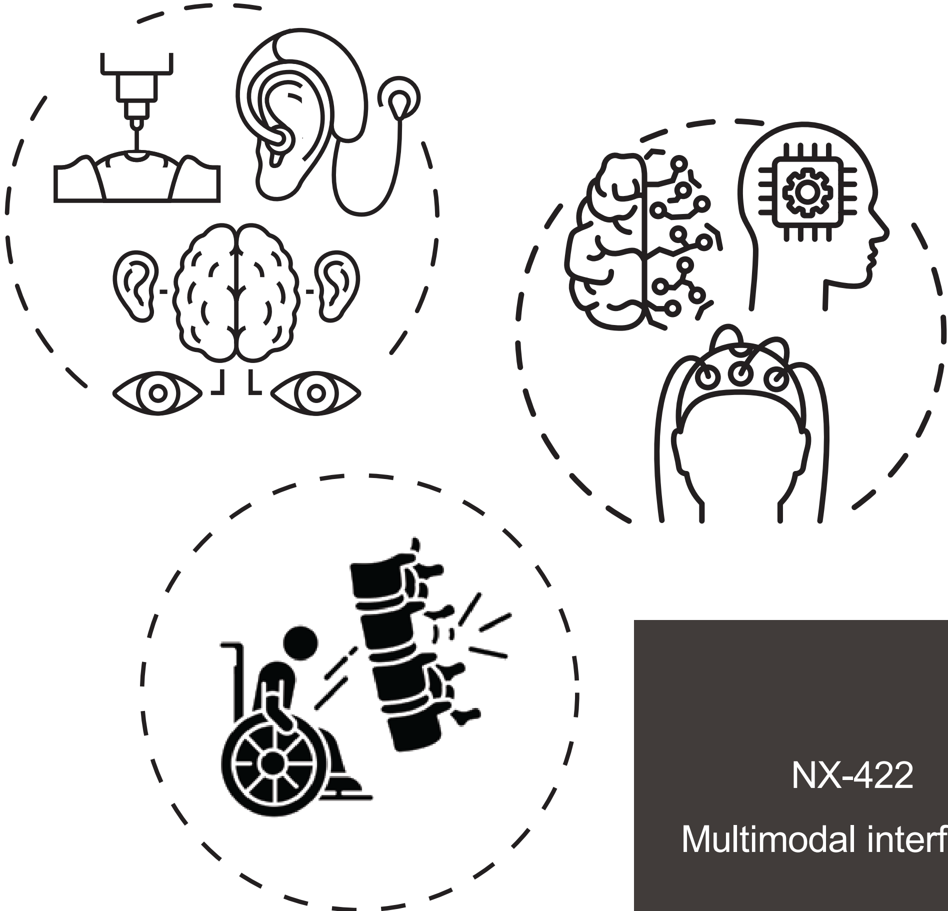


Neural Interfaces

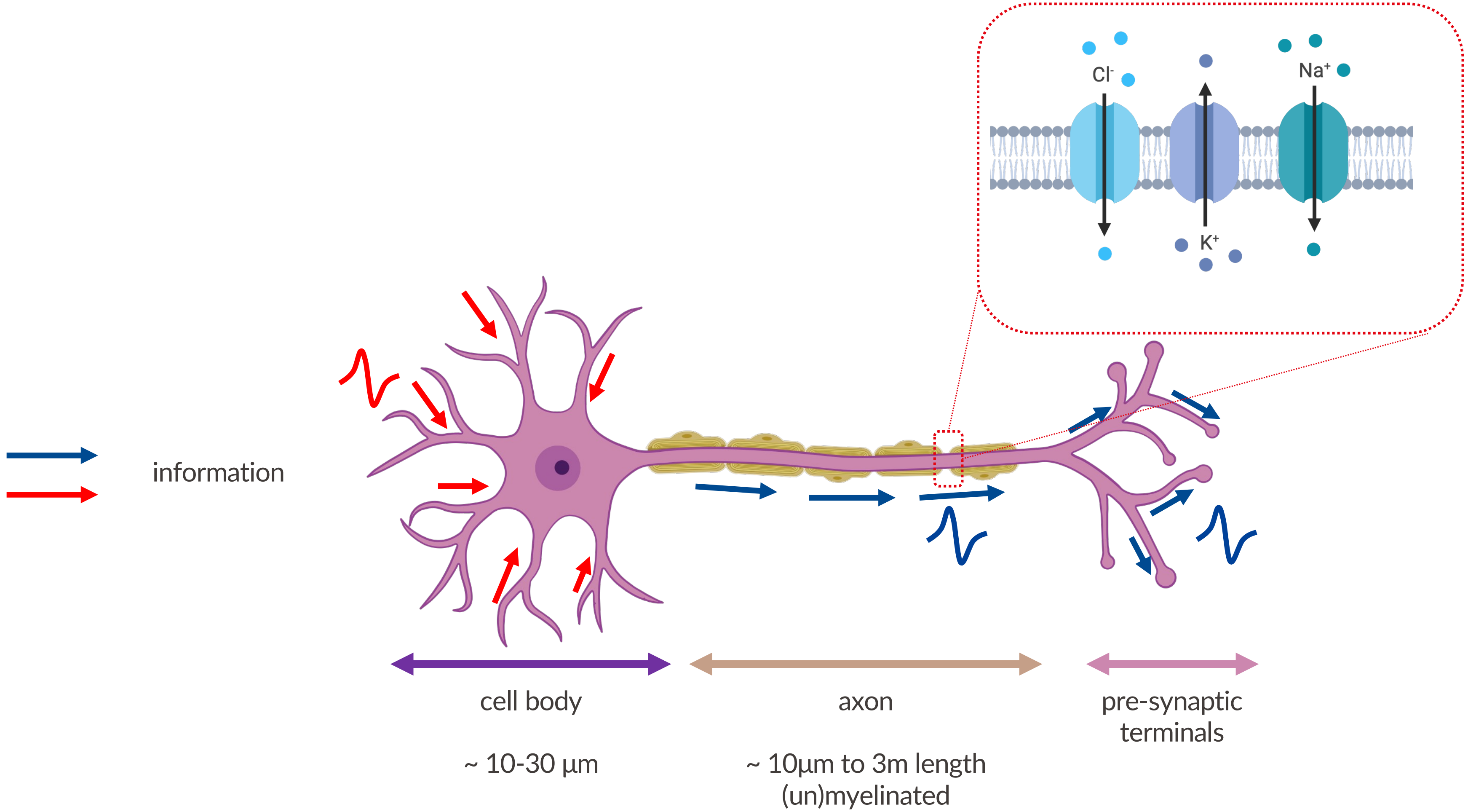
NX-422

Multimodal interfaces

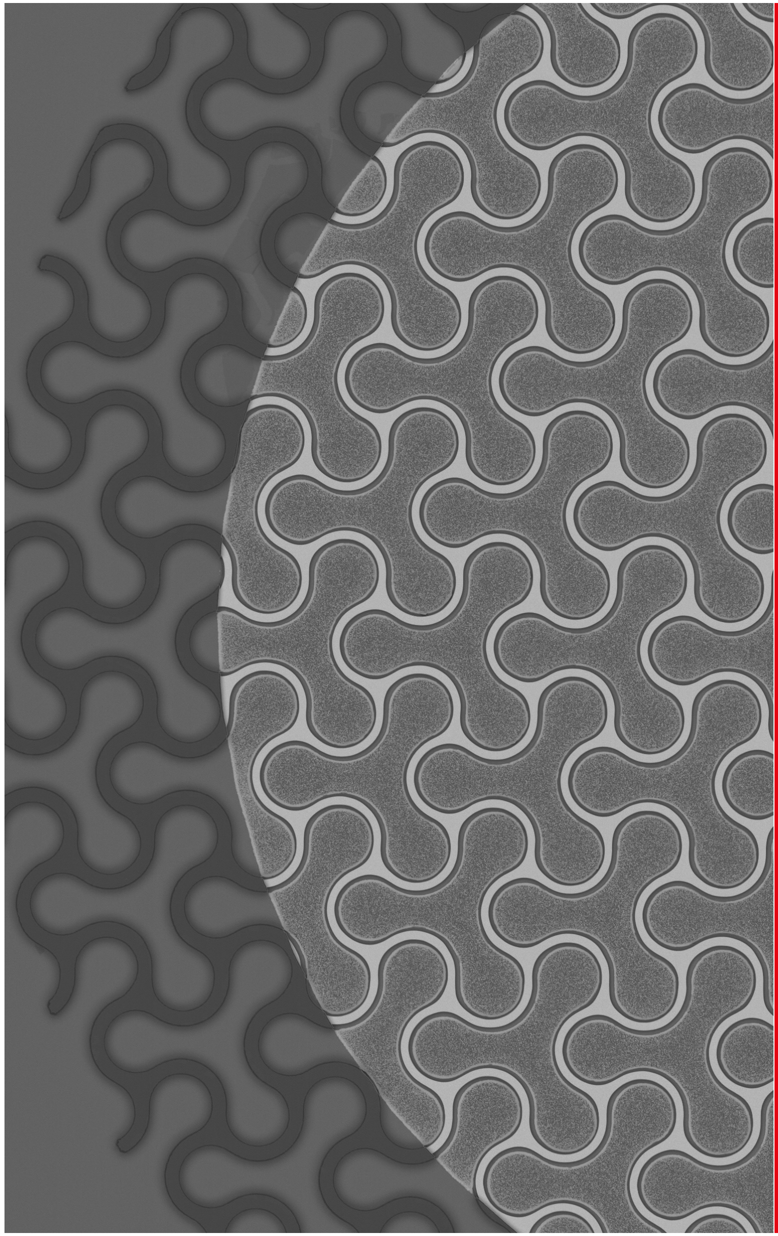
Stéphanie P. Lacour

Neuro-X Institute

The neuron



Cl-
Na+
K+
information
cell body
~ 10-30 µm
axon
~ 10µm to 3m length
(un)myelinated
pre-synaptic
terminals



Modalities of communication

Light and optogenetics

Ultrasounds

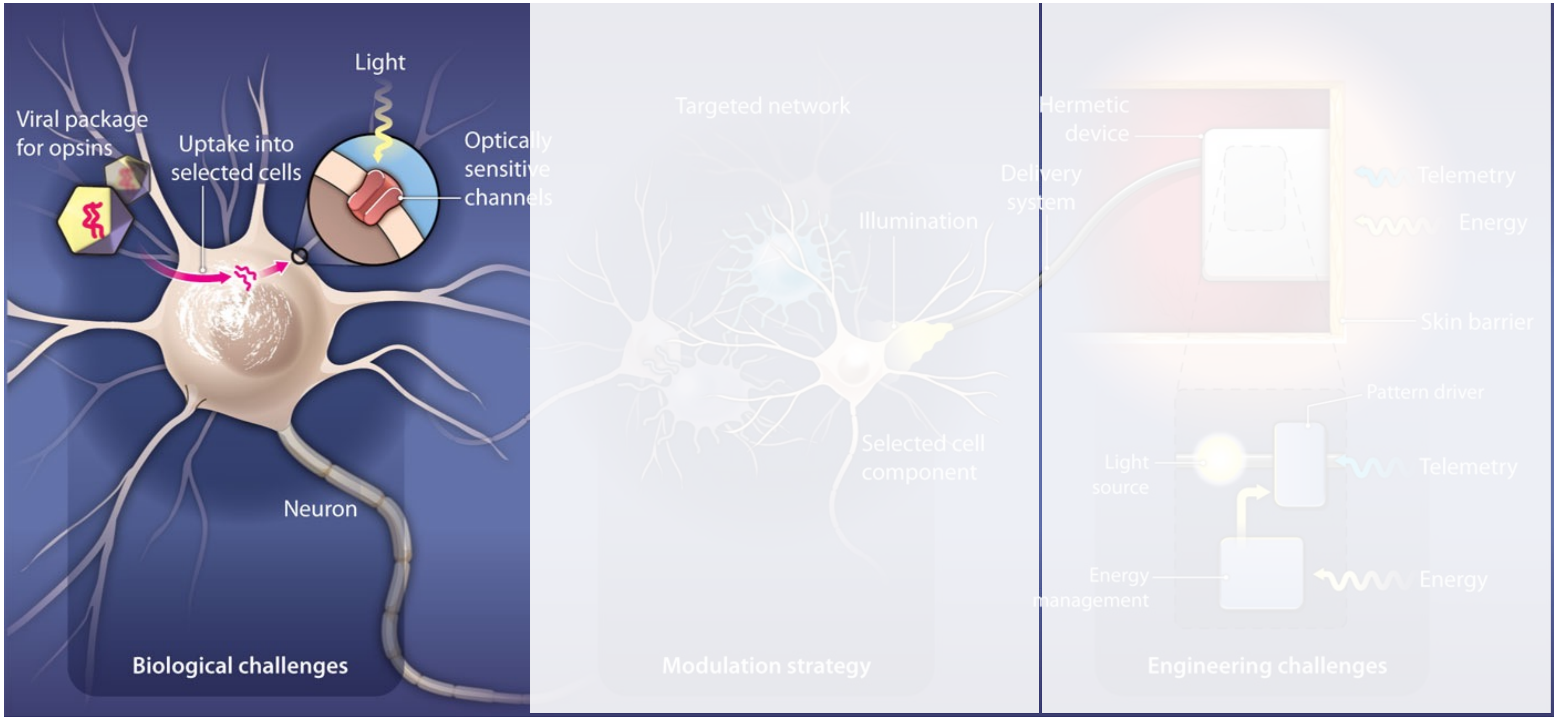
Magnetic field

Light to interrogate and modulate neural activity

[Neuronal activity is]
“an enchanted loom where millions of flashing shuttles weave a dissolving pattern.”

