



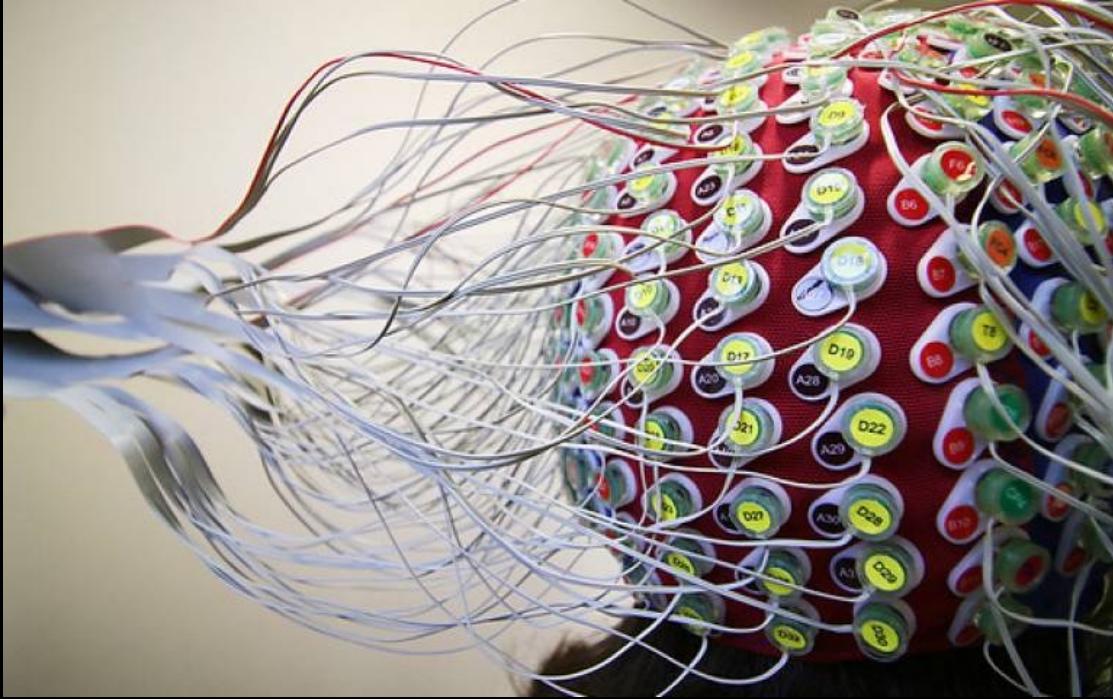
Investigating time series neural data: Experimental design & signal processing practices

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ISRC, Ulster University**

I will talk about...

- Electroencephalography and Magnetoencephalography
 - Comparison
- Brain-Computer Interfacing
 - Pipeline
 - Applications
 - Common Neural Signals
- Designing Experiments
- Pre-processing of Brain Signals
- Removing Artefacts- Independent Component Analysis
- Event Related Potential
- Time-Frequency Analysis
- Case Study 1: ALS Detection
- Case Study 2: Anytime Collaborative BCI

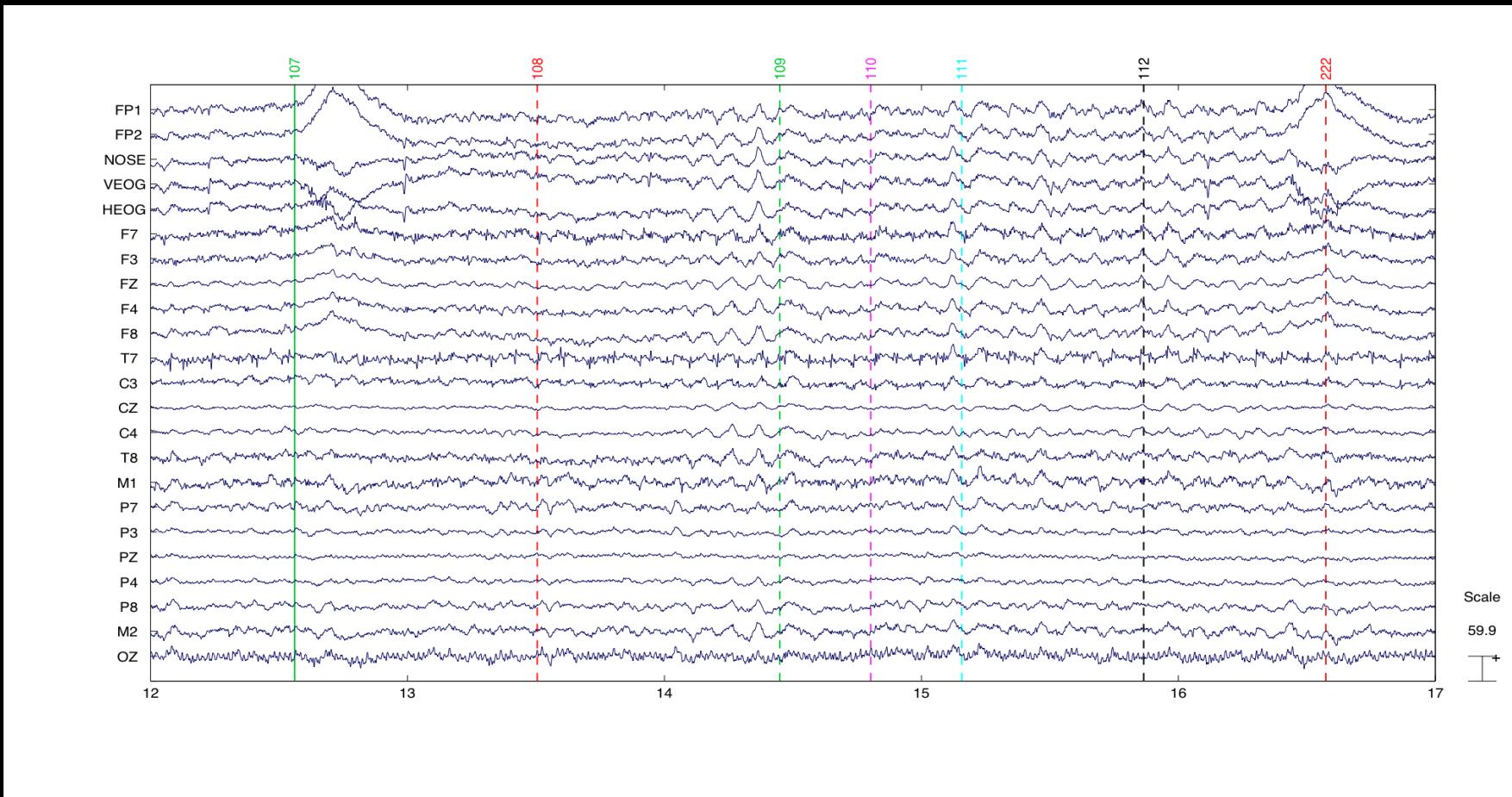
Electroencephalography - Introduction



<https://www.ucl.ac.uk/brain-sciences/news/2023/jan/brain-wave-recordings-could-reveal-cause-catatonia>

- Electroencephalogram (EEG) electrodes
- Scalp recording of electrical activity of cortex => waveform signals
- Microvolts (μ V) – small!
- Role of EEG in neuroimaging:
 - Identify neural correlates
 - Diagnose epilepsy, sleep disorders, anaesthesia, coma, brain death

EEG Recording

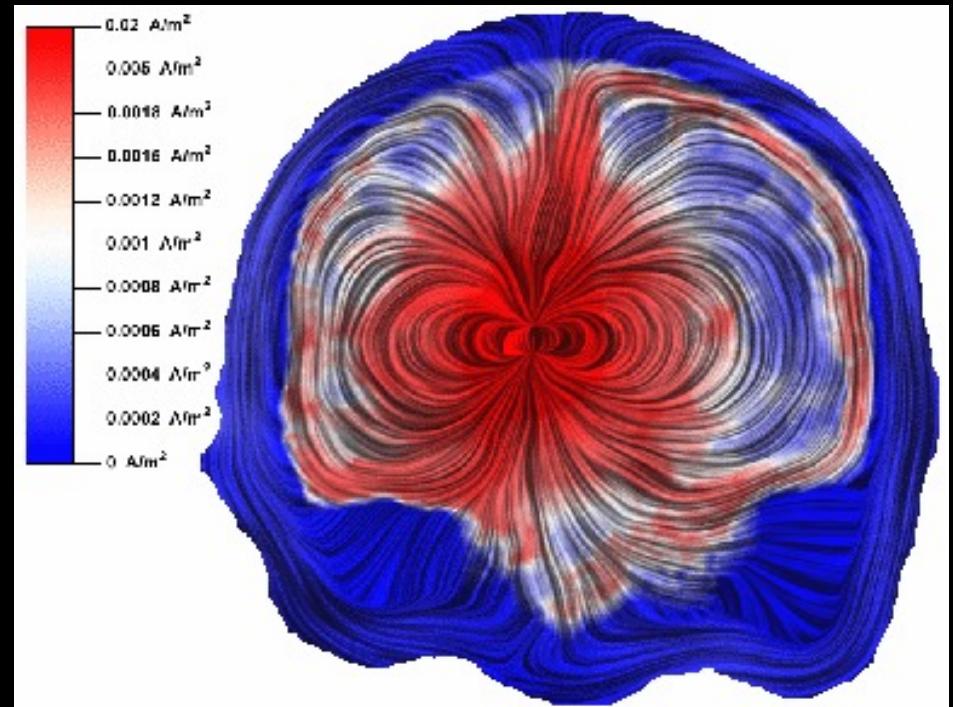


What does EEG record?

Mainly NOISE!!

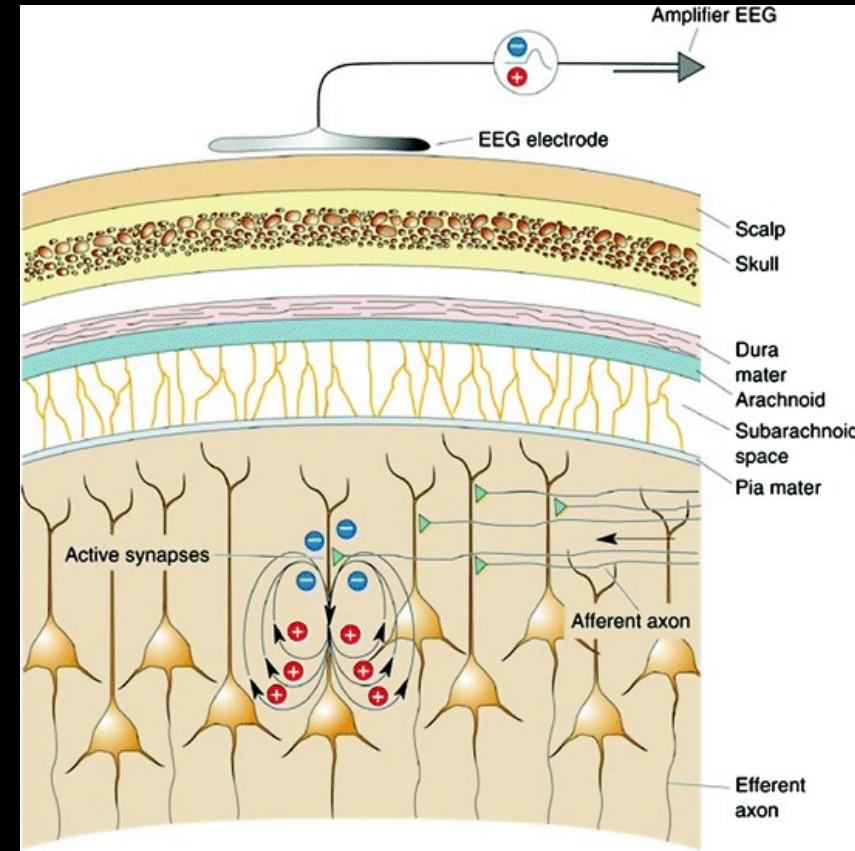
Volume Conduction

- The electrical activity flows through the tissue between the electrical generator and the recording electrode.
- The EEG is a 2-D representation of a 3-D reality, which poses a problem in localizing the sources of the electrical activity



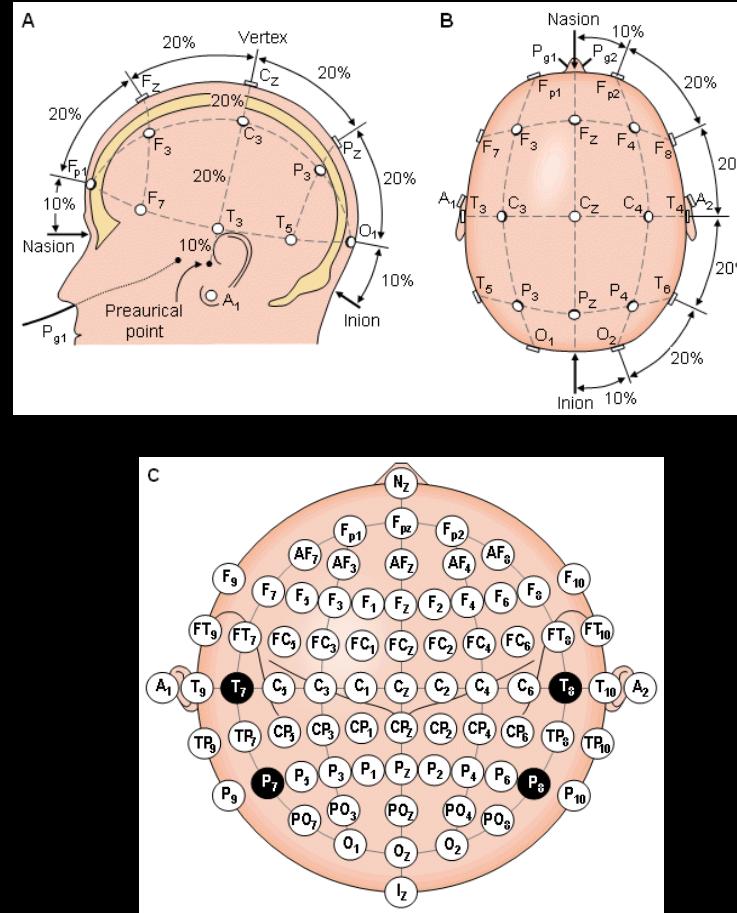
Basis of EEG Signals

- The neuronal firing inside the brain generates electrical signals.
- These electrical signals picked up from the scalp by metallic electrodes are called EEG signals.
- Summation of excitatory and inhibitory postsynaptic potentials



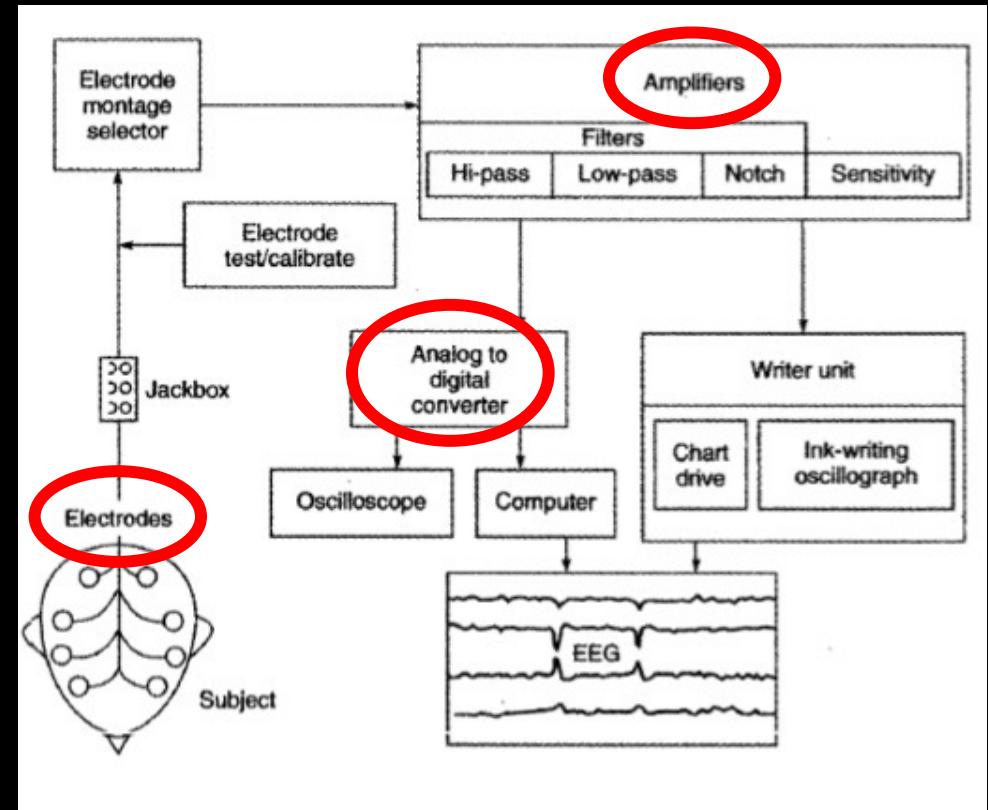
EEG Surface Recordings

- **International 10/20 or 10/10 system for placing electrodes:**
 - **A:** earlobes, **C:** central,
 - **P:** parietal, **F:** frontal,
 - **O:** occipital
- Low impedance 5-10kΩ
- Record **montages:**
 - **Bipolar** (electrodes connected to each other)
 - **Referential** (electrodes connected to one reference)



EEG Amplifier

- **Digital**
 - **Electrode array (8-256)**
 - **Amplifier** (1 per pair of electrodes)
 - **Analogue-Digital Converter:** waveform into numerical values
 - Sampling rate should be 2x your frequency of interest



Kallara 2012.

EEG Frequency Spectrum

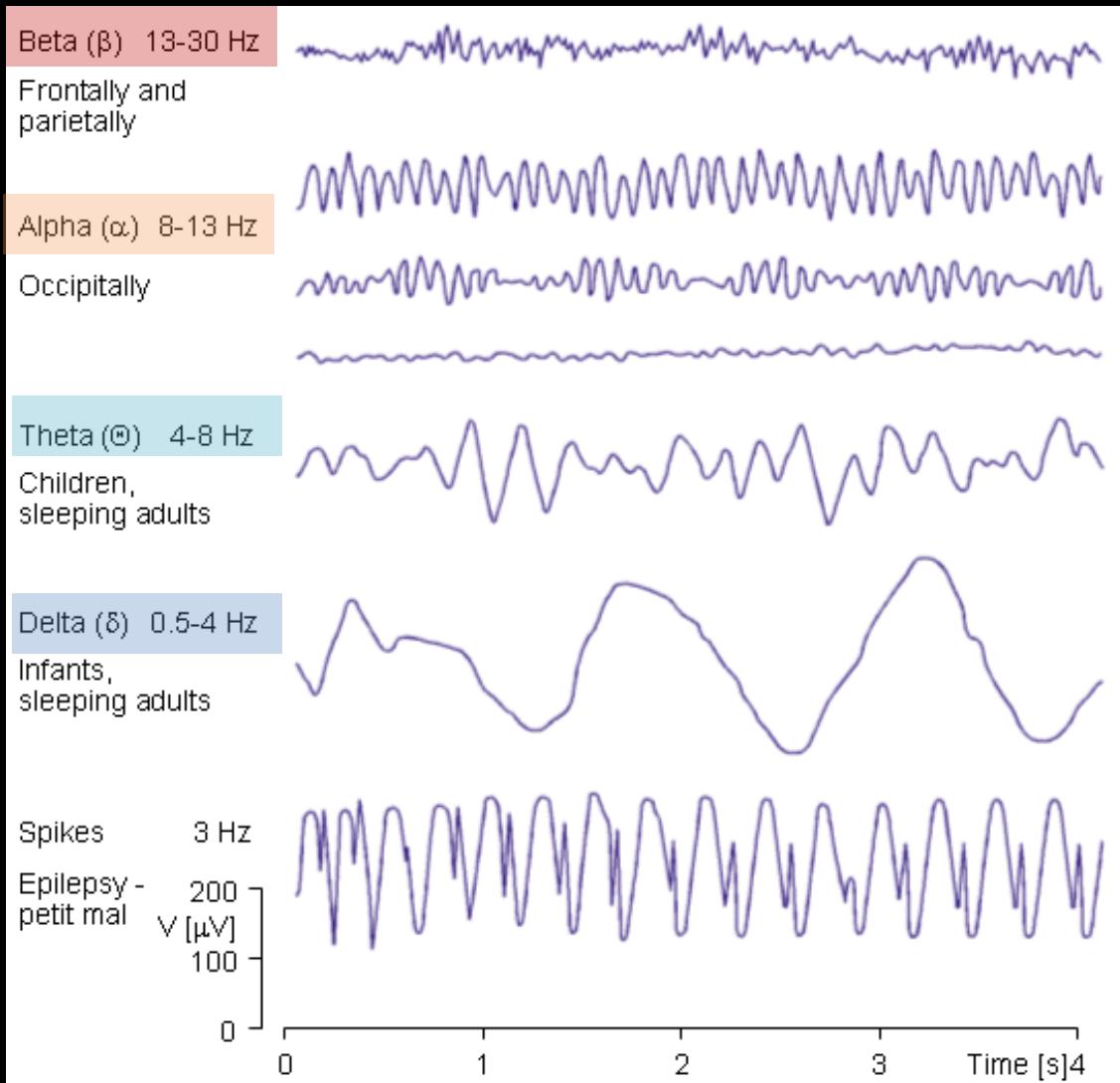
- 5-50 μ V, mostly below 30 μ V
- Sharp spike-waves, **light sleep** stages

- 5-120 μ V, mostly below 50 μ V
- **Awake**, eyes closed, mental inactivity, physical relaxation

- 20-200 μ V
 - Strictly rhythmic or highly irregular
 - Awake & drowsiness, **light sleep** stages
 - LTP and phase-encoding

- 5-250 μ V
 - Abnormality in waking adults, accompaniment of **deep sleep**

+ Gamma waves?
31-100 Hz, 10 μ V
'binding of consciousness', unity of perception



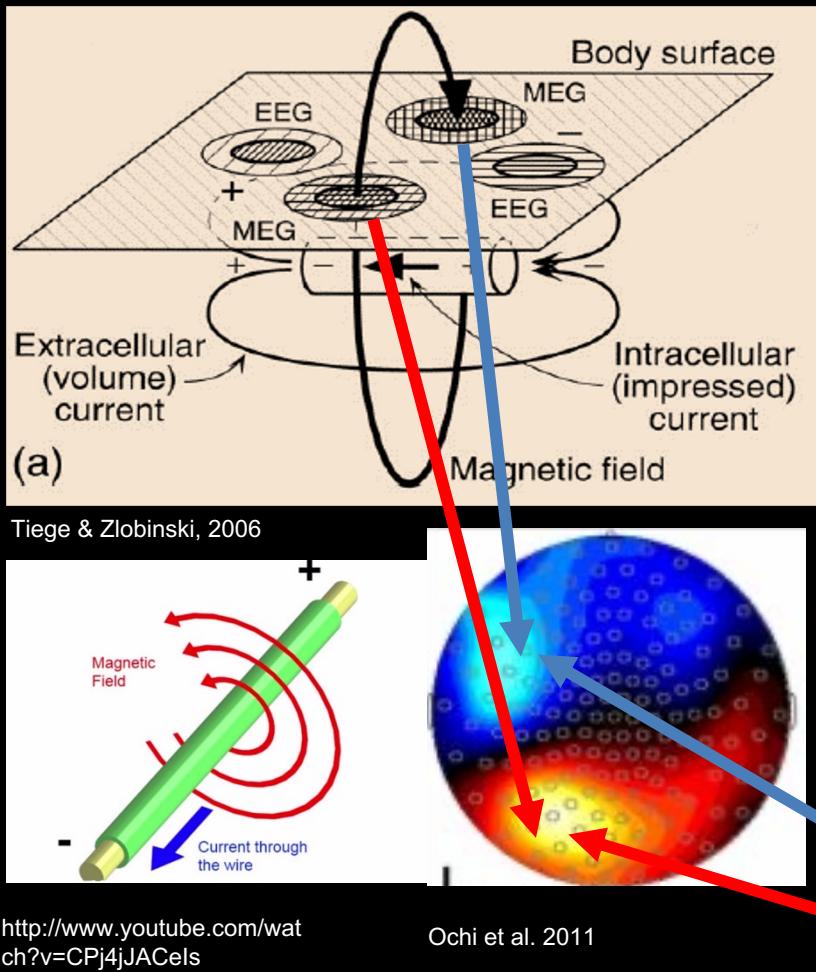
Magnetoencephalography- Introduction



<http://www.admin.ox.ac.uk/estates/capitalprojects/previouscapitalprojects/megscanner/>

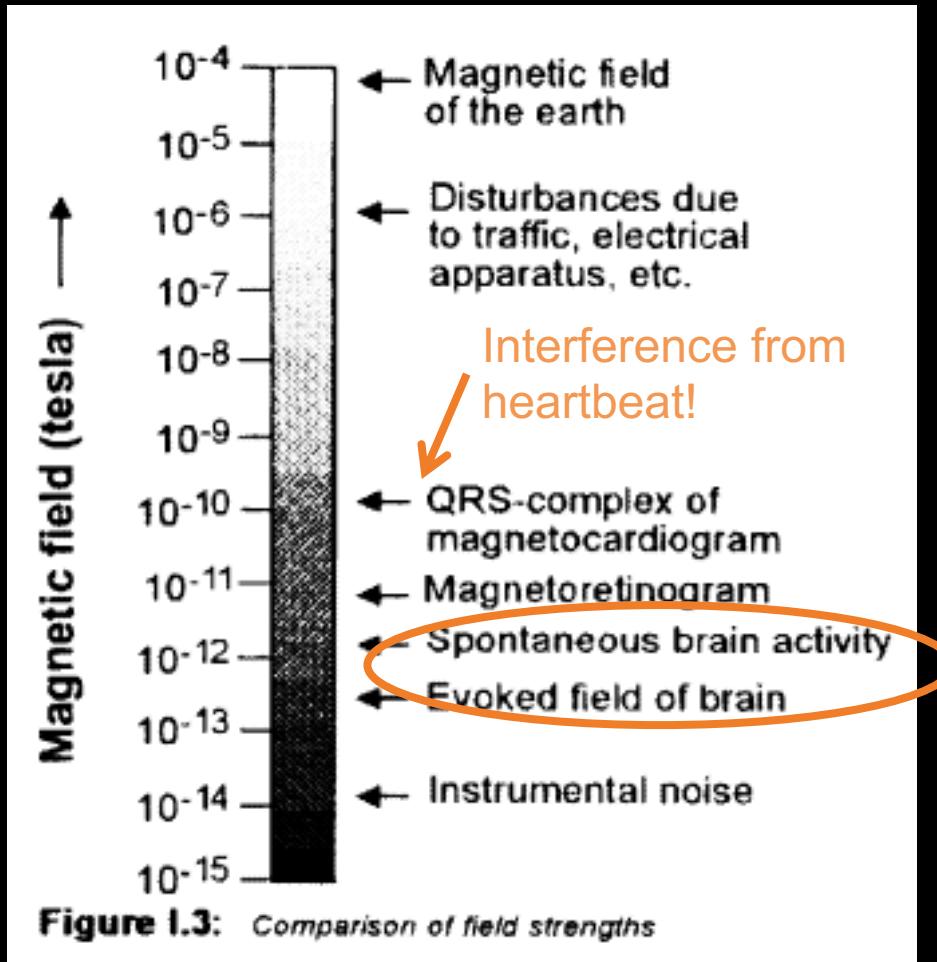
- **Magnetoencephalography (MEG)**
- Direct external recordings of **magnetic fields** created by electrical currents in cortex
- Measured in **fT** to **pT**
- Role of MEG in neuroimaging:
 - **Neural correlates** of cognitive/perceptual processes
 - **Localise** affected regions before surgery(?), determine regional and network functionality

