



# Multifunctional microrobots for biomedical applications

**Roger Sanchis Gual**

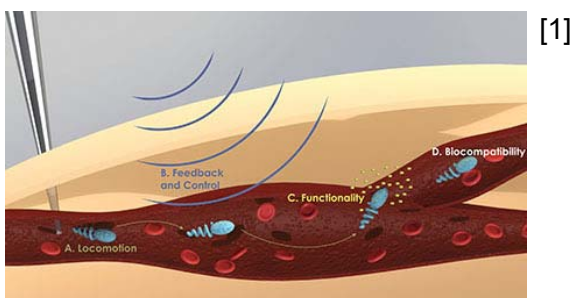
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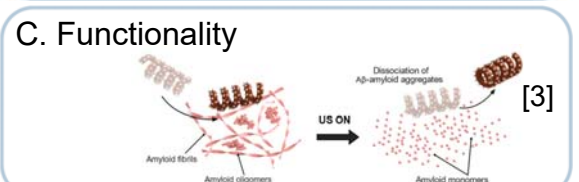
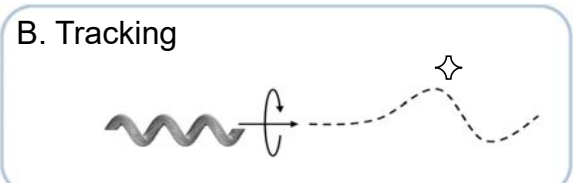
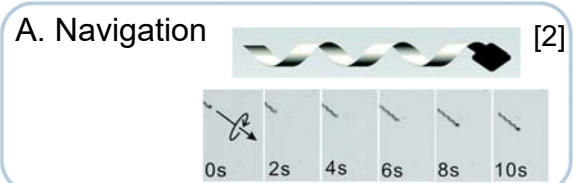
## Soft Microrobots in Medical Fields

- Made of flexible materials that allow them to bend, reducing the risk of damaging delicate surfaces.
- Accessibility to areas of the human body that are hardly reachable.
- Applications in minimally invasive surgery, in situ sensing and diagnosis, targeted drug delivery and tissue engineering.

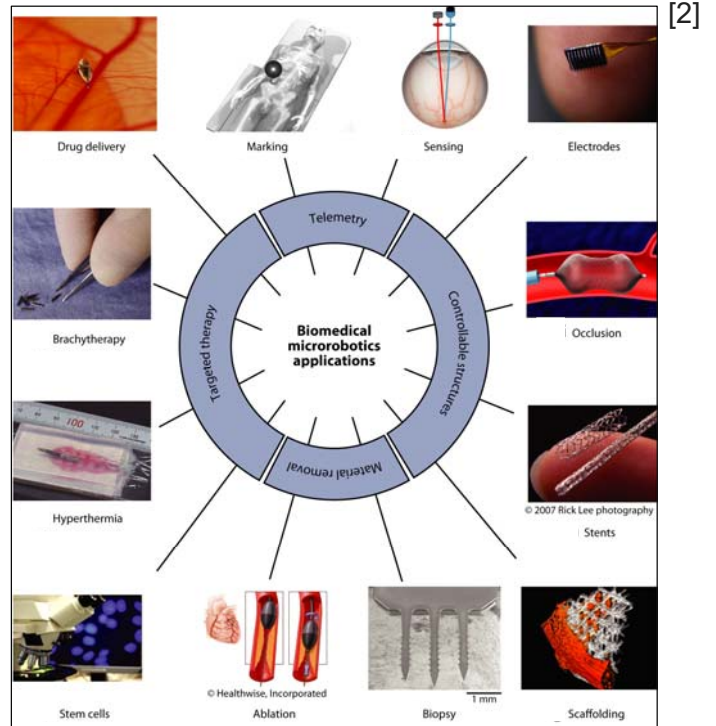
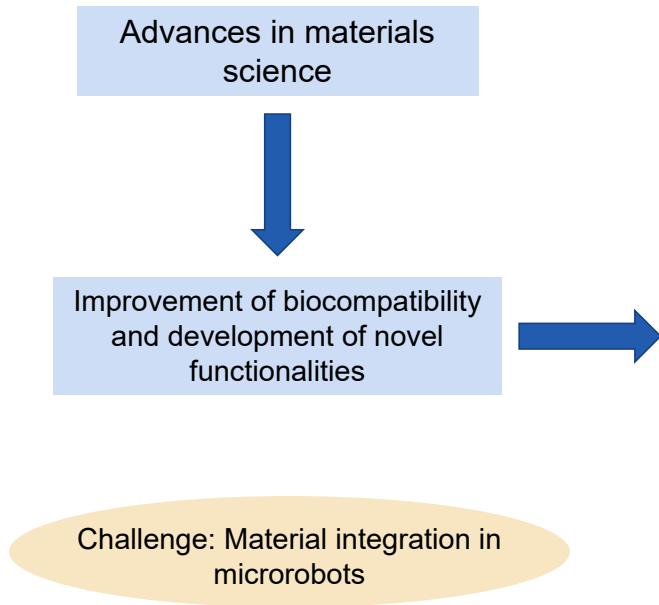


[1]

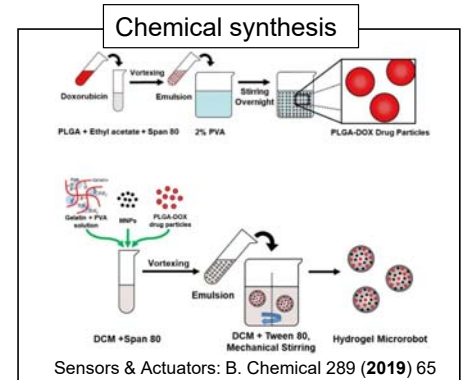
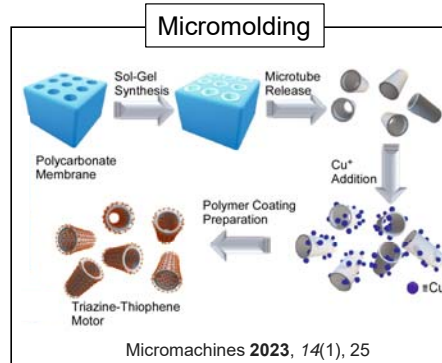
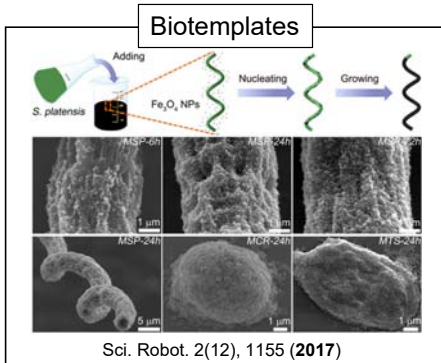
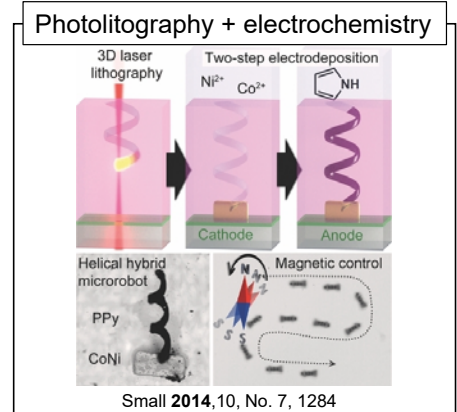
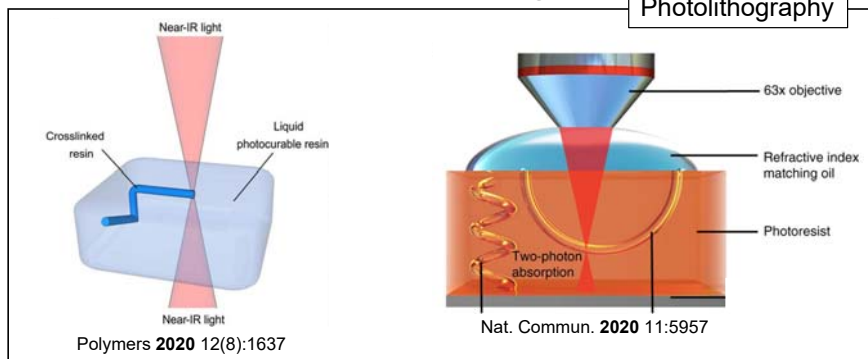
[1] *Appl. Phys. Rev.* **2019**, 6, 041305  
[3] *Nanoscale* 15 (36), 14800-14808  
[4] *Adv. Funct. Mater.*, 2212952



