Nanobots: Design, Fabrication, and Emerging Biomedical Applications

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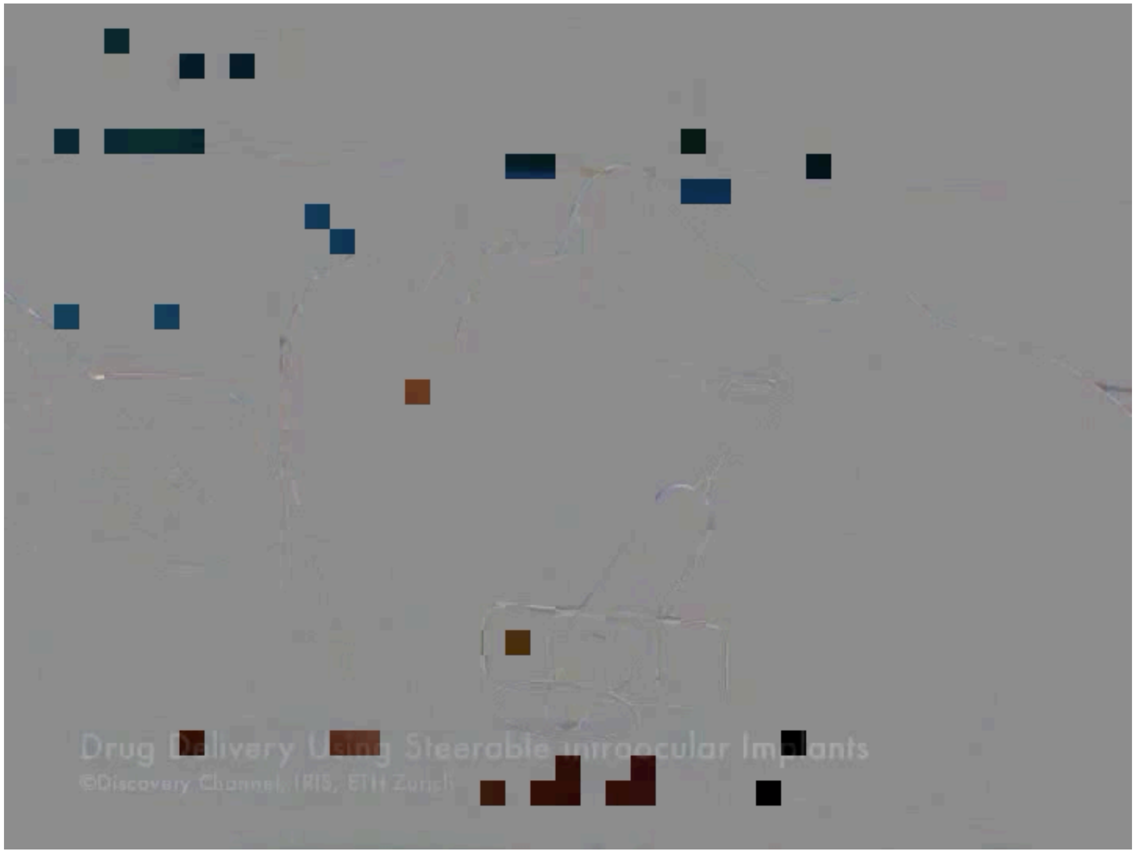
Disclosure

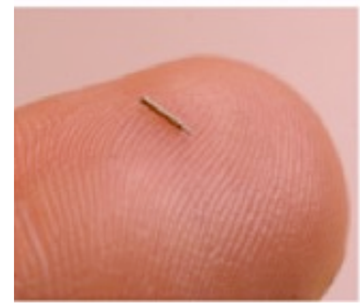
I am the Founder and a Scientific Advisor of **Allegro 3D, Inc**. that offers bioinks, bioprinters, and bioprinted tissues and medical devices.

ALLEGRO 3D™

Magnetic Micro-robots for Drug Delivery to Retinal



23-gauge needle



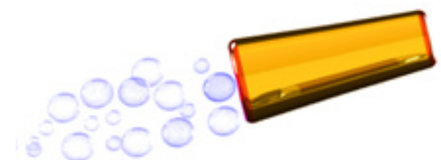
Targeted therapy with high precision and in MIS fashion

The microrobot is injected into the vitreous in the posterior eye segment using a syringe equipped with a needle through the sclera

Propulsion Mechanisms of Micro/nanoscale Robots

- Magnetic actuation

- Chemical propulsion



- Acoustic propulsion

  (e.g. ultrasound)

- Biological propulsion

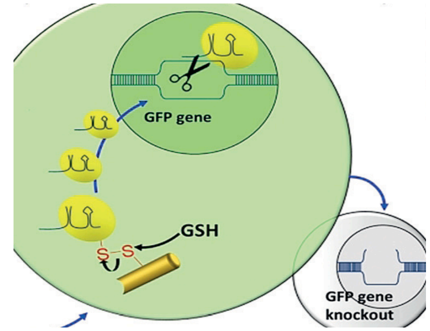
  (e.g. sperm-flagella, spermbot)

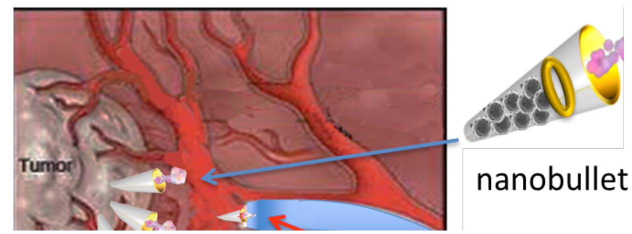
- Others: thermal, optical, electrical, etc.

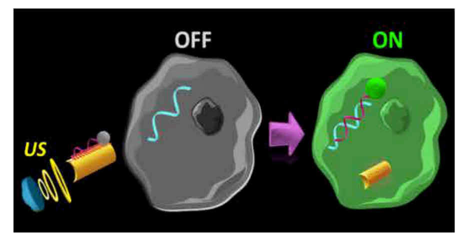
Li et al, *Science Robotics,* 2 (4), eaam6431, 2017

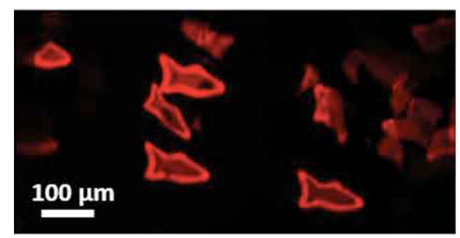
Emerging Biomedical Applications

- Targeted drug/gene delivery
- Precision surgery
- Biosensing
- Detoxification
- Others: imaging, diagnostics, etc



