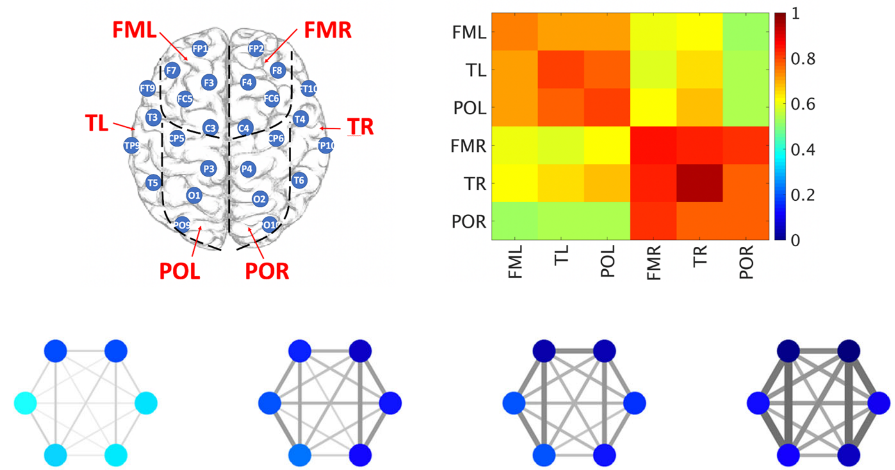
EEG Synchronization networks of Parkinson's disease patients with Freezing of Gait

effective forward motion	○	×	×
leg motion	○	○	×

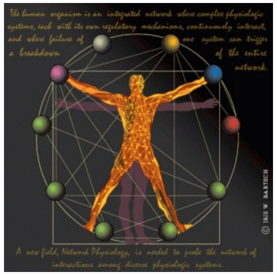
Yuki et al., Front. Human Neurosci. 16 (2022)



Asher et al., Nat. Comm. Biol. 4:1017 (2021)

Ronny Bartsch

Bar-Ilan University
אוניברסיטת בר-אילן
Tradition of Excellence



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Acknowledgements

Collaborators:

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FoG – Overview

- Freezing of Gait = FoG, Parkinson's disease = PD

FoG is a:

- significant risk factor for falls and injuries
- one of the most disabling symptoms of PD
- not universal (only about 50% of PD)
- less frequent in women
- less frequent in PD with pronounced tremor

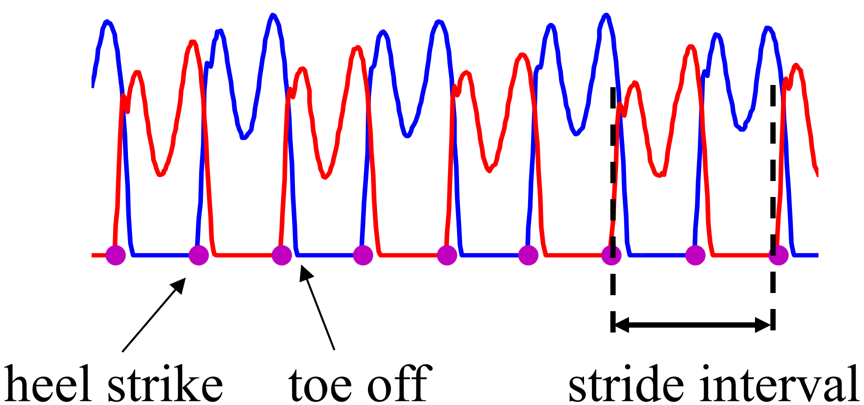
FoG trigger (most common):

- turns
- narrow passage
- gait initiation
- uneven floor (carpet, rug)

• not clear why some PD patients show FoG while others do not

Measuring locomotion and gait

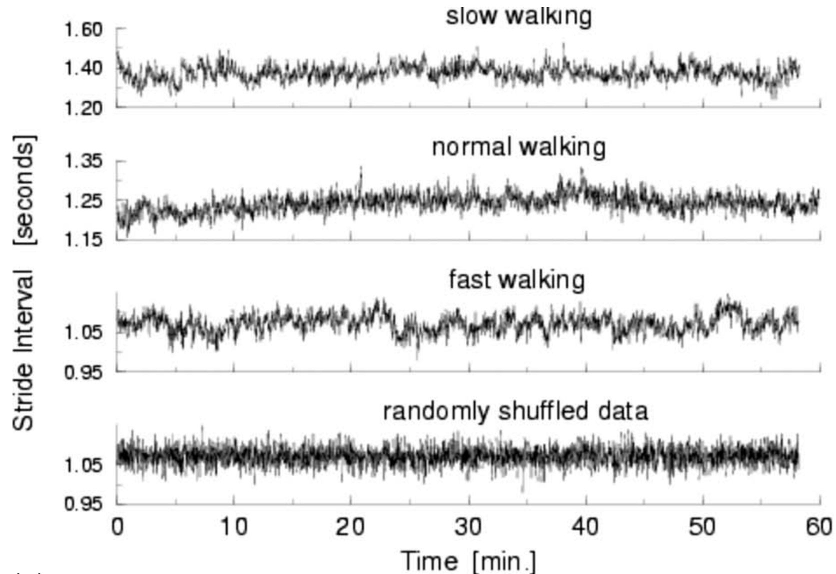
Measuring gait with force sensitive insoles



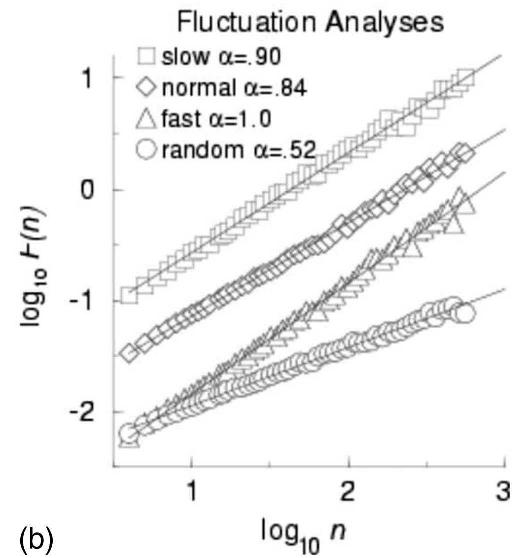
Random stride-to-stride fluctuations in PD