# Soft Microrobots in Medical Fields

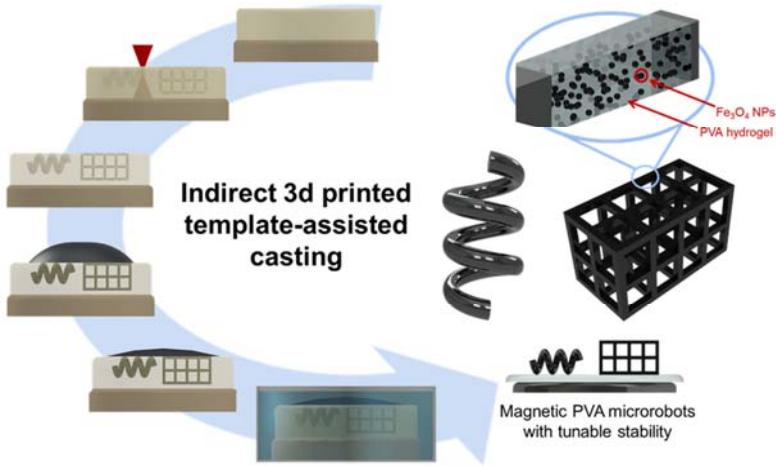


## Microrobot fabrication strategies

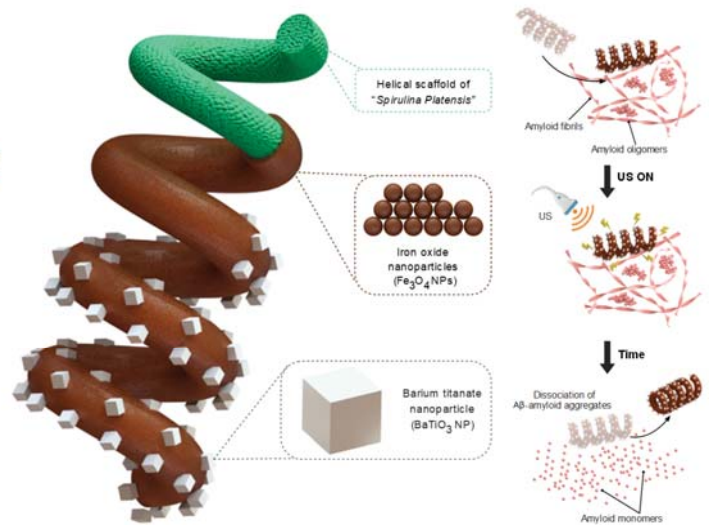


# Outline

## Indirect 3d printing for fabricating soluble material-based microrobots

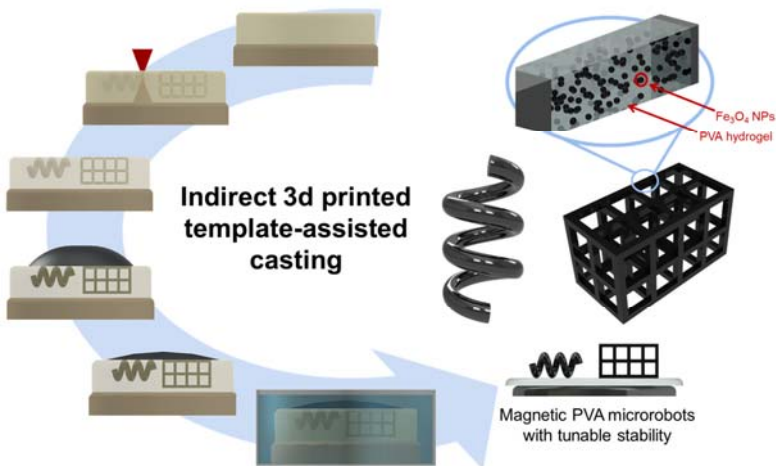


## Biotemplates as a platform for incorporating functional nanoparticles

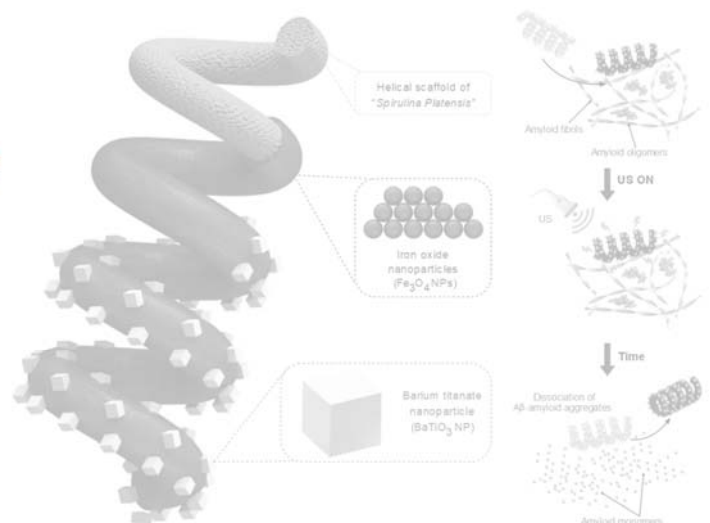


# Outline

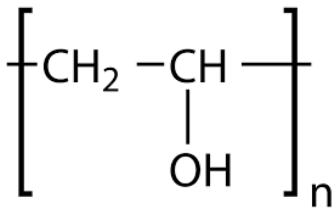
## Indirect 3d printing for fabricating soluble material-based microrobots



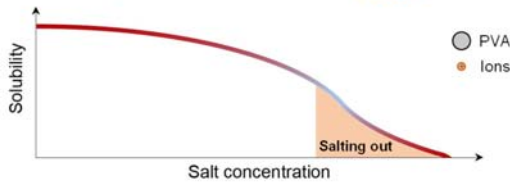
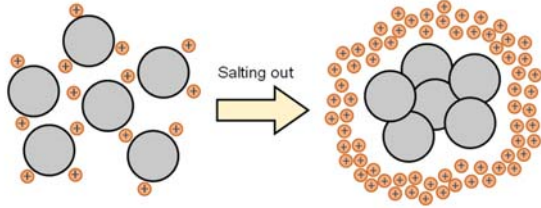
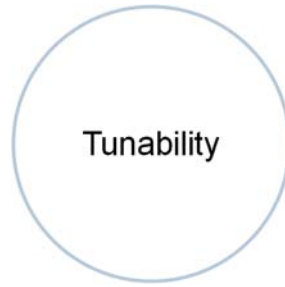
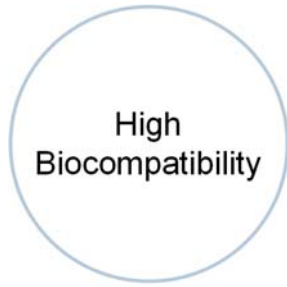
## Biotemplates as a platform for incorporating functional nanoparticles



# Poly(vinyl alcohol) (PVA)



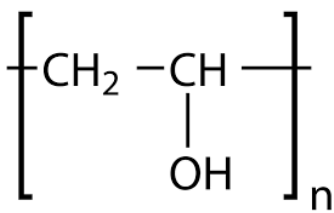
Poly(vinyl alcohol) formula



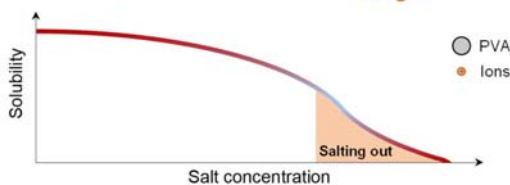
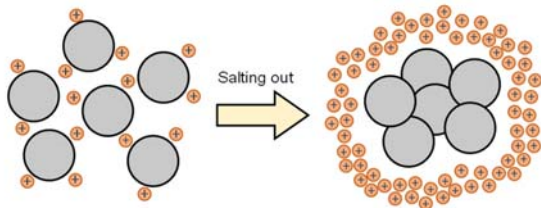
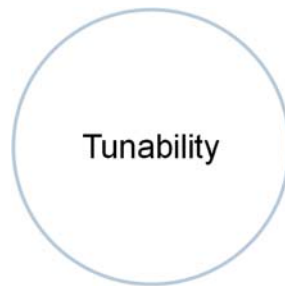
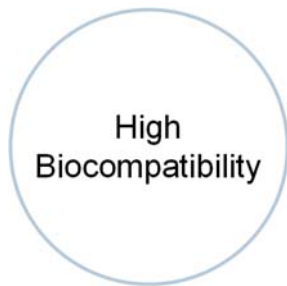
Salting out emerges as a possible solution:

- 1) This treatment helps hydrogels to remain stable in aqueous solutions
- 2) Final ion-free PVA hydrogels [3] maintain their high biocompatibility features

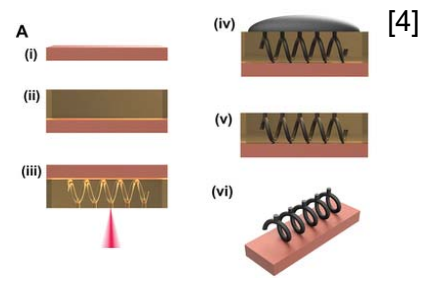
# Poly(vinyl alcohol) (PVA)



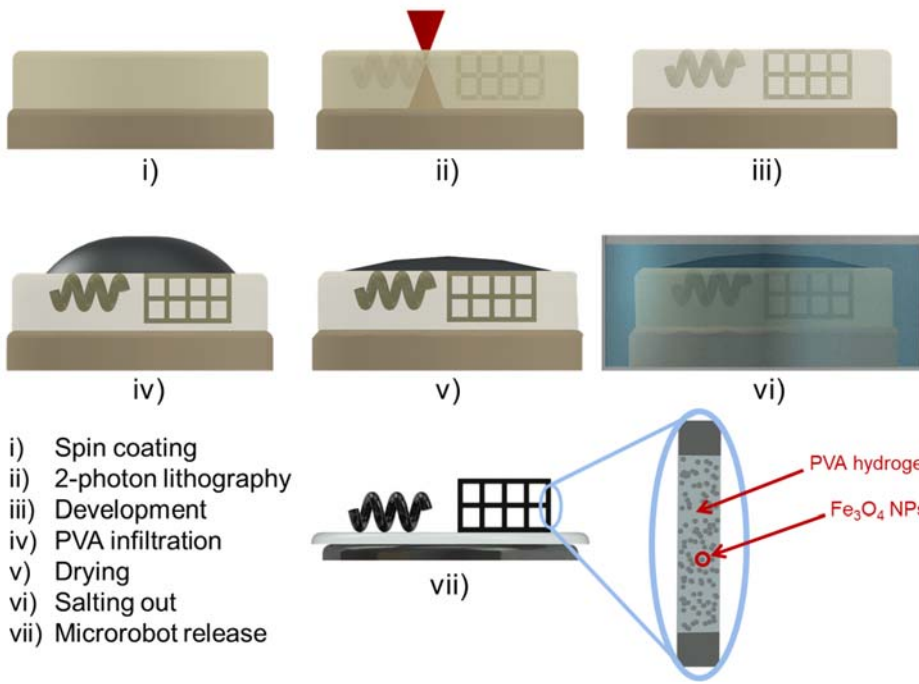
Poly(vinyl alcohol) formula



## 3D indirect printing

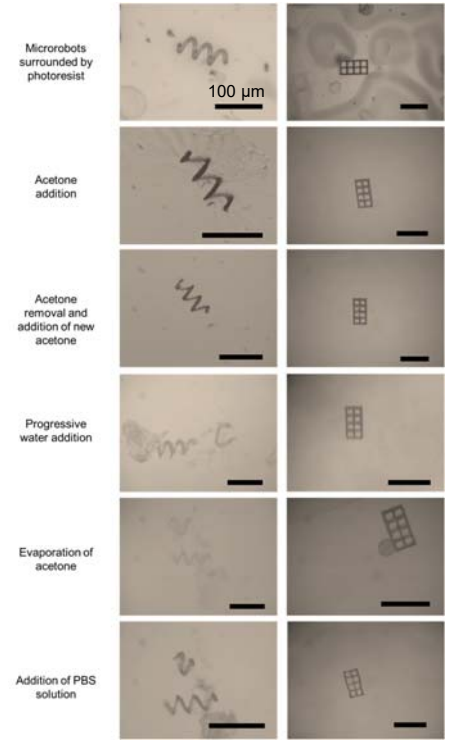


# PVA microrobot fabrication

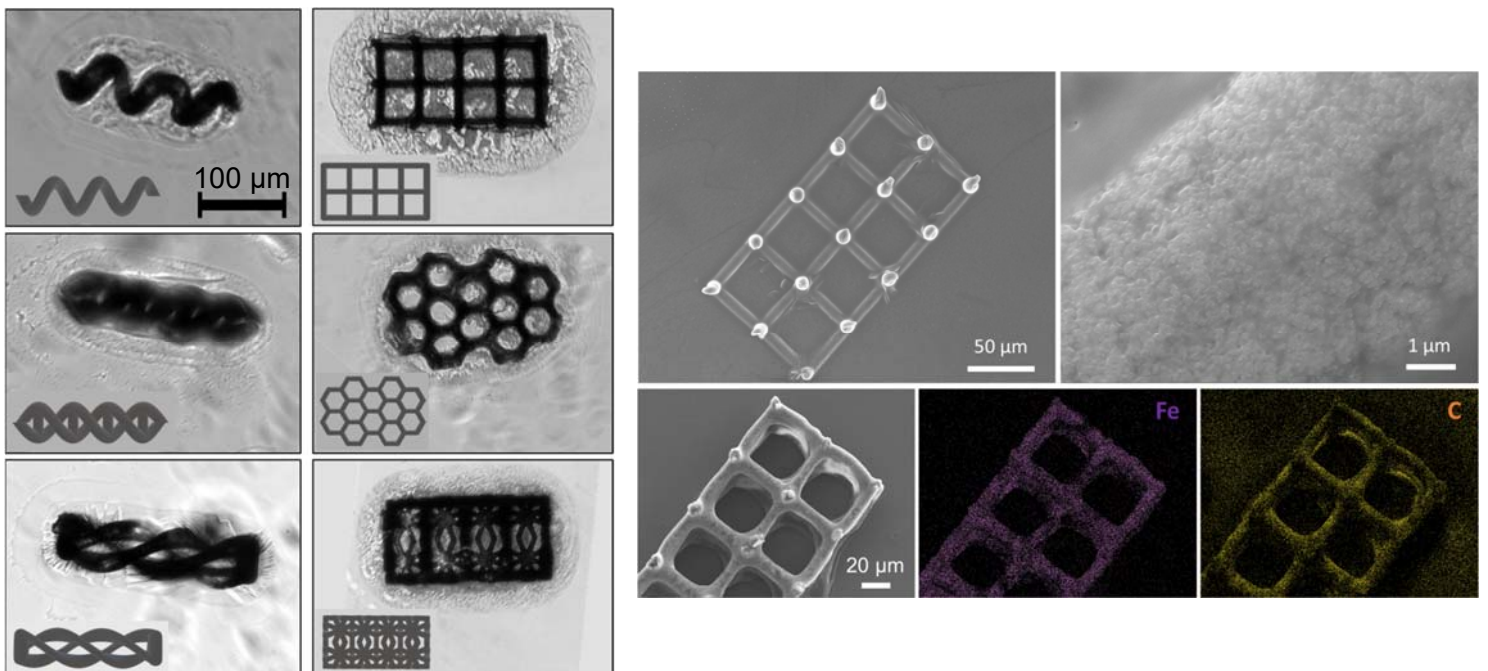


- i) Spin coating
- ii) 2-photon lithography
- iii) Development
- iv) PVA infiltration
- v) Drying
- vi) Salting out
- vii) Microrobot release

