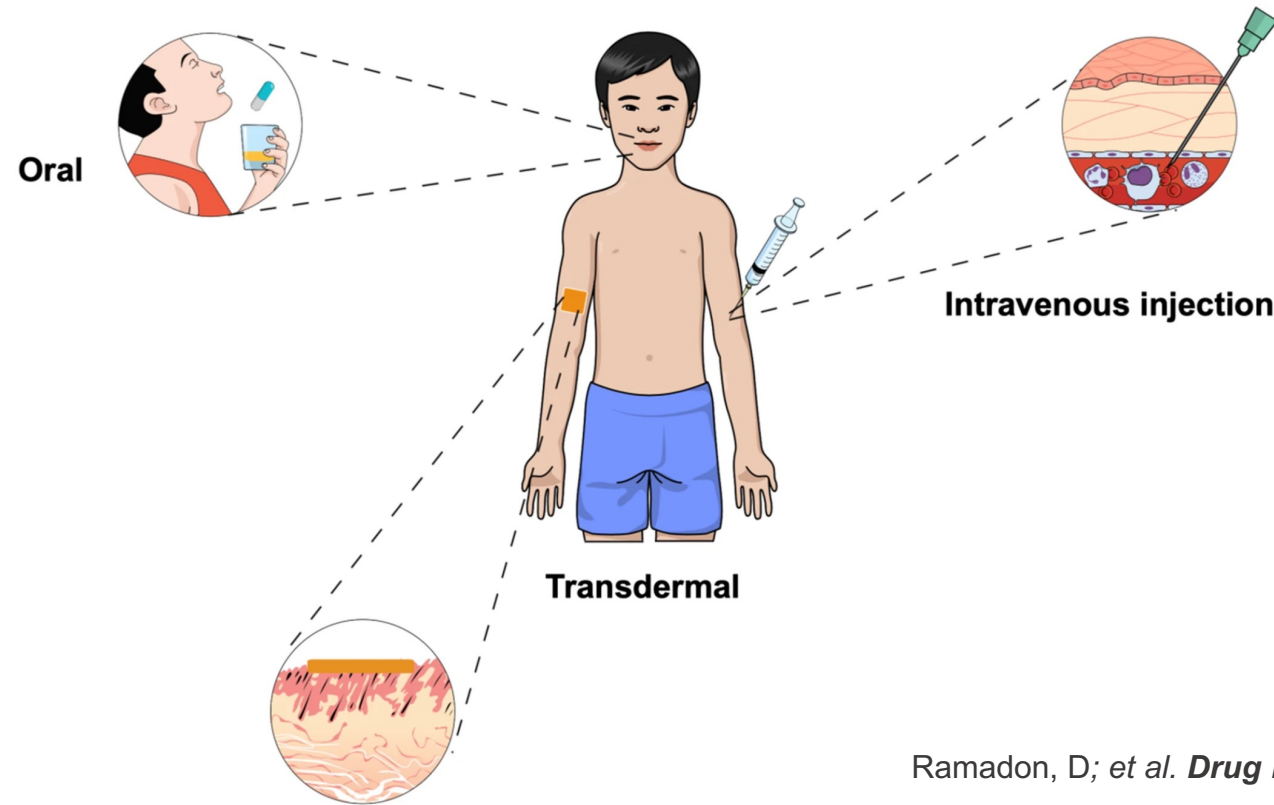


H-bonded organic frameworks as ultrasound-programmable delivery platform

Huiliang (Evan) Wang
Assistant Professor at UT Austin Biomedical
Engineering Department

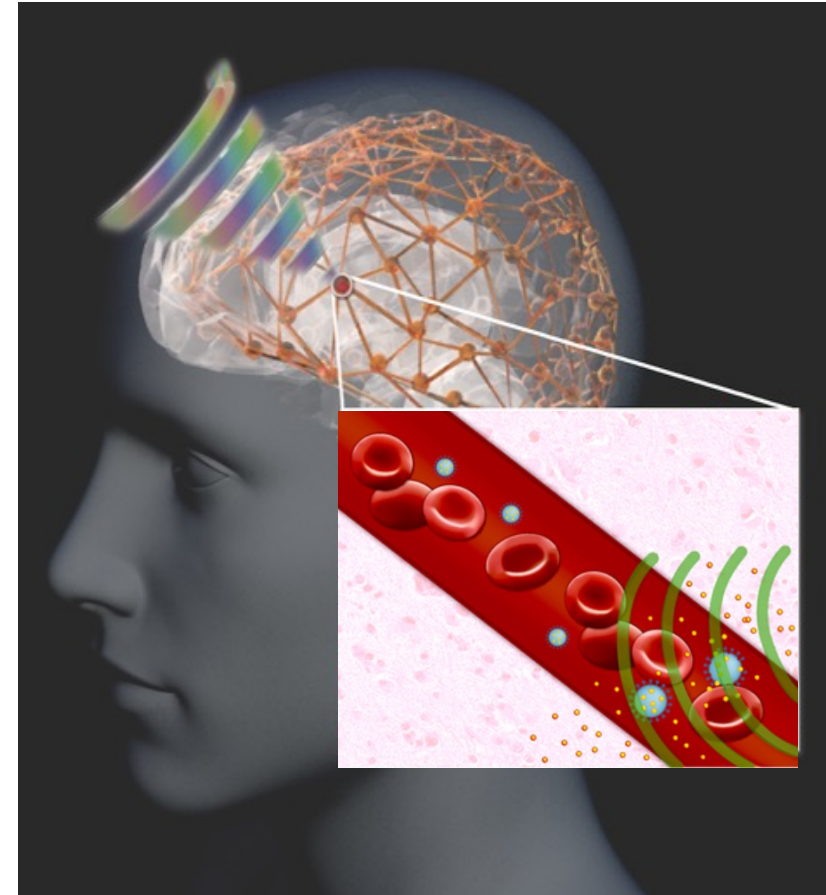
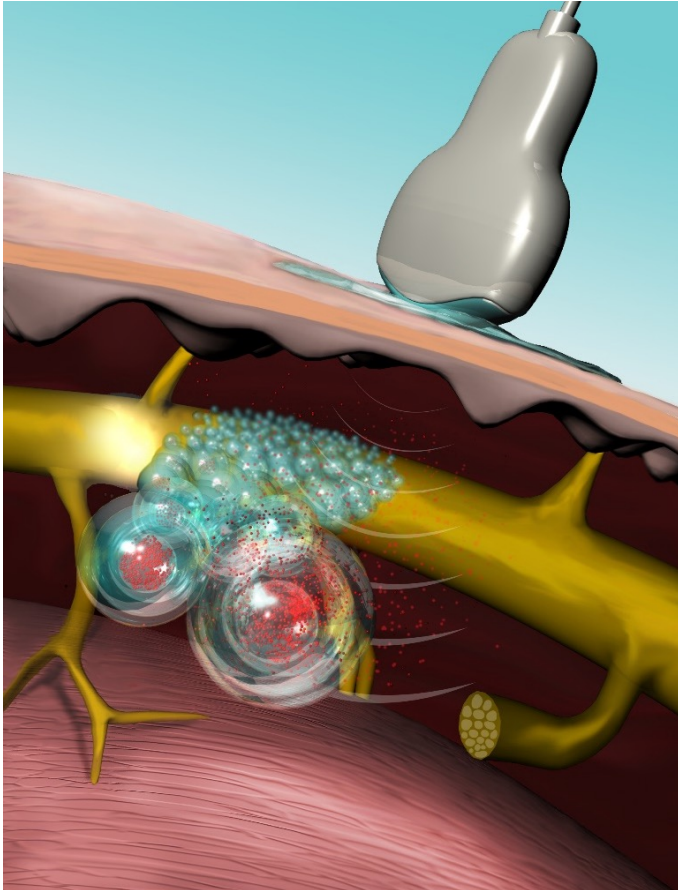
Challenges of our Current Drug Administration Methods



Ramadon, D; et al. *Drug Deliv Transl Res.* (2022)

- These drug administration methods would either lack of targeting capability (oral, intravenous) or could only target superficial areas (transdermal).
- These drug administration methods do not allow precisely temporal/repetitive control of drug release.

