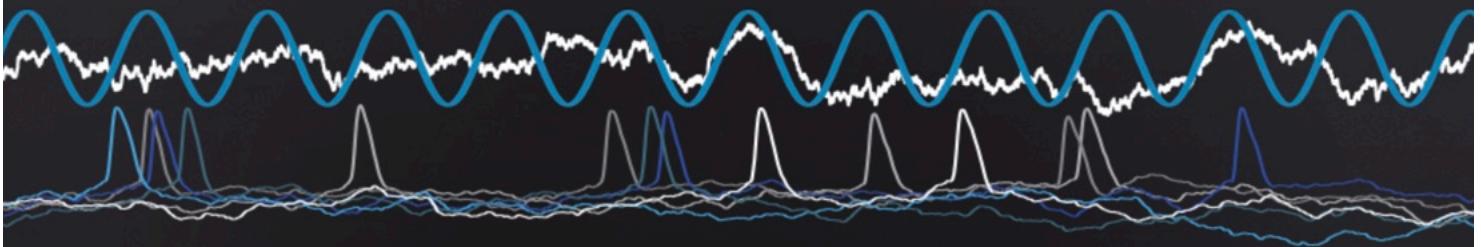


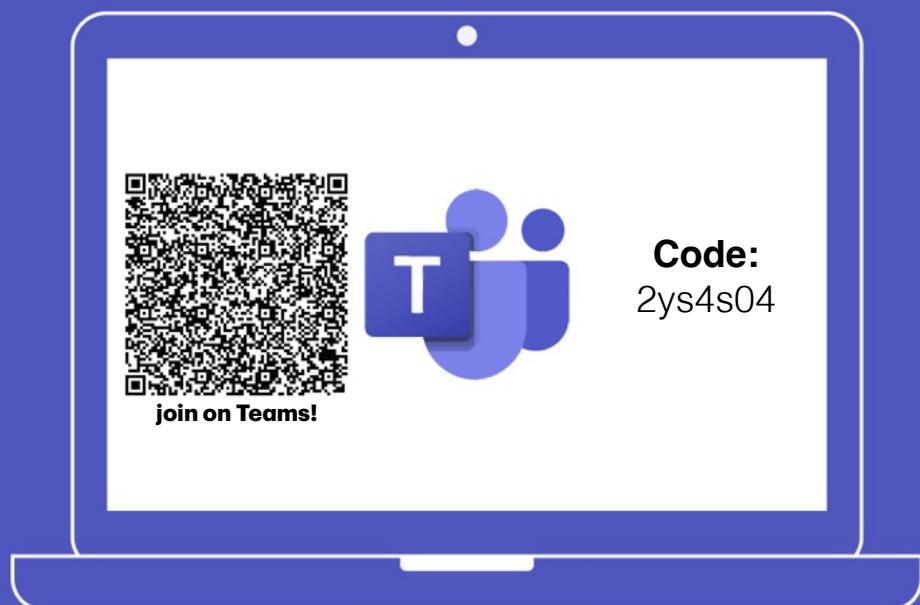
ELECTROPHYSIOLOGICAL SIGNALS



GENERATION AND CHARACTERISATION

Prof. Ing. Michele GIUGLIANO, PhD
Introductory Class

Teams - Instant messaging



Announcements; Forum/Q&A for all !

Website and GitHub repository

<https://mgiugliano.github.io/ePhysSignals>



<https://github.com/mgiugliano/ePhysSignals>

Website and GitHub repository

A screenshot of a Microsoft Teams channel interface. On the left is a sidebar with various team-related options like Activity, Chat, Teams, Assignments, Area Docente, Chatbot D..., Calendar, OneDrive, Cells, Copilot, and Apps. The main area shows a channel named "2025 BIOING_1 Segnali biologici". A post from "Michele GIUGLIANO" is highlighted with a yellow circle and a red arrow pointing to it. The post contains text about class logistics and a link to a website. Below the post is another message from Michele GIUGLIANO with the subject "Orario primo anno - bozza". At the bottom of the screen, there is a file titled "Oradio_primo_anno_Sep2...".

Math refresher, handouts, notebook

CONTENT

0. Mathematical Preliminaries - if needed (watch here)

- Mathematical functions and their graphs
- Derivatives and Integrals
- The Dirac's Delta and the Convolution Integral
- Ordinary differential equations and their solution
- Numerical solutions and the Euler forward method

1. Introduction

- Definition of "biological signal"
- Scientific motivations and innovation in medicine and neurobiology
- Examples of electrophysiological signals of the nervous system

2. EEG, Extracellular, and Intracellular Electrophysiological Signals

RESOURCES

GitHub Repository

- notebooks
- overheads

Video Material

- HowTo Google Colab: breaking the ice!
- HowTo Google Colab: intro to Markdown.

Mathematical Preliminaries

- Plotting functions on the web (web applet)
- Khan Academy on Calculus (eLearning)
- Calculus for Dummies (text book)
- Calculus 2 for Dummies (text book)
- Statistics for terrified biologists (text book)

• The Joy of X (light book)

• Infinite powers (light book)

• Why is 'x' the unknown? (TED Talk)

• The Story of Calculus - Steven Strogatz 2022 (Ulam Memorial Lecture)

Part A: mathematical functions

- Functions and their graph
- Adding a constant or multiplying by a constant
- Notable functions: straight lines, exponentials, and logarithms

Part B: Derivatives and Integrals

- Intuition for derivatives and elementary functions
- Indefinite and definite integrals

Part C: Mathematical Preliminaries

- The Dirac's Delta-function
- The Convolution Integral
- Trains of Deltas and the Sampling of a function
- Algebraic versus differential equations
- The inhomogenous case
- Numerical solutions
- The Euler's forward method
- Taylor's expansion and comparison with the analytical solution

(online) Refresher



Lectures: recorded (not streamed!)
Posted (with delay / without guarantees) on



https://www.youtube.com/@Michele_GIUGLIANO

Playlist: UNIMORE 2025 - Electrophysiological Signals

Beware of glitches!

Organisation and Practicalities

- Classes *in person* - Slides + chalk/board
- **Interactive!** I can't read your mind (yet)
- I do **NOT** mind stupid questions (really!)
- **Ask** for help, explanations, guidance, books, papers, code, hints, intuition, etc.

ATTENDANCE TRACKING: **today's code is 33333**
(for my own statistical purposes)

Download for iPhone



Download for Android



<https://www.unimore.it/it/servizi/unimore-app>

Organisation and Practicalities

- **hand-outs:** made available to you upfront (web)
- **videotaping:** mostly aimed at working students
- **hands-on:** just need a web browser (Colab) or (if interested), install **jupyter** on your device - **ask**)
- **prerequisites (ask):** math, coding, biology

Preparing for the hands-on

- <https://youtu.be/GeQAZt4iEgQ> (What is Colab?)



OR



- <https://github.com/jupyterlab/jupyterlab-desktop> (or a local python/jupyter install on your device... Ask for help if you run into trouble!)

Evaluation and Exam(s)

- **this** module: **oral**, informal, interview (~25 min)
- Overall mark = average **weighted** by CFUs of modules
- Overall mark cum laude = 32/30
- Overall mark = **rounded** to closest integer (*ceil, floor*)
- Overall mark = **requires** all modules (none skipped)
- Each module mark expires after **24 months**

Statistics from the “past”

- Average mark of “my” module: **28/30**
- % of “cum laude” for “my” module: **30%**
- Overall mark average = **26/30**

Exams and Exam sessions

- Jan 2026: 14th, 21st, 28th 8-13, 12 slots/day
- Feb 2026: 4th, 18th, 25th 8-13, 12 slots/day
- 1-2 sessions in June, TBA
- 1-2 sessions in July, TBA
- exceptionally: on appointment (1-2 slots/day)

Class organization: your call!

- Current schedule: **14:00 - 17:45**, sharp **at 14:00**
- Alternative 1: **14:15 - 18:00**, sharp **at 14:15**
- Alternative 2: **14:30 - 18:15**, sharp **at 14:30**
- Breaks: **(3 x) every 45-50 min**
- Alternative: **(1 x) every 90-100 min**



EPFL

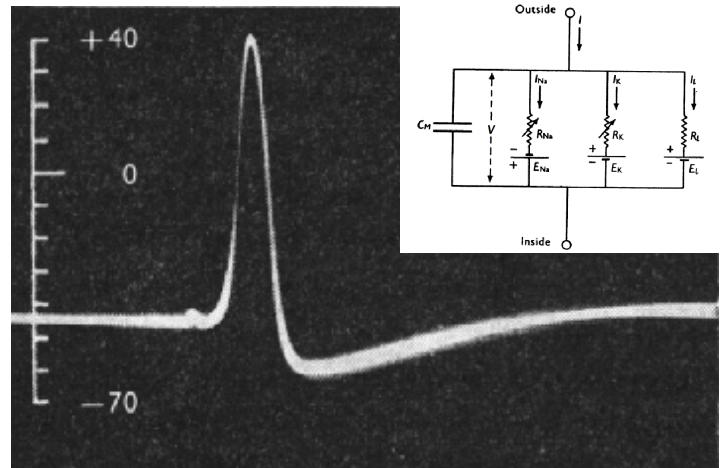
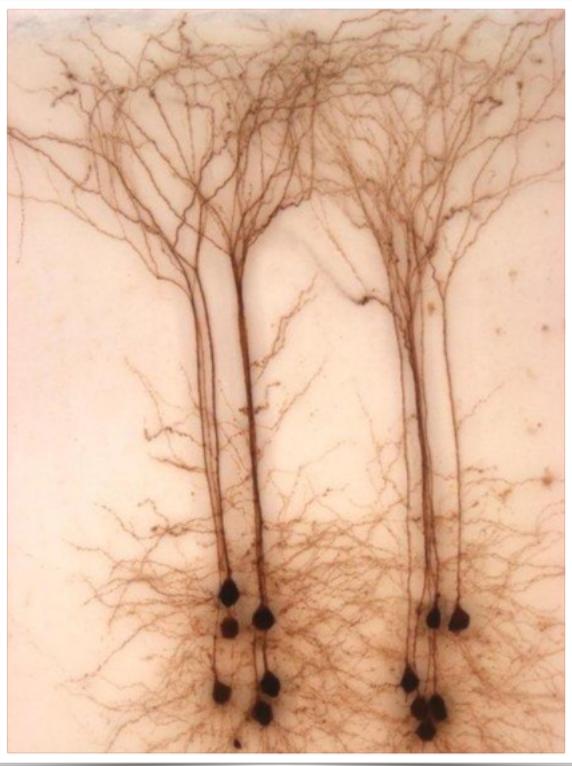


SISSA

UNIMORE

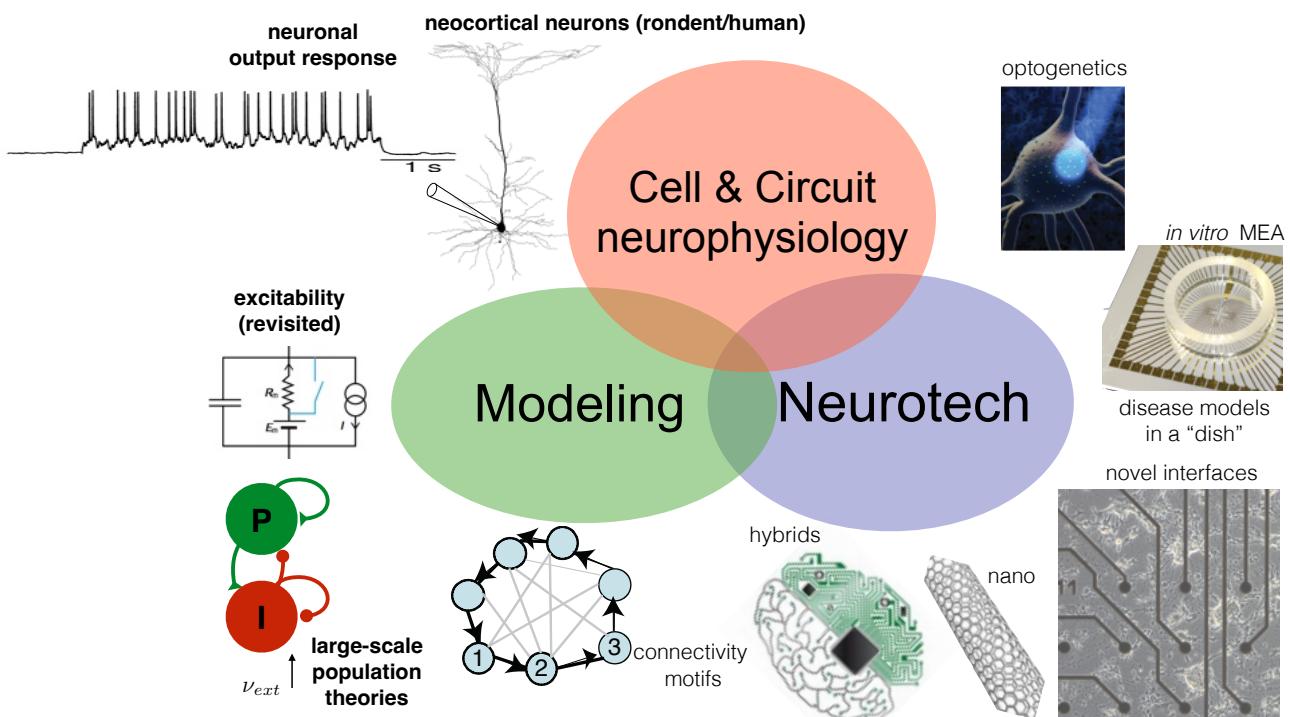


1997:	Laurea degree in Electronic/Biomedical Engineering	(Genova)
2001:	PhD in Bioengineering and Computational Neuroscience	(Milano)
2001:	Postdoc in Cellular Neurophysiology	(Bern)
2005:	Group Leader in Microcircuit Neurophysiology	(Lausanne)
2008:	Prof. of Neuroscience	(Antwerpen)
2019:	Prof. of Physiology	(Trieste)
2024:	Prof. of Bioengineering	(Modena)

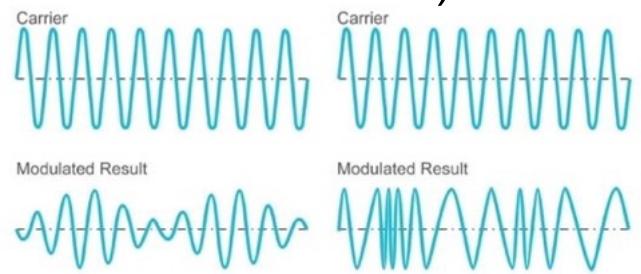
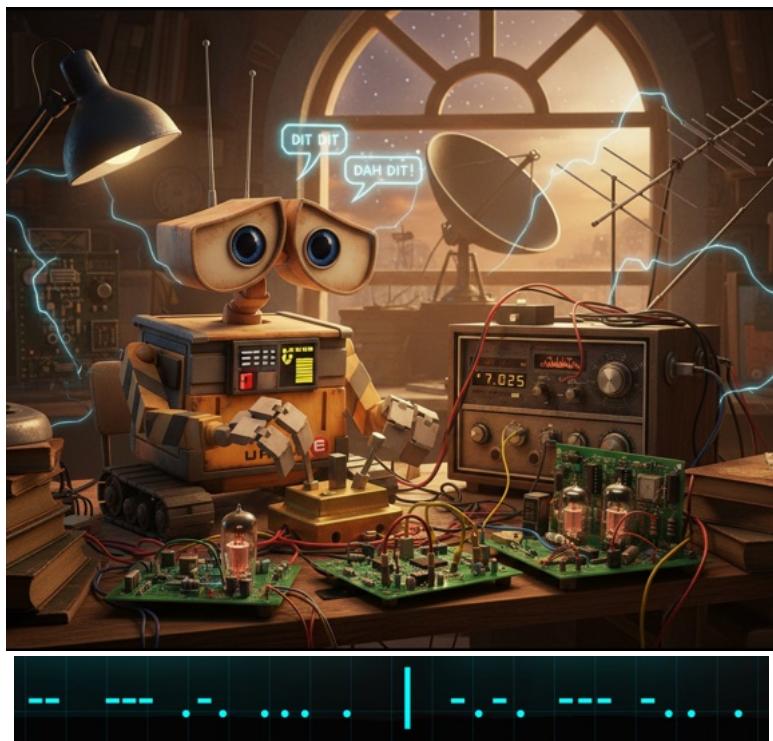


$$\frac{dV}{dt} = -\frac{1}{C_M} \{ \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_L (V - V_L) \}$$

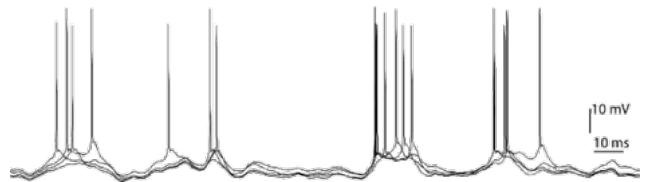
Laboratory of Neuroengineering (visits possible)



In my “free” time (have almost none)



AM, **FM**



Your self-introduction (30-60s)

- Who are you?
- What is your academic background?
- Why studying Bioengineering?
- What's your (non) academic passion?

