There's Plenty of Room at the Bottom: Opportunities and Challenges for Microrobotics

Arianna Menciassi, PhD
Scuola Superiore Sant’Anna, Pisa (Italy)

Roma, February 26th 2024
Robots are more and more outside the cages... they can be wearable ... and ...

Dustbot, robot for urban hygiene (SSSA)

MATE, wearable robot for motion augmentation (IUVO-COMAU)

... robots can work inside the body for chronic and acute interventions
ROBOTS ENTERING THE BODY WITH THEIR TIPS

ROBOTS NAVIGATING THE BODY

ROBOTS RESIDING IN THE BODY
Health and Robotics ...

No longer science fiction, robotics has emerged as a leading alternative for many healthcare applications

Dr. Daniel Kraft - "What's next in healthcare?"

Daniel Kraft is a physician-scientist, inventor and innovator. He is chair of the Medicine track for Singularity University and Executive Director for FutureMed, a program which explores convergent, exponentially developing technologies and their potential in biomedicine and healthcare

Worrell Infographic, vol. 1, no. 3, figure 01, 2015
ROBOTS ENTERING THE BODY WITH THEIR TIPS
Robotics and Minimally Invasive surgery

Robotic technologies to make surgery more accurate and less operator depending, to reach unreachable areas of the body without scars…
The beginning:
Industrial Robotics meets Clinical Imaging

A Robot with Improved Absolute Positioning Accuracy for CT Guided Stereotactic Brain Surgery

YIK SAN KWOH, MEMBER, IEEE, JOAHIN HOU, EDMOND A. JONCKHEERE, SENIOR MEMBER, IEEE, AND SAMAD HAYATI

Abstract—In this paper, we describe how a Unimation Puma 200 robot, properly interfaced with a CT scanner and with a probe guide mounted at its end effector, can be used for CT-guided brain tumor biopsies. Once the target is identified on the CT picture, a simple command allows the robot to move to a position such that the end effector probe guide points towards the target. This results in a procedure faster than one with a manually adjustable frame. But probably the most important advantage, as we show in this paper, is the improved accuracy that can be reached by proper calibration of the robot.
Medical Images make possible the typical CAD-CAM process ... in surgery
The framework today

Ion offers more.
Two exercises in the last two years:
The first one...

Medical Robots

A decade retrospective of medical robotics research from 2010 to 2020

Pierre E. Dupont¹, Bradley J. Nelson², Michael Goldfarb³, Blake Hannaford⁴, Arianna Menciassi⁵, Marcia K. O’Malley⁶, Nabil Simaan³, Pietro Valdastri⁷, Guang-Zhong Yang⁸

Robotics is a forward-looking discipline. Attention is focused on identifying the next grand challenges. In an applied field such as medical robotics, however, it is important to plan the future based on a clear understanding of what the research community has recently accomplished and where this work stands with respect to clinical needs and commercialization. This Review article identifies and analyzes the eight key research themes in medical robotics over the past decade. These thematic areas were identified using search criteria that identified the most highly cited papers of the decade. Our goal for this Review article is to provide an accessible way for readers to quickly appreciate some of the most exciting accomplishments in medical robotics over the past decade; for this reason, we have focused only on a small number of seminal papers in each thematic area. We hope that this article serves to foster an entrepreneurial spirit in researchers to reduce the widening gap between research and translation.
Two exercises in the last two years: The second one…
Main challenges and main needs

• Being targeted, i.e. helping the surgeon to reach «unreachable» areas – *targeted* therapy
• Bringing dexterity inside the body with minimal access and high performance actuators
• Being safe in interaction
• Moving towards scarless operations
Targeted therapy means...

- Target reaching
- Therapy or therapeutic tool delivery
- Minimally invasive approach
- Reduced side effects
- High accuracy, precision and reliability

Targeted therapy means...
The problem: reducing the invasiveness, augmenting the dexterity at the distal part
The problem: reducing the invasiveness, augmenting the dexterity in the distal part
The problem: reducing the invasiveness, augmenting the dexterity in the distal part

SINGLE-PORT ROBOTIC SYSTEMS
Single port modular surgery: how to deploy many degrees of freedom through a small hole
Multiarticulated platform for Minimally Invasive Aortic Valve Replacement

ValveTech: a Novel Robotic Approach for Minimally Invasive Aortic Valve Replacement

Izadyar Tamadon, Virginia Mamone, Yu Huan, Sara Condino, Claudio Quaglia, Vincenzo Ferrari, Mauro Ferrari, Arianna Menciassi

Demo Movie
The easiest navigation environment without incisions - Miniature robots navigating in the GI tract...
An endoscope with biomimetic locomotion (2000-2010)
Endoscopes and surgical tools without tails… the trend to capsule-like robots

Flexibility of traditional wired devices limits access to some target areas (i.e. limitation to targeted therapy)

Small diameter and remote districts can be reached only by wireless or softly tethered devices
The idea of bringing therapeutic and advanced diagnostic solutions where they are needed: the endoscopic capsule

Available wireless capsules: visual investigation of normally not explored areas


Active/teleoperated locomotion for giving “legs” to advanced diagnostic and therapeutic solutions
ACTIVE capsules with on-board PROPULSION

The EU VECTOR Project
Korean IMC Project

Bottleneck for active on-board propulsion

A legged capsule incorporating state-of-art batteries could only walk for less than 30 minutes along the GI tract.