Focused Ultrasound Activated Drug Release



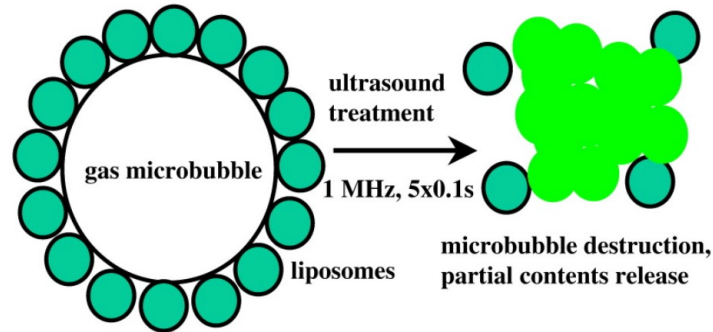
- Focused ultrasound triggered drug release can achieve spatiotemporal precision in the deep brain or body areas.

Rwei, AY; et al. **Nat Biomed Eng.** 1, 644-653, (2017)

Airan, RD; et al. **Neuron.** 100(3):728–738, (2018)

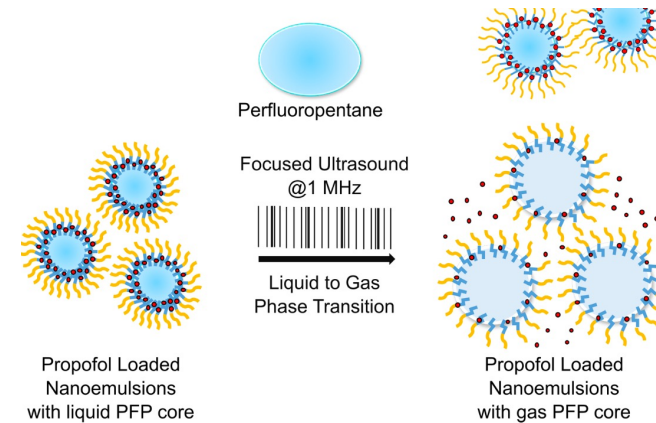
Current Ultrasound-activated Drug Release Methods and Challenges

A. Gas-phase microbubbles



Klibanov, AL; et al. *Control of drug release*.1, 12-17, (2010)

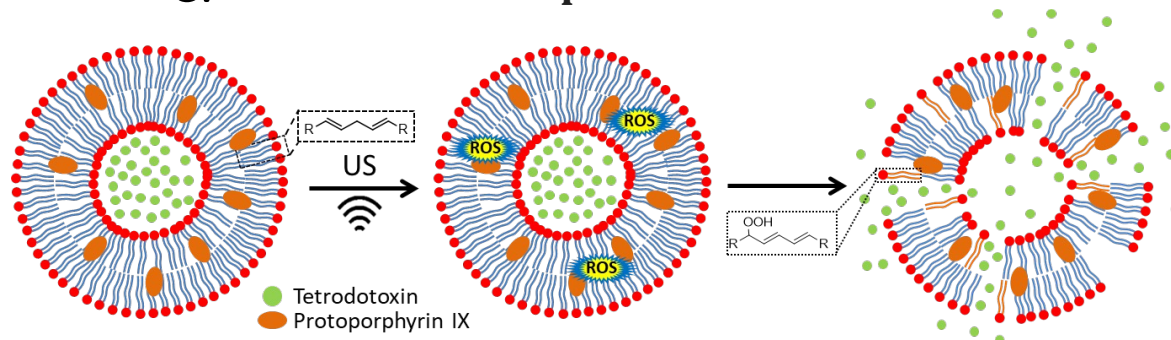
B. Liquid to gas phase change nanoemulsions



Airan, RD; et al. *Nano Let.* 17, 2, 652–659, (2017)

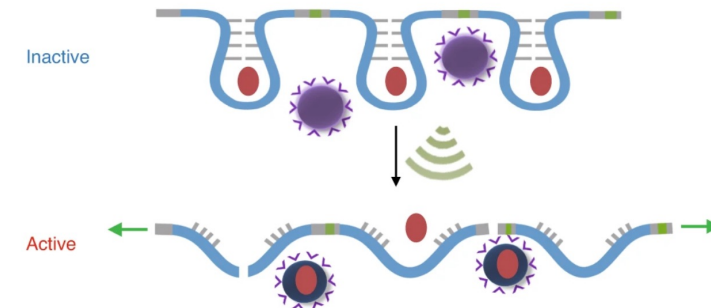
Airan, RD; et al. *Neuron.* 100(3):728–738, (2018)

C. Sonosensitizer liposomes



Rwei, AY; et al. *Nat Biomed Eng.* 1, 644-653, (2017)

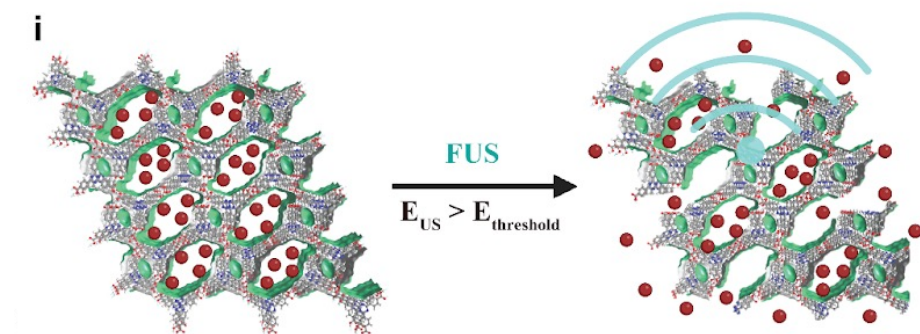
D. Multiple non-covalent H-bonds in polymer frameworks



Herrman, A et al. *Nat. Chem.*, 13, 131-139, (2021)

