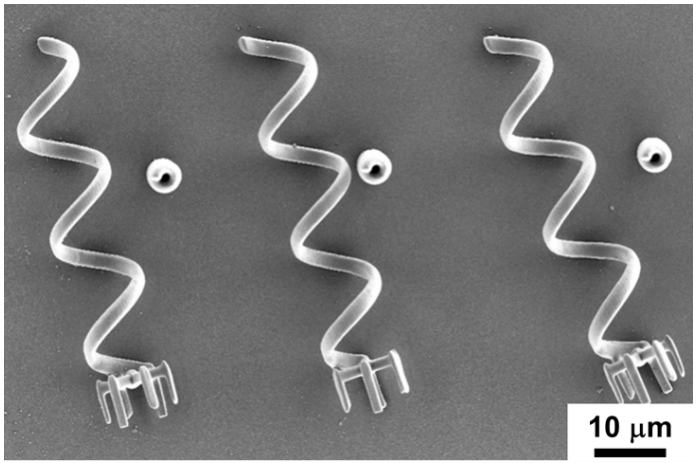
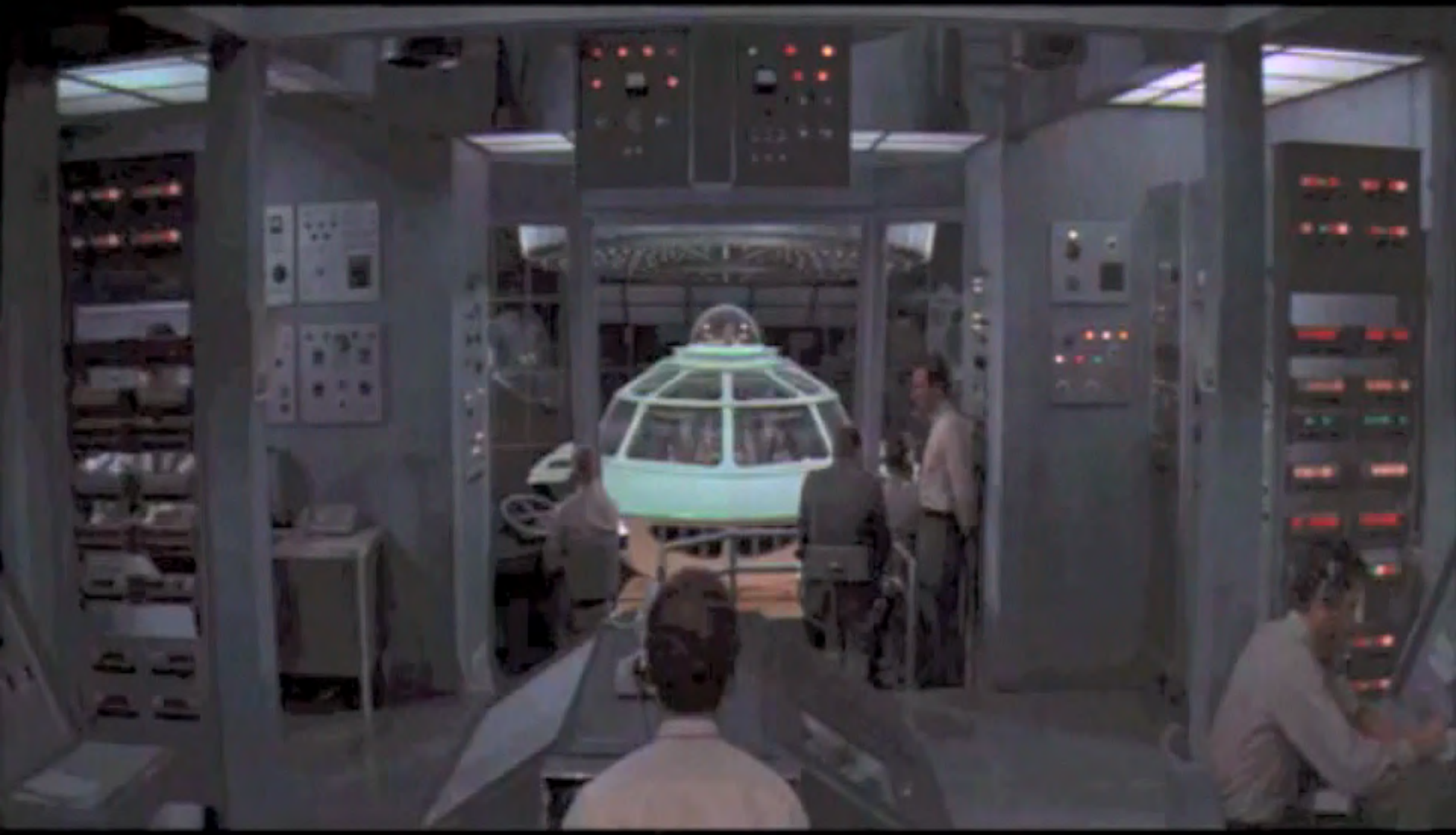
Institute of Robotics and Intelligent Systems

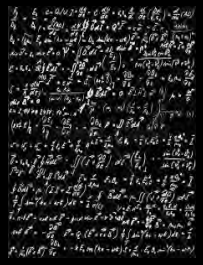


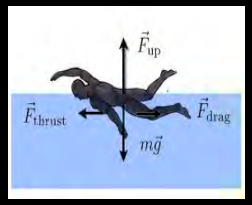
3D Printed MicroRobotics for NanoMedicine

Brad Nelson

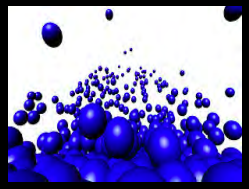
ETH Zurich
Switzerland



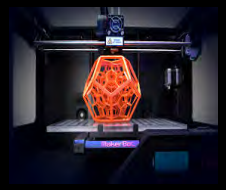




Physics



Fabrication



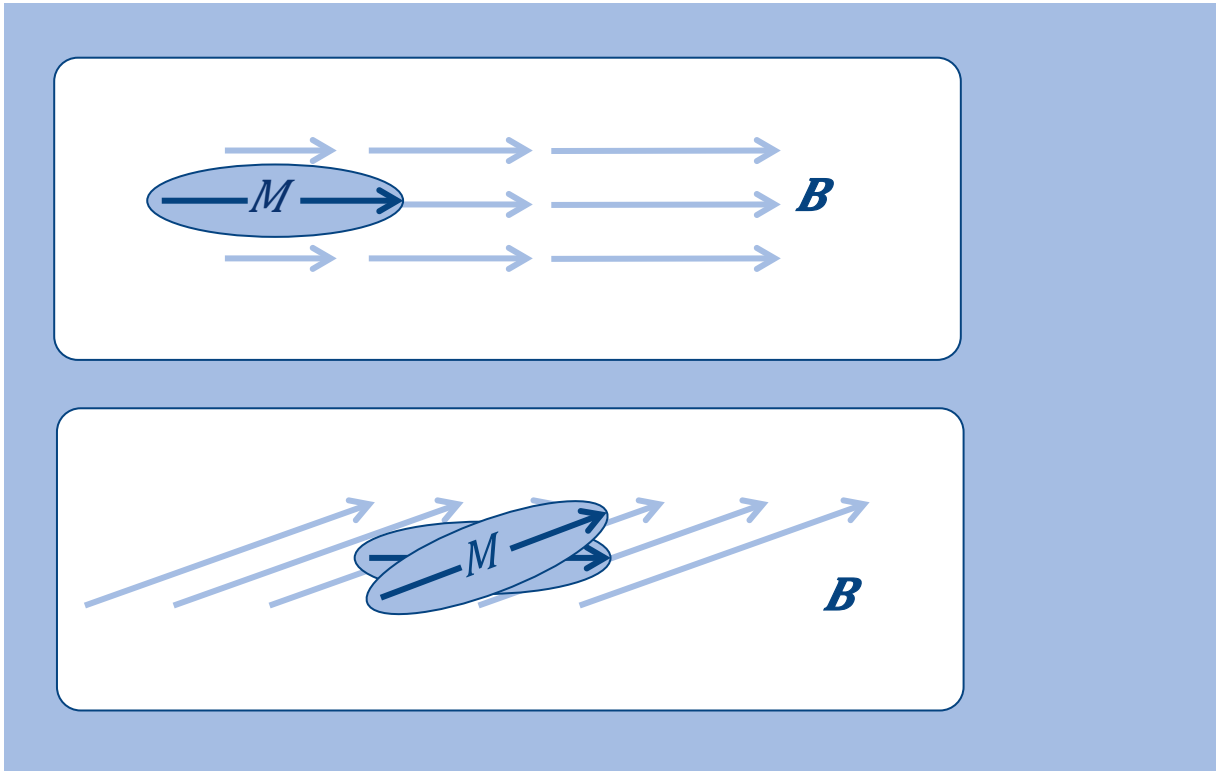
Viable Business Models

Magnetic Force

$$\vec{F}_m = V(\vec{M} \cdot \nabla)\vec{B}$$

Magnetic Torque

$$\vec{T}_m = V \cdot \vec{M} \times \vec{B}$$

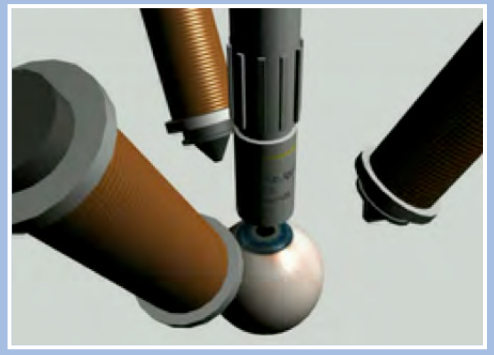


$\vec{T}_m$: Magnetic Torque [Nm]
$\vec{F}_m$: Magnetic Force [N]
V : Volume [m^3]
$\vec{M}$: Magnetization [A/m]
$\vec{B}$: Magnetic field [T]

Wireless Magnetic Steering

For small bodies, e.g. “microrobots” we assume:

- Uniform distribution of the applied field **B** throughout the body
- **M** is a single vector (body is viewed as a dipole)
- **F** = Force
- **T** = Torque

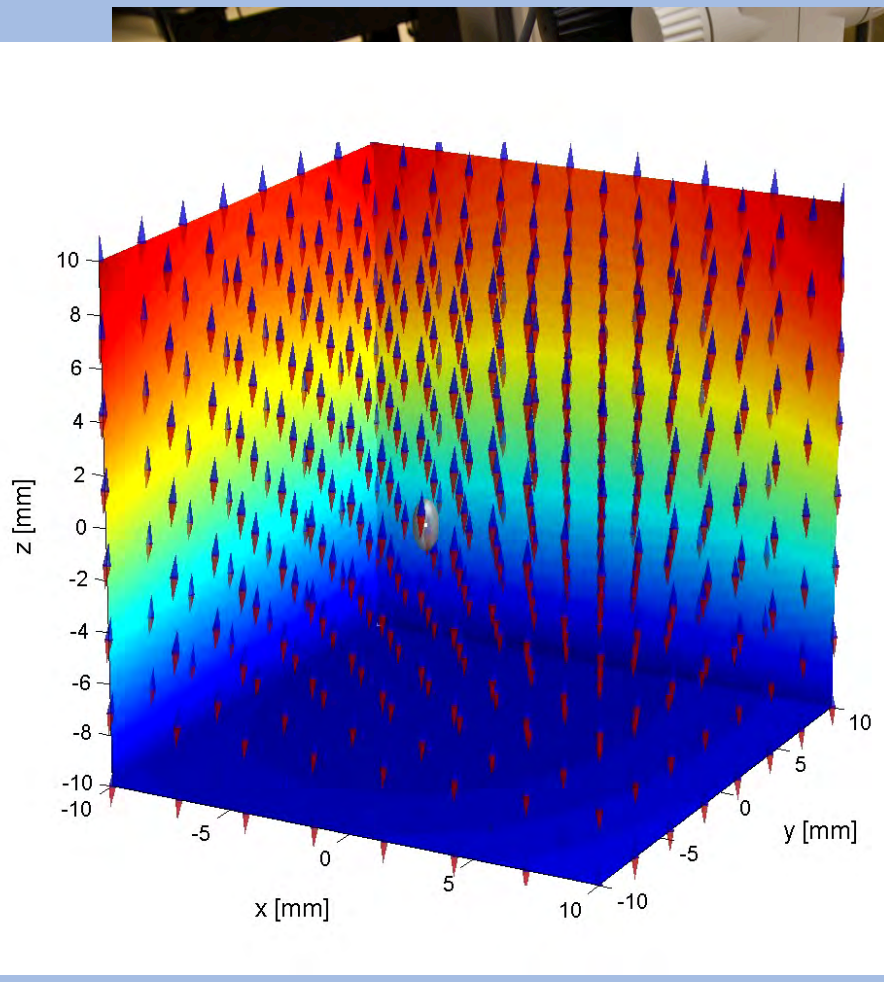


$$\begin{bmatrix}\mathbf{T}\\ \mathbf{F}\end{bmatrix} = \begin{bmatrix} Sk(\mathbf{M})\mathcal{B}(\mathbf{P}) \\ \mathbf{M}^T\mathcal{B}_x(\mathbf{P}) \\ \mathbf{M}^T\mathcal{B}_y(\mathbf{P}) \\ \mathbf{M}^T\mathcal{B}_z(\mathbf{P}) \end{bmatrix} \begin{bmatrix} i_1 \\ \vdots \\ i_n \end{bmatrix}$$

