



# 16<sup>th</sup> European School on Molecular Nanoscience

7<sup>th</sup> - 11<sup>th</sup> May 2023  
San Lorenzo de El Escorial, Madrid

## Fabrication strategies for soft biocompatible microrobots with functional capabilities

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ETH Zürich

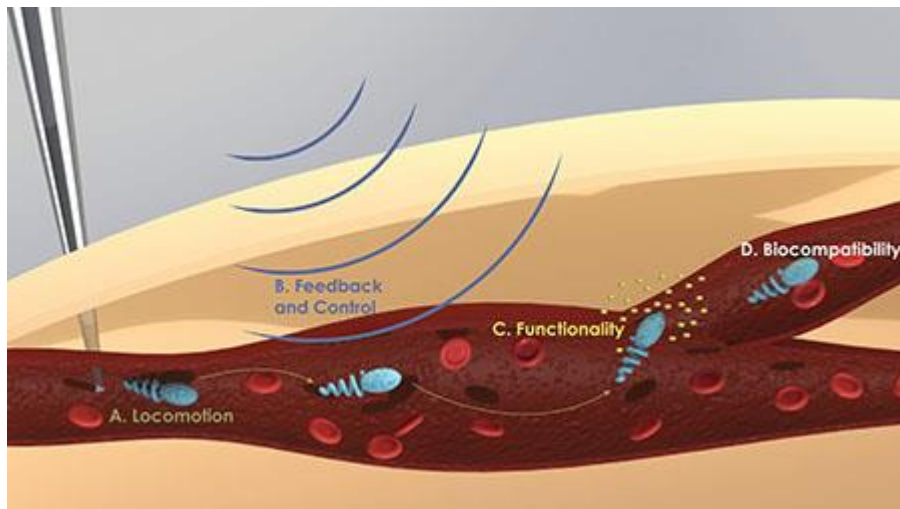
[rsanchis@ethz.ch](mailto:rsanchis@ethz.ch)

**ETH** zürich

**MSRL**  
MULTI-SCALE ROBOTICS LAB

# Soft Microrobots in Medical Fields

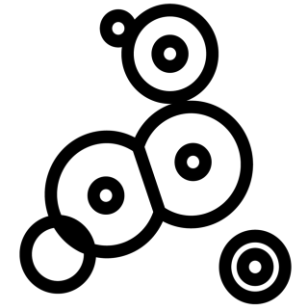
- Made of flexible materials that allow them to bend and deform, reducing the risk of damaging delicate surfaces.
- Accessibility to areas of the human body that are hardly reachable.
- Applications in minimally invasive surgery, in situ sensing and diagnosis, targeted drug delivery and tissue engineering.
- Benefits for the patient: reduction of post-operational pain, hospitalization duration, recovery time and infection risk.



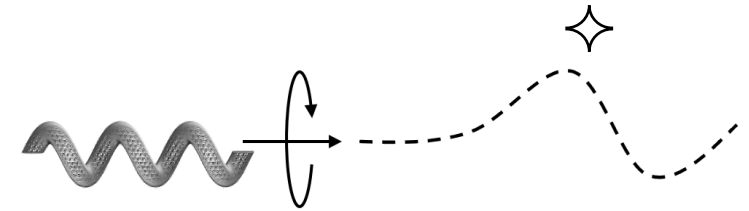
[1]

## Soft microrobot characteristics

### Biocompatibility

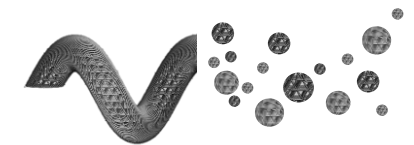


### Navigation & Controlling

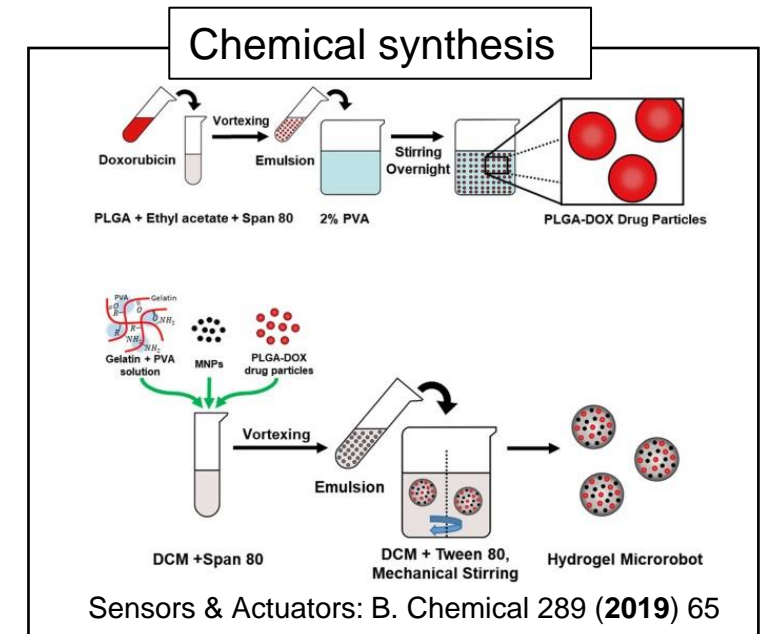
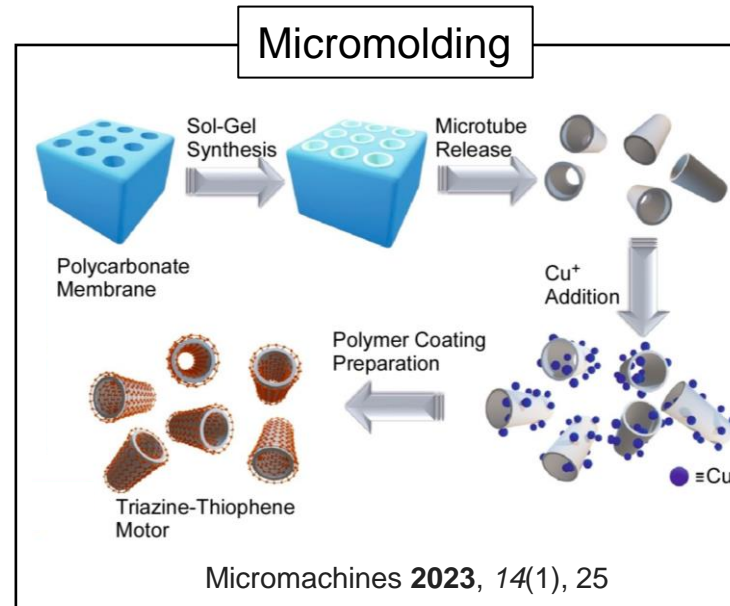
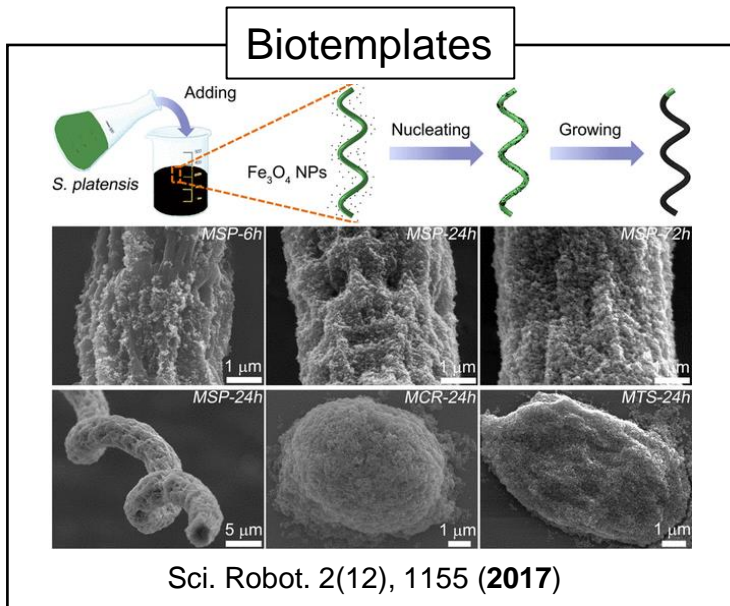
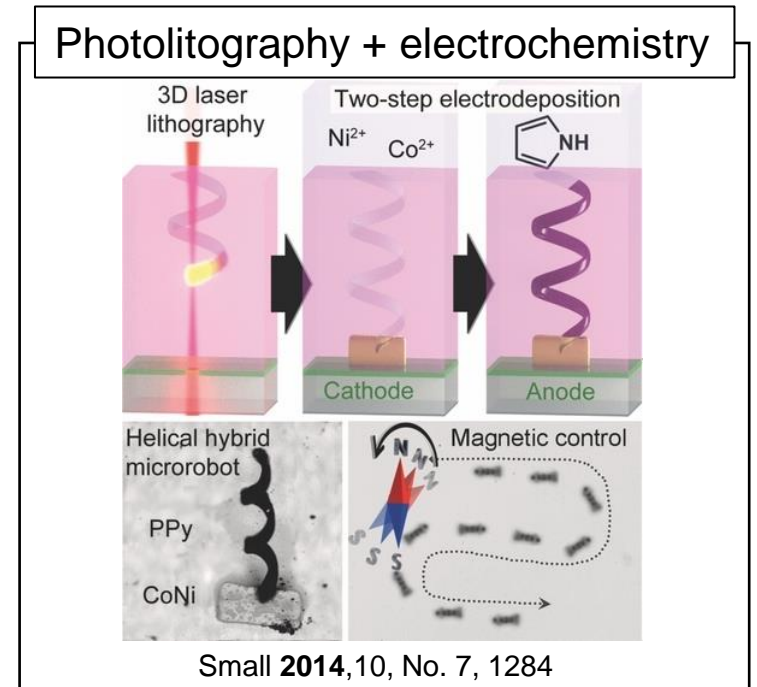
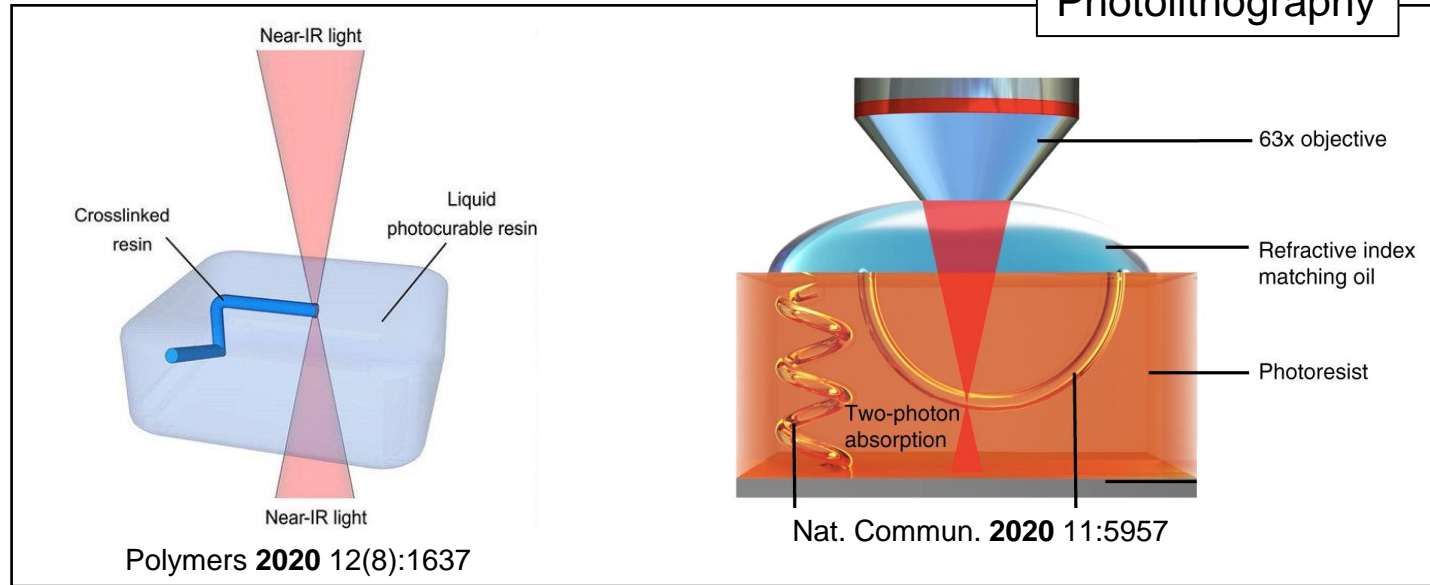


