Causality, Information Transfer and Dynamical Networks
CIDNET14, June 16-20, 2014

The reconstruction of dynamical physiological networks from time series

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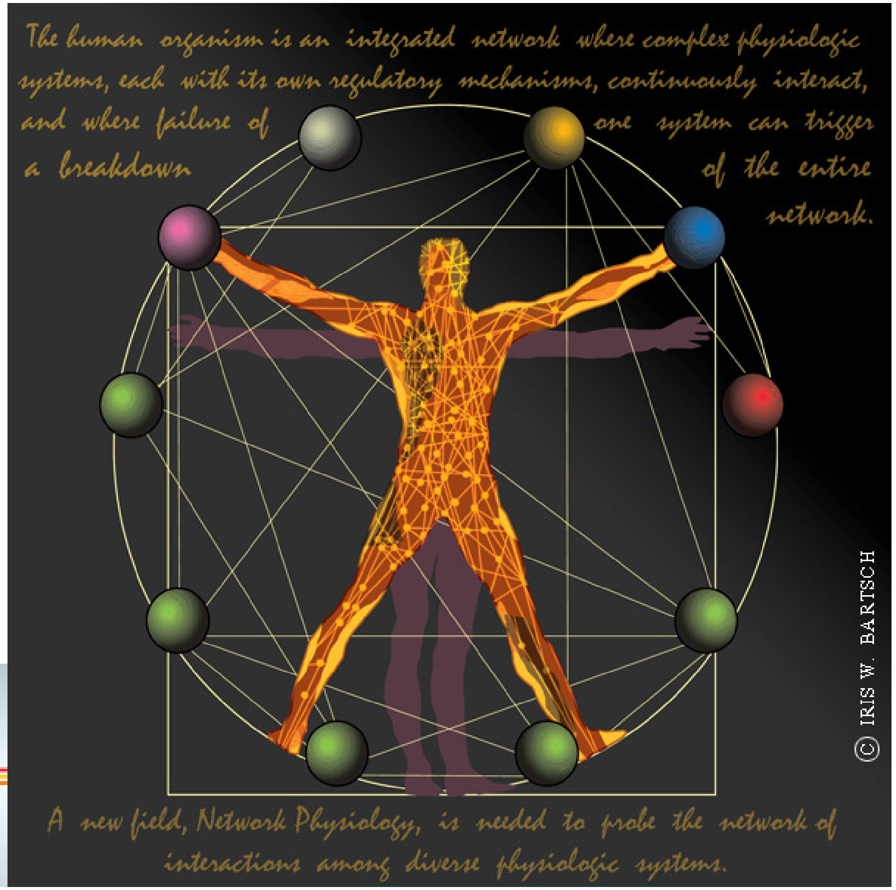
Outline of the talk

- **Introduction:** network description of complex systems based on time series analysis
- **Physiological networks reconstructed from time delay stability**
  - Pre-processing of biosignals (EEG, ECG, EMG, respiration)
  - Definition of TDS value; surrogate data tests
  - Dynamics of TDS networks during different physiological states
  - Direction of coupling / causality
- **Brain networks reconstructed from EEG phase synchronization**
- **Brain networks reconstructed from EEG amplitude-frequency cross-modulation**
- **Wikipedia networks reconstructed from cross-correlations of user-access data and event synchronization of edit data**
- Summary and conclusion

Study relations between many organs

→ Network Physiology



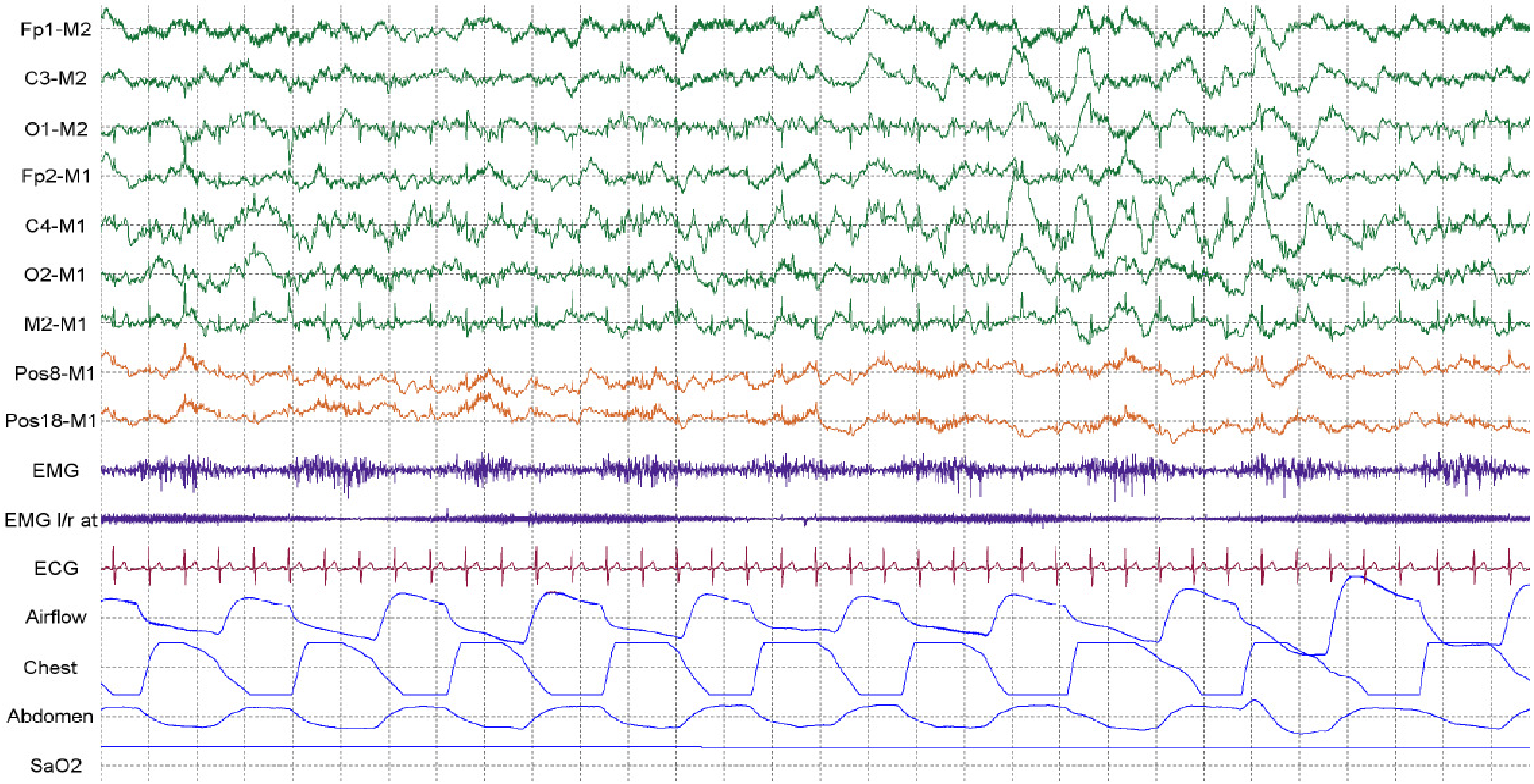
nature COMMUNICATIONS **3**, 702 (2012)

Network physiology reveals relations between network topology and physiological function

Amir Bashan[1,*], Ronny P. Bartsch[2,*], Jan. W. Kantelhardt[3], Shlomo Havlin[1] & Plamen Ch. Ivanov[2,4,5]

Medical time series data

Complex System: human being / cardiovascular system / brain



Recording from a clinical sleep laboratory (30 seconds shown)

Brain-"waves": bands in the EEG

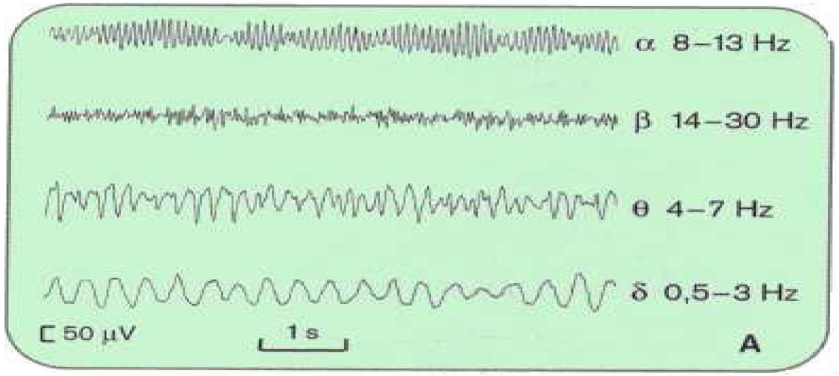
Definition of bands in EEGs
(Electro-Encephalo-Gramm):

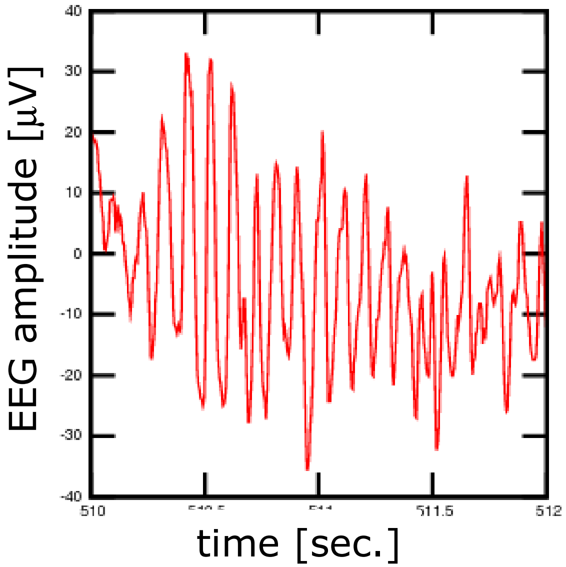
δ_1: 0.5-2Hz, δ_2: 2-4Hz,

θ: 4-7Hz, α: 7-11.5Hz,

σ: 11.5-16Hz, β: 16-22Hz

$\rightarrow$ band-pass filters





Hilbert transform:
add imaginary part

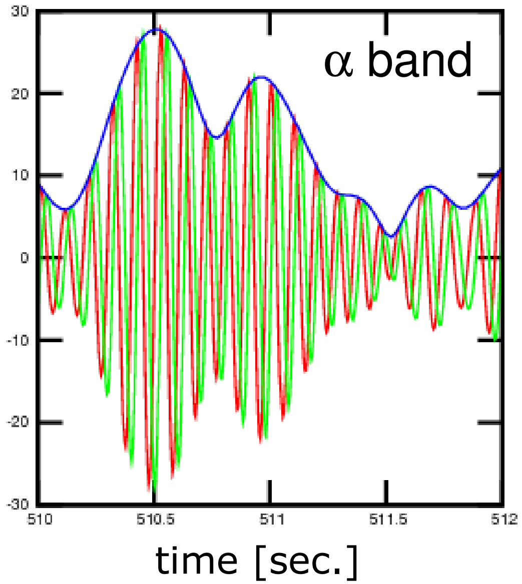
$$z(t) = x(t) + \mathrm{i}\, y(t)$$

$$y(t) = \frac{1}{\pi} \mathrm{P.V.} \int_{-\infty}^{+\infty} \frac{x(t')}{t - t'}\, dt'$$

amplitude and phase:

$$A(t) = \sqrt{x^2(t) + y^2(t)}$$

$$\varphi(t) = \arctan \frac{y(t)}{x(t)}$$



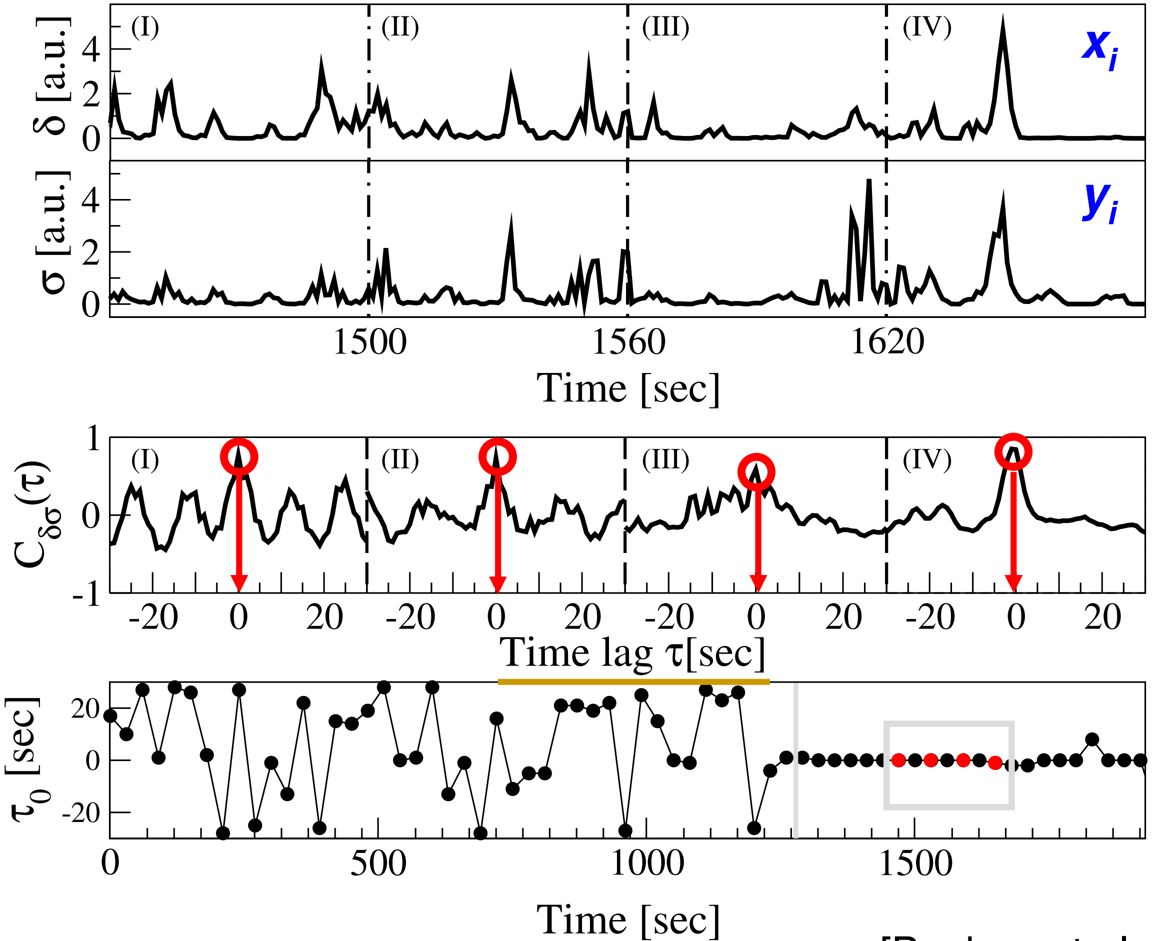
Time Delay Stability

$$C_{xy}(\tau) = \frac{1}{s_x s_y}\left\langle (x_i - \overline{x})(y_{i+\tau} - \overline{y})\right\rangle$$

1. Calculate **cross-correlation functions** for all pairs of time series, using over lapping windows of one minute duration.