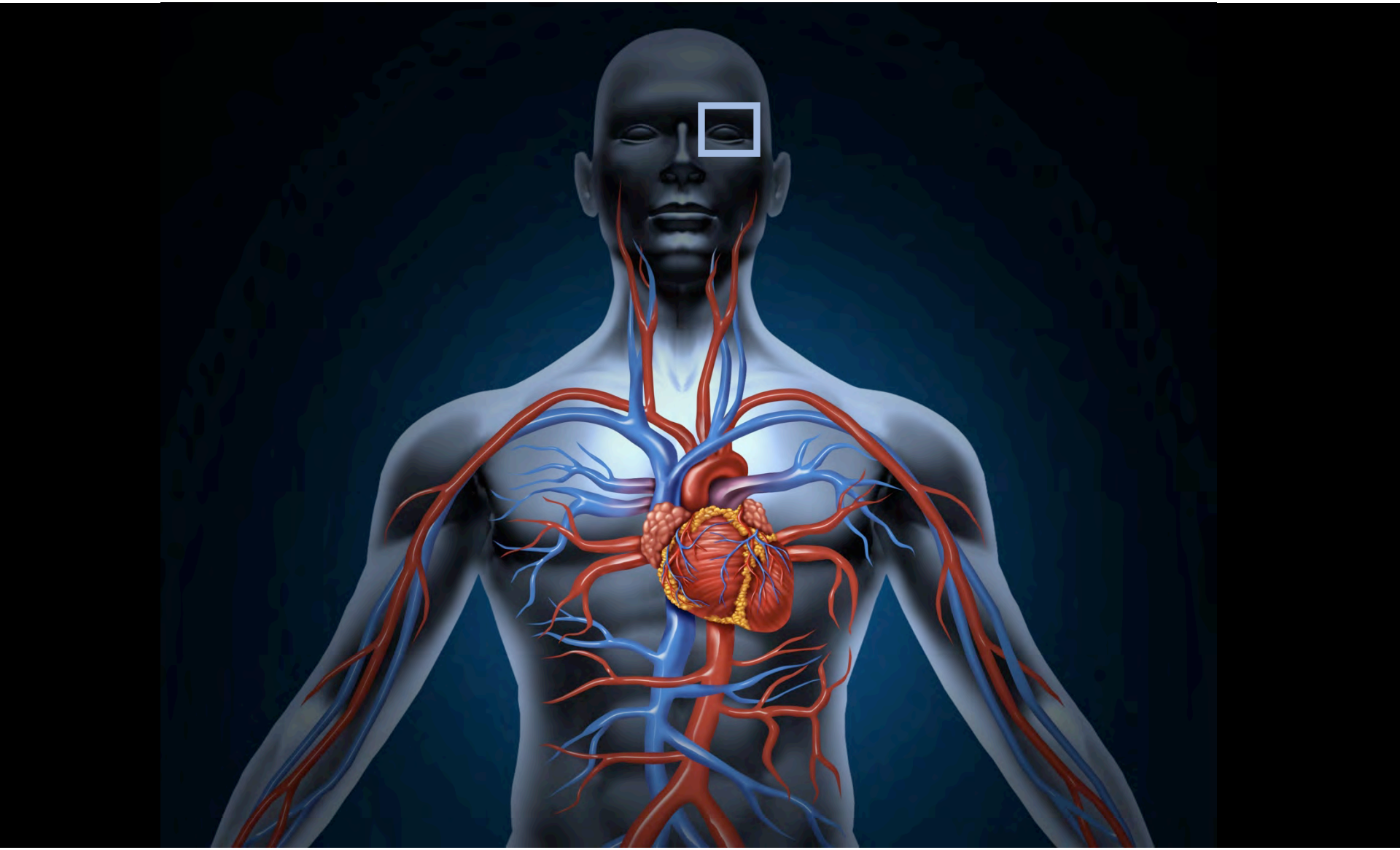
$$\mathbf{T} = v\mathbf{M}\times\mathbf{B} \qquad \mathbf{F} = v(\mathbf{M}\cdot\nabla)\mathbf{B} \rightarrow \nabla\times\mathbf{B} = 0 \rightarrow \mathbf{F} = v\begin{bmatrix} \frac{\partial\mathbf{B}}{\partial x} & \frac{\partial\mathbf{B}}{\partial y} & \frac{\partial\mathbf{B}}{\partial z} \end{bmatrix}^T \mathbf{M}$$

M. Kummer, J. J. Abbott, B. E. Kratochvil, R. Borer, A. Sengul, B. J. Nelson, "OctoMag: An Electromagnetic System for 5-DOF Wireless Micromanipulation", IEEE Trans. Rob., (26) 6, 2010

First Prototype: OctoMag

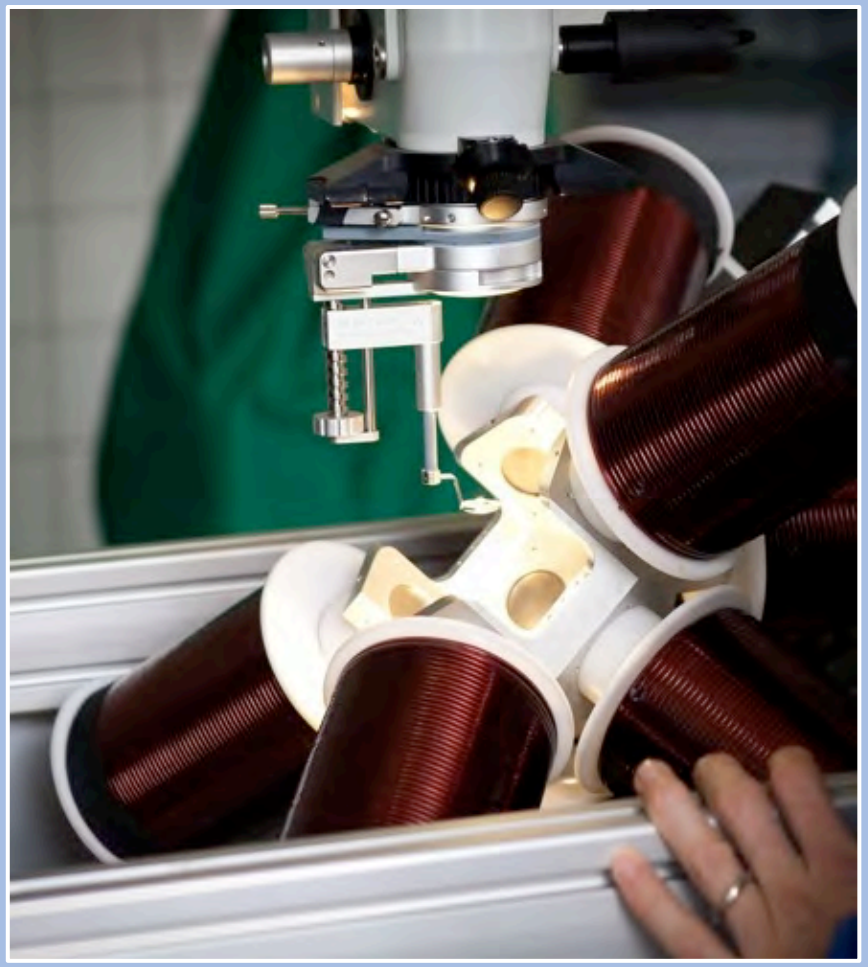


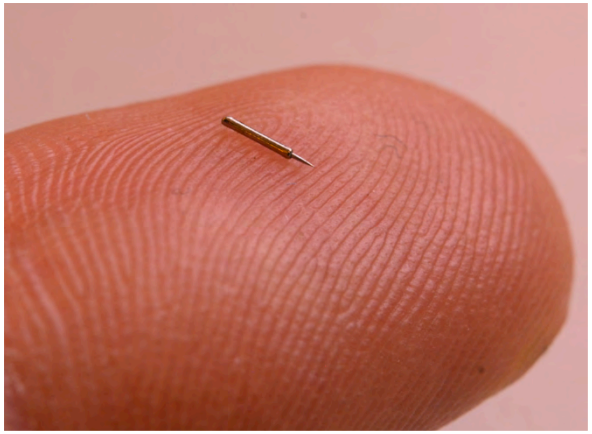
Where in the Body?