Healthy

~1/f behavior



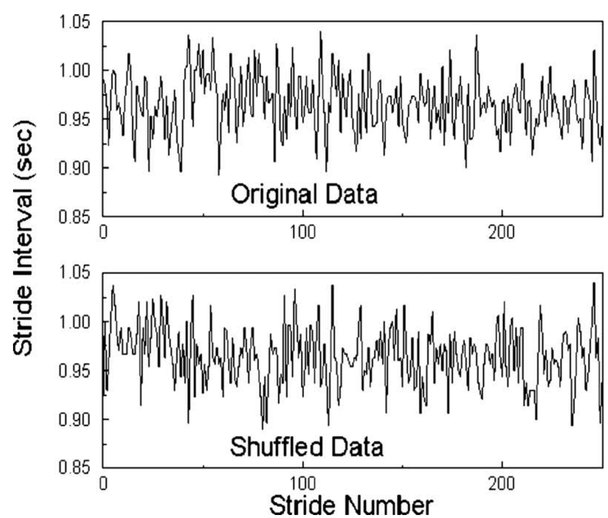
(a)

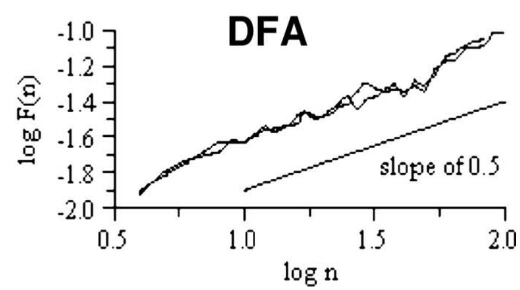


(b)

PD patient

~ white noise

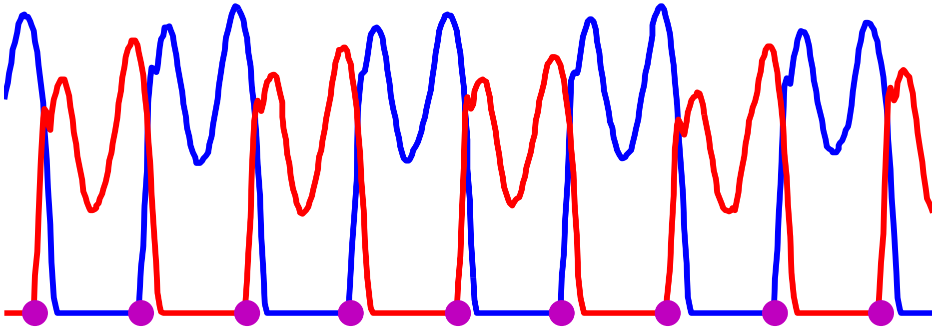




J. M. Hausdorff et al., Chaos 19, 026113 (2009)
P. Ch. Ivanov et al., PRE 79(4), 041920 (2009)

FoG – triggered by gait de-synchronization?

- study phase synchronization between both legs (ideal phase difference = 180º)



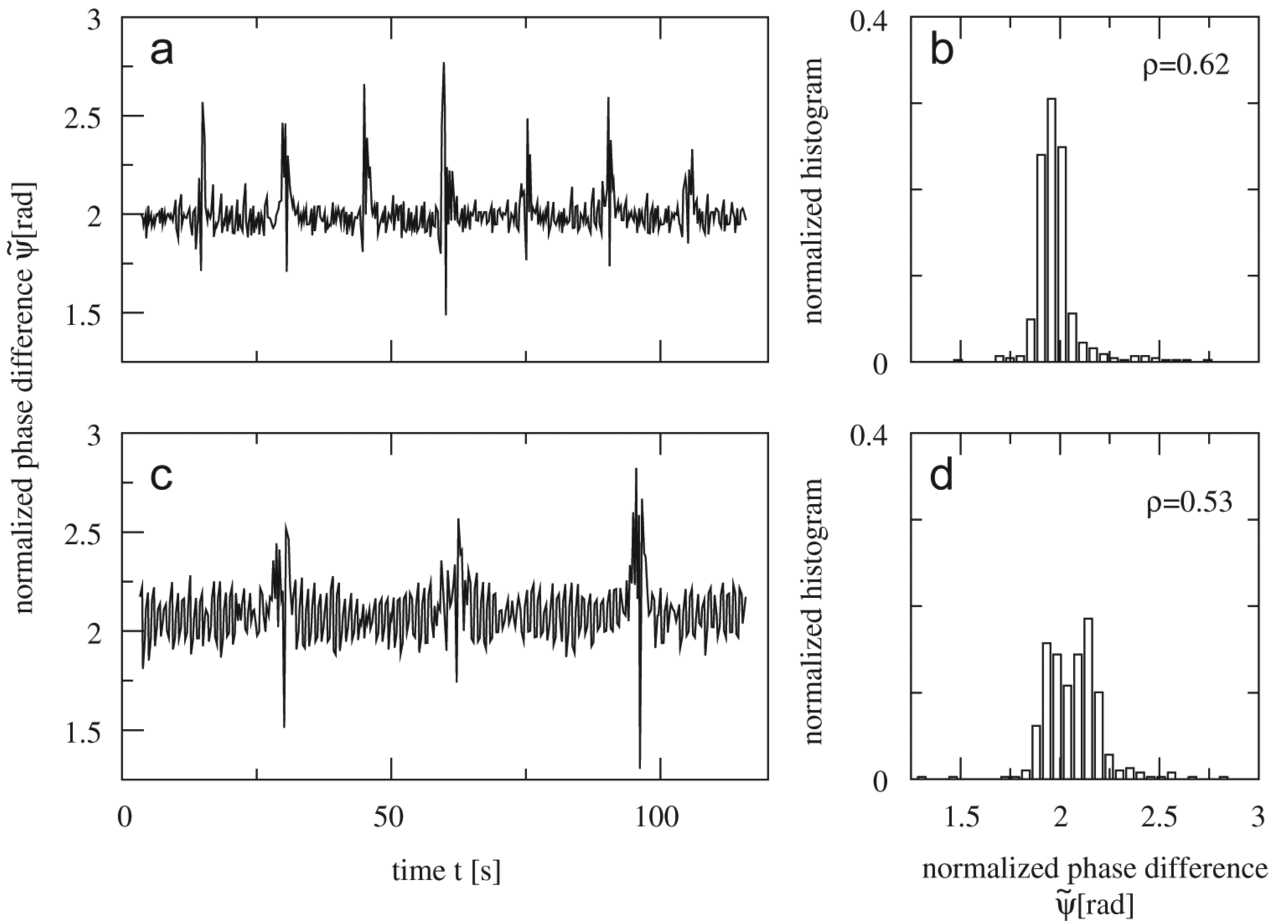
- calculate phase via Wavelet-transform (PhD Dissertation A. Guillet (F. Argoul))
- “transform” Hilbert phase to genuine phase (Kralemann et al. PRE 77 (2008))
- consider marker events (heel strikes), calculate phase via linear interpolation:

$$\Delta\phi_k^m = 2\pi \frac{t_k^{m,\mathrm{ri}} - t_k^{\mathrm{hs,le}}}{t_{k+1}^{\mathrm{hs,le}} - t_k^{\mathrm{hs,le}}}$$

FoG – triggered by gait de-synchronization?

Healthy
→ small fluctuations in phase diff

PD patient
→ large fluctuations in phase diff



Healthy (n=24; mean age: 64yrs)	PD patients (n=29; mean age: 67yrs)
$\rho = 0.62 \pm 0.01$	$\rho = 0.53 \pm 0.02$

R. Bartsch et al., Physica A 383(2), 455 (2007)

FoG – de-synchronization between legs?

instead of gait, study limb dynamics using a strange stationary bicycle

strange? - because pedals were not locked at 180 deg

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Brain Research Bulletin 61 (2003) 219–226

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Classifying lower limb dynamics in Parkinson's disease

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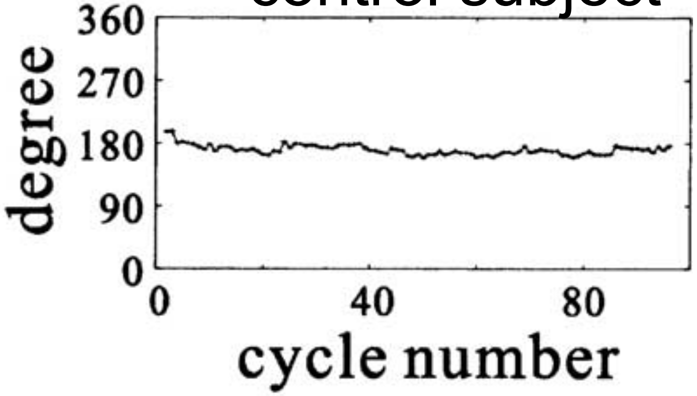
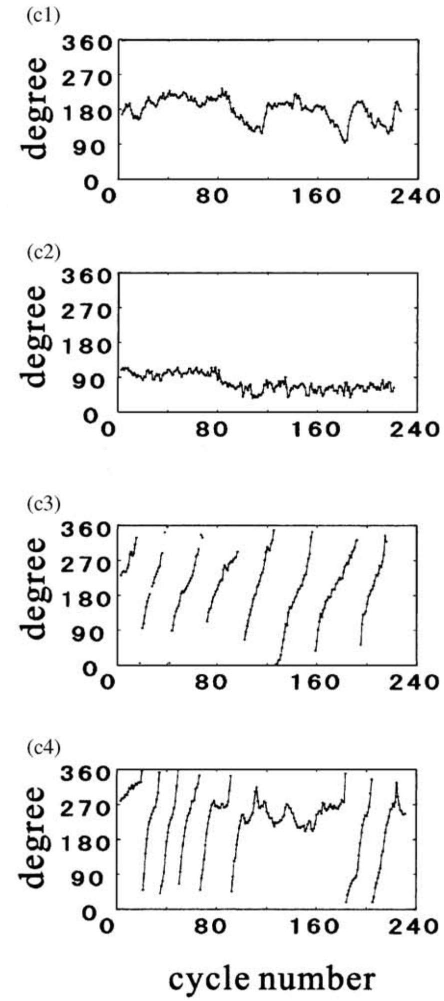
control subject





FoG-

FoG-

FoG+

FoG+

Summary: previous work on PD-related movement disorders and FoG

- focused on the analysis of gait and limb dynamics as measured by

  i) force sensitive insoles

  ii) a “strange” stationary bicycle

  iii) accelerometers (M. Baechlin et al., IEEE 14, 14(2) (2010))

  iv) EMG (A. Nieuwboer et al. Brain 127, 1650 (2004))

- other physiological signals

i) ECG – increase in heart rate during FoG (Maidan et al., Mov. Disord. **25**, 2346, 2010)

ii) Skin conductance – significant changes prior to FoG (Mazilu et al., IEEE **19**, 2015)

iii) EEG – increase in theta and beta frequency power during FoG
(e.g., Shine et al., Clin. Neurophysiol. **125**, 569, 2014 and Handojoseno et al., IEEE **23**, 887, 2015)

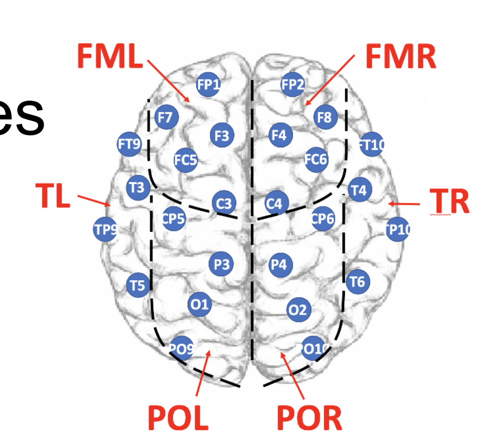
iv) EEG – increase in interhemispheric phase synchronization in PD
(Y. Miron-Shahar et al., Parkinsonism & related disorders **65**, 210, 2019.)

