

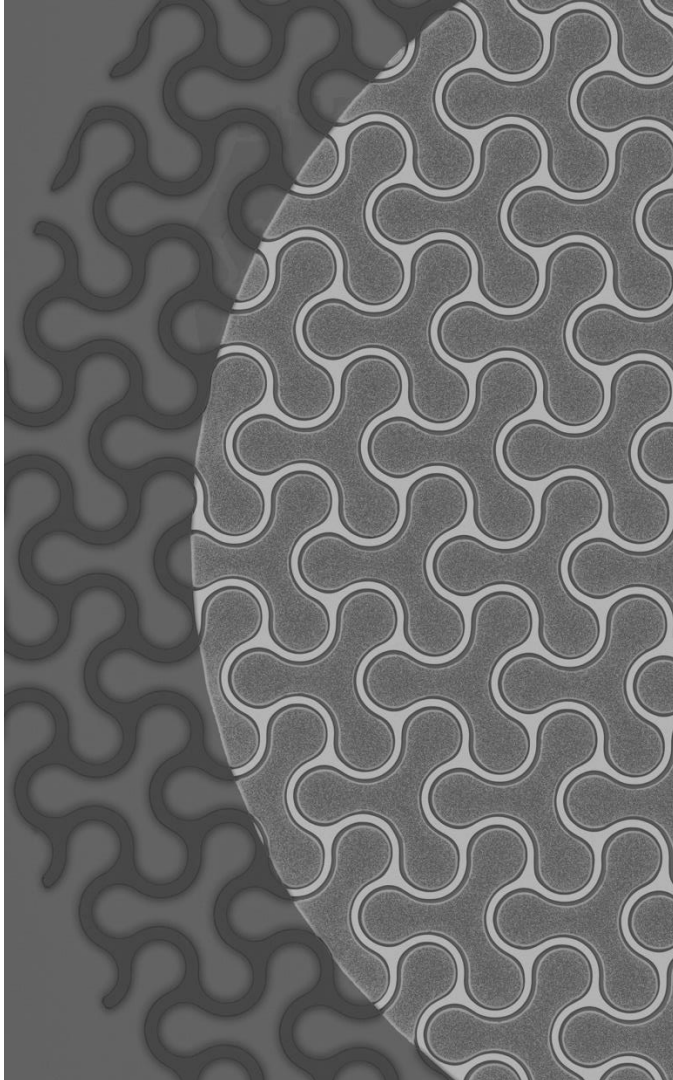
Neural Interfaces

NX-422

Multimodal interfaces

Stéphanie P. Lacour

Neuro-X Institute



Modalities of communication

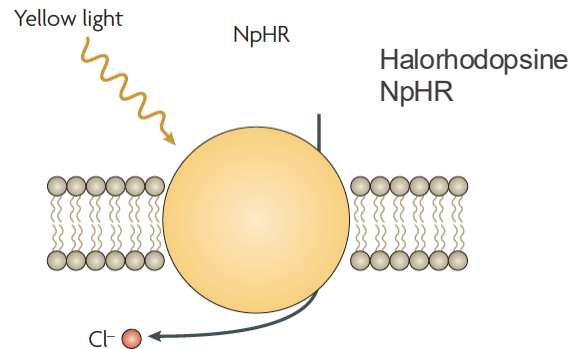
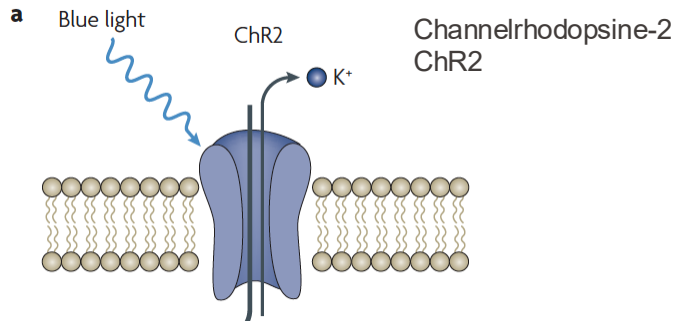
Light and optogenetics

Ultrasounds

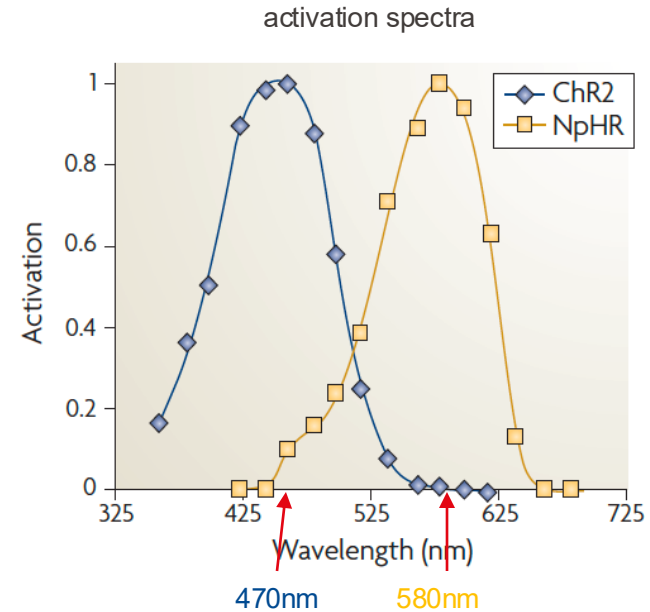
Magnetic field

Main idea: introduce light-sensitive proteins (**opsins**) into neuronal membranes, then use flashes of light to activate them with millisecond precision.

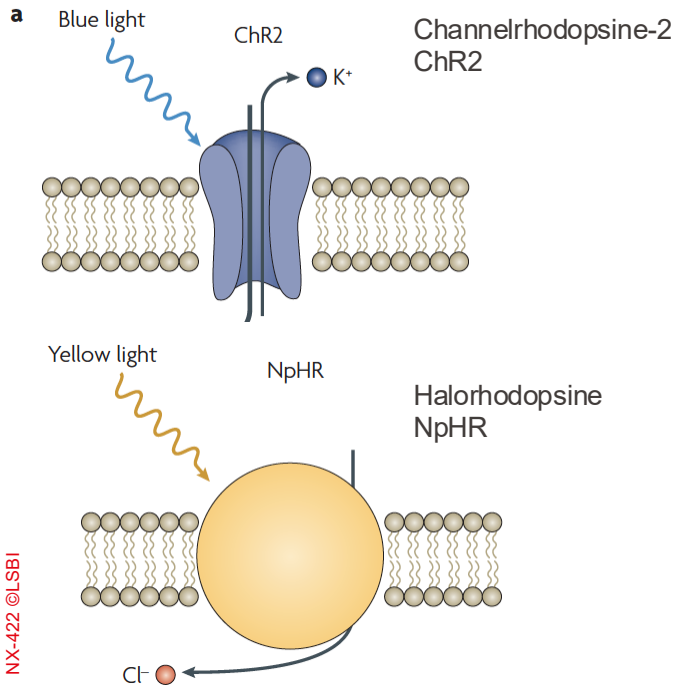
Channelrhodopsins (blue light) → open cation channels → **excite** neurons.



