Les technologies de l’électrophysiologie humaine : de Hans Berger à Elon Musk.

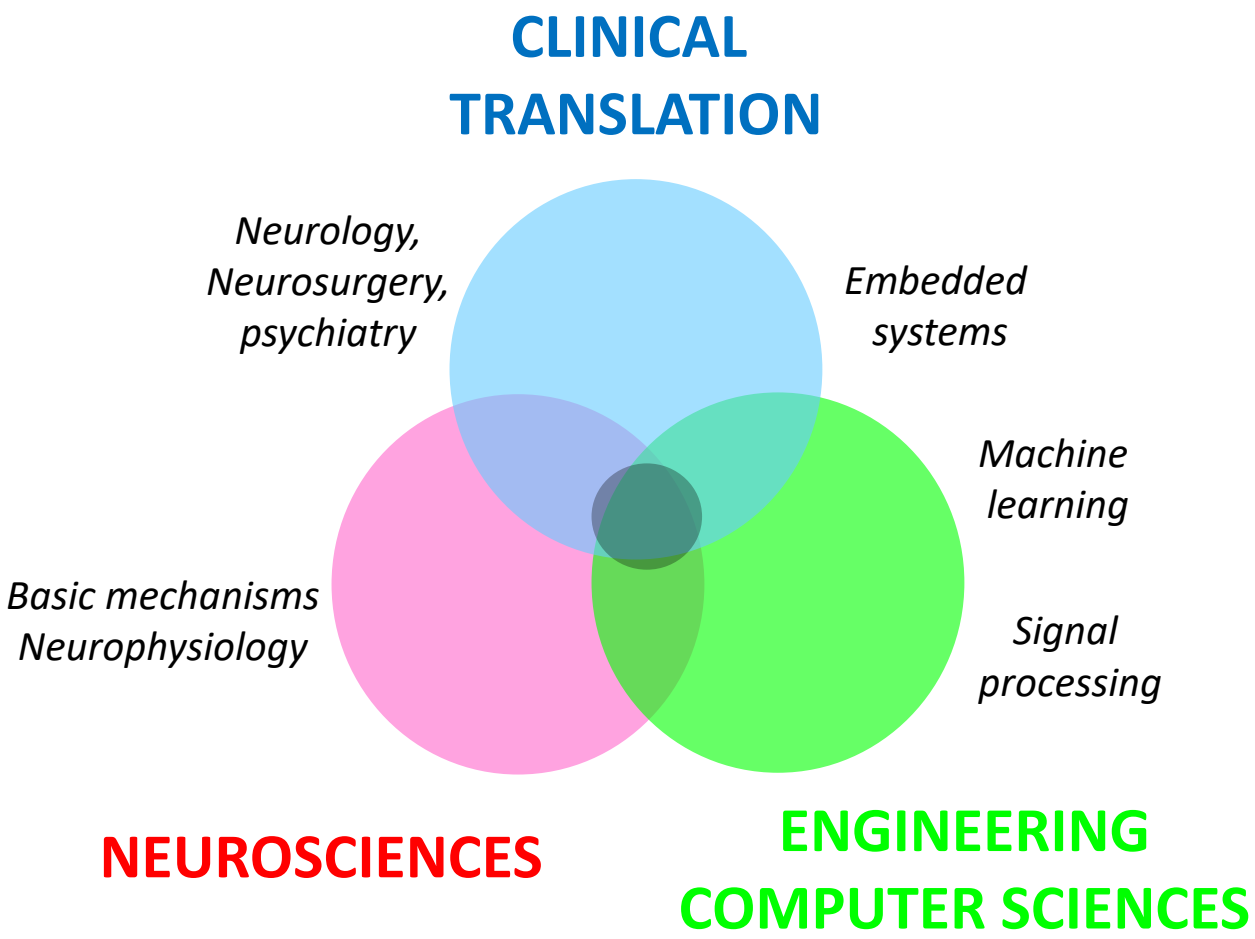
Michel LE VAN QUYEN,
Laboratoire d'Imagerie Biomédicale
U1146 INSERM / SU / CNRS 7371
Campus des Cordeliers
15 rue de l’Ecole de Médecine
75006 Paris

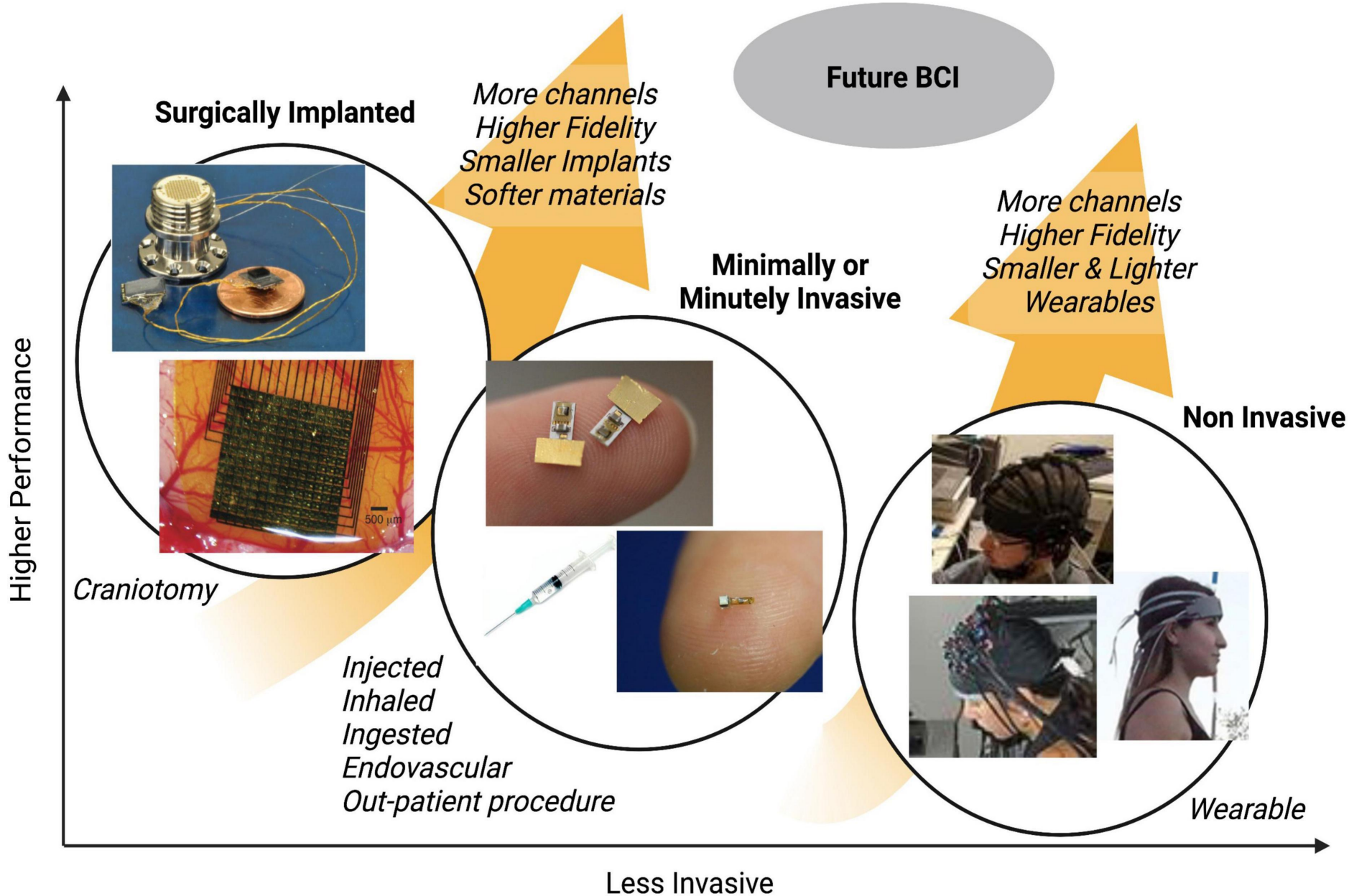




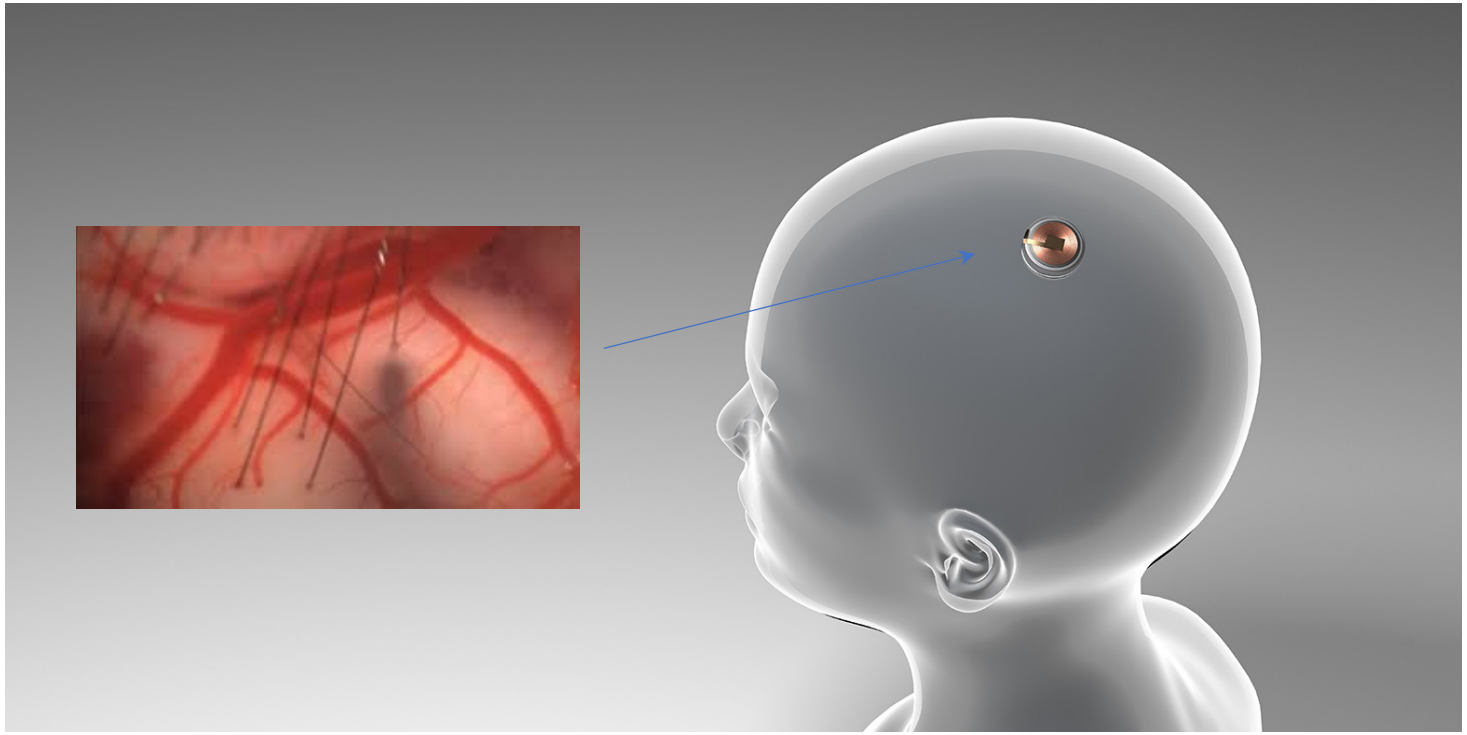
Raoul Hausmann, Tête mécanique, 1919

The neuro-technologies

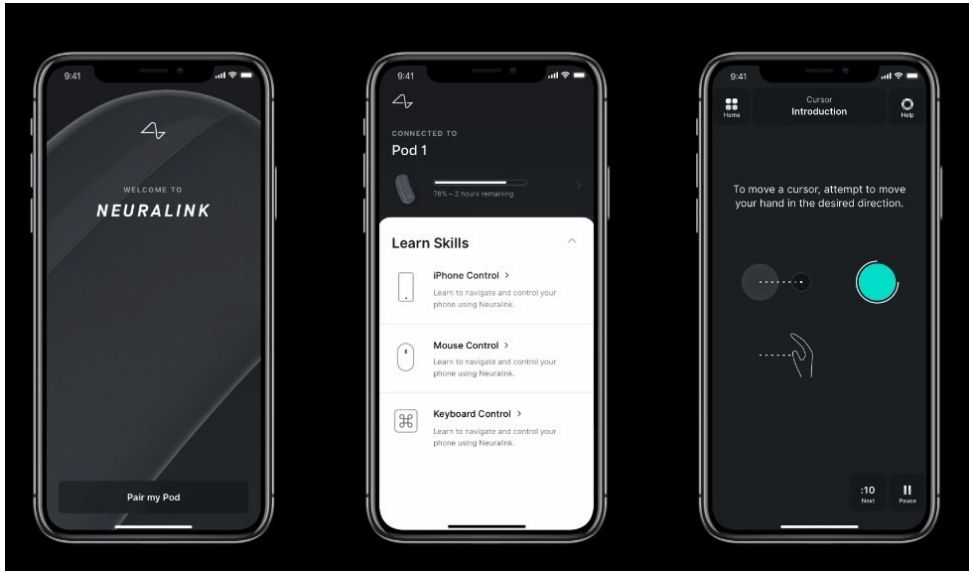




Gaudry K et al. (2021). Frontiers in Neuroscience. 15



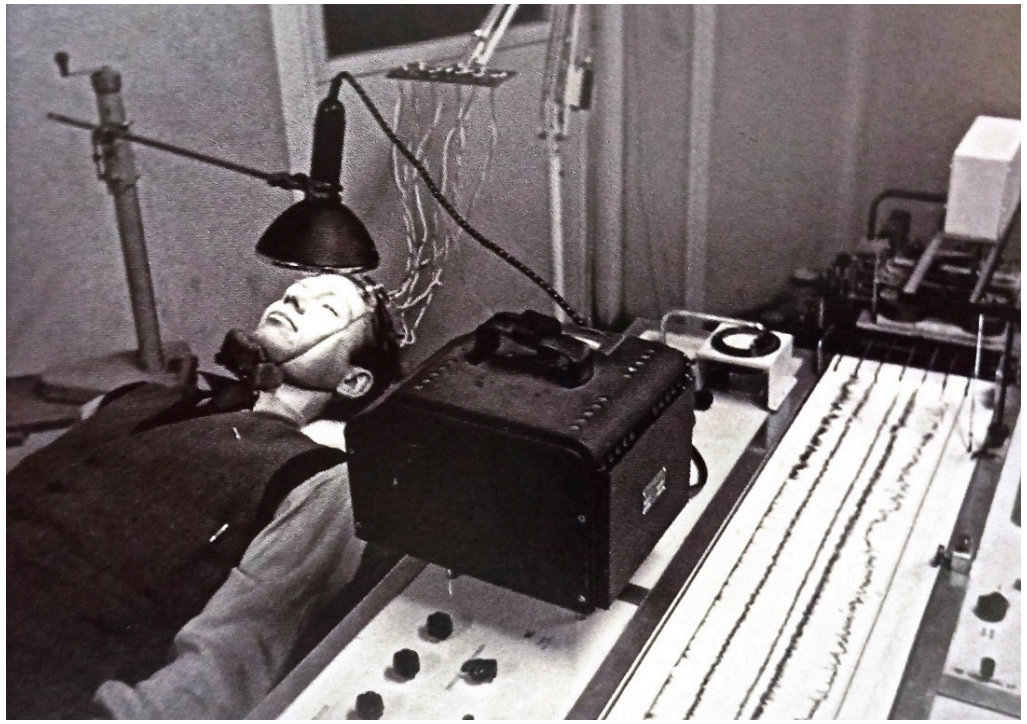
NEURALINK

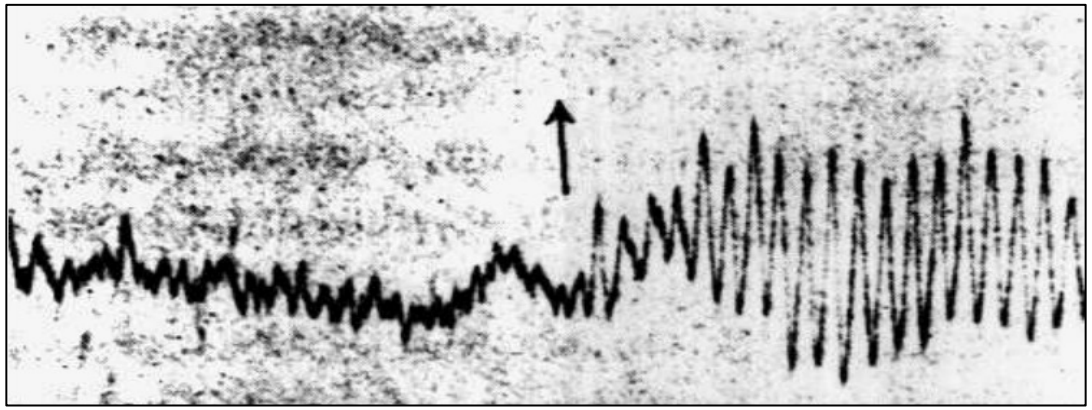

9:41
WELCOME TO
NEURALINK
Pair my Pod
9:41
CONNECTED TO
Pod 1
76% – 2 hours remaining
Learn Skills
iPhone Control
Learn to navigate and control your phone using Neuralink.
Mouse Control
Learn to navigate and control your phone using Neuralink.
Keyboard Control
Learn to navigate and control your phone using Neuralink.
9:41
Cursor
Introduction
Home
Help
To move a cursor, attempt to move your hand in the desired direction.
:10
Next
Pause

1924 Hans Berger : La découverte de l'EEG chez l'homme



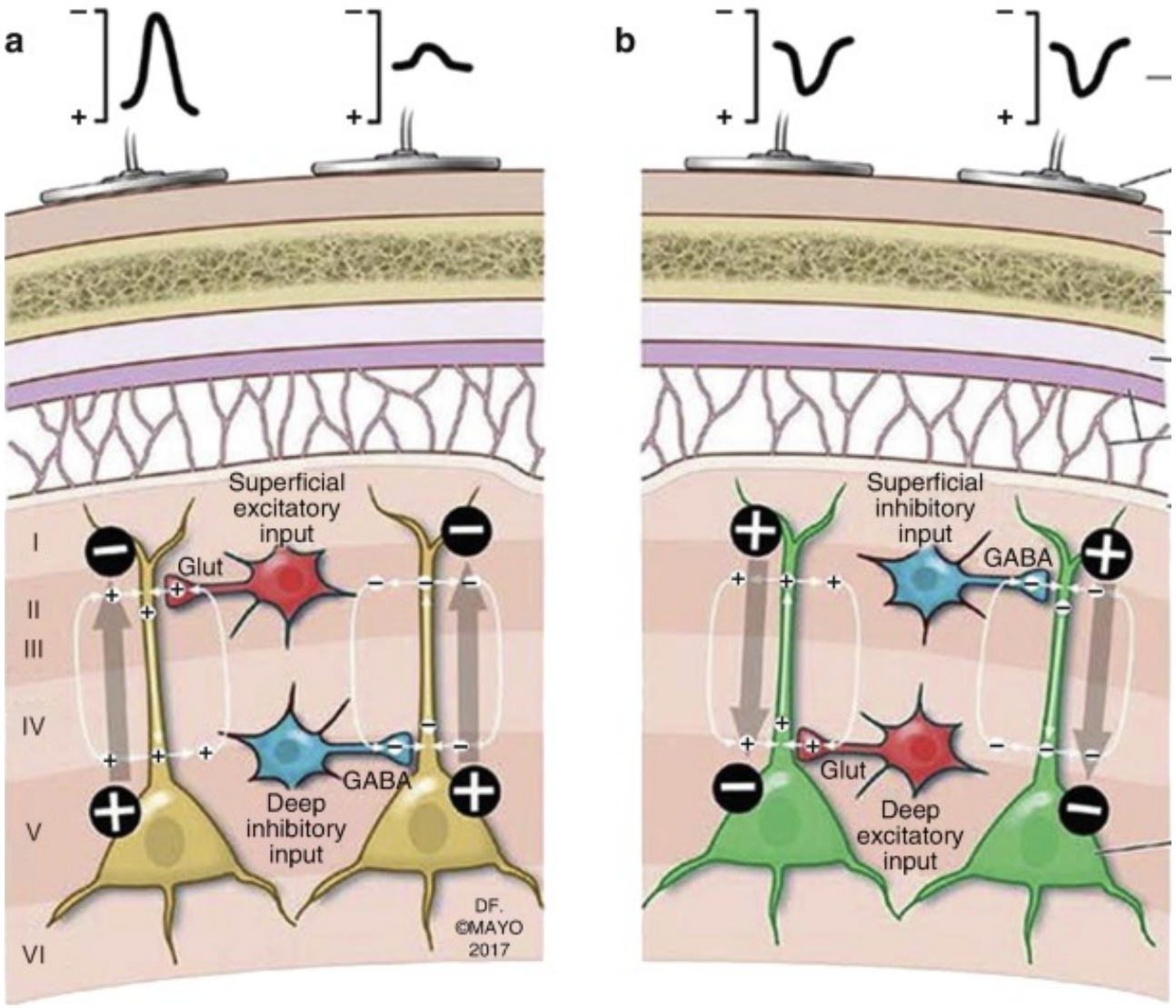


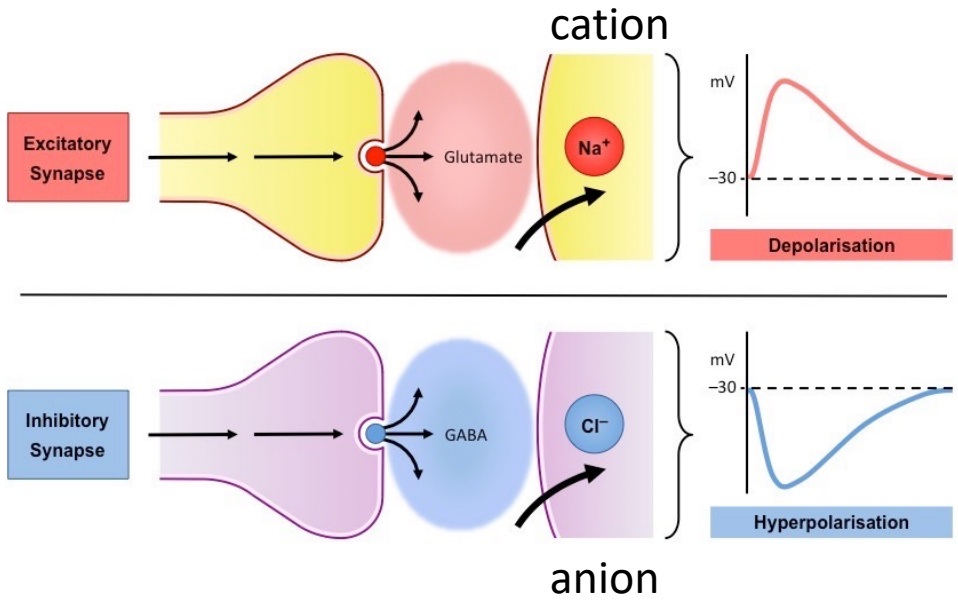




Hans Berger: Über das Elektrenkephalogramm des Menschen. In: Archiv für Psychiatrie und Nervenkrankheiten. Band 87, 1929

EEG = summation of post-synaptic potentials



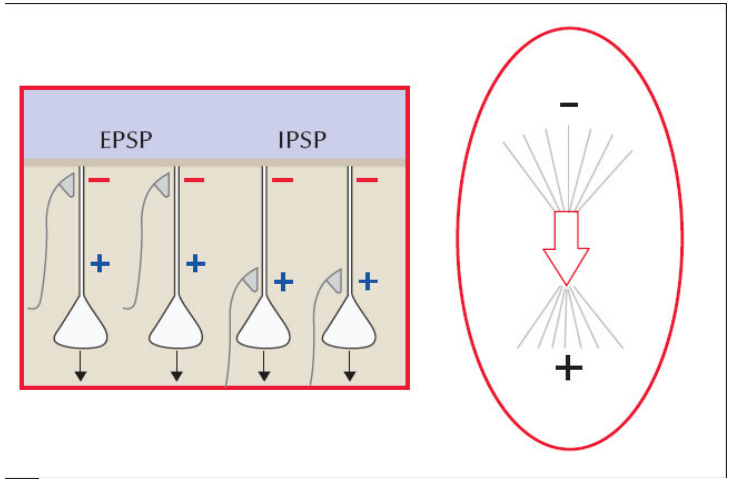


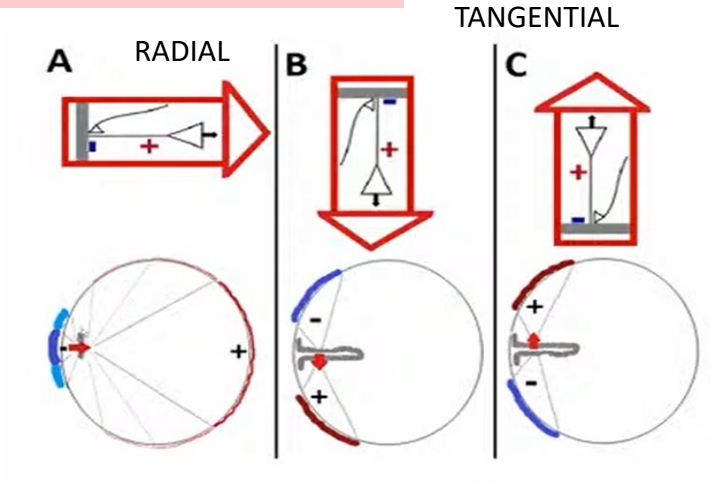
Typical EEG about 100 mV, need about 1 million neurons, a few cm2 of cortex

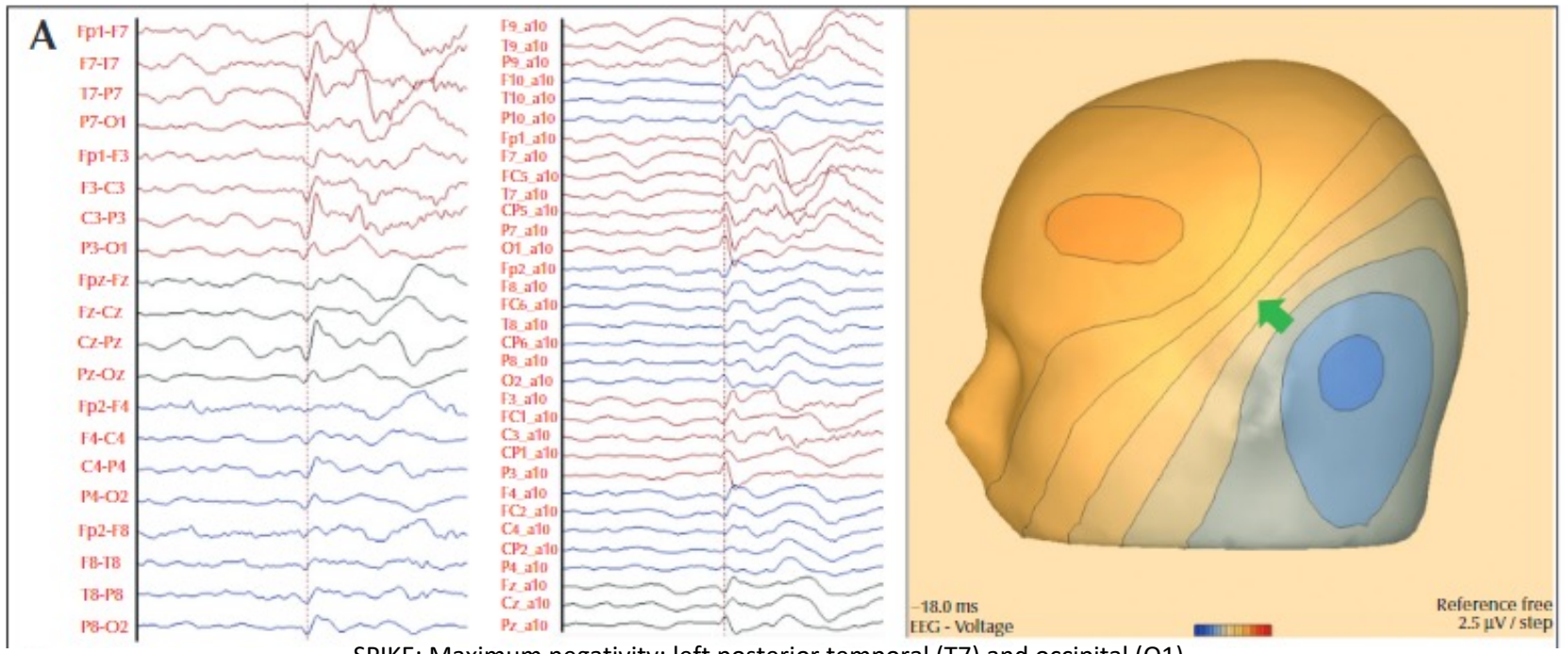
EEG = Voltage maps

Activation
=
Negative
EEG deviations







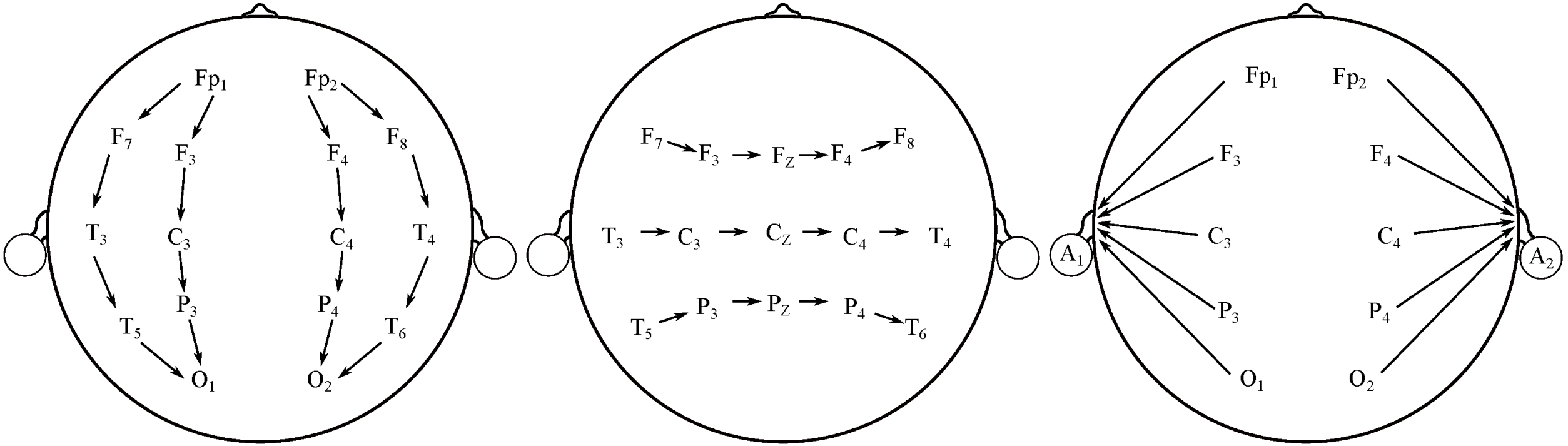


SPIKE: Maximum negativity: left posterior temporal (T7) and occipital (O1).

Sandor Beniczky

Various EEG montages for reading the EEG

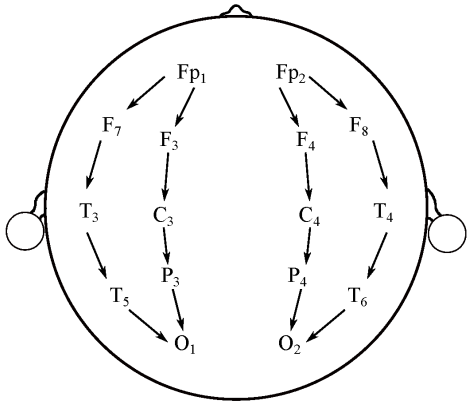
« Double banana »



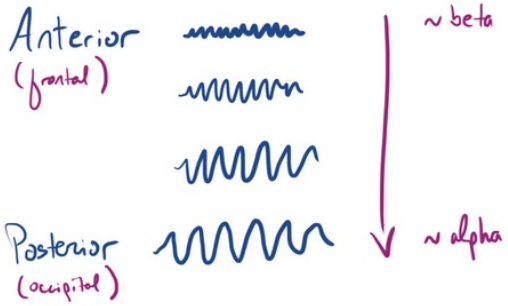
(**a**) Bipolar longitudinal montage. (**b**) Transverse bipolar montage. (**c**) Referential ear montage.

