Les technologies de l’électro-physiologie humaine :
de Hans Berger à Elon Musk

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Dynamics of neuronal ensembles in the human brain

- Living brain, in action
- Emergence of instable cooperative patterns
- Complex multi-scale activities

Simulation of a one second of a thalamocortical model having 100,000,000 neurons
Eugene M. Izhikevich and Gerald M. Edelman, PNAS 2008
Reentry and recursion in neuronal network

Reverberatory micro-circuits (Lorente de Nó)

Local networks

Thalamo-cortical loop
Local field potentials
Action potentials
Synaptic currents
GABA
AMPA
Electrodes
EEG waves

TIME
1 msec
20 msec
>100 msec

SPACE
Large-scale networks
Local network
Microscopic scale

Mesoscopic scale
Cells in a macrocolumn \(\sim (90)(100) = 8000\)

Macroscopic scale
Cortical region, cm\(^3\)
\(> 100,000-1 million\)

Human electrophysiology
Part 1: Non-invasive electrophysiology
Typical EEG about 100 µV, need about 1 million neurons, a few cm² of cortex.
Oscillating cell assemblies

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)
Evoked gamma (fixed latency)  Induced gamma (jitter in latency)

Stimulus onset

Averaging

Averaged evoked potential
<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Anatomy</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theta (4–7 Hz)</td>
<td>Hippocampus, sensory cortex and prefrontal cortex</td>
<td>Memory, synaptic plasticity, top-down control and long-range synchronization</td>
</tr>
<tr>
<td>Alpha (8–12 Hz)</td>
<td>Thalamus, hippocampus, reticular formation, sensory cortex and motor cortex</td>
<td>Inhibition, attention, consciousness, top-down control and long-range synchronization</td>
</tr>
<tr>
<td>Beta (13–30 Hz)</td>
<td>All cortical structures, subthalamic nucleus, basal ganglia and olfactory bulb</td>
<td>Sensory gating, attention, motor control and long-range synchronization</td>
</tr>
<tr>
<td>Gamma (30–200 Hz)</td>
<td>All brain structures, retina and olfactory bulb</td>
<td>Perception, attention, memory, consciousness and synaptic plasticity</td>
</tr>
</tbody>
</table>
Objets emcombrants à usage médical

Objets connectés – « wearable » - à usage à domicile
EEG et nouvelles technologies

sommeil

bien-être

dreem

mélomind

rêve

iWINKS

émotion

Thync

énergie physique

muse

halo
DEMO
Diminuer son stress

Entrainer son cerveau à se relaxer
Neurofeedback (Joe Kamiya, 1960)

Algorithmes en temps réel

Enregistrement du signal cérébral

Enregistrement du signal cérébral

Algorithmes en temps réel
Améliorer son sommeil
Le système Dreem: améliorer son sommeil

Les investisseurs historiques : Laurent Alexandre & Xavier Niel.

- 2018: levée de fonds de 35 millions de dollars (Johnson & Johnson et le Fond PSIM géré par Bpifrance).

En quatre ans, la startup a levé 57 millions de dollars.
Le système Dreem

EEG dry electrodes yielding 7 derivations (FpZ-O1, FpZ-O2, FpZ-F7, F8-F7, F7-01, F8-O2, FpZ-F8)

-250Hz with a 0.4-18 Hz bandpass filter.

- movements, position, and breathing frequency via a 3-D accelerometer located over the head

- heart rate via a red-infrared pulse oximeter located in the frontal band

- Bone conduction sounds
« Deep sleep is the most restorative sleep stage and its quality can be improved using sound... »
Slow oscillations during deep sleep

Massimini et al., 2004
Sleep, brain oscillations and memory

Hippocampo-cortical coupling mediates memory consolidation during sleep

**Diagram:**
- **Slow oscillation** (0.5-1.0 Hz; neocortex)
- **Spindle** (11-15 Hz; thalamus)
- **Sharp wave ripple** (100-300 Hz; hippocampus)

**Key Points:**
- Slow oscillation and spindle activity correlate with memory consolidation.
- Sharp wave ripples are associated with memory replay and consolidation.