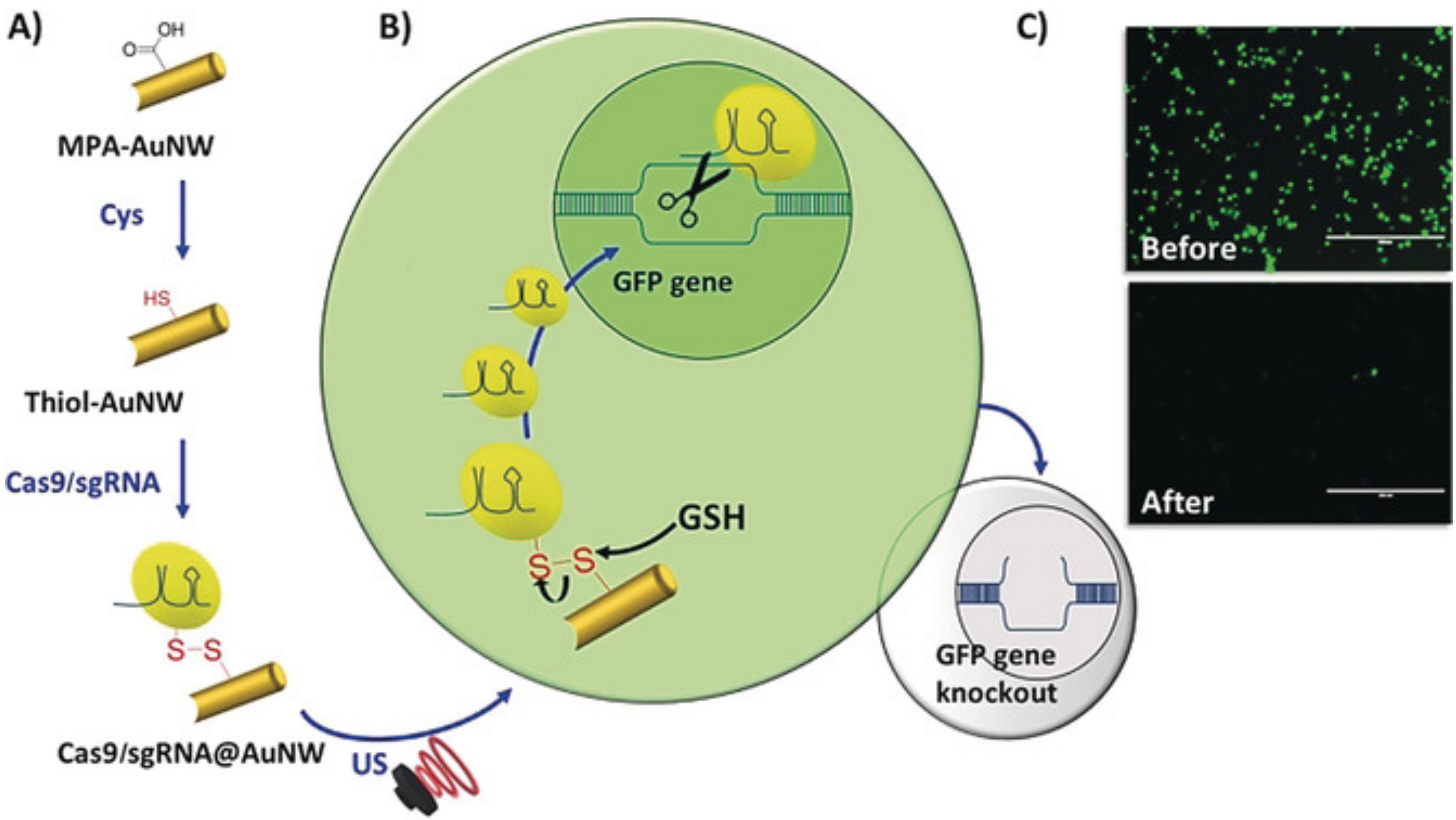






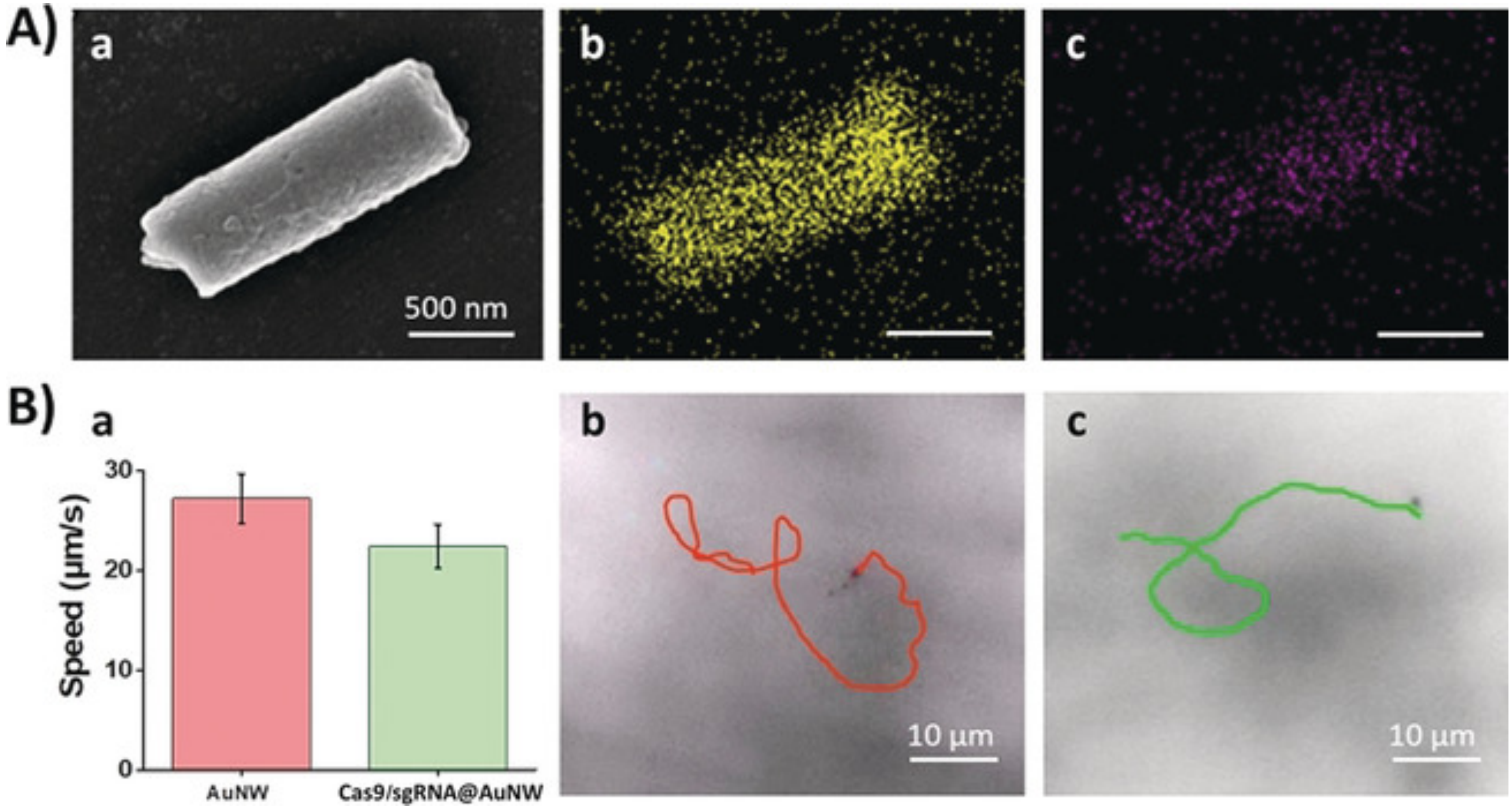
Li et al, *Science Robotics,* 2 (4), eaam6431, 2017

Intracellular Delivery of Cas9-sgRNA Complex



Cas9/sgRNA enters the nucleus to initiate site-specific gene editing for GFP knockout. The knockout effect with “turn-off” fluorescence is observed using fluorescent microscopy (c).

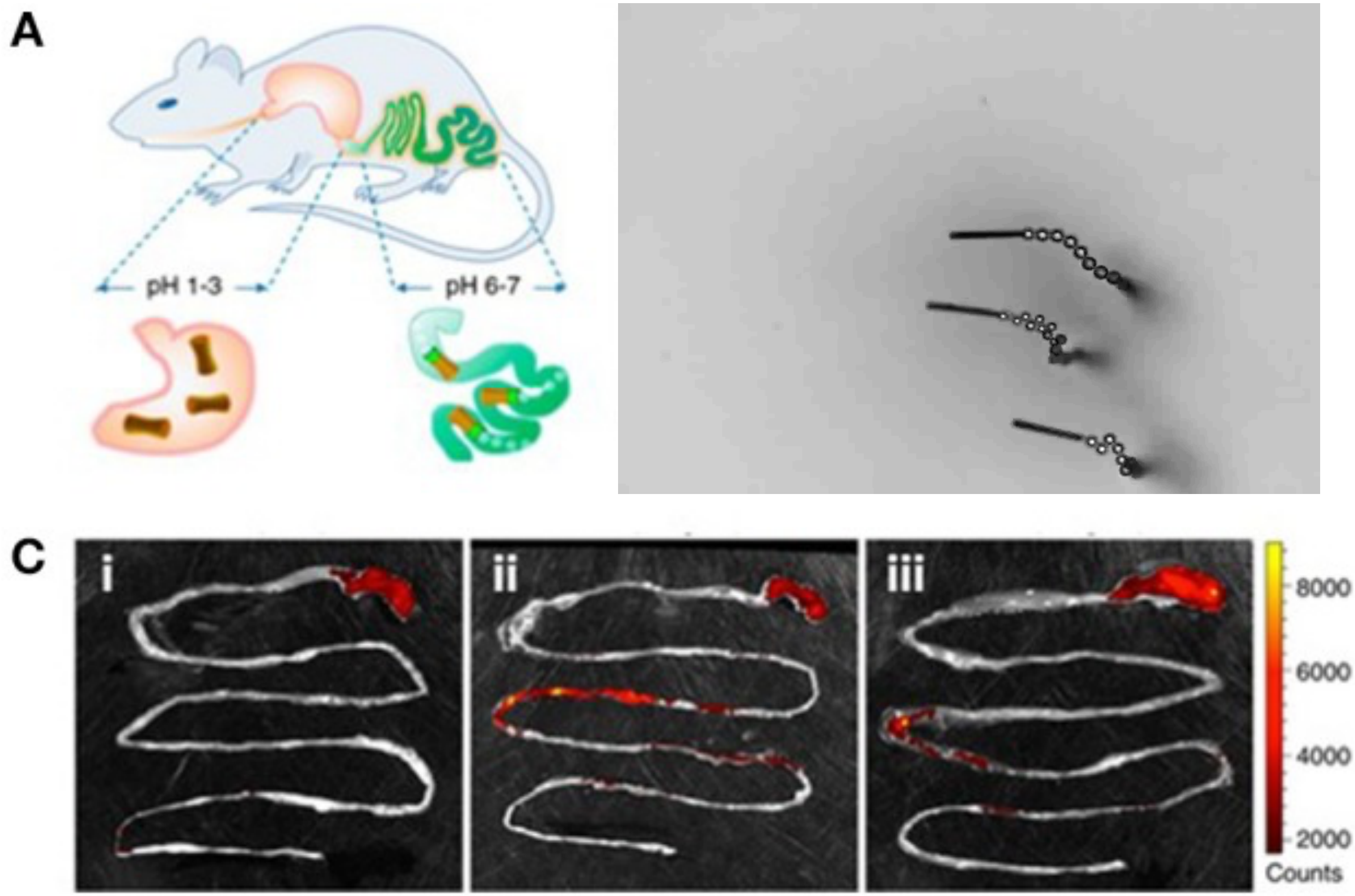
Structural and Propulsion of Cas9/sgRNA@AuNWs



A) Template-assisted electrodeposition of AuNW (a), EDX analysis (b) and N (c) content
B) propulsion of non-modified AuNWs (red) and Cas9/sgRNA AuNWs (green) under a US field (2.66 MHz). Tracking trajectories of motor (b) and a Cas9/sgRNA motor (c)