Basis of the MEG



- **Large pyramidal neurons** in layer V of cortex, arranged in parallel, similarly-oriented, perpendicular to surface, fire synchronously
- Dipolar current flow generates a **magnetic field**.
- **10,000 to 50,000** active neurons required for detectable signal
- **Scalp topography:**
 - **Influx maxima** ‘source’
 - **Efflux maxima** ‘sink’

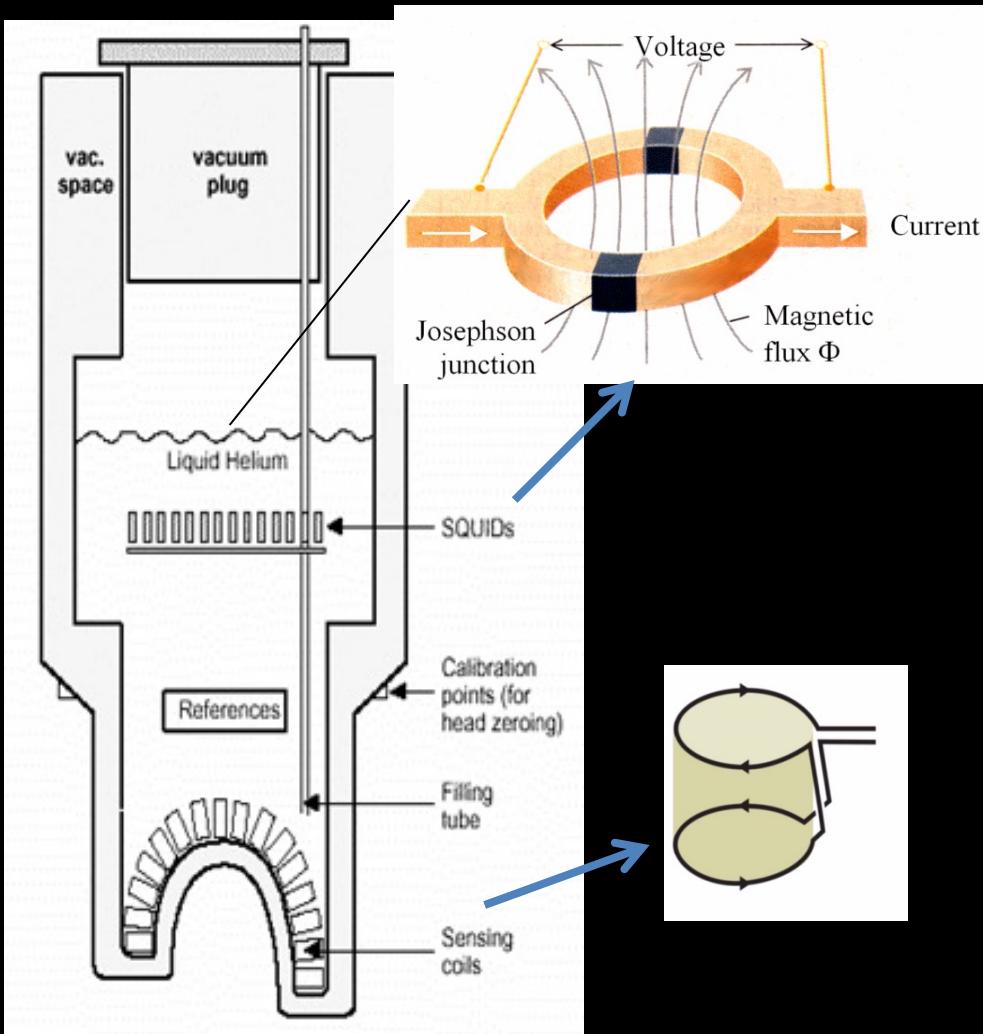
MEG: Scale of magnetic field



- MEG signal is **tiny!**
- **Interference** from electrical equipment, traffic, the earth, participant's heartbeat etc.

Requires **magnetically shield rooms** and **supersensitive magnetometers**

MEG: SQUID

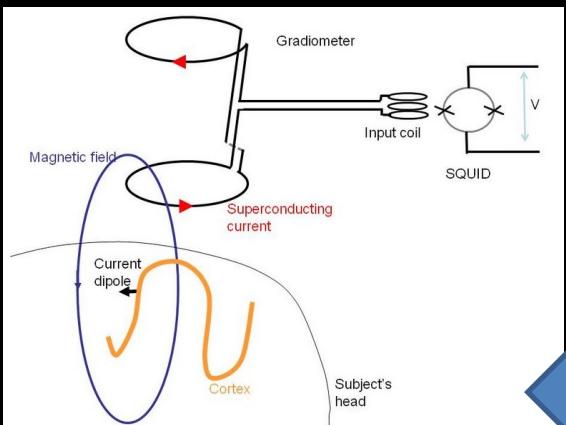
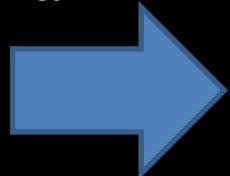


- SQUID - Superconducting QUantum Interference Device, immersed in super-cool liquid helium
- Sensitive to field changes in order of femto-Tesla (10-15)
- Superconductive ring with two Josephson junctions
- Flux transformers (coils)
 - Magnetometers
 - Gradiometers (planar/axial)

MEG: Flux Transformers

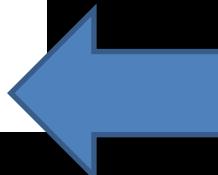
- **Magnetometer**

- consist of a **single superconducting coil**
- highly sensitive, but also **pick up environmental noise**

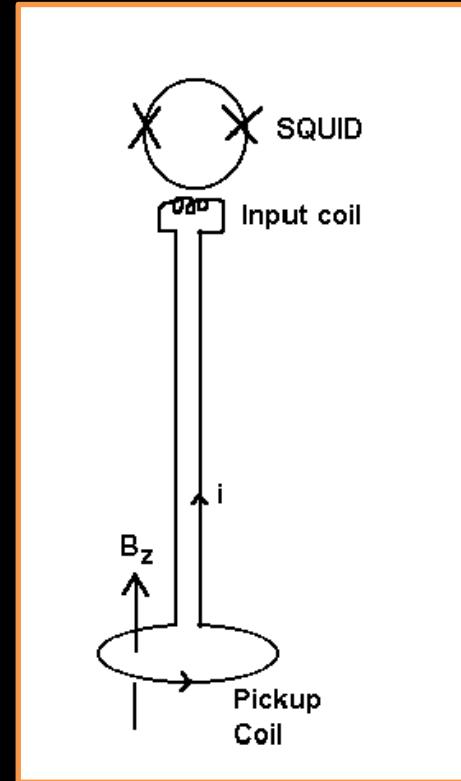


- **Gradiometers:**

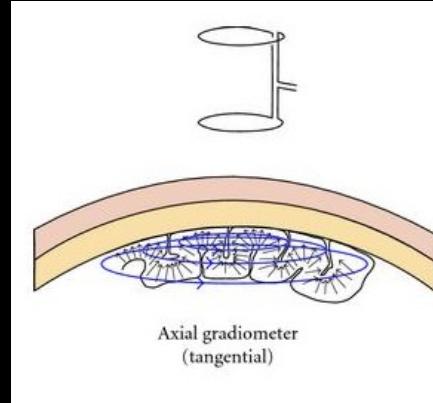
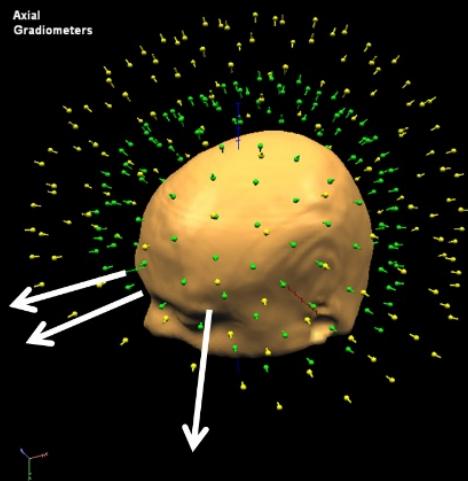
- consist of two **oppositely wound coils**
- **sources in the brain** - differentially affect the two coils



- environmental sources have the **SAME EFFECT** on both coils → **0 net current flow**



MEG: Flux Transformers

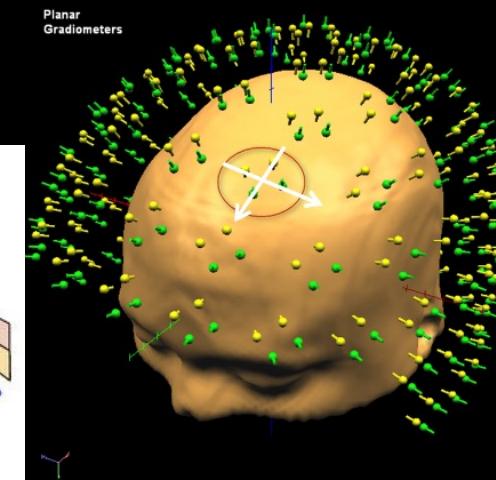
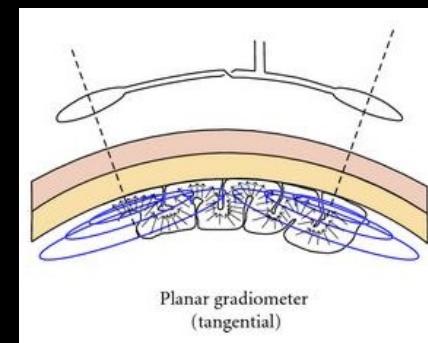


Axial Gradiometer MEG sensors...

- ...are aligned orthogonally to the scalp
- ...record gradient of magnetic field along the radial direction

Planar Gradiometer MEG sensors...

- ...two detector coils on the same plane
- ...have sensitivity distribution similar to bipolar EEG setup



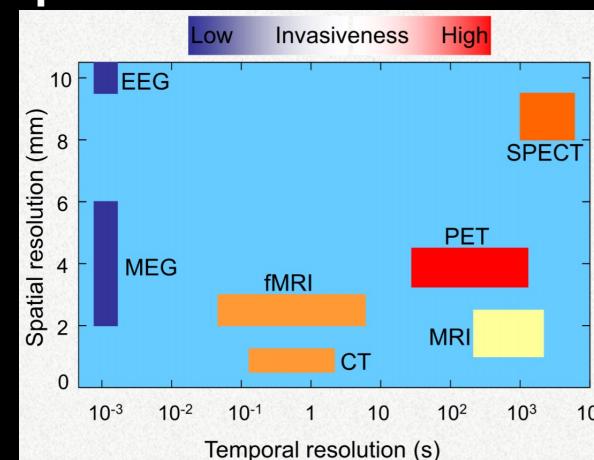
EEG and MEG

ADVANTAGES

- ✓ **Non-invasive**
- ✓ **Direct** measurements of neuronal function (unlike fMRI)
- ✓ High **temporal resolution** (1ms or less, 1000x better than fMRI)
- ✓ Easy to use **clinically** (adults, children)
- ✓ **Quiet!** (can study auditory processing)
- ✓ **Affordable**, EEG is portable
- ✓ Subjects can perform tasks **sitting up** (more natural than MRI scanner)

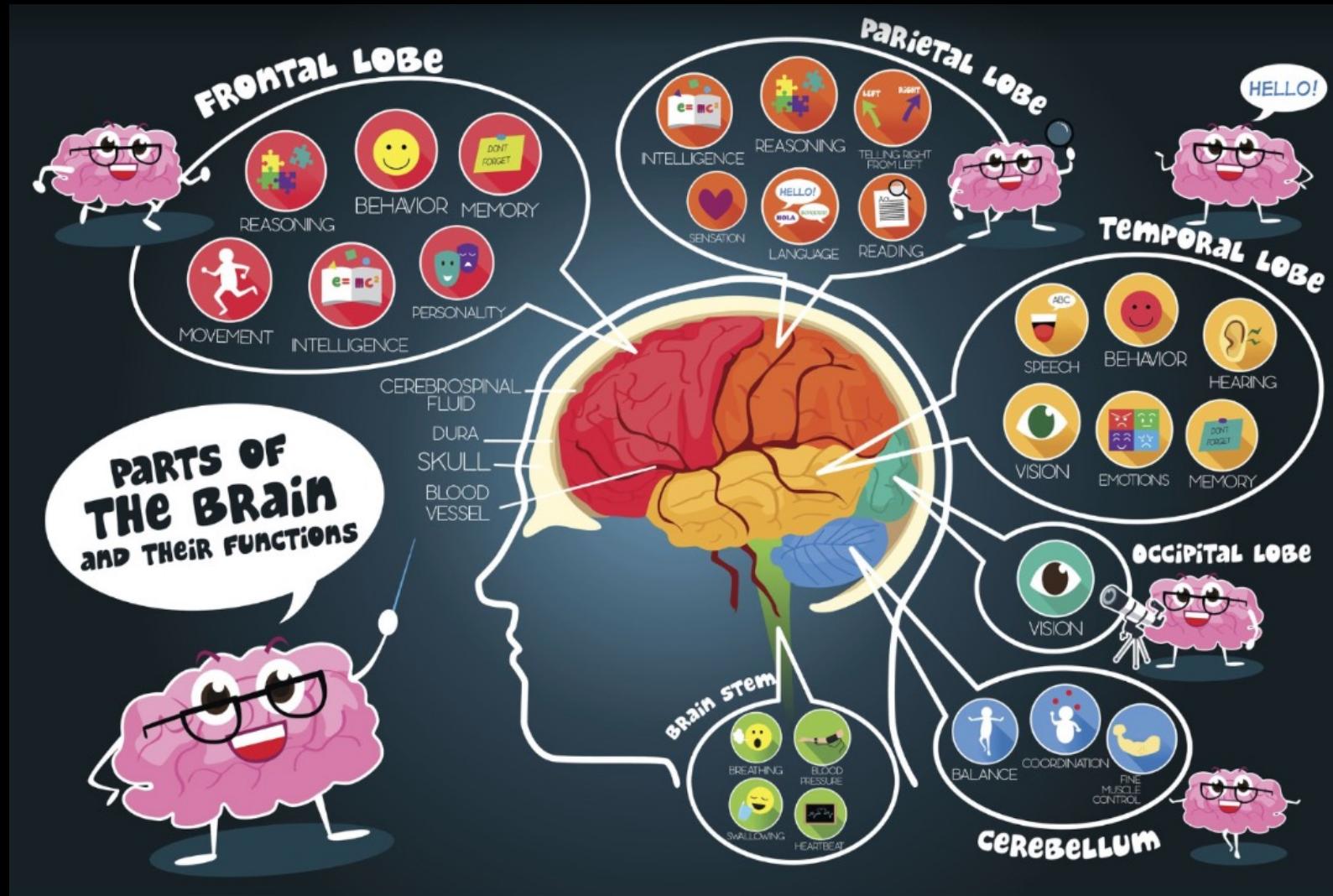
DISADVANTAGES

- ✗ Not as good **spatial localization** as fMRI, MRI, CT
- ✗ **Sensitivity depth** only ~4cm (c.f. whole brain sensitivity of fMRI)
 - Sensitivity loss proportional to square of distance from sensor
- ✗ 3D Source reconstruction is ill-posed? **forward and inverse problems**



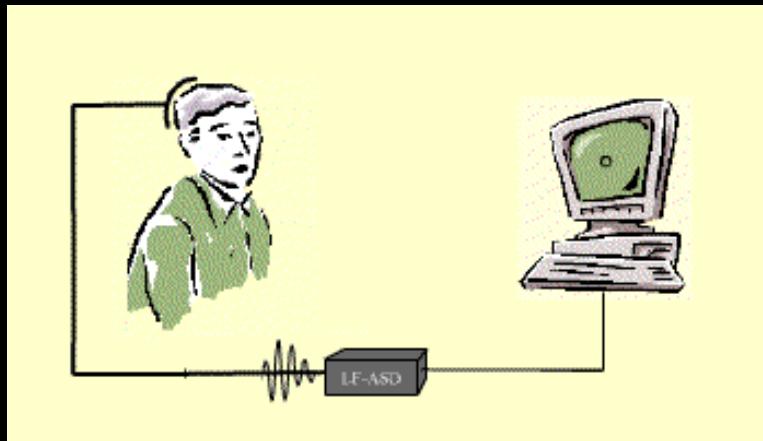
https://ngp.usc.edu/files/2013/06/Syed_EEG_MEG.pdf

EEG and MEG: Measurable Activities



Brain-Computer Interfacing

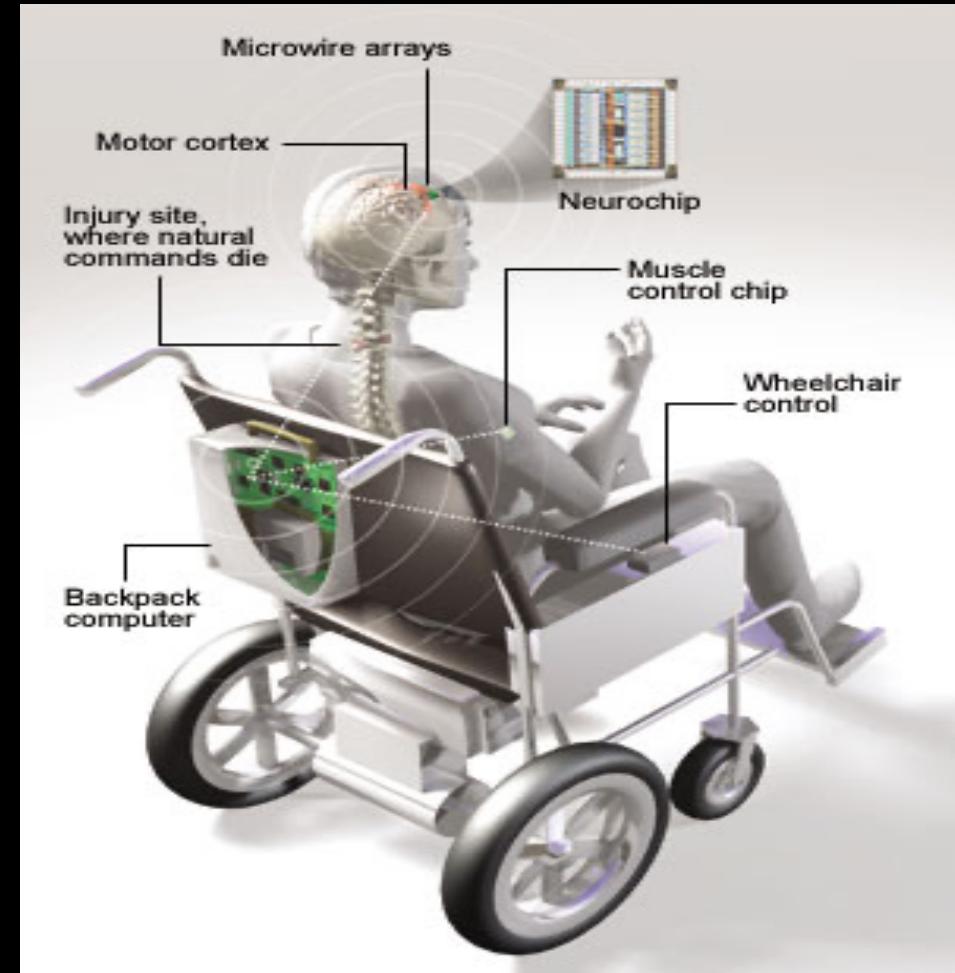
- “A Brain-Computer Interface is a communication system that do not depend on peripheral nerves and muscles” [Wolpaw et al. 2000]
- A technology which allows a human to control a computer, peripheral, or other electronic device with thought.



<http://www.ece.ubc.ca/~garyb/BCI.htm>

Brain-Computer Interfacing

- is to give disable people to communicate, to operate prostheses, and even to operate wheelchairs using brain signals.
- **Target group:**
 - Amyotrophic Lateral Sclerosis
 - Cervical spinal injury
 - Stroke paralysis
 - Cerebral palsy
 - Amputee, etc

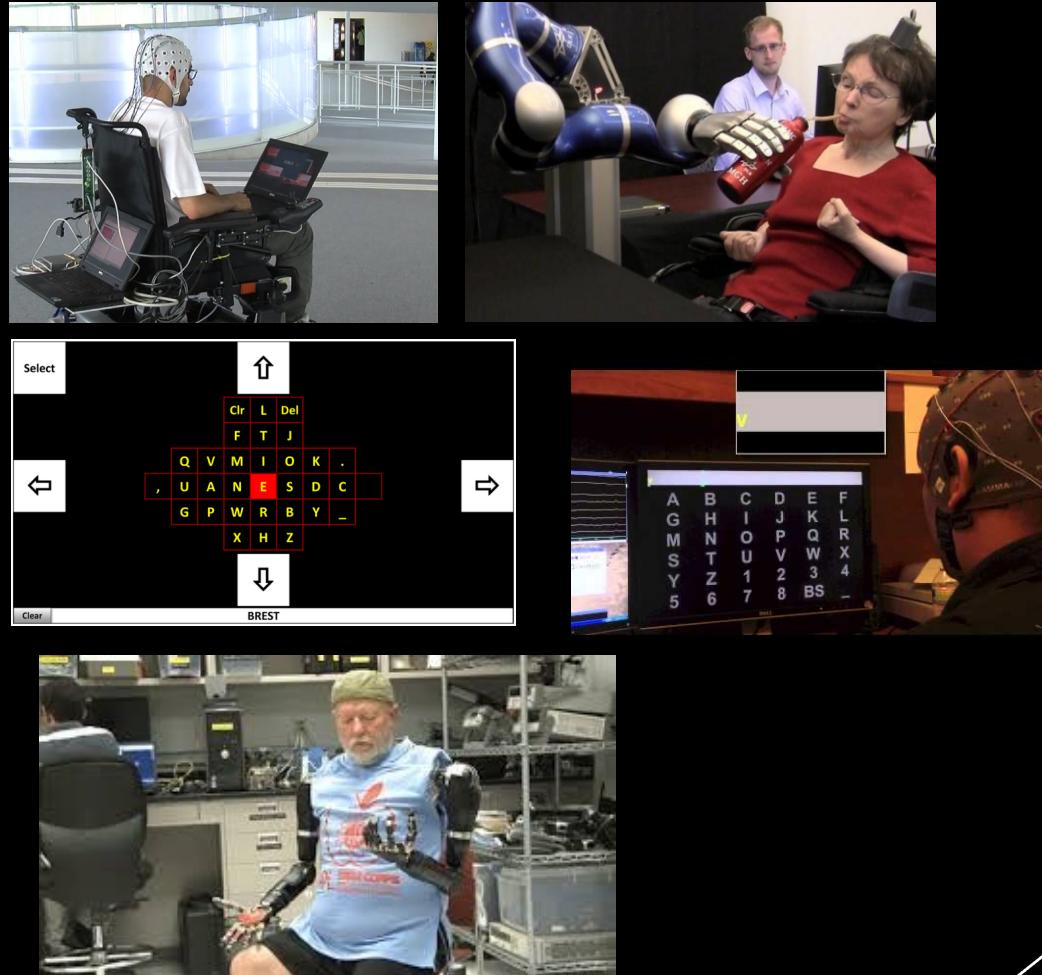


Nicolelis, 2001

Brain-Computer Interfacing

Traditionally used to allow people with disabilities to **communicate or control prosthesis**

1. Thought Controlled Wheelchair
2. Upper Limb Prosthesis
3. Cursor Control
4. Virtual Keyboard
5. BCI Speller



Brain-Computer Interfacing

... human cognitive enhancement

Neuro-Gaming



<https://www.cnet.com/videos/i-wore-the-future-with-openbcis-brain-sensing-vr-headset-galea/>

Neuro-Marketing



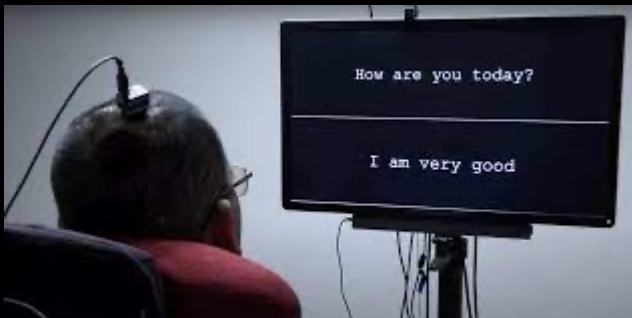
<https://www.bitbrain.com/applications/neuromarketing>

Military



<https://idstch.com/technology/biosciences/darpa-n3-developing-nonsurgical-brain-machine-interfaces-for-soldiers-to-use-his-thoughts-alone-to-control-multiple-unmanned-vehicles-or-a-bomb-disposal-robot-on-battlefield/>

