# ANALYSING THE SYNCHRONIZATION OF TIME SERIES – I

*Correlation, cross-correlation, cross-spectral analysis, coherence, imaginary coherence, (weighted) phase lag index, functional and effective connectivity*


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INSTITUTE OF BEHAVIOURAL SCIENCES


*Methodology of the electrophysiological analysis of sleep-wake states*

*15. 11. 2022.*

Oktatás, kutatás, gyógyítás: 250 éve az egészség szolgálatában

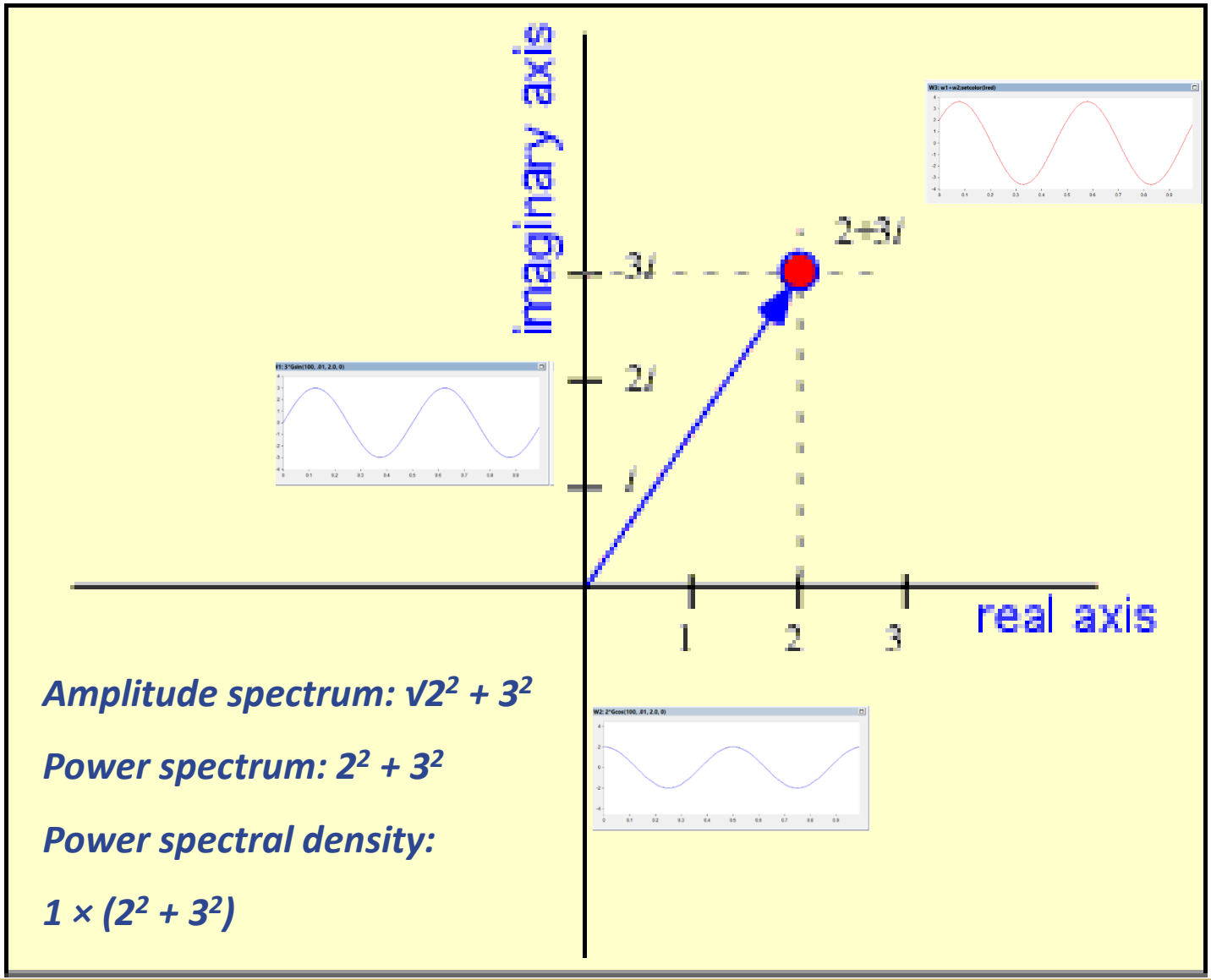

Semmelweis Egyetem
http://semmelweis.hu

ÁLTALÁNOS ORVOSTUDOMÁNYI KAR
Magatartástudományi Intézet
Pszichofiziológiai és kronobiológiai kutatócsoport

# LOOKING BACK

## Fourier spectra

# A HARMONIC IN THE DESCARTES COORDINATES



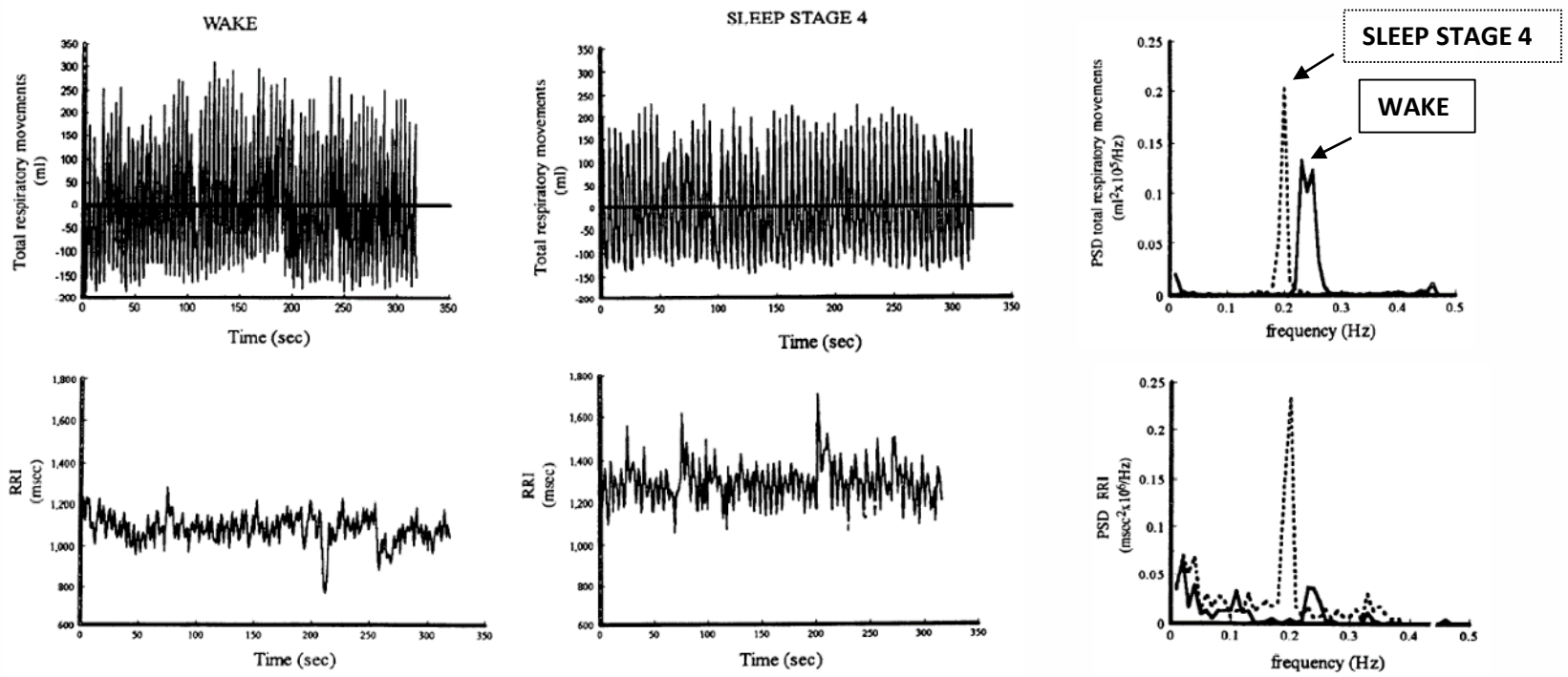

***Amplitude spectrum:*** $\sqrt{2^2 + 3^2}$

***Power spectrum:*** $2^2 + 3^2$

***Power spectral density:***

$1 \times (2^2 + 3^2)$

# EXAMPLE FOR SPECTRAL ANALYSIS: BREATHING AND HEART RATE FREQUENCIES IN WAKEFULNESS AND SLEEP



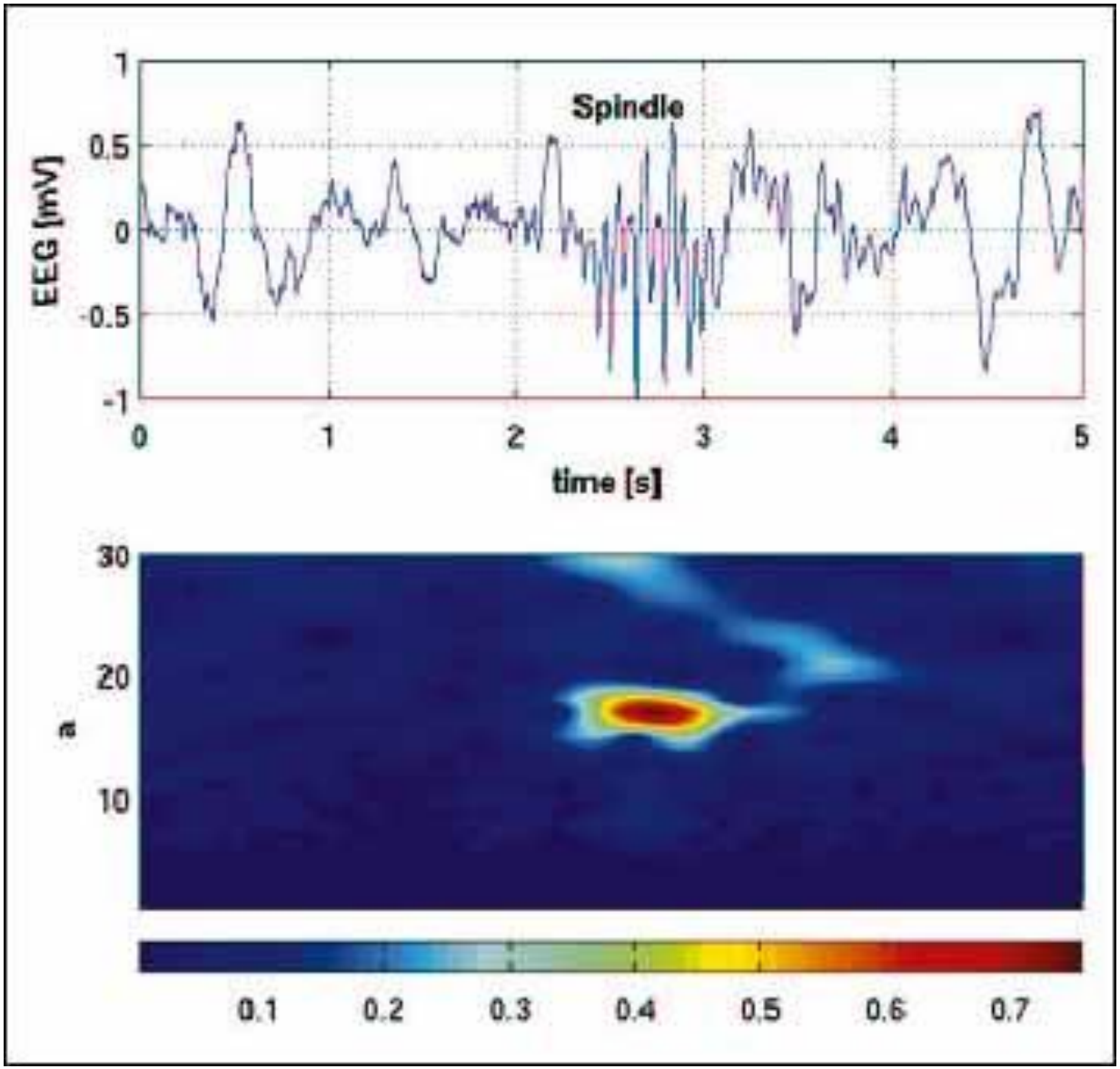

Breathing (top) and heart rate (tachogram, bottom) time series in wakefulness (WAKE) and in deep, slow wave sleep (SLEEP STAGE 4)

…as well as their power spectral densities (PSD)

Van de Borne P et al. Am J Physiol. 1995 Sep;269(3 Pt 2):H952-8.