Hansen-Bruhn et al, *Angew. Chem. Int. Ed.* 57, 2657 (2018)

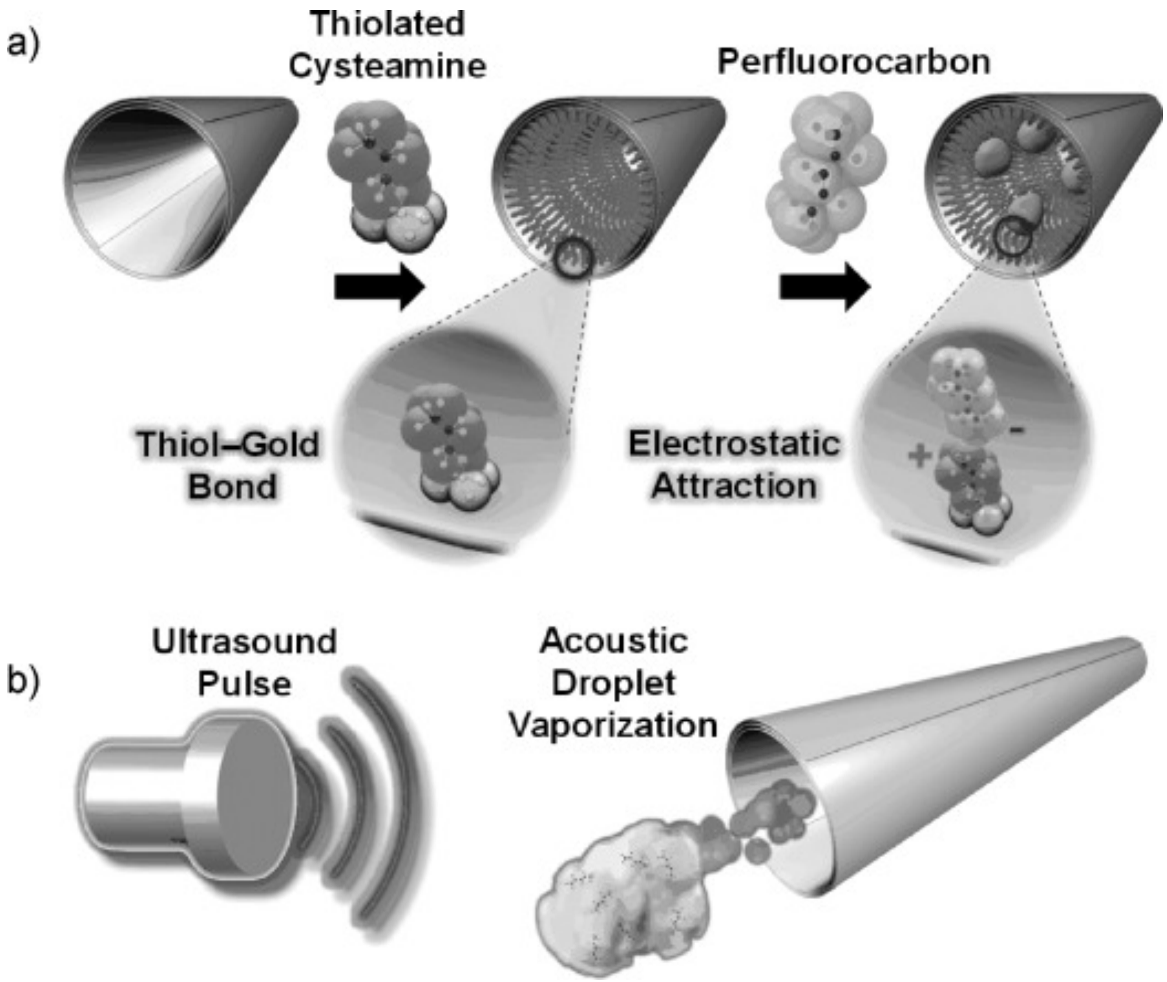
Retention of Payloads in the Gastrointestinal Tract



(B) Bubble generation at the end of the microorobot responsible for locomotion.

(C) The gastrointestinal track retention of the dye Rhodamine 6G delivered by the chemically propelled microrobot (i: control, ii: after 6 h, and iii: after 12 h of administration.

Acoustic Perfluorocarbon-loaded Micro and Nano-bullets

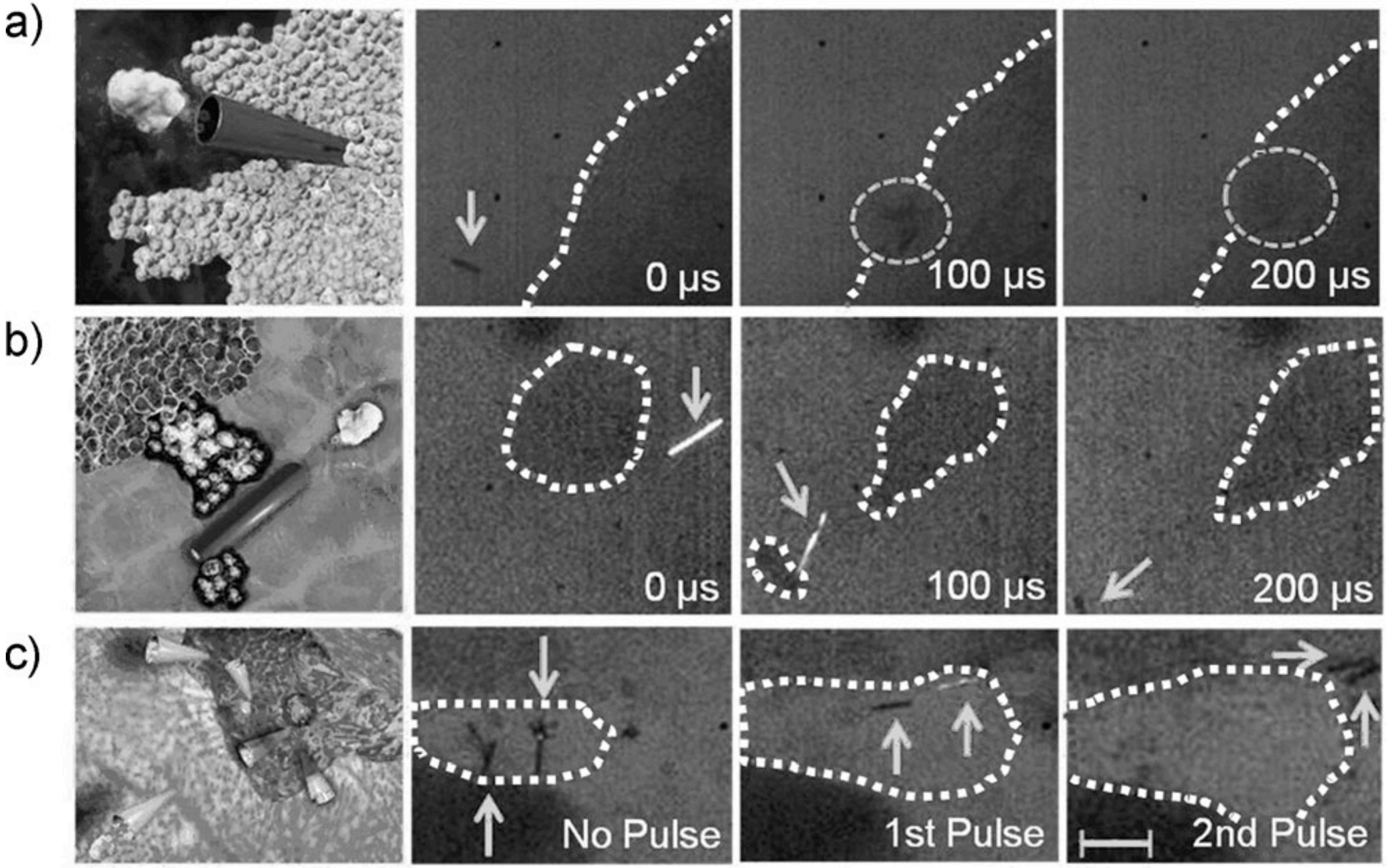


Using ultrasound (US) to vaporize biofuel (i.e., perfluorocarbon (PFC) emulsions) bound within the interior of a micro-bullet (MB) for high-velocity, bullet-like propulsion

(a) Conjugation of thiolated cysteamine to the inner Au layer of the MB (middle), electrostatic binding of the anionic PFC emulsion to the cysteamine-functionalized surface (right).
(b) Microbullet propulsion through acoustic droplet vaporization of the bound PFC by US.