→ no systematic study yet on EEG brain networks in PD during walking

EEG brain networks in PD and FoG

EEG networks:

- nodes = EEG channels or brain lobes

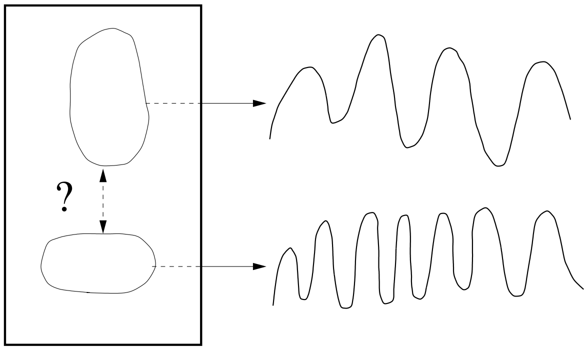


- links = interaction/coupling between EEG channels/brain lobes

How to quantify such coupling?

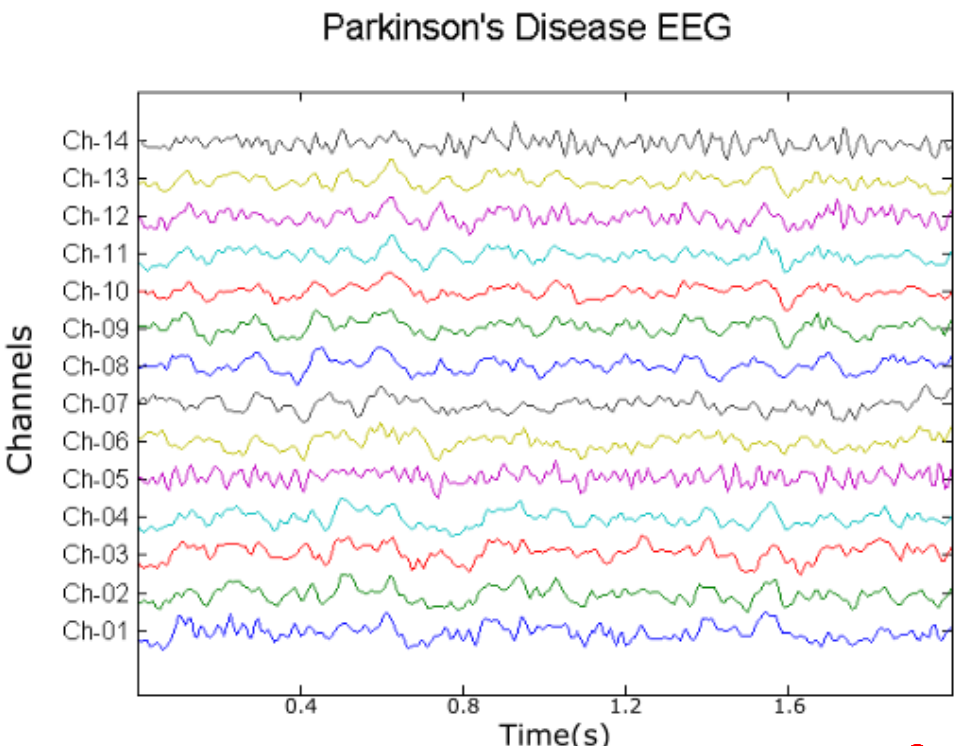
→ One possibility: Synchronization!

Phase Synchronization of coupled oscillators



well-defined frequency

M. Rosenblum et al., in Handbook of Biol Physics, Chapter 9, pp. 279-321 (2001)



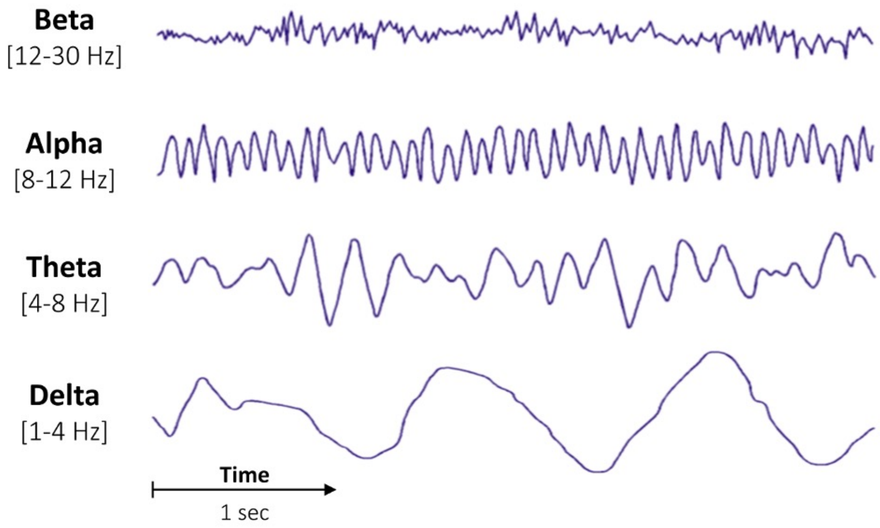
mixture of frequencies

→ need to apply a bandpass

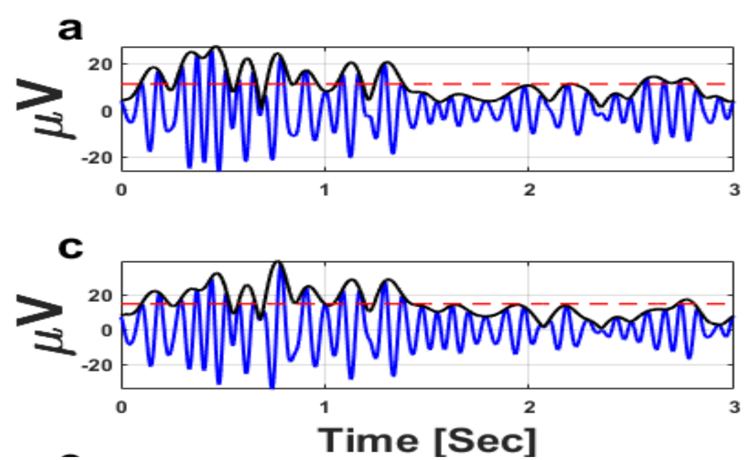
filter to extract brain wave signals

Caution! L. Xu and P. Ch. Ivanov, PRE 73, 065201 (2006)

Phase Synchronization of coupled oscillators



Example: two channels



blue = alpha oscillations

black = amplitude of the alpha signals

Extract amplitude and phase from signal

Step 1: Hilbert transform of s(t): $\tilde{s}(t) \equiv \frac{1}{\pi} P \int_{-\infty}^{\infty} \frac{s(\tau)}{t-\tau} d\tau,$

