# Biological Rhythms and Evolving Functional Brain Networks

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Third International Summer Institute
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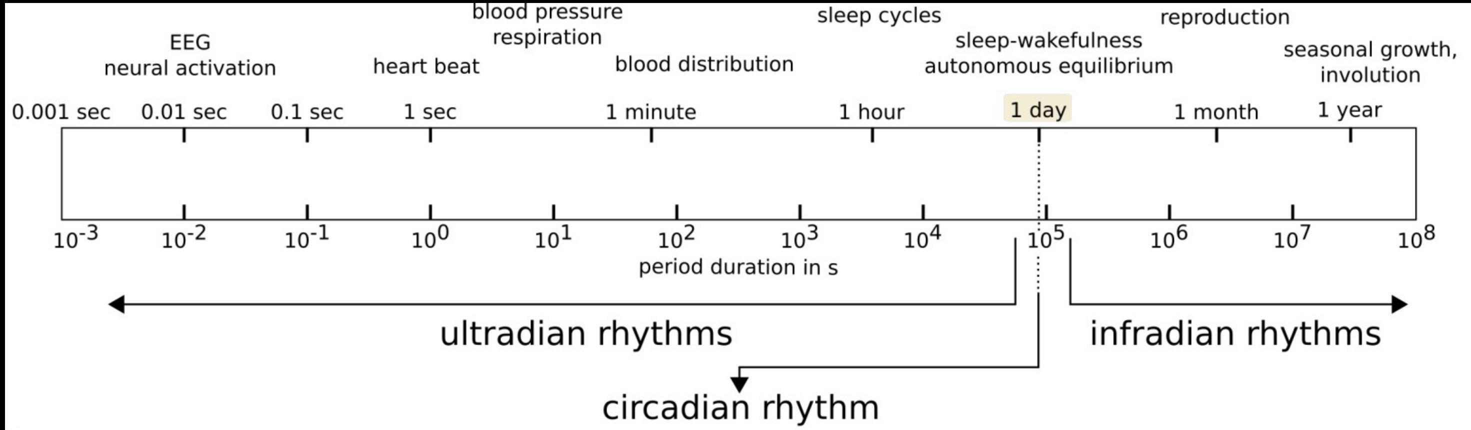
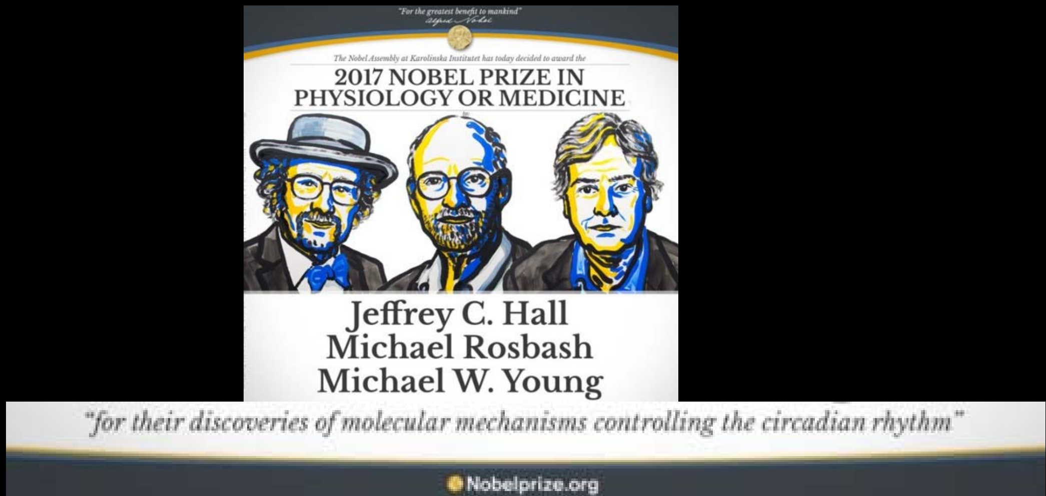
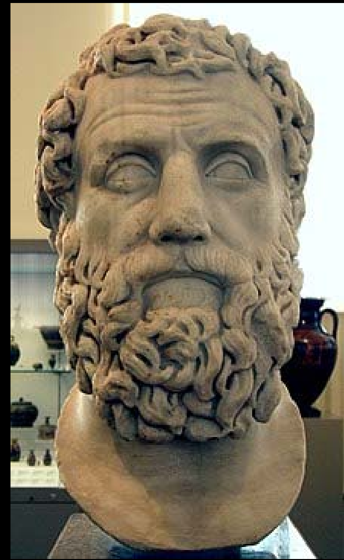
# Biological Rhythms




period lengths of biological rhythms extend over 11 orders of magnitude




θυμέ, θύμ᾽ ἀμηχάνοισι κήδεσιν κυκώμενε,
ἄνα δέ, δυσμενέων δ᾽ ἀλέξευ προσβαλὼν ἐναντίον
στέρνον, ἐν δοκοῖσιν ἐχθρῶν πλησίον κατασταθεὶς
ἀσφαλέως· καὶ μήτε νικῶν ἀμφαδὴν ἀγάλλεο
μηδὲ νικηθεὶς ἐν οἴκωι καταπεσὼν ὀδύρεο.
ἀλλὰ χαρτοῖσίν τε χαῖρε καὶ κακοῖσιν ἀσχάλα
μὴ λίην· γίνωσκε δ᾽ οἷος ῥυσμὸς ἀνθρώπους ἔχει



*Archilochos*
*(680 – 645 BC)*

My Soul, my Soul, all disturbed by sorrows inconsolable,
Bear up, hold out, meet front-on the many foes that rush on you
Now from this side and now that, enduring all such strife up close,
Never wavering; and should you win, don't openly exult,
Nor, defeated, throw yourself lamenting in a heap at home,
But delight in things that are delightful and, in hard times, grieve
Not too much – appreciate the rhythm that controls men's lives.