Microrobotic Drug Delivery for Retinal Therapies

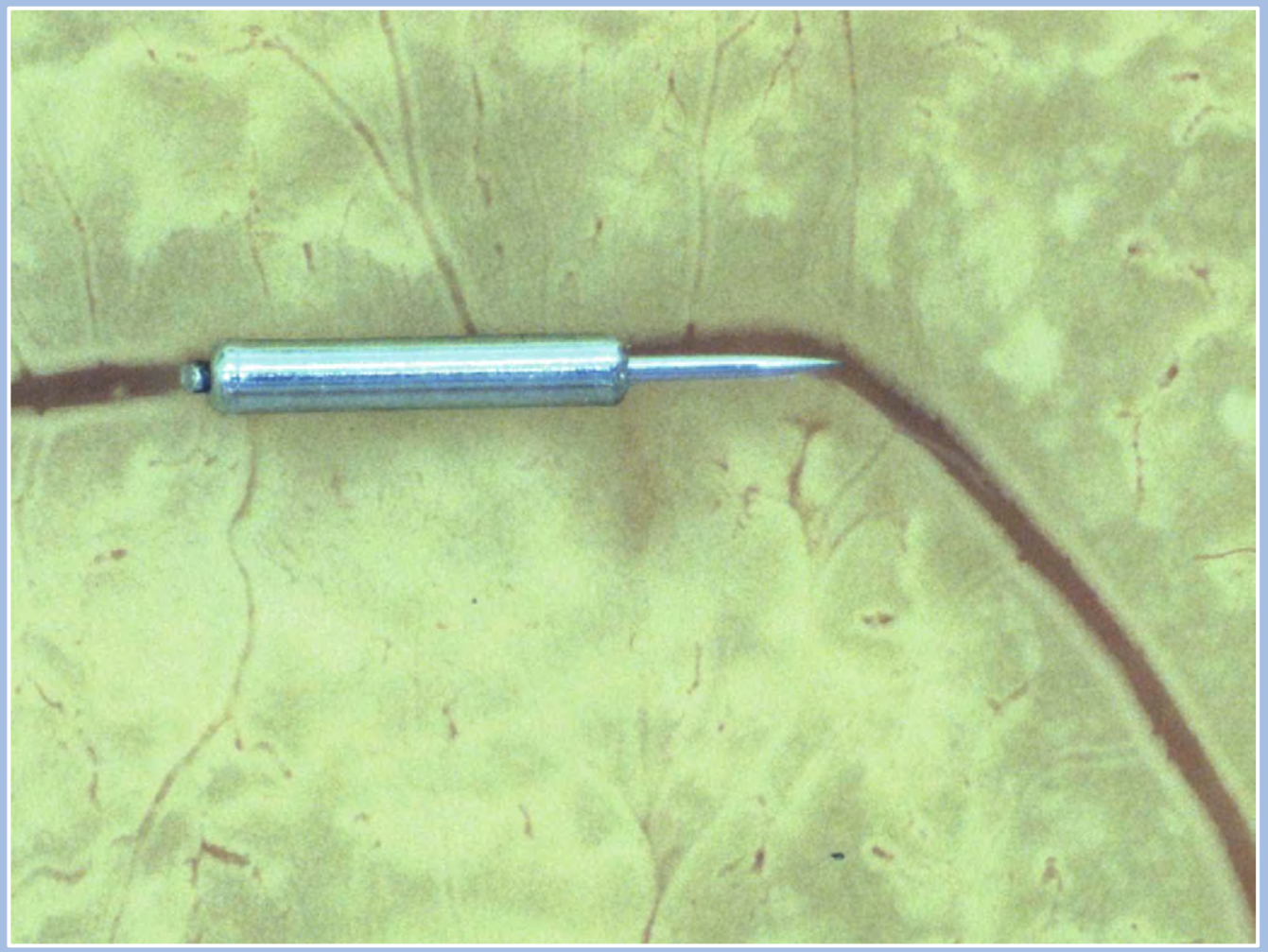
Animal Trials



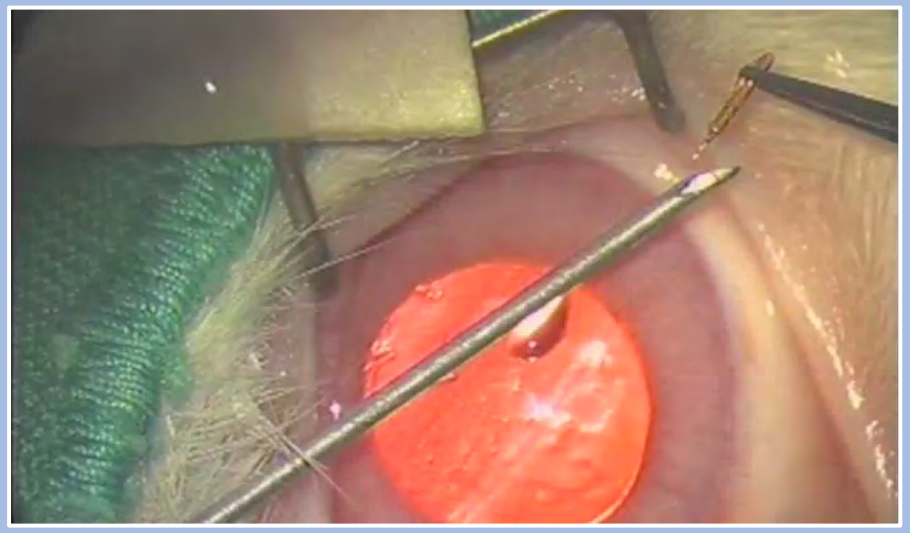


Vessel Puncture

Vessel ~125µm dia.

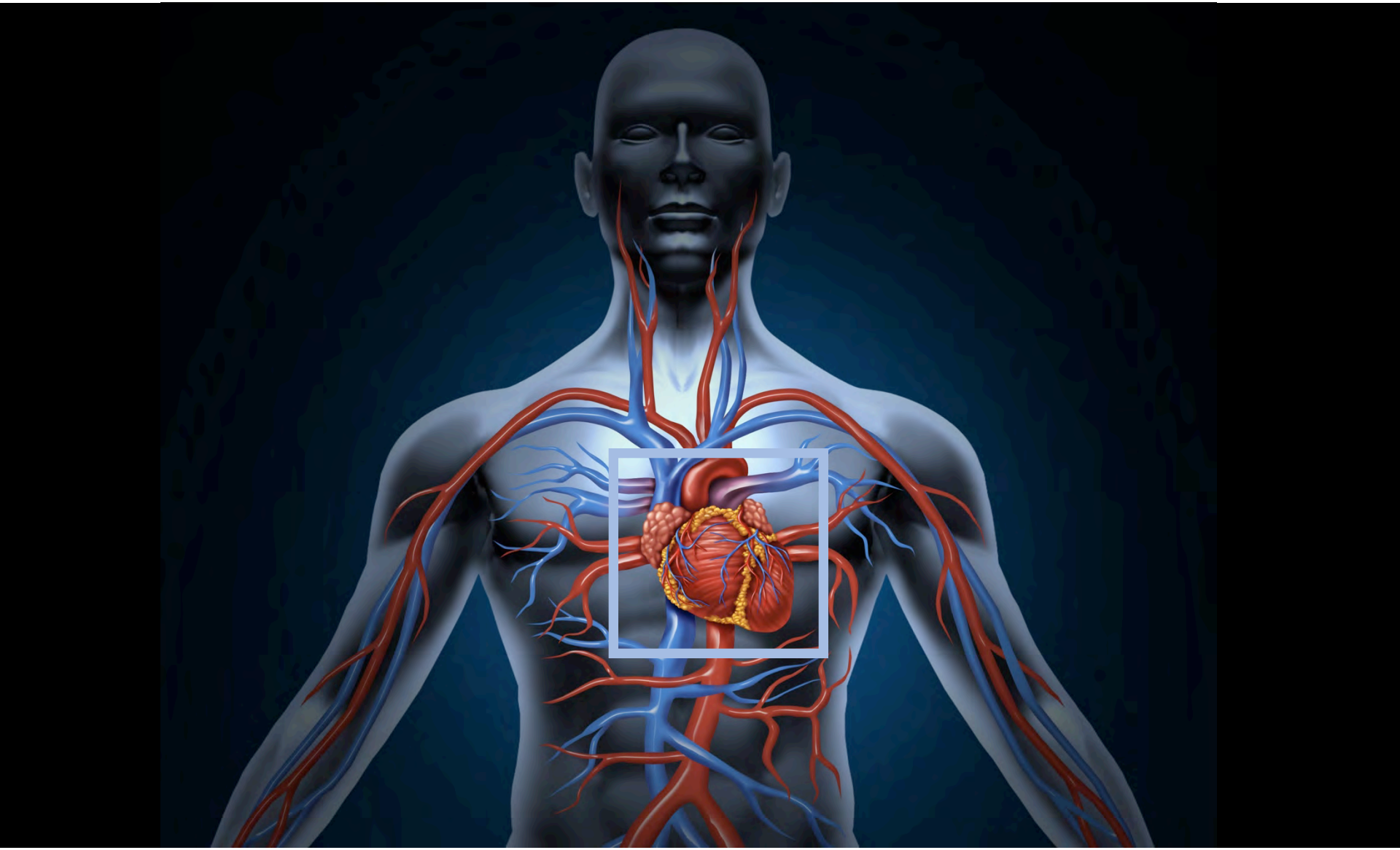


in vivo Injection and Mobility of a Microrobot



F. Ullrich, C. Bergeles, J. Pokki, O. Ergeneman, S. Erni, G. Chatzipirpiridis, S. Pané, C. Framme, B. J. Nelson, "Mobility experiments with microrobots for minimally invasive intraocular surgery", Investigative Ophthalmology & Visual Science, Vol. 54, No. 4, April 2013, pp. 2853-63.

Other Locations in the Body



Magnetically Actuated Catheter

- Magnetic Torque

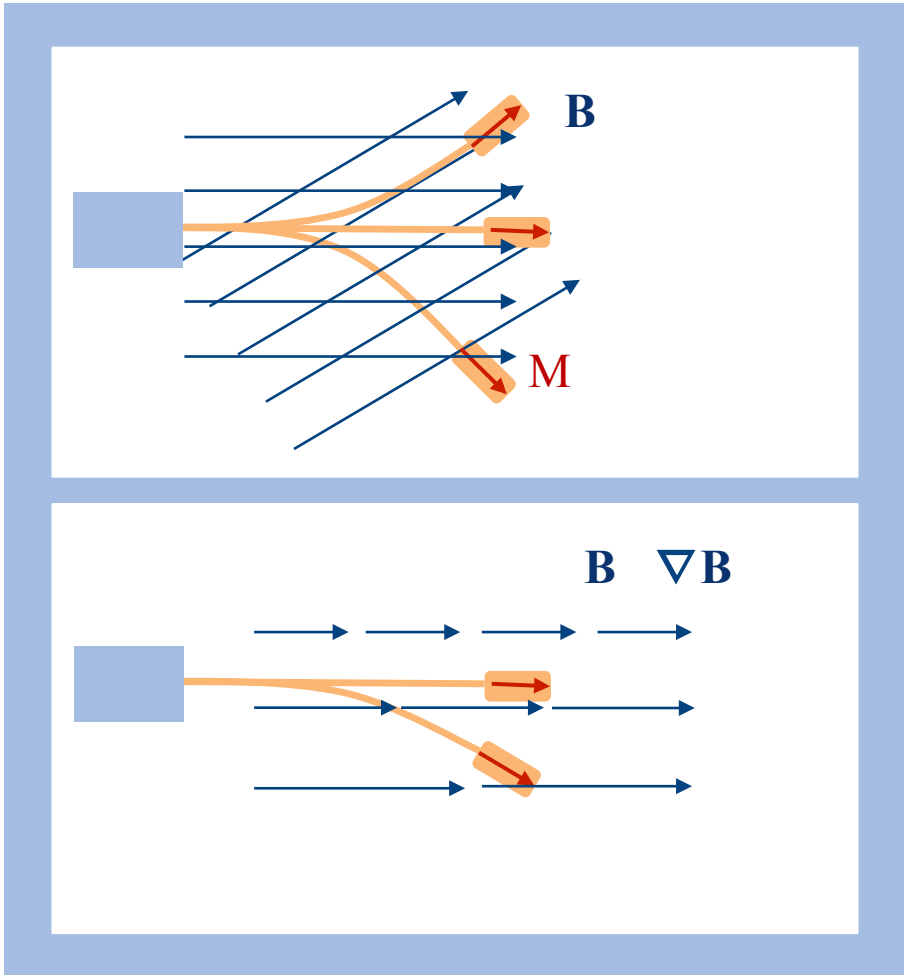
$$\mathbf{T} = \upsilon\, \mathbf{M} \times \mathbf{B}$$

- Magnetic Force

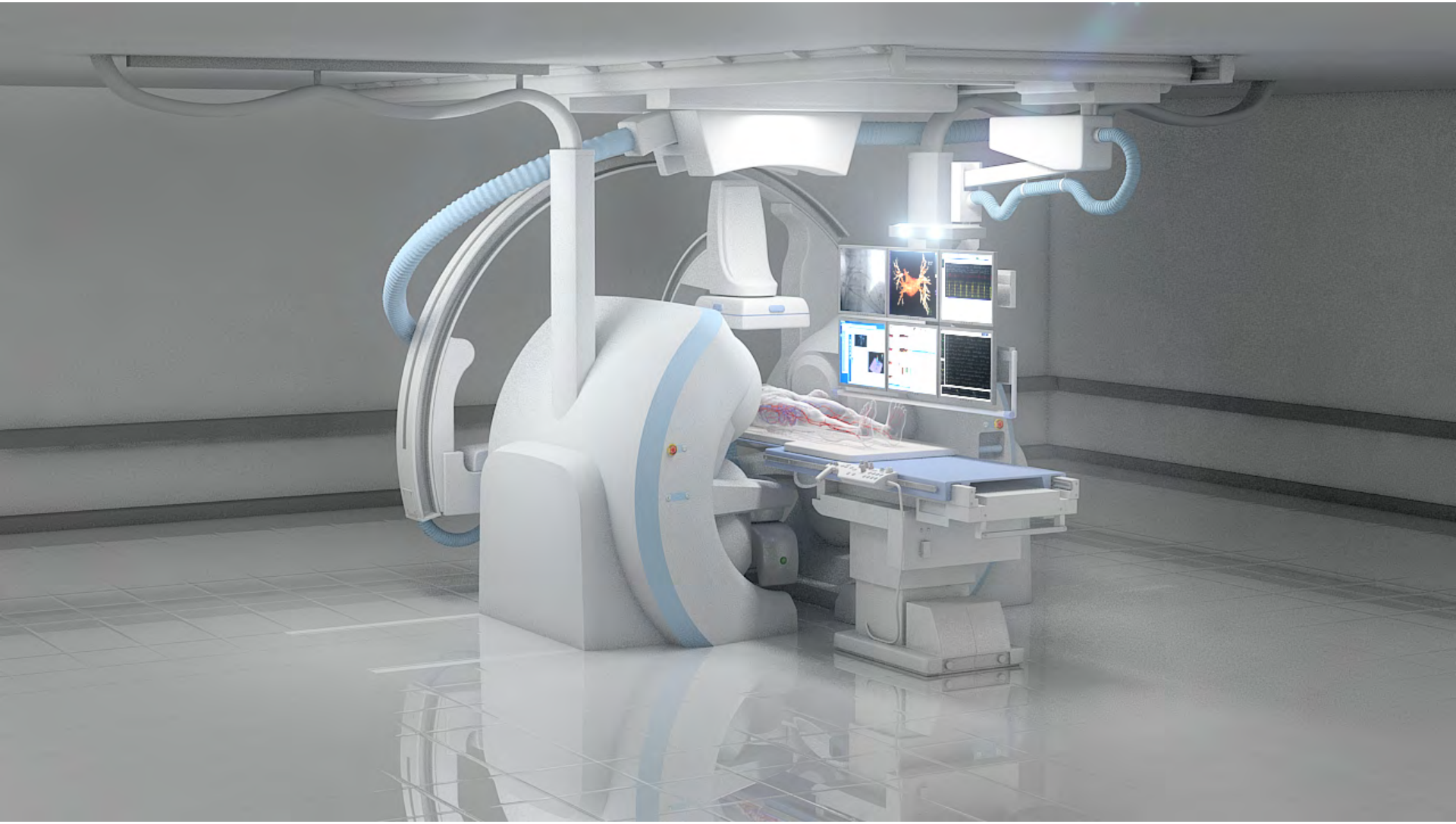
$$\mathbf{F} = \upsilon\, (\, \mathbf{M} \cdot \nabla\,)\, \mathbf{B}$$