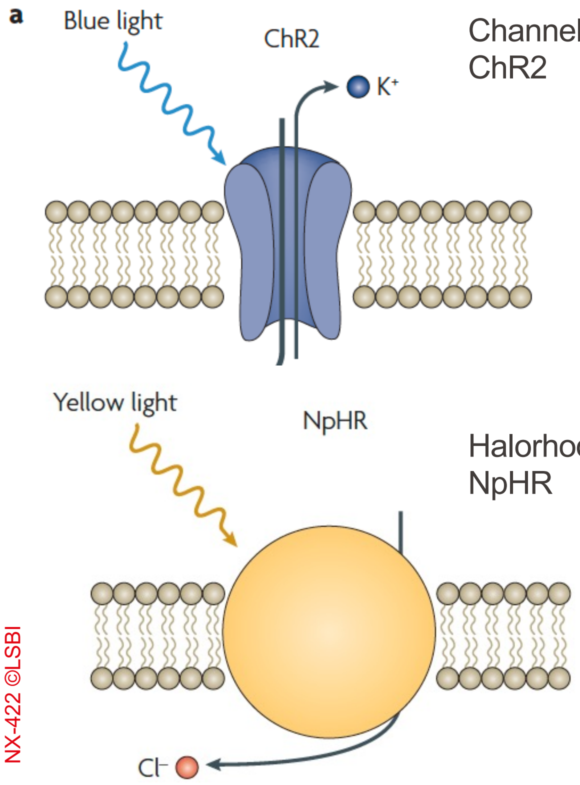
Charles S. Sherrington, 1940
English neurophysiologist
Nobel Prize, 1932

Optogenetics. Using photons to modulate neural activity



Justin C. Williams and Timothy Denison
Sci Transl Med 2013;5:177ps6

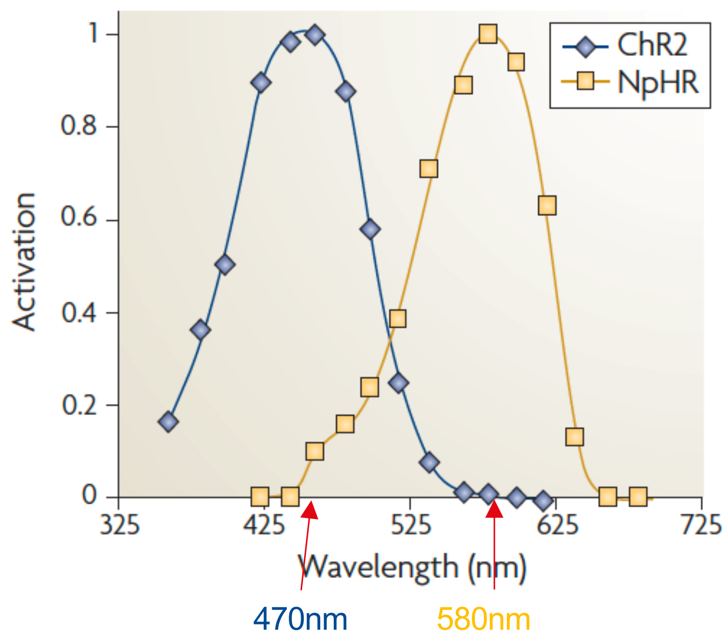
Photosensitive protein green algae



Channelrhodopsine-2
ChR2

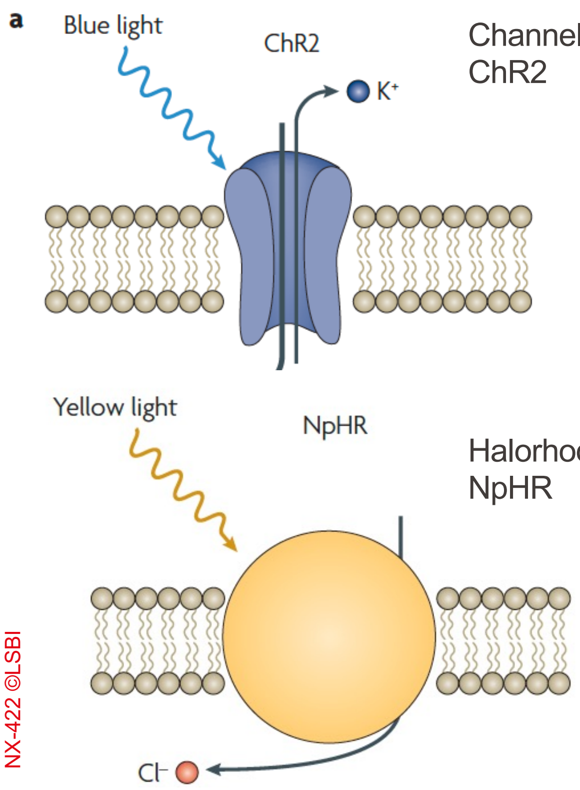
Halorhodopsine
NpHR

activation spectra



Nature Reviews|Neuroscience 2007 8 577

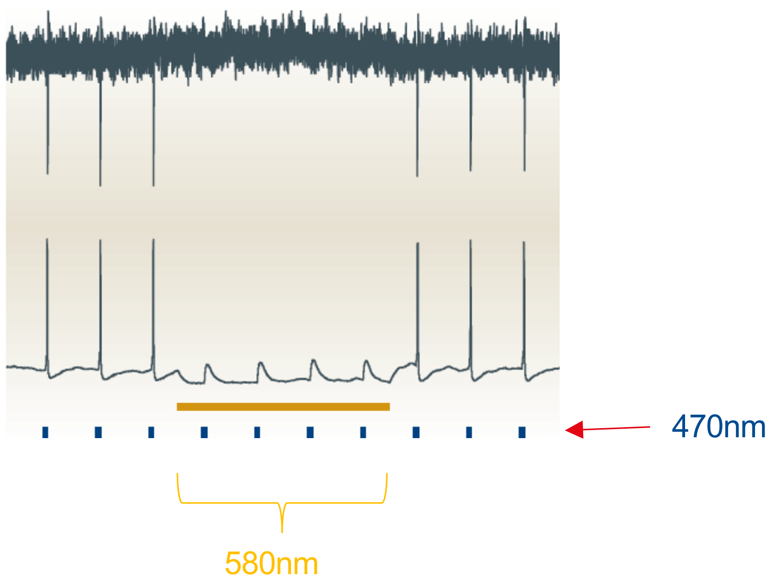
Photosensitive protein green algae



Channelrhodopsine-2
ChR2

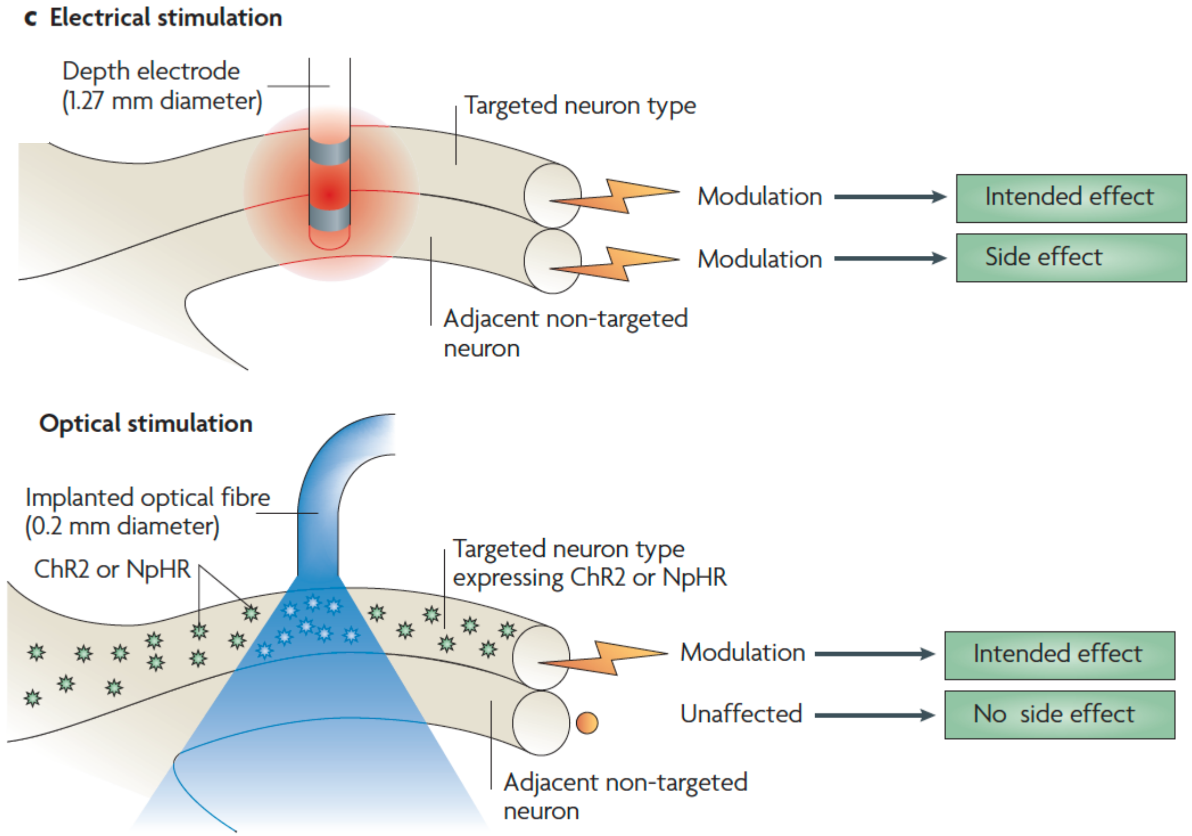
Halorhodopsine
NpHR

Activation & inhibition



Nature Reviews|Neuroscience 2007 8 577

Selectivity electrical vs optical stimulation

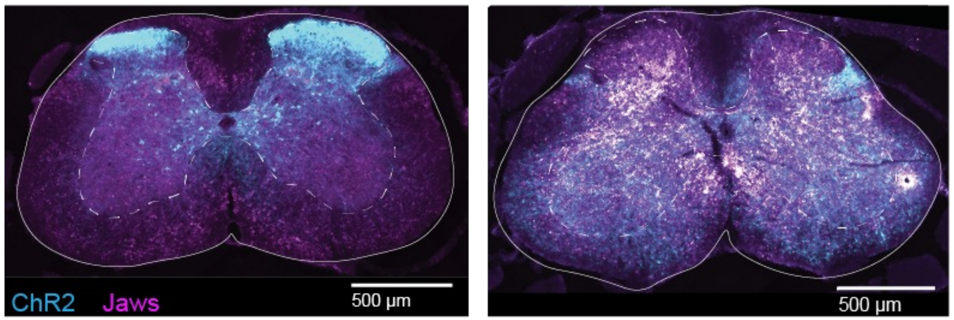


Nature Reviews|Neuroscience 2007 8 577

A unique technology

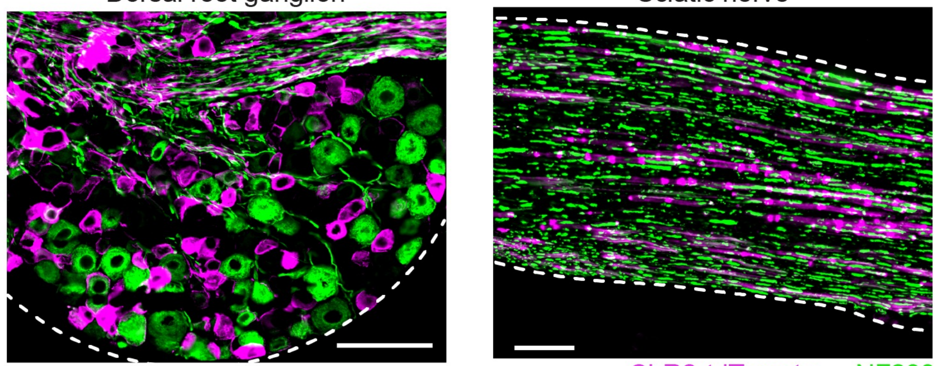
- Viral transfection
- Transgenic mice

Spinal Level L3 Spinal Level S1



Adeno-Associated Virus AAV

Dorsal root ganglion Sciatic nerve



ChR2-tdTomato NF200

Nature Biotechnology 2020
Nature Biotechnology 2021

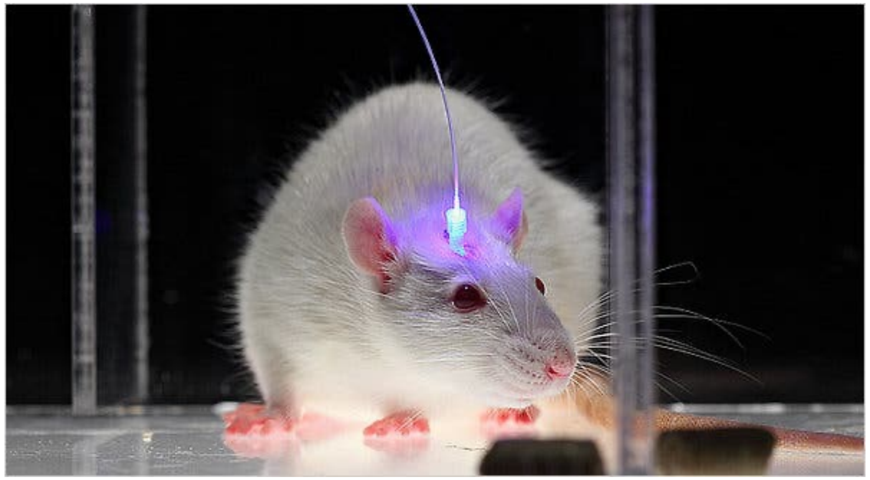
Guiding light near the neurons

- Optic fiber

\+

silica fiber
250 – 1200 nm
(UV to visible)

ceramic ferrule

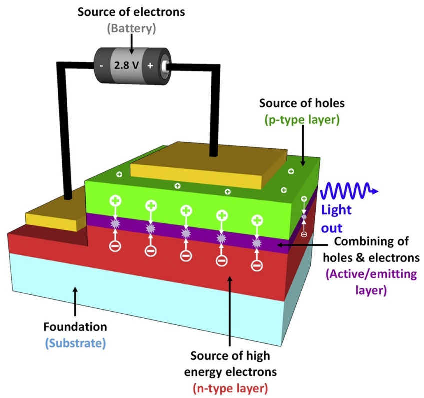


New York Times, May 16, 2011

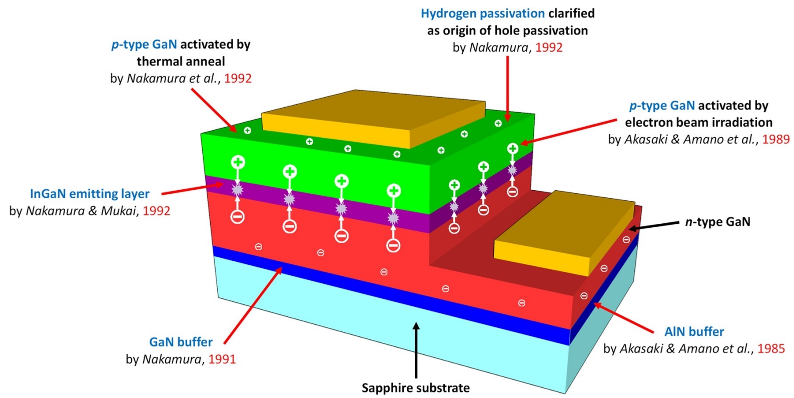
Ed Boyden, Feng Zhang …. Karl Deisseroth
Nature Neuroscience 2005 8(9) 1263-1268

Light Emitting Diodes
LEDs

2014 Nobel Prize in Physics
I. Akasaki, I. Amano, S. Nakamura
“a new light source, power efficient and sustainable, the blue LED