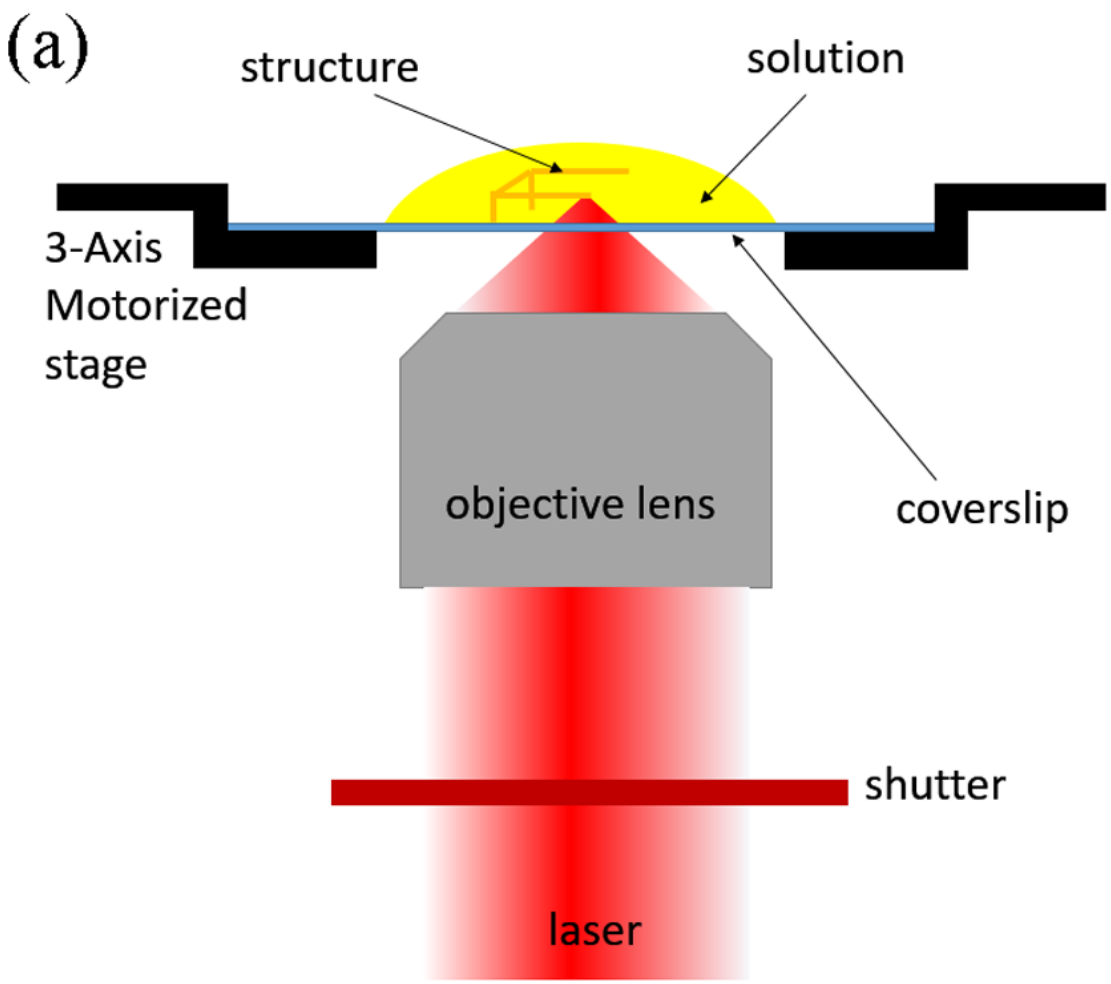
Kagan et al,, *Angew. Chem. Int. Ed.* 51, 7519 (2012)

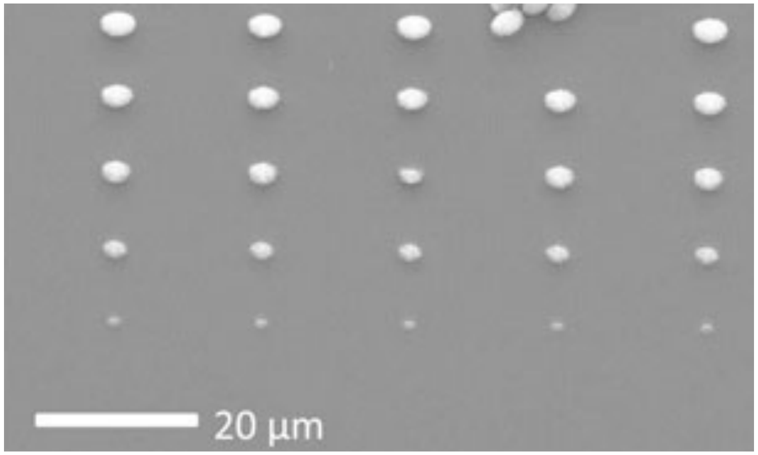
Acoustic Perfluorocarbon-loaded Micro and Nano-bullets

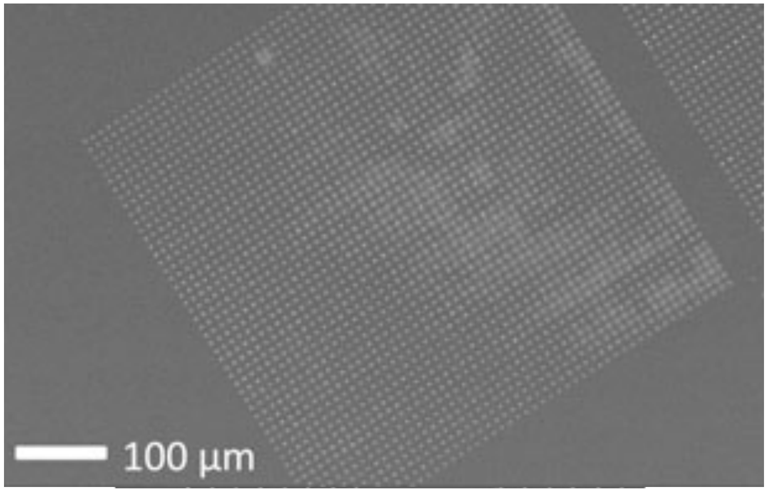


Perfluorohexane (PFC)-loaded MBs a) penetrating, b) cleaving, and c) expanding a tissue