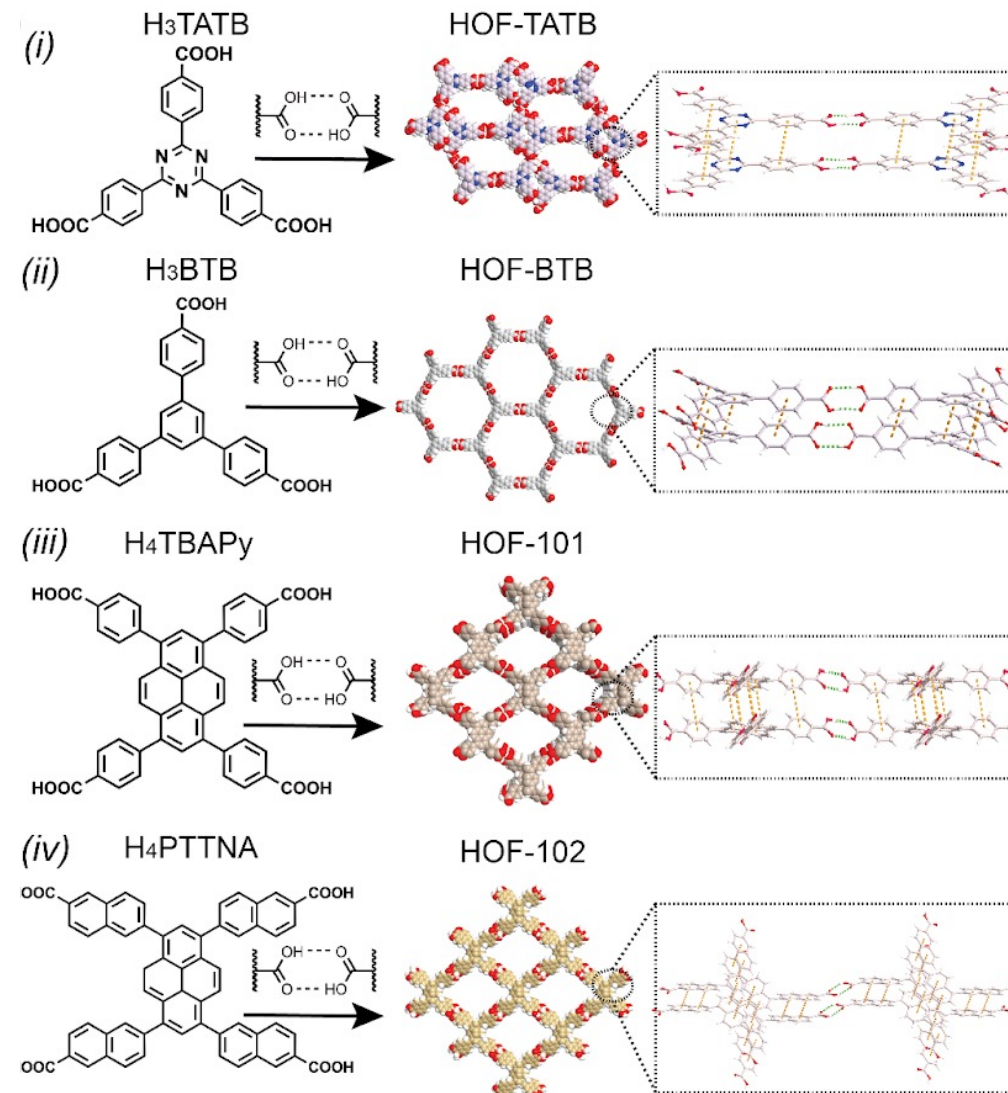
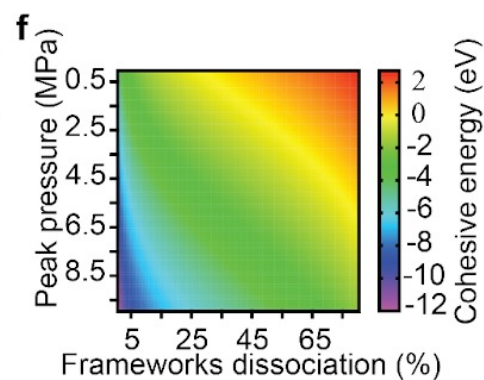
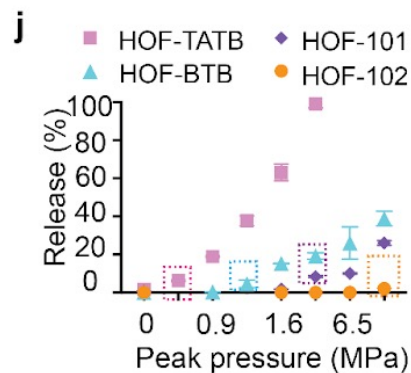
- Potential damage to the cells, stability issues, low loading capacity (A-C)
- Very high ultrasound pressure needed for drug release (D)

Ultrasound-triggered Drug Release with Hydrogen-Bounded Organic Framework (HOF) Nanoparticles