### Device Fate

- Surgical Collection
- Biodegradation



# Microrobot fabrication strategies



# Soft Microrobots in Medical Fields

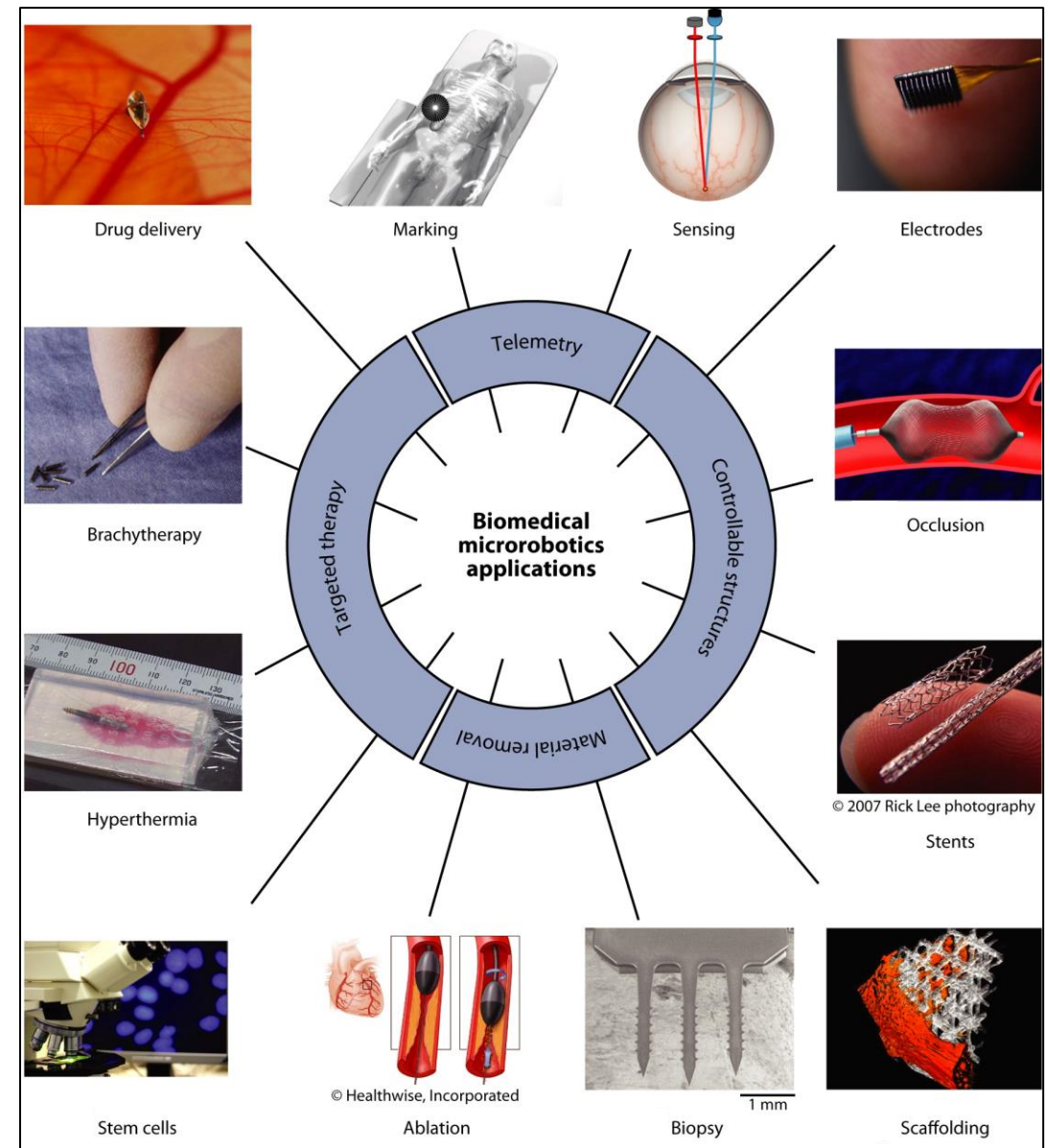
Advances in materials science



Improvement of biocompatibility and development of novel functionalities



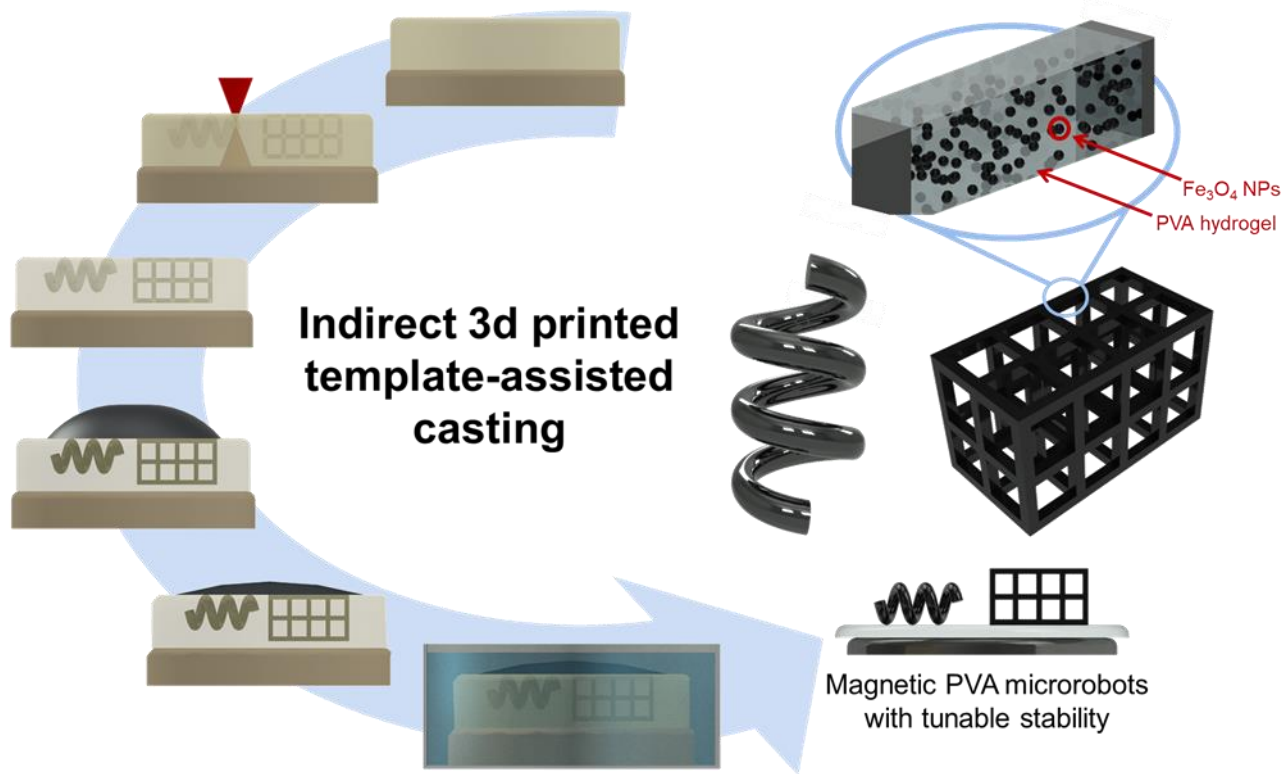
Challenge: Material integration in microrobots



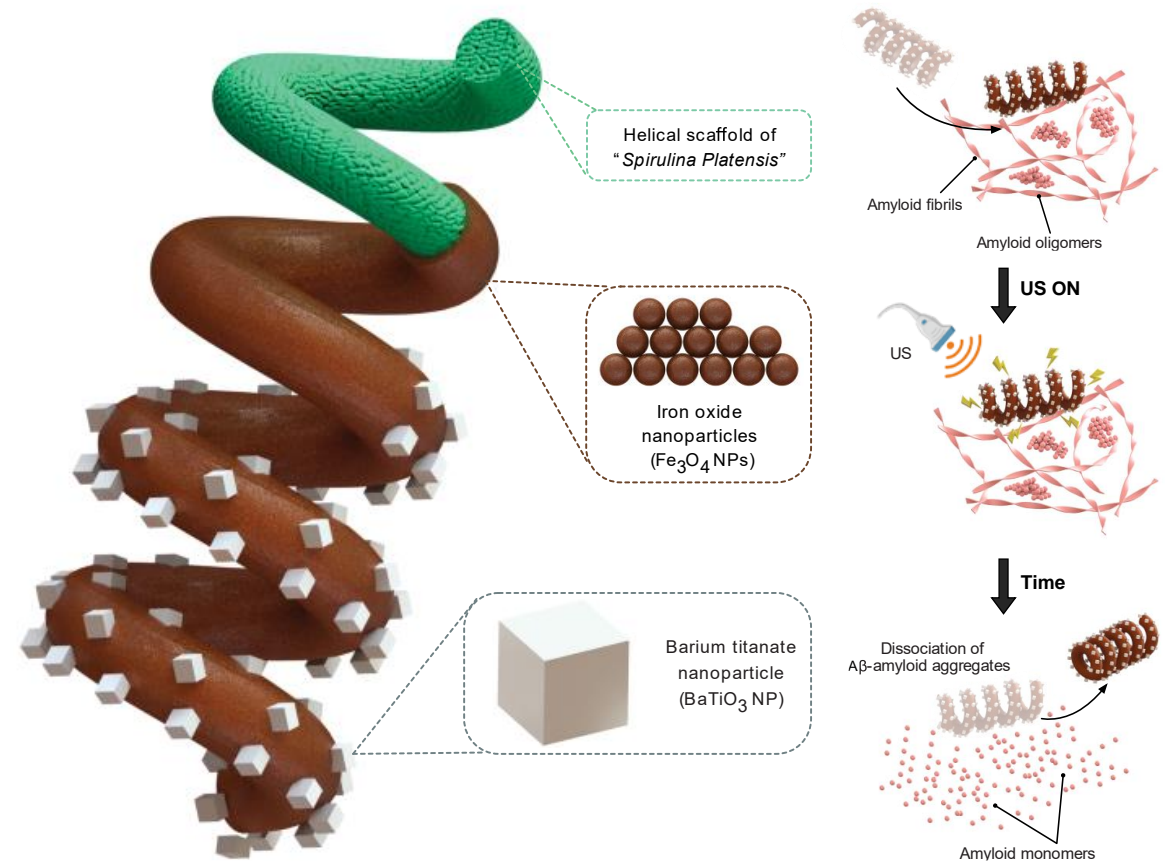
[2]

# Outline

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

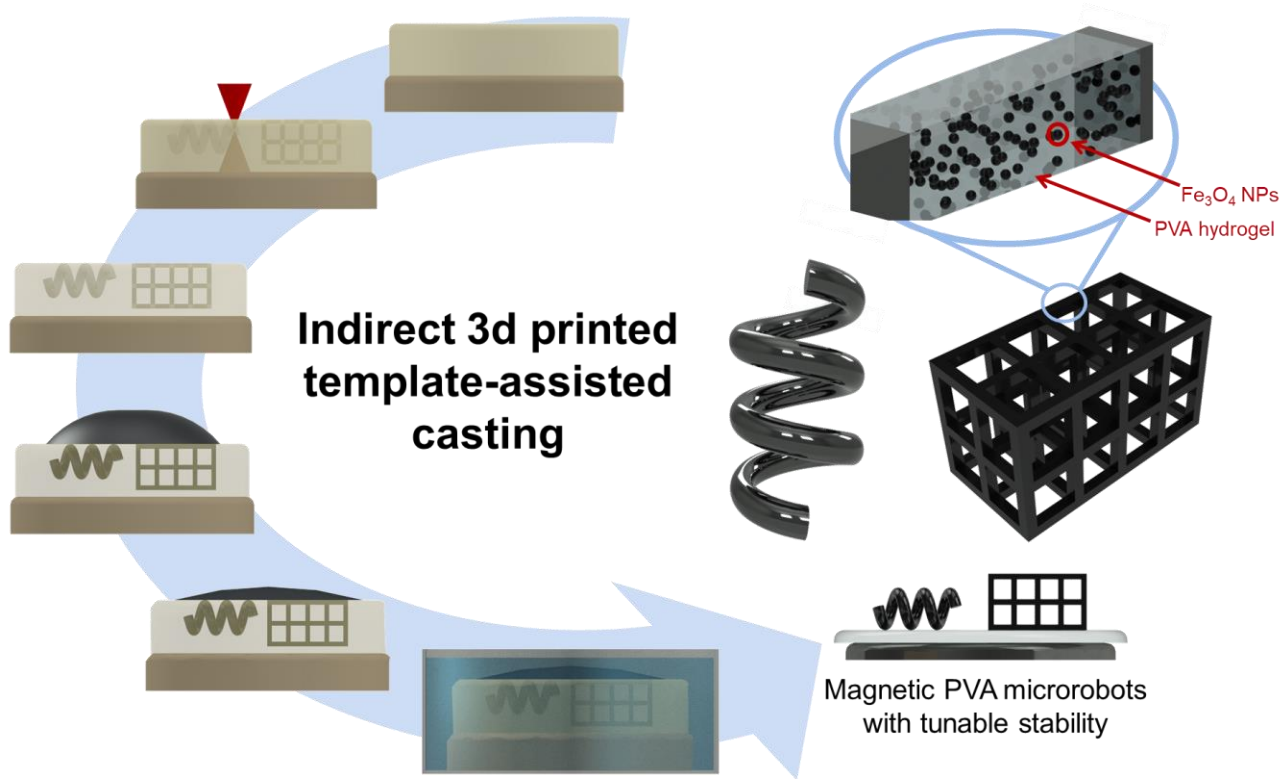


## Biotemplates as a platform for incorporating functional nanoparticles

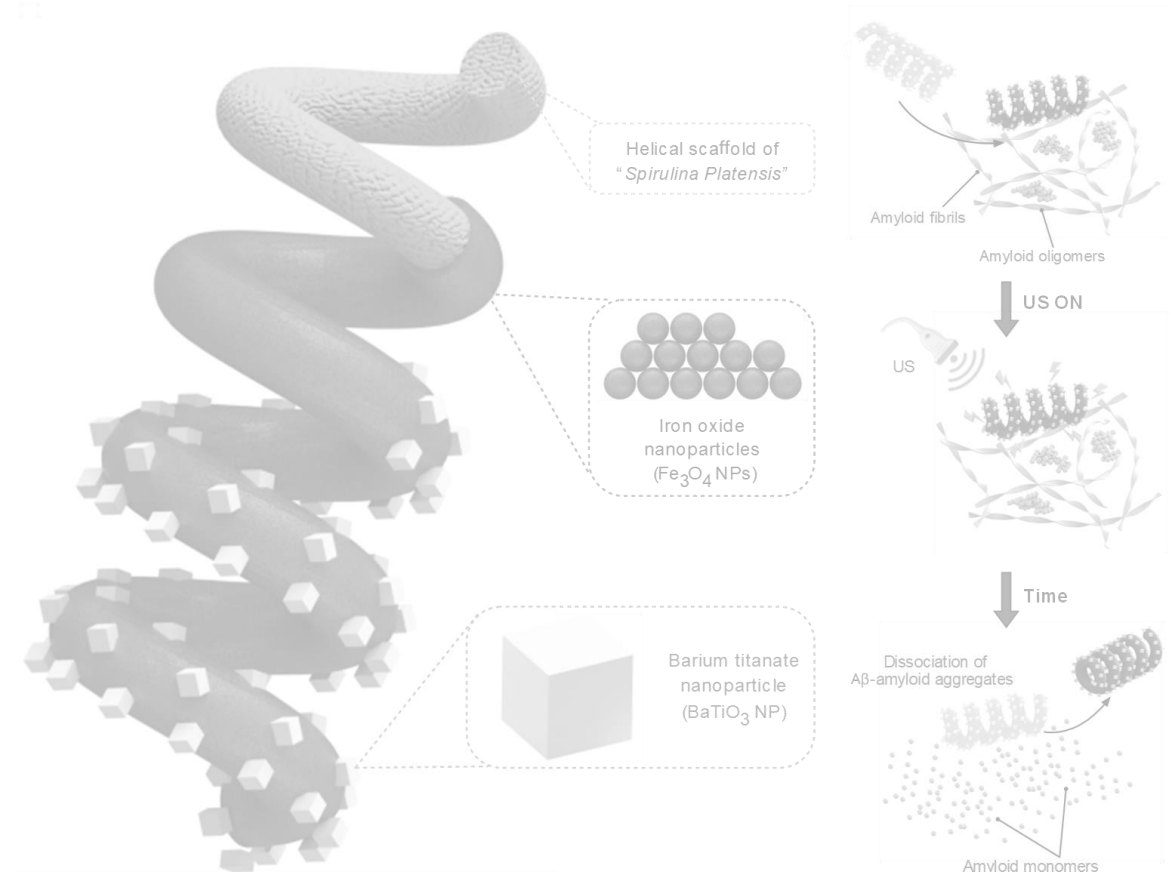


# Outline

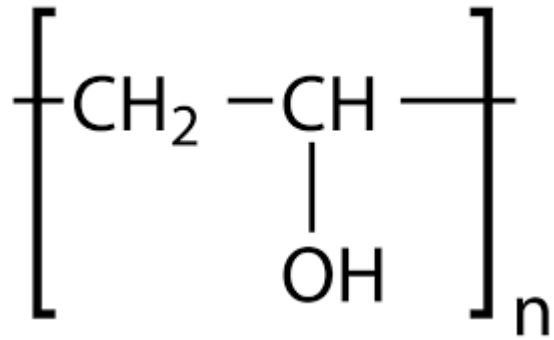
## Indirect 3d printing for fabricating soluble polymer-based microrobots



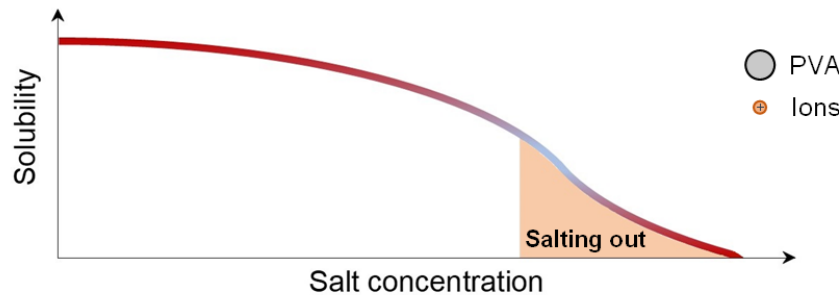
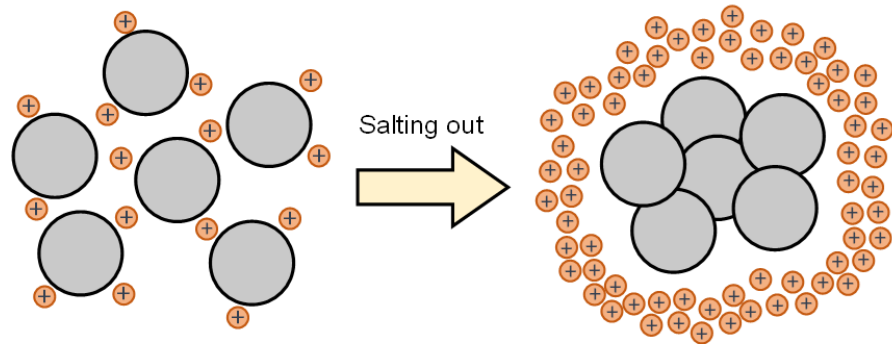
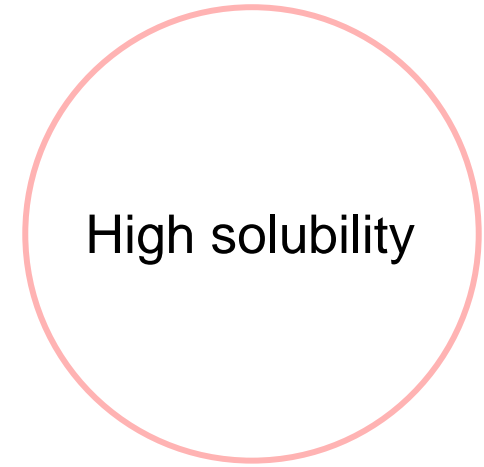
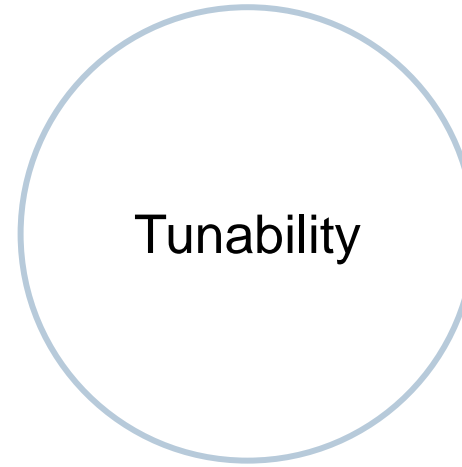
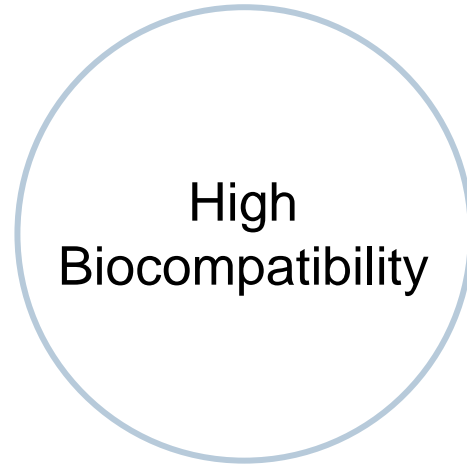
## Biotemplates as a platform for incorporating functional nanoparticles