Study Material (chapters from)

- Halnes et al., (2024) Electric Brain Signals - Cambridge Univ. Press
- Weiss TF (1996) Cellular Biophysics 1-2, MIT Press
- Bear MF, Connors B, Paradiso MA (2006) Neuroscience [...] (ch. 1-4)
- Kandel et al. (2012) Principles of Neural Science, 5th ed., McGraw Hill
- Alberts et al. (2009) Essential Cell Biology, 3rd ed., Garland Science
- Primer on “Brain Facts” (see parts 1-2, 4)
- (few) pages from Longstaff, 2007 (neurons, diversity, CNS)
- “Eye, Brain, and Vision” book by D. Hubel (ch. 1-5)

Reading material and Data sample

- Readings posted on our website (see resources)
- ECG/EMG signals posted on GitHub (see data) - follow the tutorial on YouTube and play with the data!

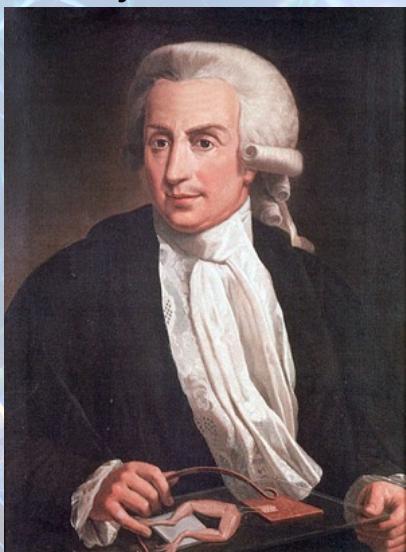
(BIOLOGICAL) SIGNALS

- A “*signal*” is physical variable (or observable), subject to **variations**.
- Variations may be (e.g.) through time **t**, through space **x,y,z,...**.
- It is represented as a scalar/vector *function* of **indep.** variable(s).
- Examples of (known) functions: $f(t) = \sin(2\pi 0.1 t)$ $g(x,y) = e^{x+y}$
- ...a collection of data points, one/more for each value of the indep. var(s).

- *scalar*: EMG (1d), mono music (1d), b/w photo (2d), b/w video (3d), MRI (3d), fMRI (4d)
- *vector*: velocity of a fly (4d → 3d), stereo music (1d → 2d), color of a RGB photo (2d → 3d)

(BIOLOGICAL) ELECTROPHYSIOLOGICAL SIGNALS

“Animal Electricity” or ...conventional Electrical phenomena??



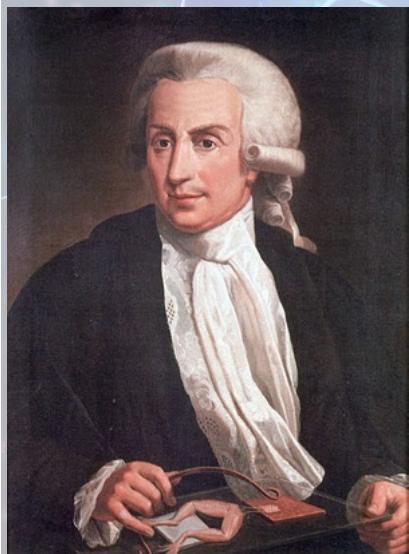
Luigi GALVANI
(1737-1798)



Alessandro VOLTA
(1745-1827)



“Animal Electricity” or ...conventional Electrical phenomena??



Luigi GALVANI
(1737-1798)



Alessandro VOLTA
(1745-1827)

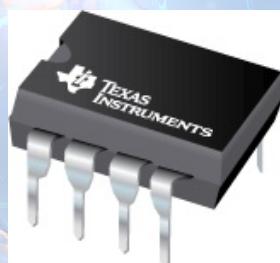
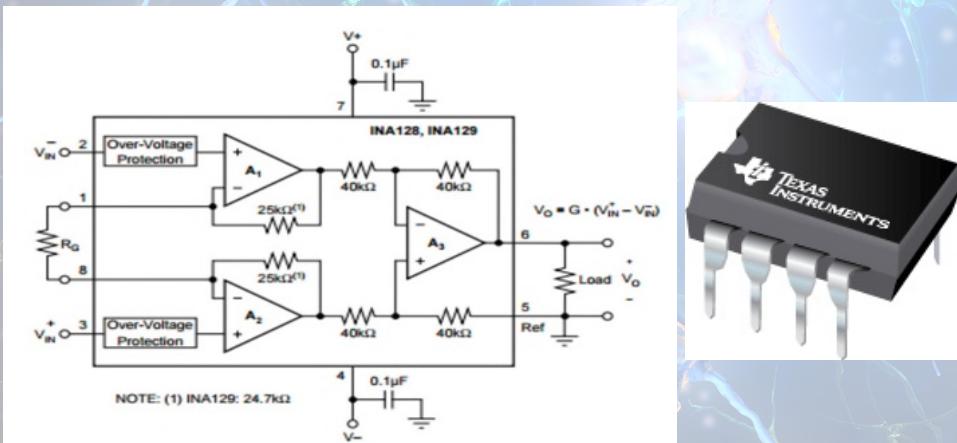
- connecting **nerves** to muscles leads to spasms...
- contacting **different metals** together creates an electric field...
- passing a **current** through frog legs, they contract!

Is Michele Giugliano... like a frog?

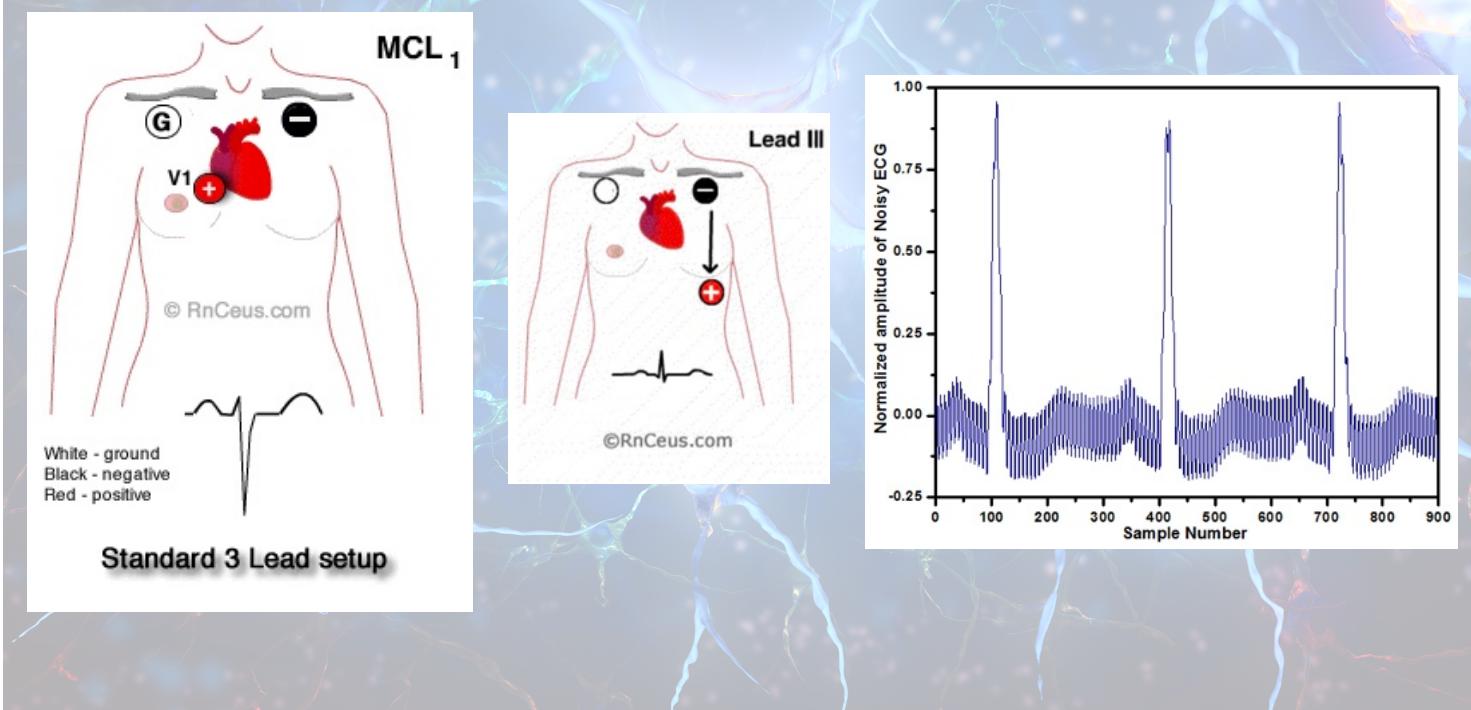
- What is Murphy's law? (Law of Engineering)
- Why would you need an electronic amplifier?
- Why better a *differential* amplifier?
- What is a ground-loop?



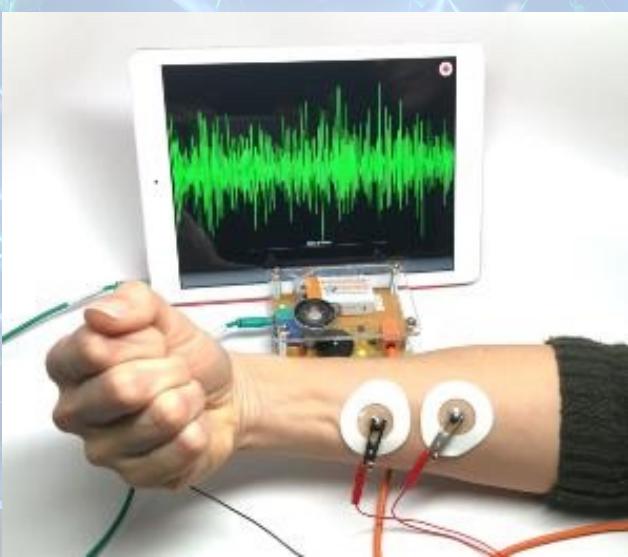
DEMO time!!!



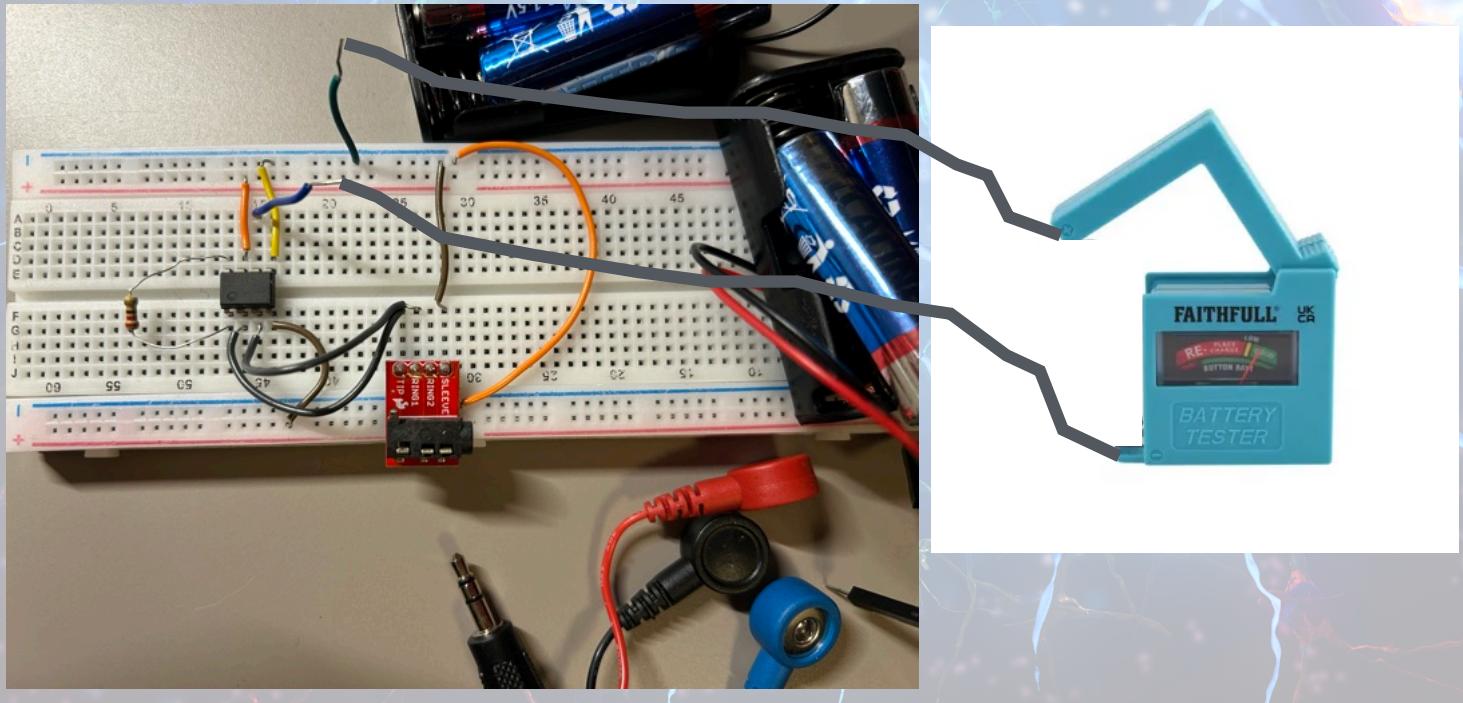
EKG - noise - signals polarity



Motor units - (surface) ElectroMyoGraphy



Is Michele GIUGLIANO like... a frog??!??



Play with my recordings! - YouTube Tutorial

- Can you plot the **EKG** and **EMG** traces? Change colors, line style, line thickness? Axis labels?
- Can you infer, from data, the sampling rate (in kHz) in both cases?
- What is the average voltage recorded for each trace? Is it zero-mean? Why? Why not?
- What is the standard deviation of each trace? What is the std dev across time, in 1s-chunks?
- Are those stationary signals? What is the power spectrum of those signals?
- Is there a clear corrupting noise? Why is it at 50 cycle/s? Can you filter it out?
- Can you infer, from data, the Analog-to-Digital conversion resolution (in bits and in mV)?
- What was my heart rate in the EKG measurements? What was the average peak amplitudes?
- What was the variability in my heart rate?
- Does it look like a EKG? Is it upside down? Why? Can you measure R-R, P-R, QT interval, S-T?

BIOLOGICAL SIGNALS: why bother??!

Basic research

Fundamental understanding of the brain, heart, pancreas, muscles...

Understanding (and treating!) dysfunctions

Epilepsy, schizophrenia, Parkinson's, Motor neuron diseases, Multiple Sclerosis, Alzheimer, Blindness, etc. ...diabetes, arhythmia, etc.

Neuroprostheses, Neuromodulators, ...Electroceutics

Retinal/Cochlear implants, (DBS) neuromodulation, BMI, pacemakers, etc.

Reverse engineering the brain

Novel computing paradigms, robotics, computer vision, ML, NeuroAI,....

Brain (dys)functions

Men ought to know that from nothing else but the brain comes joys, delights, laughter and sports, and sorrows, and griefs, despondency, and lamentations.

And by this, in a especial manner, we acquire wisdom and knowledge, and see and hear and know what are foul and what are fair, what are bad and what are good, what are sweet and what are unsavory...