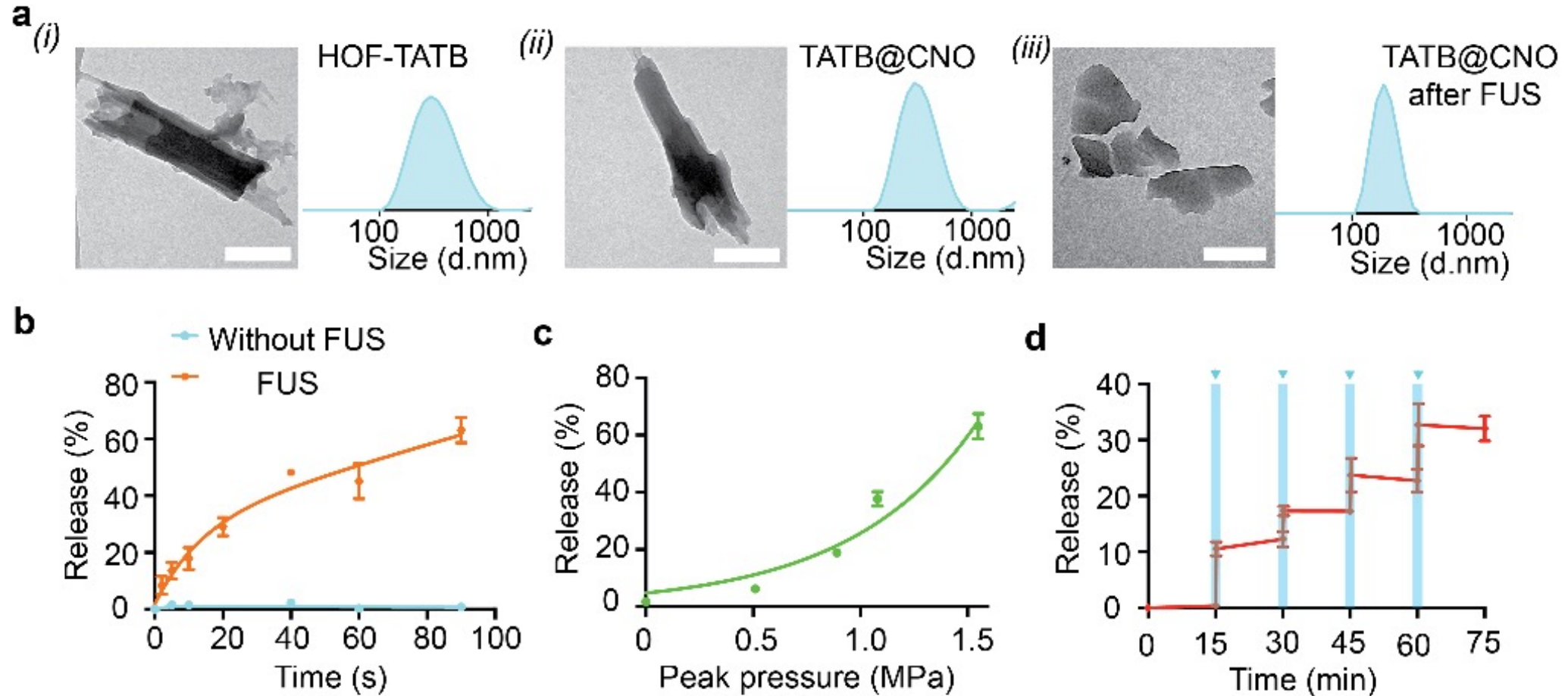
e

Cohesive energy and scission threshold of each HOFs unit				
HOFs	π - π (eV)	H-bonds (eV)	Cohesive energy (eV)	Ultrasound threshold (MPa)
HOF-TATB	-0.56	-1.65	-1.62	0.28
HOF-BTB	-0.75	-1.64	-4.10	0.50
HOF-101	-1.11	-2.22	-4.76	3.20
HOF-102	-1.11	-2.12	-9.01	7.90



Designing Hydrogen-Bounded Organic Framework (HOF) nanoparticles for ultrasound-triggered drug release

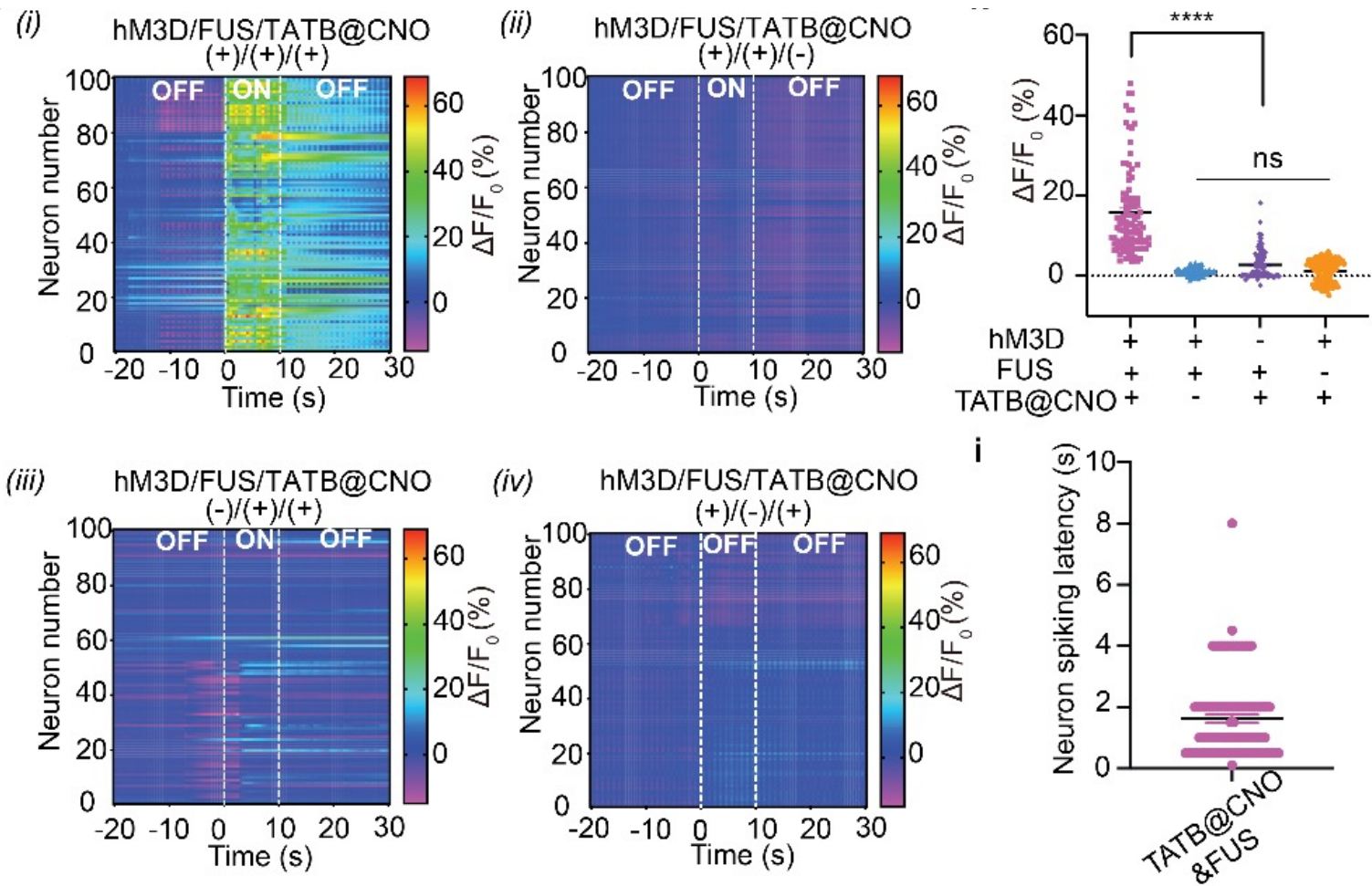
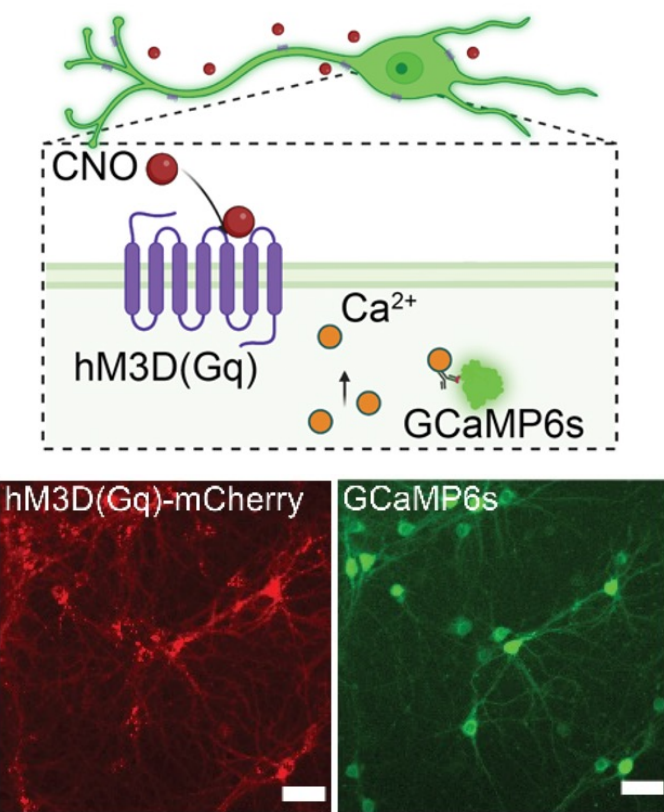
Characterizing Ultrasound-triggered Drug Release



Characterization of the size and drug release properties (threshold, repeated release) of Hydrogen-Bounded Organic Framework (HOF) Nanoparticles