# Poly(vinyl alcohol) (PVA)



Poly(vinyl alcohol)  
formula

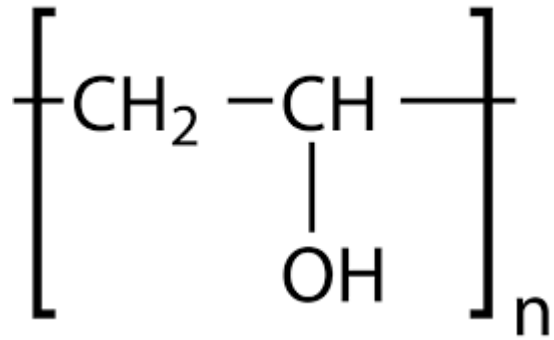


Salting out emerges as a possible solution:

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)

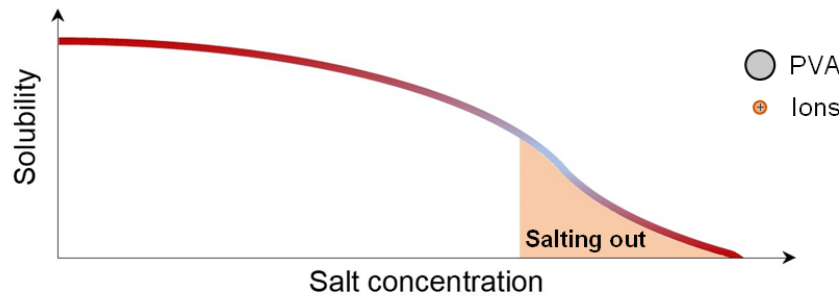
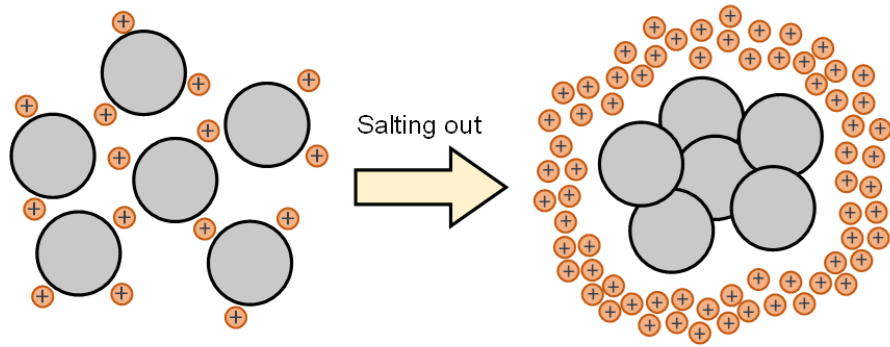


Poly(vinyl alcohol)  
formula

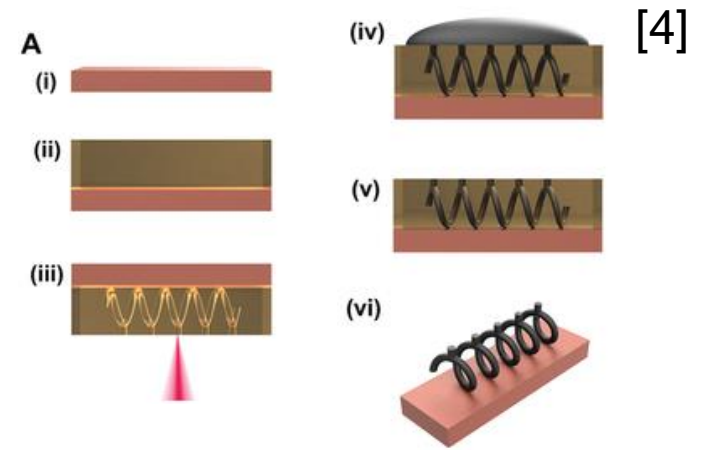
High  
Biocompatibility

Tunability

High solubility

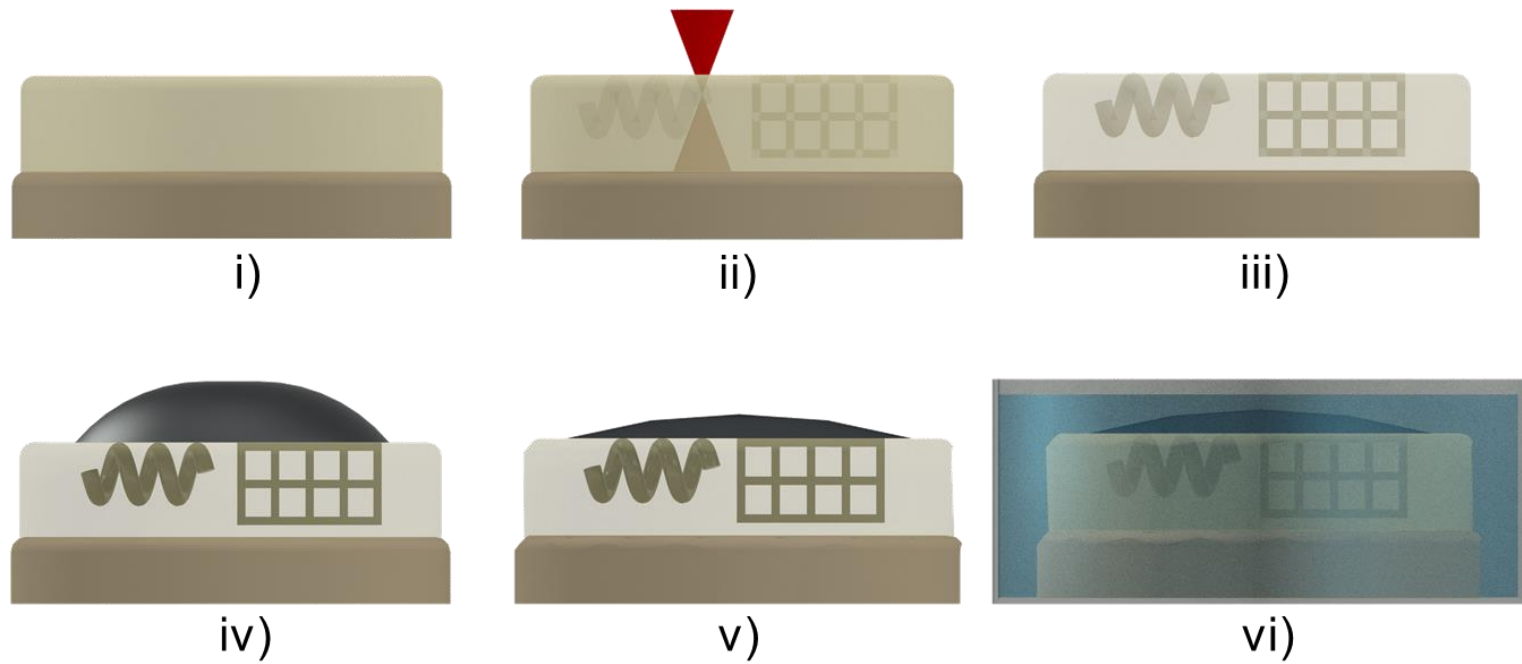


## 3D indirect printing

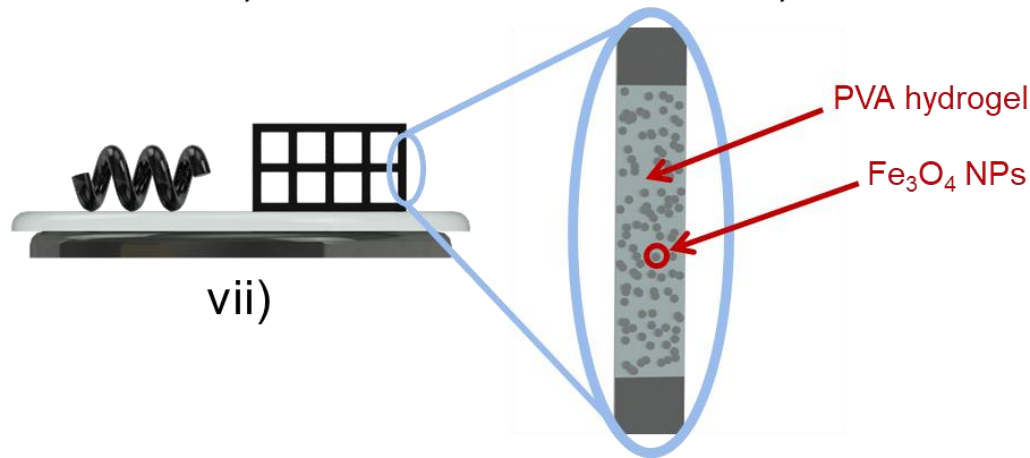




# PVA microrobot fabrication

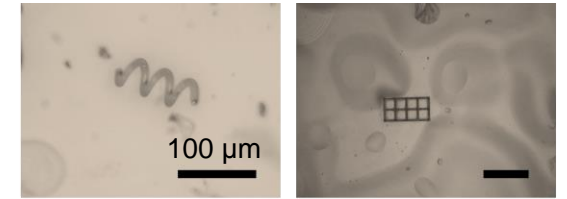


- i) Spin coating
- ii) 2-photon lithography
- iii) Development
- iv) PVA infiltration
- v) Drying
- vi) Salting out
- vii) Microrobot release

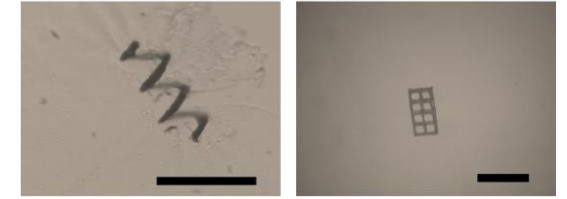


## vii) Microrobot release

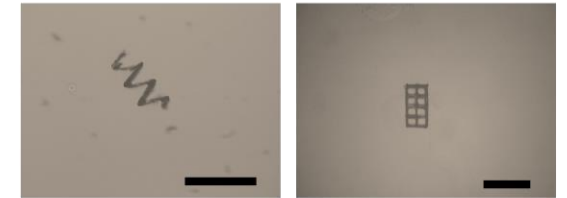
Microrobots surrounded by photoresist



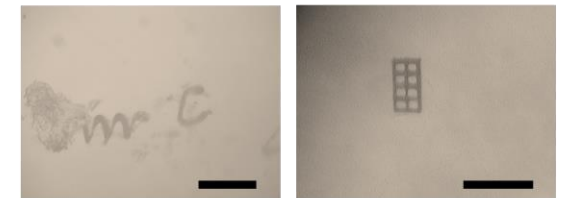
Acetone addition



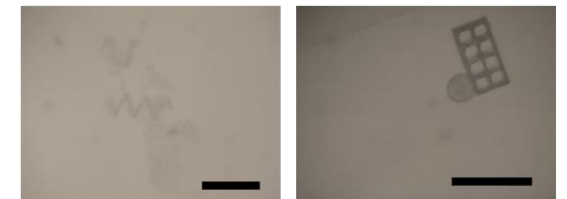
Acetone removal and addition of new acetone



Progressive water addition



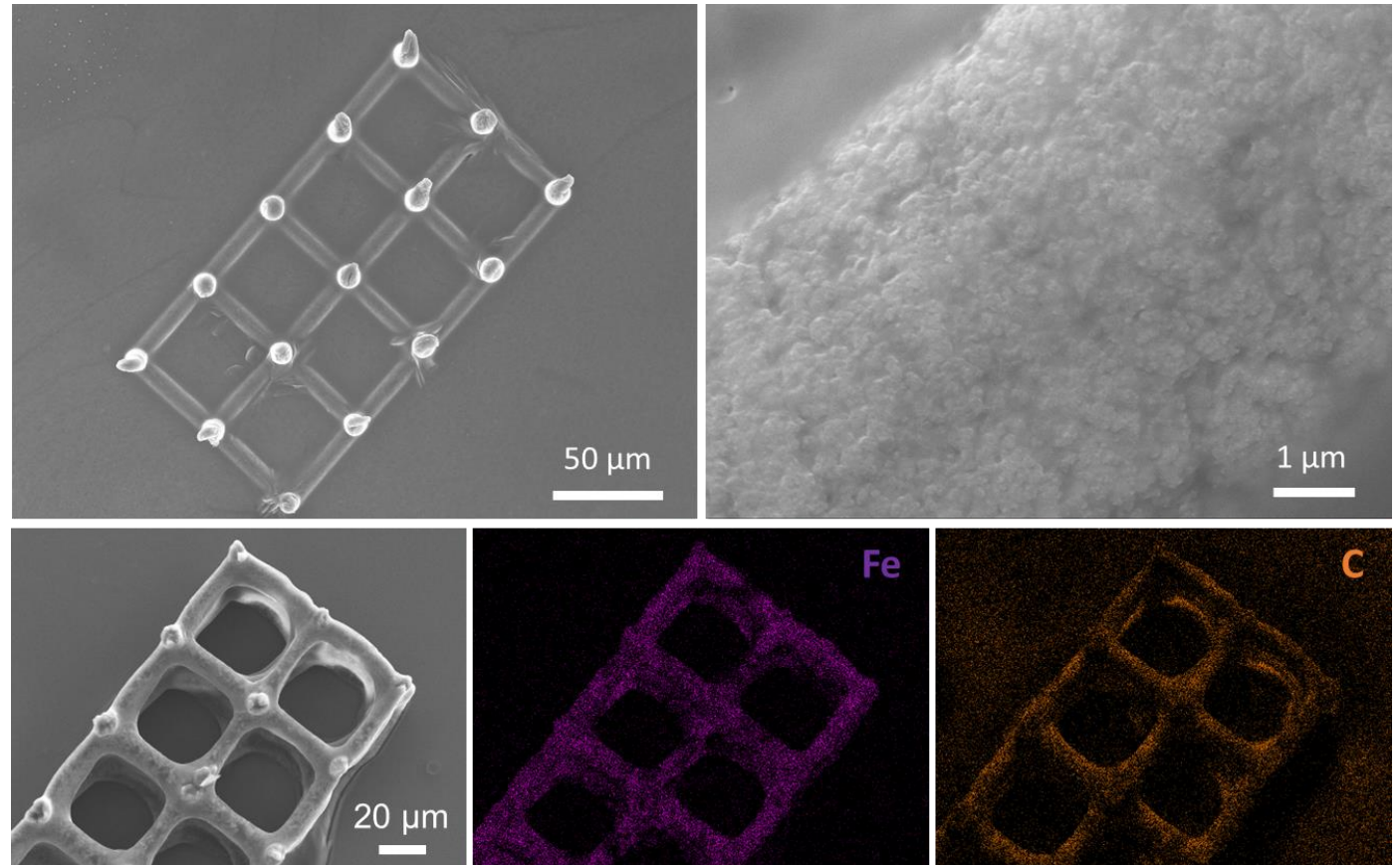
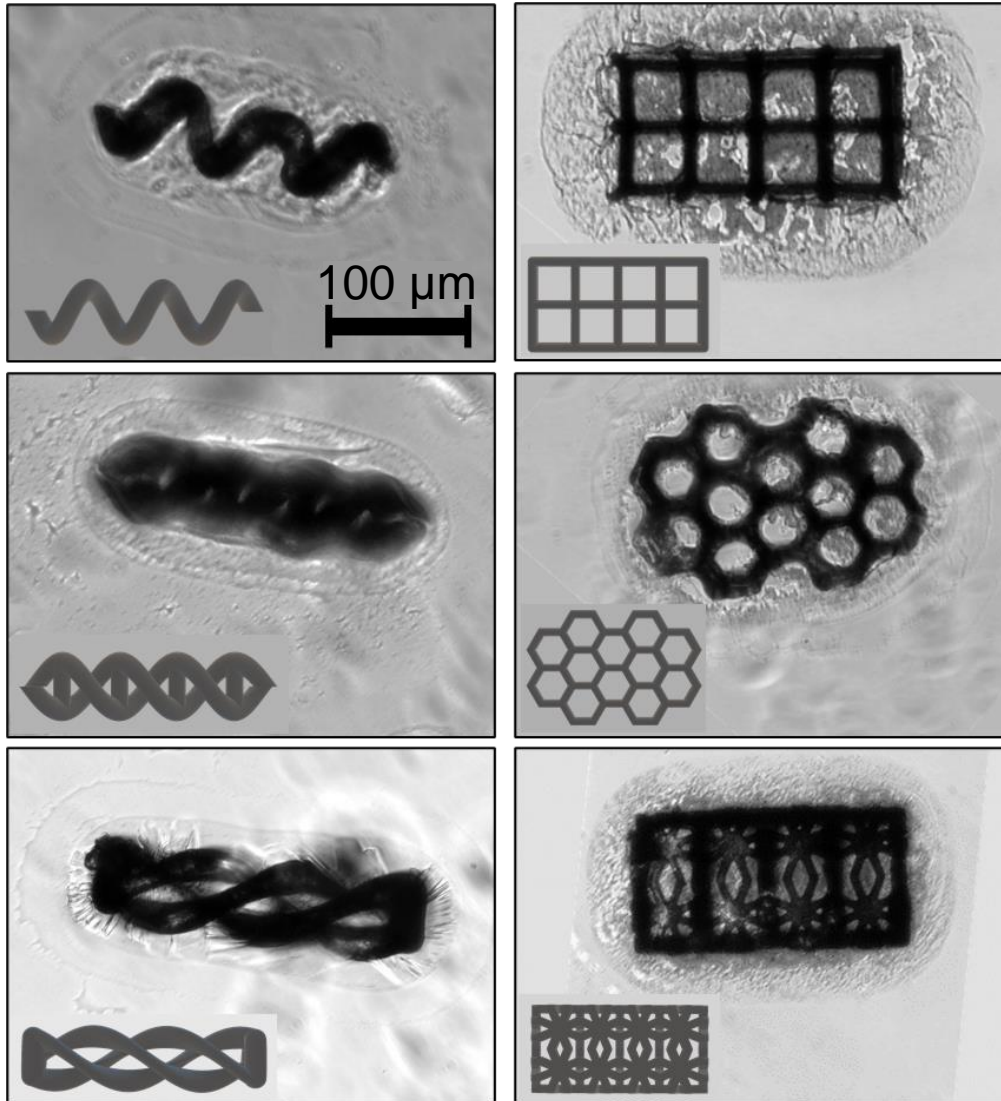
Evaporation of acetone