2. Track the **positions** (time delays) **of** the **maxima** in each cross-correlation function.

3. Identify stable relation between the two sub-systems when these **time delays** are **stable**.



[Bashan et al., Nature Commun. 2012]

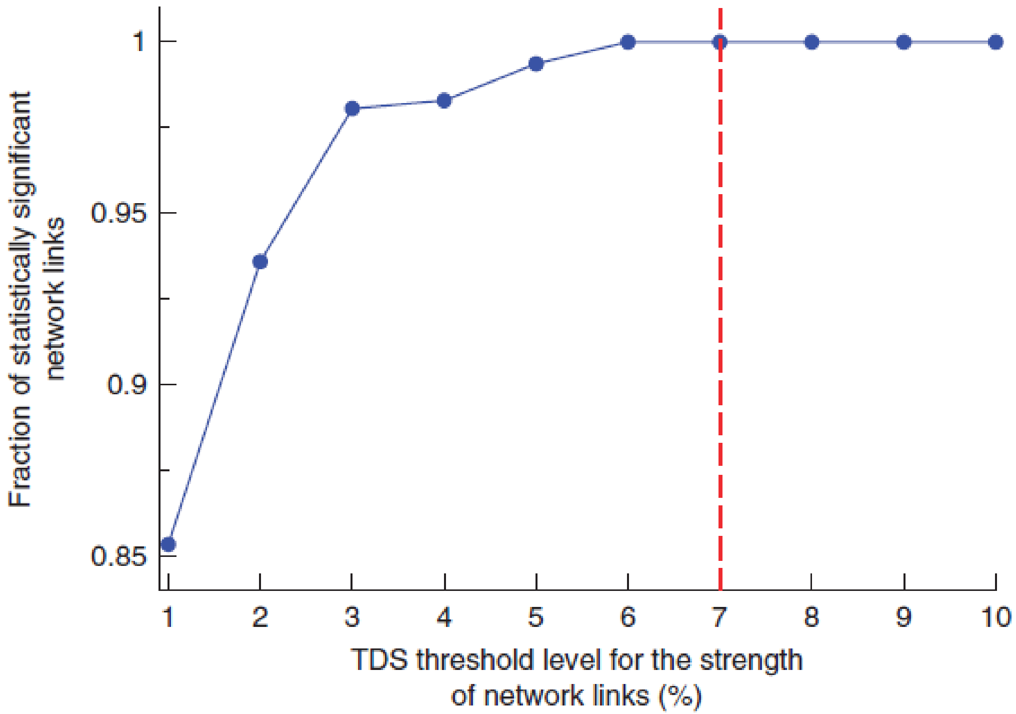
4. TDS value = percentage of time with stable link.

Surrogate data test for indentifying stable links

1. **Surrogate data:** select pairs of data channels from different subjects.

2. For each link, calculate TDS values for real data and surrogate data.

3. Compare distributions of real and surrogate TDS values using a Student's t test. The link is considered significant if $p < 0.001$.

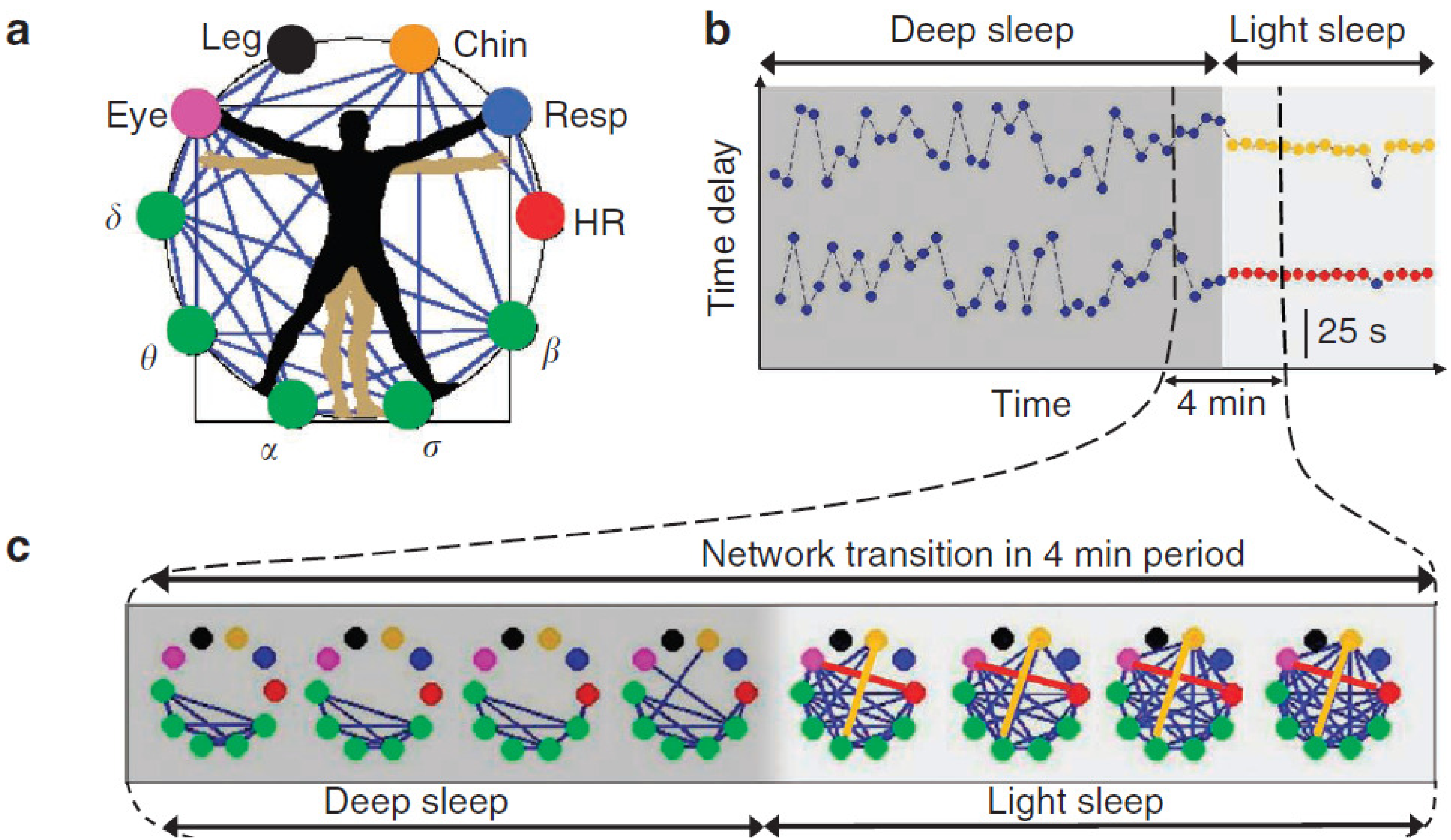


4. At a **TDS threshold of 7%**, only significant (real) links are identified. We thus replace the significance testing by the threshold procedure.

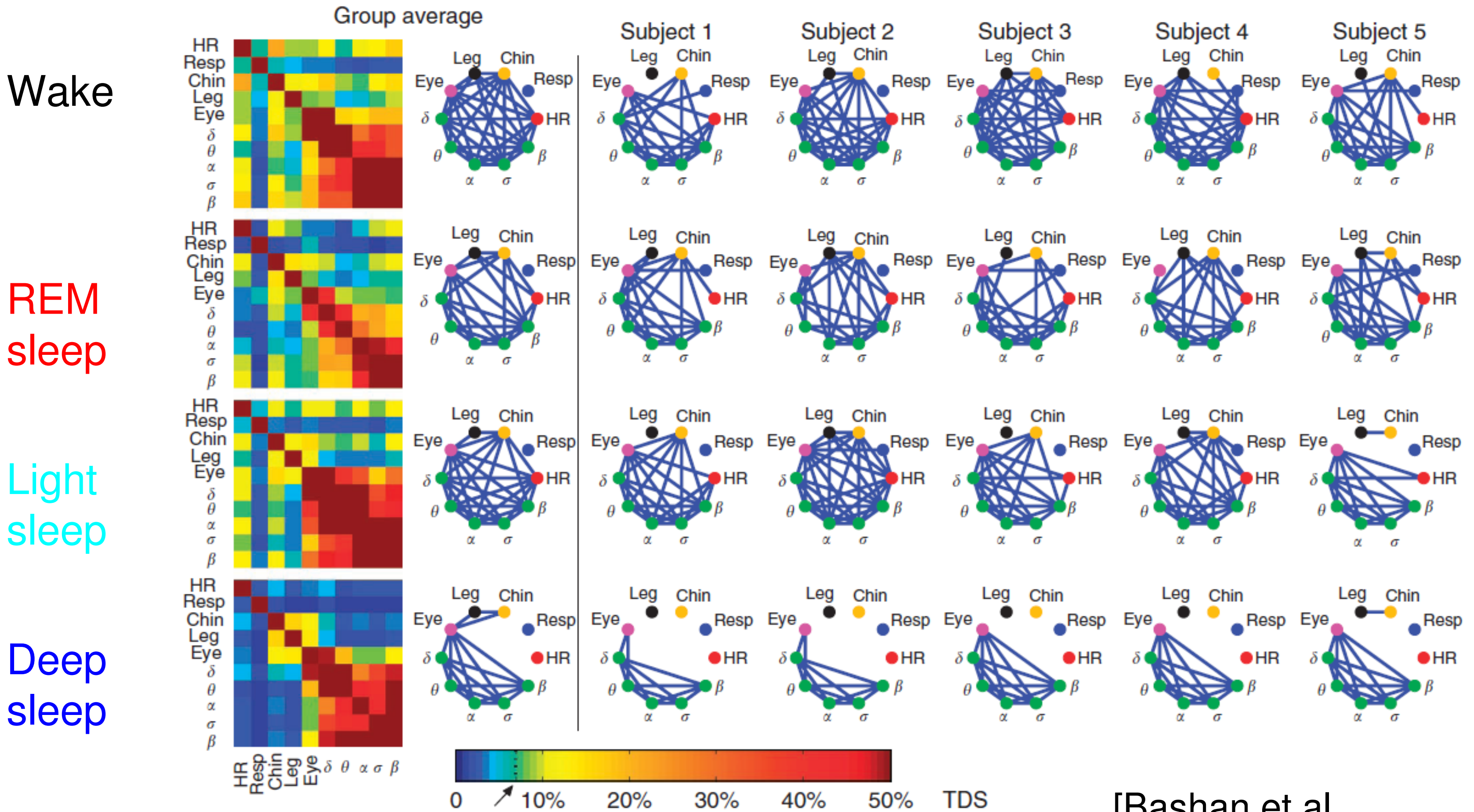
[Bashan et al., Nature Commun. 2012]

Relations between many organs change with physiological function

[Bashan et al., Nature Commun. 2012]



Dynamics of the physiological network

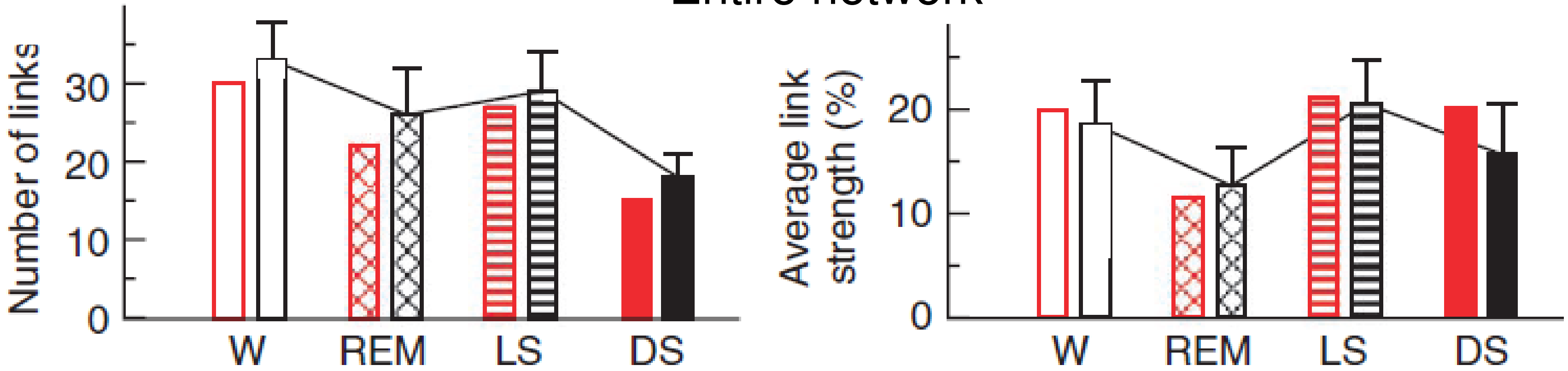


[Bashan et al., Nature Commun. 2012]

