Local neurodynamics to assess physiological and pathological network functioning

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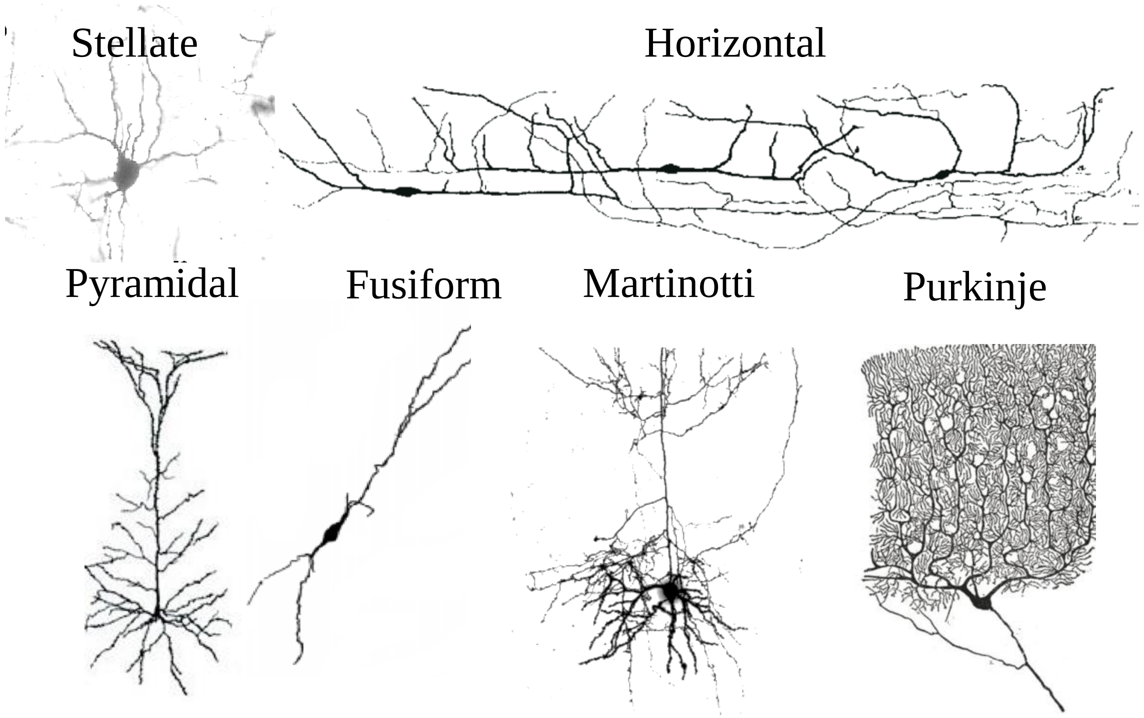
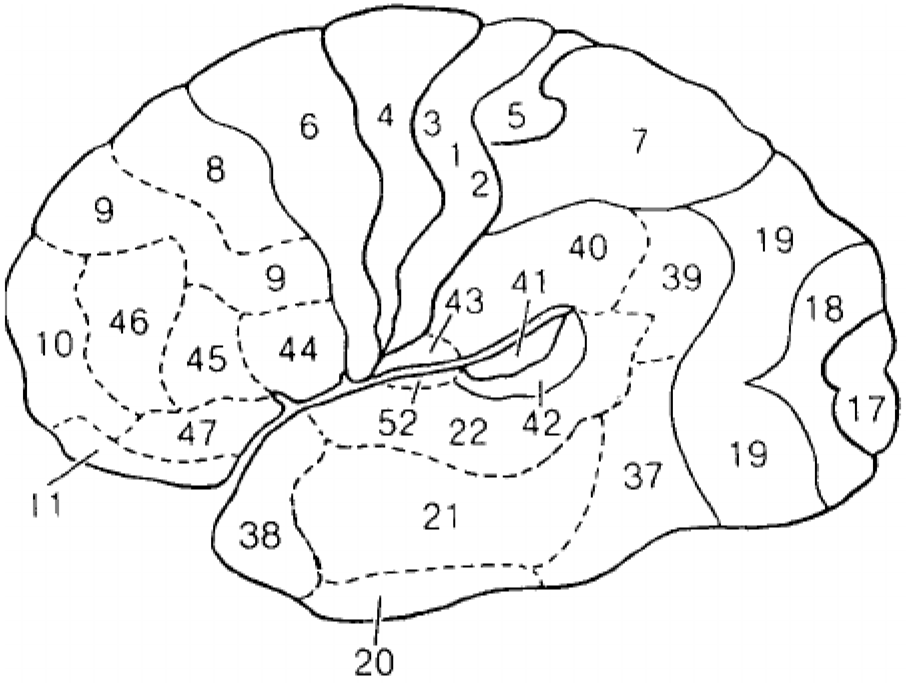
Brain parcelling according to the cytoarchitecture & Brodmann areas





Identity of a neuron:
morphology, biochemistry, function

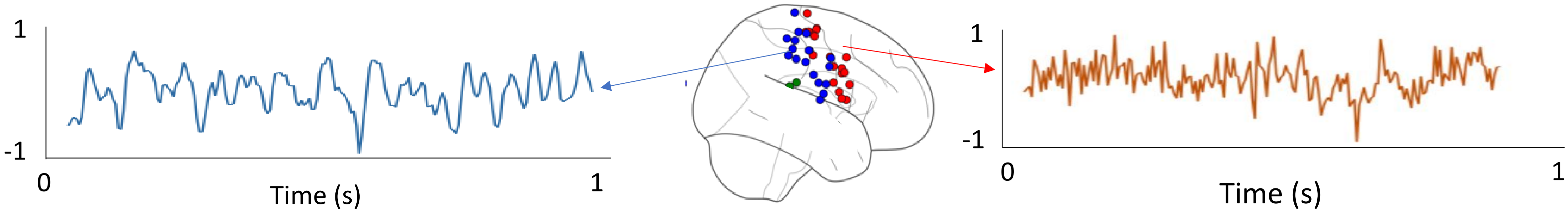
Parcelling of the cerebral cortex based on cell identity and laminar organization

Working hypothesis

Definition: neuronal pools, tightly connected within and between other pools, exhibit specific time course of neural electrical activity, hereafter **neurodynamics**.

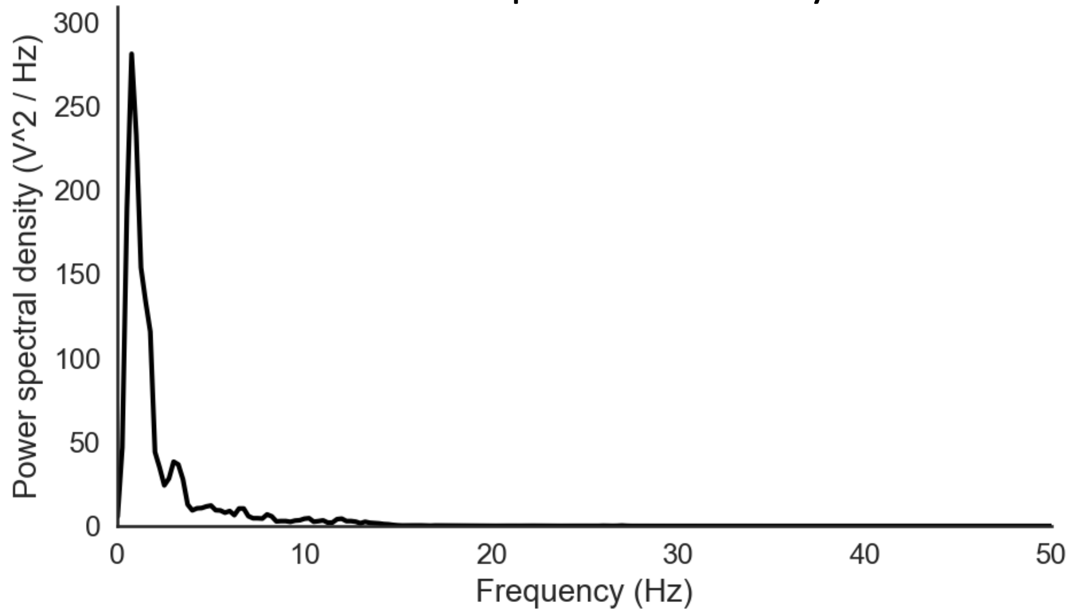
Hypothesis: as expression of different cortical areas possessing specific organizations, neuronal pools might exhibit a specific **neurodynamics.**

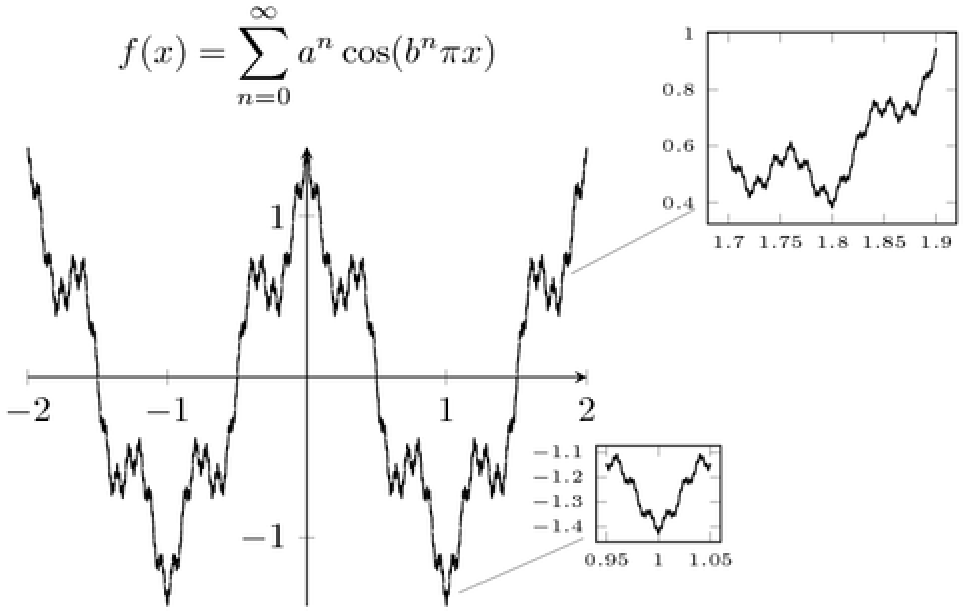
The recordings of electroencephalography (EEG), electrocorticogram (ECoG) or local field potential (LFP) could contain a **signature of the characteristics of each area**.