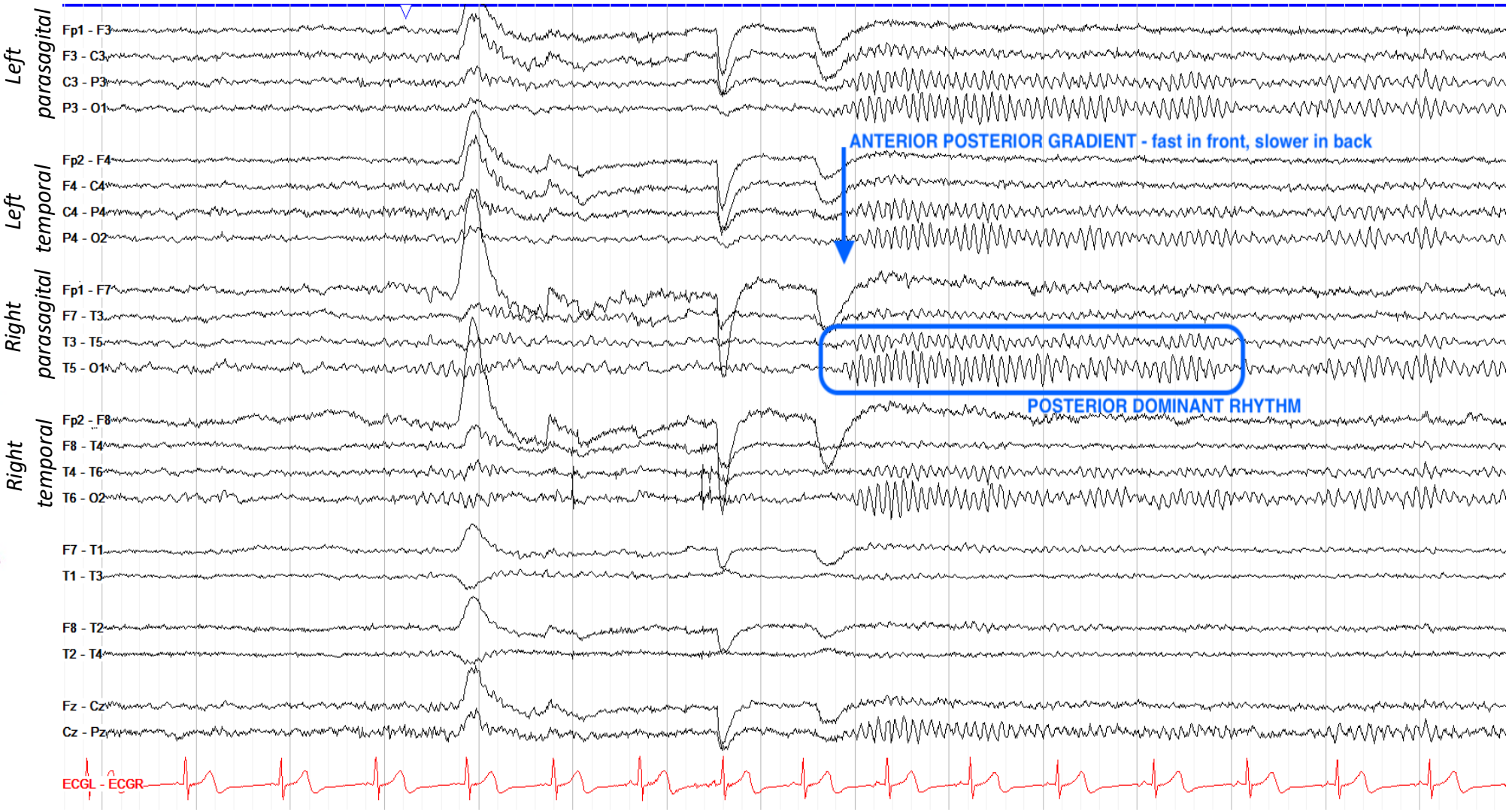
Human EEG with prominent resting state activity – alpha-rhythm

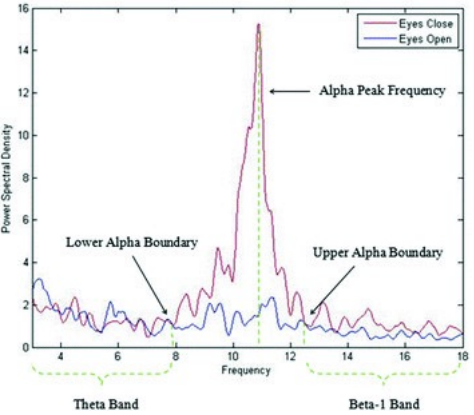
In adults, the normal PDR should be between 8.5 and 12 Hz and symmetric



Double banana



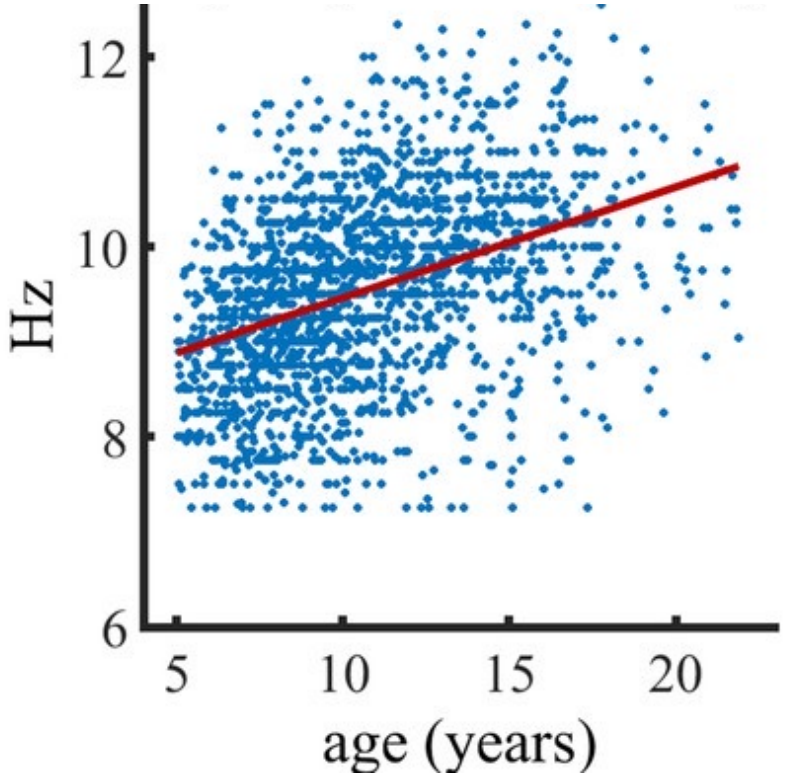




Alpha-rhythm depends on the age

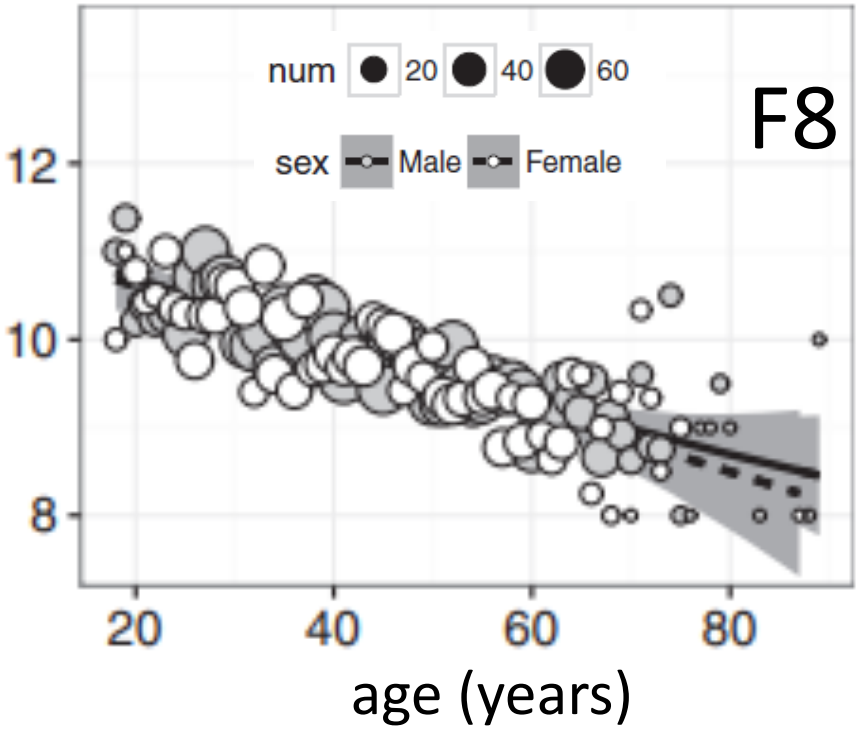
N=2529 subjects, age 5-22 years

Tröndle et al. Elife. 2022



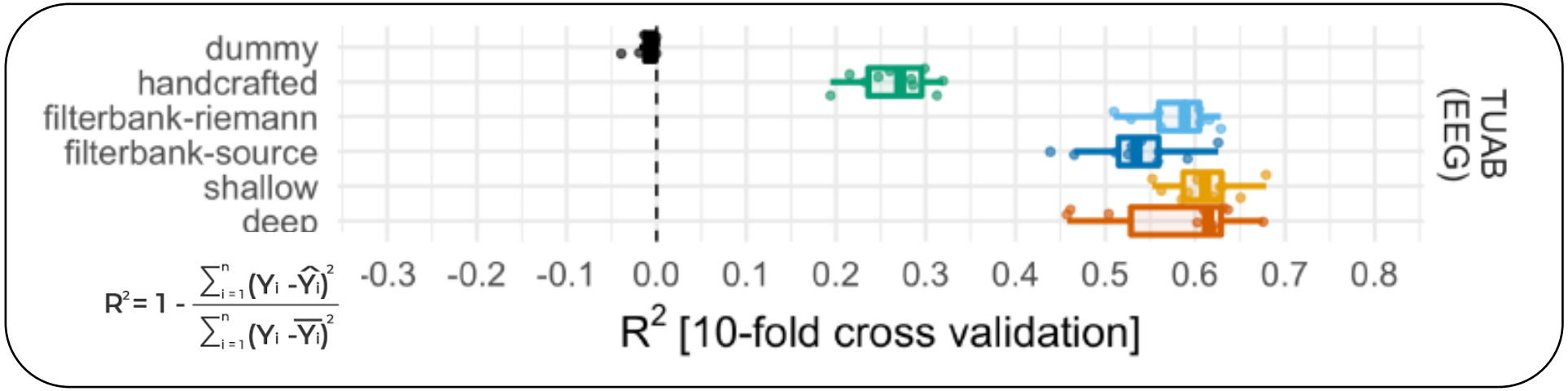
N=6029 subjects, age: 18 – 88 years

Hashemi et al., eNeuro. 2016

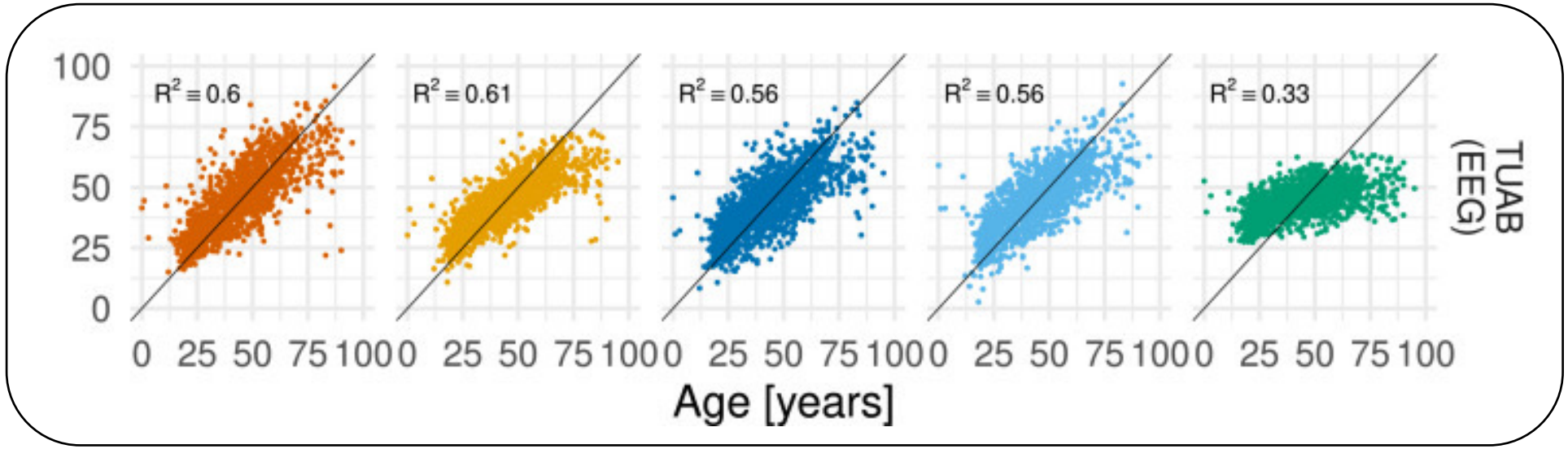


How old is your brain, really? Artificial intelligence knows

resting state



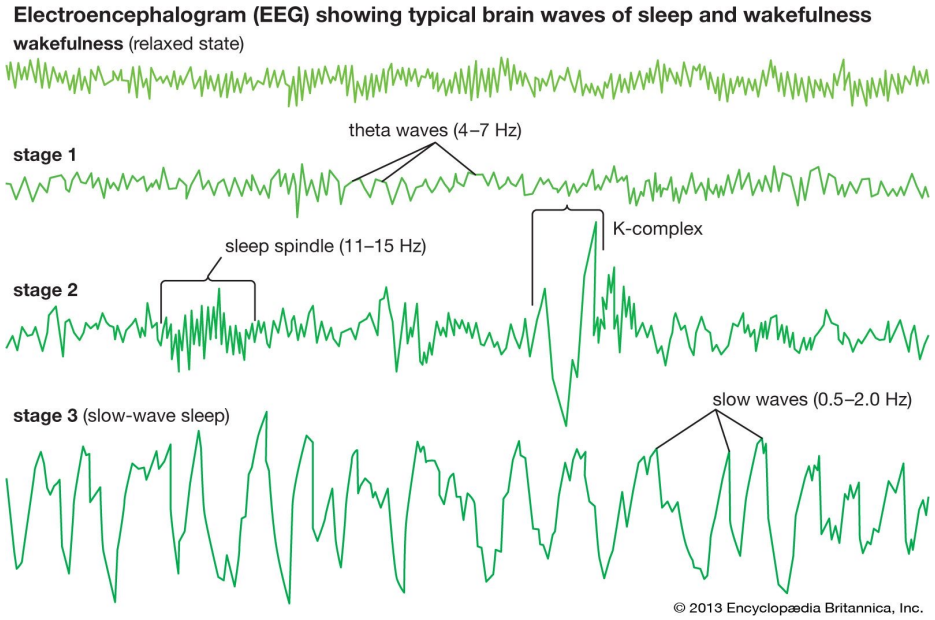
The Temple University Hospital Abnormal EEG Corpus (TUAB) 2993 recordings of resting states



the best model obtains a mean absolute error of 7-8 years between the “Brain age” and chronological age

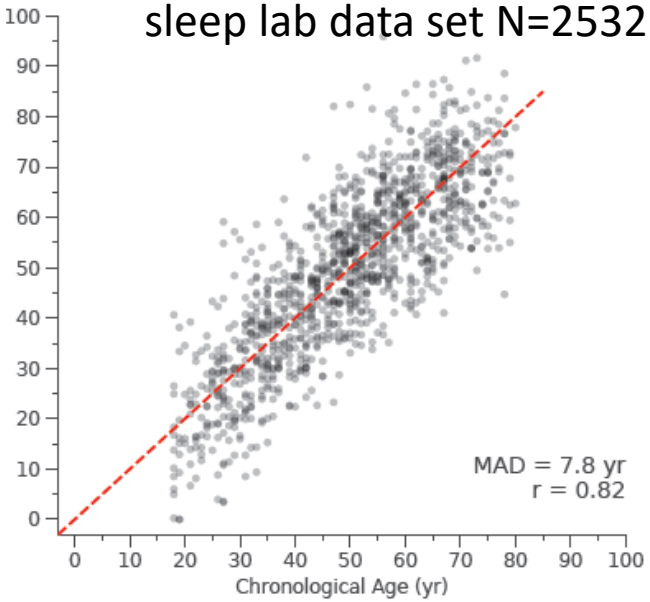
Engemann DA, Mellot A, Höchenberger R, Banville H, Sabbagh D, Gemein L, Ball T, Gramfort A. A reusable benchmark of brain-age prediction from M/EEG resting-state signals. Neuroimage 2022

Sleep EEG as a window of aging and brain health



Massachusetts General Hospital
sleep lab data set N=2532

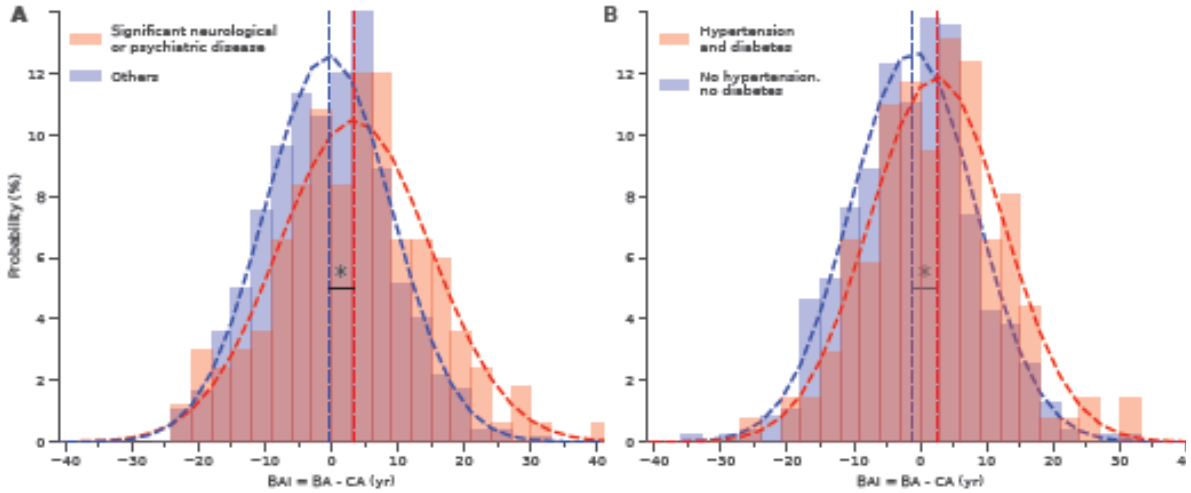
Brain Age

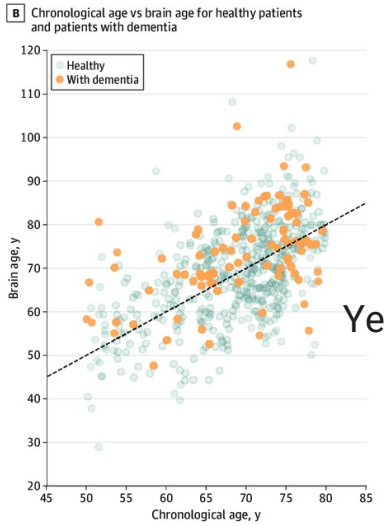


MAE=7.8 years

Sun H, …, Westover MB. Neurobiol Aging 2019

Brain Age
-
Real Age

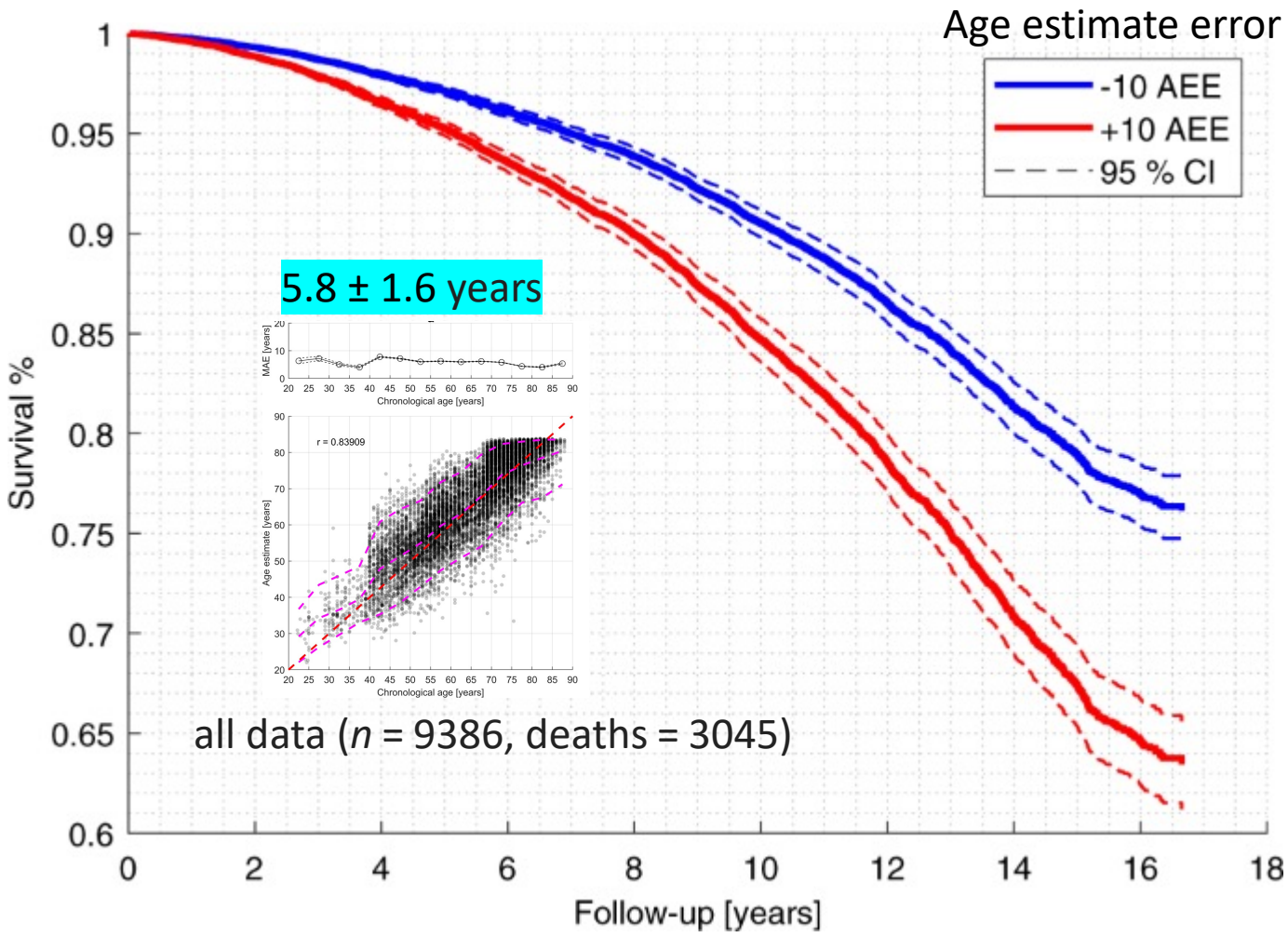




Ye EM, …Westover MB. Sleep. 2023

Age estimation from sleep studies using deep learning predicts life expectancy



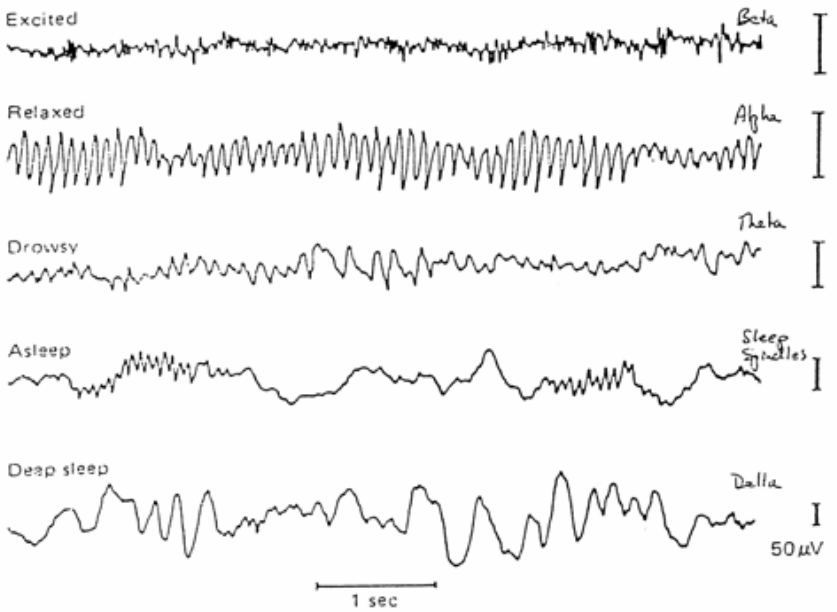


Brink-Kjaer A, …, Mignot E. Age estimation from sleep studies using deep learning predicts life expectancy. NPJ Digit Med. 2022 Jul 22;5(1):103.

L’électro-encéphalogramme (EEG)

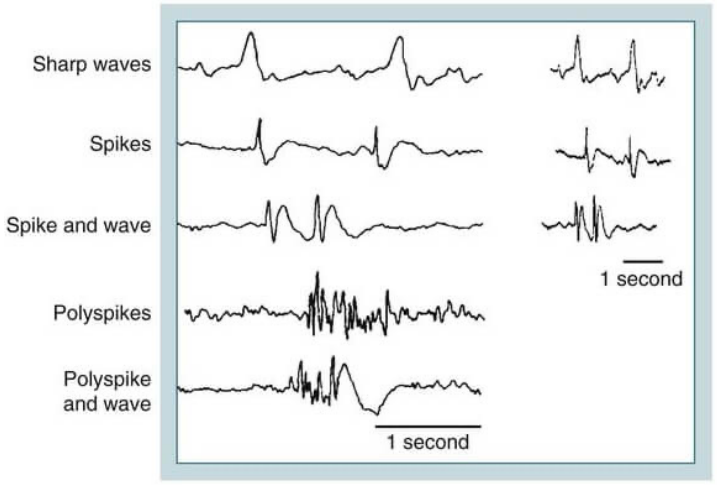


EEG normal



Limites:

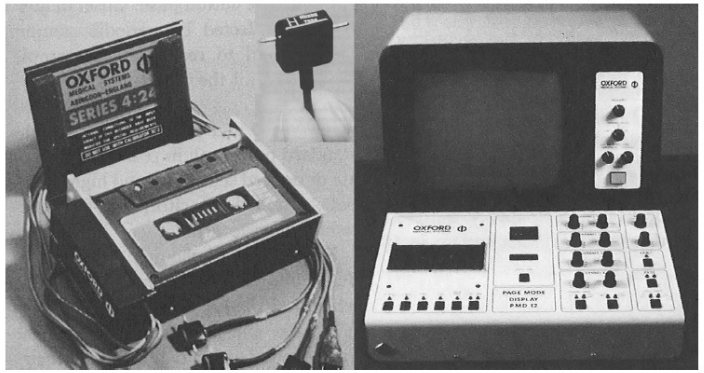
- Inconfortable et nécessite un technicien
- Sensible aux mouvements et relecture par un expert
- Enregistrement courts de 20 min à l’hôpital
- Accès difficile à des regions critiques (e.g. le lobe temporal)



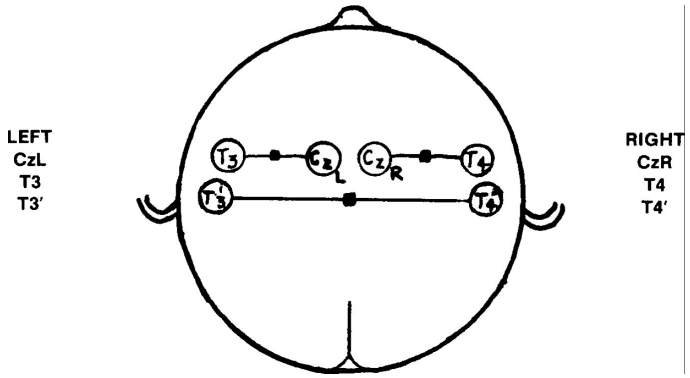
Evénements épileptiques

L’ Holter EEG

12 à 48 heures
Réalisé à domicile avec analyse du sommeil



1979, Oxford Medilog (4 canaux)

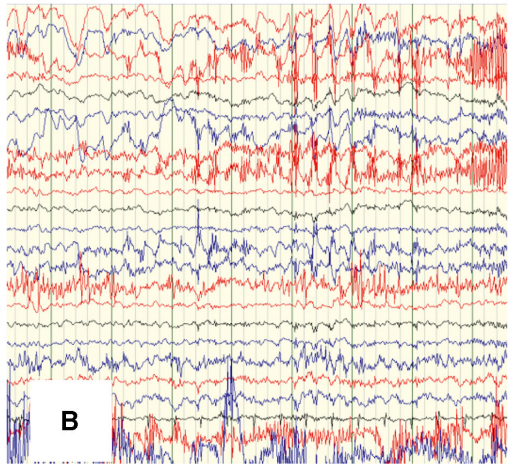


Bridgers et Ebersole (1985)
Neurology 35:1767.