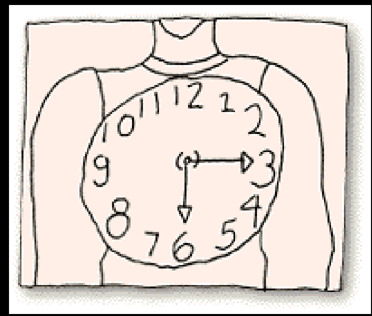
other translation:
*recognize what rhythm governs man*

*e.g. F. Halberg Chronobiology. Annu. Rev. Physiol. 31, 675, 1969.; J. Aschoff. Biological Rhythms. 1981*

# Biological Rhythms

- ultradian (90 min.)
- **circadian** (24 h.)
- circaseptan (7 d.)
- **infradian** (28-32 d.)
- circannual (1 yr.)
- 7-years

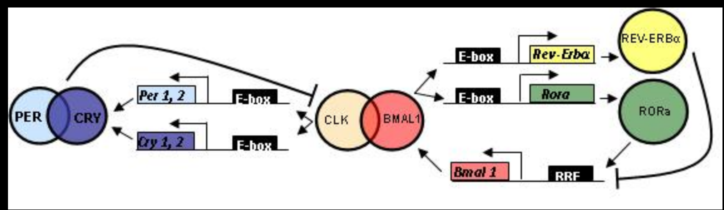





metabolism, food intake, sexuality, hormones, sleep, jet-lag, temper, ...

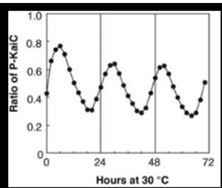
clock genes

synchronization

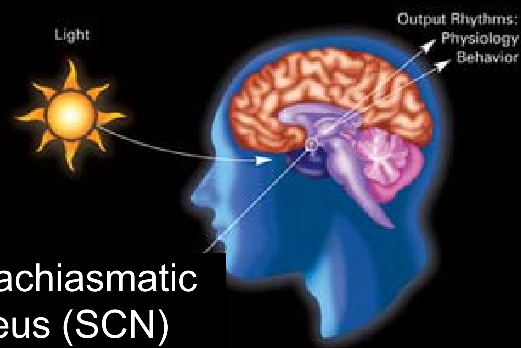



*zeitgebers* (Juergen Aschoff)

light, atmospheric conditions, medication, temperature, social interactions, exercise, eating/drinking patterns