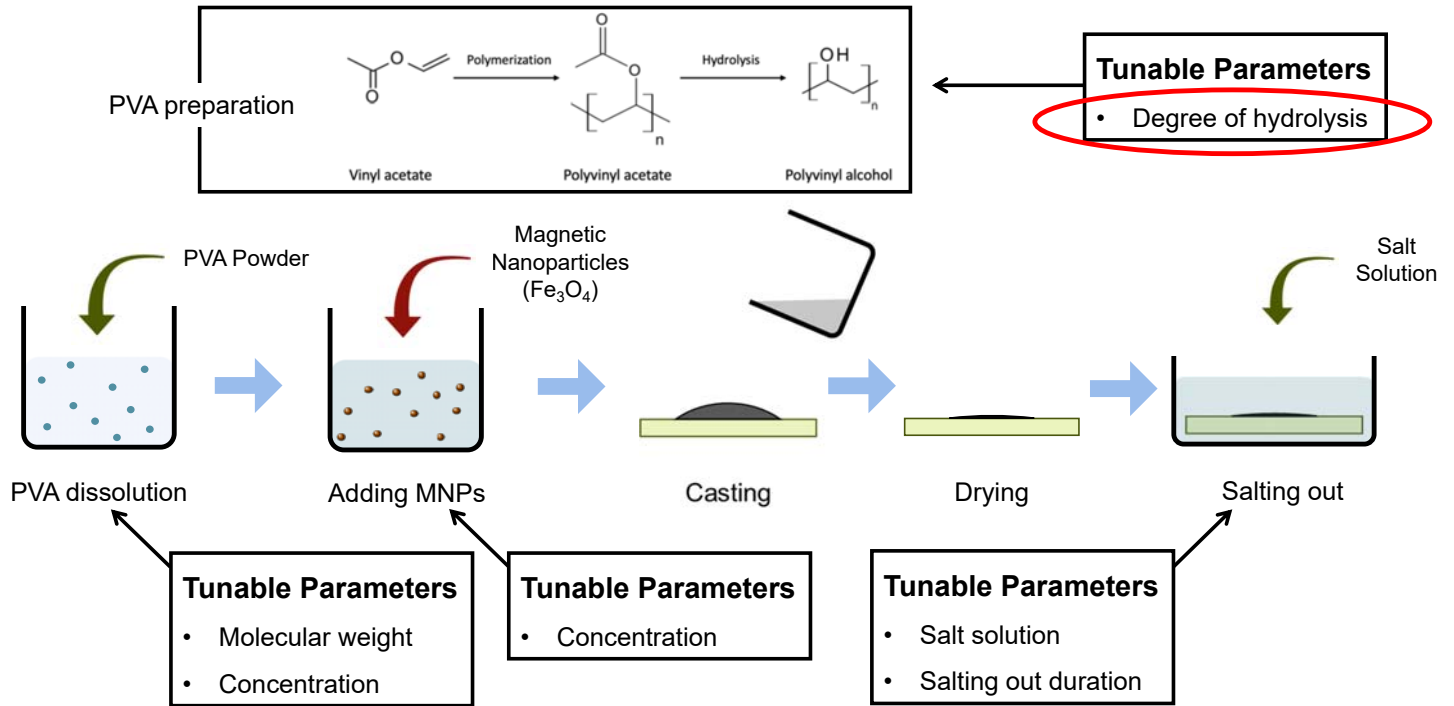
# vii) Microrobot release



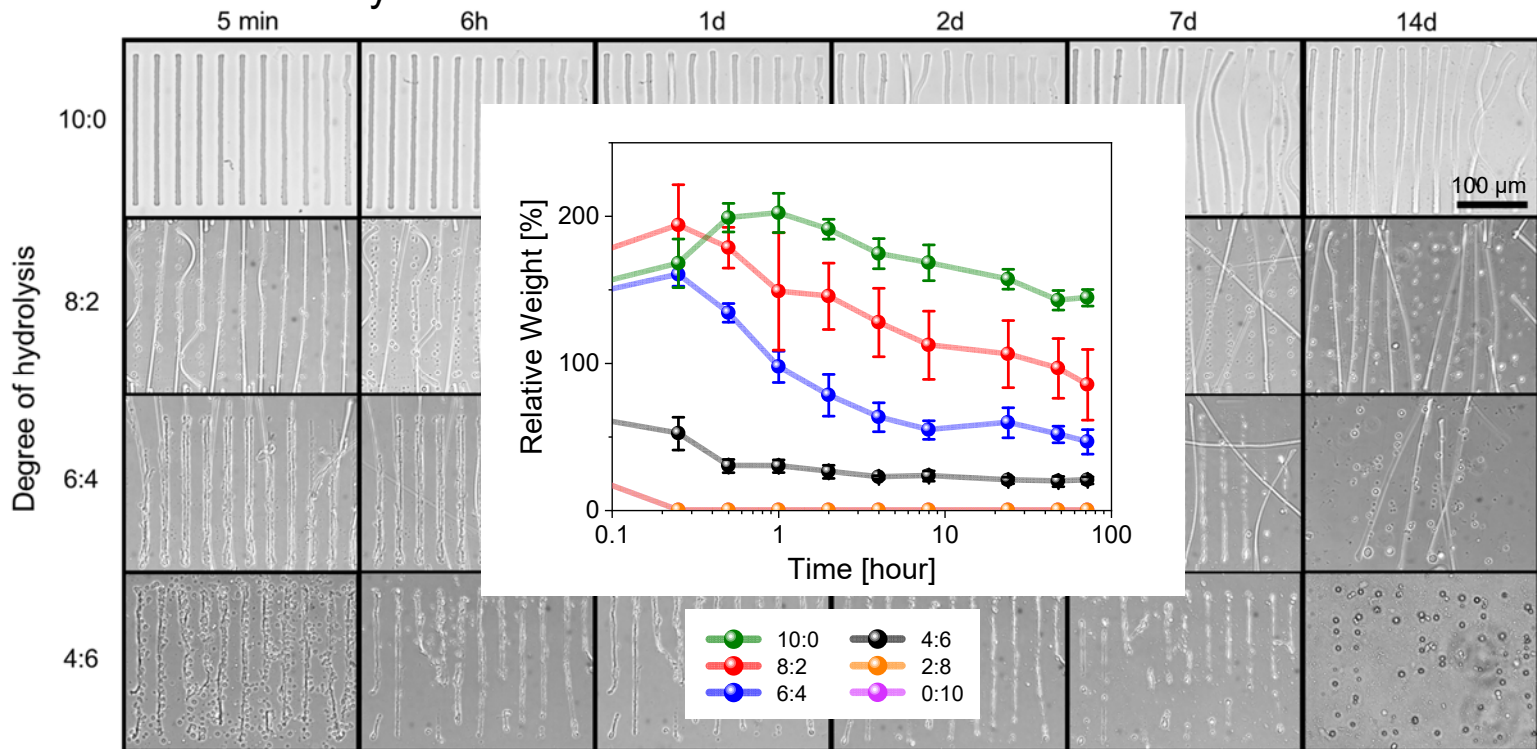
# PVA microrobot fabrication



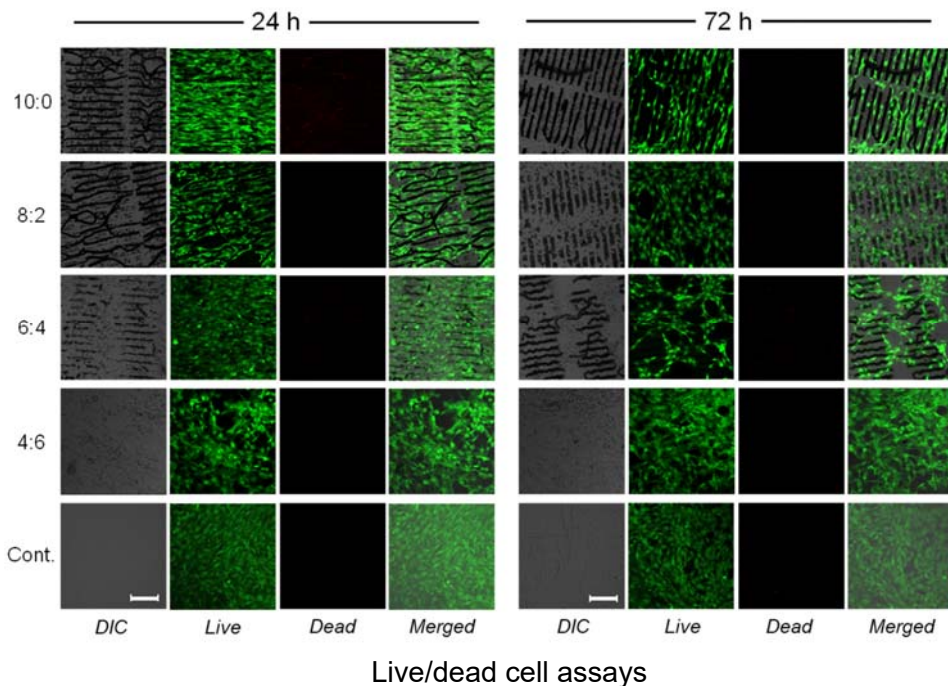
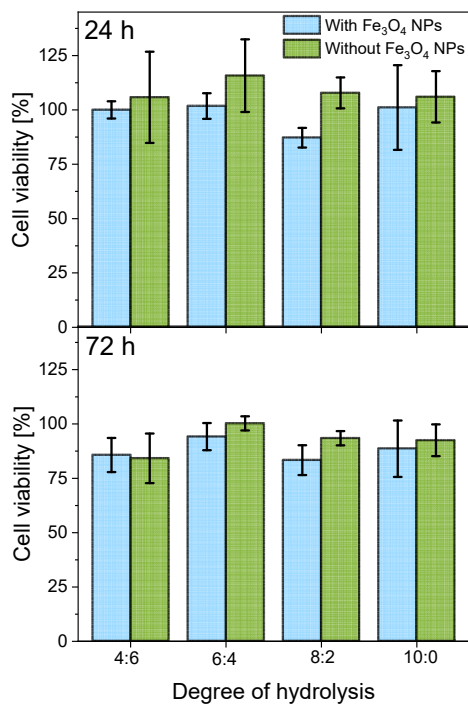
## Tunable stability



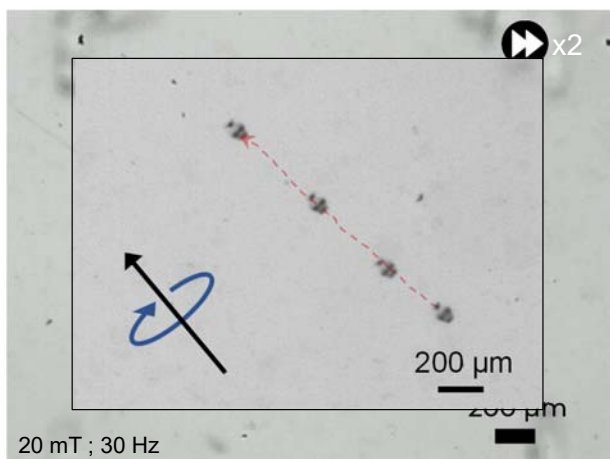
## Tunable stability



## Biocompatibility



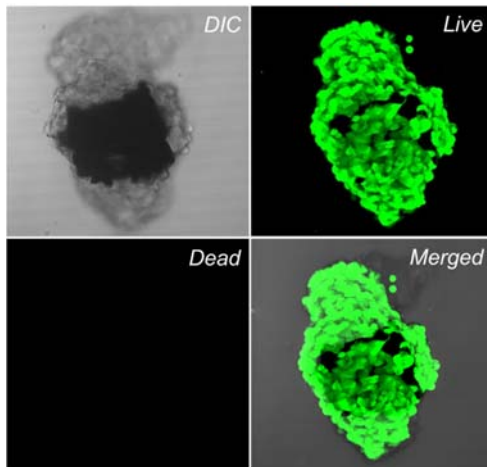
## Microrobot manipulation



Forward velocity = 65 μm/s  
Drift velocity = 11 μm/s

Forward velocity = 550 μm/s  
Drift velocity = 32 μm/s

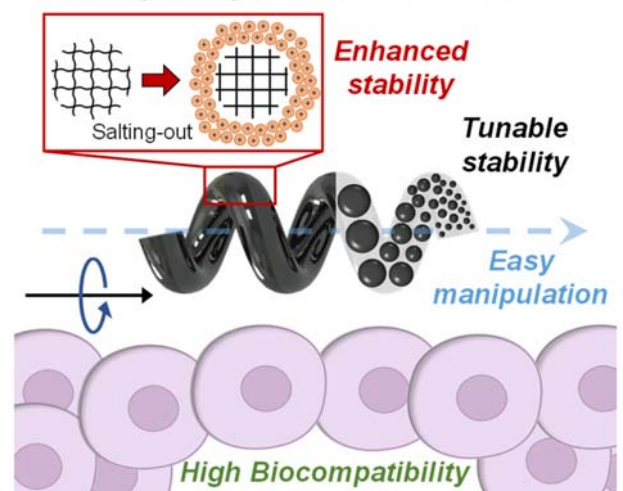