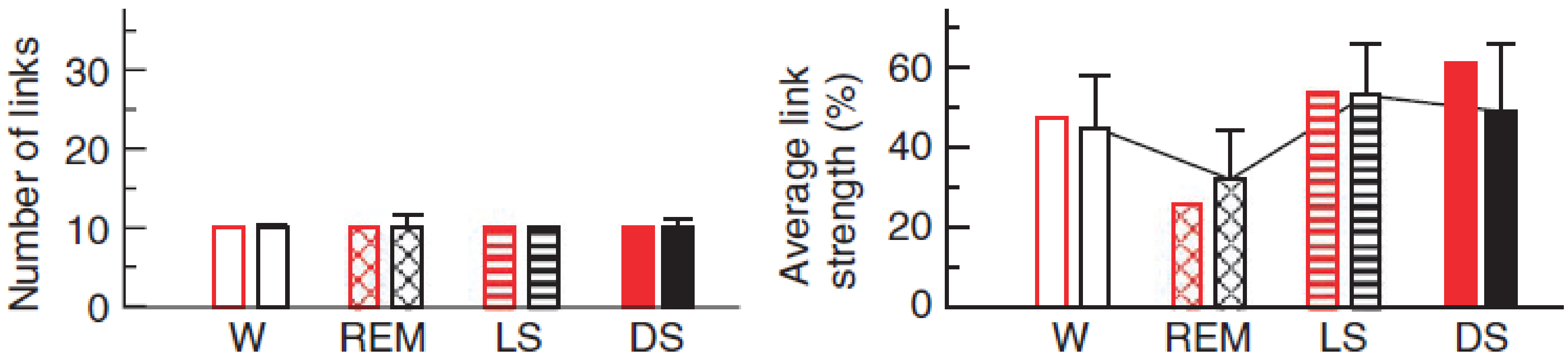
Network change across sleep stages

[Bashan et al.,
Nature Commun. 2012]

Entire network



Brain-brain network



Compare with: fluctuation scaling behavior and phase synchronization

(i) **Fluctuation scaling behavior** (type of $1/f^\beta$ noise; long-term correlations) and

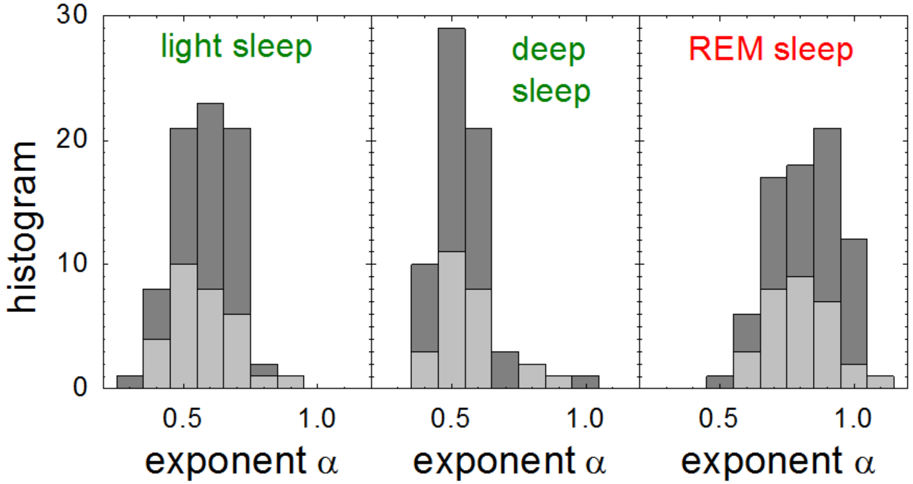
(ii) frequency of cardio-respiratory **phase synchronization** episodes

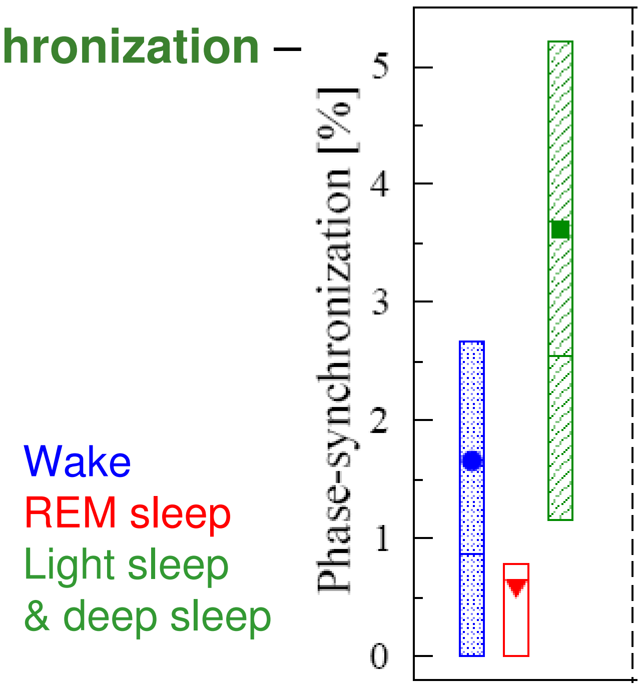
are alike for non-REM sleep (light and deep sleep)

– **nearly white noise, pronounced synchronization** –

and REM sleep / wakefulness

– **$1/f^\beta$ noise, weak synchronization**

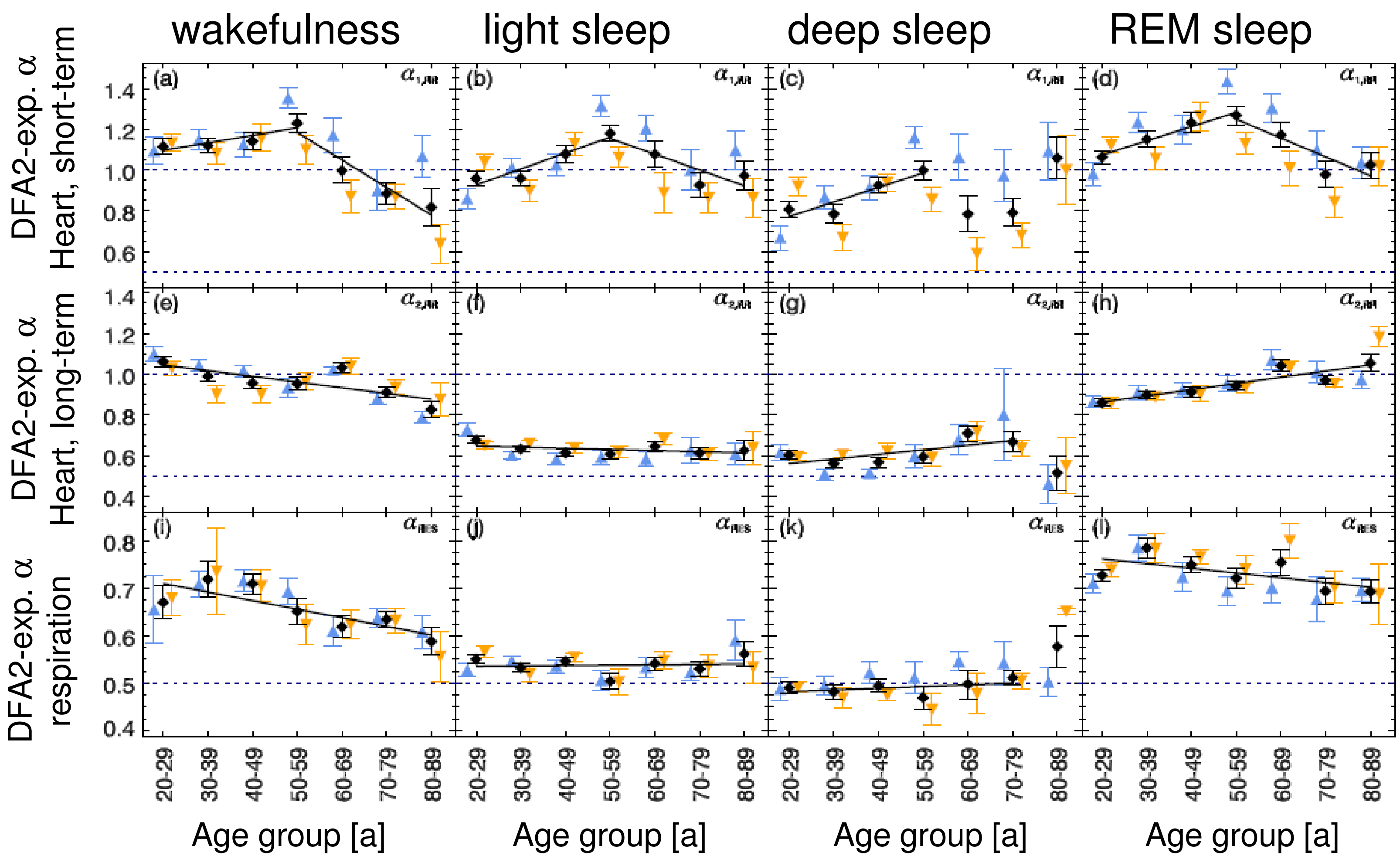




[Bunde et al., PRL 2000; Schumann et al., Sleep 2010; Bartsch et al., PNAS 2012]

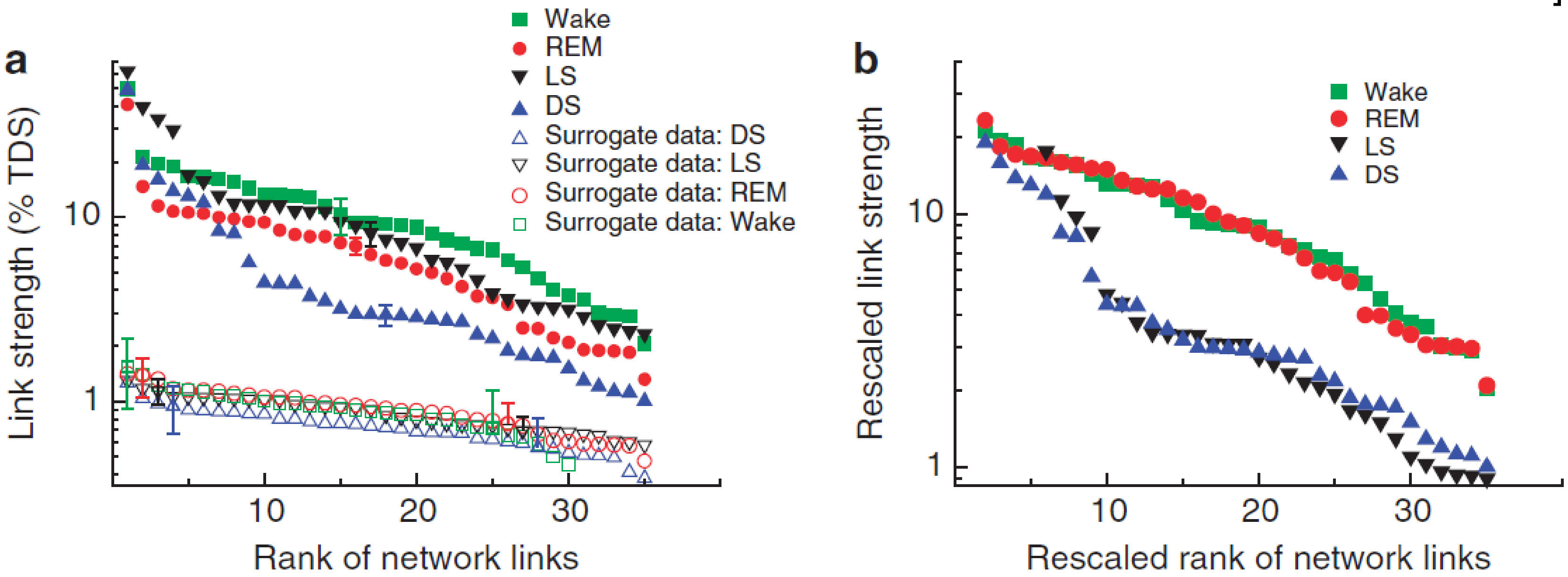
Age dependence of heart rate and respiration scaling behavior

[Schumann et al., Sleep 2010]



Rank ordered TDS link strengths

[Bashan et al.,
Nature Commun. 2012]

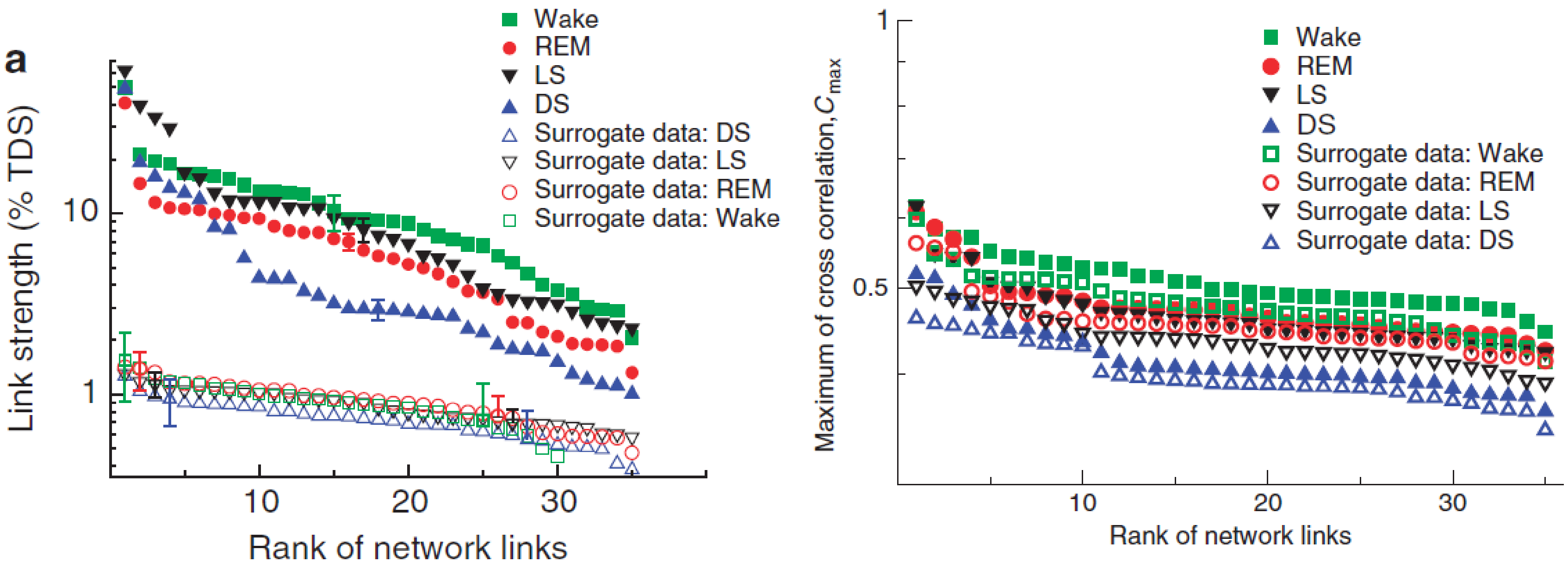


Link strengths for surrogate data are much lower than for real data.

