Ulster
University

Decoding the Brain: Neural Signal Processing and Connectivity Analysis for a Neurotechnologist

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We will learn about…

- **Brain-Computer Interfacing**
  - Applications
  - Pipeline
- **Recording Techniques**
- **Pre-processing Neural Data**
- **Removing Artefacts**
- **Event Related Potentials**
- **Time-Frequency Analysis**
- **Source Reconstruction & Brain Connectivity**
- **If time permits, My work Collaborative BCI on Decision Making****

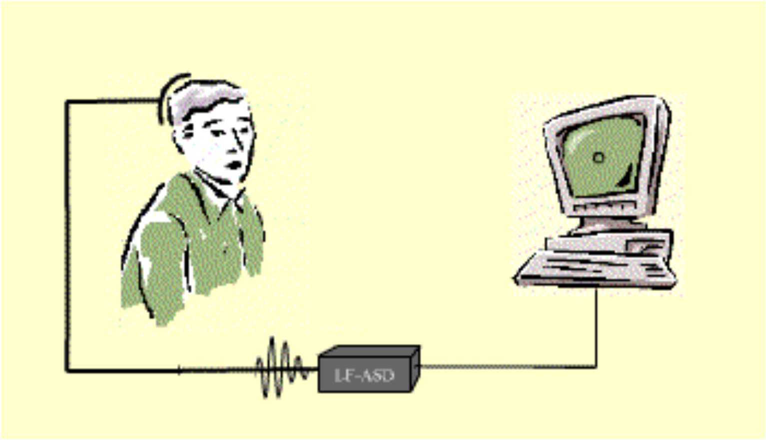
Brain-Computer Interfacing

Section

Brain-Computer Interfacing

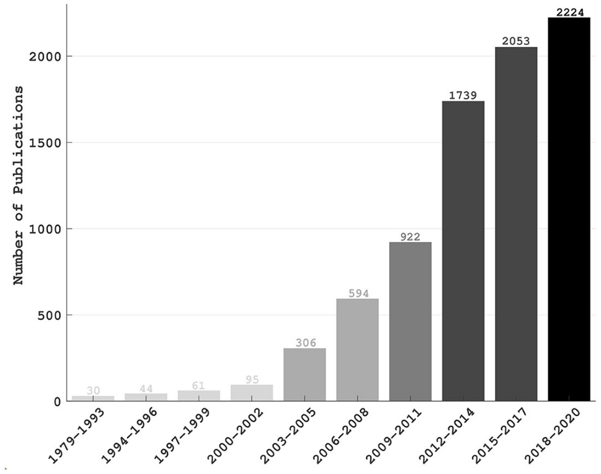
- *" A Brain-Computer Interface is a communication system that do not depend on peripheral nerves and muscles"* [Wolpaw et al. 2000]

- 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

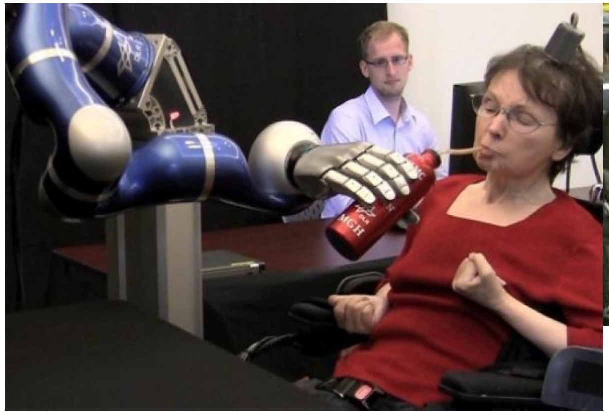
Began in the 1970s → Jacques Vidal (UCLA)



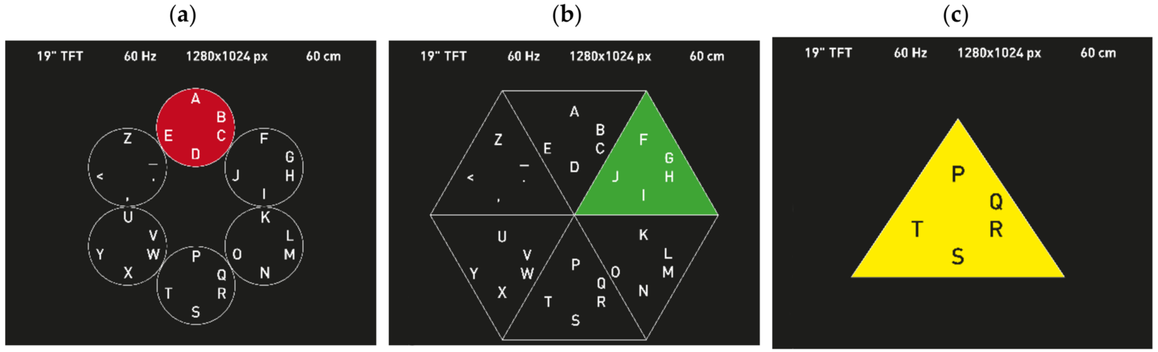
Saha et al.,

BCI Research

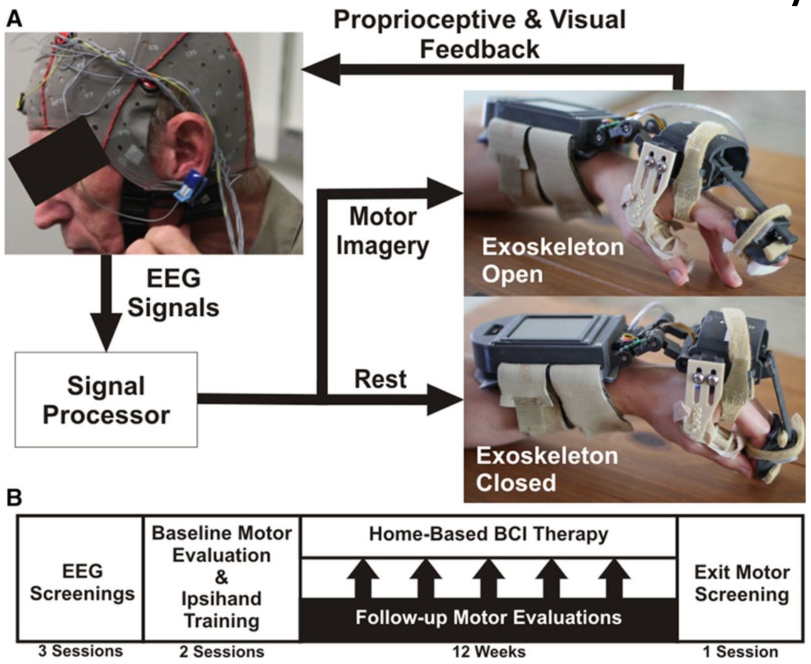
Traditionally used to allow people with disabilities to **communicate** or **control prosthesis**



Neuro-prosthesis



Assistive device



Neurorehabilitation

BCI Research

… human cognitive enhancement

Neuro-Gaming

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

Neuro-Marketing

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/

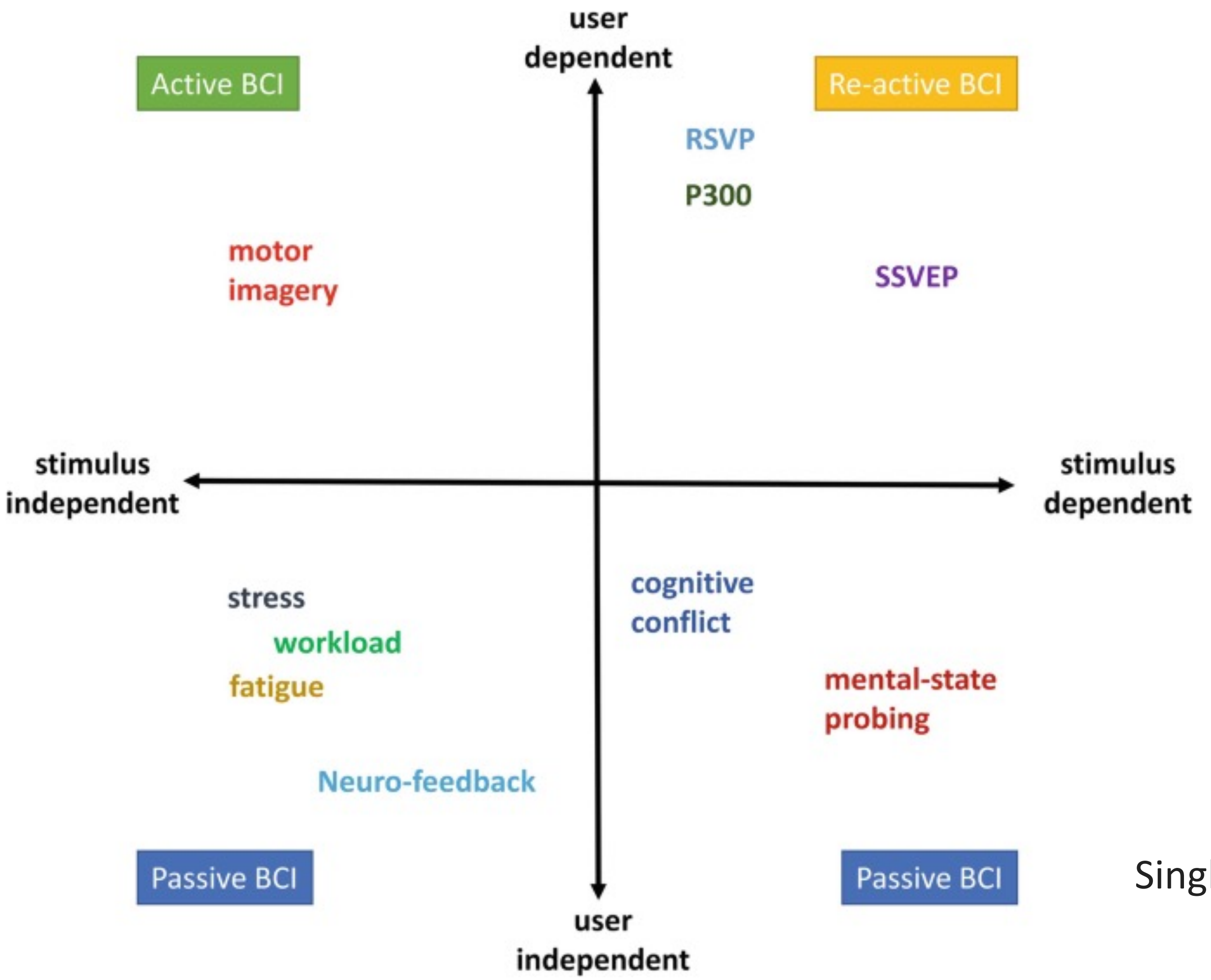
https://spectrum.ieee.org/brain-computer-interface-speech

Speech

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

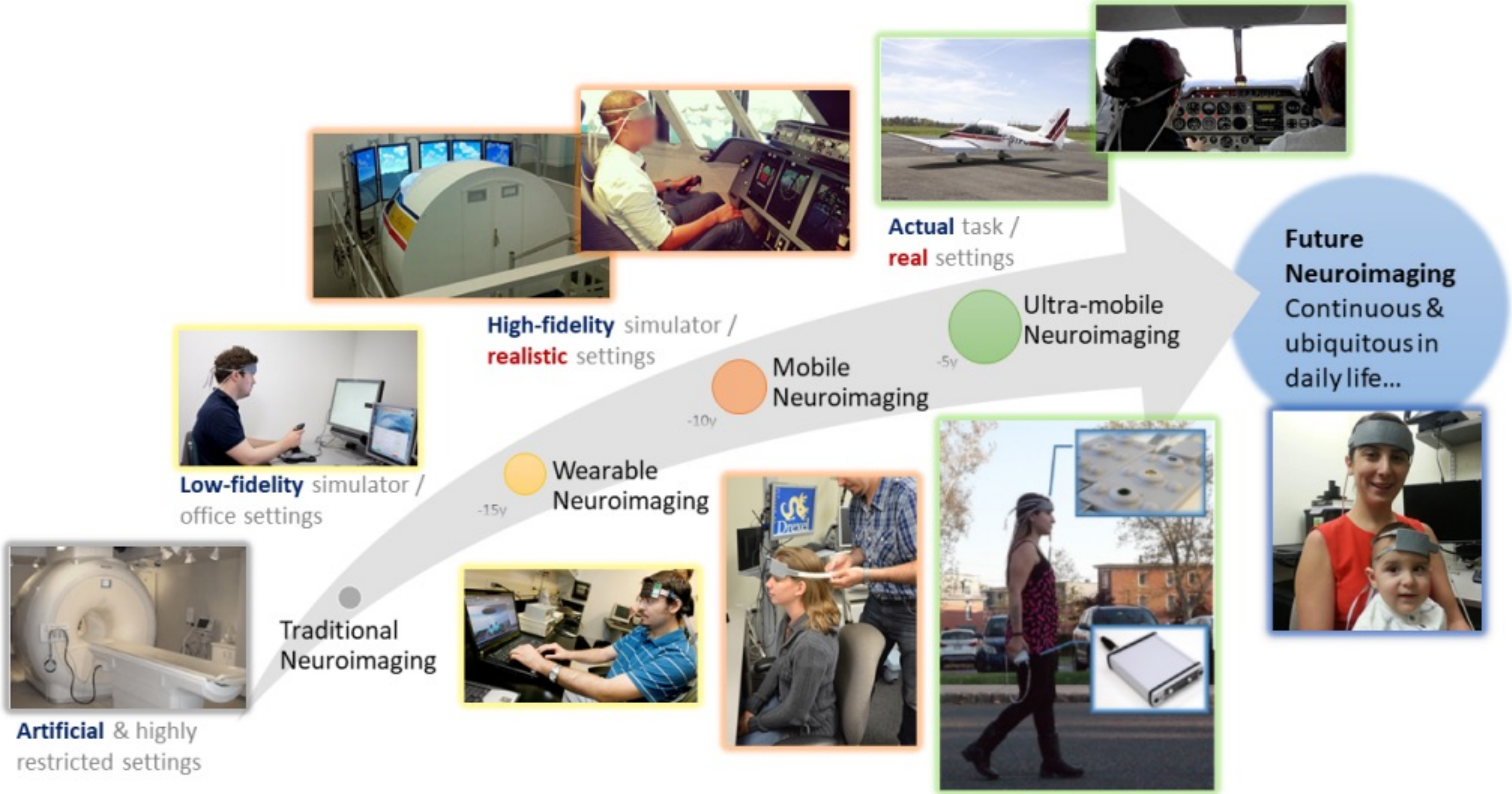
Driving

BCI have branched out…



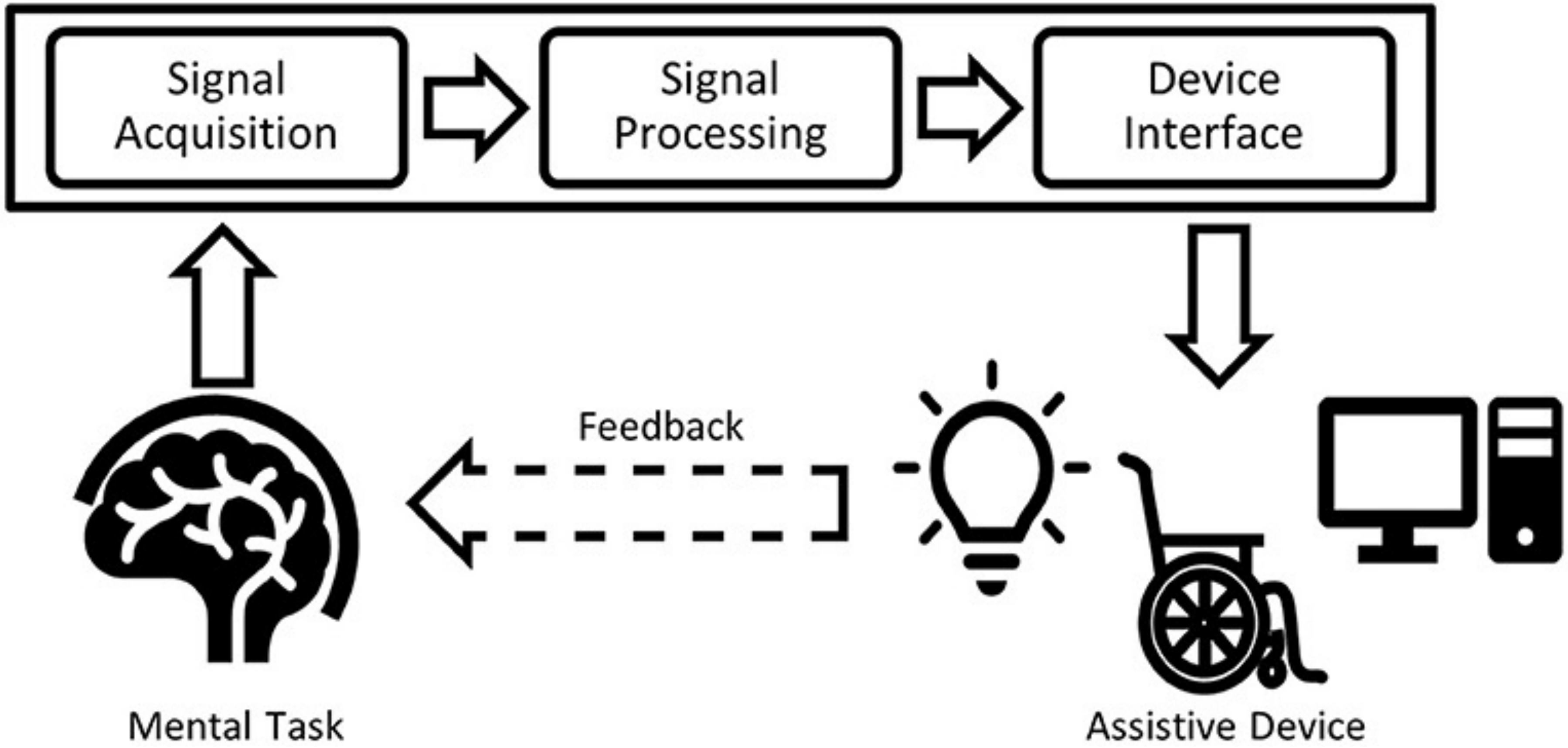
Singh, A.K., Lin, CT. (2021)

BCI in the Wild



https://ayazlab.com/research

The Pipeline



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

Recording Brain Signals

Invasive

- Electrocorticography
- Single-Unit and Multi-Unit Recording
- Local Field Potentials

Non-Invasive

- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- Functional Magnetic Resonance Imaging (fMRI)
- Near-Infrared Spectroscopy (fNIRS)

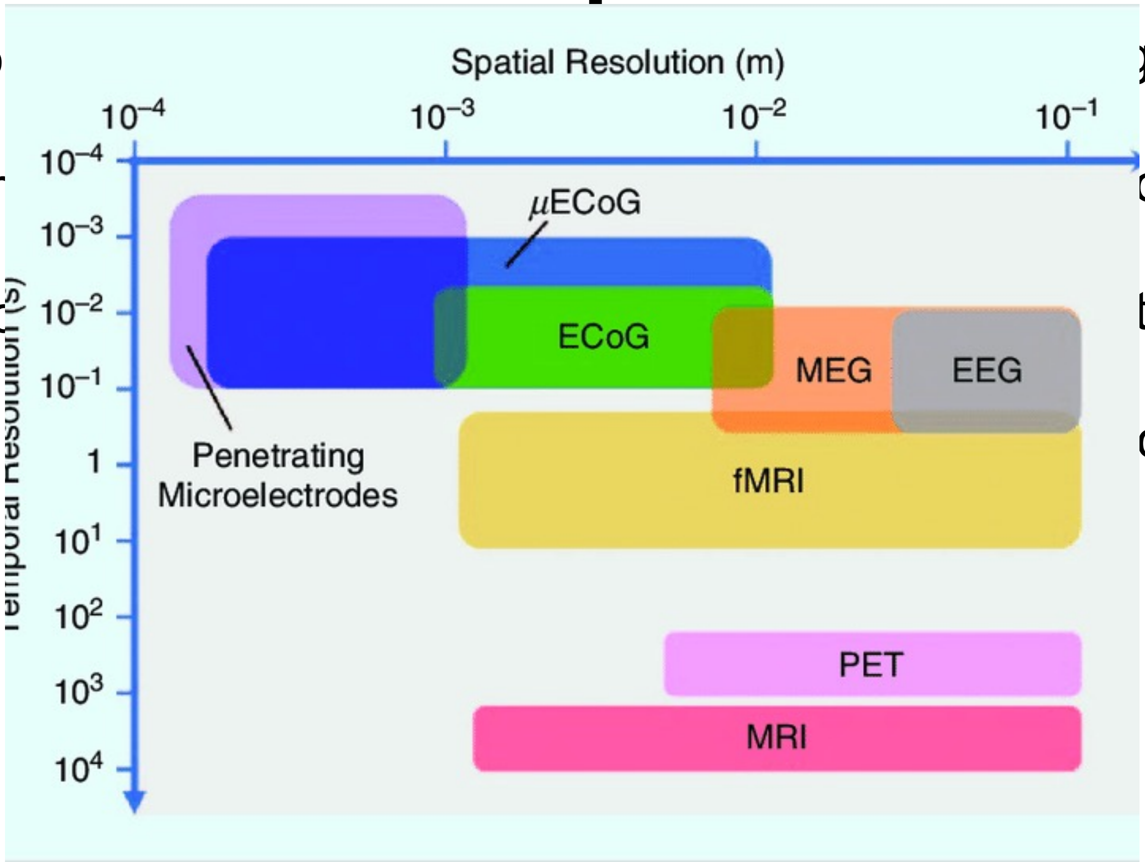
Recording Brain Signals

Invasive

- Electrocortico
- Single-Unit ar
- Local Field Pc

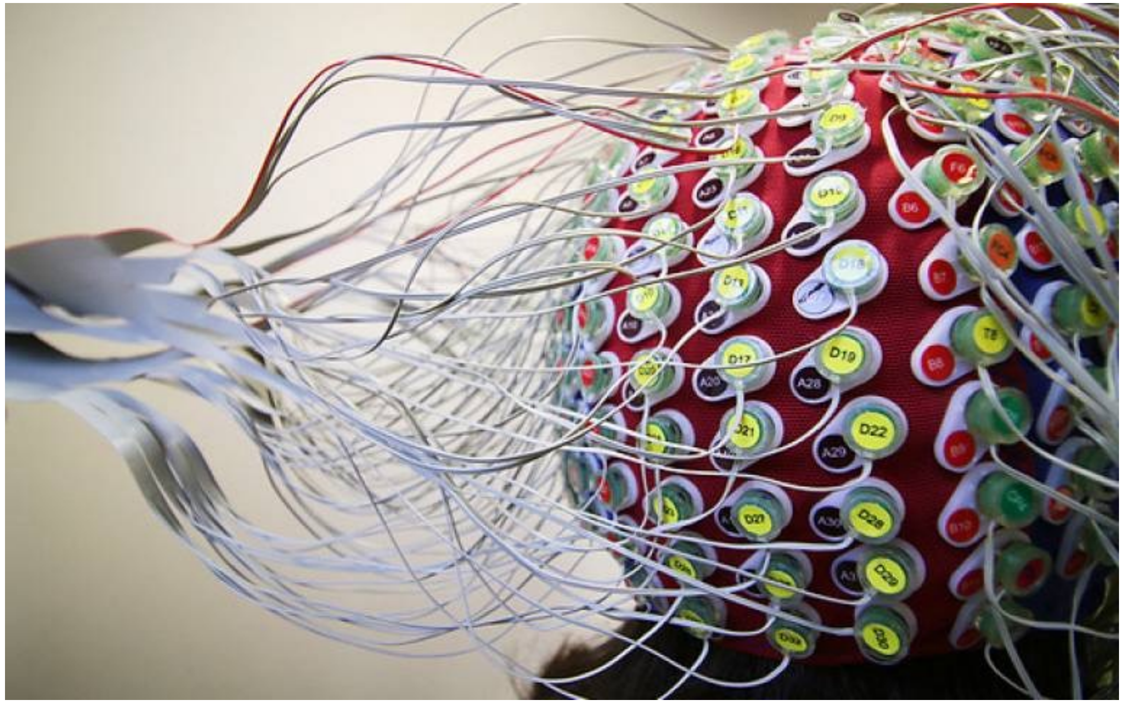
Non-Invasive

- graphy (EEG)
- ography (MEG)
- tic Resonance Imaging (fMRI)
- ctroscopy (fNIRS)