Speech



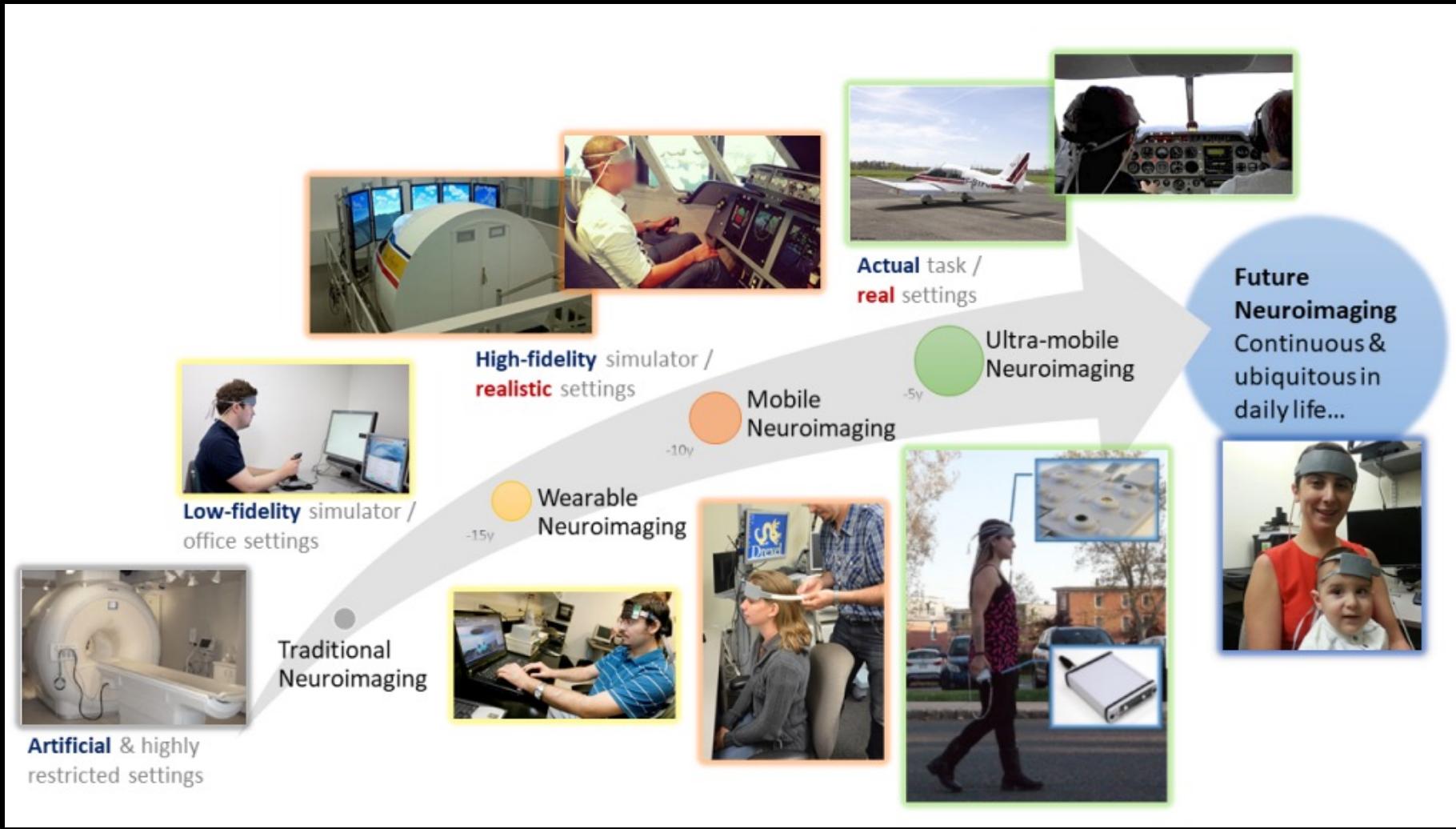
<https://spectrum.ieee.org/brain-computer-interface-speech>



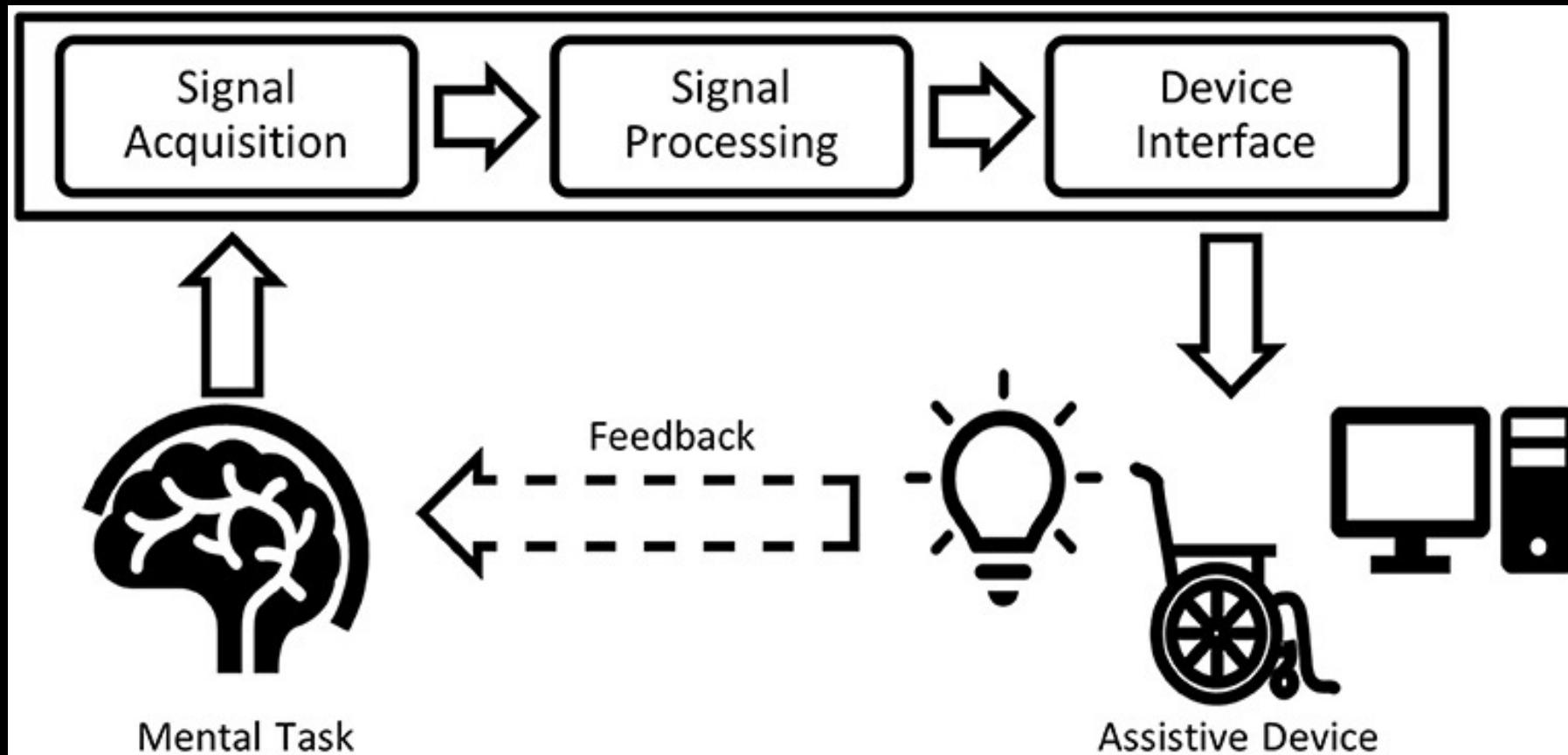
<https://www.techrepublic.com/article/mind-controlled-cars-this-brain-computer-interface-could-transform-driving/>

Driving

Brain-Computer Interfacing



A BCI Pipeline

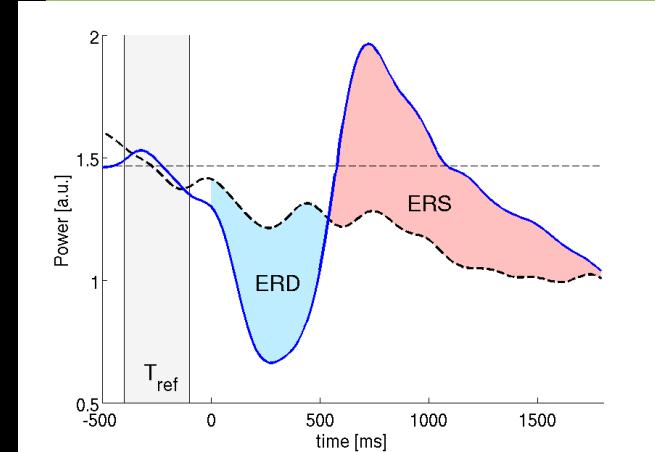
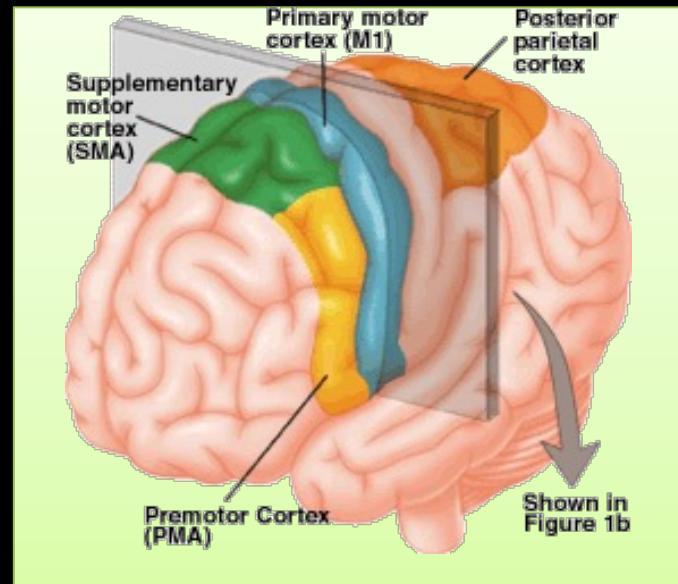
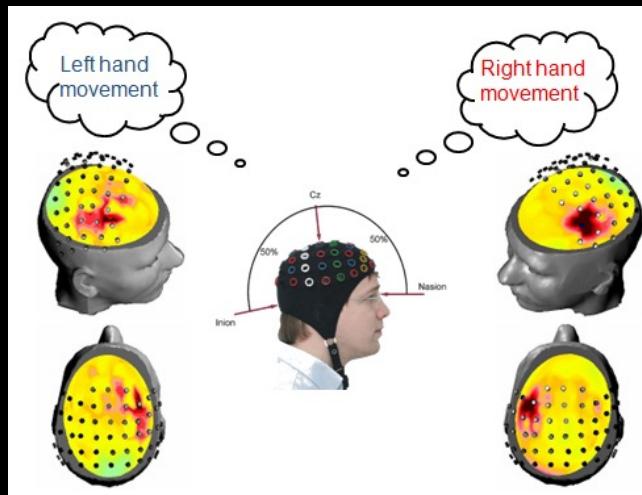


<https://www.frontiersin.org/articles/10.3389/fnhum.2021.643294/full>

BCI-Common Neural Signals

Motor Imagery (ERD/ERS)

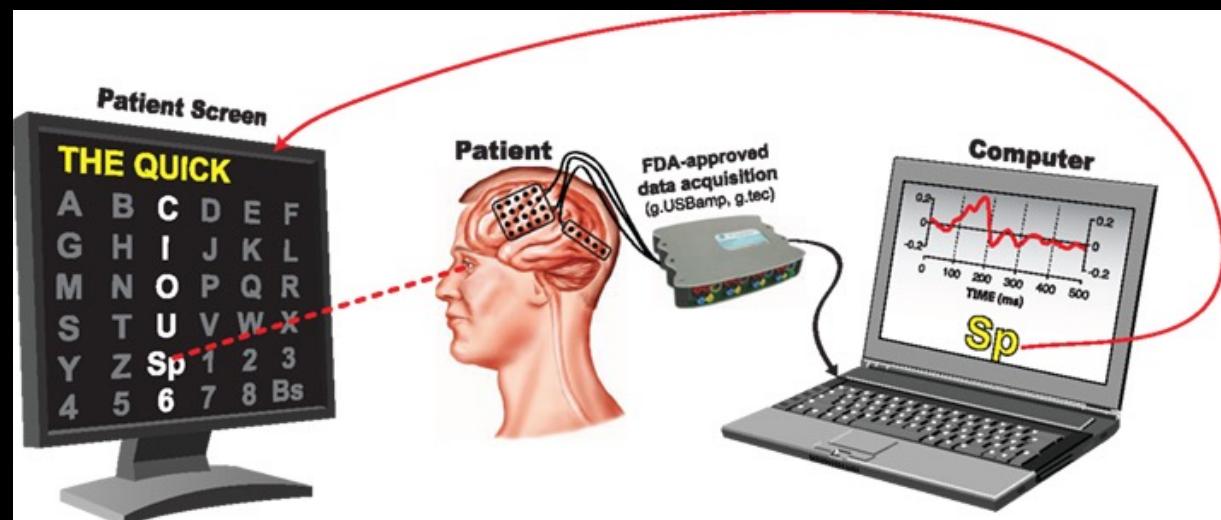
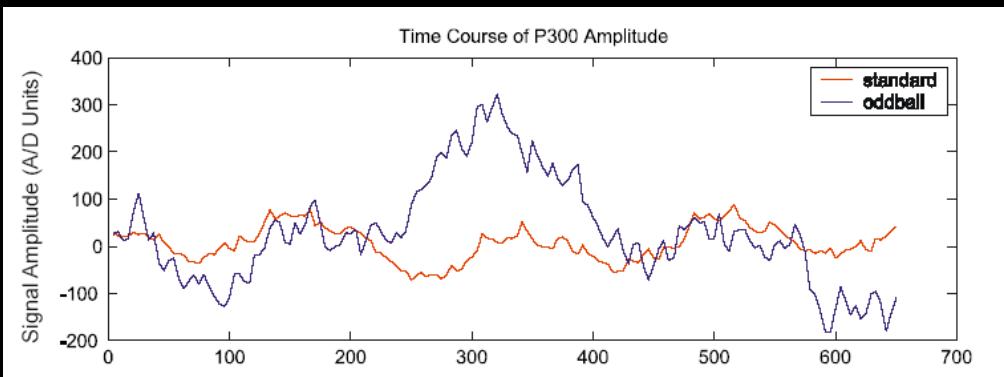
- Rolandic mu rhythm (8-12 Hz) and the central beta rhythm (16-24 Hz)
- Movement Imagination/Execution



BCI-Common Neural Signals

P300

Signal associated to the presence of uncommon targets or infrequent stimuli to which a user is paying attention

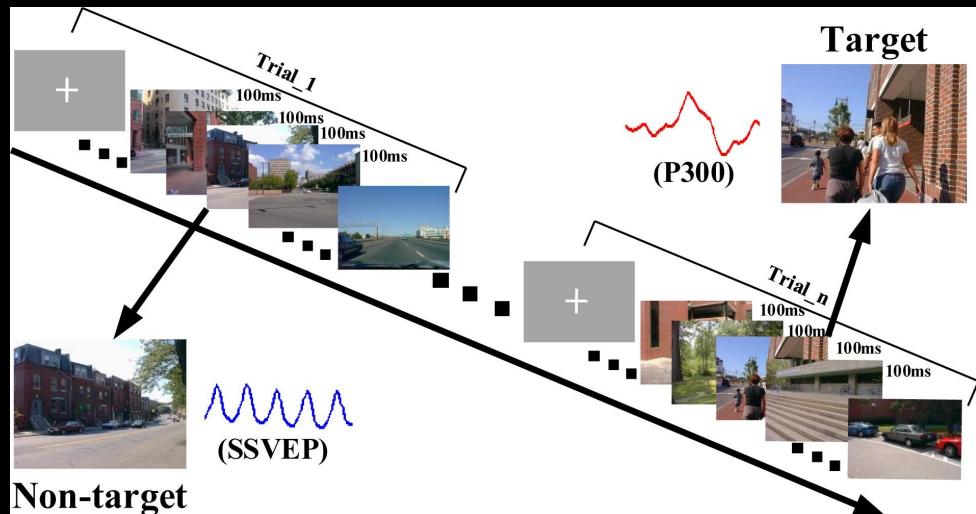


<https://www.frontiersin.org/articles/10.3389/fnins.2011.00005/full>

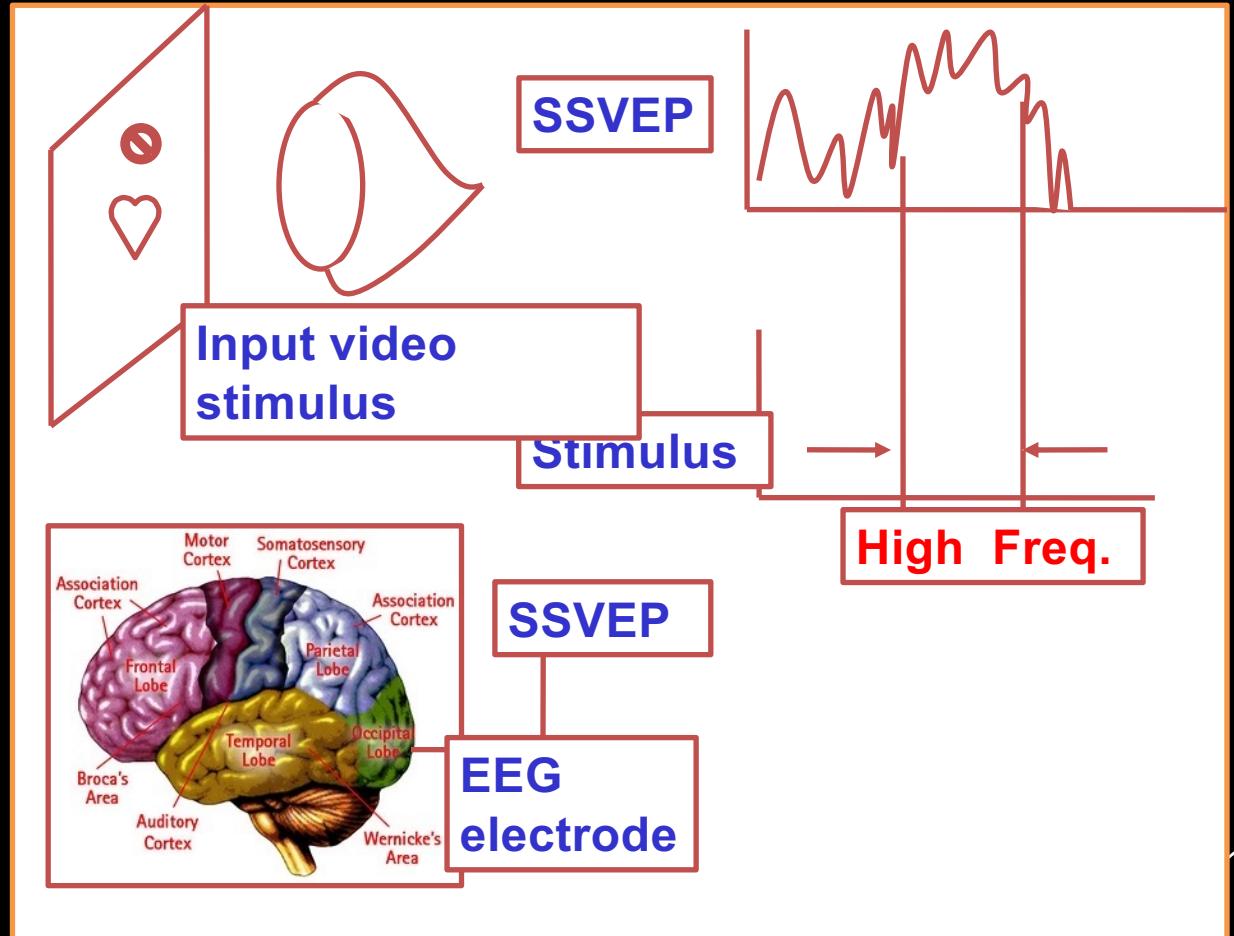
BCI-Common Neural Signals

Steady-State Visual Evoked Potential

The amplitude of the response is modulated by the frequency of the stimulus.



<https://www.frontiersin.org/articles/10.3389/fnins.2020.568000/full>



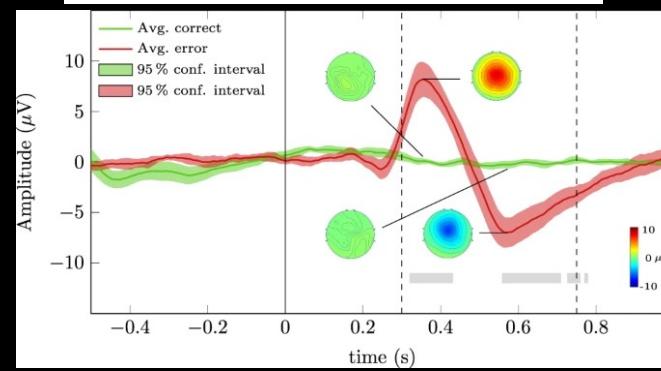
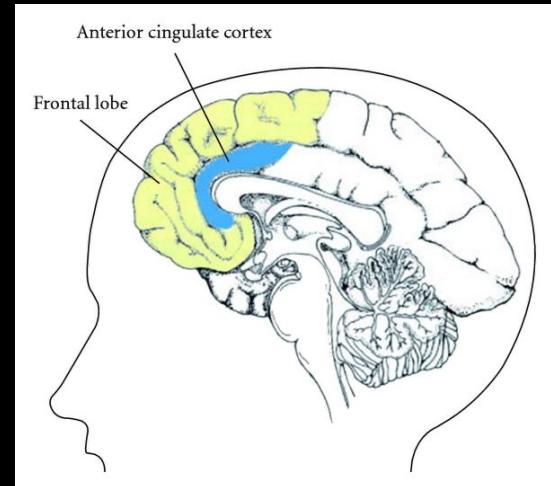
BCI-Common Neural Signals

Error Related Potential

User's awareness to erroneous response.

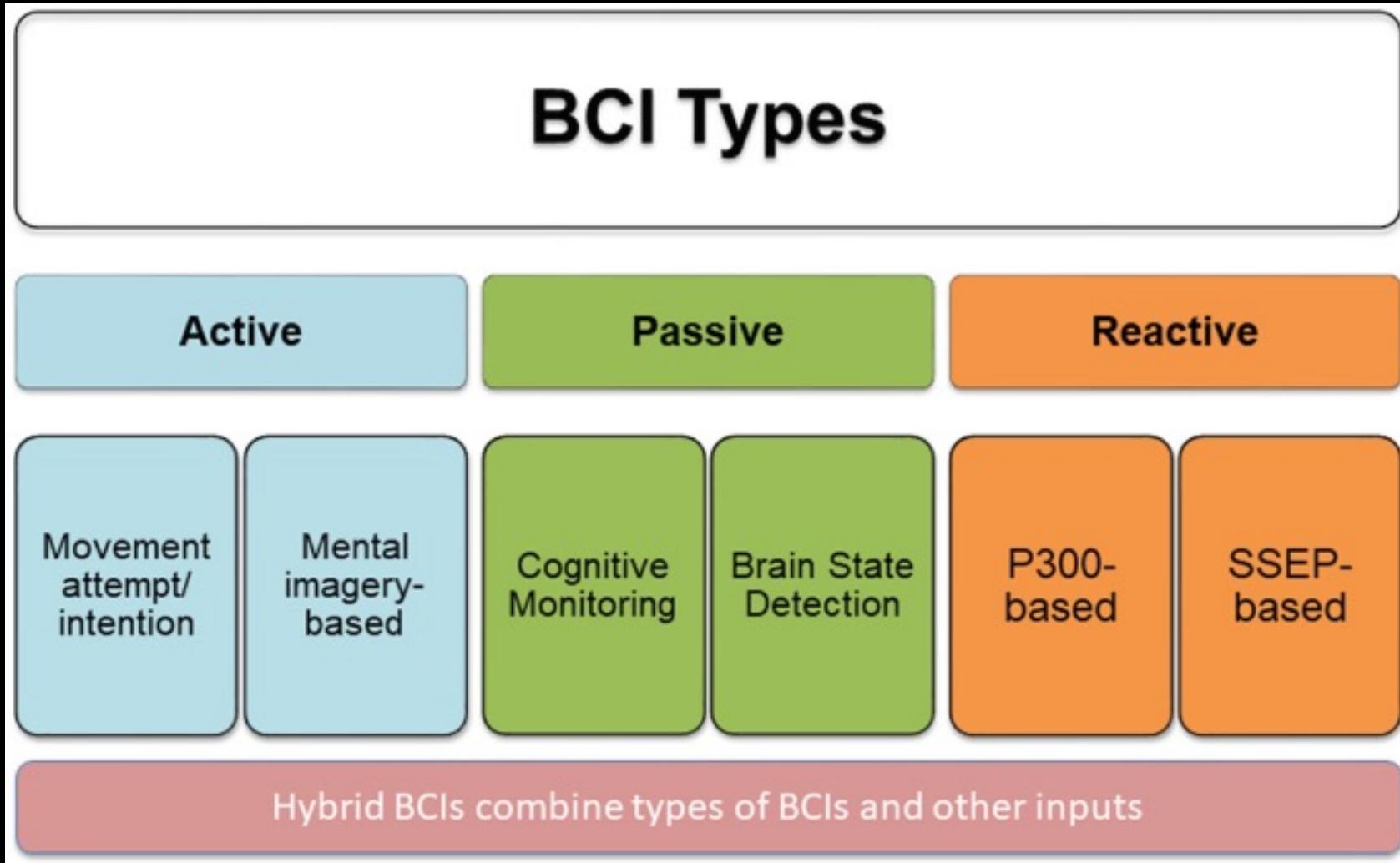
Typical occurrences that elicits ErrP:

- Choice reaction tasks
- Feedback tasks
- Observation tasks



Lopes-Dias et al., Sci. Rep., 2019

Types of BCI



Designing Experiments

- Do not underestimate the importance of good experiment design
- Produce meaningful and interpretable results
 - Implications for theories
 - Inspire new research
- Pilot test your experiment behaviourally

Event Markers

- Triggers that are sent from stimulus delivering computer to the EEG amplifier
- Recorded as separate channel
- Encode specific events such as stimulus onset or responses, etc.



https://pressrelease.brainproducts.com/wp-content/gallery/1602_ST/GUI_NavigationBar_Markers.jpg

Designing Experiments

Intra- and Intertrial Timing

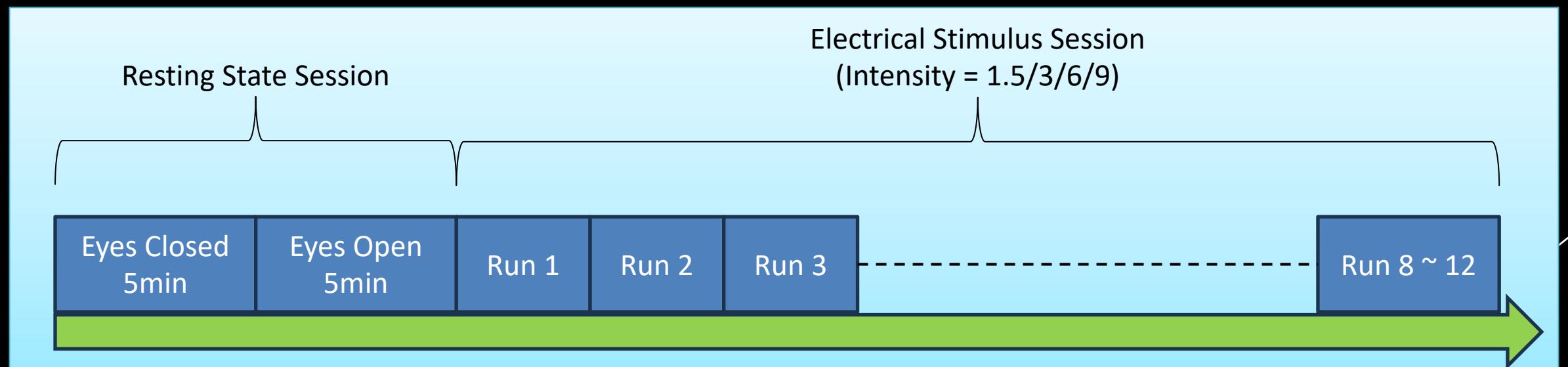
- Ideal to have experiment events within a trial separated by several hundred milliseconds
- Intervals between two trials (Inter-trial intervals):
 - Baseline normalisation
 - Frequencies to analyse
- Constant or Variable
- **Number of trials required?**
- Signal-to-Noise Ratio
- Big the effect is
- Type of analysis
- **Electrodes & Sampling Rate-** Dependent on the type of analysis

Designing Experiments - ALS

Objective: Identify neuro-markers in ALS patients and effect of electrical stimulation