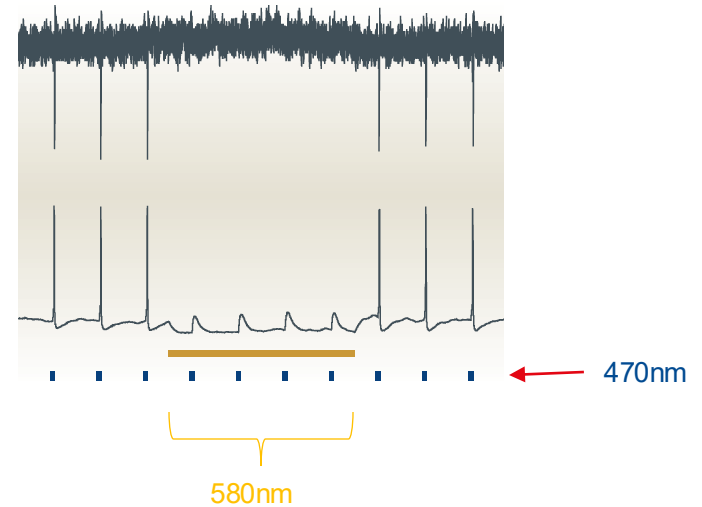
Halorhodopsins → pump Cl^-/H^+ → **inhibit** neurons



Photosensitive proteins derived from green algae



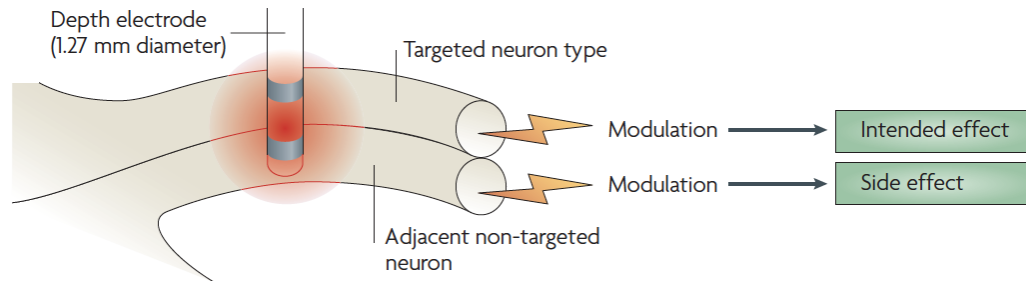
Activation & inhibition



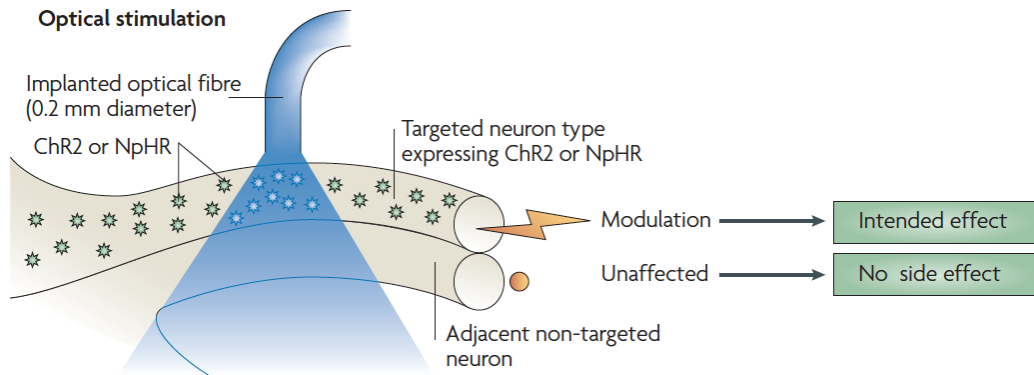
Cell-attached (top) and whole-cell current-clamp (bottom) traces from hippocampal neurons showing all-optical neural activation and inhibition. Blue pulses represent the blue light flashes used to drive ChR2-mediated activation and the yellow bar denotes NpHR-mediated inactivation.

Selectivity electrical vs optical stimulation

c Electrical stimulation



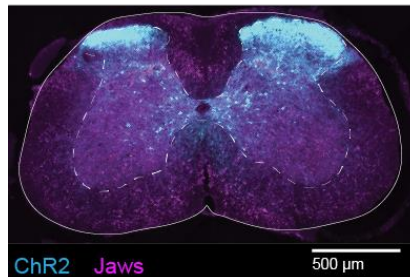
Optical stimulation



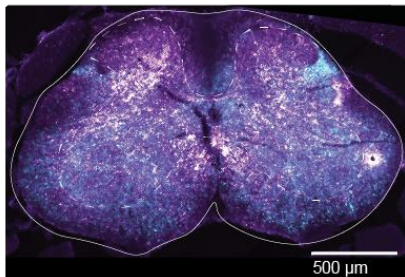
■ Viral transfection

- **Spatial/projection targeting:** control spread via injection site/volume; use retrograde adenoassociated viruses (AAV) to infect projection-defined neurons.
- **Timeline:** expression in **days–weeks**. (stability?)
- **Cons:** variability, immune response, surgical injection damage, off-target spread if dosing is high.

Spinal Level L3



Spinal Level S1



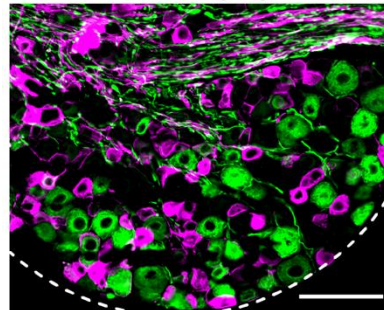
Adeno-Associated Virus AAV

■ Transgenic mice

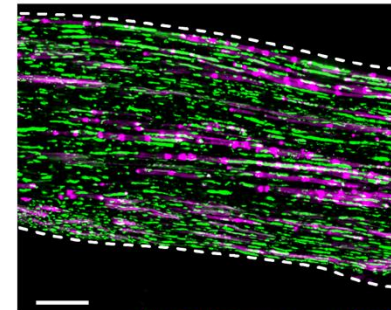


- High **reproducibility:** consistent expression across animals; no injection variability.
- **Lower surgical burden:** no intracranial injections needed
- **Stable, long-term expression:** ideal for chronic or developmental studies.
- **Mouse only**

Dorsal root ganglion



Sciatic nerve



ChR2-tdTomato NF200

How it works

- Opsins (light-sensitive proteins with specific activation spectrum):
 - Channelrhodopsins (blue light) → open cation **channels** → depolarise neurons.
 - Halorhodopsins/Arch (yellow–green light) → **pump** Cl^-/H^+ → inhibit neurons.
- Variants exist that shift color (e.g., red-shifted Chrimson) or kinetics (step-function opsins).
- Targeting the right cells: genes delivered by viral vectors or transgenic lines.
- Light stimulation: fiber optics or LEDs; timing controlled by pulse patterns.
- Measuring effects: electrophysiology, imaging, behavior readouts.