Manufacturing of Nanobots: Laser-based 3D Printing



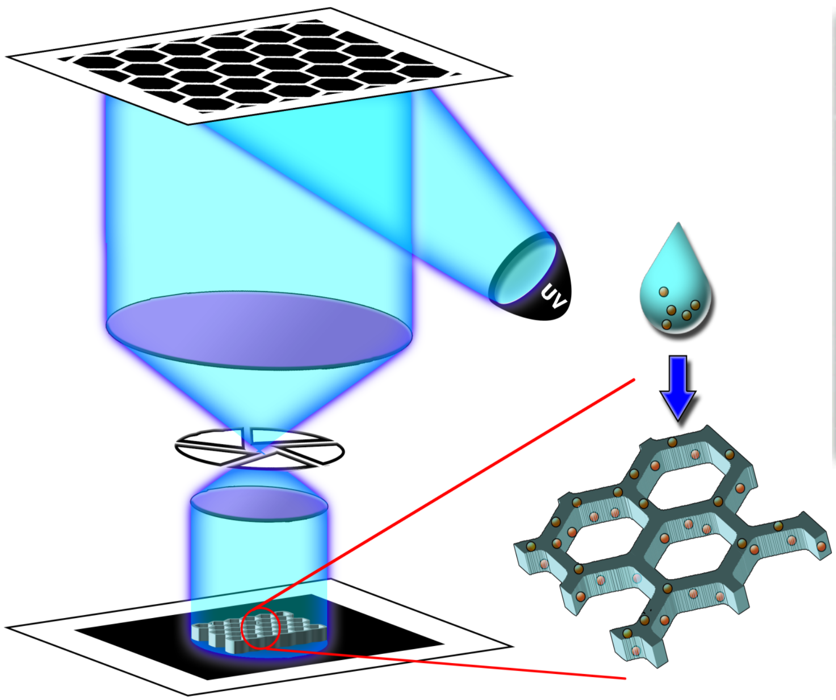


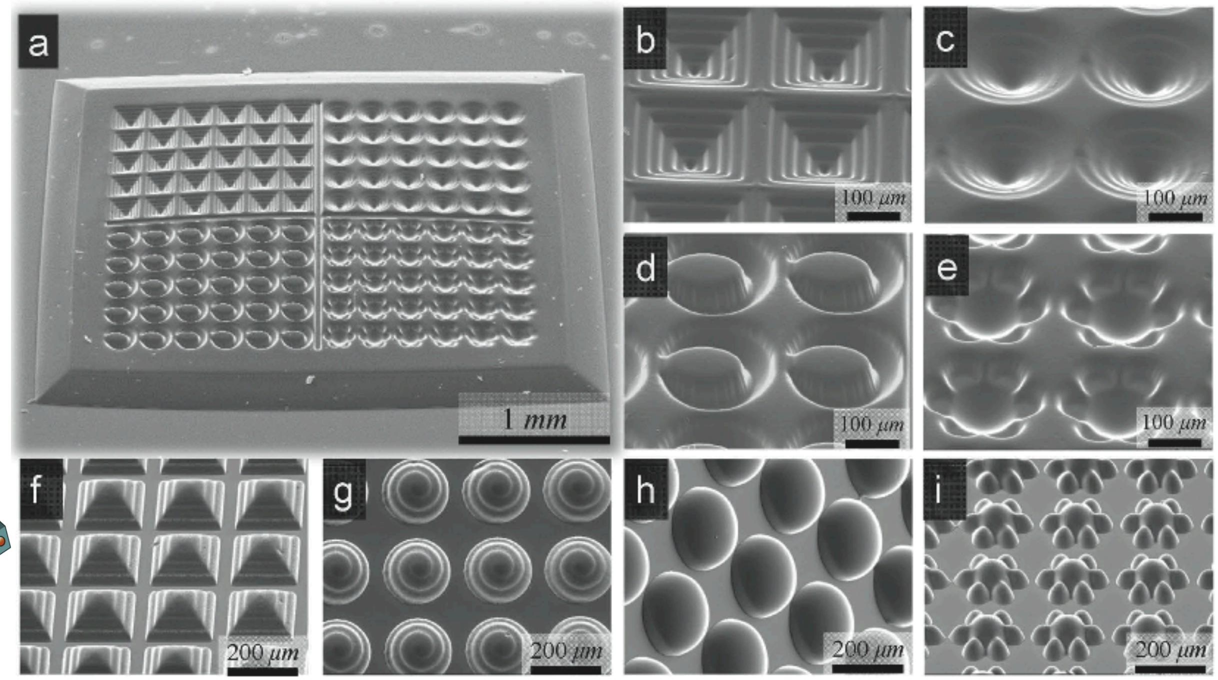


Femtosecond laser-scanning nanoscale 3D printing

Manufacturing of Nanobots: Projection-Light 3D Printing

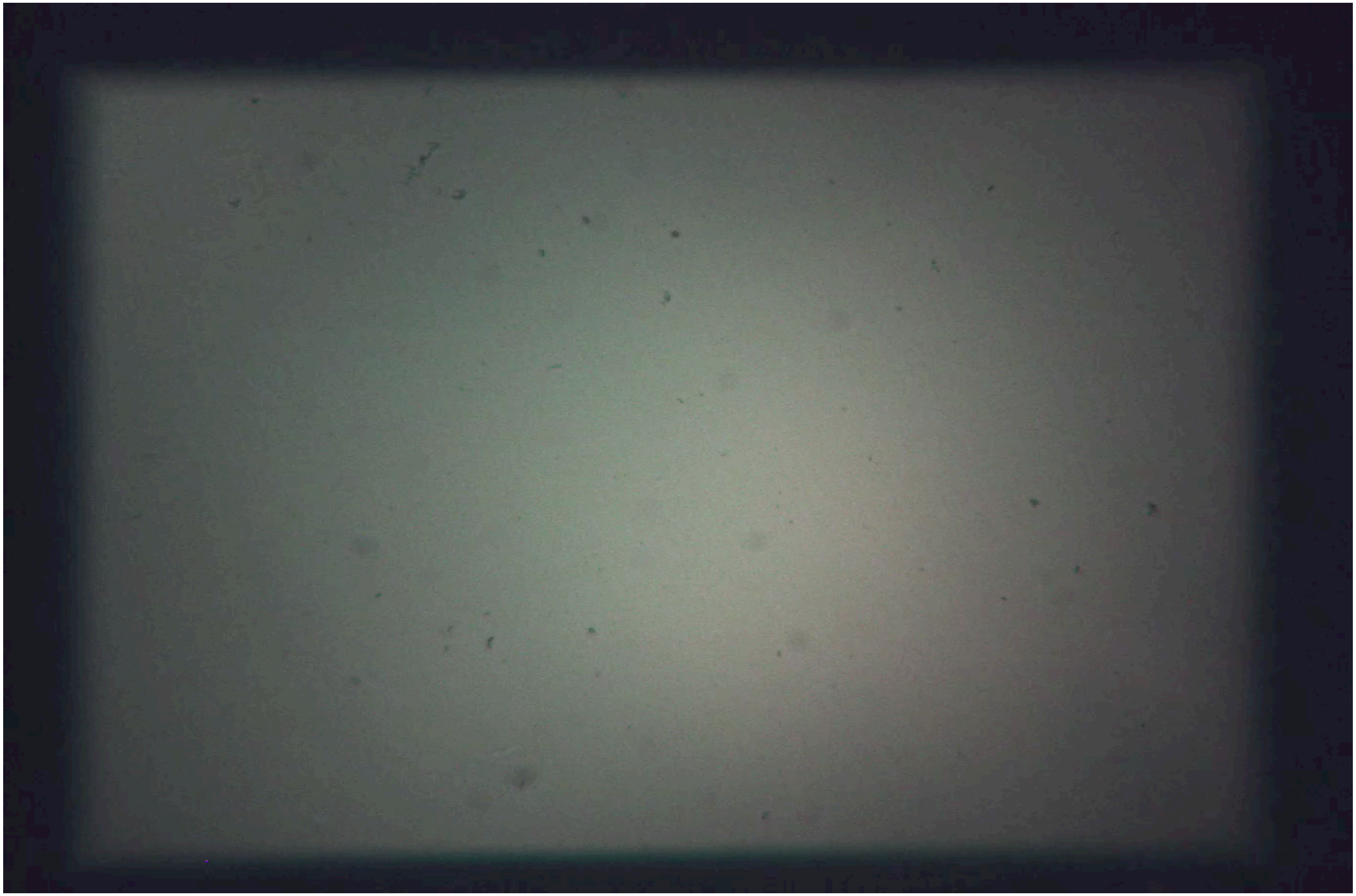
DMD chip for light projection





Digital micro-mirror device (DMD)-based projection 3D printing

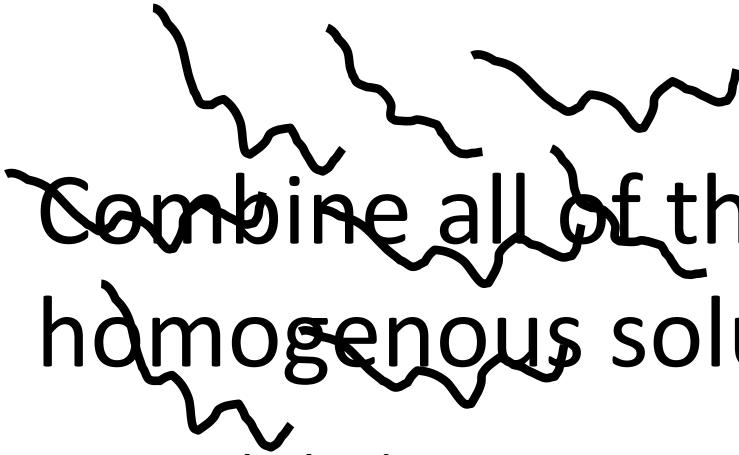
Image-guided Projection Printing of Vasculatures



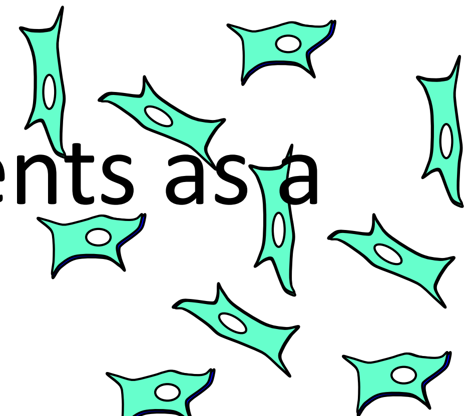
“Lightning Fast 3D Micro Printing” - by 3DTV Watcher News

Integrate XYZ within the Monomer Solution

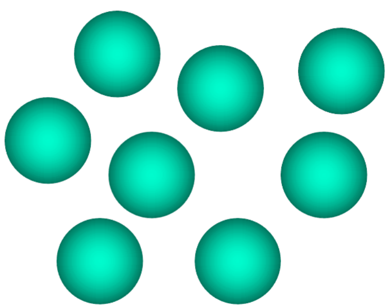
Combine all of these components as a homogenous solution