Système robuste, permettant un EEG 10-20 complet avec de bonnes performances techniques

A







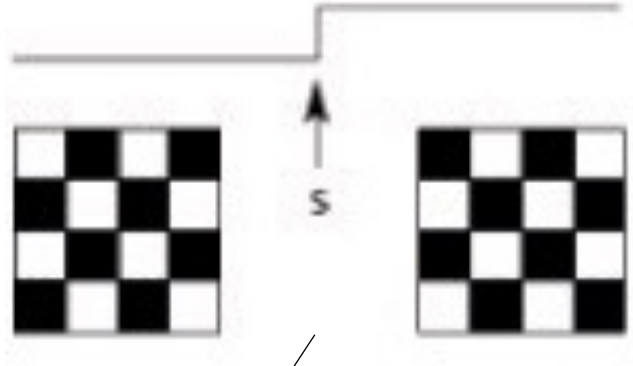
Brunnhuber et al. (2020)
Epilepsia. 2020; 61 Suppl 1

Systèmes EEG embarqués



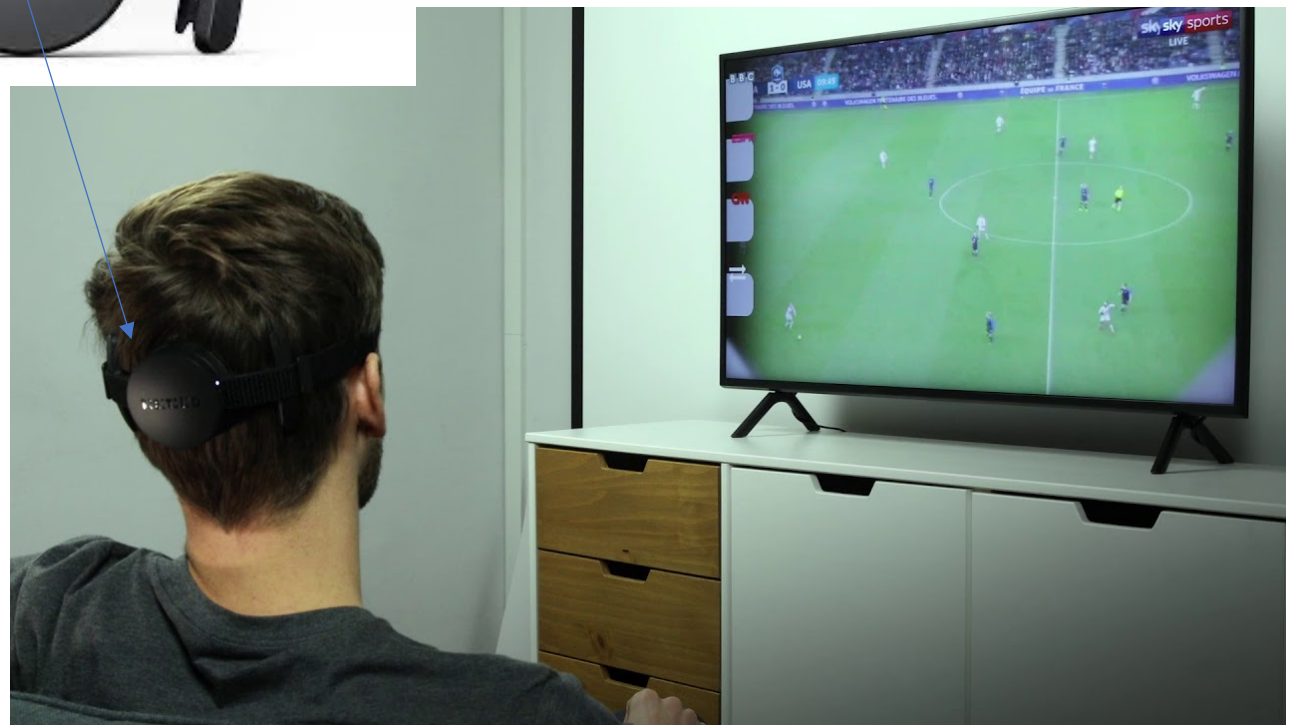
… pas de certifications DM
… pas confortable
… pas discret

Brain computer interface / Evoked potentials

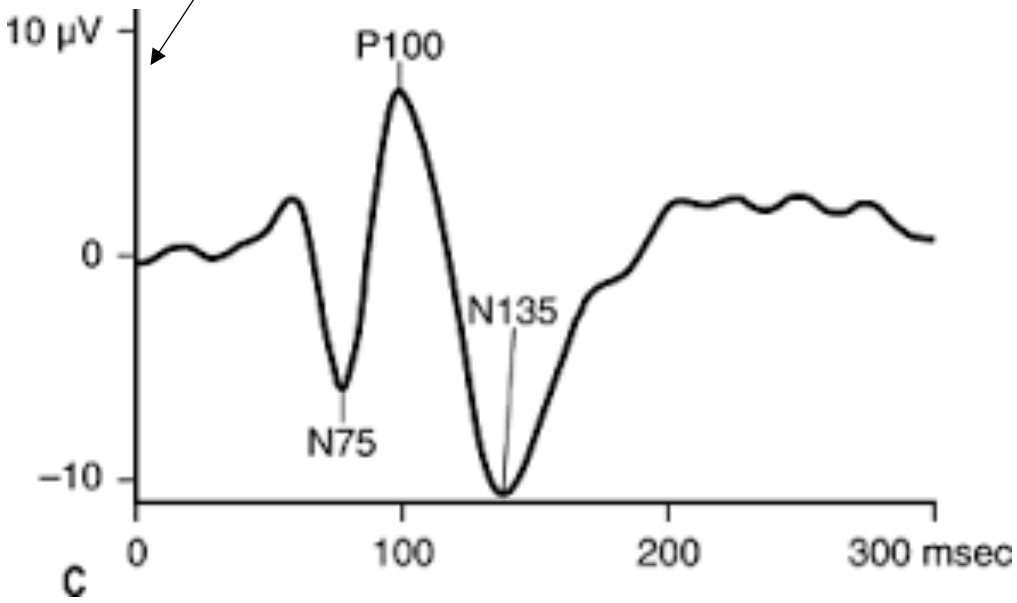




Une commande par 5 sec



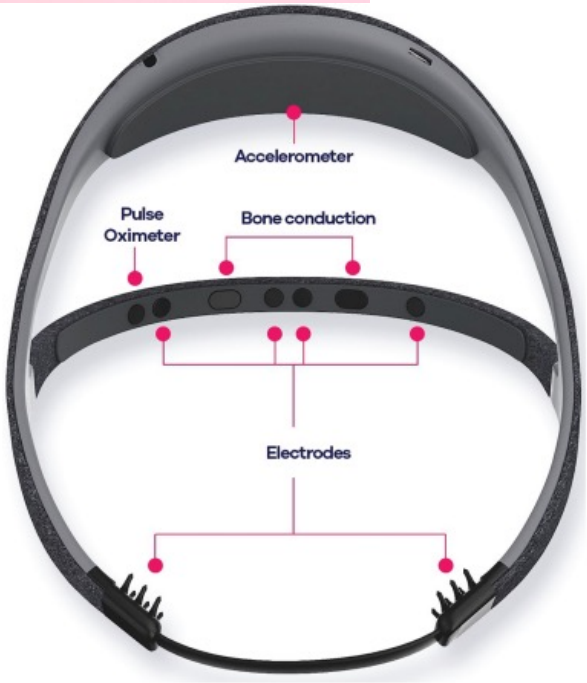
Visual evoked potentials



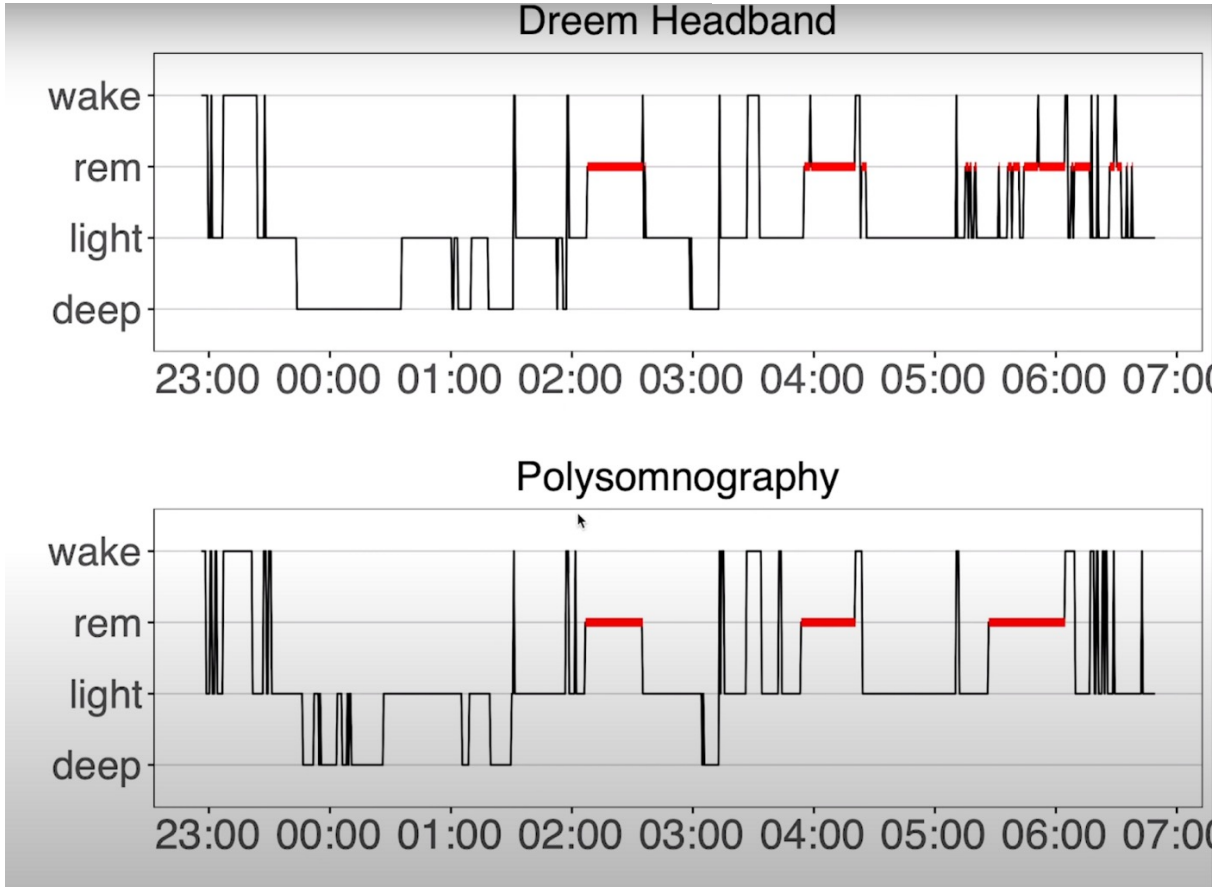
Dreem 2 EEG Headband

BEACON BIOSIGNALS



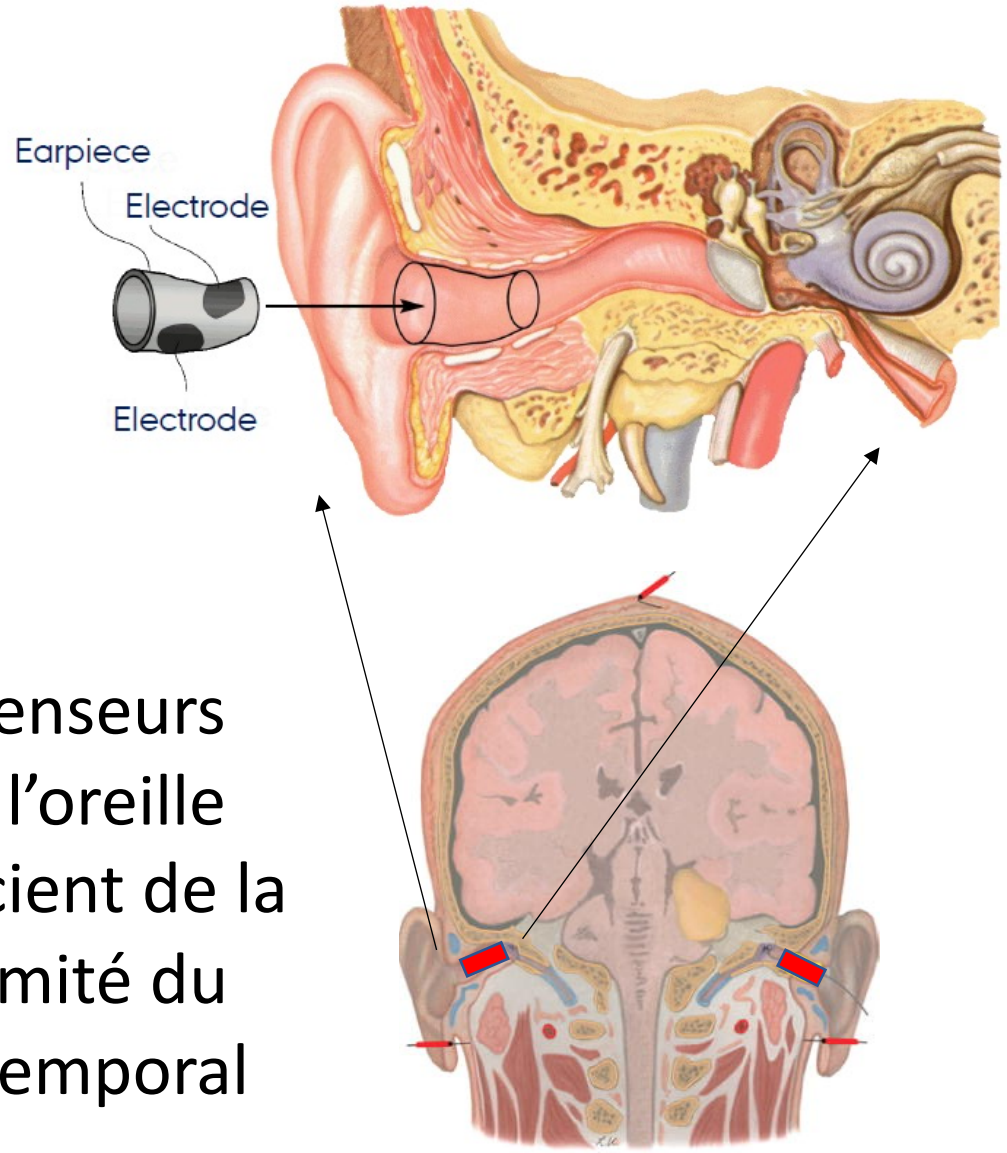


1) 7 EEG derivations: FpZ-O1, FpZ-O2, FpZ-F7, F8-F7, F7-O1, F8-O2, FpZ-F8; (2) movements, (3) sleep position, and (4) heart rate.

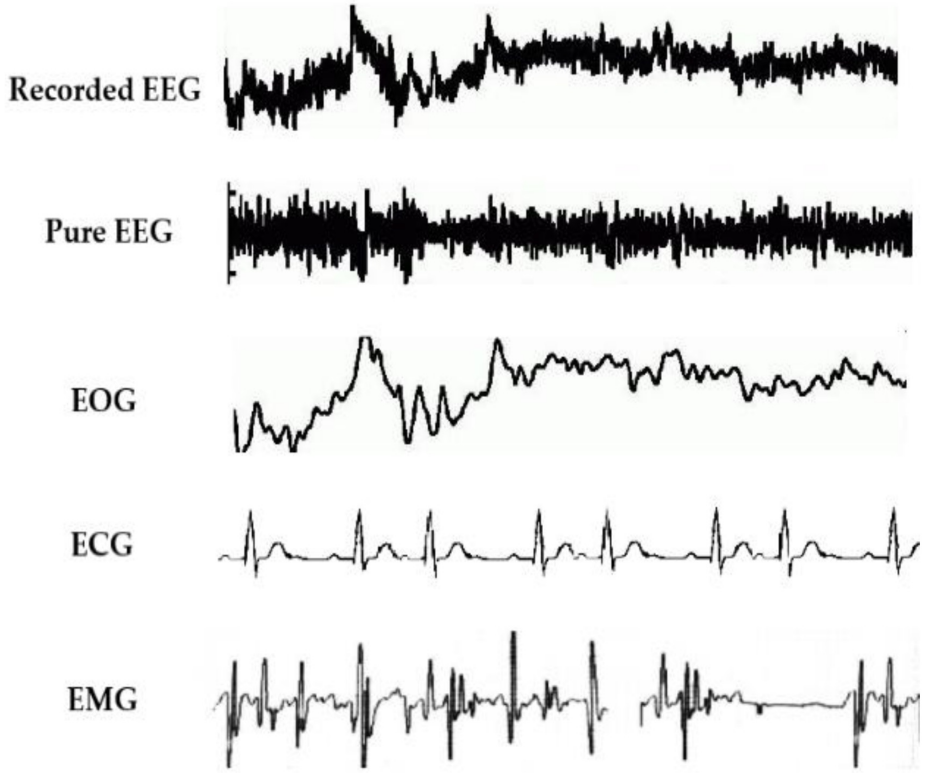


Arnal et al., The Dreem Headband compared to polysomnography for electroencephalographic signal acquisition and sleep staging, Sleep 2020

Les signaux intra-auriculaires

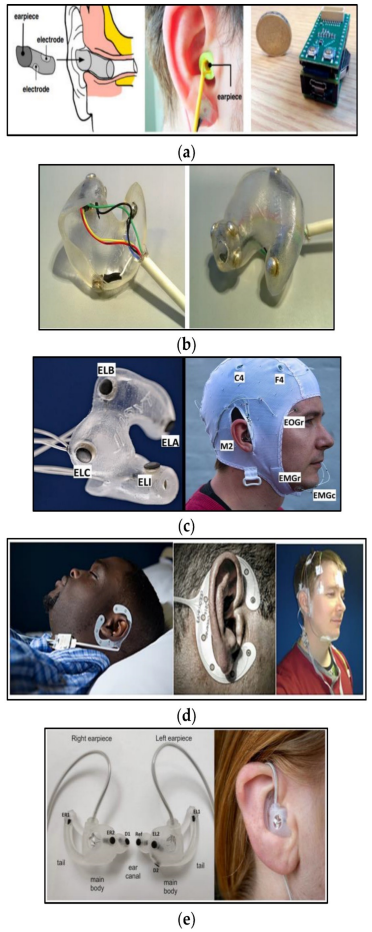


Les senseurs dans l'oreille bénéficient de la proximité du lobe temporal



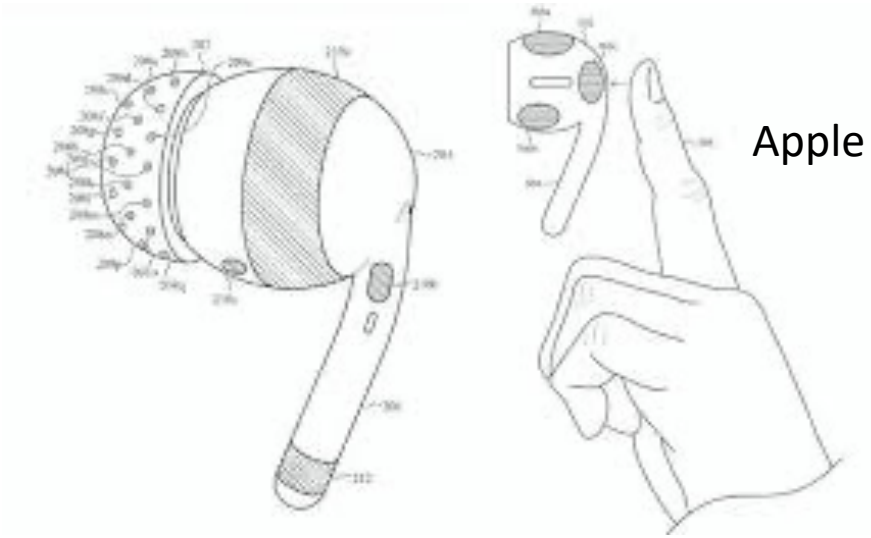
2012: Preben Kidmose, Aarhus University, Denmark

100 per-reviewed papers

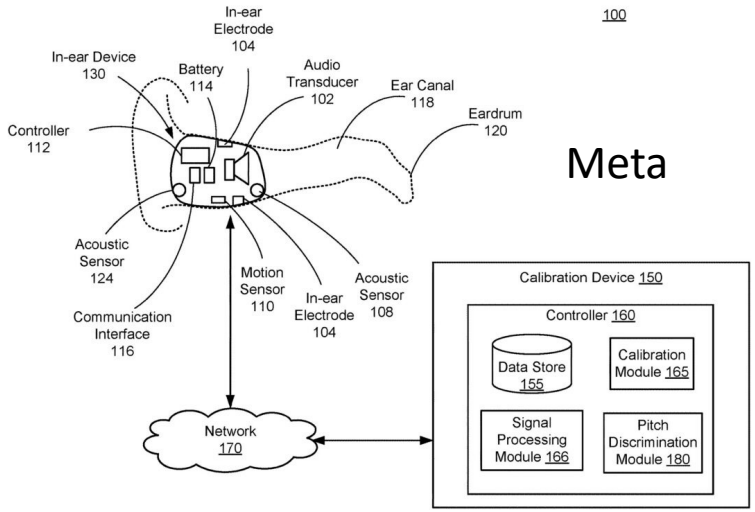




Patents



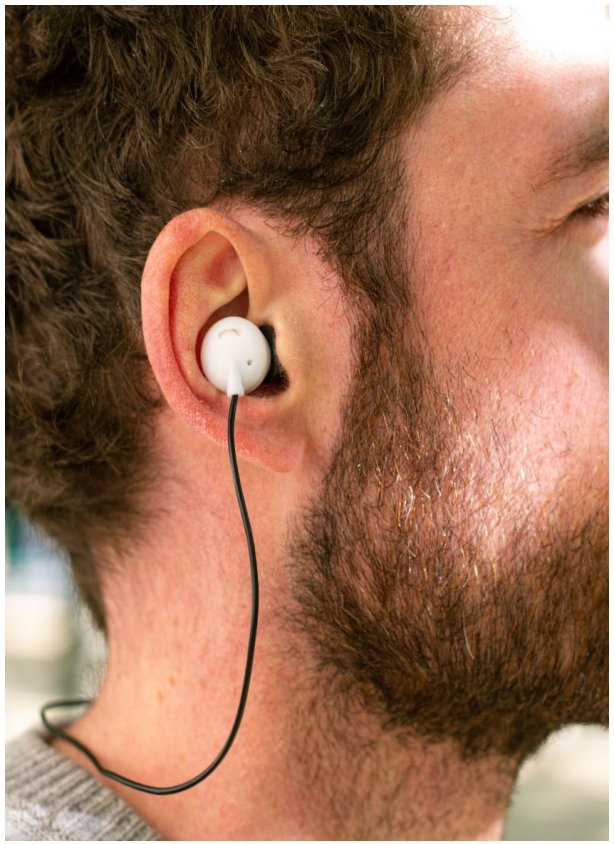
Apple

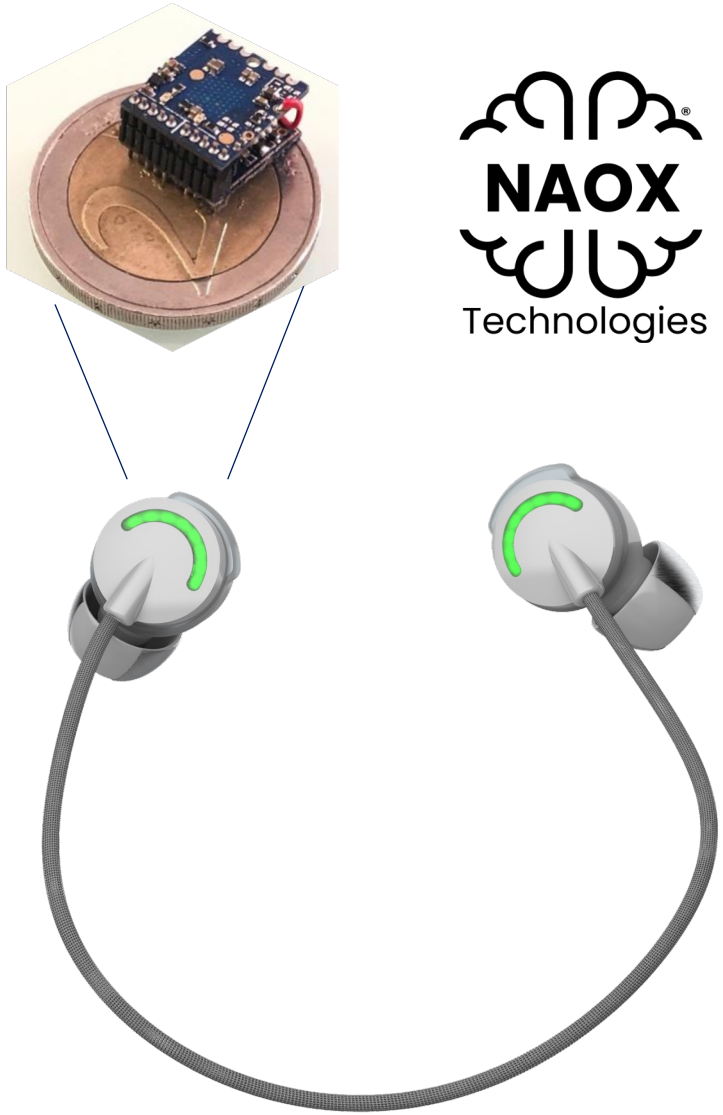


Meta

FIG. 1

An unique, non-stigmatizing form factor for longitudinal, remote patient monitoring





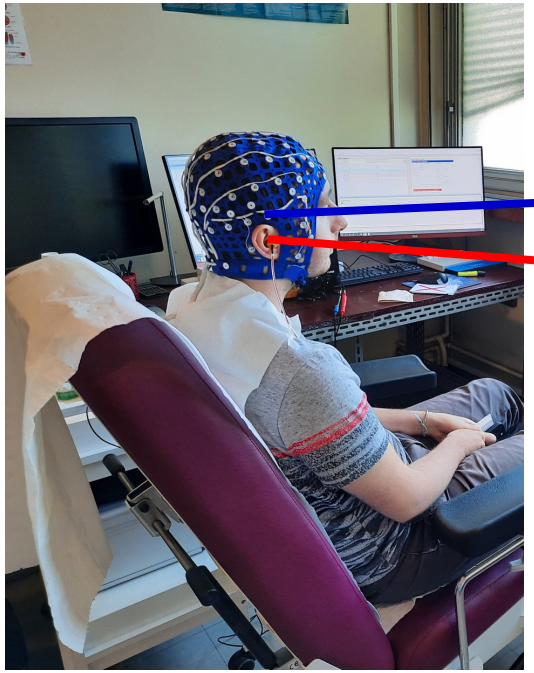
NAOX Technologies

- Une voie EEG (bipolaire, ERE-ELE)
- Echantillonnage: 250 Hz
- Poids: 20 g
- 9 heures d'enregistrement en continu (sans recharge)
- Data Stream: Bluetooth 2.4 GHz et stockage local: 64 MB
- Biocompatibilité des senseurs et performances électriques de base (IEC 60601-1;IEC 60601-1-2;IEC 80601-2-26; IEC 60601-1-11;IEC 62133)
- Bruit: < 6 µV RMS sur 1-30 Hz
- Grade médical (CE Class IIA)

Validation: L'alpha (Fermeture-Ouverture des yeux)

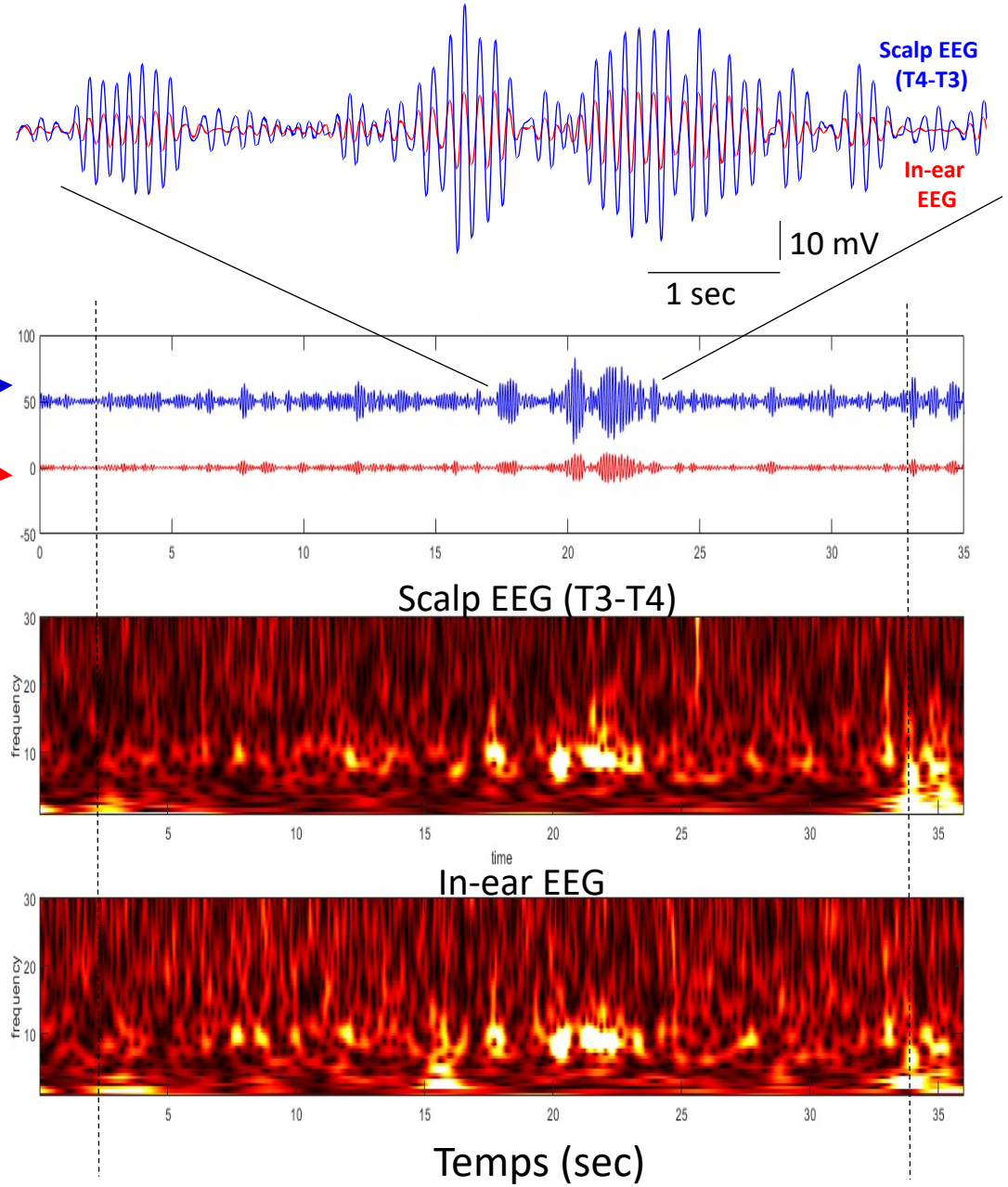
Hanane MOUMANE
Jérémy PAZUELO
protocole CER-2023,
SORBONNE UNIVERSITE

N=30 subjects

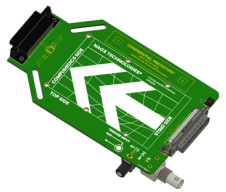


Scalp EEG (T3-T4)

In-ear EEG

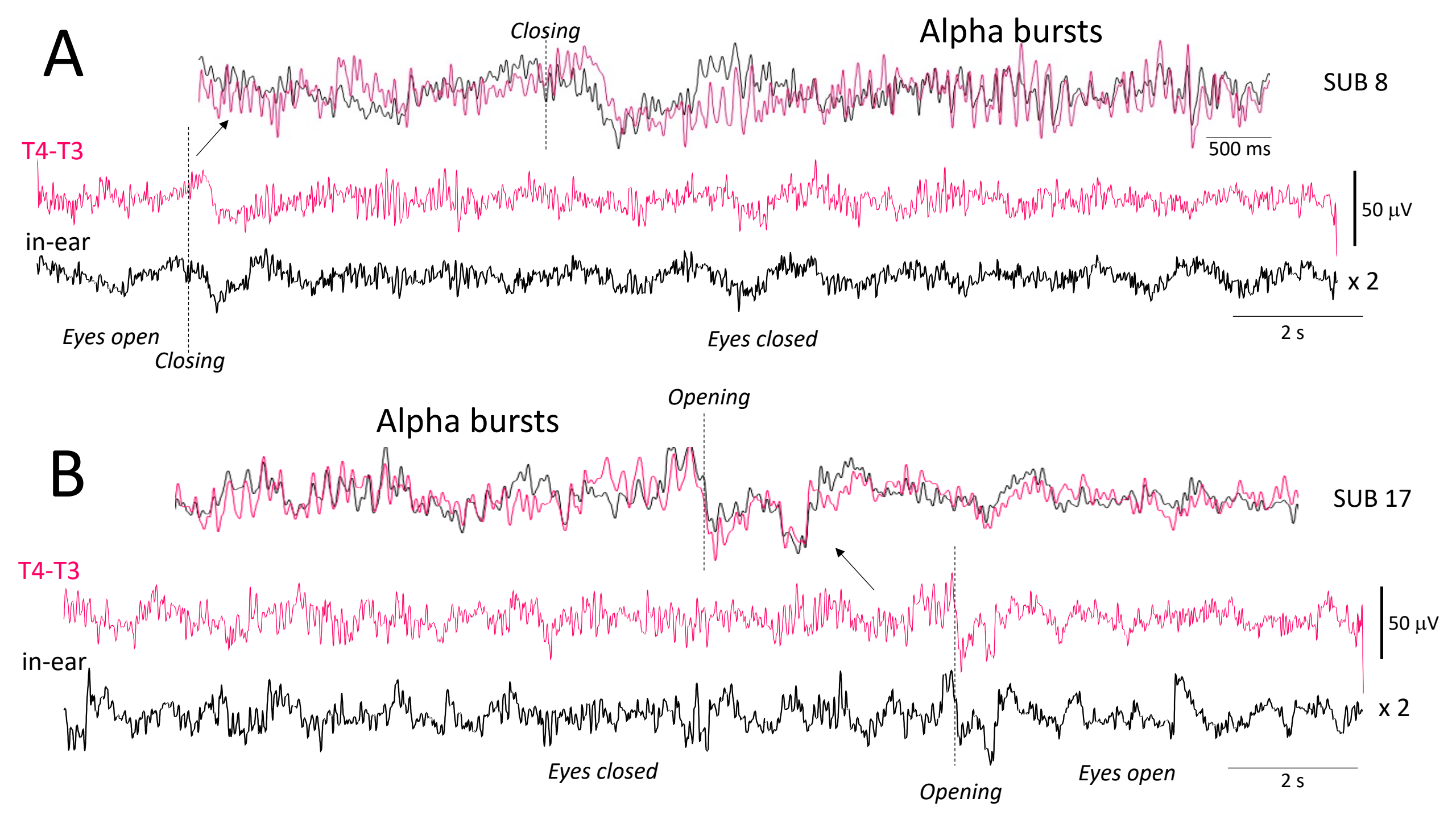


COMPUMEDICS



NAOX Technologies

Synchronisation CARD

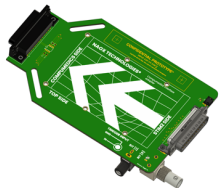

A
Closing
Alpha bursts
SUB 8
500 ms
T4-T3
50 µV
in-ear
x 2
2 s
Eyes open
Closing
Eyes closed
B
Opening
Alpha bursts
SUB 17
T4-T3
50 µV
in-ear
x 2
Eyes closed
Opening
Eyes open
2 s