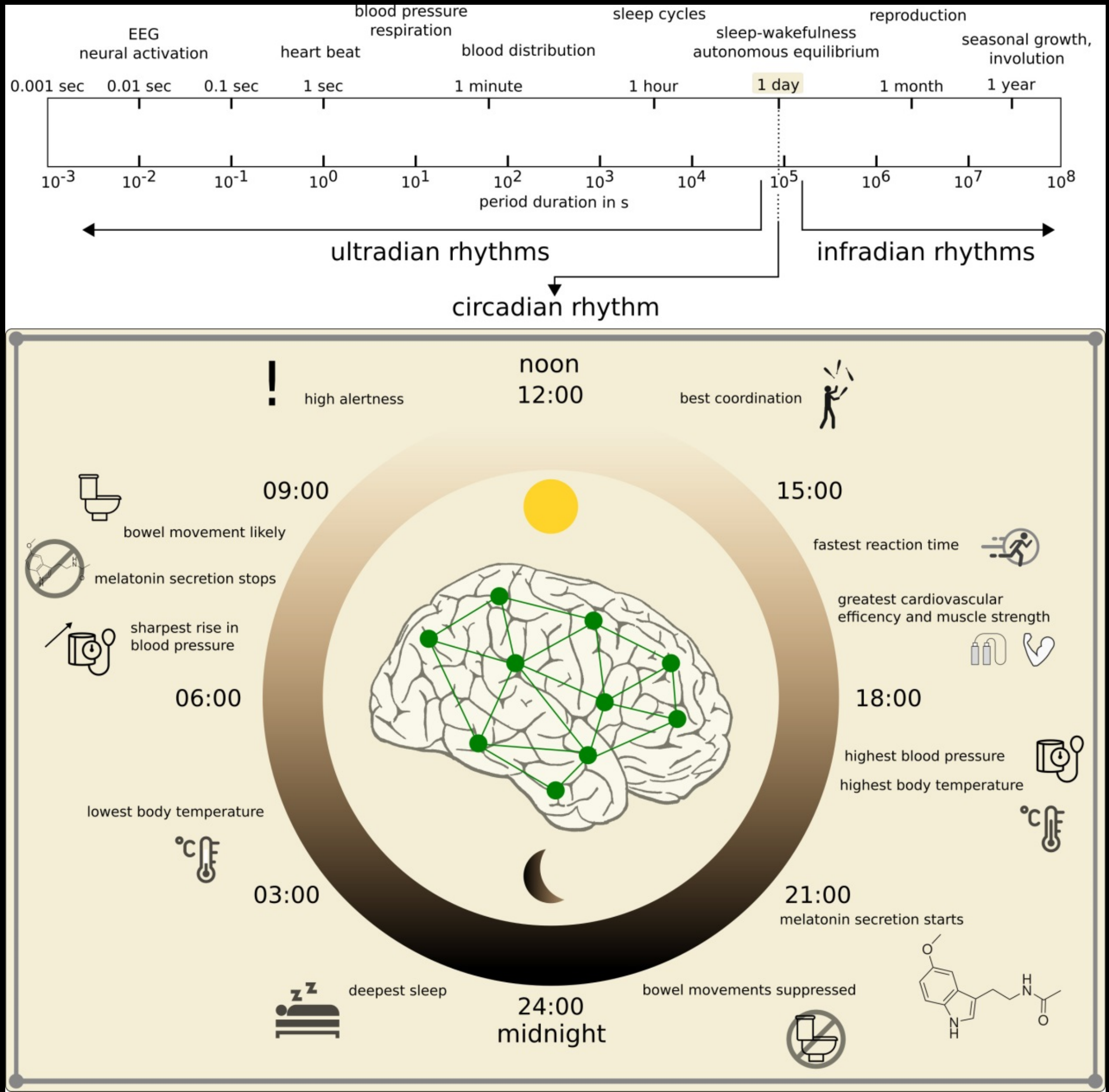

Kai protein phosphorilation cycle in cyanobacteria




suprachiasmatic nucleus (SCN)

*"almost every cell in the body contains a circadian clock"*
*(JA Mohawk, CB Green, JS Takahashi JS Central and peripheral circadian clocks in mammals". Annu. Rev. Neurosci.* ***35****: 445–62, 2013)*
*"the Kai transcription-translation cycle may be similar to that of a pendulum and an escapement mechanism that sustains the pendulum oscillation"*
*(M Nakajima et al., Science 2005)*

# Biological Rhythms and Brain Dynamics



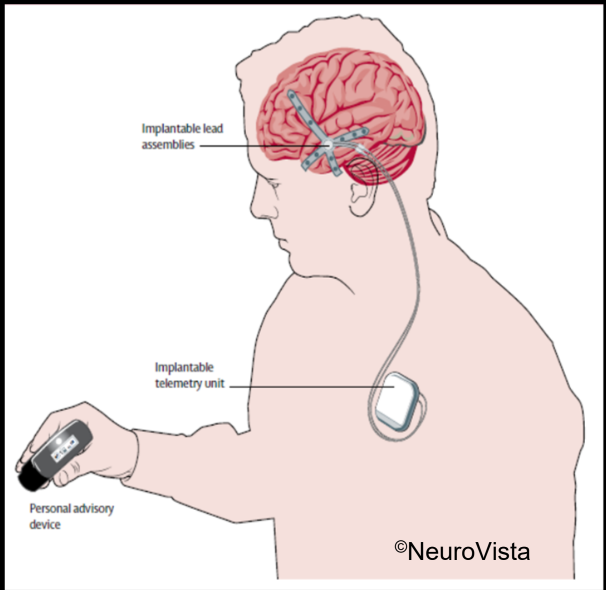

impact of circadian and various ultradian rhythms known for > 50 years

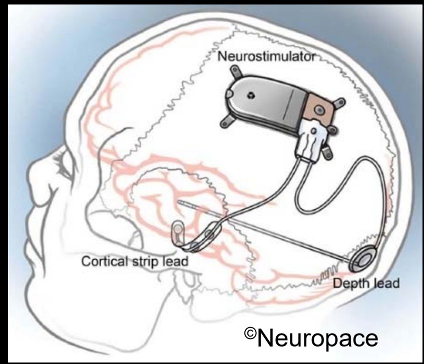
mostly EEG studies

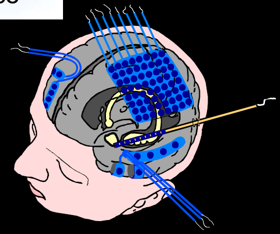
limitations:
- visual analyses
- spectral properties of EEG (modulation of classical frequency bands)
- continuous recordings rare
- limited spatial sampling

*e.g. J.N. Mills, Human Circadian Rhythms. Physiol. Rev. 46, 128–171 (1966);*
*N. Kleitman, Basic Rest-Activity Cycle-22 Years Later. Sleep 5, 311–317, 1982*

# Long-Term Recordings of Brain Dynamics



- continuous recordings (days – years)
- invasiveness (patients only)
- spatial resolution
- technical limitations (data size, storage, handling)

NeuroTec & Wyss Center

NeuroTec & CSEM & ESA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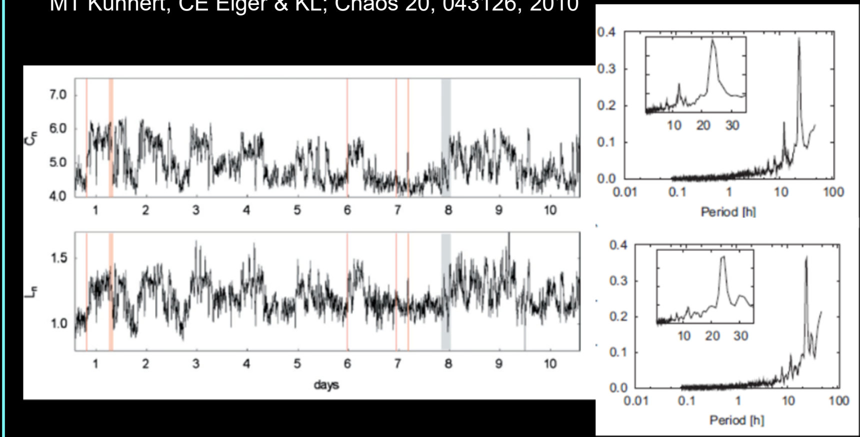
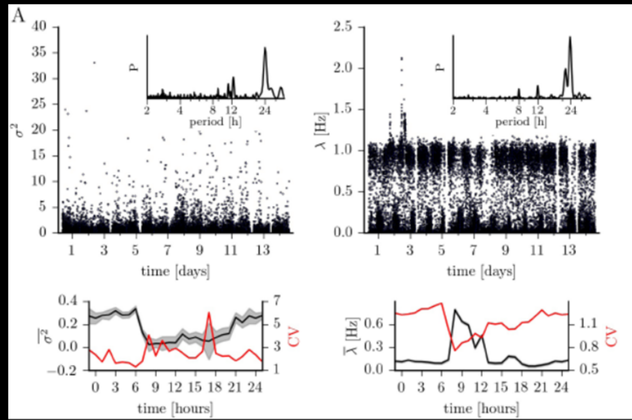
EEG and OPM-MEG