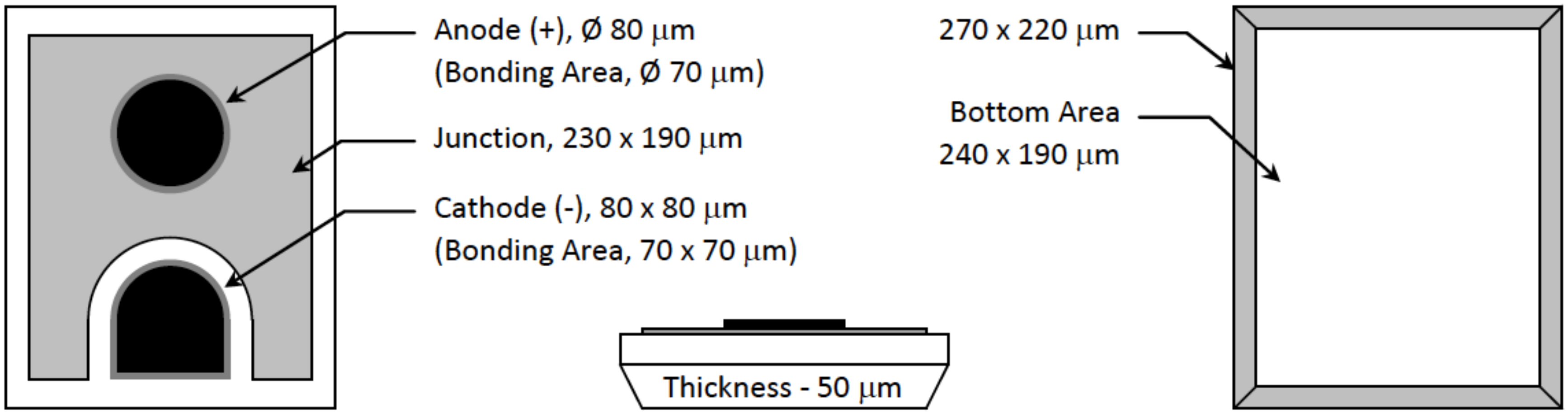
LED - heterojunction



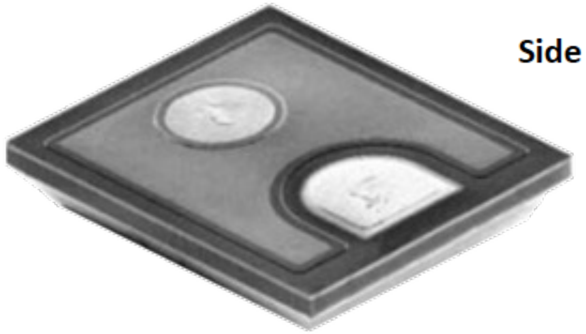
Blue LED

Comptes Rendues Physique 2018 19(3) 113-133

LED “die”

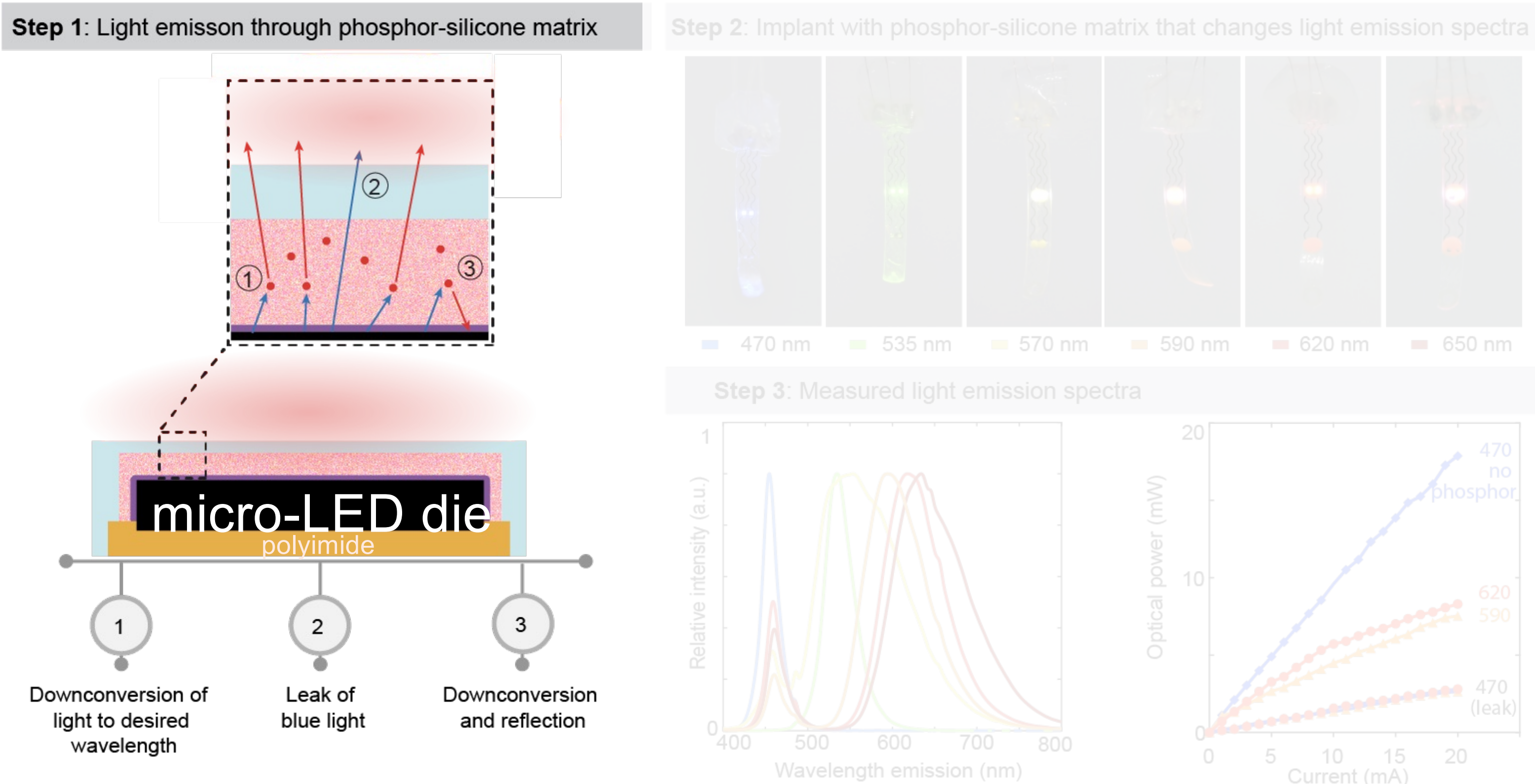


Top View **Side View** **Bottom View**



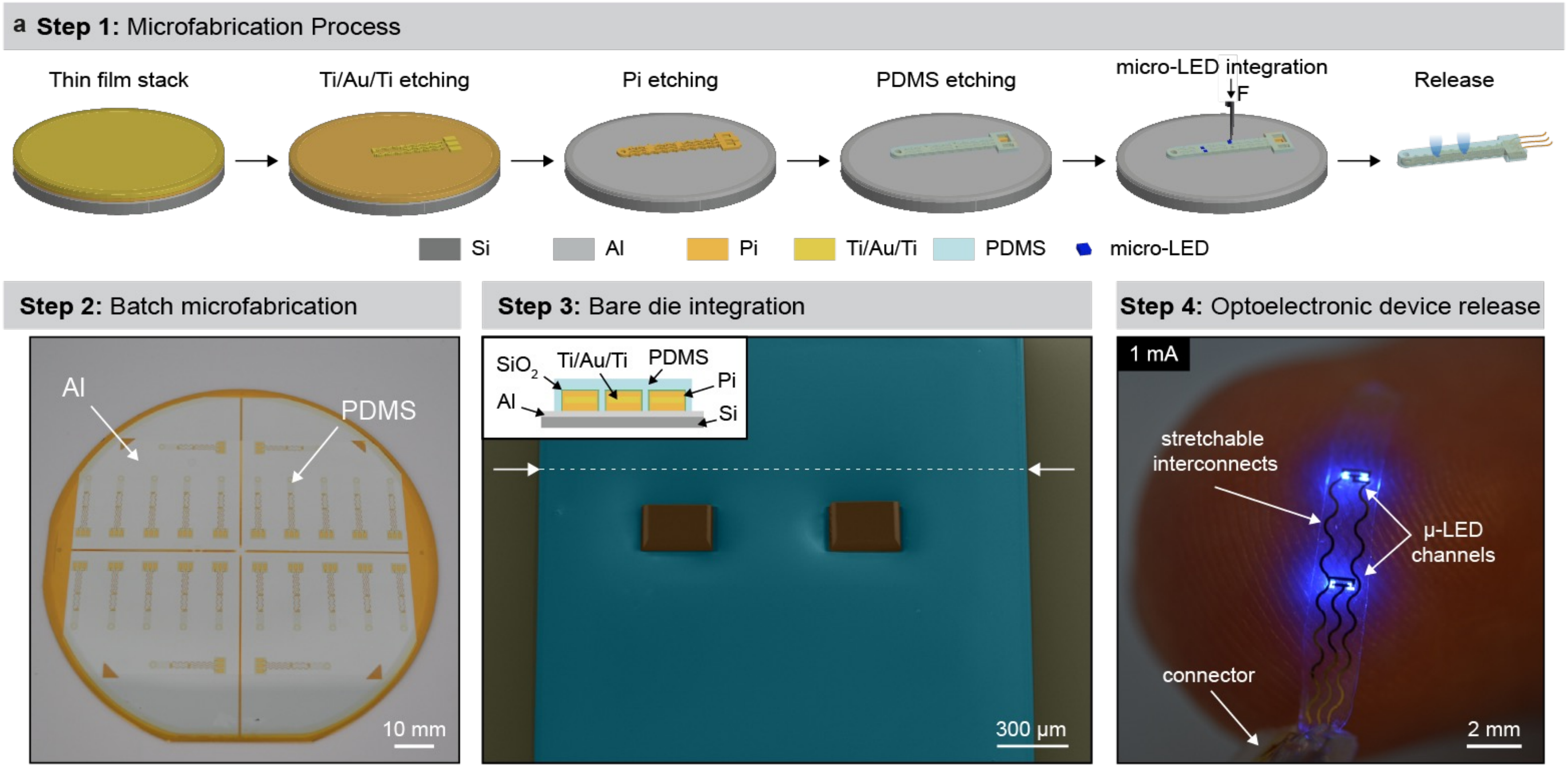
CREE InGaN LED TR2227
470nm 21mW
220x270x50 µm^3

Tailoring the wavelength



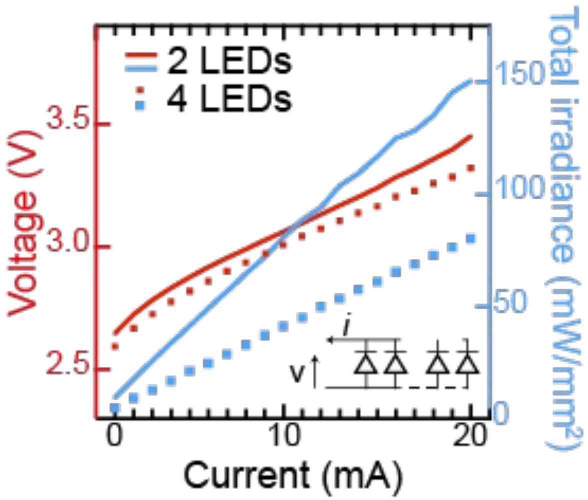
Nature Biotechnology 2020
Nature Biotechnology 2021

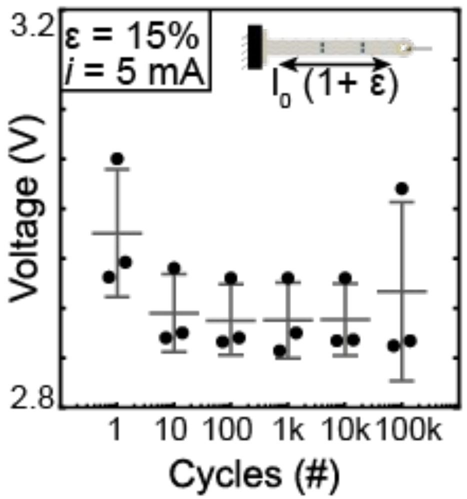
Microfabrication of an optoelectronic implant

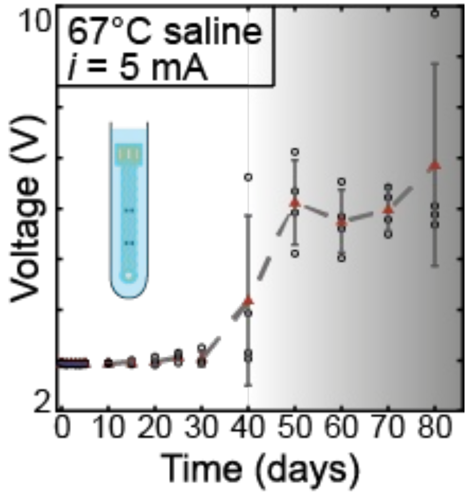


Nature Biotechnology 2020
Nature Biotechnology 2021

LED implants



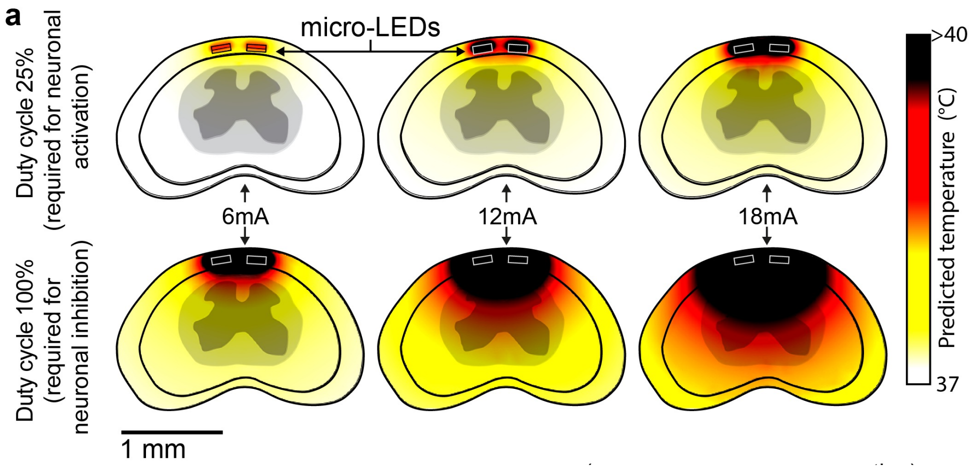


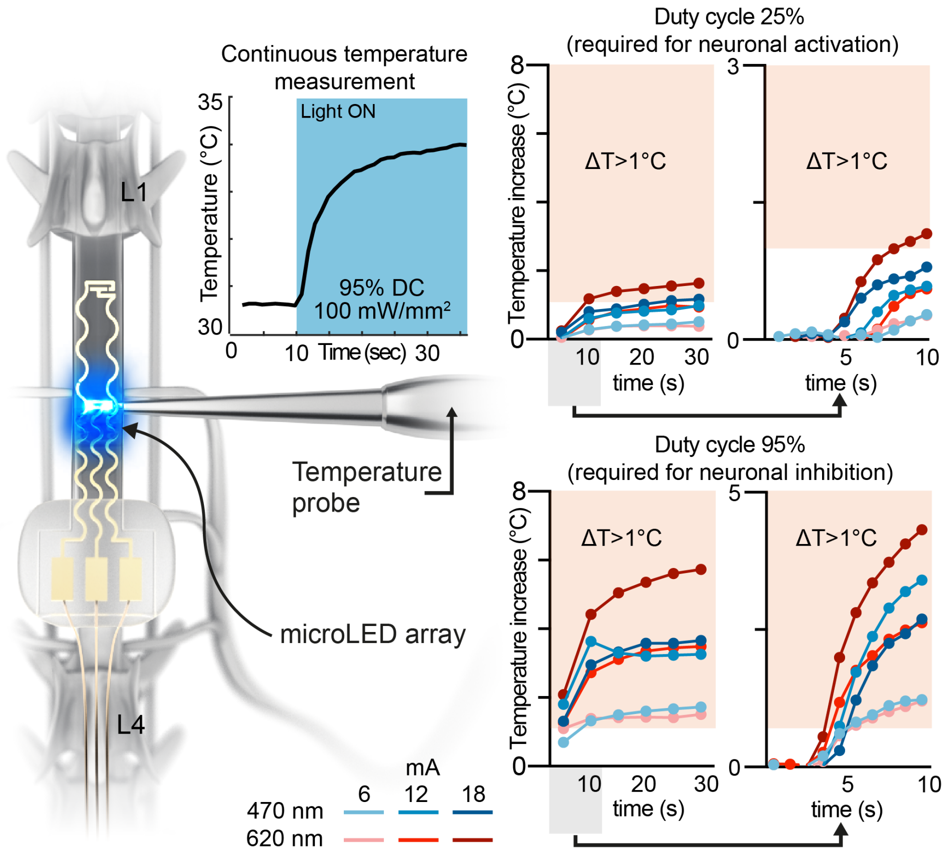


Nature Biotechnology 2020
Nature Biotechnology 2021

EPFL

Local heating!