Thukral et al., *IEEE Nanotec. Mag.* 2018

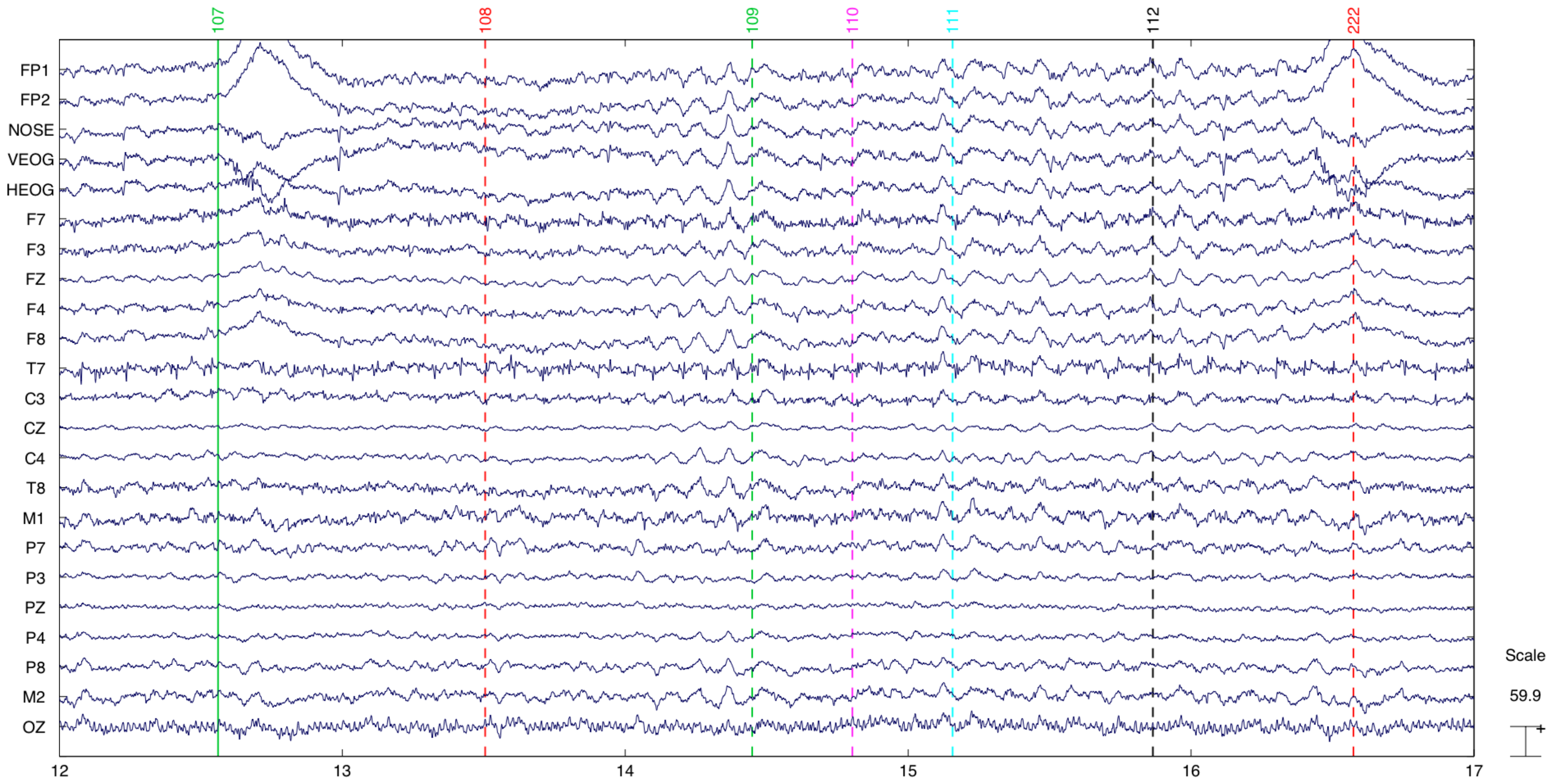
EEG Measurements



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

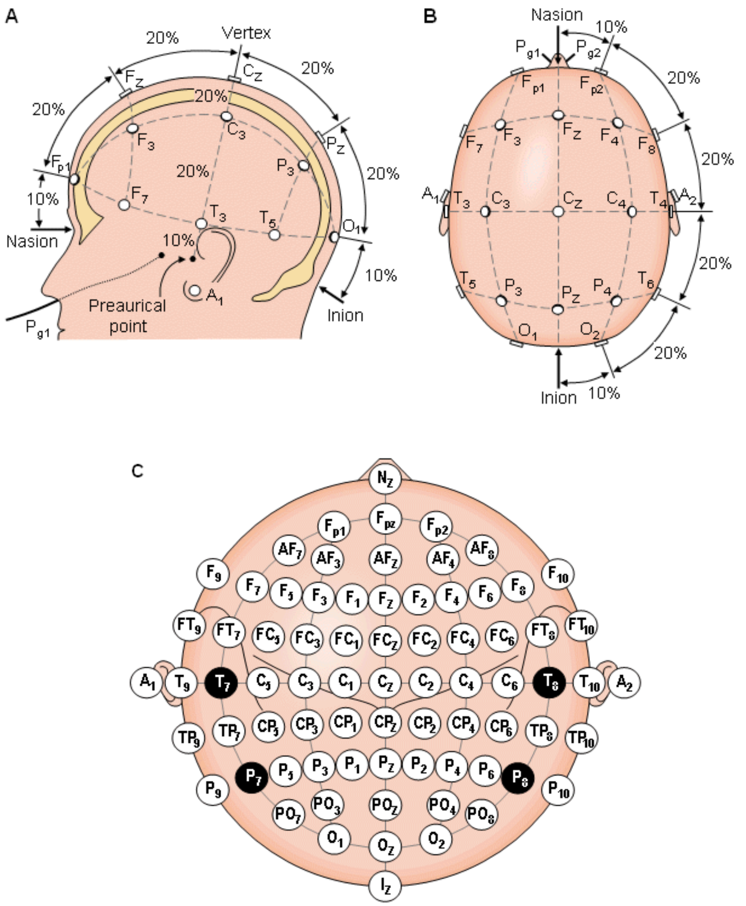
- Electroencephalogram (EEG) electrodes
- Scalp recording of electrical activity of cortex => waveform signals
- Microvolts (µV) – small!
- Role of EEG in neuroimaging:
    - Identify neural correlates
    - Diagnose epilepsy, sleep disorders, anaesthesia, coma, brain death

EEG Measurements



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)

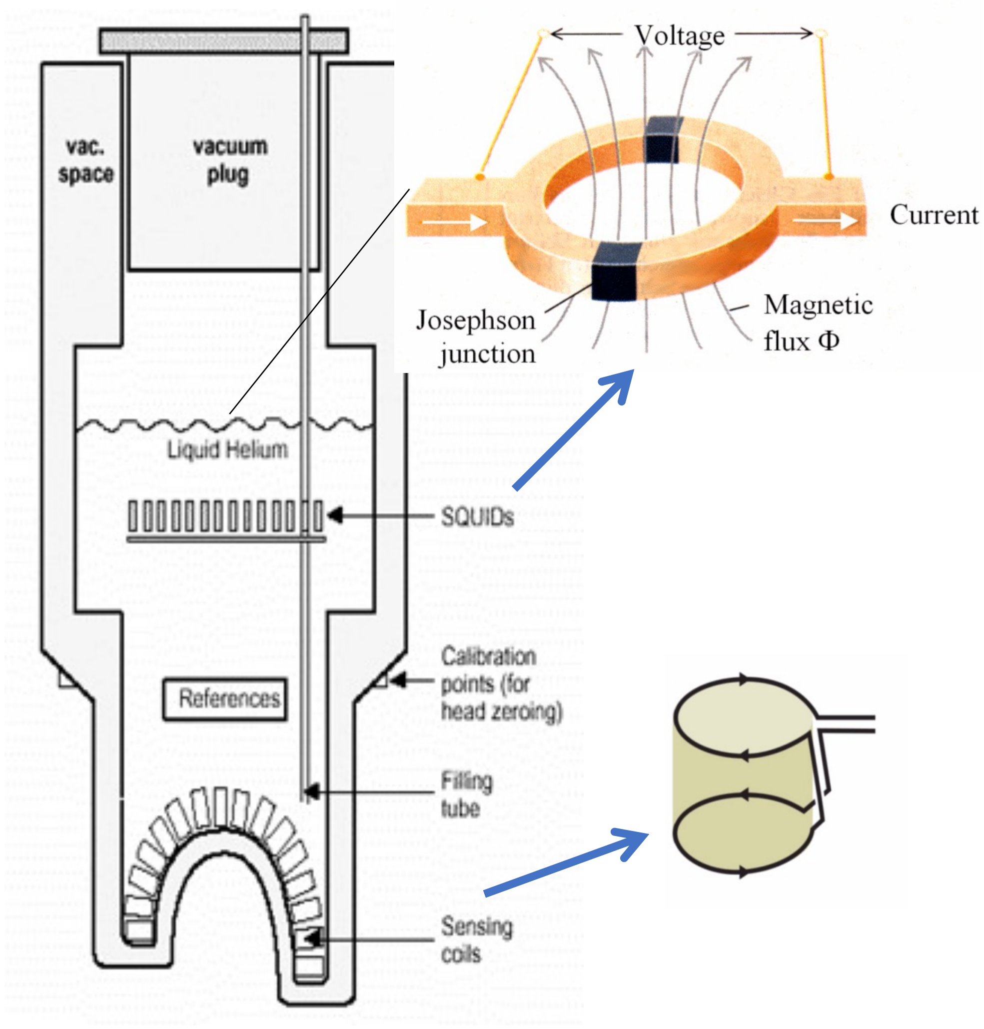


MEG- Introduction

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

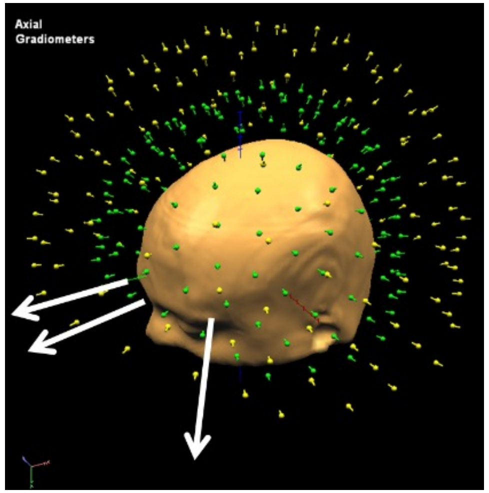
- **Magnetoencephalography (MEG)**
- Direct external recordings of **magnetic fields** created by electrical currents in cortex
- Measured in **Tesla**
- Role of MEG in neuroimaging:
  - **Neural correlates** of cognitive/perceptual processes
  - **Localise** affected regions before surgery(?), determine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

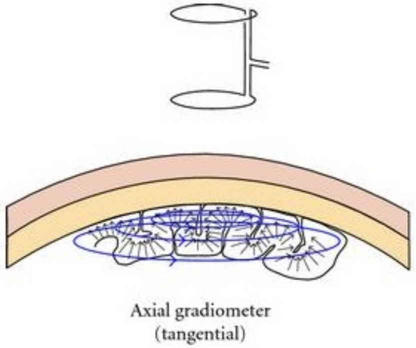
MEG- Squid



- SQUID - **S**uperconducting **QU**antum **I**nterference **D**evice, 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





Axial Gradiometer MEG sensors…

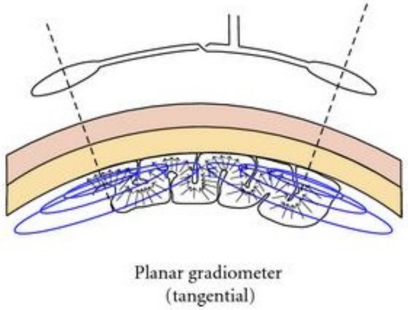
•…are aligned orthogonally to the scalp

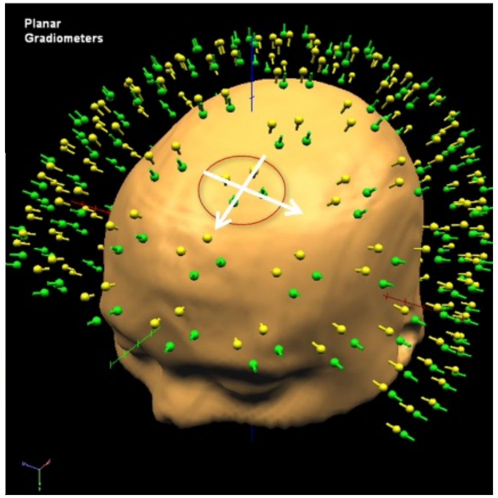
•…record gradient of magnetic field along the radial direction

Planar Gradiometer MEG sensors…

•…two detector coils on the same plane

•…have sensitivity distribution similar to bipolar EEG setup



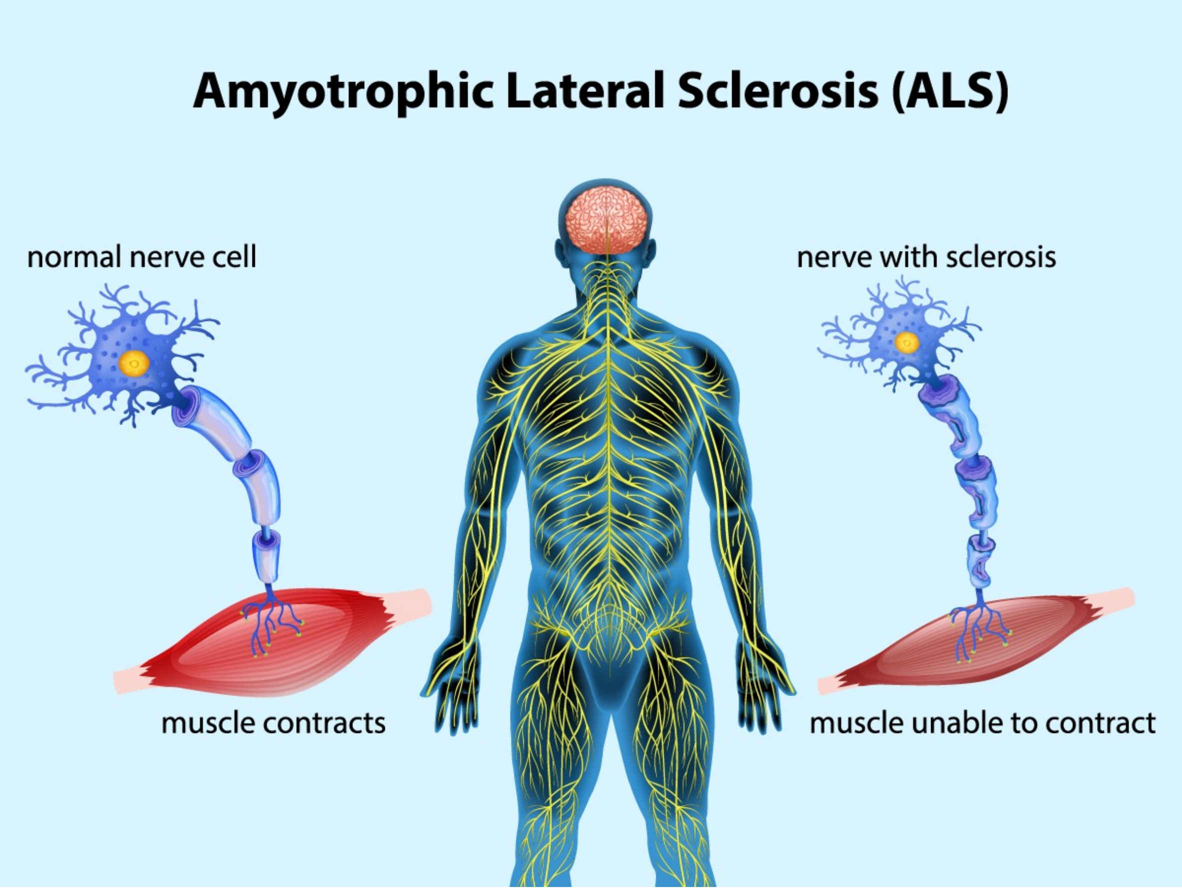


Analysing Neural Data

Section 2

Amyotropic Lateral Sclerosis

- progressive neurodegenerative disorder that affects nerve cells in the brain and spinal cord, as well as the peripheral nervous system.
- gradual loss of voluntary muscle control
- involves the degeneration of motor neurons
- precise cause of ALS remains uncertain
- Current Therapy
  - Physiotherapy
  - Osteopathy



How can BCI help?

- Communication Enhancements
  - Alternative Communication Methods
  - Eye-Tracking and Brain Signals

- Control of Assistive Devices
  - Environmental & Mobility Control

- Improving Quality of Life
  - Restoring Independence
  - Psychological Support

- Clinical and Therapeutic Application
  - Neurofeedback

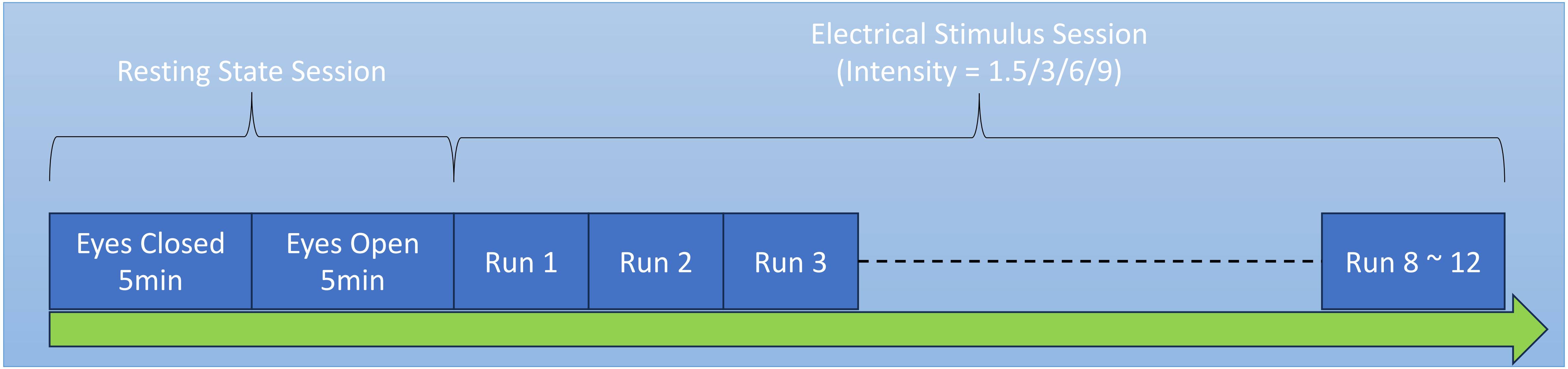
https://www.hopkinsmedicine.org/news/newsroom/news-releases/2023/11/brain-computer-interface-restores-control-of-home-devices-for-johns-hopkins-patient-with-als

Our Objective

Objective: How does brain activity differ between ALS and Healthy participants? Can therapy based on peripheral stimulation help manage symptoms or slow the progression of the disease?

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



After the experimental session…

- **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-Salpêtriere 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)

Pre-processing Neural Data

Section 3

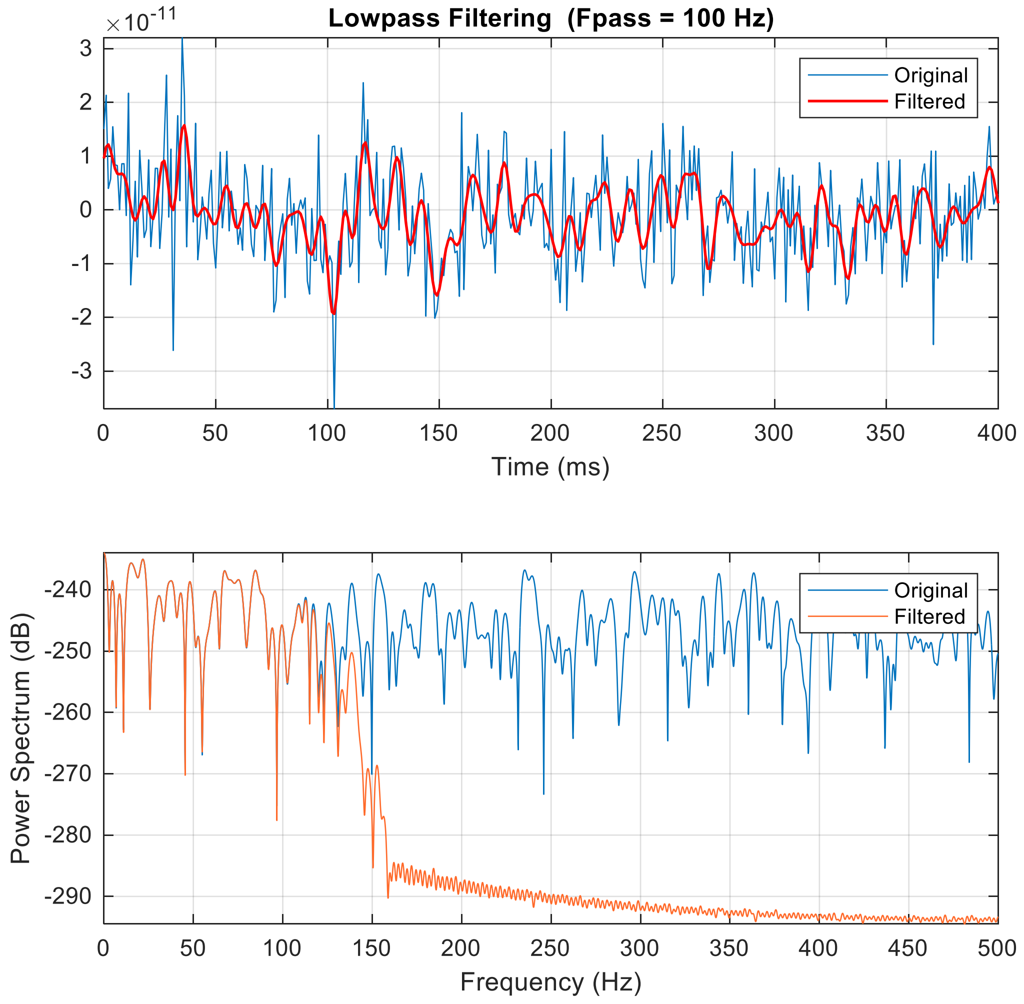
First Step – Pre-processing

Brain recordings are noisy…

- 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

Filtering

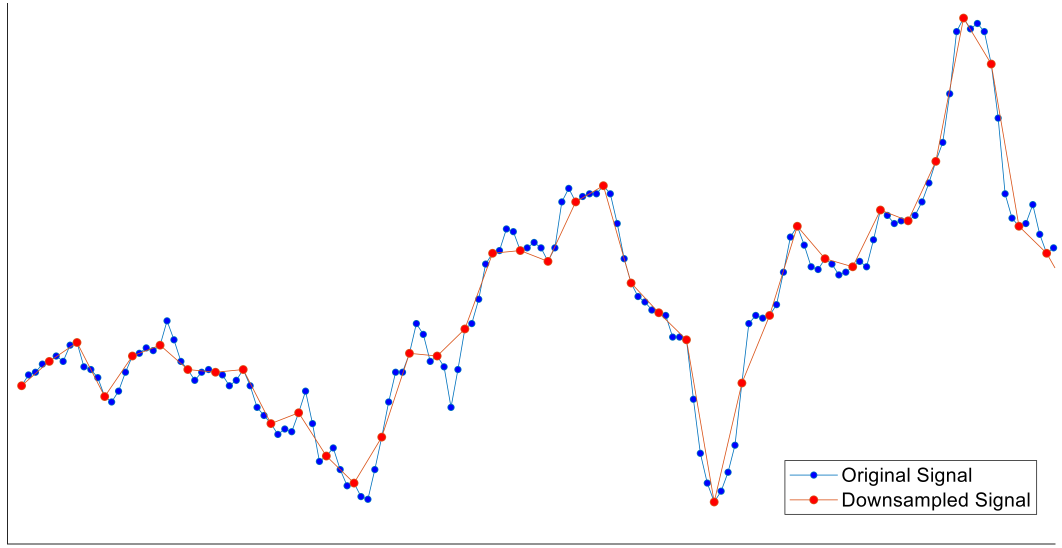
- Remove high frequency artefacts, low frequency drifts
- Notch filters at 50/60 Hz to attenuate electrical line noise
- Recommended to apply a High-pass filter at 0.1 or 0.5Hz to minimize slow drifts
- Band-pass, Band-stop, High, Low Filters
- FIR and IIR filters
    - FIR filters are more stable; less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