## Microrobot manipulation



## Conclusions

- ❖ By combining the salting-out process with an indirect 3D printing method we can create PVA microrobots that are stable in aqueous solutions.
- ❖ The stability of these PVA microrobots can be easily tuned by changing the parameters of the PVA fabrication.
- ❖ PVA hydrogels with MNPs exhibit very good biocompatibility independently of the degree of hydrolysis.
- ❖ PVA microrobots show good manoeuvrability.

### PVA hydrogel soft microrobots

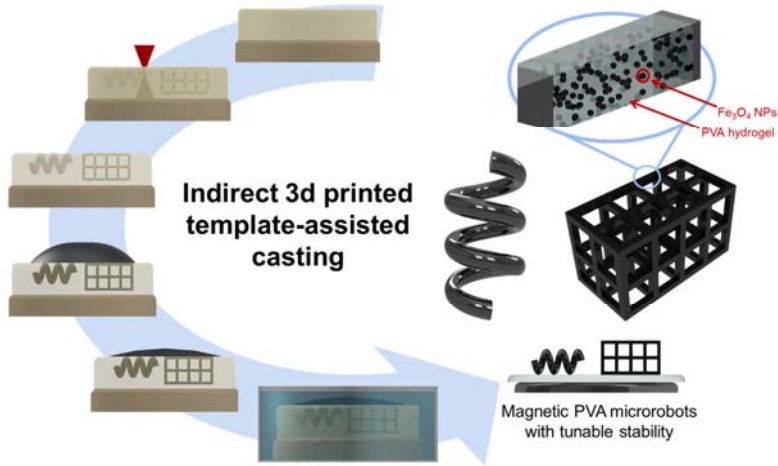


[Read the paper here: Adv. Funct. Mater. 2023, 2212952](#)