# LOOKING BACK

## WAVELET ANALYSIS



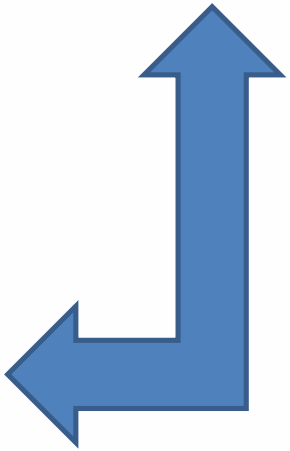

Latka M et al. J Physiol Pharmacol 2005, 56, Supp 4, 15-20

# CURRENT PROBLEM

- Depicting the synchronization (connection) between time series (eg. breathing and heart rate)
  - Is there any synchronization?
  - How strong it is?
  - What is its characteristic frequency?
- Examples
  - Activity time series of co-sleeping mother and child
  - Relationship between mood states and time-dependent physiological processes
  - Synchronization between distinct physiological signals

# A FEW BASIC CONCEPTS

- Connectivity (coupling)
  - Functional
  - Effective
  - Structural
- Synchronization
  - Linear
  - non-linear
  - mixed



# PEARSON CORRELATION

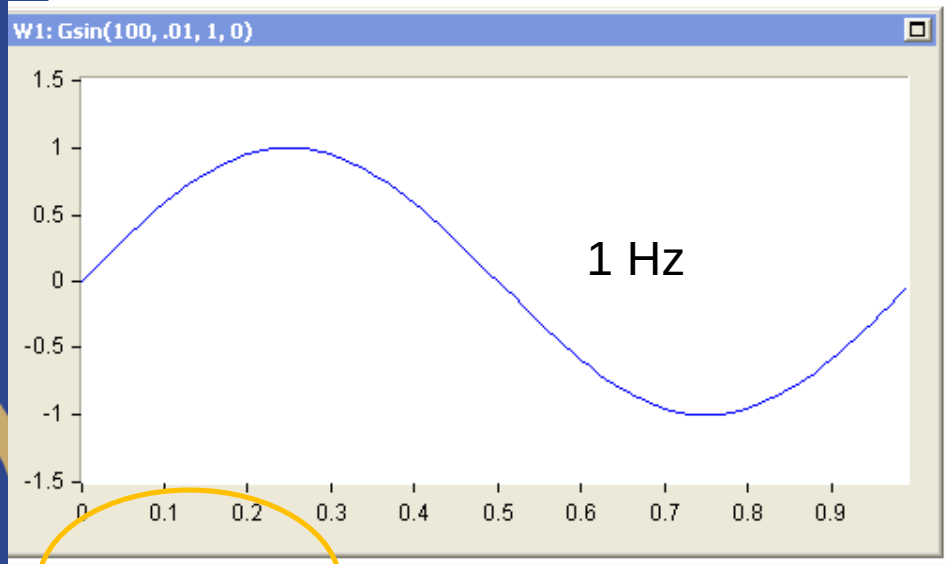
$$r_{xy} = \frac{\sum x_i y_i - n\bar{x}\bar{y}}{\sqrt{(\sum x_i^2 - n\bar{x}^2)}\sqrt{(\sum y_i^2 - n\bar{y}^2)}}.$$

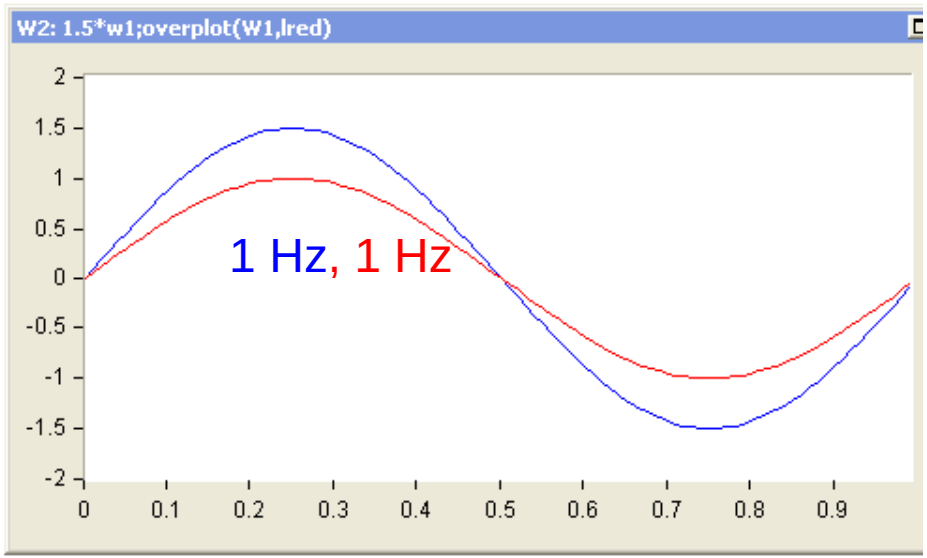
WHY EXACTLY?

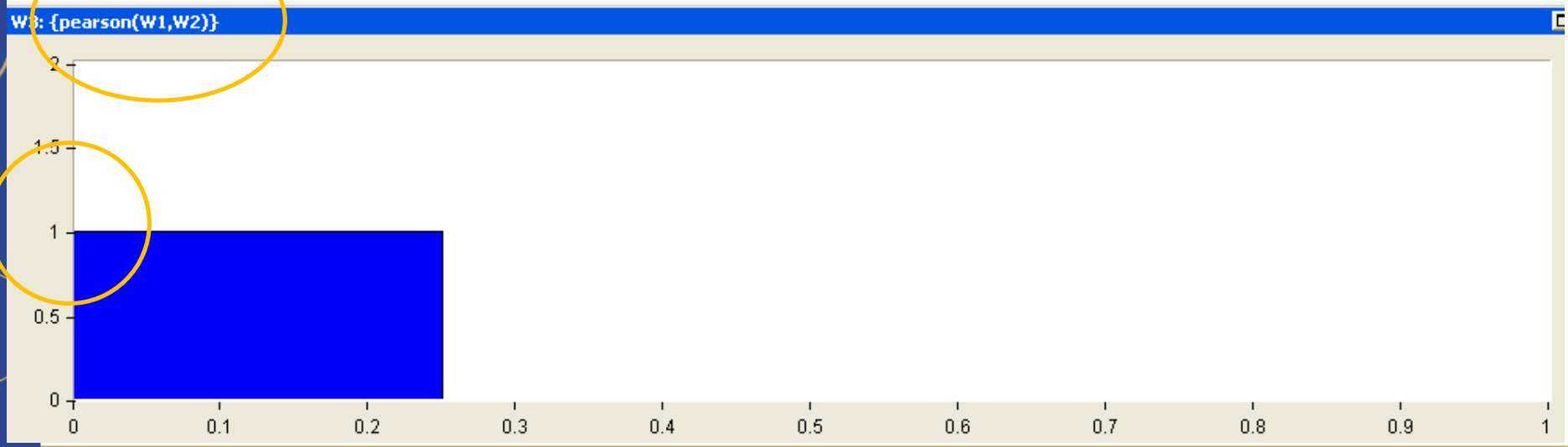
Correlation = Co-variation.

Then what is the question? Are there any more questions?

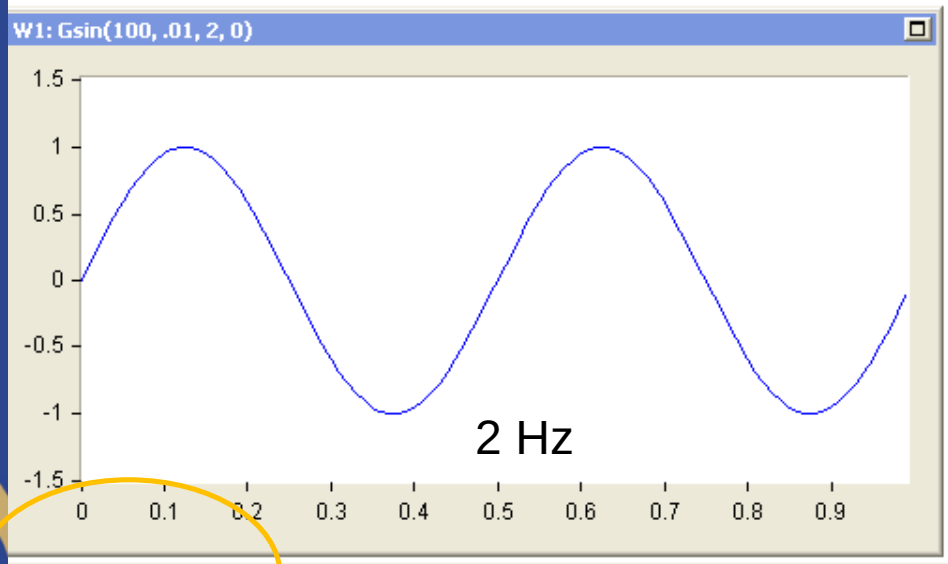
# PEARSON CORRELATION OF SINE WAVES WITH DIFFERENT AMPLITUDES, BUT IDENTICAL FREQUENCIES AND PHASES (=1)

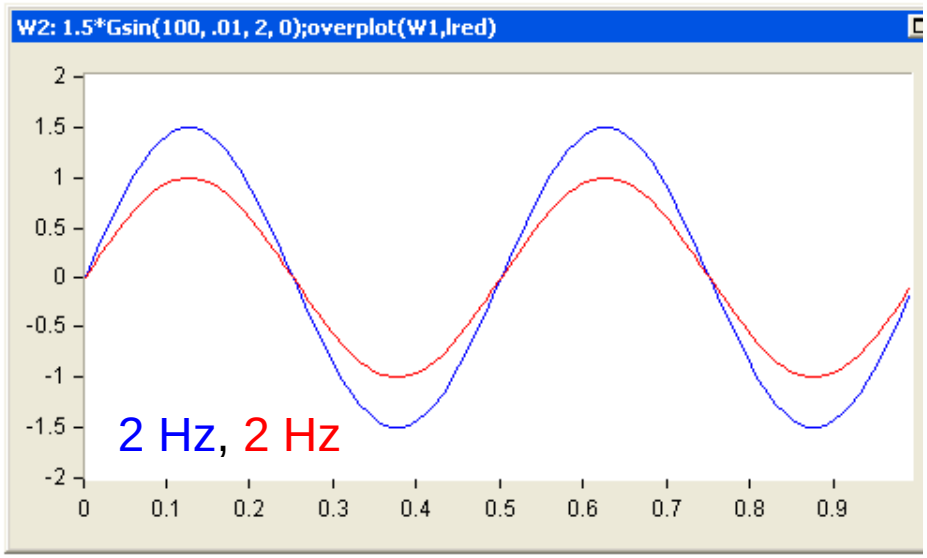


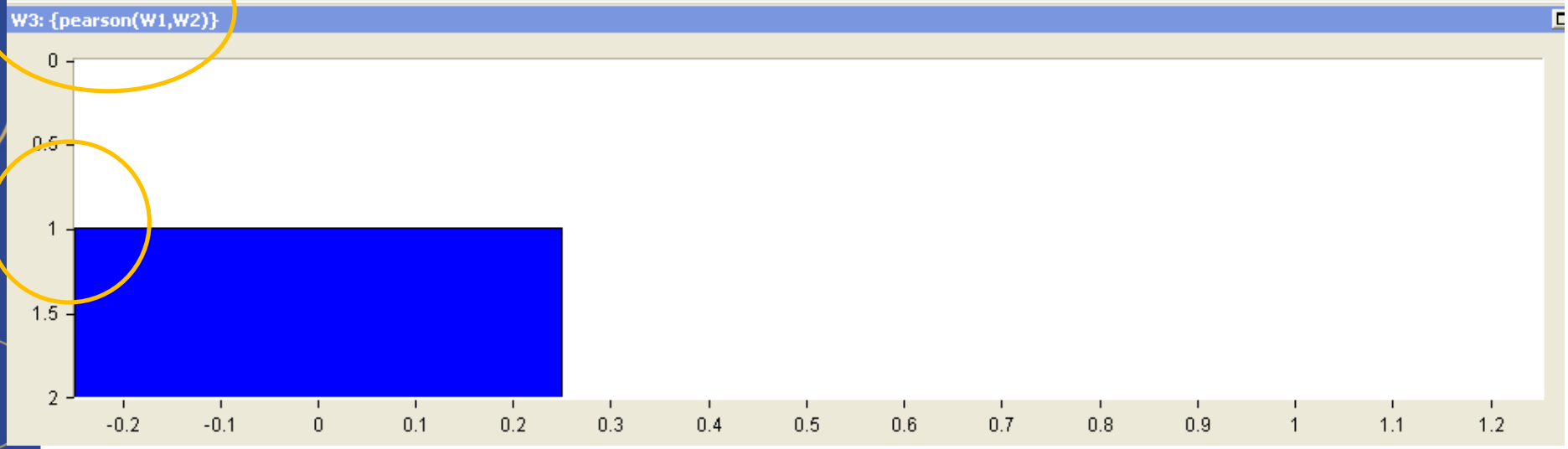



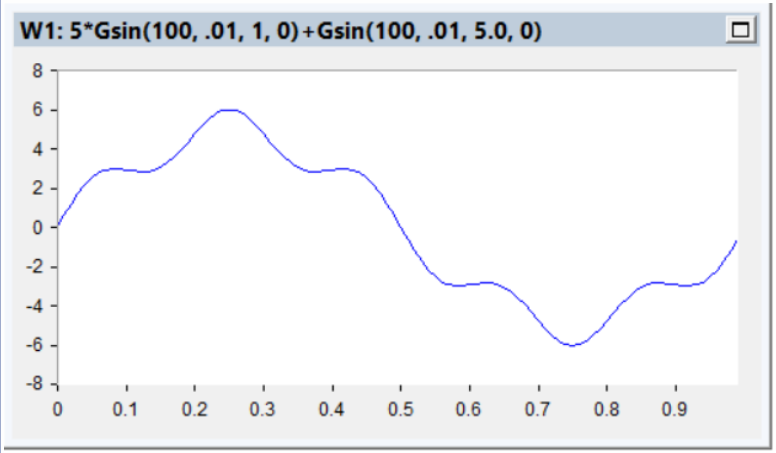
# …irrespective of their actual frequency