Addition of PBS solution

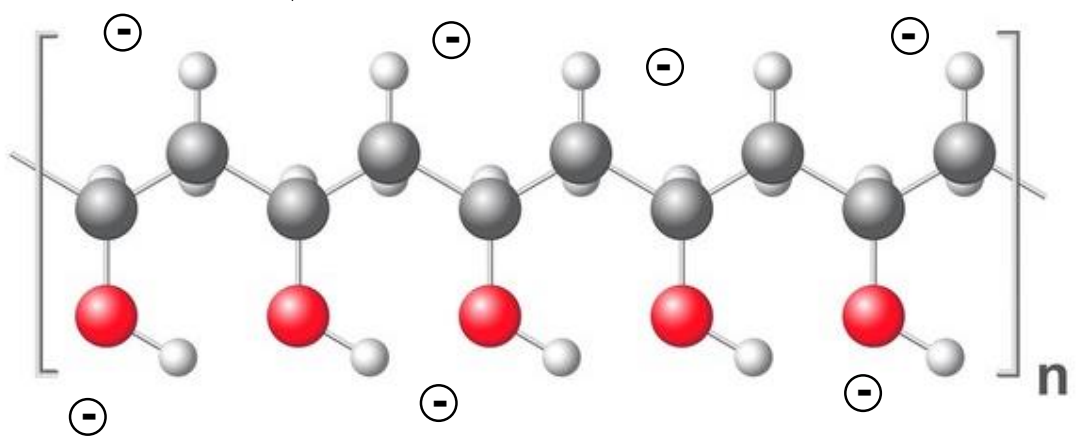
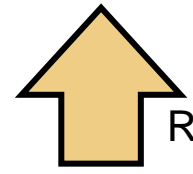
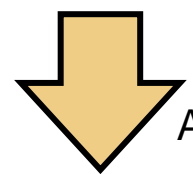
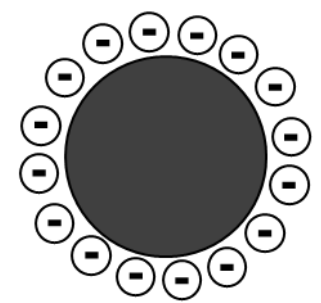
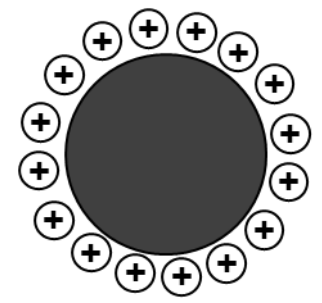
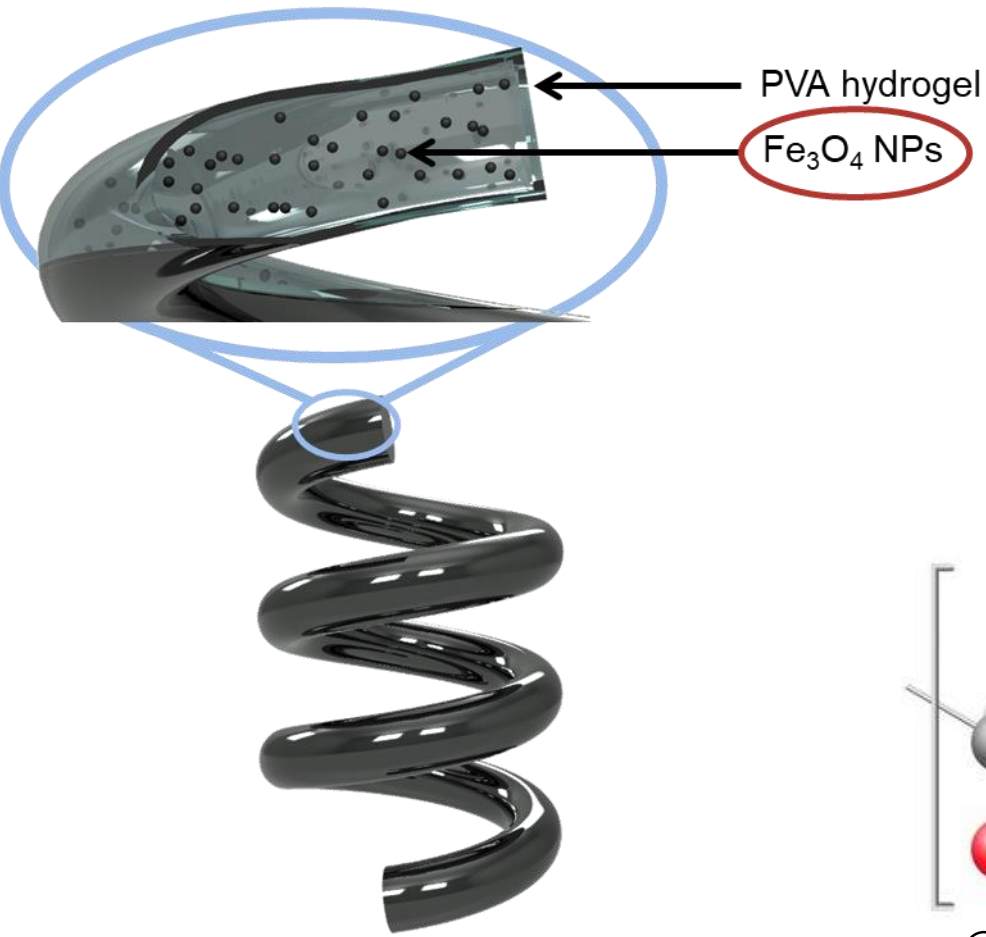


# PVA microrobot fabrication



# PVA microrobot fabrication

Positively charged MNPs (PEI, CTAB)      Negatively charged MNPs (PVP)