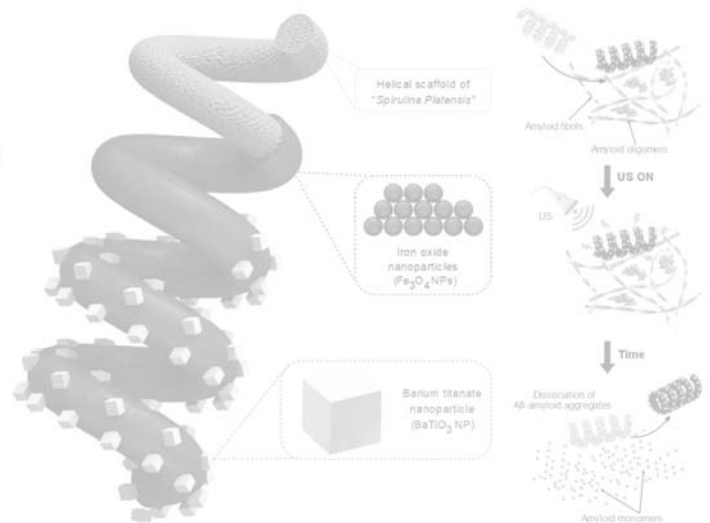


# Outline

## Indirect 3d printing for fabricating soluble material-based microrobots

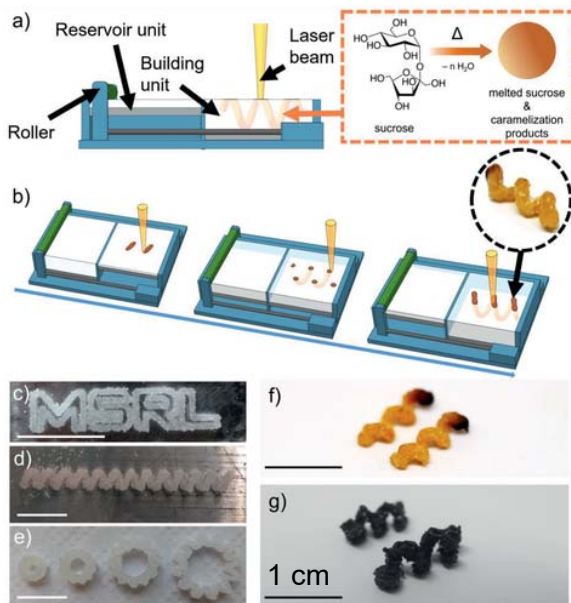


## Biotemplates as a platform for incorporating functional nanoparticles



## Caramel-based microrobots

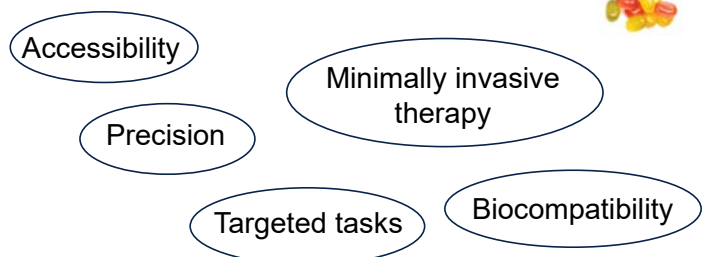
### Candybots [1]



[1] Adv.Mater.2020, 32, 2005652

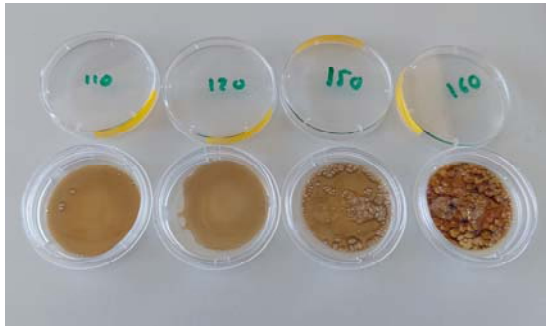


Downsize these sugar-based robots to the microscale



# Fabrication difficulties

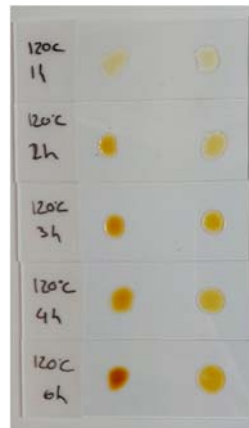
## Thermal stability of the photoresist



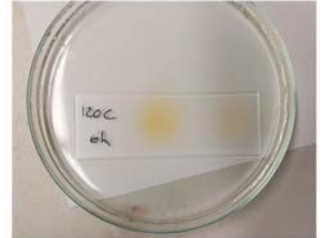
Caramelization of saccharides:

- Maltose:  $T_c = 180\text{ }^\circ\text{C}$
- Sucrose:  $T_c = 170\text{ }^\circ\text{C}$
- Glucose:  $T_c = 155\text{ }^\circ\text{C}$
- Fructose:  $T_c = 105\text{ }^\circ\text{C}$

## Solubility of the caramel



DI water immersion



# Adjustment of the protocol

C(C(C(O)CO)O)O

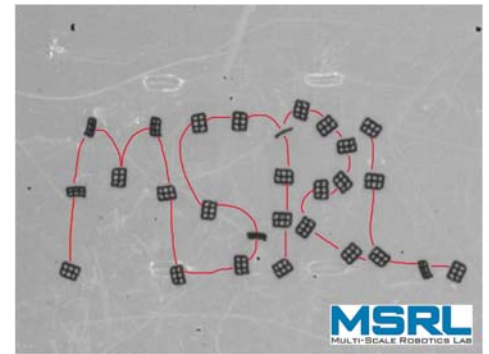
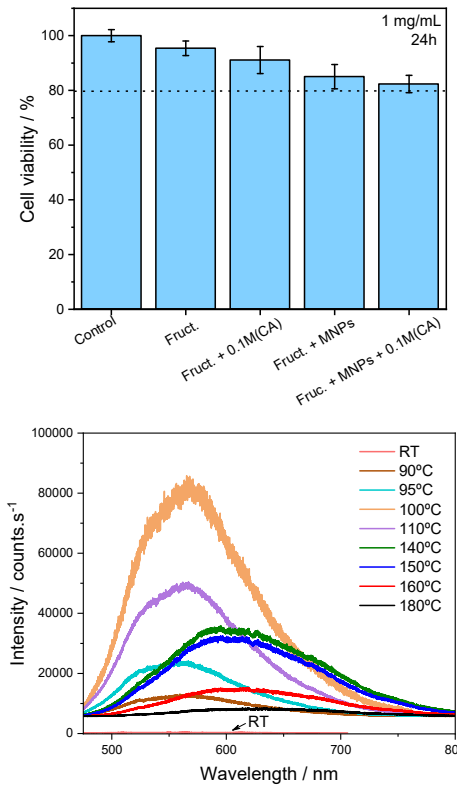
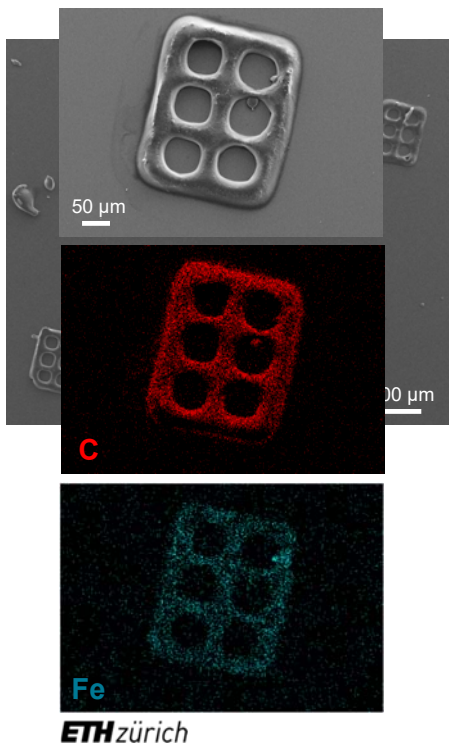
fructose

1<sup>st</sup> caramelization

Temperature / °C	Fructose (Weight %)	Fructose + Citric acid 0.1M (Weight %)
50	100	100
100	95	85
150	85	70
200	65	55

2<sup>nd</sup> caramelization

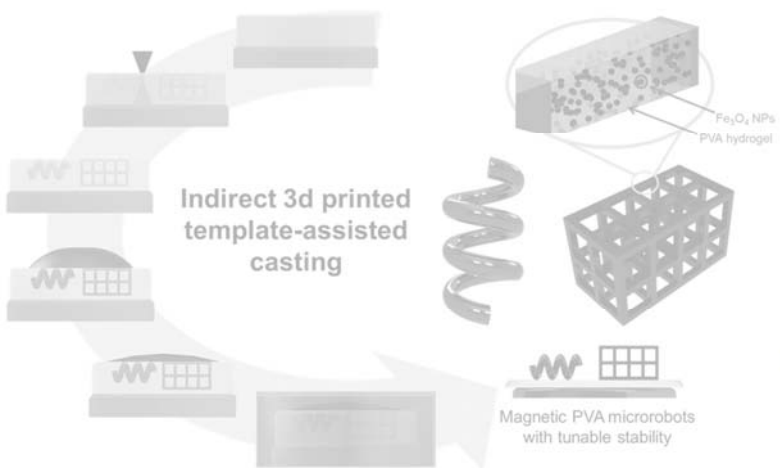
# Microstructures



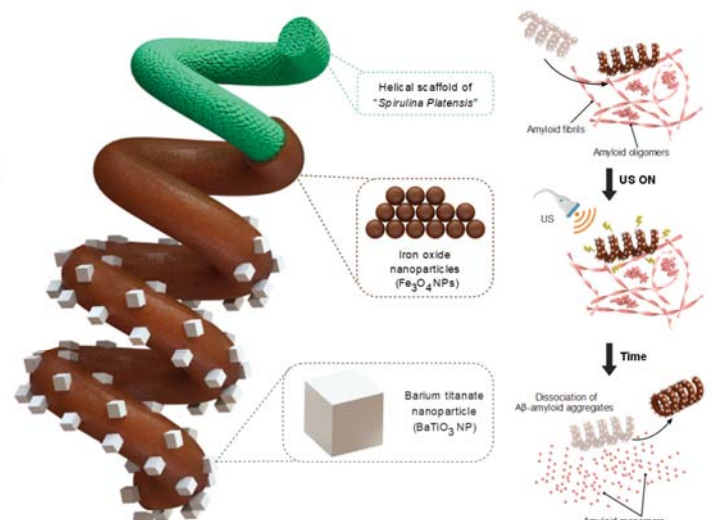
- Very high biocompatibility
- Fluorescence properties
- Good magnetic response