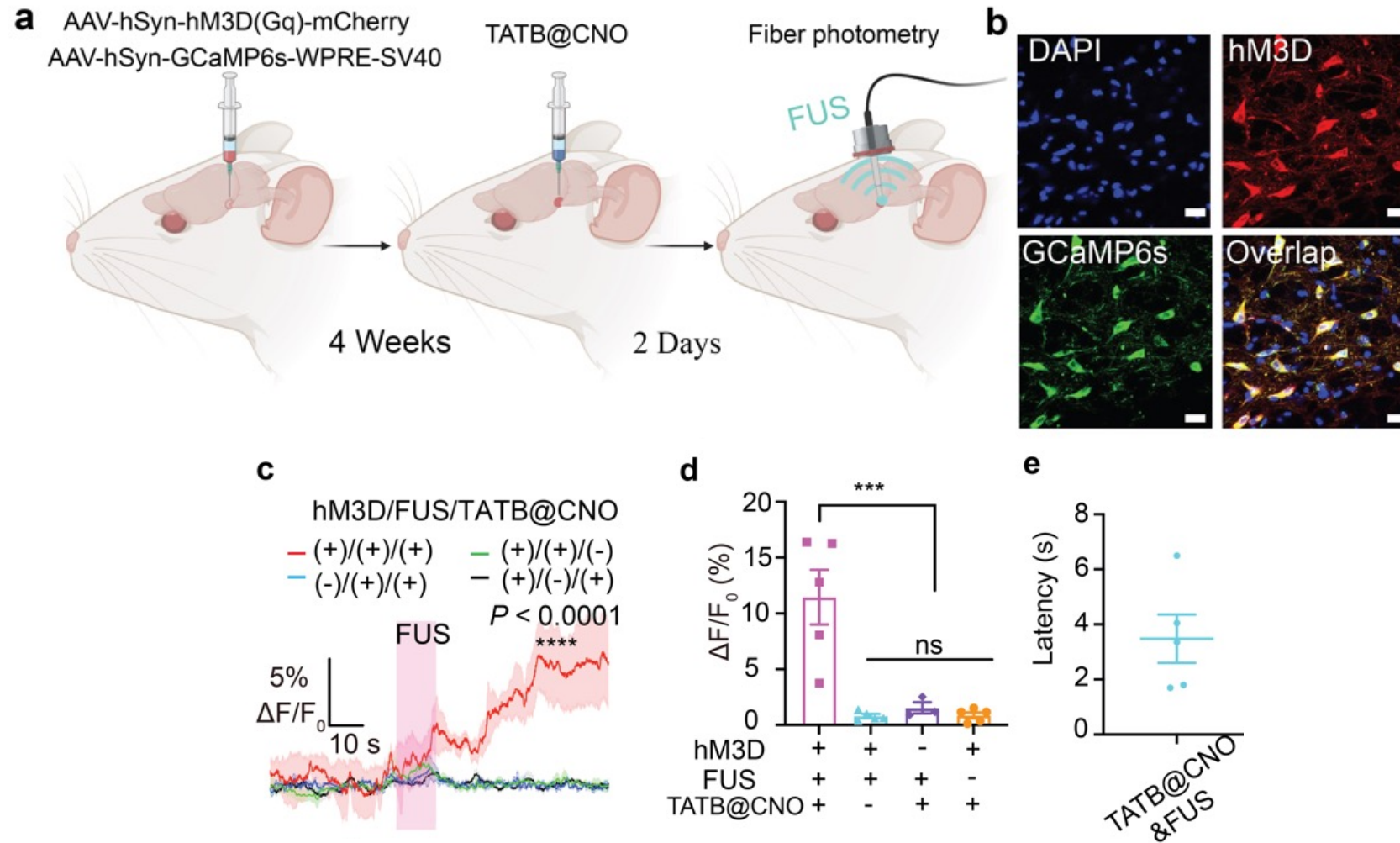
Ultrasound-triggered Drug Release for Sono-chemogenetics *in vitro*

Chemogenetics



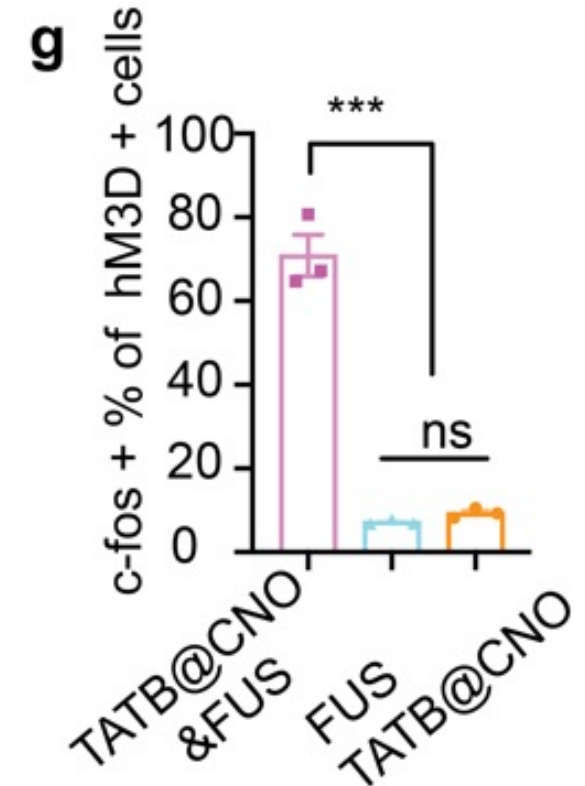
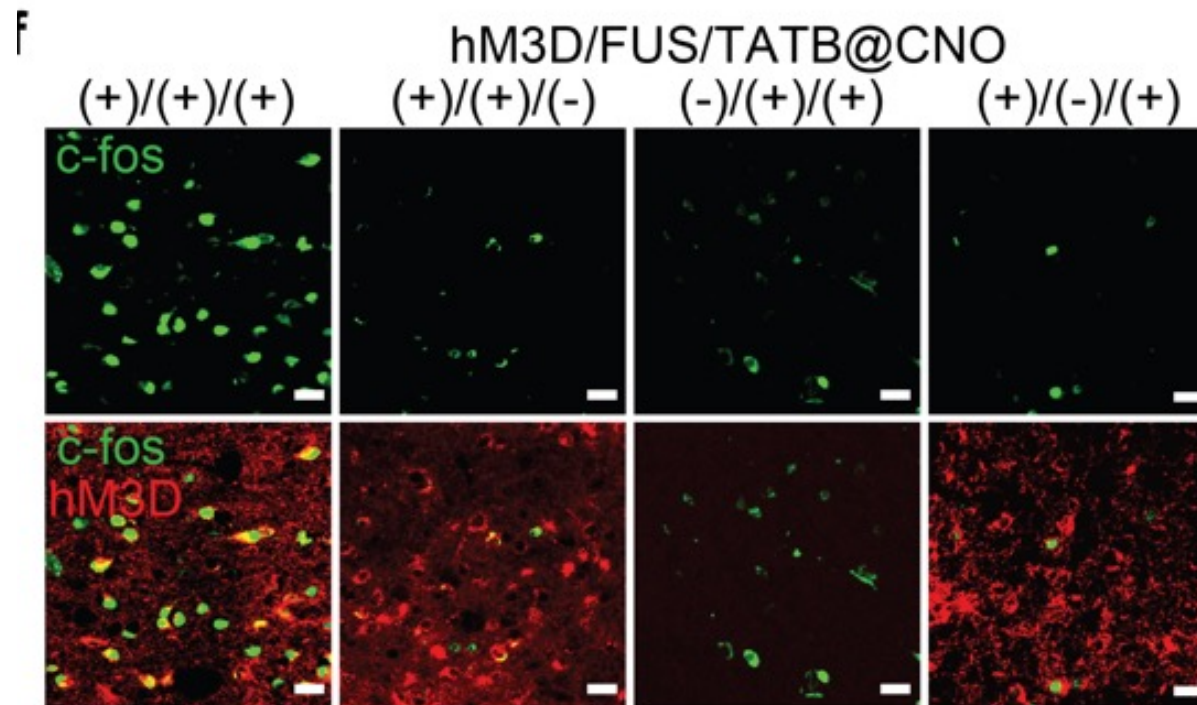
Hydrogen-Bounded Organic Framework (HOF) Nanoparticles for ultrasound-triggered drug release for Sono-chemogenetics *in vitro*