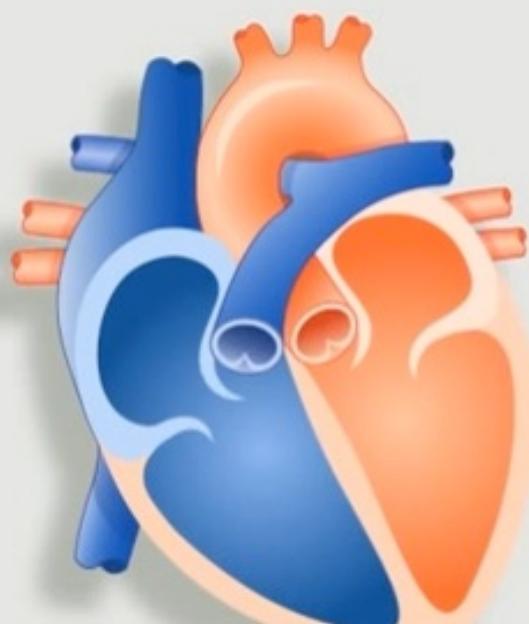
And by the same organ we become mad and delirious, and fears and terrors assail us... All these things we endure from the brain when it is not healthy... In these ways I am of the opinion that the brain exercises the greatest power in man.

Hippocrates (fourth century B.C.): “On the Sacred disease”

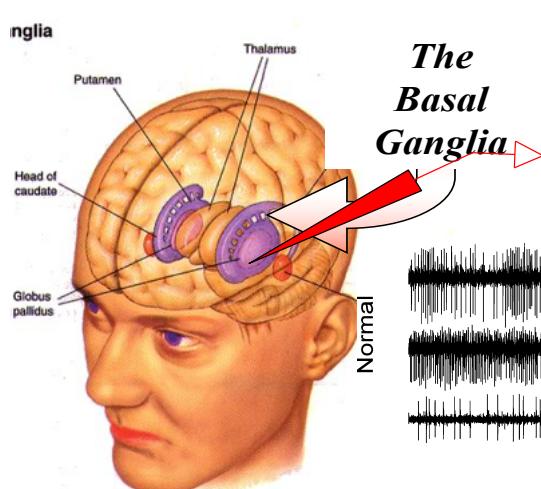
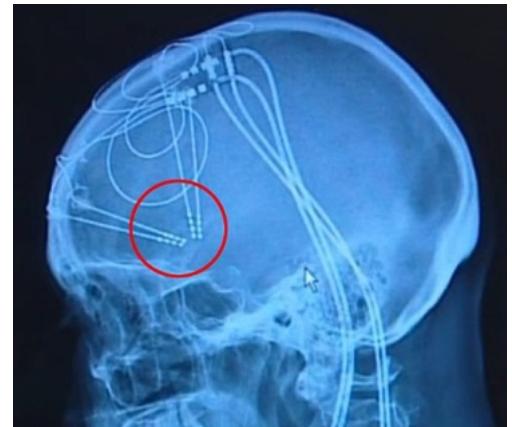
Anyone you know with...

- a heart pacemaker? an implantable defibrillator?
- a cochlear implant?
- a deep-brain stimulator?

Pacemaker



Beyond Neuropharmacology: Neuromodulation & Electroceutics



*The
Basal
Ganglia* ▶

1000900783



Courtesy of Hagai Berman, HUJI



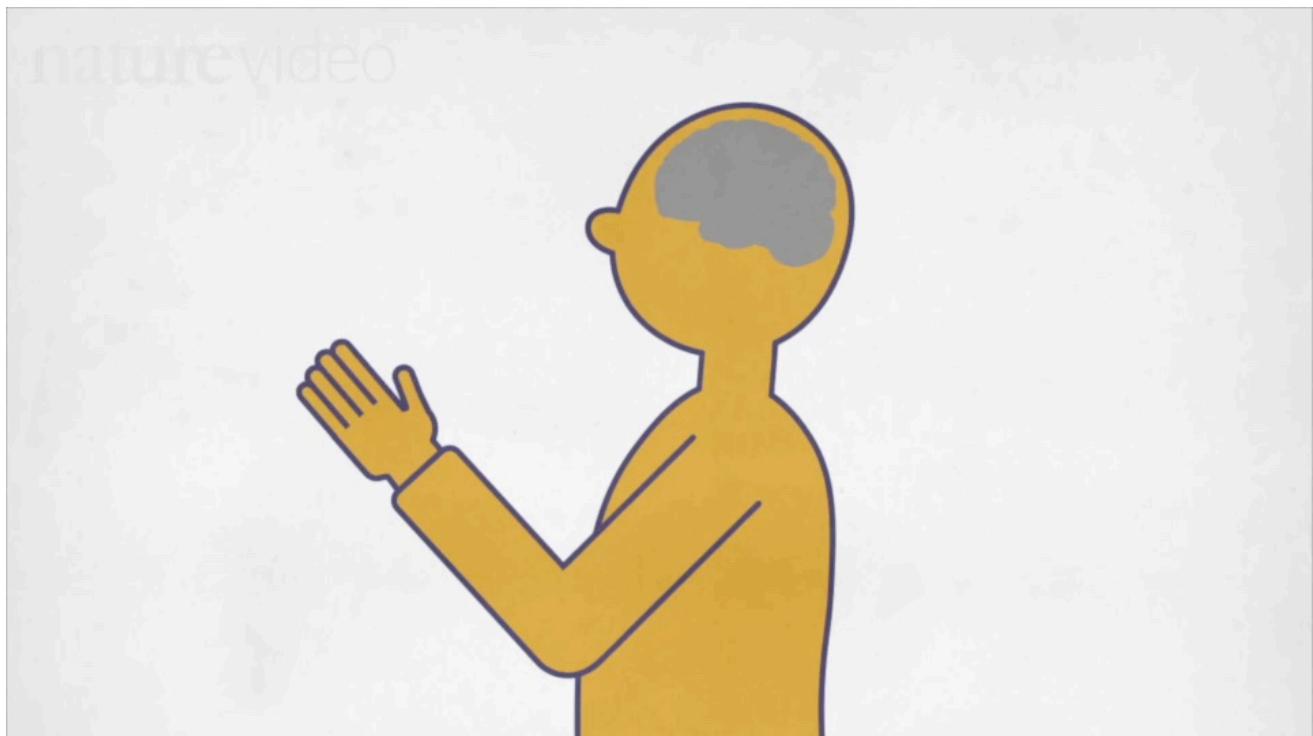
(high-frequency, electrical) Deep Brain (extracellular) Stimulation



Bionics and Neuroprosthetics

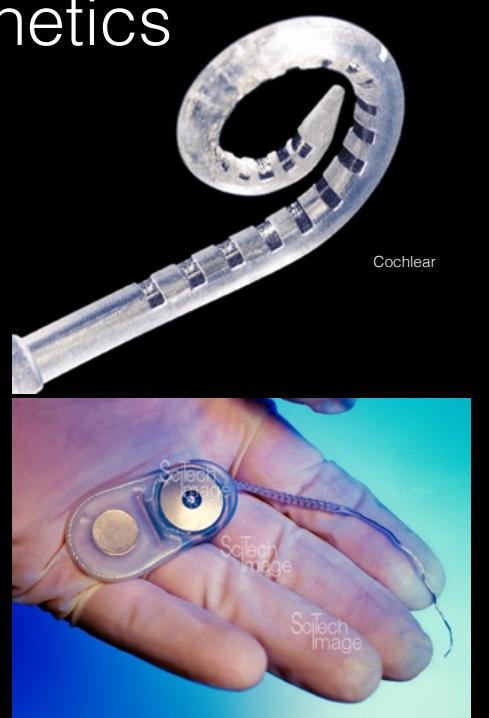
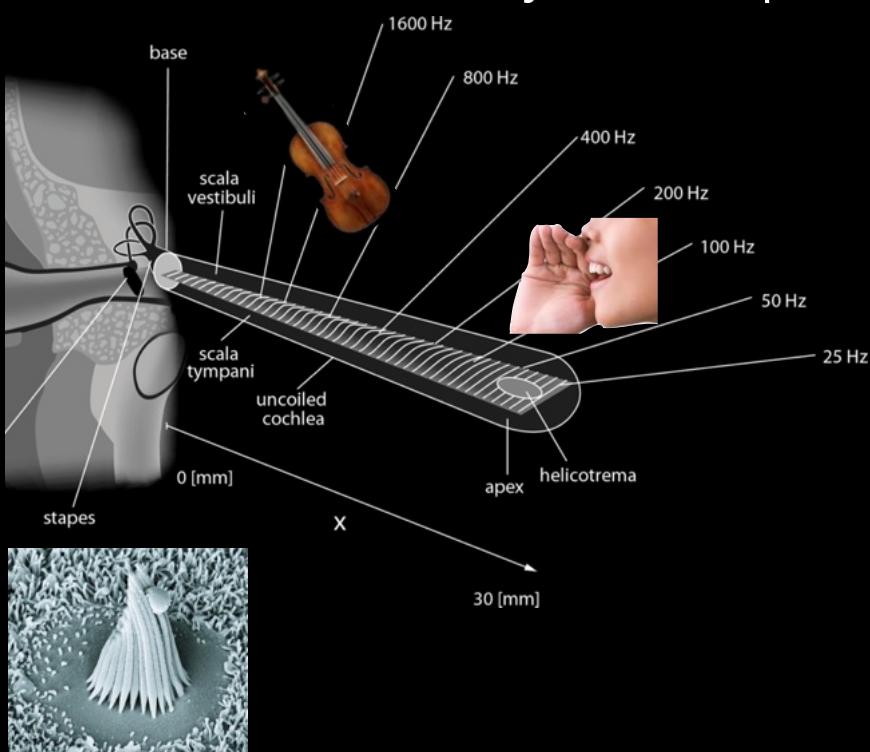


Motor (& Sensory) Neuroprosthetics

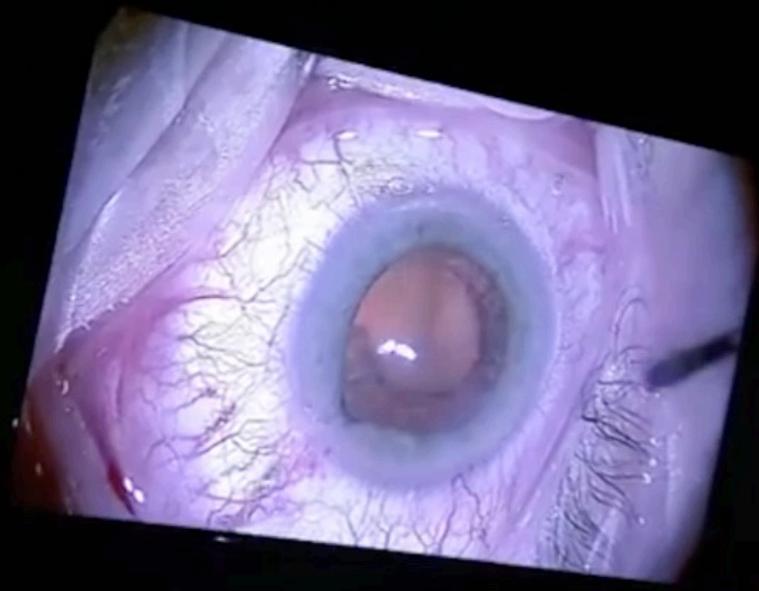




Sensory Neuroprosthetics



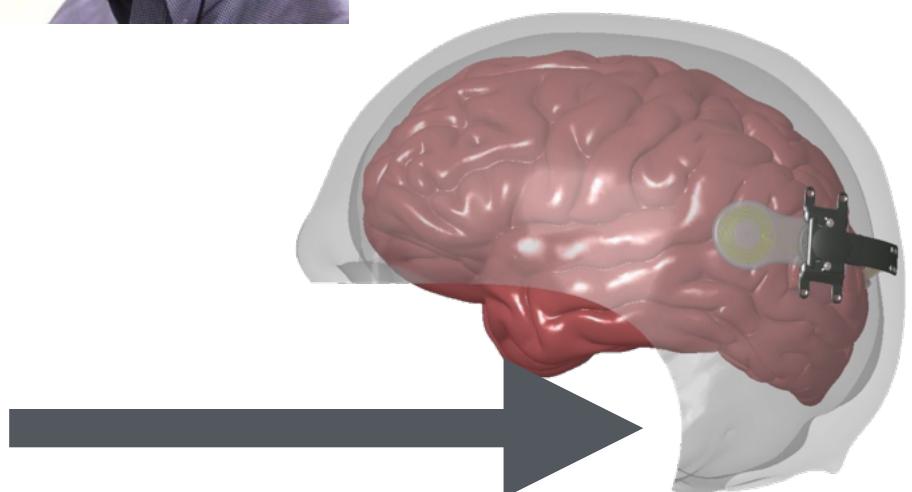
Sensory Neuroprosthetics

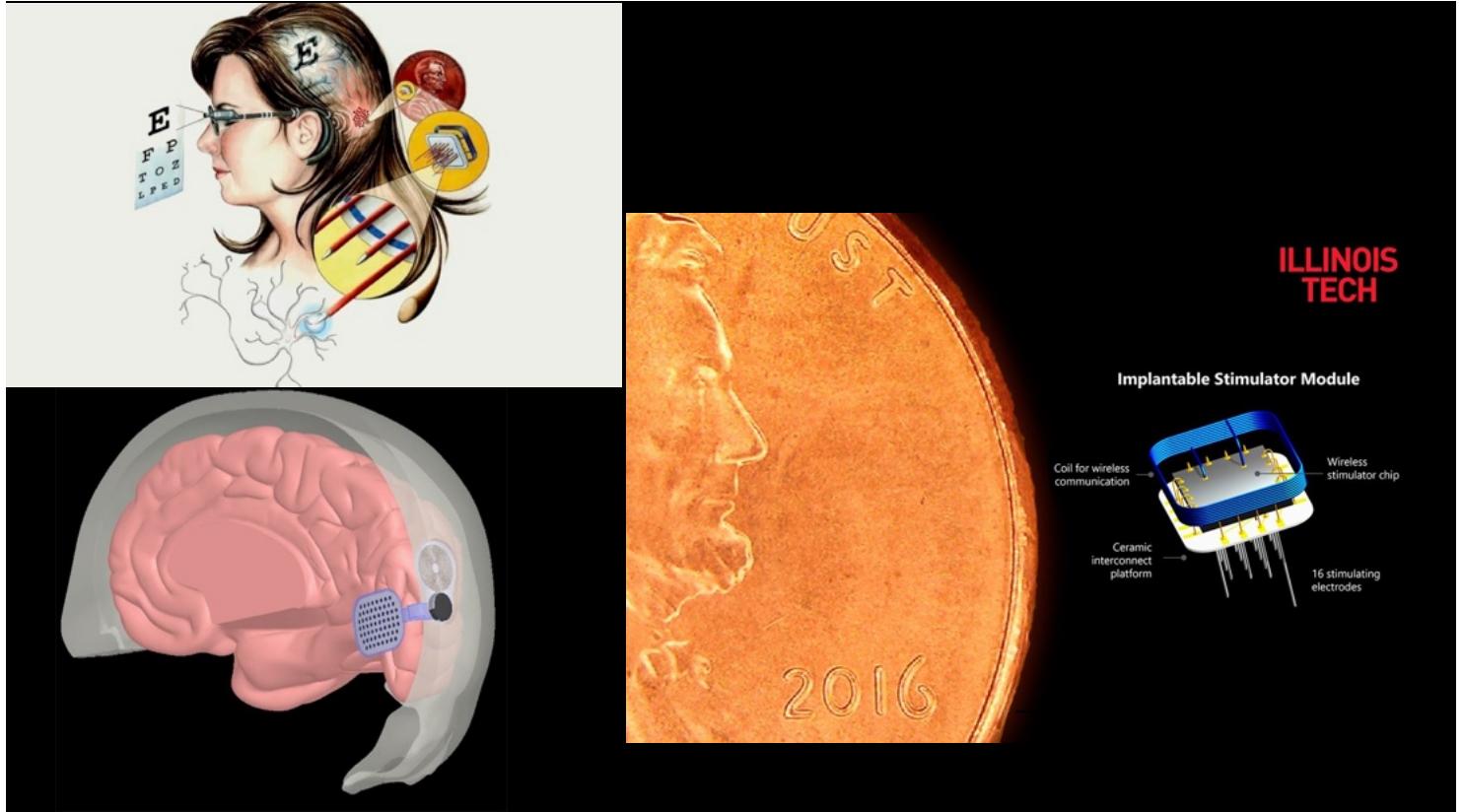


MEDTECH
'Fantastic technology and a lousy company': Second Sight's 'bionic eyes' have gone obsolete while still implanted, report finds

By Andrea Park · Feb 17, 2022 11:48am

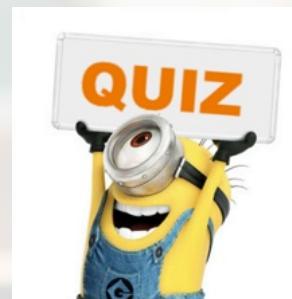
Second Sight Medical Products Implants Retinitis Pigmentosa Investigation

A close-up photograph of a human eye. A small, rectangular electronic device is attached to the cornea. The device has some text and symbols on it, including 'FP' and 'OZ'.A schematic diagram of the Second Sight bionic eye implant. It shows a cross-section of the eye with a microelectrode array placed on the retina. Labels point to the 'Pericular electronic processing unit', 'Cables', and the 'Microelectrode array responsive to electrical signal from pericular electronic processing unit'.