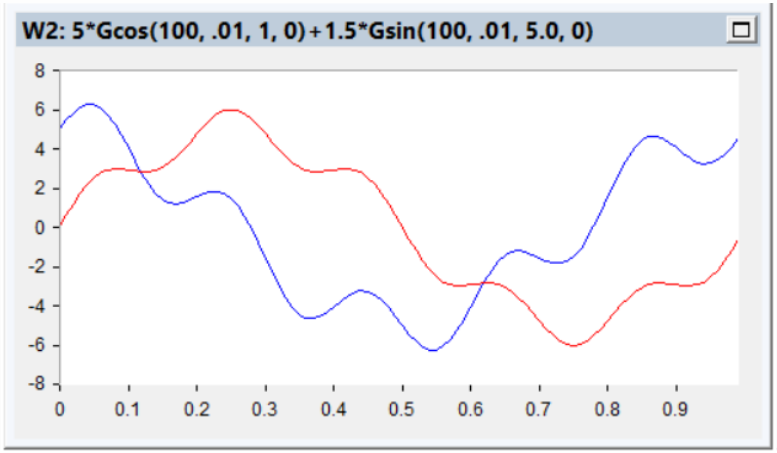


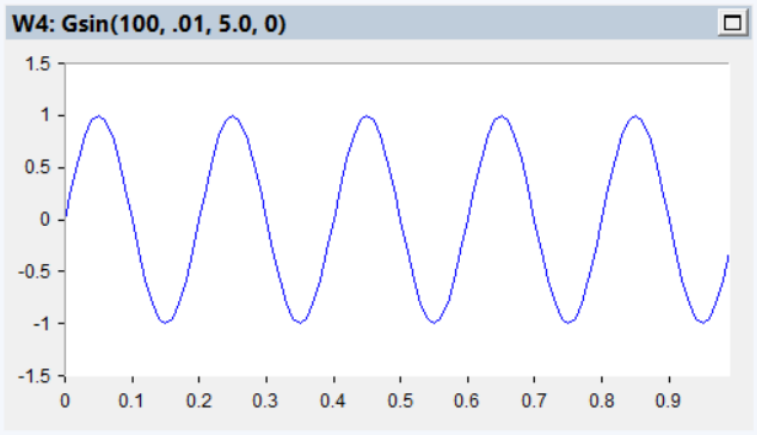
# TIME SERIES MIGHT NOT CORRELATE WITH EACH OTHER BUT THEIR HARMONICS STILL DO

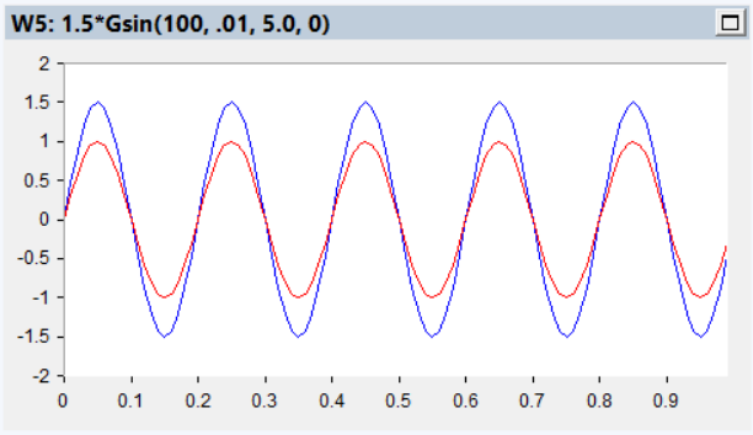



W3: {Pearson(W1,W2)}

| | 1: No Units |
|---|---|
| 1: | 0.056354 |
| 2: | |
| 3: | |
| 4: | |
| 5: | |
| 6: | |
| 7: | |
| 8: | |
| 9: | |
| 10: | |
| 11: | |



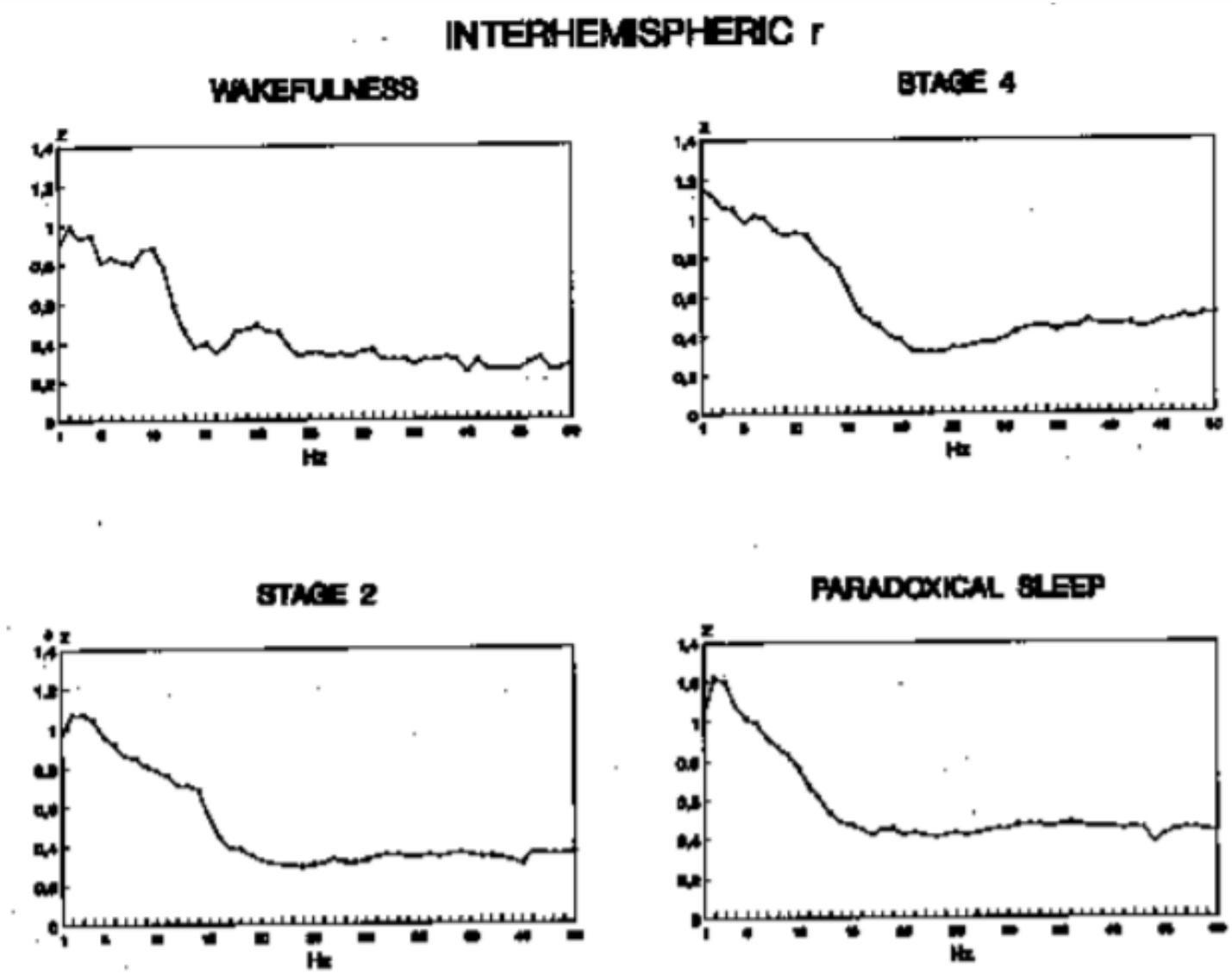




W6: {Pearson(w4,w5)}

| | 1: No Units |
|---|---|
| 1: | 1.000000 |
| 2: | |
| 3: | |
| 4: | |
| 5: | |
| 6: | |
| 7: | |
| 8: | |
| 9: | |
| 10: | |
| 11: | |