Step 2: Construct complex analytic signal (matlab: hilbert(s)):

$$S \equiv s(t) + i\tilde{s}(t) = A(t)e^{i\varphi(t)}$$

Step 3: Calculate instantaneous amplitude and phase

Amplitude

$$A(t) = \sqrt{s^2(t) + \tilde{s}^2(t)}$$

Phase

$$\phi_{mod2\pi} = arctan(\frac{\tilde{s}(t)}{s(t)})$$

Properties of Hilbert transform: Preserves the amplitude of the signal

Advantage: can be applied to any signal; needs to be narrow banded

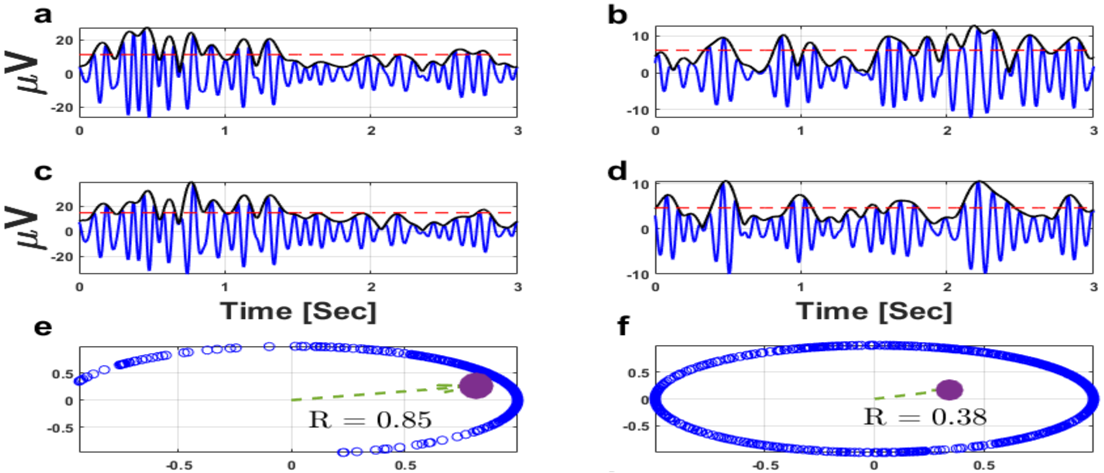
Characterization of Phase Synchronization

phase of Amplitude signal 1: ϕ_1

phase of Amplitude signal 2: ϕ_2

synch. index R in window ν

$$R(\nu) = |\langle exp[i(\phi_1(t) - \phi_2(t)]\rangle_\nu|$$

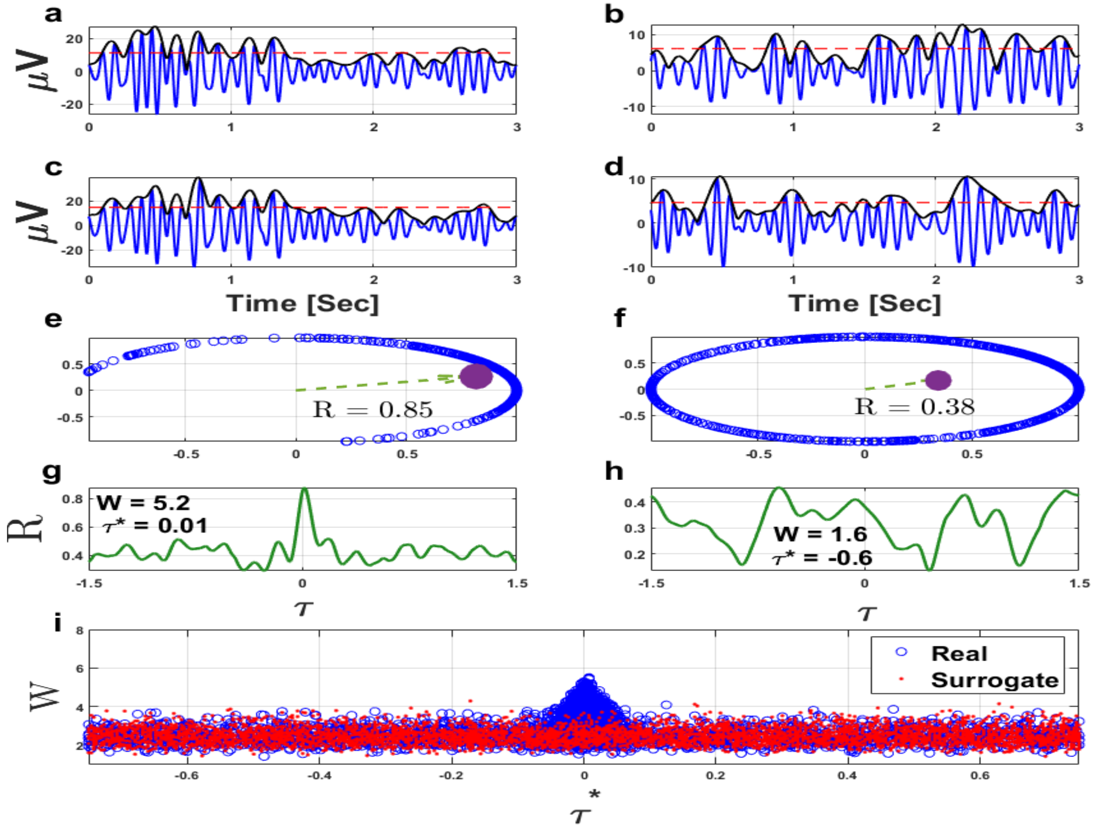


Strong synchronization   Weak synchronization

Large R index: strong phase synchronization→ strong coupling
Small R index: weak phase synchronization → weak coupling

Probing significant interactions in amplitude synchronization

- shift amplitude signals against each other, time shift τ
- calculate R as function of shift → $R(\tau)$
- calculate significance value $W = \frac{R_{max} - \langle R(\tau) \rangle}{\sigma(R(\tau))}$