Do you know Elon Musk?

- What is Neuralink doing?



← Post **Reply** **...**

 **Elon Musk**  
@elonmusk

The Blindsight device from Neuralink will enable even those who have lost both eyes and their optic nerve to see.

Provided the visual cortex is intact, it will even enable those who have been blind from birth to see for the first time.

To set expectations correctly, the vision will be at first be low resolution, like Atari graphics, but eventually it has the potential be better than natural vision and enable you to see in infrared, ultraviolet or even radar wavelengths, like Geordi La Forge.

Much appreciated, @US_FDA!

← Post **Reply** **...**

 **Neuralink** 
@neuralink

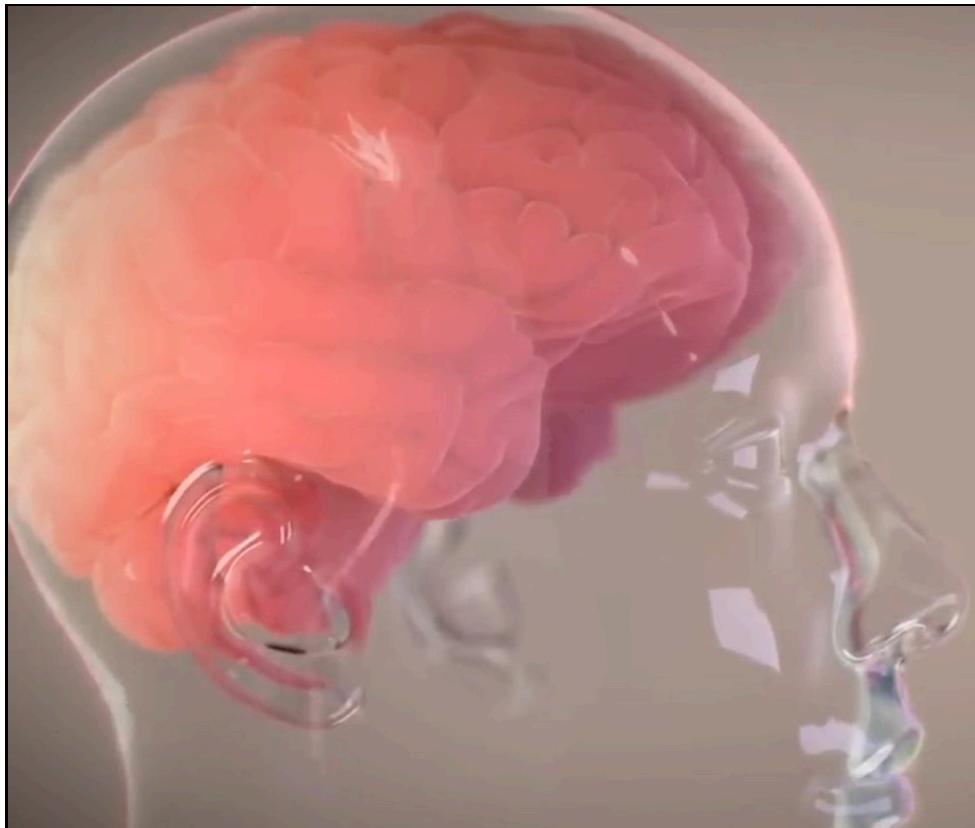
We have received Breakthrough Device Designation from the FDA for Blindsight.

Join us in our quest to bring back sight to those who have lost it. Apply to our Patient Registry and openings on our career page





From neuralink.com



9:57

 **Neuralink** 
@neuralink

We're excited to announce that recruitment is open for our first-in-human clinical trial!

If you have quadriplegia due to cervical spinal cord injury or amyotrophic lateral sclerosis (ALS), you may qualify. Learn more about our trial by visiting our recent blog post.

Replying to @neuralink
So excited

for to about
q w e r t y u i o p
a s d f g h j k l
z x c v b n m
123 space return

January 2024

THE LINK

A

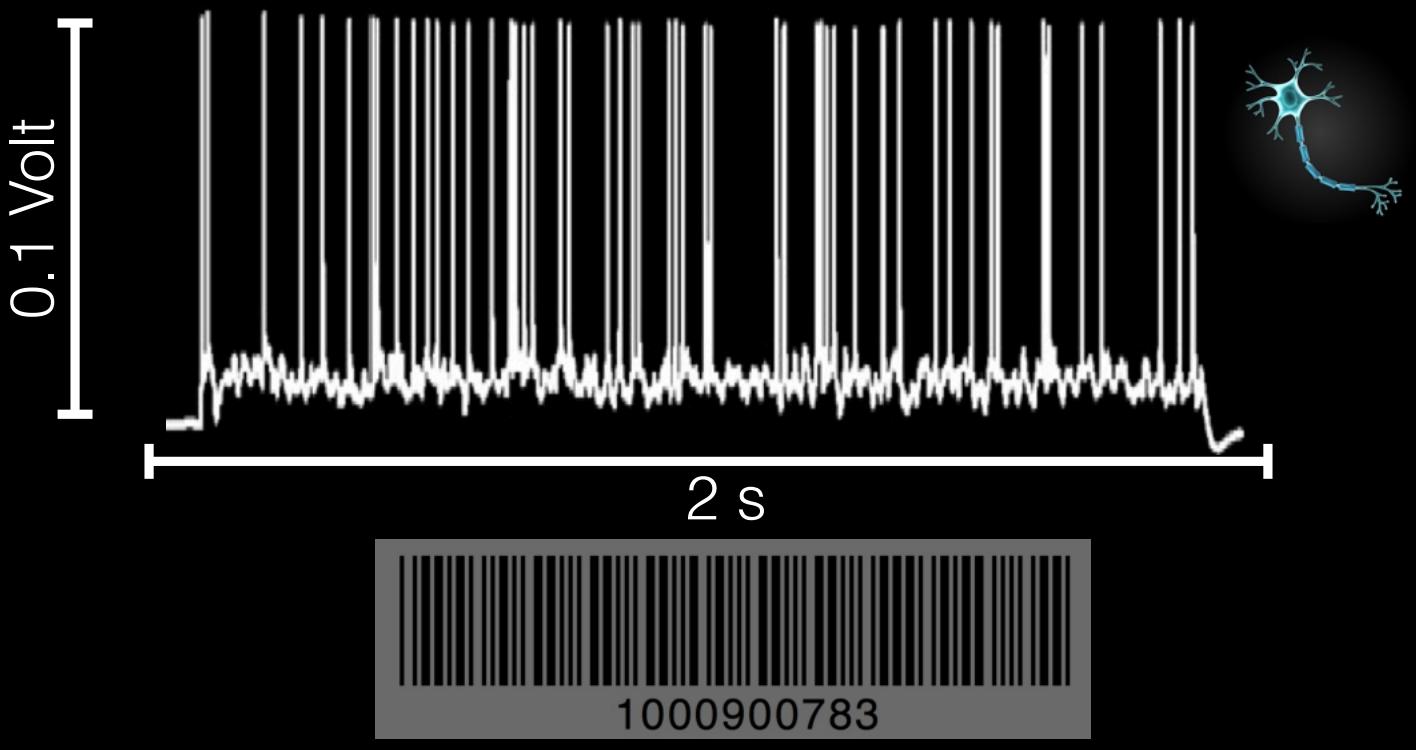


Assuming you could
...“read” thoughts

- what would you (therapeutically) use it for?
- What if you can't read but you have AI? How?



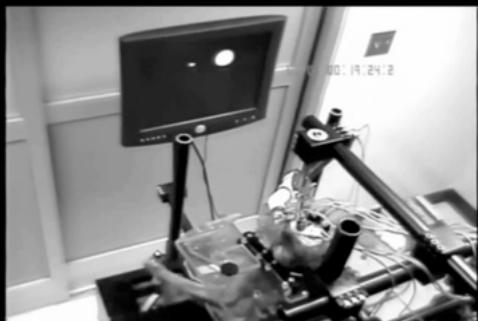
Train of impulses from a nerve cell



A ● -	J ● ---	S ● ● ●
B - ● ● ●	K - ● -	T -
C - ● - ●	L ● - ● ●	U ● ● -
D - ● ●	M --	V ● ● ● -
E ●	N - ●	W ● - -
F ● ● - ●	O ---	X - ● ● -
G - - ●	P ● - - ●	Y - ● - -
H ● ● ● ●	Q - - ● -	Z - - ● ●
I ● ●	R ● - ●	

2003 (2008)

JOYSTICK CONTROL MODE



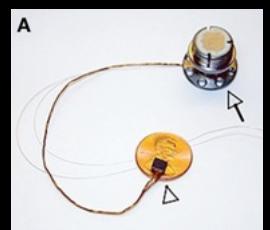
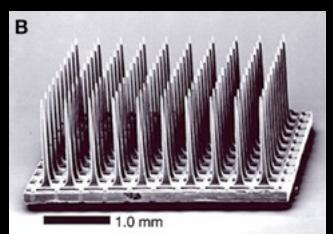
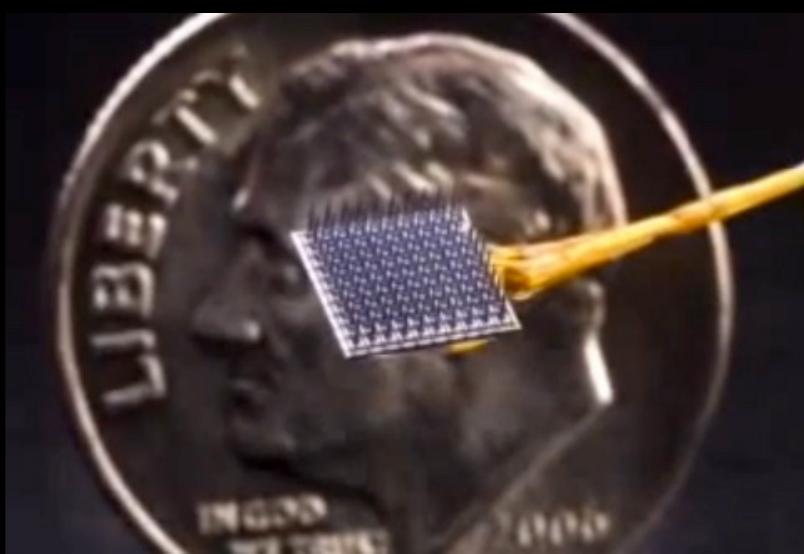
Miguel Nicolelis
Duke (US)

BRAIN CONTROL MODE



Electrical **Recordings**:
motor neuroprostheses (motor cortex)

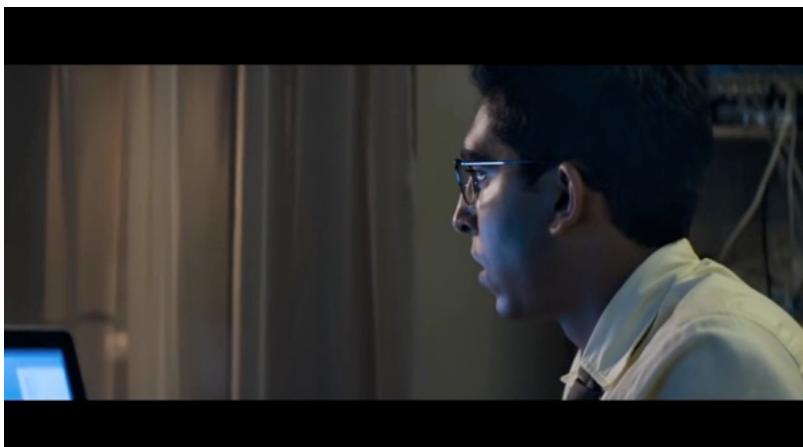
2008



Electrical **Recordings**: motor neuroprostheses (motor cortex)



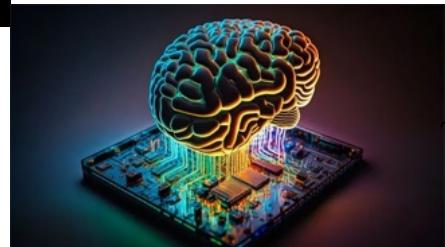
Machine Learning and Artificial Intelligence



2 gigawatt-hour (GWh) for training
~1000 households over 365 days

2 Wh/query

Neuromorphic engineering



3 Wh
~phone charger



Article

<https://doi.org/10.1038/s41467-025-64234-z>

Predictive Coding Light

Received: 29 April 2025

Accepted: 11 September 2025

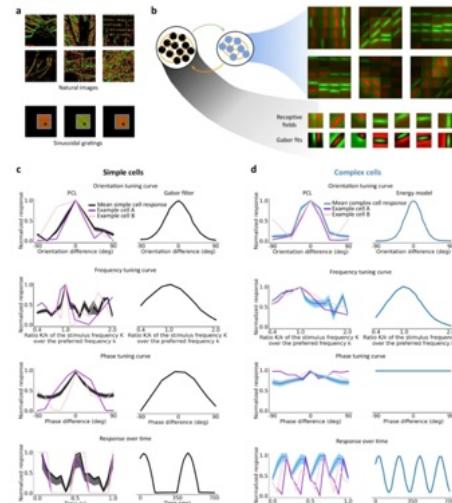
Published online: 06 October 2025

Check for updates

Antony W. N'dri¹, Thomas Barbier¹, Céline Teulière^{1,3} & Jochen Triesch^{1,2,3}

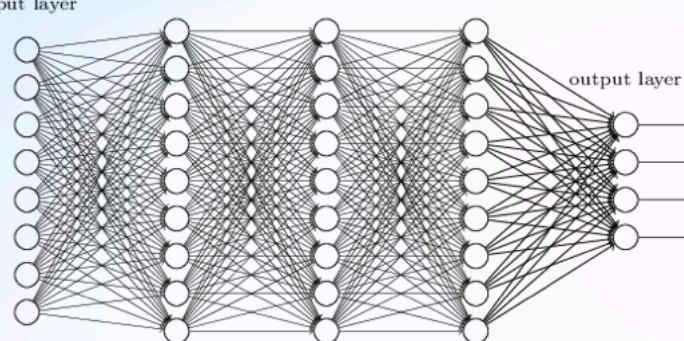
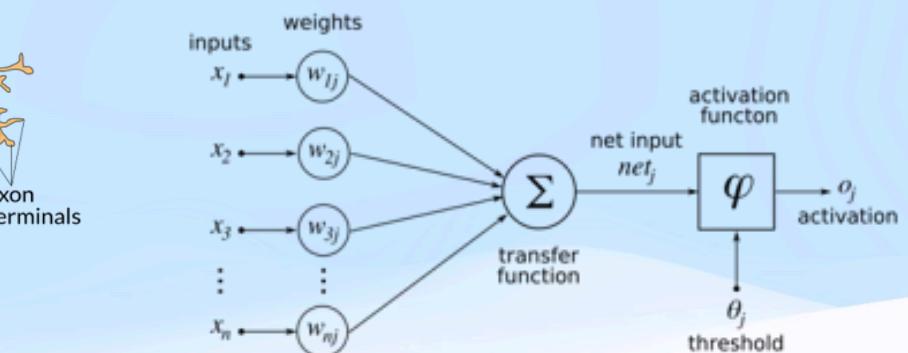
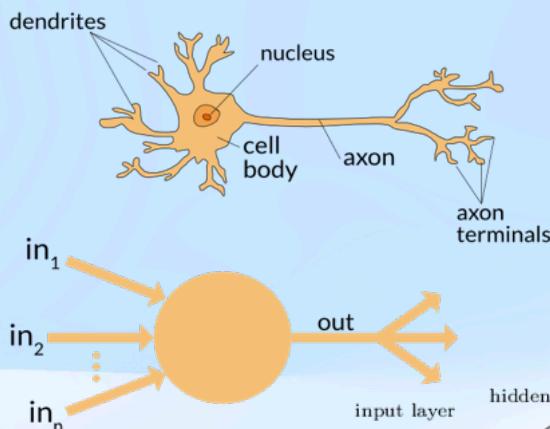
Current machine learning systems consume vastly more energy than biological brains. Neuromorphic systems aim to overcome this difference by mimicking the brain's information coding via discrete voltage spikes. However, it remains unclear how both artificial and natural networks of spiking neurons can learn energy-efficient information processing strategies. Here we propose Predictive Coding Light (PCL), a recurrent hierarchical spiking neural network for unsupervised representation learning. In contrast to previous predictive coding approaches, PCL does not transmit prediction errors to higher processing stages. Instead it suppresses the most predictable spikes and transmits a compressed representation of the input. Using only biologically plausible spike-timing based learning rules, PCL reproduces a wealth of findings on information processing in visual cortex and permits strong performance in downstream classification tasks. Overall, PCL offers a new approach to predictive coding and its implementation in natural and artificial spiking neural networks.

