducer (pMUT) and artificial cochlea using piezoelectric sensors.

Speaker:

Peer Fischer, Max Planck Institute for Intelligent Systems, Stuttgard, Germany

Title:

Wireless Actuation of Micro and Nanorobotic Systems in Real Organs

Abstract:

It is demanding to develop micro- and nanorobotic systems that can be actively propelled through "real" tissues. Systems that are relatively easy to move through liquids or liquid cavities in the body can often fail when the medium is an organ or tissue. This is also true in the case of very soft tissues, like the vitreous body of the eye. I will describe the challenges we encountered in developing micropropellers that can be driven over cm-distances through an eye, yet be located using standard OCT imaging. In the second part of my talk I will address a challenge often encountered when testing and developing new medical devices and procedures: The absence of realistic models. We have developed a full urinary tract phantom that shows high fidelity in medical imaging and that can be used for a transurethral resection of the prostate or suturing by laparoscopy. The phantoms are ideal for the development of, training on and evaluation of robotic surgery systems.

Biography:

Peer Fischer is a Professor of Physical Chemistry at the University of Stuttgart and he heads the independent Micro Nano and Molecular Systems Lab at the Max Planck Institute for Intelligent Systems in Stuttgart.

He received a BSc. degree in Physics from Imperial College London and a Ph.D. from the University of Cambridge. He was a NATO (DAAD) Postdoctoral Fellow at Cornell University, before joining the Rowland Institute at Harvard. At Harvard he held a Rowland Fellowship and directed an interdisciplinary research lab for five years. In 2009 he received an Attract Award from the Fraunhofer Society which led him to set up a photonics lab at the Fraunhofer Institute for Physical Measurement

Techniques in Freiburg. In 2011 he moved his lab to the Max Planck Institute for Intelligent Systems in Stuttgart, and since 2013 he is a Professor at the University of Stuttgart.
Peer Fischer won an ERC Grant as a consolidator in 2011 and in 2016 he won a World Technology Award. He received an ERC Advanced Grant in 2018. He is a member of the Max Planck – EPFL Center for Molecular Nanoscience and Technology, and the research network on Learning Systems with ETH Zürich. Peer Fischer is a Founding Editorial Board Member of the journal AAAS Science Robotics and a Fellow of the Royal Society of Chemistry. Professor Fischer has broad research interests including 3d nanofabrication & assembly, micro- and nano-robotics, active matter, interaction of optical, electric, magnetic, and acoustic fields with matter at small length scales, chirality, and molecular systems engineering.

Speaker:
Veronica Iacovacci, Scuola Superiore Sant'Anna, Pisa, Italy

Title:
SPECT-based Imaging of Soft Magnetic Microrobots

Abstract:
Untethered small-scale robots have great potential for biomedical applications. However, critical barriers to effective translation of these miniaturized machines into clinical practice exist. High resolution tracking and imaging in vivo is one of the barriers that limit the use of micro- and nanorobots in clinical applications. Here we present novel soft theranostic microrobots. The inclusion of radioactive compounds in soft thermoresponsive magnetic microrobots was investigated to enable their SPECT imaging. Results including single microrobot imaging of structures as low as 100 µm in diameter, as well as the tracking of shape switching from tubular to planar configurations will be presented. The employment of thermally triggered shape transformation as drug release mechanism will be described as well.

Biography:
Veronica Iacovacci obtained a PhD in BioRobotics from Scuola Superiore Sant'Anna (full marks) in June 2017, with a thesis entitled "Smart Magnetic microrsystem for targeted therapy" and she's currently a Post Doctoral fellow at the BioRobotics Institute of Scuola Superiore Sant'Anna in the Surgical Robotics and Allied technologies group. From July 2016 to January 2017 she has been visiting scientist at the Multiscale Robotics Lab (ETH, Zurich) led by Professor Bradley Nelson where she worked at the development of thermoresponsive magnetic microrobots for targeted drug delivery. her main research interests are in the field of artificial organs, towards the development of fully autonomous and implantable artificial pancreas and artificial bladder systems, advanced materials for healthcare applications, microrobots and smart magnetic microdevices for targeted therapy.