# Impact of Biological Rhythms

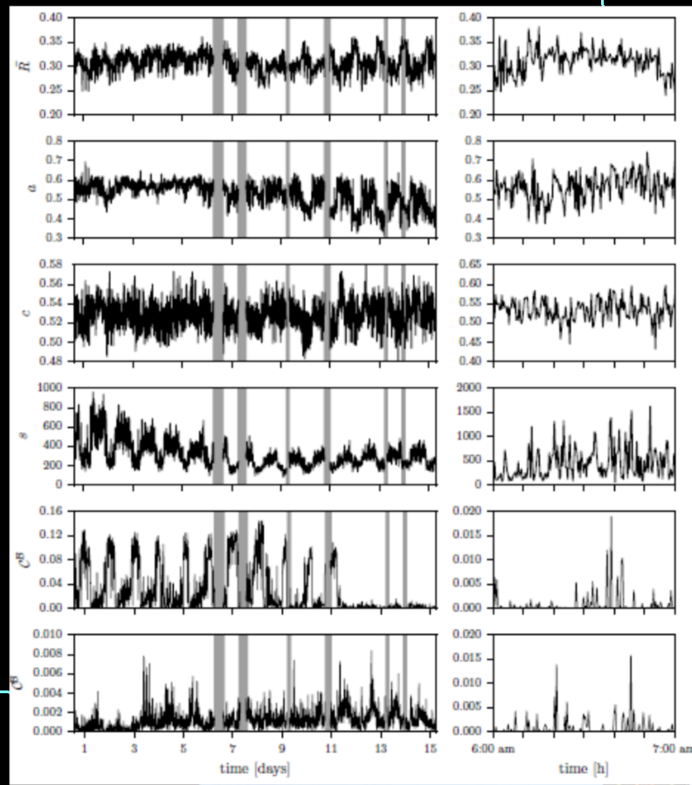
MT Kuhnert, CE Elger & KL; Chaos 20, 043126, 2010