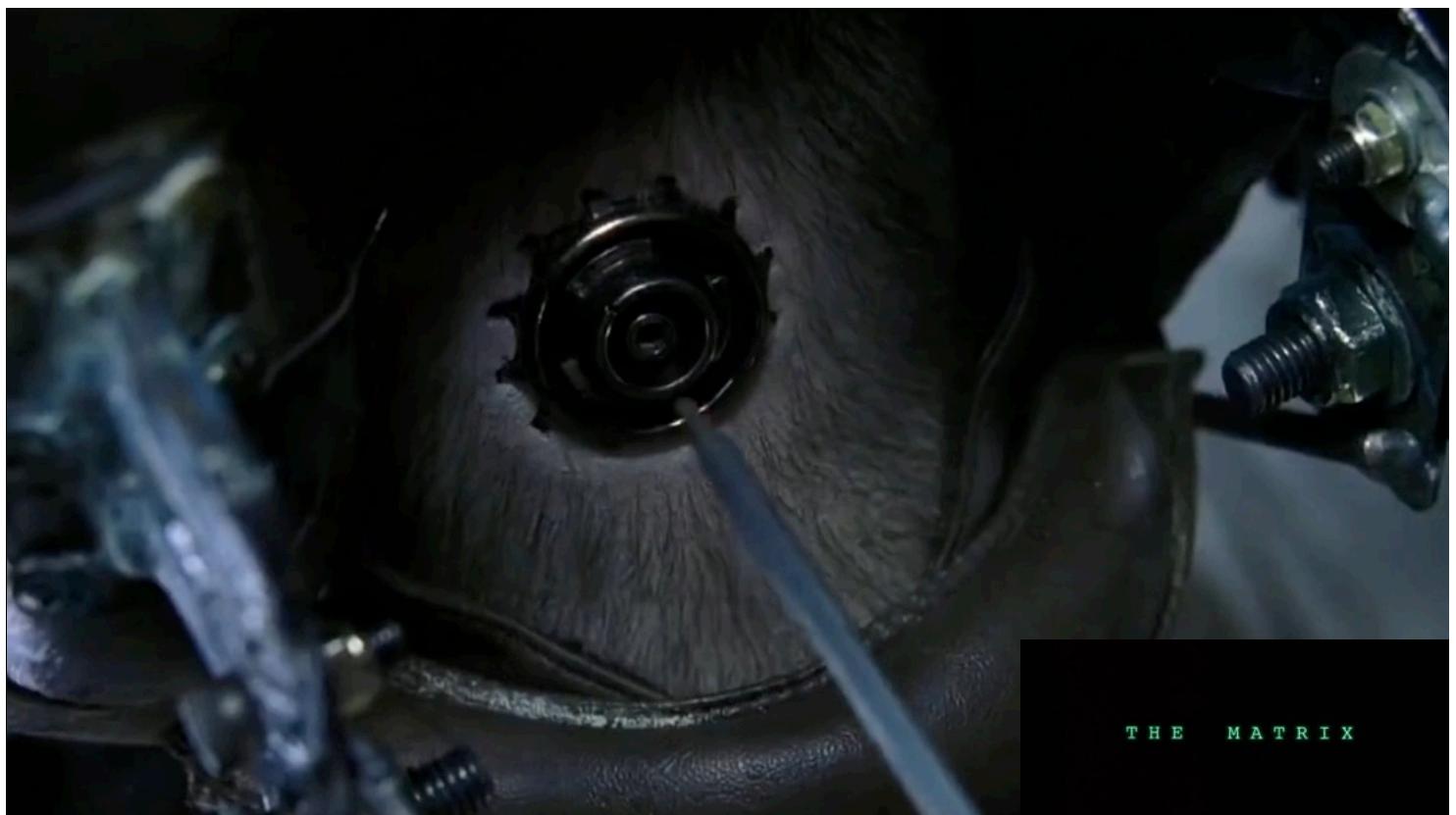
Fig. 3: Development of simple and complex cell-like receptive fields in the PCL network.



<https://www.nature.com/articles/s41467-025-64234-z>

Real neurons, Perceptron and (deep) networks





Biohybrid computation - “wetware”

BBC

Home News Sport Business Innovation Culture Arts Travel Earth Audio Video Live

3 days ago

Zoe Kleinman Technology editor

Scientists grow mini human brains to power computers

The building blocks for a biocomputer growing in a lab

It may have its roots in science fiction, but a small number of researchers are making real progress trying to create computers out of living cells.

Welcome to the weird world of biocomputing.

Among those leading the way are a group of scientists in Switzerland, who I went to meet.

<https://finalspark.com/live/>

How skin cells are turned into 'mini brains'

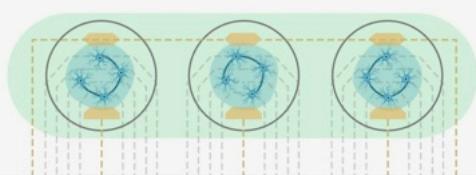
1. Human **skin cells** are turned into **stem cells**



2. The stem cells are cultured to become **clusters of neurons**, eventually becoming little spheres - collectively called **organoids**



3. After several months the **organoids** are attached to an **electrode**



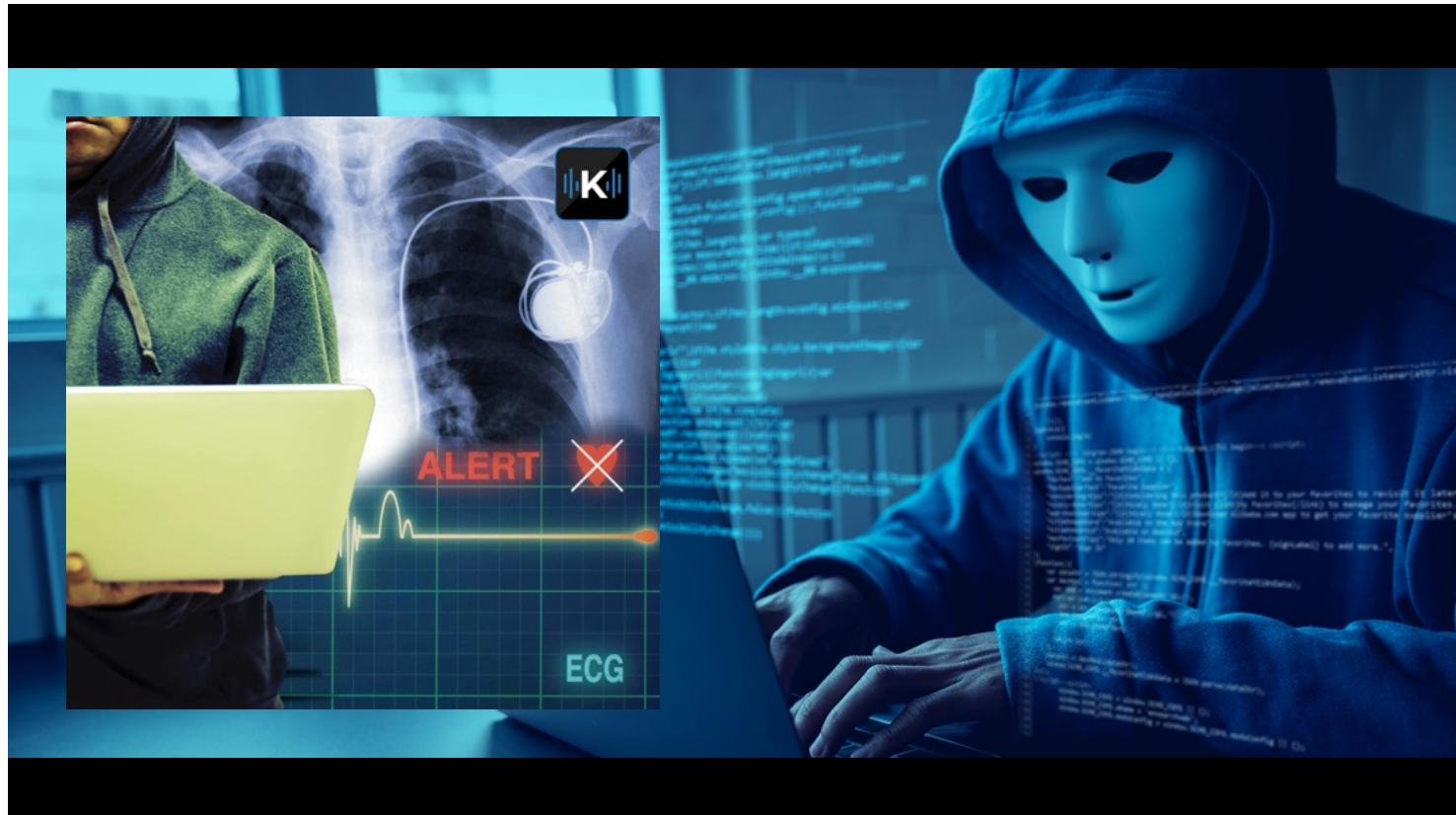
Source: FinalSpark

BBC

Biohybrid computation - “wetware”



https://www.youtube.com/watch?v=-p8BSeW_RCY



How big is big?

- What is roughly the size of a neuron (body)?
- What is the size of a DBS electrode?

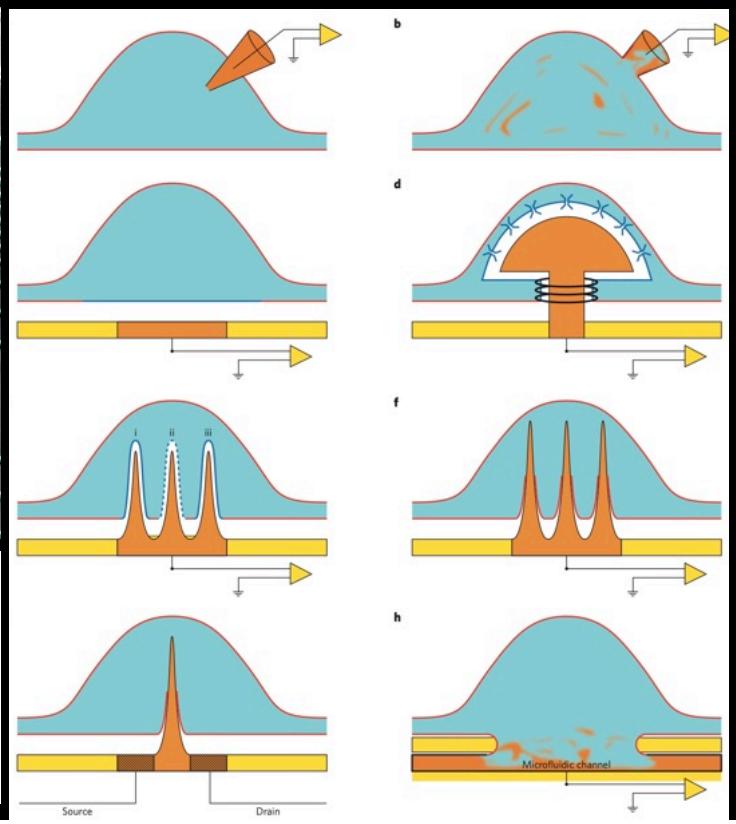
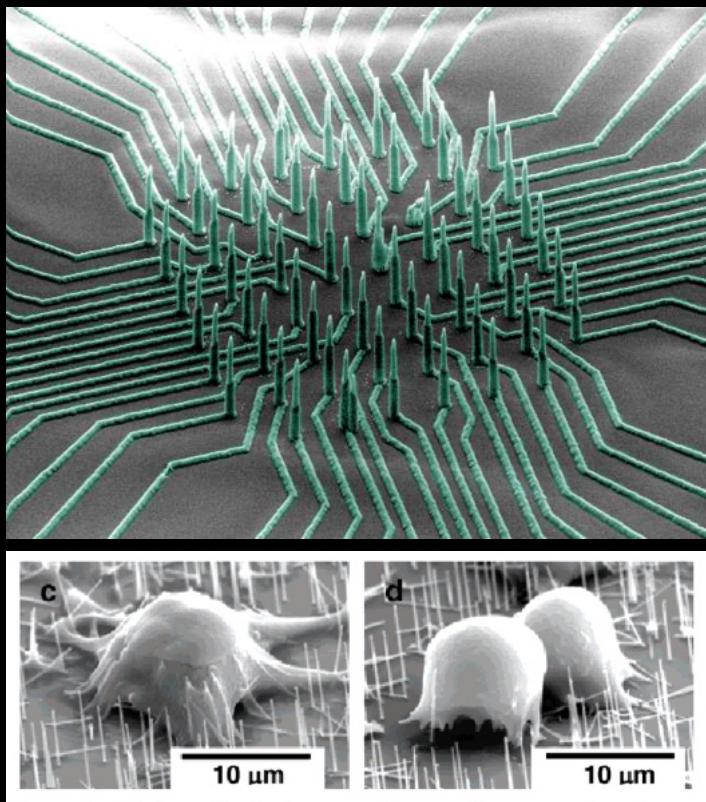


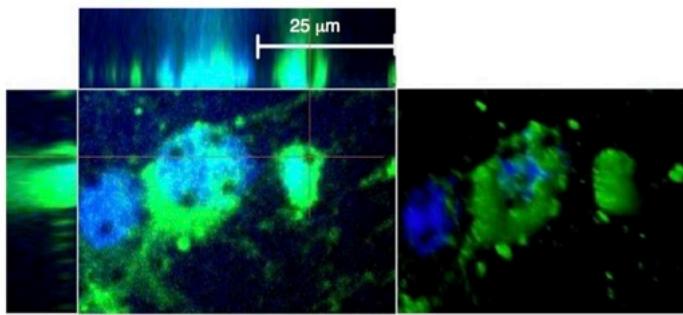
Open challenges for Neuroengineering,
Material Sciences, Nanotechnology

0.2 mm

Challenges of Neuroengineering

- **NON selective** stimulation
- Discontinuous and **NON selective** recordings
- Foreign-body tissue rejection reaction, inflammation
- **decoding** information
- design and simulate **mathematical models** of nerve cells, circuits, systems





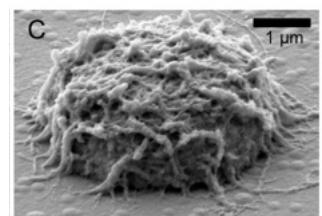
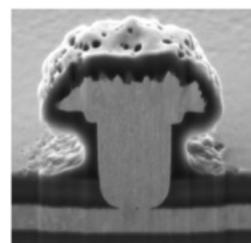
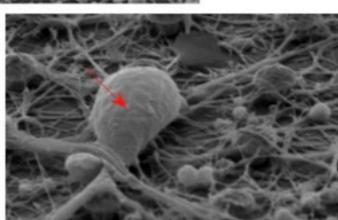
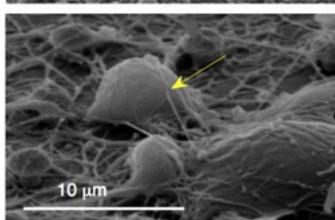
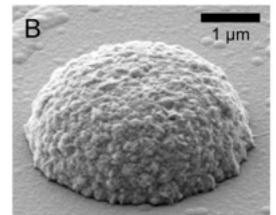
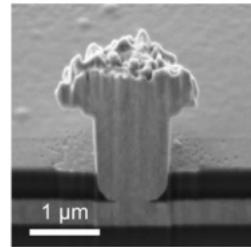
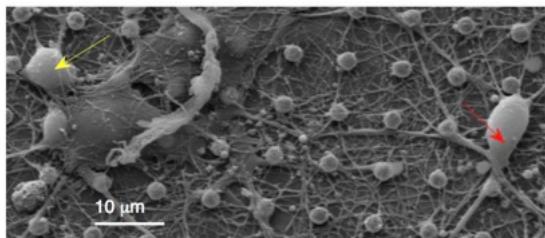
Peter
JONES