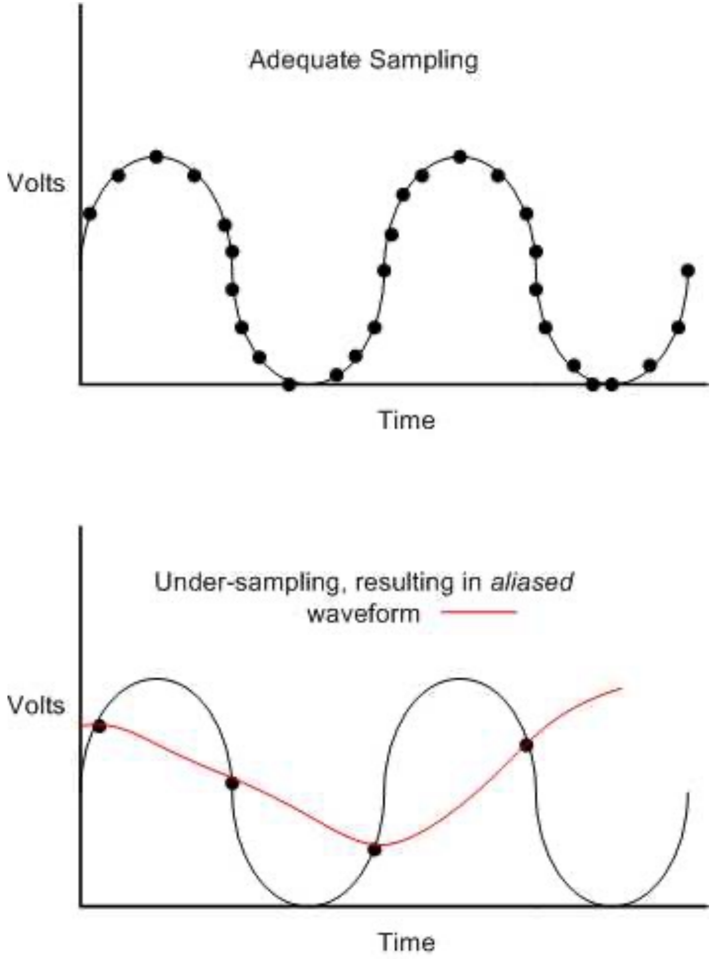
Example of filtering on the resting state signals of the ALS dataset

Downsampling

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



Spatial Filtering

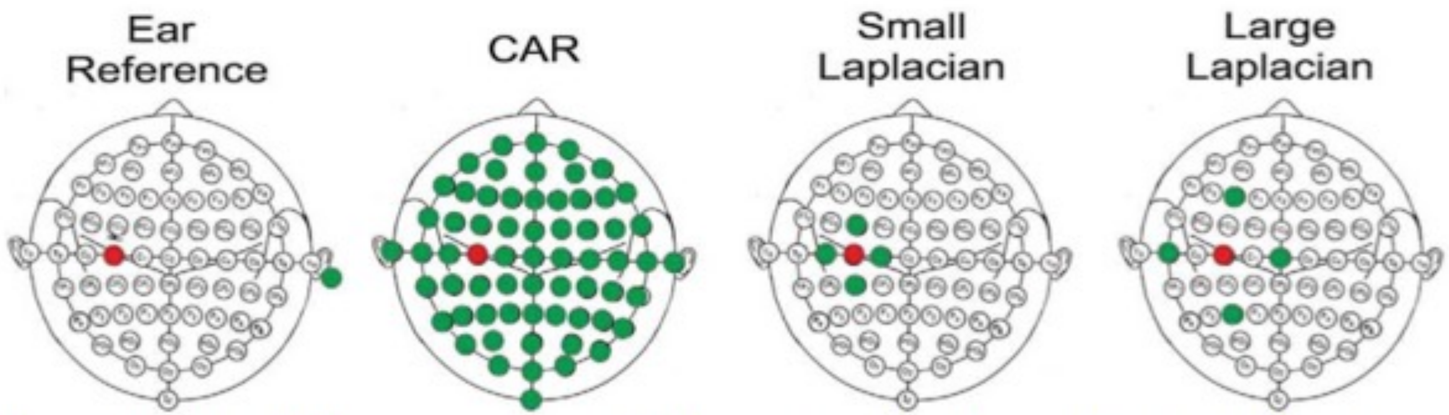
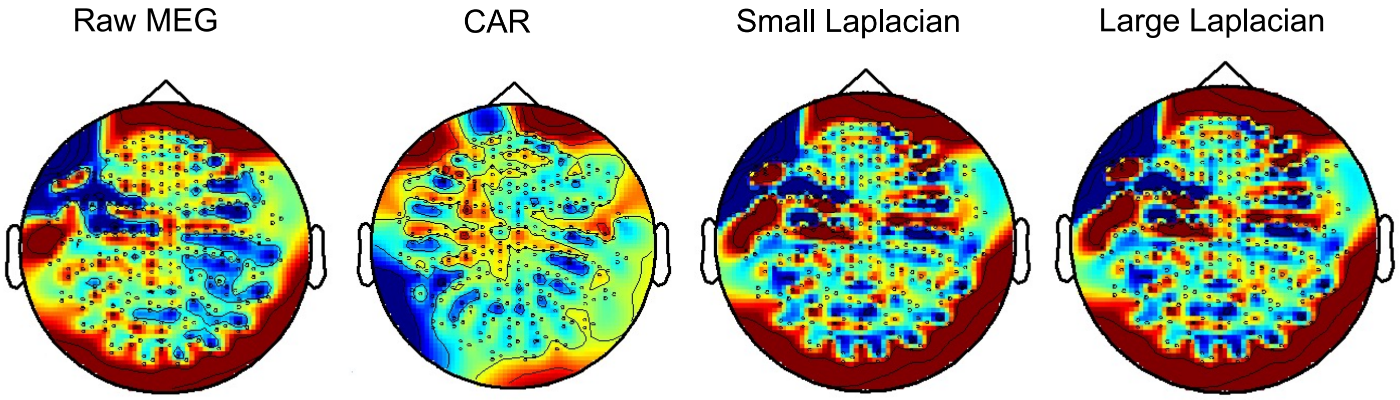


Figure 3. For a clinical EEG array, a mean or weighted mean of green electrodes would be subtracted from the red electrode for each spatial filter listed [7].

McFarland, 1997



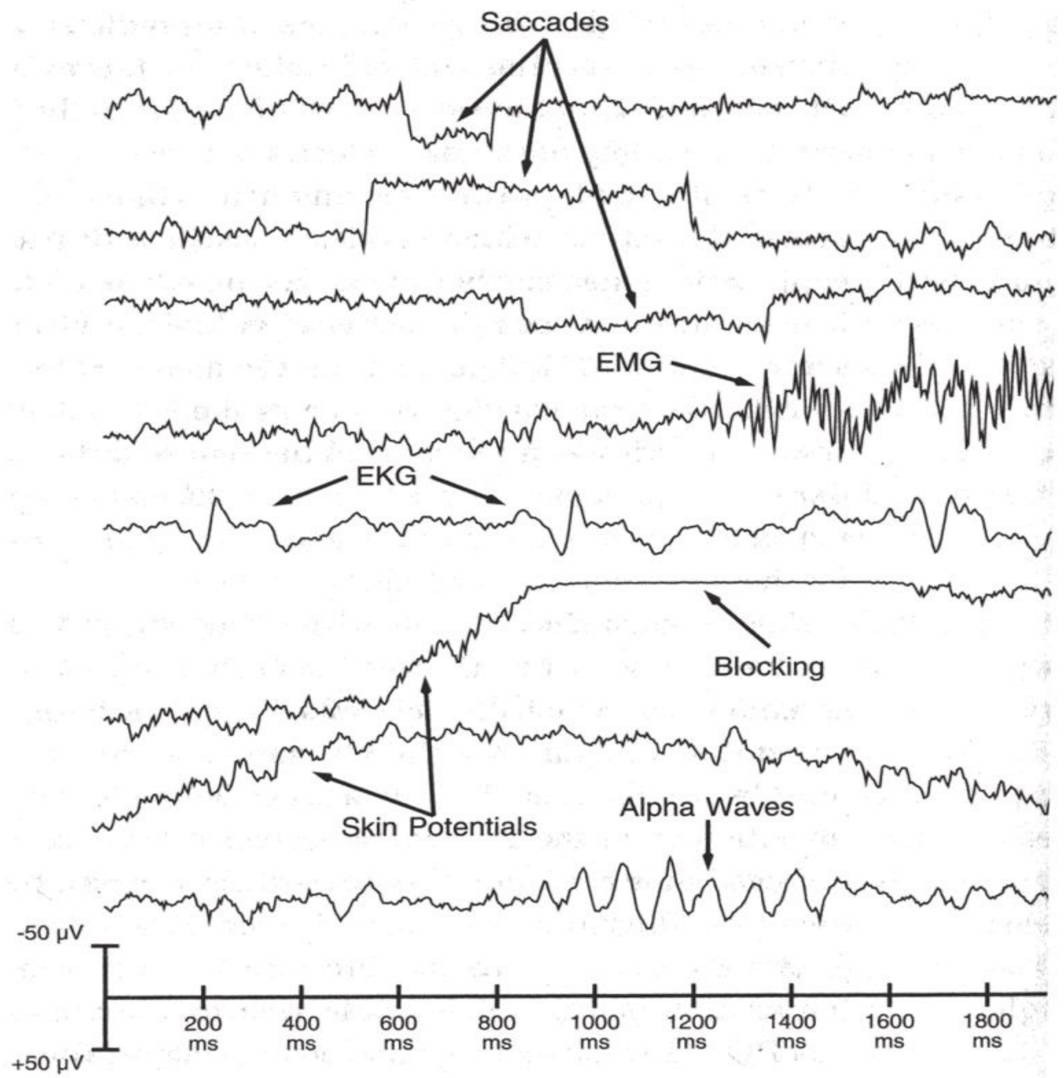
Example of spatial filtering on the resting state signals of the ALS dataset

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



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*.

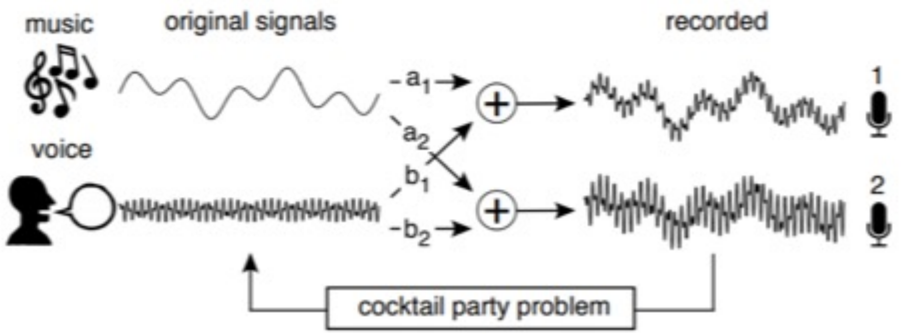
$$S = WB + E$$

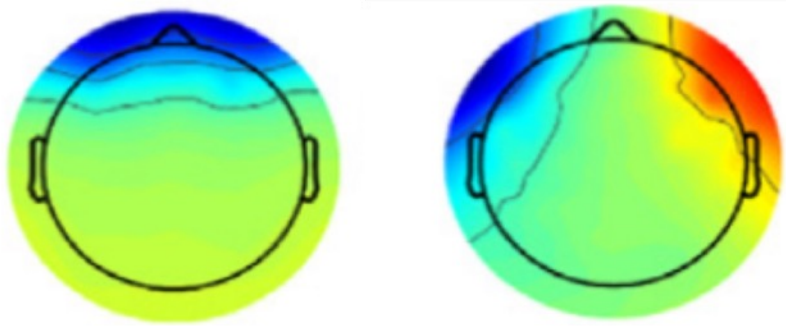
W describes the contribution of the EOG artifact in each EEG channel

Artefact Removal – Independent Component Analysis

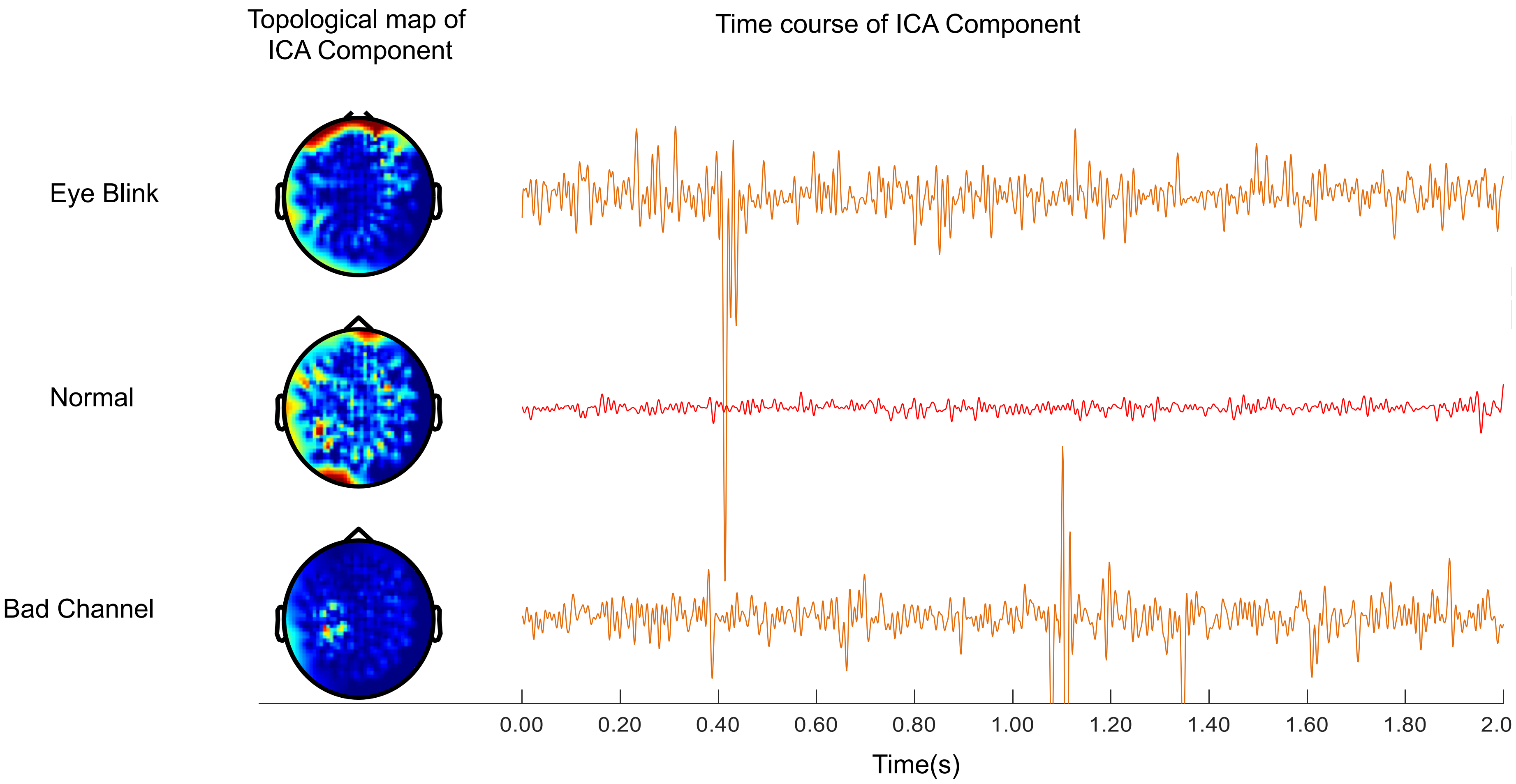
- Independent component analysis (ICA) is a blind source separation (BSS) technique that is widely used in an array of signal processing applications.

- Once the components have been identified, to remove the EOG artifacts, one can visually determine which independent component corresponds to eye-blinks or movements based on the following criteria.

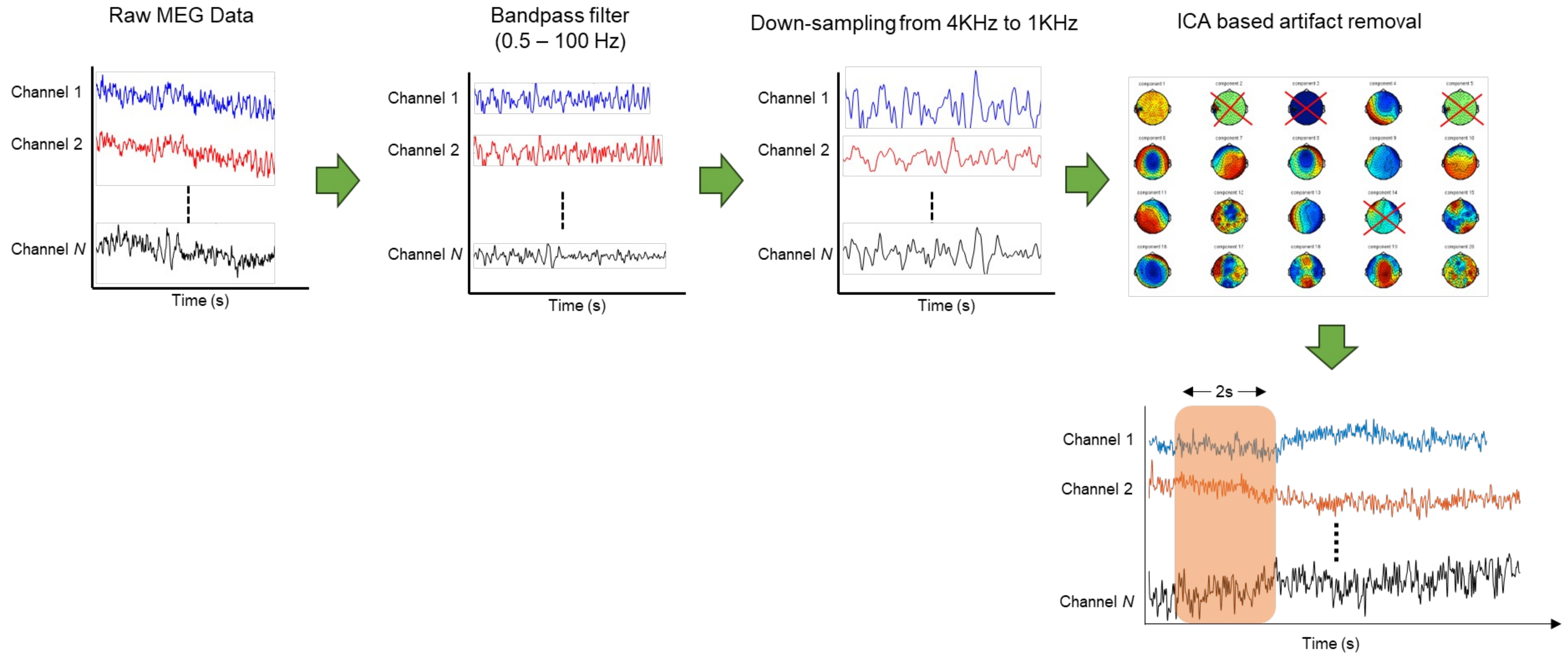




Artefact Removal – Independent Component Analysis



Our Approach



Epoching of the MEG data with 2s non-overlapping time window

Ulster University

Analysing Neural Data

Section 4

First Step – Data Processing

- **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, Wavelet Transform, Inter-trial Coherence, Cross-Frequency Coupling