Guiding light near the neurons

- Optic fiber

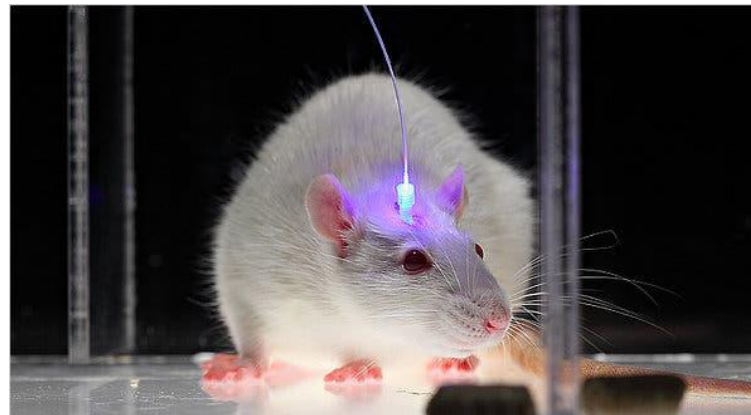


silica fiber
250 – 1200 nm
(UV to visible)

+



ceramic ferrule



New York Times, May 16, 2011

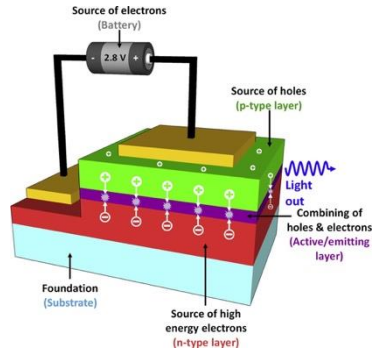
Ed Boyden, Feng Zhang Karl Deisseroth
Nature Neuroscience 2005 8(9) 1263-1268

Light Emitting Diodes LEDs

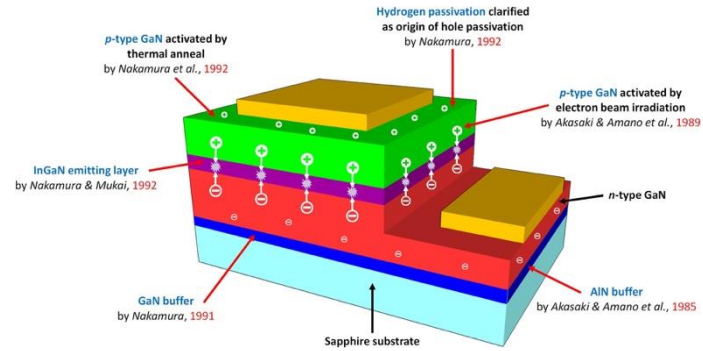
2014 Nobel Prize in Physics

I. Akasaki, I. Amano, S. Nakamura

“a new light source, power efficient and sustainable, the blue LED

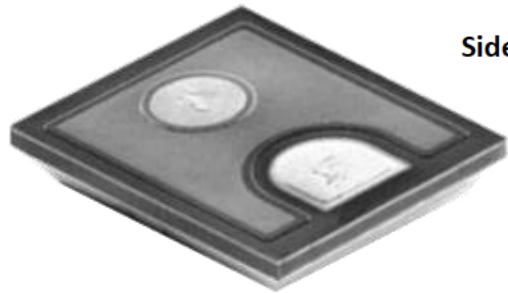
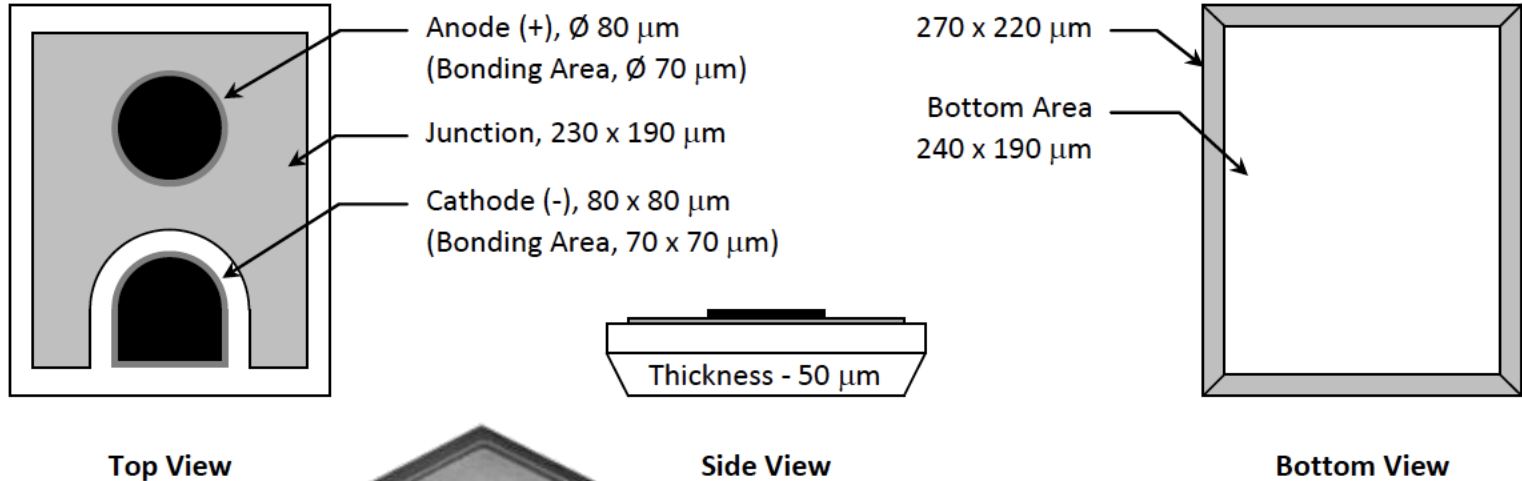


LED - heterojunction



Blue LED

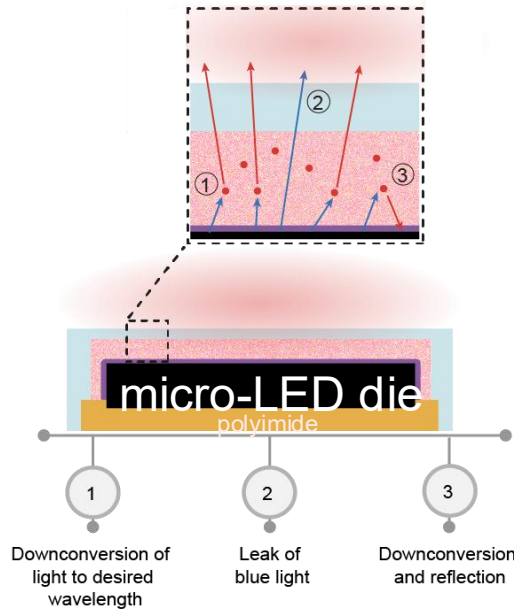
LED "die"