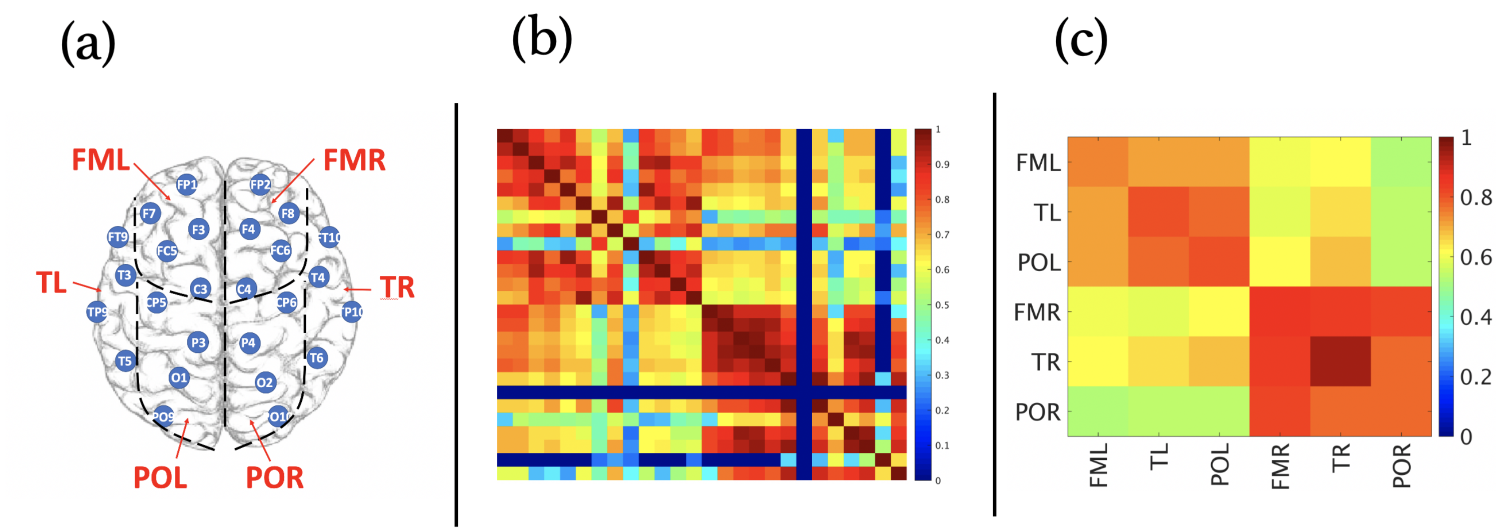


→ significant interaction if W > 2.5 and $\tau^* \in [-0.05, 0.05]\,sec$

Interaction matrices for synchronization and significance

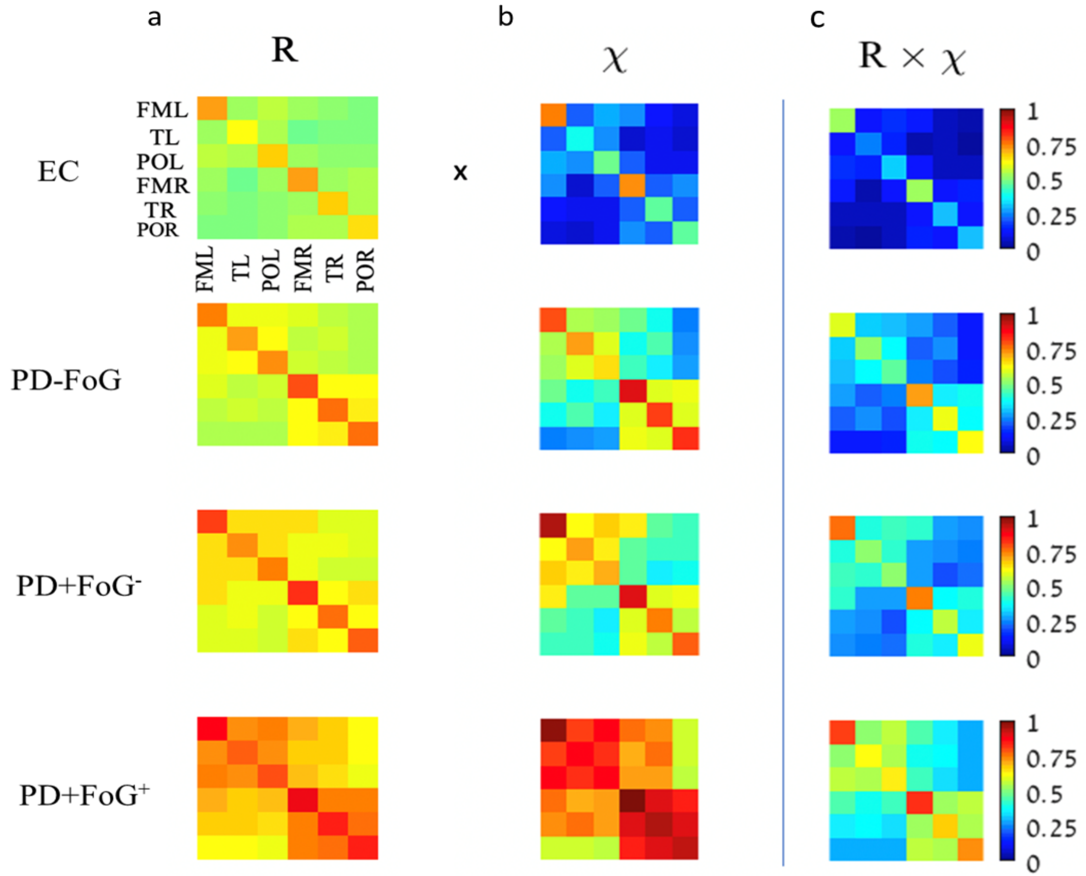
- analyze interactions between all EEG channels in the same frequency band to obtain interaction matrices