$$\downarrow \quad \nabla \times \mathbf{B} = 0$$

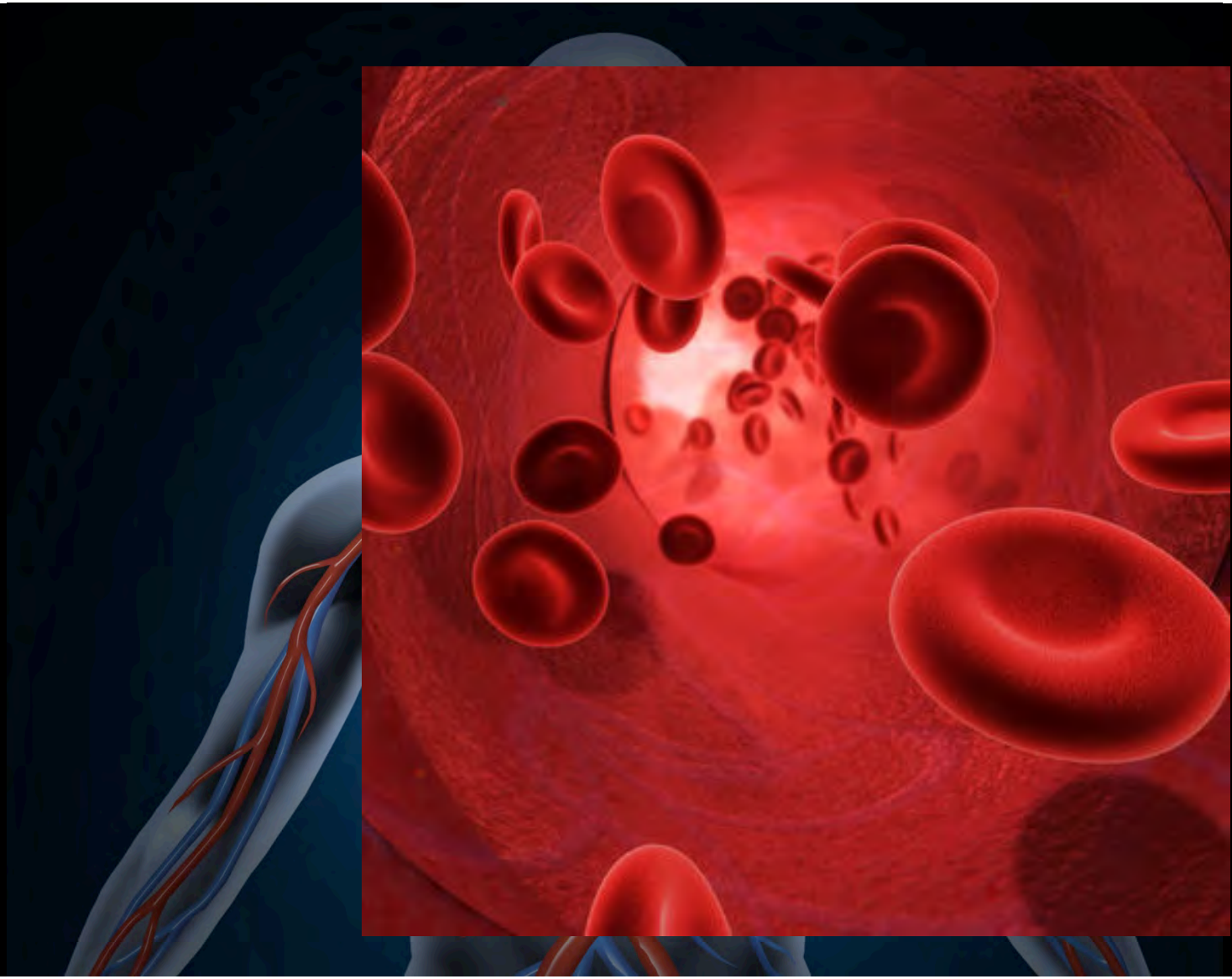
$$\mathbf{F} = \upsilon \left[\frac{\partial \mathbf{B}}{\partial x} \; \frac{\partial \mathbf{B}}{\partial y} \; \frac{\partial \mathbf{B}}{\partial z} \right]^{T} \mathbf{M}$$



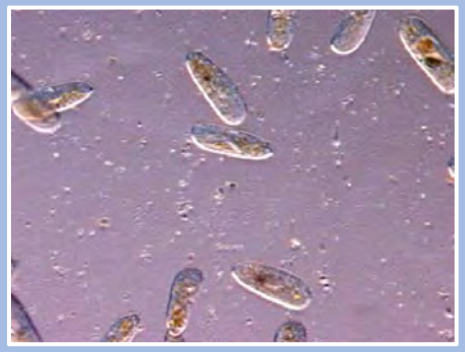
Catheter Steering for Cardiac Ablation



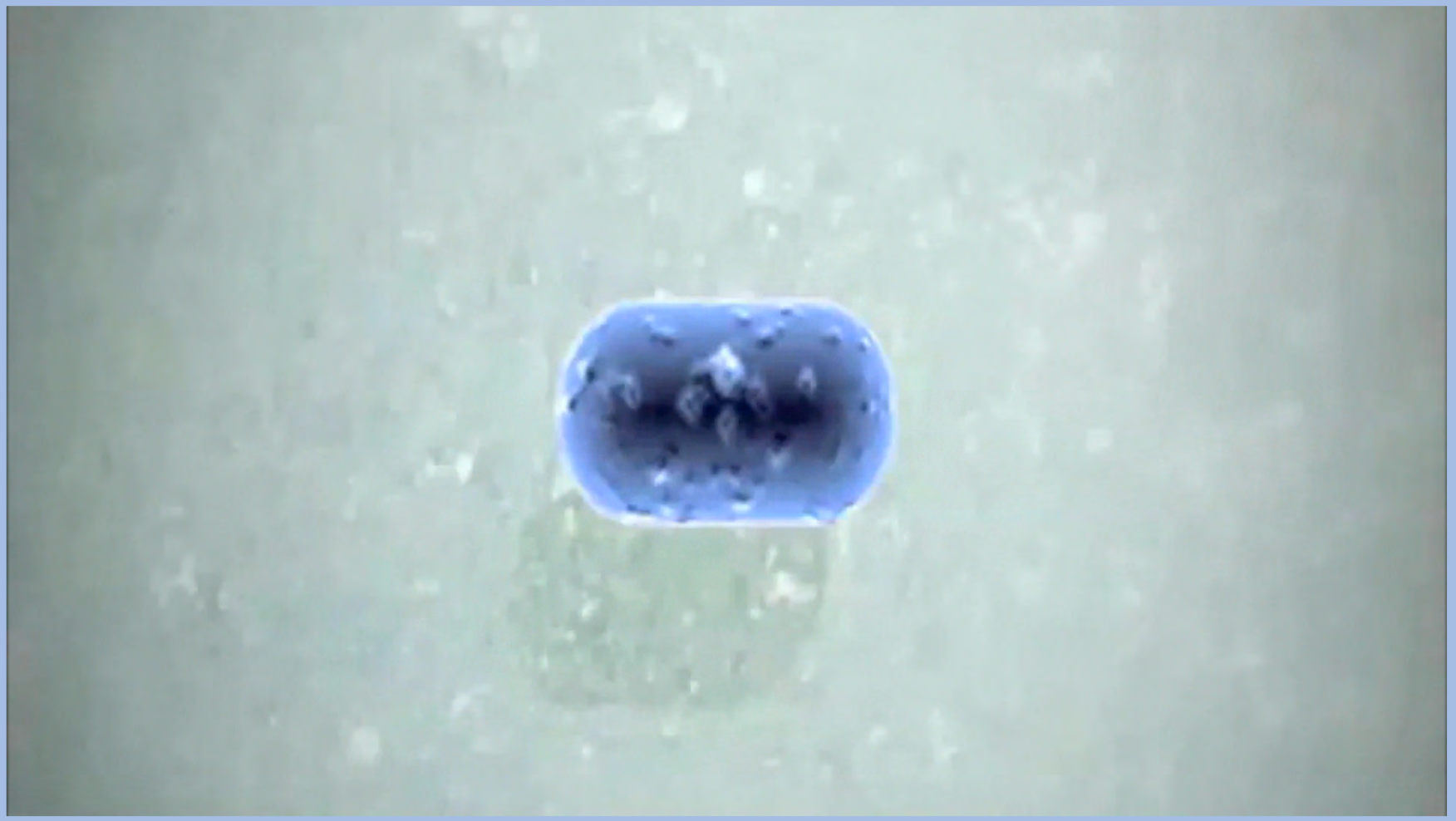
Going Smaller



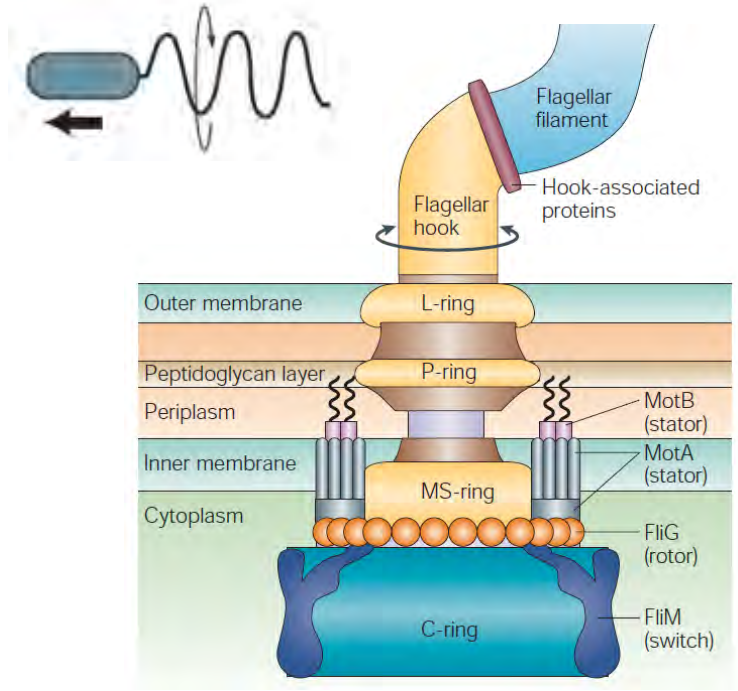
Paramecia, spermatzoa, cilia and flagella