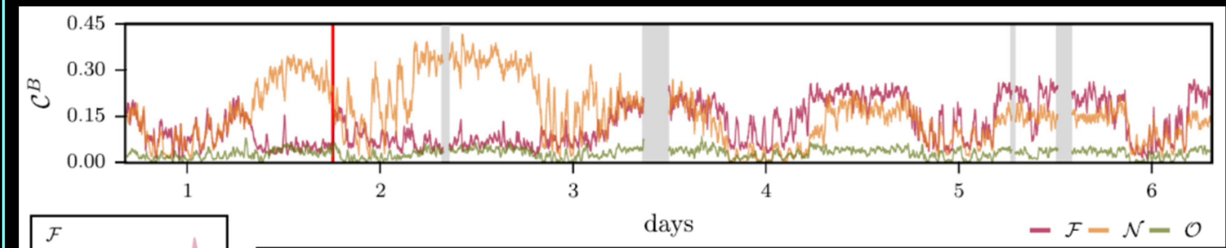

JG Kurth, T Rings & KL; Entropy 23, 309, 2021

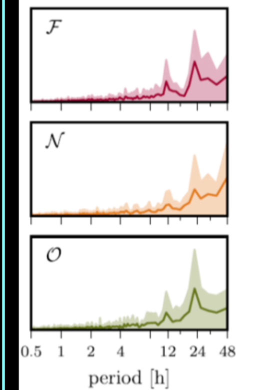



KL et al; EPJ Nonlin Biomed Phys, 5, 2, 2017

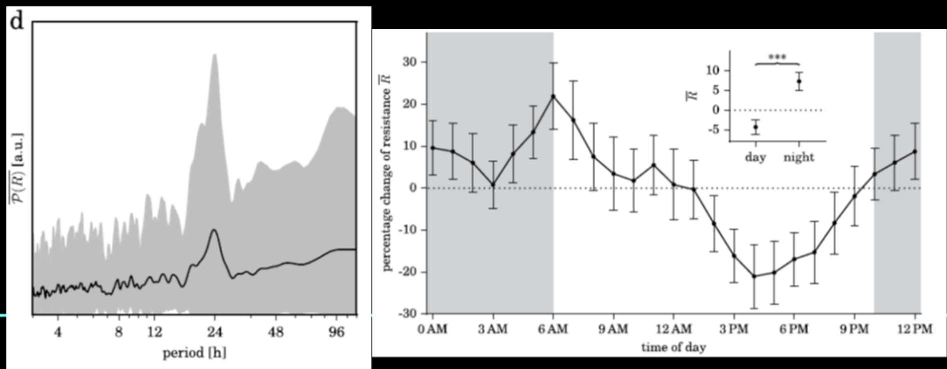



C Geier & KL; Chaos 27, 043112, 2017




T Rings et al; Sci. Rep. 9, 1744, 2019




KL et al., ***Front. Netw. Physiol. 2021***

# Biological Rhythms and Brain Network Dynamics

impact of biological rhythms on …

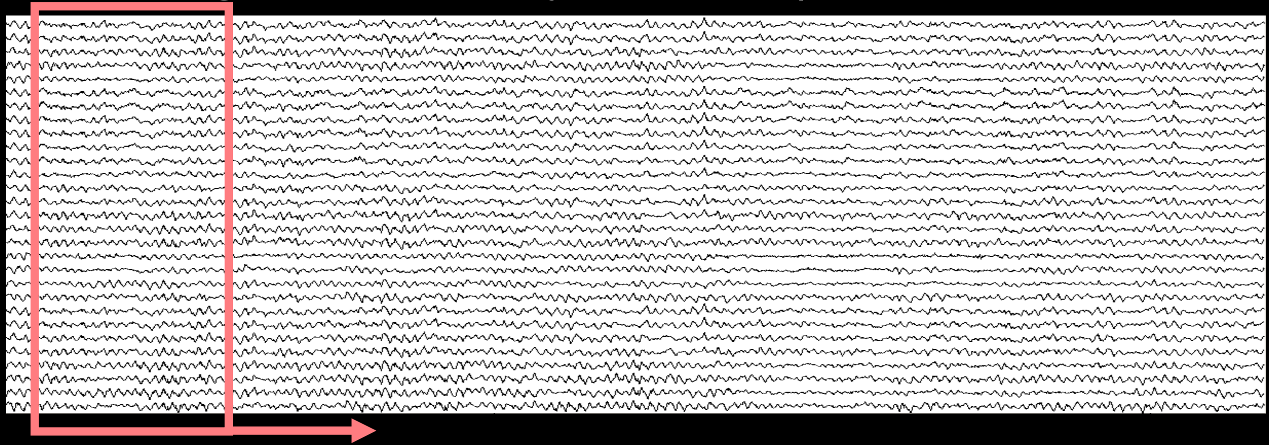
… dynamics of individual brain regions
(vertices → univariate time series analyses)

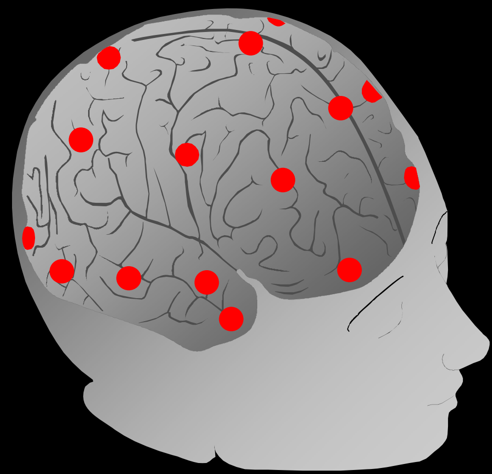
… dynamics of interactions between brain regions
(edges → bivariate time series analyses)

… dynamics of evolving functional brain networks
(network properties, from global to local)

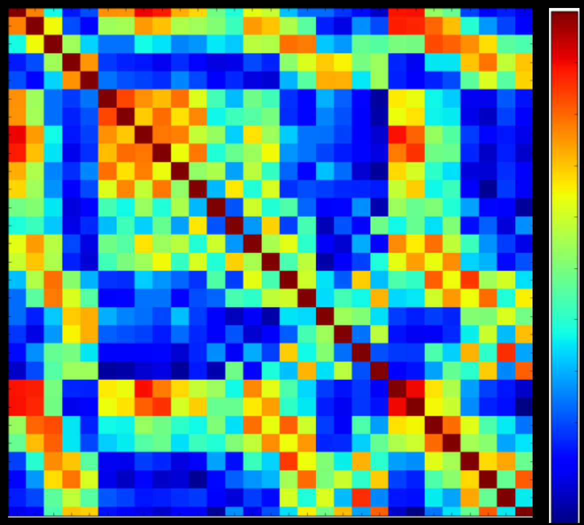
# Functional Brain Networks

recordings of brain dynamics (EEG, MEG, fMRI, …)





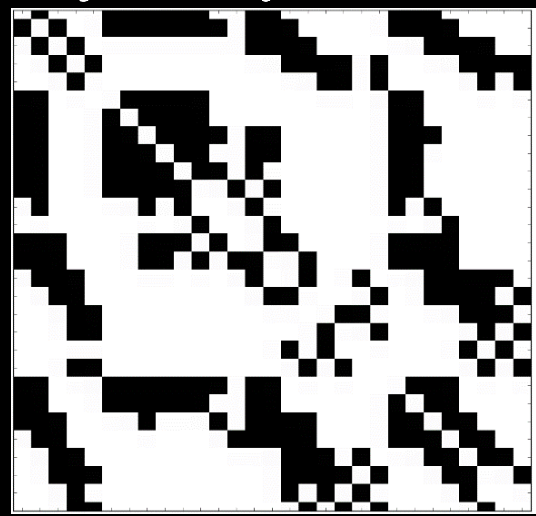
interaction matrix ***I***




***A*** = *f(**I**)*

- thresholding
- significance testing
- …

adjacency matrix ***A***




*e.g. Bullmore & Sporns, Nat. Rev. Neurosci. 10, 186, 2009;  KL et al., Physica D  267, 7, 2014*

# Characterizing Vertex Dynamics

statistical properties (mean, variance, skewness, kurtosis, …)

linear time series analysis techniques
(power spectrum-derived characteristics, autocorrelation, …)

nonlinear time series analysis techniques
(dimensions, entropies, Lyapunov exponents, …)

analysis techniques from statistical physics
(drift, diffusion, higher-order Kramers-Moyal coefficients, …)