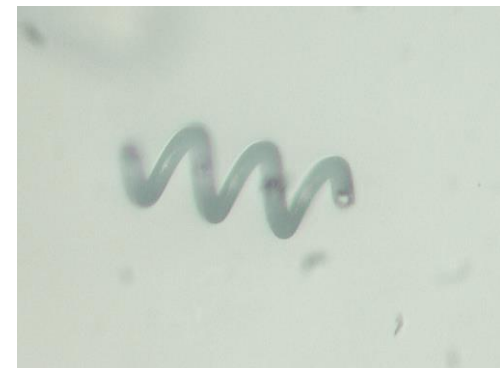


Polyvinyl alcohol

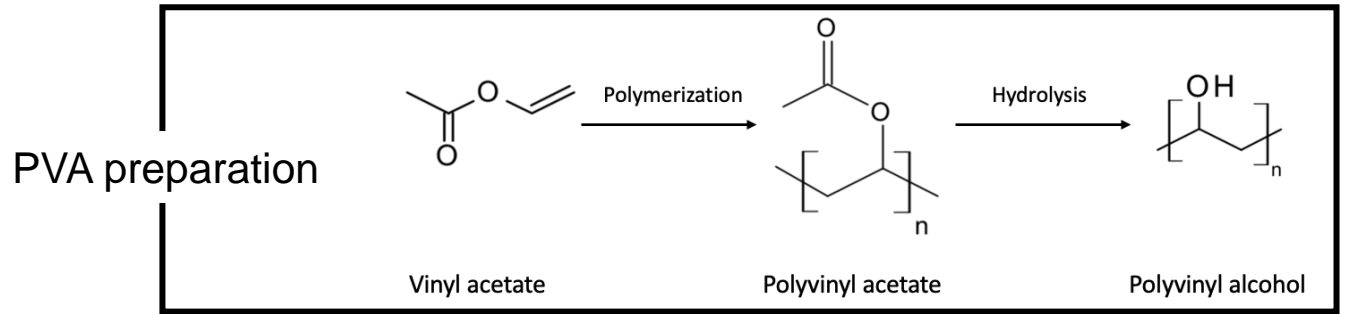
Fe<sub>3</sub>O<sub>4</sub>@PEI



Fe<sub>3</sub>O<sub>4</sub>@PVP

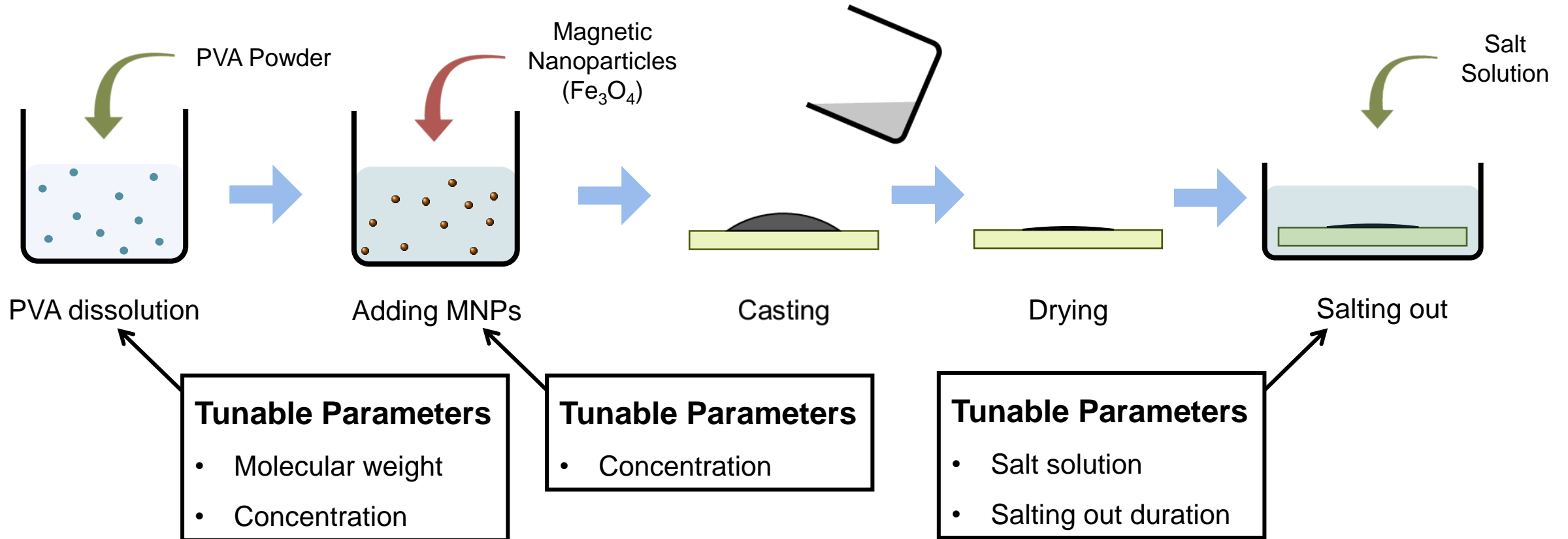


# Tunable stability

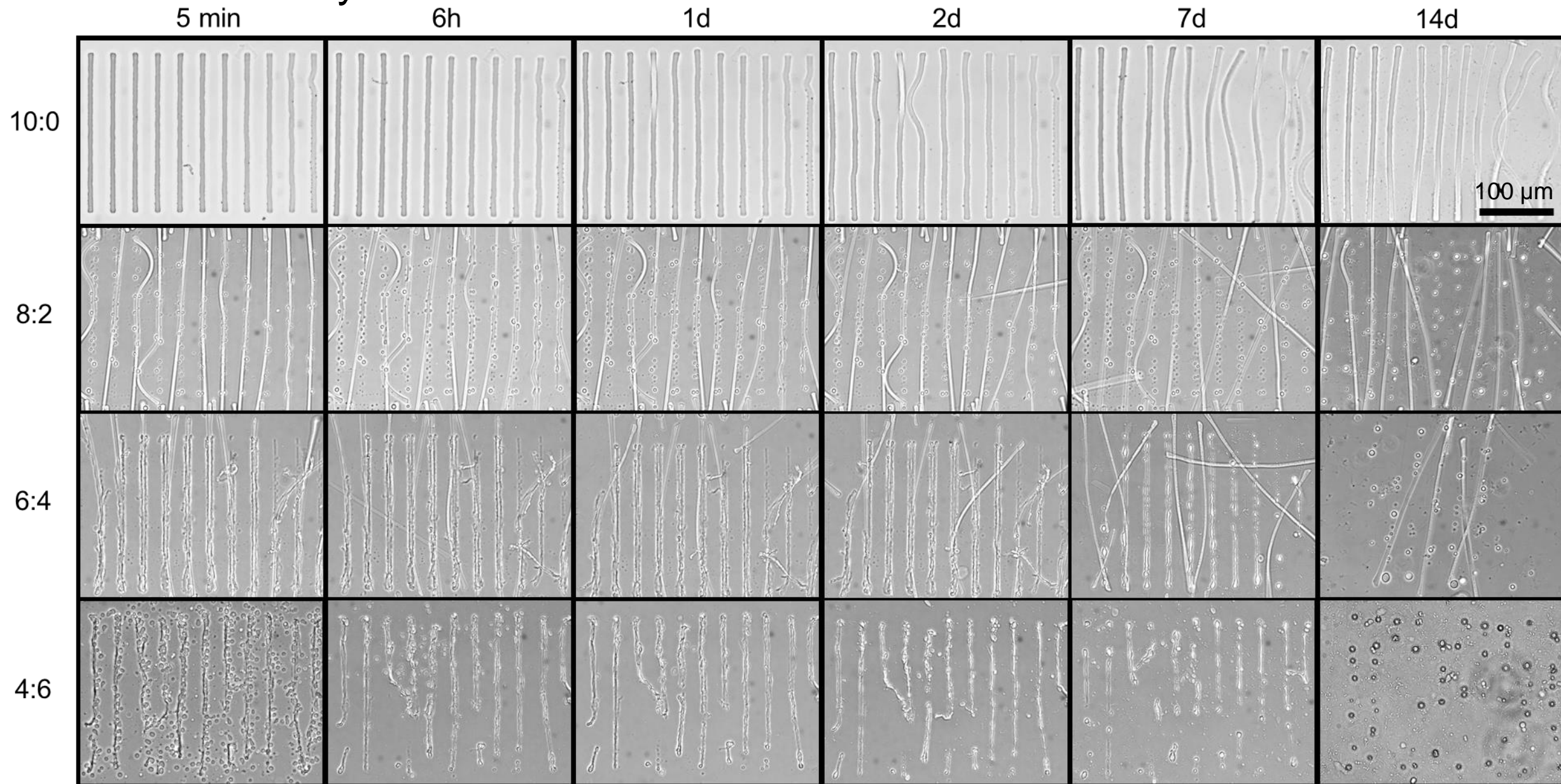


**Tunable Parameters**

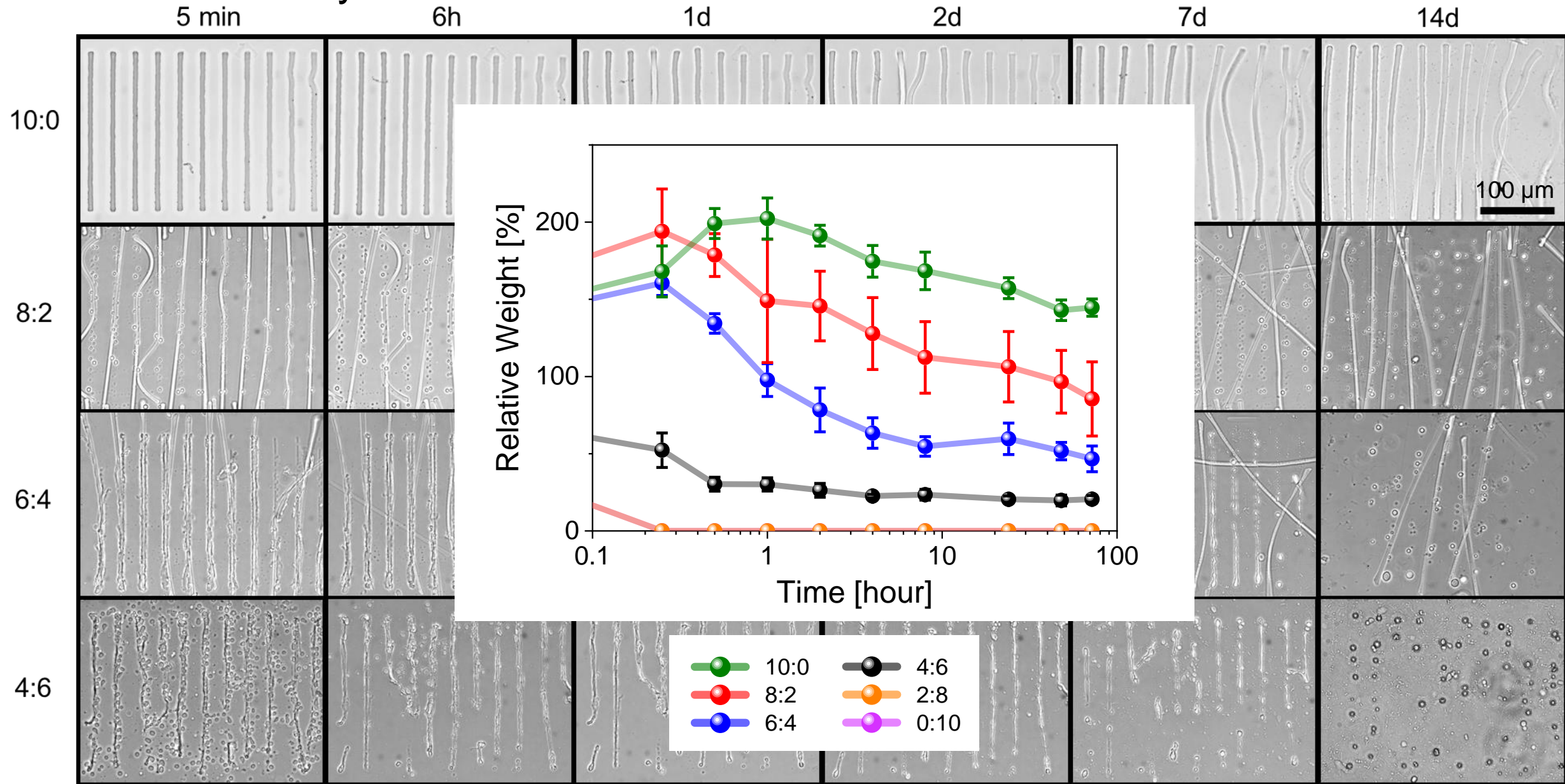
- Degree of hydrolysis



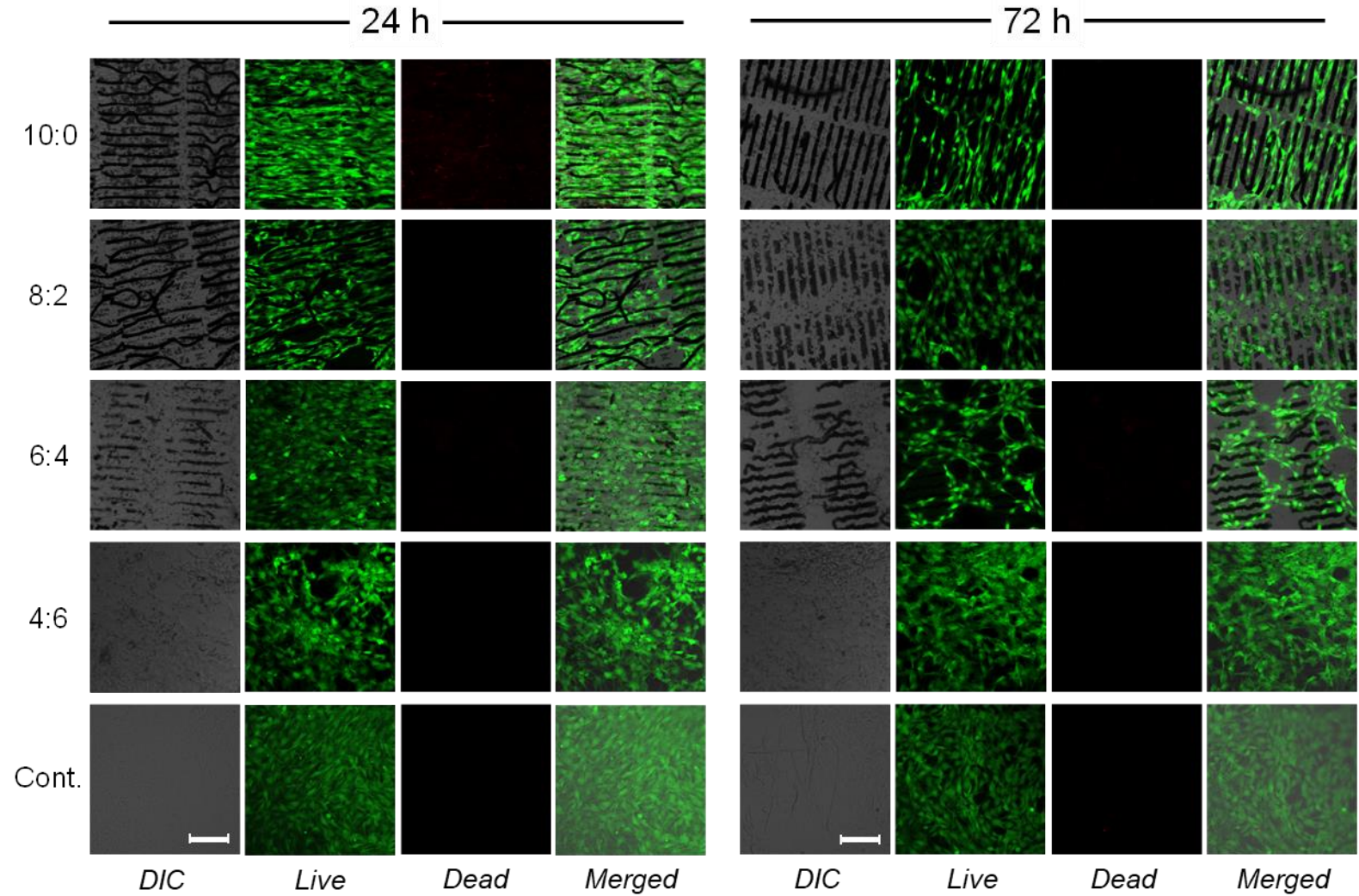
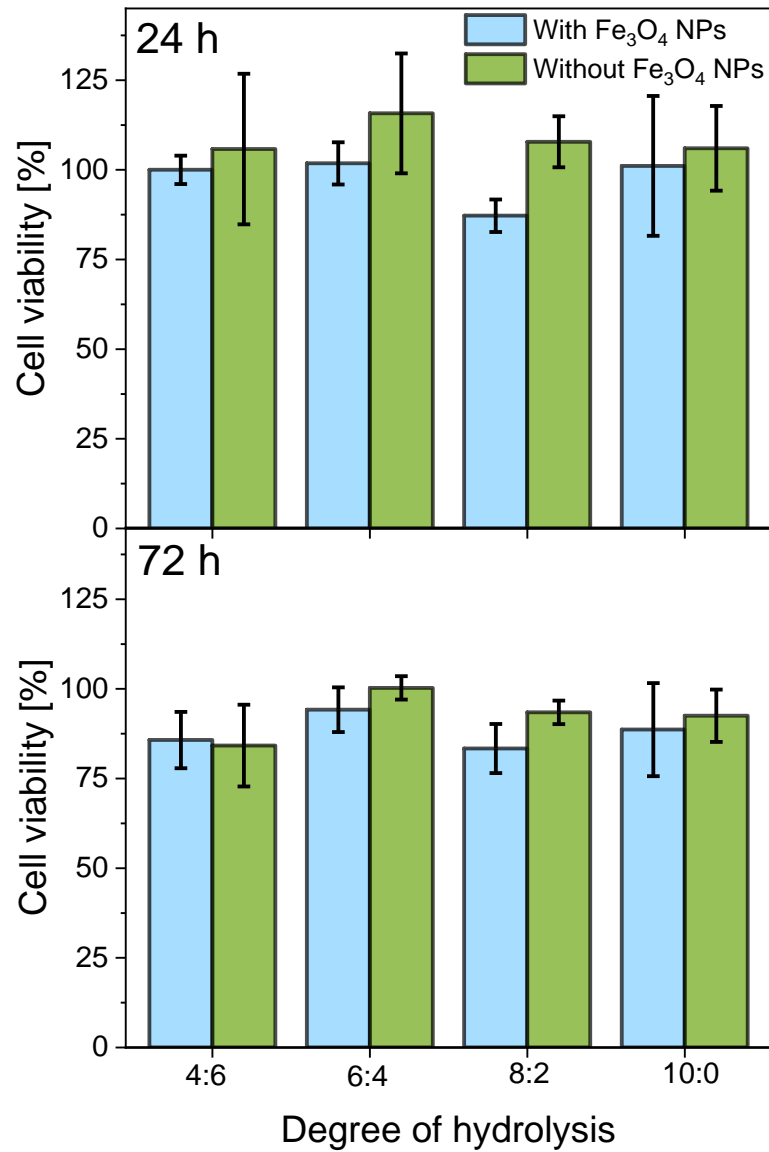
# Tunable stability



# Tunable stability

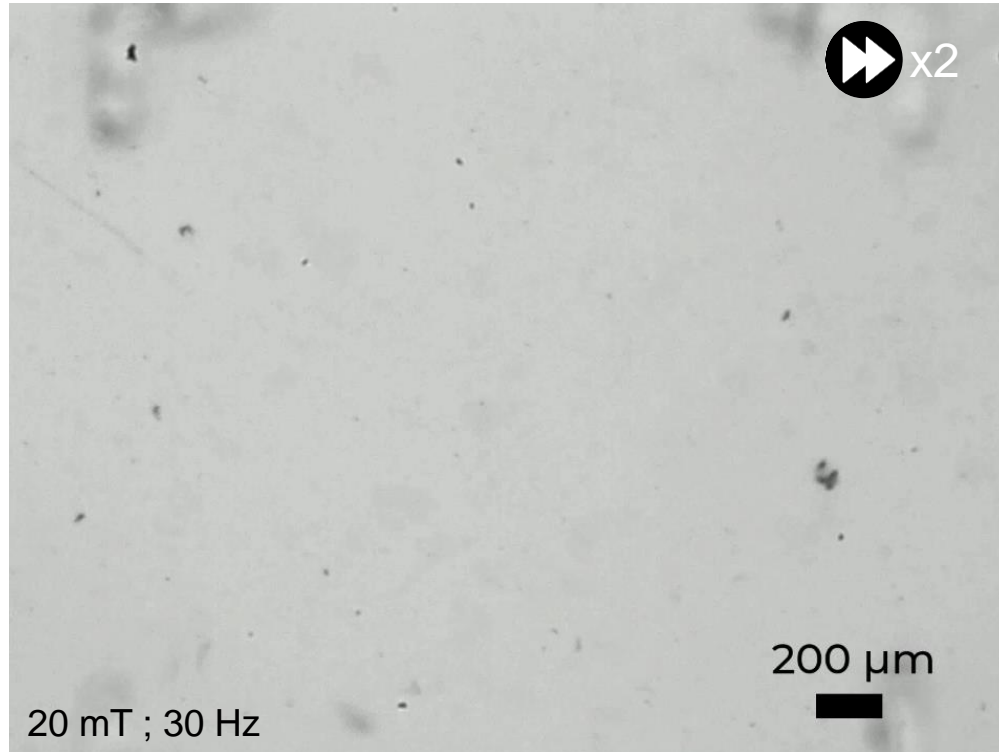


# Biocompatibility

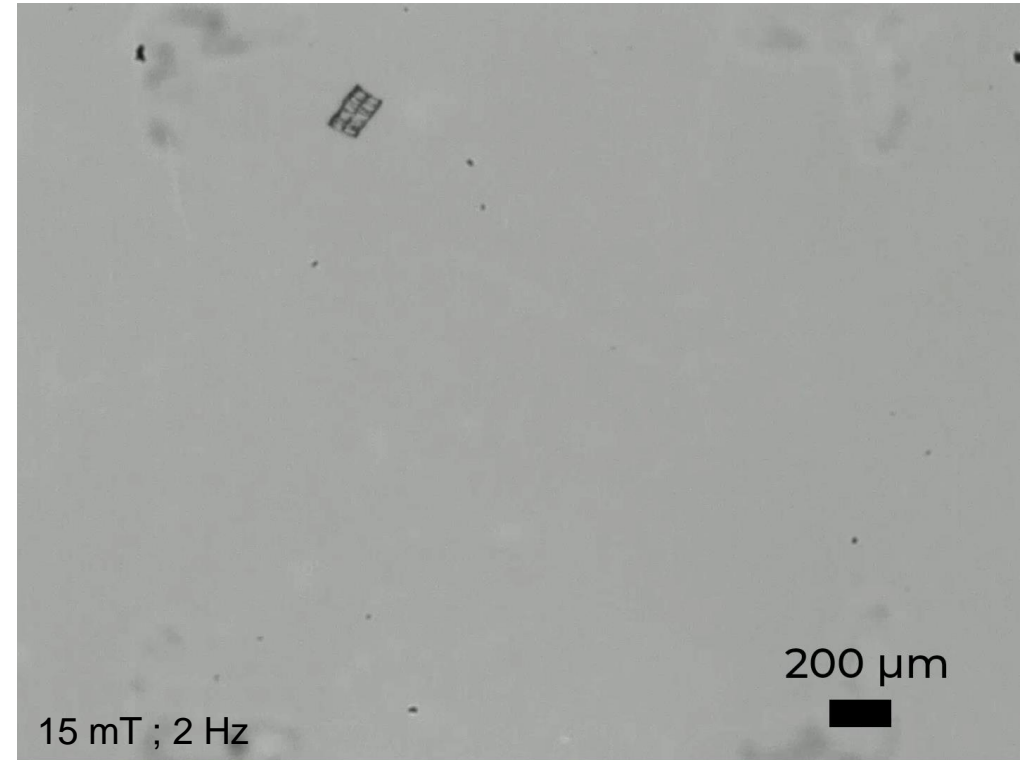


Live/dead cell assays

# Microrobot manipulation



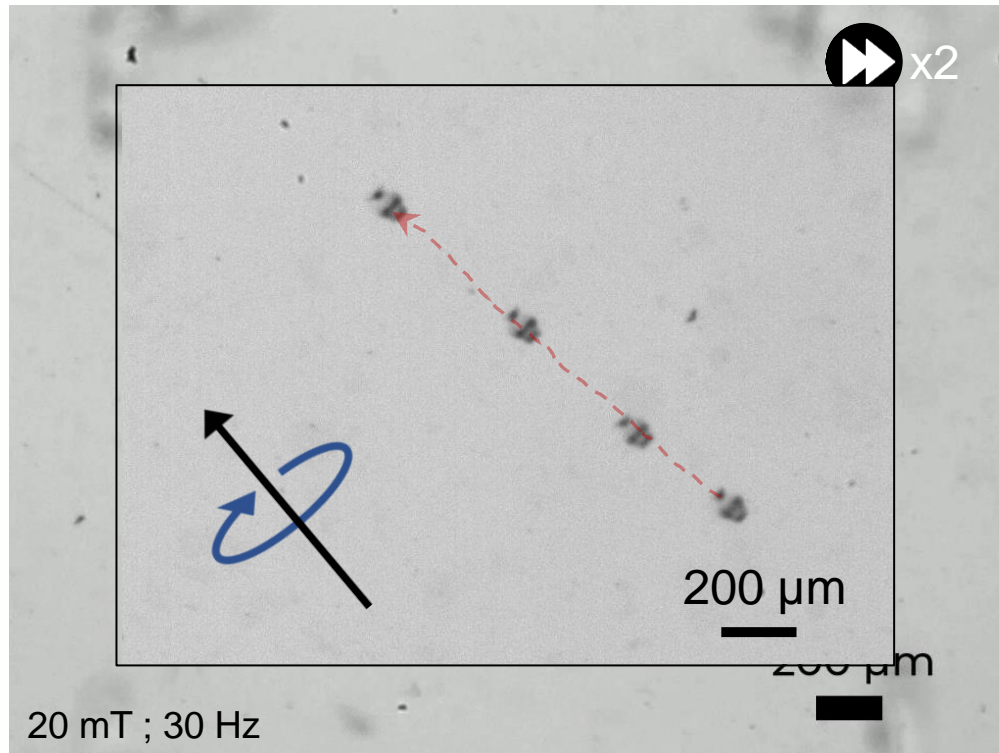
Forward velocity =  $65 \mu\text{m/s}$   
Drift velocity =  $11 \mu\text{m/s}$