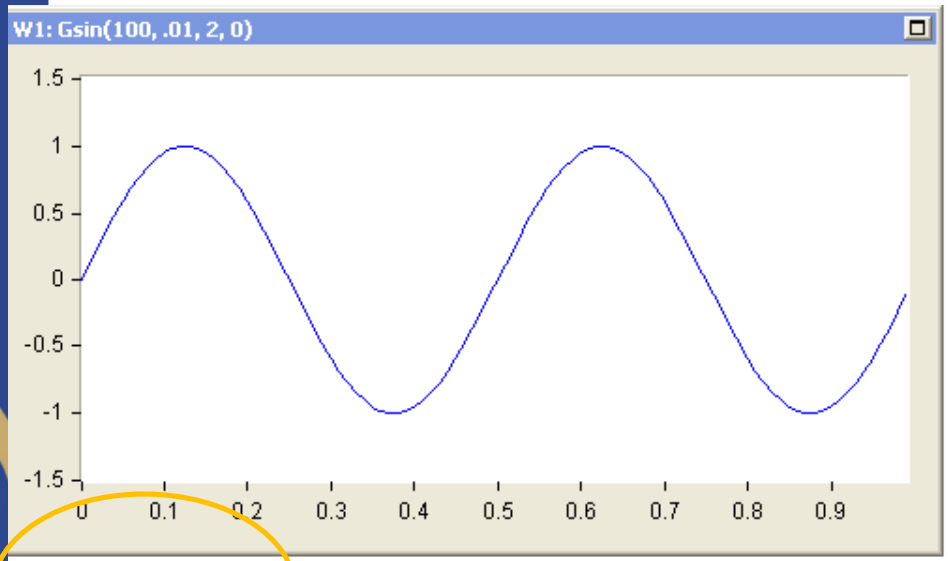
**Correlation spectrum**

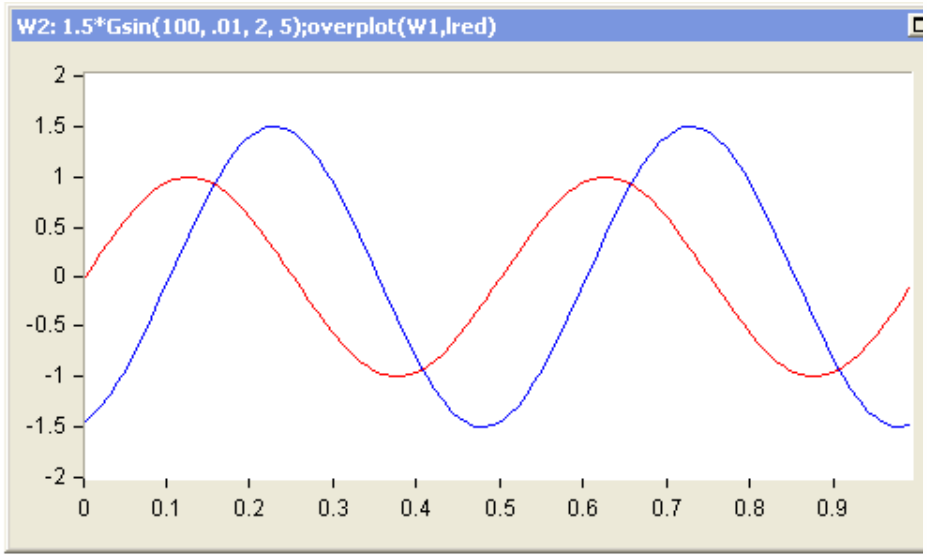
# EEG CORRELATION SPECTRA IN DIFFERENT SLEEP-WAKE STATES

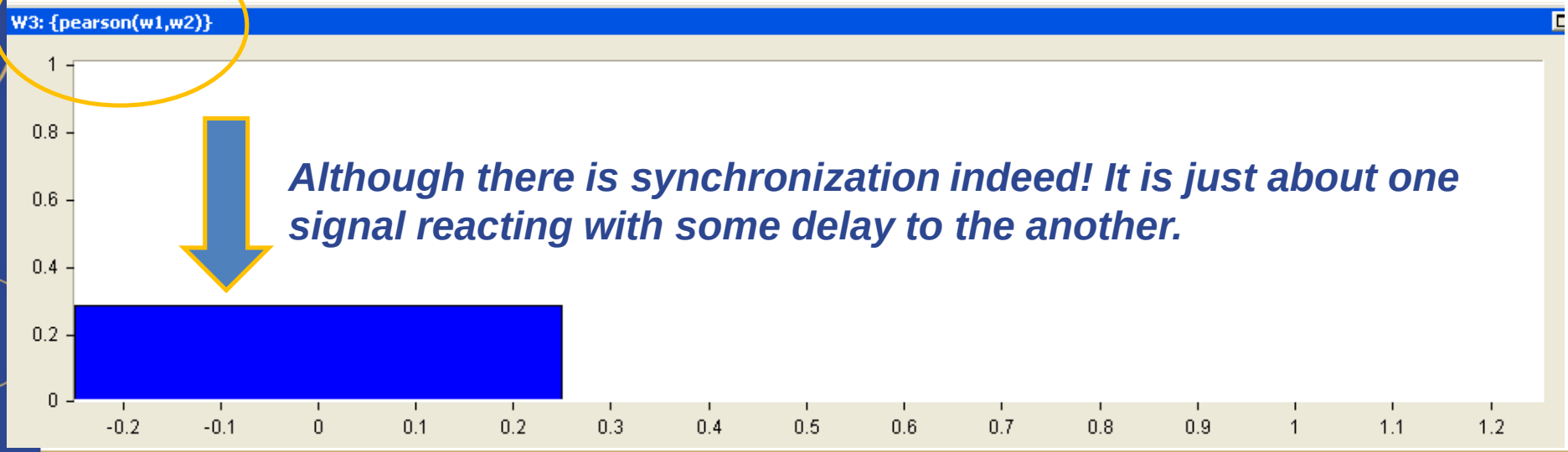



Pérez-Garci E et al. SLEEP, Vol. 24, No. 1, 2001

# WHERE DOES CORRELATION WENT?
# IT DISSAPEARED WITH A TIME DELAY



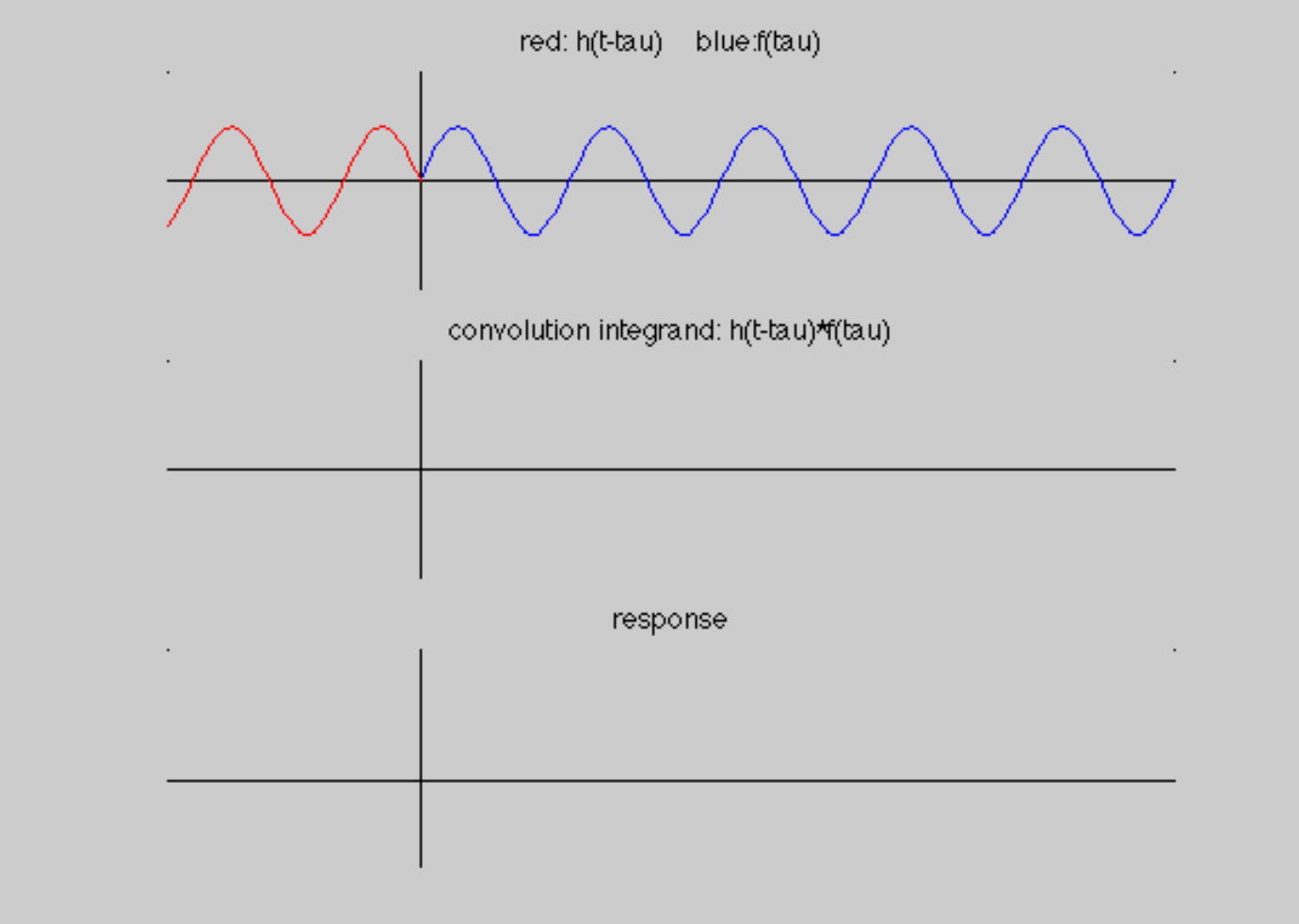




***Although there is synchronization indeed! It is just about one signal reacting with some delay to the another.***

# THE CORRELATION OF TWO TIME SERIES

- Is basically a frequency-independent measure
  - And is not constructed to distinguish between frequencies (eg. which of the harmonics instigates the correlation)
  - It can be completed by correlation between FFT (DFT) harmonics (it can be transformed to a frequency-sensitive measure ⟶ EEG correlation spectrum)
- It is amplitude free (amplitudes do not matter)!
- It is strongly phase-dependent (brokes down with delay)
  - Only 0-phase differences are well-tolerated

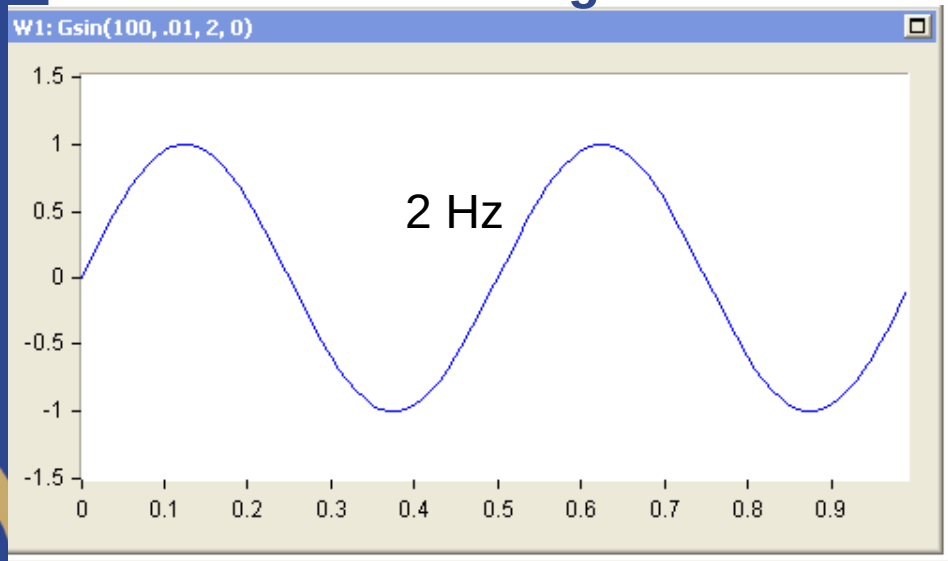
# CROSSCORRELATION = CONVOLUTION
## Convolving one time series with the another

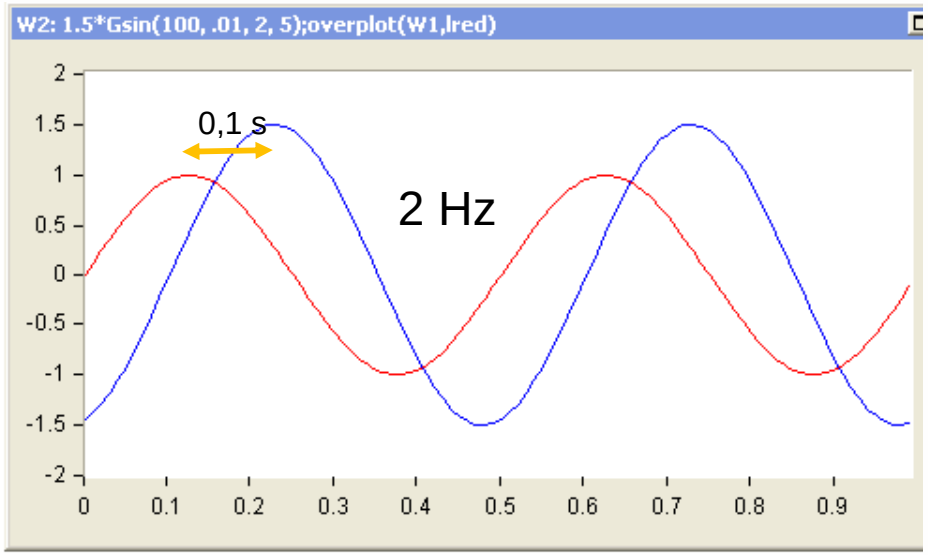


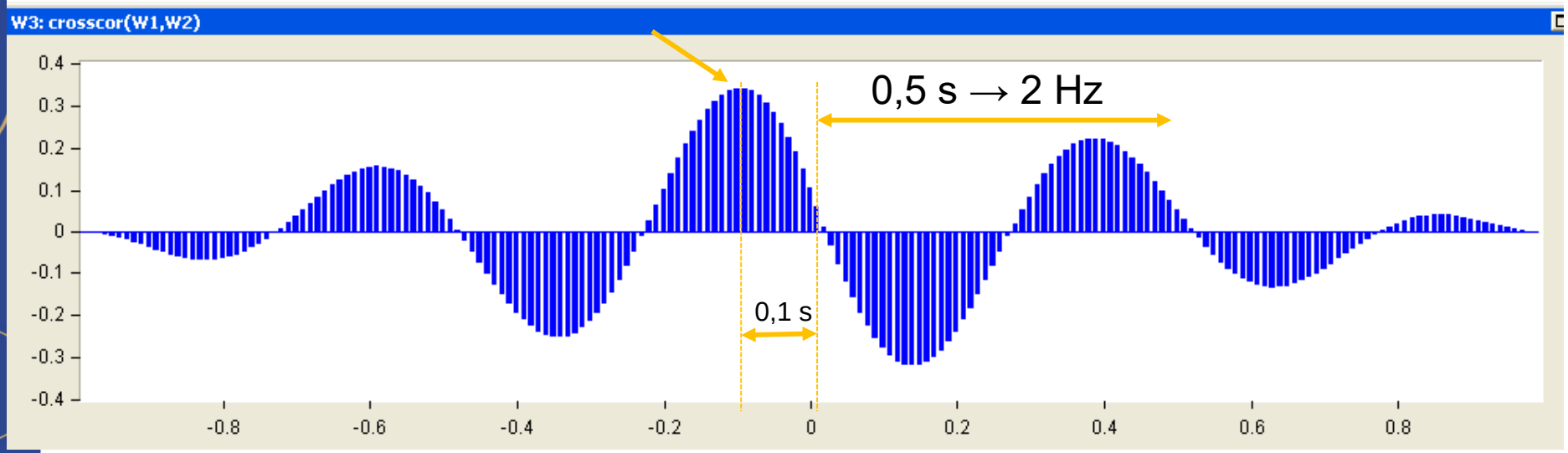

https://www.purdue.edu/freeform/ervibrations/chapter-iv-animations/convolution-integral-interpreting-resonance/