Nature Biotechnology 2020
Nature Biotechnology 2021

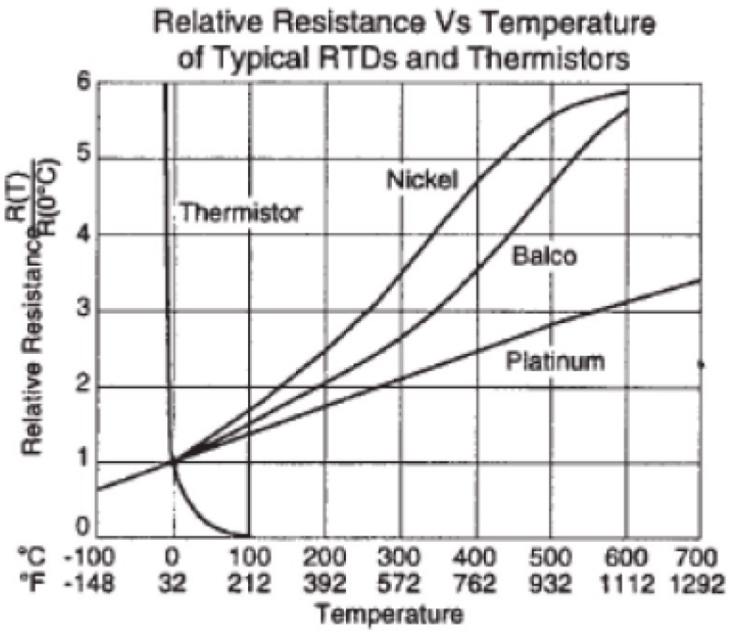
Sensing temperature

- Thin-film metallic thermistor

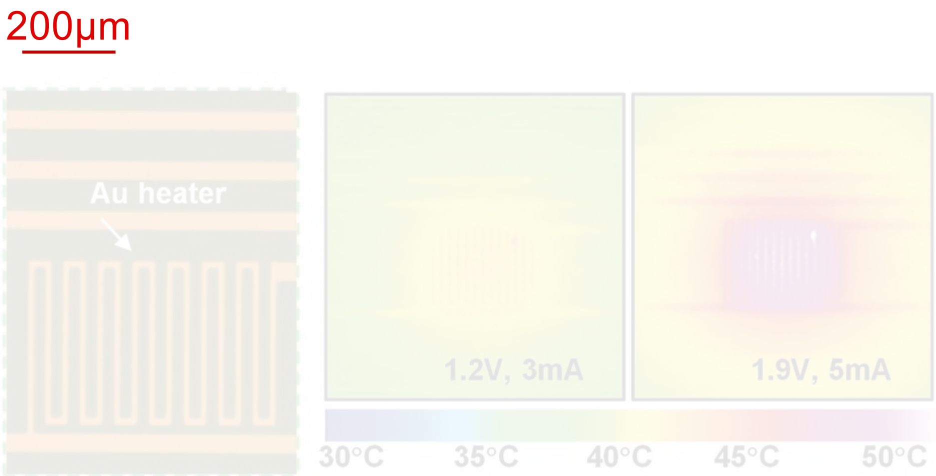
$$R = \rho \frac{L}{t\,W} \quad [\Omega]$$

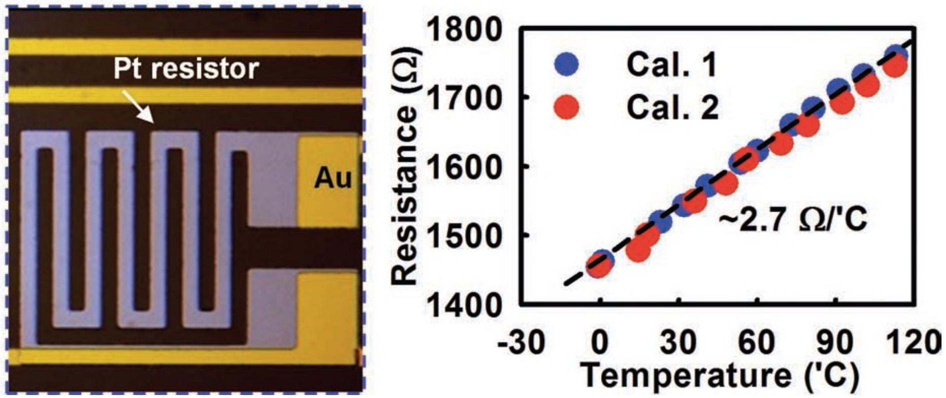
$$R(T) = R_0\ (1 + \alpha\ (T - T_0) + \beta\ (T - T_0)^2 + \ldots)$$

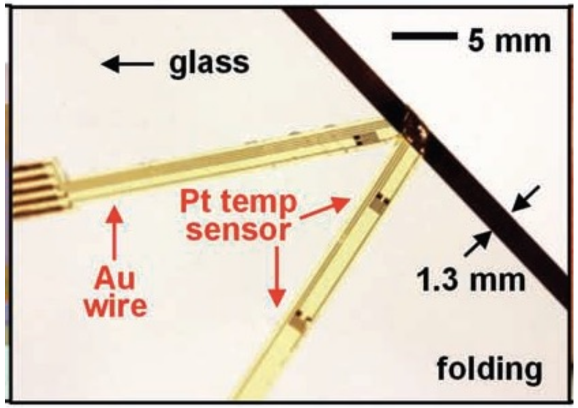
Linear approximation: $\alpha = \dfrac{R_{T1} - R_0}{\Delta T \times R_0}$

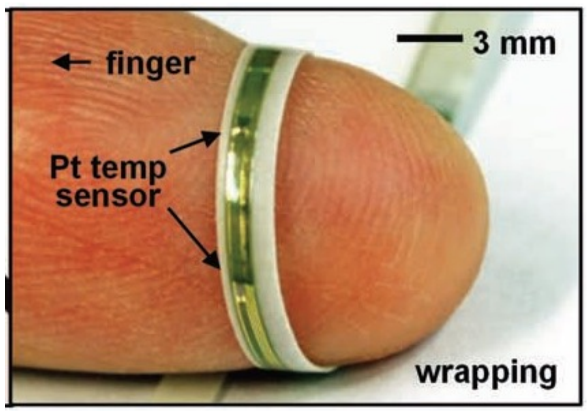


In situ temperature sensors



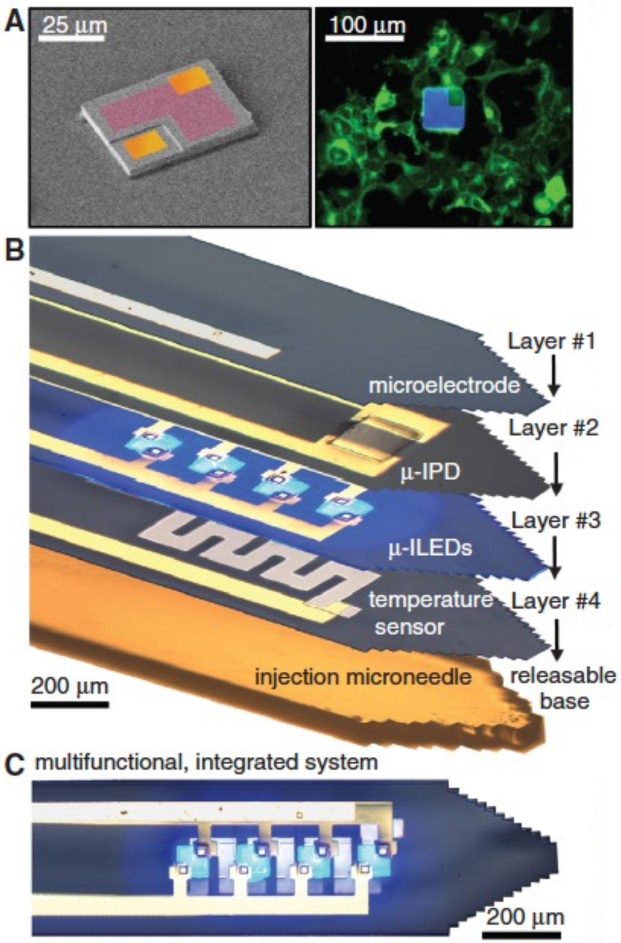


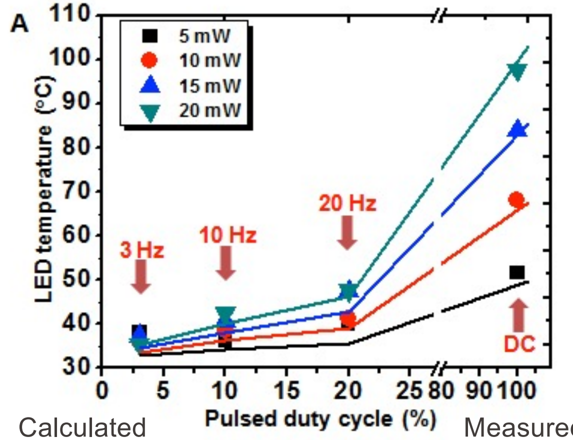




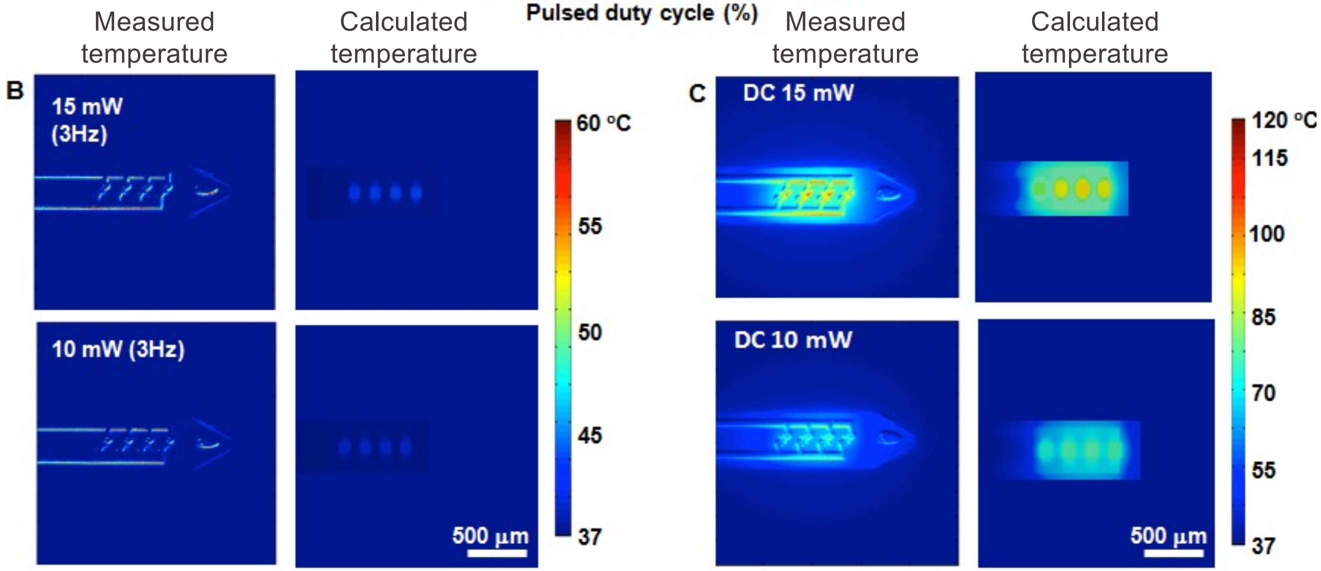
Small 2012 8(21) 3263-3268

Surface temperature of micro-LEDs during operation in air



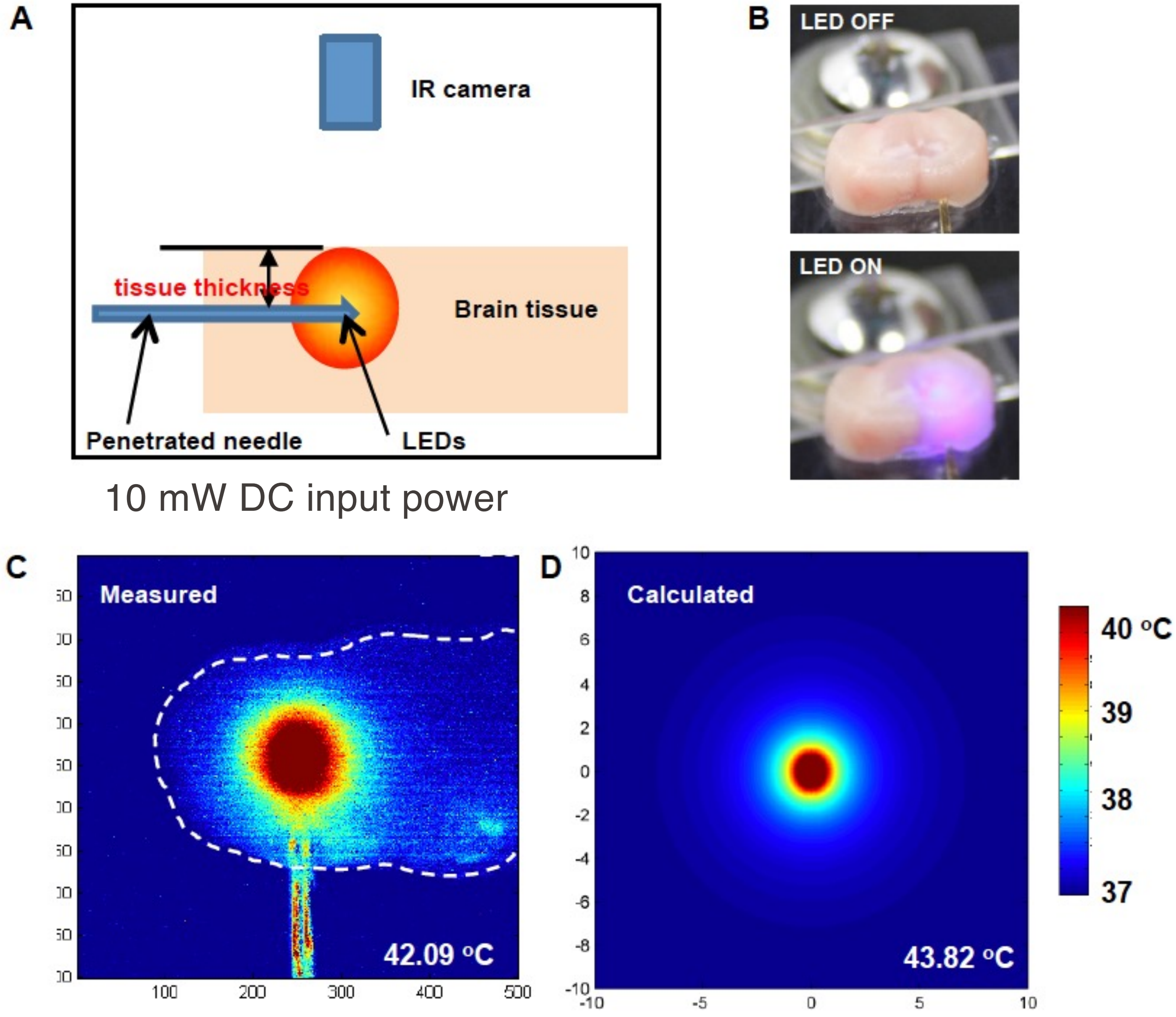


10ms pulse



Science 2013 340, 211-216

Thermal imaging

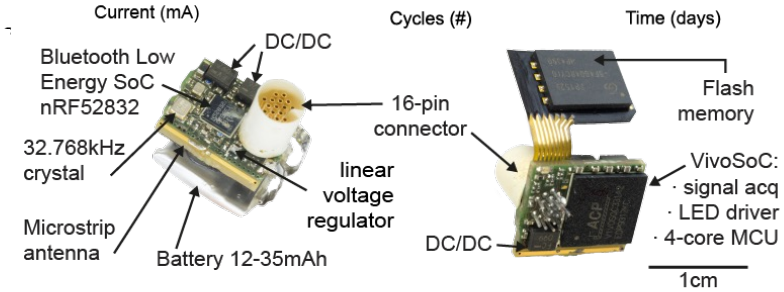


Science 2013 340, 211-216

Miniaturised electronics to drive the LED implant

Q. Huang, ETHZ

Plateforme sans fil



Tablette pour
contrôle et affichage
des données

Configurations & Ranges:

Parameter	minimum	maximum	step
# pulses	1	10 k	1
frequency	0.1 Hz	30 Hz	0.1 Hz
pulse width	1 ms	50 ms	1 ms
LED current	1 mA	60 mA	1 mA
LED selection	LED 1 / LED 2		

Nature Biotech 2022

Manipulating locomotor circuits

C. Kathe

G. Courtine

reticulospinal fibers
→hinglimb movement

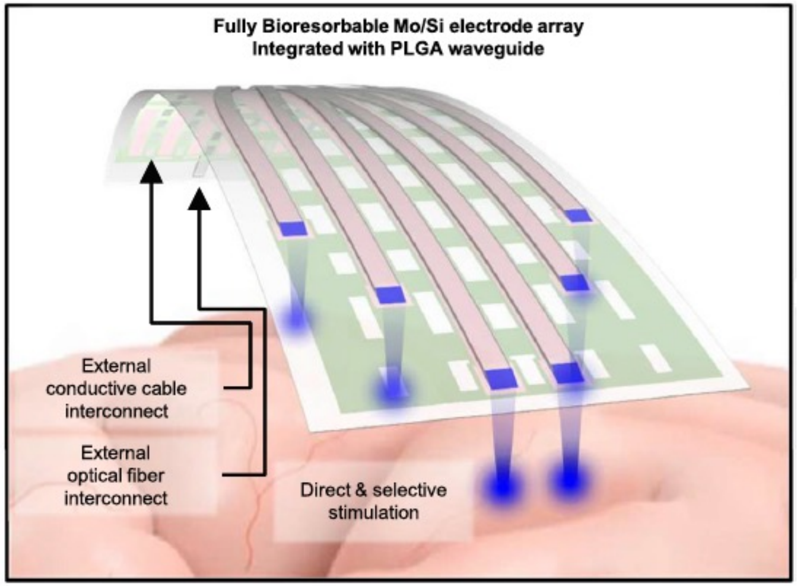
Corticospinal tract
→leg dragging and instability

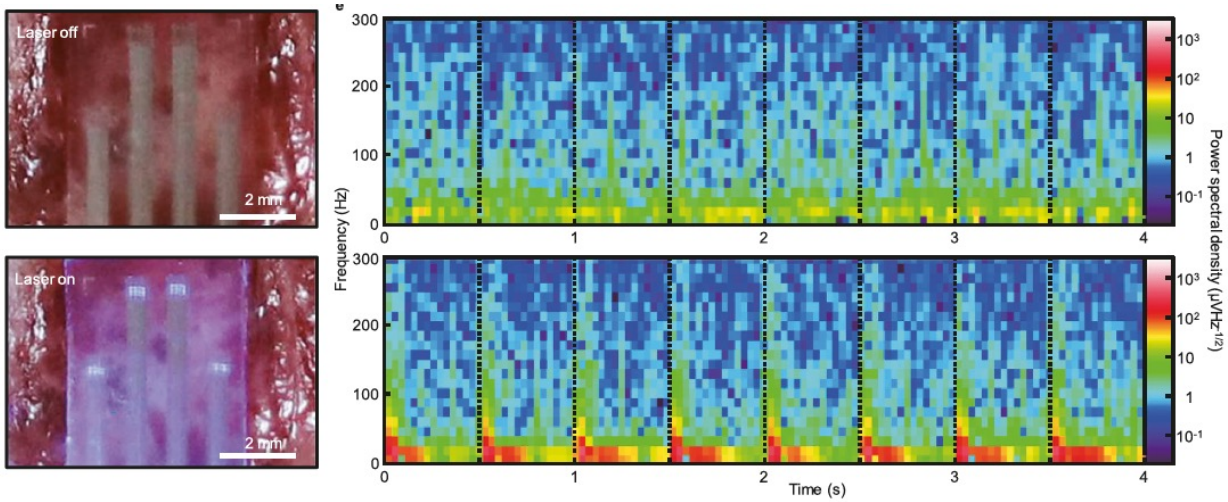
V2a interneurons
→ left-right coordination