Validation: Rythmes EEG du sommeil normal

POLYSOMNOGRAPHIE (EEG + EOG +EMG)



COMPUMEDICS

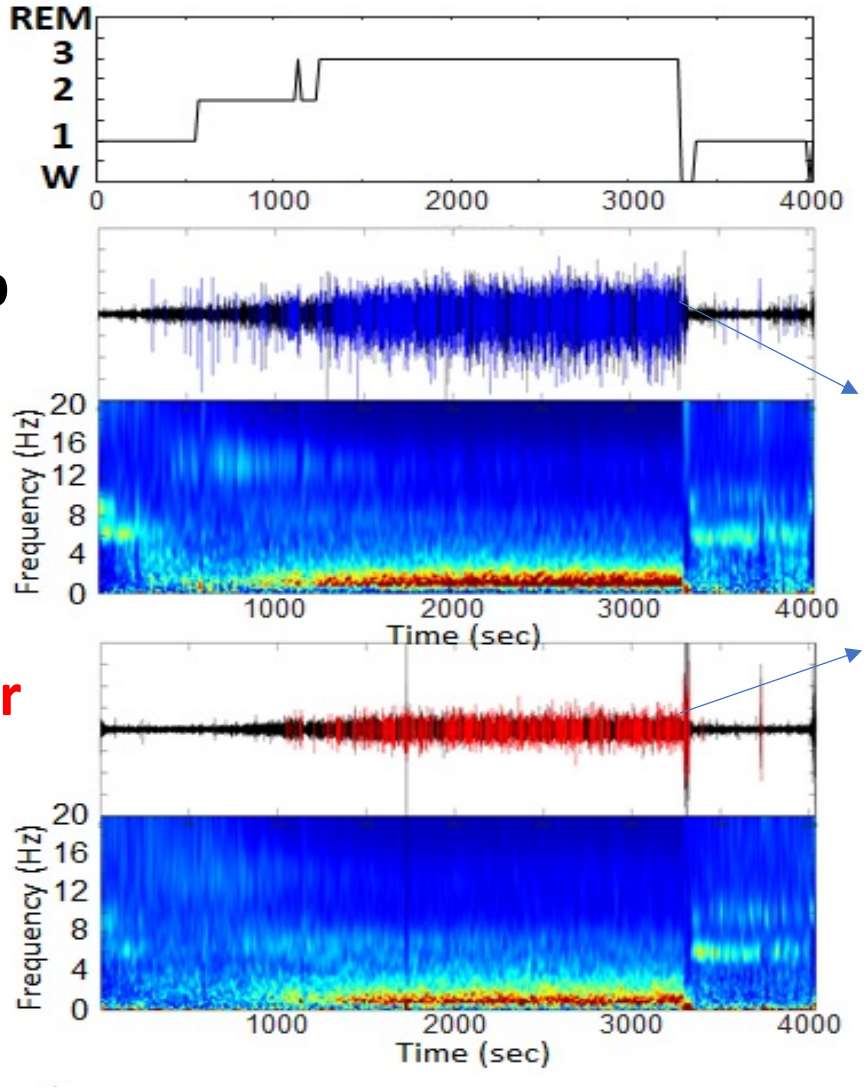


NAOX Technologies

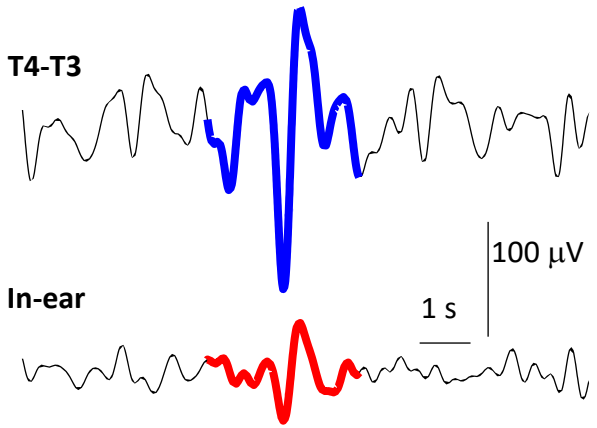
Synchronisation CARD

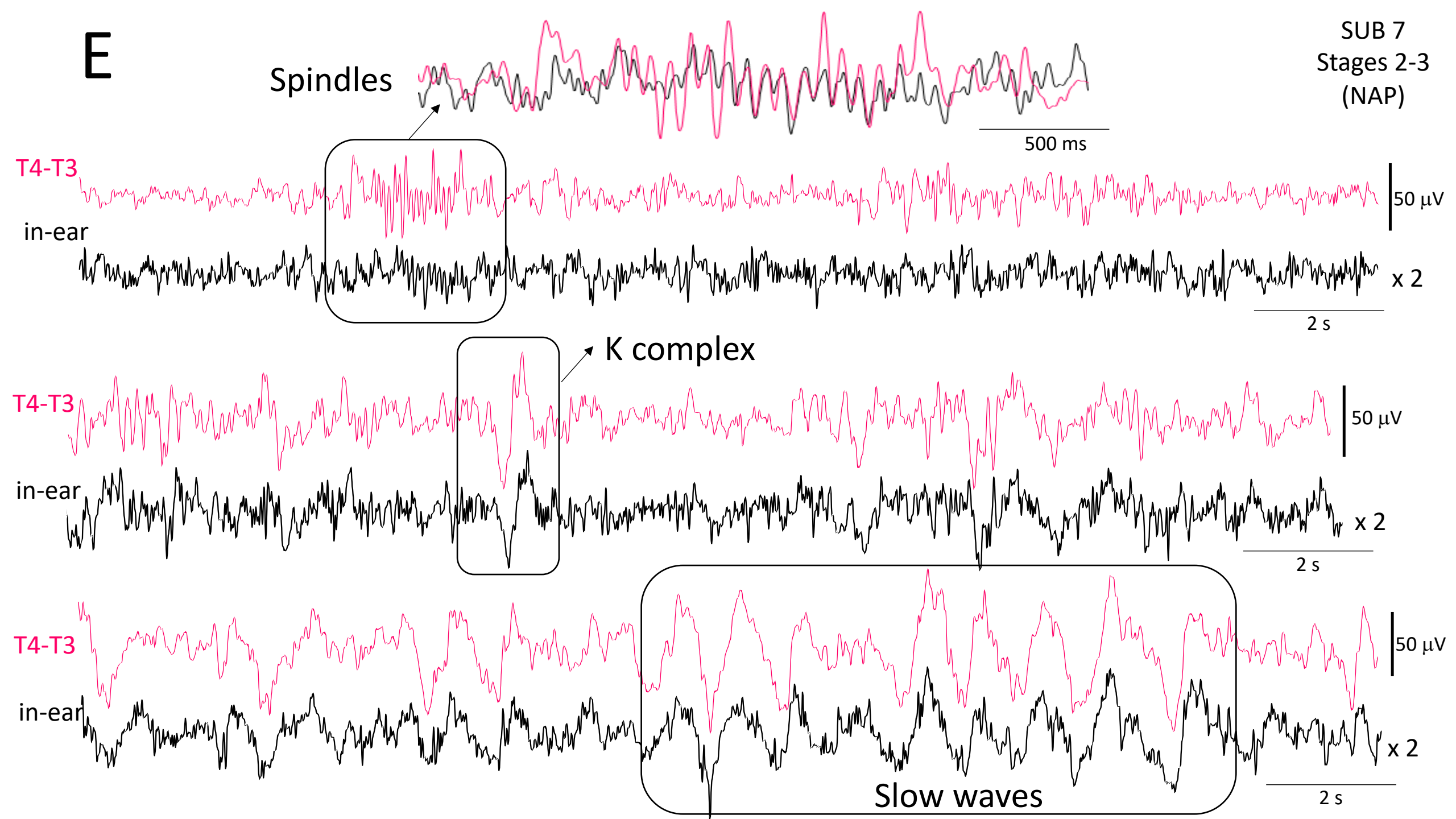
Scalp EEG

In-ear EEG



Ondes lentes (Stade 2-3)




E
Spindles
SUB 7
Stages 2-3
(NAP)
500 ms
T4-T3
in-ear
50 µV
x 2
2 s
K complex
T4-T3
in-ear
50 µV
x 2
2 s
T4-T3
in-ear
50 µV
x 2
2 s
Slow waves

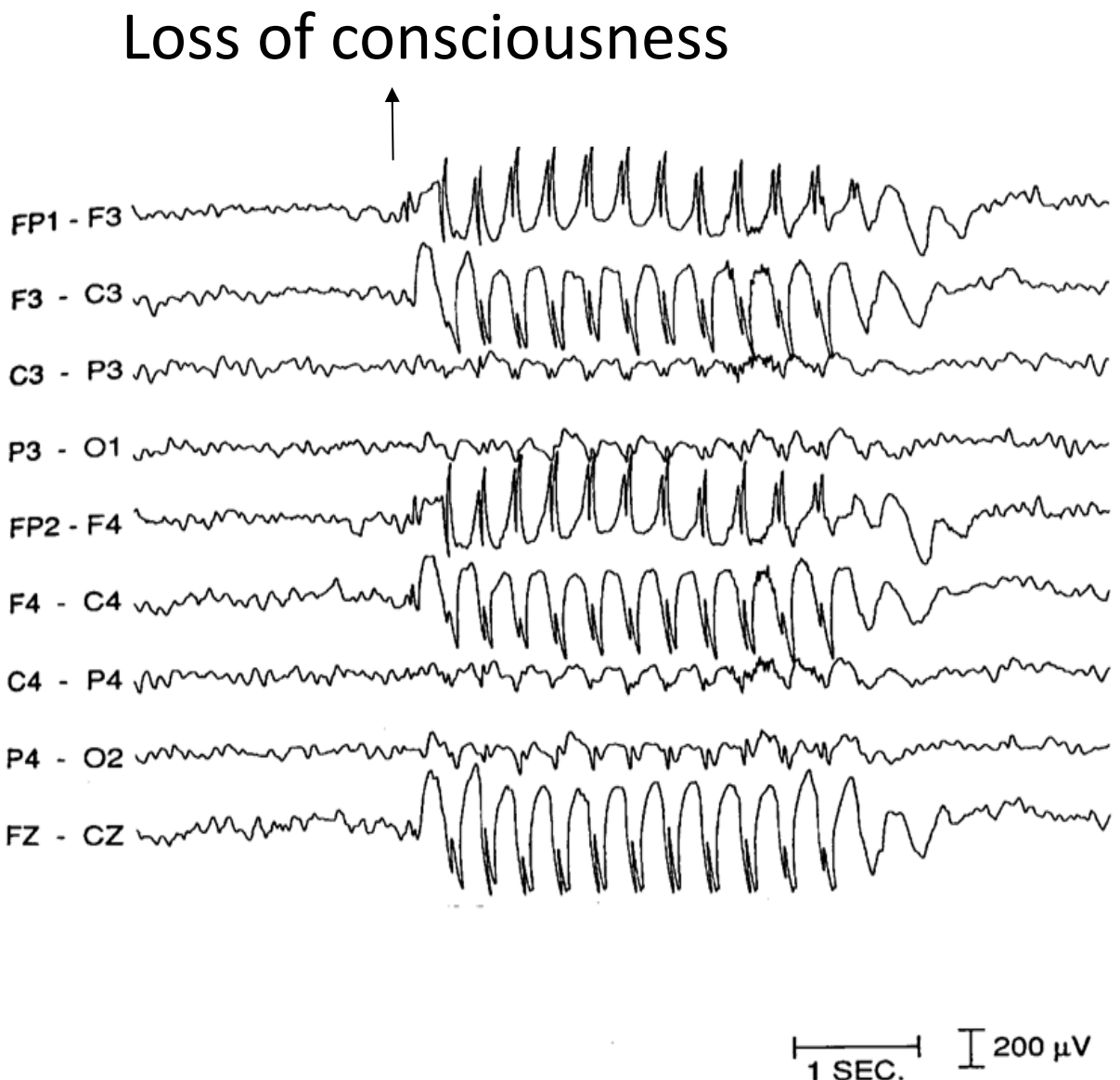
APPLICATION 1: LONG-TERM MONITORING OF EPILEPSY



- Up to 5 % of the world's population (65 M) have a seizure at some time in their lives

- Epilepsy can happen at any age, but is most common in young children and older adults

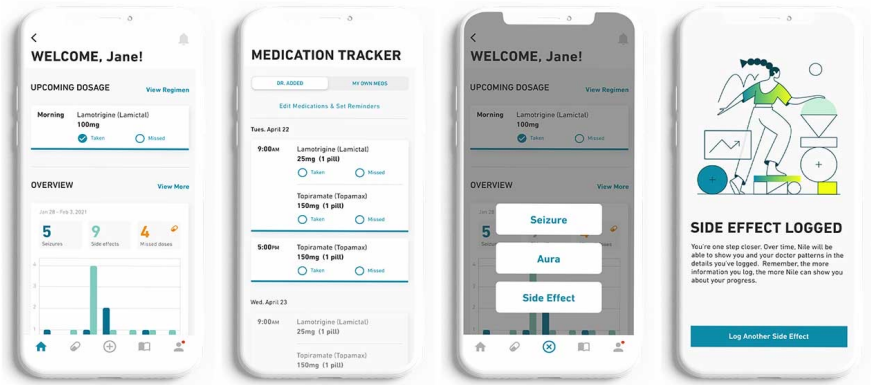
- 30% of people with epilepsy will not gain full seizure control with medication

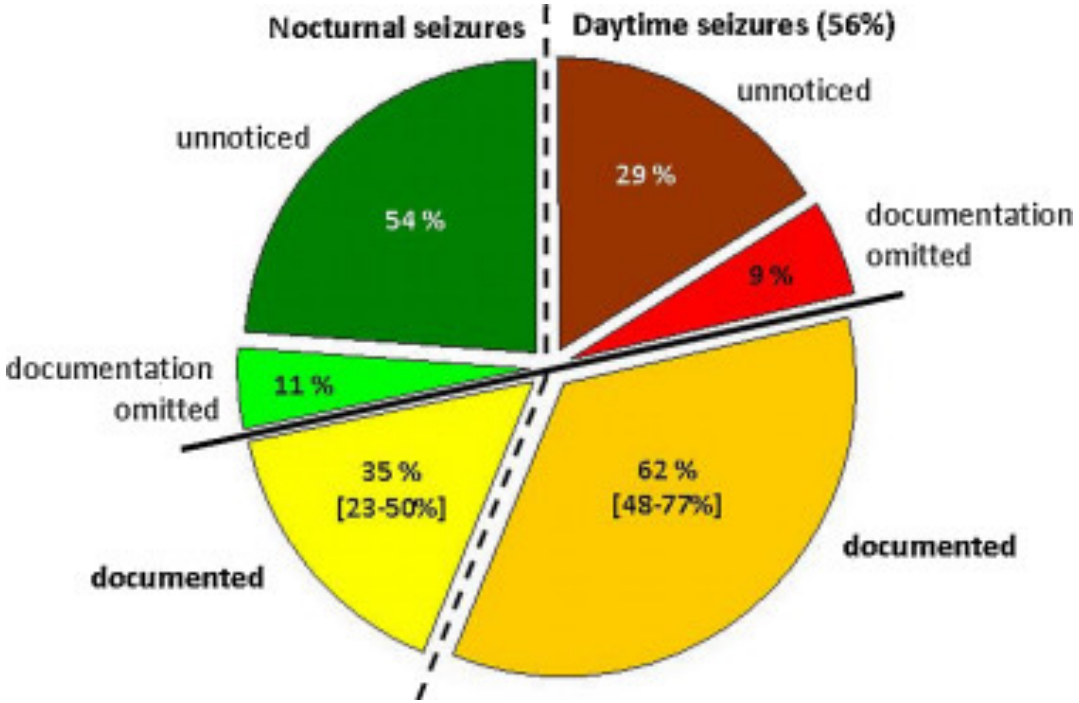


Compter les crises, au coeur du diagnostic de l’épilepsie

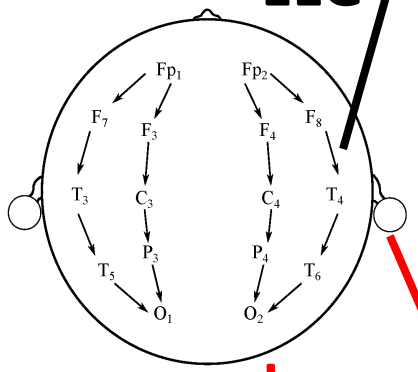
Journal des crises







Blachu et al. (2015) Seizure 29, 97-103



Scalp EEG

In-ear EEG

T6-O2
T4-T6
F8-T4
FP2-F8
P4-O2
C4-P4
F4-C4
FP2-F4
P3-O1
C3-P3
F3-C3
FP1-F3
T5-O1
F3-T5
F7-T3
FP1-F7

120 125 130 135 140 145

Frequency (Hz) 30 25 20 15 10 5

time (sec)

1 sec

1 sec

Prof. Gilles Huberfeld

HÔPITAL FONDATION
Adolphe de ROTHSCHILD
LA RÉFÉRENCE TÊTE ET COU

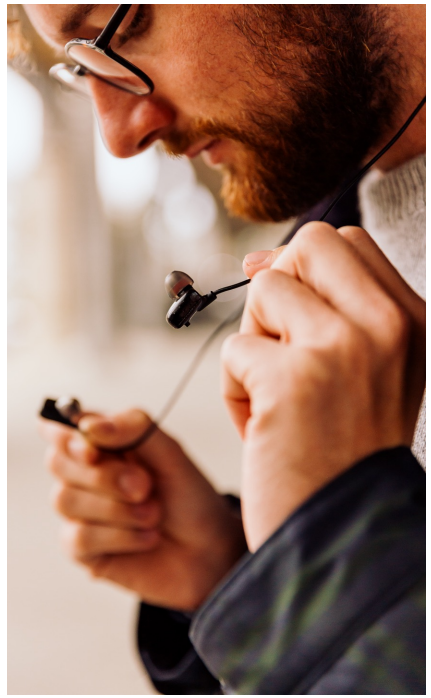
Prof. Rima Nabbout

Necker
ENFANTS MALADES
HÔPITAL UNIVERSITAIRE

NAOX
Technologies

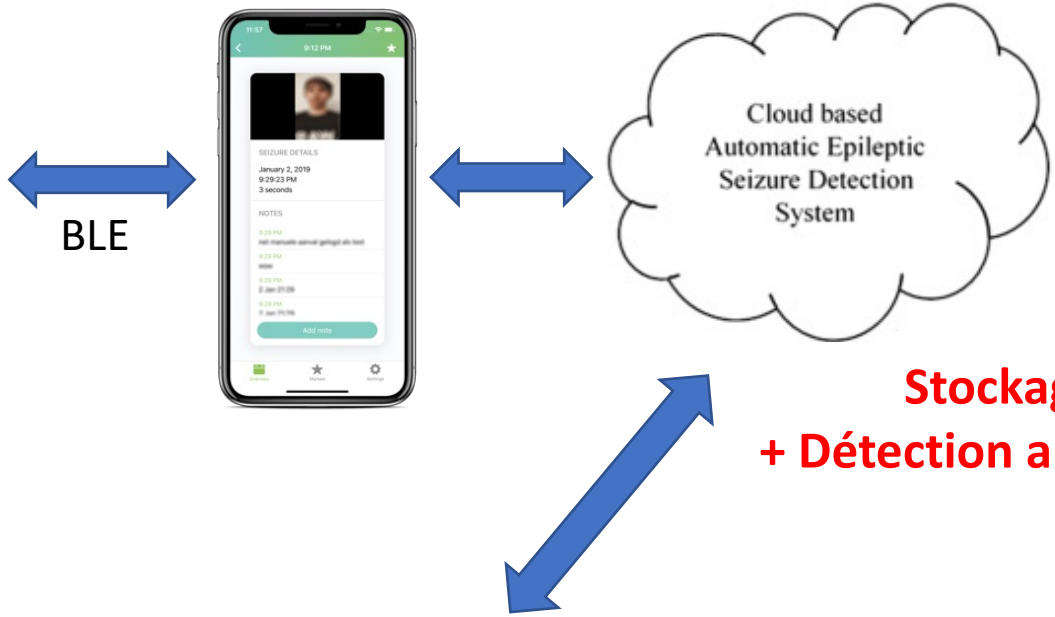
Ecouteurs Naox

- Accéléromètre
- Pousse-bouton



Une APPLI

- Information sur le traitement
- Enregistrement vidéo



Stockage des données
+ Détection automatique des crises

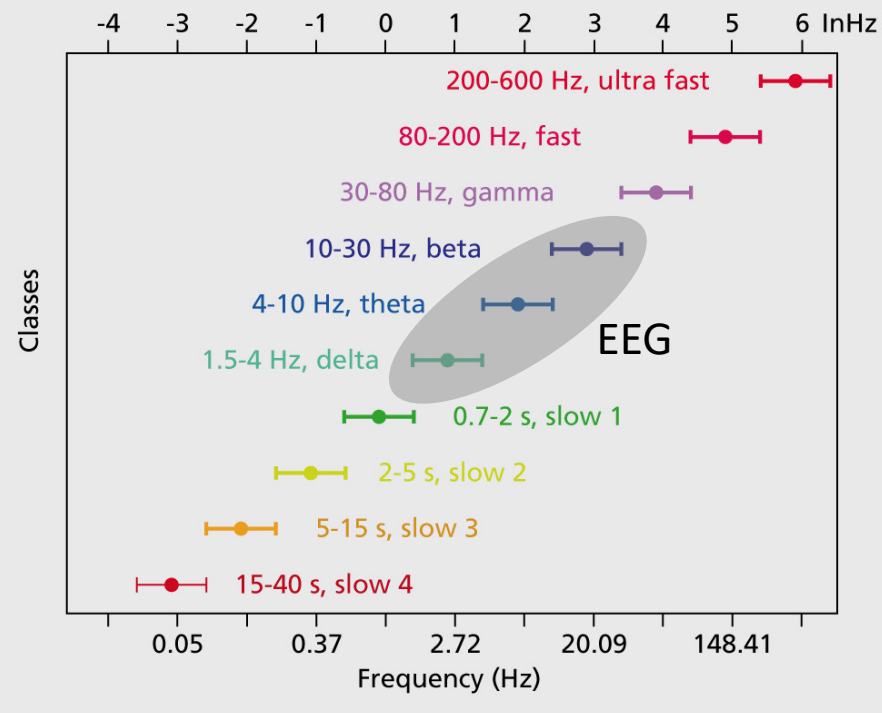
Plateforme pour les médecins

- Crises avec vidéo
- Fréquence et durée
- Cycles des crises



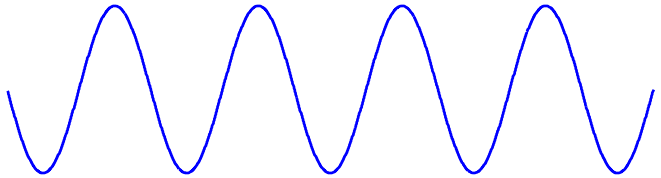
PAUSE

A system of unstable brain oscillators

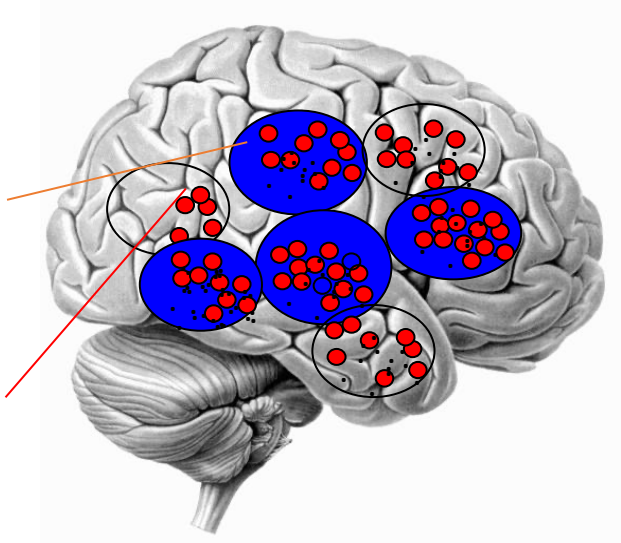


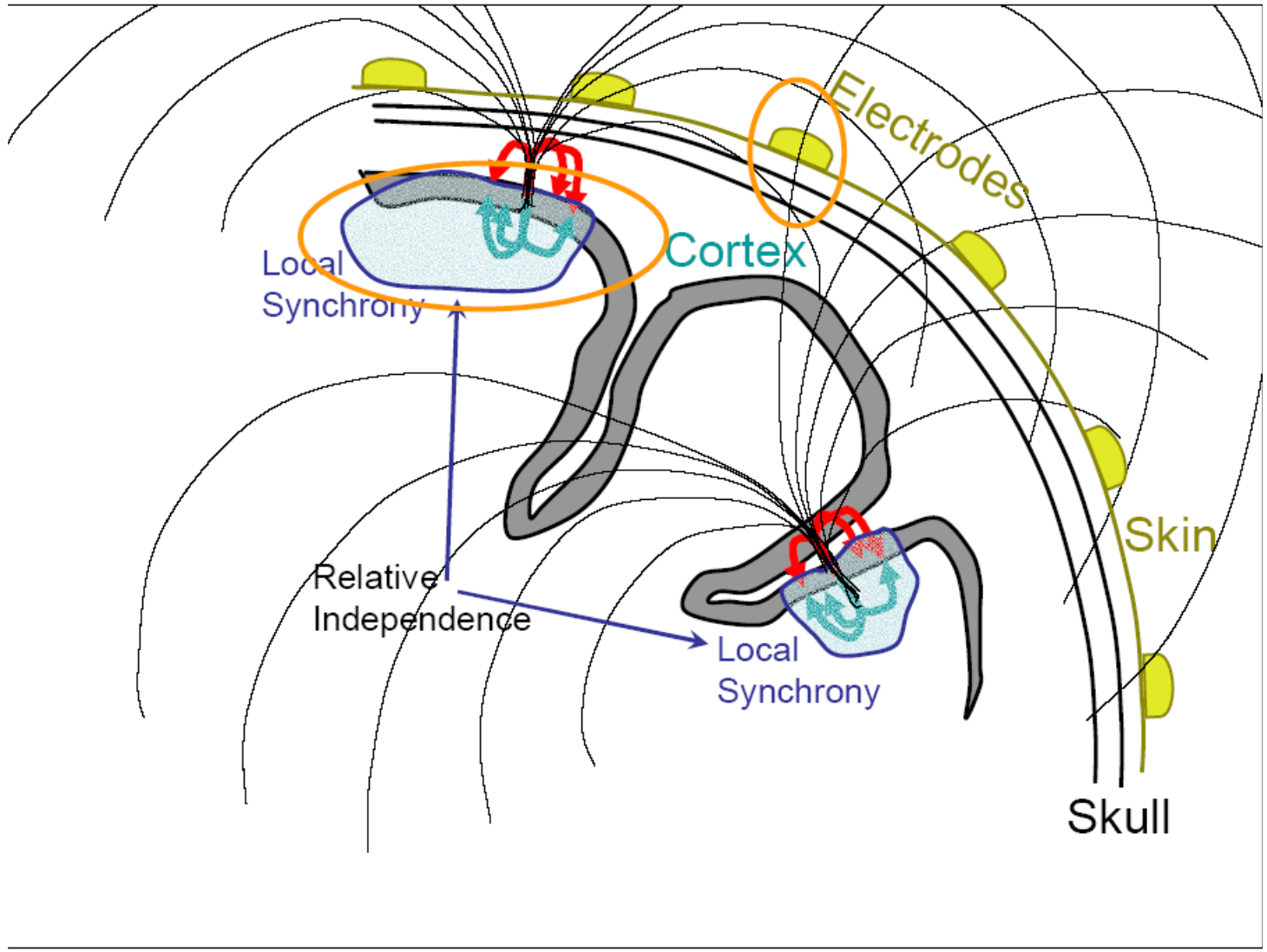
- 10 classes of oscillations (non-overlapping bands)
- Center frequencies follow an log rule
- unstable activities
- Higher frequency oscillations originate from a smaller neuronal population, whereas low frequency oscillations encompass larger populations

Large-scale slow oscillations (e.g. delta-theta)



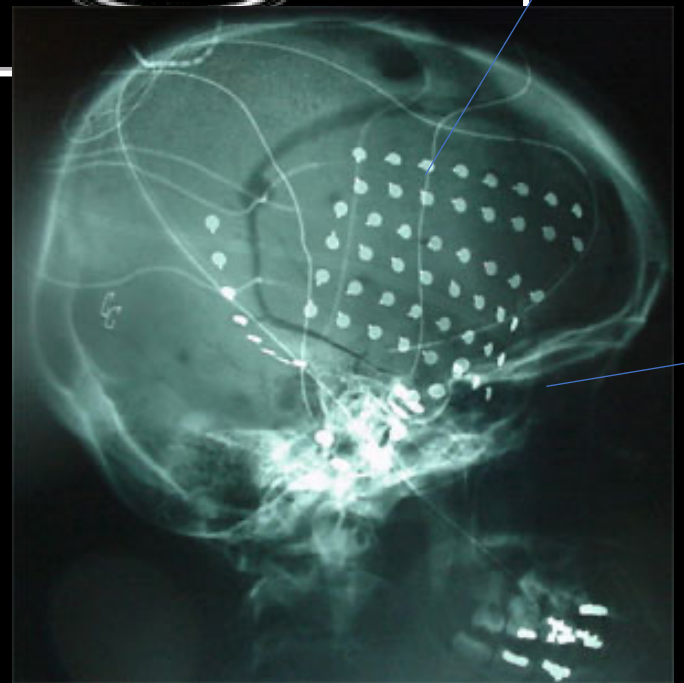
Local high frequency oscillations (e.g. gamma)



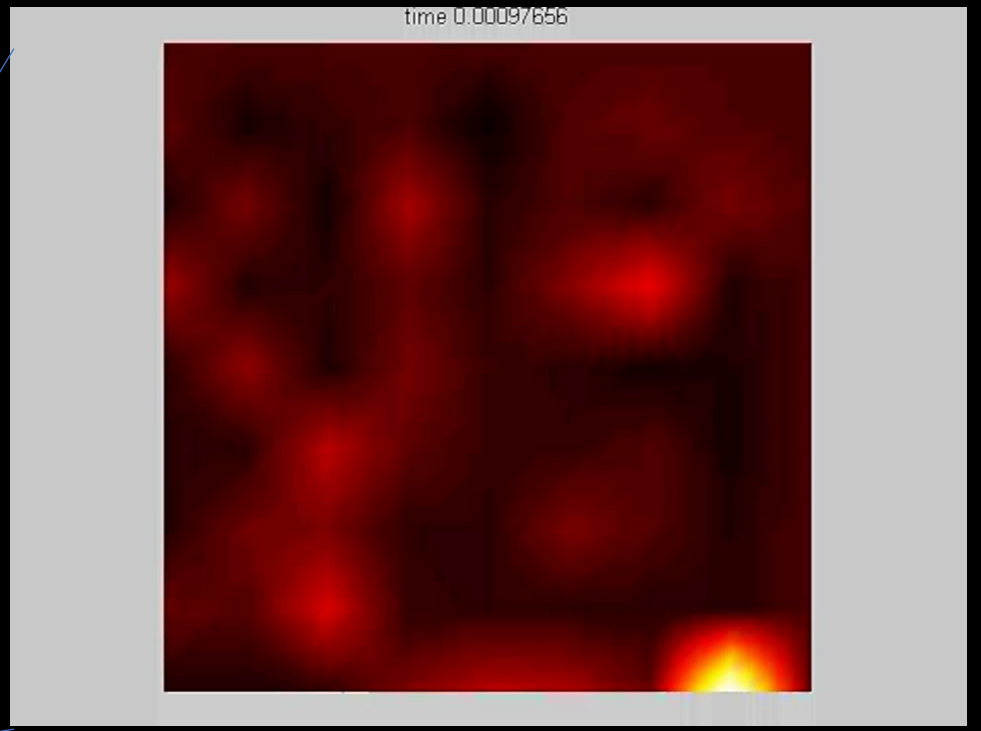

Electrodes
Cortex
Local
Synchrony
Relative
Independence
Local
Synchrony
Skin
Skull