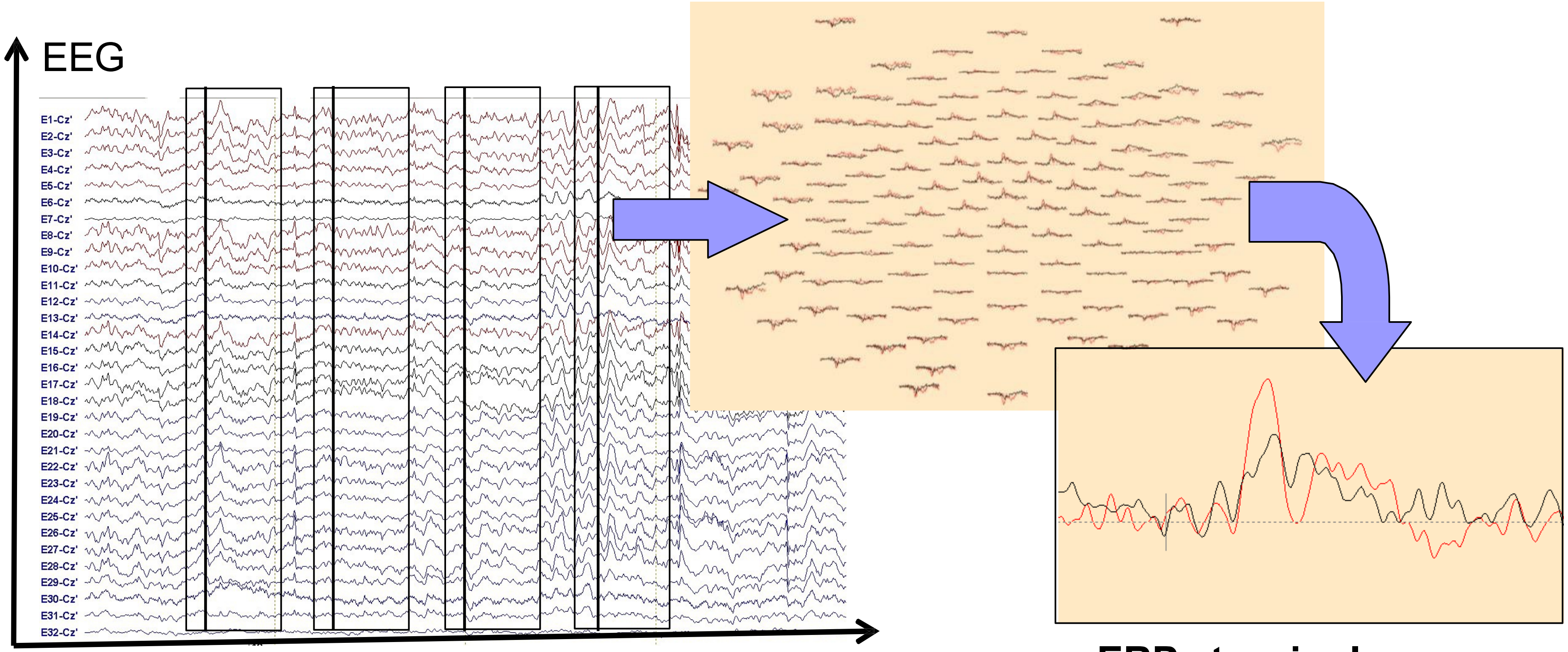
- **Brain Connectivity**

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

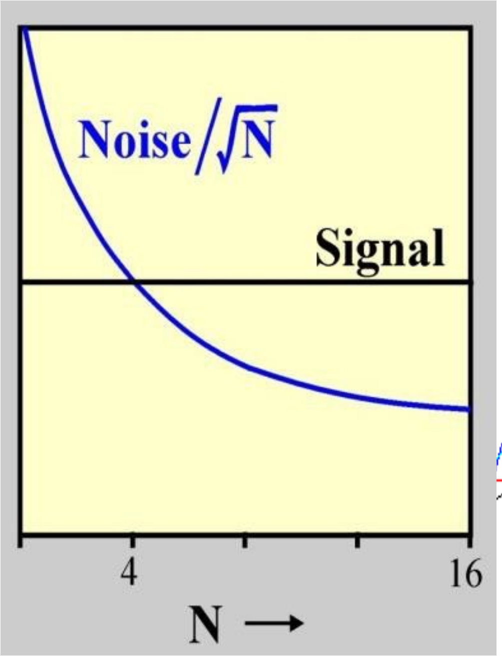
Event Related Potential

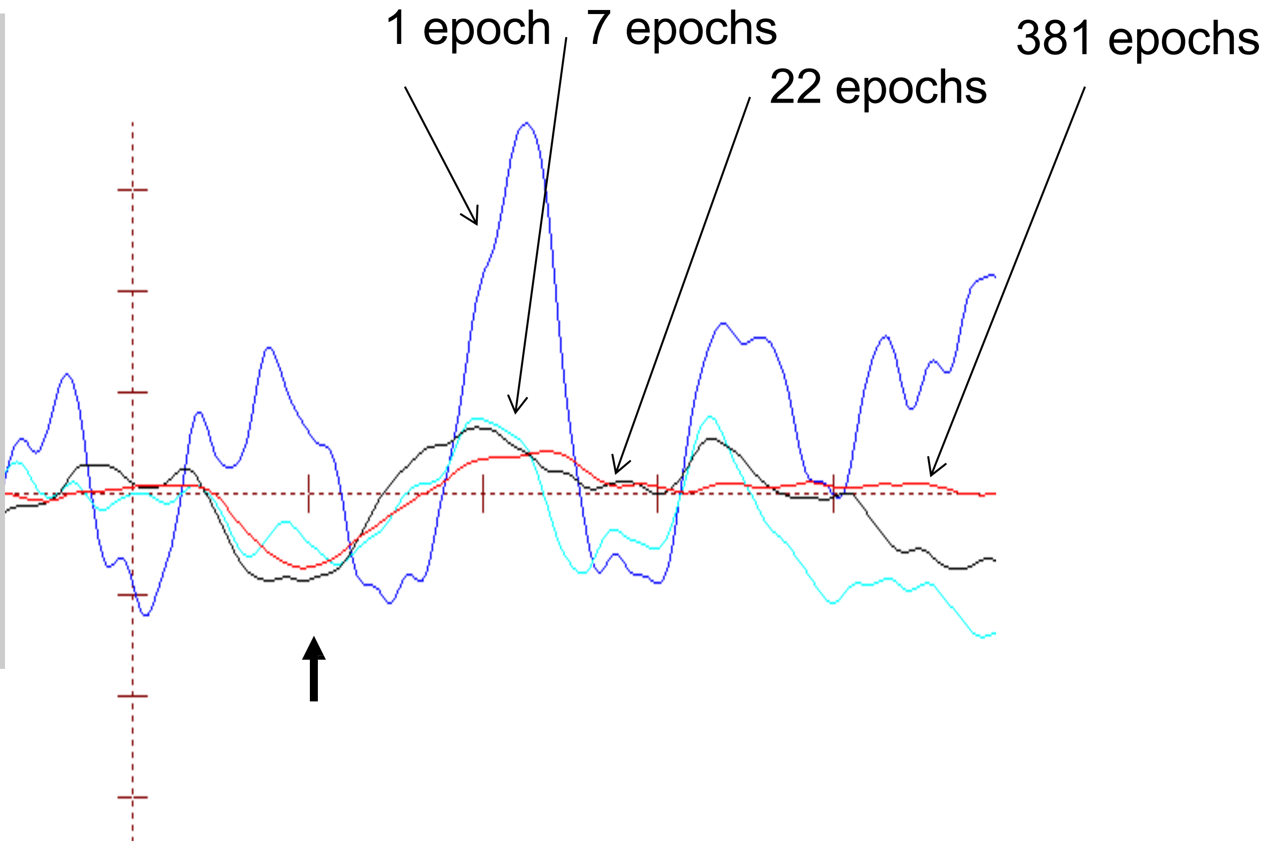
Averaged across 100 stimulus presentations



ERP at a single electrode

Event Related Potential – Effect on SNR



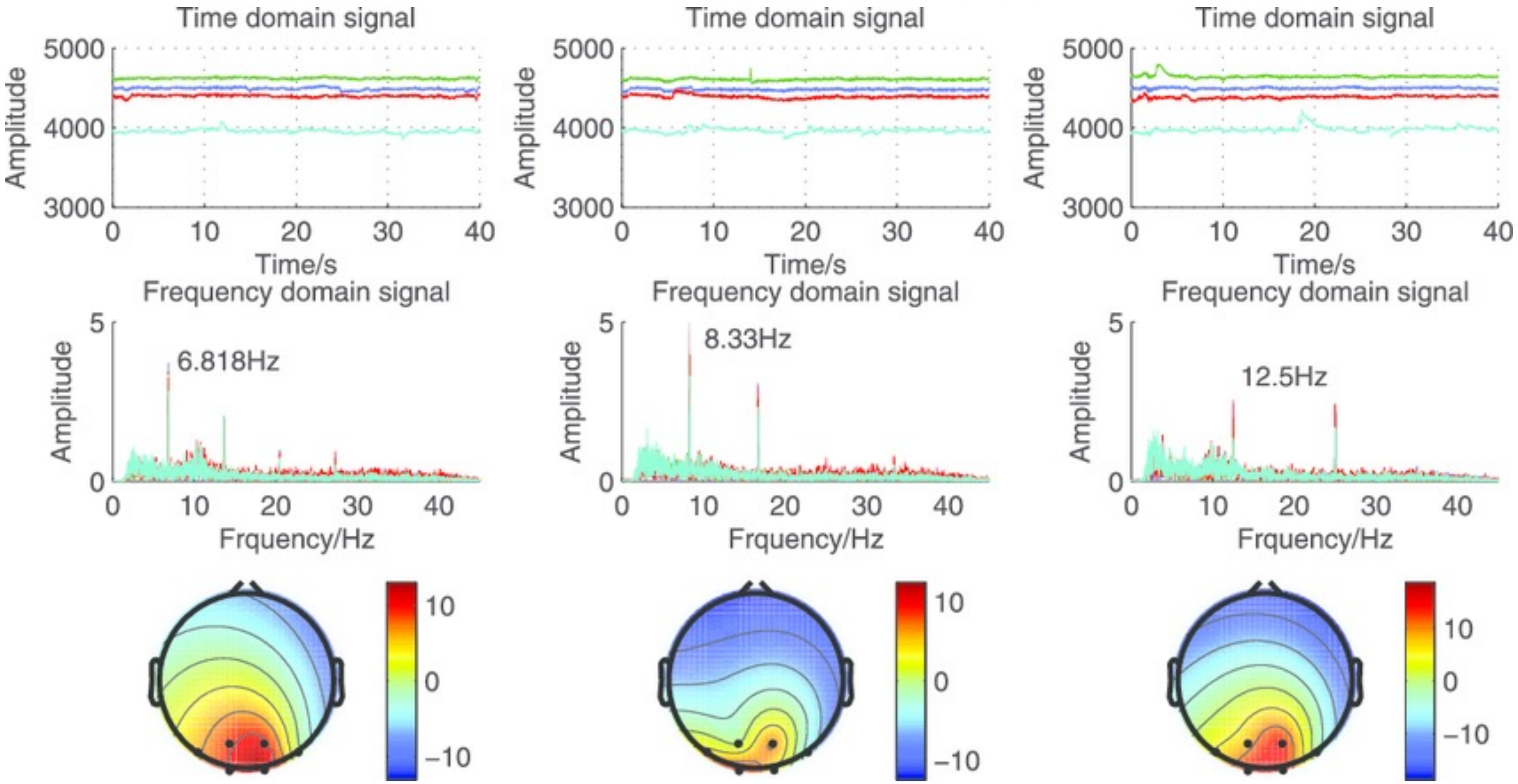


Frequency Domain Analysis

Fourier Transform:

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

Fourier Transform

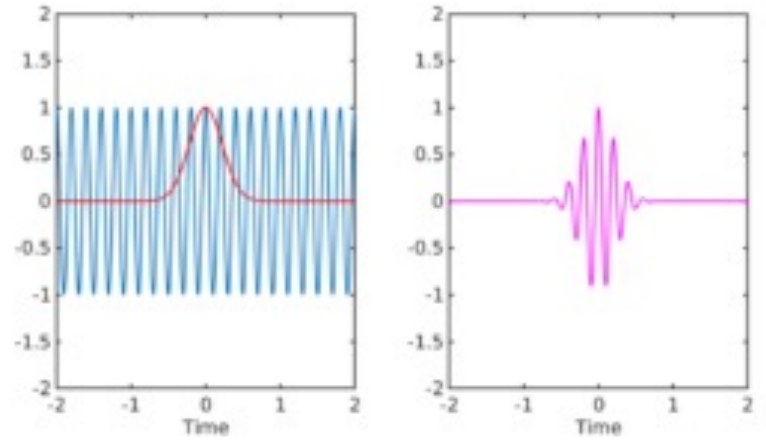


Time-Frequency Analysis

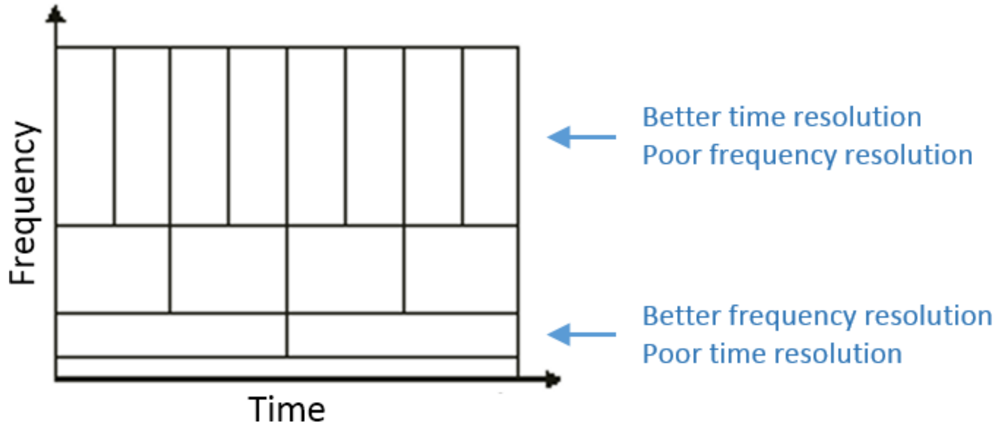
- Short-Time Fourier transform
- Wavelet Transform
- Hilbert-Huang Transform
- Stockwell Transform
- Wigner-Ville Distribution

Time-Frequency Analysis- Wavelet Transform

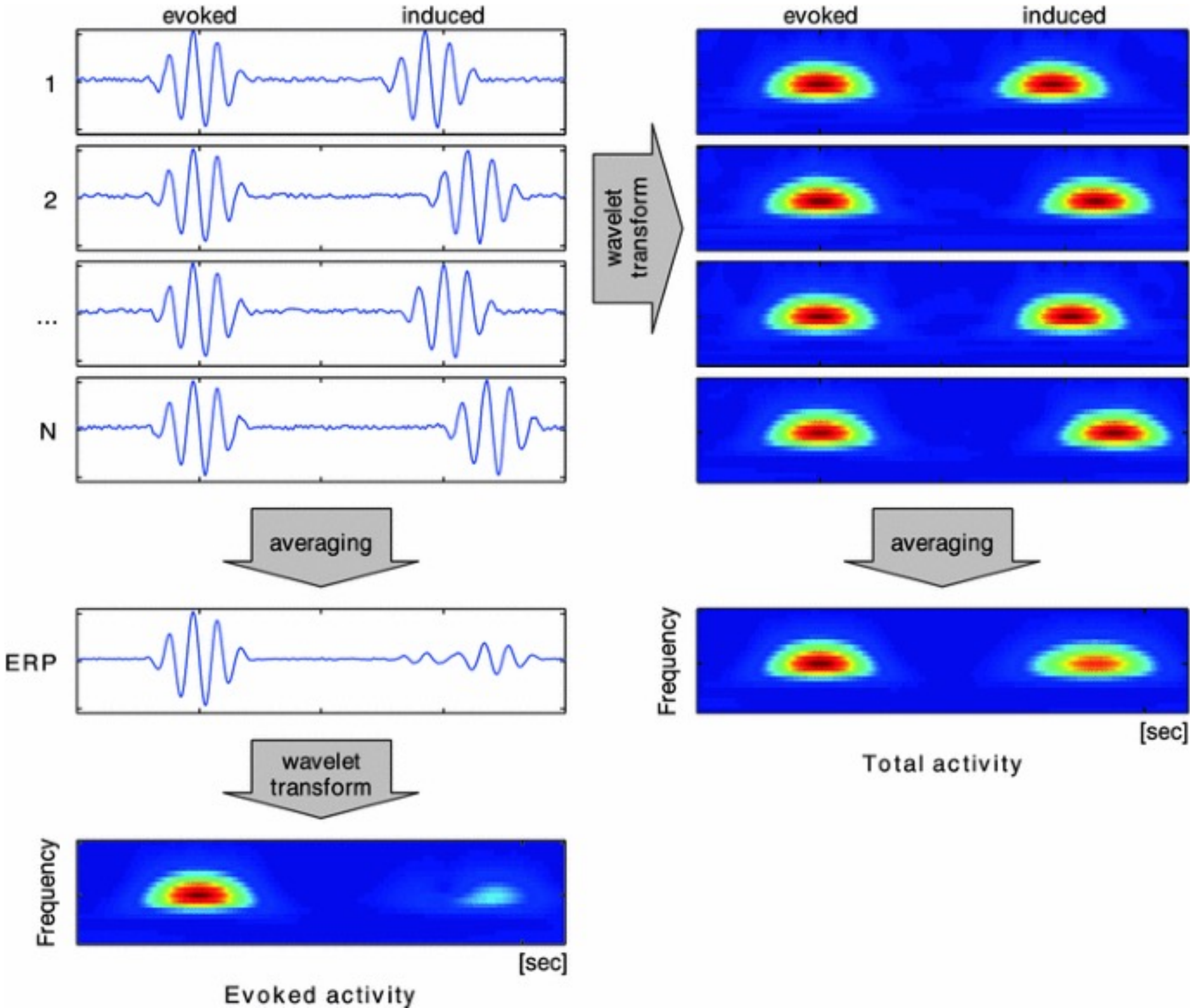
- Wavelets overcome limitations of methods such as the Fourier transform by enabling a view of changes across both time and frequency.
- shape of a sinusoid, weighted by a Gaussian kernel, and they can therefore capture local oscillatory components in the time series.
- Wavelets have variable resolution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



- 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.

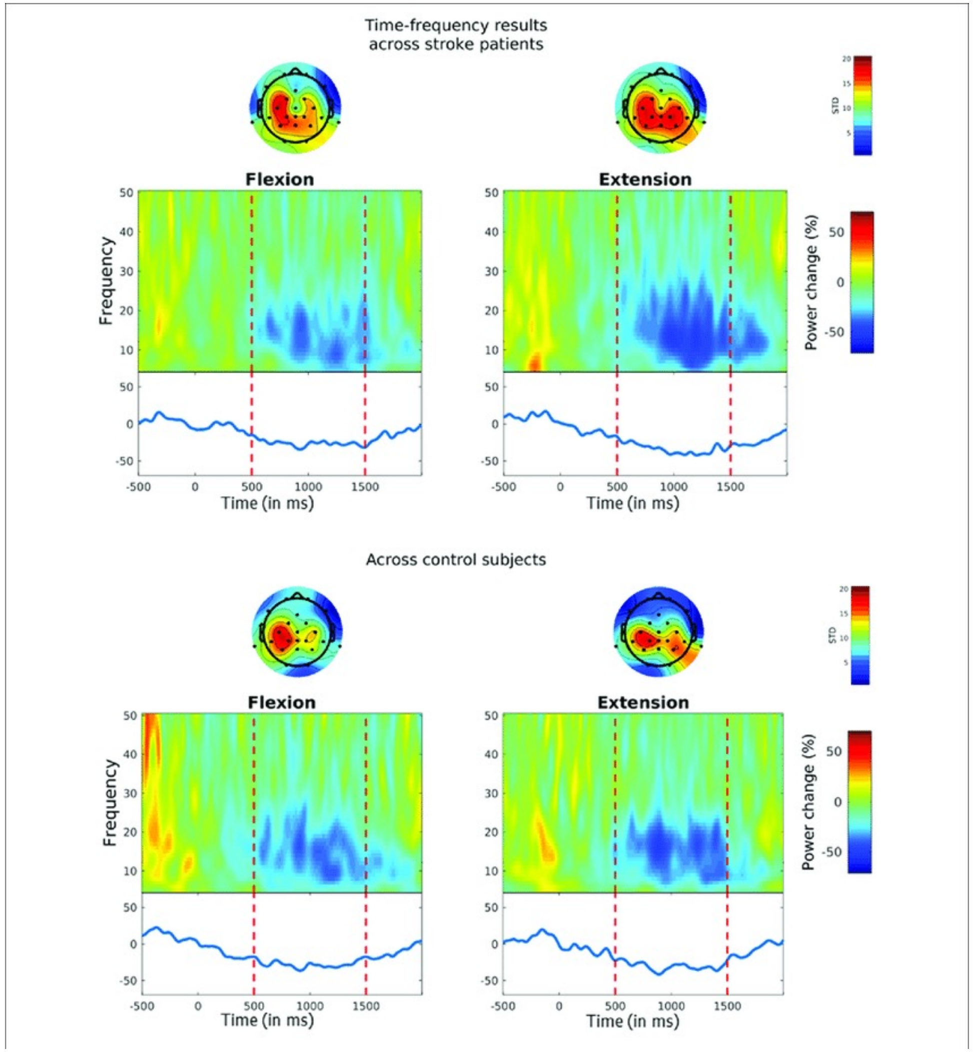


Time-Frequency Analysis – Best Approach



Hermann et al, 2013

Interpreting Time-Frequency Representation



Spychala et al, 2020

Neuro-marker identification - ALS

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

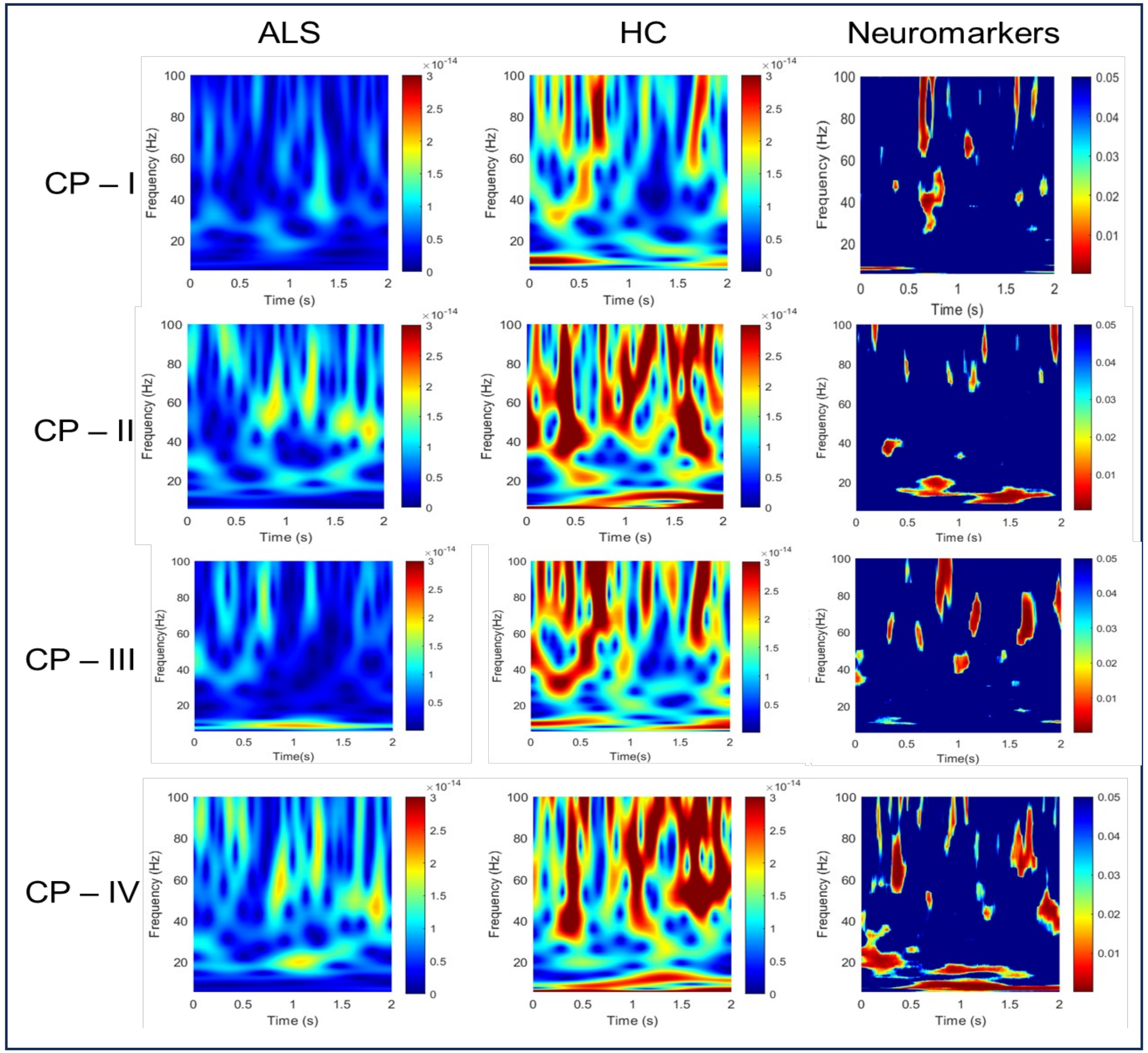
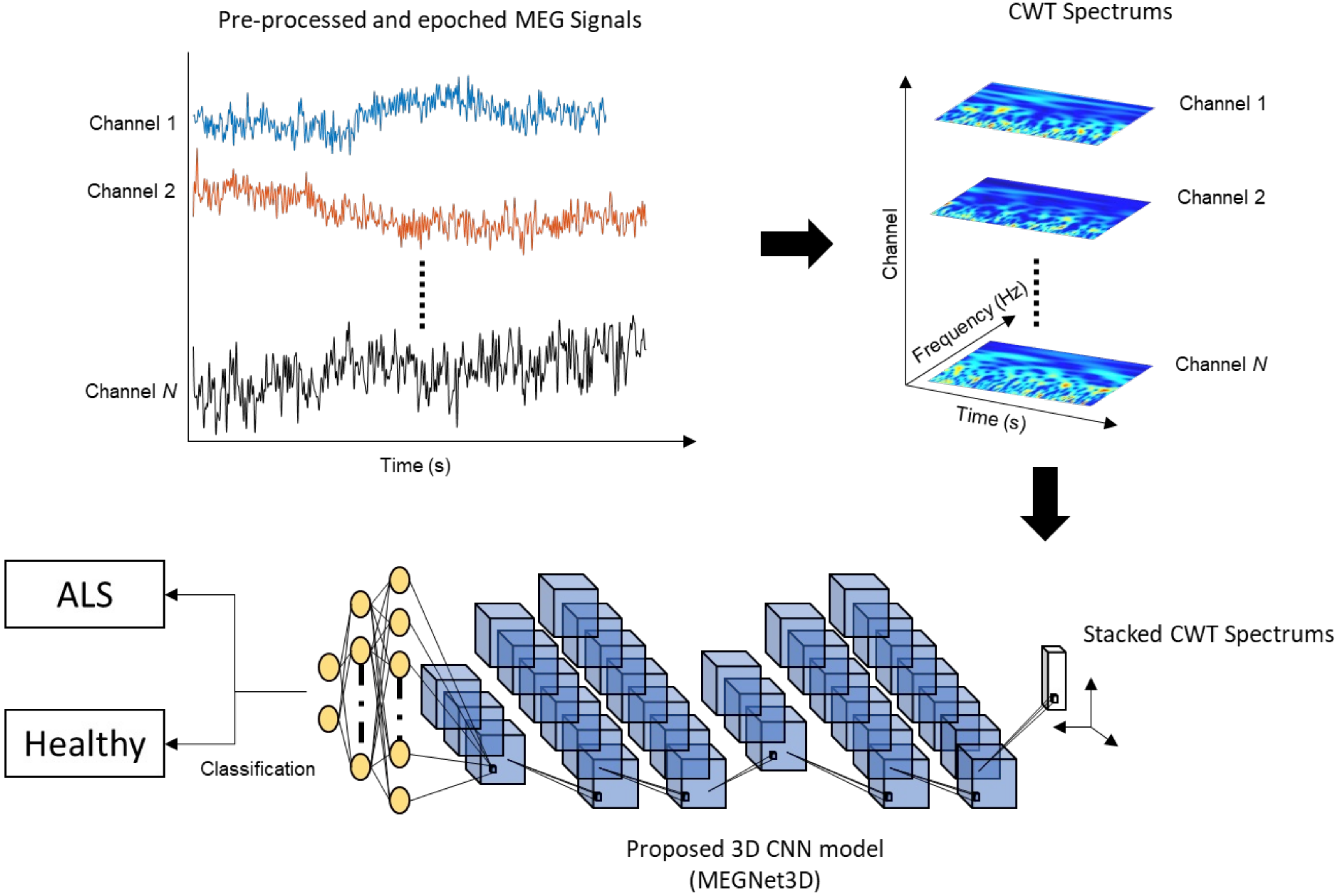
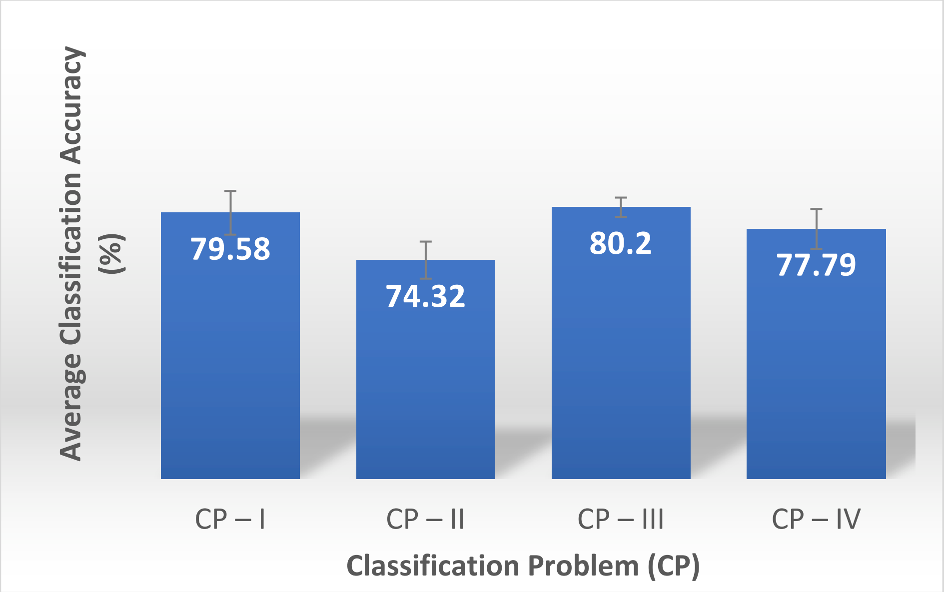