***Similarities will emerge at diff. moments and with diff. frequencies***

# CROSSCORRELATION = CONVOLUTION
## Convolving one of the series with the another

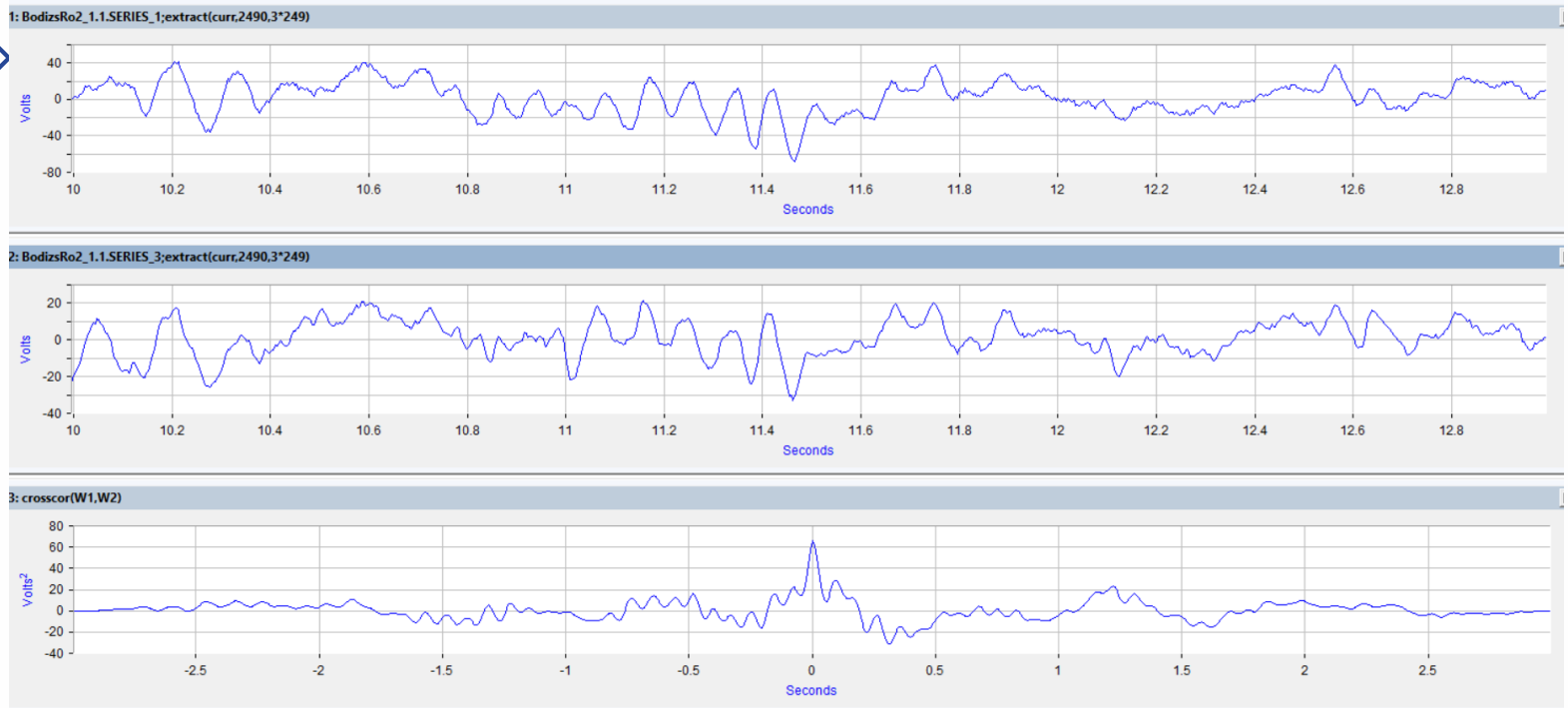


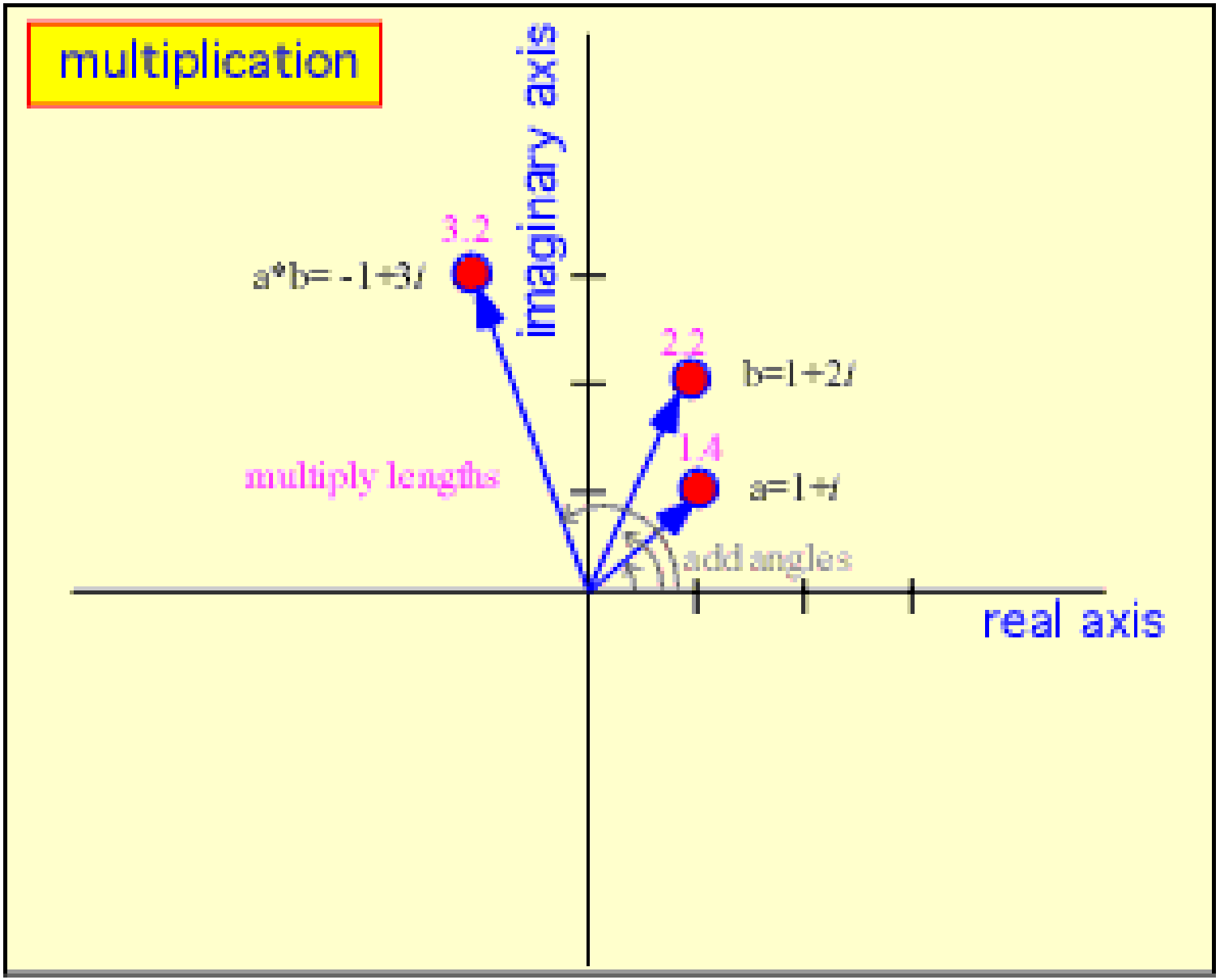




***Similarities will emerge at diff. moments and with diff. frequencies***

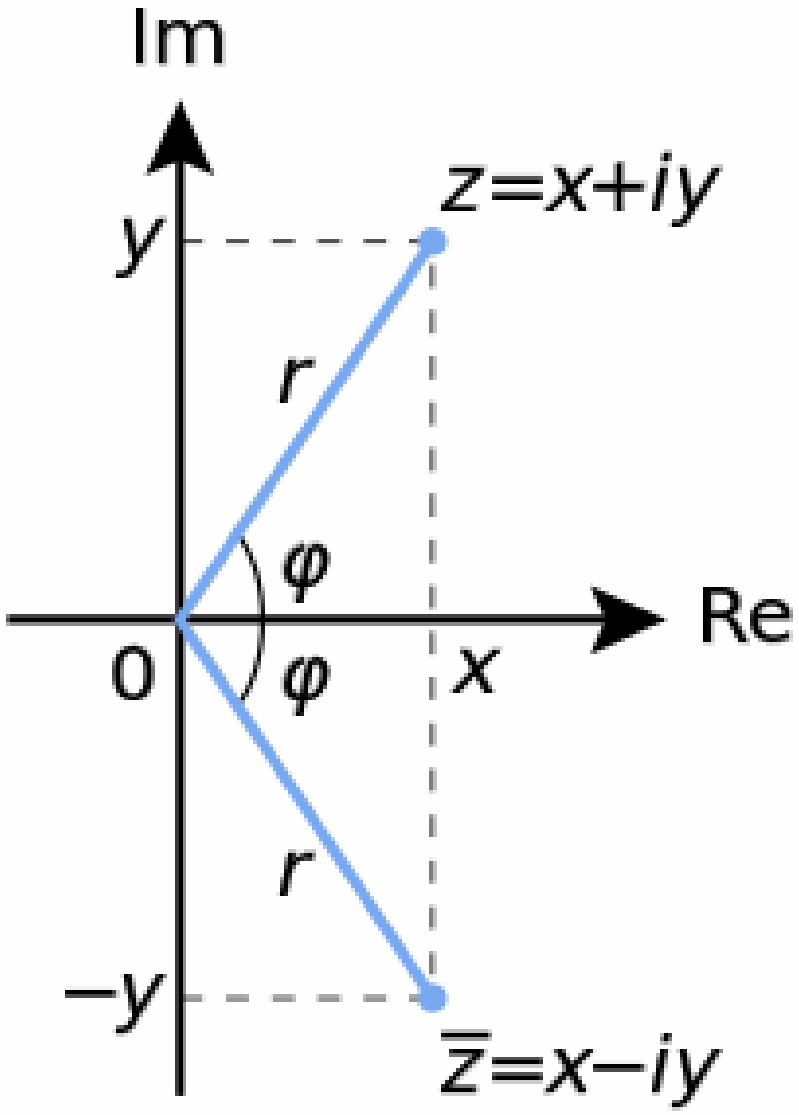
# ABOUT CROSSCORRELATION

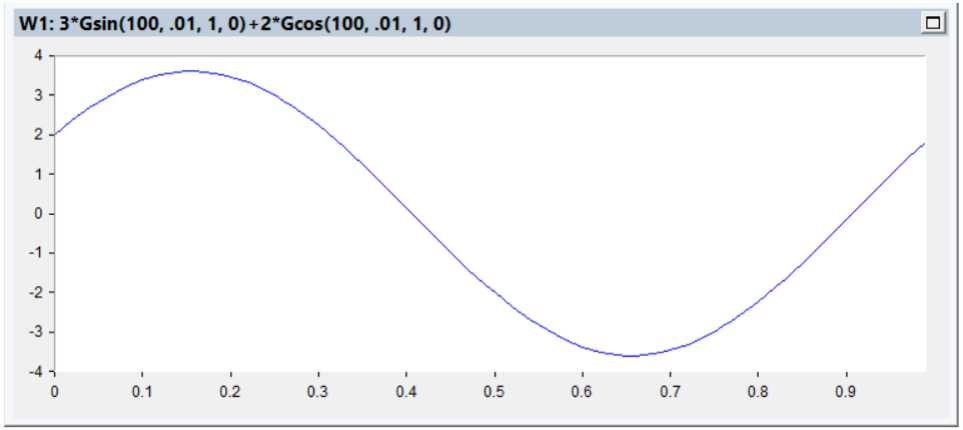
- Convolution-based method
- It might depict phase delay and common periodicity of the time series
- 

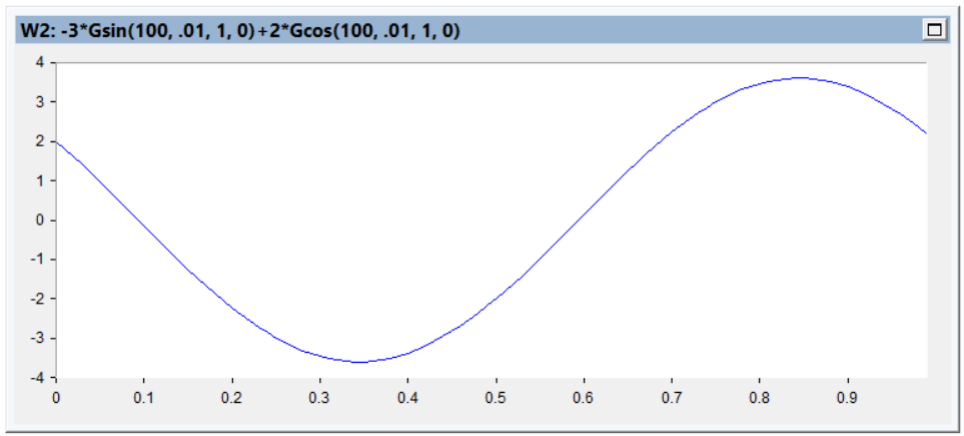
# ON THE WAY TOWARD COHERENCE-I: MULTIPLYING COMPLEX NUMBERS



# ON THE WAY TOWARD COHERENCE-II: THE COMPLEX CONJUGATE



# CROSS-SPECTRAL DENSITY - I

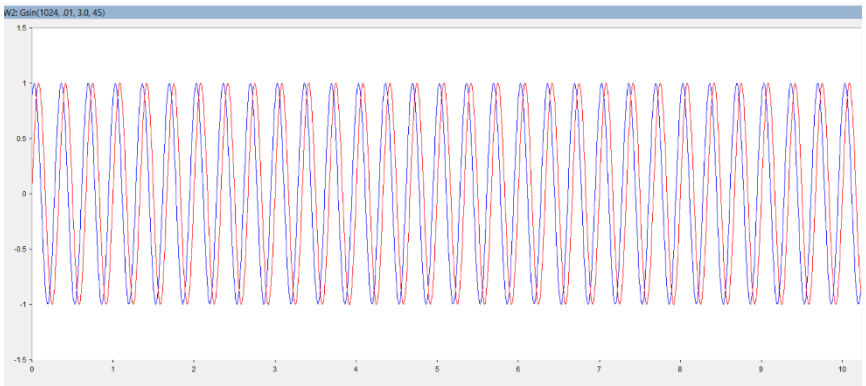
$a_1 + b_1 i$

$a_2 - b_2 i$

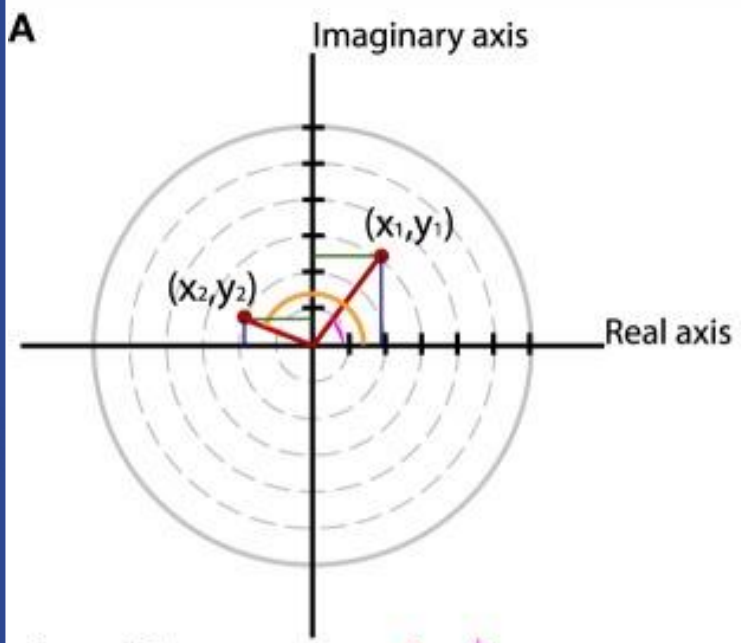
Let's take the vector multiplication of one time series with the complex conjugate of the another time series at each harmonic.

$$(a_1 + b_1 i)(a_2 - b_2 i) = a_1 a_2 - a_1 b_2 i + a_2 b_1 i - b_1 b_2 i^2 = \mathbf{(a_1 a_2 + b_1 b_2) + (a_2 b_1 - a_1 b_2)i}$$

The length of the new vector will be equal with the multiplied length of the two vectors, whereas the phase will be the difference of the two phases (because one was the complex conjugate).