Ultrasound-triggered Drug Release for Sono-chemogenetics in Mice



Sono-Chemogenetics enabled neural activation in Ventral Tegmental Area (VTA) deep brain of mice

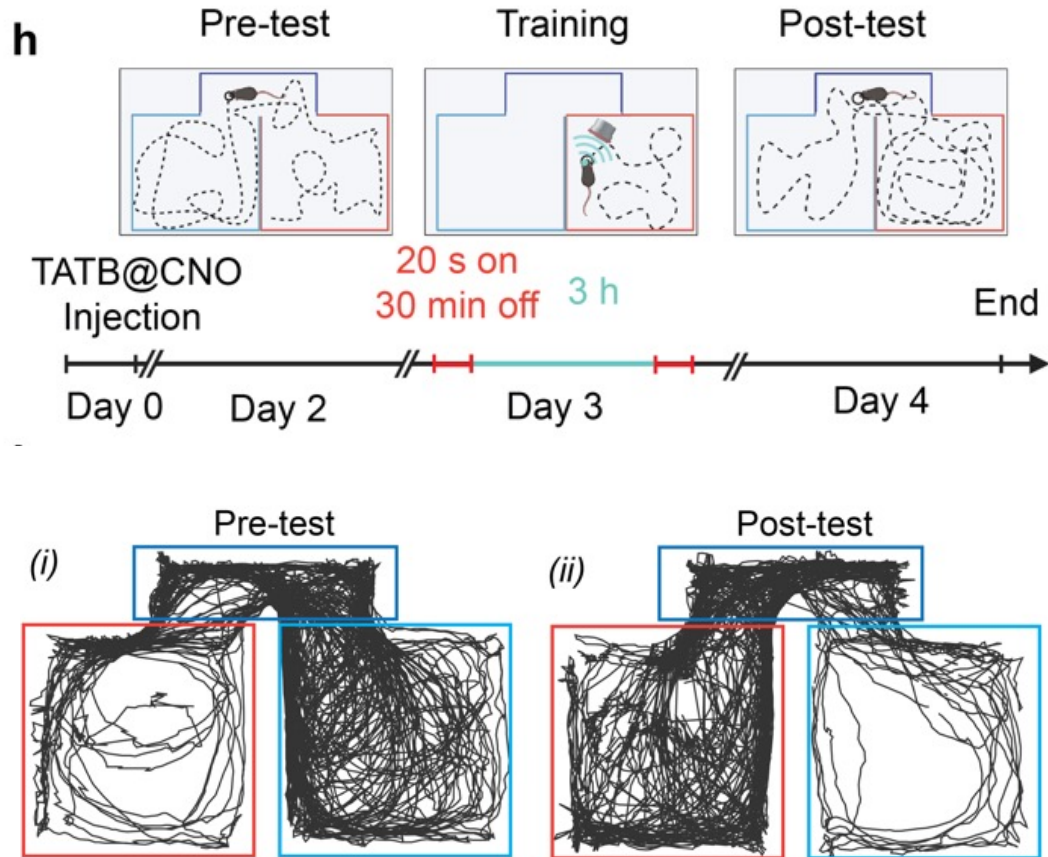
Confirming Sono-chemogenetics Neuronal activation in Mice



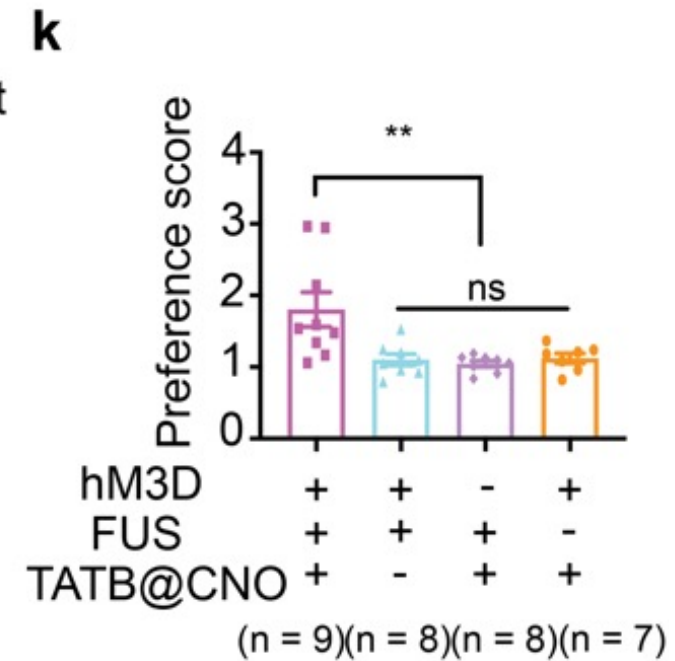
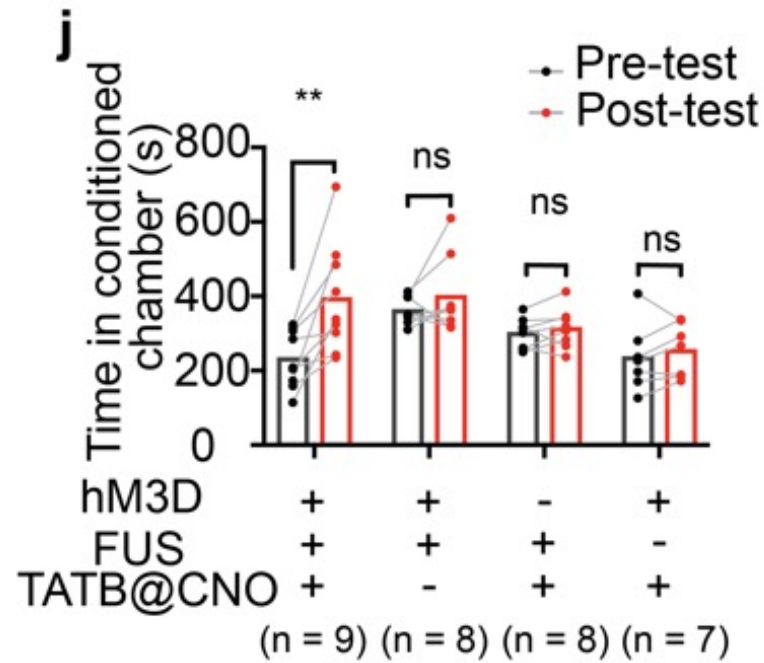
c-FOS expression observed at VTA after Sono-Chemogenetics stimulation in deep brain of mice