Speaker:
Mariana Medina-Sanchez, Leibniz-Institut fur Festkorper- und Werkstoffforschung Dresden, Germany

Title:
Sperm Microrobots and its Potential to Improve Reproductive Health

Abstract:
Medical hybrid microbiorobots which are driven by powerful microorganisms (e.g. bacteria) or motile cells (e.g. sperm cells) represent a promising approach as they combine the advantages of biological components (e.g. self-guidance mechanisms, ability to move in physiological environments and the possibility to load them with different cargoes), with the functionality of engineered microparts which serve as guidance/propulsion vehicles or to perform functions such as drilling or micrograsping, among others. To this end, our group has developed medical microbots to assist sperms with motion deficiencies to reach the oocyte, envisioning them for future in vivo assisted fertilization. We have proven the potential to guide sperms with engineered magnetic microtubes by aligning them along the external magnetic field. Sperm release was also possible using thermoresponsive polymer microtubes by a temperature change which was tuned to operate at physiological levels. We have also reported the use of helical micro-carriers, driven by an external magnetic field to transport and release viable immotile sperm cells. This is particularly interesting when sperms have no motility but are still functional and able to fertilize an oocyte (asthenozoospermia). However, with this approach there are major challenges such as identifying the most fertile sperm among the "low quality sperms", improving the coupling efficiency, the possibility to transport multiple sperms to improve the probability of fertilization, and their control and imaging in vivo, aspects that will be discussed in my presentation. We also proposed a new system where the sperm was loaded with an anticancer drug, followed by the coupling to a magnetic harness to guide it to a tumor spheroid. It also had a mechanical release mechanism which consisted in the opening of the sperm cavity once small flexible arms deform in contact to the tumor walls, releasing locally the drug-loaded sperm. This system has shown to have a great potential towards treating gynecological cancers.

Biography:

Speaker:
Arianna Menciassi, Scuola Superiore Sant'Anna, Pisa, Italy

Title:
Magnetic-based Targeted Therapy: from Accumulation to Retrieval

Abstract:
Steering and accumulation of magnetic particles in specific organs or organs portion appear as promising strategies for targeted therapy. The fundamental idea is based on the injection of magnetic responsive particles through the vasculature, on the guidance of these particles towards the target region, on the accumulation of the particles, and on the final triggering of the therapy (which can rely on hyperthermia, drug delivery, etc). Most research has been focused on accomplishing an effective

targeting and accumulation, by tuning the external magnetic sources generating magnetic forces and torques. On the other hand, there are always particles not contributing to the therapy and spreading through the vasculature with undesirable side effects, often hampering the clinical translation. In this framework, the speaker illustrates a solution for the retrieval of magnetic particles not contributing to the therapy, thus improving the overall biocompatibility of the procedure and the clinical acceptability. This strategy is based on a magnetic catheter which has been modeled, tested and fabricated for the retrieval of more than 80% of the particles not accumulated in the target area.

Biography:

Arianna Menciassi is Professor of Biomedical Robotics at SSSA and team leader of the “Surgical Robotics and Allied Technologies” group at The BioRobotics Institute. For some months between 2013 and 2014, she was Visiting Professor at the Ecole Nationale Superieure de Mecaniques et des Microtechniques (ENSMM) of Besancon (France), in the FEMTO Institute, and Visiting Professor at the ISIR Institute at the Pierre and Marie Curie University in Paris. She has considerable experience in leading interdisciplinary teams toward successful outcomes.

In terms of education, she served as preceptor to 10 postdoctoral associates, 15 PhD students and 40 graduate degree recipients. Her main research interests involve biomedical robotics, bio-hybrid systems, microsystem technology, nanotechnology and micromechatronics, with a special attention to the synergy between robot- assisted therapy and micro-nano-biotechnology-related solutions. She carries on an important activity of scientific management of several projects, European and extra-European, thus implying many collaborations abroad and an intense research activity. She is co-author of more than 270 scientific publications (more than 130 on ISI journals) and 6 book chapters on biomedical robots/devices and microtechnology.