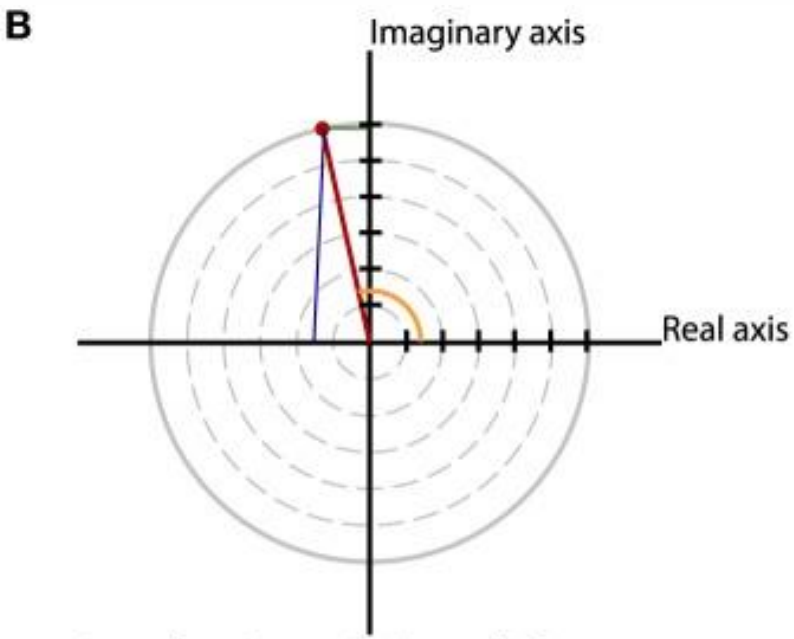



# CROSS SPECTRAL DENSITY – II




signal 1 = $x_1 + iy_1 = A_1 e^{\phi_1}$

signal 2 = $x_2 + iy_2 = A_2 e^{\phi_2}$

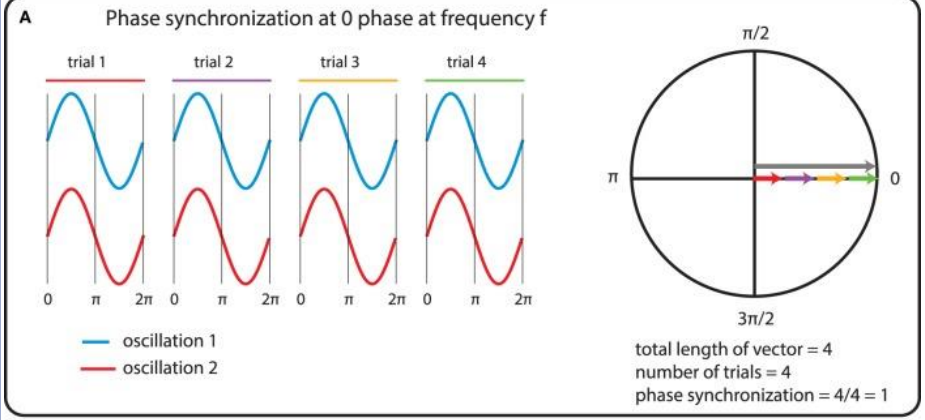


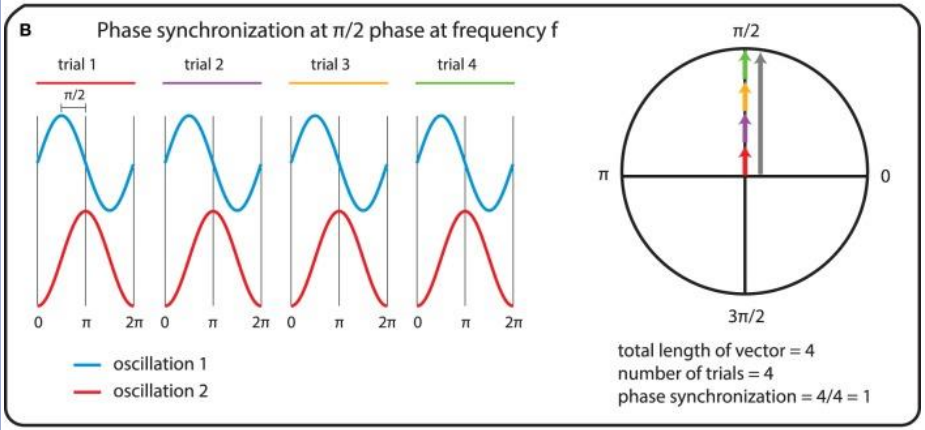

signal 1 * conj(signal 2) =

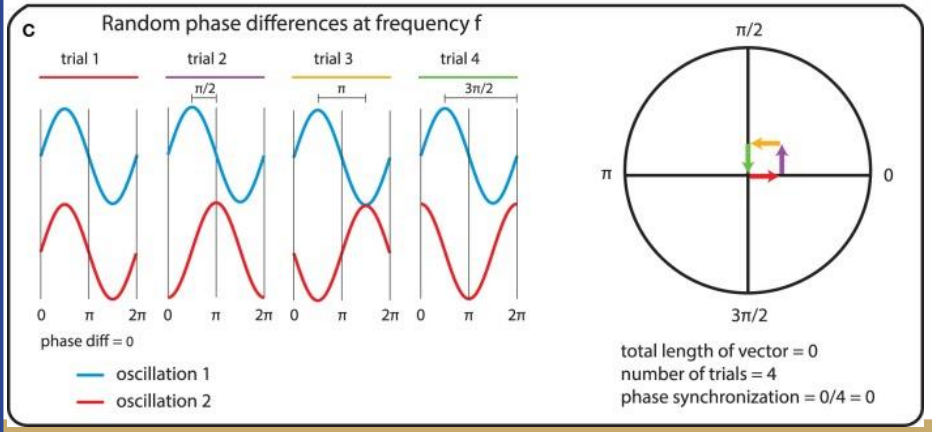
$(x_1 + iy_1) * (x_2 - iy_2) = (x_1x_2+y_1y_2) + i(y_1x_2-y_2x_1) =$

$A_1 e^{\phi_1} * A_2 e^{-\phi_2} = A_1A_2 e^{(\phi_1-\phi_2)}$

André M. Bastos and Jan-Mathijs Schoffelen
Front Syst Neurosci. 2015; 9: 175.




# THE IMPORTANCE OF THE CONSISTENT PHASE DIFFERENCES BETWEEN TWO SIGNALS

***In case of random phase differences***

***the consecutive vectors will cancel out each other.***

André M. Bastos and Jan-Mathijs Schoffelen. Front Syst Neurosci. 2015; 9: 175.

# THE CROSS SPECTRAL DESNITY OF TWO TIME SERIES

- Conveys frequency-specific information
  - It can distinguish between frequencies (which of the frequencies is decisive in synchronization)
- Amplitude-dependent measure (high input amplitudes => apparently high synchronization, ☹)
- It is a measure of phase differences
  - It not only signals the 0 phase synchronization and it explicitly tells us about phase differences (in Π values or grades) – we can derive a **Phase-Slope Index**

# ONCE AGAIN ABOUT THE ISSUE OF AMPLITUDES: let's normalize cross-spectral density!

**COHERENCE =**

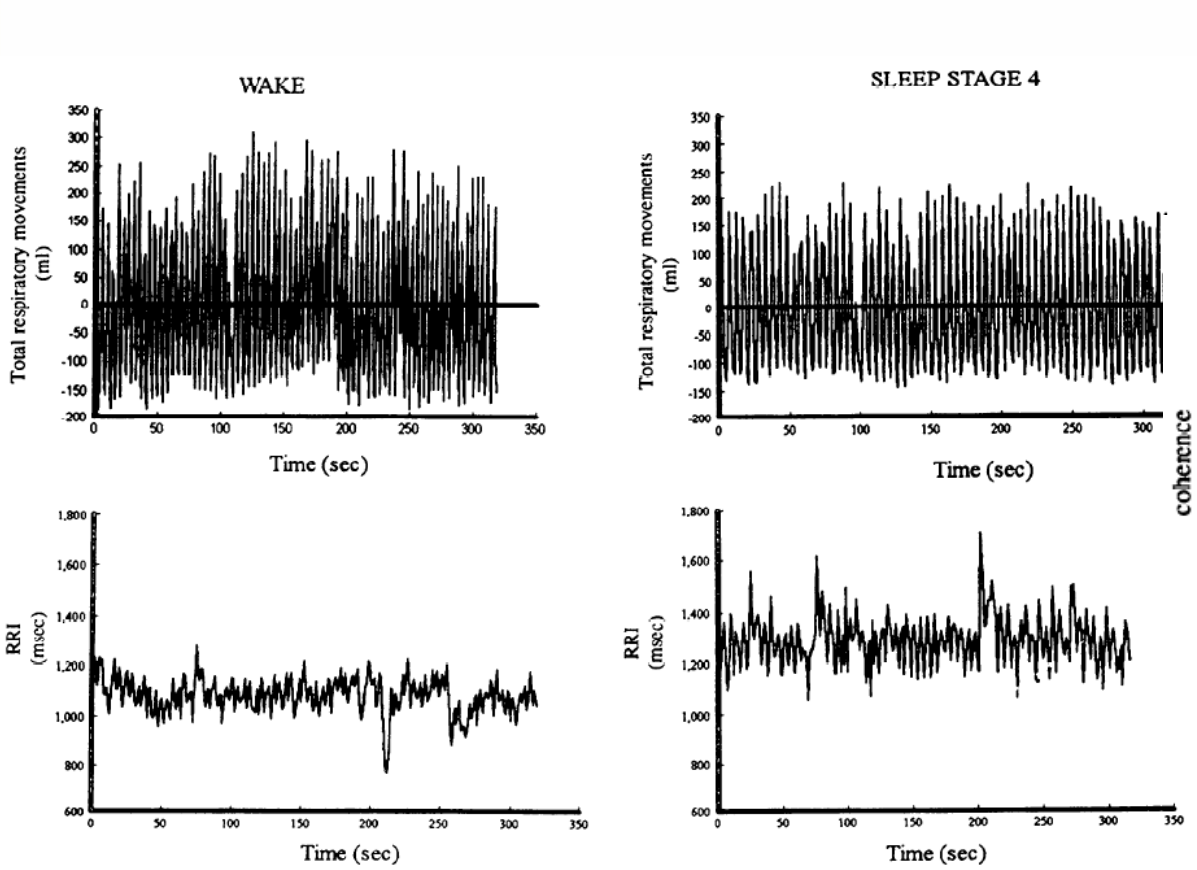
$$\frac{\text{Amplitude of CROSS SPECTRAL DENSITY}}{\text{The square root of the multiplied AUTOSPECTRAL DENSITY}}$$

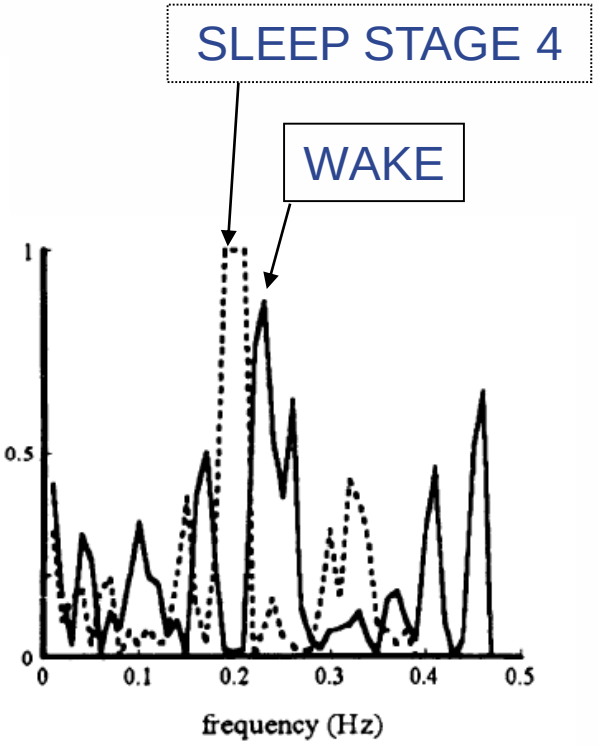
- **The numerator and the denominator has to be averaged separately!!!**
  - It can only be interpreted as a mean derived from multiple pairs of time series

$$coh_{xy}(\omega) = \frac{|S_{xy}(\omega)|}{\sqrt{S_{xx}(\omega)S_{yy}(\omega)}}$$

- Values are between 0 and 1 (from no coherence to maximal coherence)
- Frequency-specific information is conveyed
- Phase differences are not directly measured – only phase consistency is reflected