Linear & fractality measures for neurodynamics evaluation

Power spectrum density





Power Spectrum Density (PSD)

- Fast Fourier Transform (FFT):
- $F(\omega_k) = \sum_{n=0}^{N-1} f(n)\, e^{-i\omega_k n}$ with $k = 0,1,\ldots,N-1$
- Welch method: average on m FFT lines

Fractal dimension (FD)

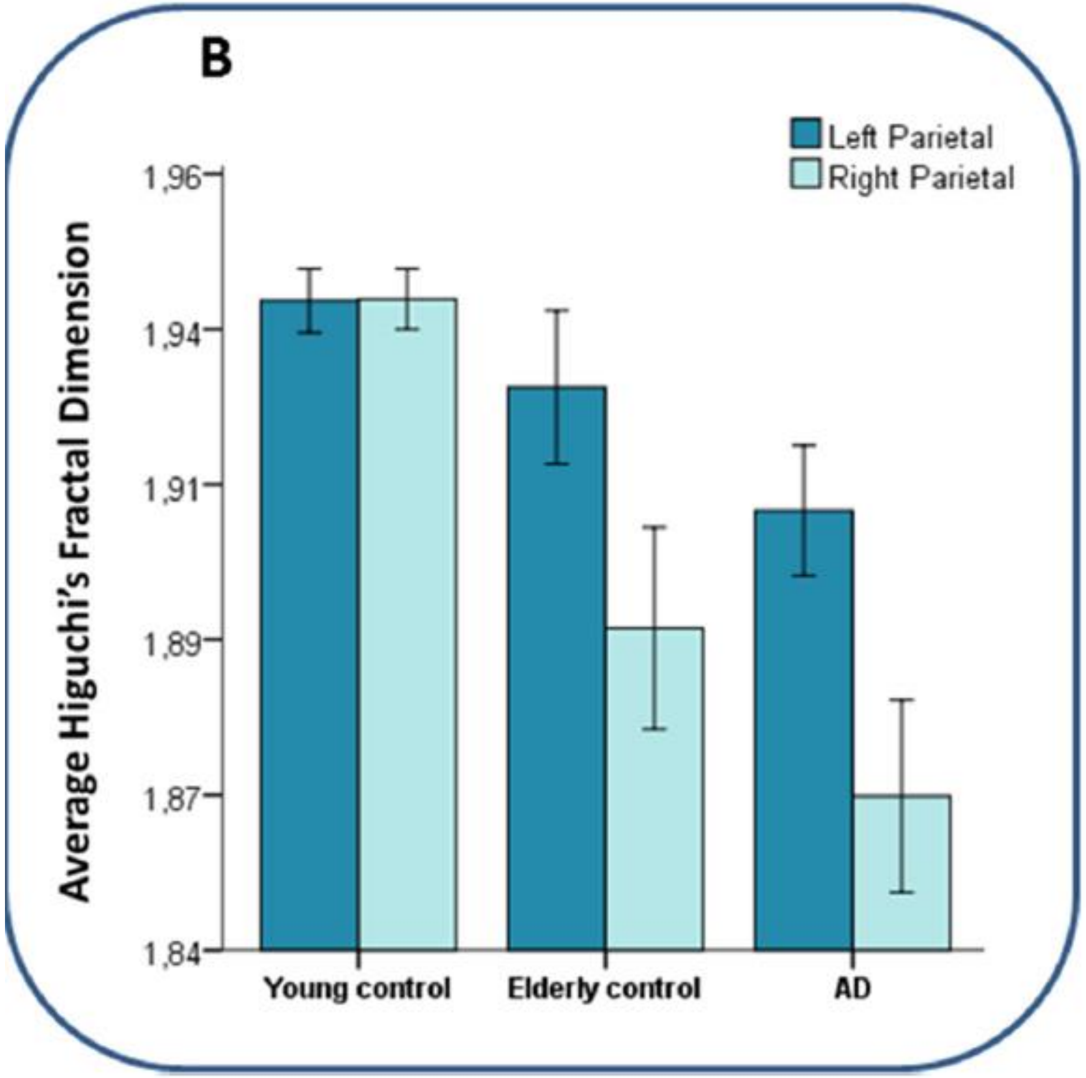
- Looking for self-similar patterns
- Fractal objects exhibit self-similarity at all scales

Evidence of distinct neurodynamics in healthy and pathological condition

Fractal dimensions decreases in healthy aging (EC) with respect to young adults (YC), where lowest complexity of neurodynamics is observed in Alzheimer's disease (AD).

The fractal dimension follows pattern

YC > EC > AD

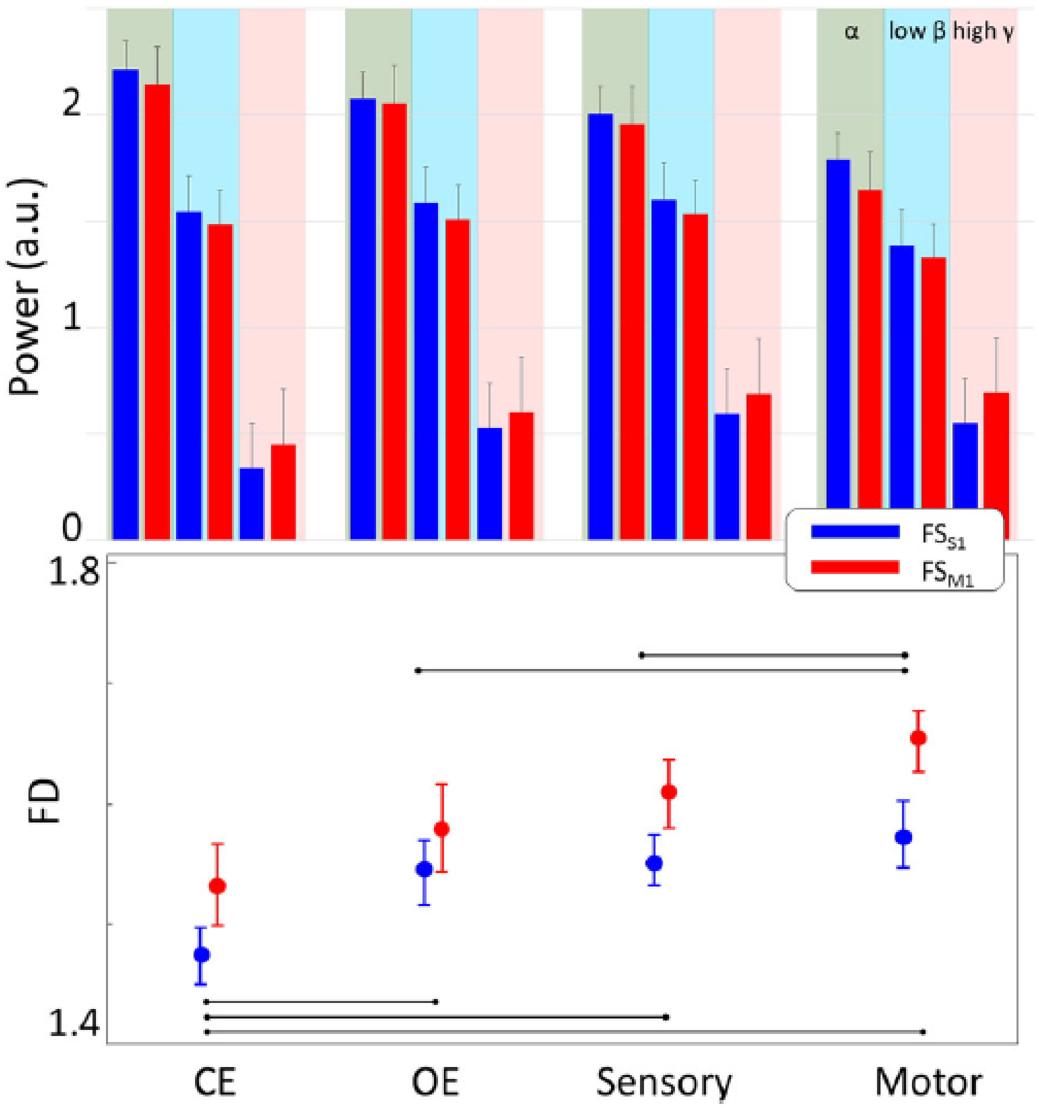


Smits et al., Brain, 2016, Plos ONE, doi:10.1371/journal.pone.0149587

Evidence of distinct neurodynamics across different cortical parcels

The neurodynamic of primary motor cortex (M1) shows significantly greater oscillations in higher frequency bands and greater complexity than the that of primary somatosensory cortex (S1).

- S1 > M1 in α frequency band (8 - 12Hz)
- M1 > S1 in β,γ freq. bands (12 - 33 Hz, 33 - 80 Hz)
- M1 > S1 with respect to fractal dimension

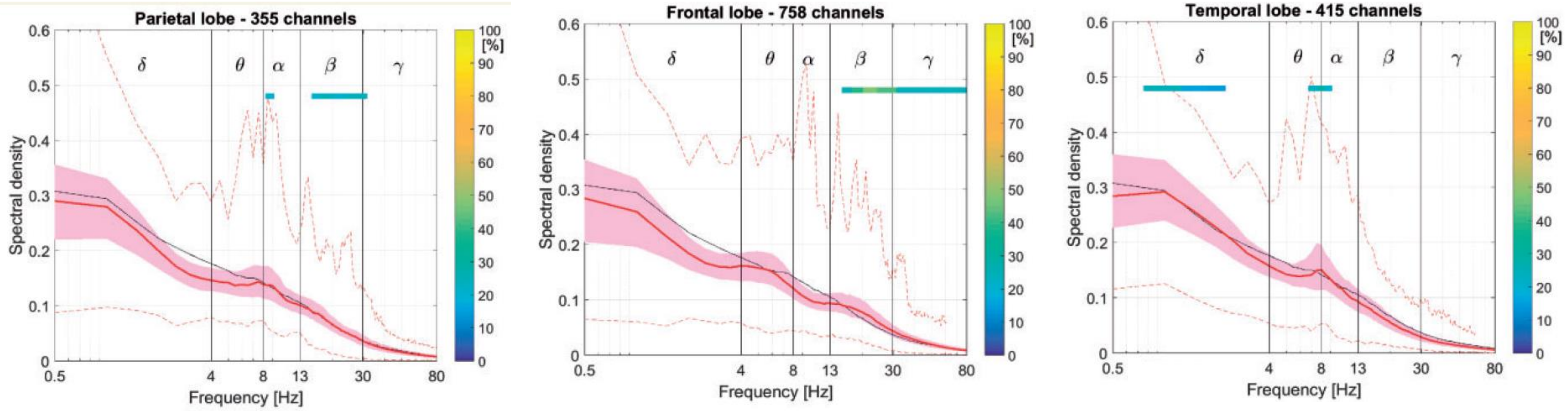


Cottone et al., Brain Structure and Function, 2016
doi.org/10.1007/s00429-016-1328-4

Evidence of distinct neurodynamics across brain regions from intracranial recordings

Neurodynamics express different oscillatory activity across lobes:

- Pariental lobe – α (8 – 12Hz)
- Frontal lobe – β, γ (12 – 33 Hz, 33 – 80 Hz)
- Temporal lobe – δ, θ (≤ 4 Hz, 4 – 8 Hz)



Frauscher et al., Brain, 2018, doi:10.1093/brain/awy035

Neurodynamics analysis with linear and fractality measures

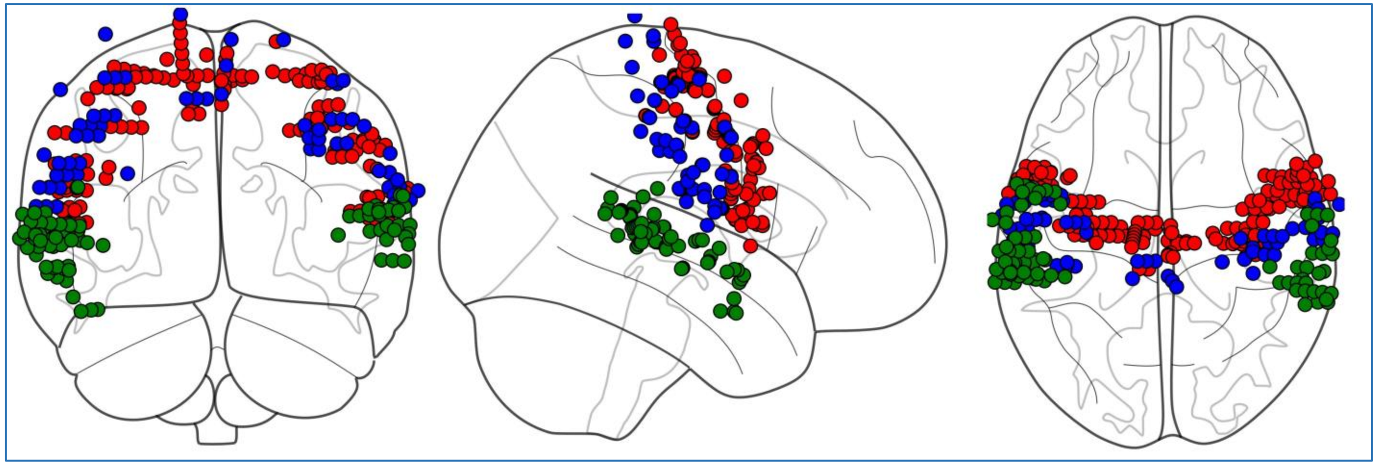
We tested the working hypothesis on the Montreal Neurological Institute (MNI) stereo-intracortical electroencephalography (sEEG) recordings.