Figure: CWT spectrums from the central motor cortex region (Cz area) for HC and ALS patients

Designing the BCI for ALS Identification



Designing the BCI for ALS Identification



IEEE SMC 2023
Oahu, Hawaii


TIME FOR A
BREAK

Going beyond Sensors – Reconstructing Sources

Section 5

Limitation of Sensor-Level Analysis

- Signals are distorted as they pass through the Cerebrospinal fluid (CSF), skull and scalp.

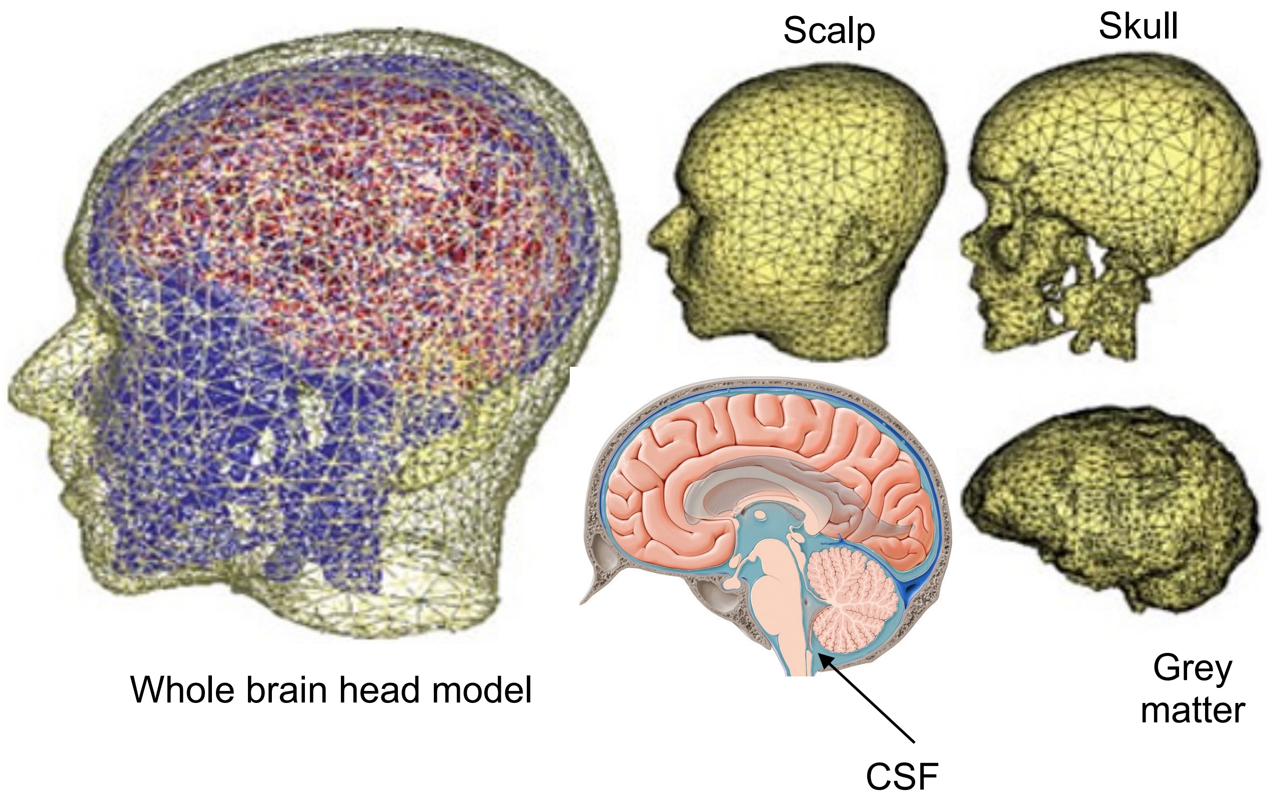
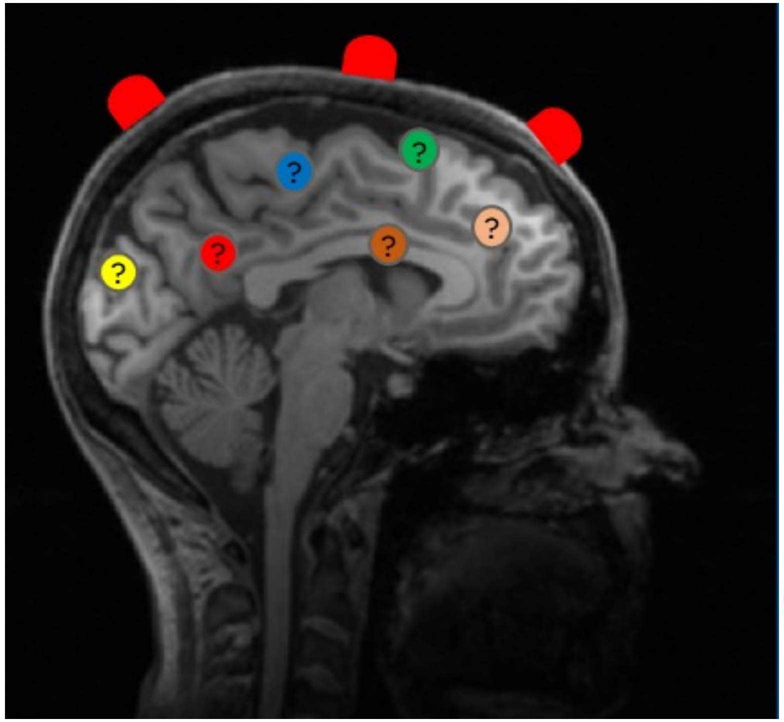


Image source: Acar et al., 2013 and KEN HUB .COM

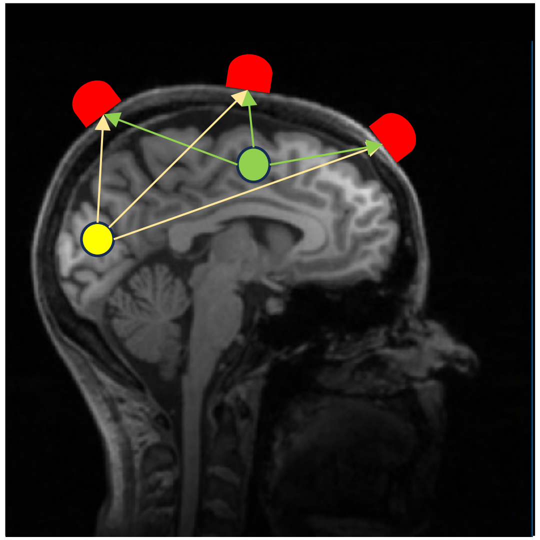
Limitation of Sensor-Level Analysis

- Difficulty in identifying the exact brain regions generating the signals.



Limitation of Sensor-Level Analysis

Signals from different brain sources can mix, making interpretation challenging.



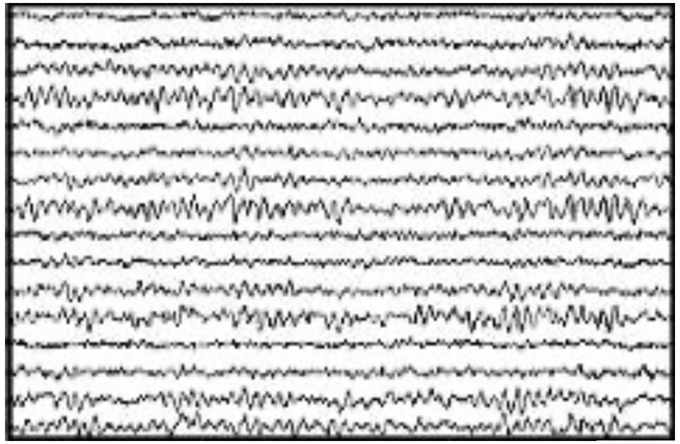


Image source: Acar et al., 2013 and KEN HUB .COM

Motivation behind Source-Level Analysis

- Source-level EEG analysis reconstructs the origin of brain signals.
- It provides a more accurate localization of neural activity, beyond what scalp-level analysis can offer.
- Improves spatial resolution, allowing for precise localization of brain activity.
- Helps in understanding the underlying neural mechanisms.
- Critical for clinical applications, such as identifying epileptic foci or brain lesions.

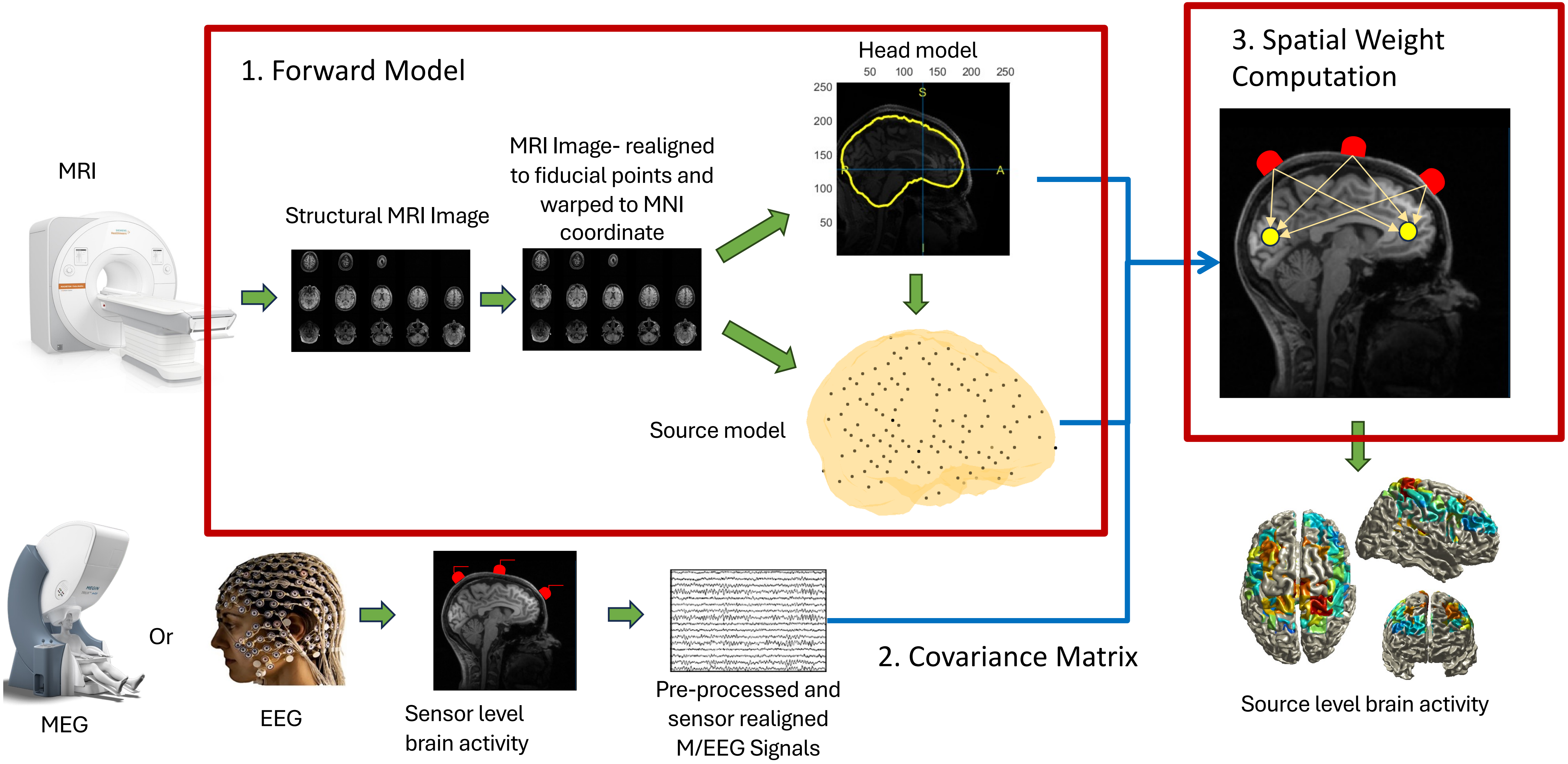
Common Techniques - Source-Level Analysis

- **Dipole Modeling:** Estimates the position and orientation of equivalent current dipoles.

- **Beamforming:** Focuses on a specific location in the brain, reducing the impact of noise from other areas.

- **Distributed Source Imaging:** Estimates brain activity over the entire brain using a distributed source model.

Source reconstruction using Beamformer method



LCMV Beamformer Algorithm

Algorithm: LCMV Beamformer for Source Reconstruction

Input:
X - Preprocessed EEG/MEG data
L - Lead Field Matrix
d - Desired Source Orientation

Output:
Reconstructed Source Activity

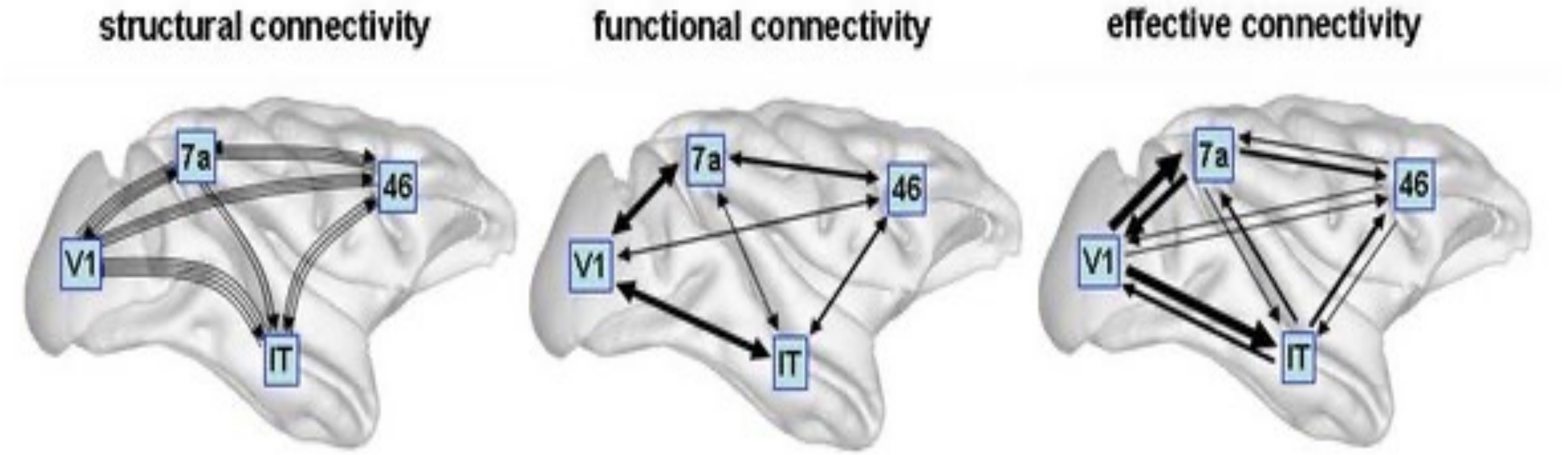
Steps:
1. Covariance Matrix Estimation:
R = (1/N) * X * X^T

2. Compute Spatial Filter Weights:
W = (R^(-1) * L * d) / (d^T * L^T * R^(-1) * L * d)

3. Estimate Source Activity:
Source_Activity = W^T * X

4. Output: Return Reconstructed Source Activity

Connectivity Analysis



Structural (synaptic) connections linking sets of neurons or neuronal elements

Statistical association or dependency between two or more anatomically distinct time-series

Causal (directed) influences between neurons or neuronal populations

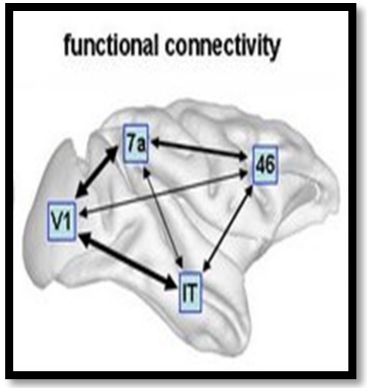
Functional Connectivity

Advantages

- No experimental control (i.e., resting-state but also useful for tasks)
  - Free from experimental confounds
  - Possible to scan participants who would find it difficult to complete a task
  - No model of what caused the data (i.e., sleep or hallucinations)

Disadvantages

- Interpretation of findings is based on correlations; descriptive
- No mechanistic insight
- Typically, dissatisfying for experimental tasks
- Typically, suboptimal for experiments with *a priori* knowledge



Phase Synchrony

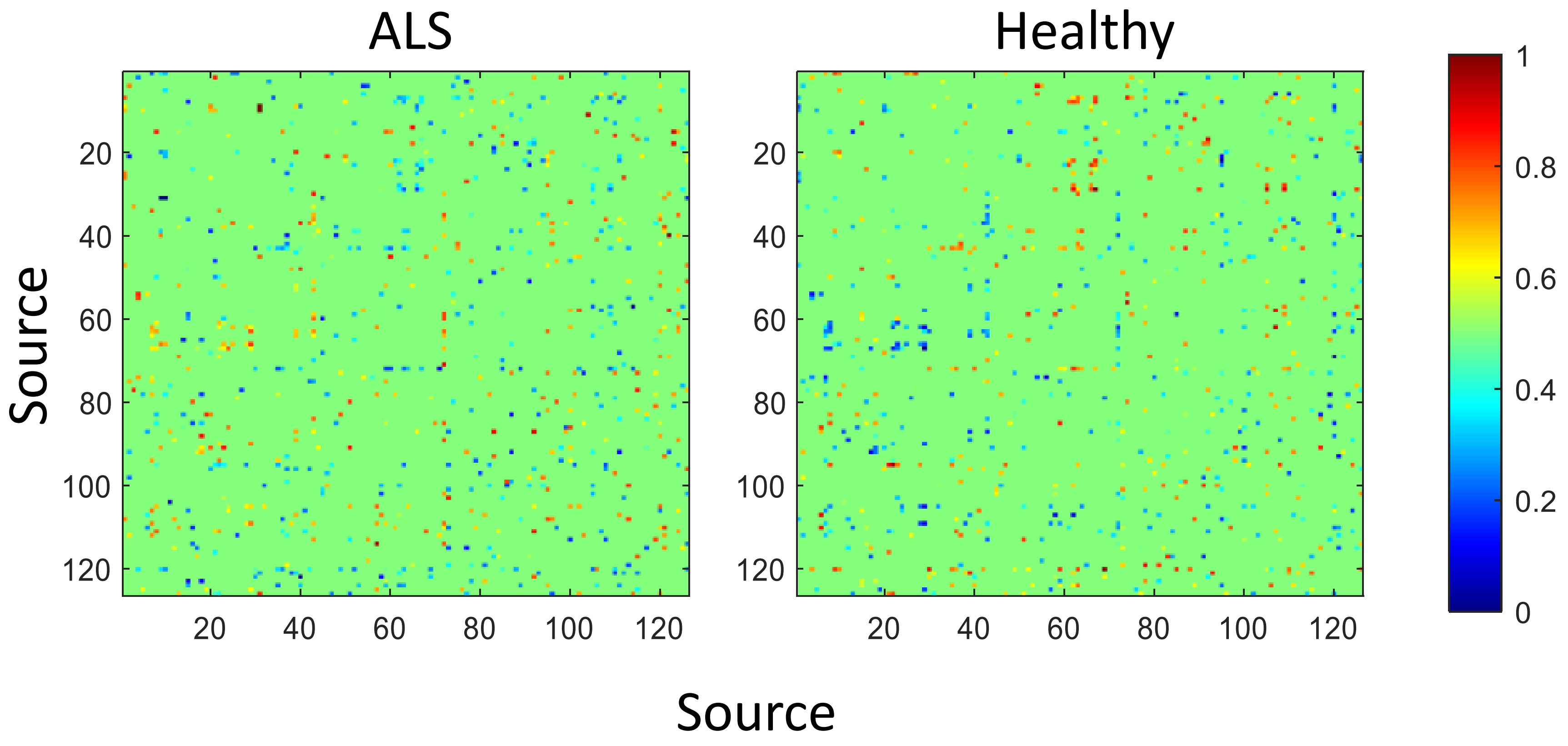
- **Phase Locking Value** is a measure of the consistency of the phase difference between two signals across trials or time. It quantifies the degree of synchronization between signals.