Example: Synchronization matrix for PD+FoG$^+$ during normal walking, alpha band



Interaction matrices for synchronization and significance

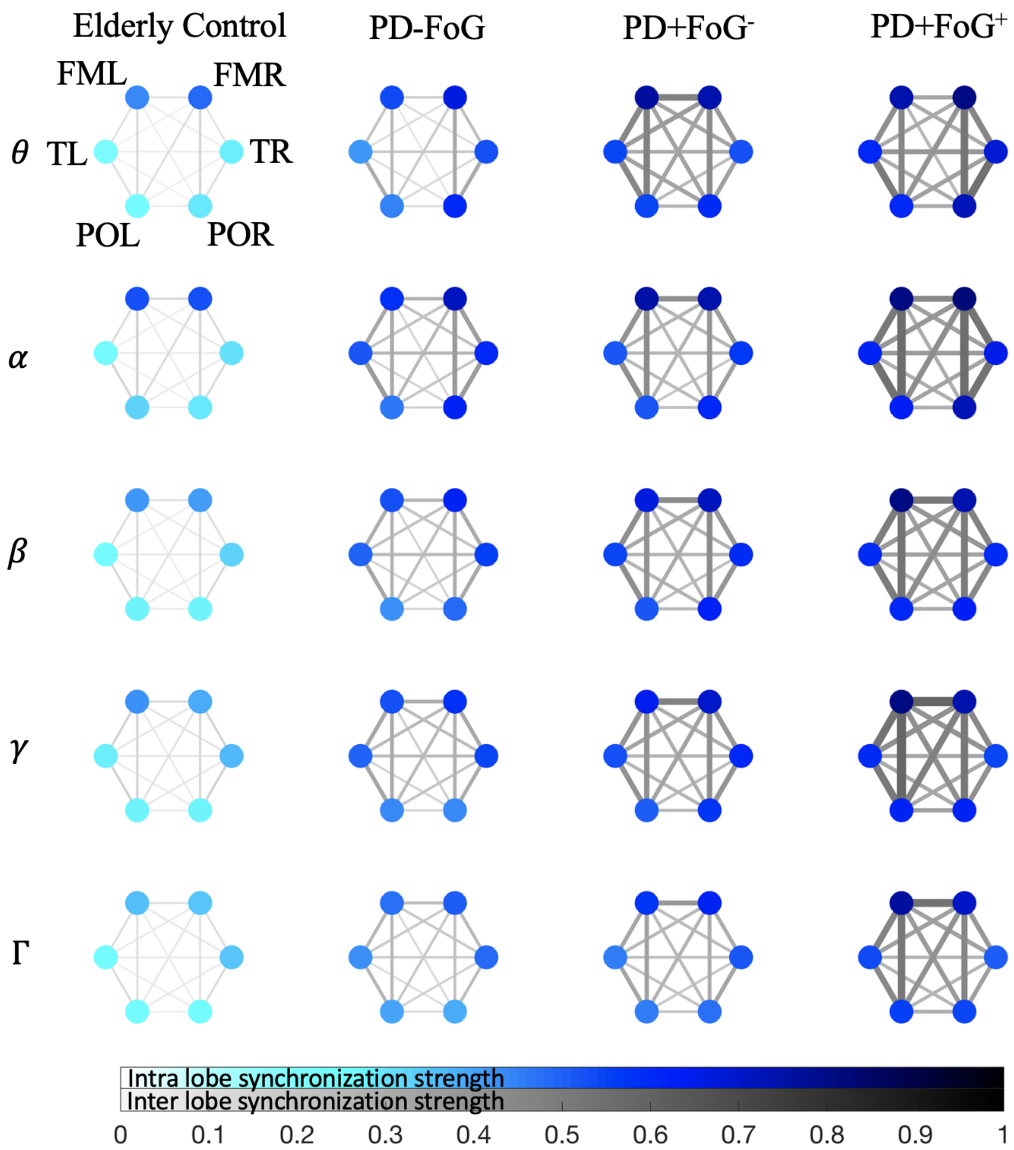
Example: Interaction matrices for alpha band