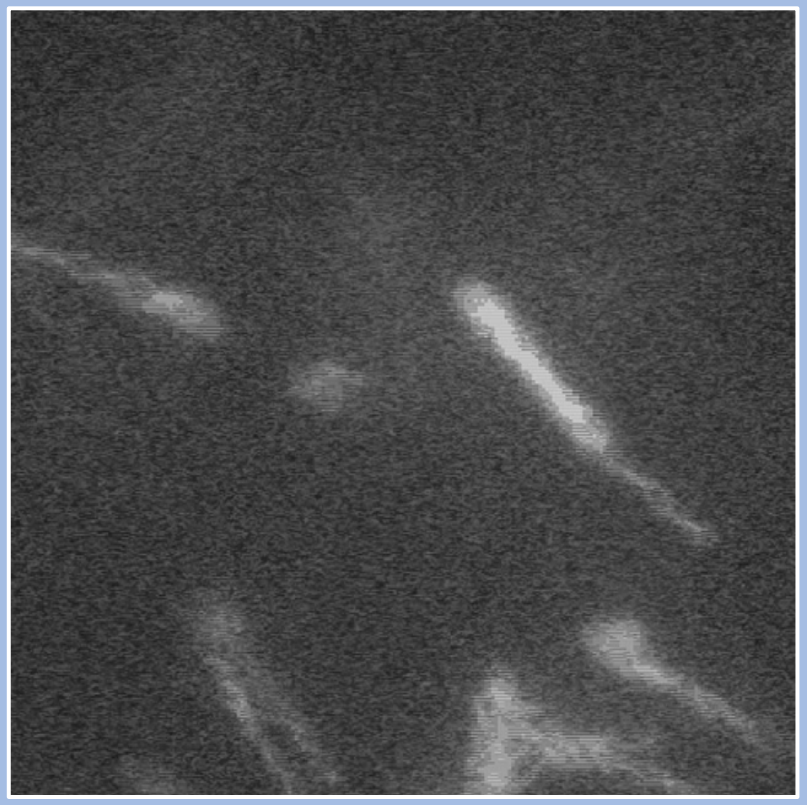
“Bacteria swim by rotating their flagellar filaments” (1973, Berg)



E. coli: “Nature’s Microrobots”

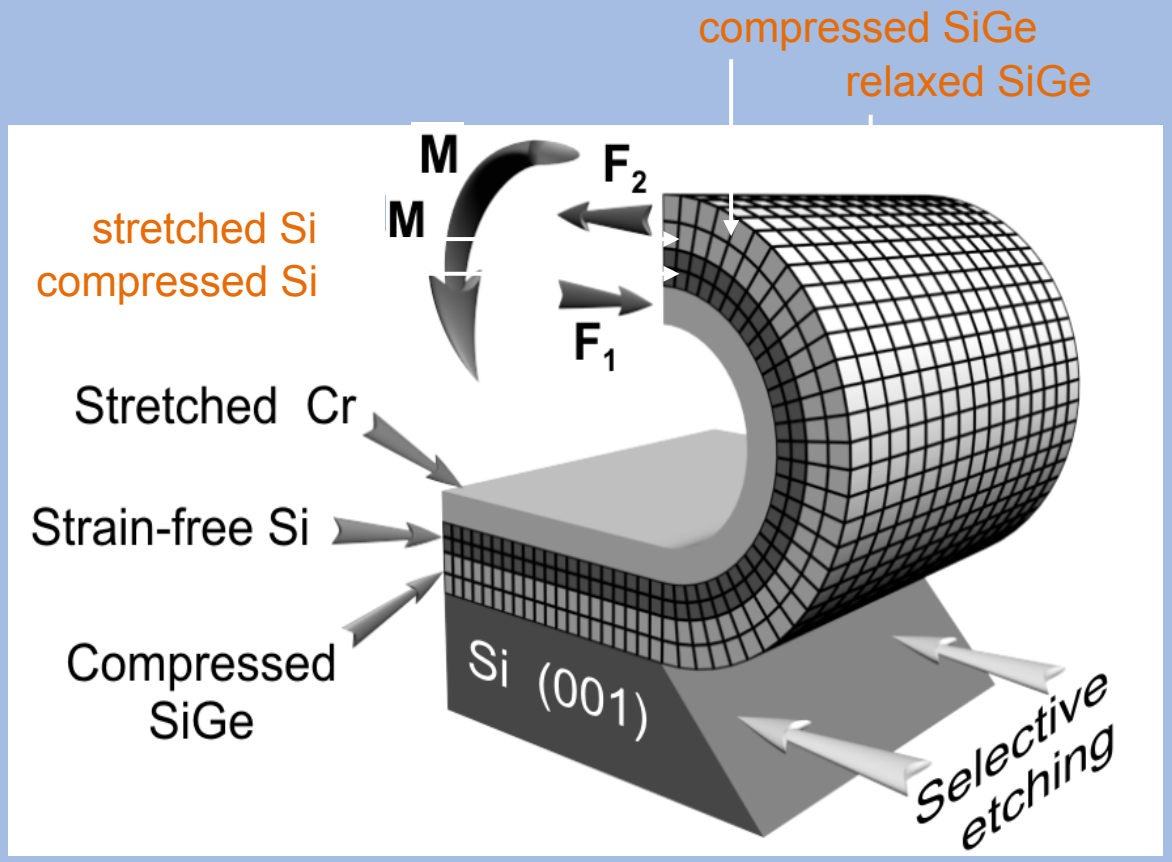


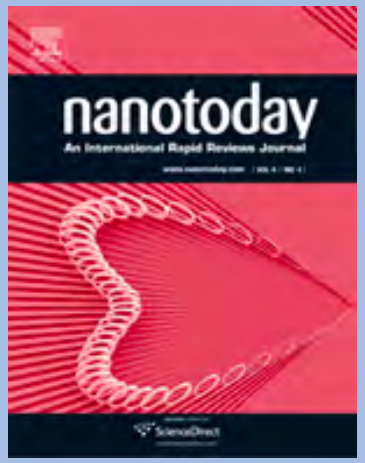
Nat. Rev. Mol. Cell Biol. 5, 1024 (2004)



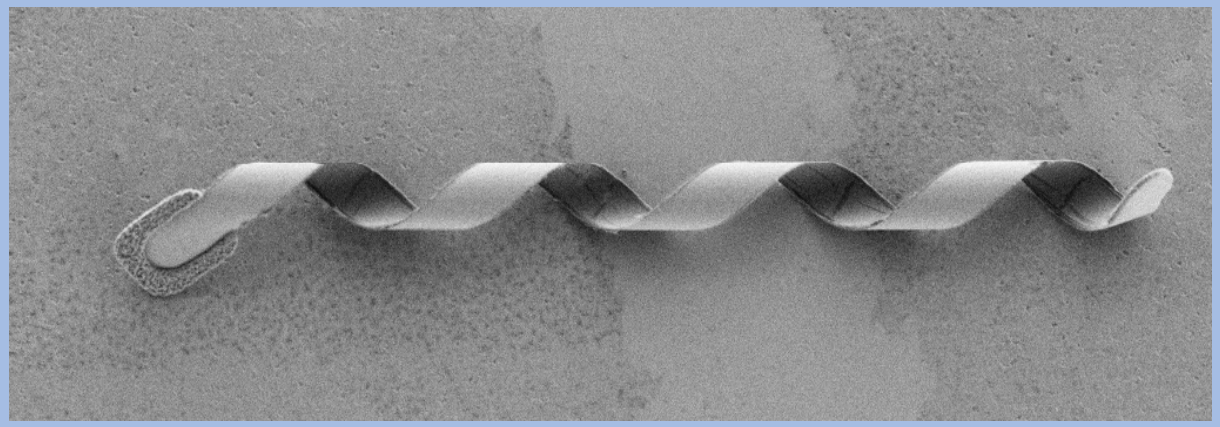
H.C. Berg (Harvard University)

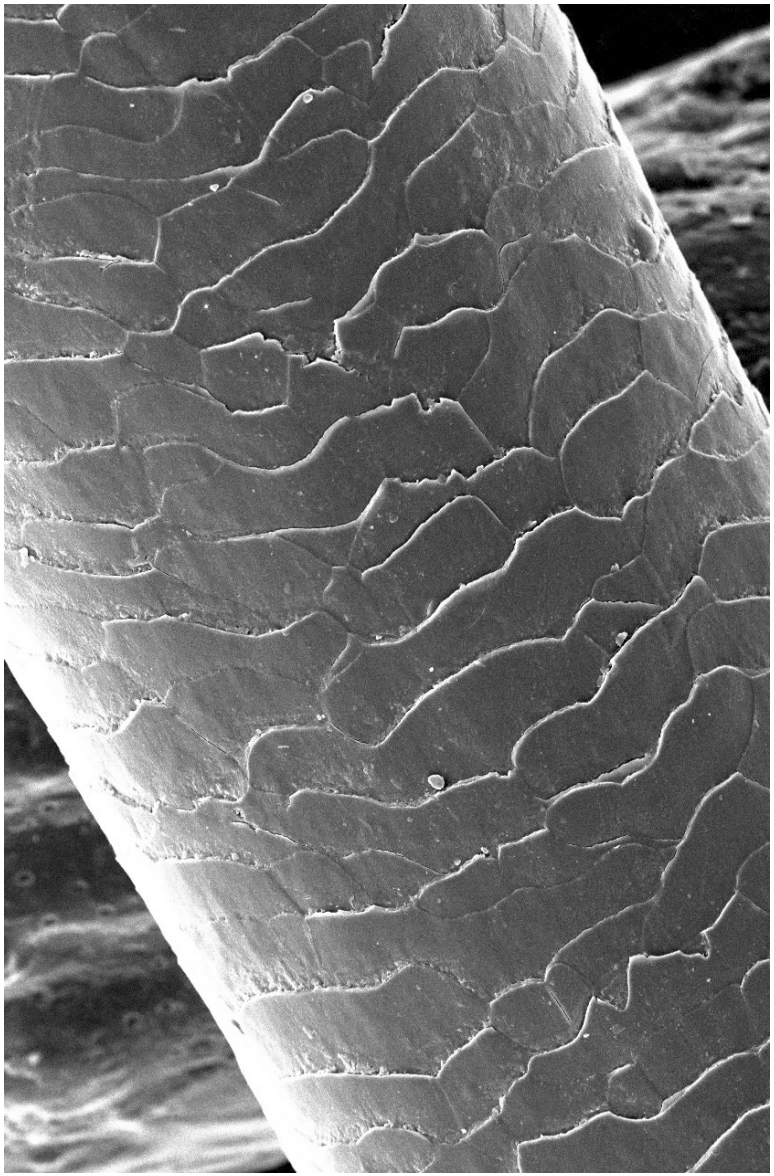
The Self-Scrolling Technique





Artificial Bacterial Flagella (ABFs)