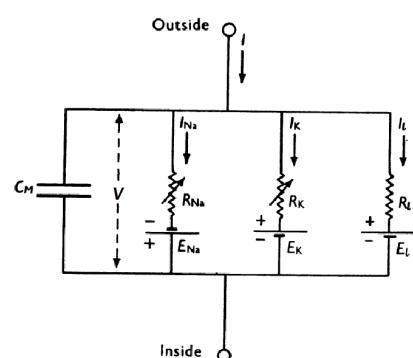
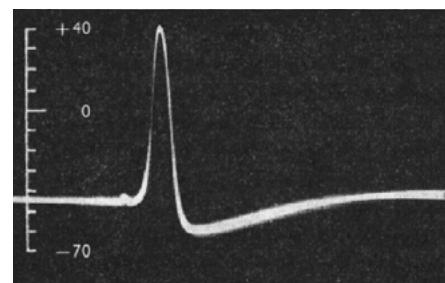
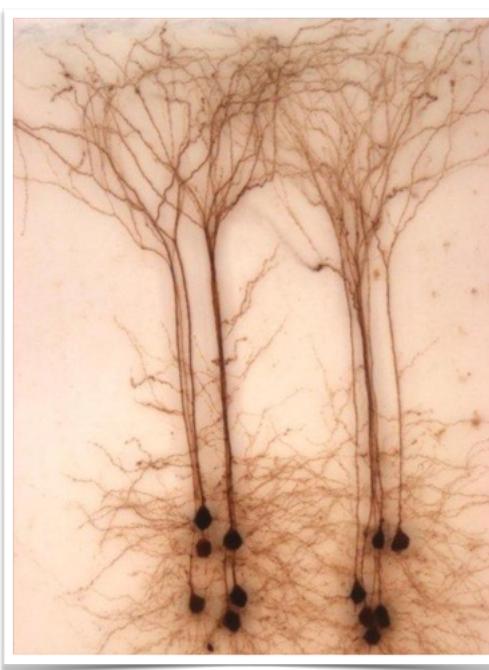
Anastasiya
MOSKALYUK



Micha
SPIRA

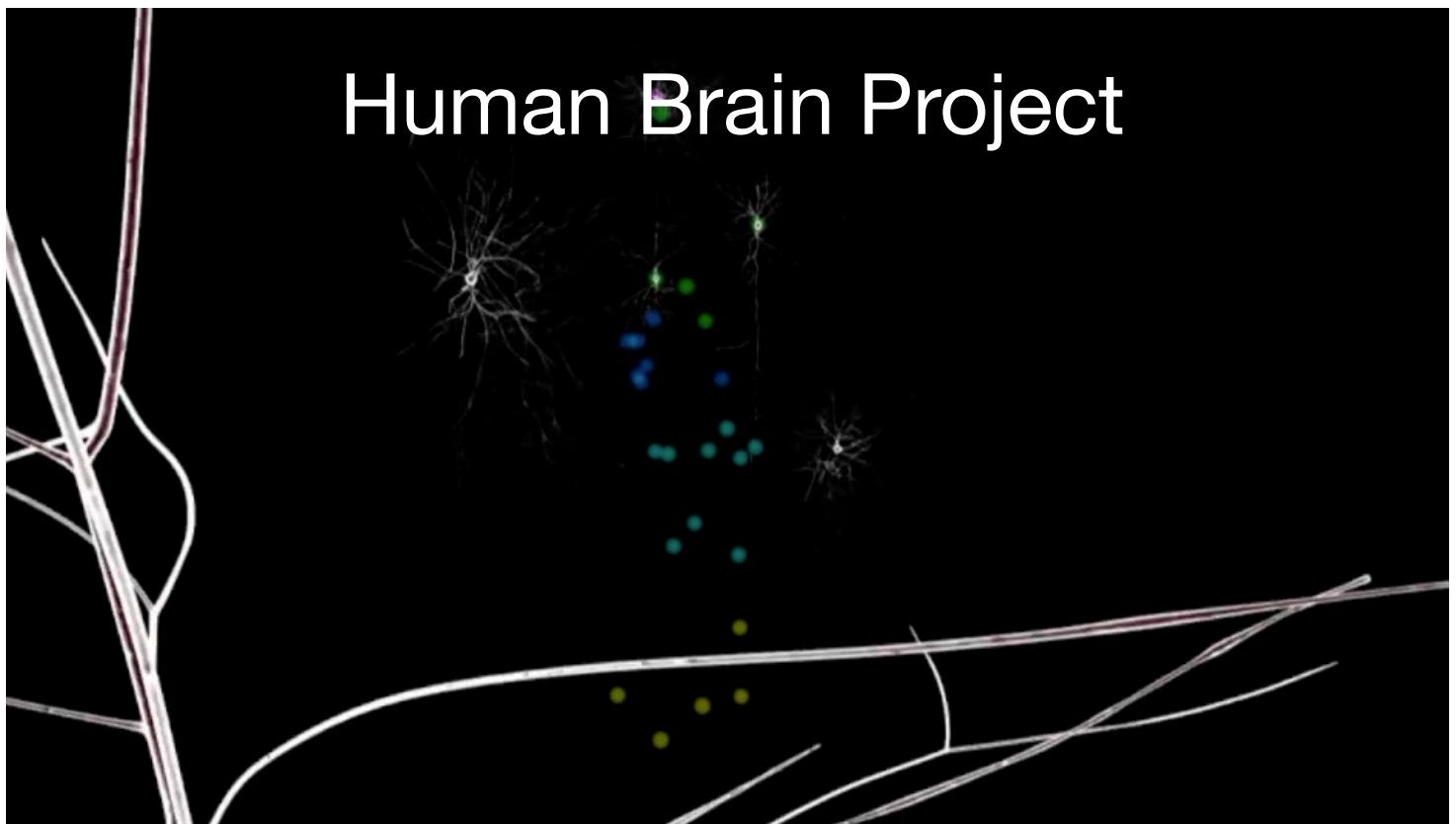


Jones et al. 2020



$$\frac{dV}{dt} = -\frac{1}{C_M} \{ \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_L (V - V_L) \}$$

Human Brain Project



High Performance Computing

- What is a super-computer?
- How would you run a “simulation” of a piece of brain on a super-computer?



Examples

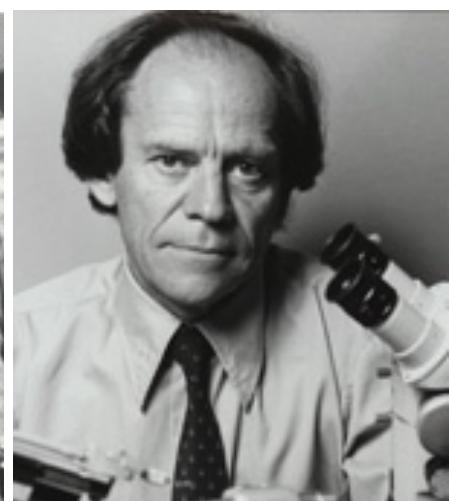
of (electrophysiological) brain signals

Mammalian Visual System

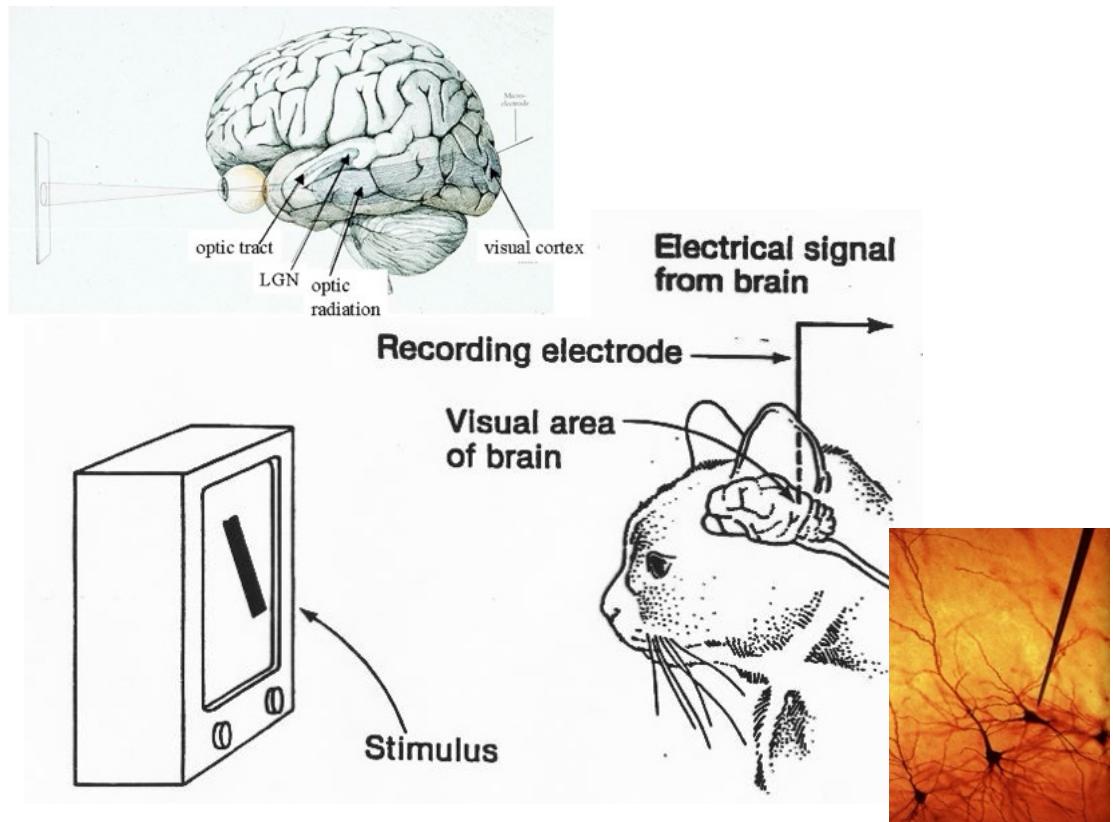
David Hubel



Torsten Wiesel



Nobel prize for Physiology or Medicine (1981)



Ganglion cell - Pay attention

- when/what is this neuron “responding” to?
- what are the features of the stimulus that... excite that neuron?
- what “computation” performed on the image?



Ganglion cells / LGN cells

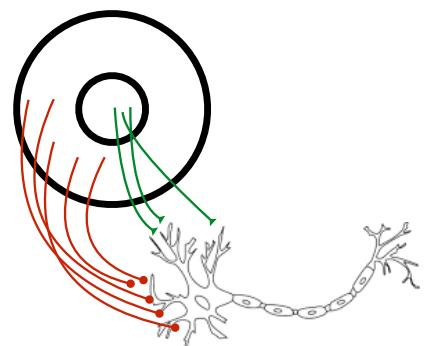
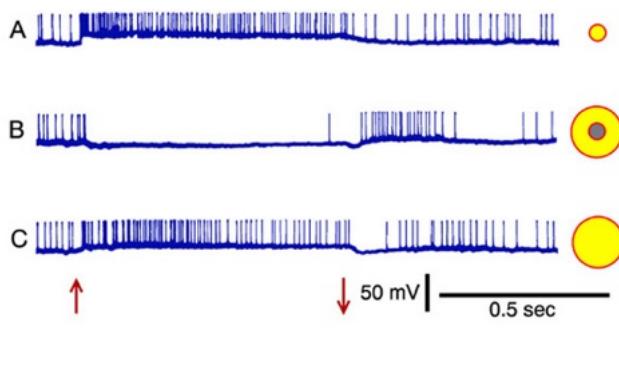
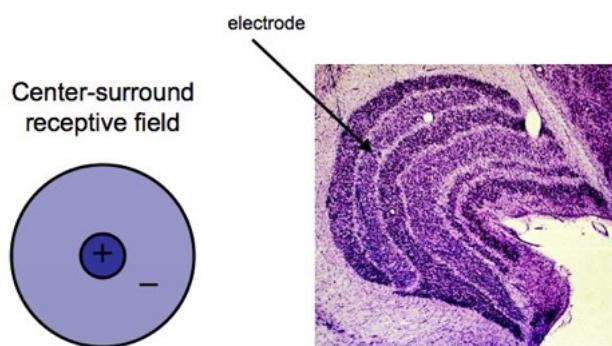
center ON - surround OFF

- exist a specific, circular receptive field
- no orientation selectivity
- cells fires action potentials spontaneously, at low rates
- cell fires action potentials when the light is in the center
- cells suppresses its firing when the light is the surround
- cells fires action potentials if light is everywhere
- firing responses are not sustained in time, fatigue, adaptation
- switching off the light over the surround causes rebound firing
- other cells show center OFF - surround ON

It is a contrast feature detector! (detects and relays info on **edges**)

Ganglion cell - Circuit?

- How would
- How could you build a similar circuit?



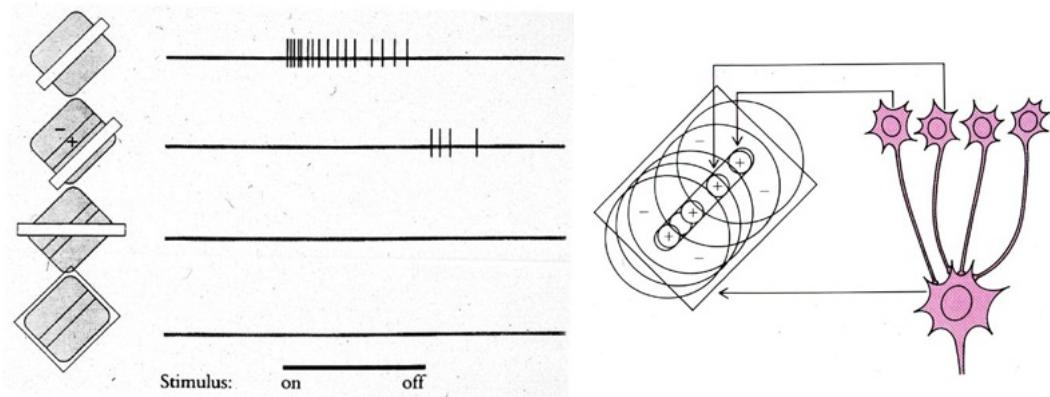
Cortical cell - Pay attention

- when/what is this neuron “responding” to?
- what are the features of the stimulus that... excite that neuron?
- what “computation”?