# EXAMPLE-I: BREATHING AND HEART RATE TIME SERIES IN WAKEFULNESS AND IN SLEEP



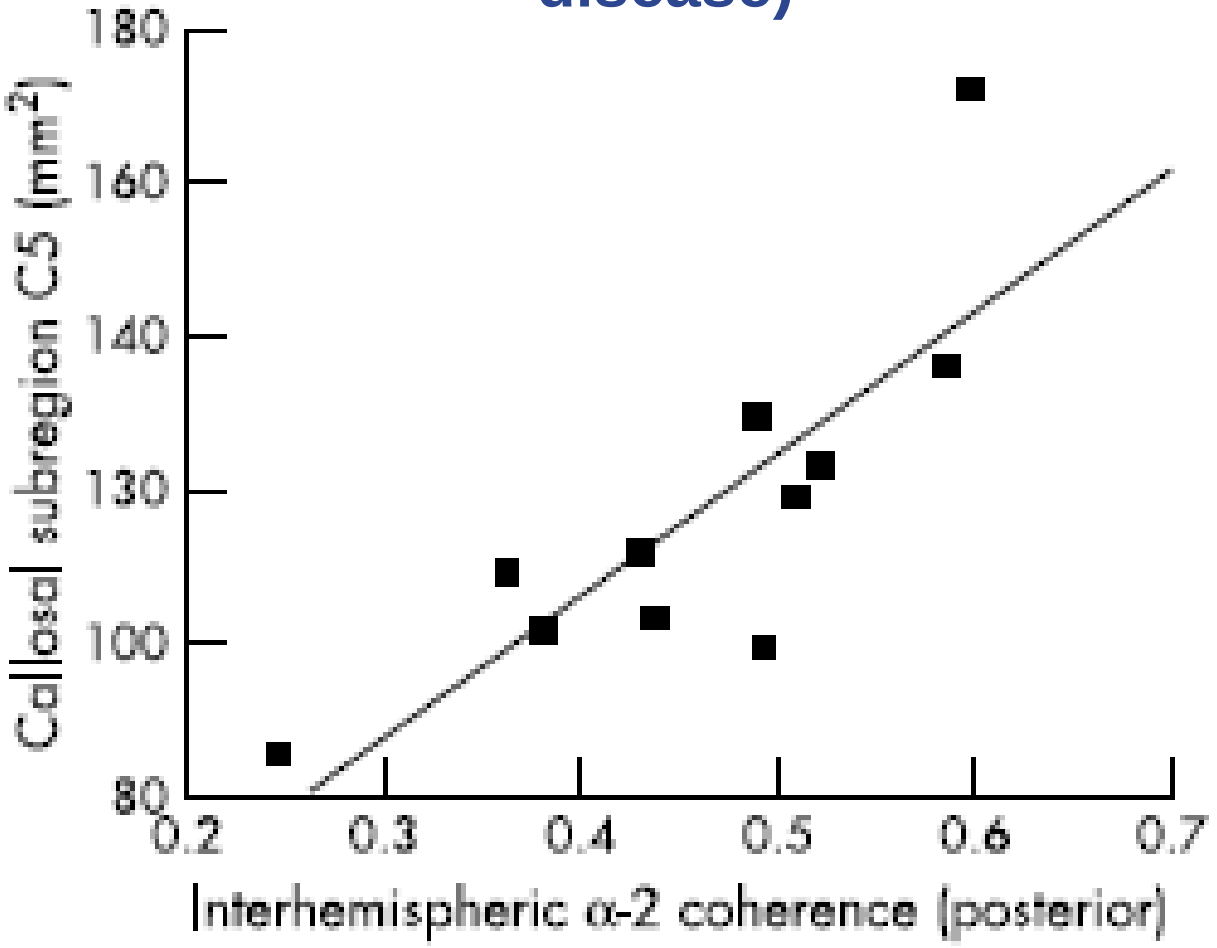




Breathing (top) and heart rate (tachogram, bottom) time series in wakefulness and in deep slow wave sleep

…as well as their coherence

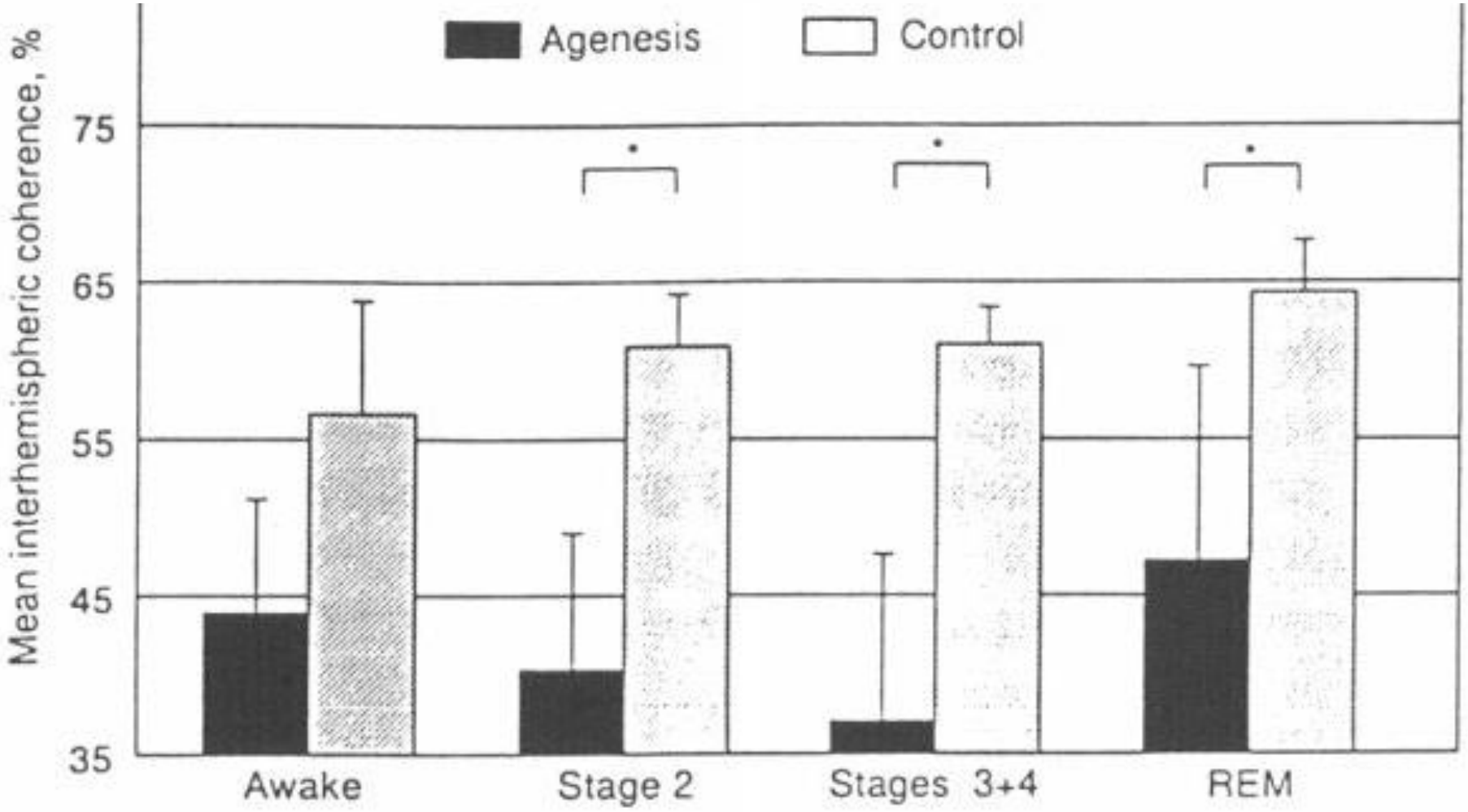
Van de Borne P et al. Am J Physiol. 1995 Sep;269(3 Pt 2):H952-8.

# EXAMPLE-II: INTERHEMISPHERIC COHERENCE OF ALPHA RANGE EEG WAVES CORRELATES WITH THE VOLUME OF THE CALLOSAL REGION (in Alzheimer's disease)




O Pogarell et al. J Neurol Neurosurg Psychiatry 2005;76:109–111.

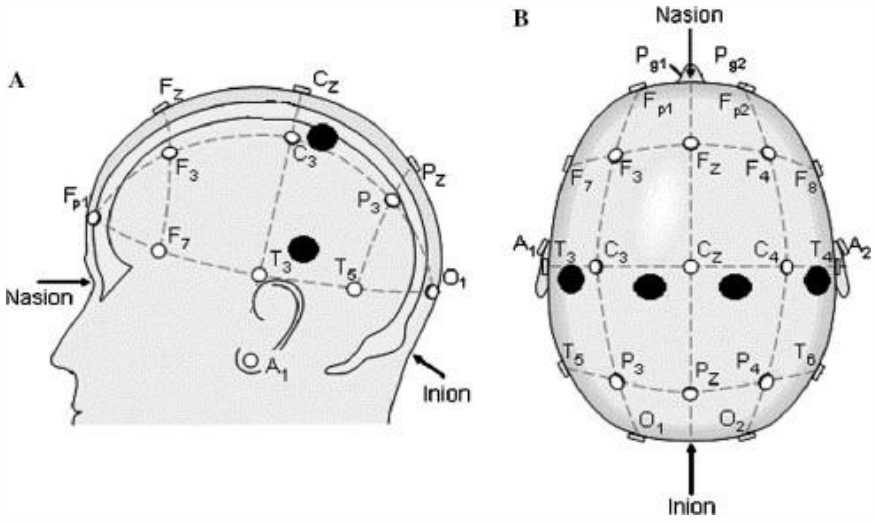
# EXAMPLE-III: DECREASED INTERHEMISPHERIC EEG-COHERENCE IN CORPUS CALLOSUM AGENESIS SYNDROME




Nielsen T et al. Eur NeuroI1993:33:173-176

# Problems with EEG coherence: active common reference

- EEG always reflects a ptential difference between two recording locations




- Monopolar reference:

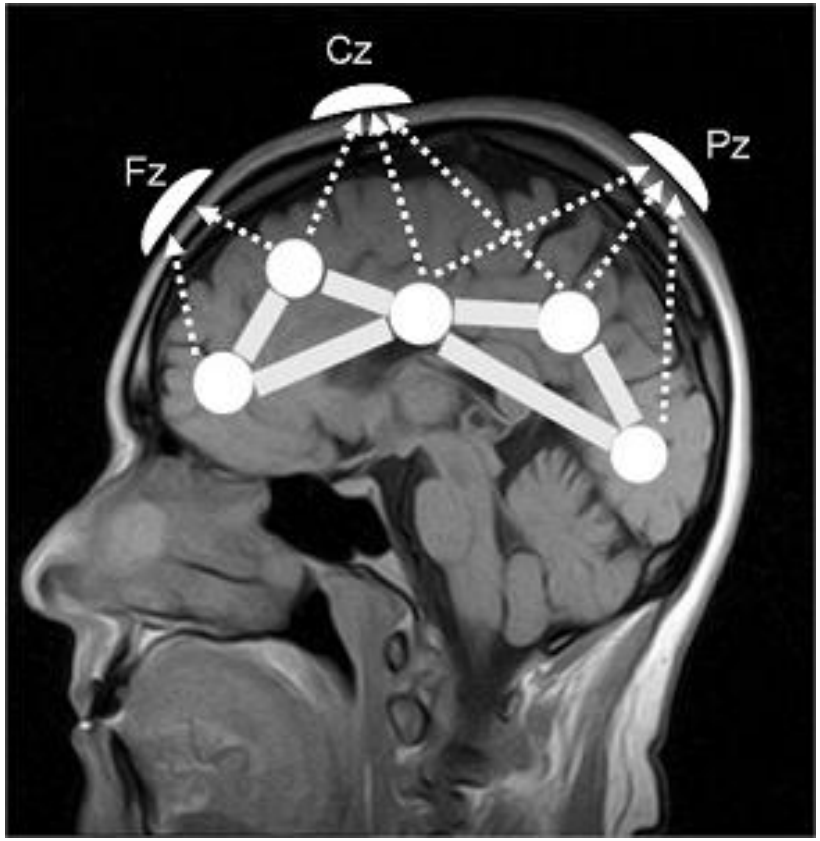
  coherence will reflect in

  part the commonalities

  cuased by the activity on

  the reference electrode

# Problems with EEG coherence: volume conduction

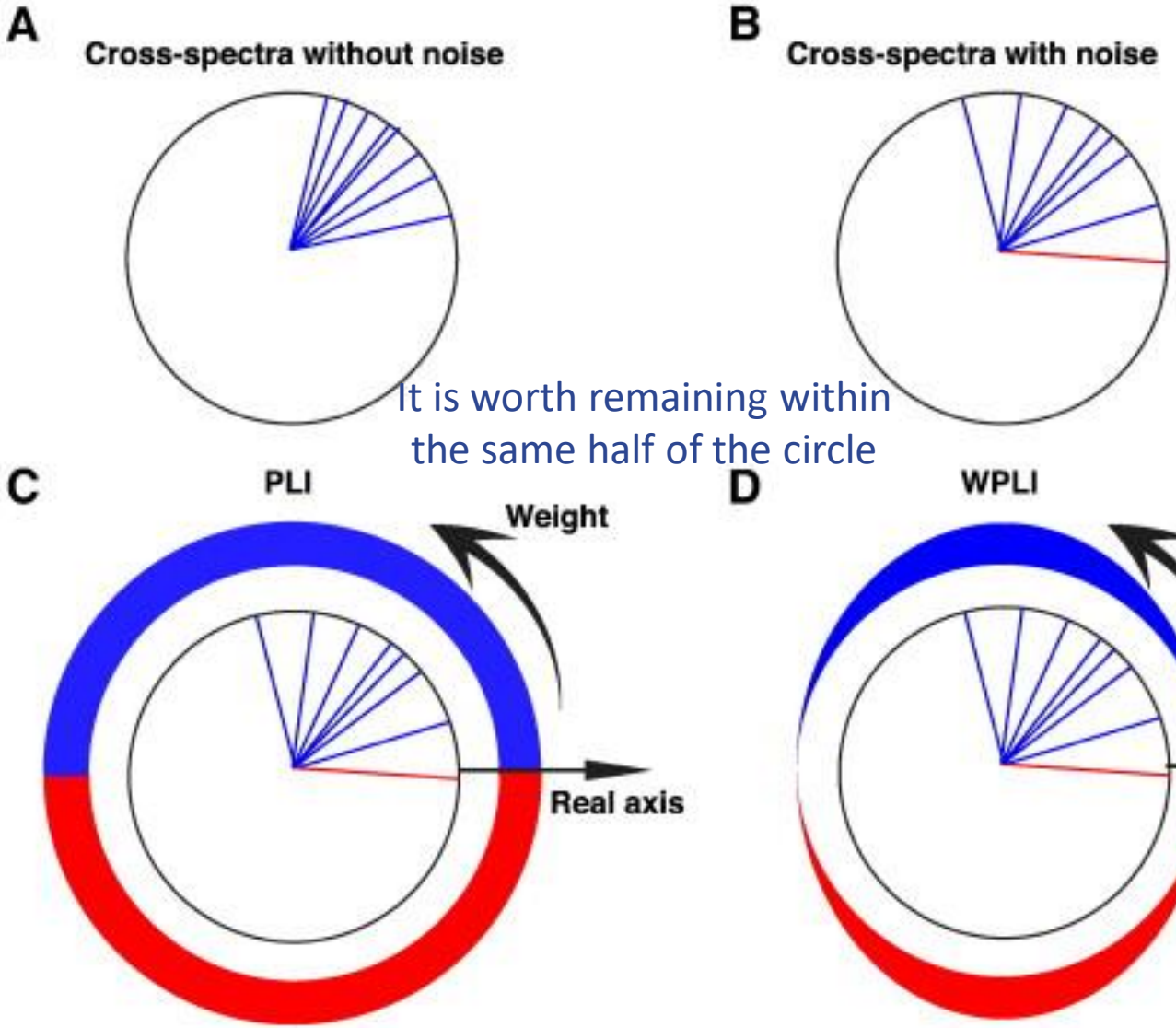



- Volume conduction: a source spreads to multiple recording locations with the speed of light
- That is, coherence reflects in part the volume conduction
- It is difficult to discern the amount of the separate sources in the signal.