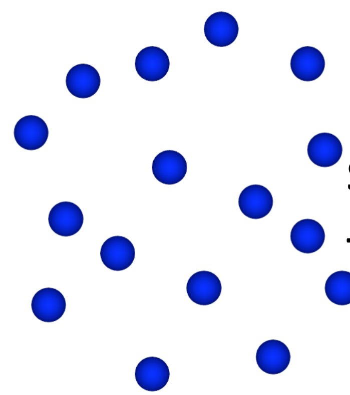
Uncrosslinked monomer



cells



controlled release microparticles



soluble bio-chemical factors

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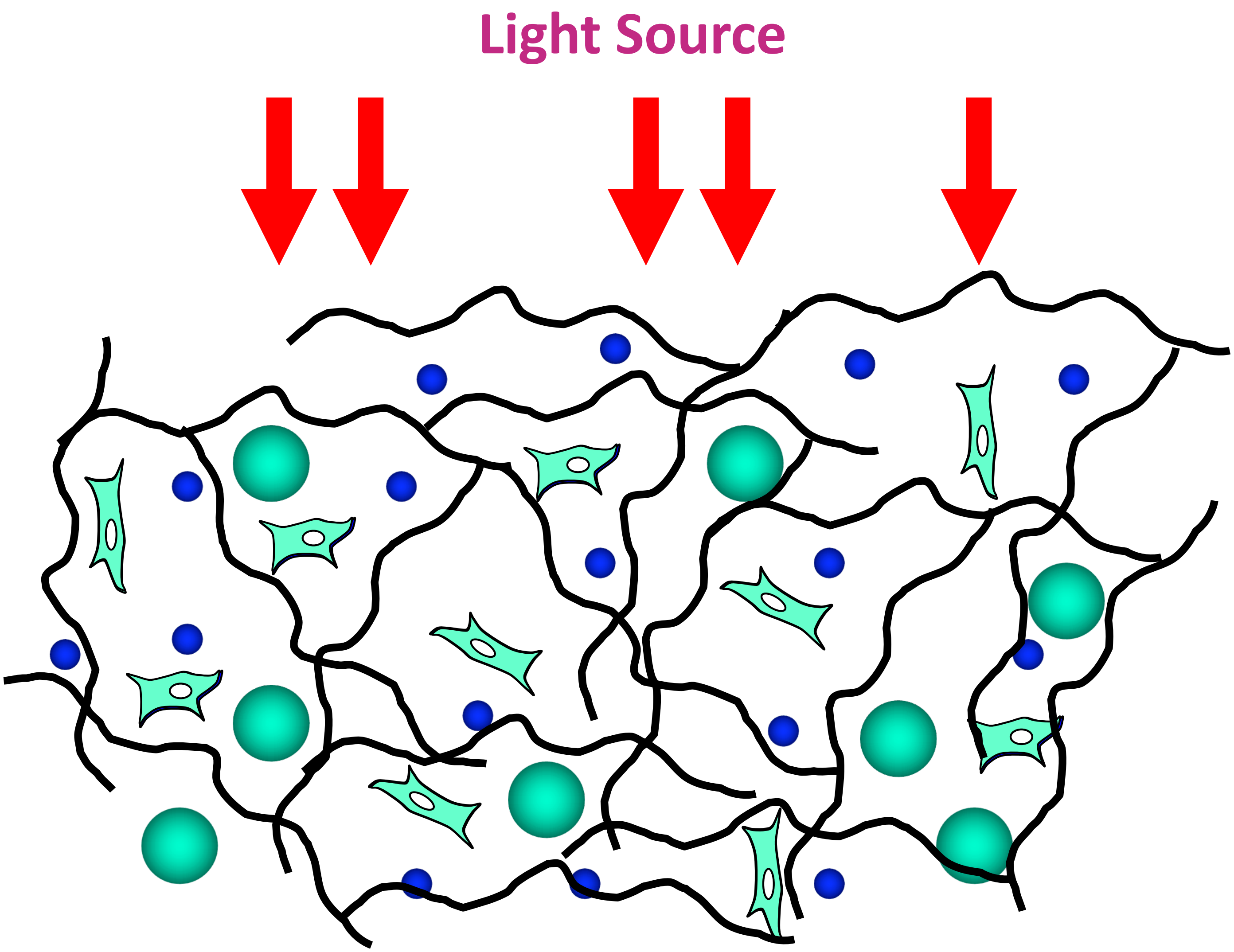
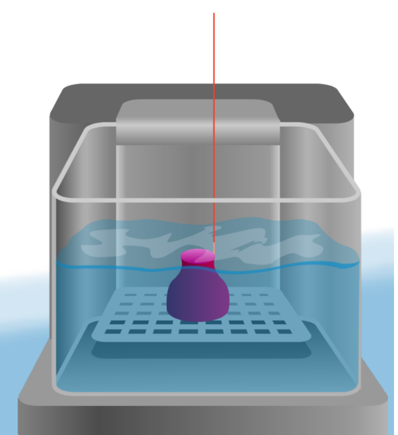
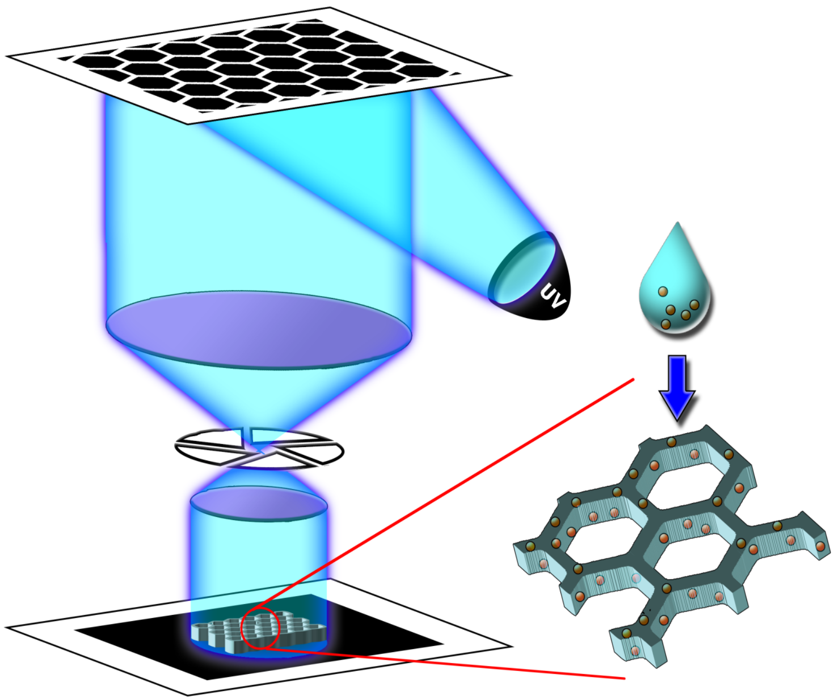
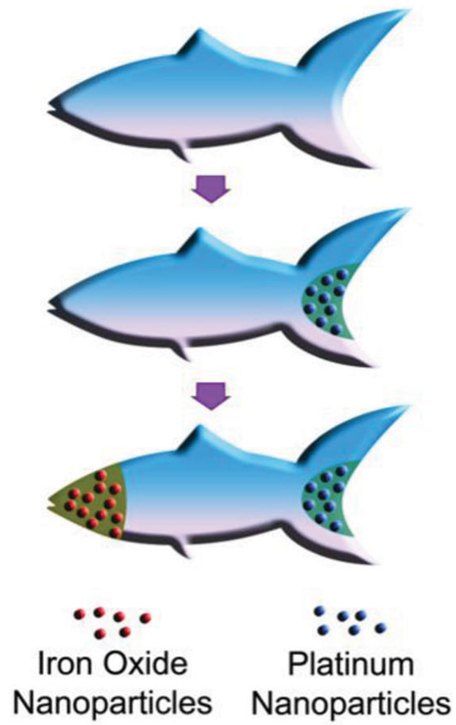
Photopolymerization to Form a 3D Device

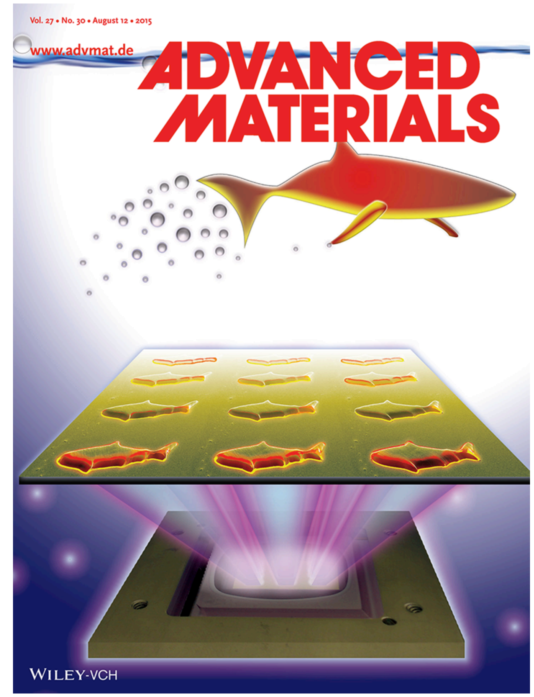




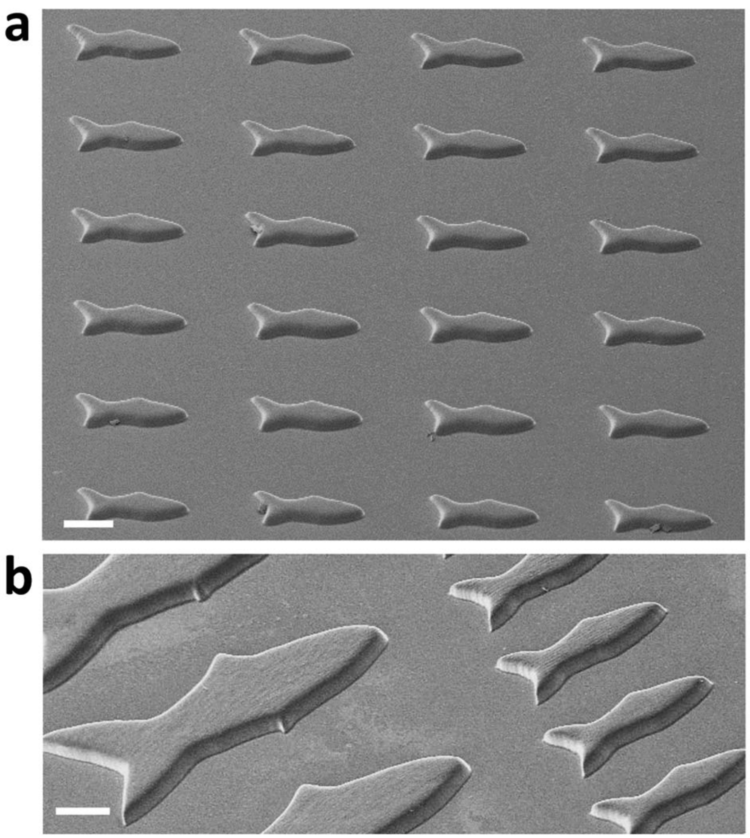
Printing Micro-Fish with Functional Nanoparticles