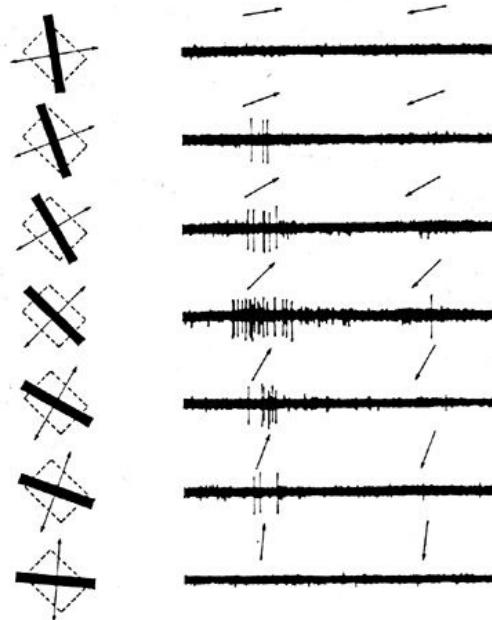
V1 (simple) cells

orientation selective, center-surround

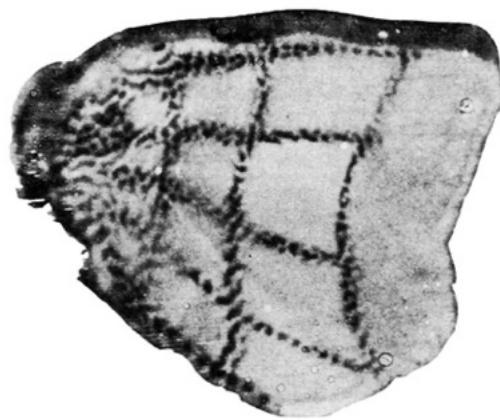
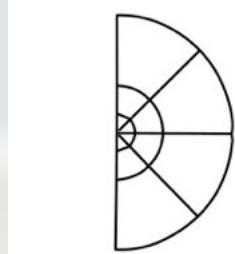
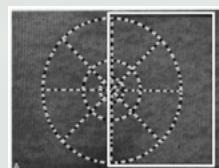


V1 cells

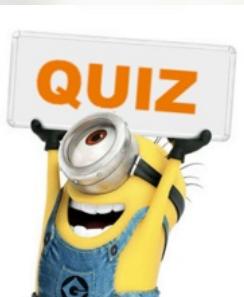
orientation and direction selective



What is Retinotopy? (Tonotopy)

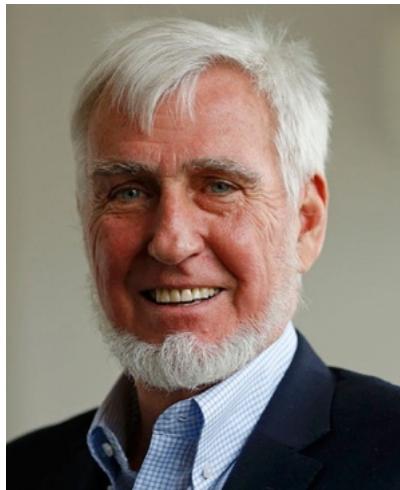


Fovea is over represented!



Hippocampus, Entorhinal Cortex: cognition/memory

O'Keefe



Moser & Moser



Nobel prize for Medicine (2014)

Hippocampal cell - Pay attention

- when/what is this neuron “responding” to?
- what “computation” is it useful for?



Hippocampal “place” cells



Hippocampal “replay” of memories?
Yes! During stillness and (non)-REM sleep!



Reading the Minds of Rats | Matt Wilson | TEDxCoconutGrove
(20 mins TED Talk)

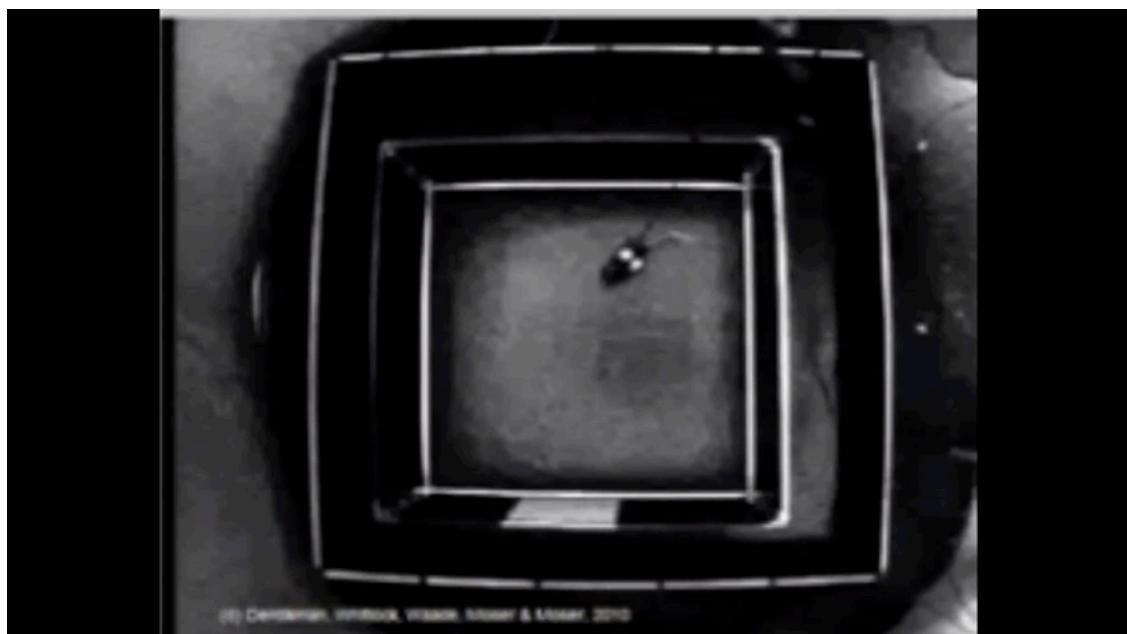
https://www.youtube.com/watch?v=Vf_m65MLdLI

Entorinal cortex - Pay attention

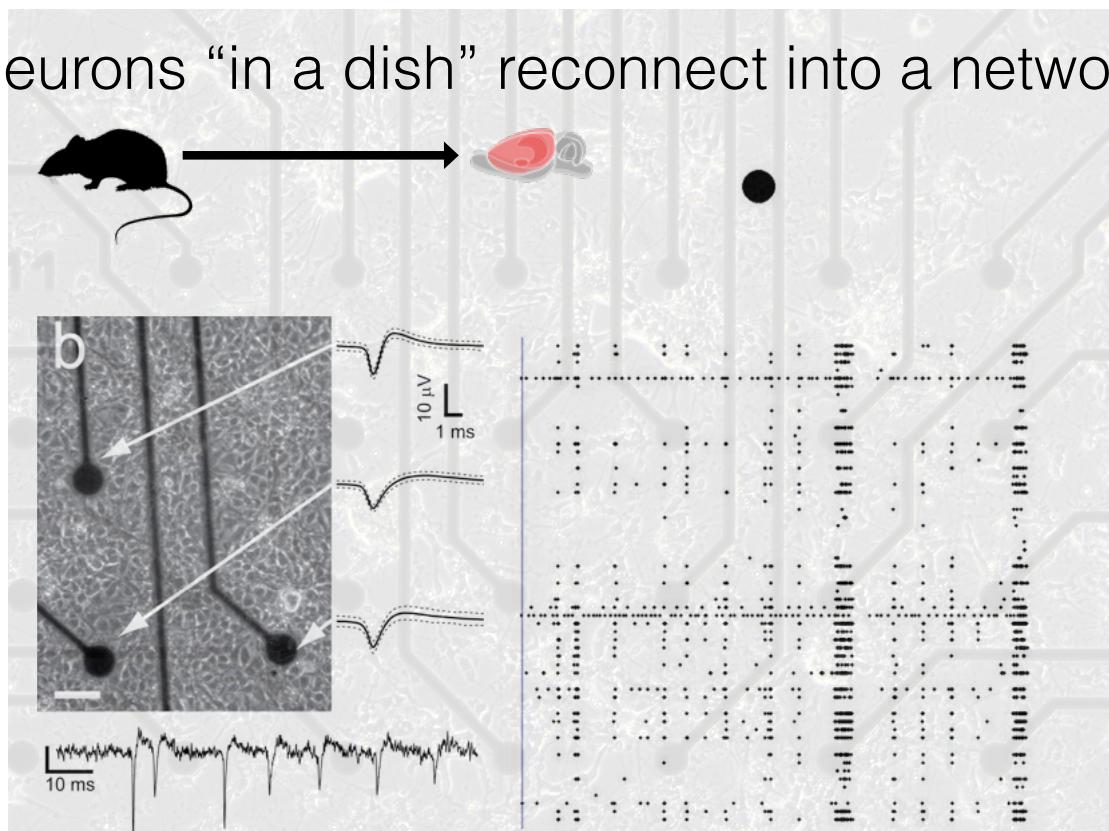
- when/what is this neuron “responding” to?
- what “computation” is it useful for?



Entorinal cortex



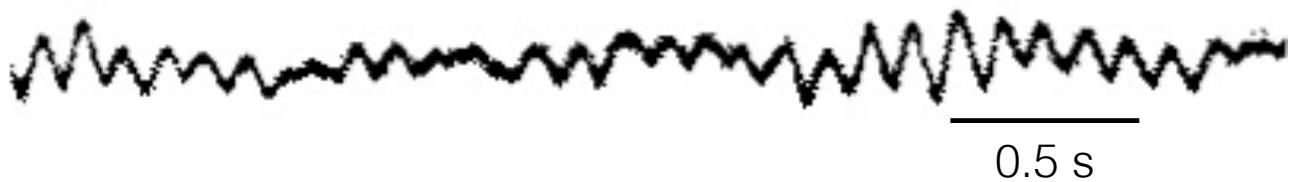
Neurons “in a dish” reconnect into a network



Electroencephalography EEG

Hans Berger

(1873-1941)



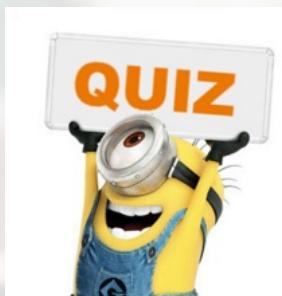
1924

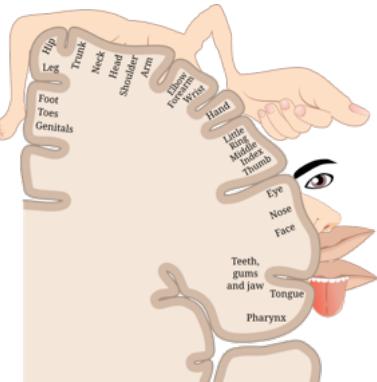
EEG Rhythms

- EEG Rhythms e.g.
 - Categorization of rhythms based on frequency
 - Beta: Greater than 14 Hz, activated cortex
 - Alpha: 8-13 Hz, quiet, waking state
 - Theta: 4-7 Hz, some sleep states
 - Delta: Less than 4 Hz, deep sleep
 - Deep Sleep
 - High synchrony, high EEG amplitude

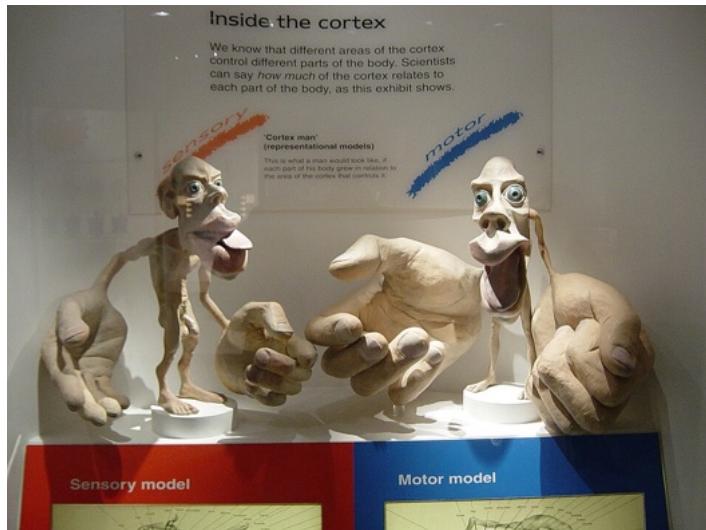
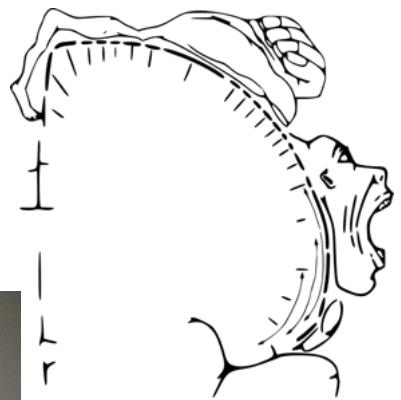
Physiological/Pathological rhythms

- What is Penfield's cortical *homunculus*?





Homunculus



- Why “hands” and “lips” are **deformed**?
- What would you experience if a wave of abnormal (synchronous) electrical activity invaded the entire cortex?
- How could it propagate from one spot to its neighbor?





Play (k)

99

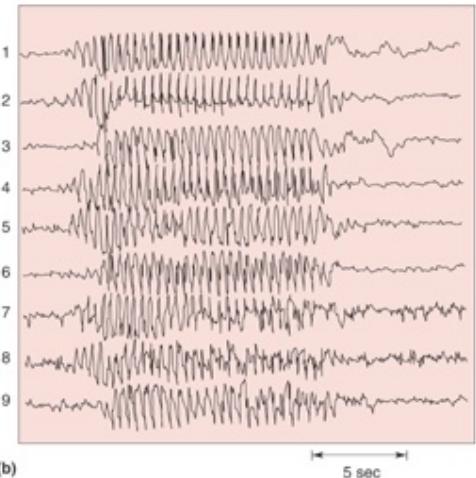
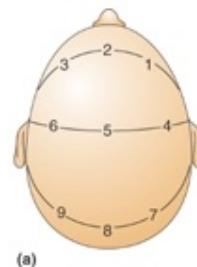
EEG signals relevance? Abnormal rhythms & synchronization epilepsy (~1% of the population)

It is a symptom, not a single disease (60% is treated by drugs): spontaneous and recurrent occurrence of **seizures**, a sudden excessive discharge of CNS electrical activity, causing unexpected changes in behavior, motor function, sensation, consciousness.

400 B.C. Hippocrates; Gospel; Witch hunting (~1400 A.D.)

Epilepsy

- seizures lasting <10 min do not cause brain damage
- no correlation to IQ, to violence..
- not necessarily inherited - unknown causes
- *petit mal* (absence seizures)
- *grand mal* (tonic-clonic seizures)



Seizure classifications

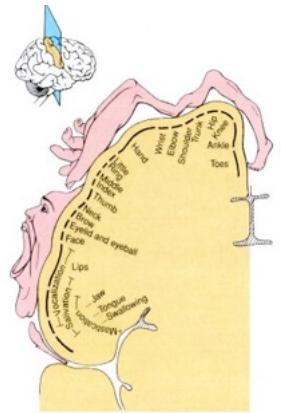
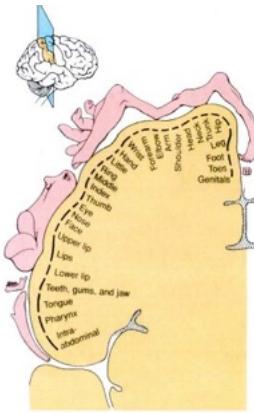
- **Focal s. (known also as “partial”, spatially constrained)**
restricted to only one part of the cortex
- **Generalized s. (involving thalamo-cortical circuits??)**
spread to the entire cortex, simultaneous
- **Simple s.**
consciousness is unaffected (full awareness, although possible impairments in speech)
- **Complex s.**
consciousness is impaired during the event (memory system, emotion processing,...)
- **Motor s.**
motor areas are involved - tonic - clonic - atonic
- **Sensory s.**
sensory areas are involved

(focal, motor) Seizures

Partial seizure



Here, not spreading to other areas.



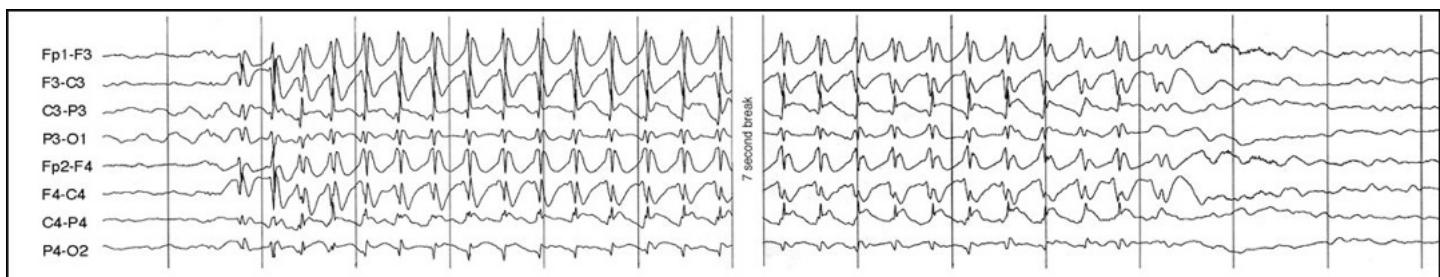
Cortical homunculus (Penfield's)

intermittent (clonic) motor activity, consciousness unaffected, unilater character, localization

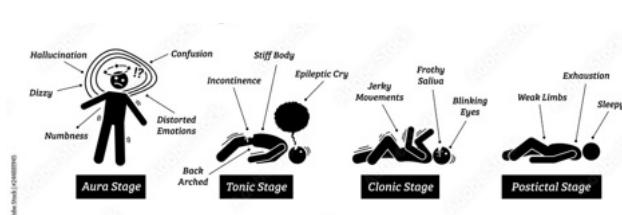
Any idea why it is intermittent ???