POWER!
Which solutions for a real scarless intervention and limiting actuation/powering problems at distal level?
Which solutions for a real scarless intervention and limiting actuation/powering problems at distal level?

William Gilbert, 1600
De Magnete, Magneticisque Corporibus, et de Magno Magnete Tellure (On the Magnet and Magnetic Bodies, and on That Great Magnet the Earth)

Magnetic endoscopic capsules, magnetic retraction systems, magnetic catheters, magnetic particles for drug delivery and drug targeting…
The easiest navigation environment - Miniature robots navigating in the GI tract…
…wireless magnetic dragging is not for free: localization issues open!

M. Salerno et al., «A discrete-time localization method for capsule endoscopy based on on-board magnetic sensing», Measurement Science and Technology 23 (1), 2011

and also Jake Abbott, Pietro Valdastri, etc…
From the GI tract... from cm-size lumen...

... to mm-size lumen... to the vascular system

ROBOTS NAVIGATING THE BODY
There’s Plenty of Room at the Bottom

Richard P. Feynman

I imagine experimental physicists must often look with envy at men like Kamerlingh Onnes, who discovered a field like low temperature, which seems to be bottomless and in which one can go down and down. Such a man is then a leader and has some temporary monopoly in a scientific adventure. Percy Bridgman, in designing a way to obtain-higher pressures, opened up another new field and was able to move into it and to lead us all along. The development of ever higher vacuum was a continuing development of the same kind.

I would like to describe a field, in which little has been done, but in which an enormous amount can be done in principle. This field is not quite the same as the others in that it will not tell us much of fundamental physics (in the dots on the fine half-tone reproductions in the Encyclopaedia. This, when you demagnify it by 25 000 times, is still 80 angstroms in diameter—32 atoms across, in an ordinary metal. In other words, one of those dots still would contain in its area 1000 atoms. So, each dot can easily be adjusted in size as required by the photoengraving, and there is no question that there is enough room on the head of a pin to put all of the Encyclopaedia Britannica.

Furthermore, it can be read if it is so written. Let’s imagine that it is written in raised letters of metal; that is, where the black is in the Encyclopaedia, we have raised letters of metal that are actually 1/25 000 of their ordinary size. How would we read it?

If we had something written in such a way, we could
Main Challenges:

- For catheters: flexibility, maneuverability and tip control.

- For microrobots: control, biocompatibility, tracking (+ many others!)

Microparticles in the blood flow (Fantastic Voyage)
3D Printing of Small-Scale Soft Robots with Programmable Magnetization

HMD Ansari et al., Advanced Functional Materials, 2023
3D Printing of Small-Scale Soft Robots with Programmable Magnetization

Mohamed Hossam Abd-El Moati, Valentina Iacovacci, Stefano Pram, haoula Oukir
Gianni Borghesan, Pauline Tandon, Emmanuel Vander Poorten, Arianna Menciassi

HMD Ansari et al., Advancement Functional Materials, 2023
Magnetic catheters with programmable magnetization

- Distributed magnetic particles – miniaturization
- Magnetic anisotropy – programmed bending – patient-specific
- 3D printing – different materials, sizes, shapes – versatile

Ansari et. al. *Actuators*, 2023

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Robot-assisted guidance of the magnetic catheter

Robot assisted catheterization
• Automatic insertion using catheter driver
• EPM path defined using several waypoints
• EPM moved along the path based on visual feedback of the operator
• Success rate = 83.3% (5/6)
Main Challenges:

- For catheters: flexibility, maneuverability and tip control.

- For microrobots: control, biocompatibility, tracking (+ many others!)

• Space constraints
• Need for higher spatial resolution
• Need for higher temporal resolution
• Need to shift from microscope-based lab settings to tissue-compliant imaging modalities
• Lower contrast mismatch between microrobots and tissue

* Microparticles in the blood flow (Fantastic Voyage)
Let’s focus on challenges for microrobots in the vasculature.
(Magnetic) Microrobots for in vivo applications – Open Challenges

So far, most microbot experiments have been done in vitro under conditions very different from those in the human body. Many devices rely on toxic fuels, such as hydrogen peroxide. They are simple to steer in a Petri dish, but harder to control in biological fluids full of proteins and cells, and through the body’s complex channels and cavities.