# Outline

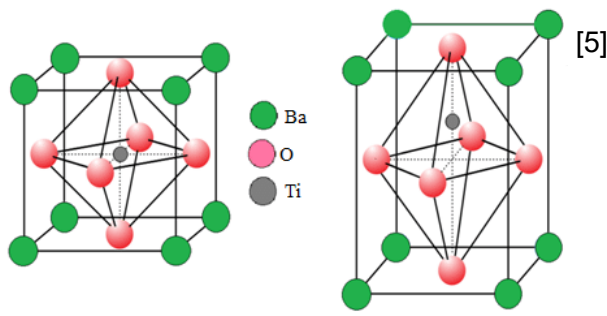
## Indirect 3d printing for fabricating soluble material-based microrobots



## Biotemplates as a platform for incorporating functional nanoparticles



# Piezoelectric BaTiO<sub>3</sub> nanoparticles



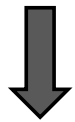
centrosymmetric

noncentrosymmetric

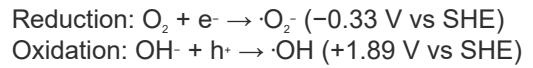
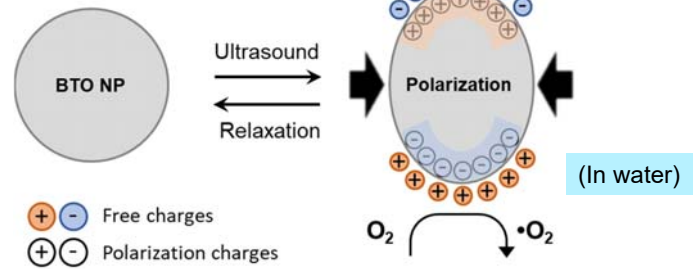


Mechanical stimulation

No effect



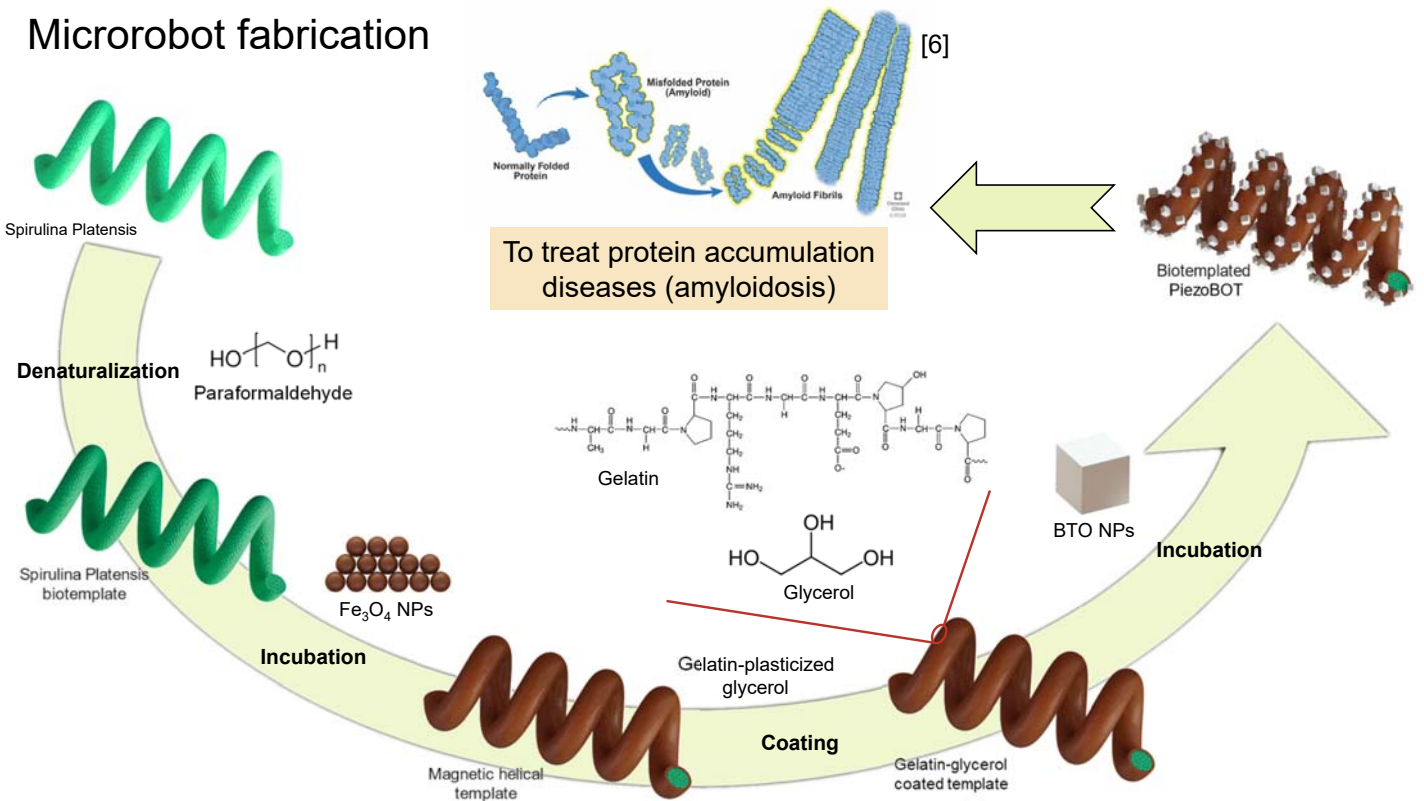
Formation of electric dipoles



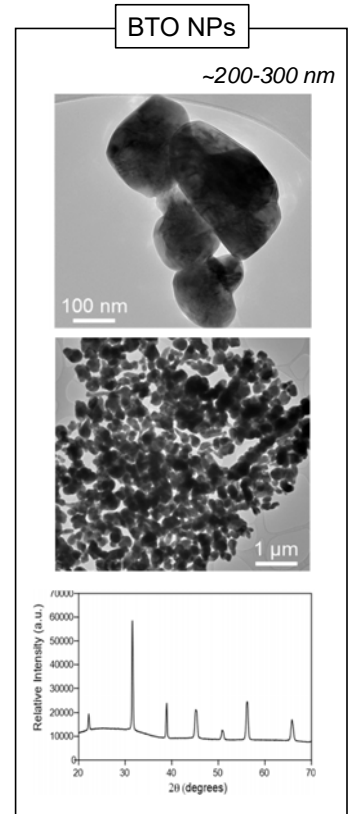
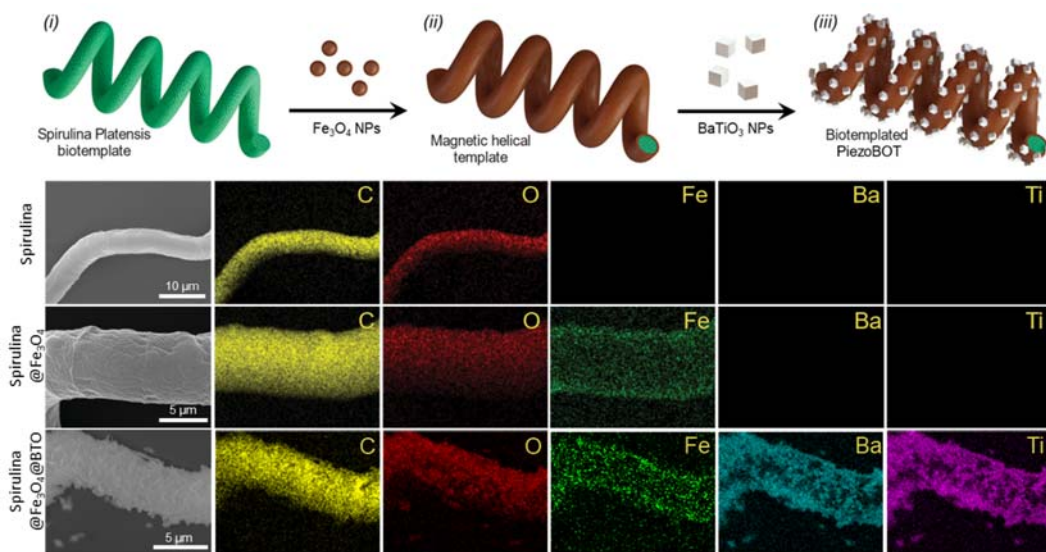
Dye degradation, cancer cell therapy, **protein dissociation**