Dataset that we selected: precentral, postcentral and superior temporal gyri.

Number of subjects and channels analyzed: {55, 284} out of total dataset{106, 1792}

Number of subjects and channels by gyri:

- precentral: {34, 141}
- postcentral: {21, 64}
- superior temporal: {26, 79}



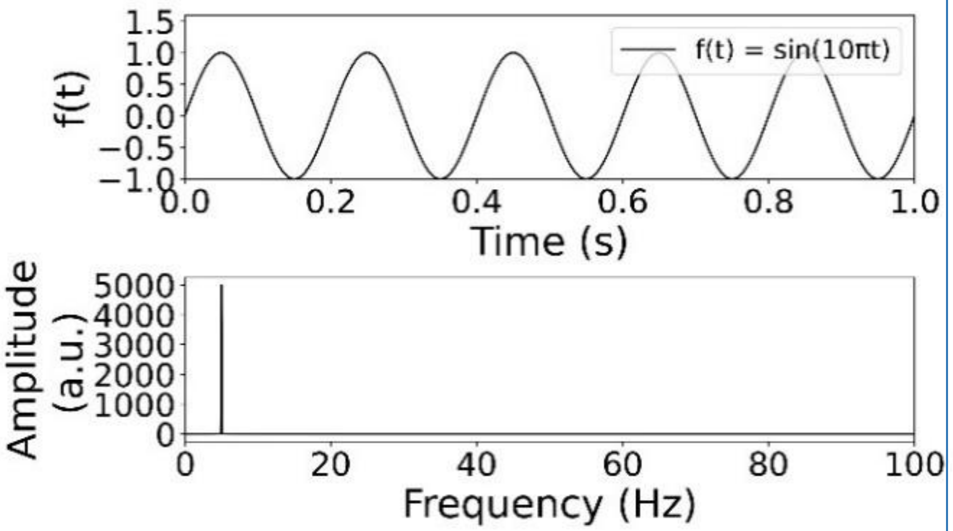
Armonaite et al., Submitted to Nature Scientific Reports, 2023

Methods: analysis of oscillatory components (1/2)

Power Spectrum Density (PSD)

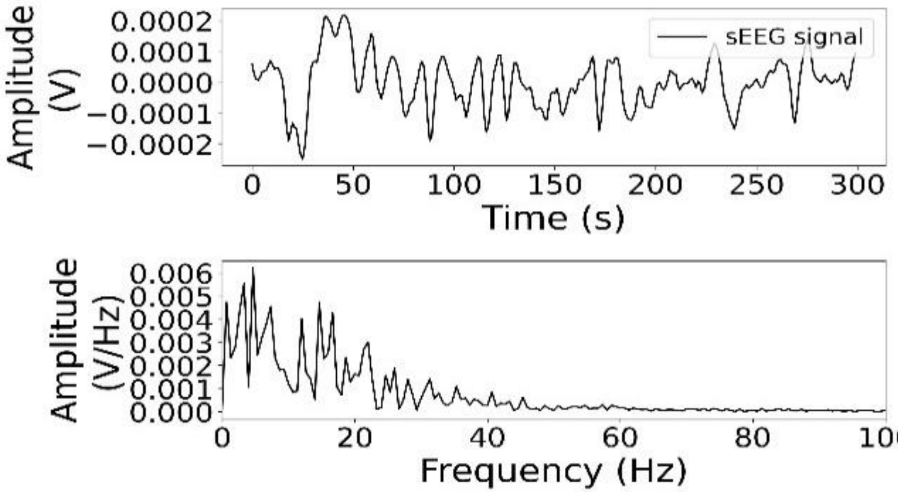
- Fast Fourier Transform (FFT): $F(\omega_k) = \sum_{n=0}^{N-1} f(n)\, e^{-i\omega_k n}$ with $k = 0,1,\ldots,N-1$
- Welch method: 256 FFT lines, 50% overlapping, Hanning windowing

Sinusoid



Top. A periodic, **sinusoidal wave** with characteristic frequency equal to 10 Hz and sampling rate equal to 1000 samples/s. **Bottom.** The absolute value of FFT amplitude is shown, which results into a sharp peak at 10 Hz. The x-axis is cut at 100 Hz.

EEG

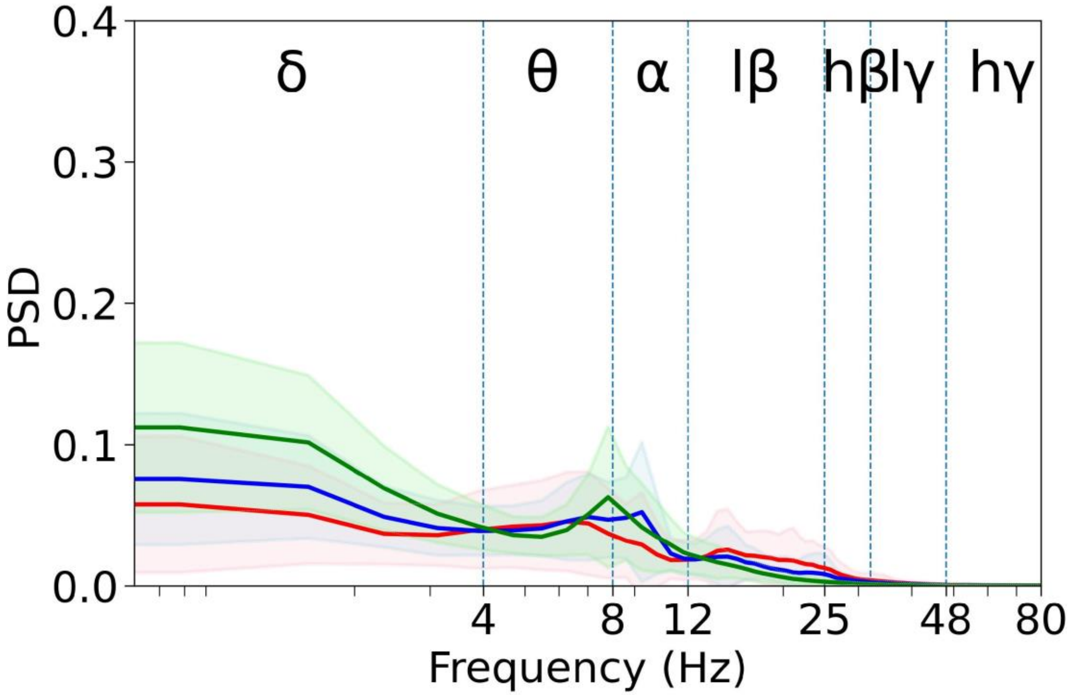


Top. A portion of arbitrarily selected **sEEG signal from M1** as an example, which contains many periodic components and noise. **Bottom.** The absolute value of FFT amplitude is presented, where various frequency components can be observed.

Methods: analysis of oscillatory components (2/2)

Power Spectrum Density (PSD)

- Normalize the PSD so that the area under the curve equals 1.
- Divide the PSD into seven frequency bands.

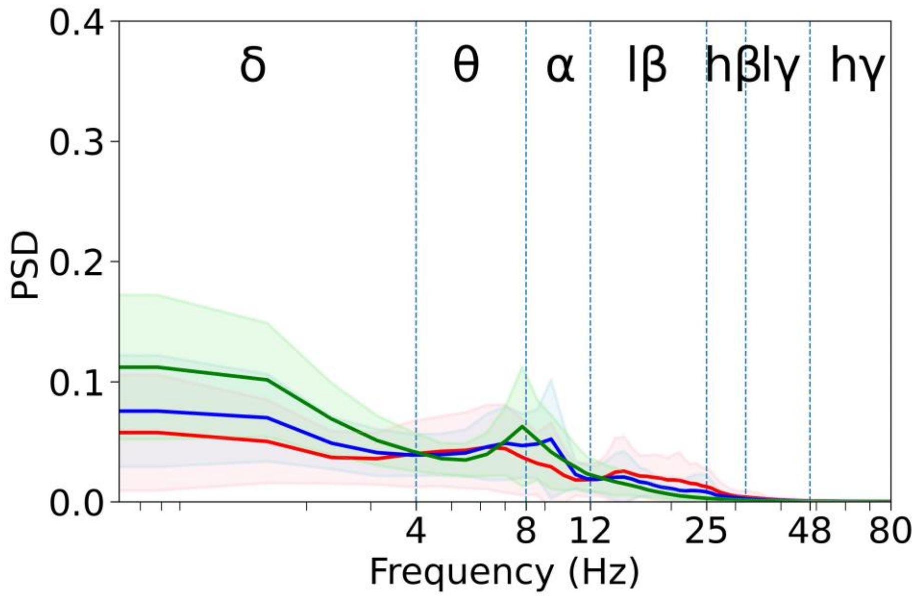


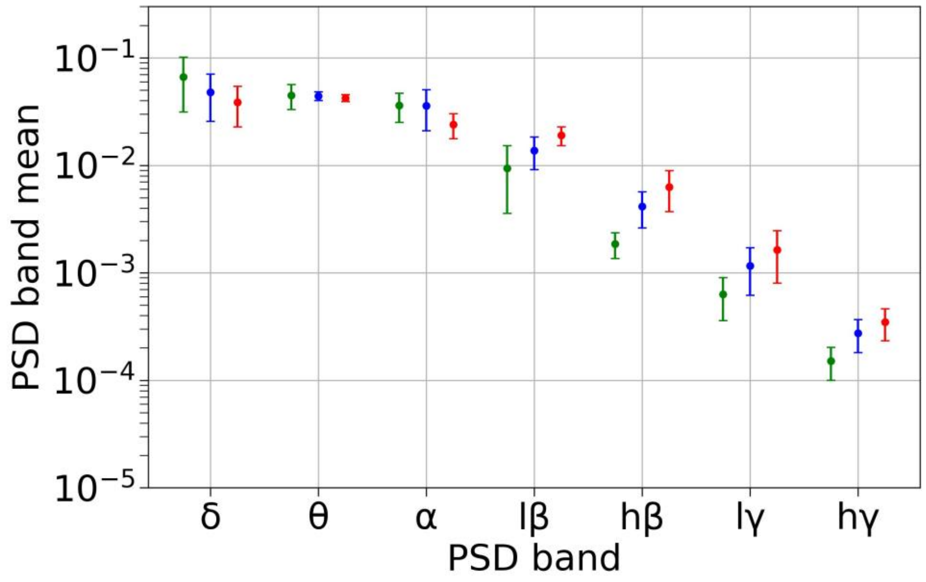
PSD of three primary areas. The Greek letters indicate different frequency bands. X-axis is given in logarithmic scale.

Band	Symbol	Frequency range (Hz)
Delta	δ	≤ 4
Theta	θ	3 – 8
Alfa	α	8 – 12
Low-beta	lβ	12 – 26
High-beta	hβ	26 – 33
Low-gamma	lγ	33 – 49
High-gamma	hγ	49 – 80

Results: comparison of oscillatory activity in 3 parcels and 4 states (1/2)

Wake





Comparison of the normalized PSD (averaged across all channels) between:

- superior temporal (green),
- postcentral (blue),
- precentral (red).

Comparison of the mean PSD (with std. deviation) evaluated on each of the 7 standard frequency bands.