PV^{ON} proprioceptive neurons
→perturbation of proprioception during walking

Nature Biotechnology 2021

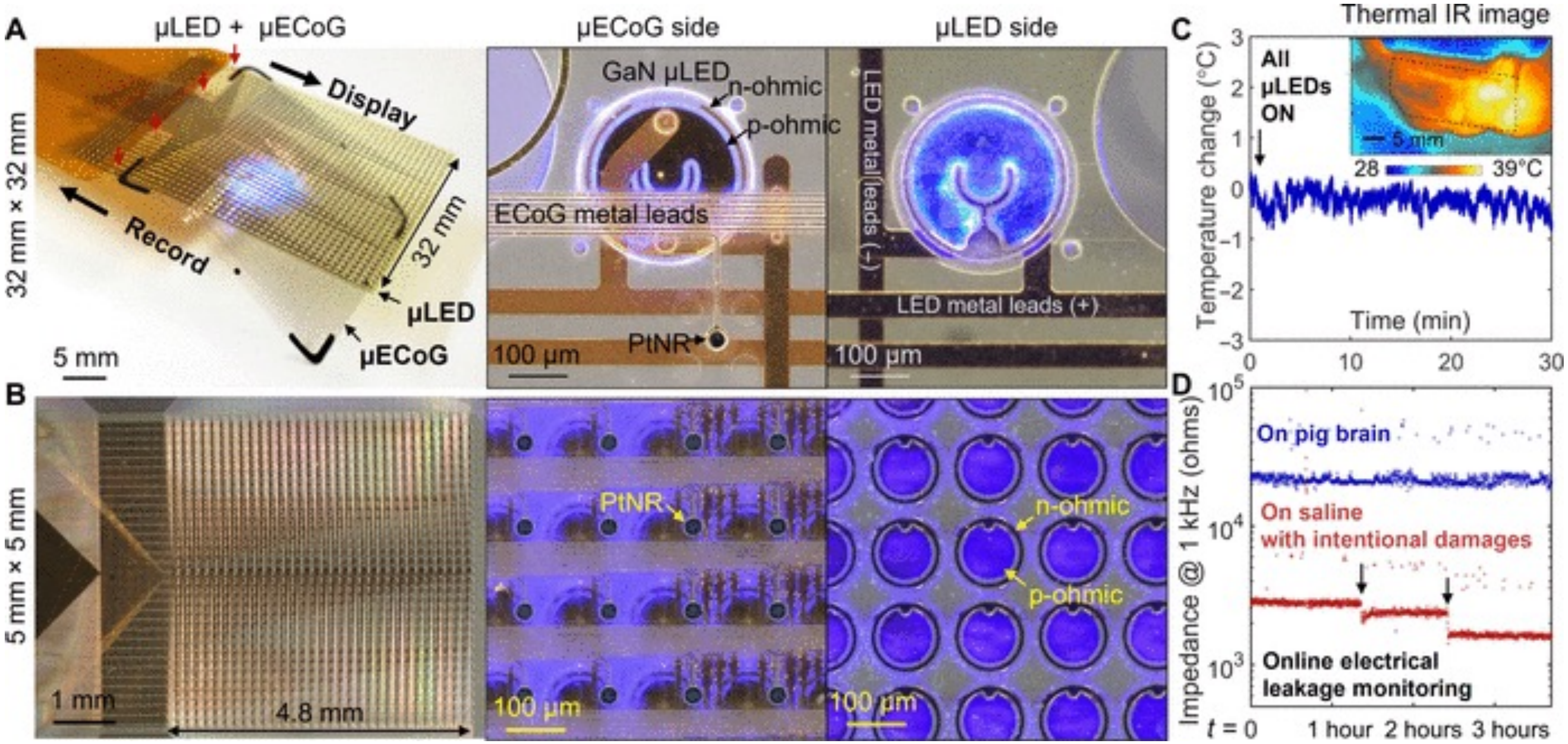
Optical stimulation and recording





EPFL

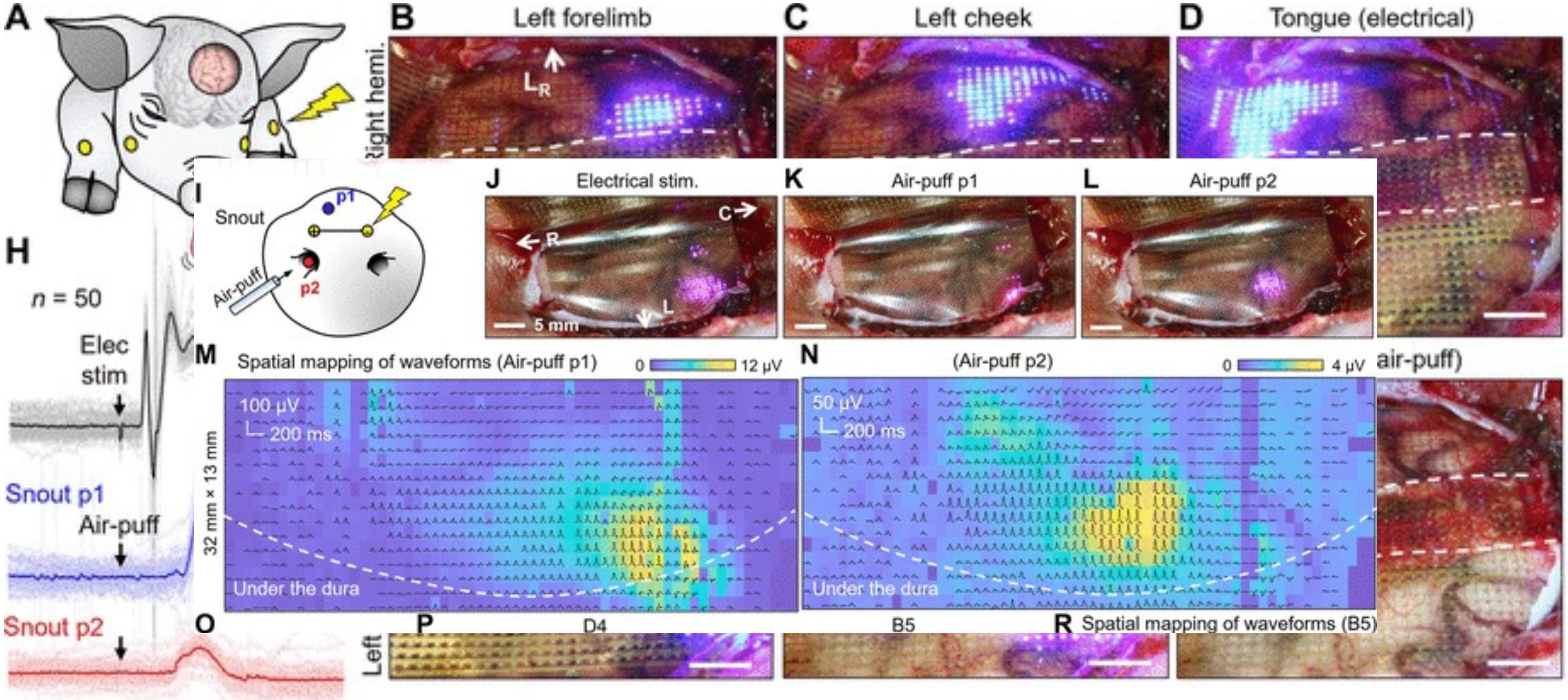
Using light to see neural activity



Science Trans. Med. **2024**

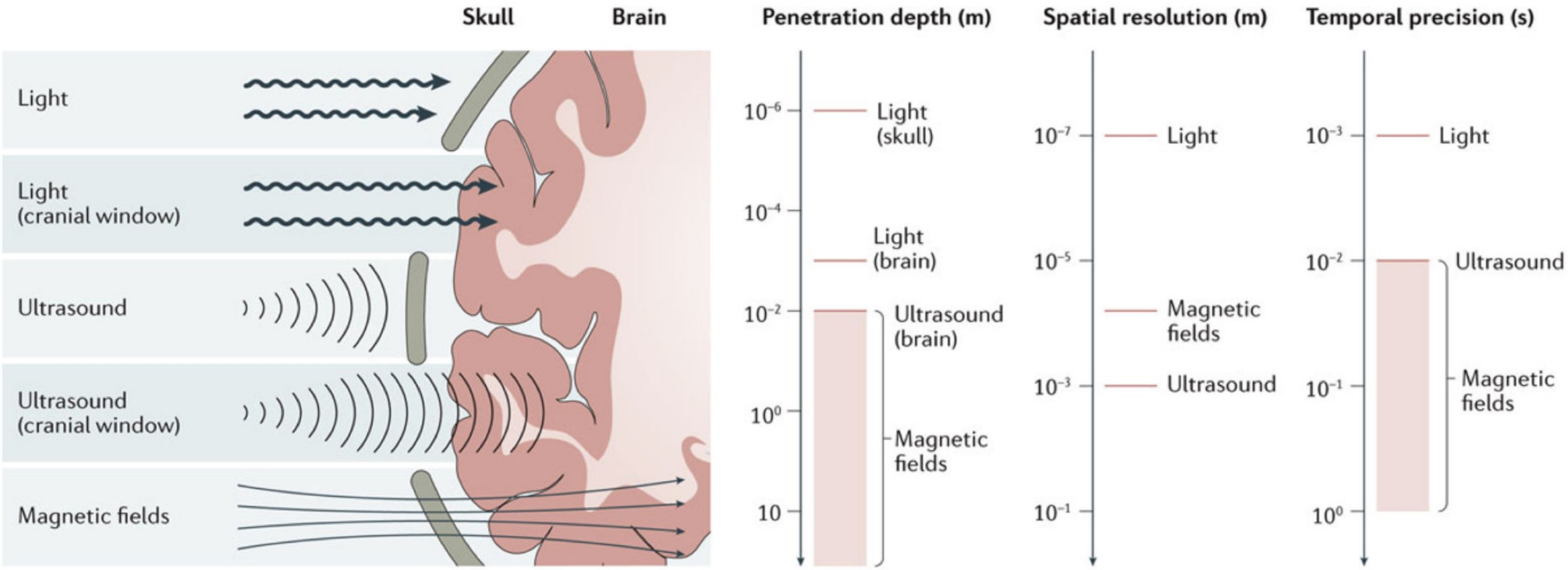
EPFL

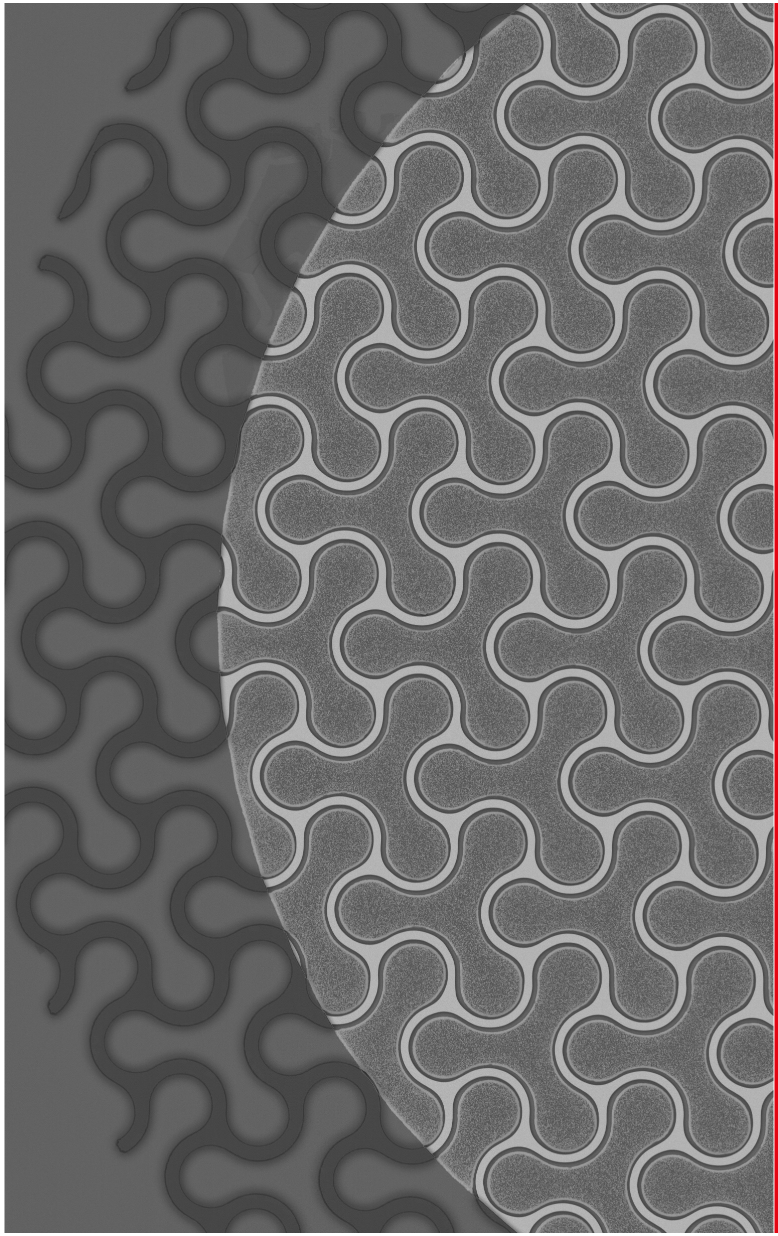
Using light to see neural activity



Science Trans. Med. **2024**

Pénétration des ondes dans les tissus





Modalities of communication

Light and optogenetics

Ultrasounds

Magnetic field

Ultrasound imaging

- **First medical ultrasound scanner**– 1952
    - Imaging organs in depth
    - Piezoelectric transducers
    - Anatomy: desnity, modulus of compressibility, tissue structures

Ultrasound imaging

- **First medical ultrasound scanner**– 1952
  - Imaging organs in depth
  - Piezoelectric transducers
  - Anatomy: desnity, modulus of compressibility, tissue structures
- **Doppler effect**

Ultrasound imaging

- **Premier échographe médical** – 1952
  - Imagerie en profondeur
  - Transducteurs piézoélectriques
  - Anatomie: Masse volumique, module de compressibilité, structures des tissus

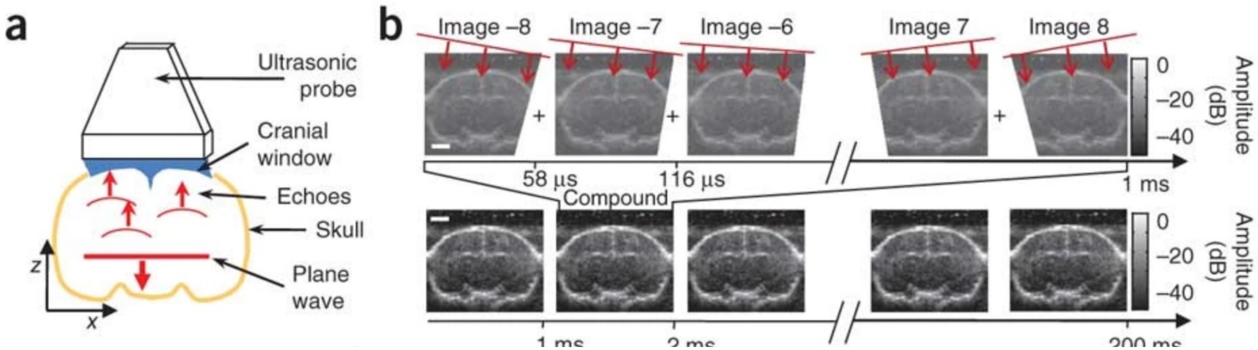
- Effet Doppler
  - Ultrasound; travel speed in blood vessels
  - Mapping according to direction and speed of blood flow

- **Ultrafast Doppler**
  - in vivo exploration of the dynamics of the vascular network, from large to small vessels, right through to neurovascular coupling

Functional imaging using ultrasounds

Track neuronal activity via blood flow, thanks to neurovascular coupling

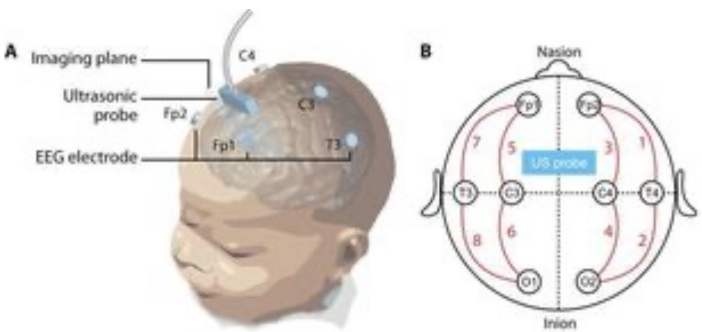
- f_D proportional to the axial blood velocity with respect to the *z* axis (mm/sec)
- **Signal intensity** depends on blood volume

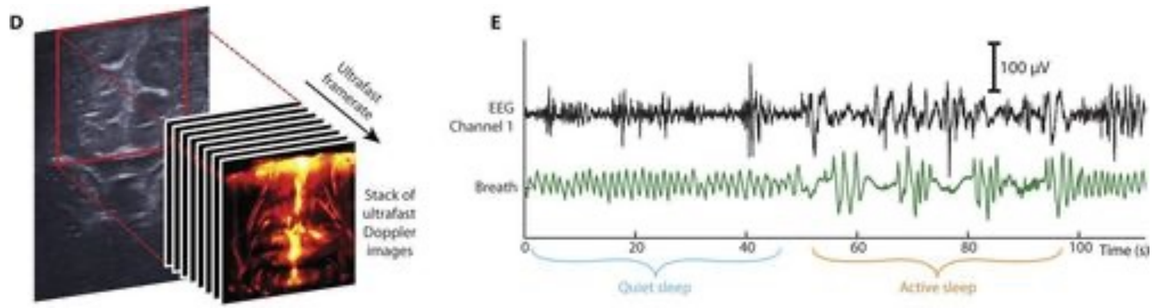


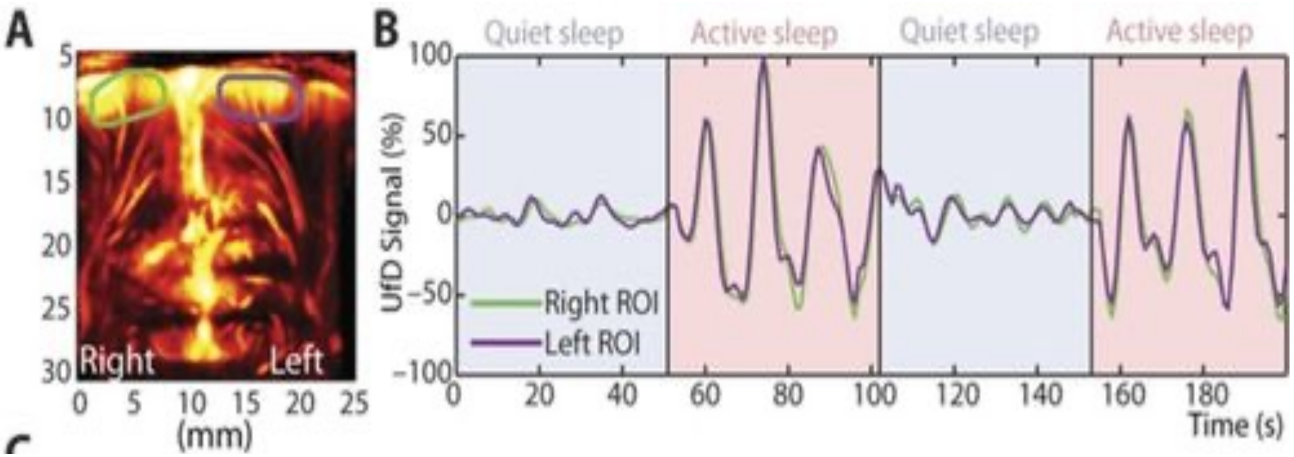
M. Tanter

EPFL

Imaging newborn cortex



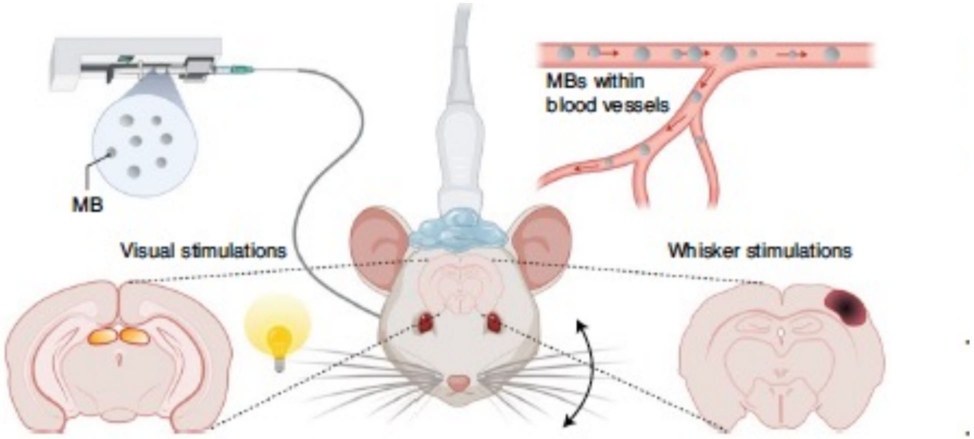


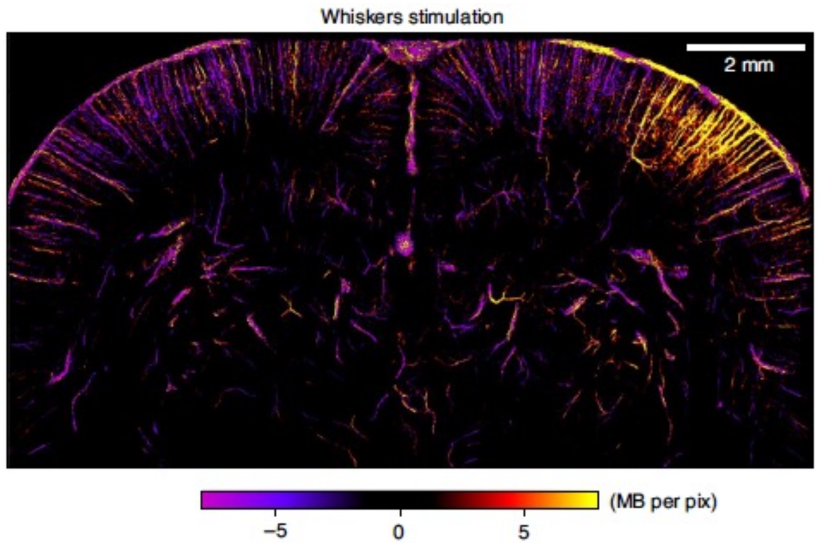


Science Trans. Med. | 2017 9 411

Using micro-bulles to enhance imaging resolution

- Micrometer-resolution ultrasonic localization microscopy





Localization of intravenously injected microbubbles
spatial resolution: 6.5 µm
temporal resolution: 1 sec

Nature Methods | 2022 19 1004-1012

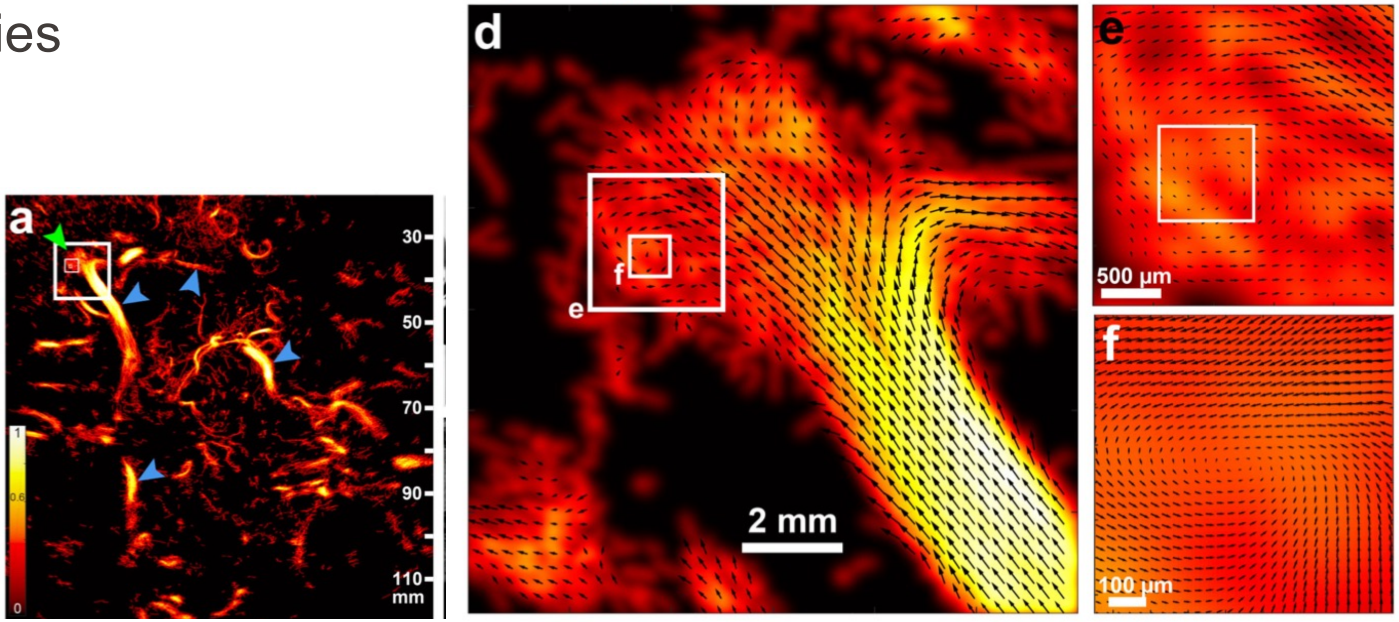
Transcranial ultrasound imaging of the human cortex