(generalized) Absence Seizures

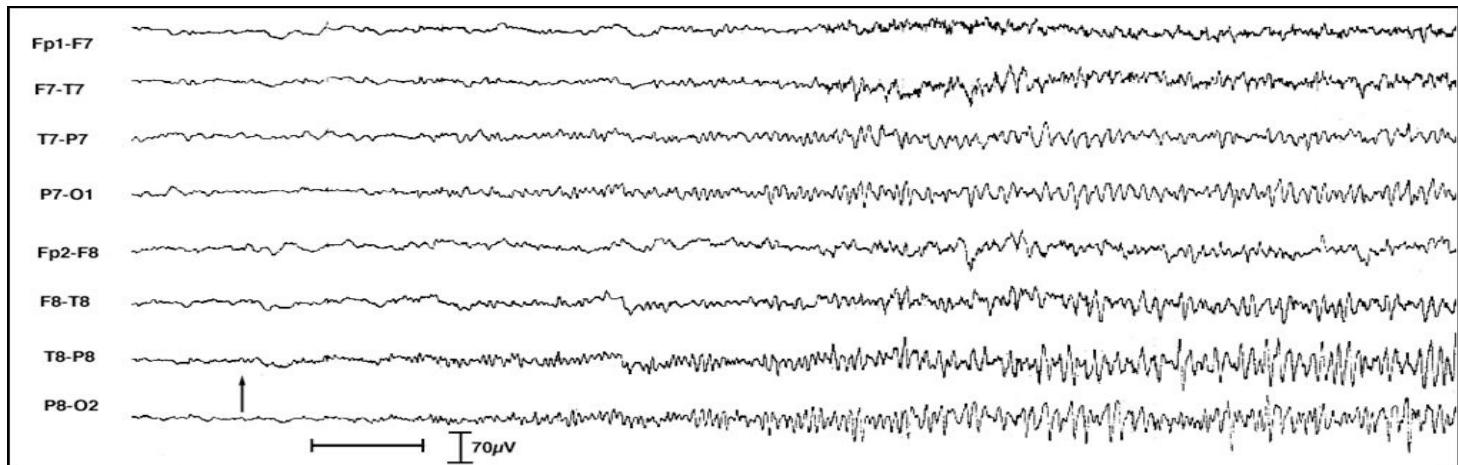
- 2 - 30 seconds episodes, absence, twitching eye movements
- 1-2 times - 100 times a day
- prepubertal age
- stereotypical spike & wave, 3 Hz



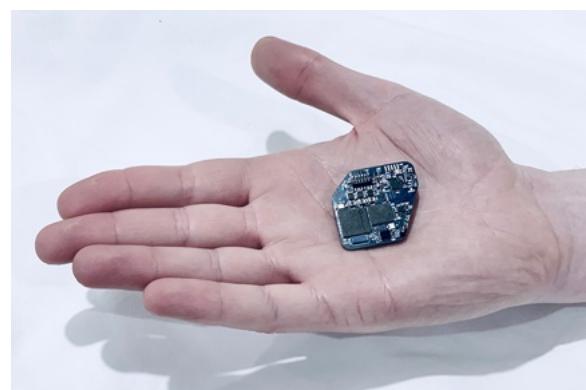
Generalized seizure



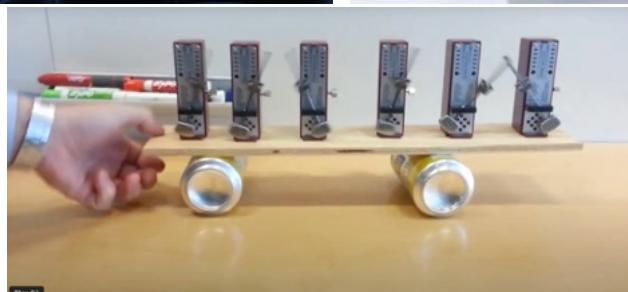
Generalized seizure



Brain pacemakers... for epilepsy

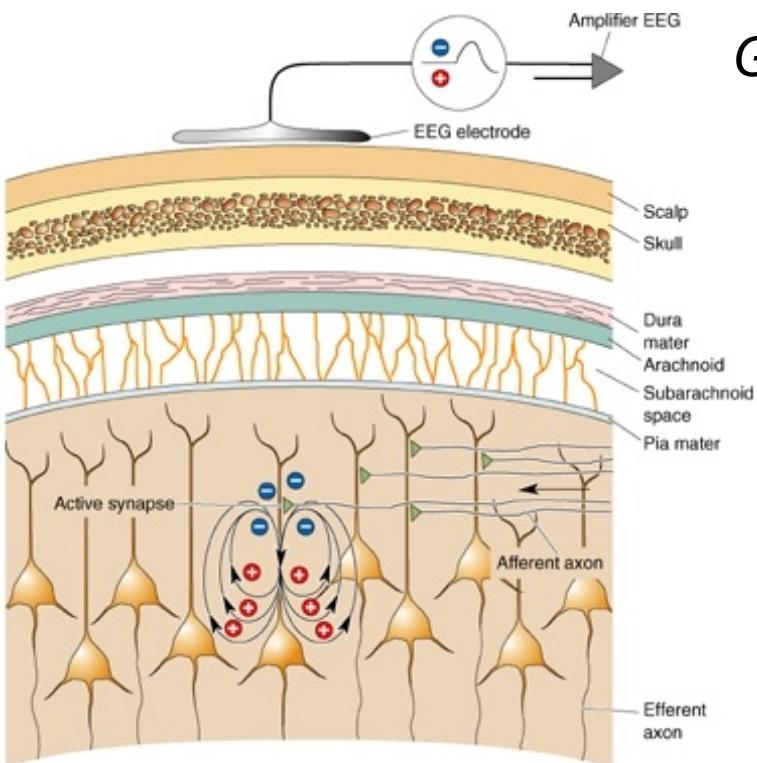


WAND chip, UC Berkley

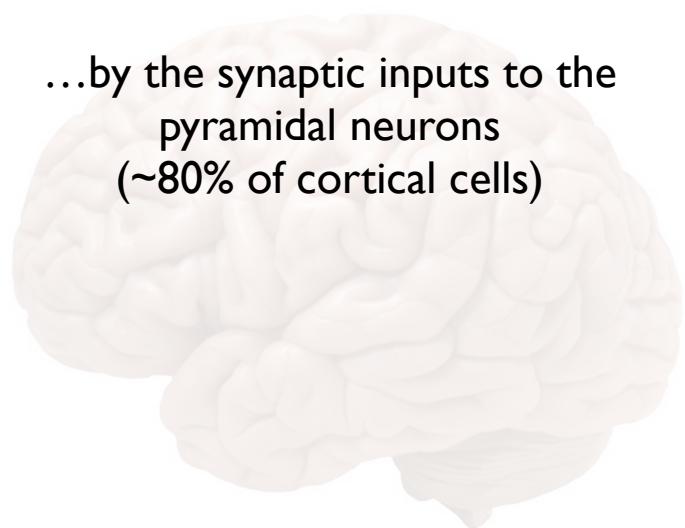


Robert Desimone

Generation of EEG?

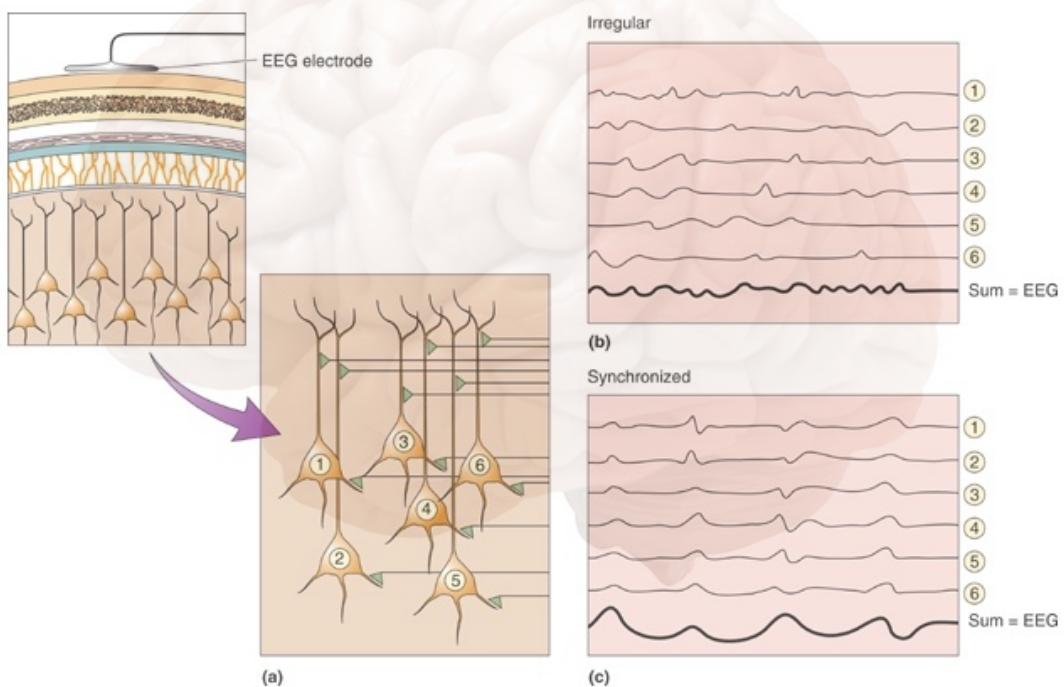


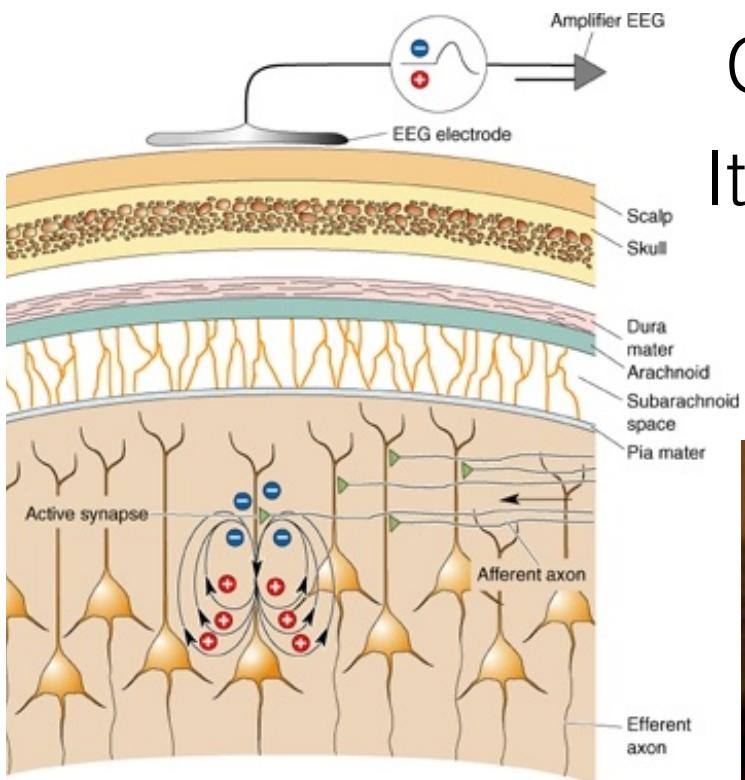
...by the synaptic inputs to the pyramidal neurons
(~80% of cortical cells)



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Rhythms in EEG: how?



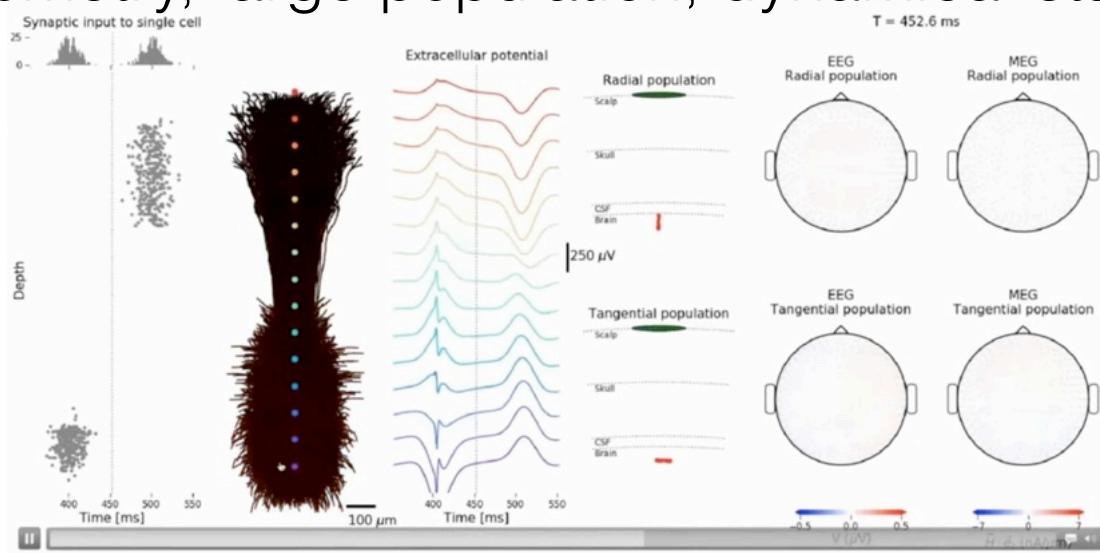


Complex generation!
It calls for an **in-depth**
understanding!



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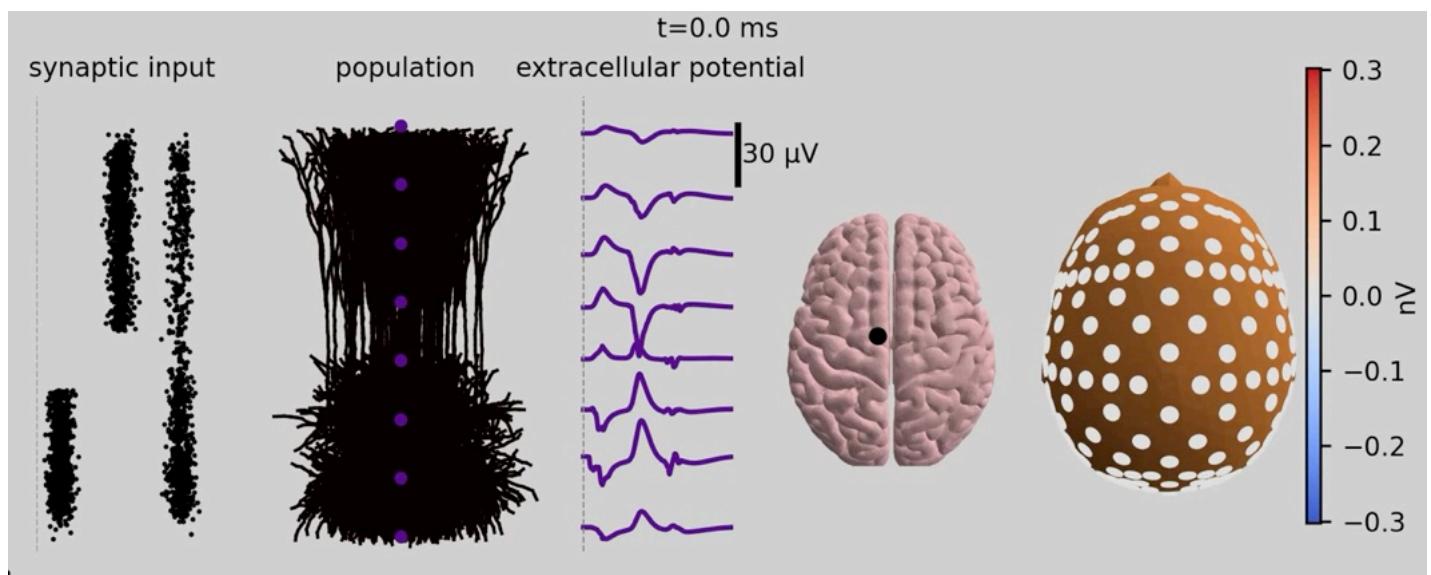
Intracellular signals, extracellular signals,
geometry, large population, dynamical state...



Næss et al, NeuroImage, 2021

Animation by Torbjørn V. Ness

Courtesy of G. Einevoll



Torbjørn V. Ness's YouTube Channel