To enter clinical trials, microbots must clear two major hurdles. First, researchers need to be able to see and control them operating inside the body — current imaging techniques have insufficient resolution and sensitivity. Second, the vehicles need to be biocompatible and be removed or stabilized after use. Achieving both aims would set the stage for further improvements — in steering and mobility, materials and capabilities.

We call on microrobotics researchers, materials scientists and bioimaging and medical specialists to work together to solve these problems. And regulatory agencies need to put in place directives for testing therapeutics that are based on microbots.

Medical microbots need better imaging and control

Mariana Medina-Sánchez and Oliver G. Schmidt set priorities for more realistic tests of tiny machines that could be used to diagnose and treat conditions.
Micro & Nanorobotics towards in vivo applications: challenges

- Imaging
- Locomotion Control
- Biocompatibility and safety
- Therapy delivery
- Innovative materials
- Protocols for tests
How facing the bio-distribution of magnetic particles in the body? How managing the magnetic particles not contributing to the therapy?
How facing the bio-distribution of magnetic particles in the body? How managing the magnetic particles not contributing to the therapy?
(Magnetic) Microrobots for in vivo applications – Open Challenges

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X. Wang et al., 2018.
H. Ceylan et al., 2019.

**Development of fully degradable structures**

**Loaded drugs and magnetic particles are biodistributed in the body after degradation**

Intravascular magnetic catheter to retrieve micro and nanoagents from the bloodstream

TARGET: ORGANS FEATURED BY TERMINAL CIRCULATION (e.g. LIVER, KIDNEY, PANCREAS)

To face these issues, we developed an intravascular magnetic microcatheter able to capture unaccumulated nanoparticles, thus preventing side effects.

MODULAR CATHETER STRUCTURE

Iacovacci, V., et al. ICRA 2019
\[ \nu_p = \nu + \zeta f(H)(H \cdot \nabla)H \]

\[ \zeta = \frac{\mu_0(1+\chi_f)}{6\pi\eta_f} \frac{V_{mag}}{\tau_h} \]

\[ f(H) = \begin{cases} \frac{3(\chi_p-\chi_f)}{(\chi_p-\chi_f)+3(1+\chi_f)} & M_{sp} \geq \frac{3(\chi_p-\chi_f)}{(\chi_p-\chi_f)+3(1+\chi_f)} \\ \frac{M_{sp}}{H} & \frac{3(\chi_p-\chi_f)}{(\chi_p-\chi_f)+3(1+\chi_f)} > \frac{M_{sp}}{H} \end{cases} \]

**Magnetic module design – FEM modeling**

- **SPHERICAL PARTICLE**
- **POINT DIPOLE APPROXIMATION**
- **LAMINAR FLOW IN A CHANNEL**

**PARTICLE IN A FLUIDIC AND MAGNETIC FIELD SIMPLIFIED MODELING**

- **CATHETER DIAMETER (12 F, 15 F)**
- **MAGNET NUMBER, GROUPING**
- **PARTICLES DIMENSION**

Iacovacci, V., et al. ICRA 2019
Experimental validation

• BLOOD MIMICKING FLUID
• PHYSIOLOGICAL FLOW RATE

ICP-MS ANALYSIS to quantify the collected samples Iron content

MAGNETIC NANOPARTICLES

MICROPUMP → FLUIDIC CIRCUIT → MAGNETIC RETRIEVAL MODULE → COLLECTION SYSTEM

BLOOD-LIKE FLUID RESERVOIR

MULTIPLE PASSAGE TESTS

500 nm NP

Capture Efficiency [%]

Capture Efficiency [%]

Capture test repeat

Capture test repeat

500 nm NP

250 nm NP

EXTENSIVE CAPTURE EFFICIENCY FOR MULTIPLE USAGE (MASSIVE DOSES)

OPTIMAL CORRESPONDANCE AMONG FEM PREDICTION AND EXPERIMENTAL DATA

iakovacci, V., et al. ICRA 2019

NO SIGNIFICANT HEMORHEOLOGICAL ALTERATION (BLOOD CELLS COUNT AND HEMATOCRIT)
So far, most microbot experiments have been done in vitro under conditions very different from those in the human body. Many devices rely on toxic fuels, such as hydrogen peroxide. They are simple to steer in a Petri dish, but harder to control in biological fluids full of proteins and cells, and through the body's complex channels and cavities.