- Understanding cerebral hemodynamics
- Correlating vascular anomalies and neurological pathologies

a aneurism

➤ large vessels

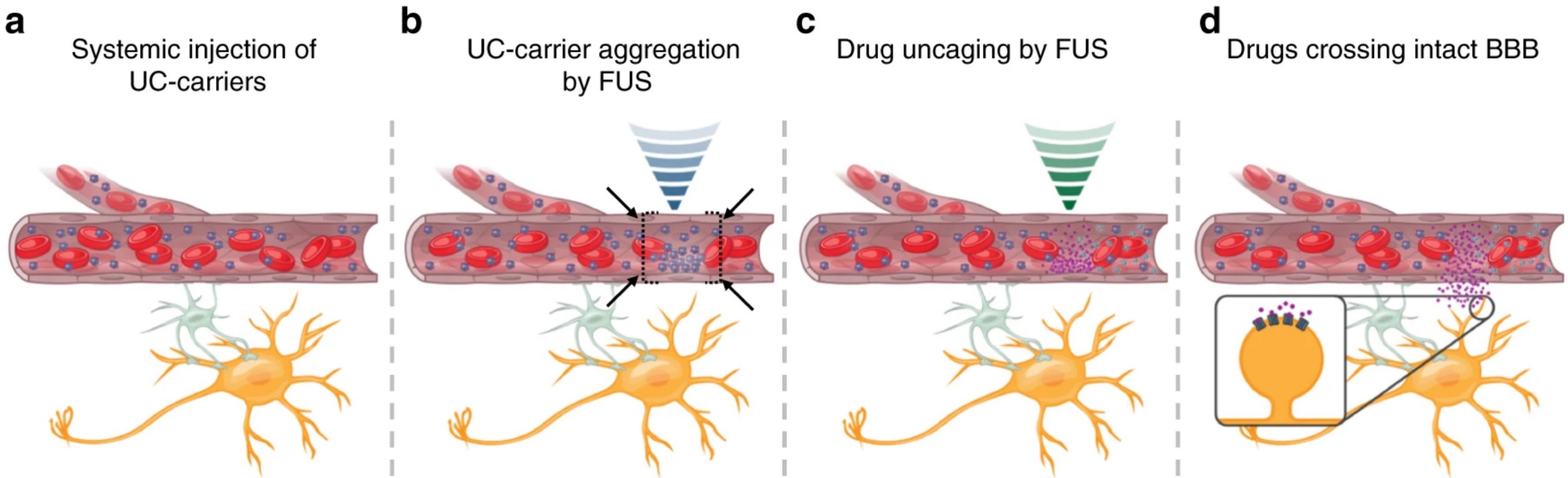
f v~ 0 cm/s



microbulles 2-9µm

Nature Biomed. Eng. | 2021 5(3) 219-228

Allow passage through the blood-brain barrier (BBB)

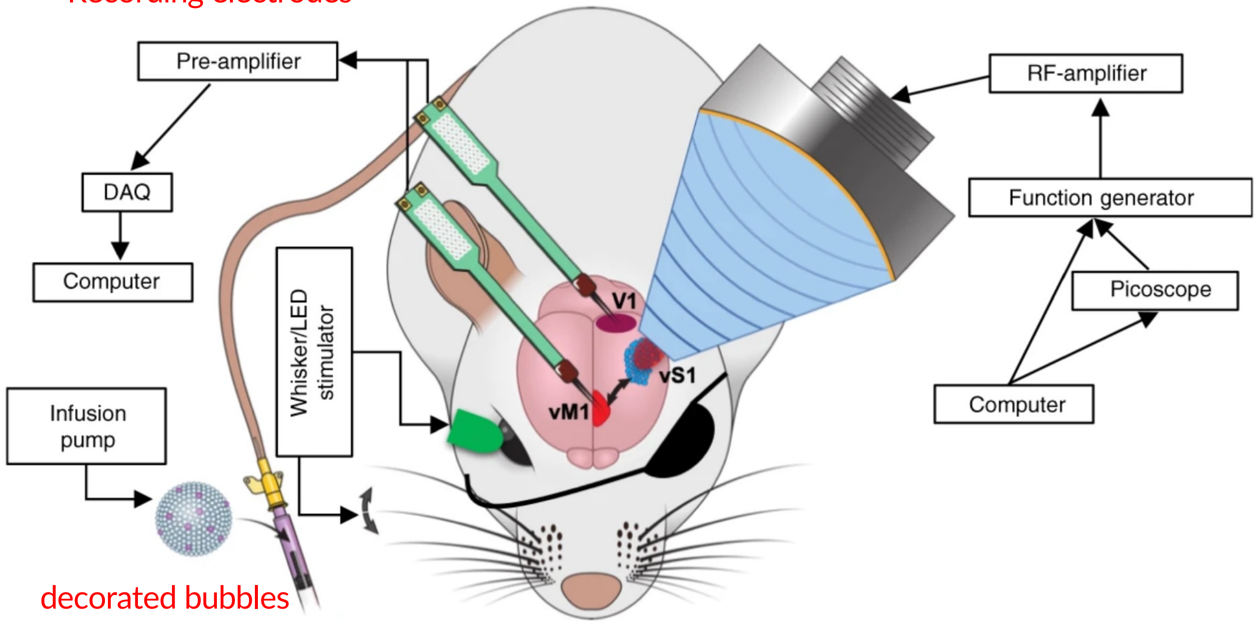


Nature Comm. | 2020 11 4929

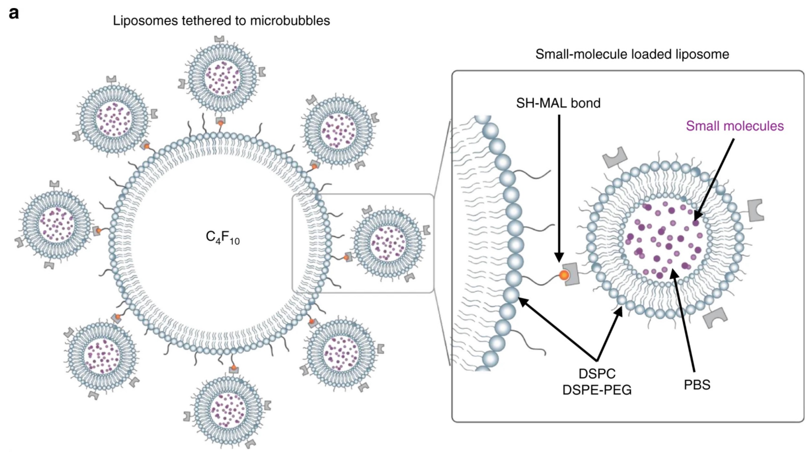
Experimental platform

Recording electrodes

non invasive US stimulation



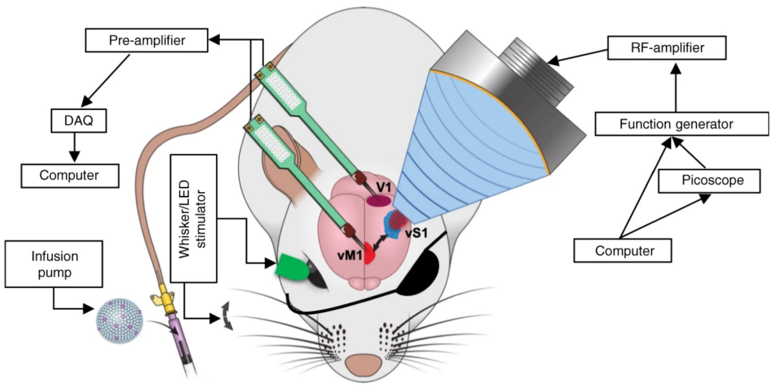
decorated bubbles

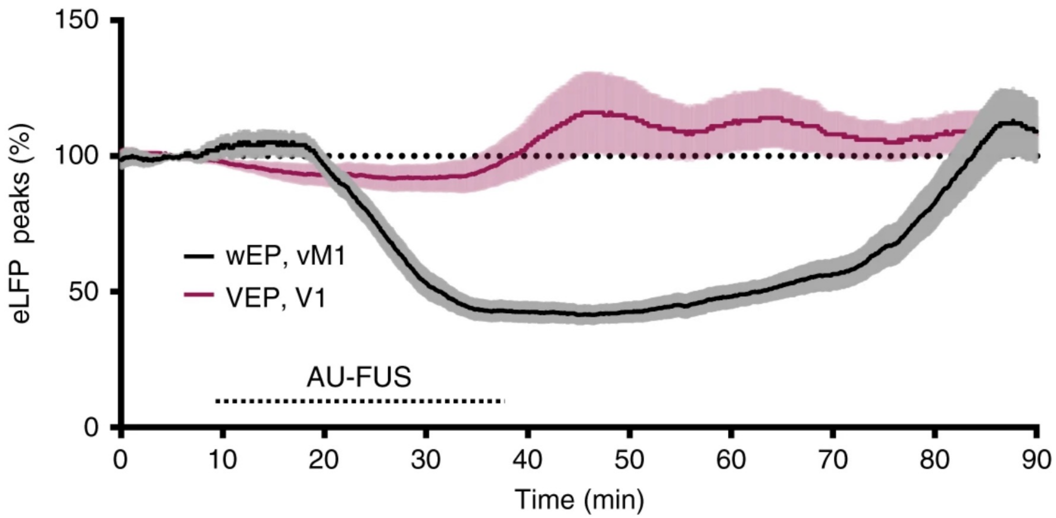


Decorated bubbles with suspended molecules in saline solution

Specific modulation of neuronal circuit receptors

vS1 - vSM1 circuits: focal inhibition of vibrissae sensory cortex (vS1), via release of the GABA receptor agonist muscimol

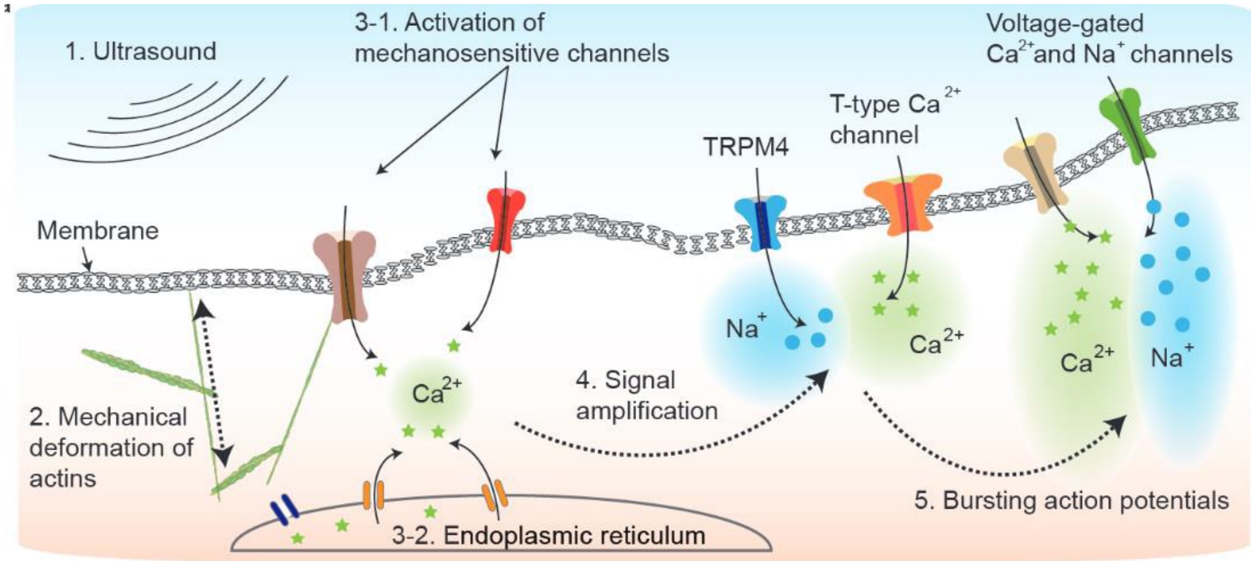




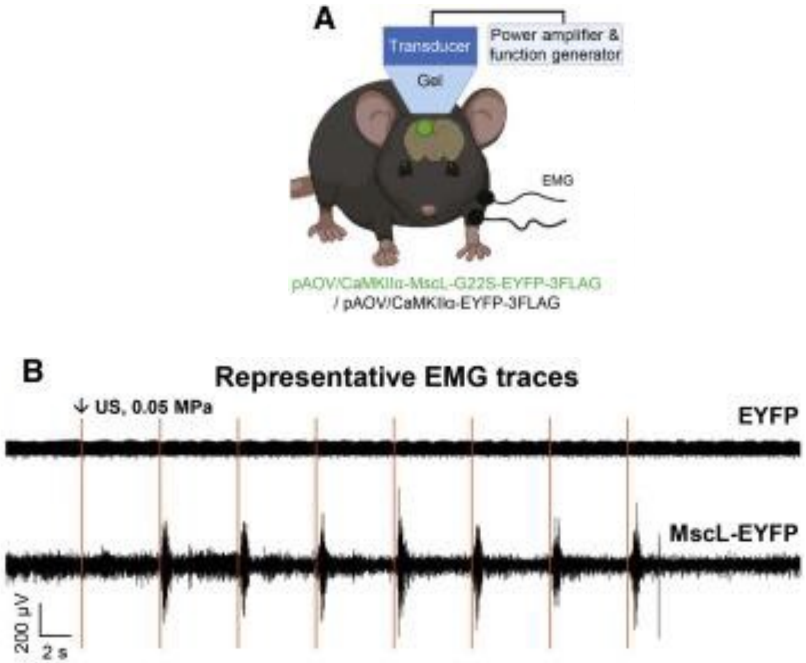
Test: whiskers movement
➞ 3ms delay between vS1 and vM1 (normal)
➞ inhibition of vS1 via fUS, reduced activity in vM1