- **Phase Lag Index** measures the asymmetry in the distribution of phase differences between two signals, minimizing the effect of volume conduction.

- **Coherence** is a measure of the linear relationship between two signals as a function of frequency. It indicates the degree to which two signals are synchronized in both phase and amplitude.

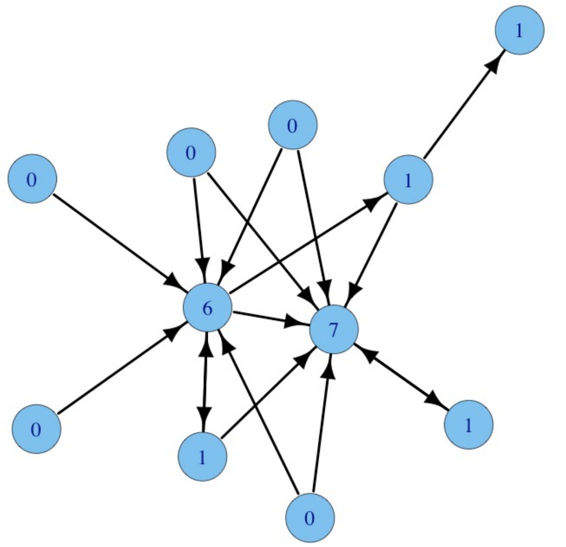
Brain Connectivity

Coherence → Imaginary Part

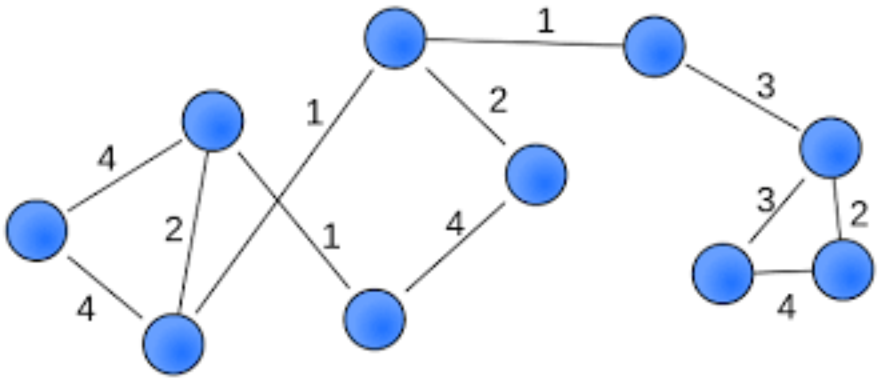


Measuring Brain Connectivity

Node degree refers to the number of connections (edges) that a particular node (or vertex) has to other nodes in the network..



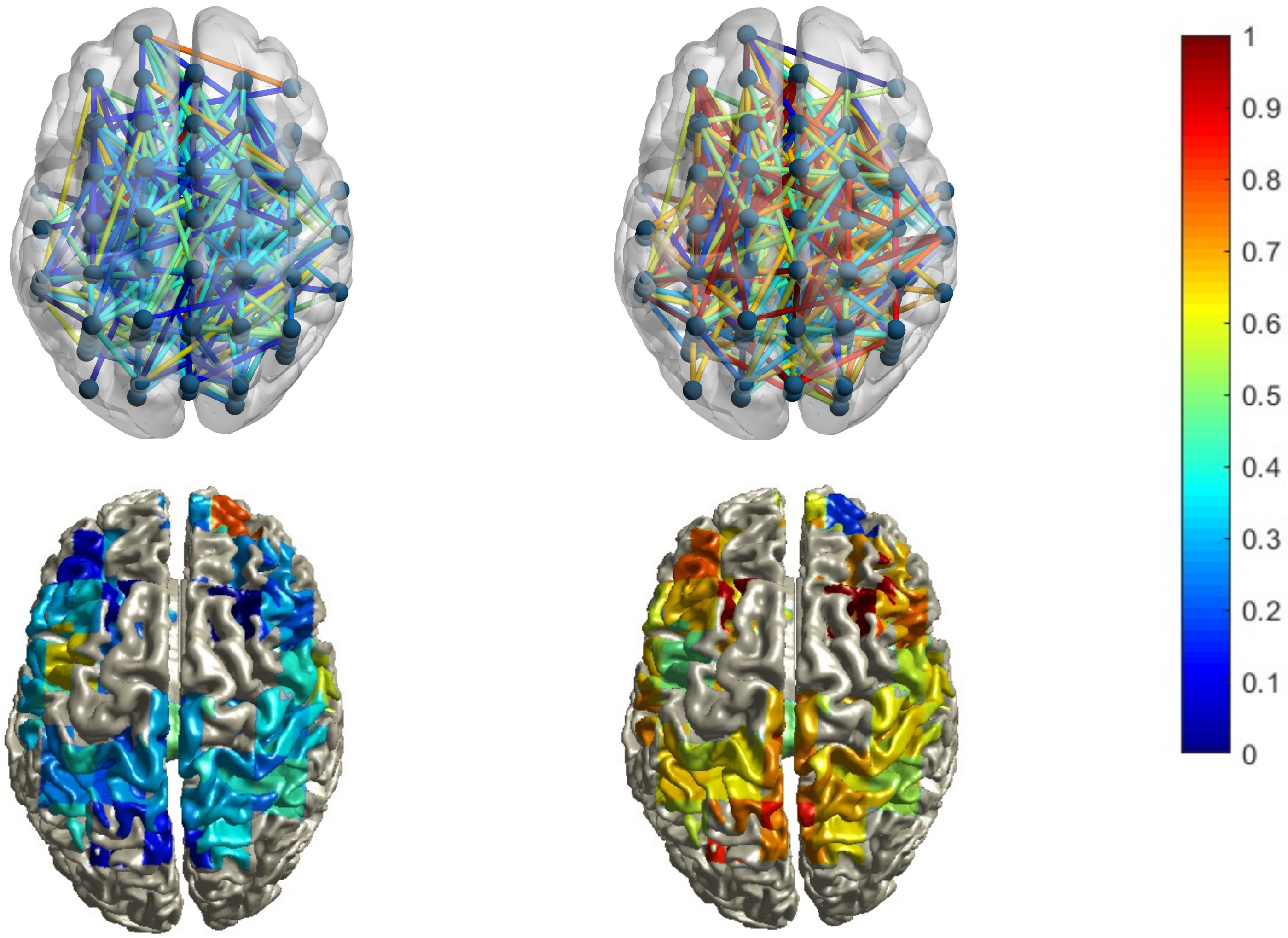
Node Strength sums the weights of these connections.



Connectivity Analysis on the ALS Dataset

Node Degree Connectivity Network

Node Strength Connectivity Network

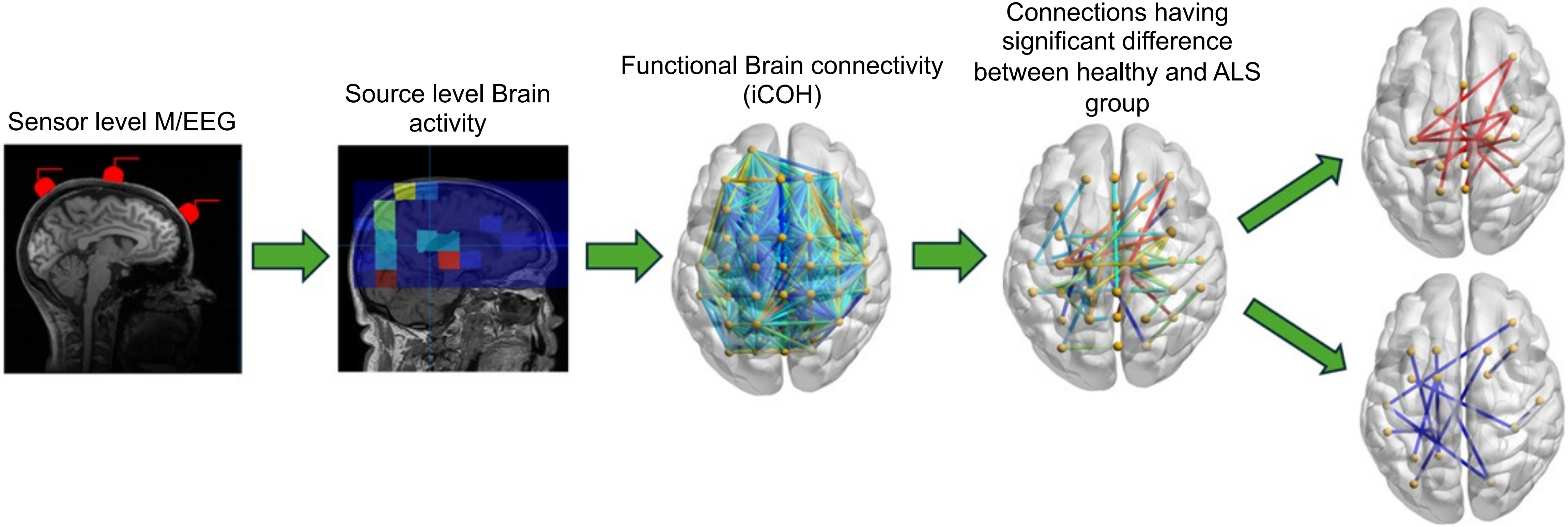


ALS

Healthy

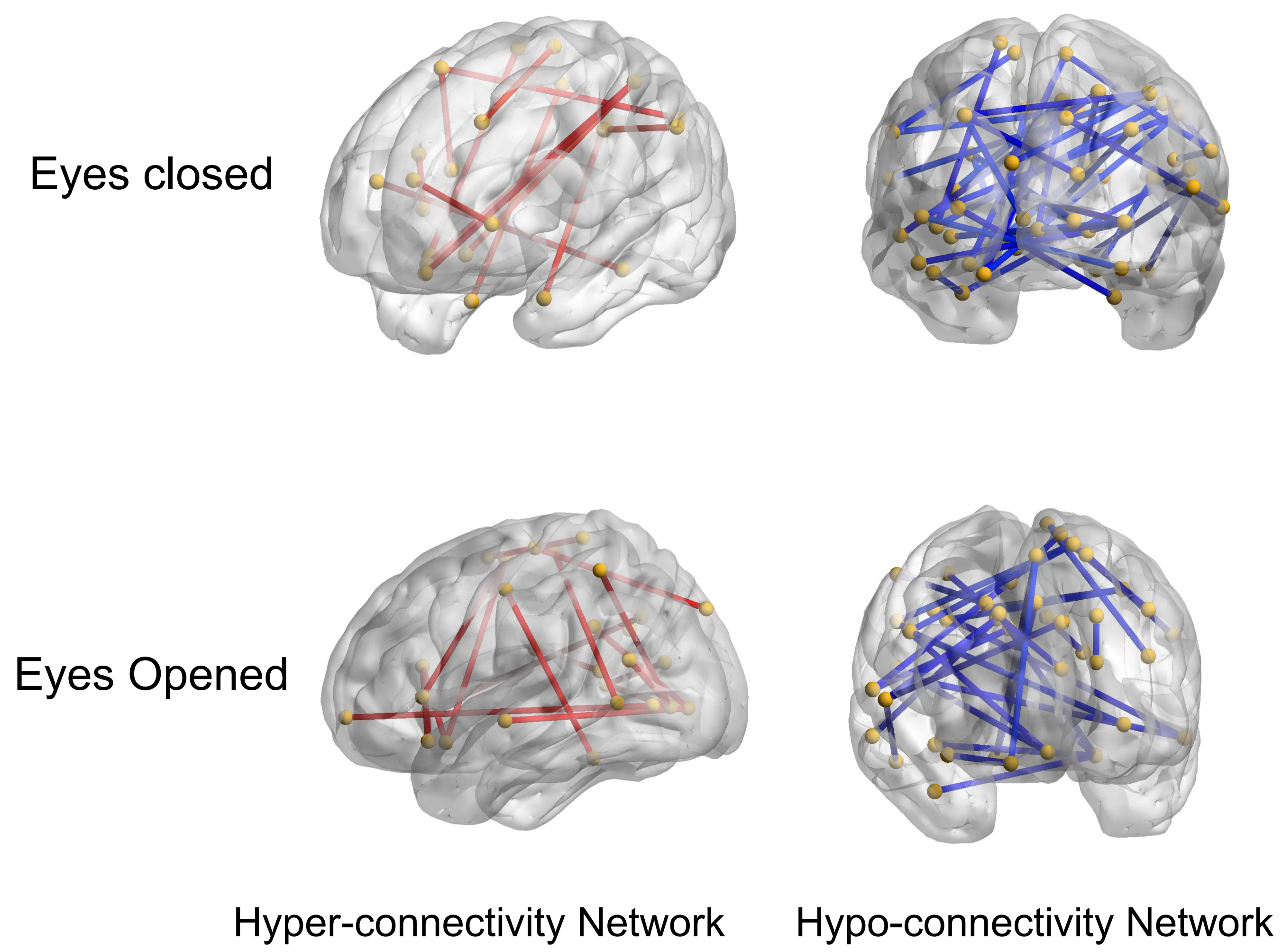
Connectivity between ALS and Healthy Group

Resting State



Our Interpretation

Differential Connectivity



- The left brain (red connections) highlights regions where the ALS group shows **hyper-connectivity** compared to the healthy group.
    - This hyper-connectivity could be compensatory, where the brain tries to maintain functionality despite ongoing neurodegeneration due to the disease.
- The right brain (blue connections) illustrates areas where there is **hypo-connectivity** in ALS compared to healthy controls, meaning
    - This hypo-connectivity might correspond to the degeneration of neural pathways, loss of neurons, or disruption of normal connectivity due to the progression of ALS.

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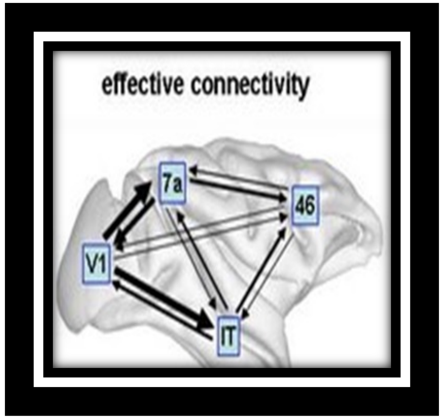
Effective Connectivity

Advantages

- To infer neurobiological mechanisms underlying cognitive function
- To infer causal or mechanistic function
- To infer experimental modulation
- To bridge the gap between rodent work and human work

Disadvantages

- Interpretation of findings is based on correlations; descriptive
- No mechanistic insight
- Typically, dissatisfying for experimental tasks
- Typically, suboptimal for experiments with *a priori* knowledge




TIME FOR A
BREAK

Collaborative BCI for Decision Making

Section 6

Making Decisions in Group

- **Most animals and humans live within groups. Why?**

A group can do things that individuals alone can't:

- **Augmented action capabilities:** Members of a group can join forces to do something that is beyond the strength or endurance of a single individual

- **Increased sensing capabilities:** A group has a much higher probability of finding resources and noticing danger

- **Increased cognition and intelligence:** groups show emergent cognition and intelligent behaviours which are more powerful than those of the individual members.

"OK, all those in favour of delegating decision-making, shrug your shoulders"

http://archive.timesandseasons.org/2015/07/small-group-dynamics/index.html

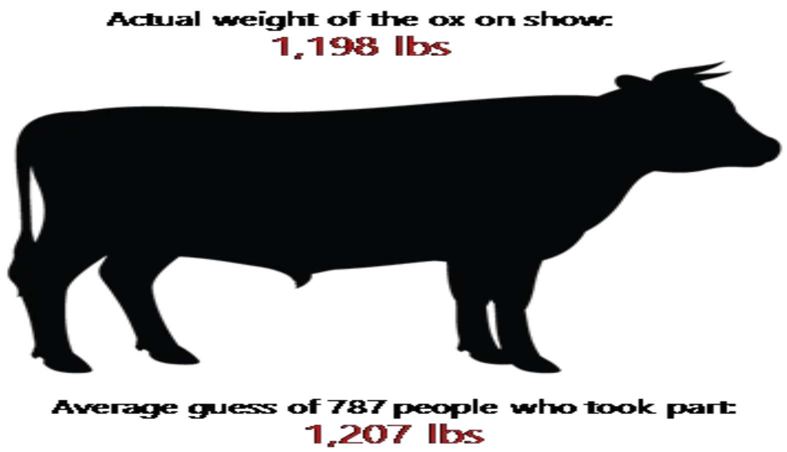
Wisdom of Crowd

- Sir Francis Galton, 1907 → Surowiecki J. (2004)

- Collective intelligence emerges from the aggregation of individual judgments, opinions, or decisions within a large group.

Key Characteristics
- Diversity of Opinion
- Decentralization
- Aggregation

Examples:
- Market Predictions
- Crowdsourcing



Surowiecki, J. (2004). *The Wisdom of Crowds: Why the Many Are Smarter Than the Few and How Collective Wisdom Shapes Business, Economies, Societies, and Nations*. New York: Doubleday.

French, C. W. (2002). *Review of James Surowiecki's 'The Wisdom of Crowds'*

Group and Individual Decision Making

Pros

- Improved Decision Time (Bang & Frith, 2017)
- Reduction of cognitive Biases (Charness & Sutter, 2012)
- Enhanced Collaboration (Bhattacharyya, 2021)
- Better Handling of Complex Problems (Islei & Lockett, 1991)

Cons

- Groupthink and Conformity Pressures (Kroon et al., 1992)
- Slower Decision-Making Process (Islei & Lockett, 1991)
- Less Accountability(Viscusi et al., 2011)
- Risky Shifts (Ezernik, 2014)

More discussion about it in Bang & Frith, 2017

'We make a great team! But you guys really need to contribute more.'

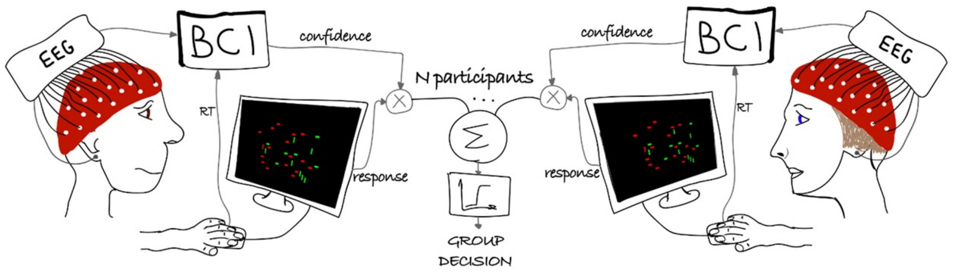
"That's an excellent suggestion, Miss Triggs. Perhaps one of the men here would like to make it."

Group Decision Making

Standard Approach – Majority Voting

Disadvantages
- Metacognitive Failure-Overconfidence (Bahrami et al., 2012)
- Psychological Entrapment (Kamedi & Sugomeri, 1993)
- Second guessing (Viscusi et al., 2011)
- Risky Shifts (Ezernik, 2014)

Mitigation Strategies
- Deliberation & Participation
- Feedback mechanism
- Weighing Decisions
    - Minority Inclusion
    - Adding objectivity → Neurotechnology (cBCI)

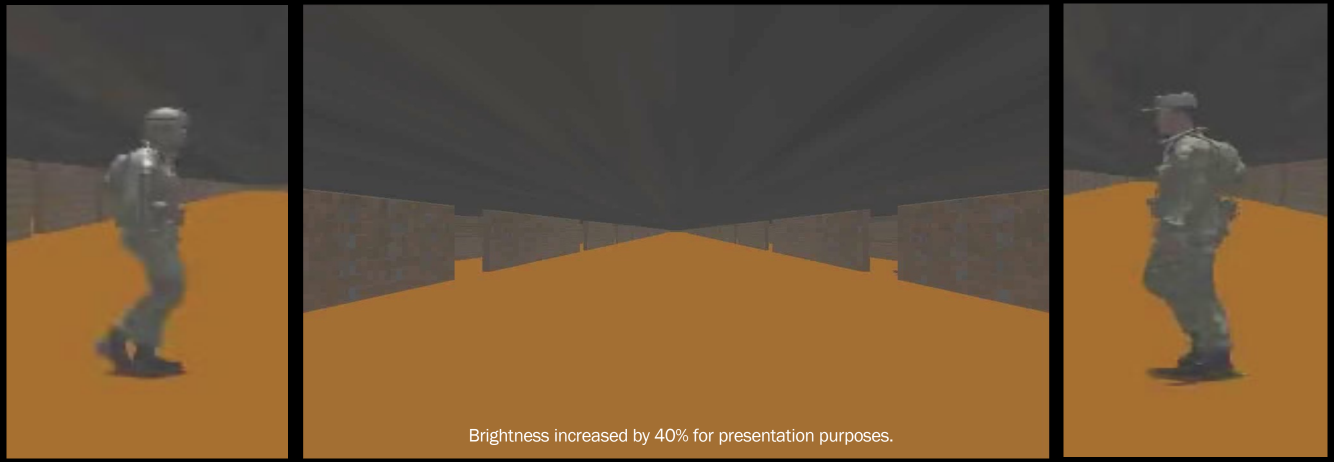


Anytime Collaborative BCI

❑ **Dynamic Environment- Patrol Experiment**

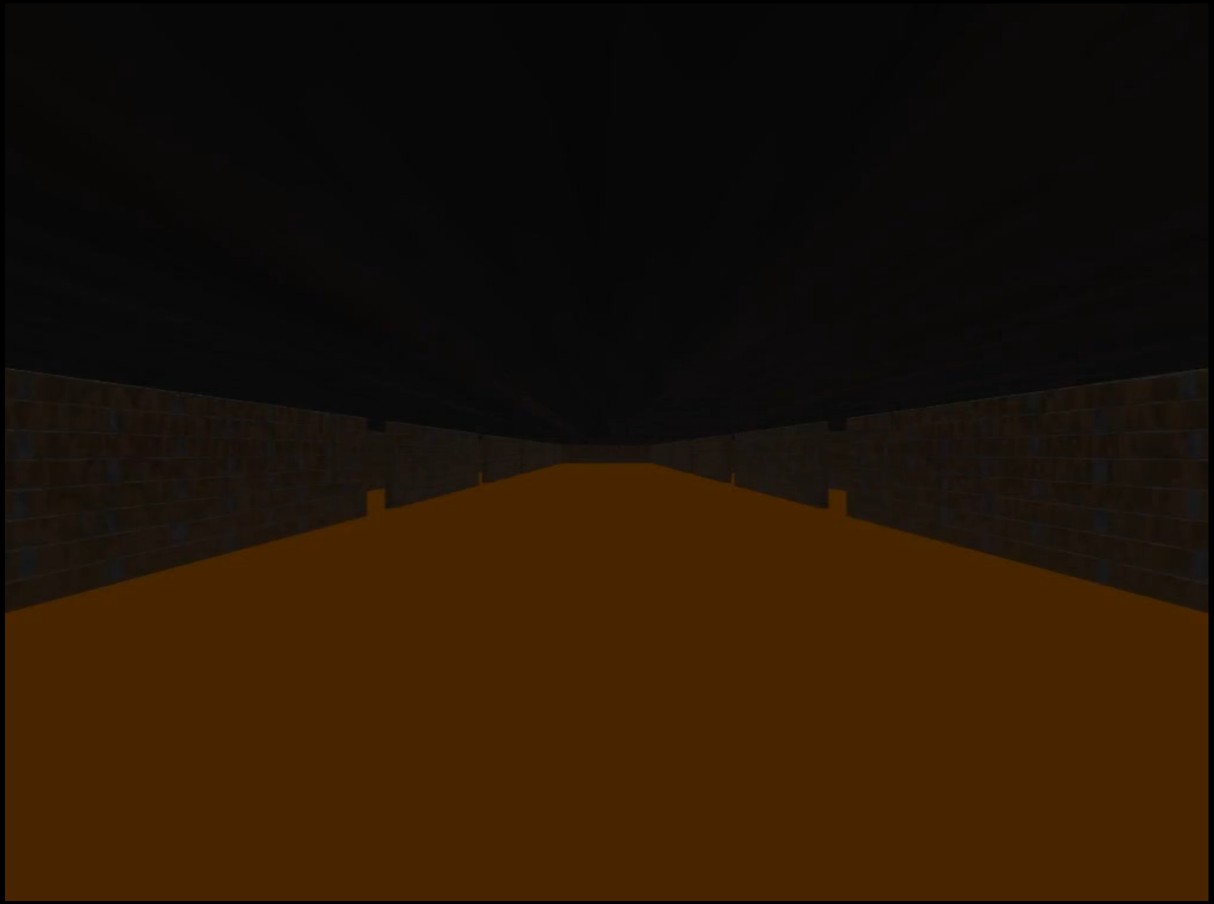
- We generated a dynamic environment where a soldier is walking along a corridor with multiple doorways present on both sides (Corridor/Patrol Experiment)