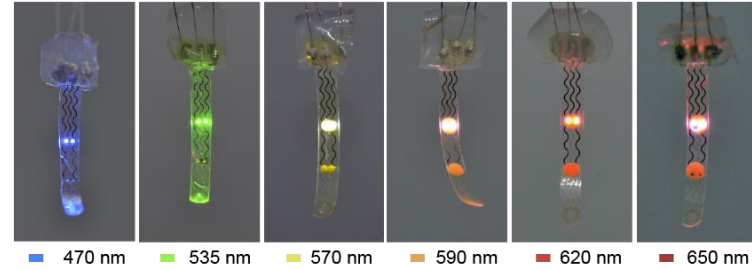
CREE InGaN LED TR2227
470nm 21mW
 $220 \times 270 \times 50 \mu\text{m}^3$

Tailoring the wavelength

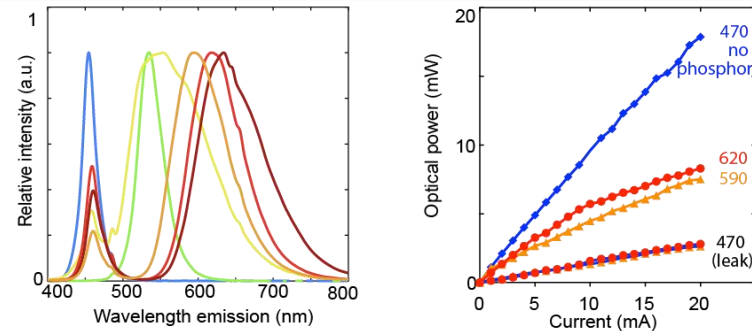
Step 1: Light emission through phosphor-silicone matrix



Step 2: Implant with phosphor-silicone matrix that changes light emission spectra

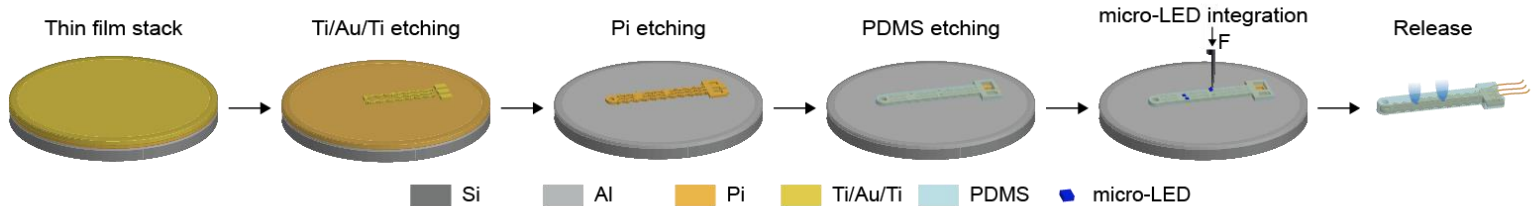


Step 3: Measured light emission spectra

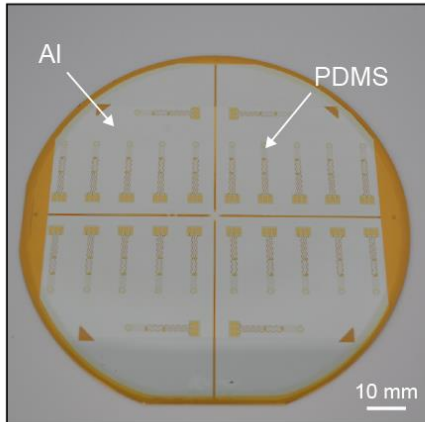


Microfabrication of an optoelectronic implant

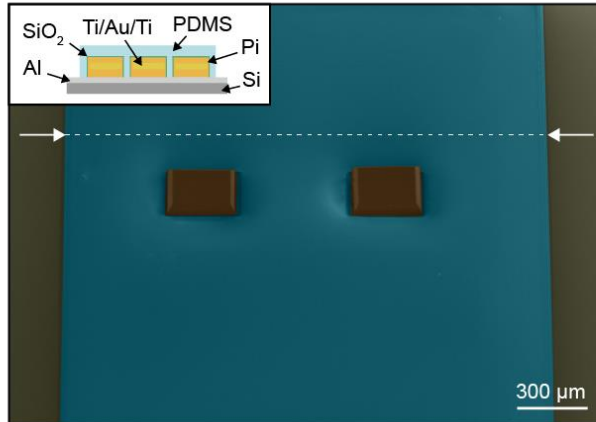
a Step 1: Microfabrication Process



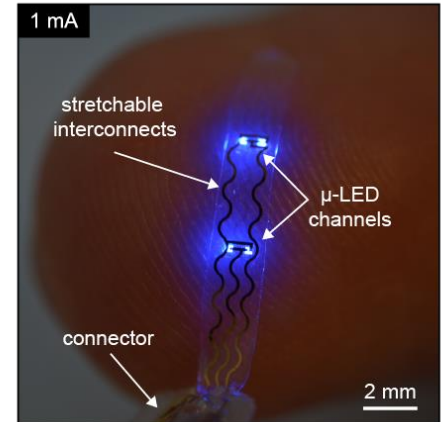
Step 2: Batch microfabrication



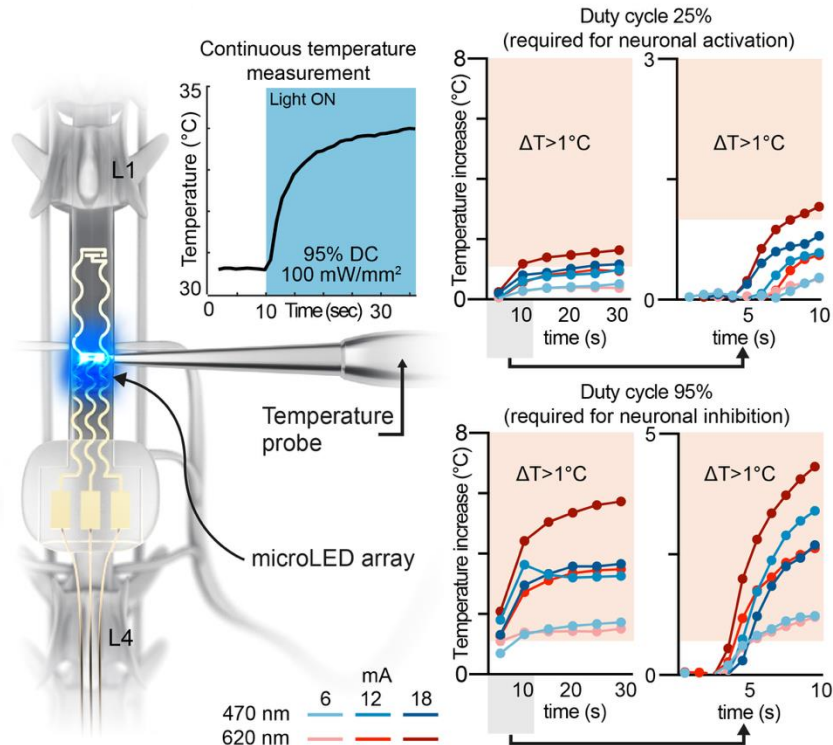
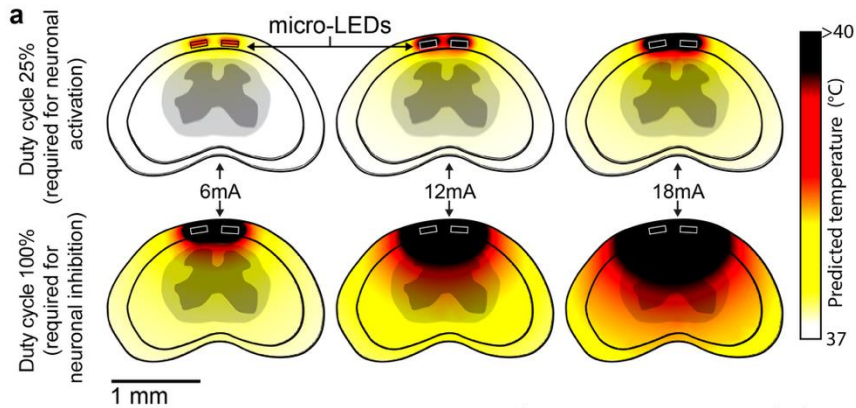
Step 3: Bare die integration



Step 4: Optoelectronic device release



Local heating!