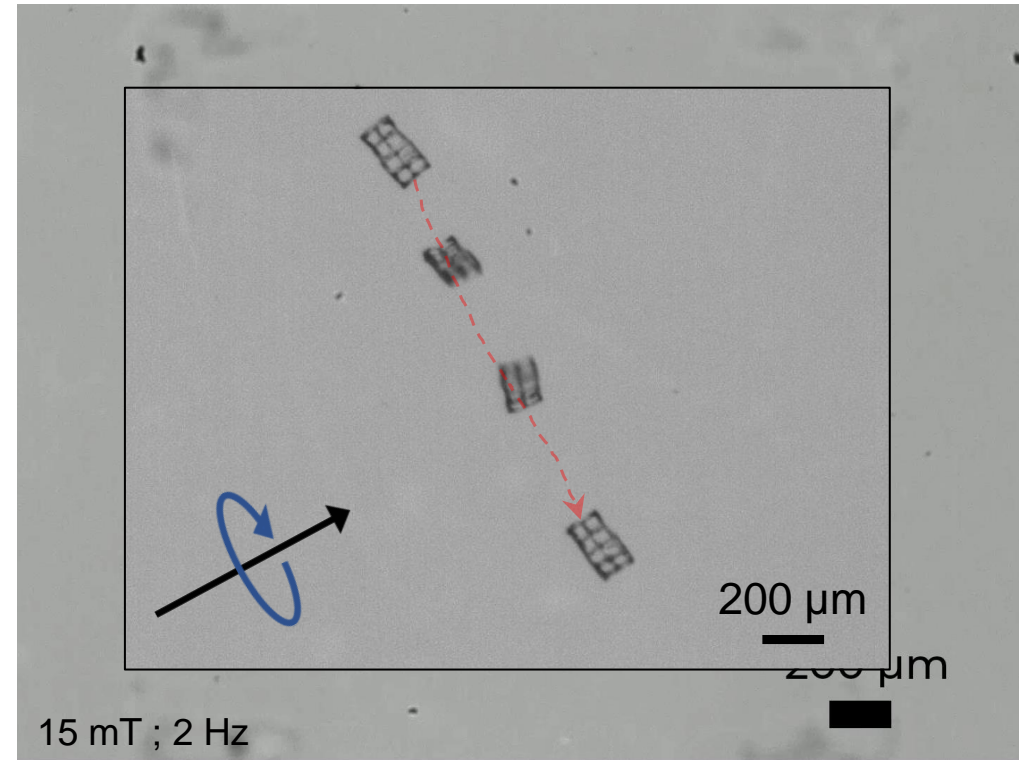
Forward velocity =  $550 \mu\text{m/s}$   
Drift velocity =  $32 \mu\text{m/s}$



# Microrobot manipulation

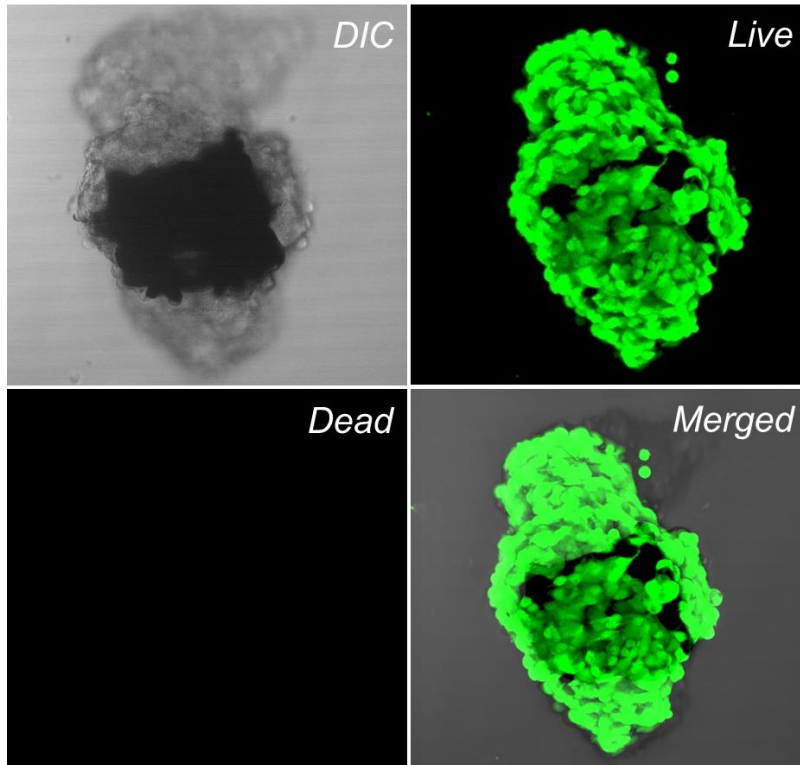


Forward velocity =  $65 \mu\text{m/s}$   
Drift velocity =  $11 \mu\text{m/s}$



Forward velocity =  $550 \mu\text{m/s}$   
Drift velocity =  $32 \mu\text{m/s}$

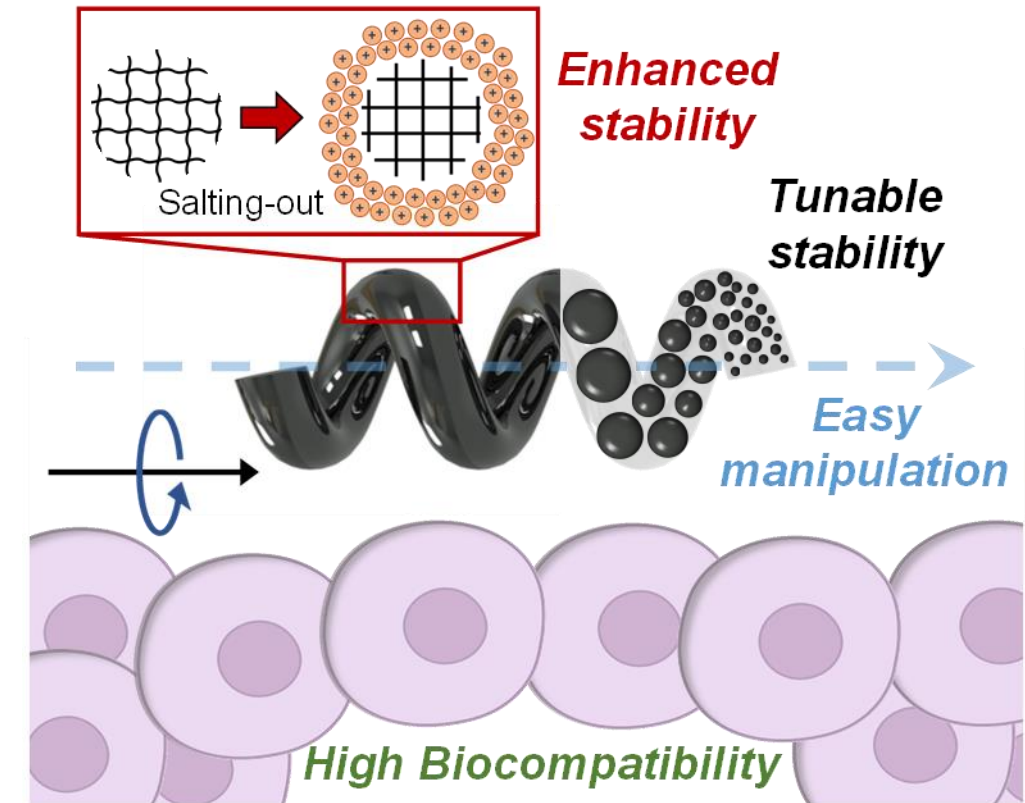
# Microrobot manipulation



# 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.

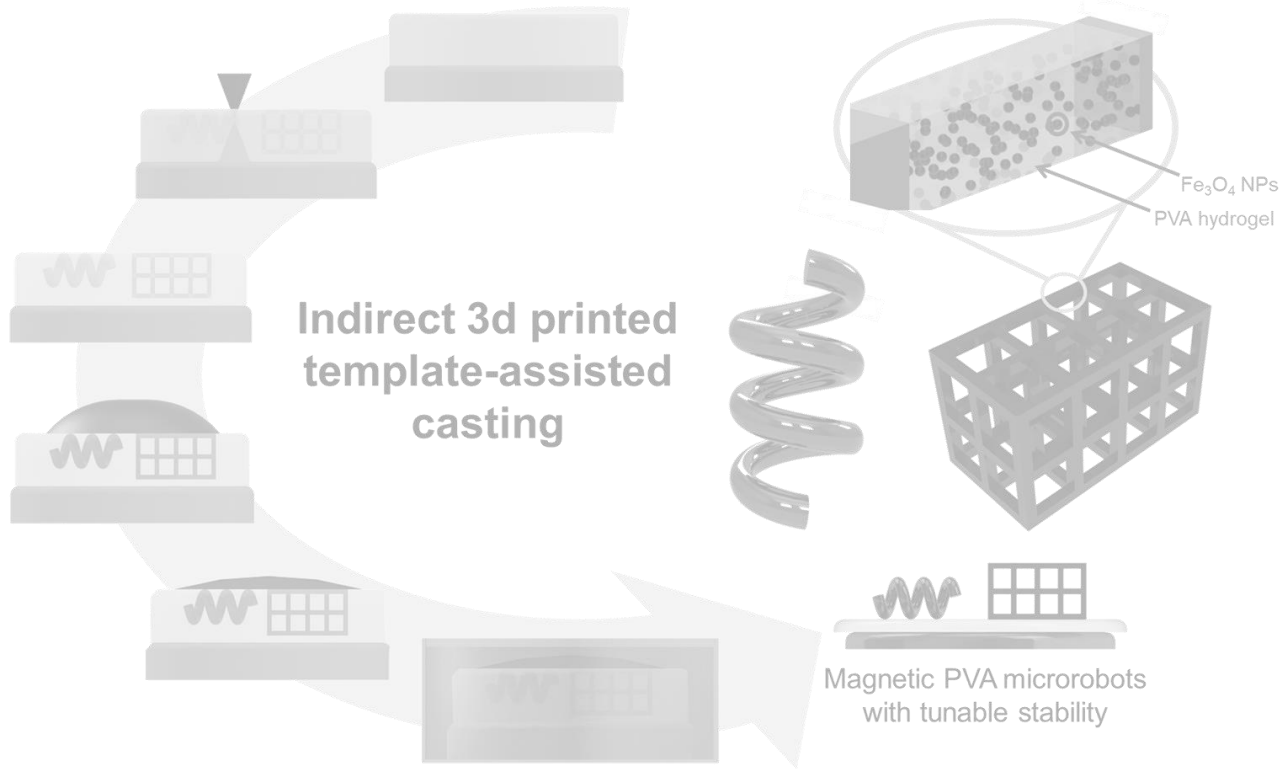
## PVA hydrogel soft microrobots



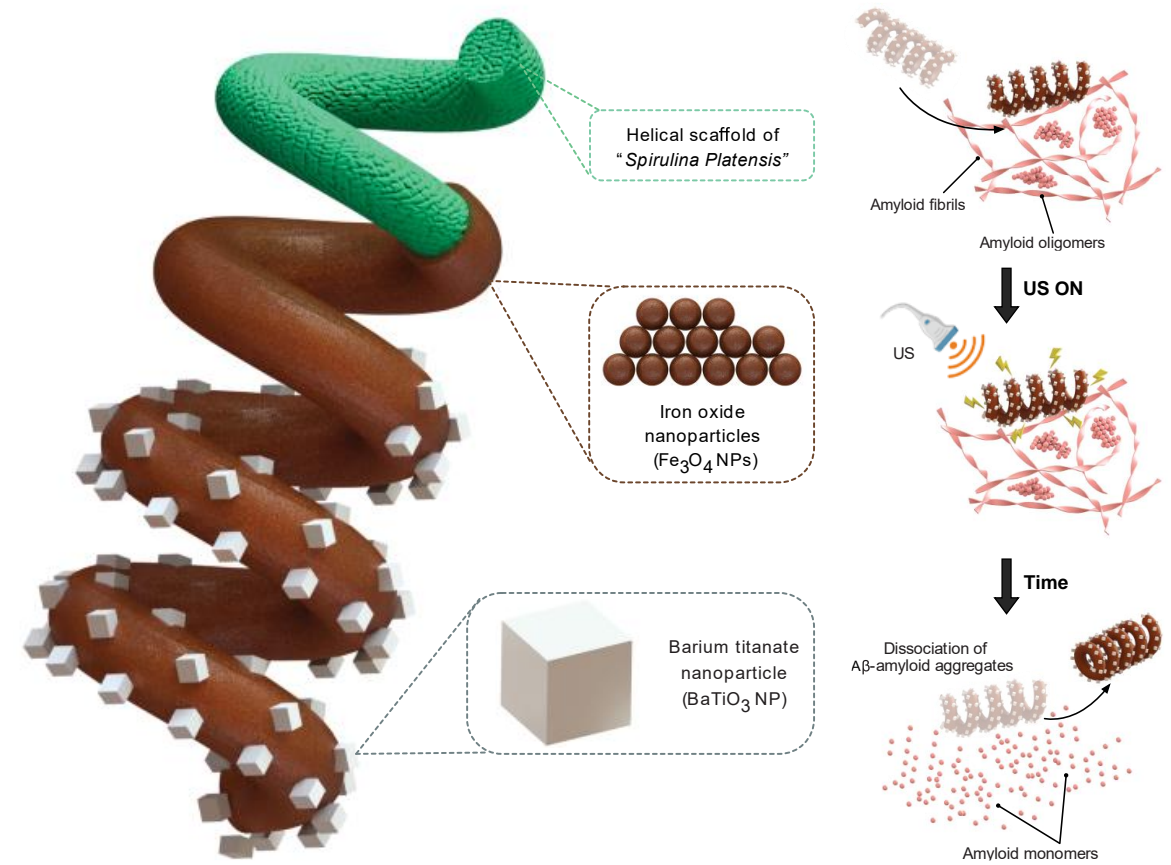
[Read the paper here: Adv. Funct. Mater. 2023, 2212952](#)

# Outline

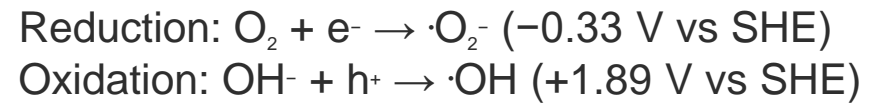
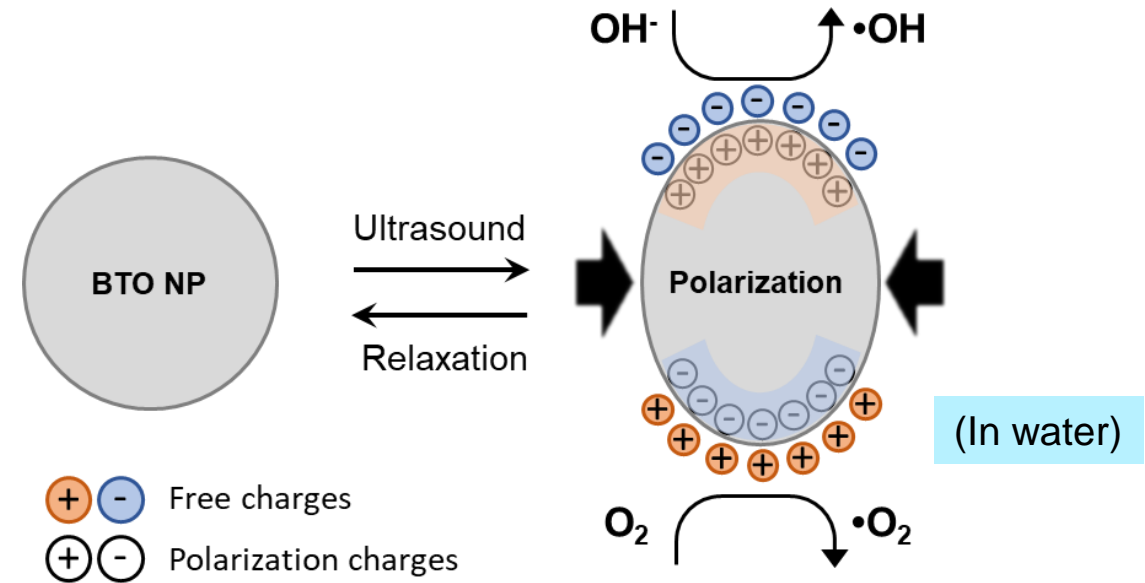
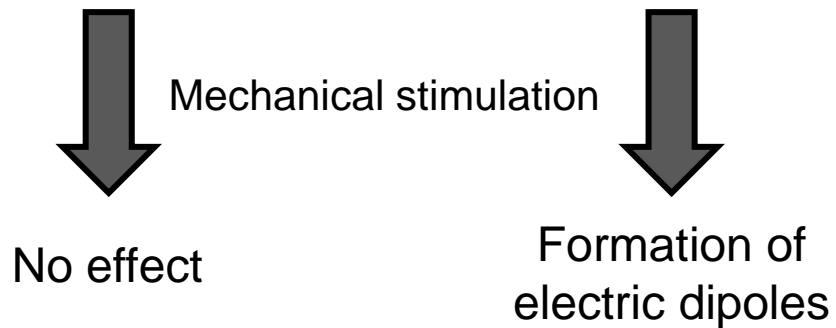
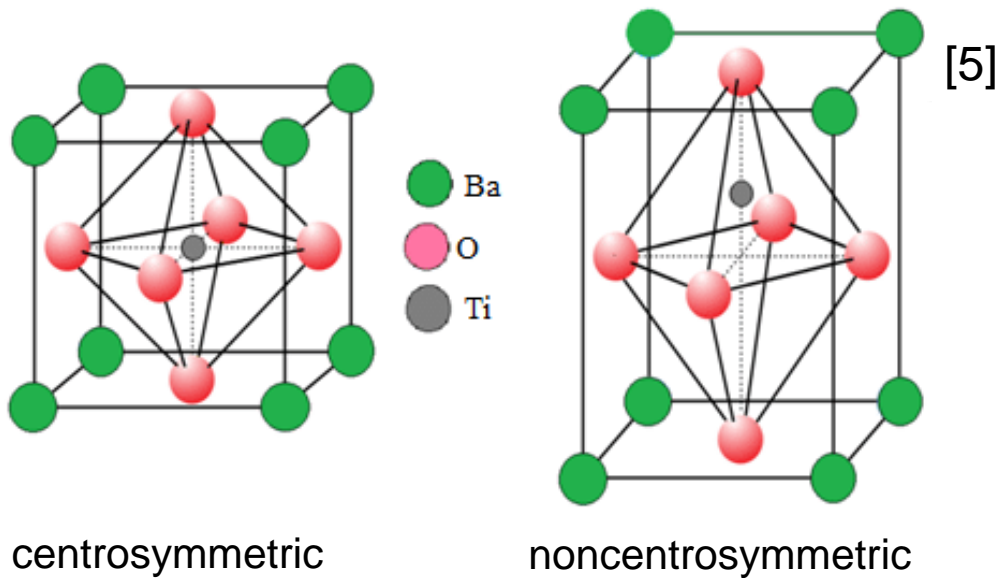
## Indirect 3d printing for fabricating soluble polymer-based microrobots