Sono-chemogenetics Behavior Control in Mice

- Conditioned Place Preference (CPP)

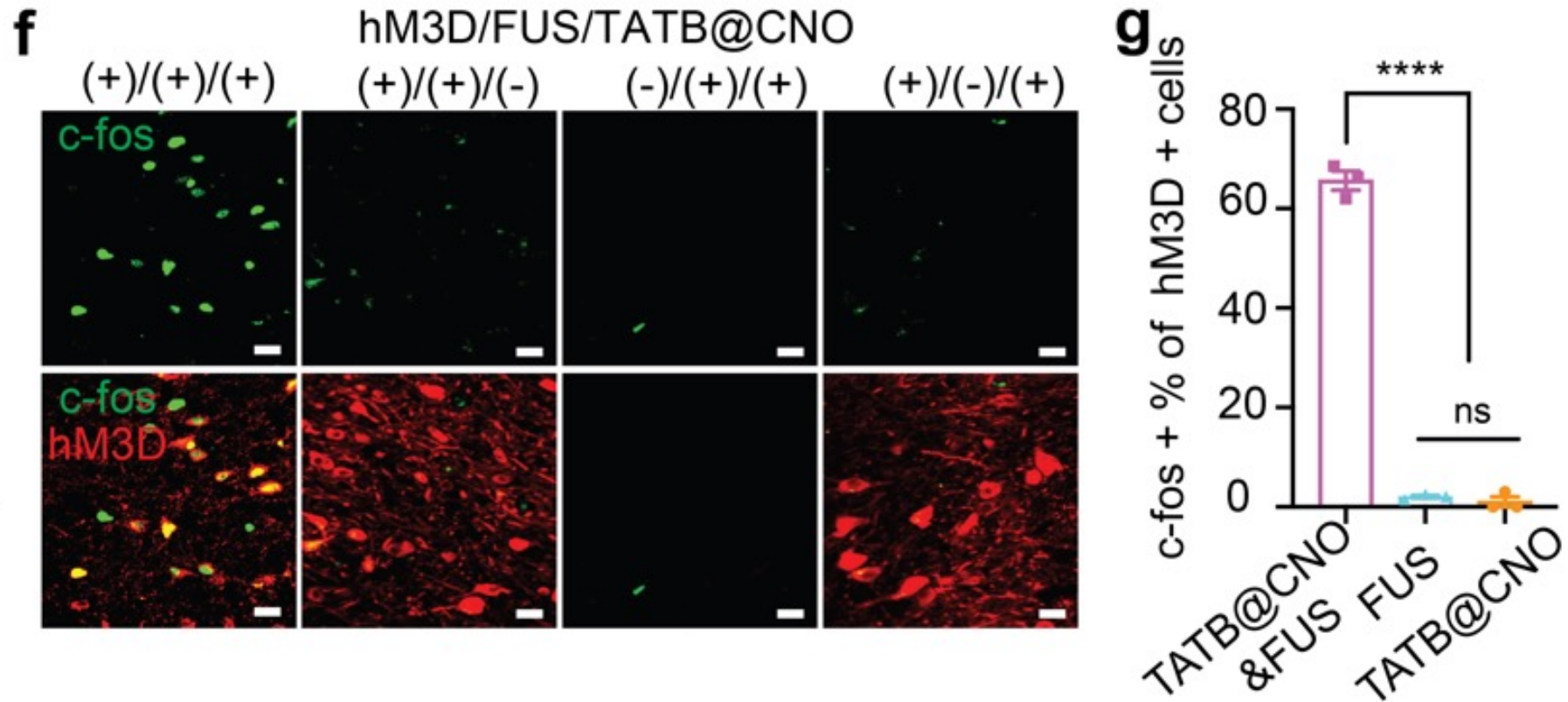


Chamber A: Conditioned chamber



Sono-Chemogenetics enabled neural activation in deep brain of mice for place preference behavior control

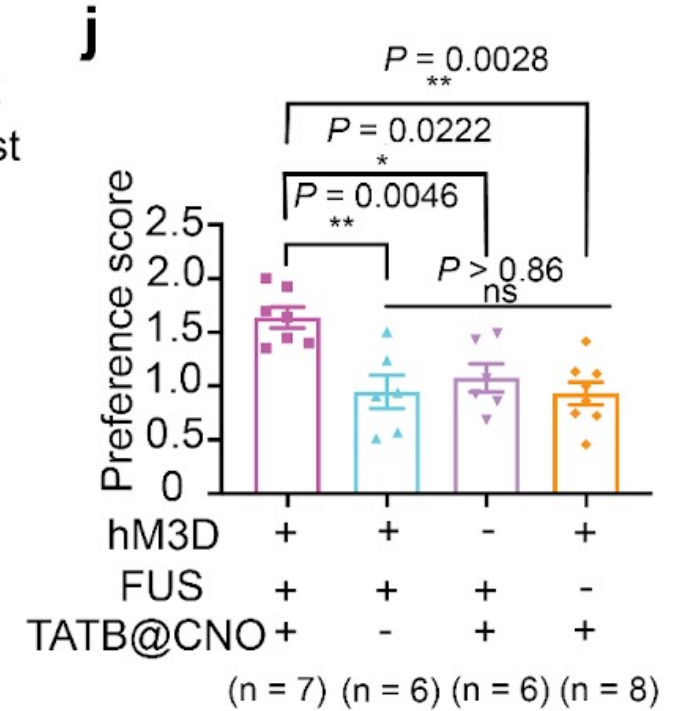
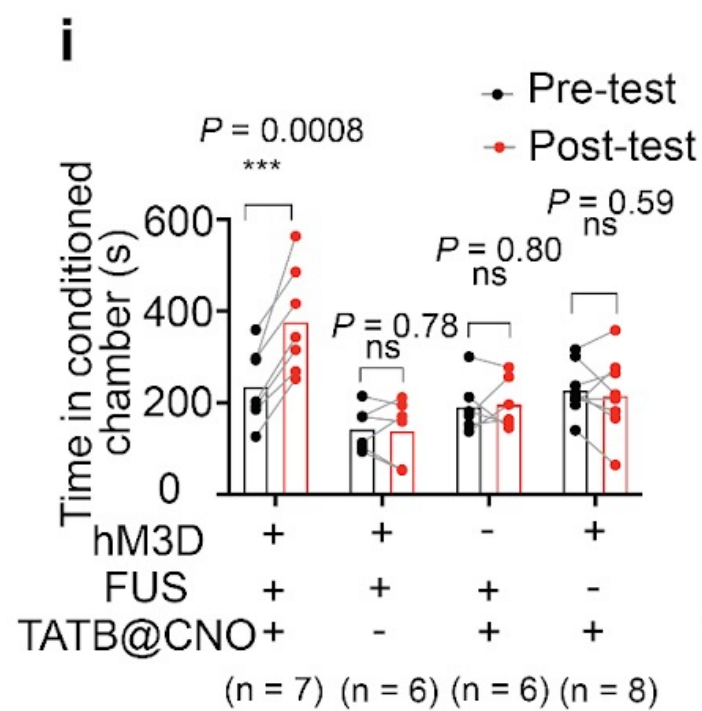
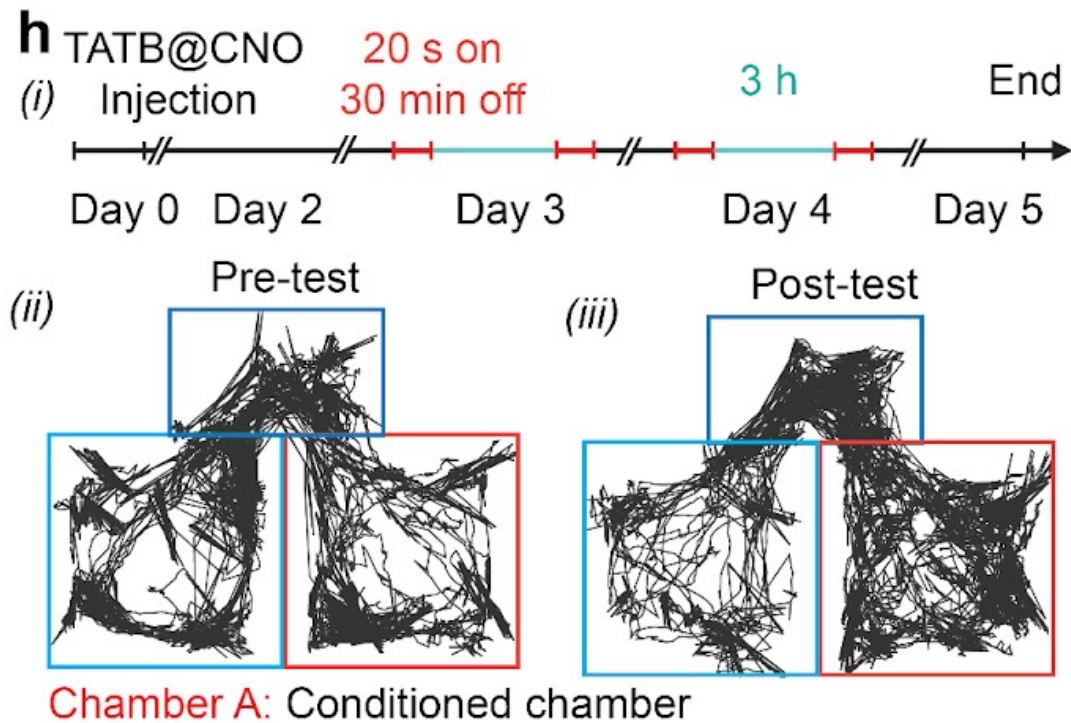
Confirming Sono-chemogenetics Neuronal activation in Rats