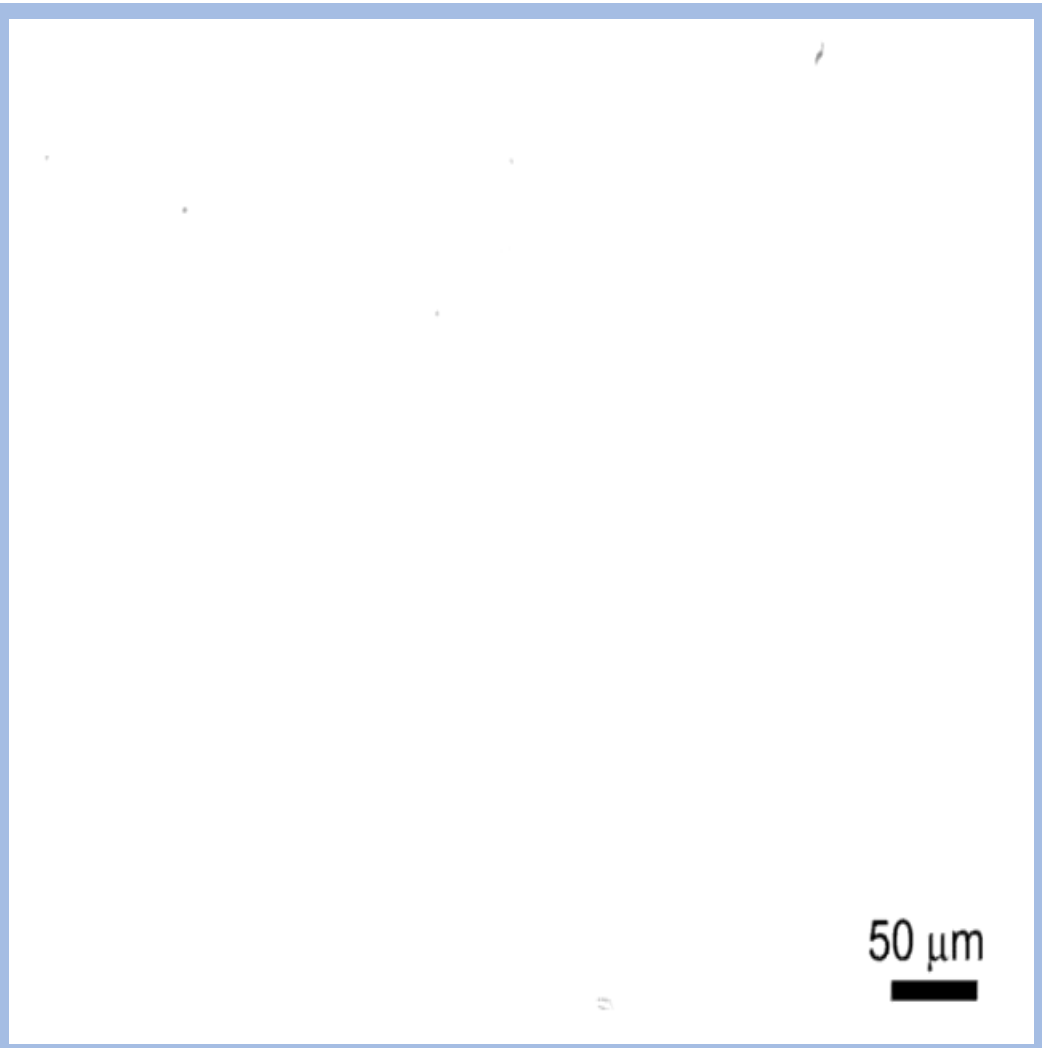




Artificial Bacterial Flagella

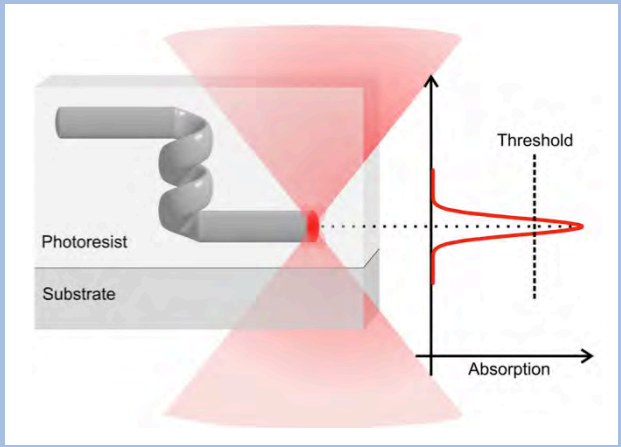
2012 Guinness Book of World Records

Synchronized Swimming



Biocompatible ABFs?

- Polymer materials
  - Non-cytotoxic
  - Bioerodable
  - Functionalizable
  - Low-cost

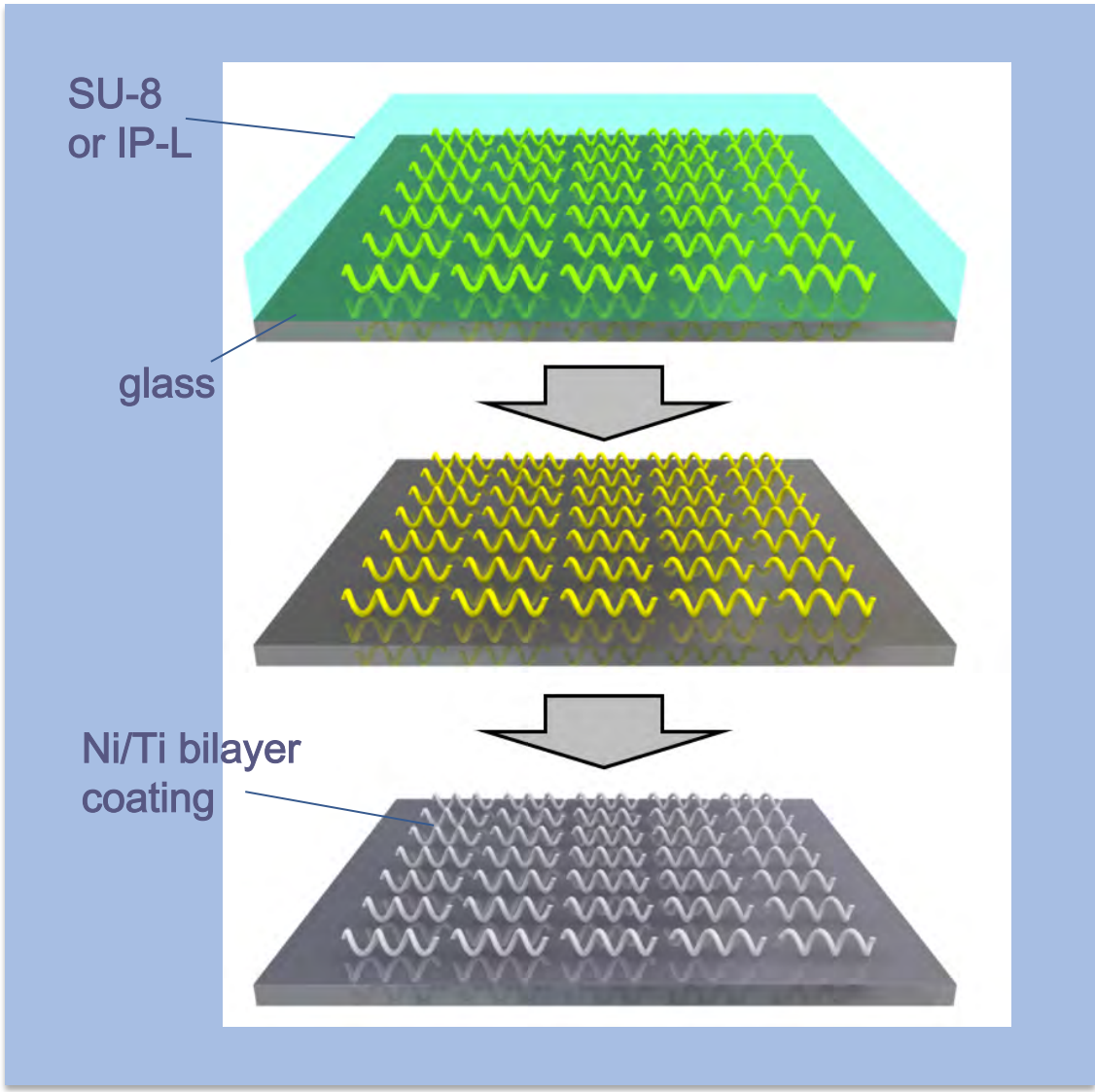


Two-photon-photopolymerization

Nanoscribe

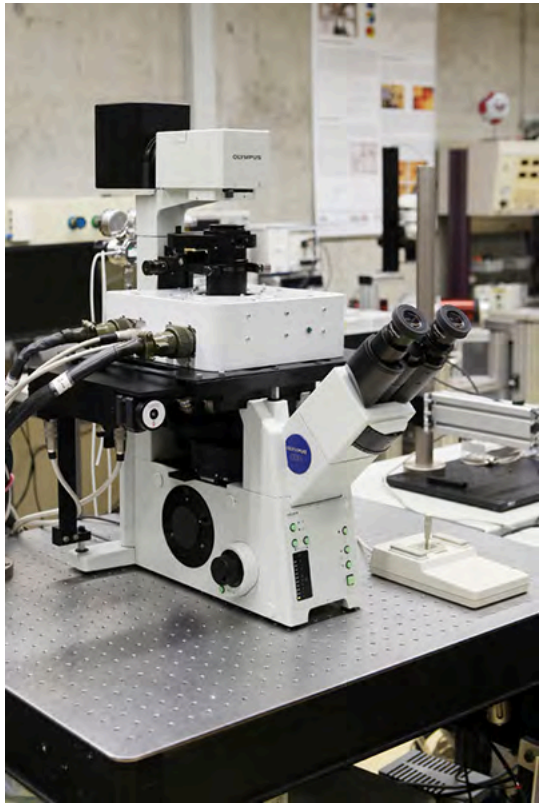
Biocompatible ABFs?

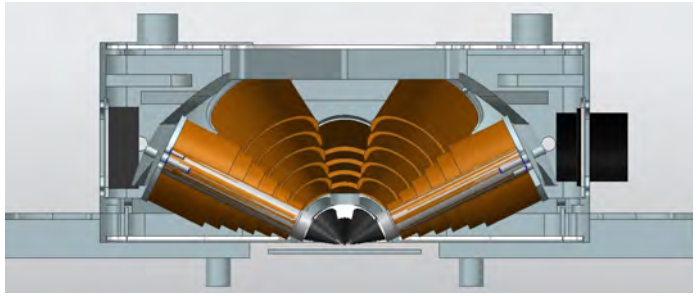
- Polymer materials
  - Non-cytotoxic
  - Bioerodable
  - Functionalizable
  - Low-cost