Nature Comm. | 2020 11 4929

Ultrasound modulation

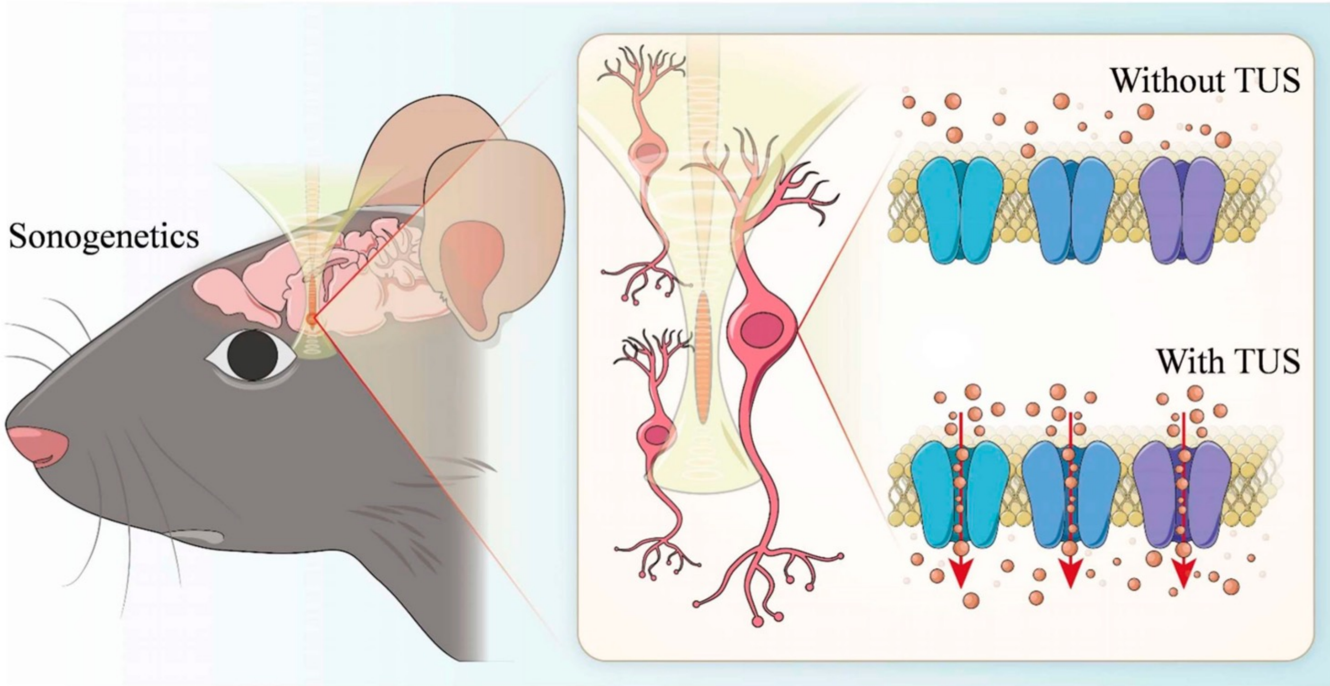


Qiu et al., 2020, CellReports



Muscle activity (EMG) depends on:
- US stimulation intensity
- stimulation cycle
- stimulation burst duration

Sonogenetics



Genetic engineering:
UltraSound-sensitive proteins;
Modulation of Na+, Ca2+ channels via ultrasound

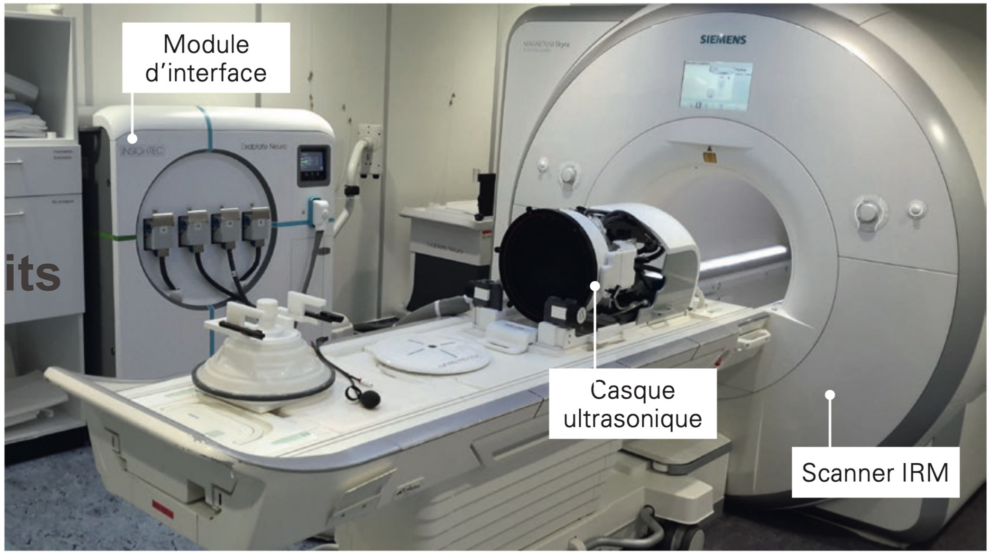
Depolarization induced by mechanical deformation of the cell membrane?

FUS image-guided high-intensity focused ultrasound treatment

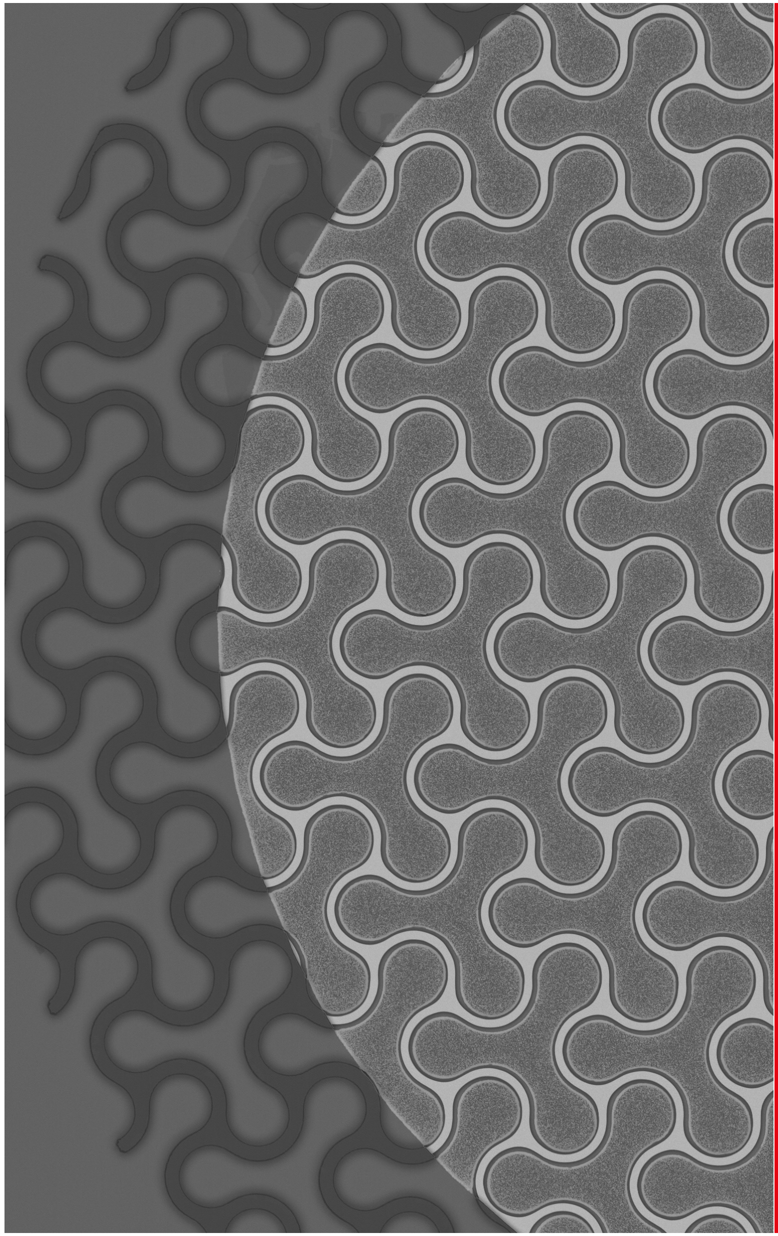
- Non-invasive technique creating small therapeutic lesions in a specific MRI-guided area of the brain

- Sound waves 0.2 - 4MHz & high intensity local vibration
  - local heating
  - targeted necrosis
- Zone 2-6mm diameter
  - spatial resolution 1mm
- **Interruption of abnormal neuronal circuits**

- Main conditions:
  - Essential tremor
  - Parkinson



HUG



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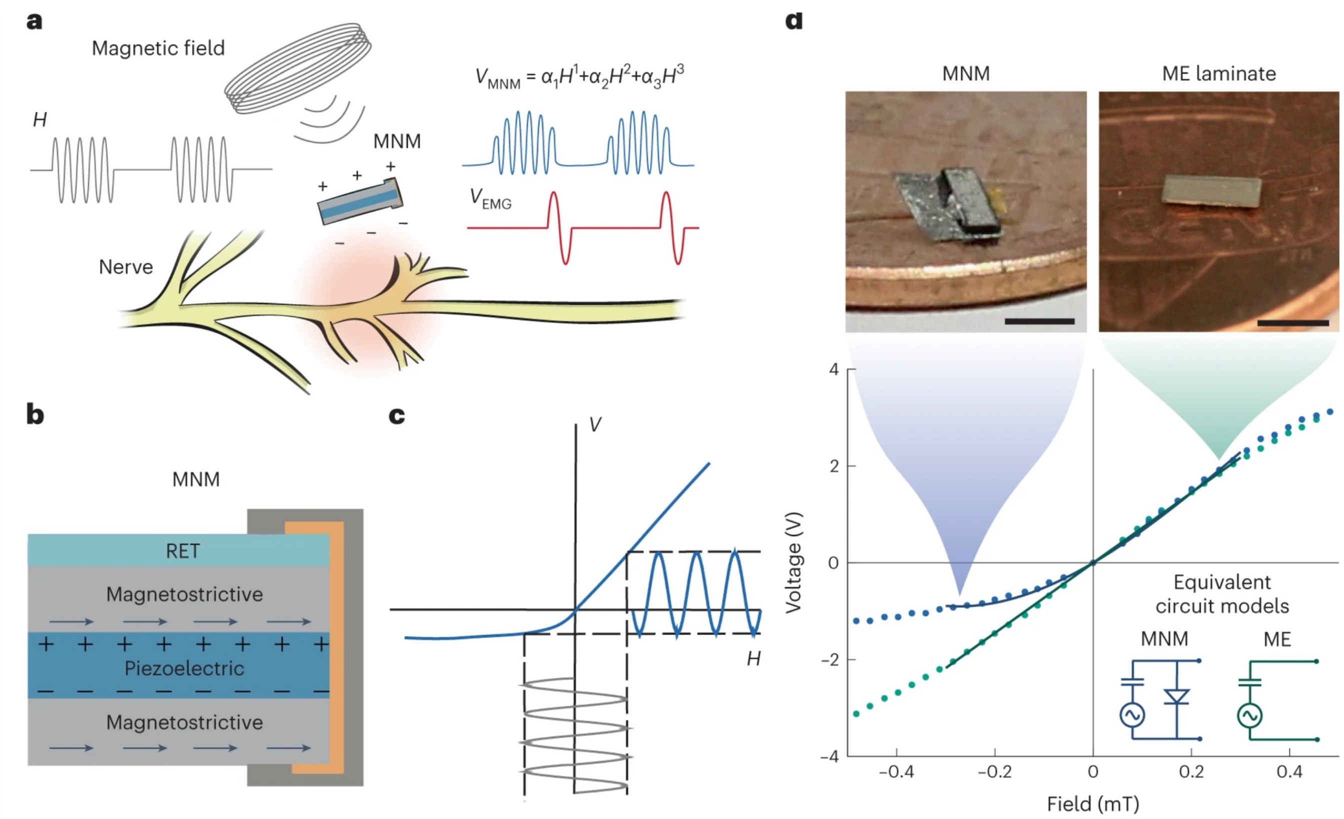
Remote stimulation induced by magnetic field

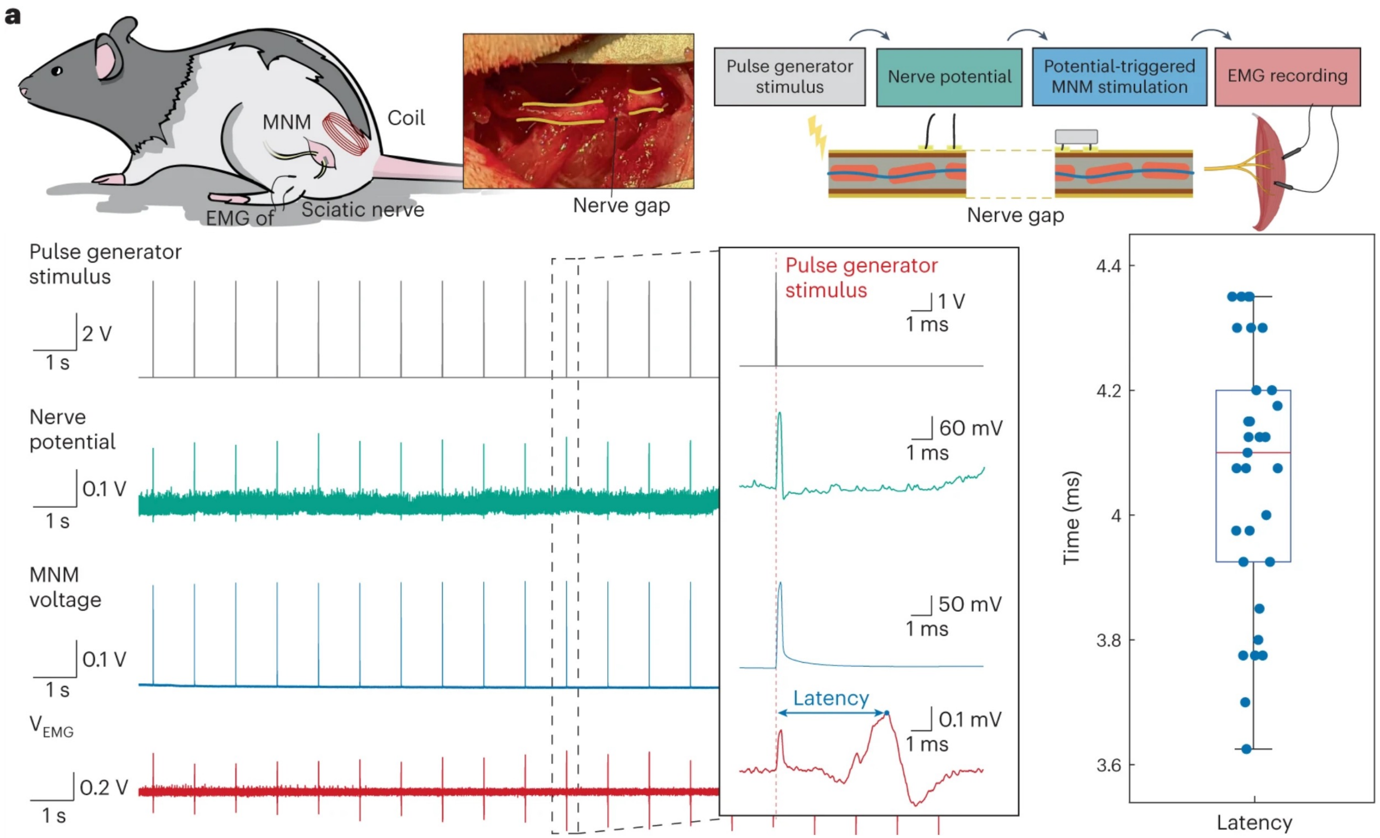


$$V_{ME} = \alpha H d$$

ME magnetoelectric material
MNM magnetoelectric non linear metamaterial
RET rectifying electron transport

Nature Materials 2024 23 139-146

Restoring communication after nerve damage



Nature Materials 2024 23 139-146

Take-home messages

- Implementation of different transduction modes
  - **Optogenetics**: selective and rapid, but still difficult to apply in humans
  - **Ultrasound**: versatile, indirect measurement and modulation of brain activity; micro-lesions
  - **Magnetic field**: in-depth interaction; pre-clinical stage only