**Neuroanatomy:**
- Neocortex
- Hippocampus
- Acetylcholine, cortisol, etc.
Deep sleep disruption

Impaired memory

Aβ Steals Shuteye: People with low amyloid (left) generate slow oscillations (red) from the medial prefrontal cortex more robustly than people with intermediate (middle) and high (right) amyloid loads. [Image courtesy of Mander et al., Nature Neuroscience.]
Hypothesis:
Boosting sleep slow oscillations = Boosting the beneficial effect of Sleep

Sensory stimulation for enhancing slow wave oscillations
Auditory Closed-Loop Stimulation of the Sleep Slow Oscillation Enhances Memory

Hong-Viet V. Ngo,1,2,3 Thomas Martinetz,2 Jan Born,1,4* and Matthias Mölle1,4

1Institute of Medical Psychology and Behavioral Neurobiology, and Center for Integrative Neuroscience, University of Tübingen, 72076 Tübingen, Germany
2Institute for Neuro- and Bioinformatics
3Graduate School for Computing in Medicine and Life Sciences
4Department of Neuroendocrinology
University of Lübeck, 23538 Lübeck, Germany
Clinical study: Closed loop auditory stimulation during sleep

Auditory closed-loop stimulations (inspired by Ngo's protocol) during N3 over 1,000 nights

A

B

In phase stimulation accuracy
Arousals
Part 2:
Invasive electrophysiology
Low spatial sampling of scalp EEG
Studying human brain activities from within

- Diameter: 1.0 mm & contact spacing: 10 mm
- Temporal resolution: 1 kHz
- Spatial resolution: < cm³

Gamma frequency band (40-120 Hz)
Intracranial markers of epilepsy

Interictal spikes,
High frequency oscillations
precursors
Electrographic seizures & Clinical seizures

Electrodes
time

Uses of detection
- Diagnose seizure
- types and foci
- Evaluate for surgery
- Seizure warning
- Responsive therapy
- Treatment evaluation
Cook et al. (2013) Lancet Neurol 12: 563–71
Speech synthesis from neural decoding of spoken sentences

Gopala K. Anumanchipalli, Josh Cartier & Edward F. Chang

Nature 568, 493–498 (2019)  Download Citation

"Ship building is a most fascinating process."
Speech synthesis from neural decoding of spoken sentences

UCSF
Micro-electrodes

Spatial resolution: <1 mm
Temporal resolution: 0.05 ms

LFP (<400 Hz)
MUA (>400 Hz)

Broad band signals (0-20 kHz)

- Spatial resolution: <1 mm
- Temporal resolution: 0.05 ms
Spike and LFP: two different phenomena
....the spike amplitude decreases rapidly with distance from the soma
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
BRAIN GATE (John Donoghue, Brown University)

Hochberg et al., Nature 485, 2012
Figure 4: 1. The inserter approaches the brain probe with a thread. i. needle and cannula. ii. previously inserted thread. 2. Inserter touches down on the brain probe surface. 3. Needle penetrates tissue probe, advancing the thread to the desired depth. iv. inserting thread. 4. Inserter pulls away, leaving the thread behind in the brain probe. iv. inserted thread.

Figure 6: Thread implantation and packaging. A. An example peri-operative image showing the cortical surface with implanted threads and minimal bleeding. B. Packaged sensor device ("System B") chronically implanted in a rat.
NeuroGrid: intraoperative recording of cortical micro-circuits

Micro-electrodes

PEDOT:PSS

Diameter: 20 µ
Thickness: 4 µ
Spacing: 100 µ

Electrodes de Panaxium

Khodagholy Nat Neurosci 2016
Oscillations gamma (80-200 Hz) évoquées par des stimulations des doigts

Taro Kaiju et al. Front. Neural Circuits, 2017
BRAIN COMPUTER INTERFACES