Values of link strengths are similar for **wake** and **light sleep** (LS),
but lower for **REM sleep** and **deep sleep** (DS).

Shape of rank-ordered link-strength distributions are similar for **wake** and **REM**,
but different for non-REM (**light sleep** and **deep sleep**).

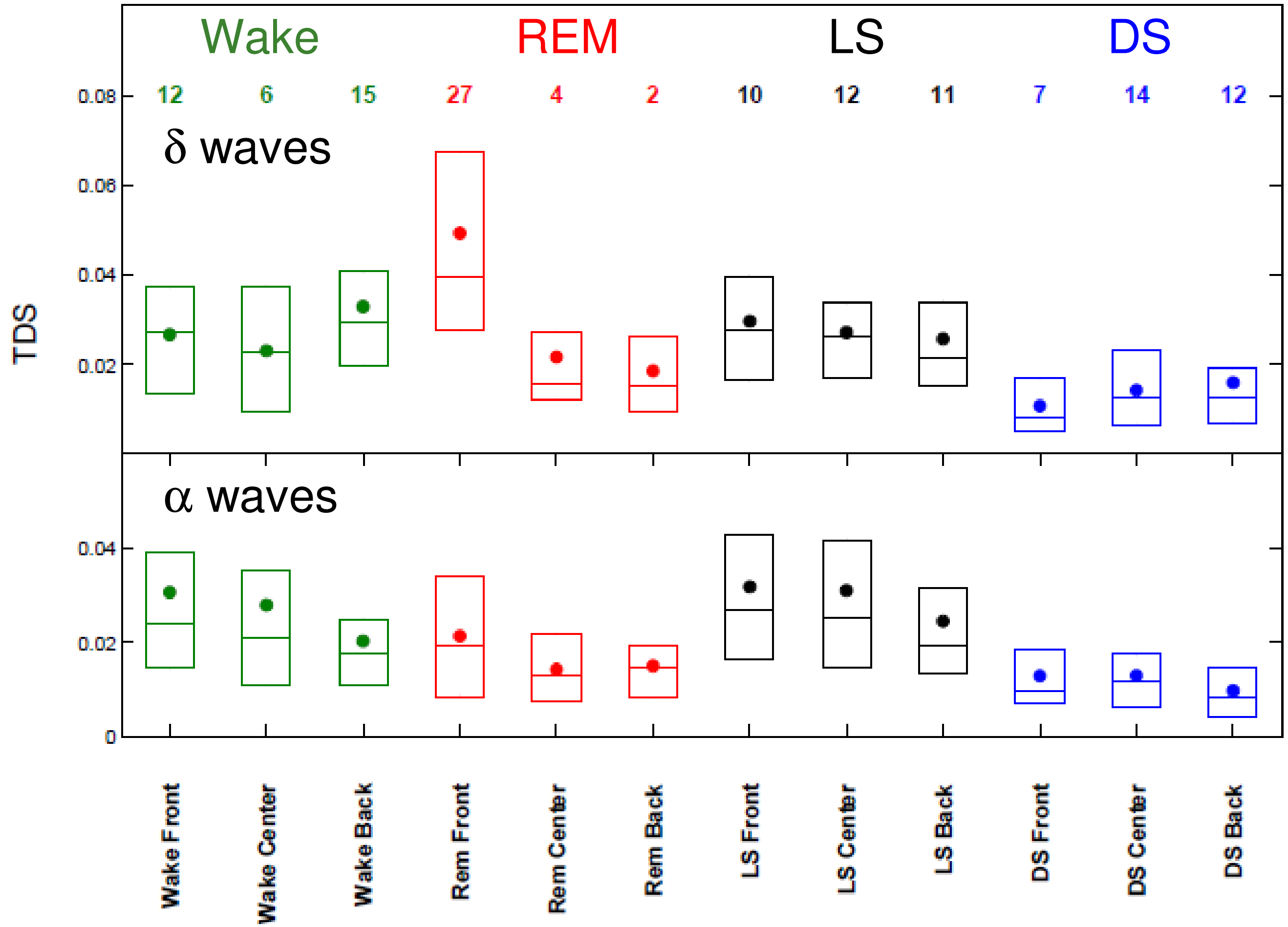
Comparison with results for cross correlation maximum



The value of the cross-correlation function (maximum) cannot identify links reliably.

[Bashan et al., Nature Commun. 2012]

Link between respiration and the brain

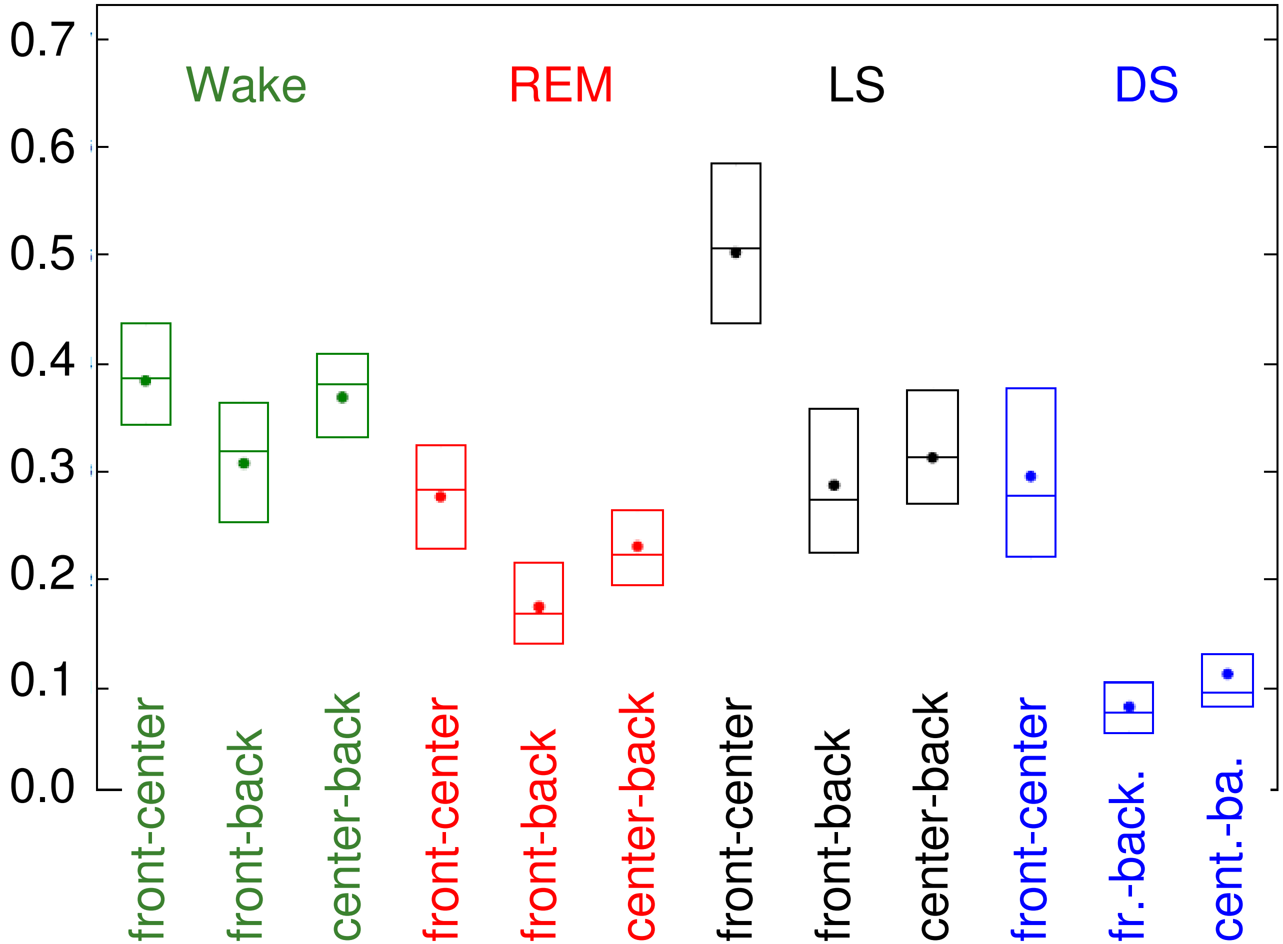


Dominating in # subjects (out of 33)

Observation: Coupling of respiration and frontal δ brain waves is enhanced during REM sleep.

[Zakashansky, Bashan, Havlin, Bartsch, Kantelhardt; work in progress, 2014]

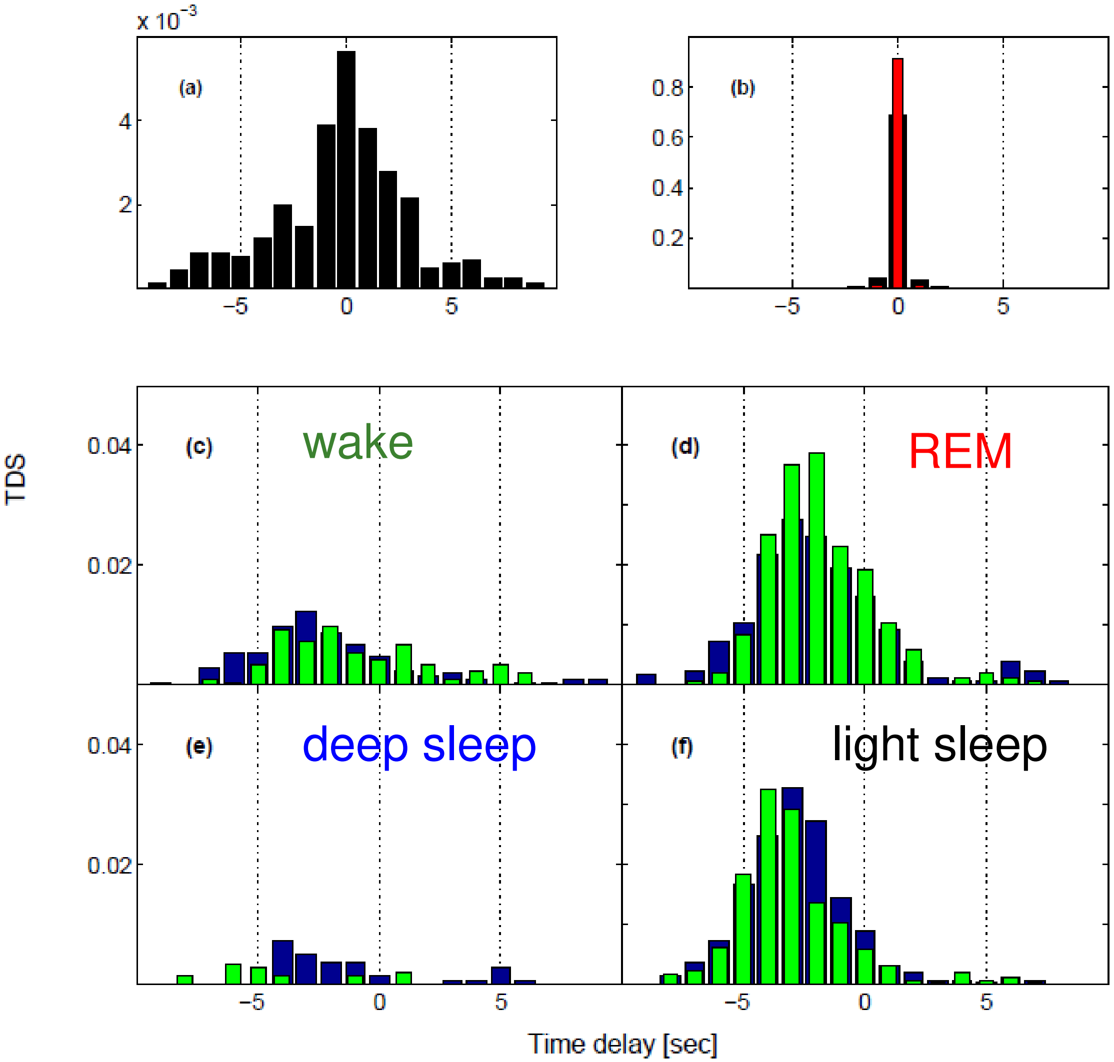
TDS relations between EEGs recorded in different parts of the brain



Observation: During non-REM sleep the connections of the back brain are significantly weaker relative to the center-to-front connection.

[Zakashansky, Bashan, Havlin, Bartsch, Kantelhardt; work in progress, 2014]

Non-zero TDS delay → direction / causality?