→ increase in EEG interactions with disease severity

→ most pronounced within the same lobe and same hemisphere

Brain networks across different frequency bands

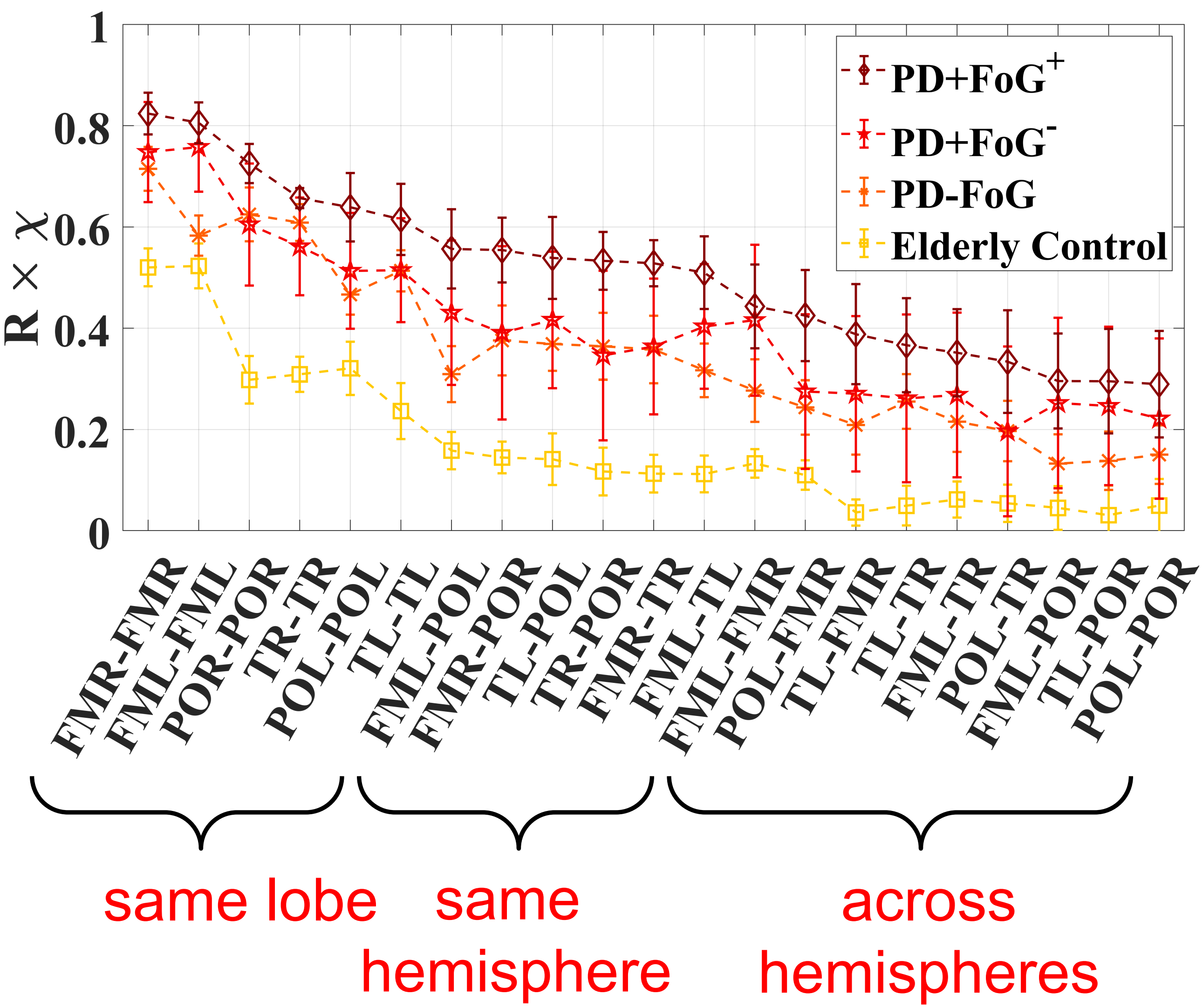


→consistent pattern across different frequencies

→difference is more pronounced for higher frequencies

Interaction strength across lobes and hemispheres

Example: ranking plot of matrix elements for alpha band

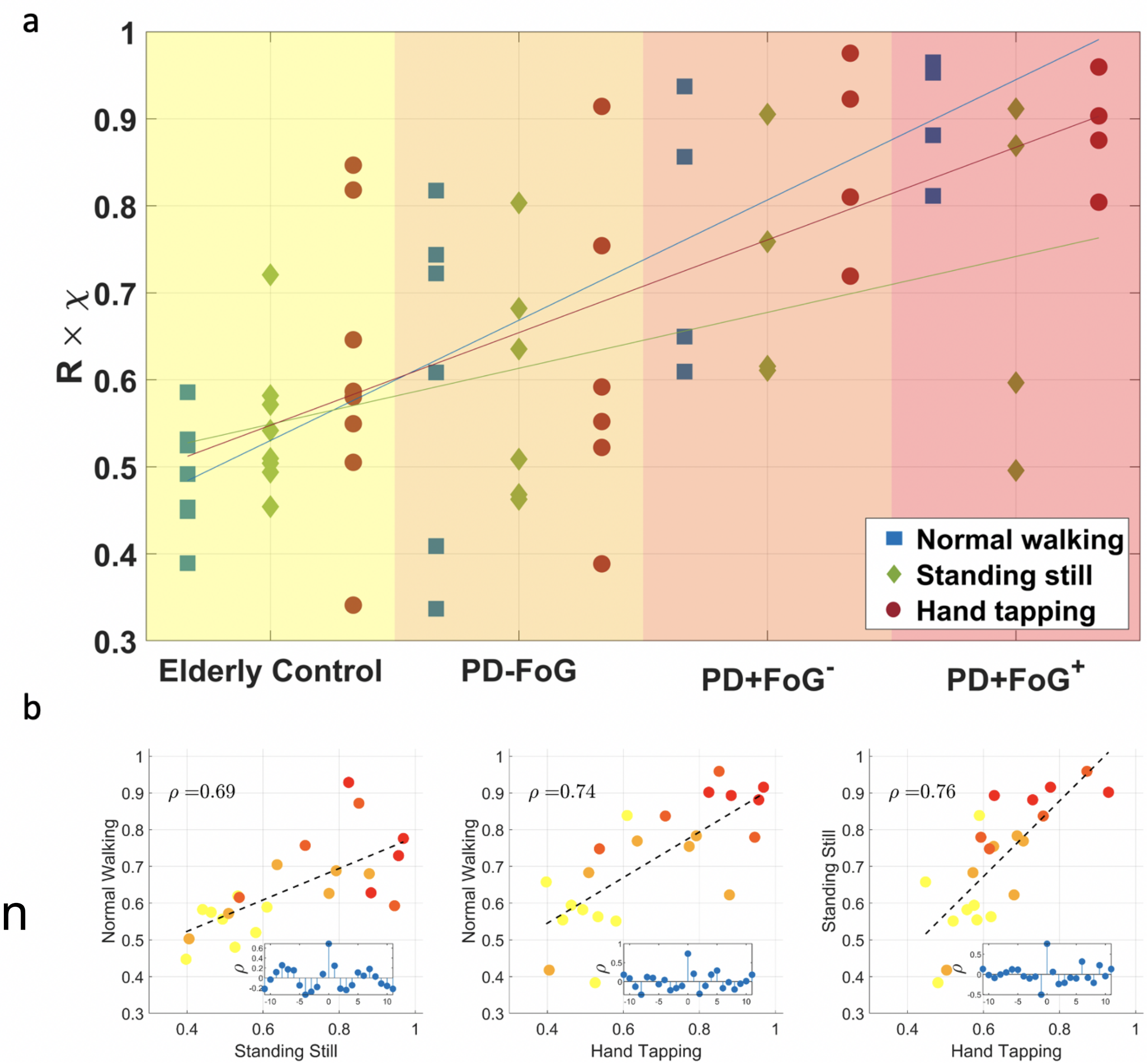


Intra-lobe interaction in frontal lobe for different motor tasks

Each dot is for an individual subject for a given task

alpha band results

significant cross-correlations between tasks



Summary

- ✓ Significance measure to distinguish between physiological and spurious synchronization
- ✓ Strength of network links/interactions in EEG amplitudes shows dramatic increase for PD patients in more advanced stages of the disease
- ✓ overall increase in EEG synchronization for advanced PD is analogous Alzheimer’s disease; increased brain activity in AD could be related to a compensation mechanism due to the process of neurodegeneration
- ✓ EEG amplitude synchronization is similar in PD-FoG and PD+FoG- although both groups are generally quite different in clinical terms
- ✓ Perhaps: FoG risk changes on daily basis where cortical areas switch between ’prone-to-FoG’ vs. non-FoG states (this could be monitored by EEG synchronization networks and treated by DBS)