Studying human brain activities from within

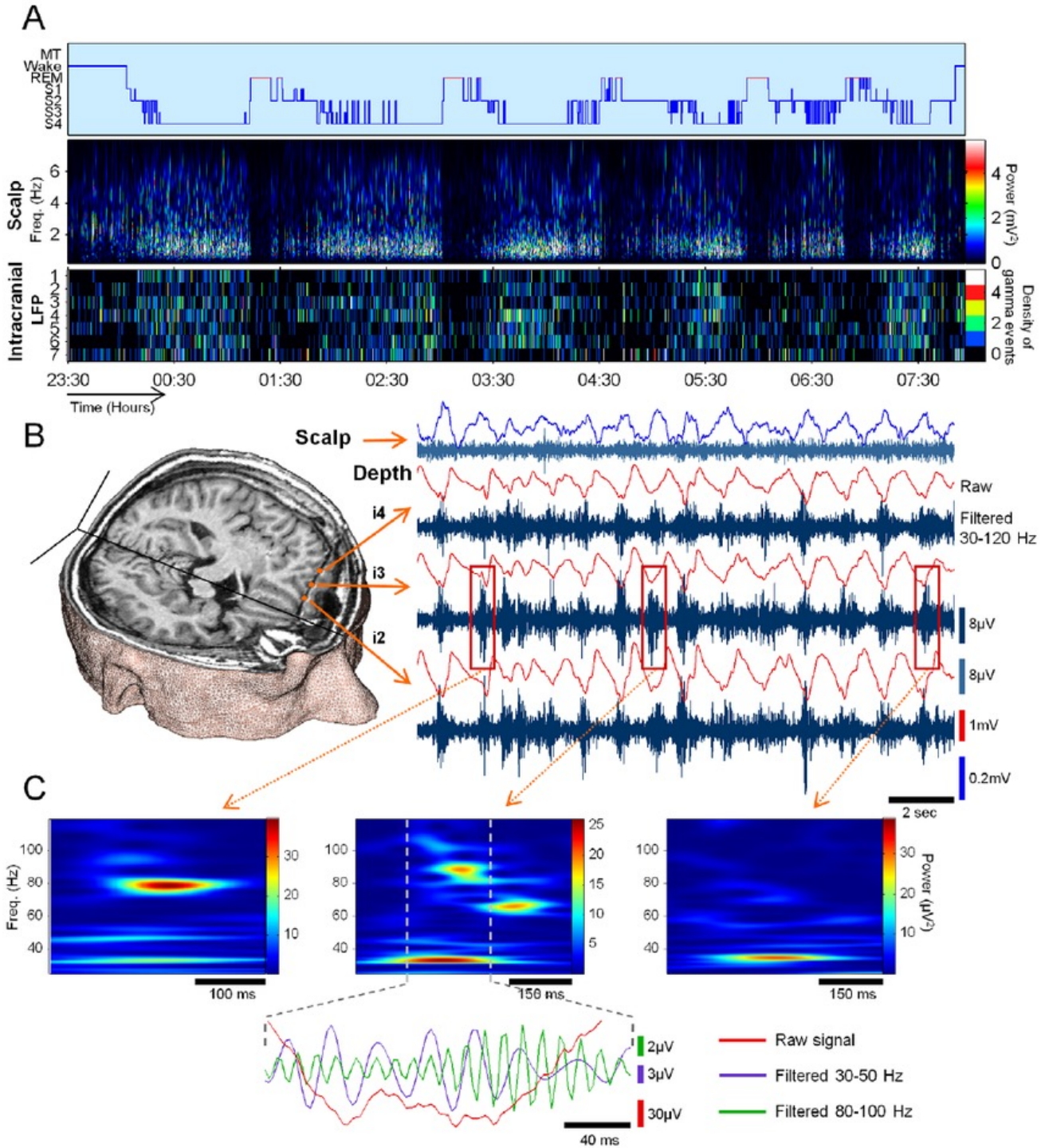




gamma frequency band (40-120 Hz)



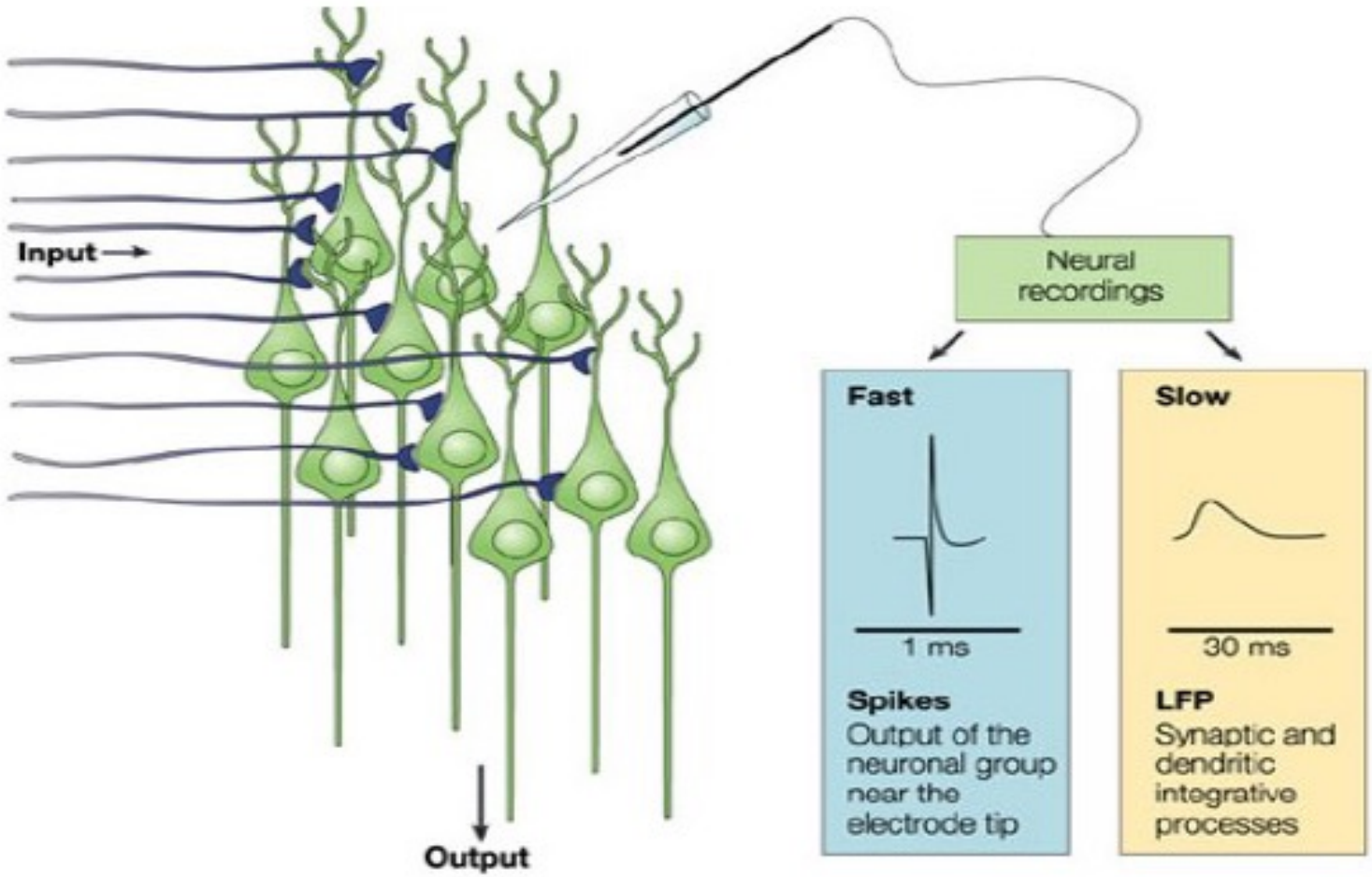
- Diameter: 1.0 mm & contact spacing: 10 mm
- Temporal resolution: 1 kHz
- Spatial resolution : < cm^3



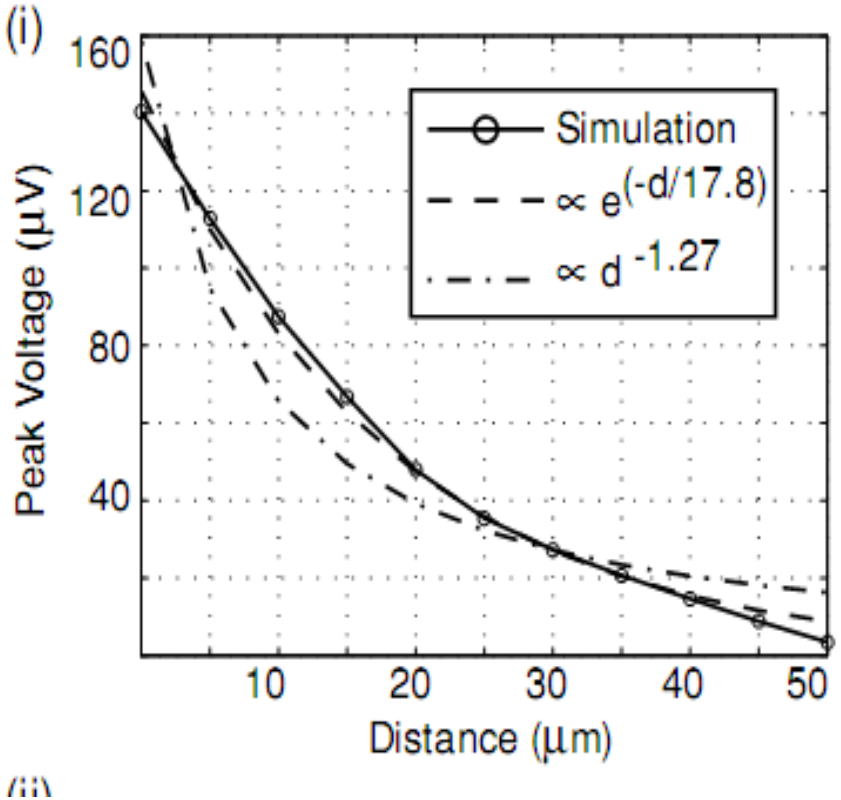
Human gamma oscillations during slow wave sleep

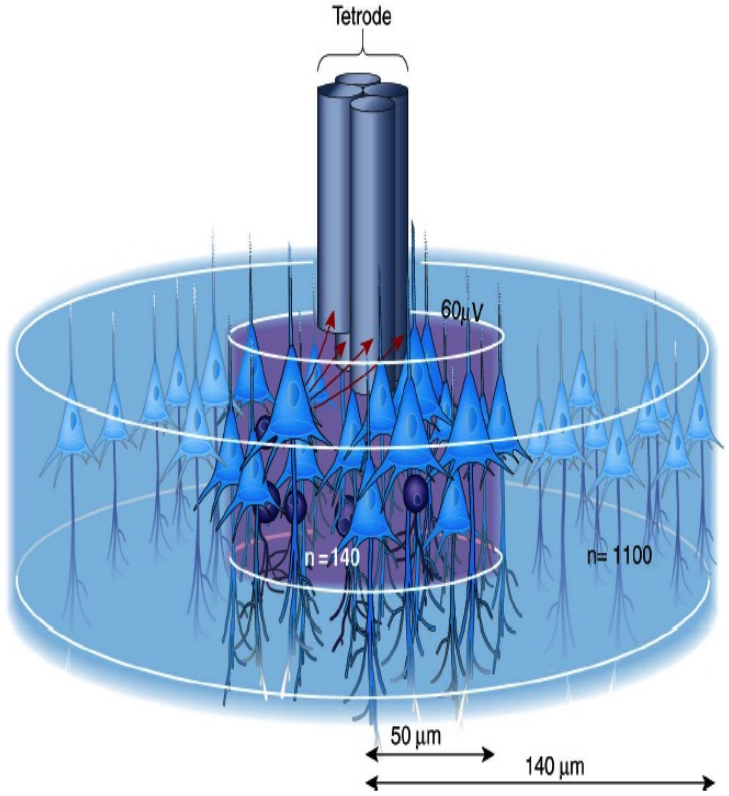
Valderrama M, Crépon B, Botella-Soler V, Martinerie J, Hasboun D, Alvarado-Rojas C, Baulac M, Adam C, Navarro V, Le Van Quyen M.. PLoS One. 2012

Spike and LFP: two different phenomena



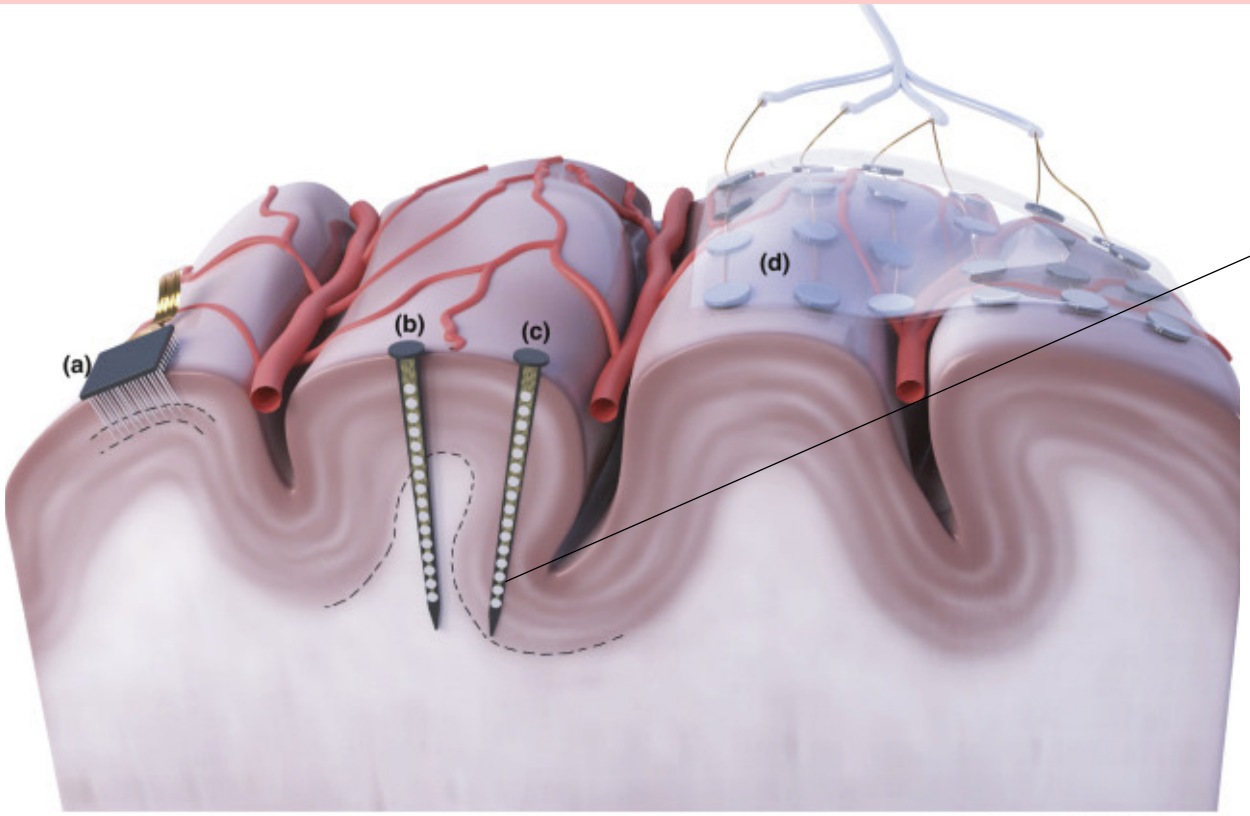
Detecting spikes from far away is difficult

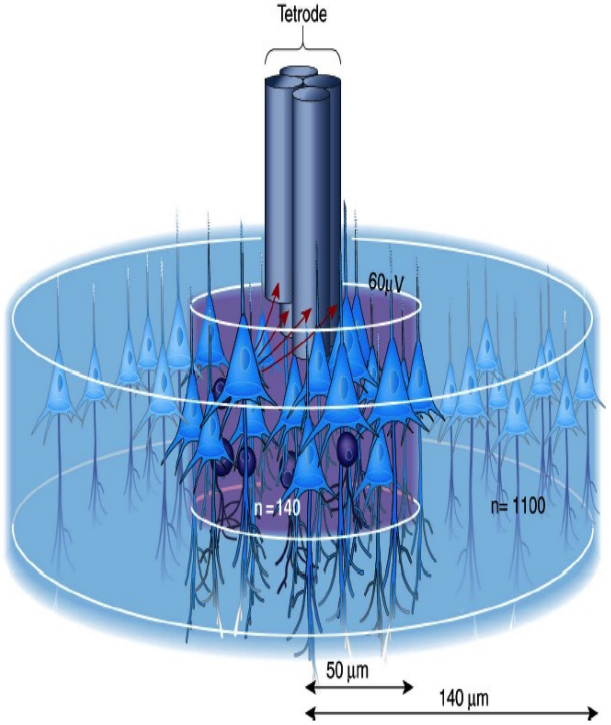




Gold, Henze and Koch,
J Computational Neuroscience 2007

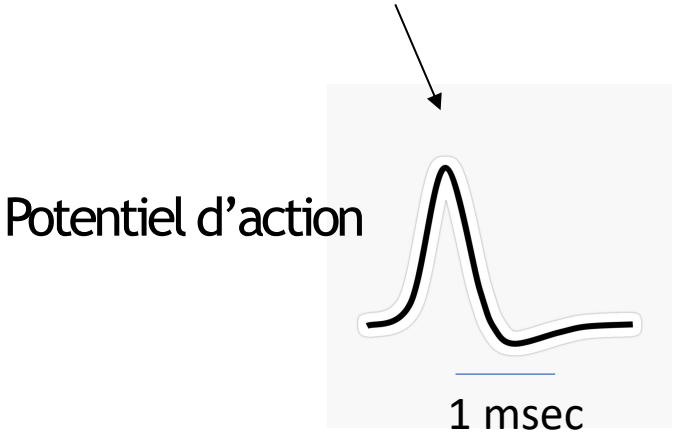
Les micro-électrodes à haute impédance

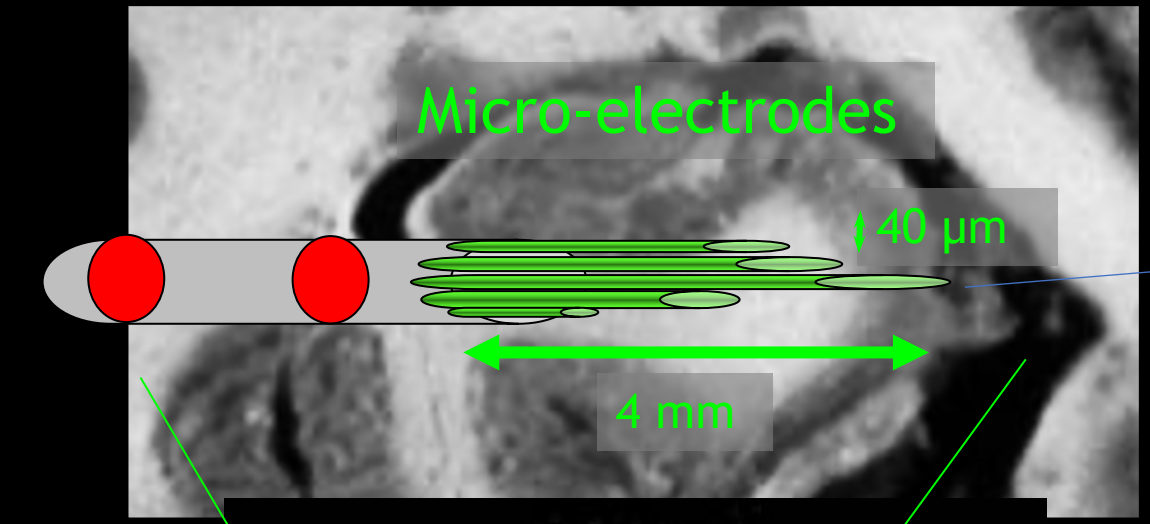




MUA

petite surface conductrice (de quelques µm)
en métal (en or, iridium, Pt)





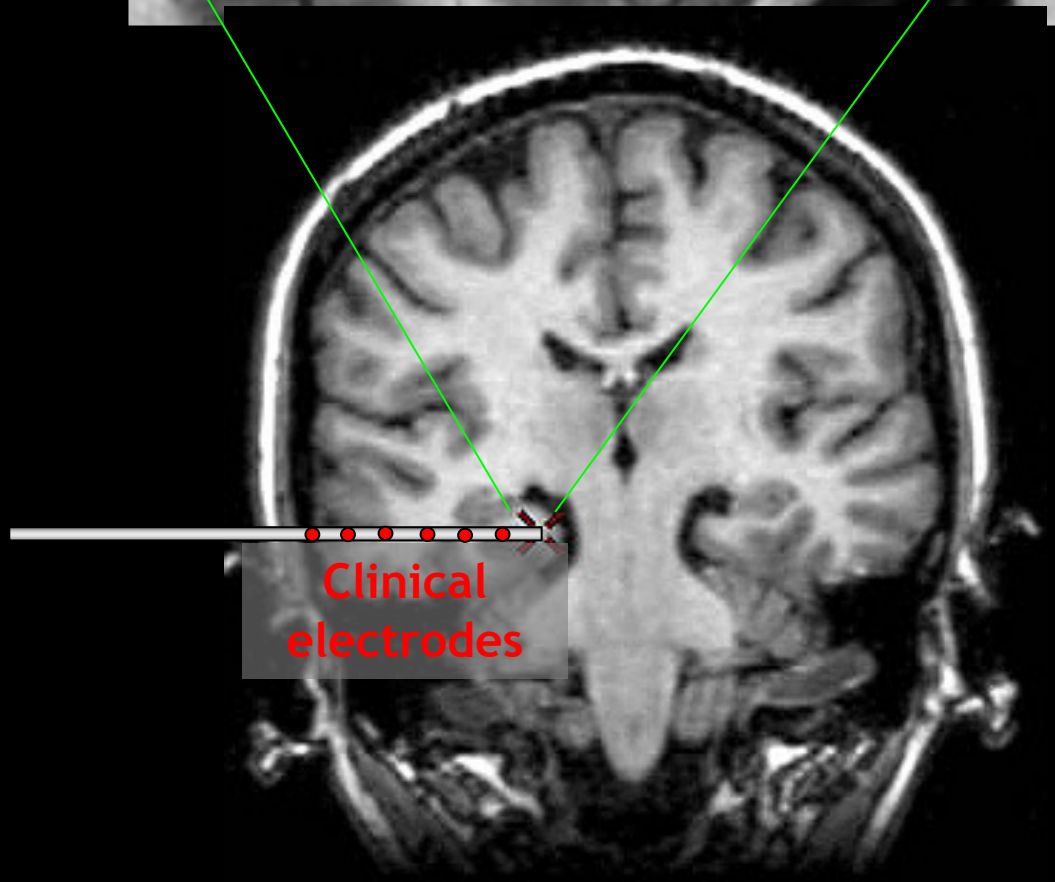
Broad band signals (0-20 kHz)

50 mV
1 s

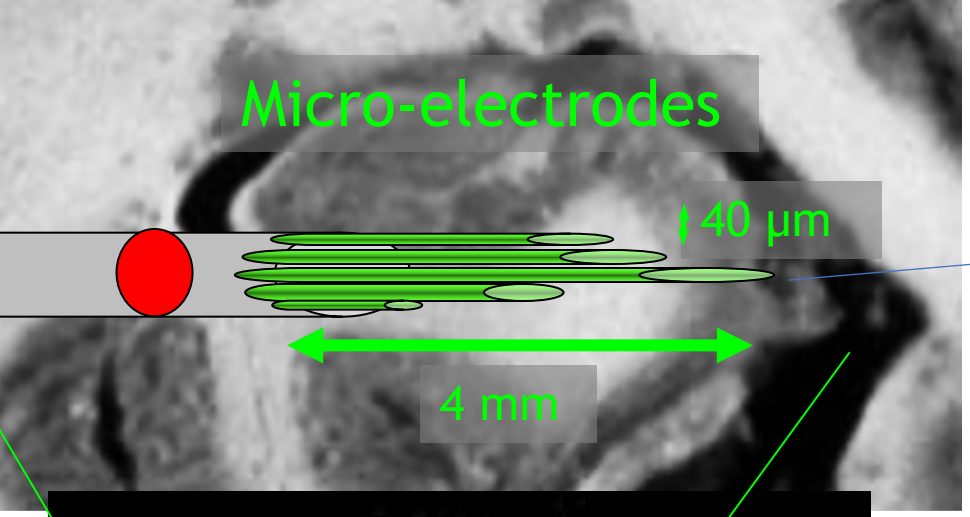
LFP (<400 Hz)

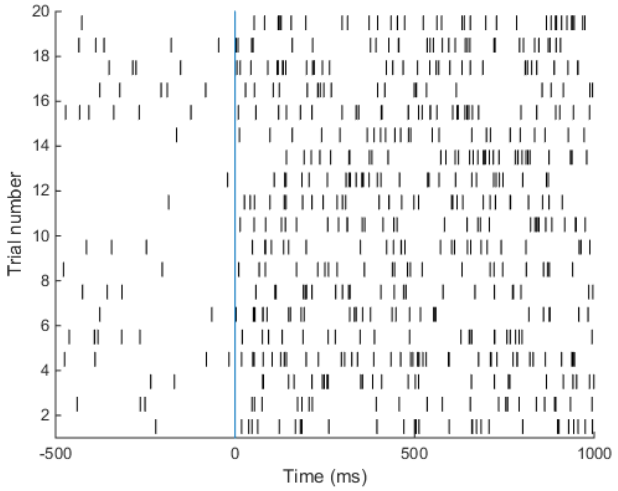
MUA (>400 Hz)





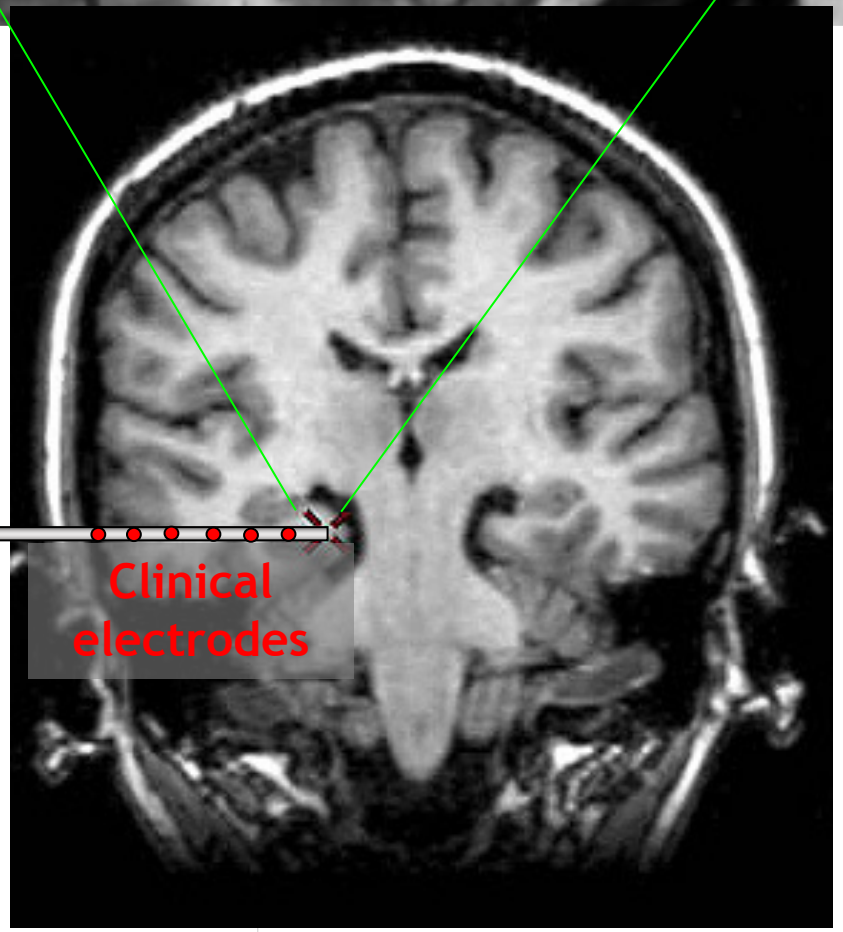
- Spatial resolution: <1 mm
- Temporal resolution: 0.05 ms

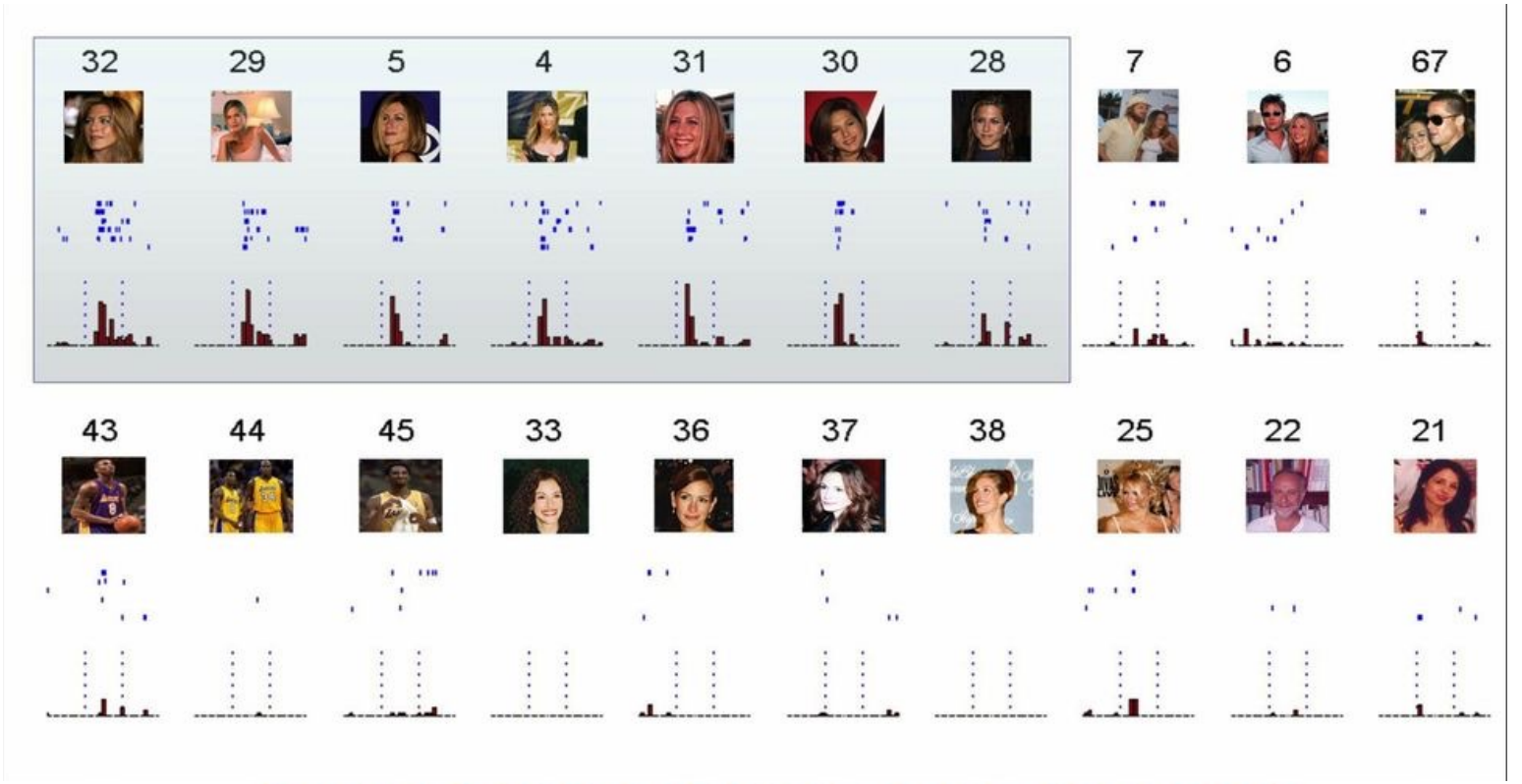




Jennifer Aniston' s neurons



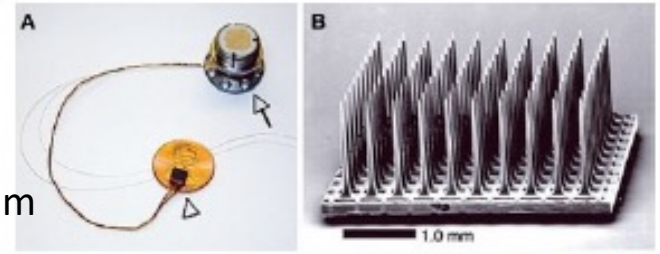




Quiroga, R. Q., Reddy, L., Kreiman, G., Koch, C., & Fried, I. (2005).
Invariant visual representation by single neurons in the human brain. Nature, 435(7045), 1102.