Results: comparison of oscillatory activity in 3 parcels and 4 states (2/2)

Same comparison of:

- PSD and
- mean band PSD

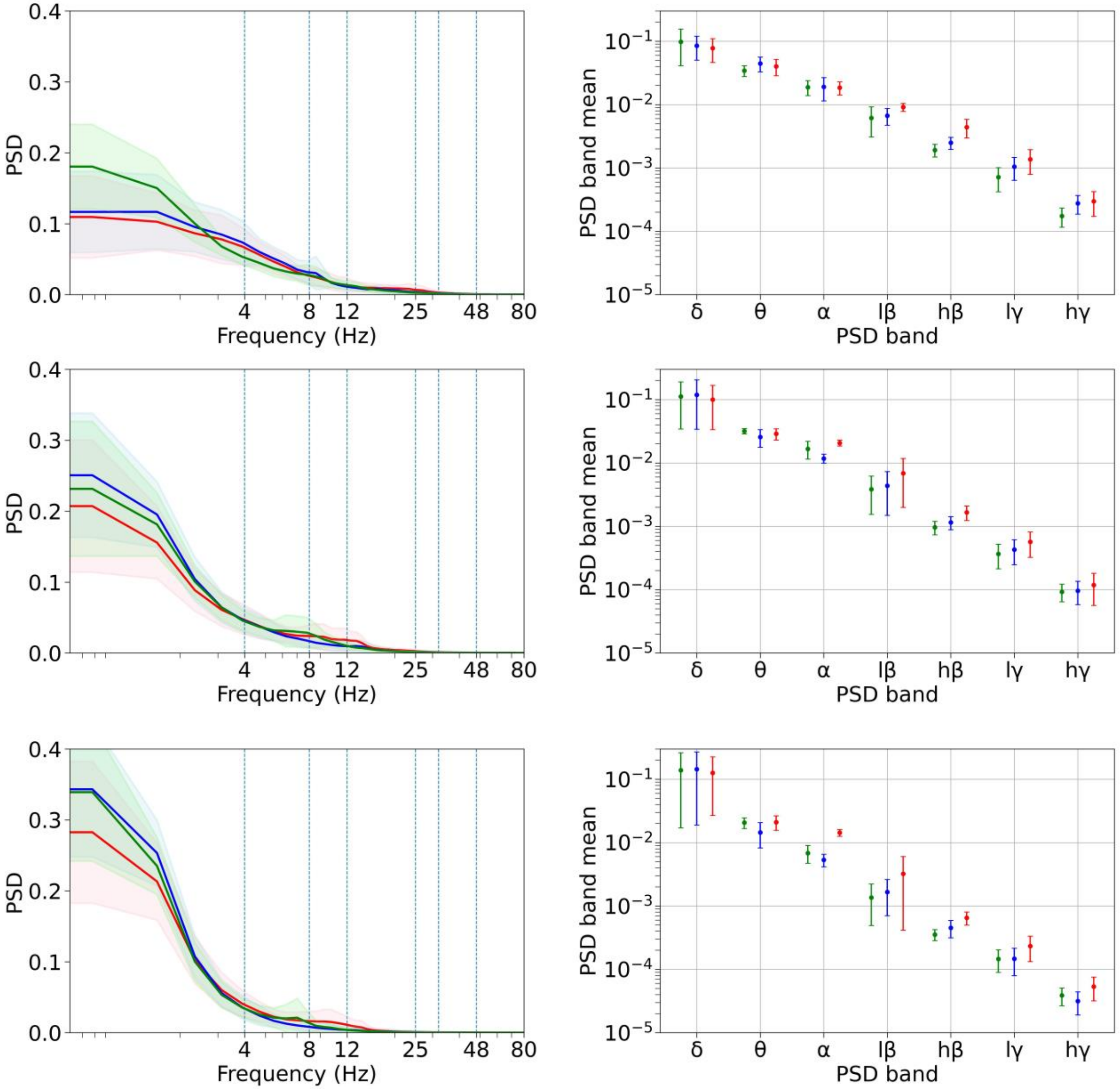
for sleep stages:

- REM,
- N2,
- N3.

REM

N2

N3



- superior temporal (green)
- postcentral (blue)
- precentral (red).

Methods: Higuchi fractal dimension (HFD) (1/2)

HFD is a more accessible and intuitive method to detect the characteristics of a complex and irregular time series.

- The estimation of HFD of an N-length signal X(i) with i=1,2,3,…,N, is based on down sampling it into k-length sequences, where sub-sequences X_k^m are obtained (k is a constant integer, m=1, 2, 3,…, k).
- Consider given N-length time series {X(1), X(2), X(3),…, X(N)}.
- For a time interval equal to k, we obtain k sets of new time series series

  X_k^m: X(m), X(m+k), X(m+2k),…,X(m+[(N-m)/k)])
- Then we calculate the length $L_m(k)$ of the curve as follows:

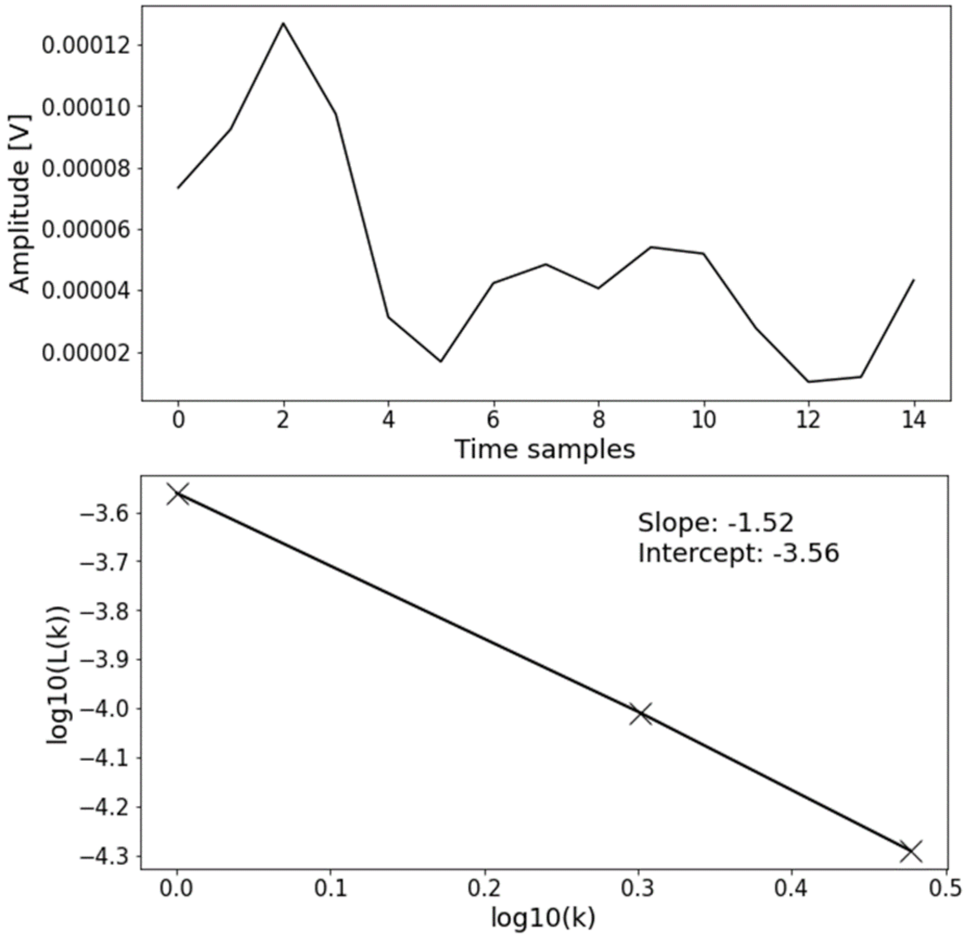
$$L_m(k) = \left[\left(\sum_{i=1}^{int\left(\frac{N-m}{k}\right)} |X(m+i\,k) - X(m+(i-1)k)| \right) \frac{N-1}{int\left(\frac{N-m}{k}\right) k} \right] \frac{1}{k}$$

Methods: Higuchi fractal dimension (HFD) (2/2)

- Length of the curve L(k) is evaluated by averaging the k sets of $L_m(k)$ values, as:

$$L(k)=\frac{1}{k}\sum_{m=1}^{k} L_m(k)$$

- If there exist a limit for $L(k) \propto k^{-D}$, then the curve is fractal with dimension equal to D.
- D value is calculated by evaluating all k values up to the maximum k and by least-square method fitting the log(L(k)) versus log(k) curve.
- If the power spectrum density PSD(f) $\propto$ $f^{-\beta}$, then $\beta = 5\text{-}2D$, for $1 \leq \beta \leq 3$ and $1 \leq D \leq 2$.



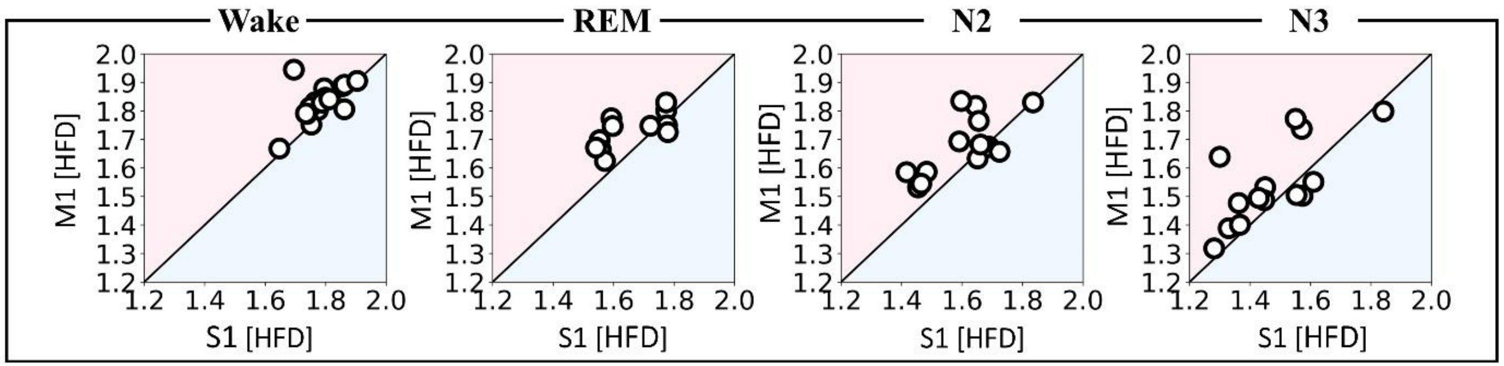
Top. Signal sample of 15 time points
Bottom. log10(average length of the curve) vs log10(k). The crosses mark the three k values.

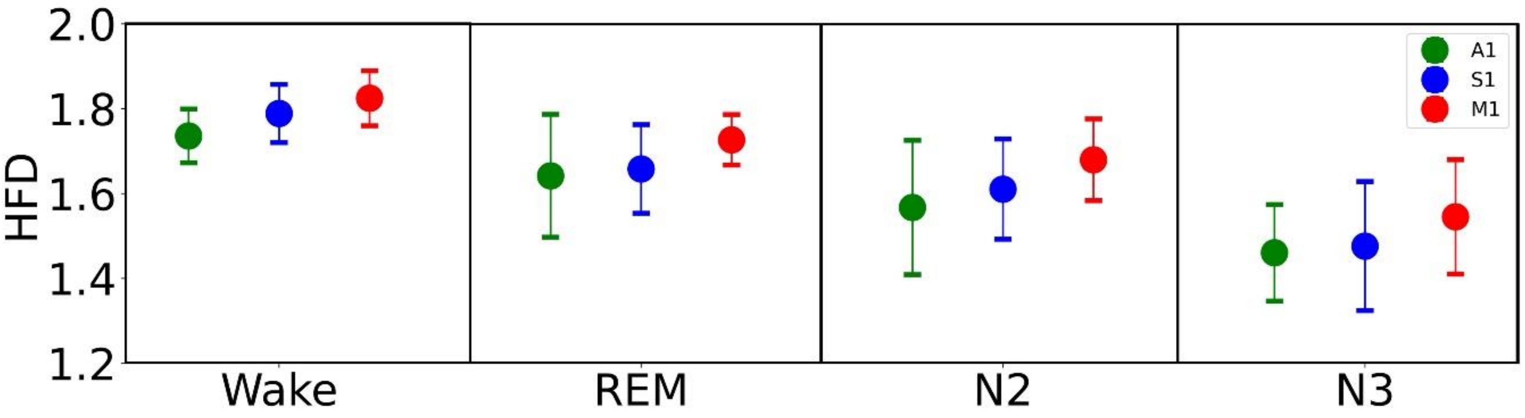
Results: HFD

Comparisons of β values across 3 cortical parcels and 4 wake/sleep states

Comparison HFD of local neurodynamic in pairs of regions and across population

- The scatterplots of HFD between subjects for each couple of brain areas: S1 vs M1 [16 subjects]; A1 vs M1 [9 subjects].
- In each plot, a point above (below) the diagonal has HFD of the source on x axis lower (higher) than that of the source on y.
- The mean HFD estimated across population in wakefulness, REM, N2 and N3 sleep stages.
- For each subject we considered a representative of all available channels within the A1, S1 and M1 regions.
- The Higuchi fractal dimension was evaluated at k_{max}=35 in each state.



