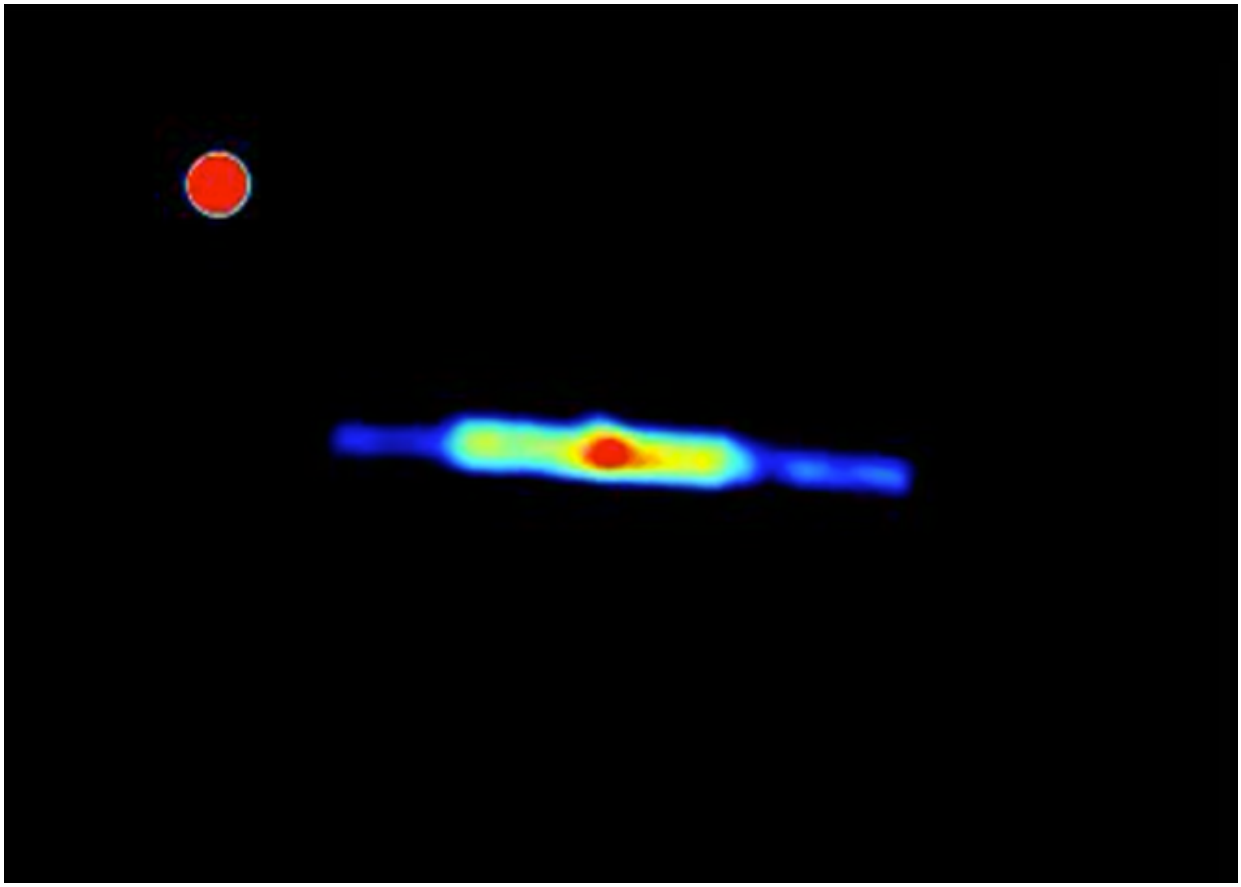
**Docket #:** S19-430

# Sono-Optogenetics: a method for non-invasive optogenetics via nanoscale light sources

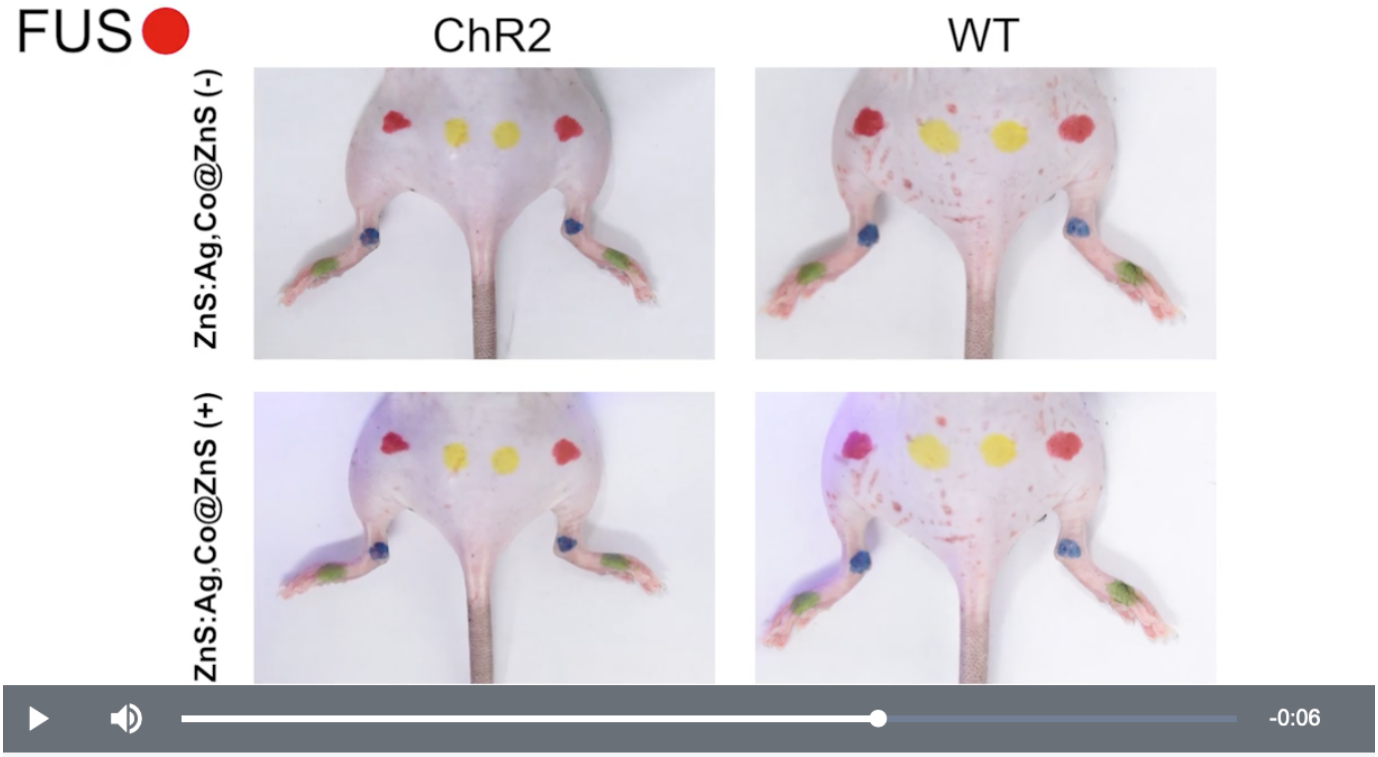
The Hong Neurotechnology Lab at Stanford University developed ultrasound-activated nanoscopic light emitters (mechanoluminescent nanoparticles) that are delivered via the blood stream, unlike conventional optogenetics approaches that require invasive fiber optic implants. After injection of nanoparticles into the bloodstream, photoexcitation light penetrating into the superficial blood vessels charges the nanoparticles circulating in the blood, and focused ultrasound activates the nanoparticles for light mission. The nanoparticles can be repeatedly charged and discharged with minimal to no loss of luminescence intensity and provide the least invasive technique for optogenetic neuromodulation and any other approaches that require the delivery of light in deep tissues, such as photodynamic therapy, photothermal therapy, and photovoltaic powering.



**FUS triggered emission of 470-nm light sonoluminogens in an artificial circulatory system.**

**Stage of Development – Proof of Concept (in vivo)**

Hong and his team demonstrated unilateral limb activation via sono-optogenetic stimulation in mice using the mechanoluminescent nanoparticles with non-invasive, brain penetrant focused ultrasound (FUS) through intact scalp and skull. There was negligible intracranial heating, and no noticeable tissue damage nor pathological lesion in organs of mice injected with mechanoluminescent nanoparticles, suggesting good biocompatibility.




**FUS triggered emission of 470-nm light in an artificial circulatory system..**

## Applications

- Optogenetics
- Photodynamic and photothermal therapy