c-FOS expression observed at VTA after Sono-Chemogenetics stimulation in deep brain of rats

Sono-chemogenetics Behavior Control in Rats

- Conditioned Place Preference (CPP)

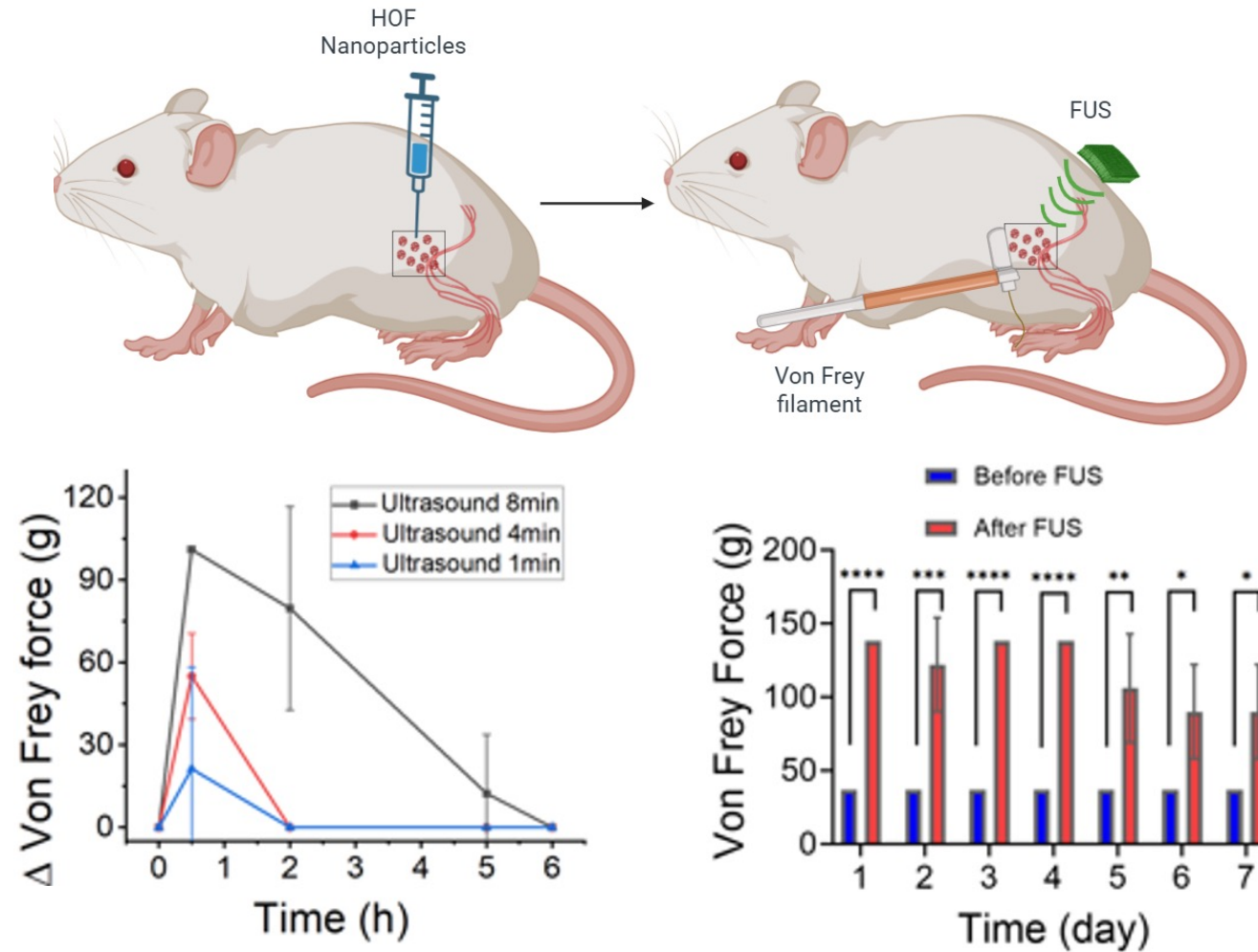


Sono-Chemogenetics enabled neural activation in deep brain of rats for place preference behavior control

Summary of this Work

- We determined that focused ultrasound enables well-defined manipulation of Hydrogen-bonded organic framework (HOFs) at the molecular level for precisely controlled release of chemicals
- We applied these HOFs based drug delivery system for non-invasive, deep brain (up to the depth of 9 mm) drug activation for modulating neural activity and animal behavior.

Ongoing work: Ultrasound-activated Local Drug Release for Local Anesthesia



unpublished

Ultrasound-triggered HOF@lidocaine drug release at sciatic nerve for increasing the pain threshold over a week

Acknowledgements



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