Points to consider

- ALS patient needs to be compared with Healthy (Control) group
- Resting state needs to be recorded before electrical stimulation sessions
- Different intensities of stimulation

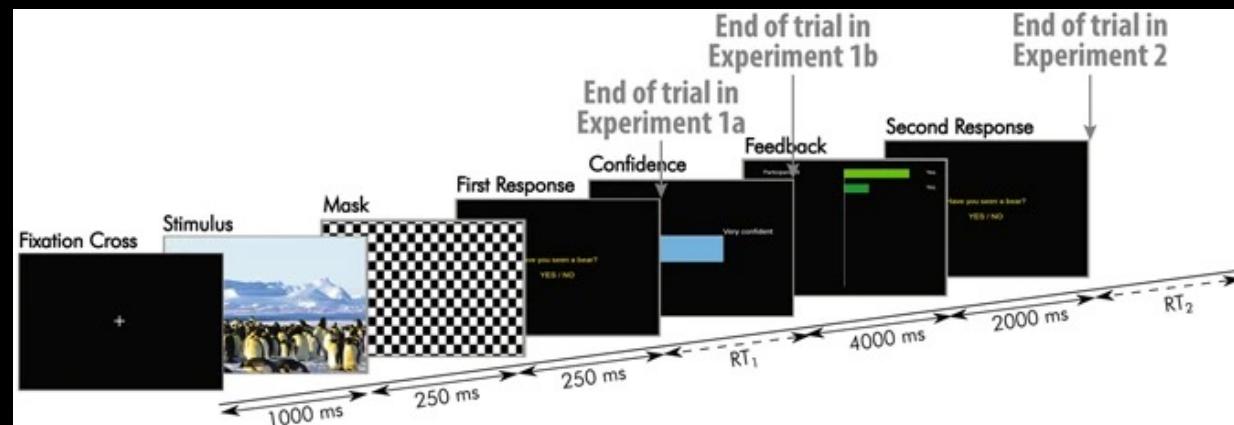


Designing Experiments – Decision-Making

Objective: Identify neural correlates of decision confidence from realistic visual-search task to improve group decision making

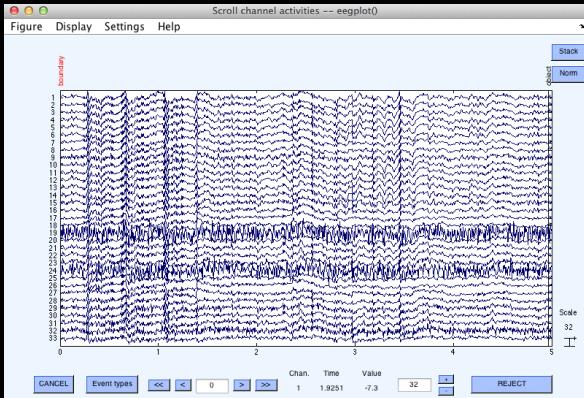
Points to consider

- In each trial, participants had to decide whether a “target” was present amongst a number of non-targets or “distractors”;
- All participants see the same sequence of stimuli
- Subjective degree of confidence to be recorded
- Change of mind incorporated



<https://www.nature.com/articles/s41598-017-08265-7>

Processing Pipeline



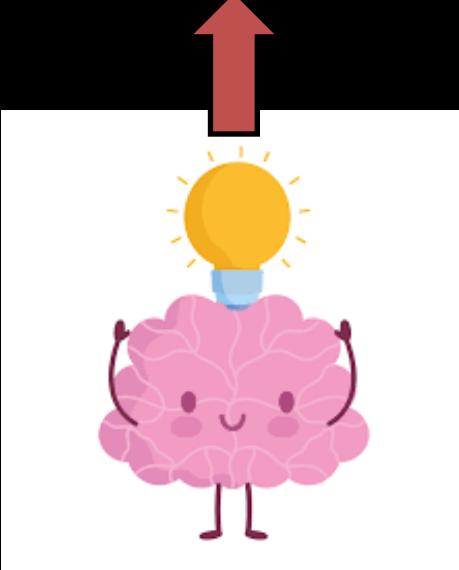
Pre-processing



Processing
(Analysis)

Time Consuming
Tedious
Signal Processing
Do it well, Do it once

Hypothesis driven
Exploratory
Often done multiple times

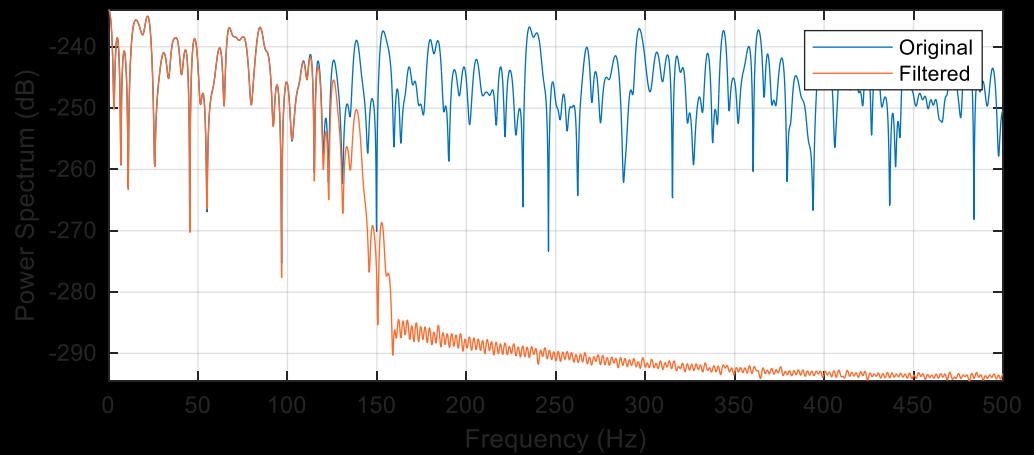
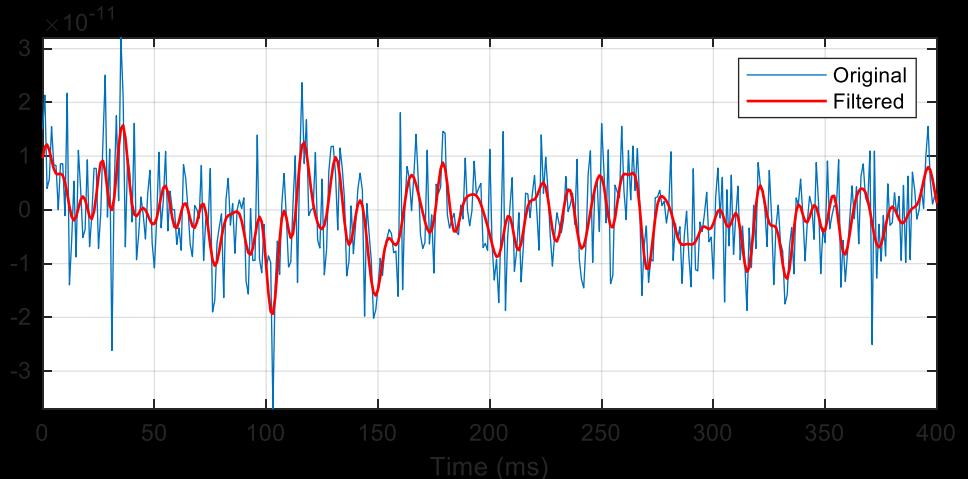


Pre-processing

- Refers to any transformation or reorganisation of signals before analysing the data and after collecting the data.
- Steps involved:
 - Filtering
 - Epoch extraction
 - Trial Rejection
 - Spatial Filtering
 - Re-referencing
 - Interpolating bad electrodes

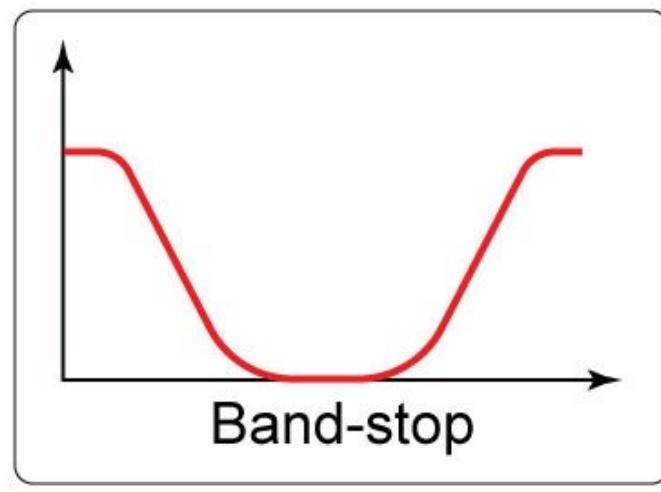
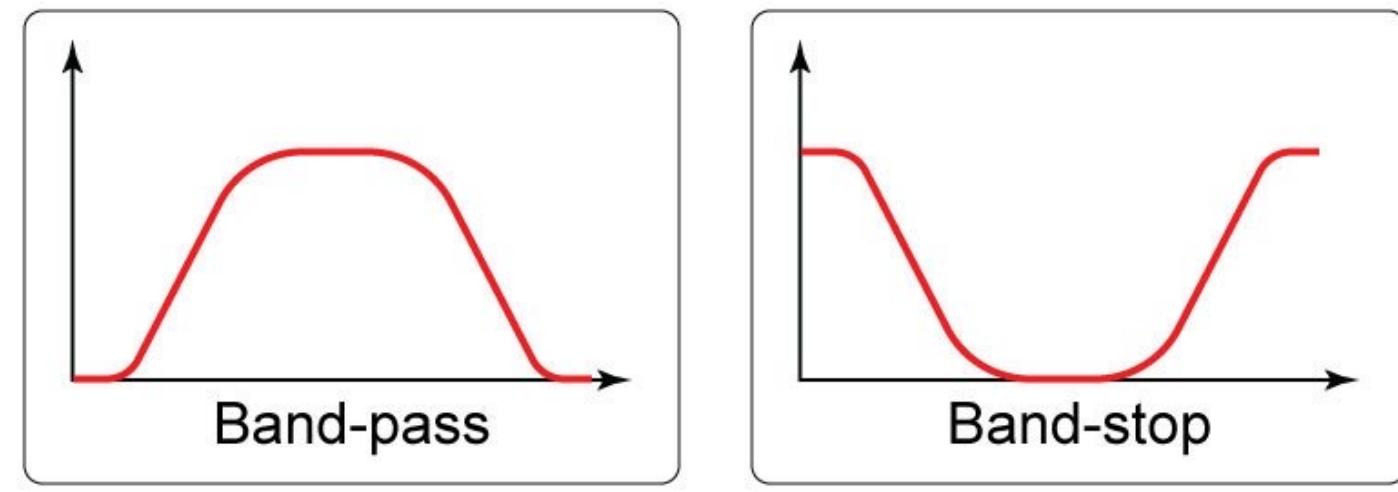
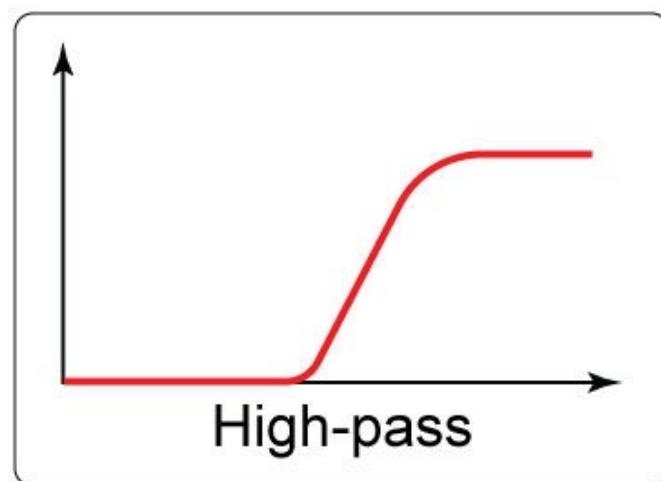
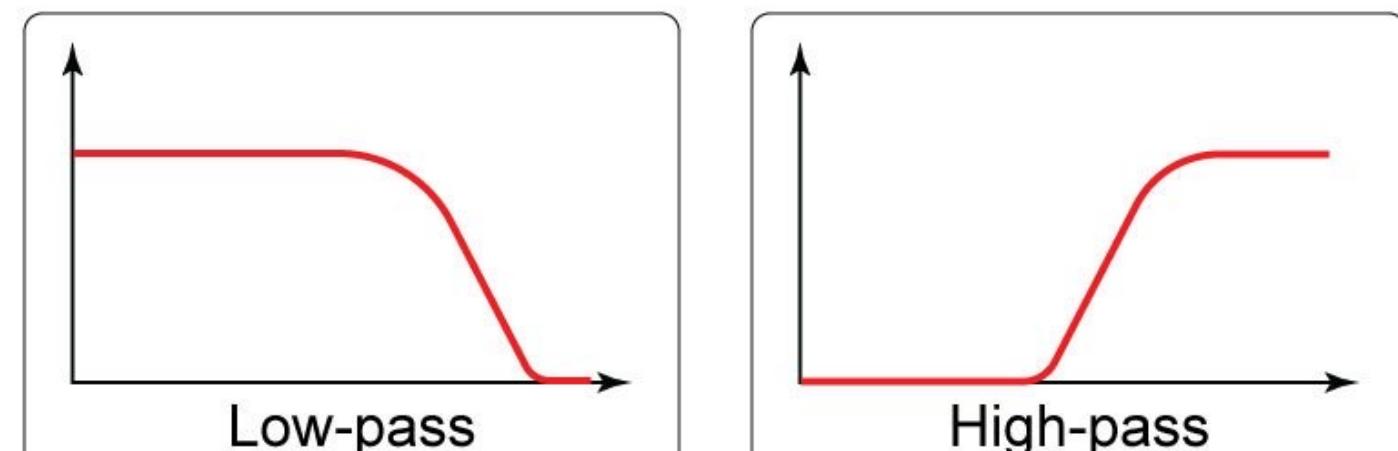
Pre-processing: Filtering Operation

- Remove high frequency artefacts, low frequency drifts
- Notch filters at 50/60 Hz to attenuate electrical line noise
- Recommended to apply a High-pass filter at 0.1 or 0.5Hz to minimize slow drifts
- Band-pass, Band-stop, High, Low Filters
- FIR and IIR filters
 - FIR filters are more stable; less likely to introduce nonlinear phase distortions
 - Computational costs higher to IIR



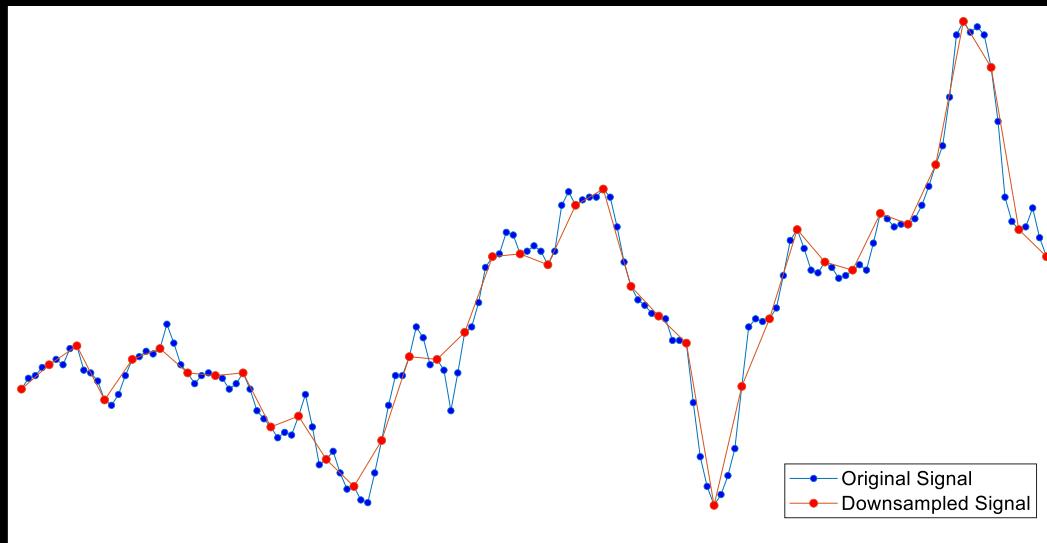
Example of filtering on the resting state signals of the ALS dataset

Pre-processing: Filtering Operation

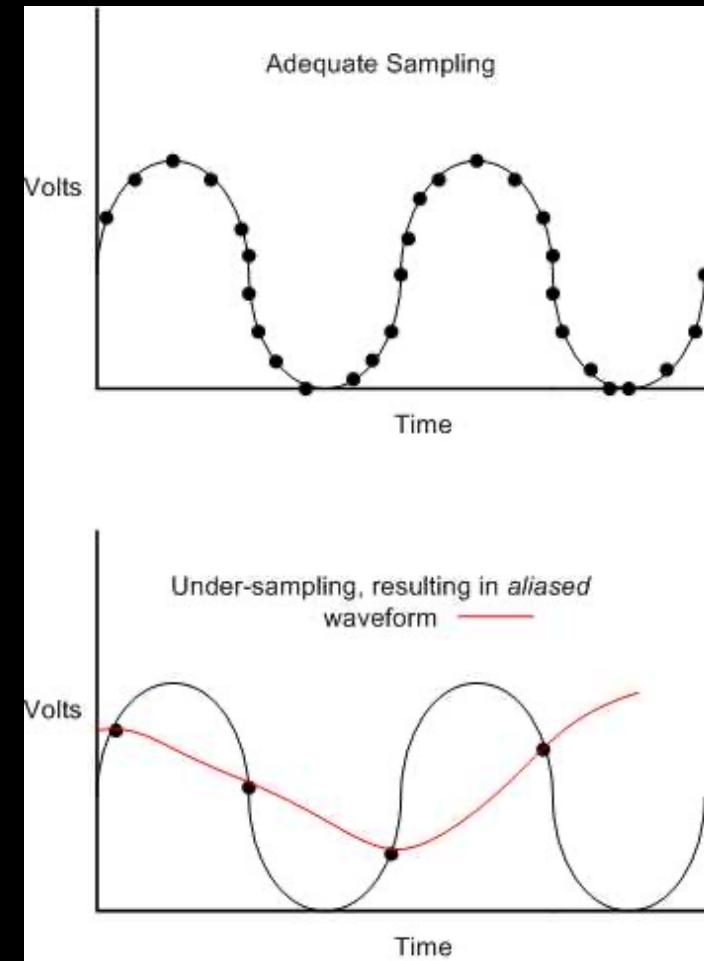


Pre-processing: Downsampling Operation

Nyquist Theory – minimum digital sampling frequency must be $>$ twice the maximum frequency in analogue signal



Example of downsampling on the resting state signals of the ALS dataset



Pre-processing: Spatial Filtering

- Bipolar: the voltage difference between two electrode pairs

- Laplacian

$$V_i^{Lap} = V_i^{ER} - \sum_j g_{ij} V_j^{ER} \quad \text{where} \quad g_{ij} = (d_{ij} \sum_j \frac{1}{d_{ij}})^{-1}$$

- Common Average Referencing (CAR)

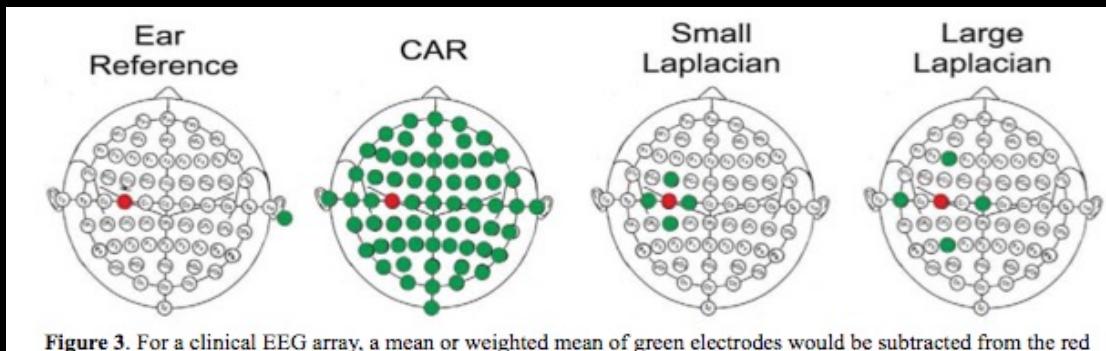
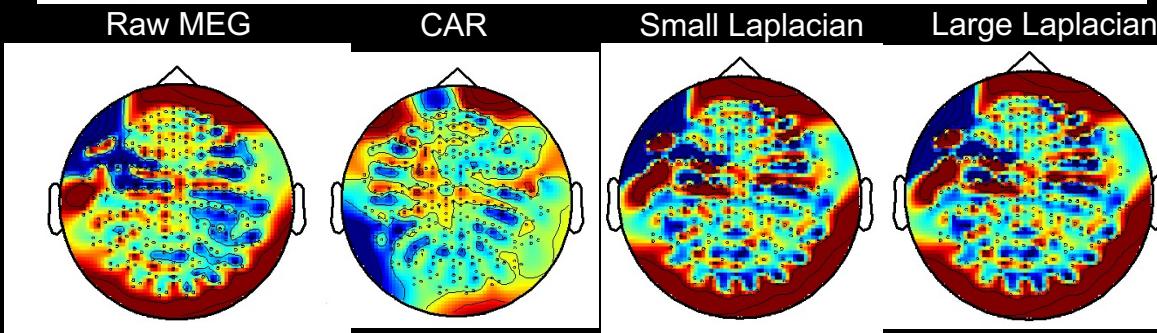


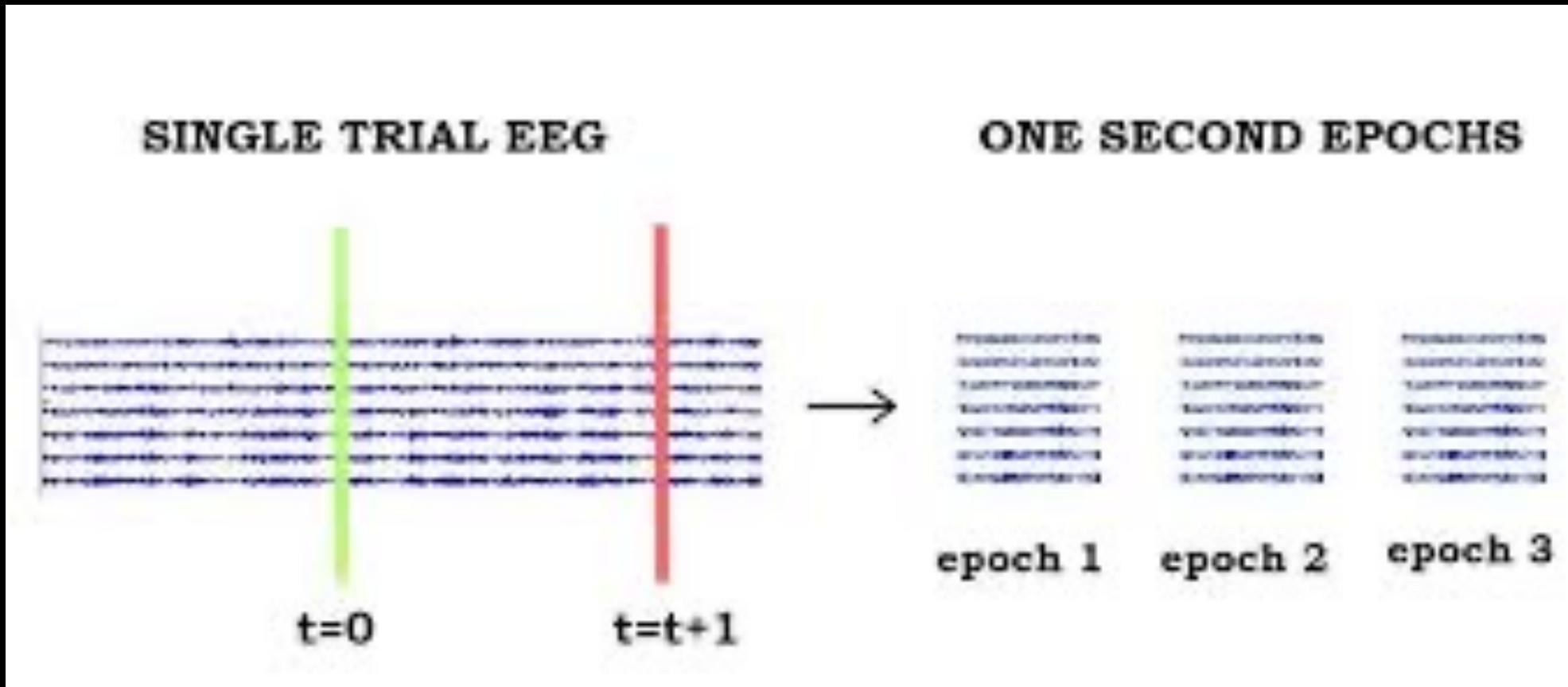
Figure 3. For a clinical EEG array, a mean or weighted mean of green electrodes would be subtracted from the red electrode for each spatial filter listed [7].