Distributions of stable delay times between

(a) α brain activity in two locations on the scalp

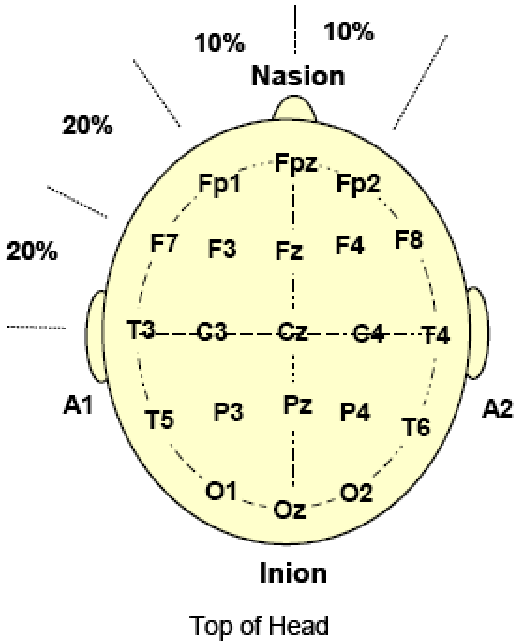
(b) respiratory rate and brain activity

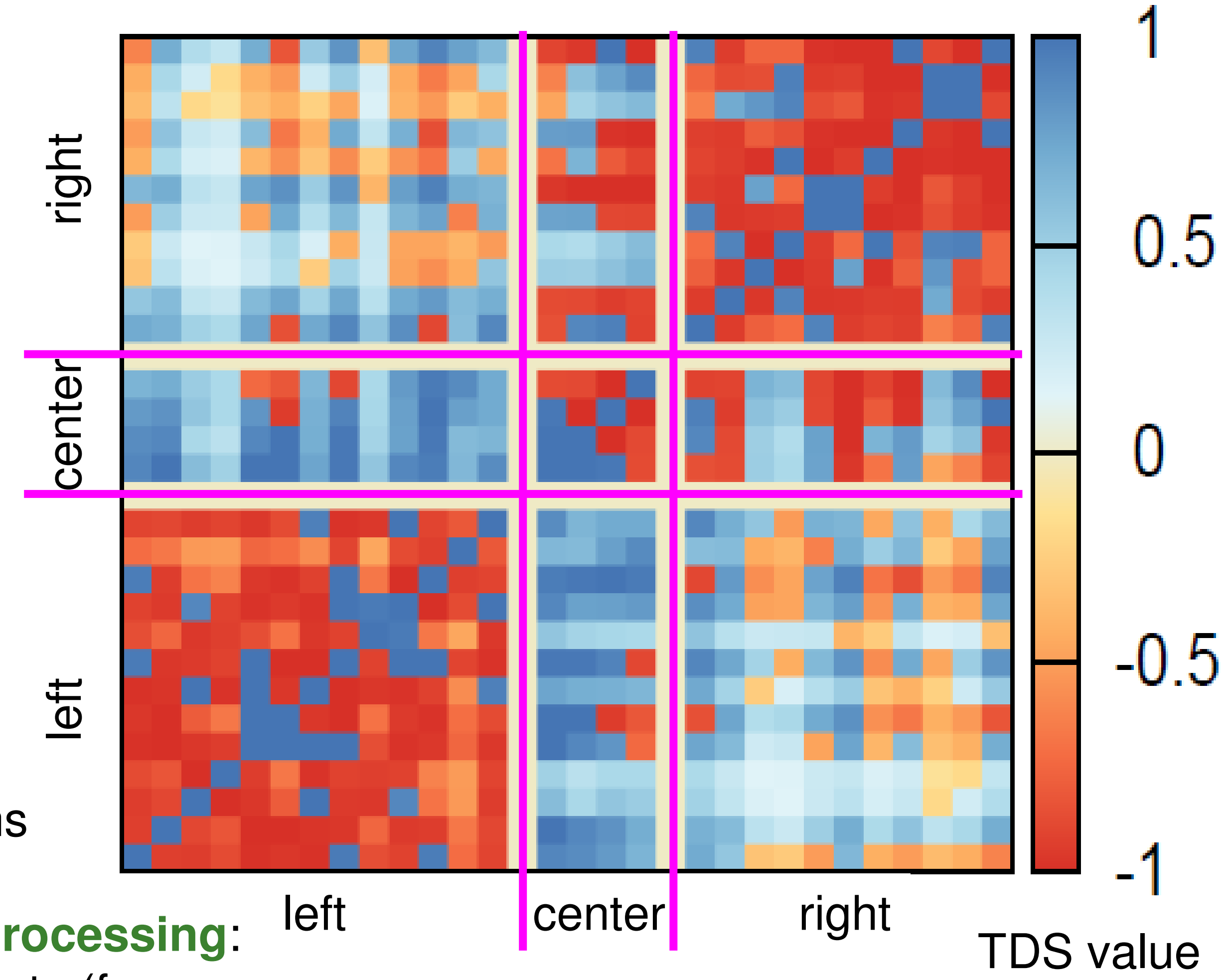
(c-f) invasive blood pressure and brain activity.

blue: healthy subjects, green: apnea patients

[Zakashansky, Bashan, Havlin, Bartsch, Kantelhardt; work in progress, 2014]

Matrices of TDS between 30 EEG electrodes





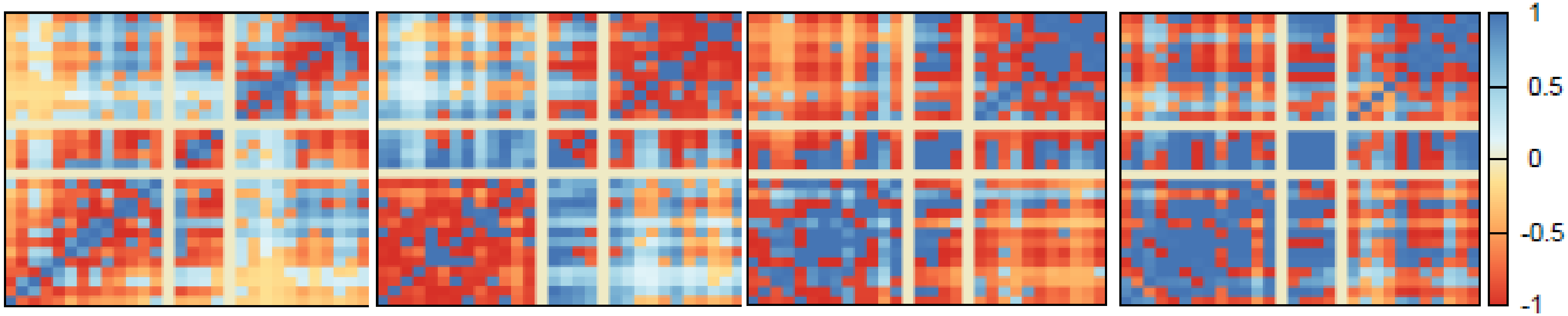
Exercise: walking with turns for 4 minutes, patient with Parkinson's disease. **Pre-processing**: elimination of 2-4 components (from EEGLAB independent component analysis)

[Meier, Miron, Plotnik, Kantelhardt; work in progress, 2014]

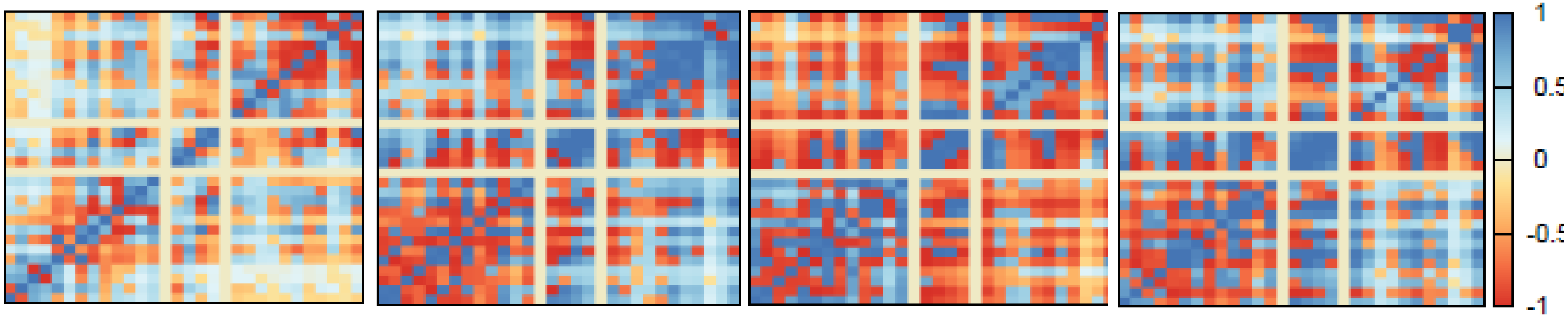
Comparison across EEG bands and exercises

TDS value

Walking with turns: no freezing-of-gait episodes in this patient



Walking through narrow passage: **many freezing-of-gait episodes**



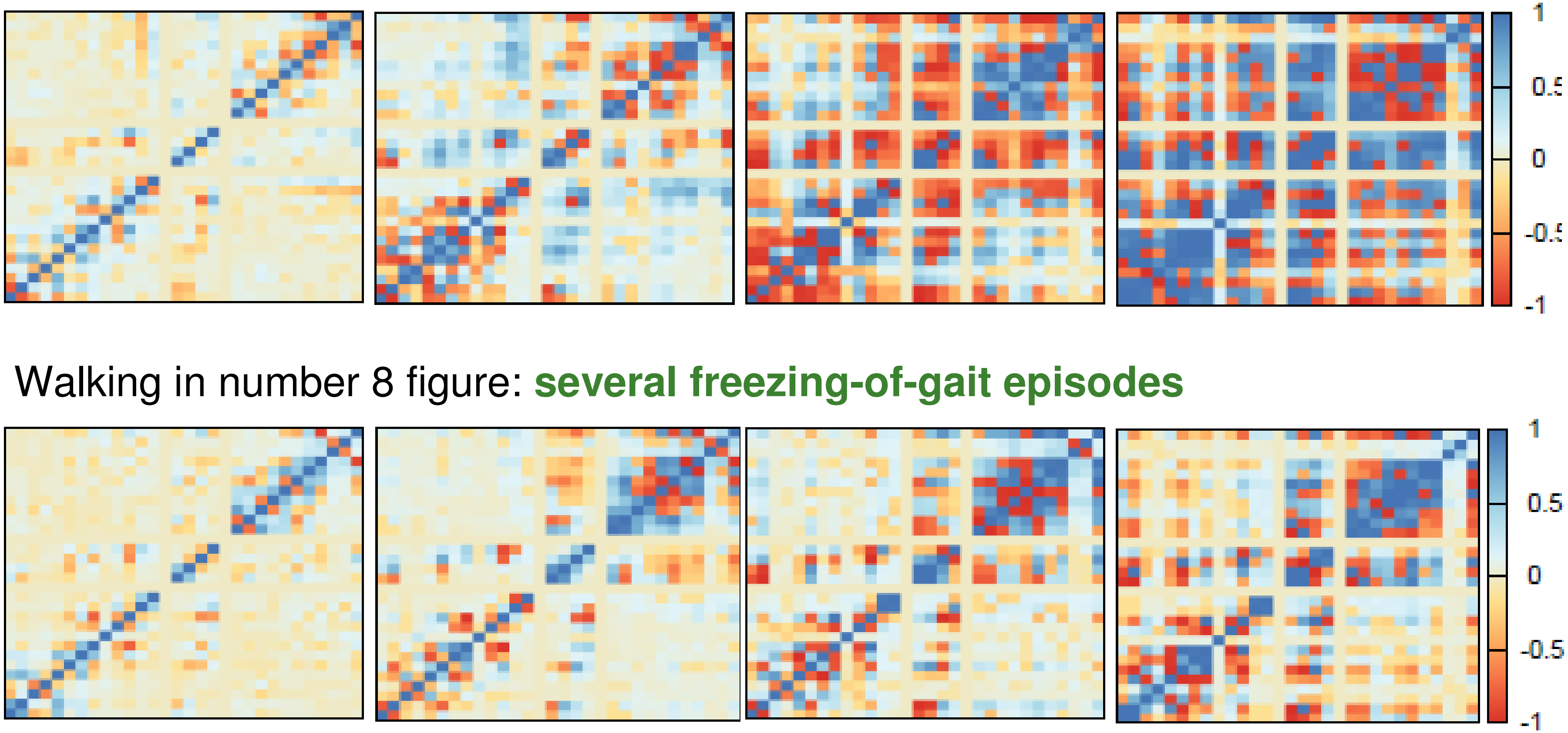
ϑ: 4-7Hz α: 7-11.5Hz σ: 11.5-16Hz β: 16-22Hz

[Meier, Miron, Plotnik, Kantelhardt; work in progress, 2014]

Comparison across EEG bands and exercises

Walking with turns: no freezing-of-gait episodes in this patient

Walking in number 8 figure: **several freezing-of-gait episodes**



ϑ: 4-7Hz α: 7-11.5Hz σ: 11.5-16Hz β: 16-22Hz

[Meier, Miron, Plotnik, Kantelhardt; work in progress, 2014]

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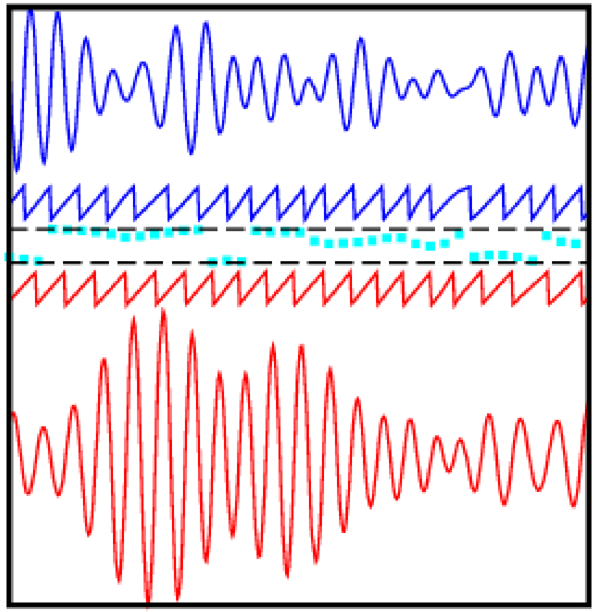
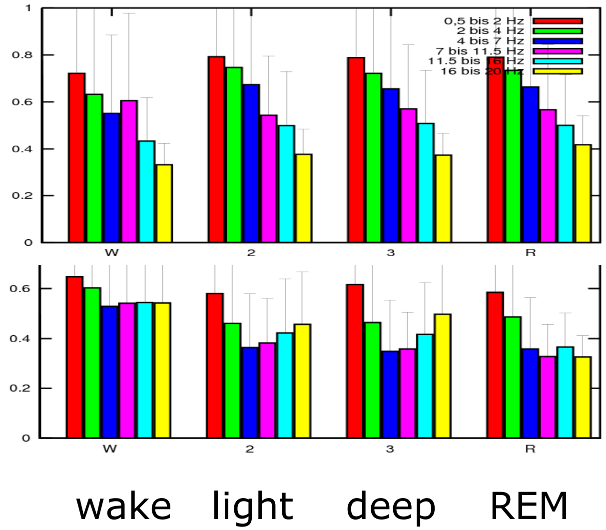
EEG phase synchronization analysis

Extraction of local EEG phases:



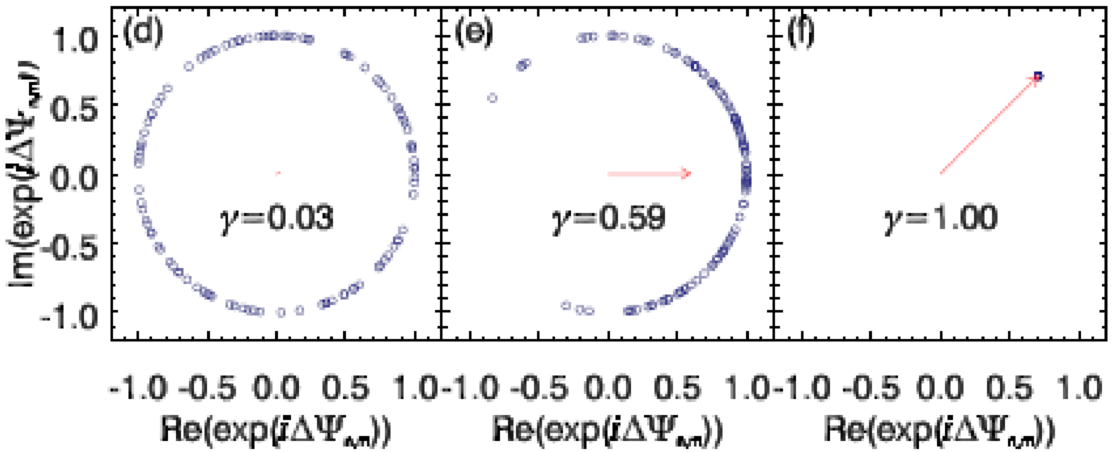
Phase synchronization between **left and right** part

between **front and back** of the brain

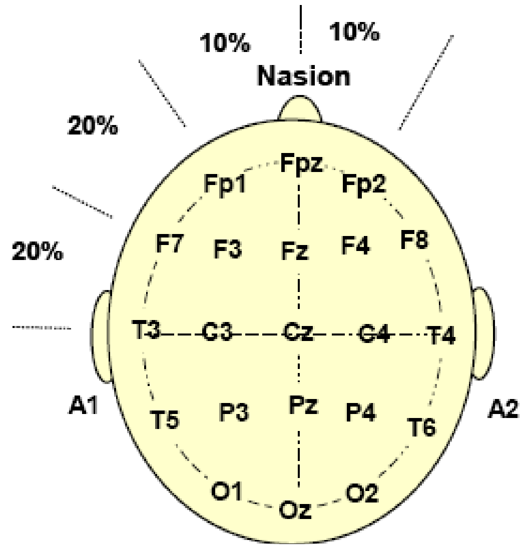


Synchronization coefficient γ:

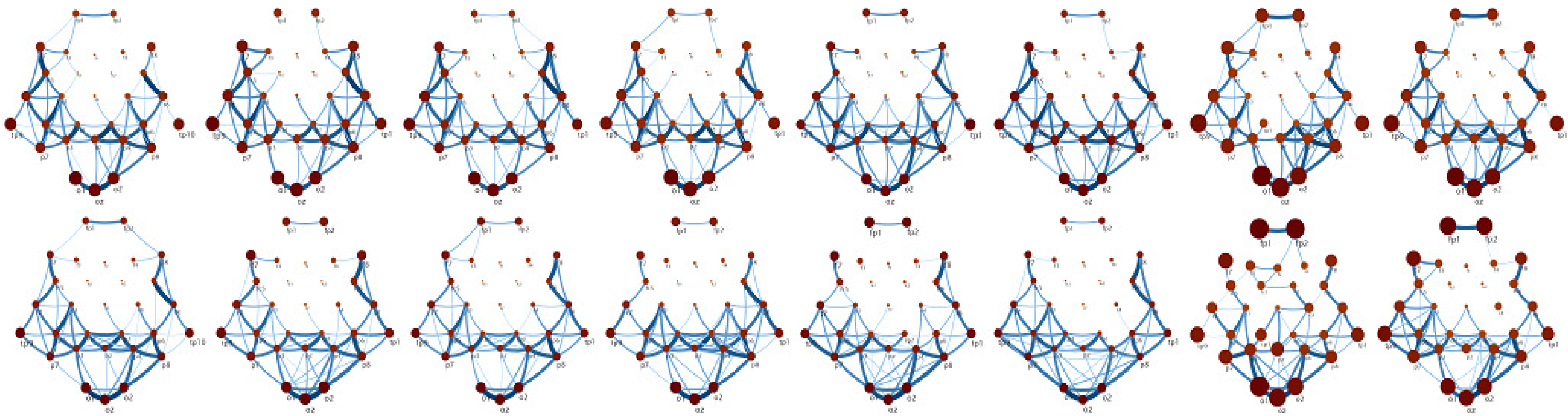
$$\gamma = \left| \left\langle \exp\left[i(\varphi_k^{(1)} - \varphi_k^{(2)}) \right] \right\rangle \right|$$



EEG phase synchronization network analysis



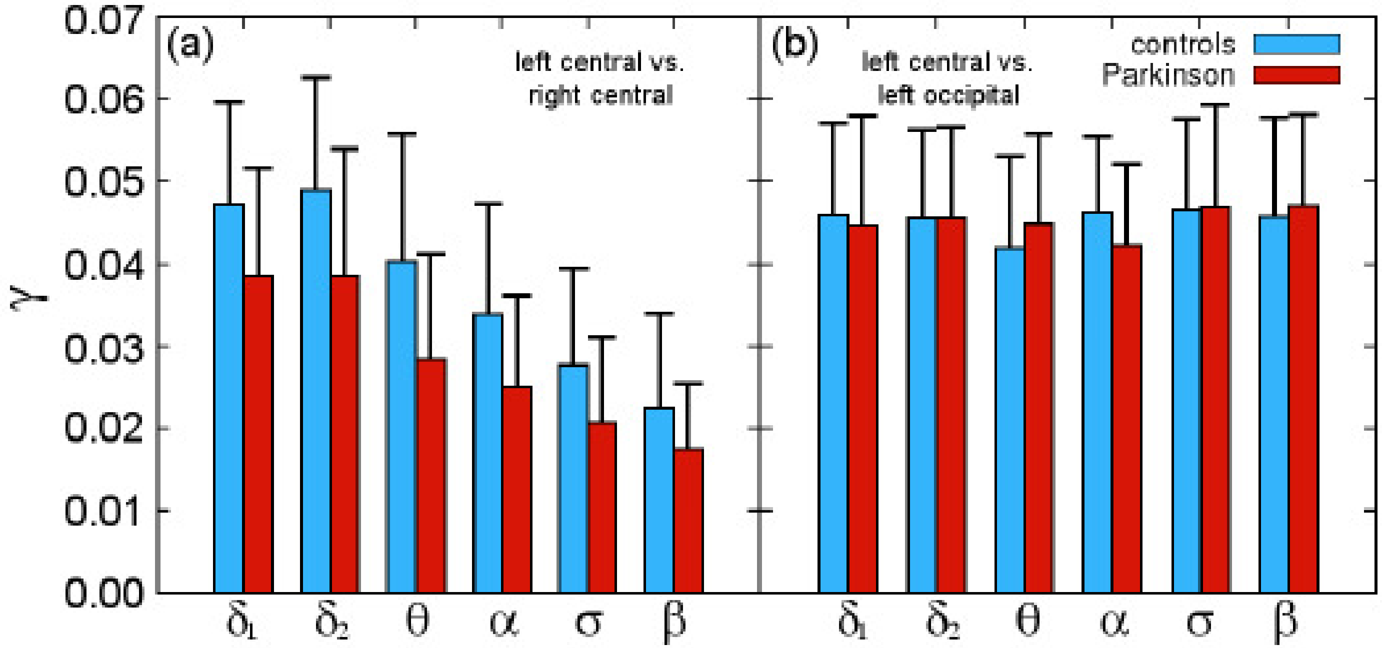
Data from EEG recordings with 32 electrodes, duration 56h. Analyse synchronization between α waves and β waves in each pair of electrodes. **Synchronization matrix → network description**.



Top: α band, bottom: θ band. Experiments: 1. alternating hand tapping, 2. hand tapping only left, 3. hand tapping only right, 4. simultaneous hand tapping, 5. sitting in rest, 6. standing in rest, 7. walking, 8. walking in place

Synchronization analysis for Parkinson patients and age-matched controls

10 Parkinson patients (average age 61 years) compared with age-matched healthy controls recorded in the same sleep laboratories.
Synchronization between left and right part of the brain is weaker in Parkinson patients in all considered bands and sleep stages.



[Stumpf et al., EPL 2010]

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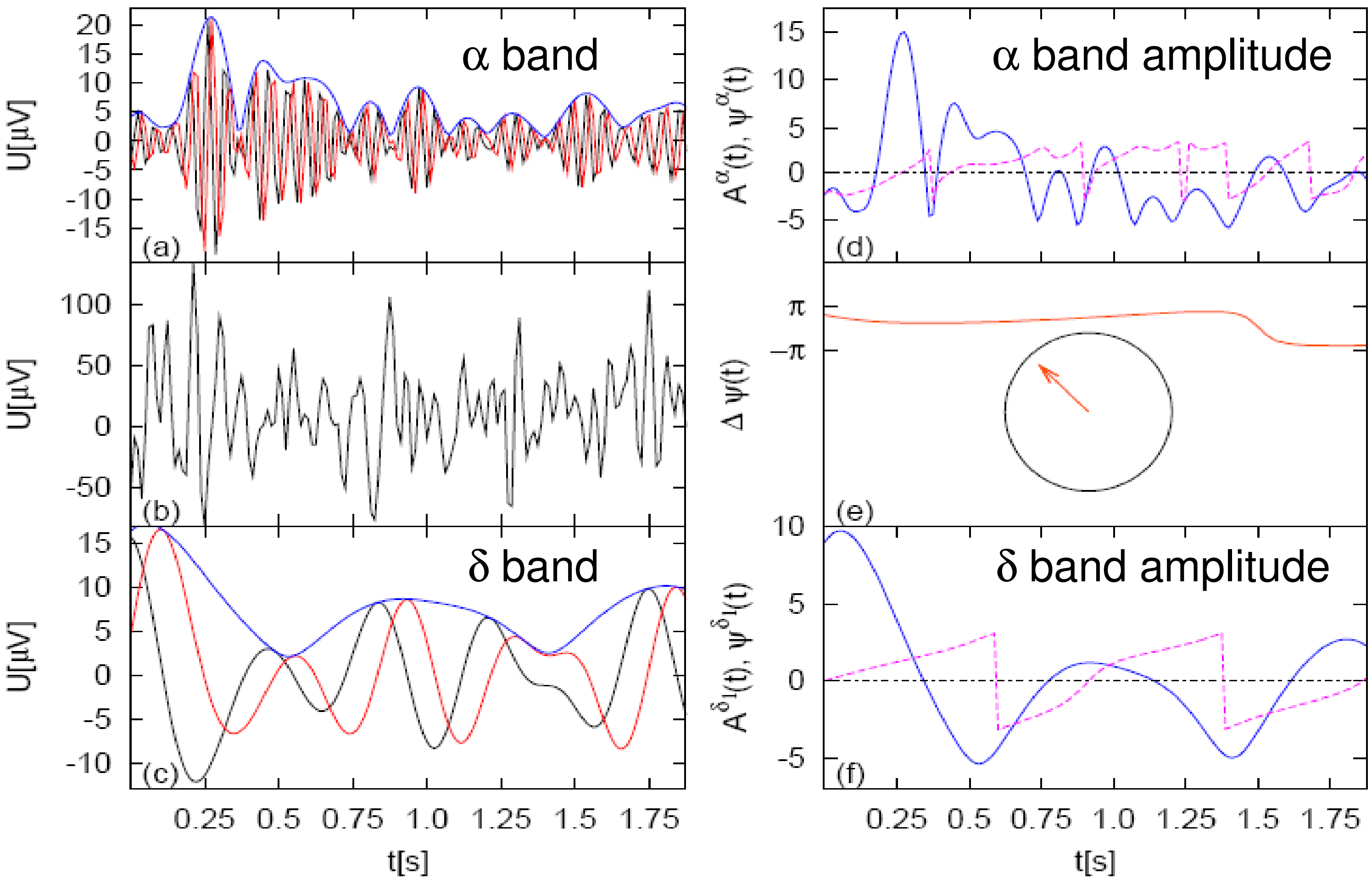
Methodology of double Hilbert transform

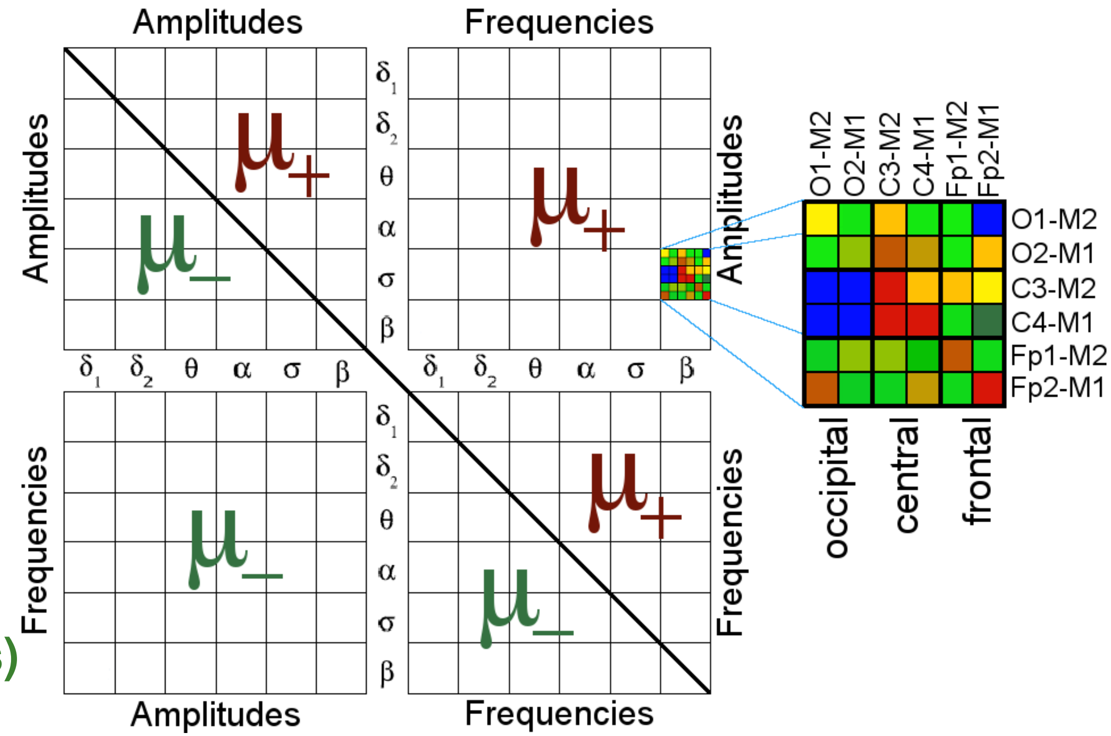


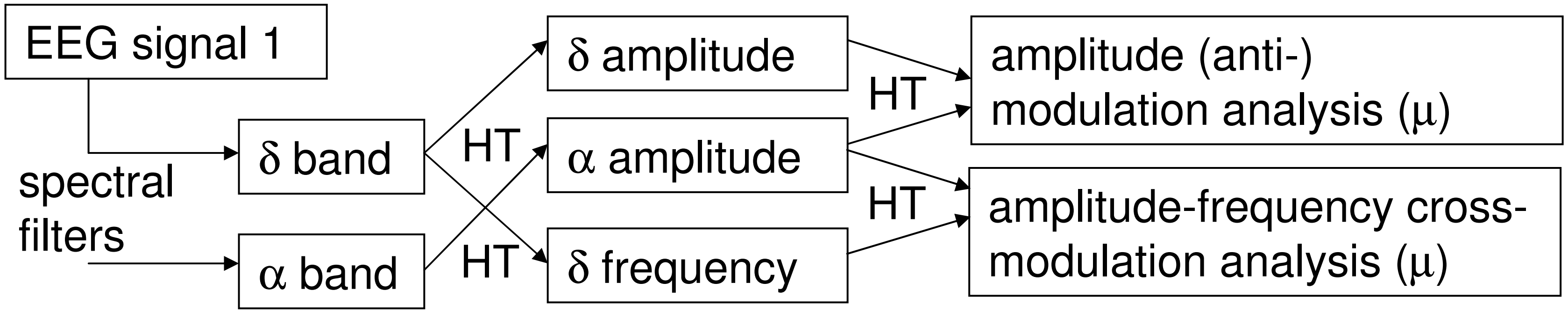
[Gans et al., PRL 2009]