## Biotemplates as a platform for incorporating functional nanoparticles



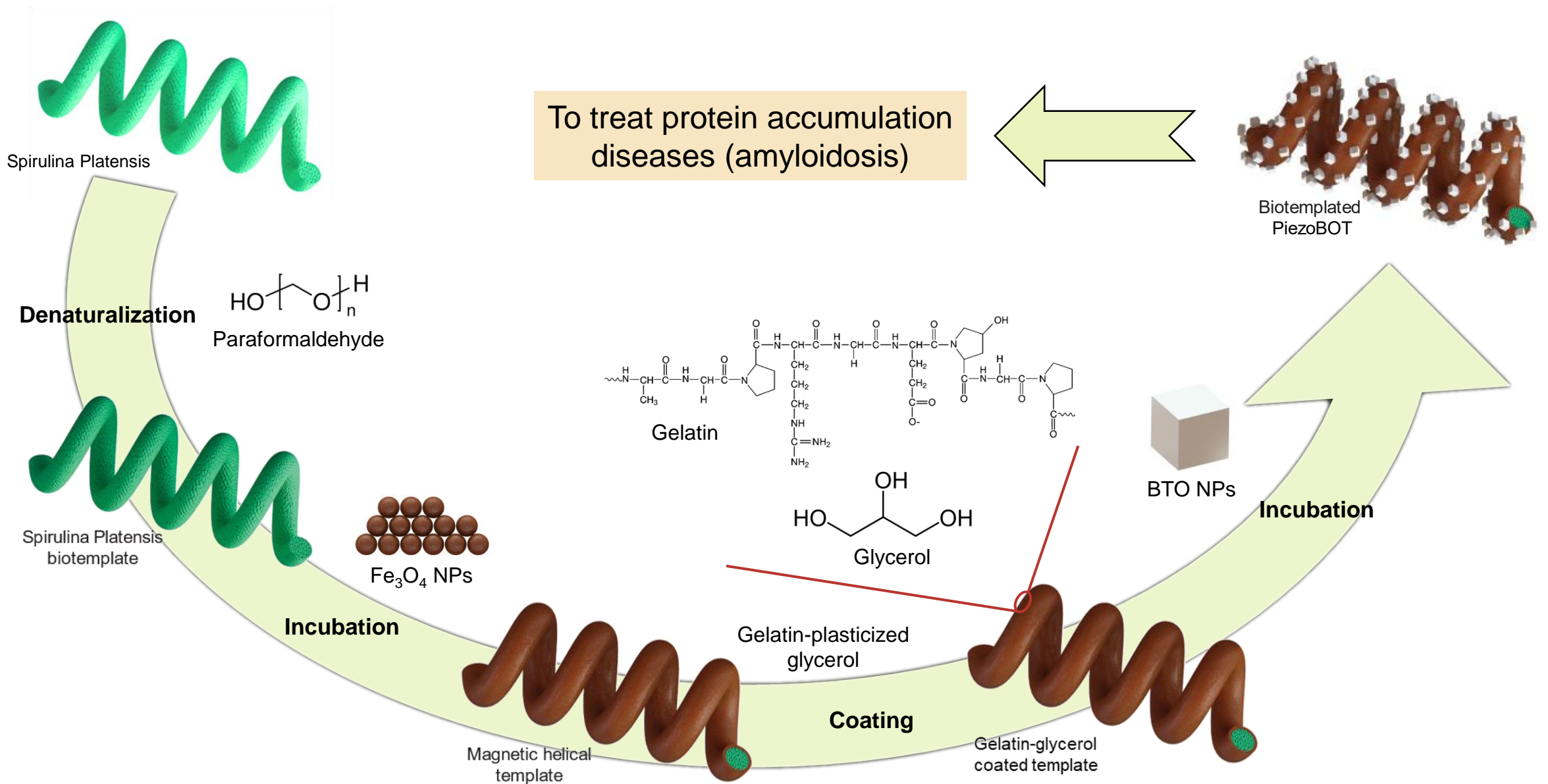
# Piezoelectric BaTiO<sub>3</sub> nanoparticles



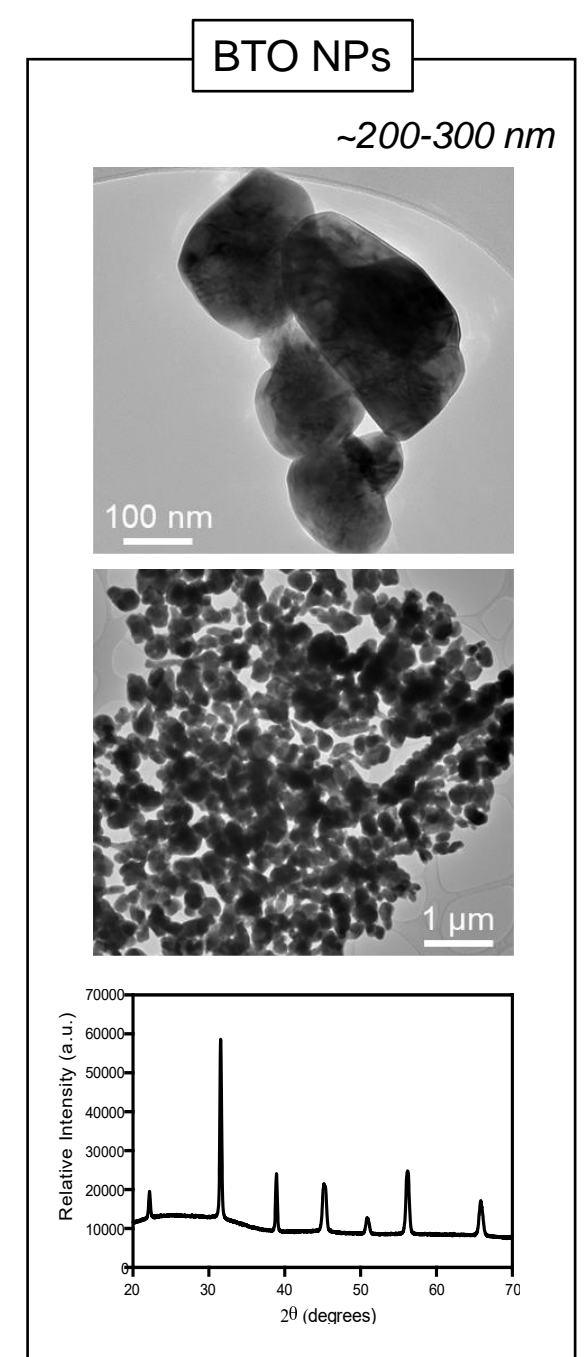
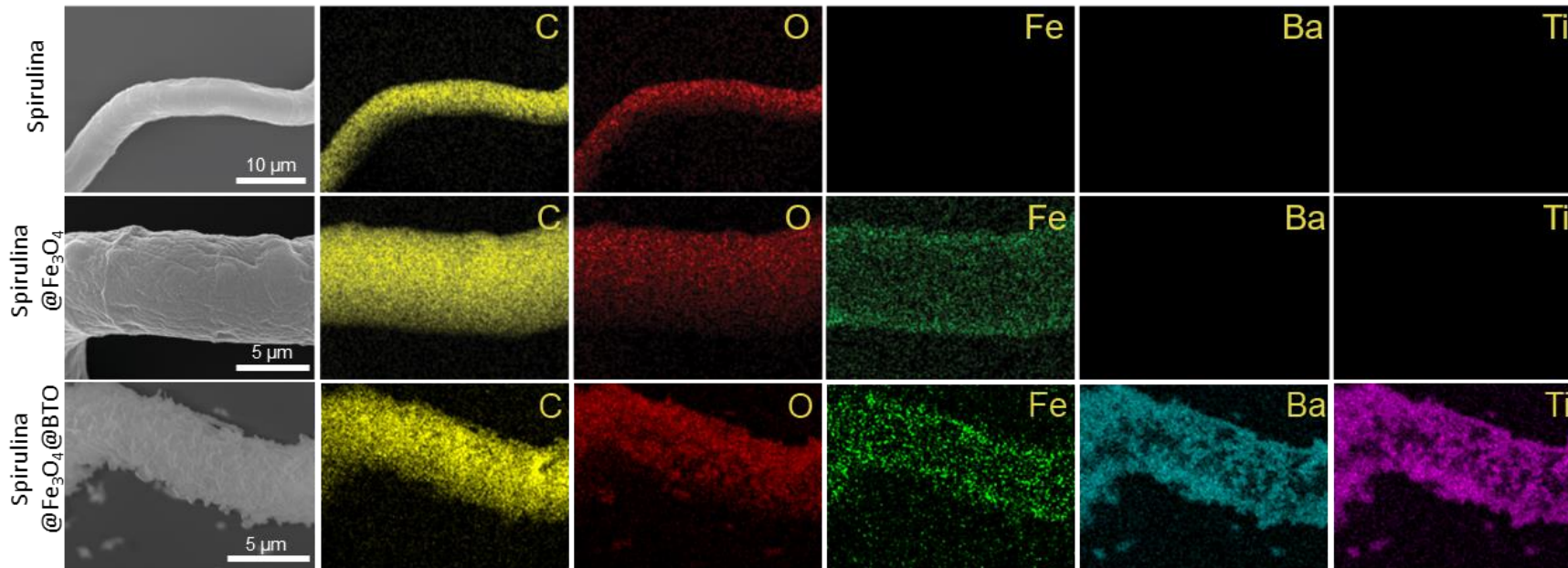
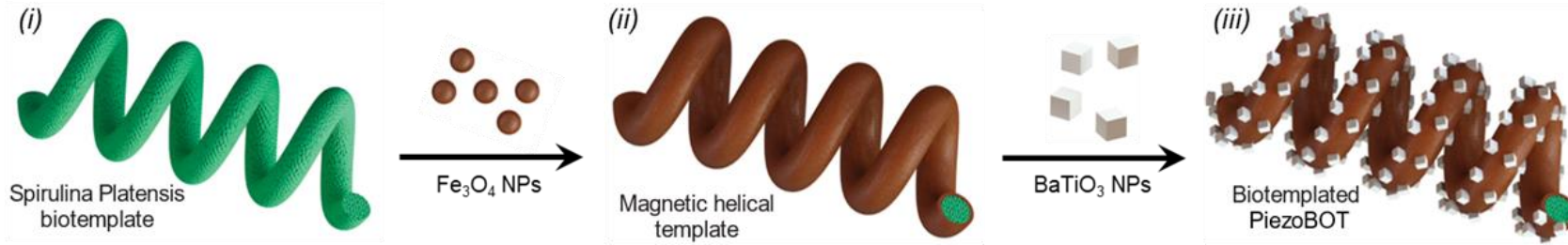
Dye degradation, cancer cell therapy,  
**protein dissociation**

Limitations:  
aggregation, bioabsorbability

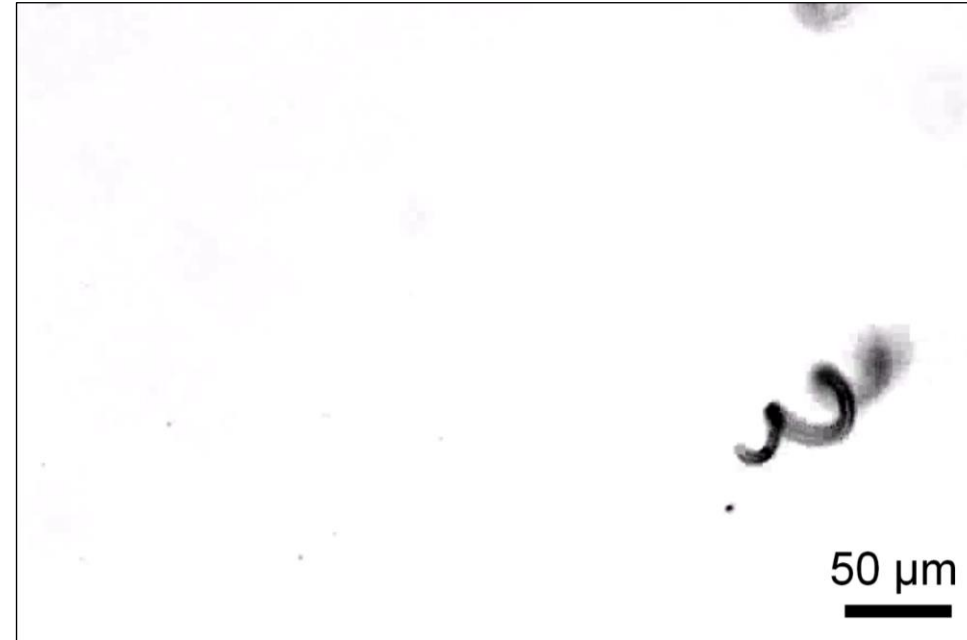
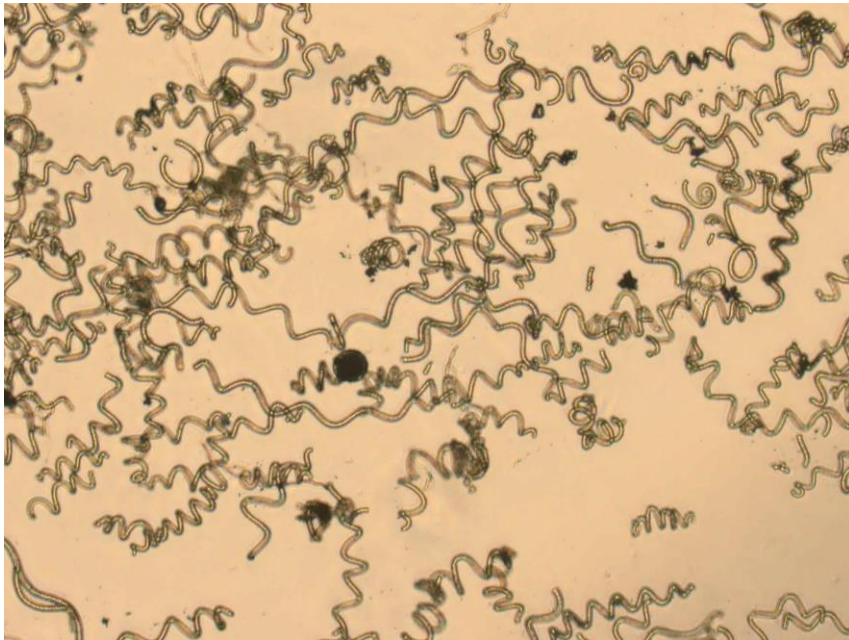
# Microrobot fabrication