- Task: Decide whether the characters appearing wear a helmet or a cap



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

Anytime Collaborative BCI



Designing more complex experiments

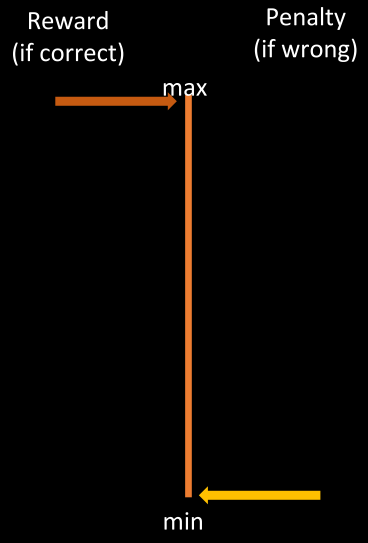
Dynamic Environment- Outpost Experiment

- **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).**



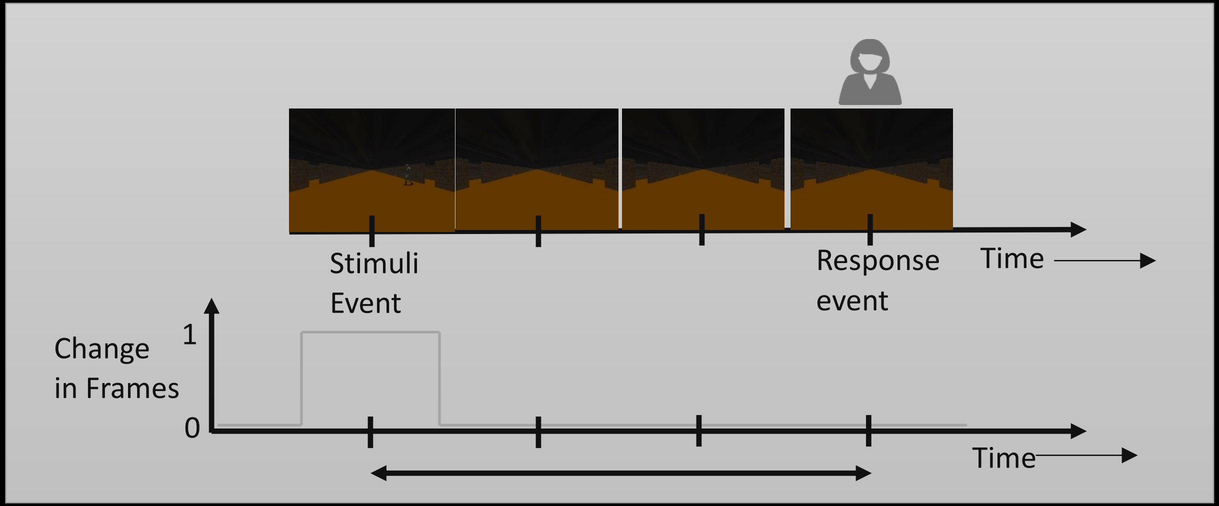
Bhattacharyya et al. Scientific Report (2021)

Towards Anytime cBCI

Reconstructing the response times

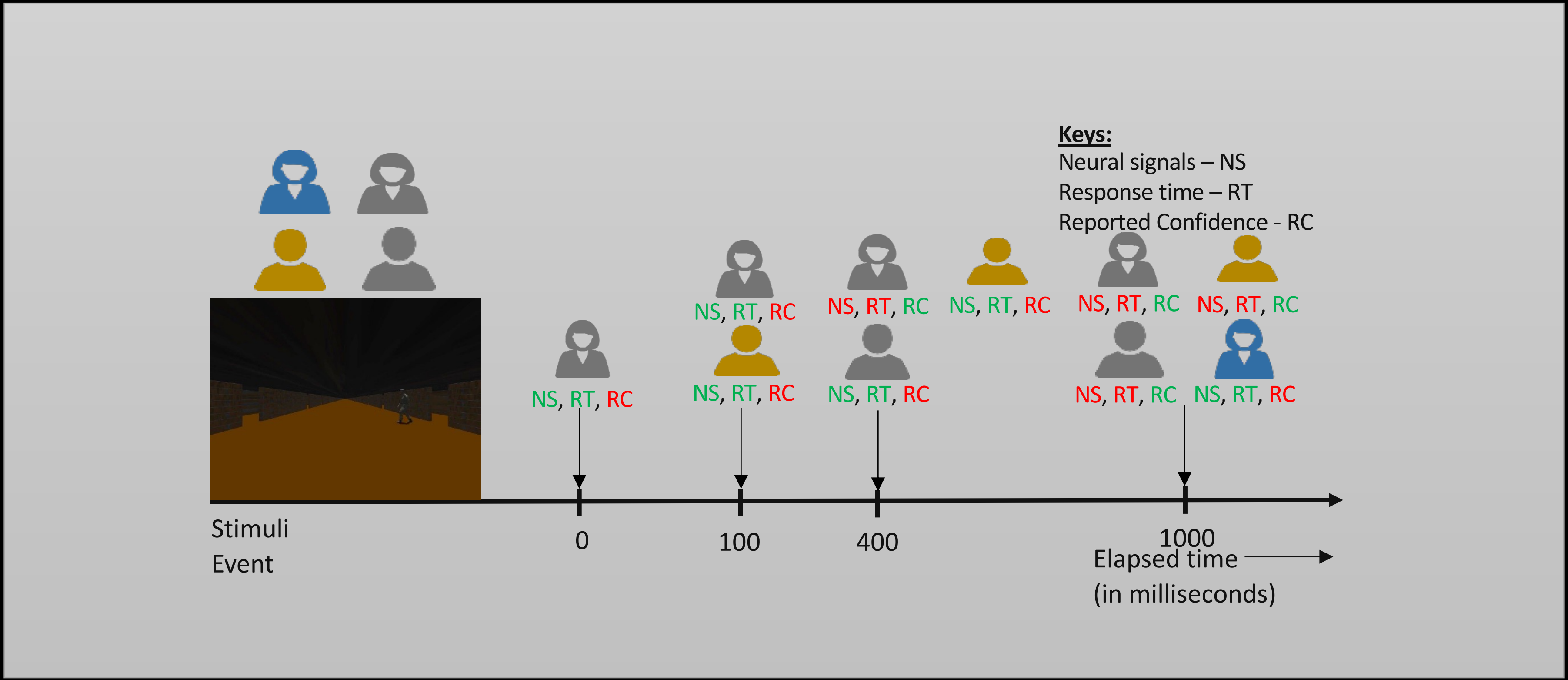
- **Key issue:** In real life we know when a participant has a reaction (button press) but we don't know what caused it and when. So, **RT is not readily available**.
- Implemented an **automated system** to detect a **sudden change in video frames** preceding the user's response.

sudden change frame ≅ stimulus onset



Bhattacharyya et al. Scientific Report (2021)

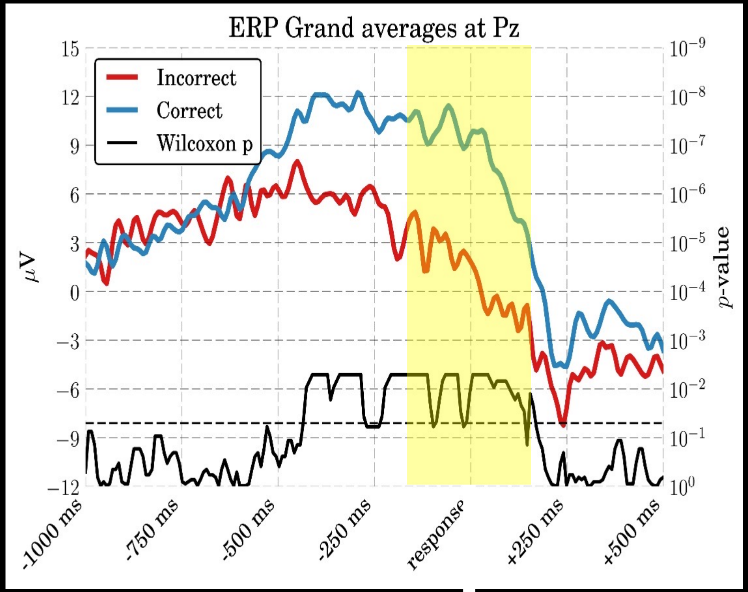
The anytime cBCI



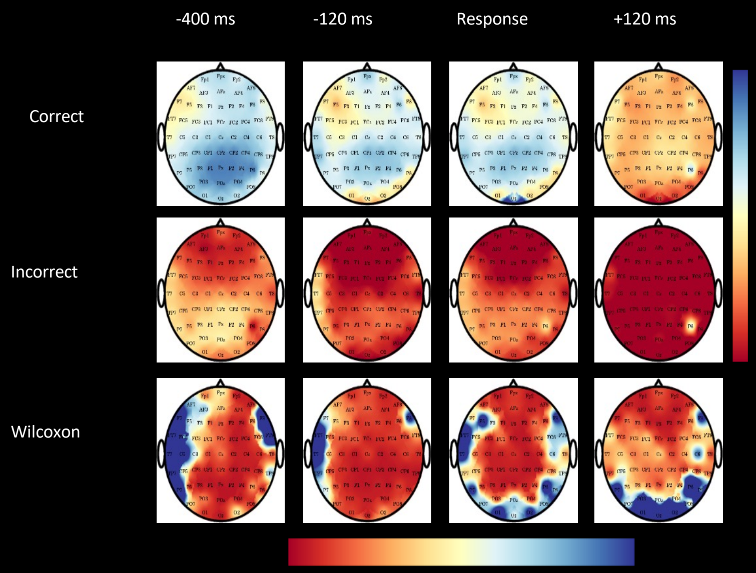
At **every 100ms** after the first response, the system searches for other members in the group who has responded.

Bhattacharyya et al. Scientific Report (2021)

Evidence of Neural Markers



Decision-Related Potential (DRP)



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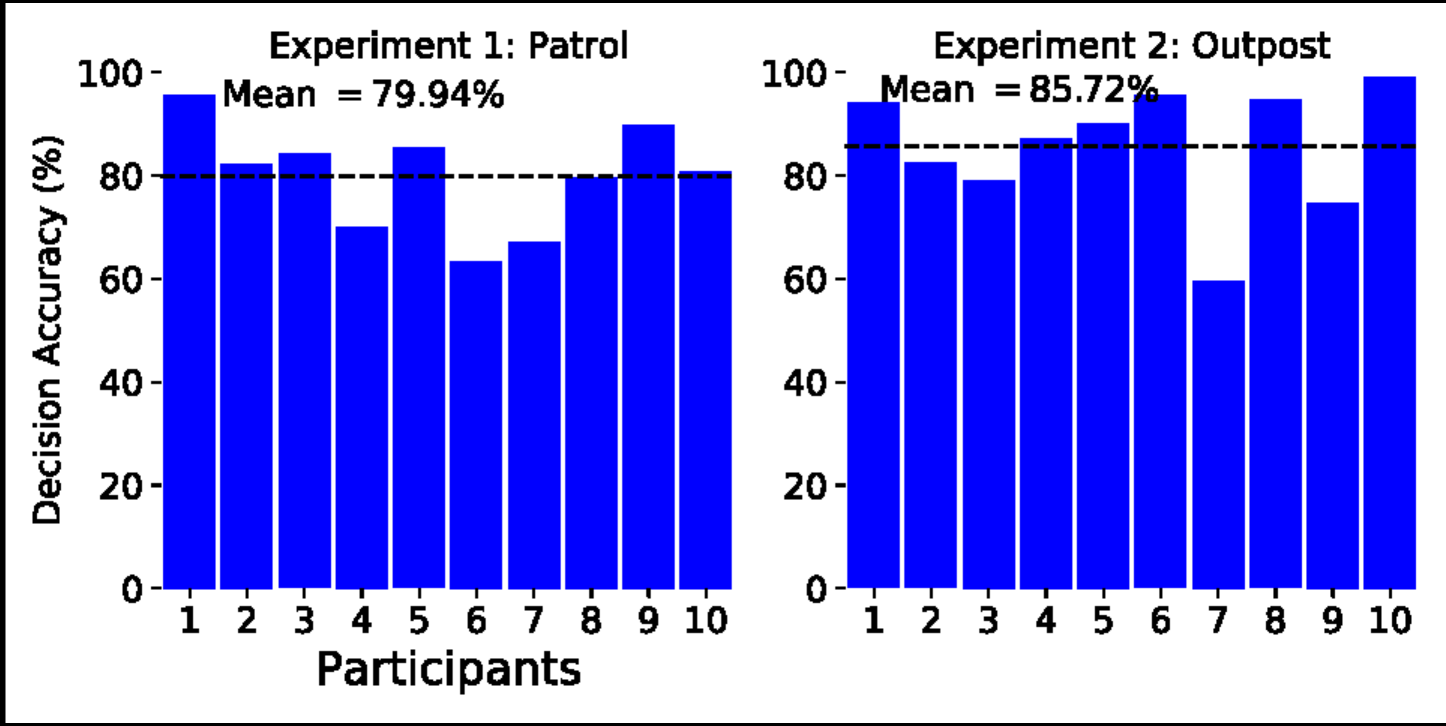
Decision accuracy is…

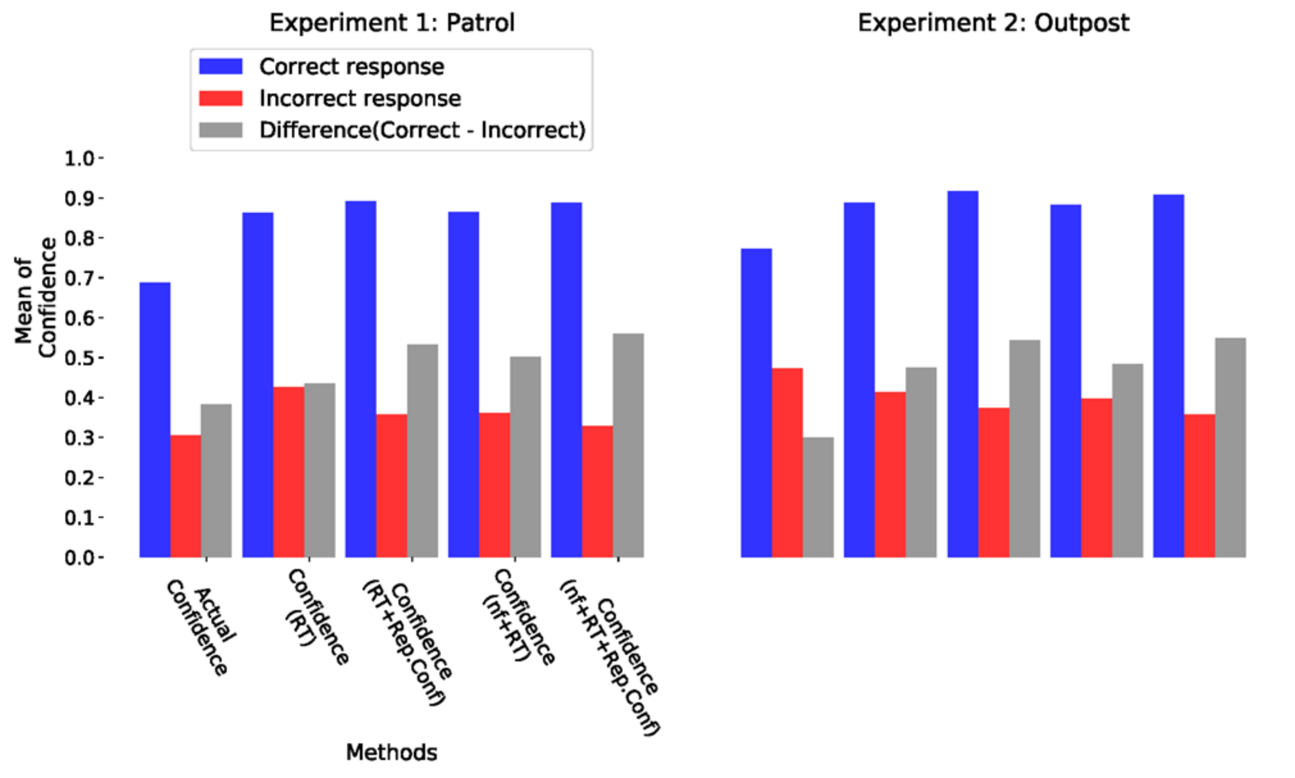


Bhattacharyya et al. Scientific Report (2021)

Subjective and objective confidence

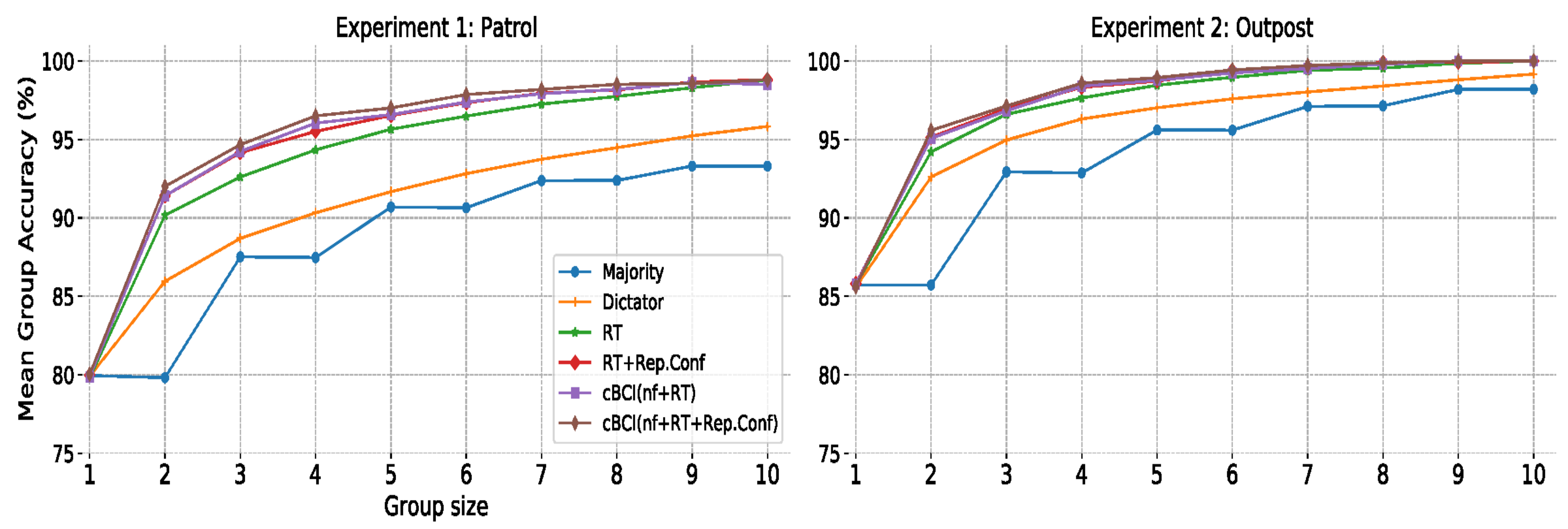
Objective confidence using-

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



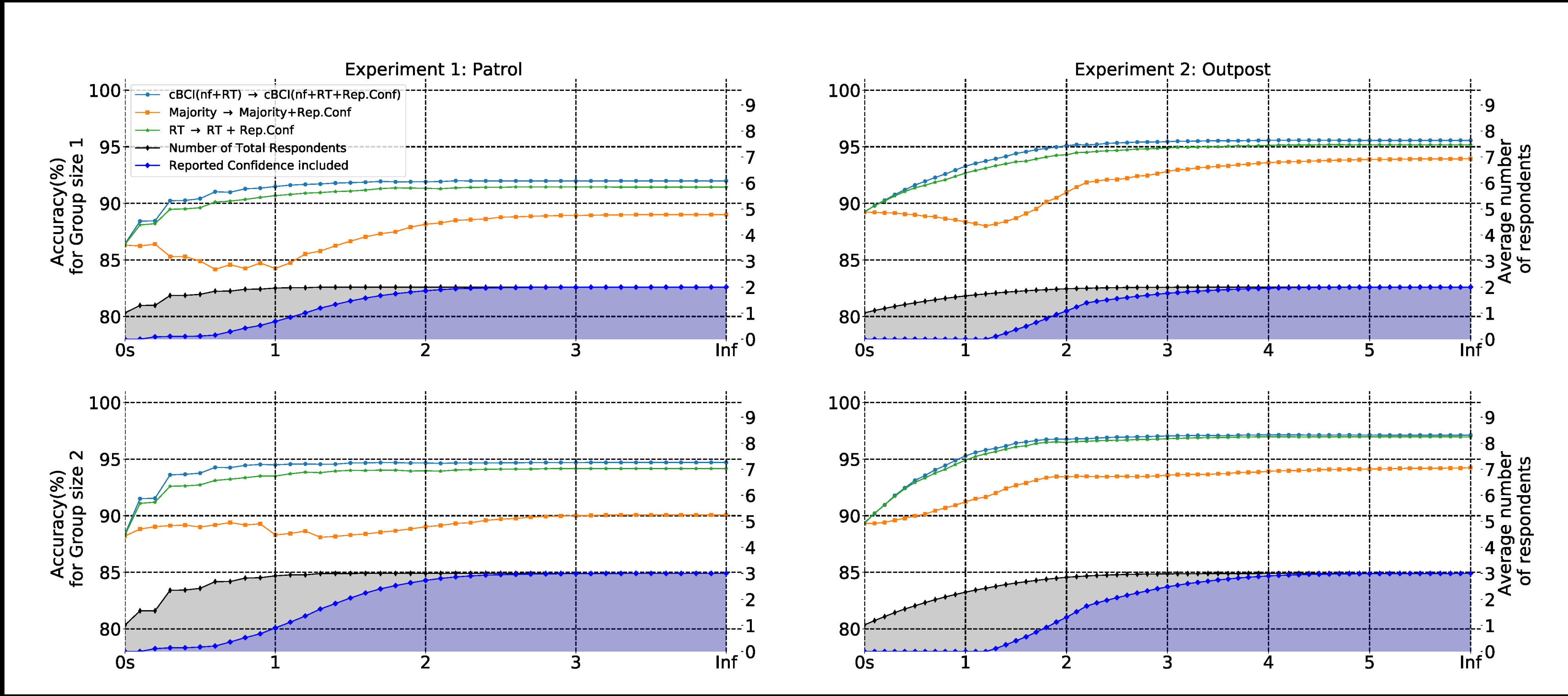
Bhattacharyya et al. Scientific Report (2021)

cBCI works better



Bhattacharyya et al. Scientific Report (2021)

Optimal time vs accuracy

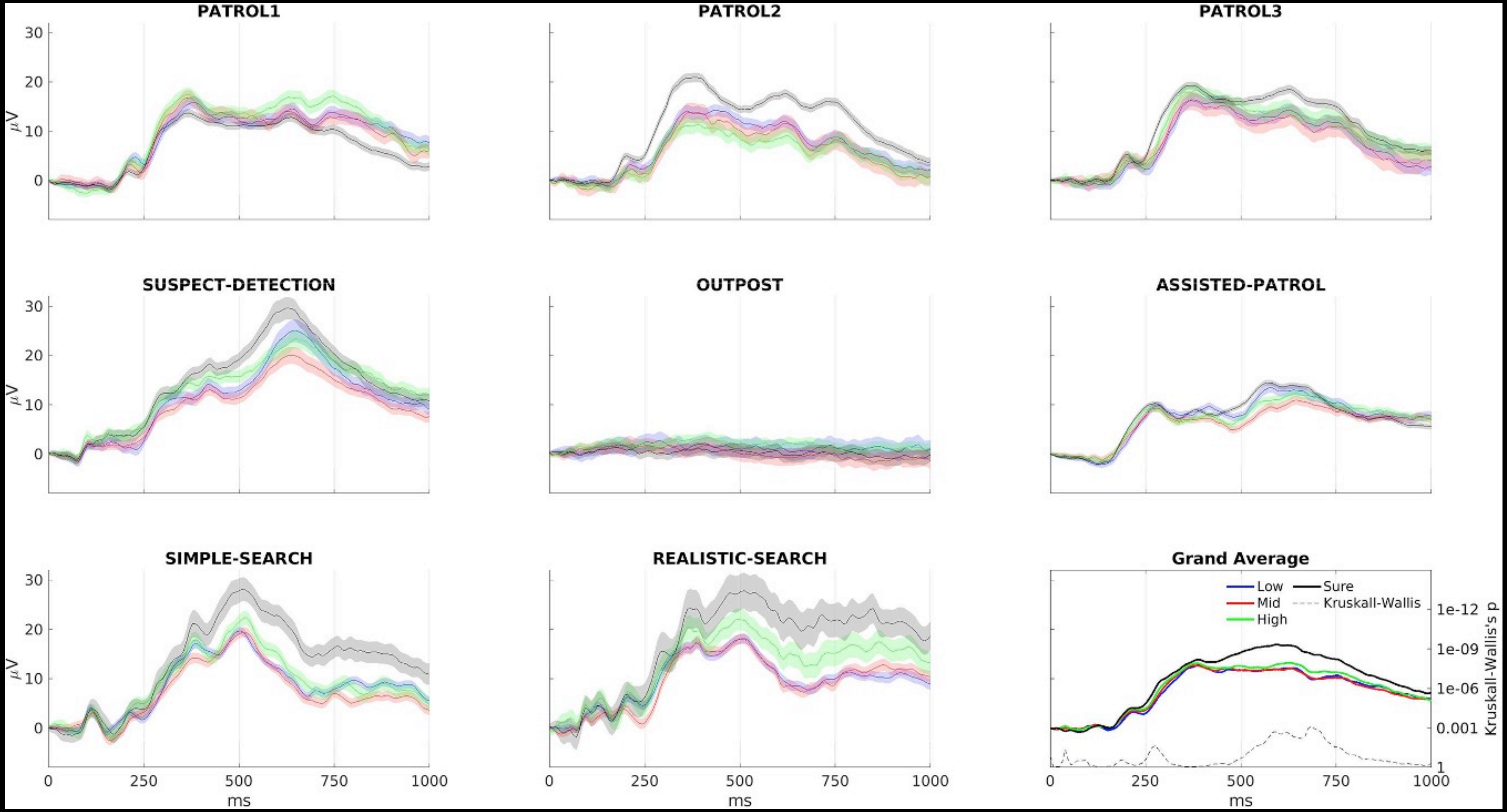


- Interestingly, after a rather rapid transient, accuracy tends to plateau.
- Near optimal decisions can be obtained well before all participants have responded and reported their confidence.