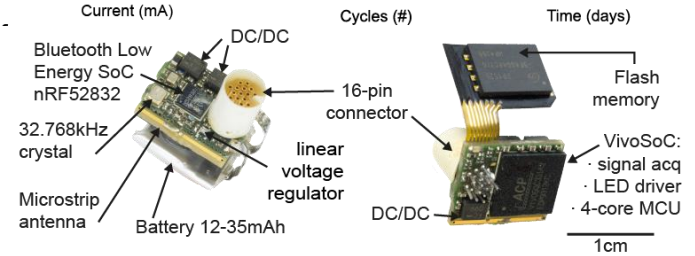
Miniaturised electronics to drive the LED implant



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		



Manipulating locomotor circuits



C. Kathe



G. Courtine

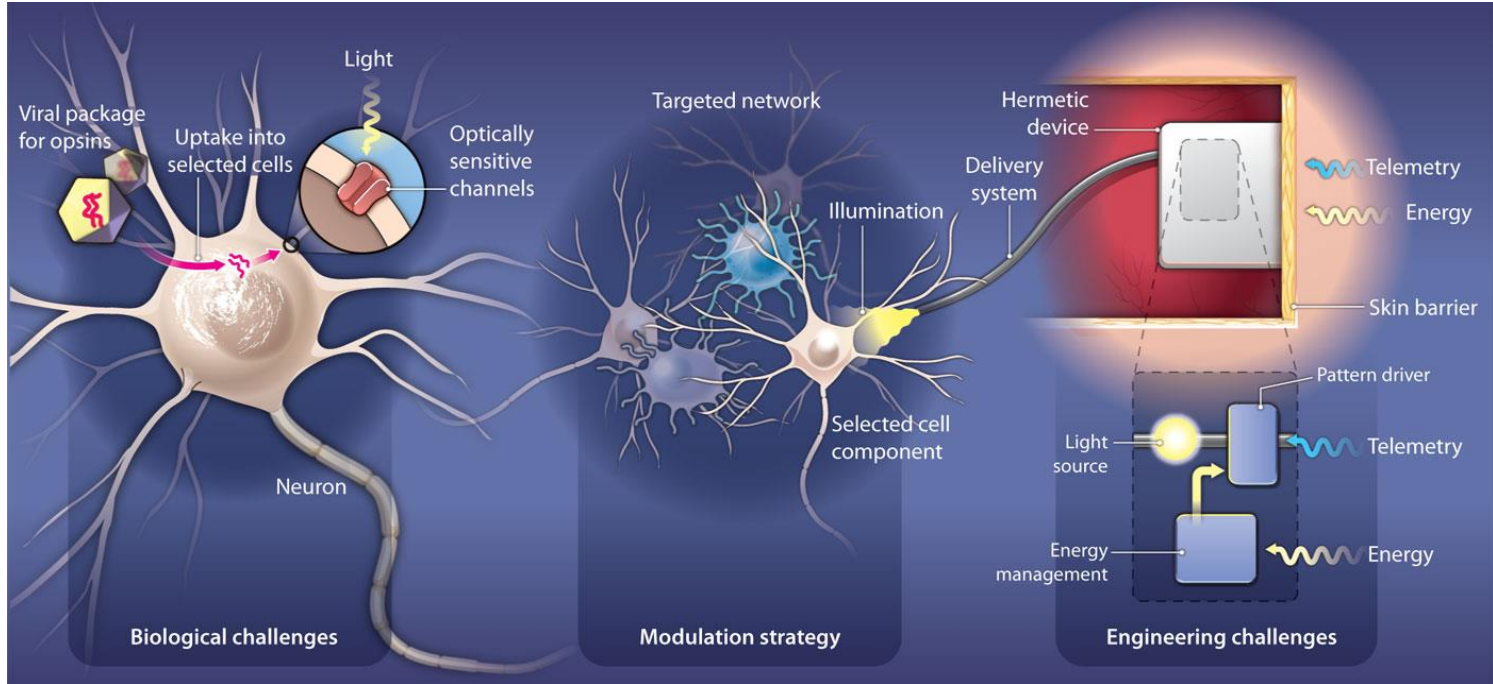
reticulospinal fibers
→ hindlimb movement