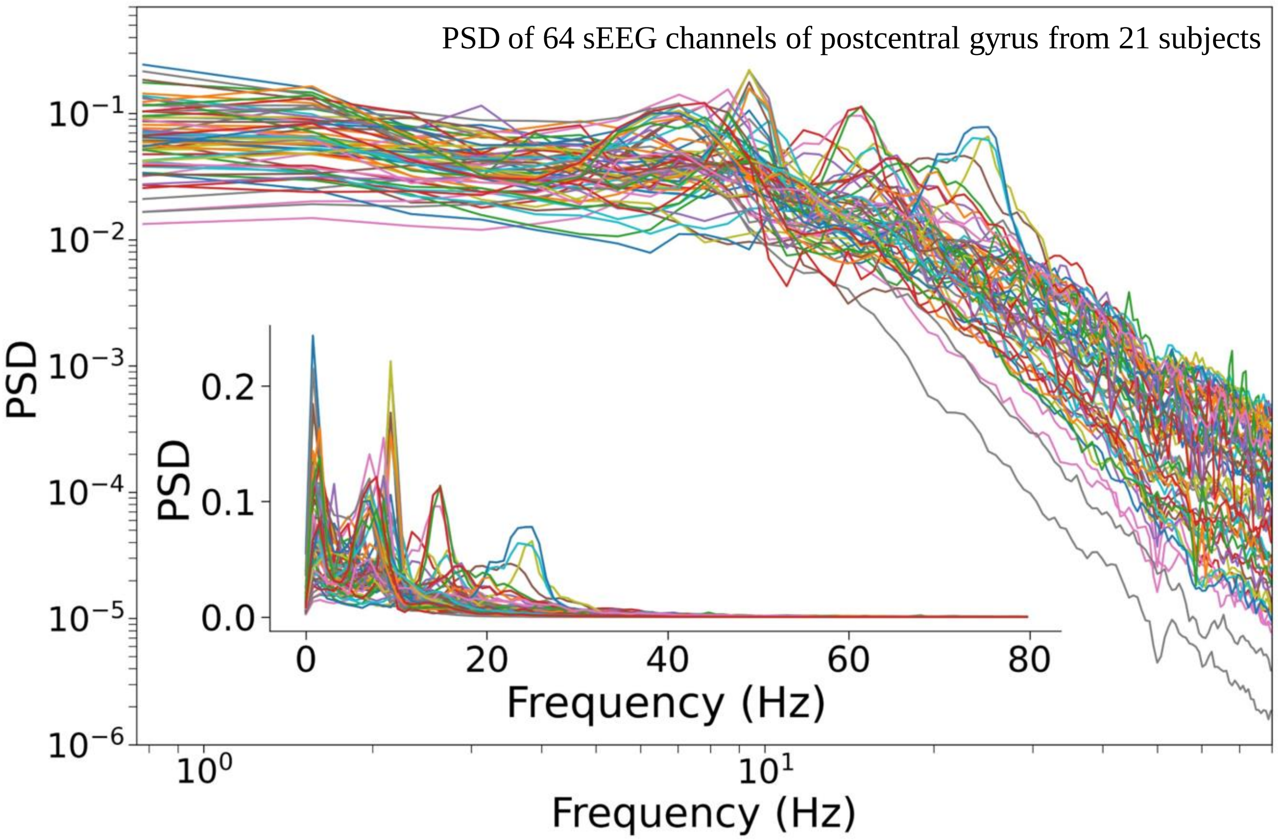


Armonaite et al., Cerebral Cortex, 2022

Methods: analysis of non-oscillatory component (1/2)

Looking of power-law behavior of PSD

- $P(f) \sim 1/f^{\beta}$.
- Estimation of β: linear fit of PSD vs frequency in a log-log scale



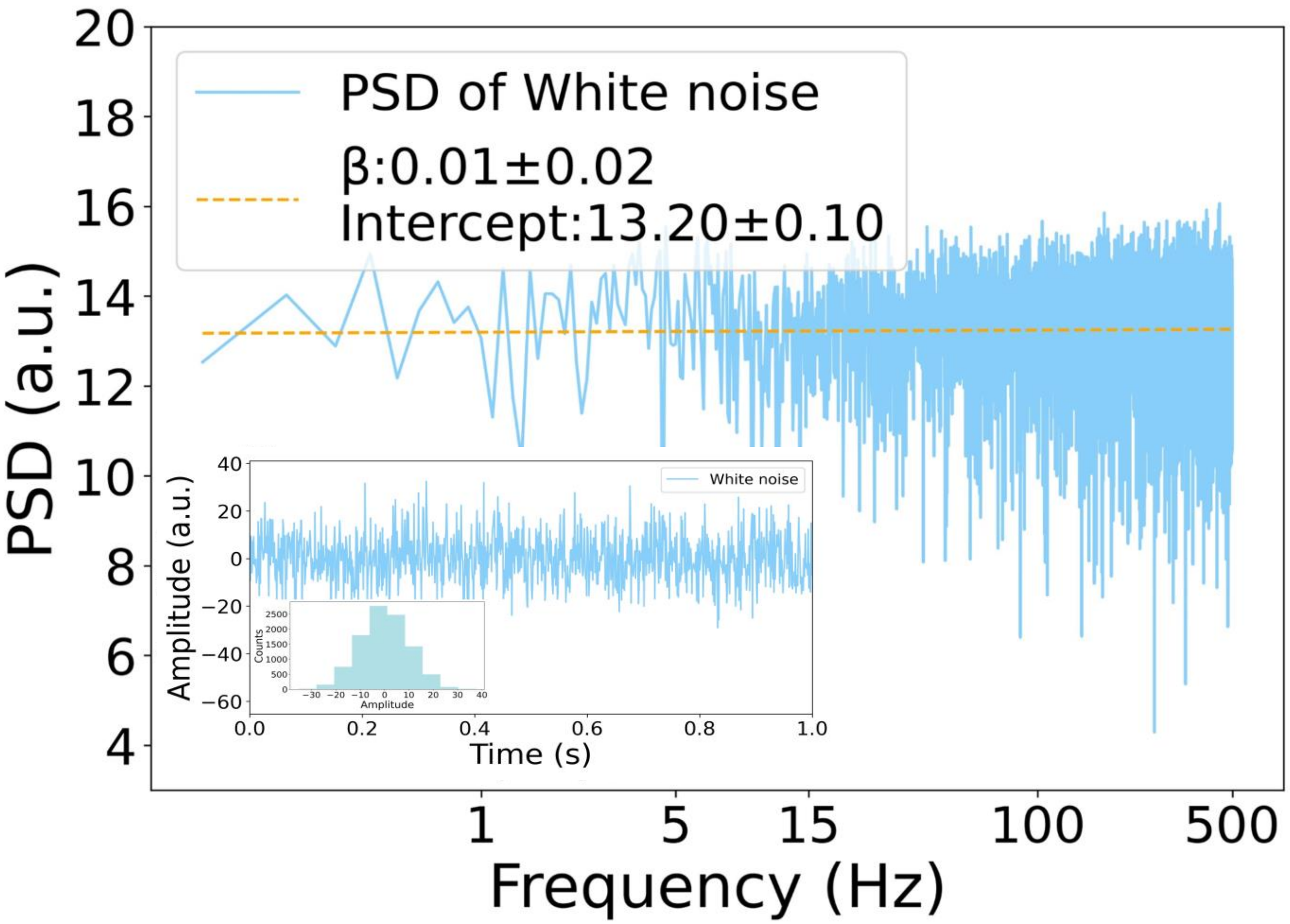
- Main figure: PSD on a log-log scale shows two about linear (power-law) behaviours: at low and high frequencies.
- Inset figure: PSD on linear scale showing typical peaks.
- Peaks might surge the "linear" slope on both sides.

Armonaite et al., Submitted to Nature Scientific Reports, 2023

Methods: analysis of non-oscillatory component (2/2)

Example of white noise:

Power spectrum is flat for all frequencies

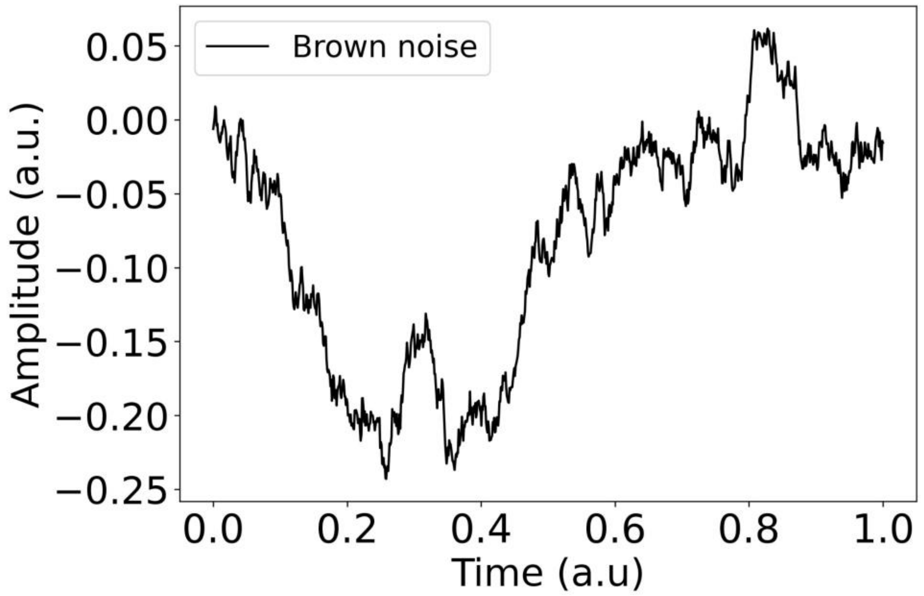


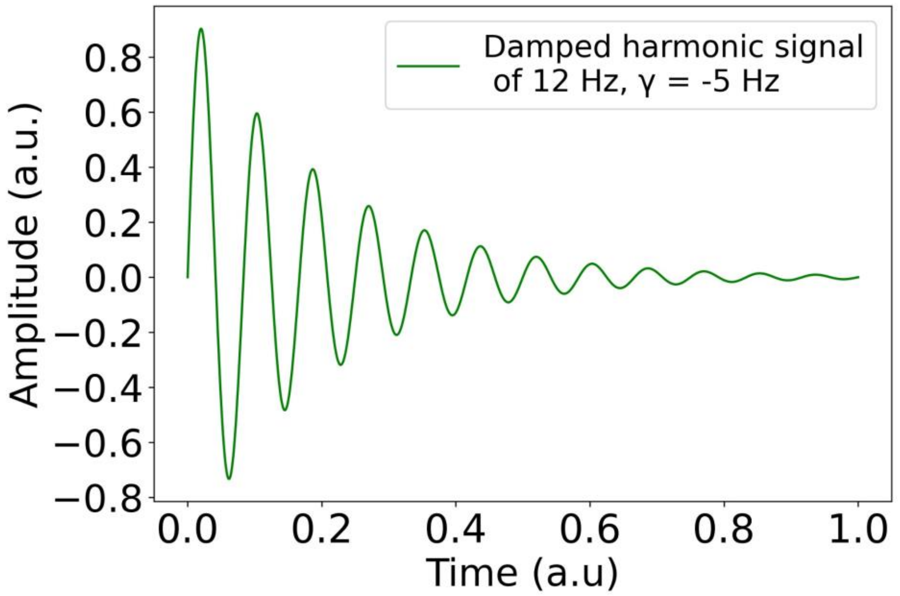
Armonaite et al., Submitted to Nature Scientific Reports, 2023