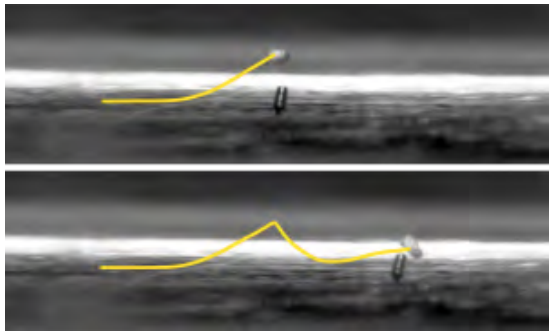


Generating Magnetic Fields and Field Gradients

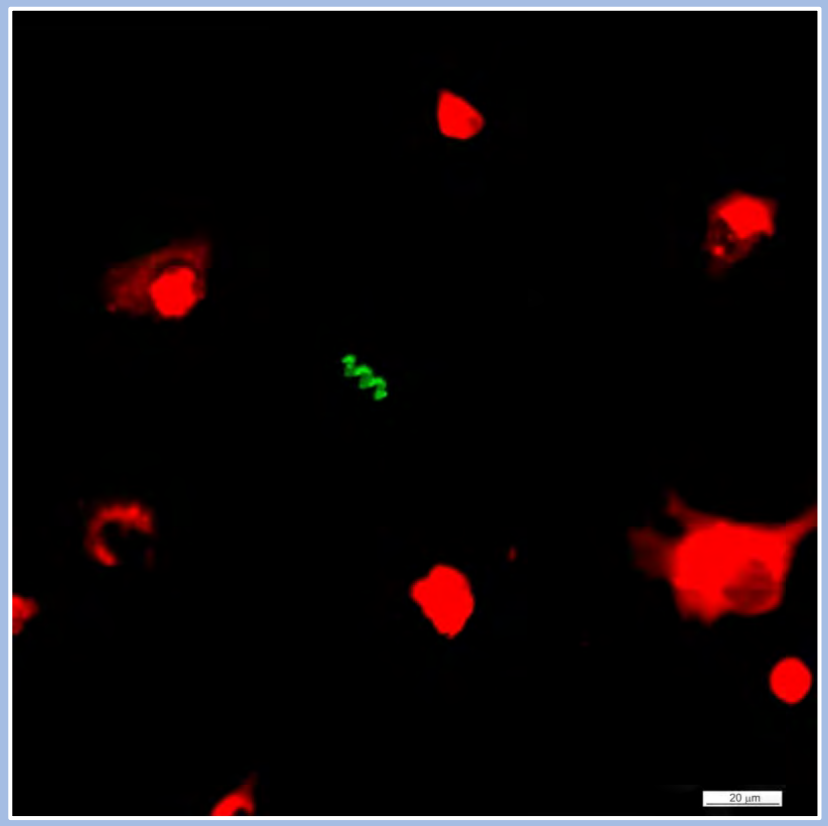
MagnebotiX

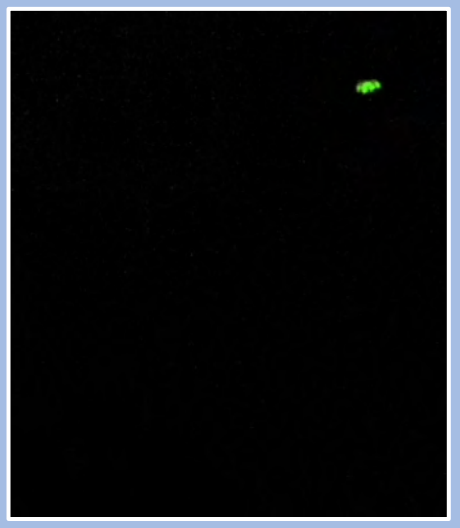


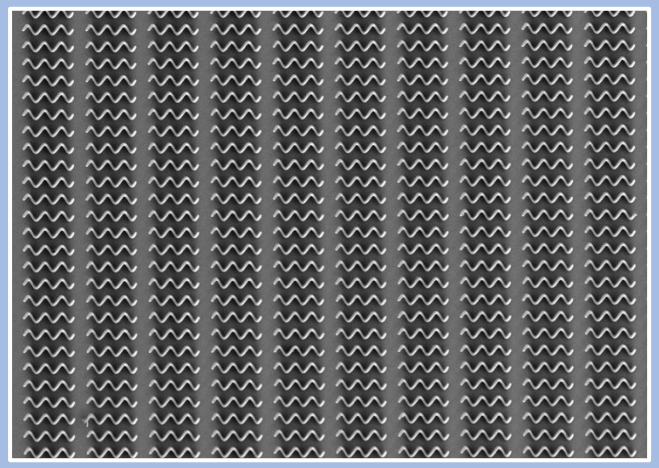




Delivering Drugs to Individual Cells

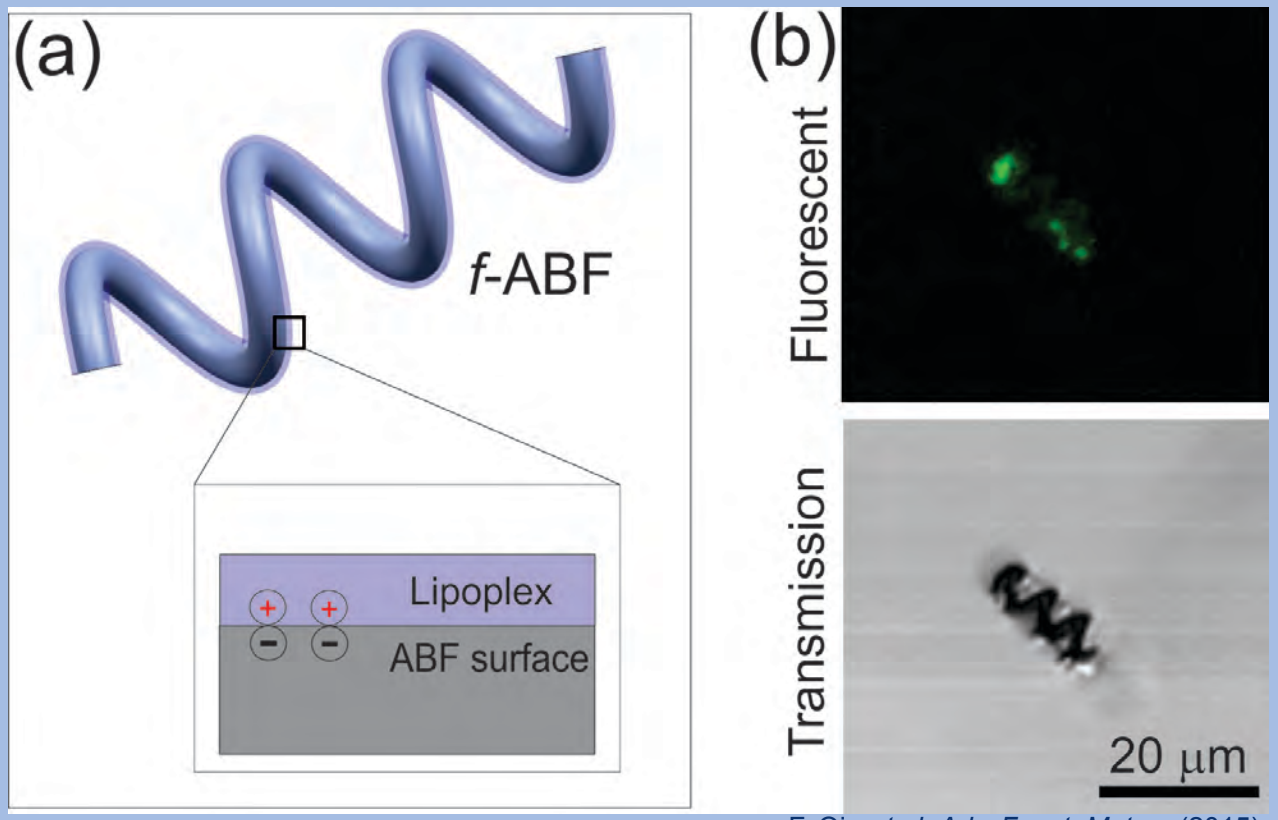






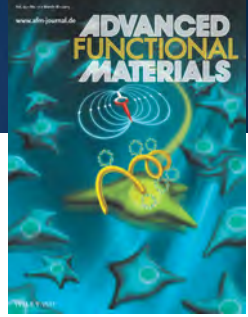
ABFs Functionalized with Lipoplexes

- (a) Functionalization of ABFs with lipoplexes
  - Lipoplexes are mixtures of cationic lipids and DNA, transfection agents
  - Size of ABFs: Diameter 5 um, Length16 um, Ni/Ti layer (25 nm/ 15 nm)
- (b) Confirmation of lipoplexes on ABFs by CLSM
  - DNA was marked using green fluorescence (fluorescein)

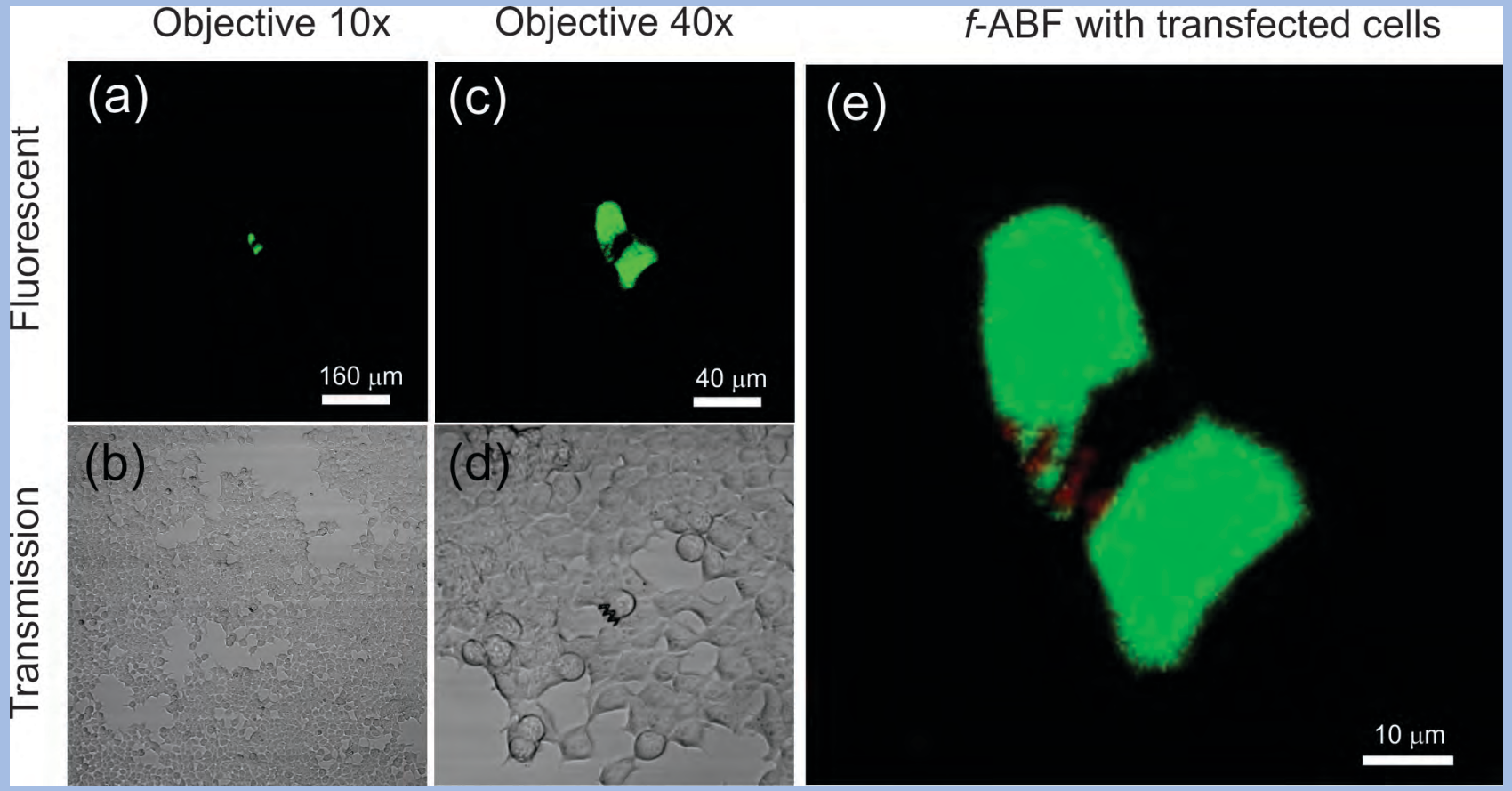


F. Qiu *et al. Adv. Funct. Mater.*, (2015)

Cell Transfection and Gene Expression

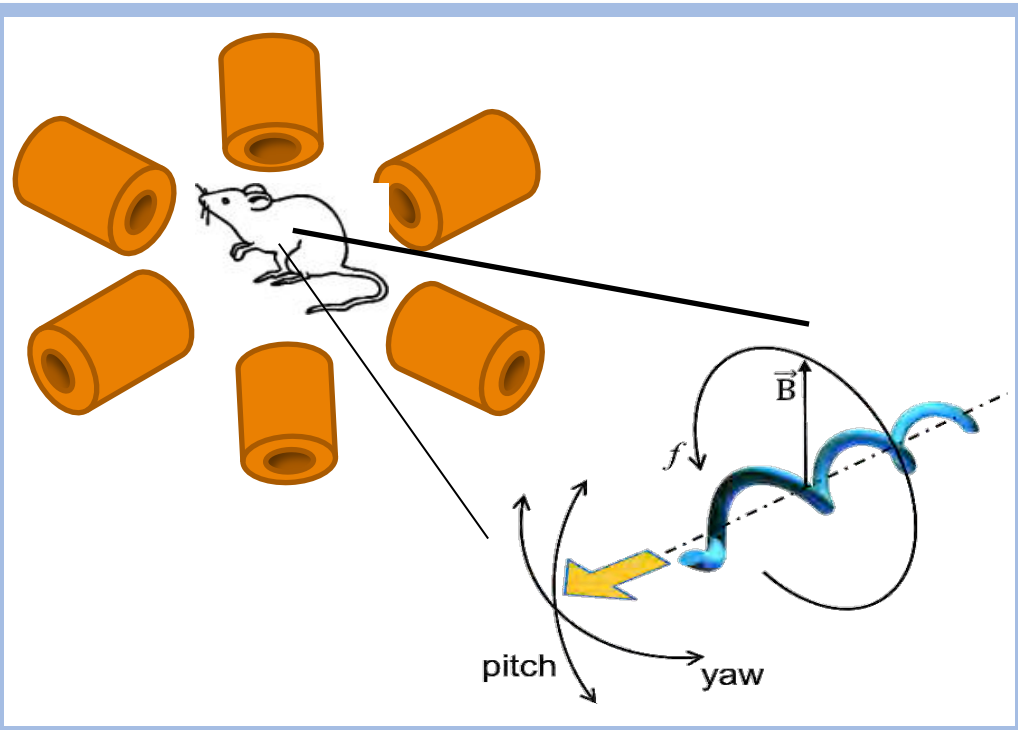


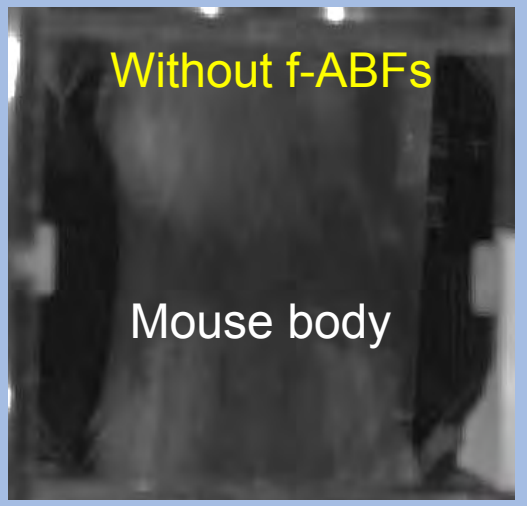
- Only targeted cells were transfected by DNA carried on ABFs
- Cells expressed the Venus protein encoded in DNA