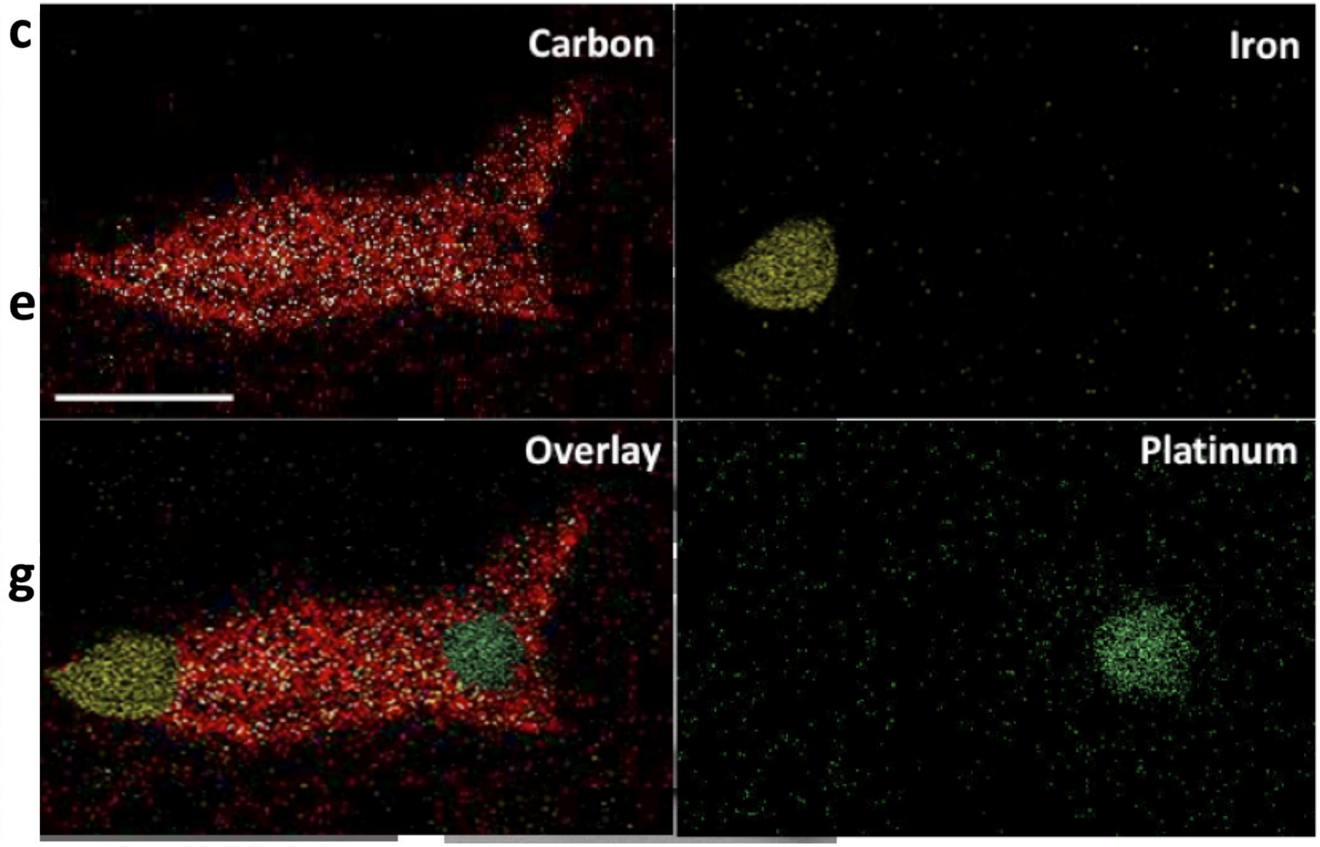




Direct Printing a School of Micro-Fish



Various Fish Array



EDS measurement showing different compositions of the fish

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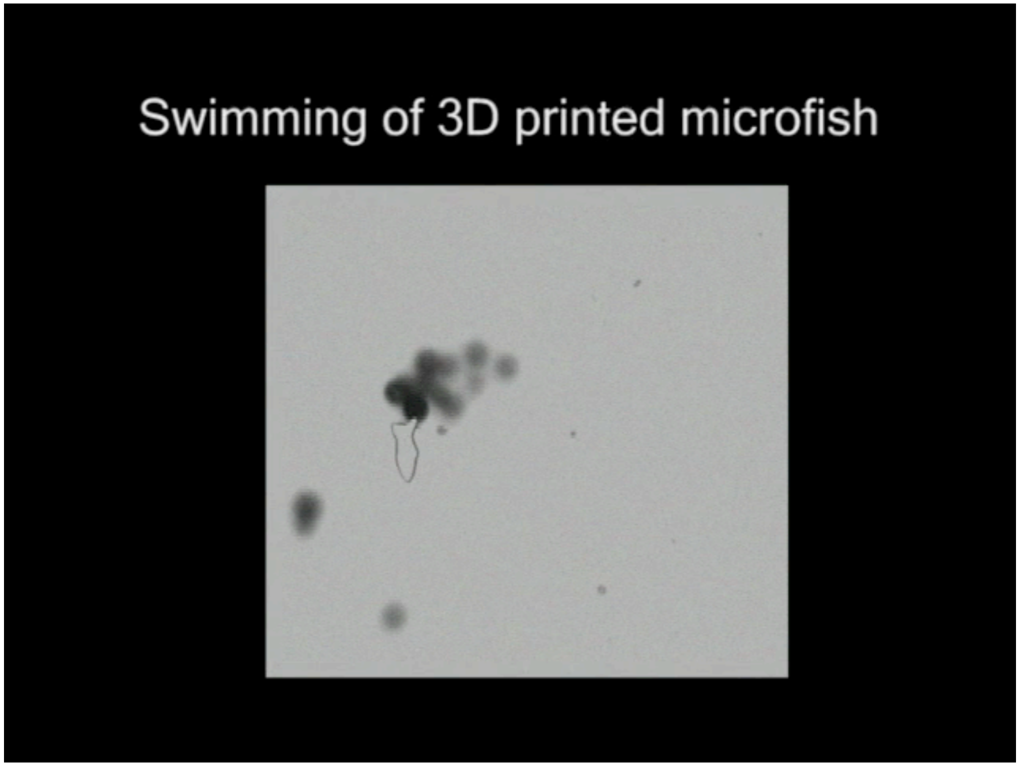
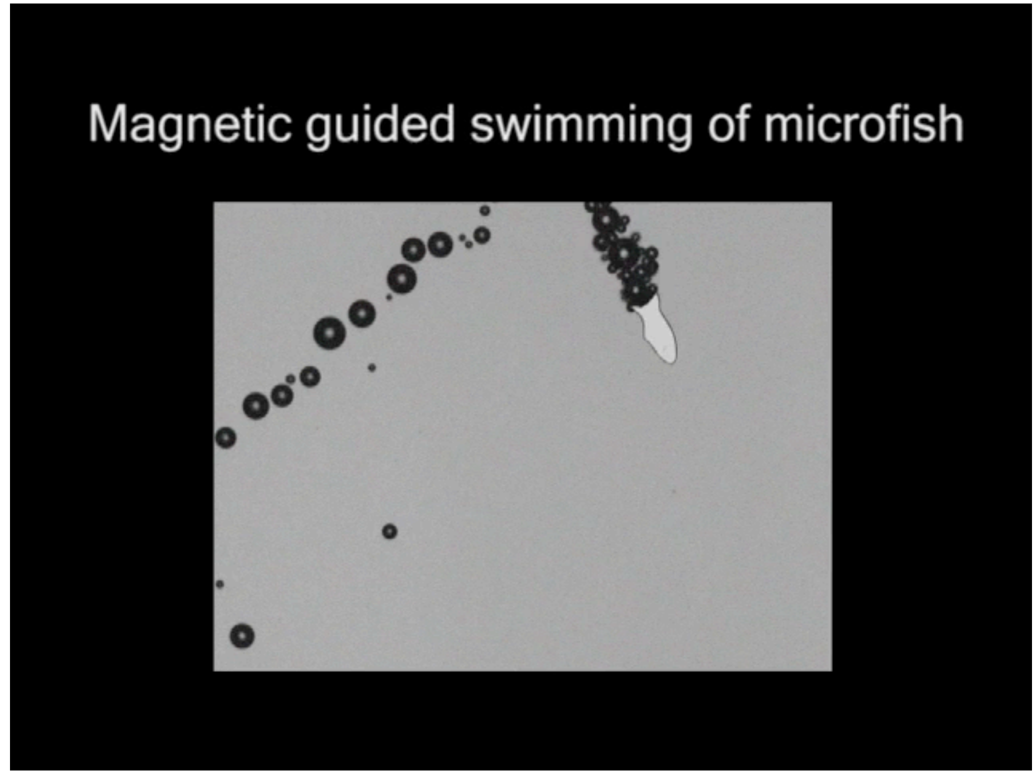
3D-printed Micro-fish in Motion