Test: harmonic oscillations can surge power-law (1/3)

Analysis how harmonic oscillations can surge a linear slope β

- Comparison between true scale-free process (Brownian noise) and harmonic periodic oscillation



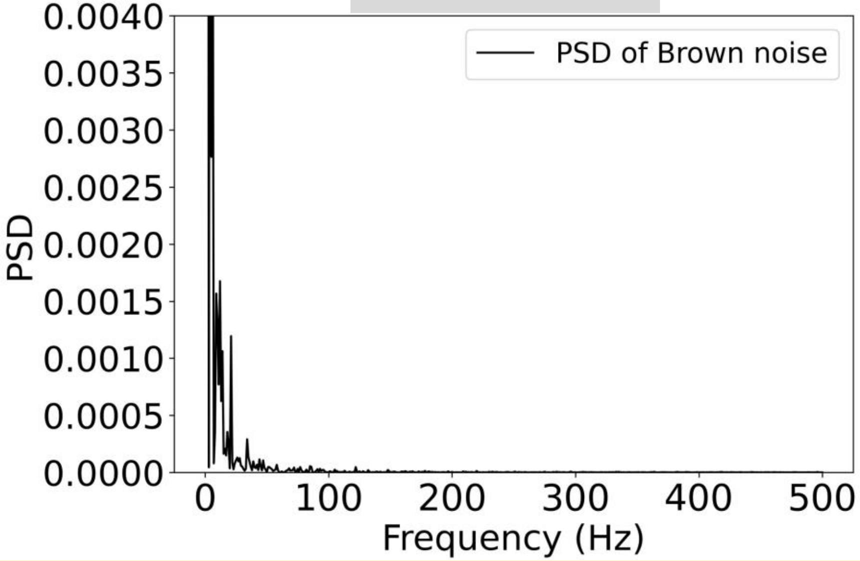


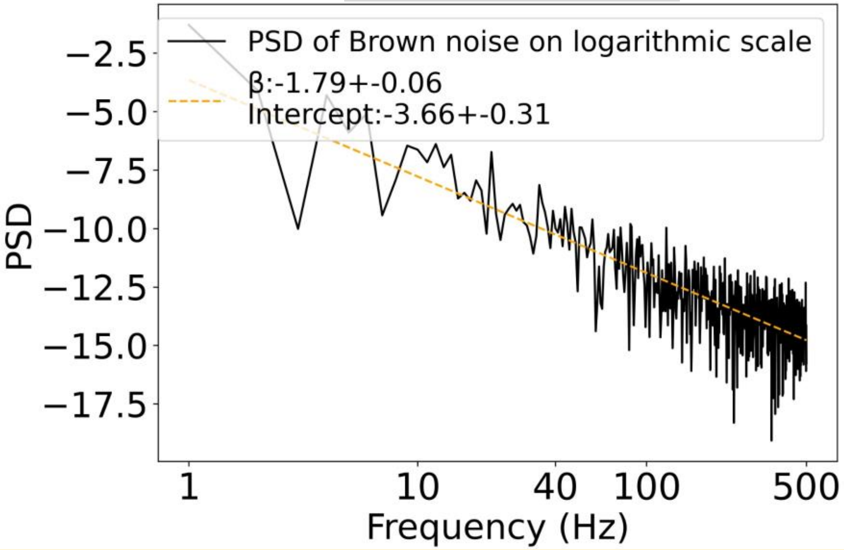
Left. Brown noise: an ideal example of scale-free activity fluctuation, generated as a random walk with iterative process.
Right. Damped sinusoidal wave $A(t) = \sin(\omega t)e^{-\gamma t}$, with $\omega = 2\pi f$ and γ exponential decay rate, which impacts the width of the peak in the power spectrum.

Test: harmonic oscillations can surge power-law (2/3)

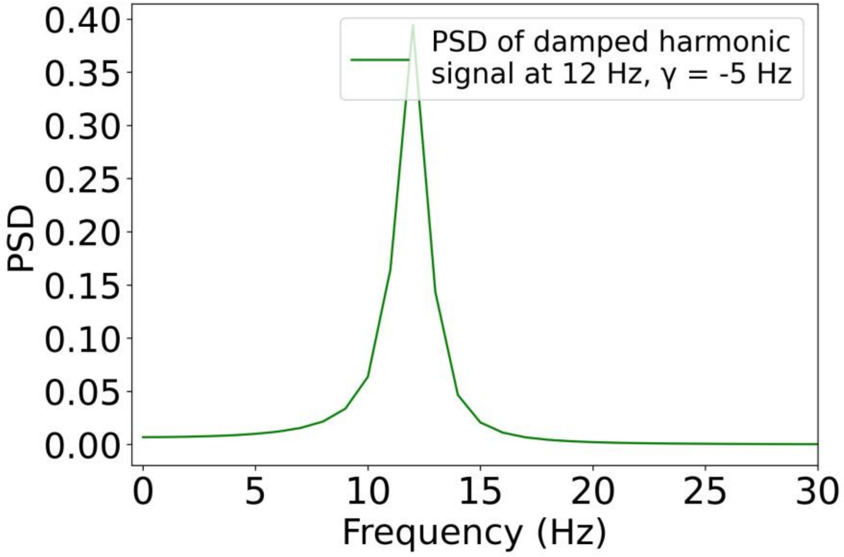
linear scale **log-log scale**

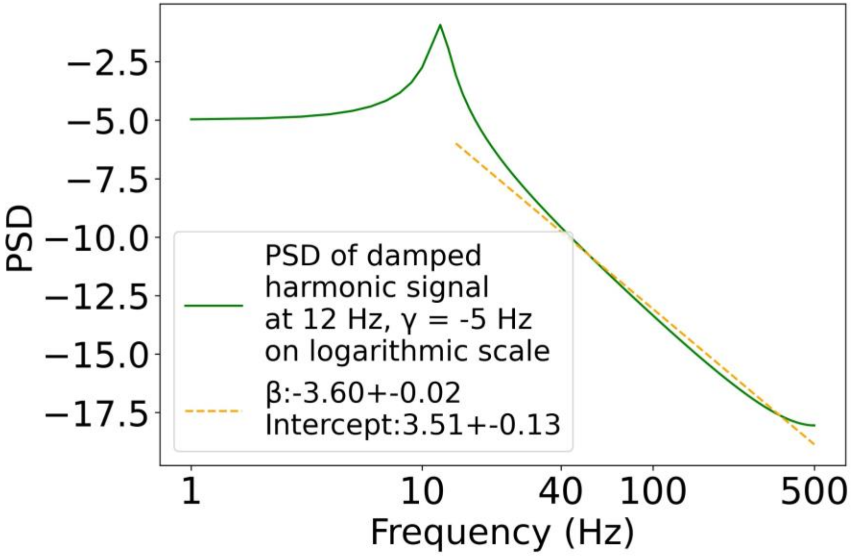
- PSD of **Brownian noise**
- Linear behavior on log-log scale.
- The single slope is indicated as β.





- PSD of **damped oscillator**
- Peak at 12Hz with a width
- The non-zero slope in damped harmonics is meaningless.
- The x-scale is truncated at 30 Hz (out of 500 Hz)

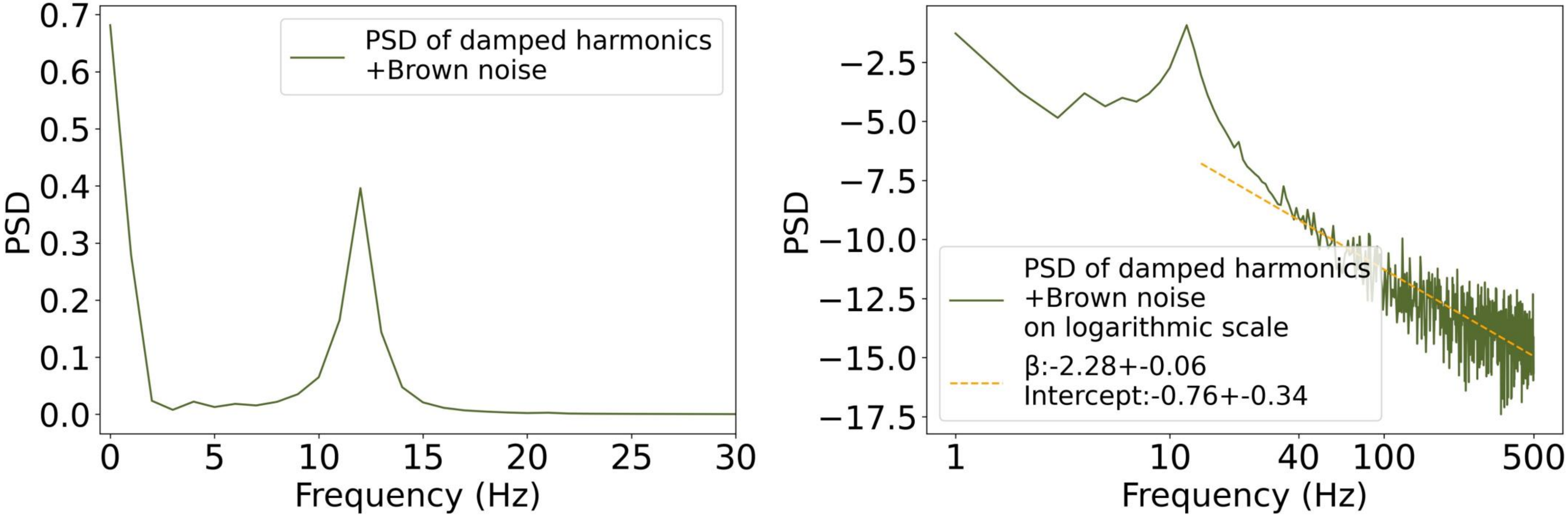




Test: harmonic oscillations can surge power-law (3/3)

PSD of the sum of Brownian noise + damped harmonic signal

- Brownian noise at any scale has a slope of 1.80 +/- 0.06
- The slope of Brownian noise mixed with harmonic oscillator increases to 2.28+/-0.06



Left. The PSD of the summed Brown noise and damped harmonic signal in a linear scale
Right. The PSD of the summed Brown noise and damped harmonic signal on log-log scale.
The dashed yellow line indicates the best fit with least square method, and the slope is represented as β.