Corticospinal tract
→ leg dragging and
instability

V2a interneurons
→ left-right coordination

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

Optogenetics. Using photons to modulate neural activity



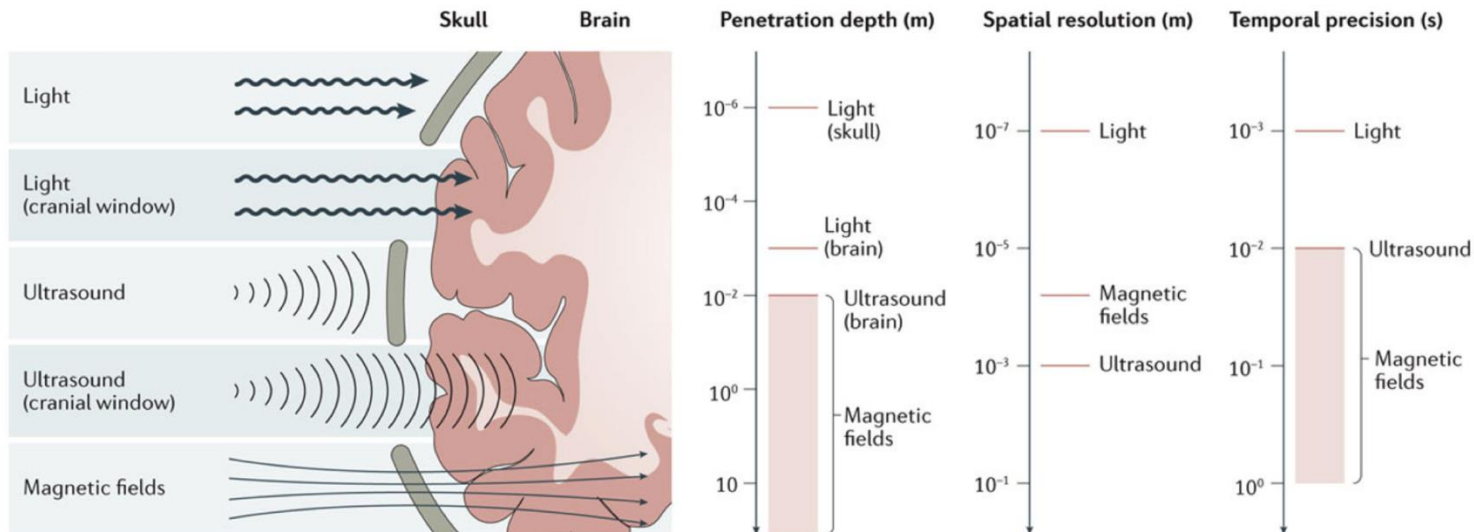
Optogenetics vs Electrical interfacing

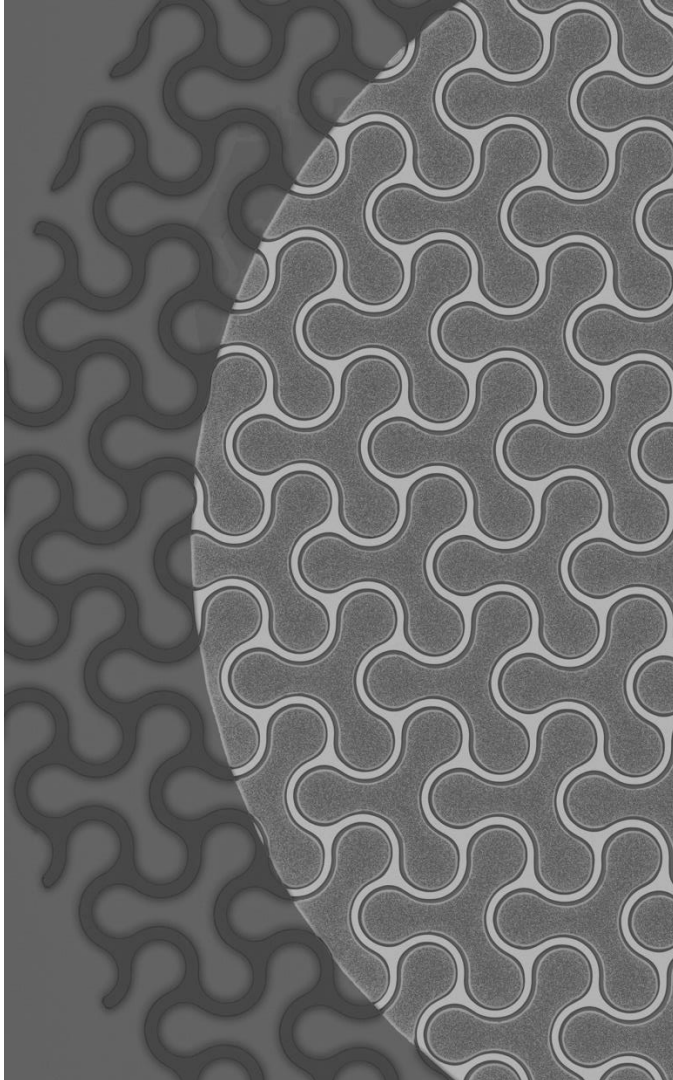
- **Cell-type specificity:** restrict expression to desired cell population → stimulate only what you want
- **Excitation/inhibition:** **excite** (ChR/Chrimson) or **directly inhibit** (NpHR/Arch/GtACR) by choosing the opsins.
- **Spectral multiplexing:** leverage opsin activation spectrum to independently perform different function.
- **Low electrical artifact:** no electrical stimulation pulses → stim artifact in electrophysiology recordings.

BUT:

- **Requires gene delivery:** viruses/transgenics need time and expression needs controlling.
- **Light limits:** scattering/absorption reduce depth.
- **Hardware implants:** fibers/ μ LEDs more invasive than simple electrodes.
- **Heating limits efficacy:** duty cycle limited by temperature rise → limit to operation.

Pénétration des ondes dans les tissus





Modalities of communication

Light and optogenetics

Ultrasounds

Magnetic field

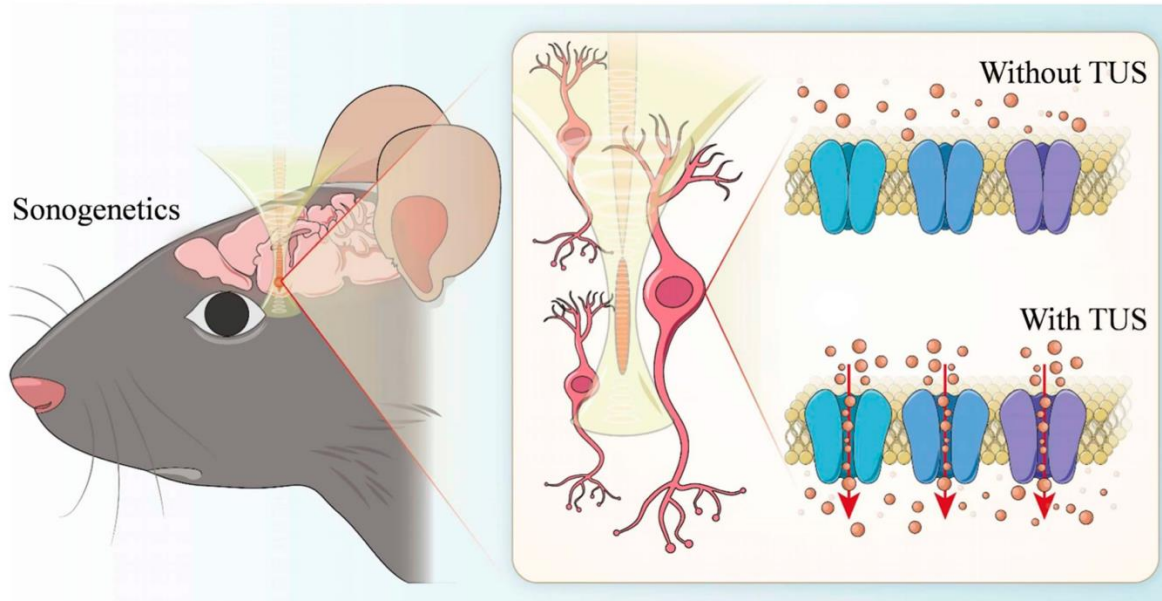
- Selectively stimulating specific neurons in the brain non-invasively
- Ultrasound lacked the ability to target specific cell types.
- **Sonogenetic** approach by expressing mechanosensitive channel MscL-G22S in neurons, allowing them to respond to low-intensity ultrasound.
- Evoked significant neuronal activation and muscular responses in targeted brain regions without widespread activation in non-target areas.