…

*e.g. Box & Jenkins Time Series Analysis: Forecasting and Control., 1976; Boashash, Time Frequency Signal Analysis And Processing (2003);*
*Kantz & Schreiber, Nonlinear Time Series Analysis, 2003;*
*Tabar, Analysis and Data-Based Reconstruction of Complex Nonlinear Dynamical Systems: Using the Methods of Stochastic Processes, 2019*

# Characterizing Edge Dynamics

linear time series analysis techniques
(cross-correlation, coherence, …)

nonlinear time series analysis techniques
(synchronization-based techniques,
information-theory-based techniques, …)

analysis techniques from statistical physics
(higher-order Kramers-Moyal coefficients, …)

…

*e.g. Lütkepohl, Introduction to Multiple Time Series Analysis (1993);*
*Pikovsky, Rosenblum, Kurths, Synchronization - A universal concept in nonlinear sciences (2001);*
*L Rydin Gorjao, J Heysel, KL, MRR Tabar. Analysis and data-driven reconstruction of bivariate jump-diffusion processes. Phys Rev E 2019*

# Characterizing Functional Brain Networks (II)

clustering coefficient, average shortest path length, assortativity, synchronisability, …

communities, motifs, modularity

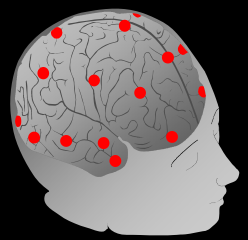
degree, degree distribution, centralities for vertices and edges

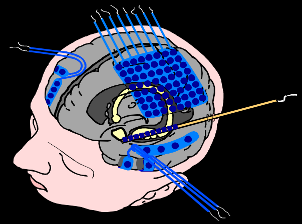
…

*e.g. Bullmore & Sporns, Nat. Rev. Neurosci. 10, 186, 2009; Newman, Networks: An Introduction. OUP. 2010;*
*KL et al., Physica D 267, 7, 2014*

# Long-Term Recordings of Brain Dynamics

exemplary data sets





**A**
scalp EEG
male subject, 81 y,
no epilepsy
recording duration: 7 d
19 sensors
(10-20-system)
sampling rate: 256 Hz

**B**
invasive EEG
male subject, 55 y,
epilepsy
recording duration: 14 d
88 sensors
(frontal and temporal)
sampling rate: 250 Hz

*KL et al.*, ***Front. Netw. Physiol. 2021***

# Long-Term Recordings of Brain Dynamics

steps of analysis

freq. band: 1 - 45 Hz; moving window (20 s → approx. stationary)

***node dynamics***:
statistical moments → *Gaussian distributed?*
variance ($\sigma$), skewness (*s*), kurtosis (*k*)

***edge dynamics***:
(non-redundant) pairwise ***strength of interactions***
- mean phase coherence (*R*)
- correlation ($\rho$) → *functional connectivity*

***network characteristics***:
clustering coefficient and centrality (nodes and edges)

Lomb-Scargle periodograms of resulting time series

*KL et al.*, ***Front. Netw. Physiol. 2021***

# Impact of Biological Rhythms – Results I

**scalp EEG (A)**

- periods:
  dominant: 24 h
  (+ 12, 8, 6, 4 h, 90 min, 60 min)

- location:
  variable, mostly fronto-central

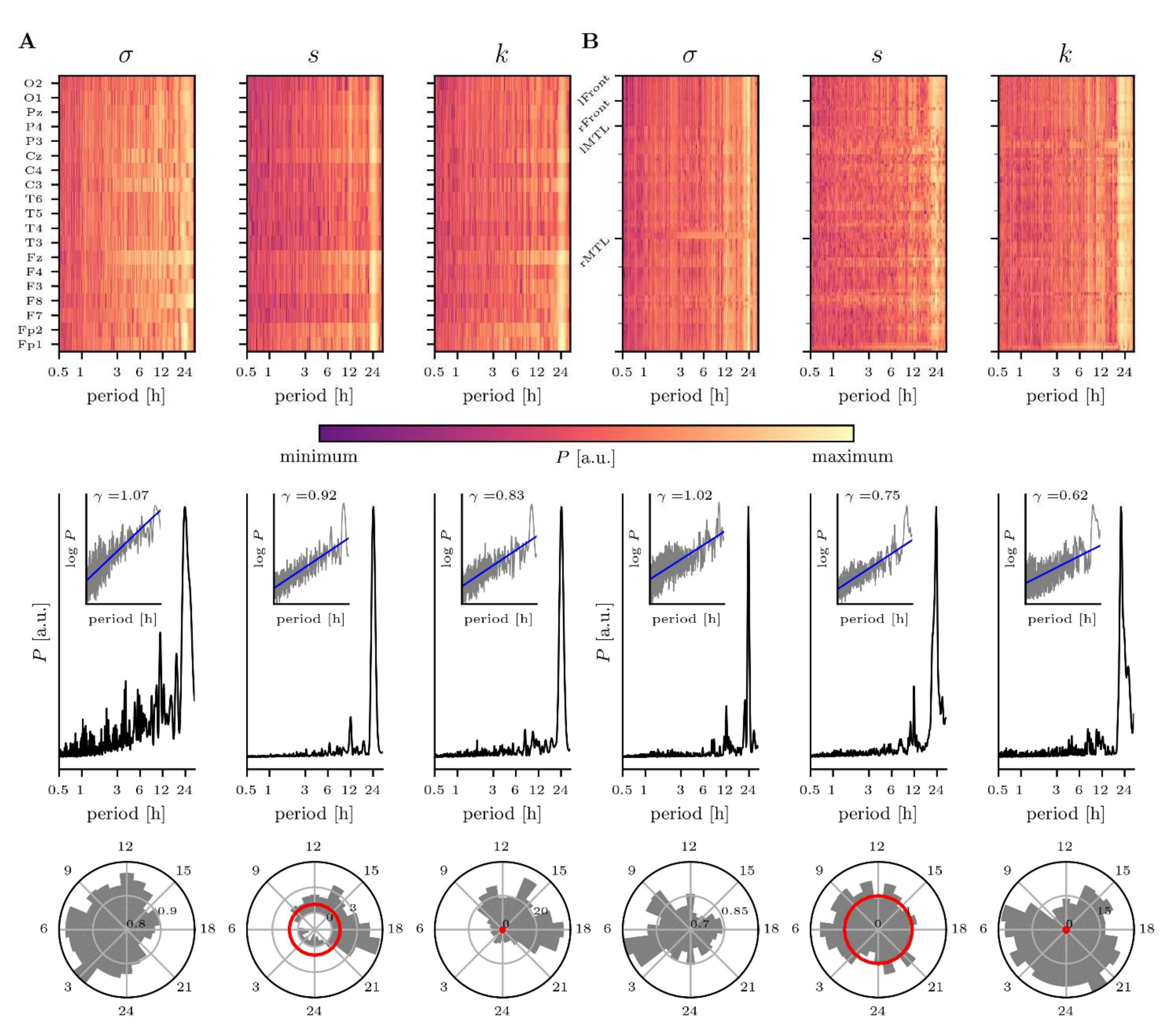
- daytime – strong deviation from Gaussianity