Cross-modulation of amplitudes and frequencies

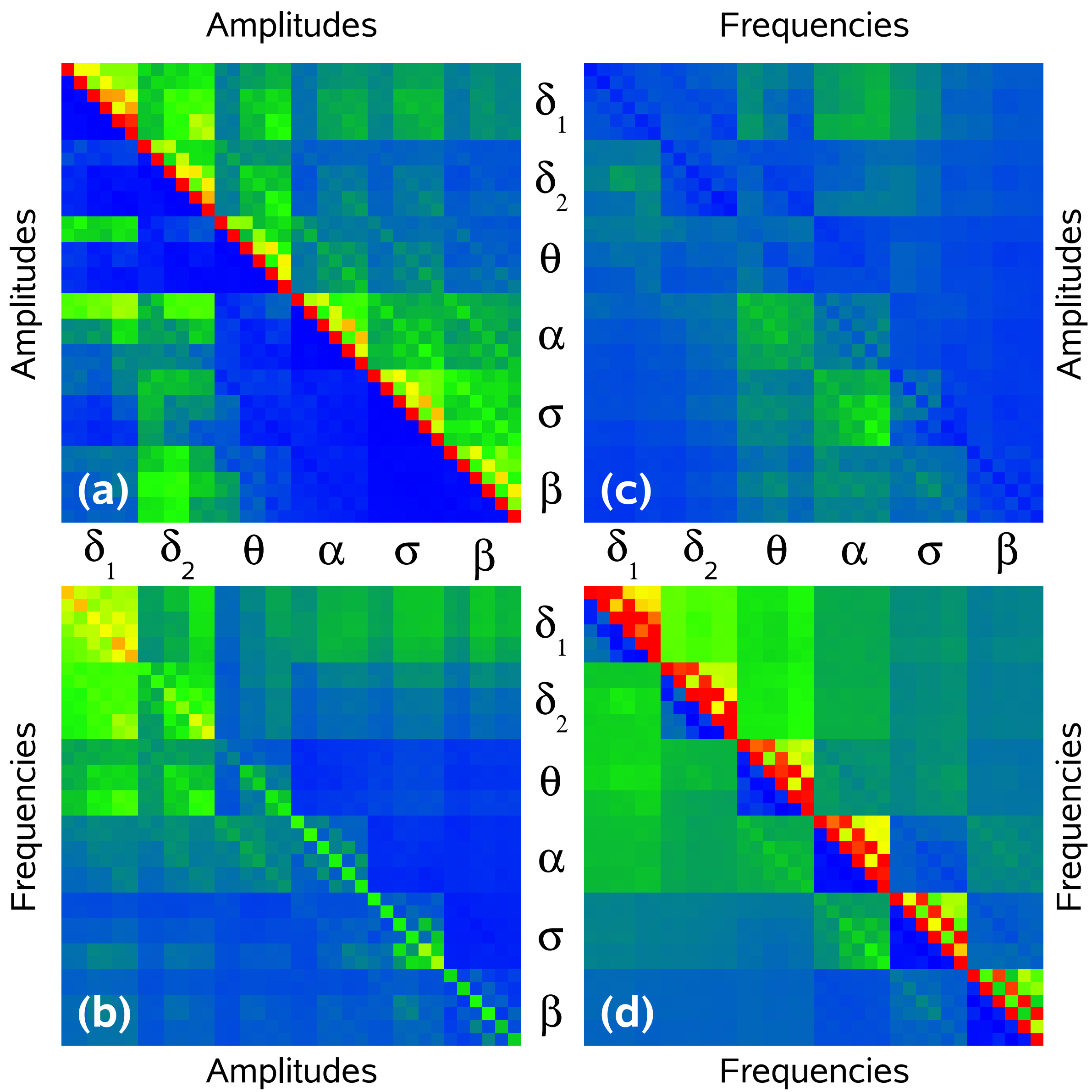
6 simultaneous EEG recordings x 6 bands
⇒ 36 amplitude signals and 36 frequency signals (nodes).

Separate consideration of positive and negative modulation ⇒ 72 x 72
= **5184 coefficients (links)**

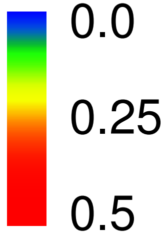




Cross-modulation of amplitudes & frequencies

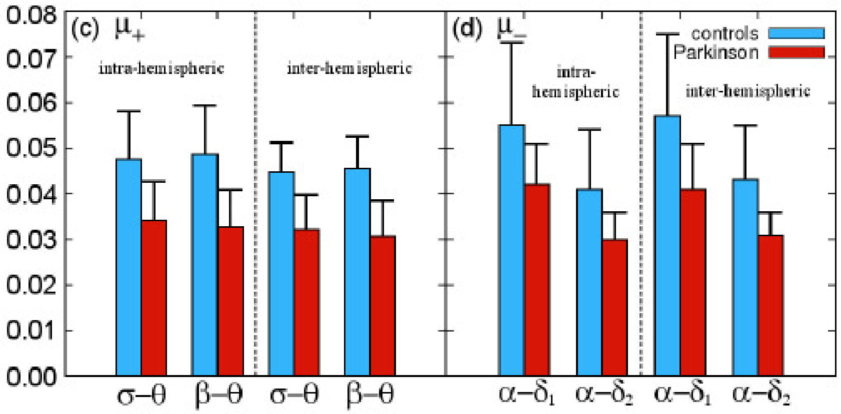


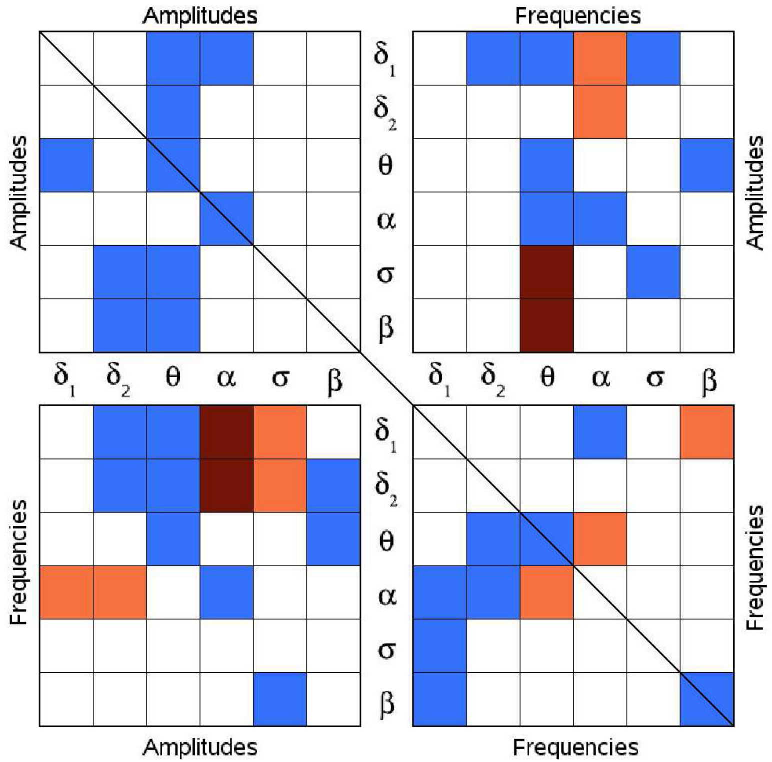
color scale for γ



[Gans et al., PRL 2009]

Significant differences between patients with PD and healthy controls





Results are rather independent of electrode position and intra-/inter-hemisphere measurements. They challenge physiologists and physicists to find a meaningful interpretation for the specific interaction decreases in patients with PD and for the complex interactions in healthy subjects.

Significance levels for differences: $p < 0.05$, $p < 0.01$, and $p < 0.001$.

[Stumpf et al., EPL 2010]

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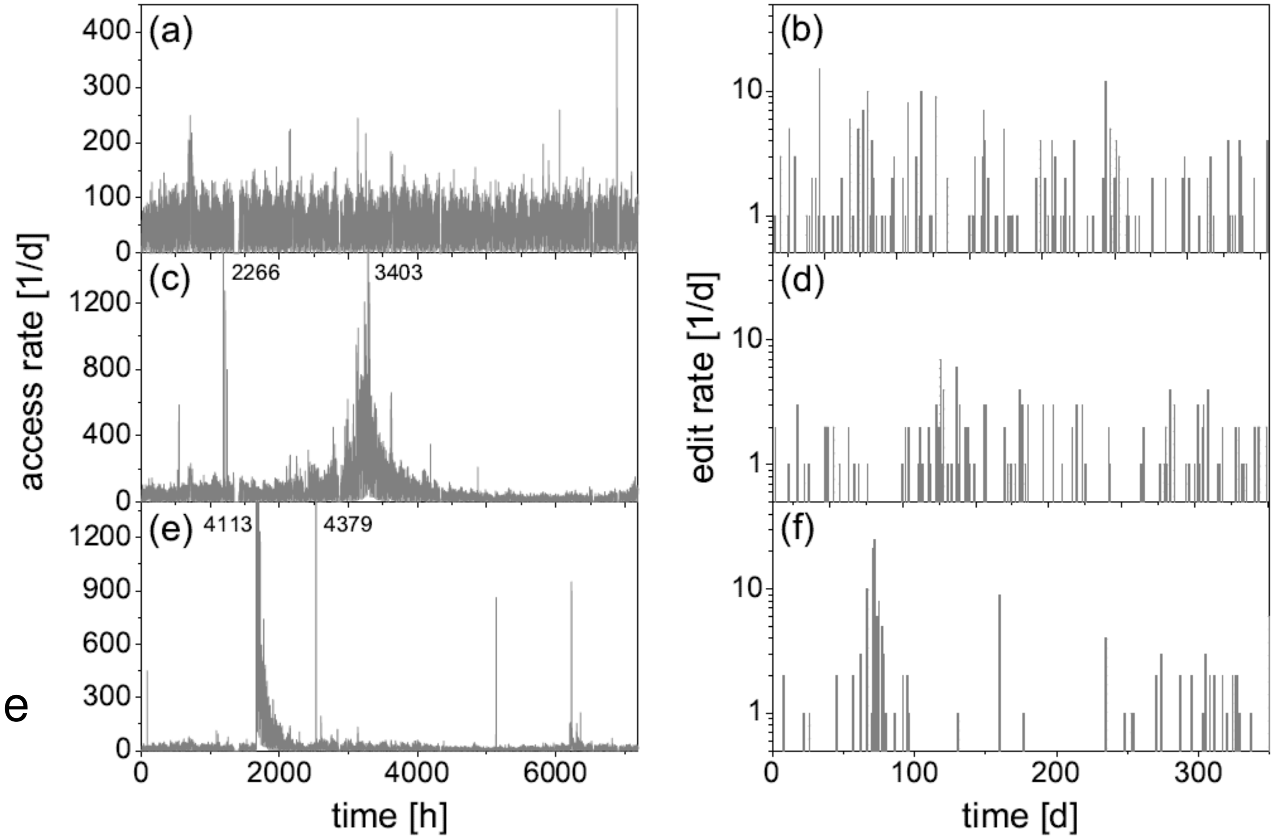
Wikipedia data base

[Kämpf et al., Physica A 2012]

Node = article (specific topic)

Available data:
1. hourly access frequency (number of article down-loads for each hour in ≈ 300 days)

2. Edit events (time stamps for all changes in the article pages)

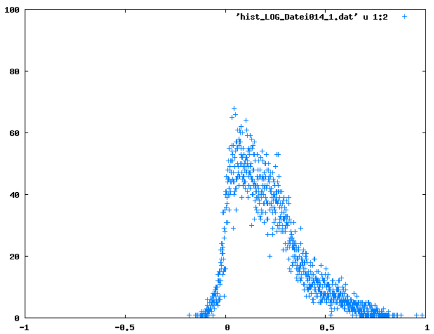


Examples of Wikipedia access time series for three articles with (a,b) stationary access rates ('Illuminati (book)'), (c,d) an endogenous burst of activity ('Heidelberg'), and (e,f) an exogenous burst of activity ('Amoklauf Erfurt'). The left parts show the complete hourly access rate time series (from January 1, 2009, till October 21, 2009; i.e. for 42 weeks = 294 days = 7056 hours). The right parts show edit-event data for the three representative articles.