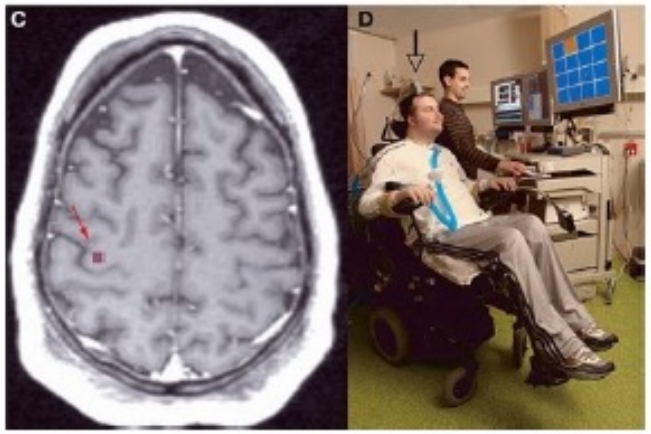
Utah electrode arrays

96 microelectrodes with 400-µm spacing, covering an area of 4 × 4mm

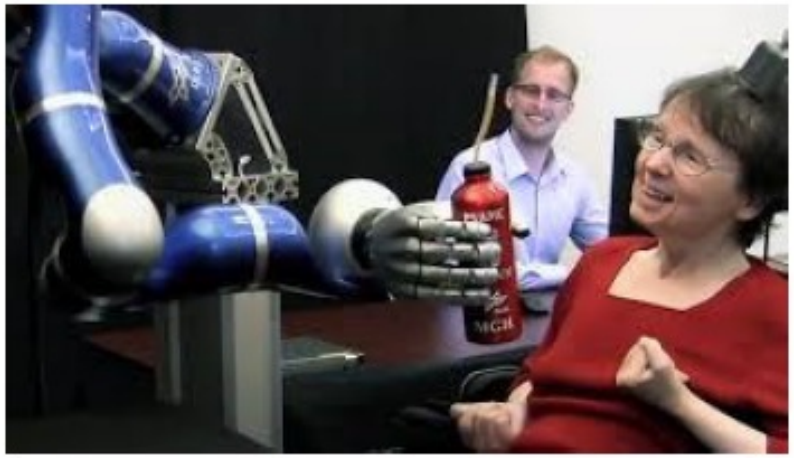


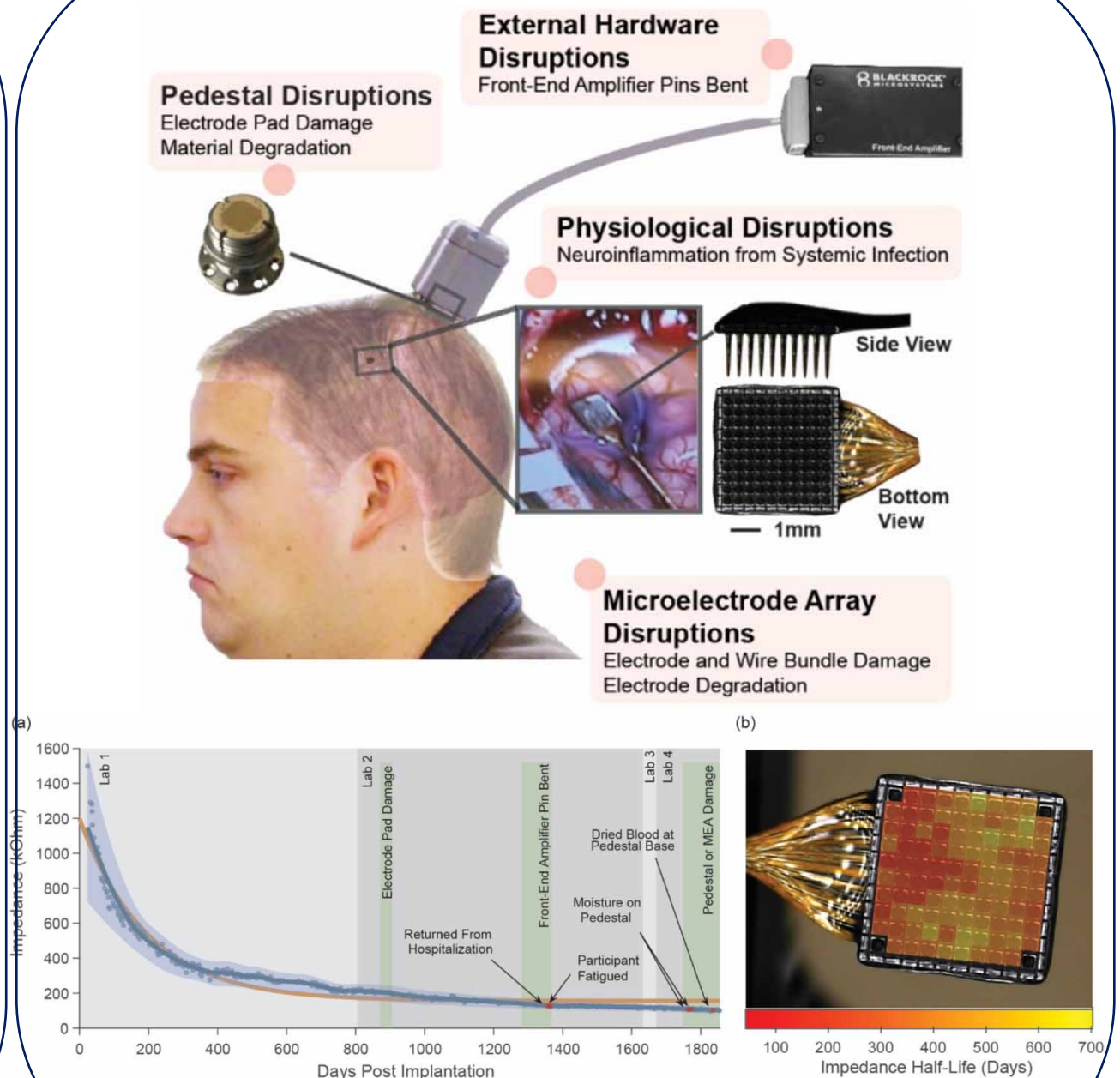
2005
Matt Nagle

Patients tétraplégiques



2006

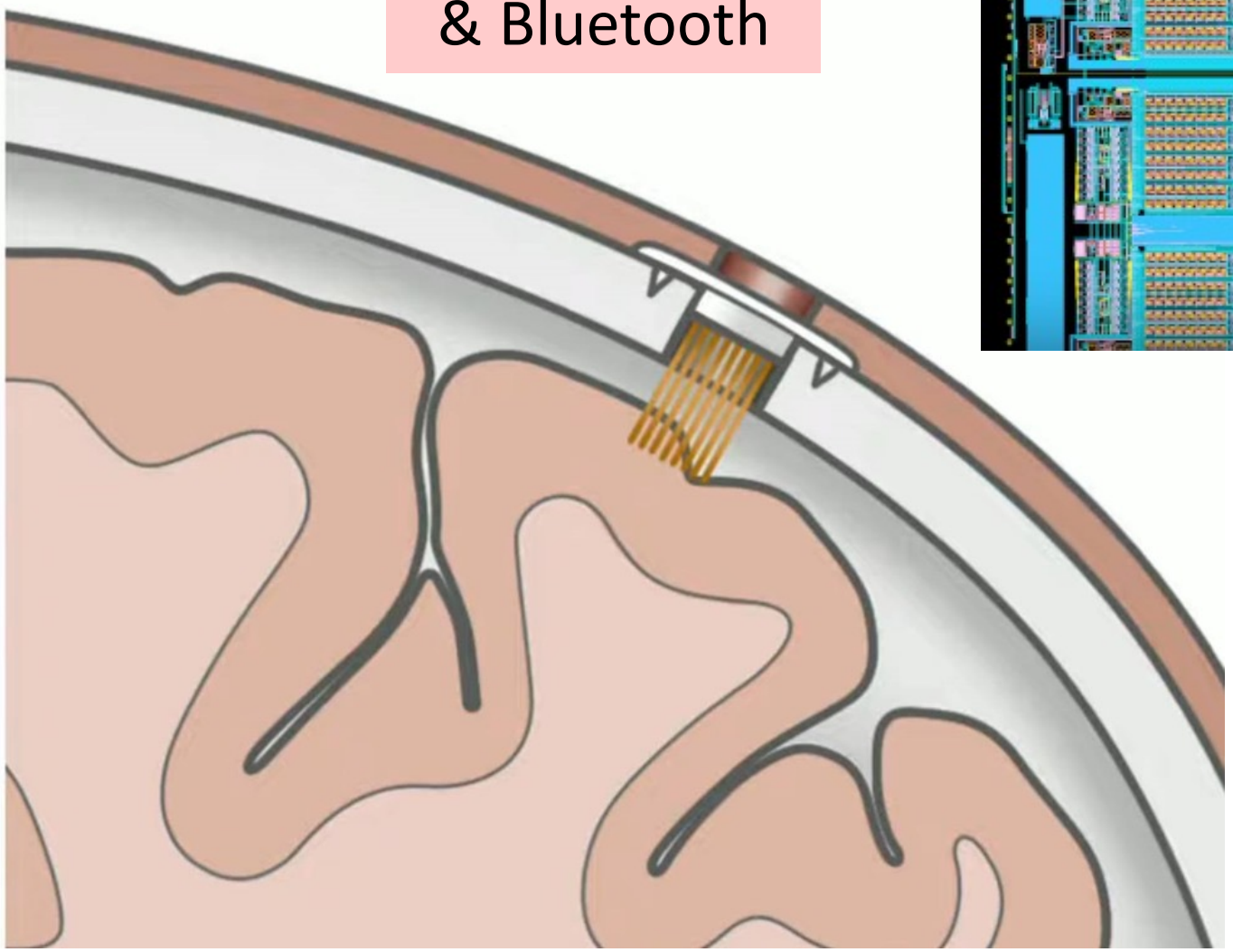


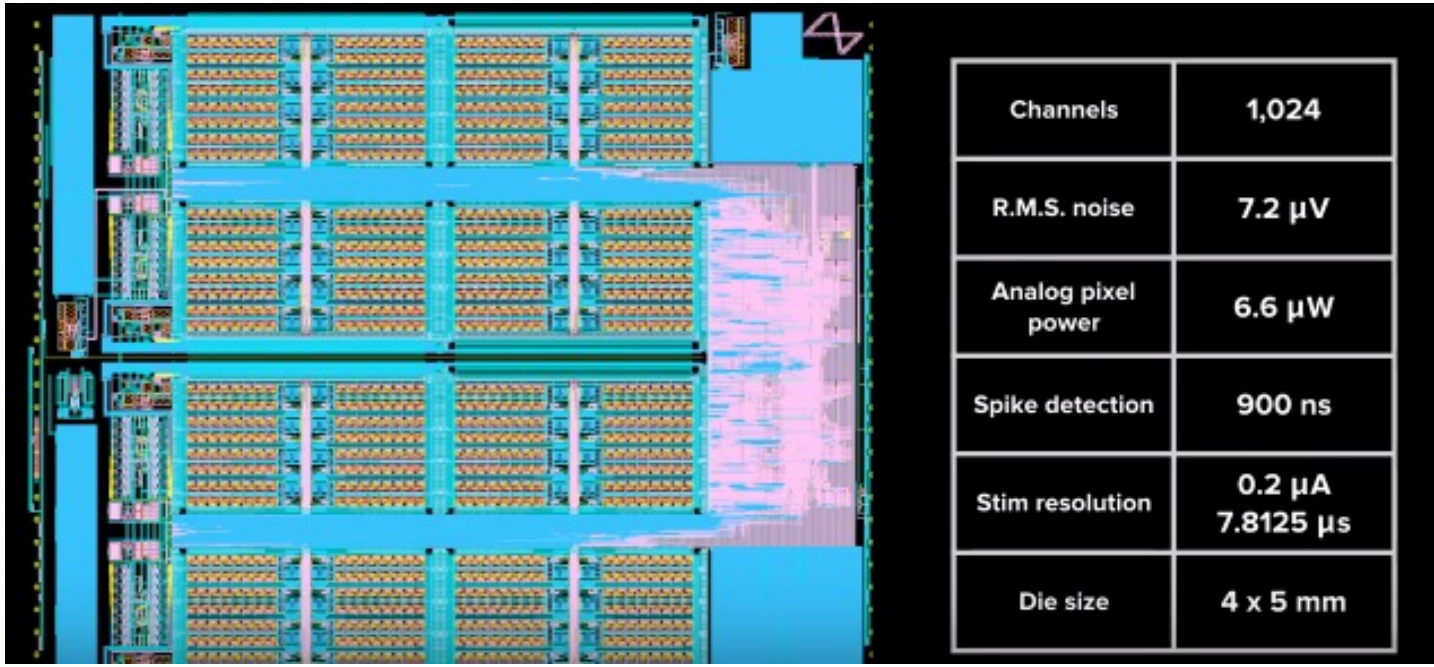


Colachis et al. J Neural Eng. 2021;18

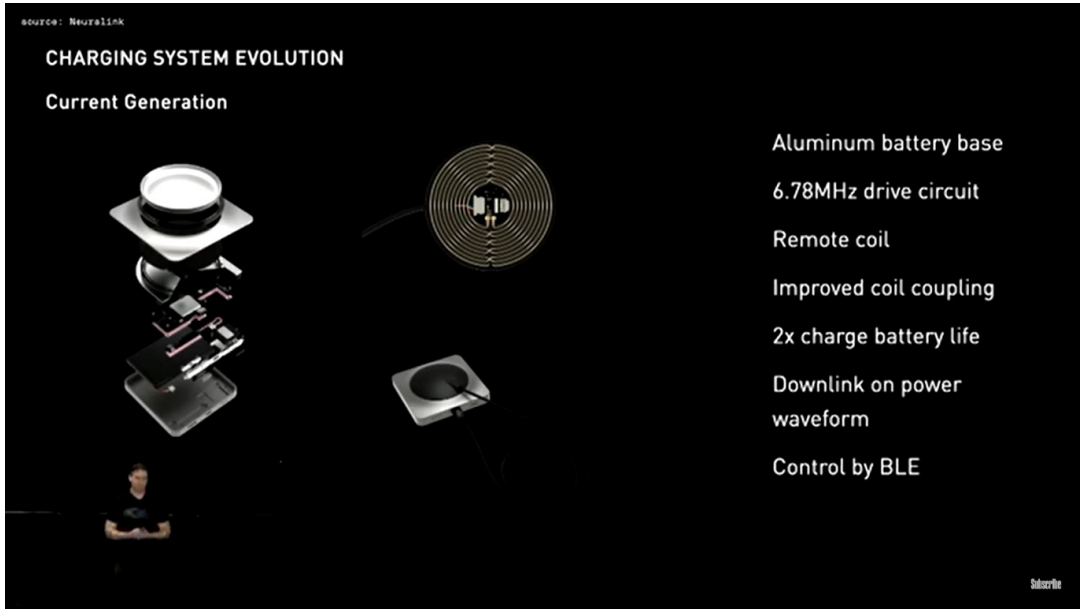
NEURALINK

1024 channels & Bluetooth

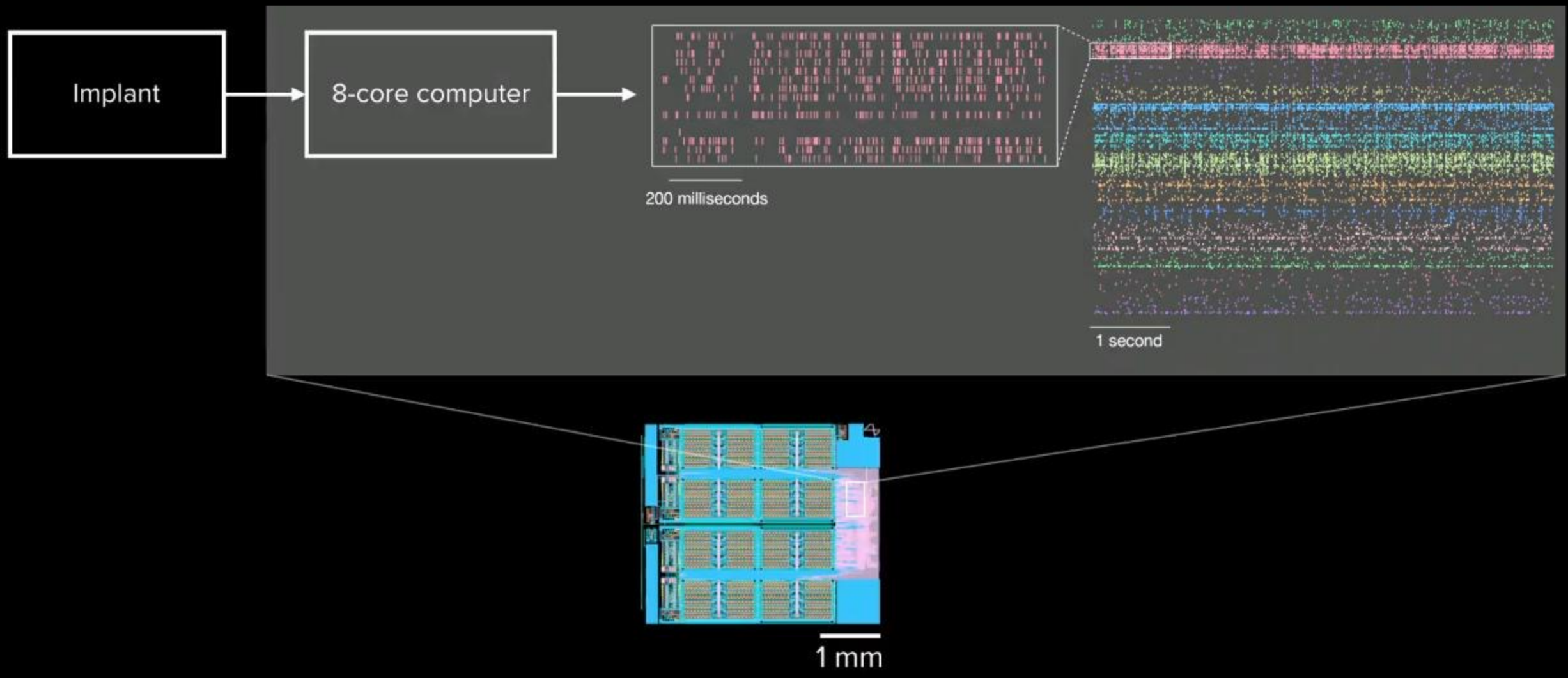


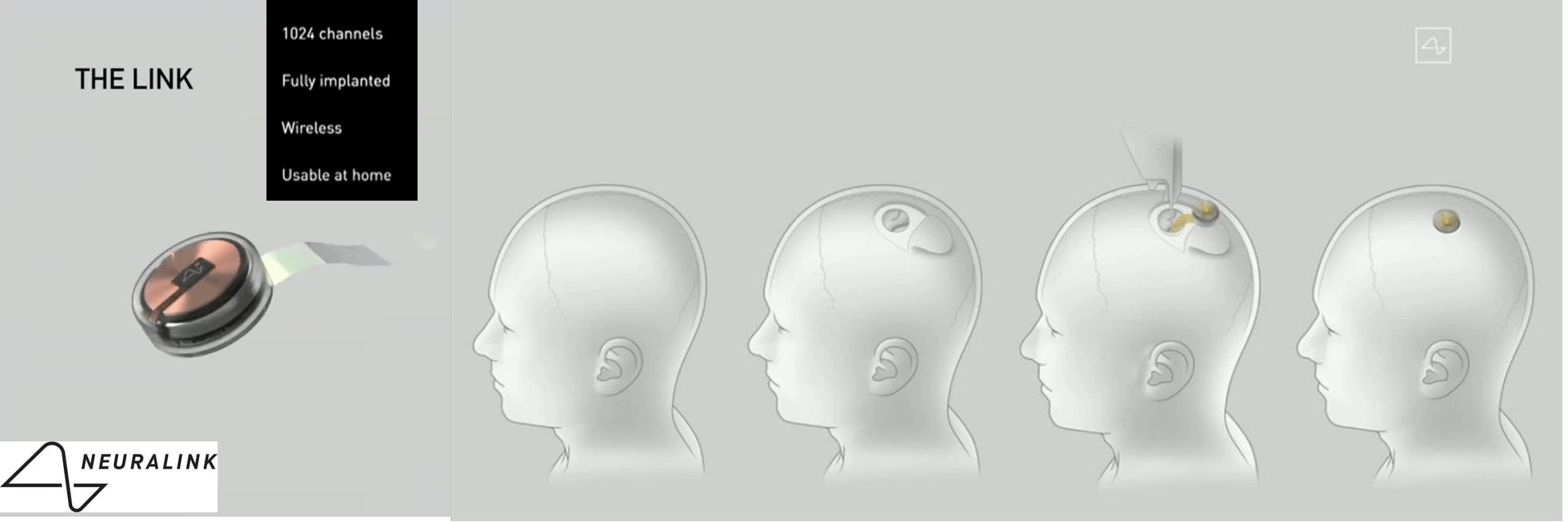


Channels	1,024
R.M.S. noise	7.2 µV
Analog pixel power	6.6 µW
Spike detection	900 ns
Stim resolution	0.2 µA 7.8125 µs
Die size	4 x 5 mm



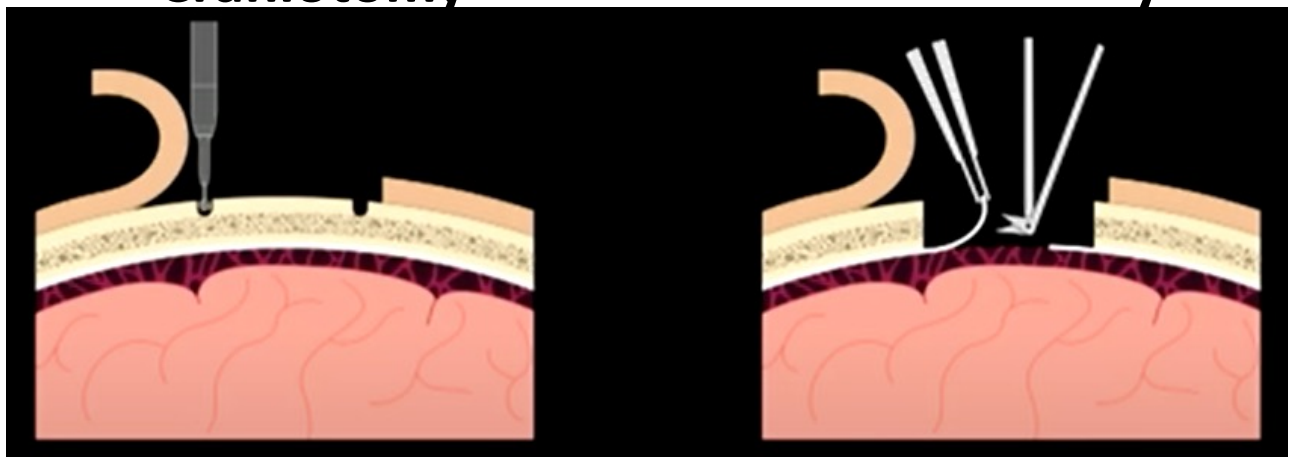
ON-CHIP SPIKE DETECTION

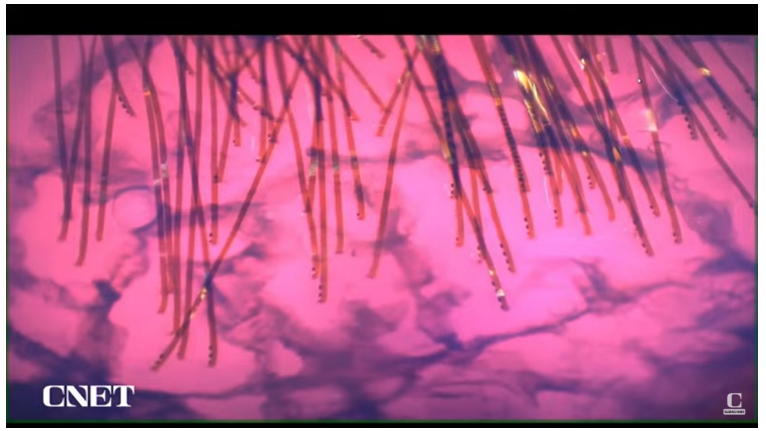




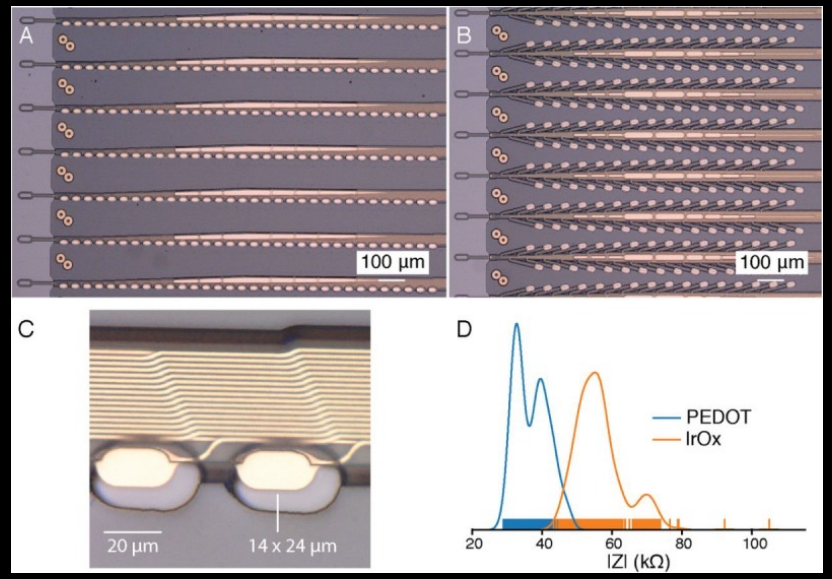
Craniotomy

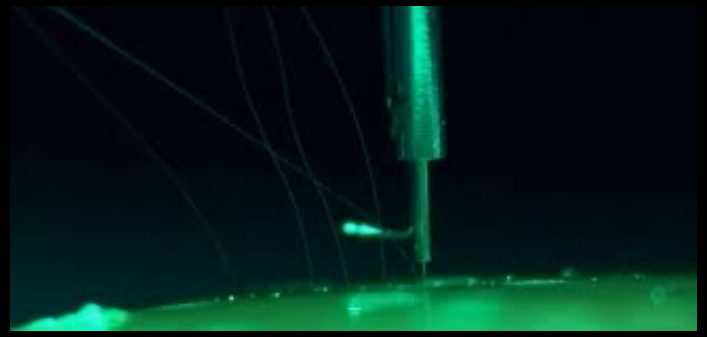
Durectomy





Threads= 32 electrode contacts spaced by 50 µm

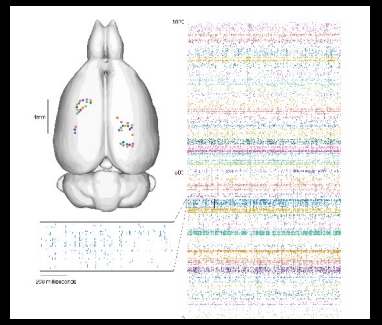






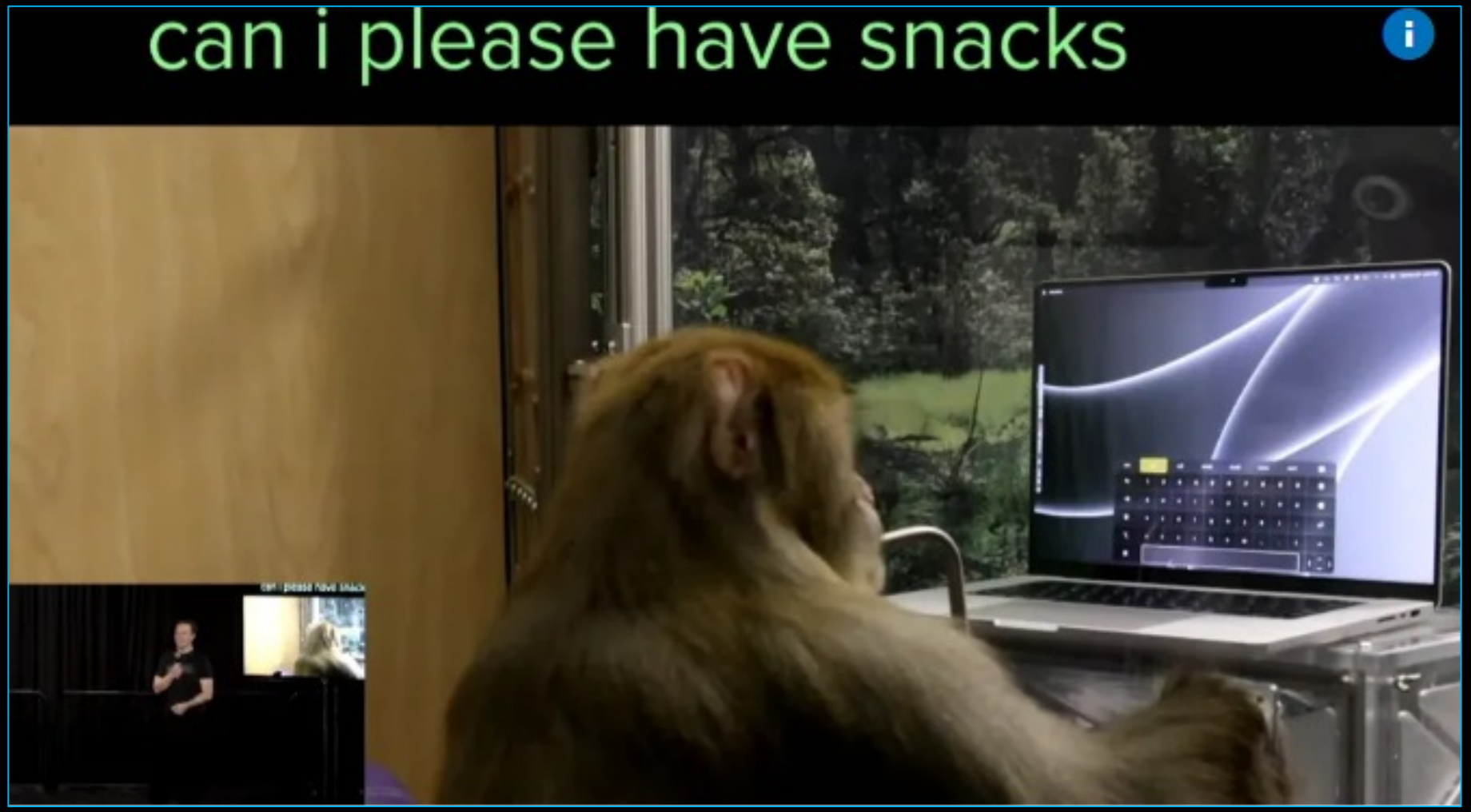
Musk E; Neuralink. J Med Internet Res. 2019 Oct 31;21(10):e16194.