Methods: analysis of non-oscillatory component

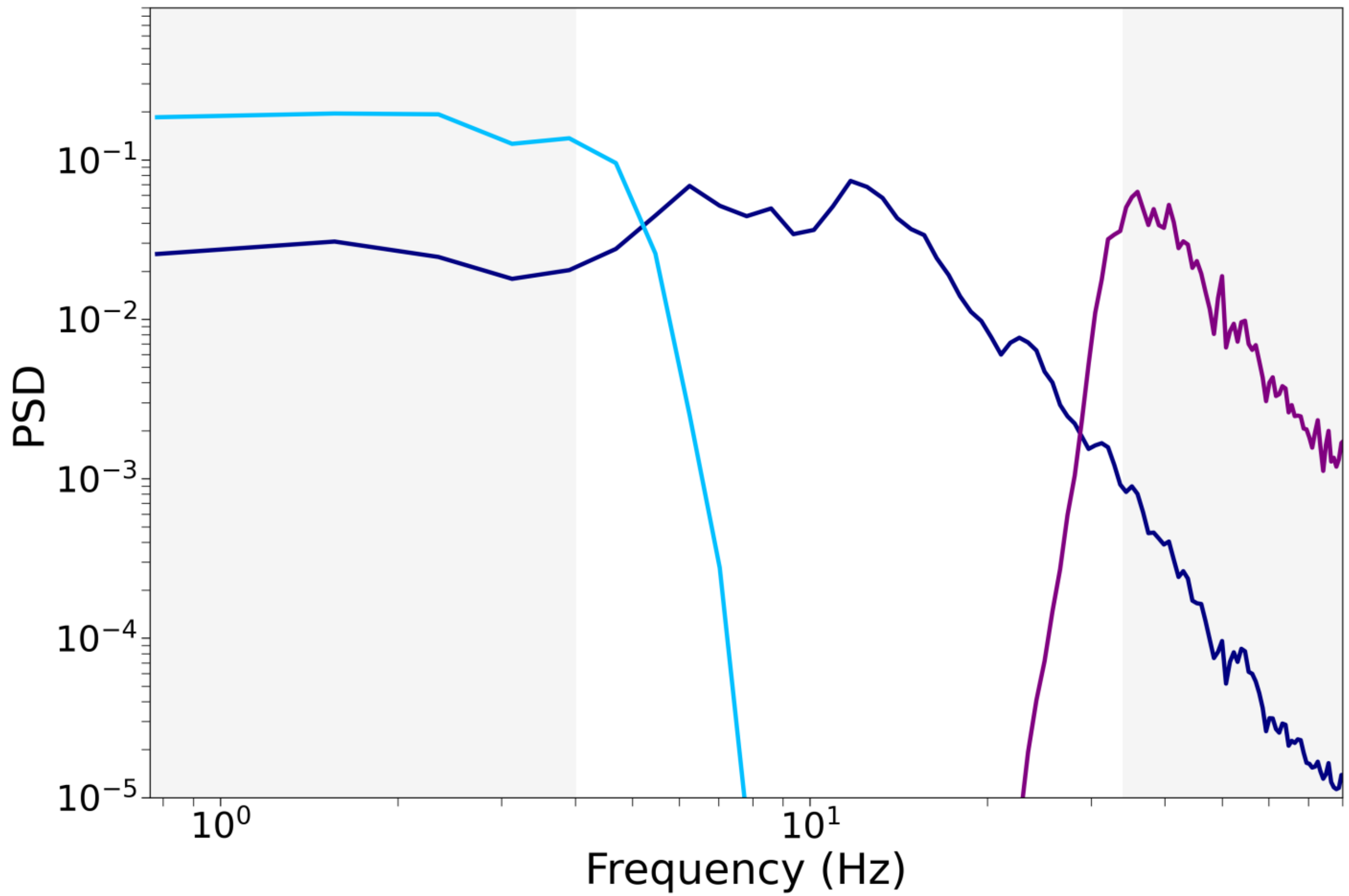
Filtering oscillatory components

- Low- and high-pass Butterworth filters with frequency response:

$$|H(n, j\omega)| = \frac{1}{\sqrt{1+\left(\frac{\omega}{\omega_c}\right)^{\pm 2n}}},$$

with order *n* and ω_c cut-off freq.

- Filtering of each sEEG channel

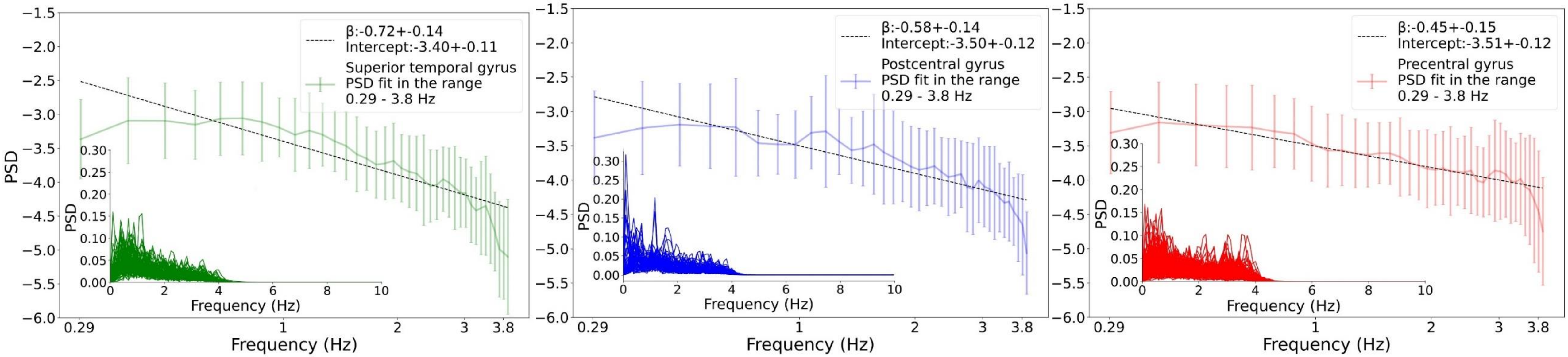


An example of channel from postcentral gyrus showing the methodology to remove the oscillatory activity (in theta, alpha and low beta bands) by applying the low- and high- pass filters on each channel. Both axes are given in logarithmic scale.

Armonaite et al., Submitted to Nature Scientific Reports 2023

Results: three parcels are distinct in terms of β (1/3)

β value in the <u>low</u> frequency range: δ (≤ 4 Hz) range. **Wakefulness**



- We applied Butterworth filter with a cut off value of 4 Hz on all signals from three gyri:
  Left panel superior temporal, **Middle panel** postcentral, and **Right panel p**recentral.
- We calculated PSDs using 2048 line for FFT and then averaged them across population.
- We calculated the power law index of PSD in a log-log scale in the 0.29 – 3.9 Hz frequency range using least square method.
- The inset figures show the PSD filtered below 4 Hz in a linear scale.
- The linear fit was calculated by using the weighted least square method, where to each ordinate $y_i = log(PSD(f_i))$ is associated the weight $w_i = 1/\Delta y_i^2$ with Δy_i the uncertainty on y_i.

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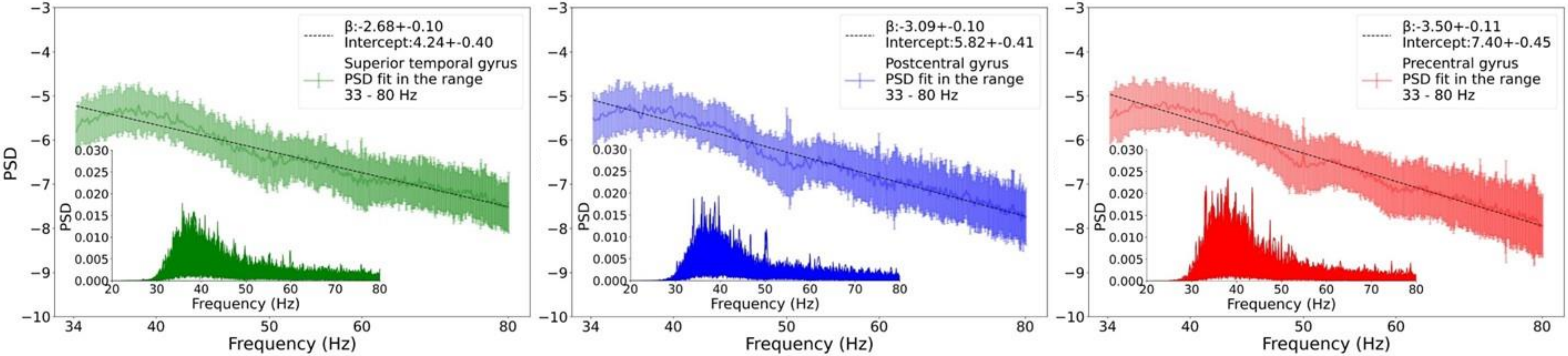
Results: three parcels are distinct in terms of β (2/3)

β value in the high frequency range: hβ-γ (33-80 Hz) range. | **Wakefulness**



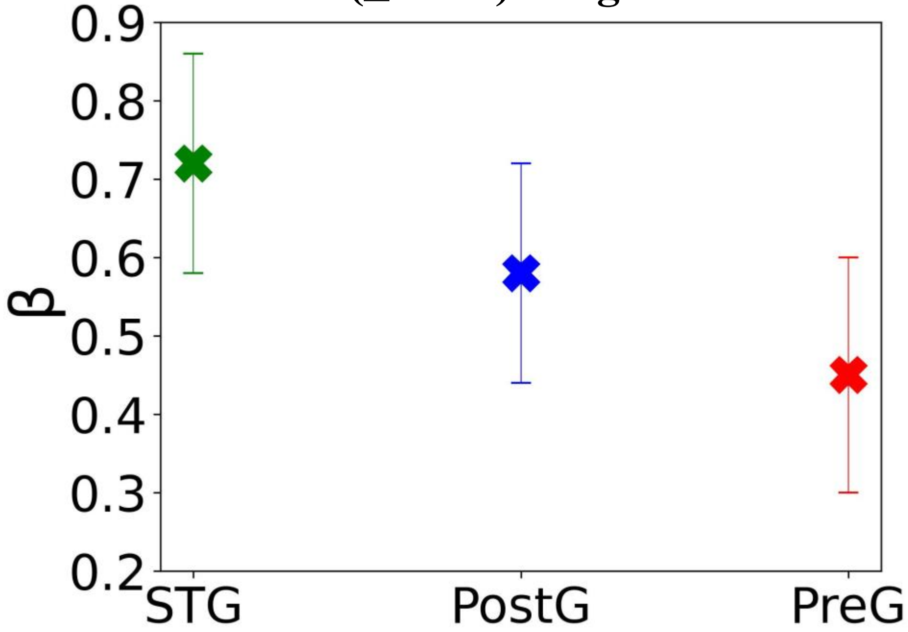
- We applied a high-pass Butterworth filter with a cut off of 33 Hz on all channels from 3 brain areas.
- We calculated their PSDs using 2048 lines FFT and then averaged them across population.
- Mean PSD & std deviation are shown in the panels: **Left.** superior temporal, **Middle.** postcentral and **Right.** precentral gyrus.
- We fit the mean PSD in a log-log scale vs frequency in order to evaluate the power-law β index as in the low frequency range.

Armonaite et al., Submitted to Nature Scientific Reports 2023

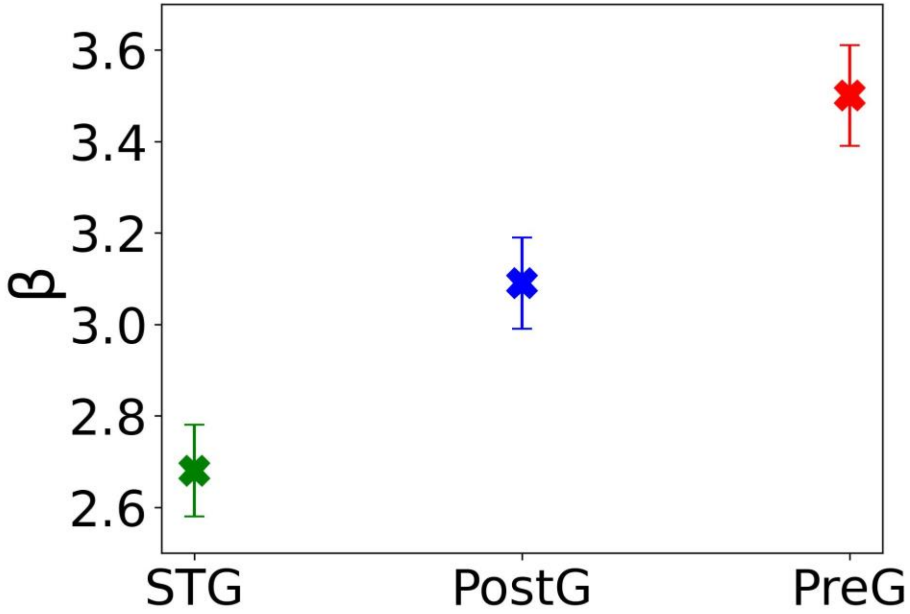
Results: three parcels are distinct in terms of β (3/3)

Comparison of β value in <u>low</u> and <u>high</u> frequency ranges between the investigated areas. **Wakefulness**

δ (≤ 4 Hz) range



hβ-γ (33-80 Hz)



Left. The β value of the mean PSD across all the channels in three gyri: superior temporal, postcentral and precentral evaluated at the **0.29 – 3.8 Hz** frequency range.
Right. The β value of the mean PSD across all the channels in the frequency range **34 – 80 Hz** in three gyri.
The β values for the three regions are indicated in the legend.