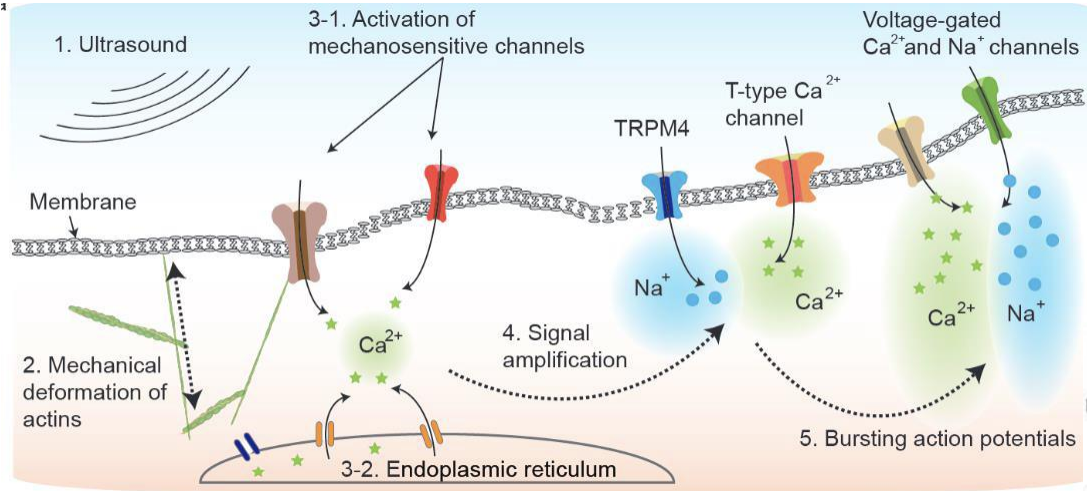
Genetic engineering:

UltraSound-sensitive proteins;
Modulation of Na^+ , Ca^{2+}
channels via ultrasound

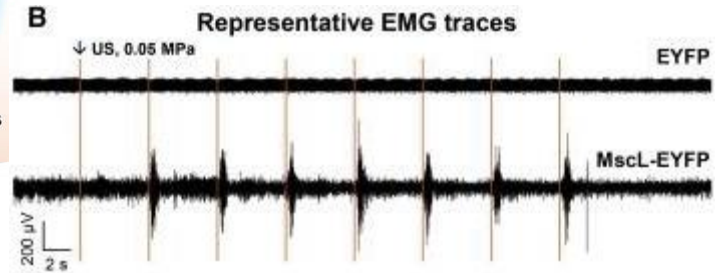
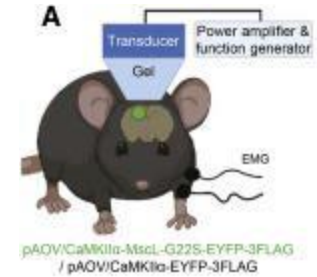
Depolarization induced by
mechanical deformation of
the cell membrane?

No established mechanistic
theory yet





Qiu et al., 2020, CellReports



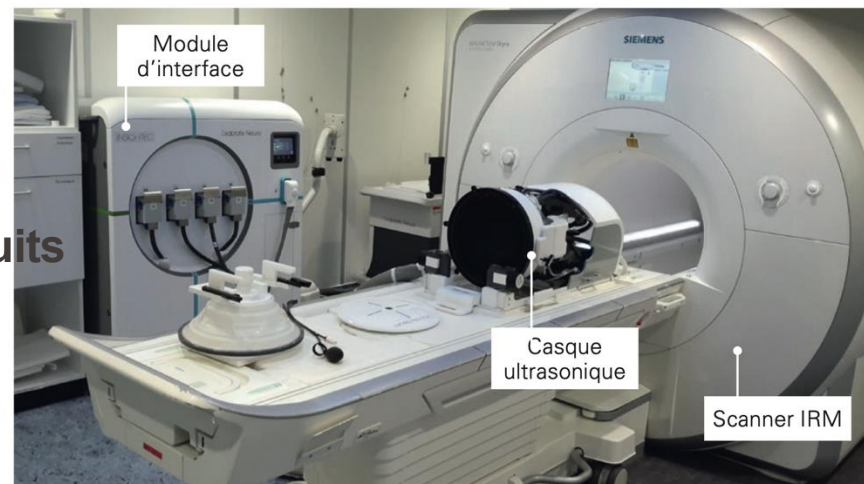
Muscle activity (EMG) depends on:

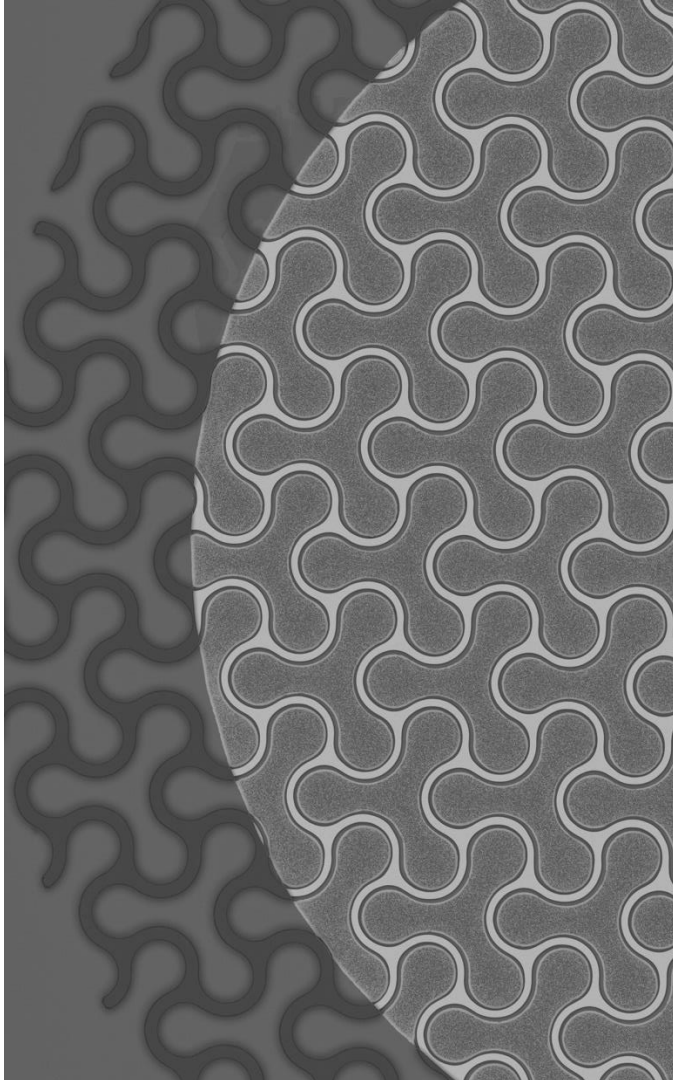
- US stimulation intensity
- stimulation cycle
- stimulation burst duration

FUS image-guided high-intensity focused ultrasound treatment

(NOT neural “interfacing”)