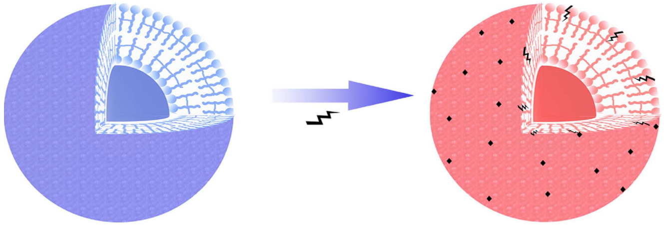


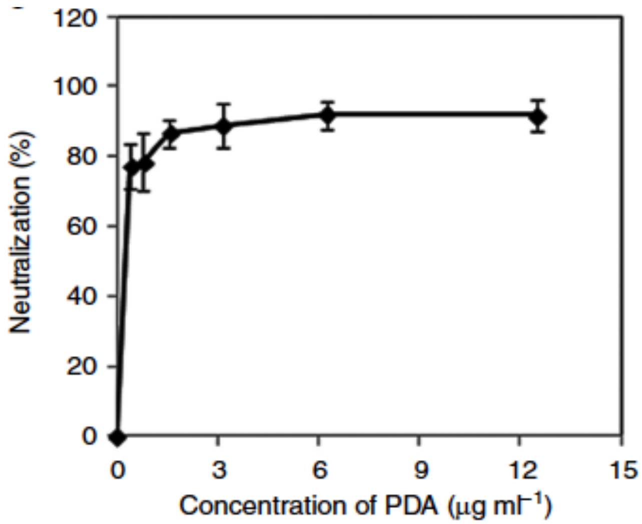


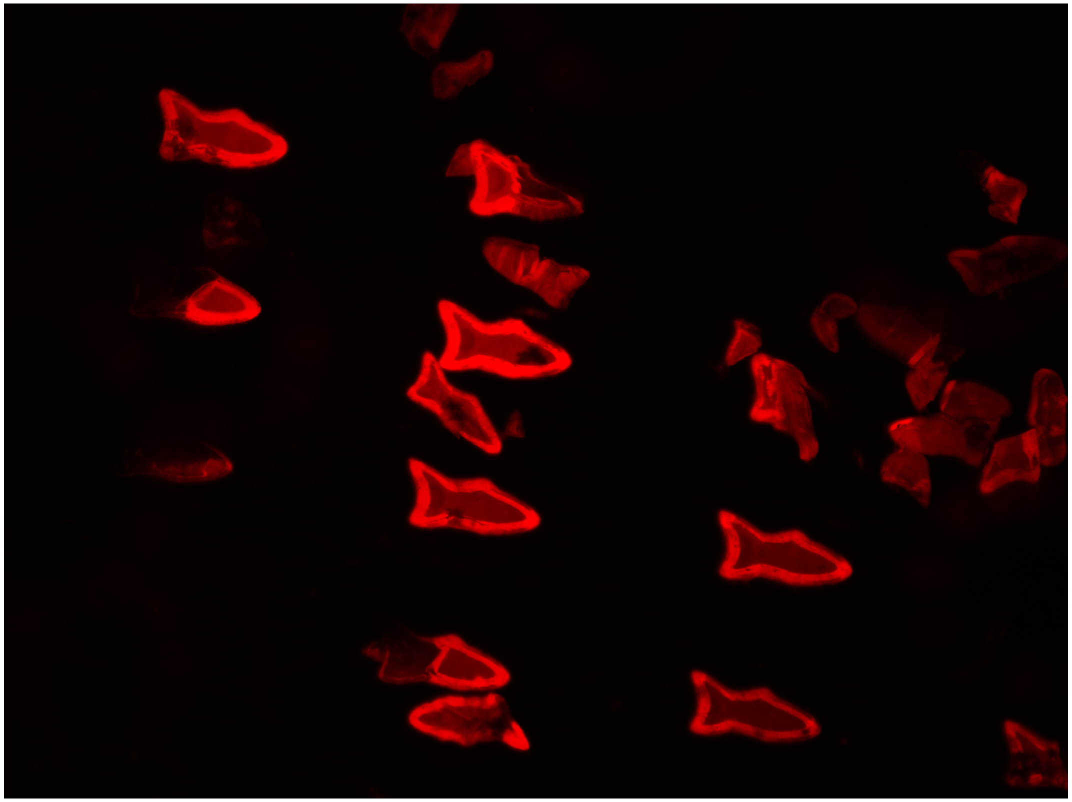
Self-driven micro-fish due to bubble generation at the tail

Adding magnetic nanoparticles in the fish head for magnetic guidance

3D-printed Micro-fish to Remove Toxin





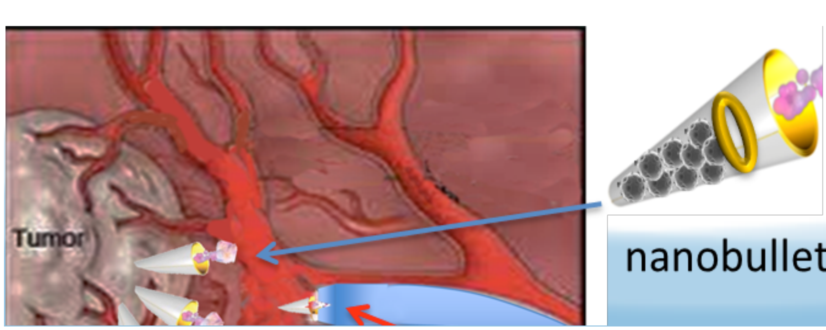


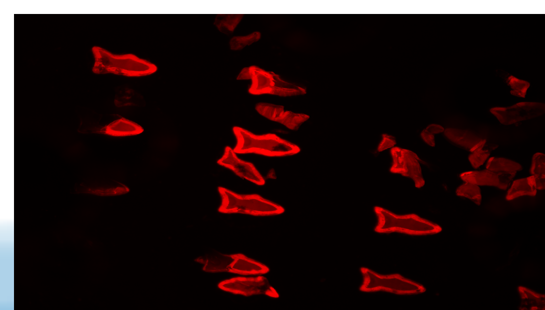
Embedding polydiacetylene (PDA) nanoparticles in the fish body to sense, attract, and capture toxins for blood detoxification

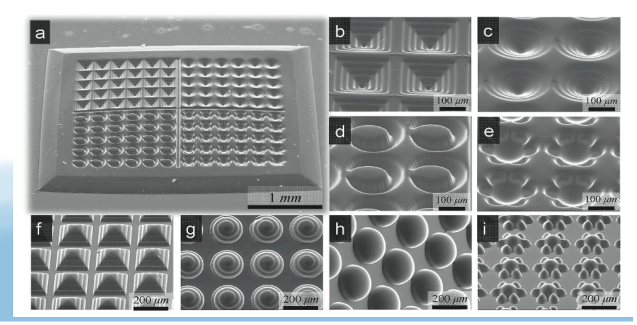
Gou et al, *Nature Communications*, *5, 3774* (2014)
Zhu et al, *Advanced Materials*, 27, 4411 (2015)
Press report by *The Wall Street Journal*, *The Washington Post*, *Forbes*, etc.

Summary

- Nanobots can be powered by various mechanisms: chemical, magnetic, acoustic, biological, optical, etc.
- Nanobots enable targeted drug delivery, in vivo sensing, precision surgery, detoxification, imaging, diagnostics, etc.
- Light-based 3D printing is a powerful method for manufacturing functional micro- and nano-bots:
  - ✓ controlling 3D shape,
  - ✓ integrating different nano-elements,
  - ✓ encapsulating biological cells,
  - ✓ using printable bioinks that are biocompatible, deformable, biodegradable, etc.



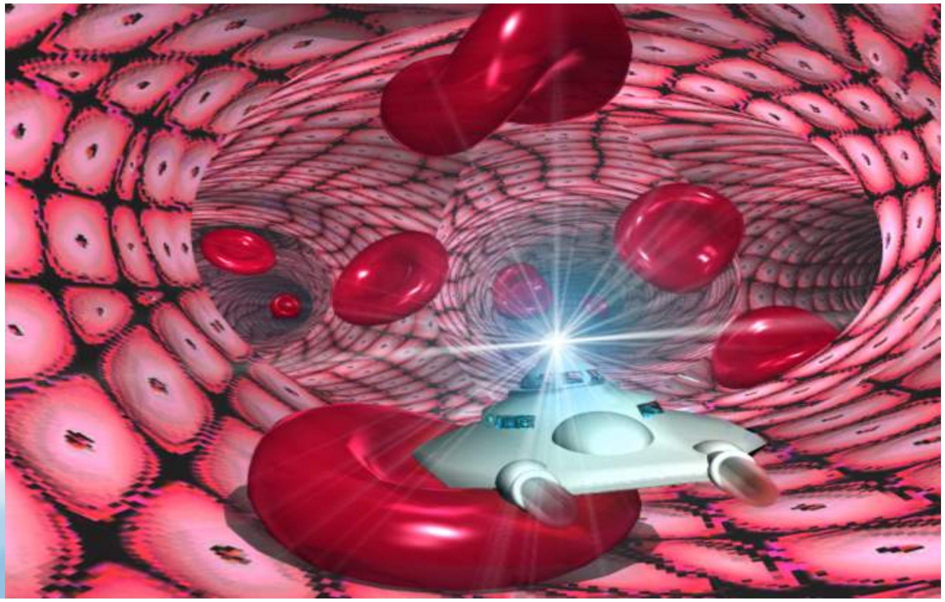




Future Perspectives

- New design principles, materials, and propulsion mechanisms are needed for safe and sustainable operation in the human body (e.g. biocompatible, degradable, deformable, responsive)
- Monitoring/tracking nanobots inside the body could be challenging (swarm intelligence?)
- Scalable nanomanufacturing methods need to be developed for high-quality, cost-effective, reproducible manufacture of functional nanobots.
- Convergence of nanotechnology with bio-, cognition-, info- and other fields will further empower nanobots research.

Fantastic Voyage



BioNano

A Nano-baby: Dept. of NanoEngineering at UC San Diego

- Established in 2007, now with 31 faculty, $15M research expenditure
- Offers BS (ABET-accredited), MS, PhD degrees in Nanoengineering
- Enrolls 671 BS, 86 MS, and 188 PhD students (NanoE and ChemE)