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Results: three parcels are distinct also during sleep (1/3)

Sleep stages: REM, N2, N3

Comparison of β value in hβ-γ frequency range between the investigated regions.

- The PSD mean across all channels in high frequency range after applying a high-pass Butterworth filter with a cut off value of 33 Hz.
- PSDs calculated using 2048 lines FFT and then averaged them across population.
- The power-law index is evaluated by fitting the mean PSD in the 34 – 80 Hz range using least square method.

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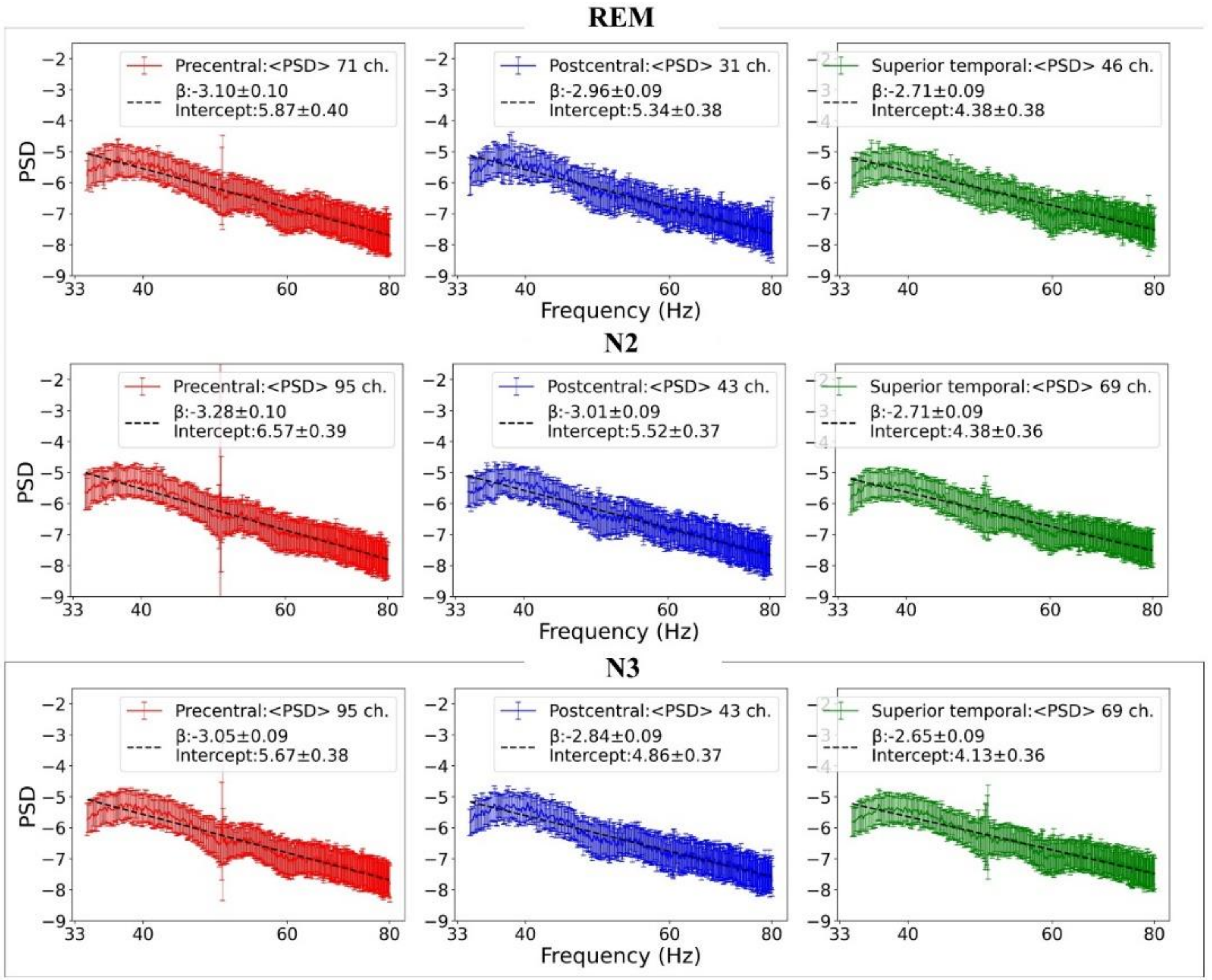
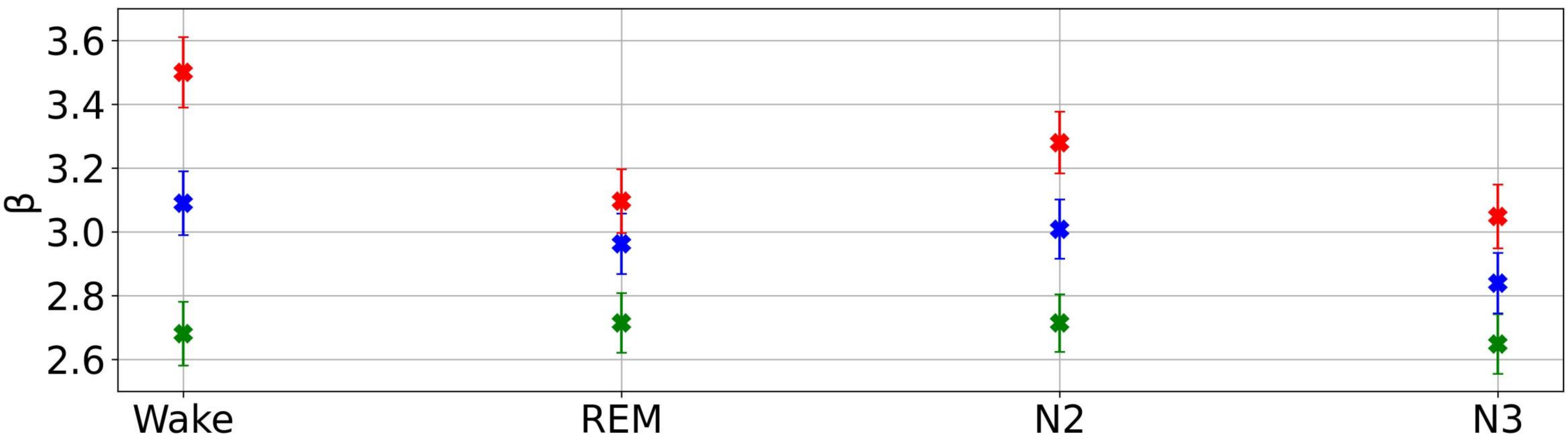


Results: three parcels are distinct also during sleep (2/3)

Comparisons of β values across 3 cortical parcels and 4 wake/sleep states



The β values of the PSD in the frequency range 34 – 80 Hz in three gyri: superior temporal, postcentral and precentral is presented in wake, REM, N2 and N3 stages.

- **The regions are distinguishable within the error even in deep sleep.**
- **The stability of β value in a region across stages could imply the fixation of the scale-free activity.**

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Conclusions: towards mapping the cortex via local neurodynamics

- ✓ In awake & across sleep stages, despite huge changes in local neurodynamics, **a defined relationship is present between different cortical areas**
- ✓ Primary **motor cortex** expresses in all states the **highest complexity**
- ✓ Primary somatosensory cortex expresses a higher complexity than auditory cortex, probably expression of the inseparable relationship with primary motor cortex
- ✓ The **fractal dimension allows us to take into account the temporal dynamic patterns of neurodynamics**

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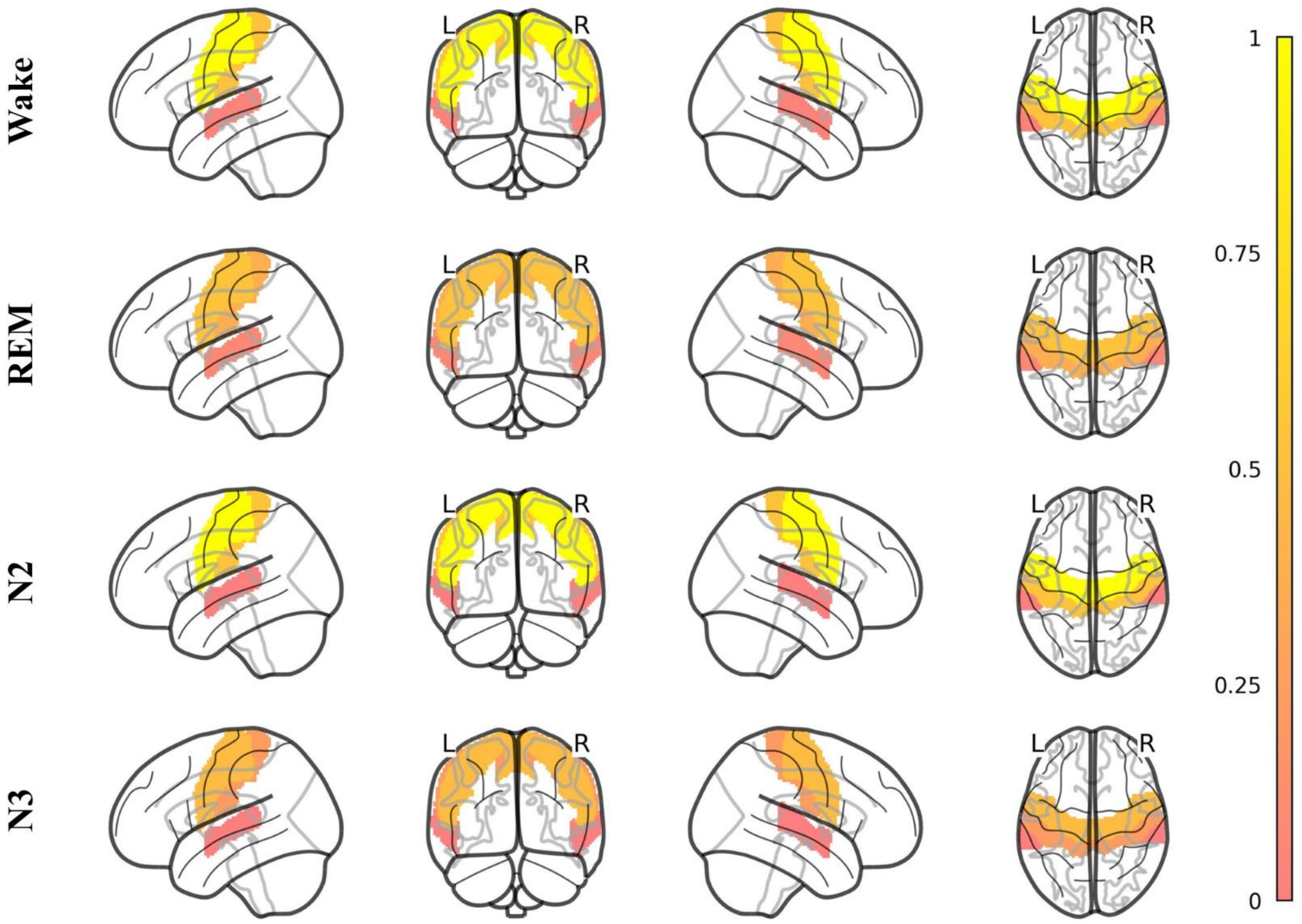

Perspectives

We are working to proceed in the direction of better understanding:

- ✓ the relationship between complex behavior and behavior in frequency ranges,
- ✓ how synchronization relates to neurodynamics,
- ✓ how to related hierarchical network structures and neurodynamics,
- ✓ how neurodynamics can inform neuromodulation,
- ✓ whether such advances can enhance sensitivity to pathology indicating compensatory treatments.