She is also inventor of 25 patents, national and international. She served in the Editorial Board of the IEEE-ASME Trans. on Mechatronics and she is now Topic Editor in Medical Robotics of the International Journal of Advanced Robotic Systems; she is Co-Chair of the IEEE Technical Committee on Surgical Robotics, she is the Nanotechnology Technical Committee representative of the steering committee of the IEEE Transactions on Nanobioscience.

Speaker:

Bradley Nelson, ETHZ Zurich, Zurich, Switzerland

Title:

Microrobots: From the Bench, to in vivo, to the Clinic

Abstract:

In this talk I will discuss our lab’s strategy for translating research into clinical application. Our main approach is to perform proof-of-concept studies in our lab. Once satisfied that we have a promising solution to a particular medical problem, we then usually test our ideas in ex vivo tissue and iterate on our design. The next step can be in vivo studies, if justified. Finally, application of our technology in the clinic represents the ultimate goal. Over the years we have primarily worked with ophthalmic therapies and cardiac ablation procedures. In my talk I will discuss the challenges faced, which are much more than simply optimizing our technology.

Biography:

Brad Nelson has been the Professor of Robotics and Intelligent Systems at ETH Zürich since 2002, where his research focuses on microrobotics and nanorobotics. Fundamentally, he is interested in how to make tiny intelligent machines that are millimeters to nanometers in size.
He studied mechanical engineering at the University of Illinois and the University of Minnesota, worked as a computer vision researcher at Honeywell and a software engineer at Motorola, served as a United States Peace Corps Volunteer in Botswana, Africa, and then obtained a Ph.D. in Robotics from Carnegie Mellon University. He was an Assistant Professor at the University of Illinois at Chicago and an Associate Professor at the University of Minnesota before moving to ETH.

Prof. Nelson has over thirty years of experience in the field of robotics and has received a number of awards for his work in robotics, nanotechnology, and biomedicine. He was named to the "Scientific American 50", Scientific American magazine's annual list recognizing fifty outstanding acts of leadership in science and technology. His lab is the undefeated international champion in Robocup's Nanogram Soccer League, and he is in the Guinness Book of World Records for the "Most Advanced Mini Robot for Medical Use." His research group has won more than a dozen best paper awards at various international conferences and in international journals.

Prof. Nelson serves on the advisory boards of a number of academic departments and research institutes across North America, Europe, and Asia and is on the editorial boards of several academic journals. He has been the Department Head of Mechanical and Process Engineering at ETH, Chairman of the ETH Electron Microscopy Center, and is a member of the Research Council of the Swiss National Science Foundation. He is also a member of the board of directors of three Swiss companies.

Speaker:

Salvador Pané, ETHZ Zurich, Zurich, Switzerland

Title:

Magnetoelectric Stimulation of Cells with Small-scale Robots

Abstract:

Traumatic injury and neurodegenerative diseases in central nervous system result in neuronal damage or apoptosis. Unfortunately, neurons in adult human brain have limited capability of regeneration. Neural progenitor cells can be induced to differentiate into neurons and form functional neuronal networks. However, targeted delivery of therapeutic cells and their differentiation at specific sites remains challenging. Untethered small-scale robotic devices are promising for biomedical applications such as targeted therapy delivery and minimally invasive interventions. Here, we present highly integrated magnetoelectric micromachines featuring remote electrical stimulation for cell differentiation. The micromachines consist of multiferroic composite materials, which have the ability to generate an electric field under the application of an external magnetic field. The magnetoelectric small-scale swimmers comprise a magnetostrictive component that allows for both the magnetic locomotion of the device, and also for the activation of the piezoelectric component, which ultimately serves as the cell electrostimulator. The microrobots can swim by actuation of rotating magnetic fields in different liquid environments that mimic the human body fluids.

Biography:

Salvador Pané i Vidal (Barcelona, 1980) is currently a Senior Research Scientist at the Multi-Scale Robotics Lab (MSRL) at ETH Zurich. He received a B.S. (2003), M.S (2004) and a PhD in Chemistry (2008) from the Universitat de Barcelona (UB) in the field of the electrodeposition of magnetic composites and magnetorresistive alloys. He became a postdoctoral researcher at IRIS in August 2008, Research Scientist in 2010. He has authored or co-authored 31 articles in international peer-reviewed journals including 2 "Advanced Functional Materials "(I.F. = 10.18), 1 "Small" (I.F.: 7.33), 1 "Nanoscale" (I.F. = 5.91) and 3 "Electrochemistry Communications" (I.F.: 5.16); and several books for education in science.