**iEEG (B)**

- periods:
  dominant: 24 h
  (+ 12, 8, 4 h)

- location:
  variable

- daytime and nighttime strong deviation from Gaussianity




KL et al., ***Front. Netw. Physiol.* 2021**

# Impact of Biological Rhythms – Results II

**scalp EEG (A)**

- periods:
  dominant: 24 h + triplets (17-19 h + 27-30 h)
  (+ 3.5 and 12 h)

- different impact on short- and long-range connections

- global synchrony weaker during nighttime

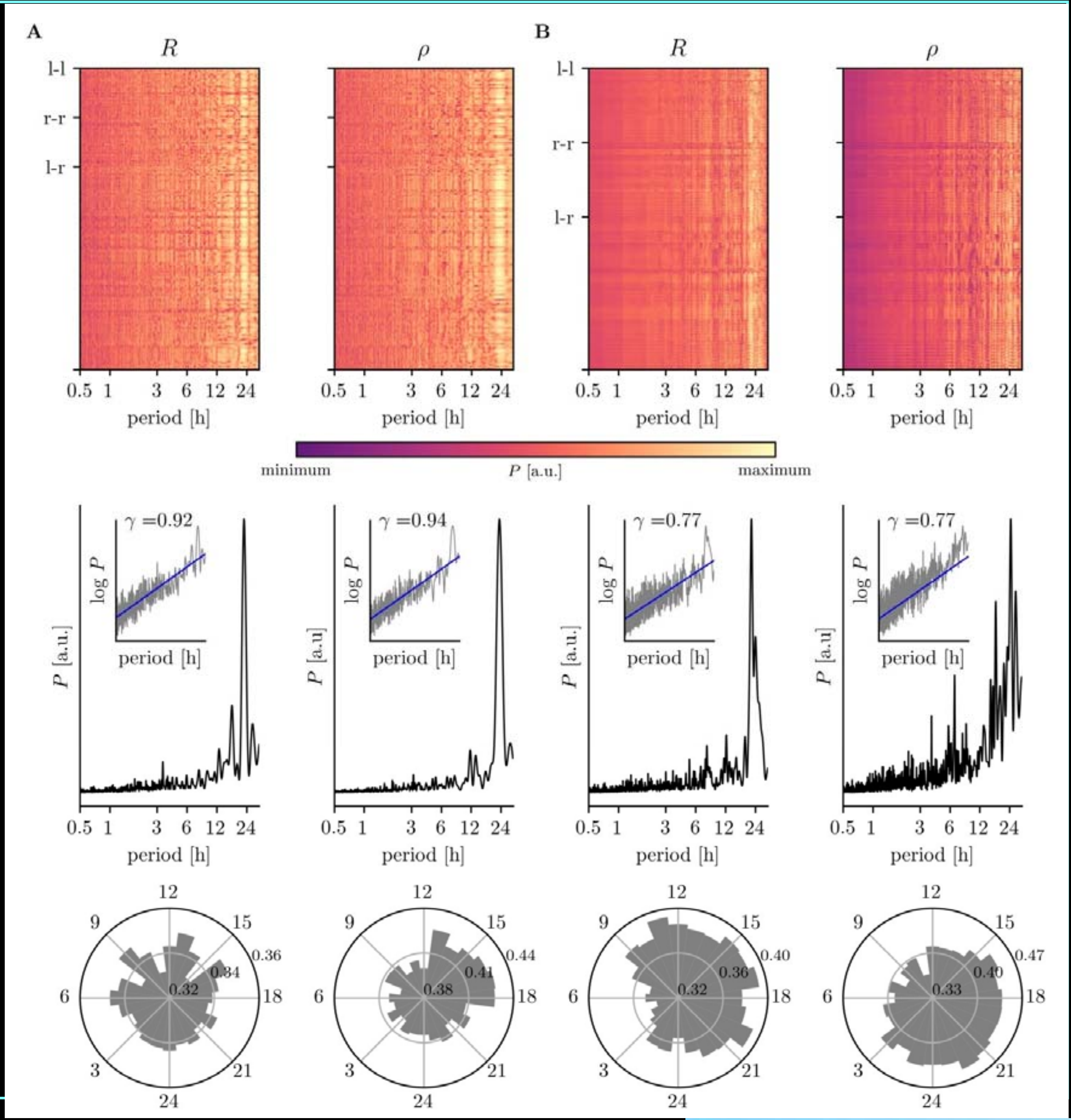
**iEEG (B)**

- periods:
  dominant: 24 h + triplets (17-19 h + 27-30 h)
  (+ 5+8 h (*R*), 4+7 h (ρ)

- different impact on short- and long-range connections

- global synchrony weaker during nighttime

- diurnal cycle: *R* 3-6 h ahead of ρ !