# Microrobot fabrication



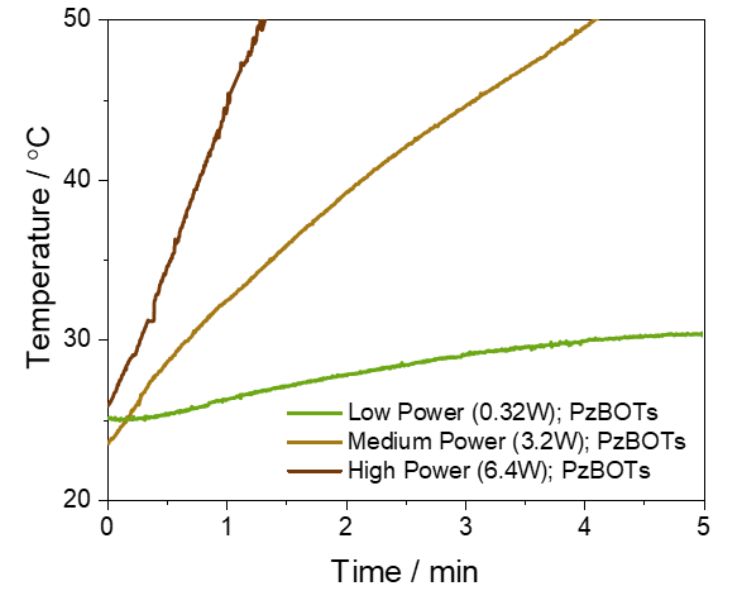
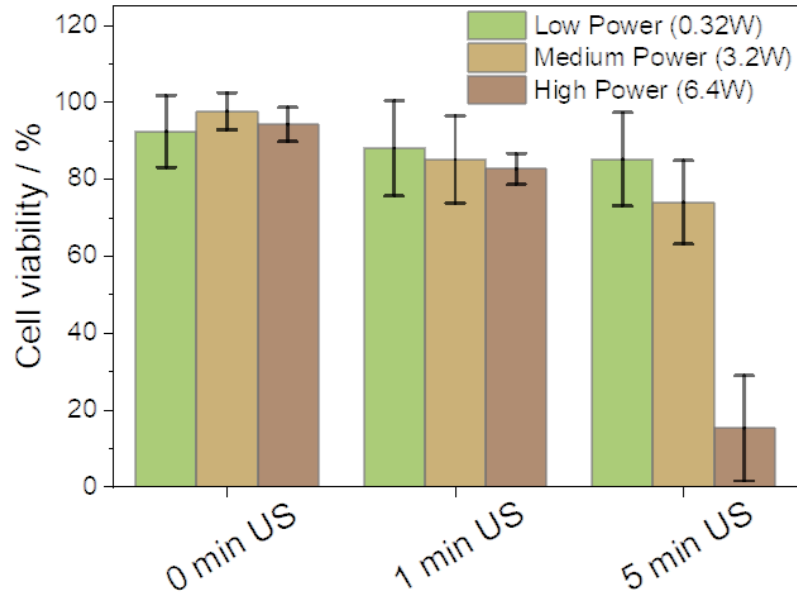
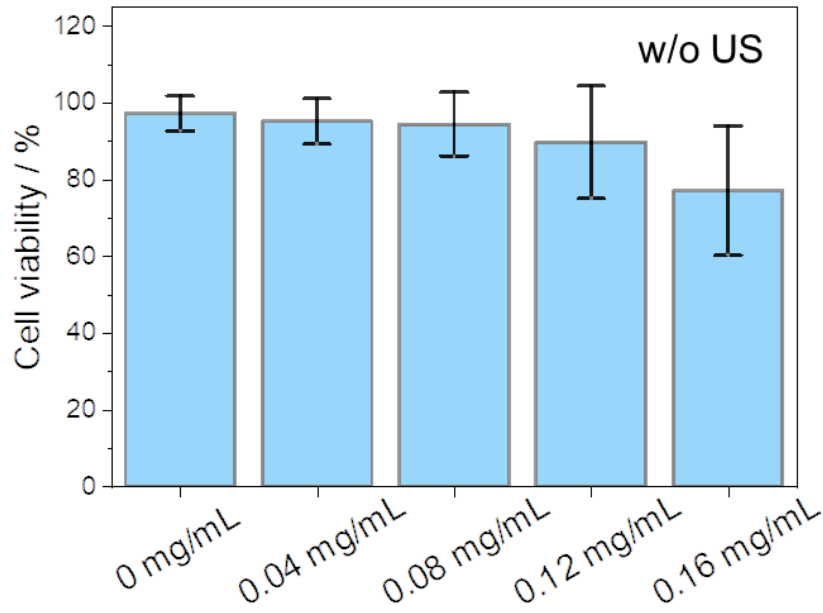
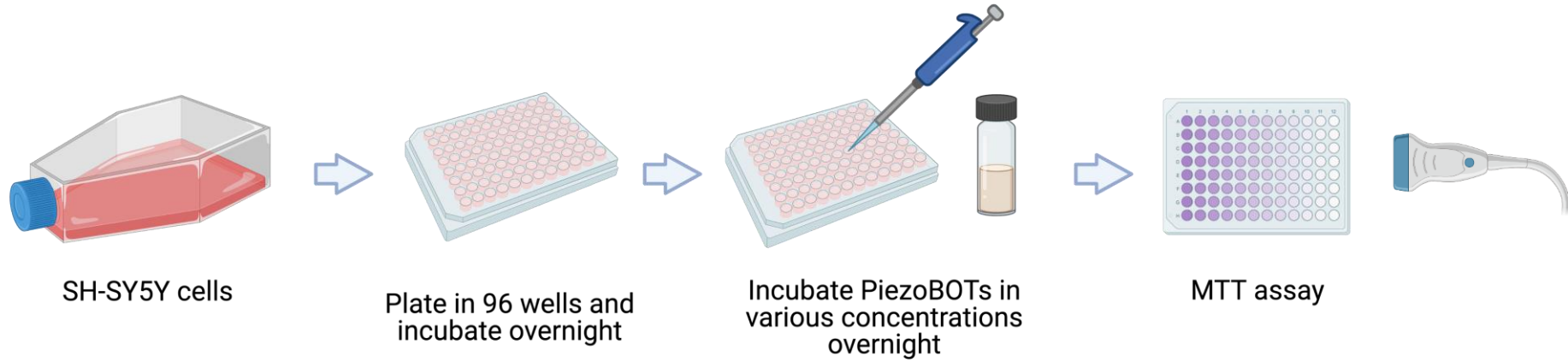
# Microrobot manipulation



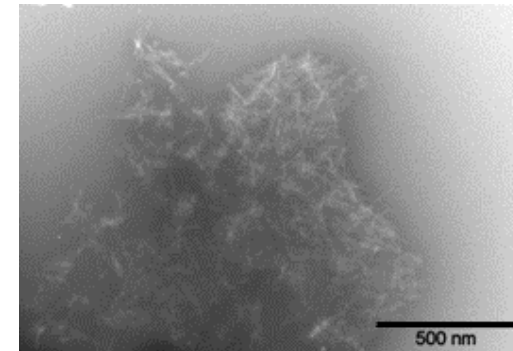
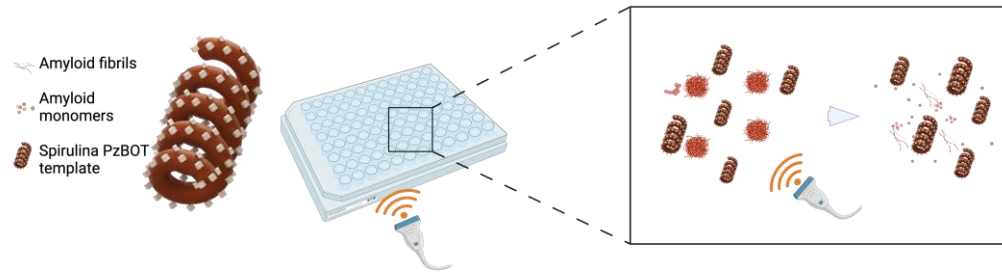
Good magnetic response and easy manipulation



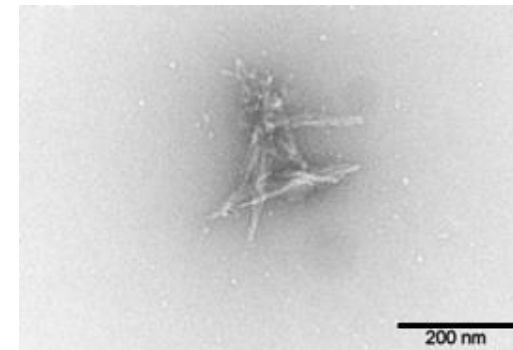
# Biocompatibility



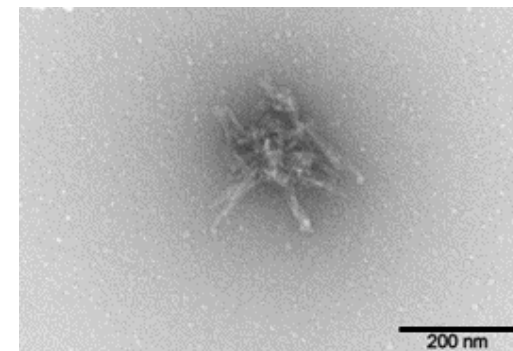
# Protein degradation



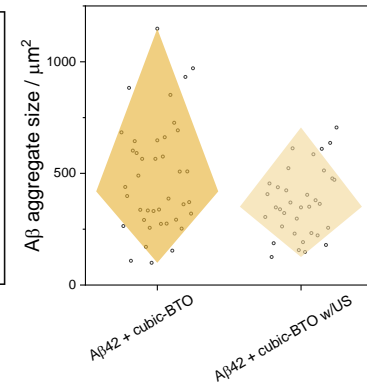
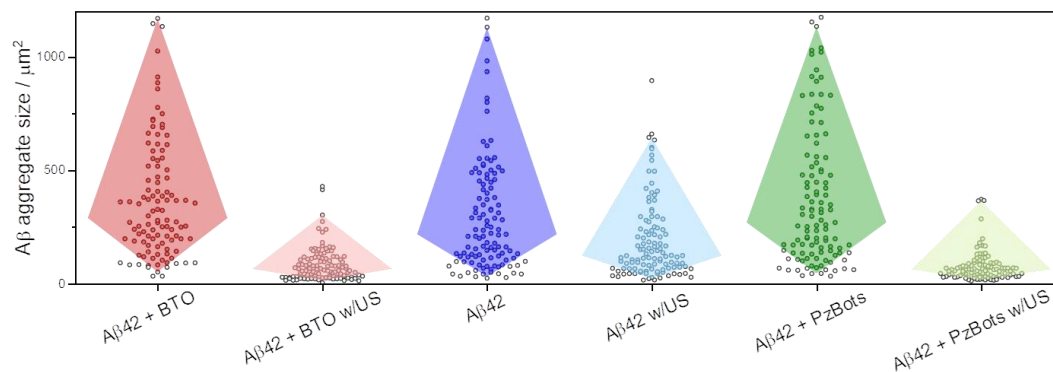
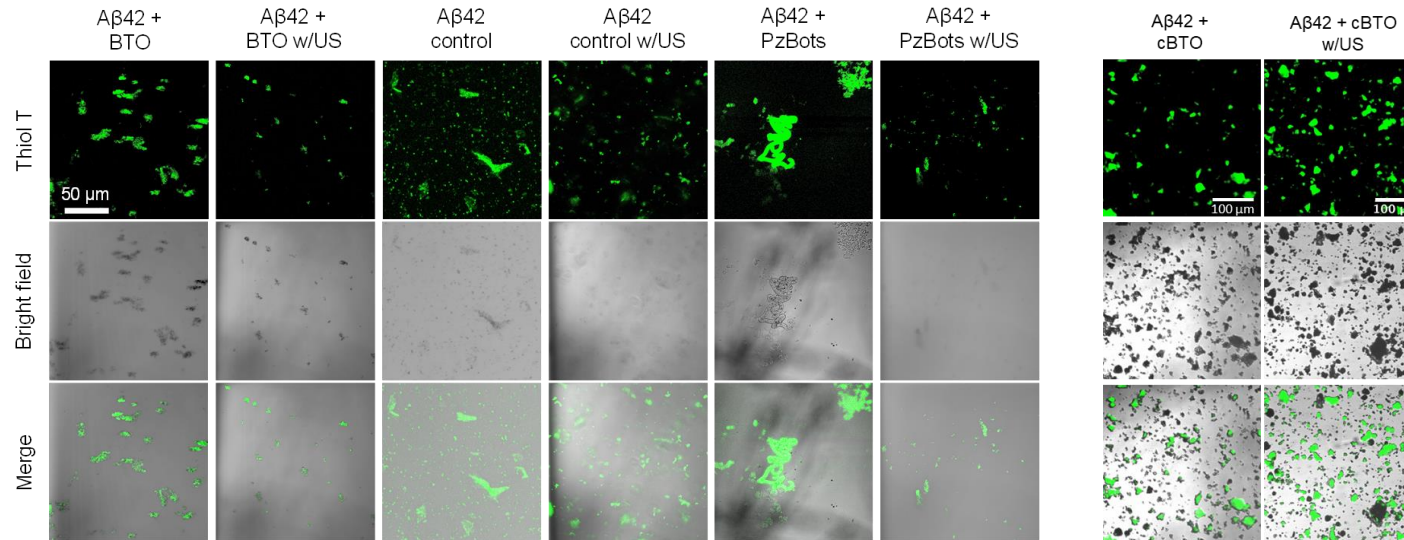
Aβ42 control w/US



Aβ42 + BTO w/US

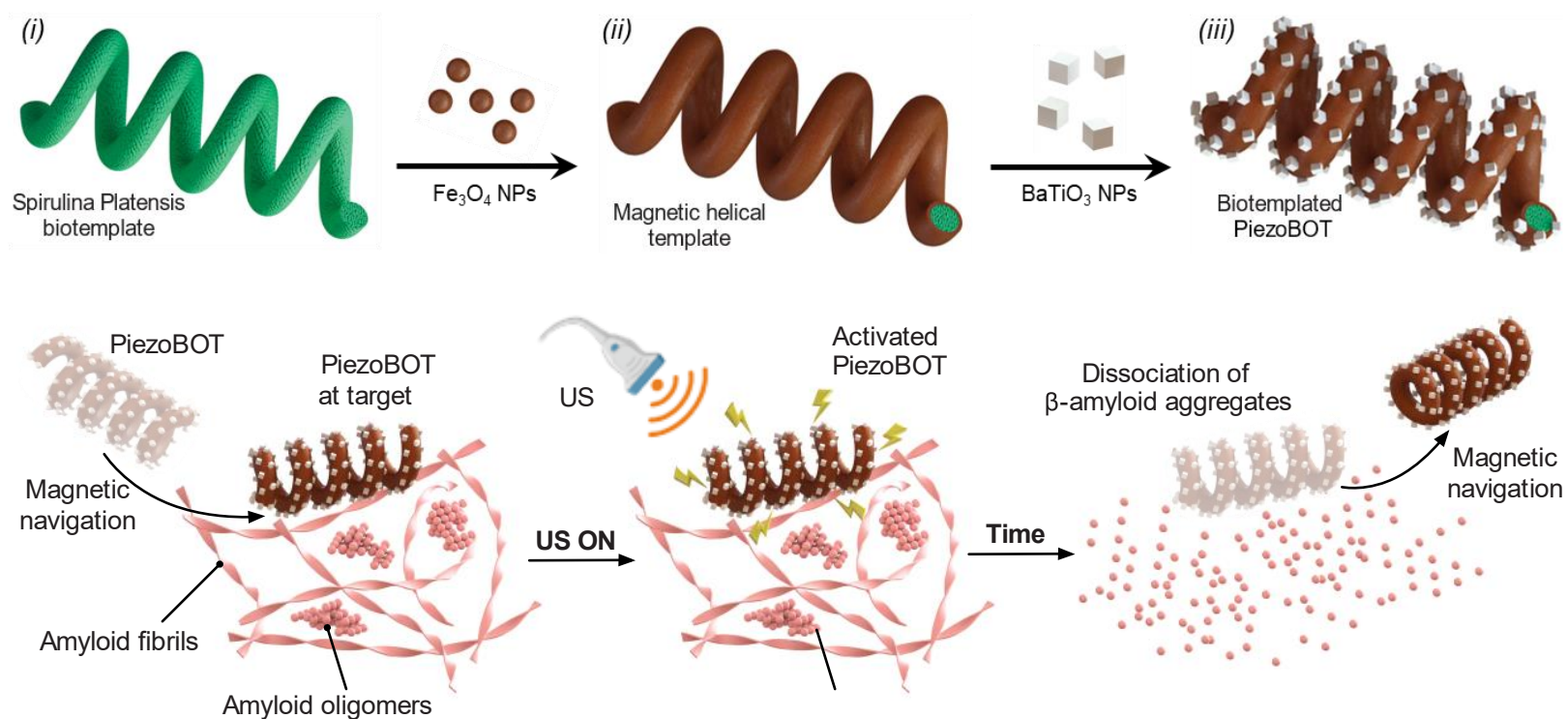


Aβ42 + PzBots w/US



# 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.



# Acknowledgments

Shen Ning

Towa Ueno

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Lukas Hurtle

Fabian Landers

Joaquin Llacer-Wintle

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Dr. Semih Sevim

Dr. Hao Ye

Dr. Carlos Franco

Dr. Xiangzhong Chen

Prof. Hongsoo Choi

Prof. Josep Puigmartí-Luis

Prof. Bradley Nelson

Prof. Salvador Pané

## Thanks for your kind attention