McFarland, 1997



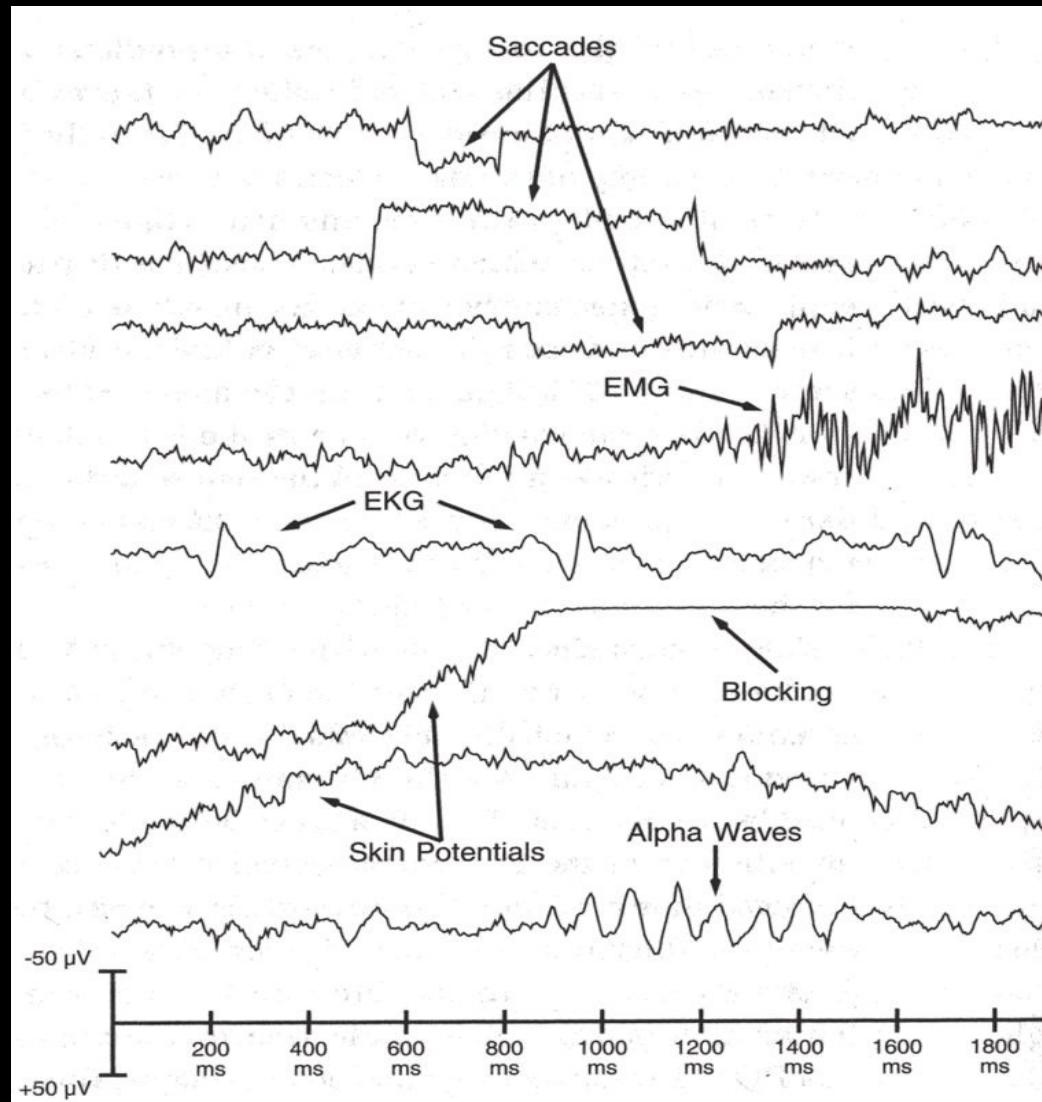
Example of spatial filtering on the resting state signals of the ALS dataset

Pre-processing: Epoching



Pre-processing: Artefact Removal

- Blinks
- Eye-movements
- Muscle activity
- EKG
- Skin potentials
- Alpha waves



Pre-processing: Artefact Removal

- **Blinking**
 - Avoid contact lenses
 - Build ‘blink breaks’ into your paradigm
 - If subject is blinking too much – tell them
- **EMG**
 - Ask subjects to relax, shift position, open mouth slightly
- **Alpha waves**
 - Ask subject to get a decent night’s sleep beforehand
 - Have more runs of shorter length – talk to subject in between
 - Jitter ISI – alpha waves can become entrained to stimulus

Pre-processing: Artefact Removal

EOG/Blinks

- most common contaminants of the EEG signal.

Linear Regression

- The main assumption in this approach is that each EEG channel can be expressed as the sum of noise-free EEG signal and a fraction of the source artifact available through EOG electrodes.
- Let S be the recorded EEG signal which can be expressed as the sum of noise-free EEG signal E and EOG or eye blink signal B multiplied by a weight matrix W .

$$S = WB + E$$

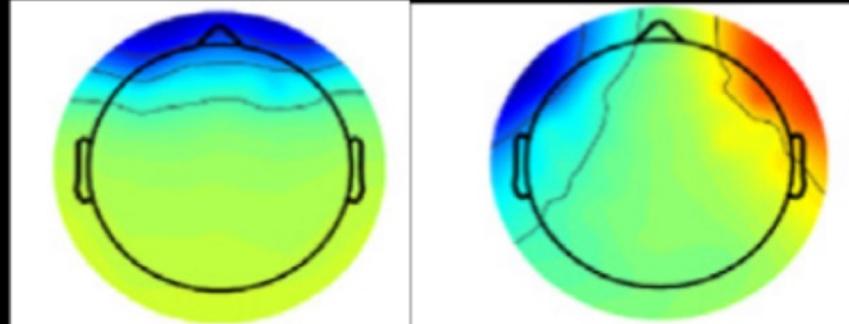
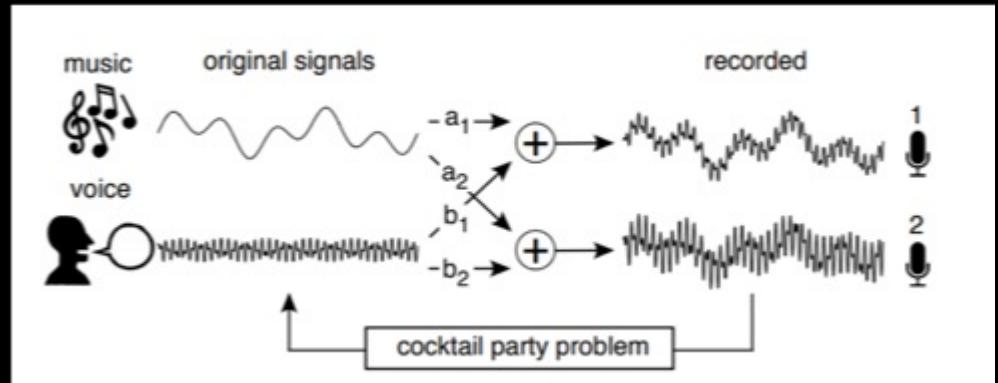
W describes the contribution of the EOG artifact in each EEG channel

Pre-processing: Artefact Removal

EOG/Blinks

ICA

- Independent component analysis (ICA) is a blind source separation (BSS) technique that is widely used in an array of signal processing applications.
- Once the components have been identified, to remove the EOG artifacts, one can visually determine which independent component corresponds to eye-blanks or movements based on the following criteria.

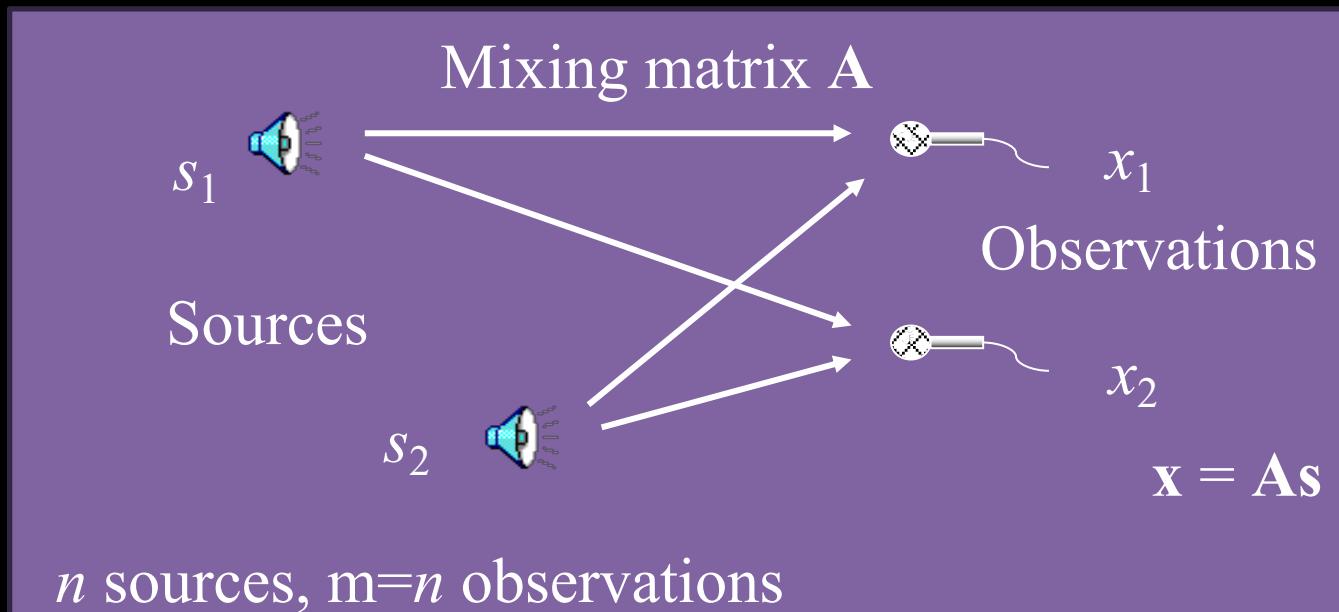


Presence of frontal topography (for blinks, shown on left) and bilateral with opposite sign frontal topography (for horizontal eye-movements, shown in right) in scalp map (adapted from here).

Independent Component Analysis

“Independent component analysis (ICA) is a method for finding underlying factors or components from multivariate (multi-dimensional) statistical data. What distinguishes ICA from other methods is that it looks for components that are both statistically independent, and non-Gaussian.”

A.Hyvarinen, A.Karhunen, E.Oja
‘Independent Component Analysis’

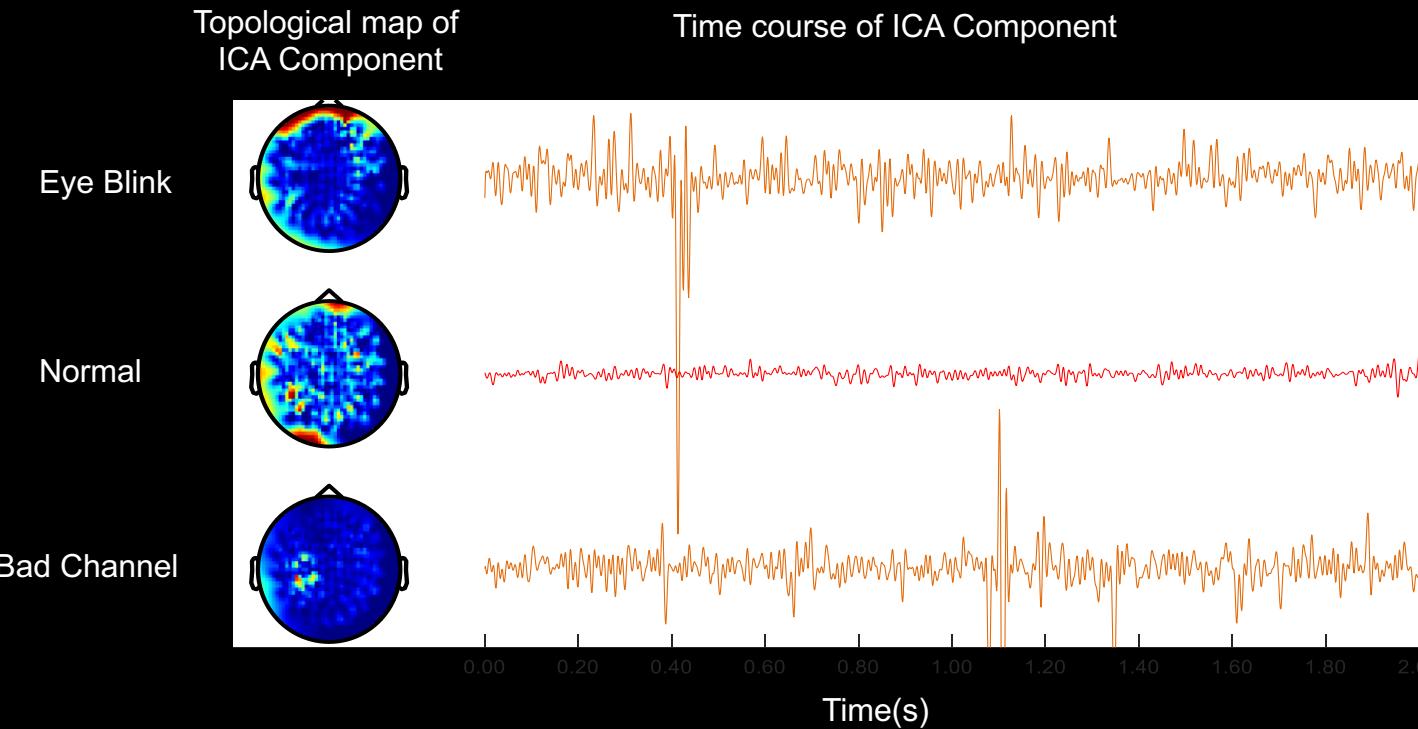


Pre-processing: Artefact Removal

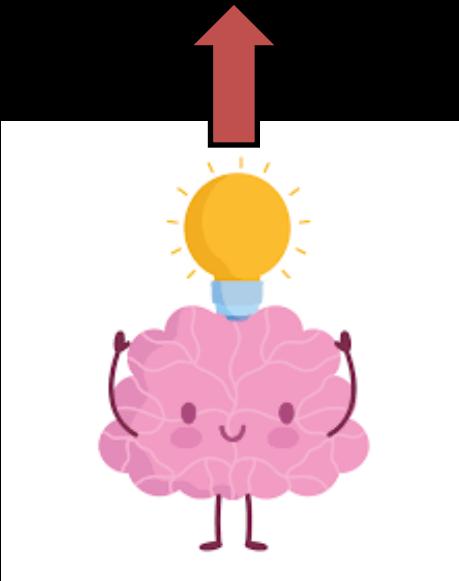
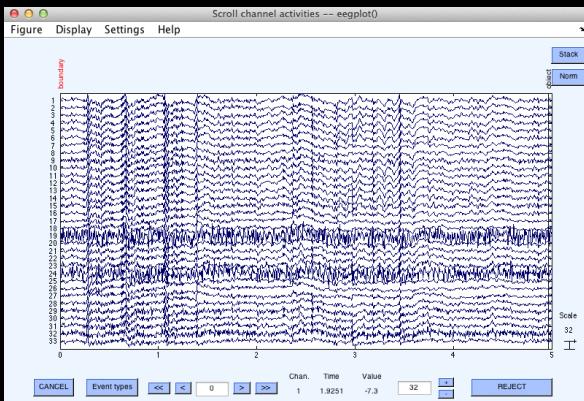
EOG/Blinks

ICA

Example of ICA decomposition from ALS dataset



Processing Pipeline



Pre-processing

Time Consuming
Tedious
Signal Processing
Do it well, Do it once



Processing
(Analysis)

Hypothesis driven
Exploratory
Often done multiple times

Common Brain Signal Analysis

- **Time Domain** – Event-Related Potentials, Amplitude & Latency Measurement, Single Trial Analysis, Cross-Correlation & Coherence
- **Frequency Domain** – Power Spectral Density, Fast Fourier Transform, Spectral Coherence , Cross-Spectral Density , Event related Spectral Perturbation, Band Power
- **Time-Frequency Domain** – Short-Time Fourier Transform, Inter-trial Coherence, Cross-Frequency Coupling
- **Brain and Functional Connectivity**

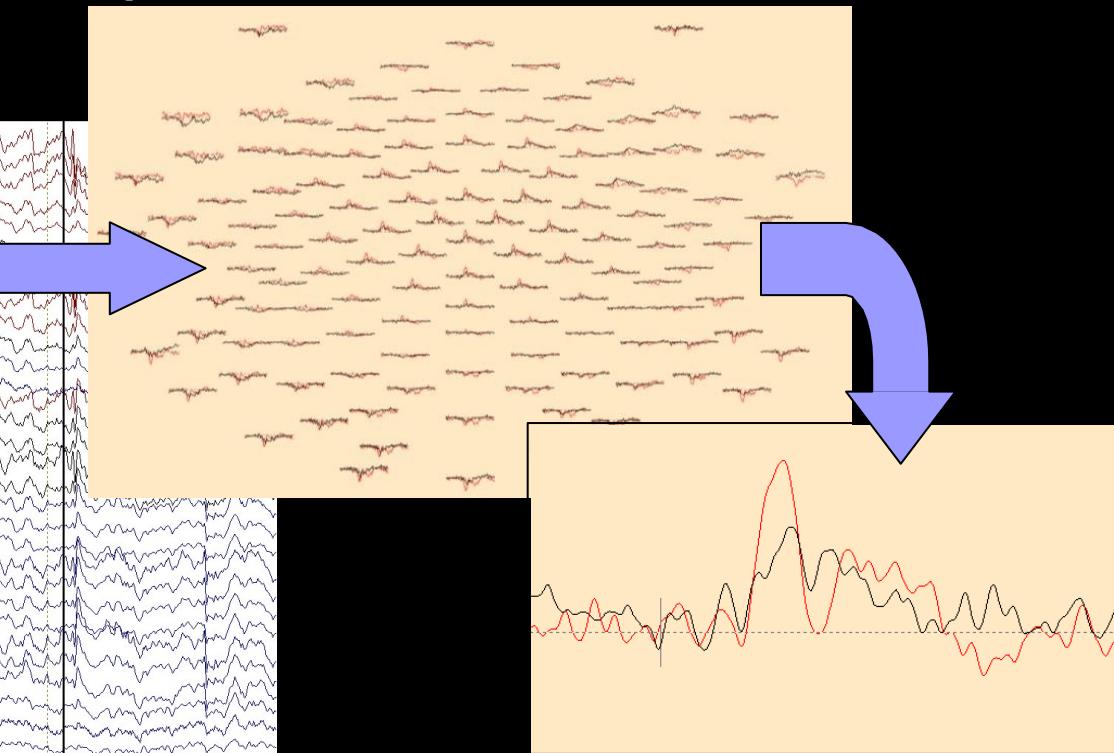
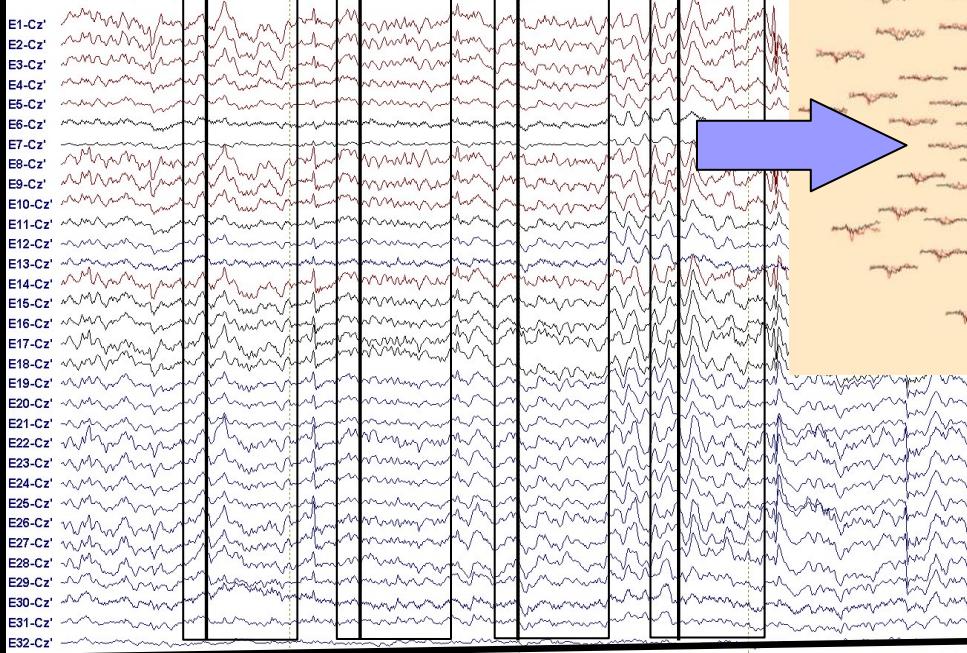
Event Related Potential

- Averaging technique used to study the electrical activity time-locked to an event.
- Needs a considerable amount of trials
- Comprises a mixture of different brain rhythms, depending on the filters applied.
- Only about 20% of the evoked activity is shown
 - Other approaches to study electrical brain activity: Time-frequency analysis

Event Related Potential

Averaged across 100 stimulus presentations

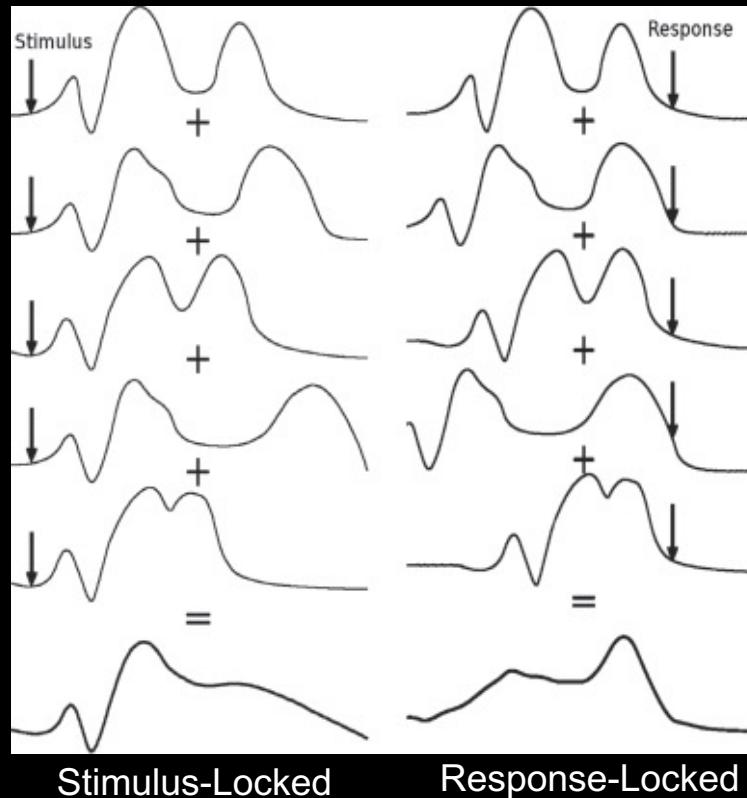
EEG



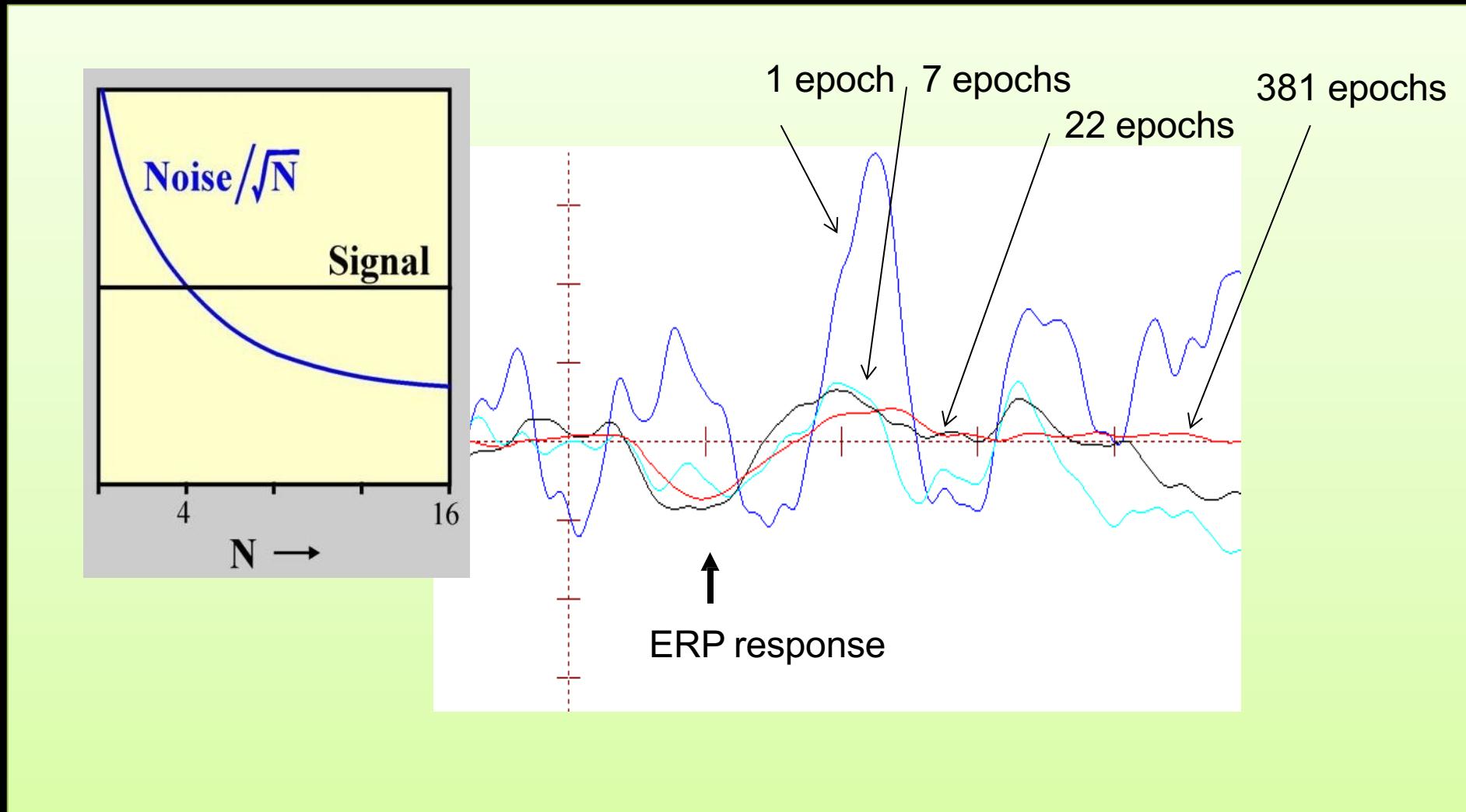
ERP at a single electrode

Event Related Potential

Stimulus-Locked and Response-Locked



Effect of averaging on SNR

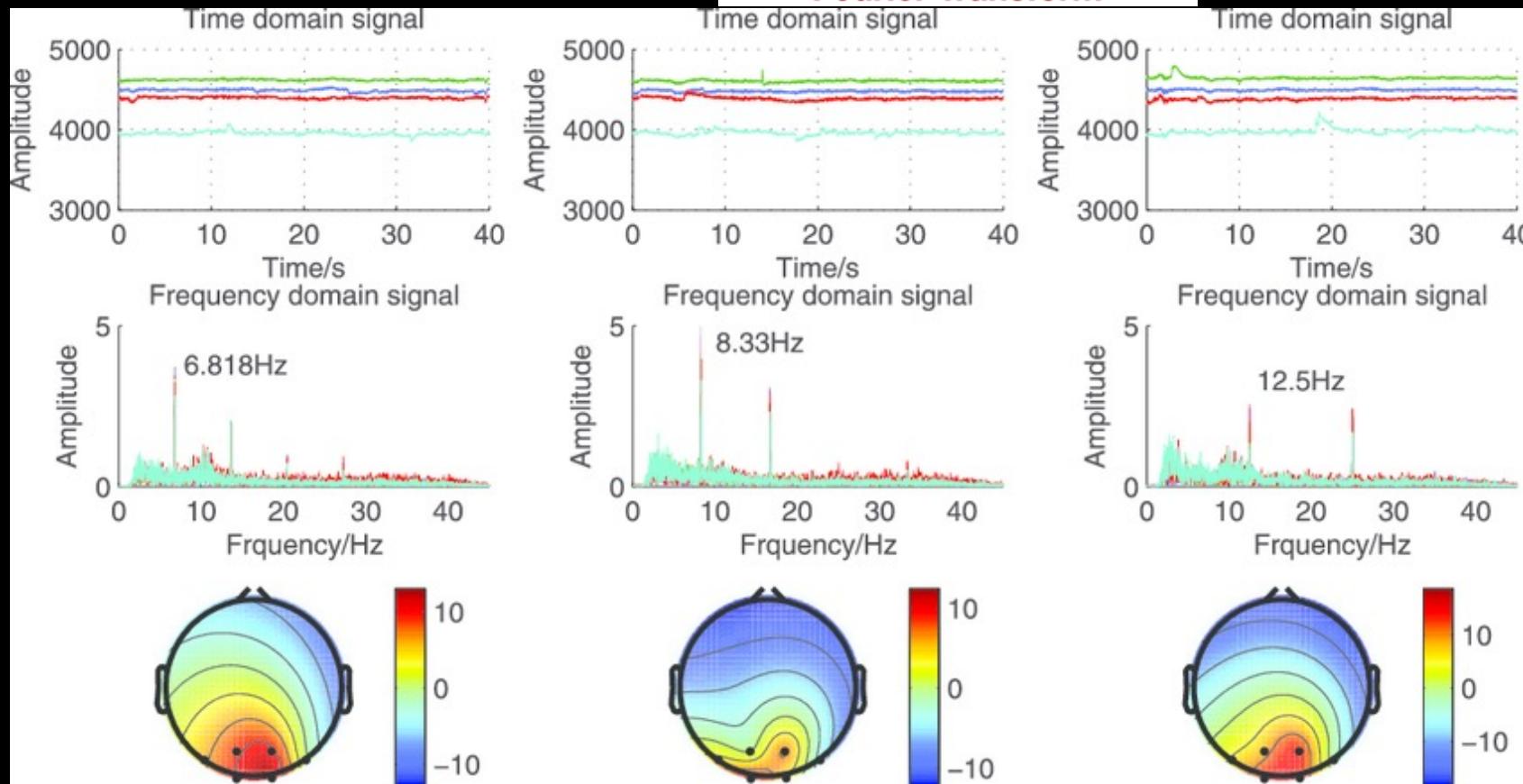


Frequency Domain Analysis

Fourier Transform:

$$F(j\omega) = \int_{-\infty}^{\infty} f(t)e^{-j\omega t} dt$$

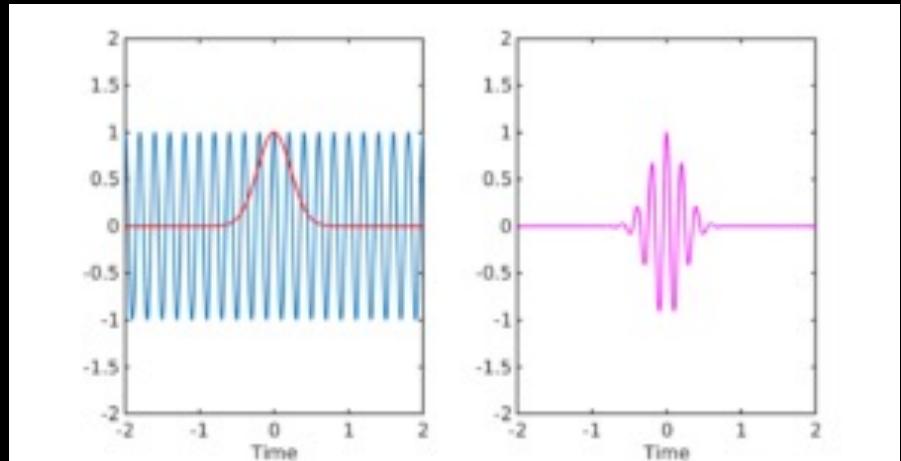
Fourier Transform



Time-Frequency Domain Analysis

Morlet Wavelet

- Wavelets overcome limitations of methods such as the Fourier transform by enabling a view of changes across both time and frequency.
- shape of a sinusoid, weighted by a Gaussian kernel, and they can therefore capture local oscillatory components in the time series.
- Wavelets have variable resolution in time and frequency.