KL et al., ***Front. Netw. Physiol. 2021***

# Impact of Biological Rhythms – Results III

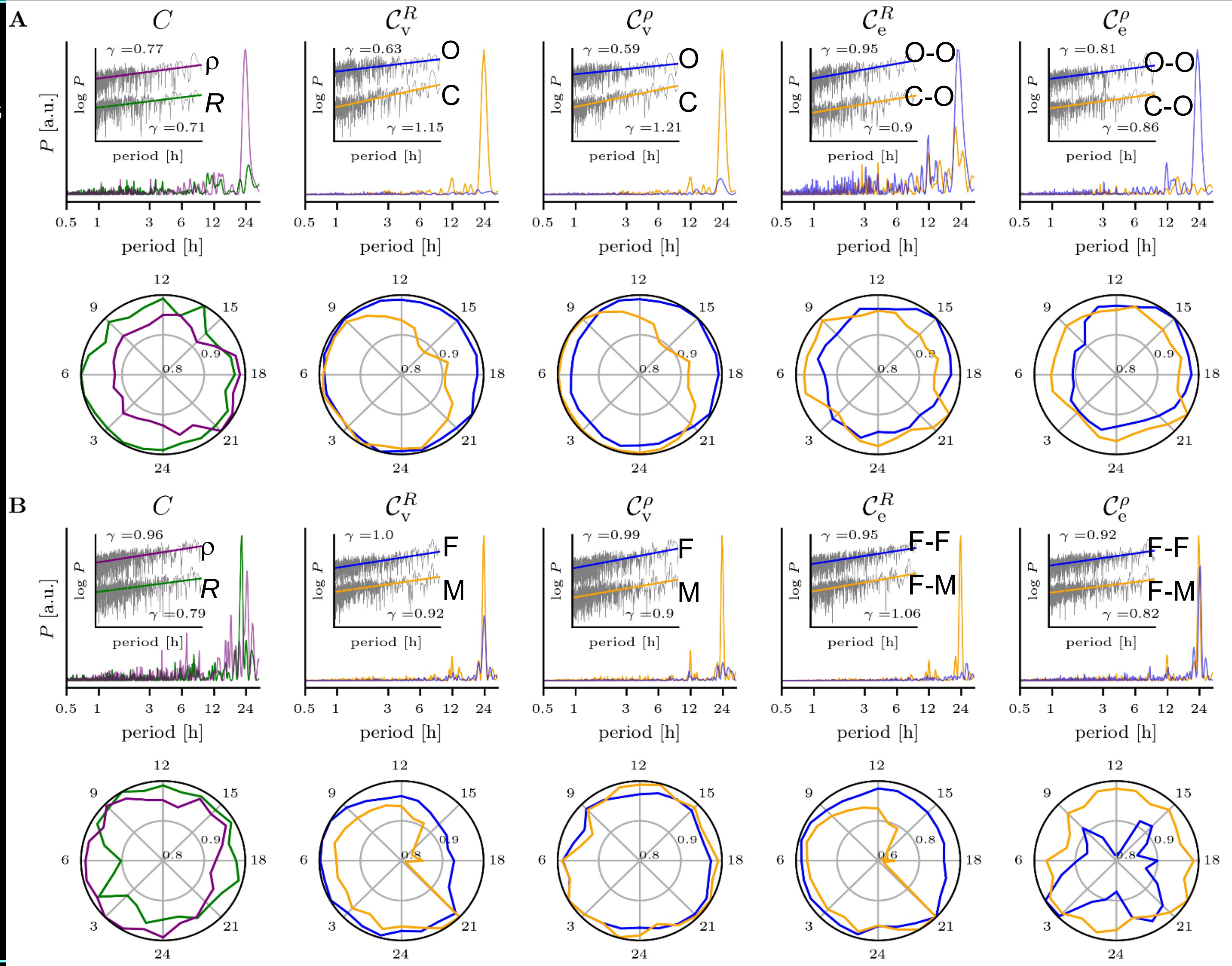
**scalp EEG (A) and iEEG (B)**

different impact of biological rhythms dependent on network construction (*R* or ρ)

- periods (scalp EEG): 24 h + triplets (21-28 h)

- periods (iEEG): 24 h + ultradian rhythms triplets and quartets

centralities:
nodes:
scalp EEG: central (C) und occipital (O)
iEEG: left frontal (F) and right mesial (M)




*KL et al.*, ***Front. Netw. Physiol. 2021***

*see Poster by Timo Bröhl*

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# Summary: Impact of Biological Rhythms

suitability and reliability of analysis techniques that assume Gaussian distributed data

reproducibility of studies on

- (patho-)physiological synchronization
- *functional connectivity* (EEG/MEG/fMRI)
- functional brain networks (EEG/MEG/fMRI)

interpretability of findings from repeated measurements/long-term recordings

impact of infradian rhythms (age-dependent changes) largely unknown

KL et al., ***Front. Netw. Physiol. 2021***