Bhattacharyya et al. Scientific Report (2021)

Prediction of Decision Confidence

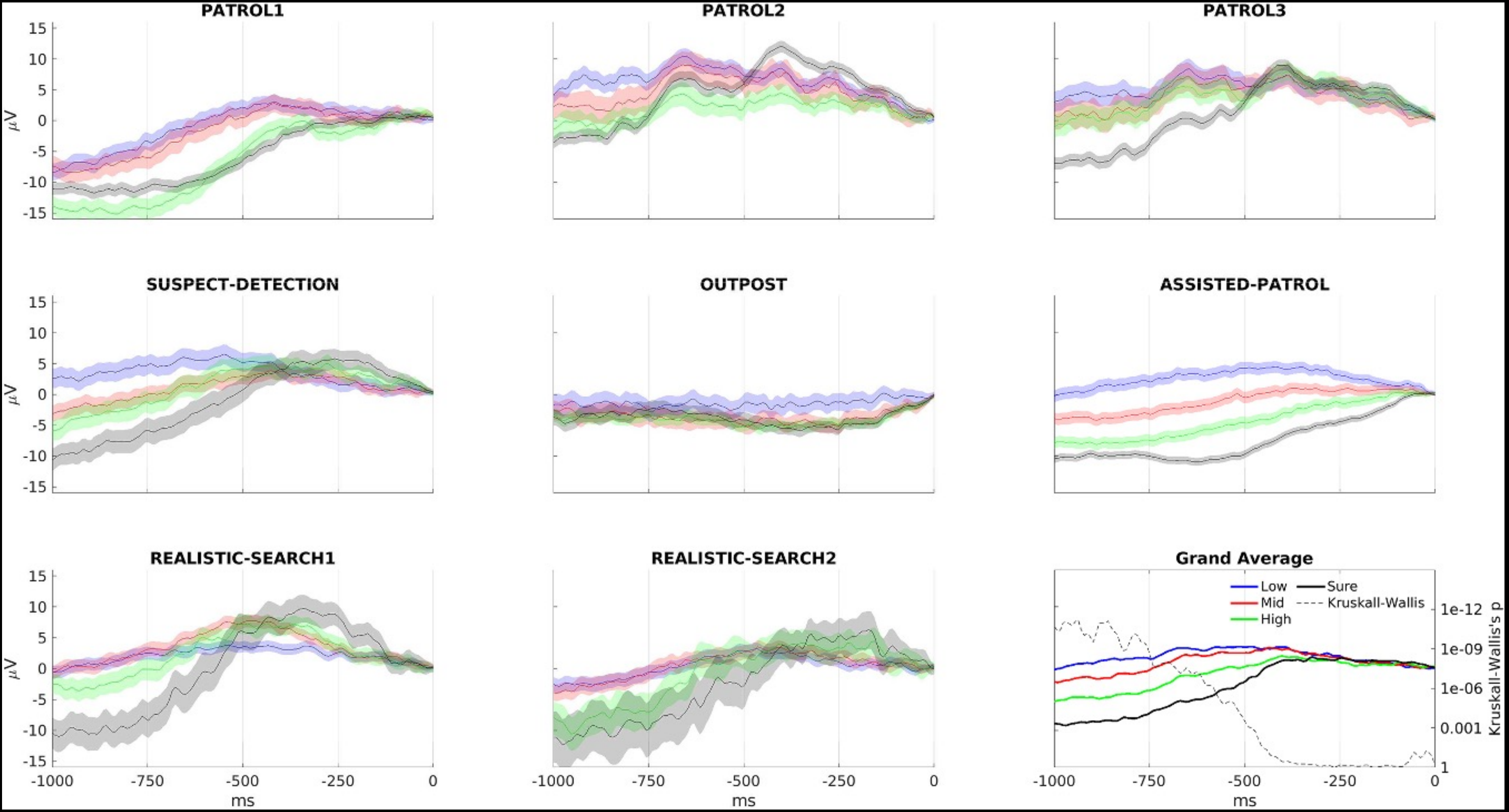
- Stimulus-Locked Event



Fernandez-Vargas et al. JNE(2021)

Prediction of Decision Confidence

- Response-Locked Event

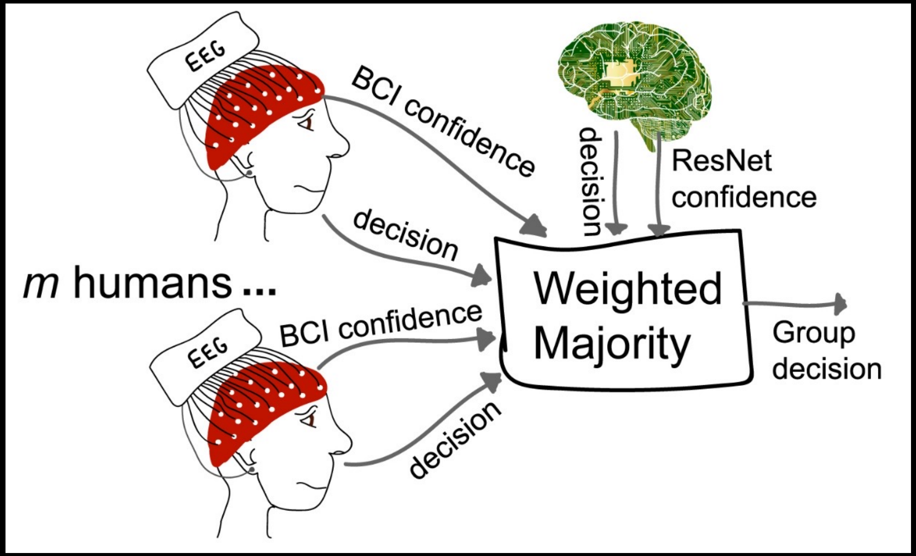


Fernandez-Vargas et al. JNE(2021)

Human-Machine teaming-preliminary work

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

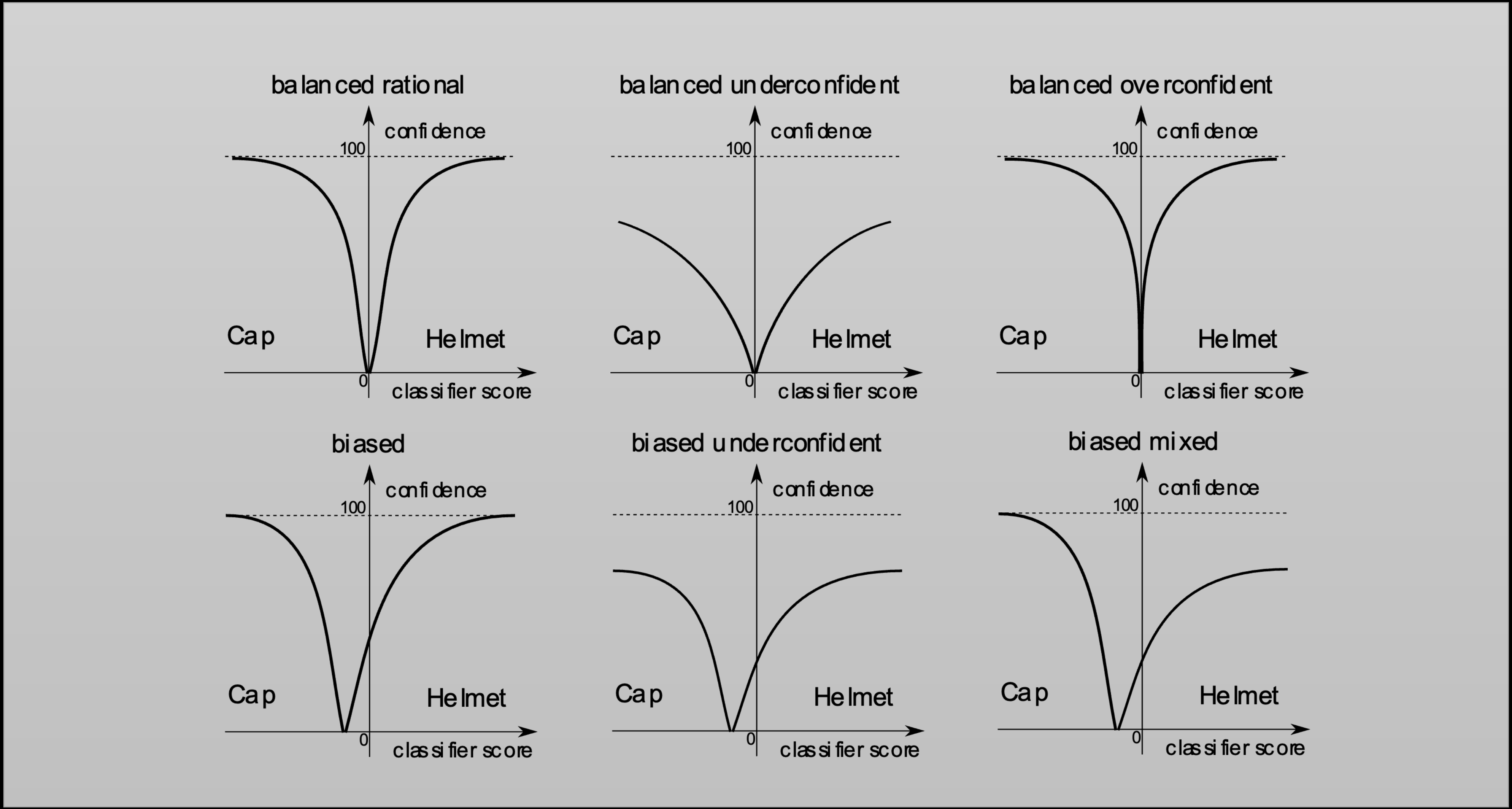
AI as additional team member



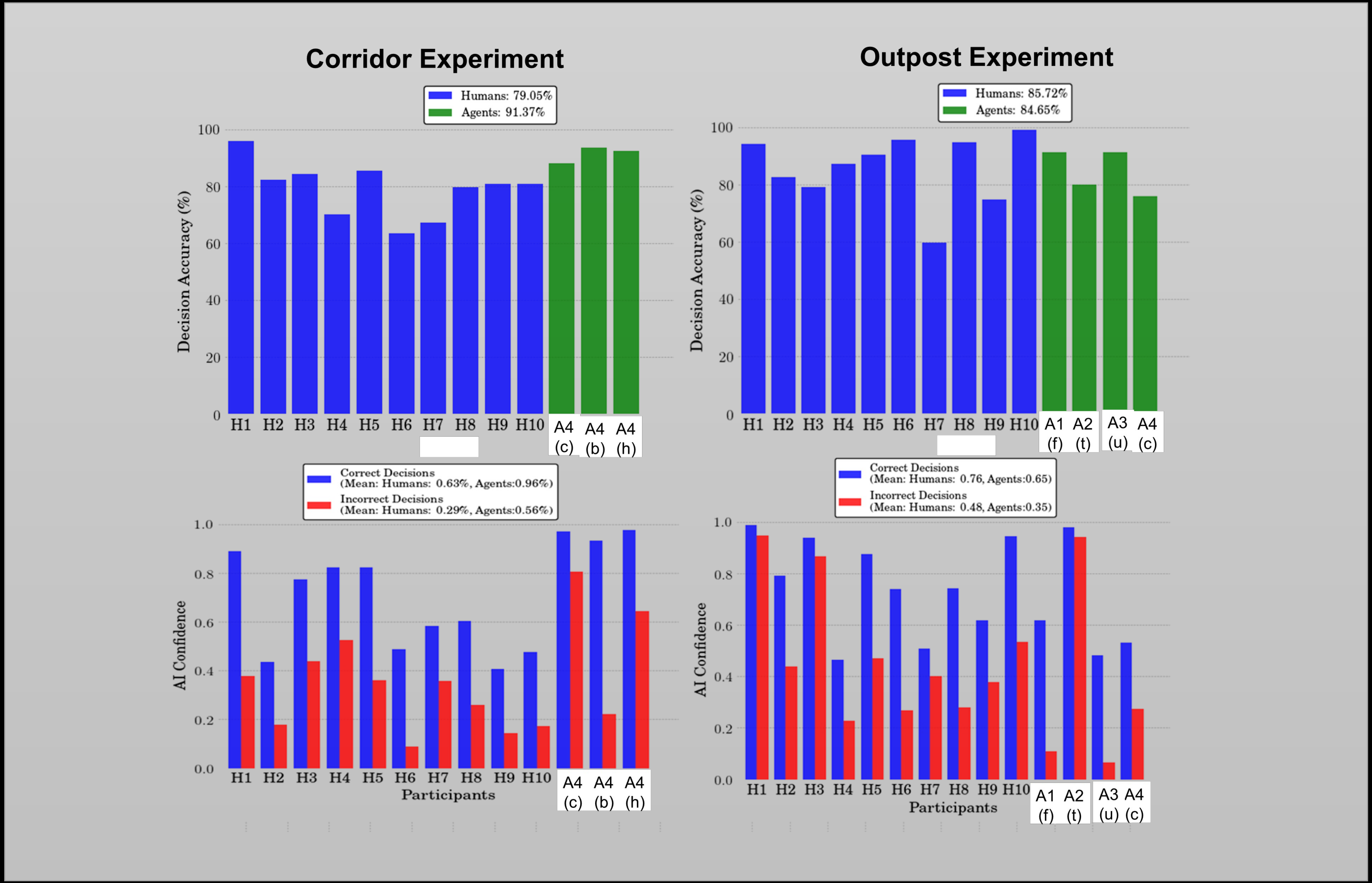
Re-simulating the patrol and outpost experiment

Valeriani et al. PlosONE (2019)

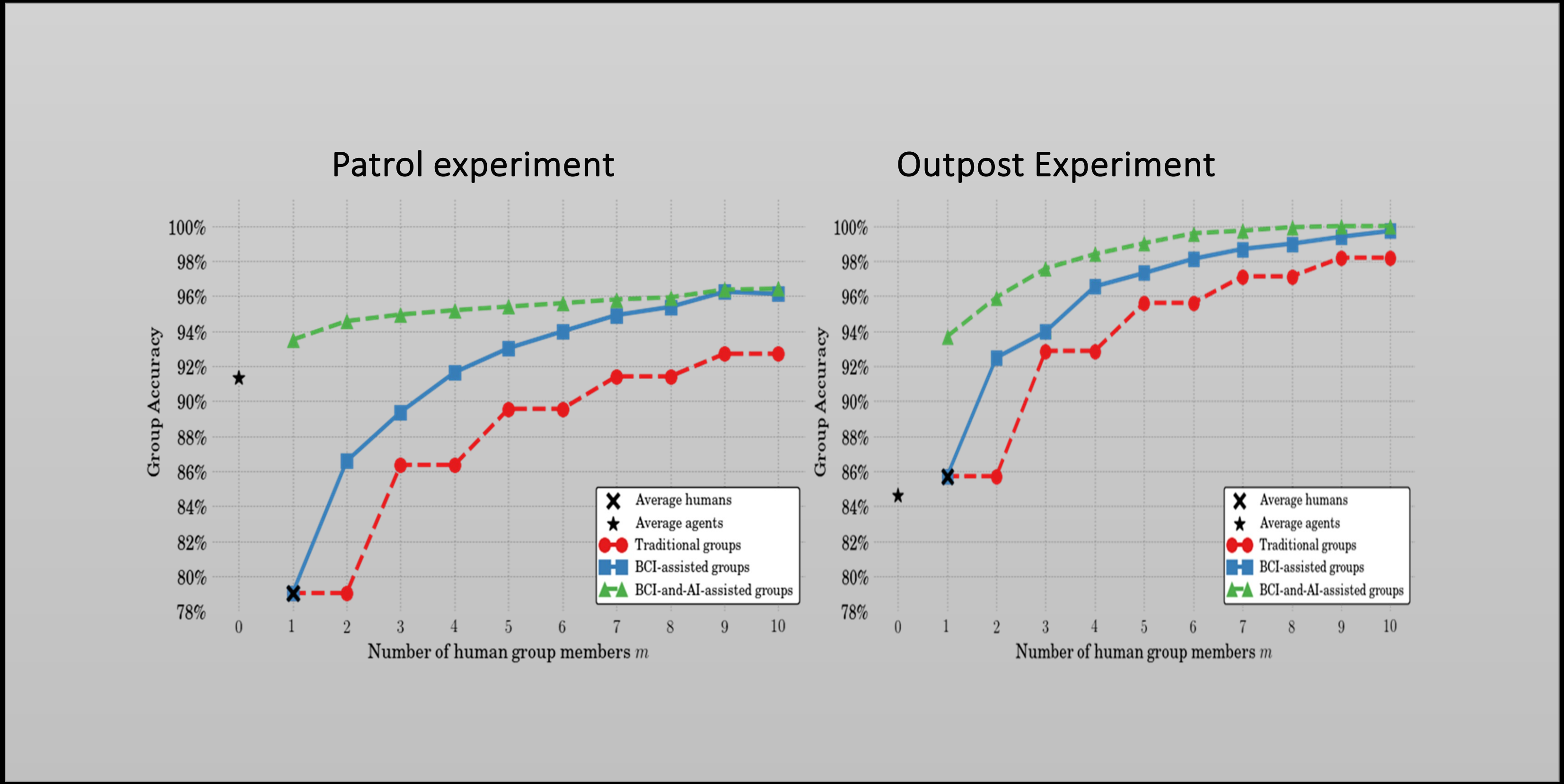
Confidence functions for AI



Behavioral results of humans and agents



group results of humans and agents



Thanks to…

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

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Collaborators


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Luca Citi


Caterina Cinel


Davide Valeriani


Jacobo Fernandez-Vargas


Christoph Tremmel

THAN K YOU for listening

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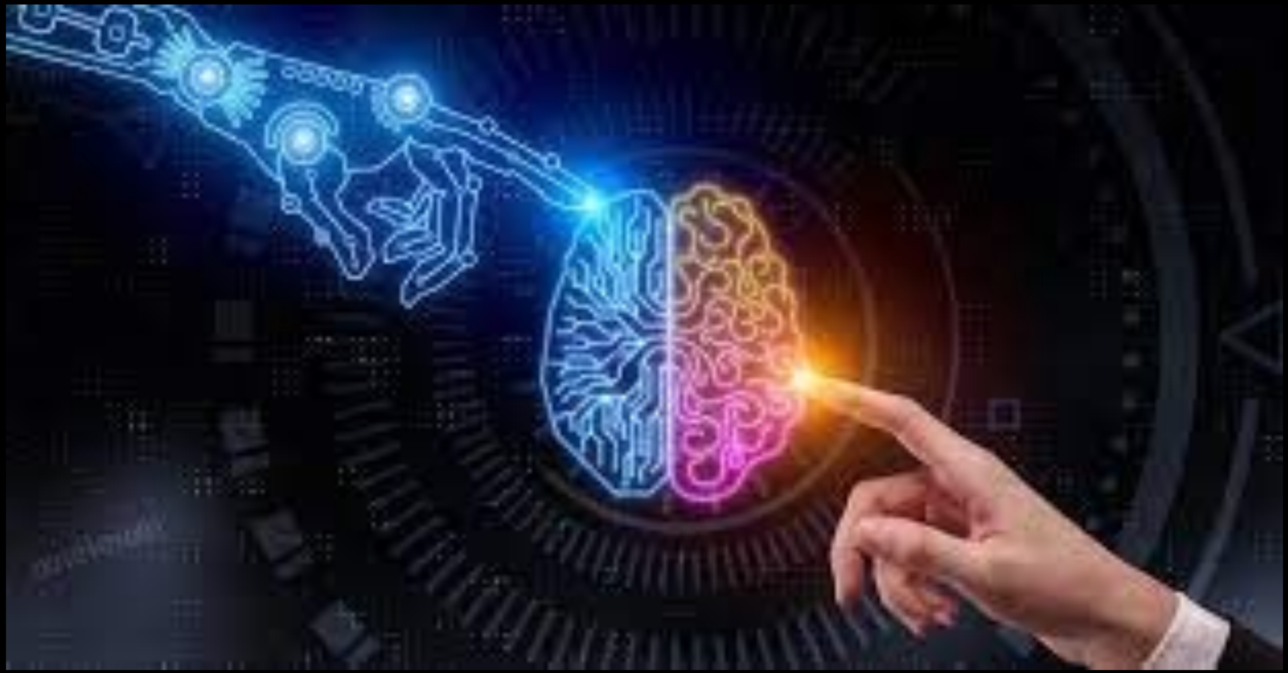
Take-home message



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