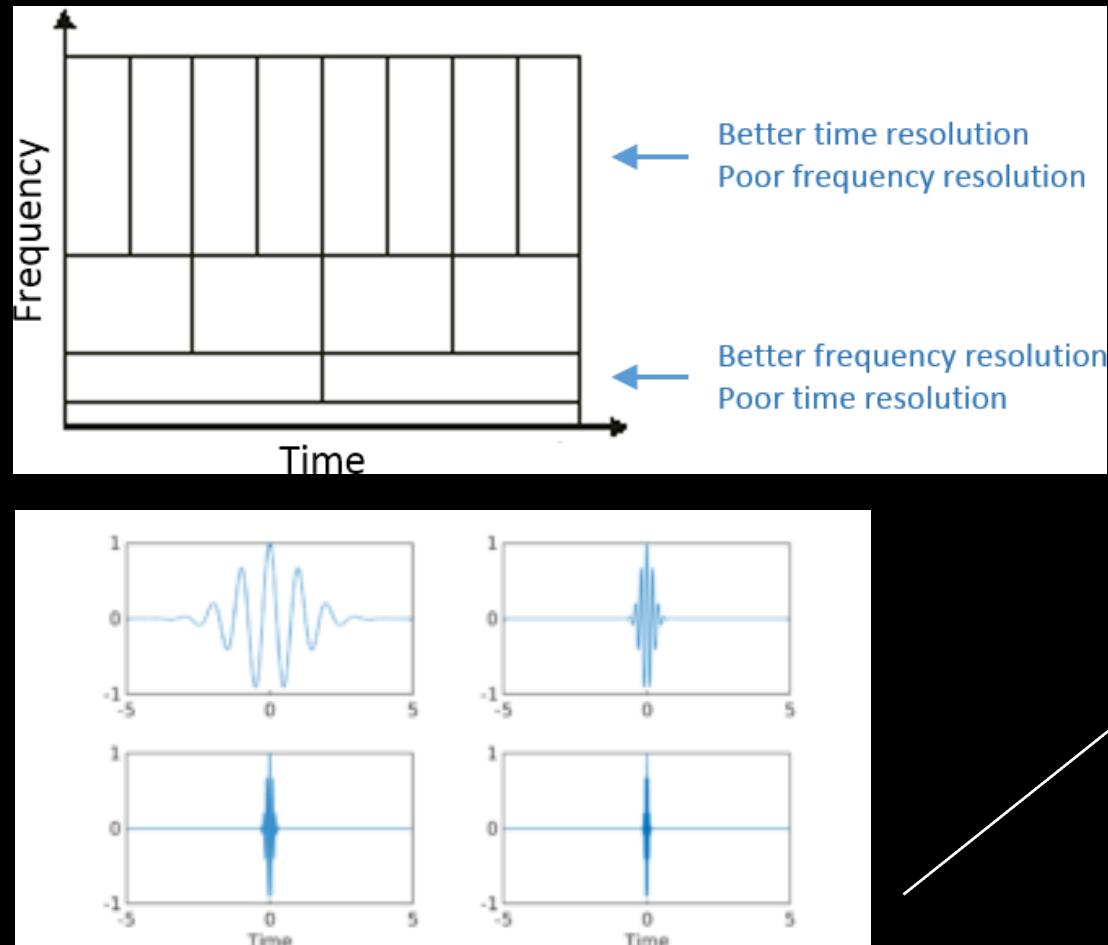


Time-Frequency Domain Analysis

Morlet Wavelet

- Wavelet transformation then essentially involves convolving the complex wavelet with the EEG signal and moving it along the time axis (known as **translation**) and doing this with wavelets of varying frequencies (known as **scaling**).
- **higher frequency** wavelets can achieve **better localization** in time, while **low frequency** wavelets lose some information in time as they are stretched out.

wavelets of frequency 1, 5, 10 and 20 Hz →

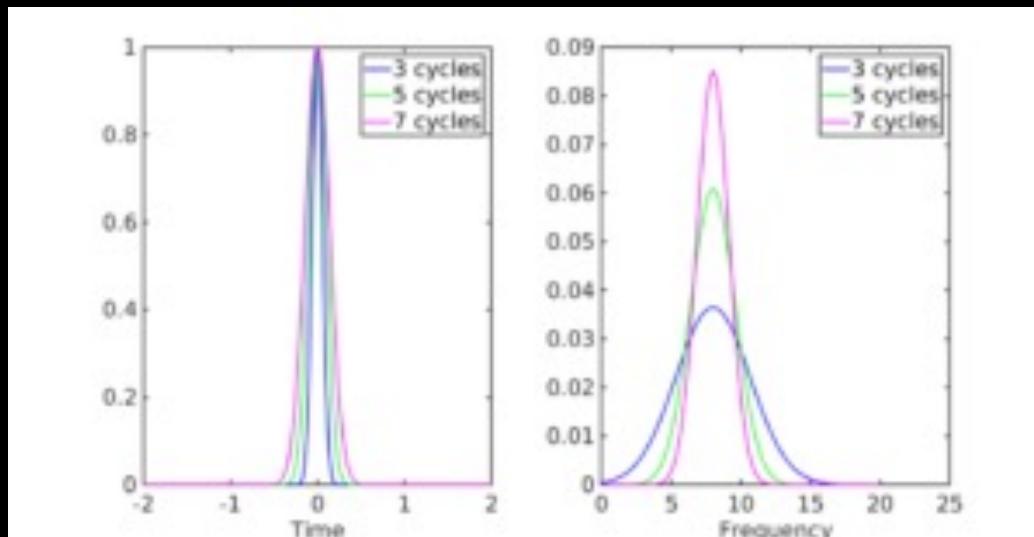


Time-Frequency Domain Analysis

Morlet Wavelet

- Most important parameter-**number of cycles**
- As the number of cycles is increased the width of the Gaussian increases.
- When we take the FFT of these Gaussians, we see that the Gaussian with lower number of cycles is spread more in the frequency domain compared to the Gaussian with higher number of cycles.

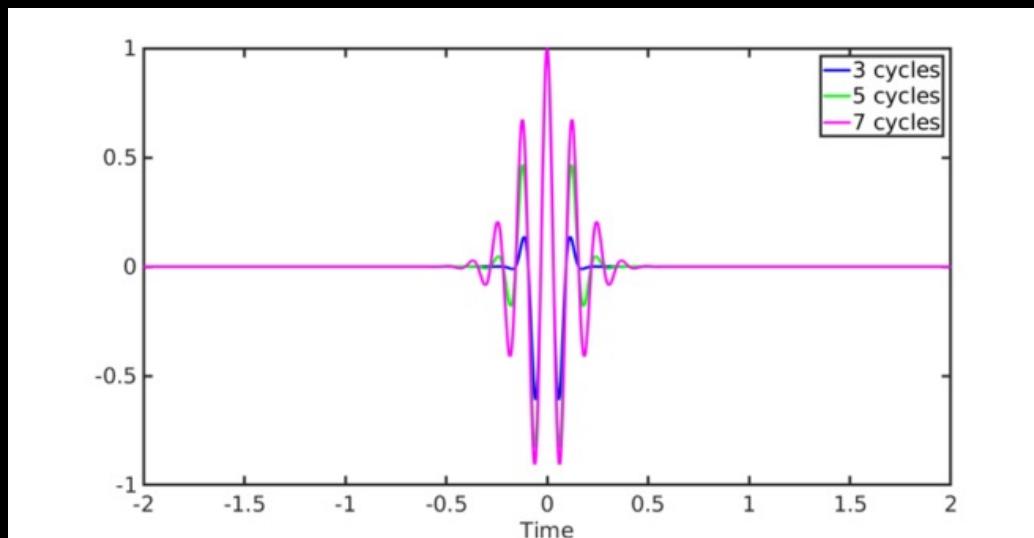
$$\sigma = \frac{n}{2\pi f}$$



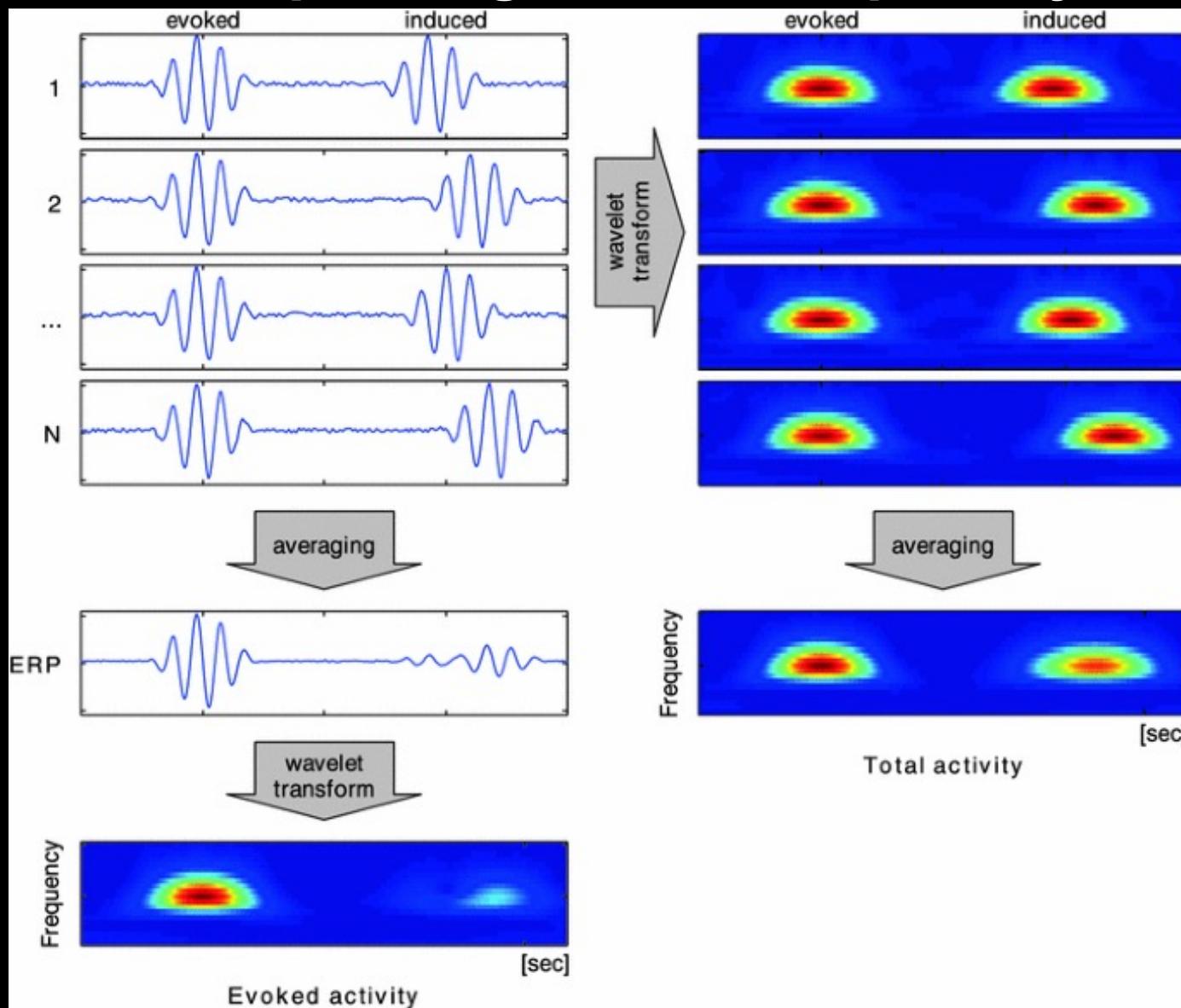
Time-Frequency Domain Analysis

Morlet Wavelet

- **Choosing the number of cycles (n)**
- the wavelet with higher n has wider spread than wavelet with lower n, which can be interpreted as poorer temporal localization as n increases.
- For temporal-focussed analysis, choose lower n
- For frequency-focussed analysis, choose higher n



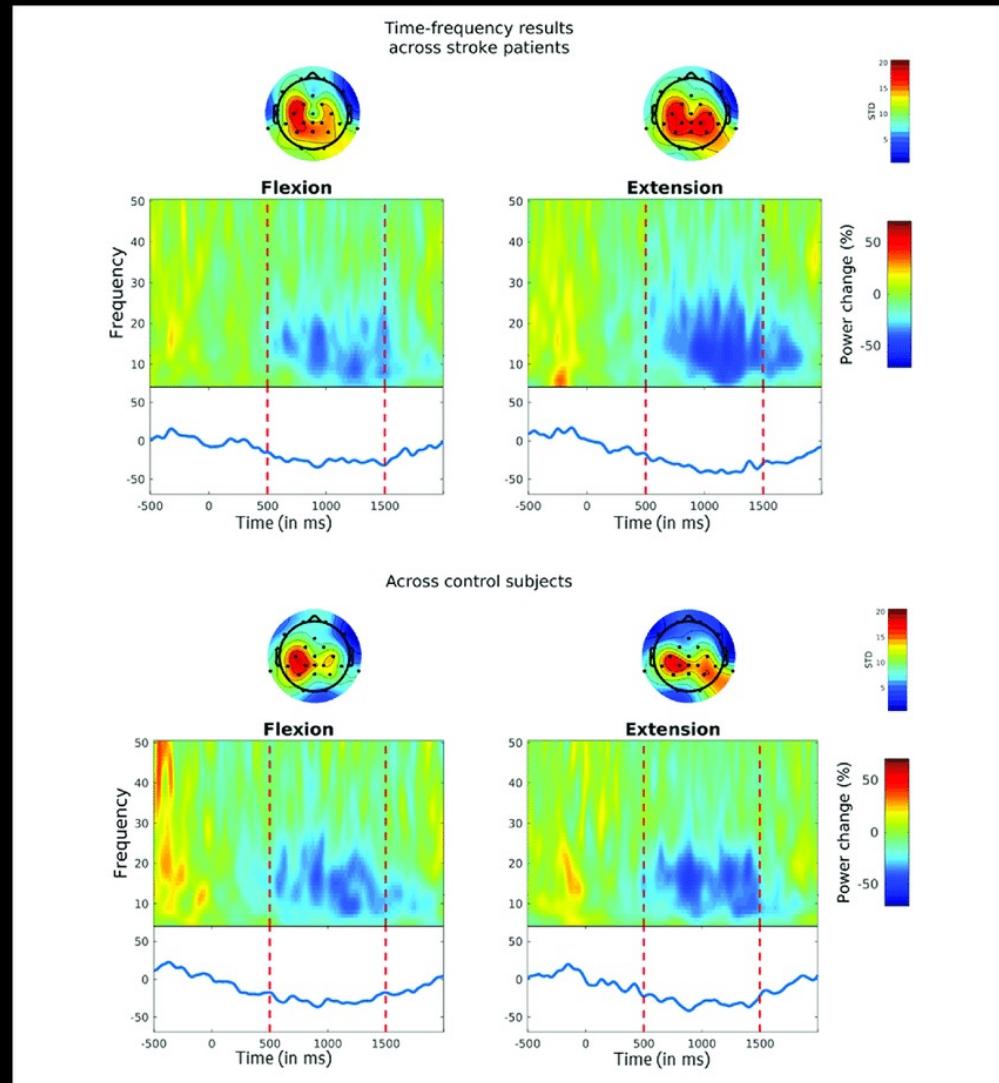
Interpreting Time-Frequency



Hermann et al, 2013

Interpreting Time-Frequency Representation

Event-related desynchronization (ERD) during MI. Time-frequency (TF) plots show the percentage change in power from baseline (i.e. from -0.5 s to 0 s) for MI flexion trials (left panels) and MI extension trials (right panels). MI started at time point zero and was performed for 1.5 s. Vertical lines indicate the chosen time interval for the statistical analysis (i.e. from 0.5 s to 1.5 s). The solid blue line on the bottom reflects MI-related power changes within the 10 – 25 Hz SMR frequency range.



Case Study 1: ALS Detection

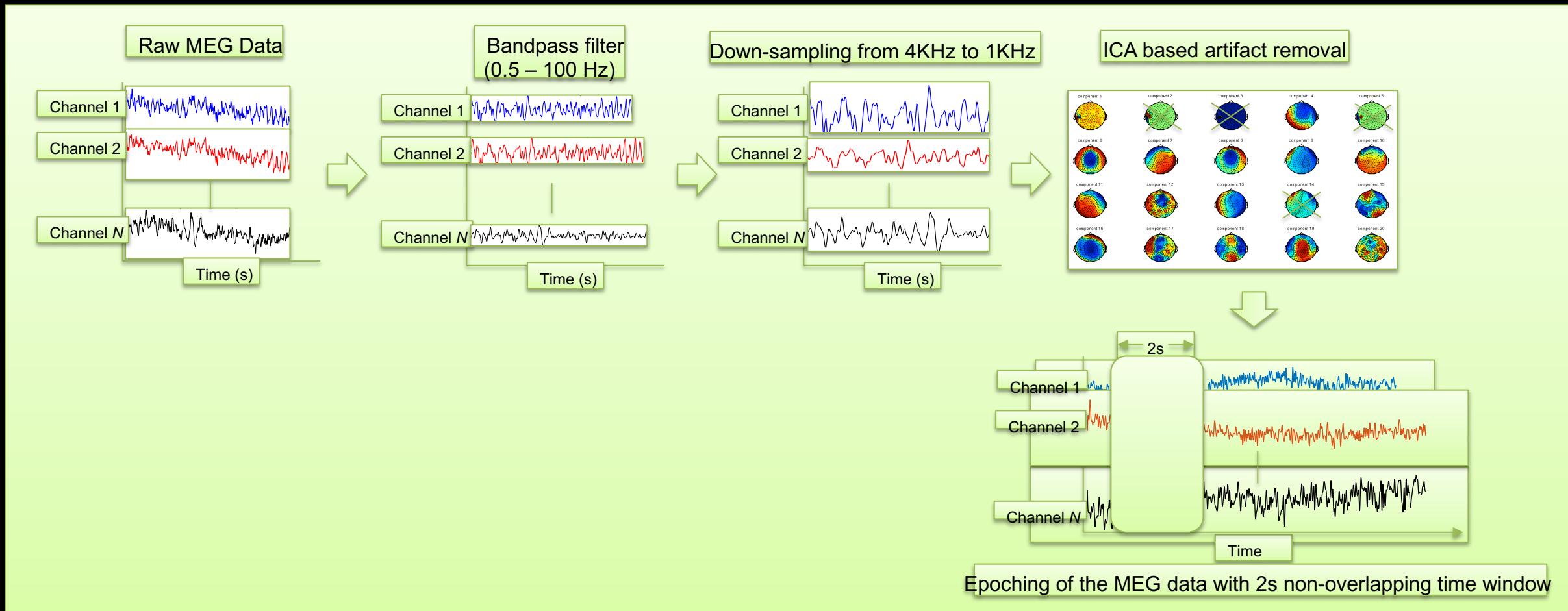
❑ Dataset description

- **26 Healthy individuals (HC) with average age of 60 years**
- **26 ALS patients with an average age of 63.8 years** and an average ALS functional rating scale – revised (ALSFRS-r) score of 39.8.
- **Center for Neuroimaging Research (CENIR), France; ethics committee of Pitié-Salpêtrière Hospital (CPP Ile de-France VI)**
- MEG recording details:
 - Device – Elekta Neuromag
 - Number of Magnetometers (MAG) – 102
 - Number of orthogonal planer Gradiometers (GRAD) – 204
 - Sampling frequency – 4000 Hz
- MEG recording paradigm:
 - Resting state without any motor activity
 - Eye Opened (5 minutes)
 - Eye Closed (5 minutes)