2020



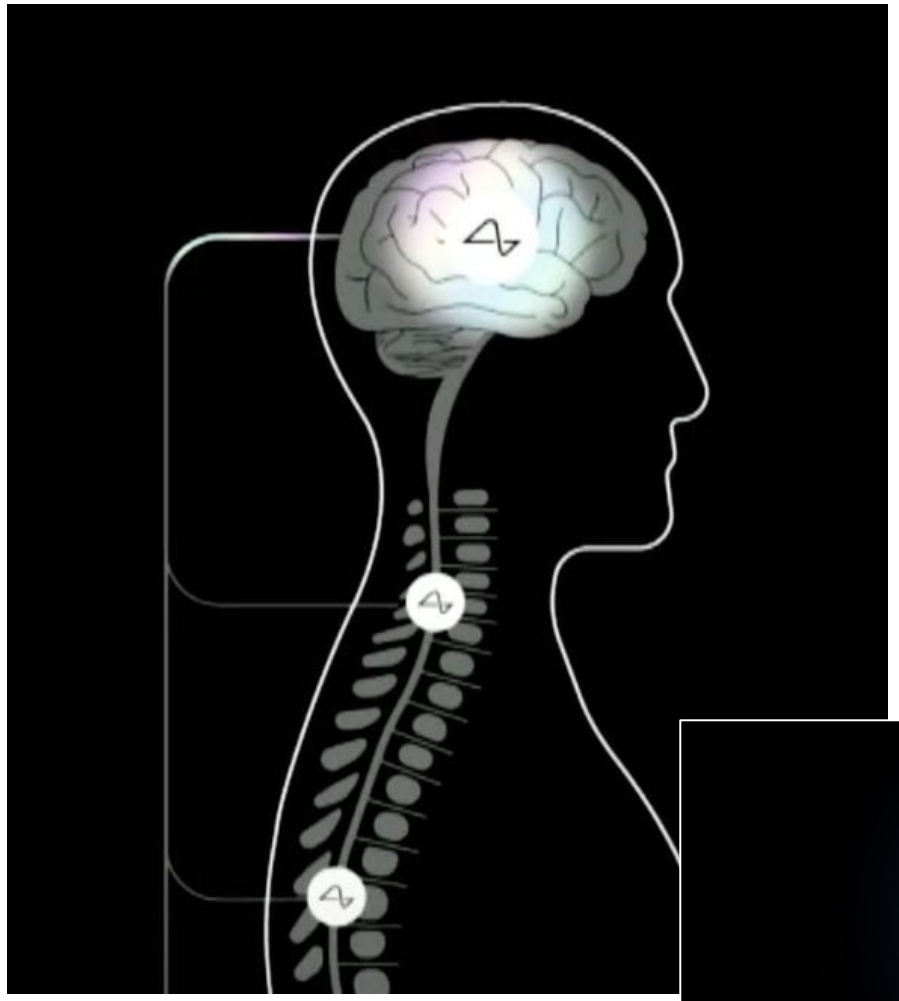


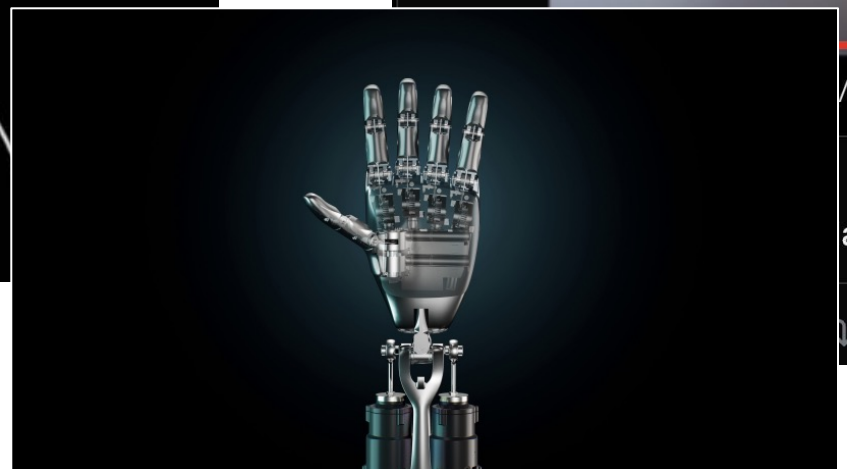




"**Show** and **Tell**" **event, 30 Novembre 2022**

FDA approval on 25 May 2023:
PRIME Study (Precise Roboticallly Implanted Brain Computer interface)





Optimus robot limbs

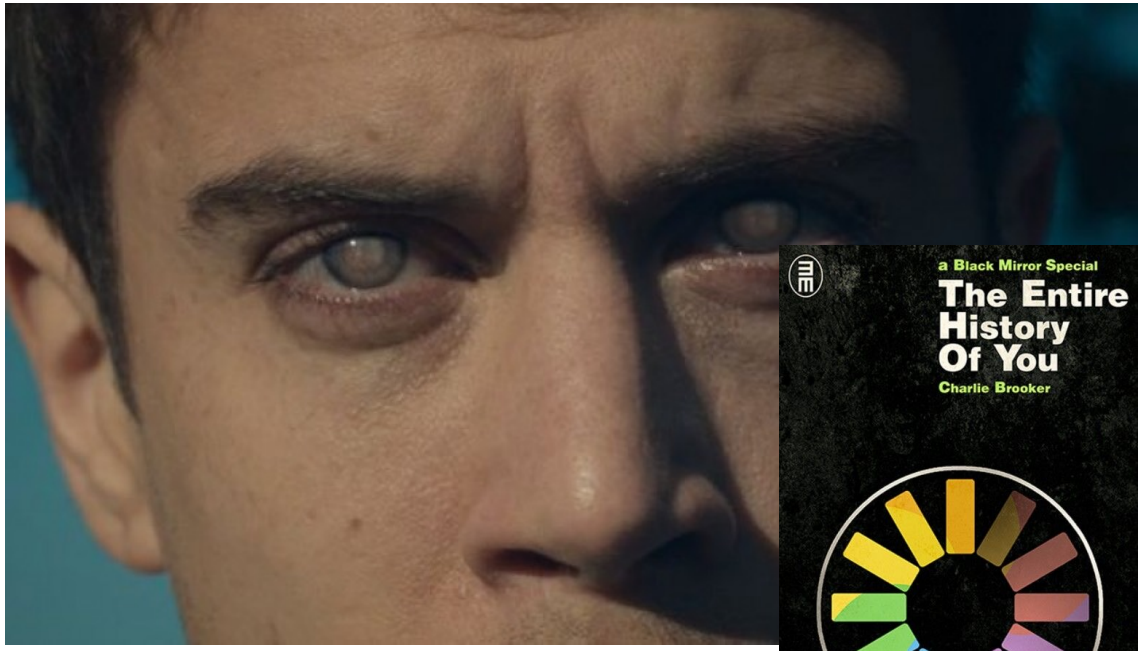


Réparation / augmentation / transformation



Bénéfices pour les patients

Black Mirror: « Toute ton histoire »



Transhumanisme

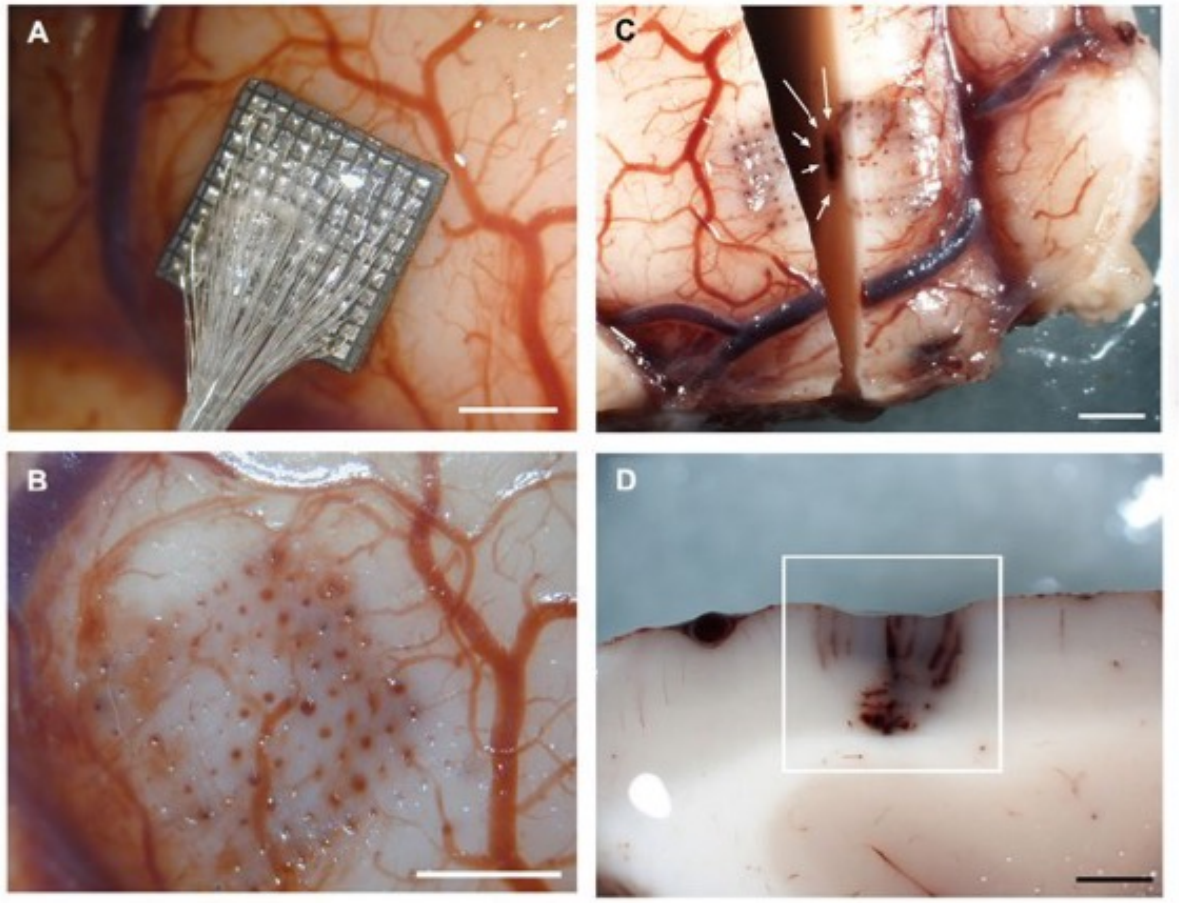




Risques de manipulations

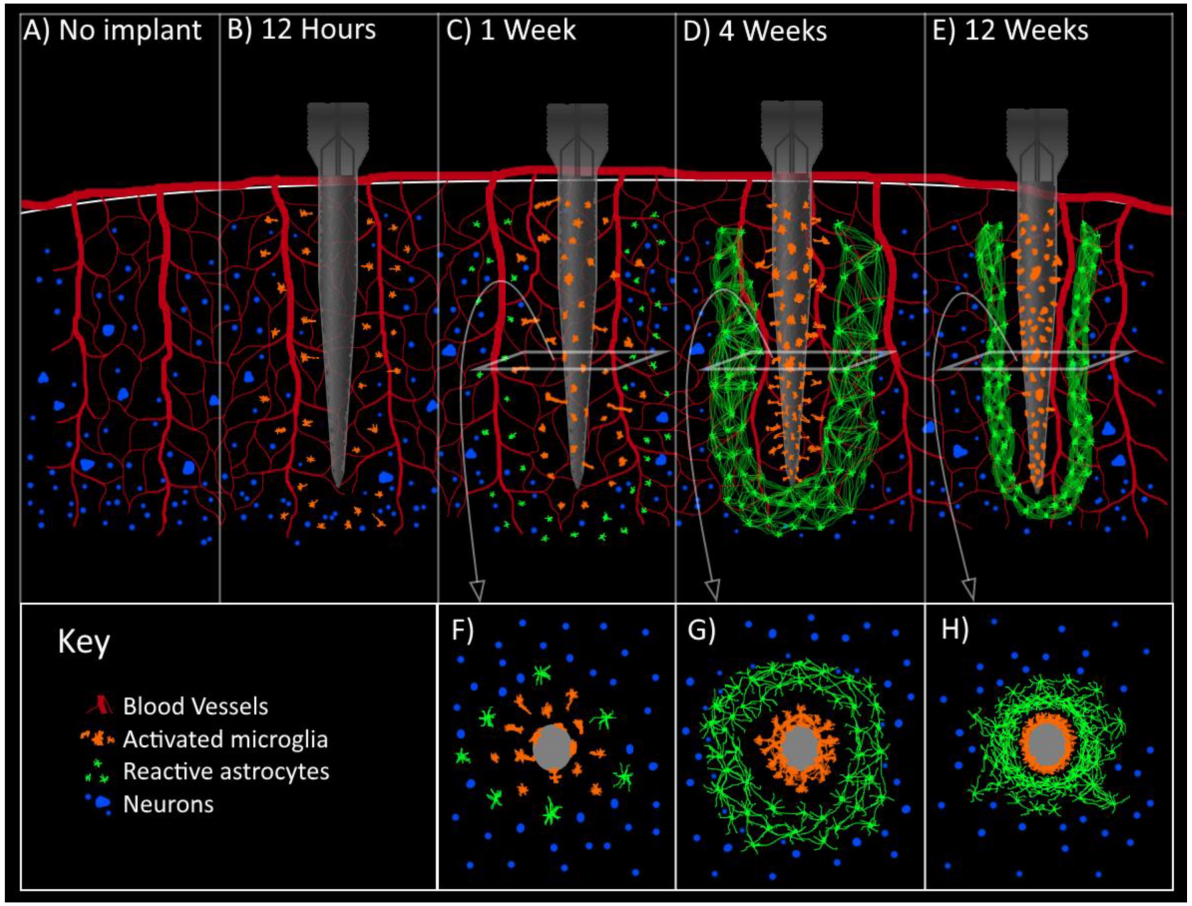
Neuroethical considerations of high-density electrode arrays

Risques de lésions et de micro-hémoragies



Fernández E, Greger B, House PA, Aranda I, Botella C, Albisua J, Soto-Sánchez C, Alfaro A, Normann RA.
Acute human brain responses to intracortical microelectrode arrays: challenges and future prospects. Front Neuroeng. 2014 Jul 21;7:24.

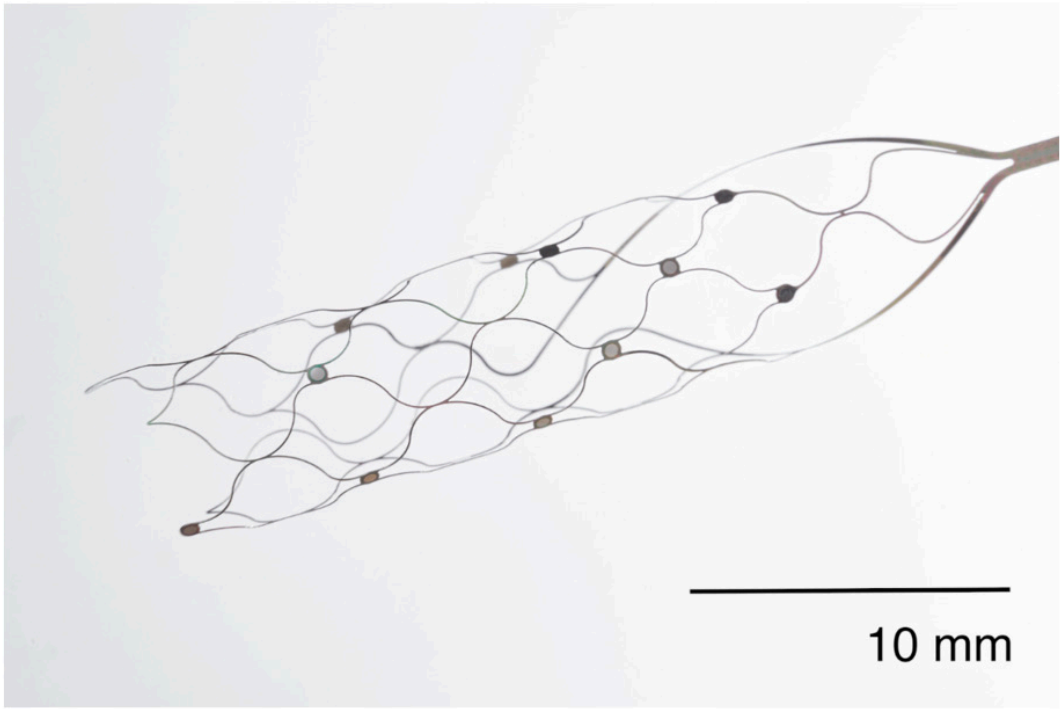
Risques de gliose

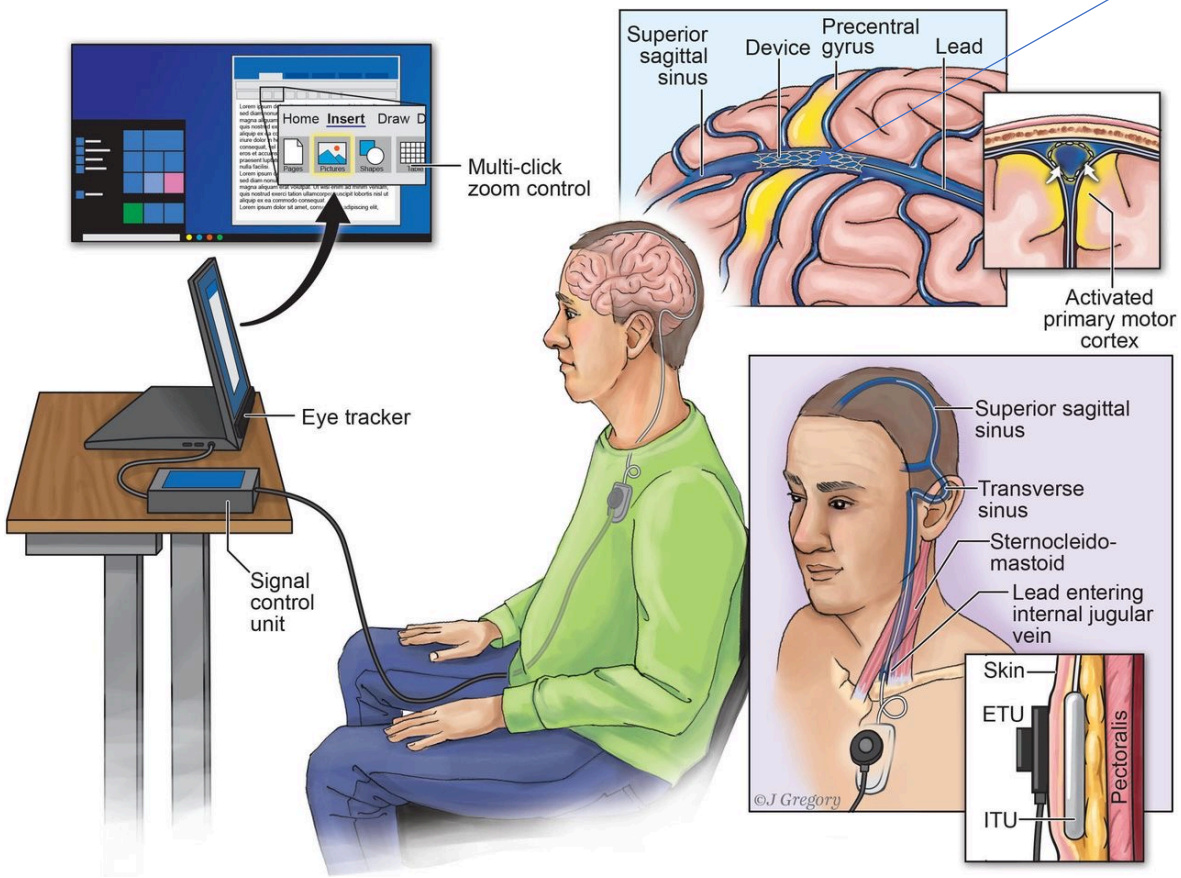


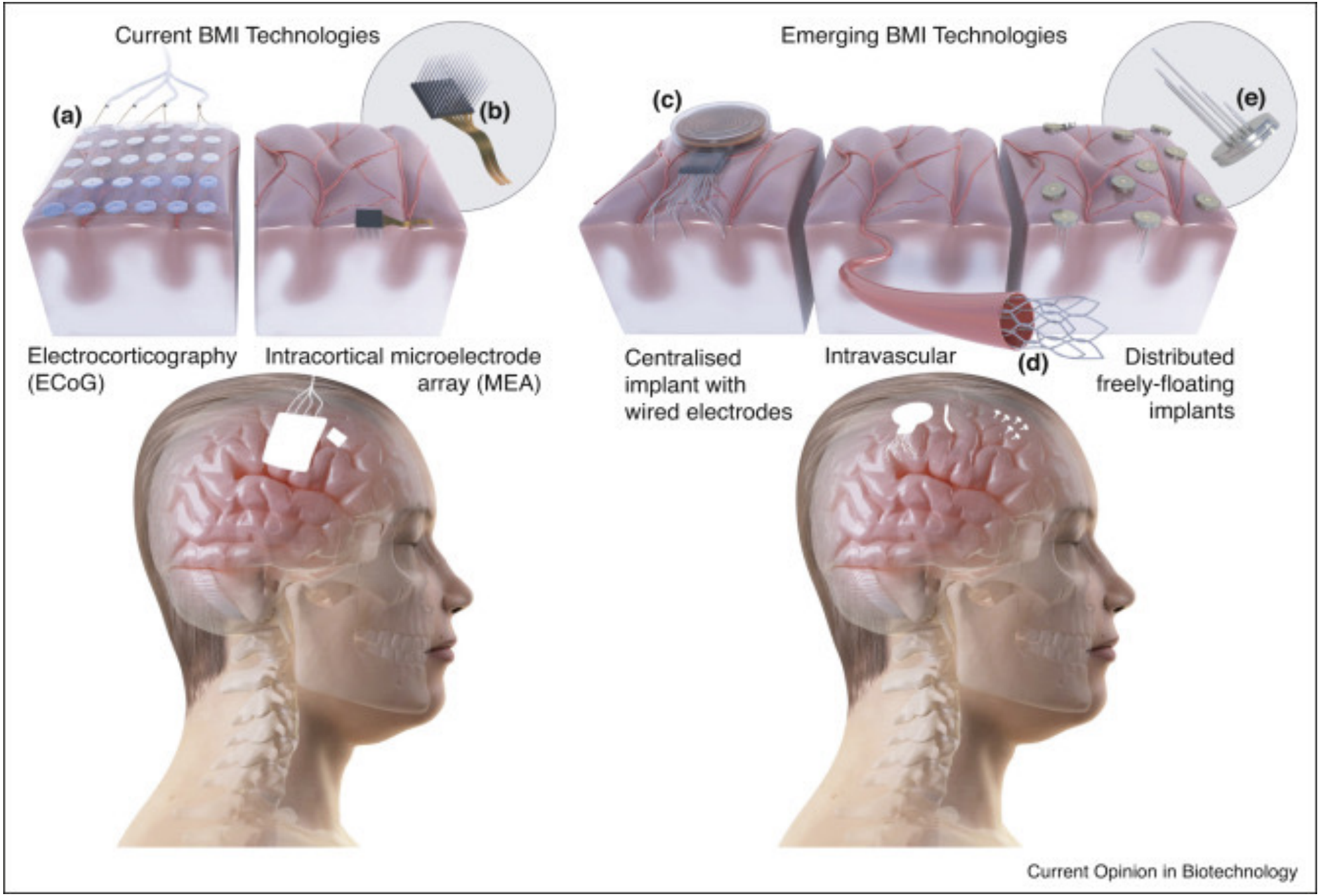
Campbell A, Wu C. Chronically Implanted Intracranial Electrodes: Tissue Reaction and Electrical Changes. Micromachines (Basel). 2018 Aug 25;9(9):430.

synchron

Stentrode






Current BMI Technologies
Emerging BMI Technologies
(a)
(b)
(c)
(d)
(e)
Electrocorticography (ECoG)
Intracortical microelectrode array (MEA)
Centralised implant with wired electrodes
Intravascular
Distributed freely-floating implants
Current Opinion in Biotechnology

Les neuro-technologies : de Hans Berger à Elon Musk.

1924



2023



Implants
of microelectrodes



Wearable
neuro-technology
for brain monitoring

Laboratoire d'Imagerie Biomédicale

NAOX Technologies





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HÔPITAL FONDATION
Adolphe de ROTHSCHILD
LA RÉFÉRENCE TÊTE ET COU

Necker
ENFANTS MALADES

PROGRAMME MESSIDORE

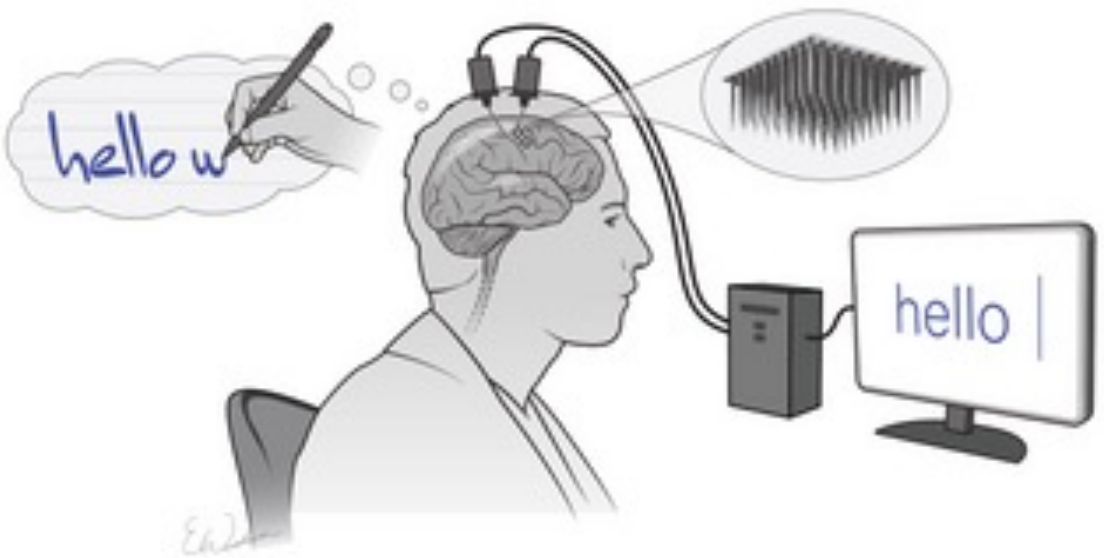
Inserm

institut imagine
GUÉRIR LES MALADIES GÉNÉTIQUES

NOUS RECRUTONS !

michel.le-van-quyen@inserm.fr

Frank Willett et al., (2021) High-performance brain-to-text communication via handwriting, Nature Vol 593

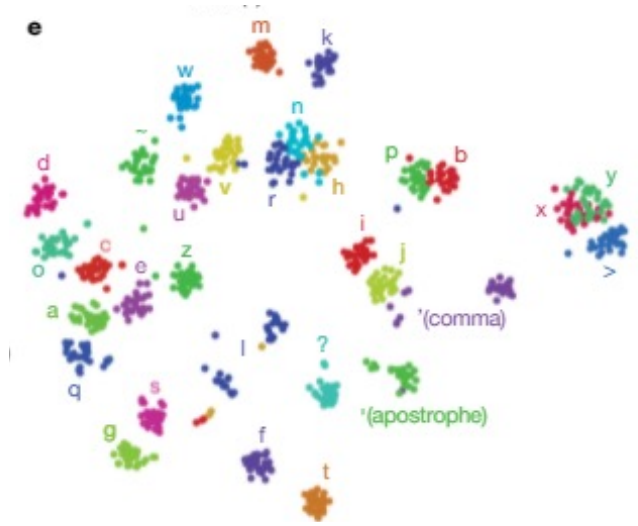




>BrainGate2 participant nicknamed T5 who has a spinal injury

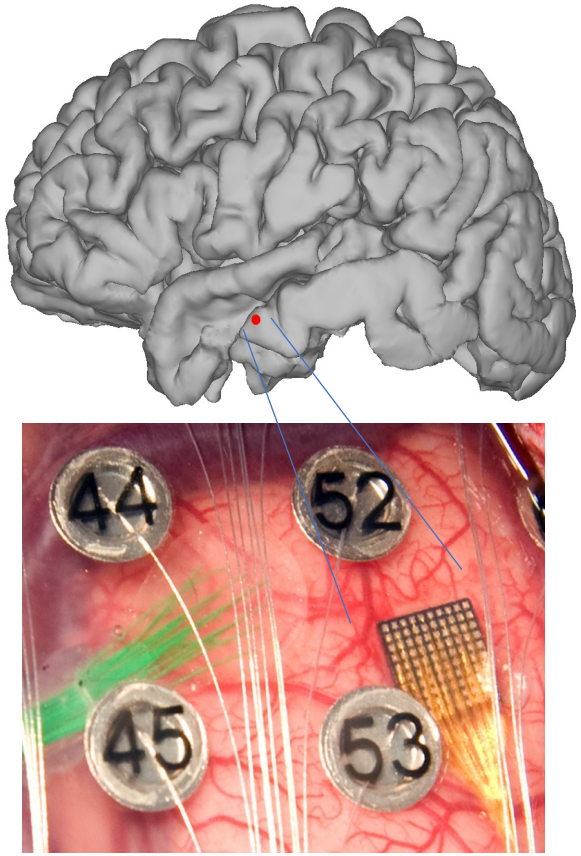
>brain-implant system trained to decode the neural signals for handwriting from a paralyzed man enabled a computer to type up to 90 characters per minute with 94 percent accuracy.