Limitations: aggregation, bioabsorbability

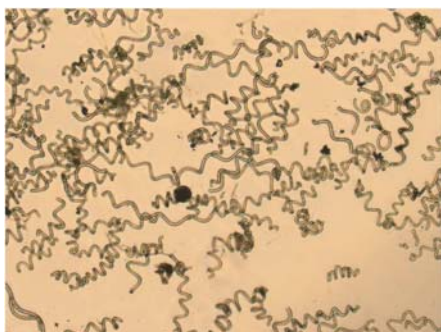
# Microrobot fabrication



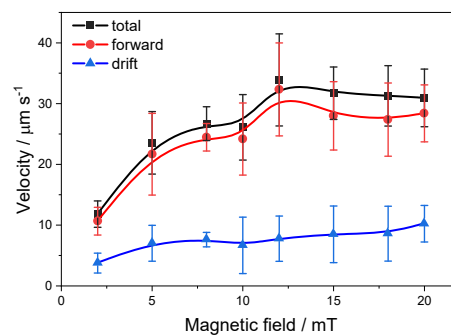
## Microrobot fabrication



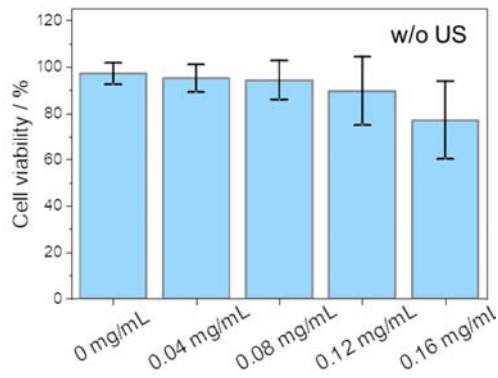
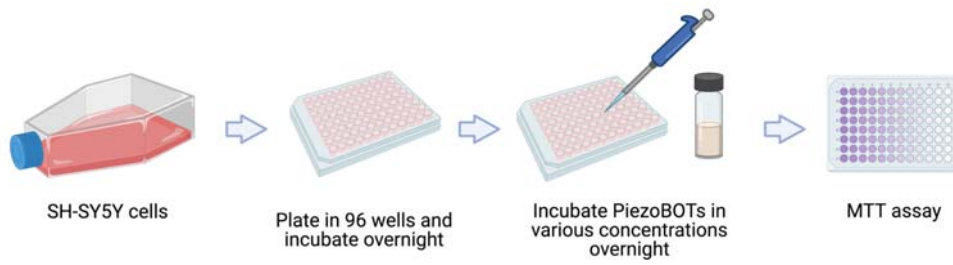
## Microrobot manipulation



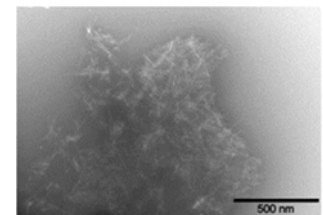
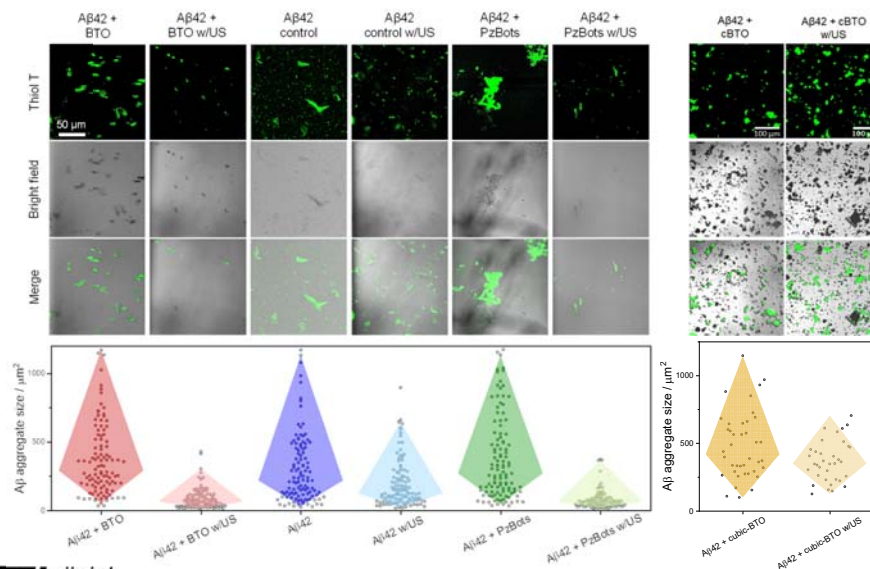
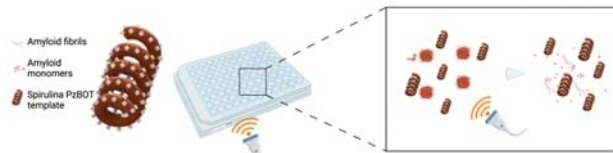
Good magnetic response and easy manipulation



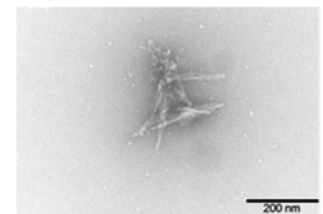
# Biocompatibility



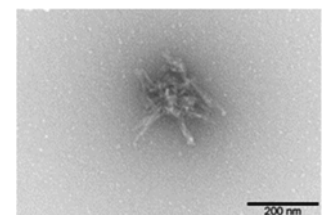
# Protein degradation



Aβ42 control w/US



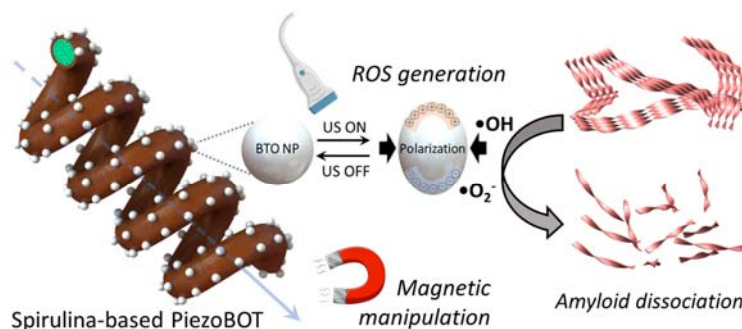
Aβ42 + BTO w/US



Aβ42 + PzBots w/US

## Conclusions

- ❖ BTO NPs were integrated into biotemplates to prepare microrobots with ultrasound piezocatalytic capabilities.
- ❖ The ROS species generated by the piezoelectric effect reduces the peptide aggregate size by more than 80%.
- ❖ These biocompatible PiezoBOTS are an excellent platform for conducting minimally invasive amyloidosis therapy.



[Read the paper here: \*Nanoscale\*, 2023, 15 \(36\), 14800-14808](#)

## Acknowledgments



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Prof. Bradley Nelson

Lukas Hurtle

Dr. Hao Ye

Prof. Salvador Pané

Fabian Landers

Dr. Carlos Franco

Joaquin Llacer-Wintle

Dr. Xiangzhong Chen

Yanming Xia

## Thanks for your kind attention