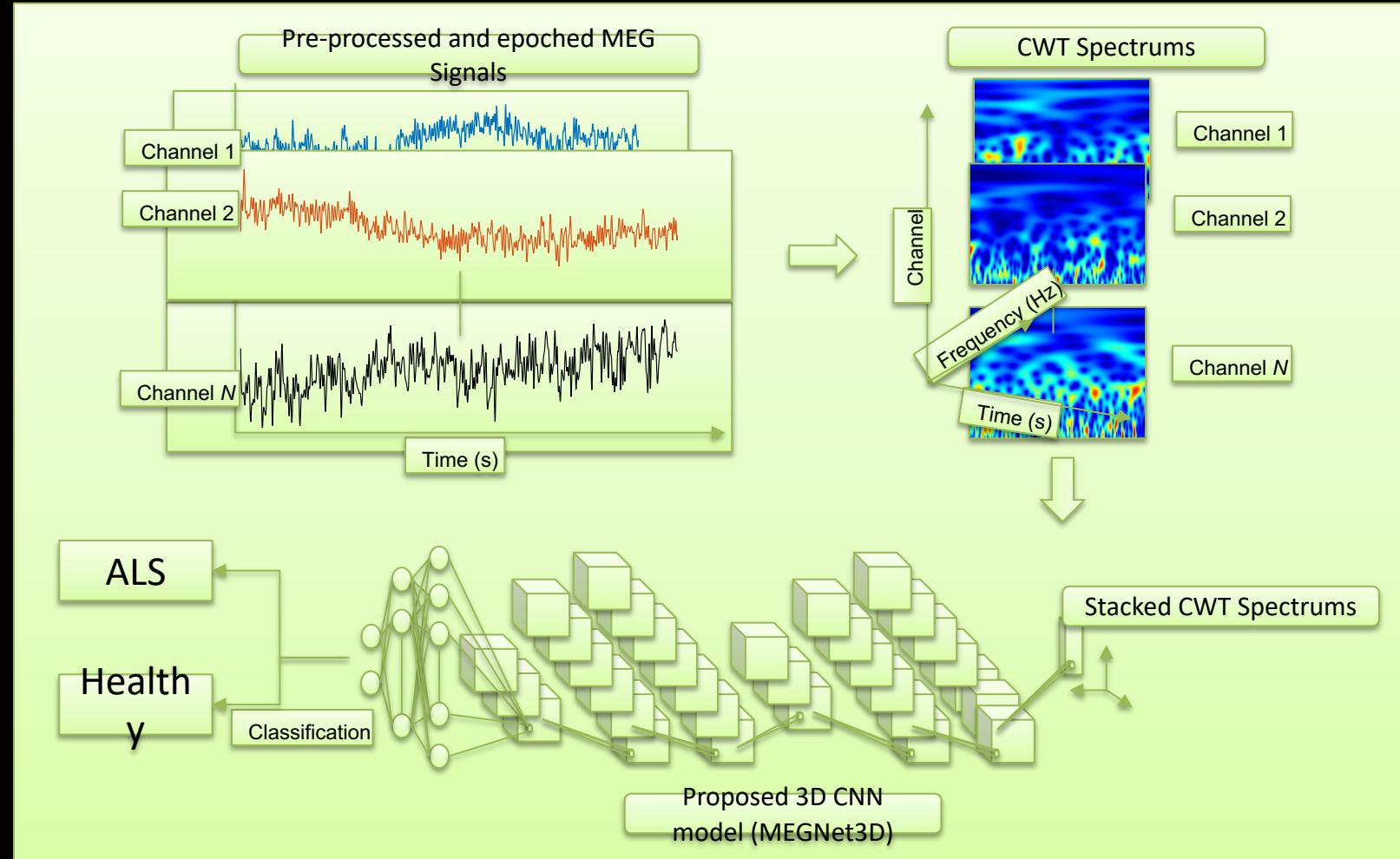
Case Study 1: ALS Detection

□ Data pre-processing pipeline



Case Study 1: ALS Detection

□ Proposed ALS detection framework



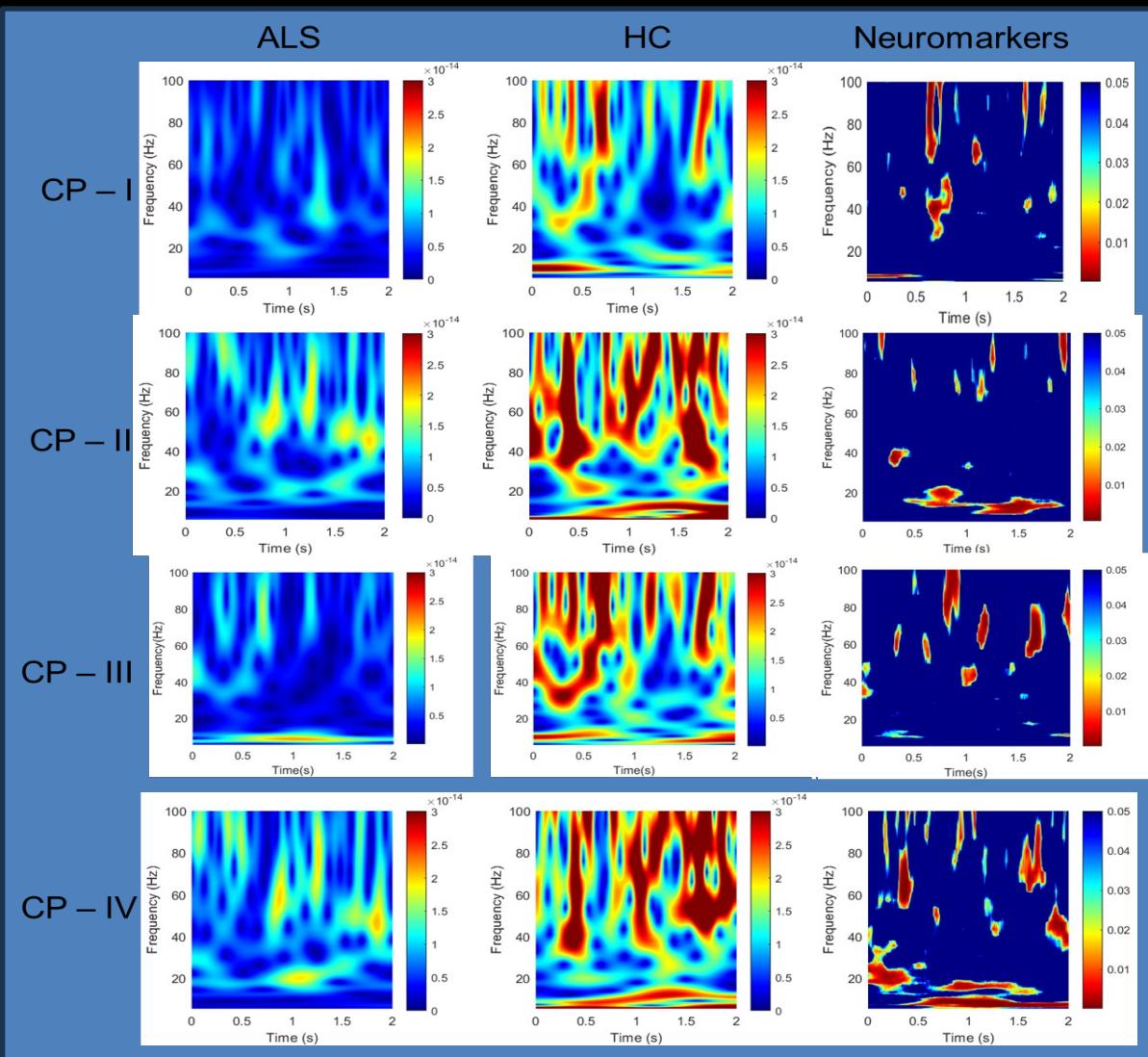
Case Study 1: ALS Detection

□ Time Frequency Analysis

Table: Different Classification Problems

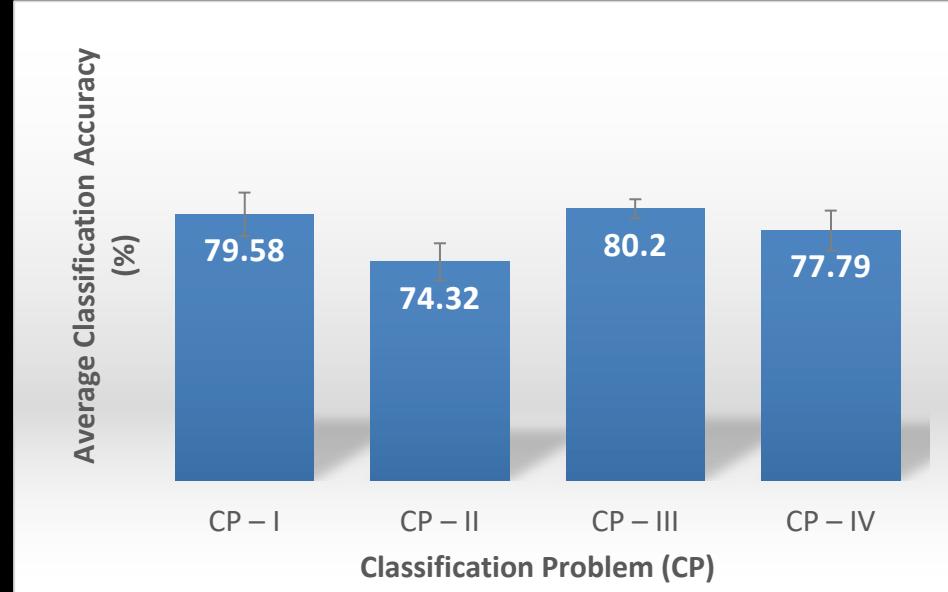
Classification Problem (CP)	Sensor Type	Eyelid Position
CP - I	MAG	Eye Closed
CP - II	MAG	Eye Opened
CP - III	GRAD	Eye Closed
CP - IV	GRAD	Eye Opened

Figure: CWT spectrums from the central motor cortex region (Cz area) for HC and ALS patients



Case Study 1: ALS Detection

□ Classification Result



Case Study 1: ALS Detection



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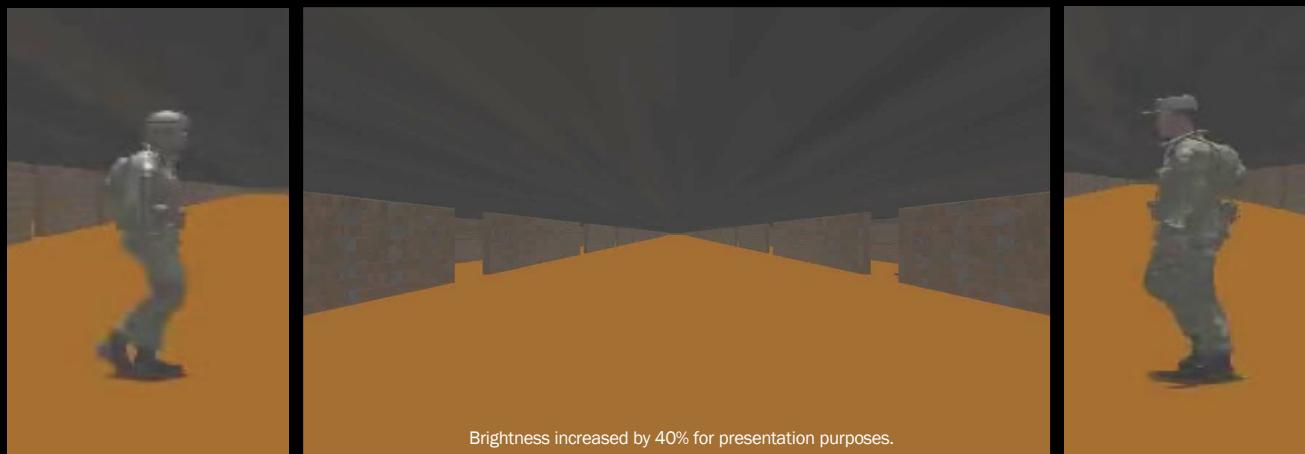
Dr. Muskaan Singh,
Lecturer in Data Analytics
Intelligent System Research
Center,
Ulster University, UK
Email: m.singh@ulster.ac.uk



Case Study 2: Anytime Collaborative BCI

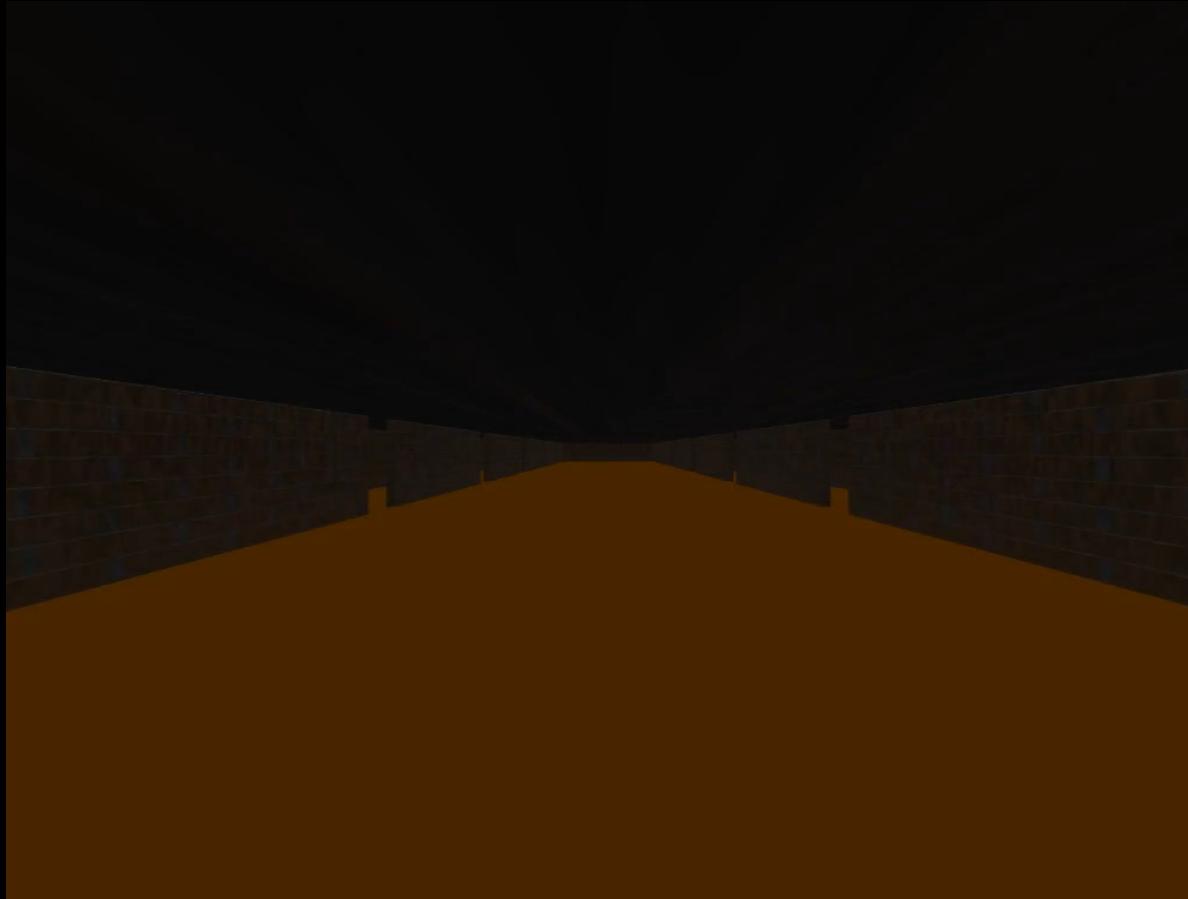
□ Dynamic Environment- Patrol Experiment

- We generated a **dynamic environment** where a soldier is walking along a corridor with multiple doorways present on both sides (**Corridor/Patrol Experiment**)
- **Task:** Decide whether the characters appearing wear a helmet or a cap



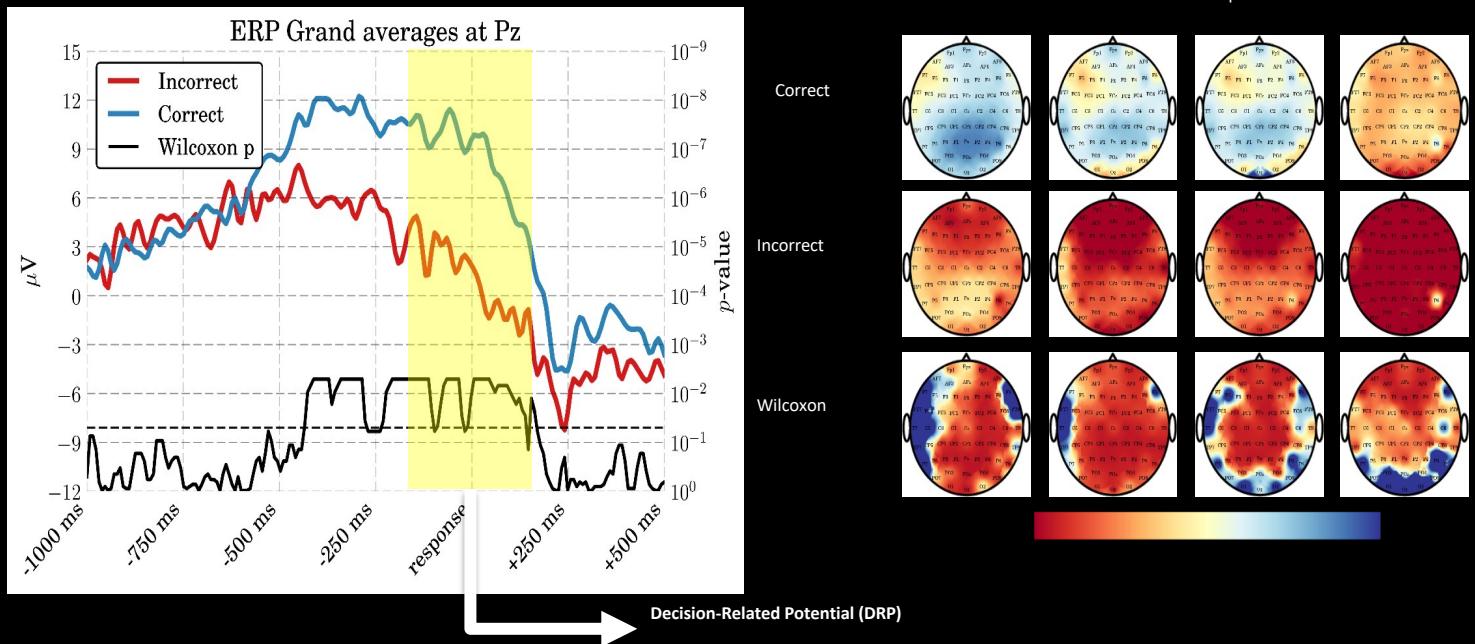
Bhattacharyya et al., NER'19,
Bhattacharyya et al. Scientific
Report (2021)

Case Study 2: Anytime Collaborative BCI



Case Study 2: Anytime Collaborative BCI

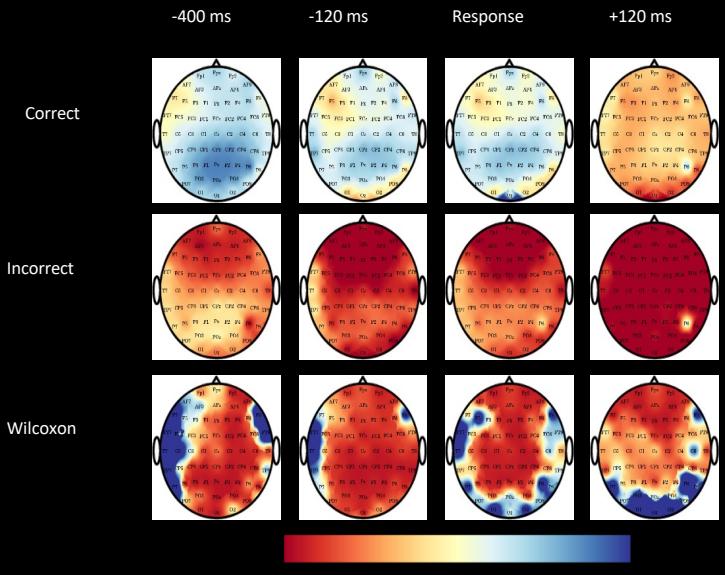
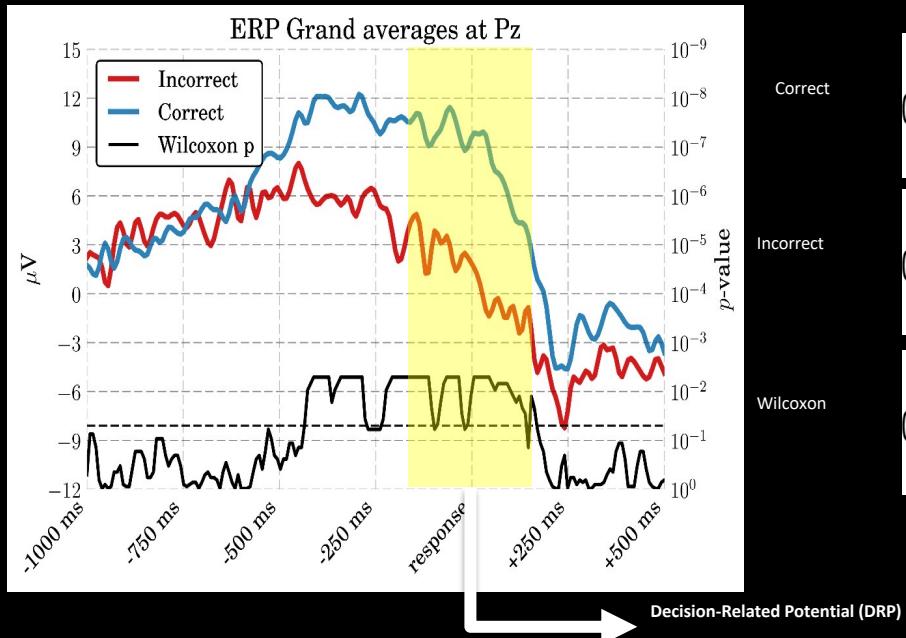
Evidence of Neural Marker



Bhattacharyya et al. Scientific Report (2021)

Case Study 2: Anytime Collaborative BCI

Evidence of Neural Marker



Designing more complex experiments

Dynamic Environment- Outpost Experiment

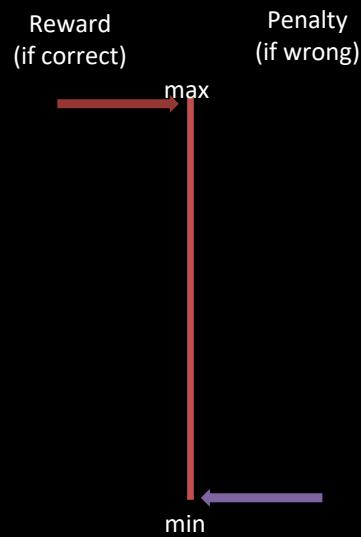
- User stationed at an outpost.
- Observes a character moving in.
- **Task:** decide whether the person is wearing a helmet or a cap, Report self-confidence
- **Reward and penalties** proportional to the correctness of the decision and the time taken by the user to respond



Bhattacharyya et al. Scientific Report (2022)

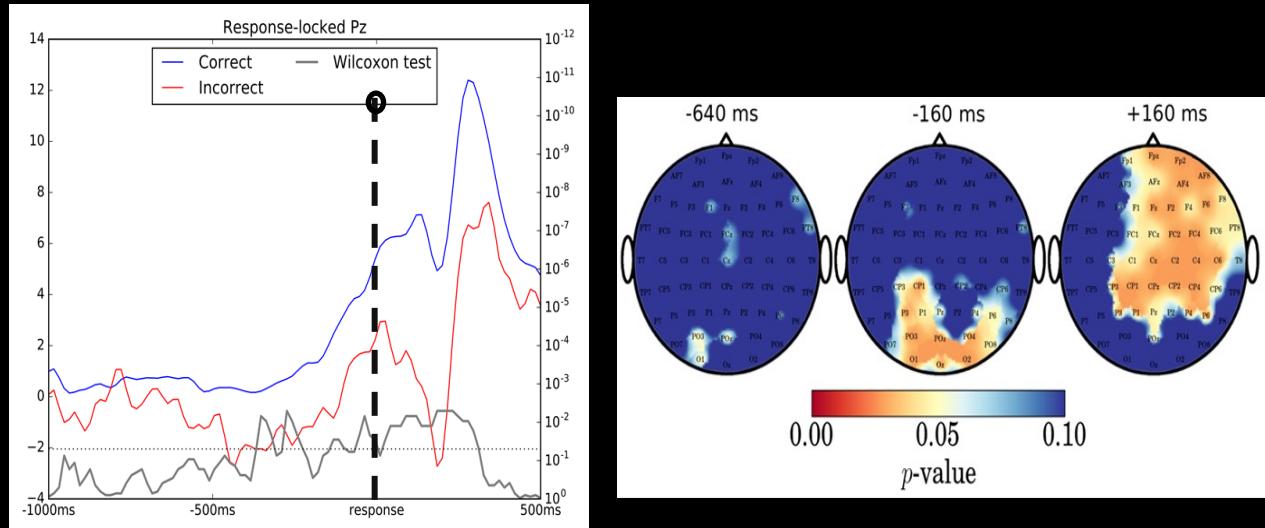
Reward system

- **Reward system:** The faster the response, the more points you score (for a correct response).



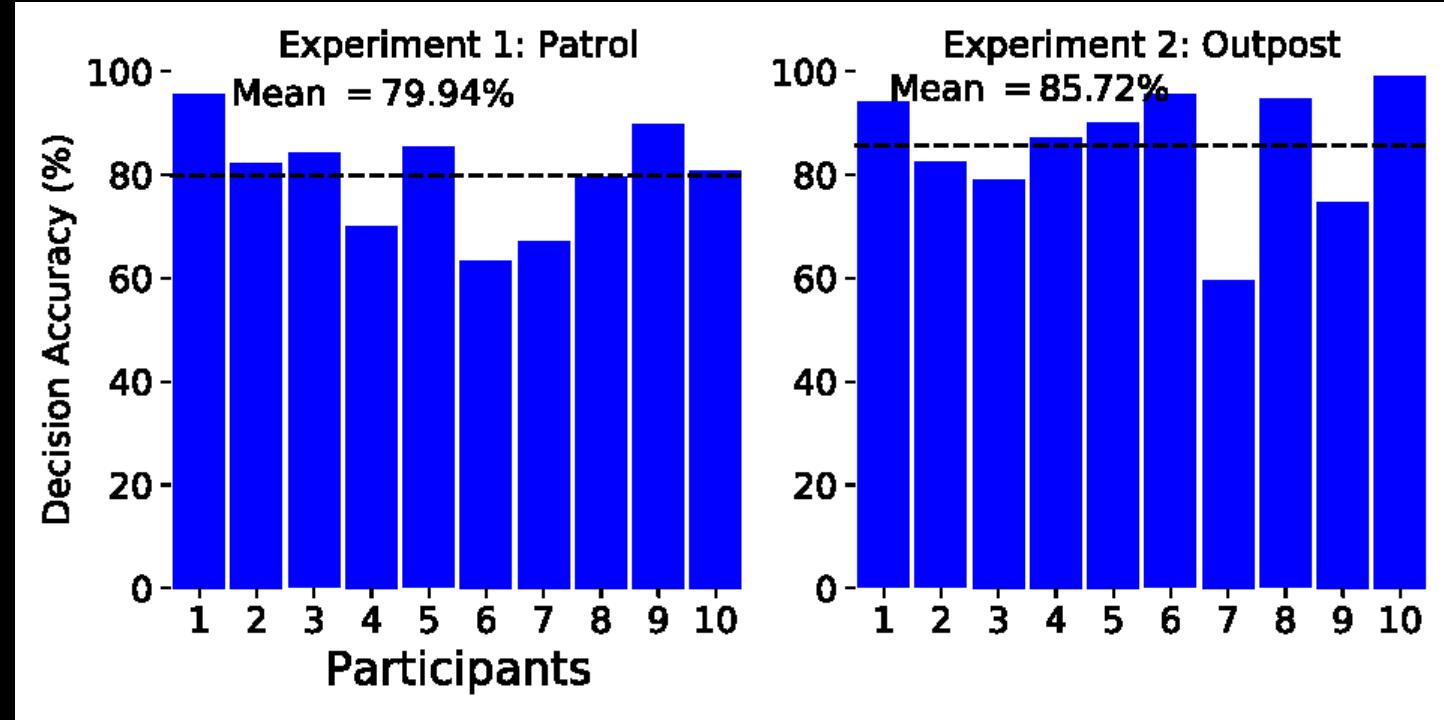
Bhattacharyya et al. Scientific Report (2021)

Similar but weaker neural markers



Bhattacharyya et al. Scientific Report (2021)

Decision accuracy is...