Dr. Pané is currently working on bridging chemistry and electrochemistry with robotics at small scales. In the field of micro- and nanororobotics, his major focus has been the miniaturization of magnetic materials and conductive polymers and hydrogels for targeted drug delivery. He is the head of the IRIS electrochemistry laboratory at ETH, which he established in 2010. At present, he teaches a course on nanorobotics and supervises eight on-going PhD theses. He has established successful international collaborations with several research groups (Autonomous University of Barcelona, University of Barcelona, University of Würzburg, Bogaziçi University, University of Orléans, Michigan State University) and companies (AEON Scientific, Happy Plating).

Dr. Pané is also the coordinator for the MANAQA project (Magnetic Nanoactuators for Quantitative Analysis), which is funded by the EU commission under the Seventh Framework Programme (FP7/2007-2013) under Information and Communication Technologies (ICT). The duration of the project is 36 months, starting from August 1st 2012. The MANAQA project brings together six academic and industrial partners from five different countries.

Speaker:

Samuel Sanchez, Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

Title: *Enzyme-powered Nanorobots Towards their Applications in vivo: Enhanced Delivery, Sensing and Imaging*

Abstract:

The combination of biological components and artificial ones emerges into what we called hybrid machines/bots. Alike bacteria or small swimmers found in nature, artificial nanobots convert bio-available fuels to generate propulsion force to swim at the nanoscale. One of the dreams in nanotechnology is to engineer small vehicles which can eventually be applied in vivo for medical purposes. Major advances have been demonstrated towards that end, however, questions like -how to swim at the nanoscale, how to achieve motion control and how to image these nanobots- need to be properly addressed.

Here, I will present our recent developments in the field of nanomotors that can autonomously swim and perform complex tasks in vitro. Our hybrid "bots" combine the best from the two worlds: biology (enzymes) and (nano)technology (nano- micro-particles) providing swimming capabilities, remote control, multifunctionality and actuation. I will present some of the proof-of-concept applications such as the efficient transport and the enhanced release of drugs into cancer cells and spheroids, sensing

capabilities and the use of molecular imaging techniques for their tracking and localization. We will present our first preliminary results of enzyme nanomotors in vivo imaged by PET-CT.

Biography:

Samuel (PhD Chemistry, UAB, 2008) is since January 2015 ICREA Professor and Group Leader at the Institute for Bioengineering of Catalonia (IBEC) in Barcelona. In 2009, he worked at NIMS, Japan and from 2010 until 2013, he was Group Leader at the Institute for Integrative Nanosciences, IFW Dresden, Germany. He received several awards: Guinness World Record® 2010 and 2017 for smallest jet engine; IFW-IIN Research Prize 2011 for outstanding scientist; ERC Starting Grant 2012 “Lab-in-a-tube and Nanorobotic Biosensors”, ERC Proof-of Concept 2016 (Microcleaners) and 2018 (Lab-in-a-patch); MIT TR35 as “Innovator of the year under 35” Spain 2014; Princess of Girona Scientific Research Award 2015; "Joven Relevante" Award by the Círculo Ecuestre de Barcelona and National Research Award for Young Talent from the Catalan Foundation of Research and Innovation (FCRi).

Samuel Sánchez is leader of the “Smart Nano-Bio-Devices” group, working in the multidisciplinary field of Nanosciences with interest in self-powered micro- and nano-systems, small-scaled robots, integrated and flexible nano-(bio)-sensors, active drug delivery systems and 3D (Bio) Printed Soft Robotics. Sánchez’s group has been consolidated as one of the leading groups in catalytic nano-motors from fundamental aspects to various proof-of-concept applications. Currently, the main research lines in the group are: 1. Nanofabrication of self-powered micro- and nanorobots using nanotechnology and new fabrication tools for biomedicine and environmental applications. 2. 3D Printing and 3D BioPrinting for soft robotics and biomedical engineering. 3. Fabrication of ultracompact and flexible devices for biosensing. 4. Physics of active colloids near surfaces.