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Microrobots imaging – state of the art

- X-ray
- Y-ray
- Reflection-based
- Fluorescence-based
- MRI
- MPI
- B-mode
- Doppler
- US-APA
Microrobots US imaging – examples

B-MODE IMAGING OF SUB-MILLIMETRIC ROBOTS

Sanchez et al., IEEE BioRob, 2014
Yu et al., Nat. Comm, 2019

LOW CONTRAST RESOLUTION IN HIGHLY ECHOGENIC MEDIA

Sanchez et al., IEEE BioRob, 2014
Yu et al., Nat. Comm, 2019
Motion-based analysis can help

OPPORTUNITIES OFFERED BY DOPPLER IMAGING

INTERFERENCE WHEN OTHER OBJECTS ARE MOVING
Microrobots US imaging – examples

Selective motion filtering can improve tracking stability and precision

ACOUSTIC PHASE ANALYSIS (APA)

\[ d \ll \lambda \]

Sub-resolution events

Echoes

Frame #1

Frame #2

Analytic echo signal

\[ E(t) = A(t) e^{\varphi(t)} \]

Acoustic intensity

Acoustic phase

Target Motion projection on pulse axis

\[ \varphi(t) = \frac{4\pi}{\lambda} u(t) \]
Different microrobot locomotions induce different phase feedback

\[ \varphi(t) = \frac{4\pi}{\lambda} u(t) \]
Experimental setup for real-time imaging and tracking
Vibrations detection algorithm

1. Fourier analysis
   Analyze the frequency components of the acoustic phase

2. Frequency filtering
   Isolate vibrations at microrobot frequency

3. Phase filtering
   Isolate vibrations in-phase with the magnetic field

4. Overlap with B-mode
Tracking soft vibrating microrobots in tissues


- Magnetic fields
- US probe
- Imaging plane
- Microrobot
- Linear motion
- Vibrations
- Chicken breast
- Microrobot
- Markers
- Imaging plane

- B-mode
- B-mode + Filtered Motion Image
- MR centroid positions

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<td>MR vibration frequency</td>
<td>3 Hz</td>
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<tr>
<td>MR linear velocity</td>
<td>1 body-length/s</td>
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<td>Position tracking err.</td>
<td>0.25 body-length</td>
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<tr>
<td>Tracking frame rate</td>
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Rotations detection algorithm

1. **Temporal analysis**
   Analyze the differential phase in the time domain

2. **Block-matching**
   Cross-correlate the mean differential phase with a rotation template

3. **Derive microrobot features**
   Localize the maximum in the cross-correlation map and identify size of motion diagram

4. **Overlap with B-mode**
Tracking rotating microrobots in vascular phantom

Rotating Microrobot

Magnetic field sequence

\[ B(t) = \begin{cases} 
B_x = |B| \cdot \sin(2\pi f_{rot}t) \\
B_y = |B| \cdot \cos(2\pi f_{rot}t) 
\end{cases} \]

MR diameter \(550\ \mu\text{m}\)
MR vibration frequency \(5\ \text{Hz}\)
MR Rotation frequency \(1.5\ \text{Hz}\)
Flow rate \(3\ \text{mL/s}\)
Position tracking err. \(130\ \mu\text{m}\)
Tracking frame rate \(3\ \text{fps}\)

Use APA feedback for control

Closed-loop control architecture

Microrobot states

User interface

Microrobot blind localization

Graphical interface

Manual interface

Control system (open-loop)

Visual feedback

1. System start: MR not vibrating
2. Controller start: supervised search mode
3. MR found: set optimal imaging plane
4. Teleoperation start: visual-servoing mode

Closed-loop control performances

Microrobot teleoperation in tissue-mimicking vascular phantom

Robustness to disturbances from tissues and physiological flow

System performances

Average tracking error $\mu$

Precision $\mu < 1$ body-length

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At a glance comparison between APA and Doppler

**Static background conditions**

**Disturbance**: fluid flow motion

**Disturbance**: tissue motion

**Disturbance**: fluid flow in bifurcation

Motion detection by US imaging: Could more traditional solutions work?

APA requires specific US imaging devices (need for RF data) and low temporal performances (few Hz)

Difficult translation

There exist other motion detection strategies with higher output rates and based on standard Bmode

One option is OPTICAL FLOW
Comparison between APA and Optical Flow

The comparison between the two techniques was carried out considering:

- Different microrobot dimensions (from 1200 to 250 µm in diameter)
- Different locomotion patterns (rolling and vibration from 5 to 1 Hz)
- Different environmental conditions (vascular and tissue-like)

Comparison between APA and Optical Flow

Optical Flow consistently achieved submillimetric tracking accuracies in all tested conditions (error $< 0.6$ body length for rolling $\sim 1$ body length for vibration)

Spatial performances are comparable to US-APA with no need for RF data

Major increase in output rate from 1-2 Hz up to 40 Hz

Conclusions

- Many challenges are still ahead, but motivations are strong!
- It is time to think about more advanced paradigms for microrobotic control, application, human interaction…
- Open research platforms and published datasets are key for developing / testing new methodologies
- Identifying the correct balance between AI methods and physical modelling in the miniature/micro domain
Thank you for your attention!