# THEN LET'S DISREGARD THE REAL AXIS (X) : IMAGINARY COHERENCE

- In the formula of coherence function we use the imaginary part of the vector (instead of vector length)
- 0 and 180 grade phase differences is just eliminated from coherence
- As a consequence, there is no volume conduction and common reference problem
- Unfortunately, this method is strongly biased toward 90 grades phase differences, indeed it still considers real axis values in the denominator

# (WEIGHTED) PHASE LAG INDEX – (W)PLI




It is worth remaining within the same half of the circle

Imaginary part values are the weights (weighted averaging)

Cornelius J. Stam

Vinck M et al. NeuroImage 2011;55(4):1548-1565

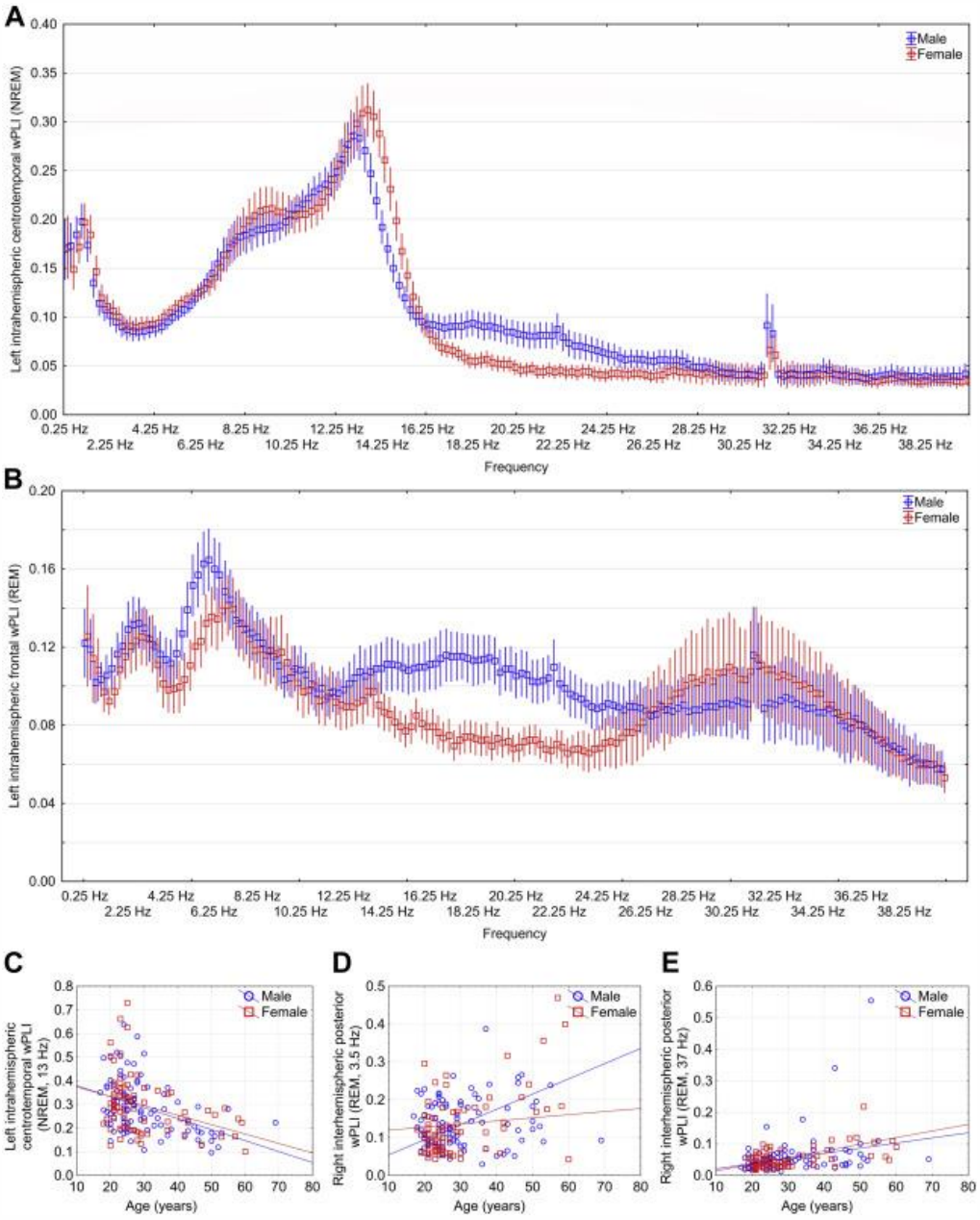
# PHASE LAG INDEXES

## PLI

- The **modulus** of the **sign** function of cross spectral density
- In case of the values scattered **around the real axis** result is close to 0
- It is in fact based on a **distribution**

## WPLI

- Correction of the formula of coherence function with **weights derived from the imaginary axis**
- If vectors are **close to the real axis**, their imaginary parts are low
- It is the normalized mean of **weighted vectorial multiplications**




# WPLI IN USE:

## Sex differences and age effects in sleep-EEG functional connectivity

Ujma PP et al. Neurobiology of Aging 2019;78:87-97.

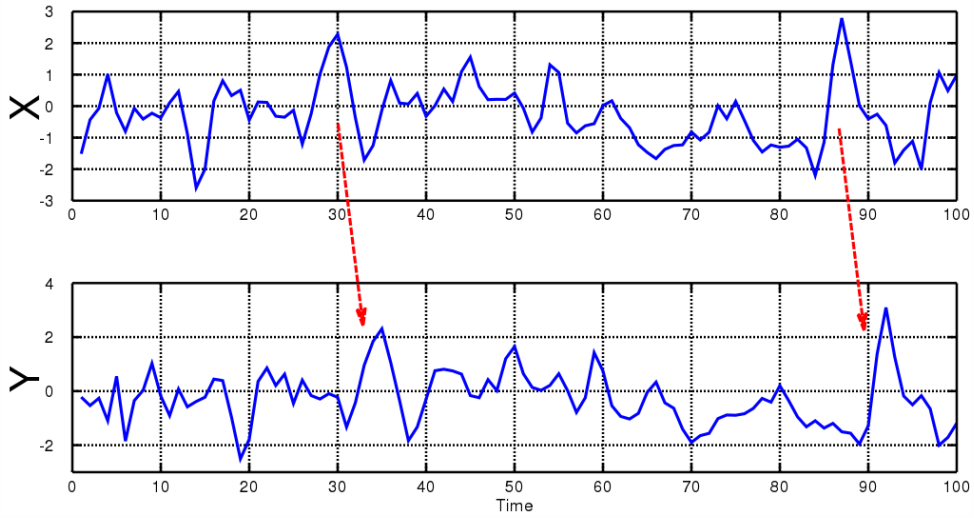
# DIRECTION IN FUNCTIONAL CONNECTIVITY-I: Granger-causality

In what measure can a time series be predicted based on its own past (simple linear regression)?

And if we consider the past of another time series as well (multiple linear regression)? Will the prediction improve significantly?

No – there is no directed connectivity

Yes – there is directed connectivity (we can foresee the future of a time series based on the past of another)

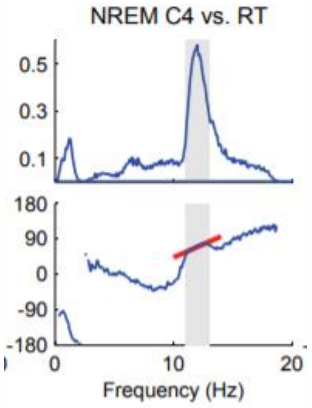


# DIRECTION IN FUNCTIONAL CONNECTIVITY-II: Phase-Slope Index (PSI)

- Interactions are time consuming
- If propagation speed is equal for different frequency oscillations
- Then: phase differences between the transmitter and the receiver increase in a frequency-dependent manner

- **<u>Slope of the phase angle derived from the cross spectral density</u>**

Nolte G et al. Phys Rev Lett 2008




NREM sleep: right central EEG and right anterior thalamic LFP coherence: increased values in the slpindle range

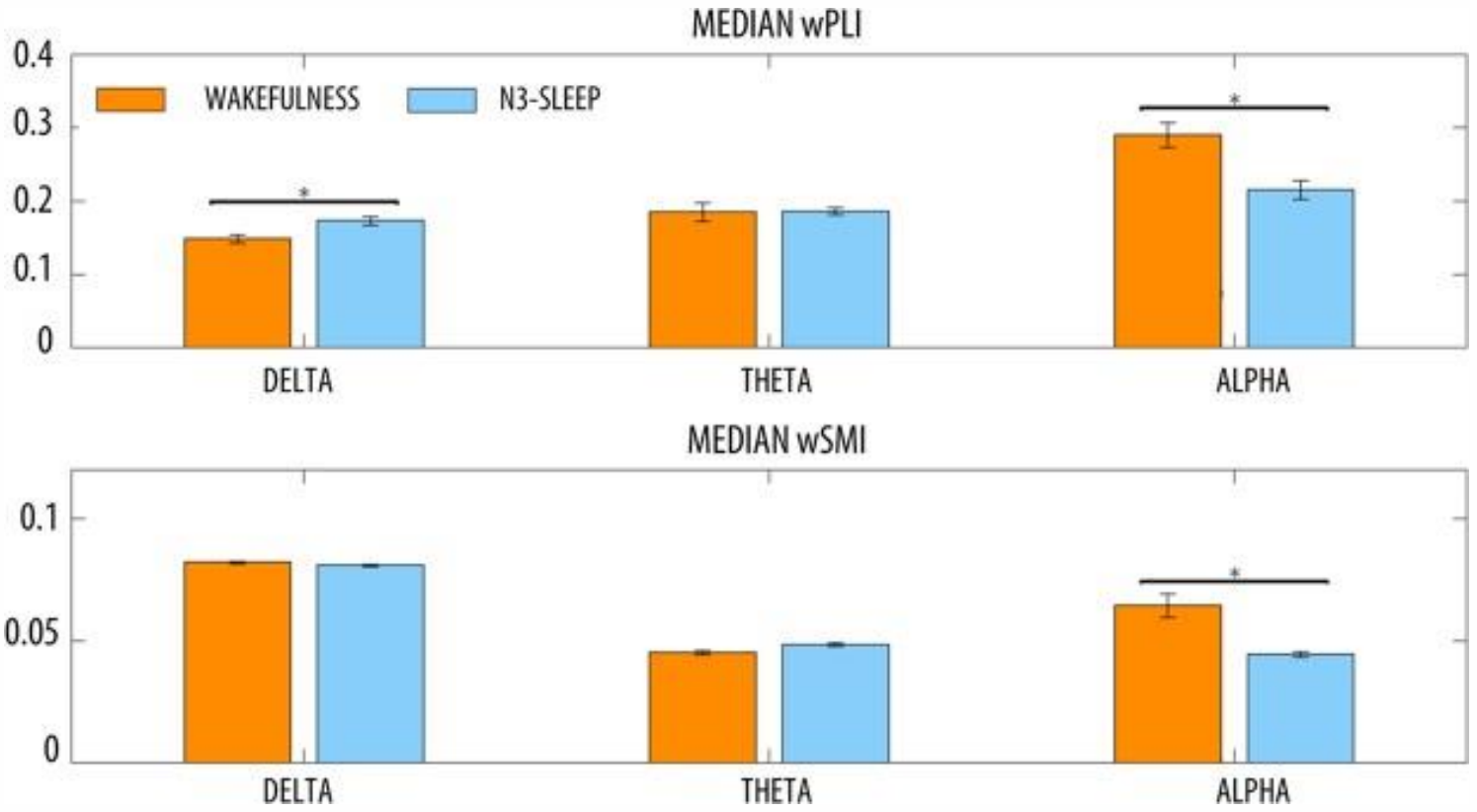
Calculating the PSI from the phase angles of the cross spectral density

Tsai et al. Neurosci Lett 2010

# WHAT ARE THE PROBLEMS WITH LINEAR METHODS AND UNIDIRECTIONALITY?

- Non-linear interactions (eg. Large increases above a certain threshold) result in misrepresentations in linear connectivity
- Can we really exclude unidirectionality in neural interactions?
  - Just very rarely and hypothetically (see for example the case of thalamo-cortico-thalamic interactions)

# MUTUAL SYMBOLIC INFORMATION




It can complete WPLI-measurements

Sci Rep. 2019; 9: 8894.

# CLOSING REMARKS

- We could still discuss:
  - Instantaneous phase differences – Hilbert transformation (perhaps during the last lecture)
- Questions? ☺