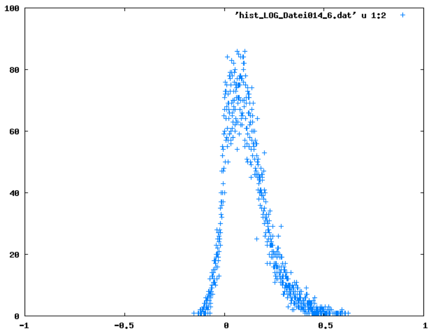
Network reconstruction I: cross-correlation

- Determine a **correlation coefficient for each pair of access time series** (measured at hourly resolution), total length of time series is 300 days.
- Calculate cross-correlation function for each day (24 h) with zero time-delay
- Determine the **median** of these values for four weeks – outlier-days with artifacts and very strong / weak correlations are automatically disregarded
- Compare with **surrogate data** obtained by considering different days in both time series several weeks apart, applying an identical procedure

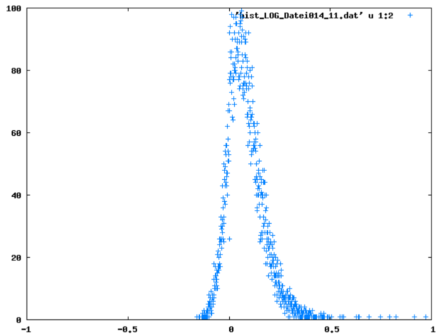
Distributions of strength of significant (reliable) links among all articles with direct incoming or outgoing link to the article "Heidelberg":



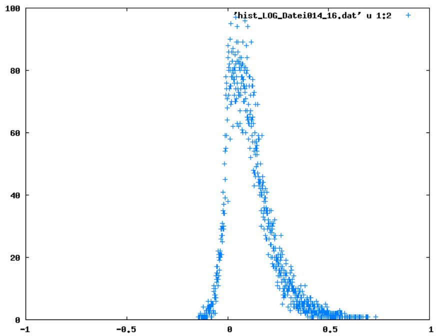
weeks 1-4



weeks 6-9



weeks 11-14

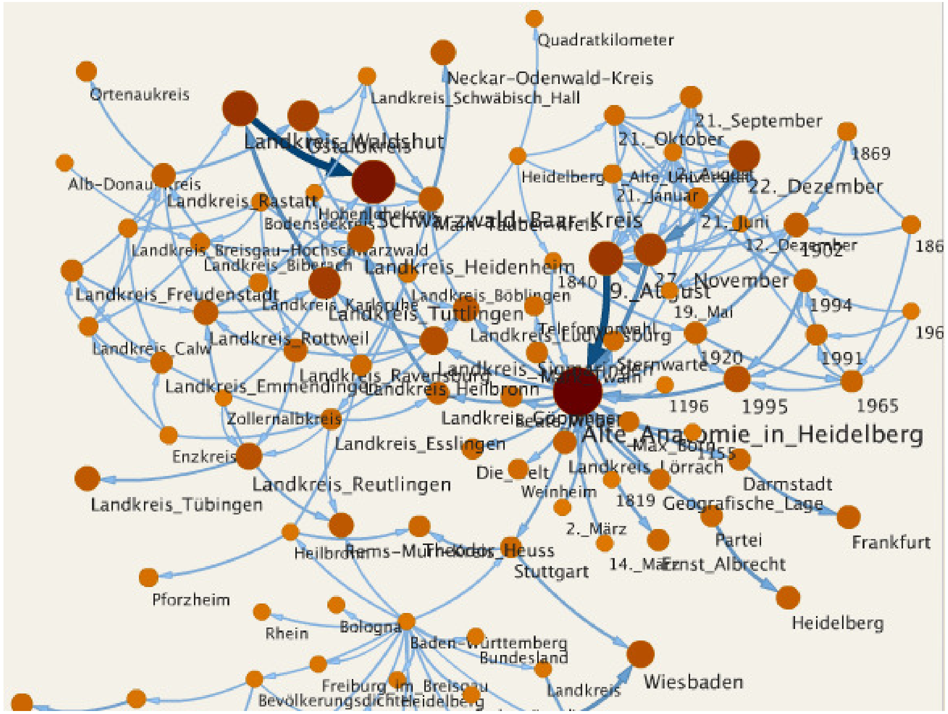


weeks 16-19

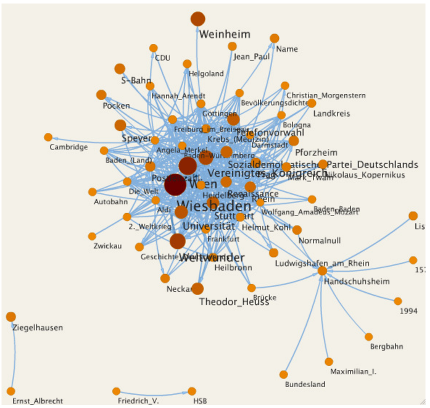
Example of recon-structed network

Select groups of 200 articles, beginning with a central node (in this example: Heidelberg). Link strengths are determined from time series with length 300 days (7200 h).

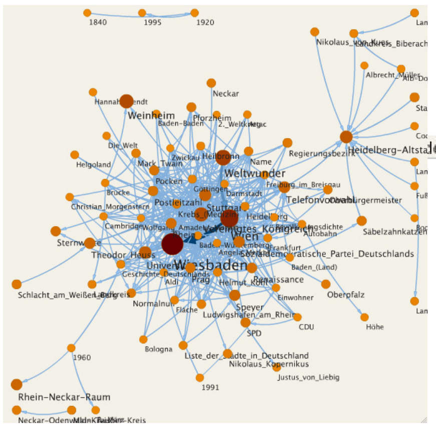
Tool: mapequation.org



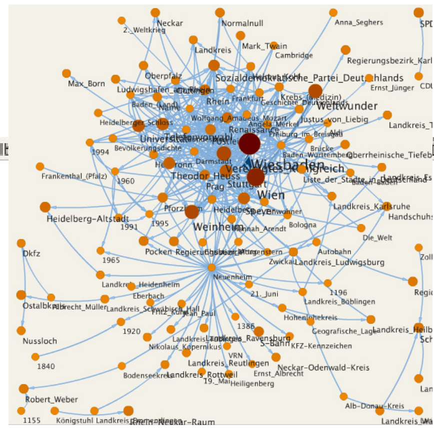
Evolution of the network:



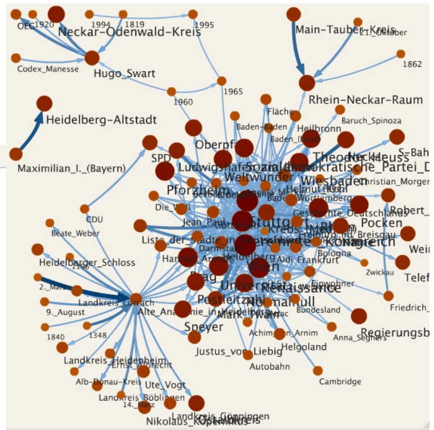
weeks 1-4



weeks 6-9



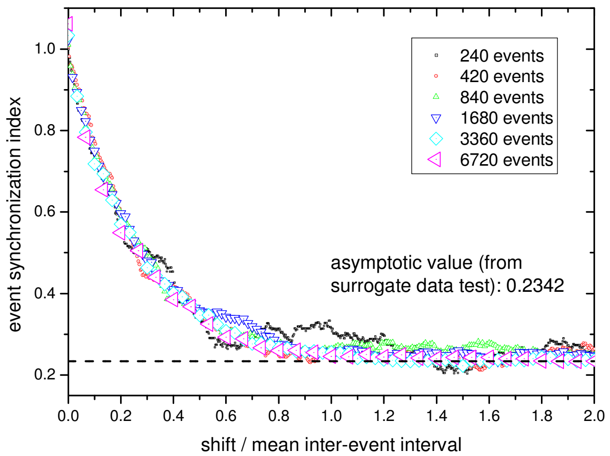
weeks 11-14



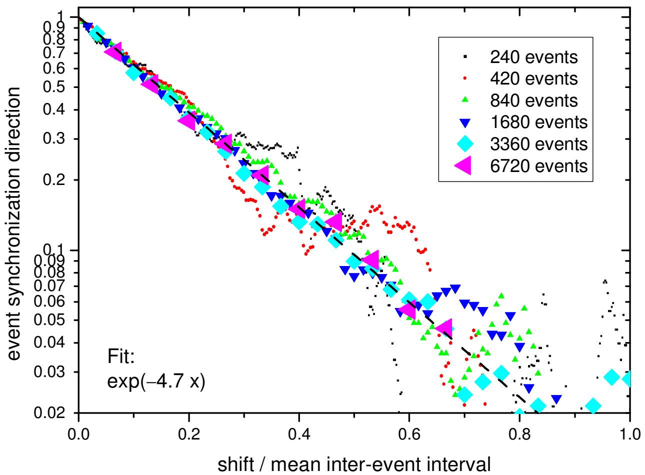
weeks 16-19

Network reconstruct. II: event synchronization

- Edit data consist of **events** – no continuous time series → methodology needed for event correlation analysis. Approach taken from climate network research [Quiroga et al., PRE 2002, Malik et al., Clim. Dyn. 2011]
- Two edit events from different articles are considered as synchronized if their temporal distance is below half of the minimum of the temporal distances of both events to the previous and following events regarding the same article. The sign of the time delay leads to a definition for the **direction of event sync.**
- **Surrogate data** tests determine significance levels depending on the total number of edit events for both considered articles.



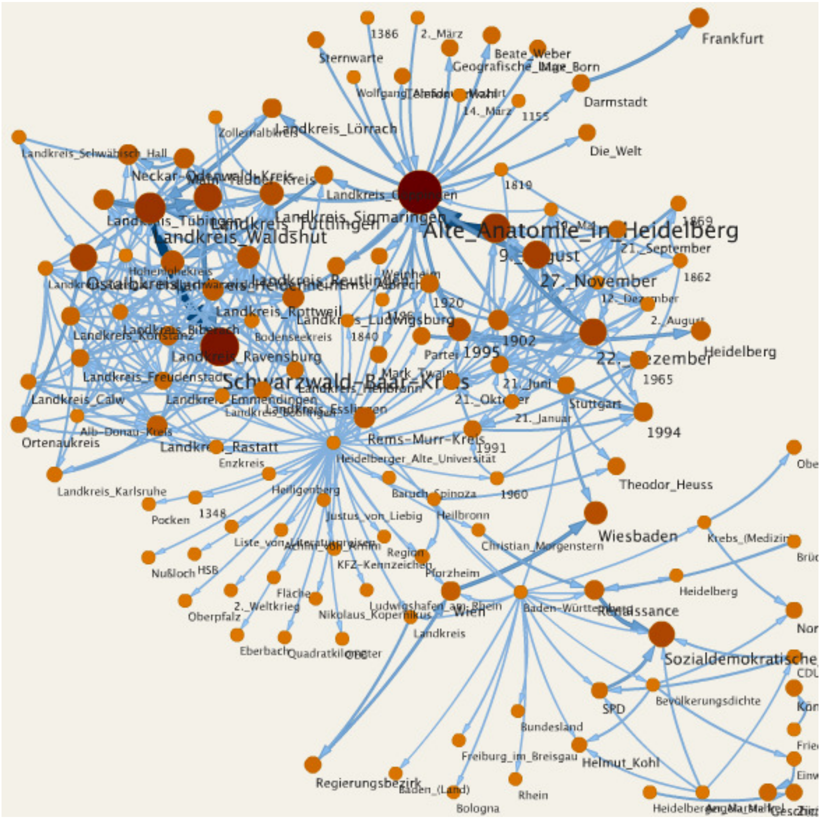
Surrogate data test: decays of event synchronization and synchronization direction with time delay of series of random events



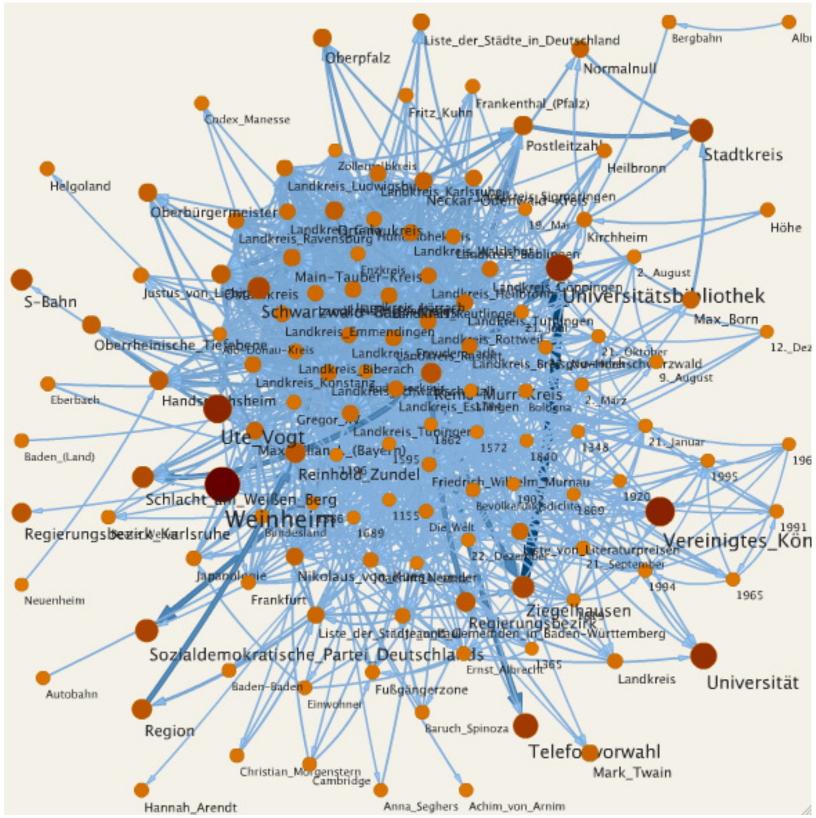
Examples of reconstructed networks

Select groups of 200 articles, beginning with a central node. The link strengths are determined from time series with length 300 days (7200 h).

Access network



Edit network



Summary

- The human organism is an integrated network where complex physiological systems continuously interact.
- Identifying and quantifying dynamical networks of diverse systems with different types of interactions is a challenge.
- Time delay stability analysis can determine changing link strengths between different kinds of time series and reconstruct the network.
- Across physiological states, the network undergoes topological transitions associated with fast reorganization of physiological interactions on time scales of a few minutes.
- We observe increased numbers of links and increased link strengths between organs and to the brain during wakefulness and light sleep compared with REM sleep and deep sleep.
- Intra-brain time-delay stability relations become more asymmetric in patients with Parkinson’s disease during freezing-of-gait episodes.

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