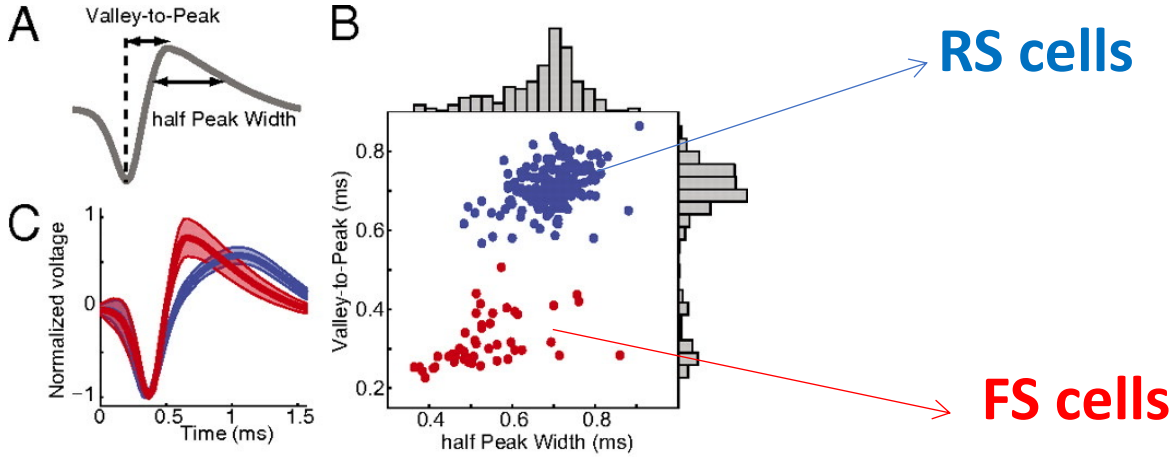
> Smartphone tipping: 115 characters per minute

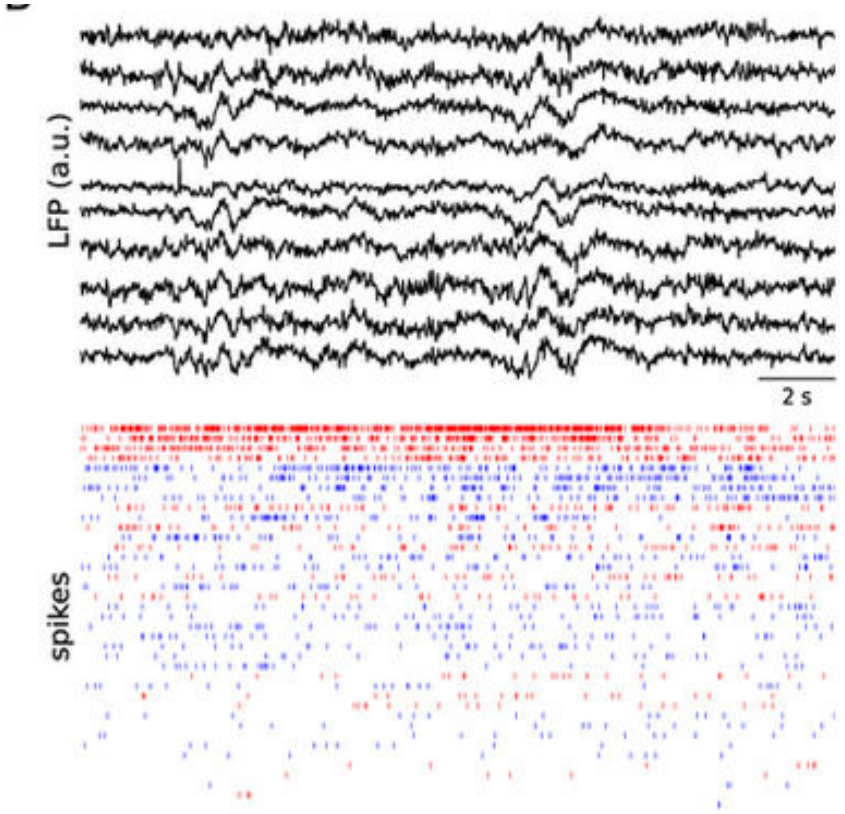


t-distributed stochastic neighbour embedding (t-SNE)

96 microelectrodes
with 400-µm spacing,
covering an area of 4 × 4mm







Le Van Quyen et al. (2016) PNAS

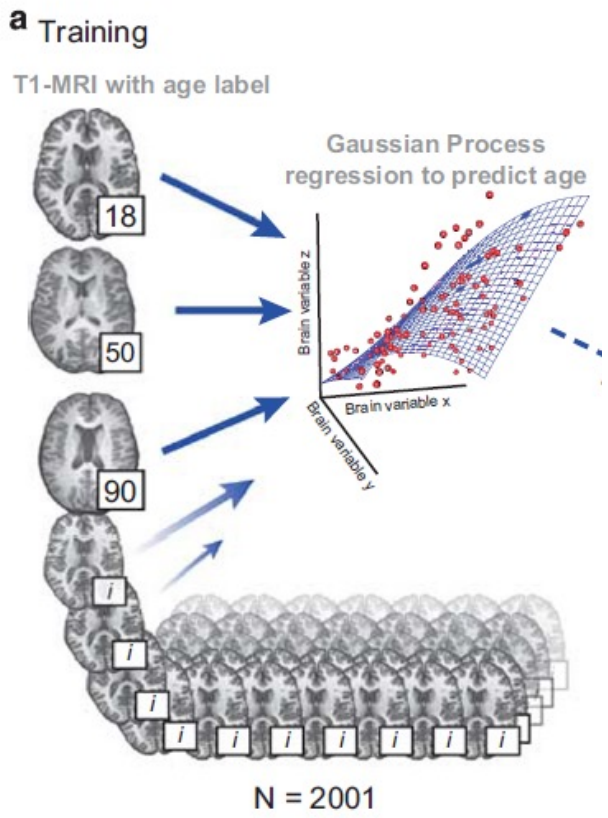
Peyrache et al. (2011) PNAS 109

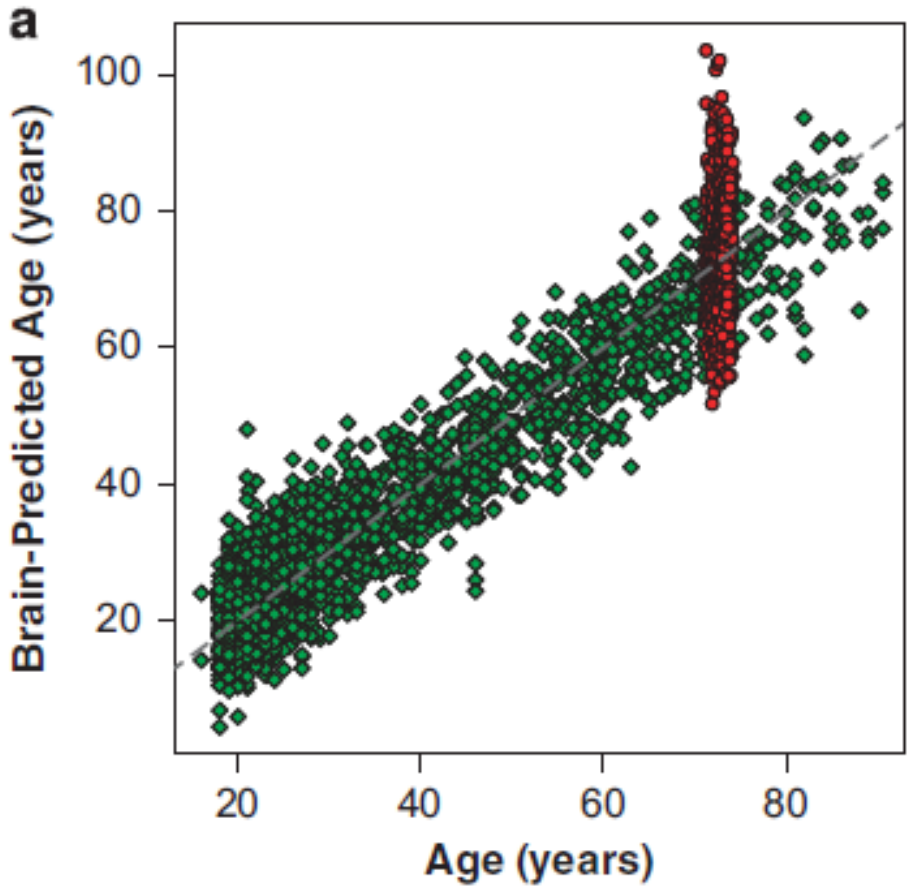
ORIGINAL ARTICLE

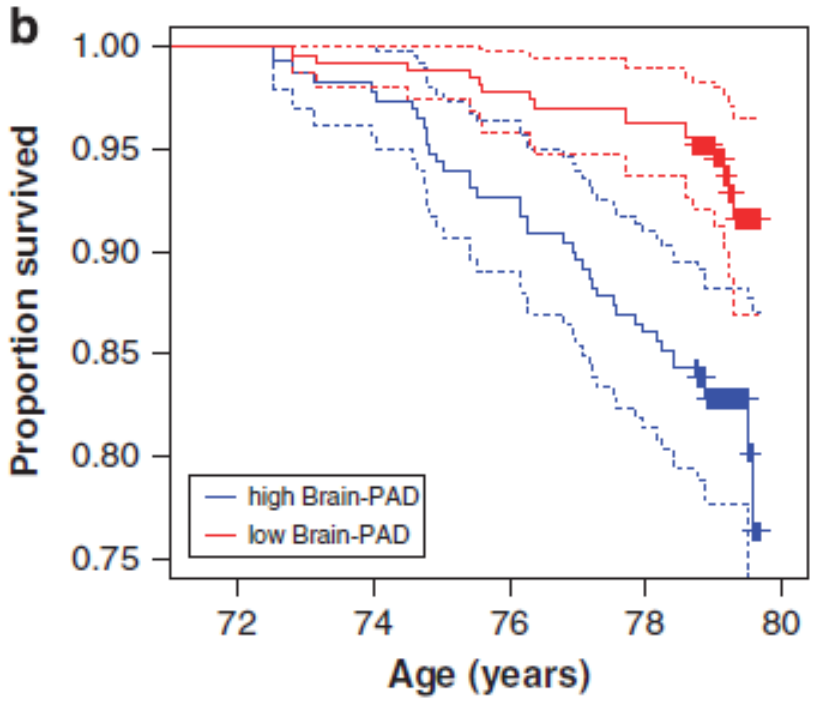
Brain age predicts mortality

Cole et al. Molecular Psychiatry (2018) 23, 1385–1392

JH Cole[1], SJ Ritchie[2,3], ME Bastin[2,4], MC Valdés Hernández[2,4], S Muñoz Maniega[2,4], N Royle[2,4], J Corley[2,3], A Pattie[2,3], SE Harris[2,5], Q Zhang[6], NR Wray[6,7], P Redmond[3], RE Marioni[2,5,7], JM Starr[2], SR Cox[2,3], JM Wardlaw[2,4], DJ Sharp[1] and IJ Deary[2,3]







The mean absolute error of prediction was 5.02 years and the root mean square error was 6.31 years.

Do try this at home: Age prediction from sleep and meditation with large-scale low-cost mobile EEG

Hubert Banville*[1,2], Maurice Abou Jaoude[2], Sean U.N. Wood[2], Chris Aimone[2], Sebastian C. Holst[3], Alexandre Gramfort[1], and Denis-Alexander Engemann[1,3,4]

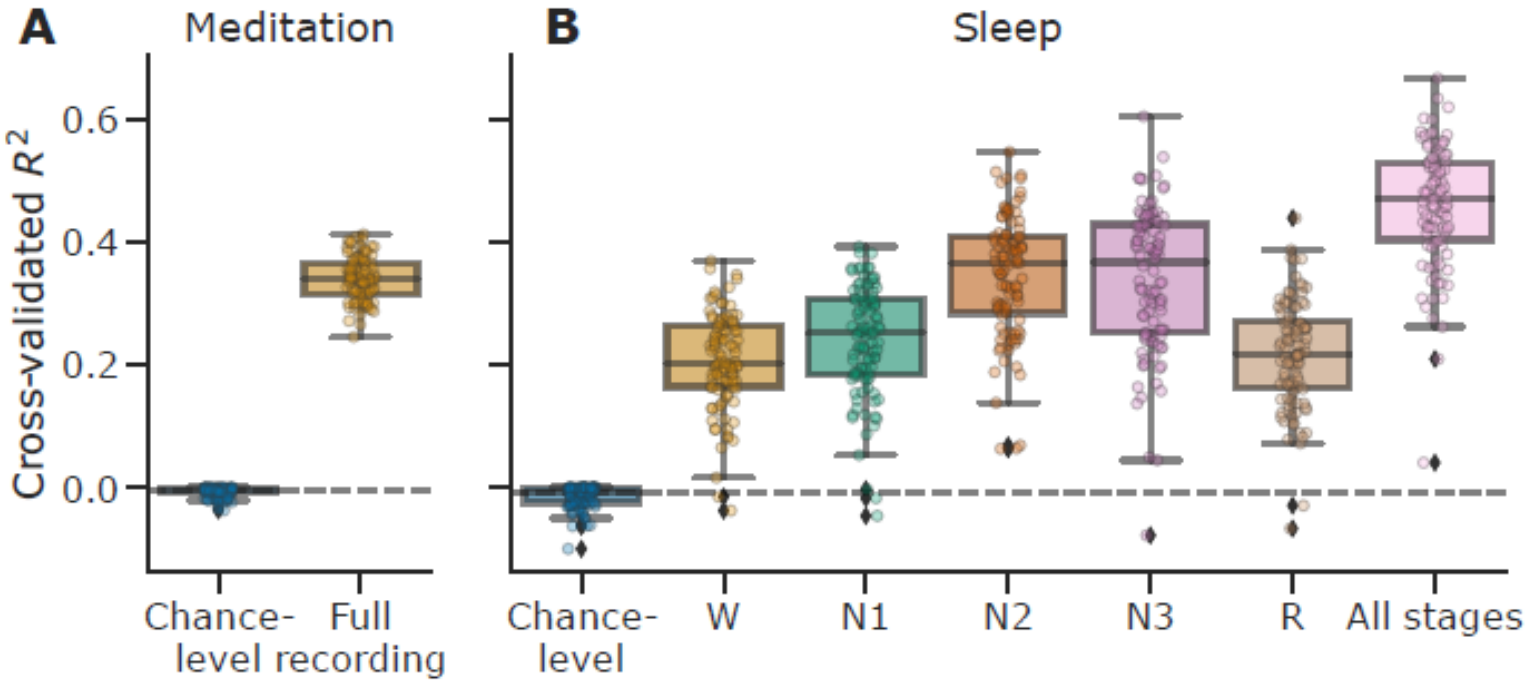
[1]Université Paris-Saclay, Inria, CEA, Palaiseau, France
[2]InteraXon Inc., Toronto, Canada
[3]Roche Pharma Research and Early Development, Neuroscience and Rare Diseases, Roche Innovation Center Basel, F. Hoffmann–La Roche Ltd., Basel, Switzerland
[4]Max Planck Institute for Human Cognitive and Brain Sciences, Department of Neurology, Leipzig, Germany

Table 1: Description of the datasets used in this study.

Dataset	Type	Nb of sessions	Nb of subjects	Duration in minutes (mean ± std)	Age (mean ± std)	% female (sessions)
MMD	meditation	4191	4191	13.88 ± 6.52	44.92 ± 14.22	39.11
MMD-long	meditation	497	4	23.06 ± 8.72	54.51 ± 11.61	12.88
AMUSeD	sleep	1020	1020	456.89 ± 75.05	43.78 ± 13.52	49.02
AMUSeD-long	sleep	539	4	461.73 ± 65.62	57.64 ± 13.17	20.22

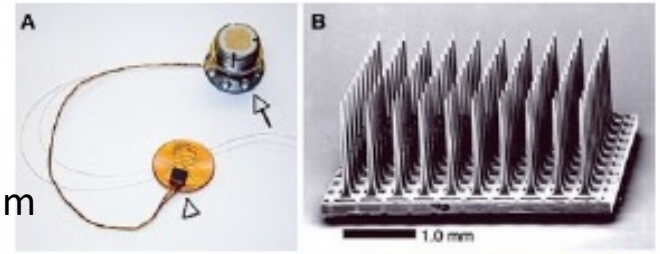
```
r_squared = 1 - (sum((test_labels - predicted_labels).^2)
      / sum((test_labels - mean(test_labels)).^2));
```



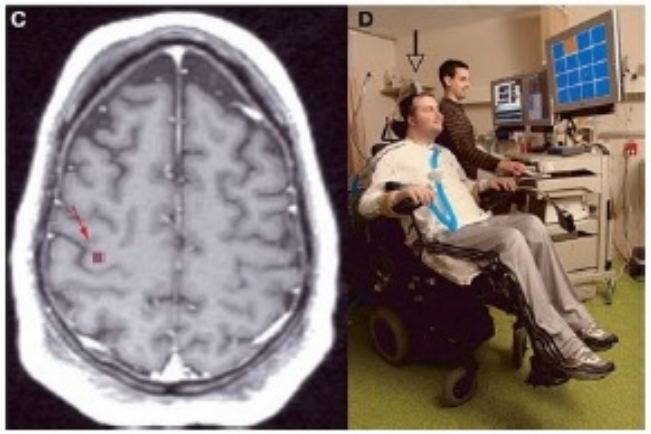


Utah electrode arrays

96 microelectrodes with 400-µm spacing, covering an area of 4 × 4mm

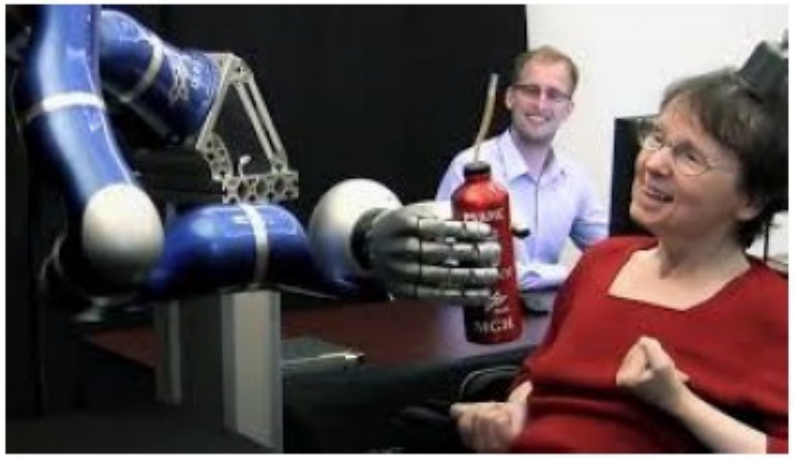


2005

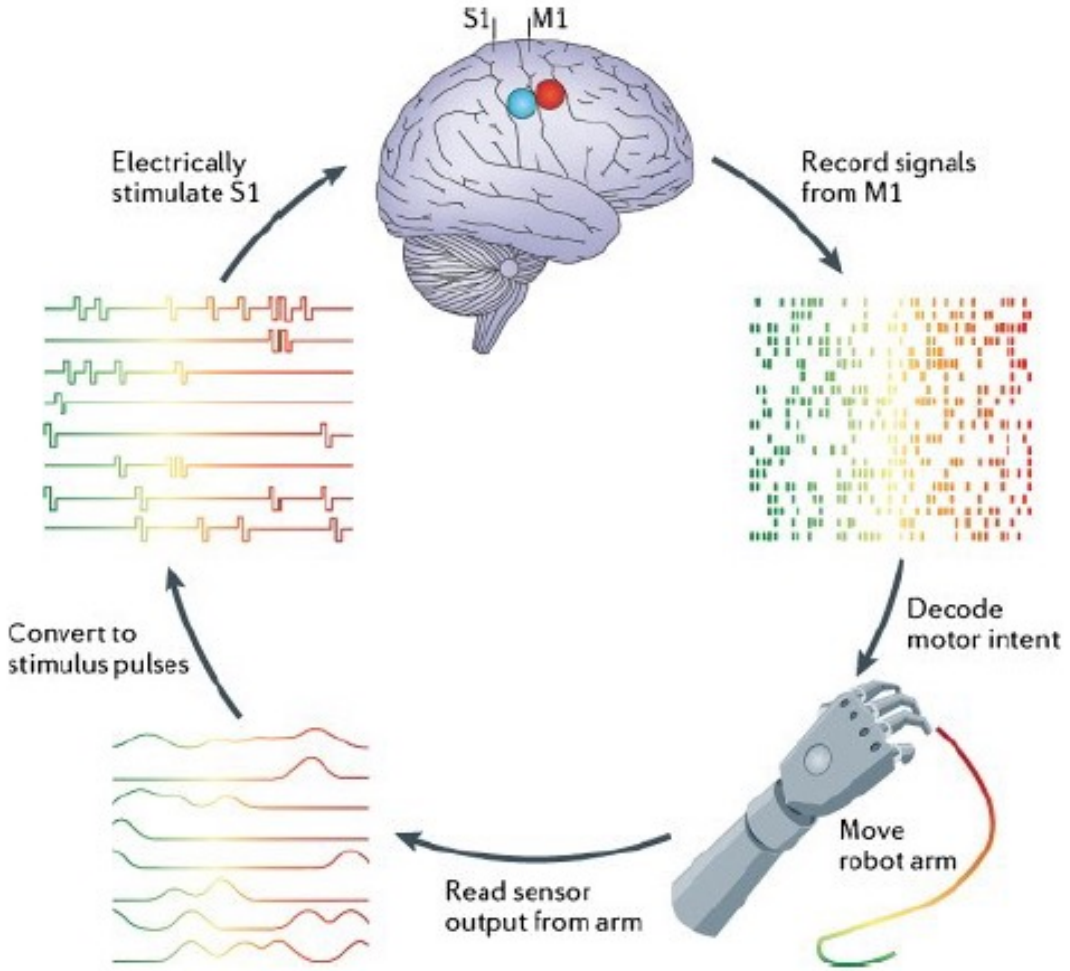


Patients tétraplégiques

2006

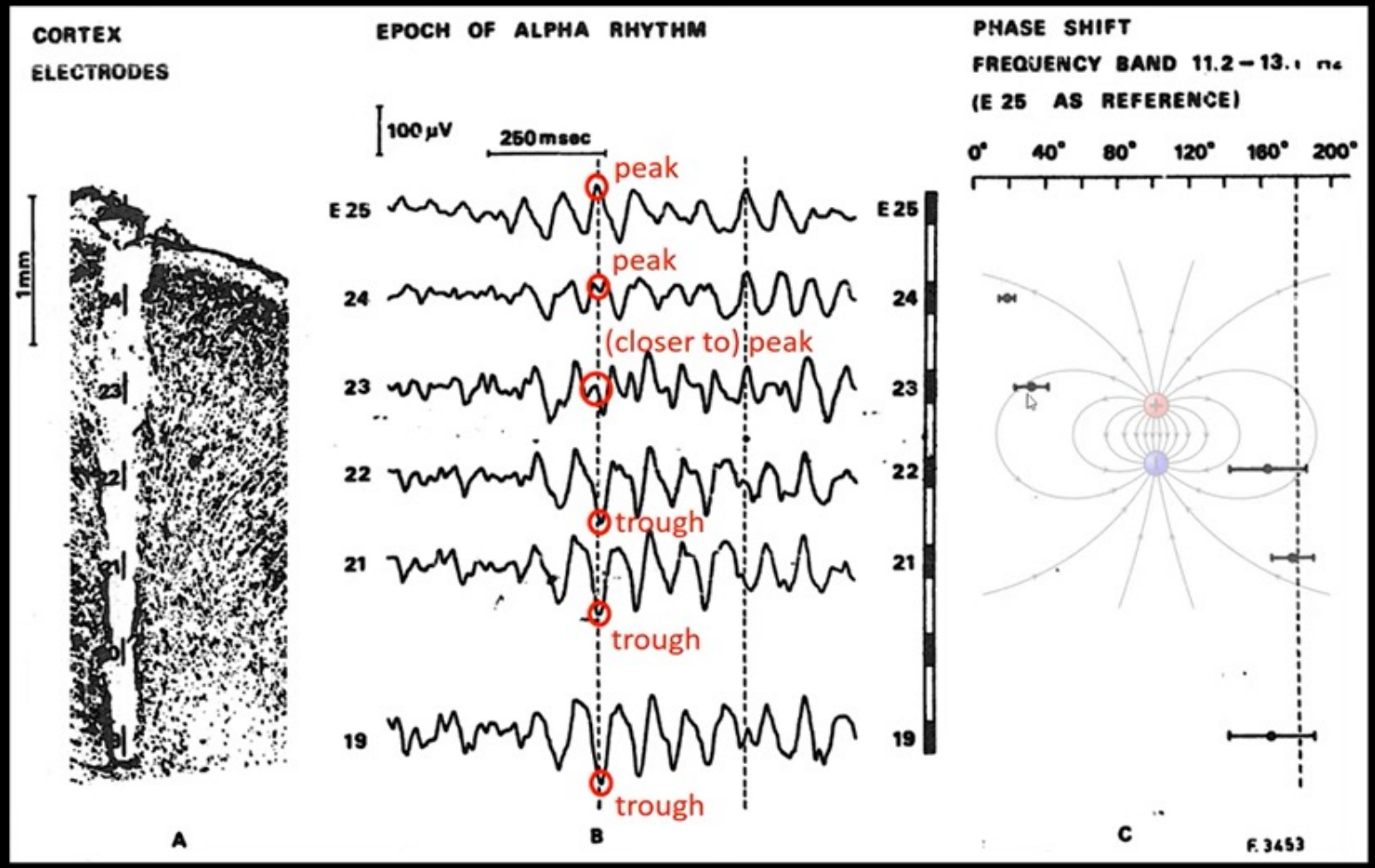


Bidirectional BCI



Hochberg et al., Nature 485, 2012

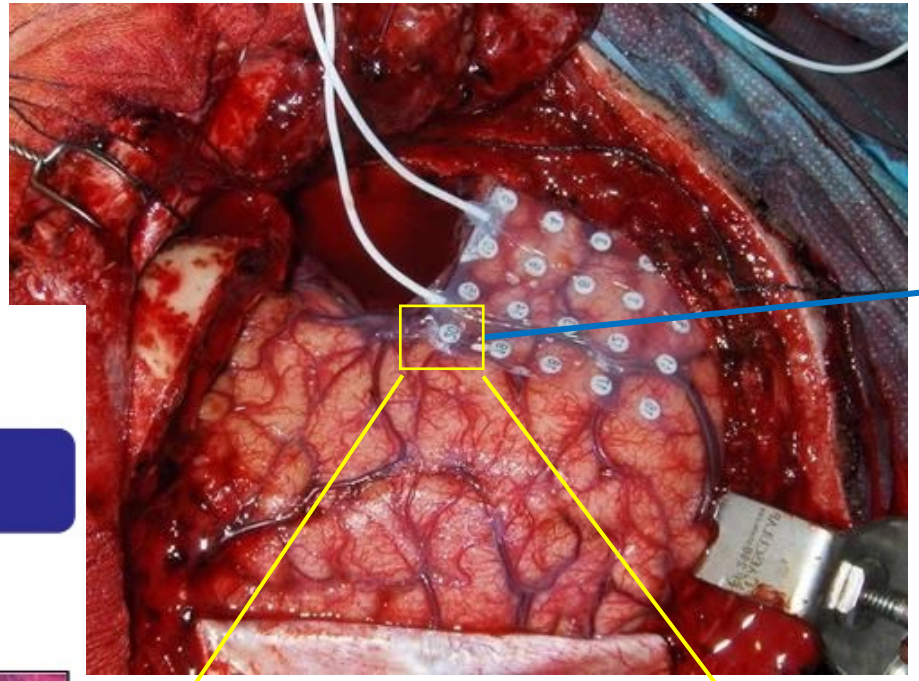
The source of alpha oscillation is in the cortical laminar structure

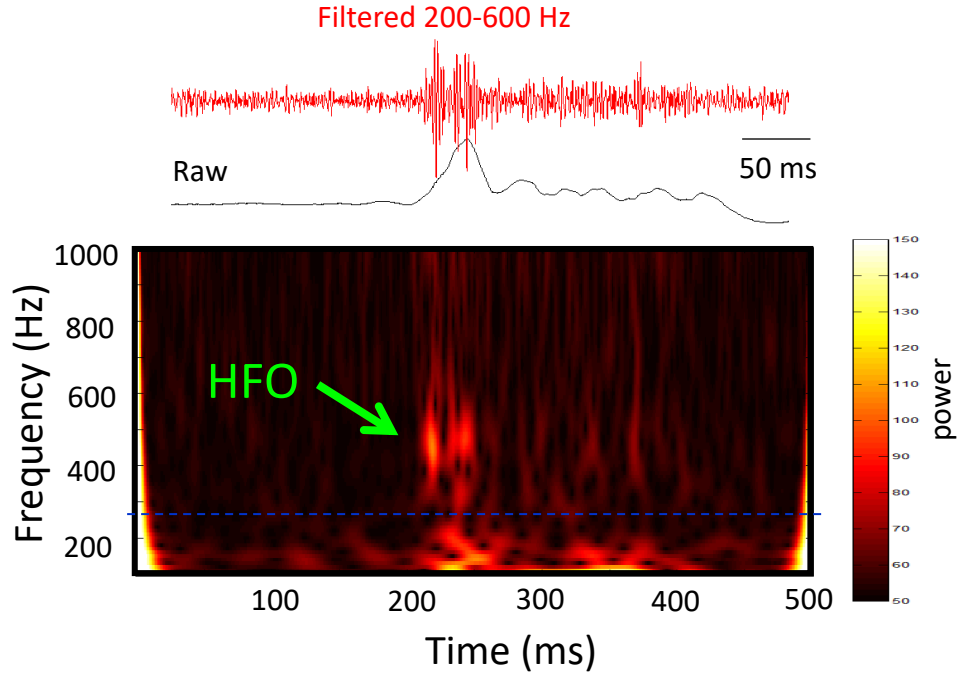




Lopes da Silva and Storm van Leeuwen (1977)

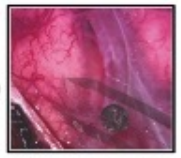
Macro-electrodes ECoG





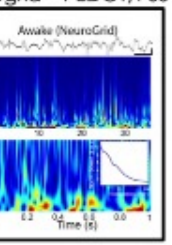
> 2024
µECoG

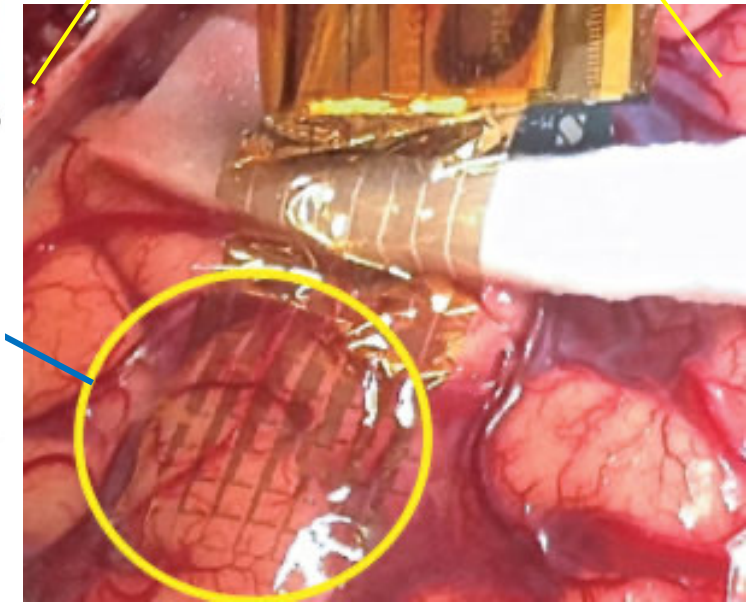
Diameter: 10 µm
Thickness: 4 µm
Spacing : 100 µm
4 000 µm



Khodagholy Nat Neurosci 2016

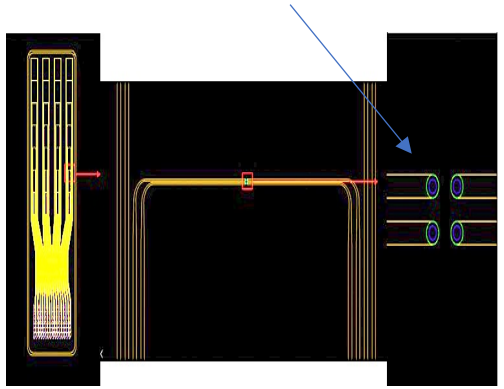
ogrid – PEDOT/PSS



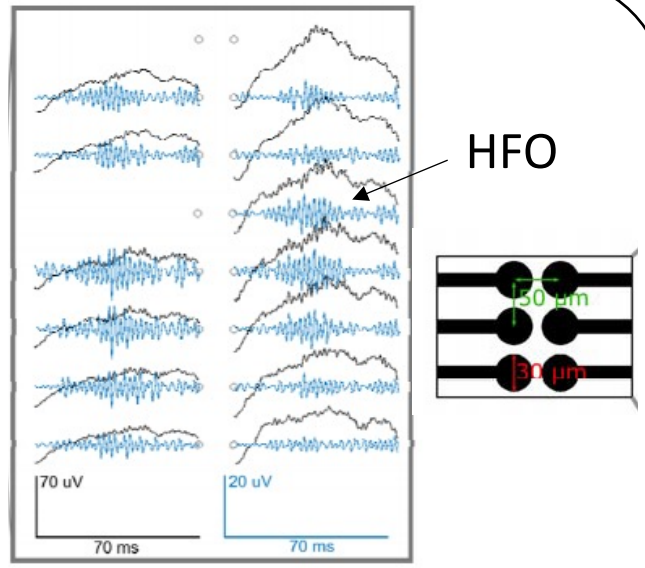


Electrodes de Panaxium

Diamètre: 10 µm



10 rangés de 3 tetrodes



Yang et al., 2020 (medRxiv)
Massachusetts General Hospital, Boston

IMPROVING STIM

4096 Channels

Time-division Multiplexed Control

28 nm

± 2.5V

Monopolar and Bipolar Output

Automatic Charge Balancing

Integrated Arm® Cortex®-M23 core

DMA-enabled Peripherals