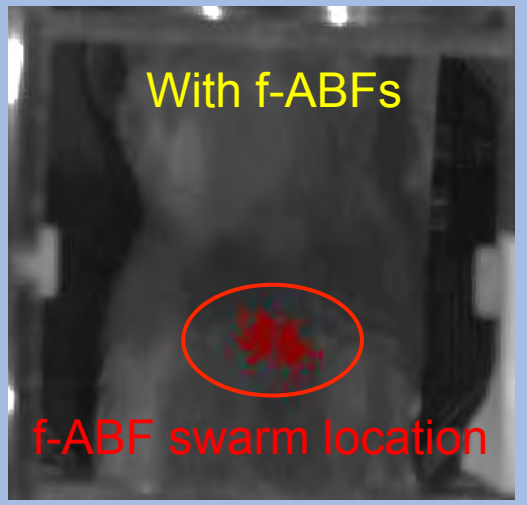


F. Qiu *et al. Adv. Funct. Mater.*, (2015)

in vivo Swimming

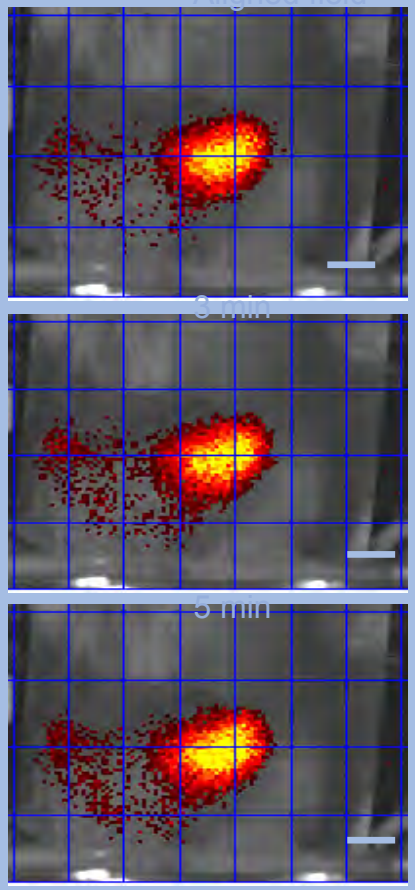


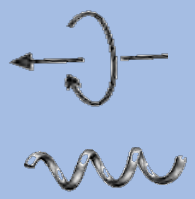


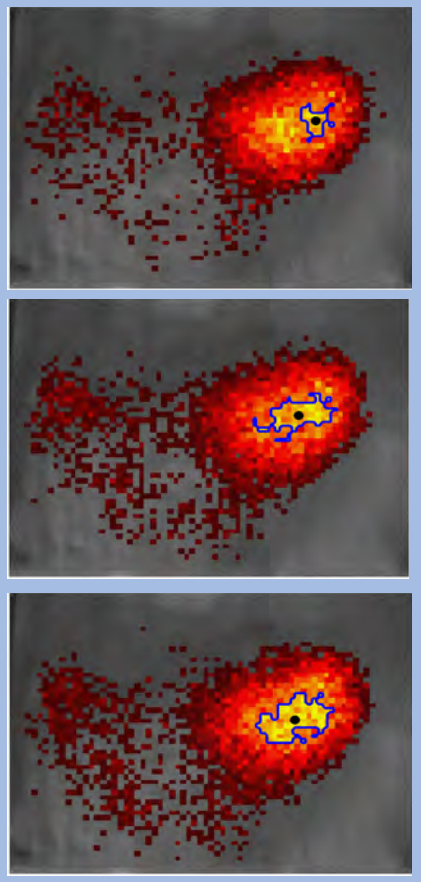


- NIR-797 dye served as a tracking probe for an *in vivo* imaging system (IVIS)
- A swarm of f-ABFs were inject into the peritoneal cavity
- The swarm localized in a mouse body (red cloud)

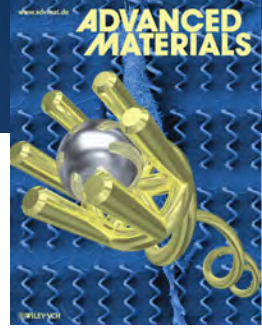
in vivo Swimming of Swarms





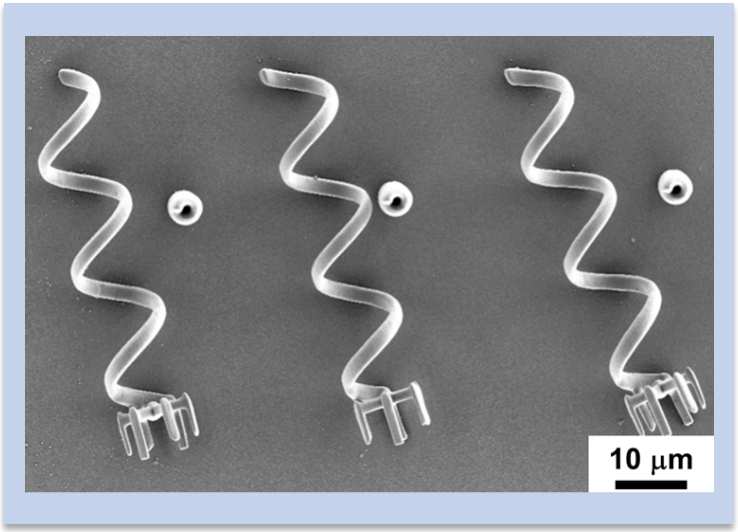


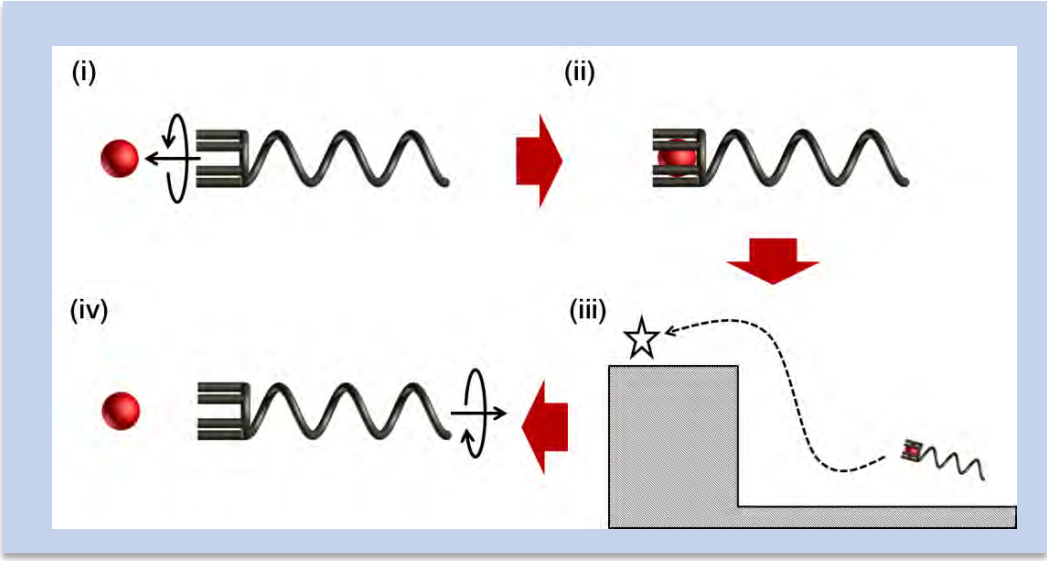
Micromanipulation



Microswimmers with end effectors

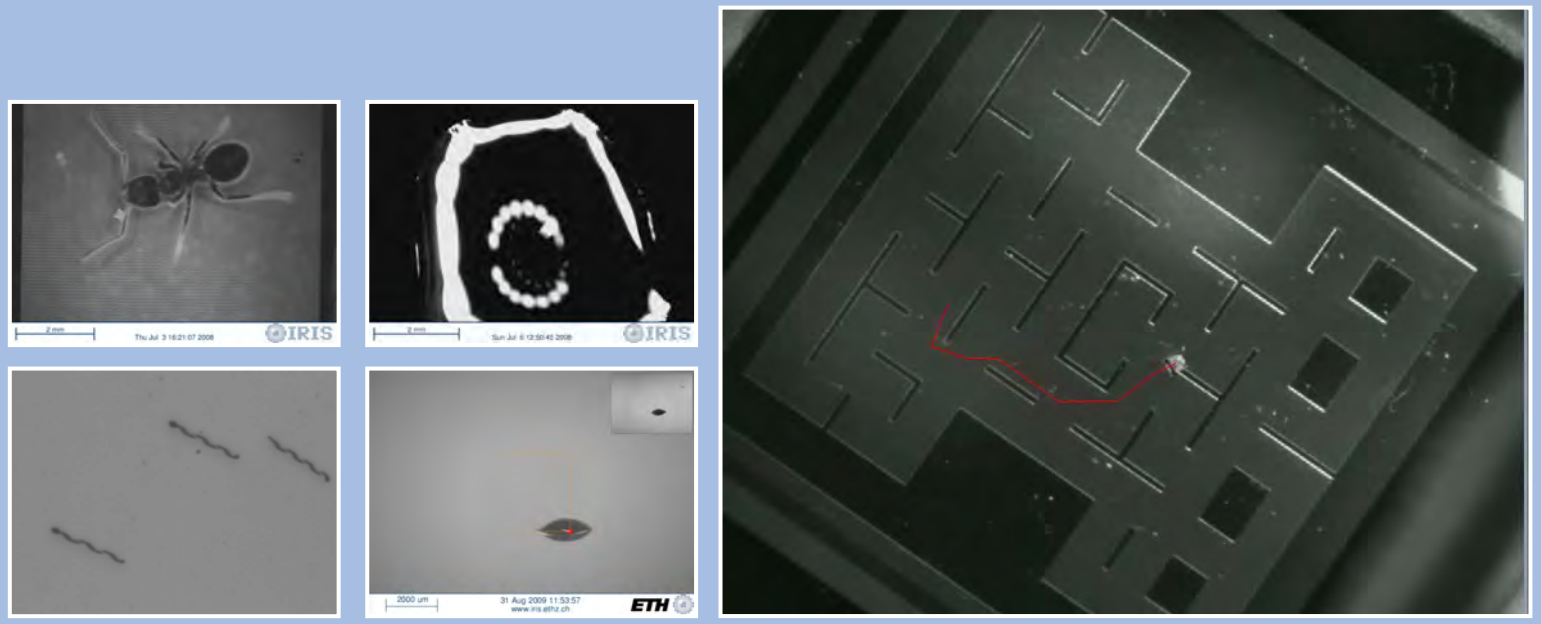
- Microhands fabricated at the ends of helical bodies
- Load and release using fluid drag





Summary

- A primary application area for micro and nano robotics is medicine, biology, manufacturing, and, perhaps, environmental monitoring
- The Micro/Nanorobotics Community has made tremendous progress in a decade
  - Power, locomotion, fabrication
  - Addressing appropriate therapies
- The potential is huge, but the timeline uncertain
- The field is in its infancy



The MSRL Team

Li Zhang
Brad Kratochvil
Salvador Pane
Felix Beyeler
Yu Sun
Jake Abbott
Lixin Dong
Eniko Enikov
Ge Yang
Berna Ozkale
Ayoung Hong
Markus Hoop

Ruedi Borer
Brigitte Geissmann
Karl Vollmers
Stefano Fusco
Dominic Frutiger
Sascha Stoeter
Zoltan Nagy
Didi Xu
Christos Bergeles
Franziska Ullrich
Chengzhi Hu
Andrew Petruska

Kaiyu Shou
Olgac Ergeneman
Michael Kummer
Martin Probst
Ninja Oess
Michael Flückiger
Dominik Bell
Chauncey Graetzel
Jonas Goldowsky
Sam Cherreyron
Roel Pieters
Xiangzhong Chen

Kathrin Peyer
Serdar Sezen
Michael Greminger
Shan Guan
Jens Tapproge
Berk Yesin
Arif Zeeshan
Yu Zhou
Kartik Sivaraman
Andre Lindo
Hen-Wei Huang
Fajer Mushtaq

Dimitris Felekis
Hsi-Wen Tung
Simone Schürle
Vanda Pocepcova
Sandro Erni
Barmeshwar Vikramaditya
Arunkumar Subramanian
Juho Pokki
Famin Qiu
Naveen Shamsudin
George Chatzipirpiridis
Carlos Alacantra

Robotics
Biomedical Engineering
MEM
Nanotechnology
Mechanical and Electrical Engineering
Computer Science
Materials
Physics
Chemistry
Medicine
Business, …