- 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





Modalities of communication

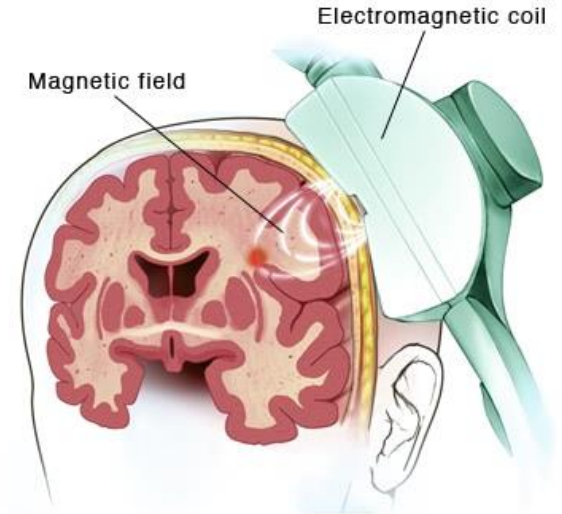
Light and optogenetics

Ultrasounds

Magnetic field

Transcranial magnetic stimulation

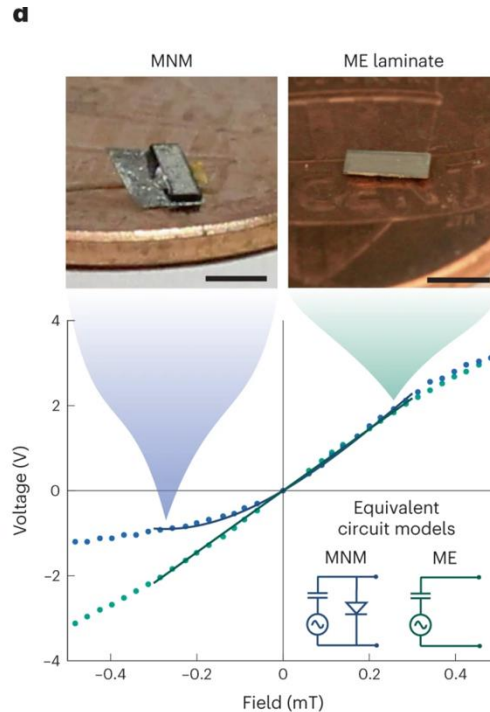
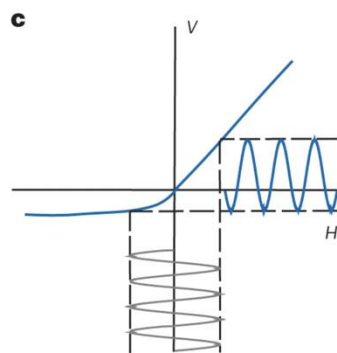
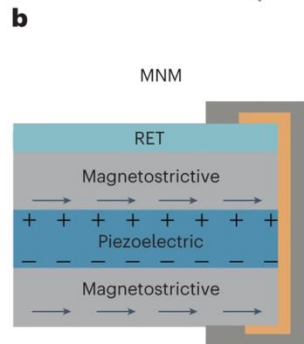
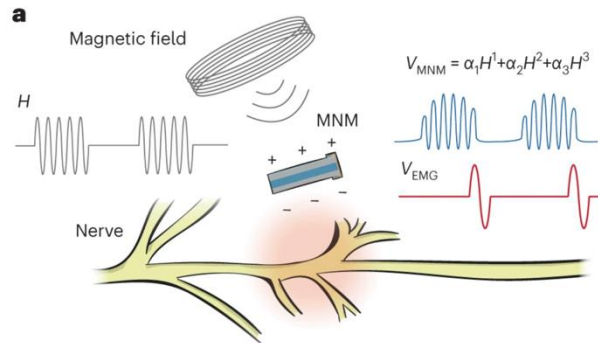
- Transcranial magnetic stimulation (TMS) uses external magnetic fields to stimulate nerve cells in the brain .
- FDA approved for drug-resistant depression, OCD, migraines and to help people stop smoking.
- An electromagnetic coil is placed against the scalp and delivers magnetic pulses that stimulate the brain region involved in mood control.
- Although the biology of why TMS works isn't completely understood, It's thought to activate regions of the brain that have decreased activity during depression.



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Remote stimulation induced by magnetic field

- AC magnetic field → large penetration depth
- Magnetostriction → mechanical deformation
- Strain in Piezo → conversion to electric field
- RET layer (e.g. p-n junct.) → rectify to DC
- AC magn. Bursts → DC pulsing!

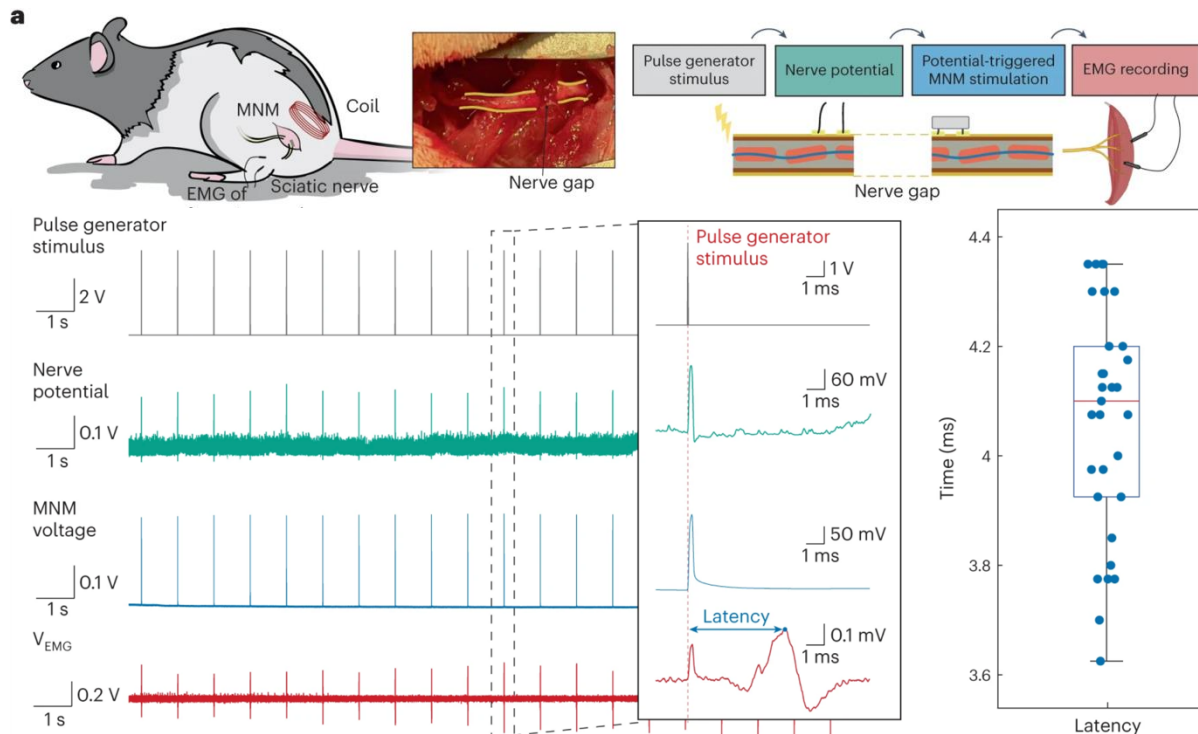


$$V_{ME} = \alpha H d$$

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

Restoring communication after nerve damage

A unique example
Not really “magnetic” interfacing



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 penetration; pre-clinical stage only