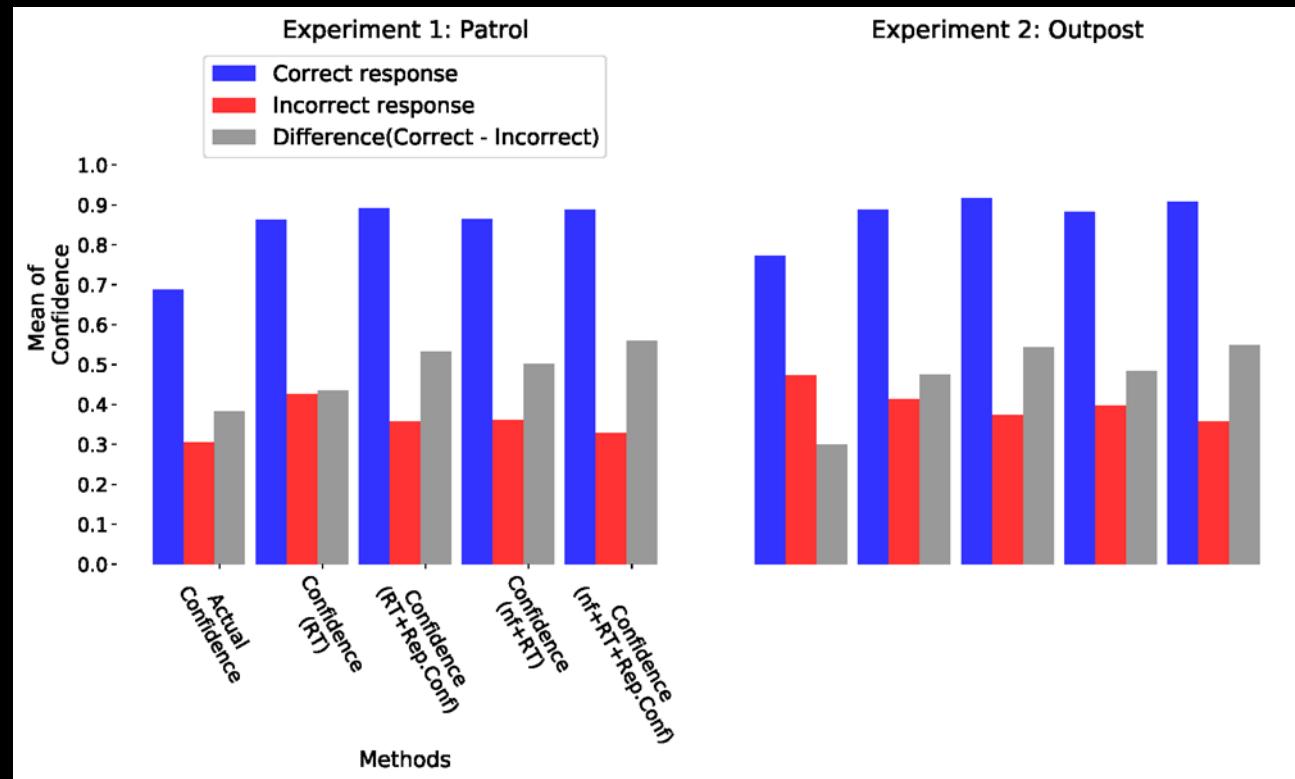


Bhattacharyya et al. Scientific Report (2021)

Subjective and objective confidence

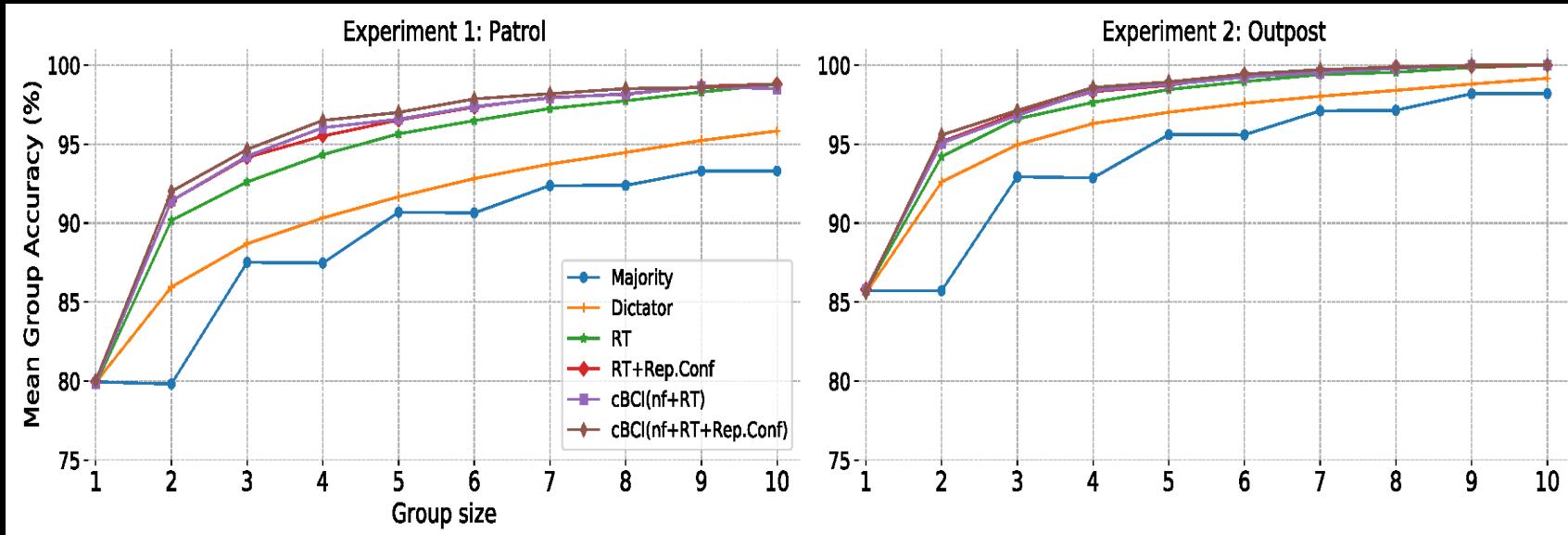
Objective confidence using-

- Only RT
- RT + Reported Confidence
- Neural Features + RT
- Neural Features + RT + Reported Confidence



Bhattacharyya et al. Scientific Report (2021)

cBCI works better



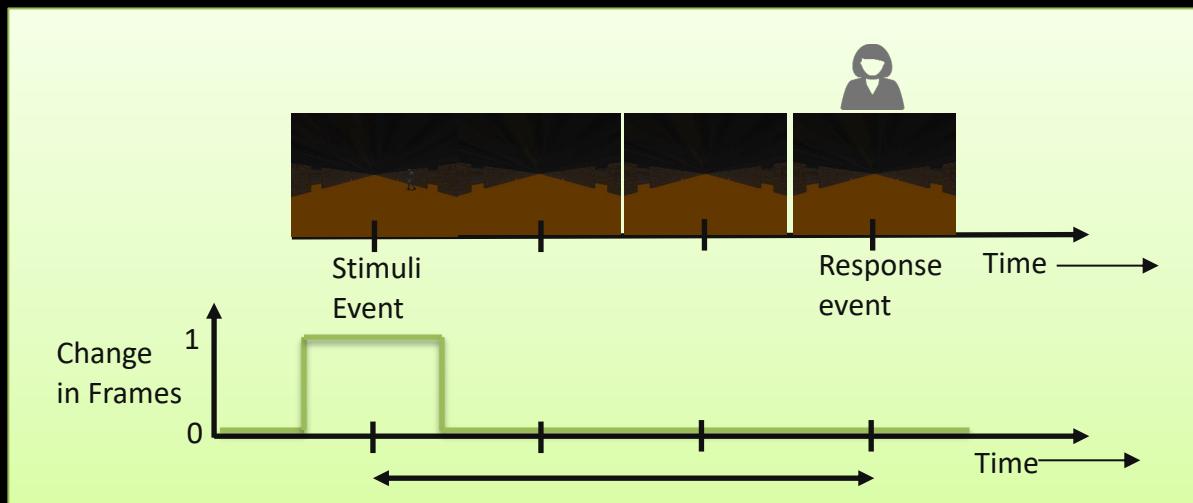
Bhattacharyya et al. Scientific Report (2021)

Towards Anytime cBCI

Reconstructing the response times

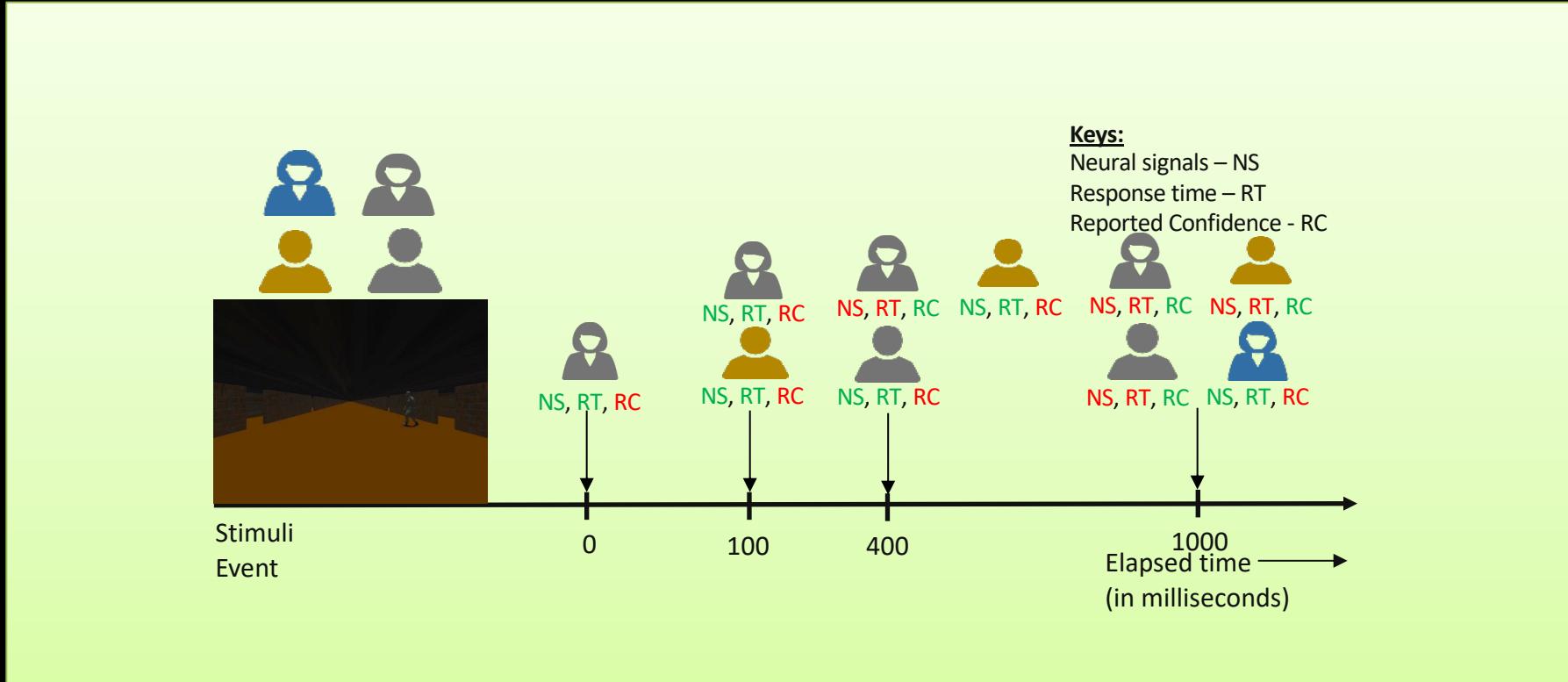
- **Key issue:** In real life we know when a participant has a reaction (button press) but we don't know what caused it and when. So, **RT is not readily available.**
- Implemented an **automated system** to detect a **sudden change in video frames** preceding the user's response.

sudden change frame \cong stimulus onset



Bhattacharyya et al. Scientific Report (2021)

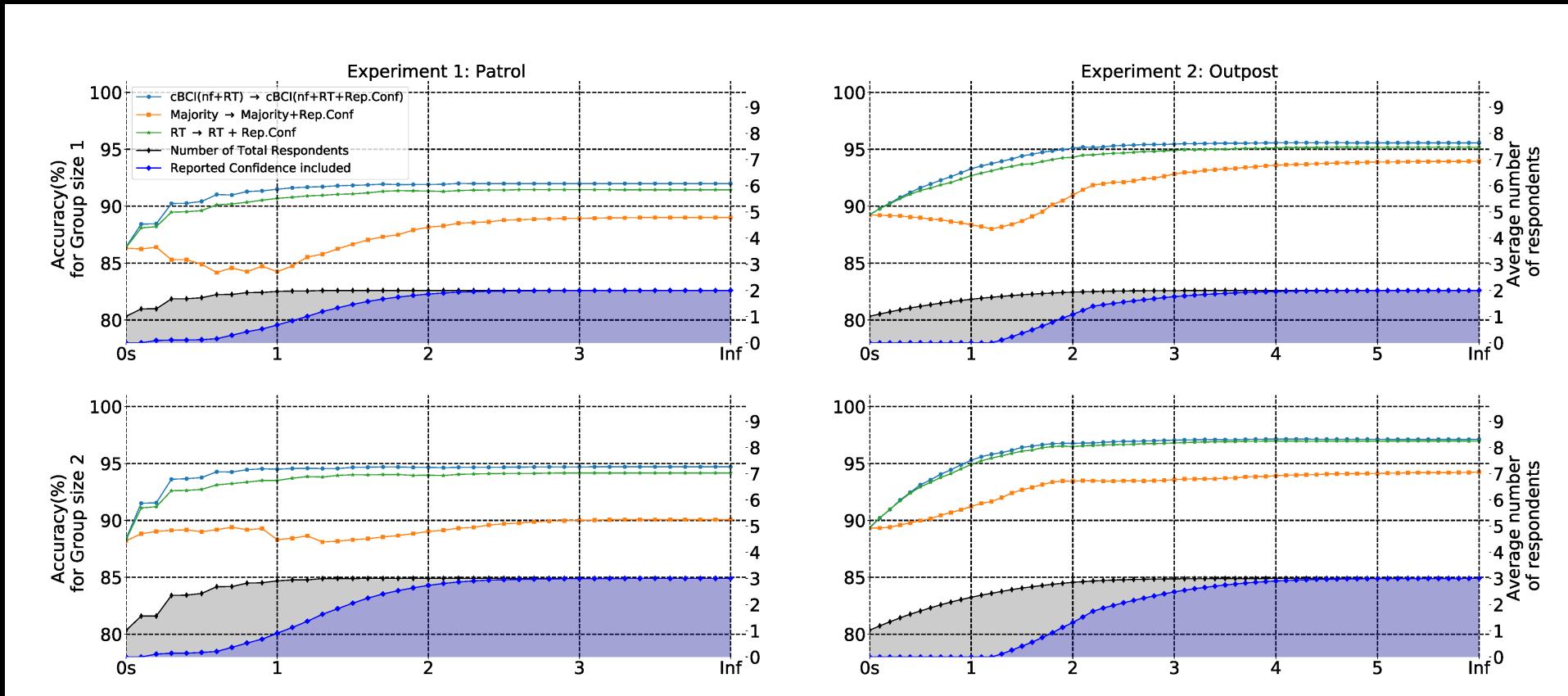
The anytime cBCI



At **every 100ms** after the first response, the system searches for other members in the group who has responded.

Bhattacharyya et al. Scientific Report (2021)

Optimal time vs accuracy

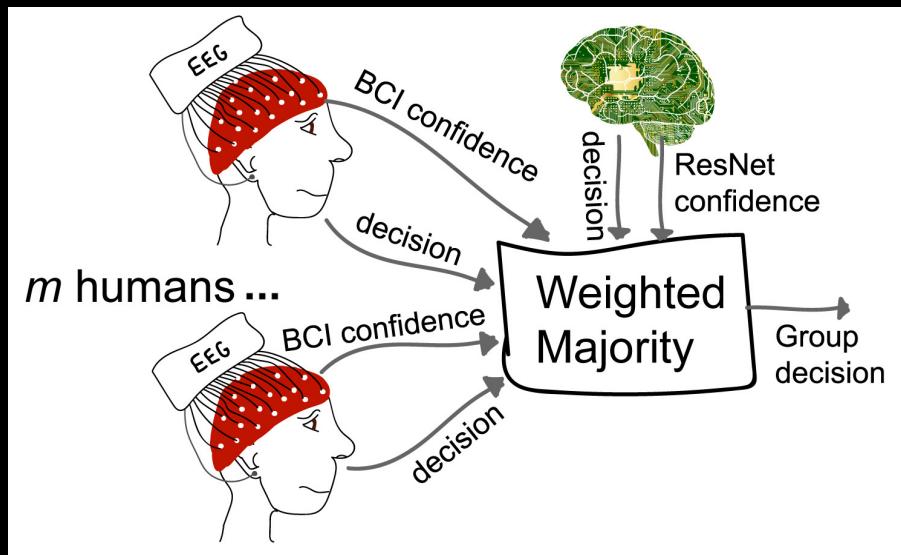


- Interestingly, after a rather rapid transient, accuracy tends to plateau.
- Near optimal decisions can be obtained well before all participants have responded and reported their confidence.

Human-Machine teaming-preliminary work

What happens if we replace some human team members with **artificial intelligence (AI) agents?**

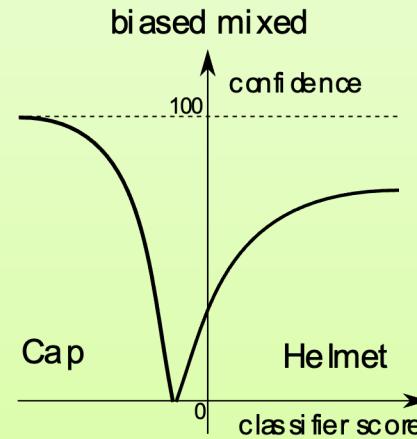
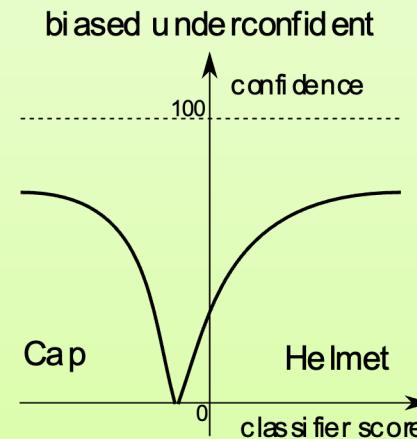
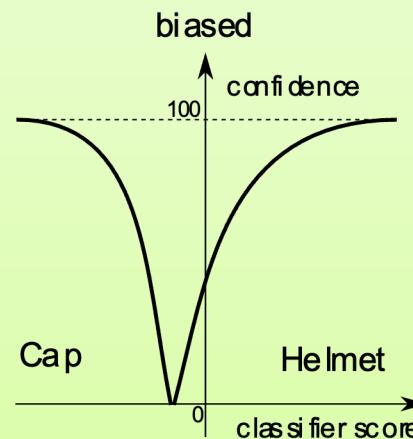
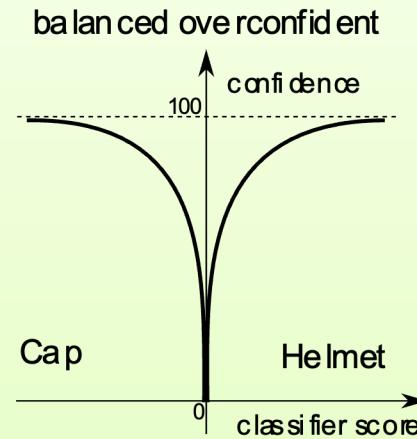
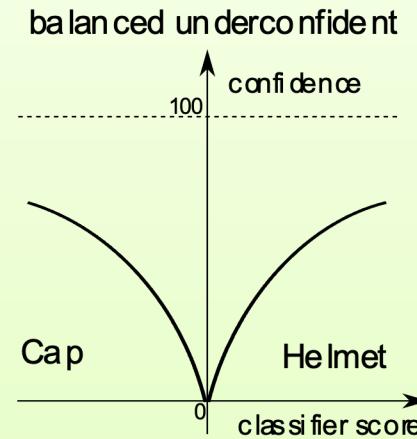
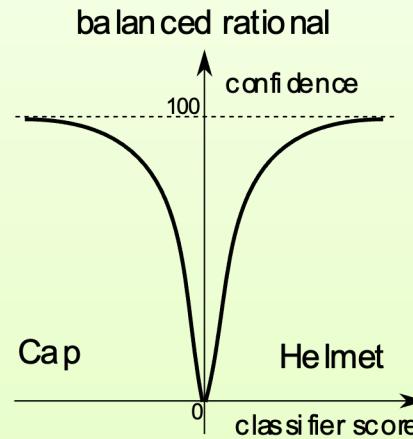
AI as additional team member



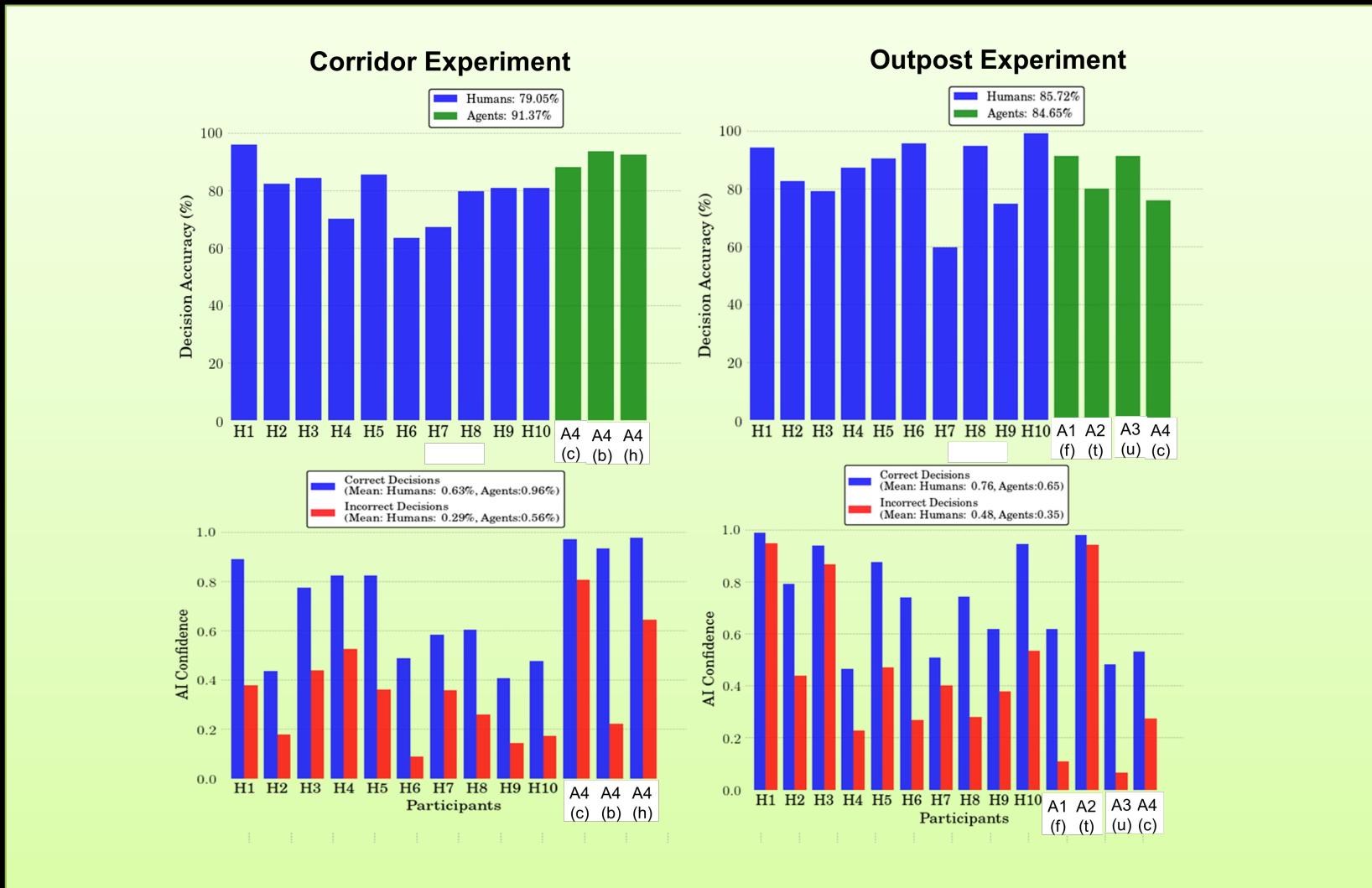
Re-simulating the patrol and outpost experiment

Valeriani et al. PlosONE (2019)

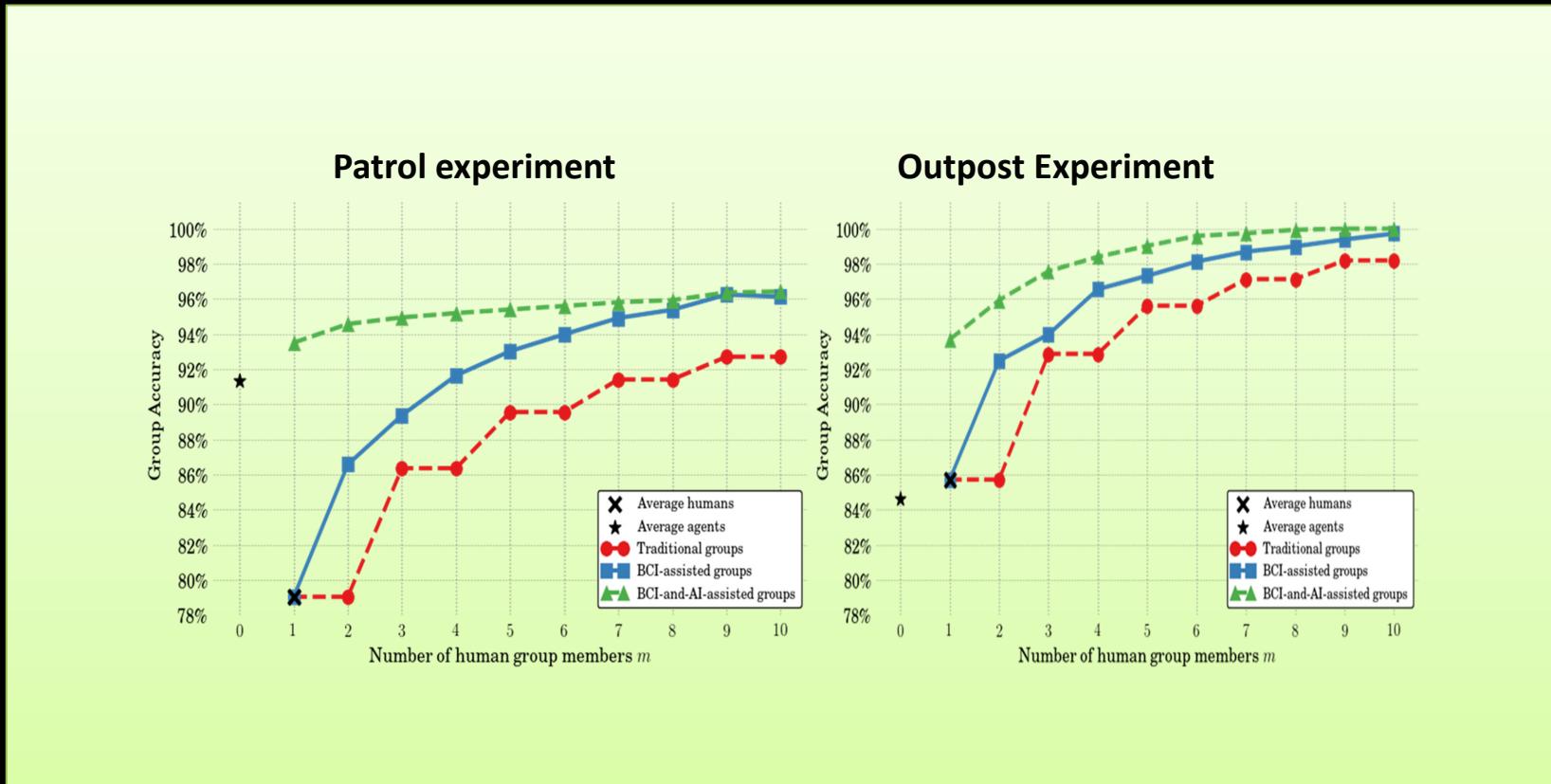
Confidence functions for AI



Behavioral results of humans and agents



group results of humans and agents



Thanks to...

DSTL (UK Ministry of Defense) – TIN and BARI project

US Department of Defense – BARI Project

Collaborators



Riccardo Poli



Luca Citi



Caterina Cinel



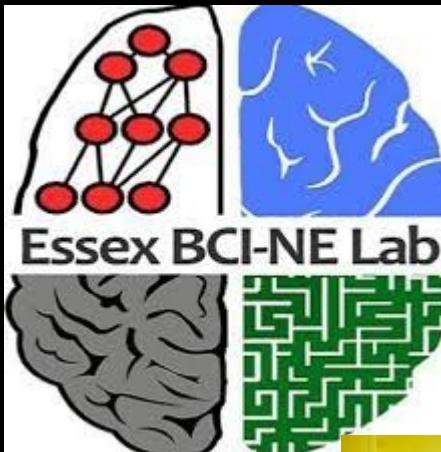
Davide Valeriani



Jacobo
Fernandez-
Vargas



Christoph
Tremmel



THANK YOU FOR LISTENING

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Take-home message