- Photovoltaic powering of implantable devices
- Any application that needs a "light source" deep in the body

## Advantages

- Non-invasive – eliminates the need for surgical delivery of optical fiber or LED light source.
- Deeper penetration (a few centimeters) in biological tissues including the brain, compared to standard light sources used in optogenetics (0.2 millimeters).
- "Rechargeable" - by photoexcitation light in superficial blood vessels during circulation and turned on by focused ultrasound to emit light in the broadly defined optical spectrum (400-1700 nm) repetitively in the intact tissues for

optogenetic stimulation and other applications that need a light source deep in the body.

## Publications


- Wu, X., Jiang, Y., Rommelfanger, N.J. et al. Tether-free photothermal deep-brain stimulation in freely behaving mice via wide-field illumination in the near-infrared-II window. *Nat. Biomed. Eng* (2022).
- Nicholas Weiler. Researchers control brain circuits from a distance using infrared light. *Wu Tsai Neurosciences Institute News* (2022).
- Wu, Xiang, Xingjun Zhu, Paul Chong, Junlang Liu, Louis N. Andre, Kyrstyn S. Ong, Kenneth Brinson et al. "Sono-optogenetics facilitated by a circulation-delivered rechargeable light source for minimally invasive optogenetics." *Proceedings of the National Academy of Sciences* 116, no. 52 (2019): 26332-26342. https://doi.org/10.1073/pnas.1914387116
- Collins, Nathan. "Engineers develop a less invasive way to study the brain." Stanford Engineering News, 16 December 2019. https://engineering.stanford.edu/magazine/article/engineers-develop-less-invasive-way-study-brain


## Patents

- Published Application: WO2021108674
- Published Application: 20220330832

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