Electromagnetic Brain Mapping
Functional Connectivity

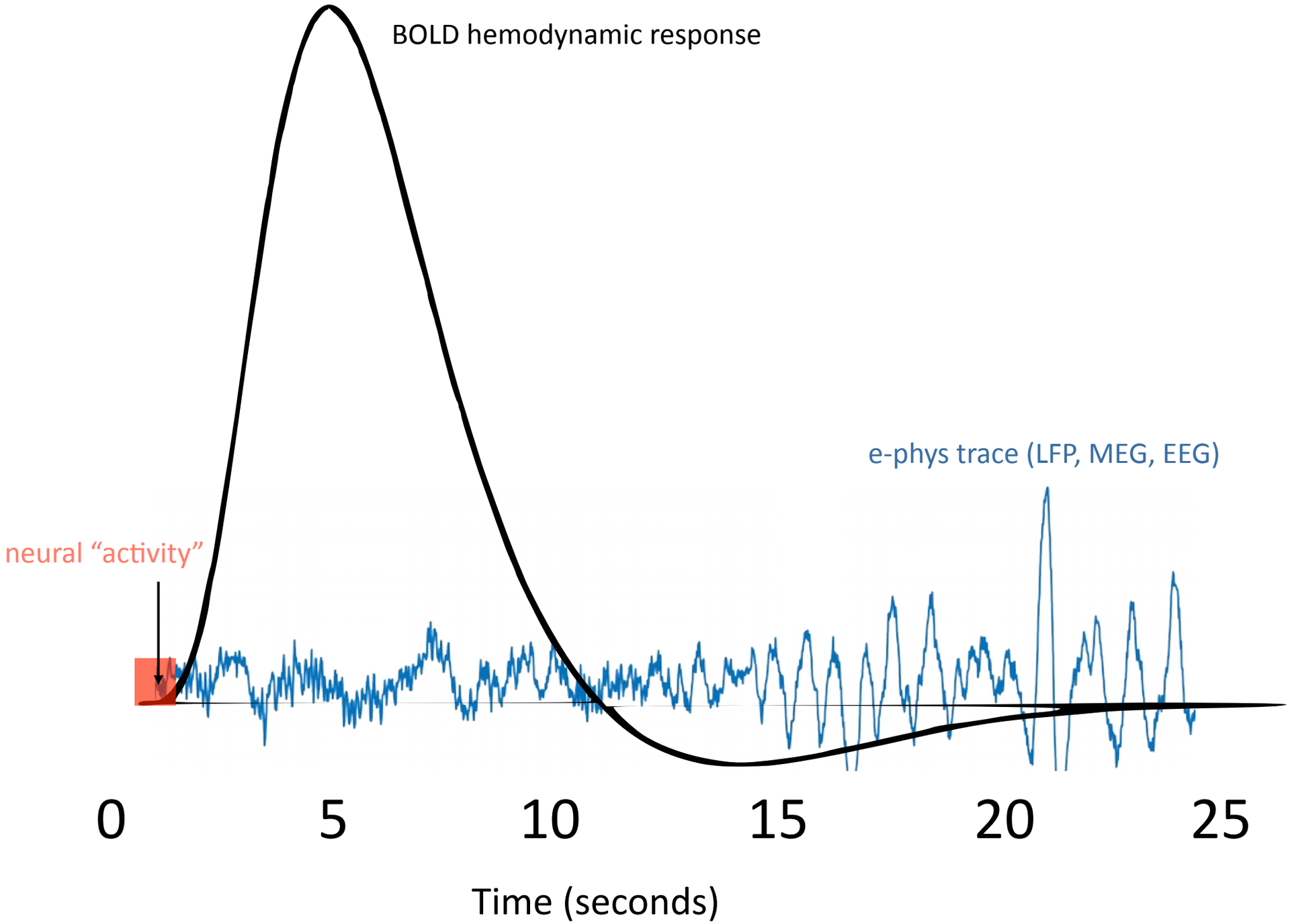
Sylvain Baillet

McConnell Brain Imaging Centre
Montreal Neurological Institute
McGill University

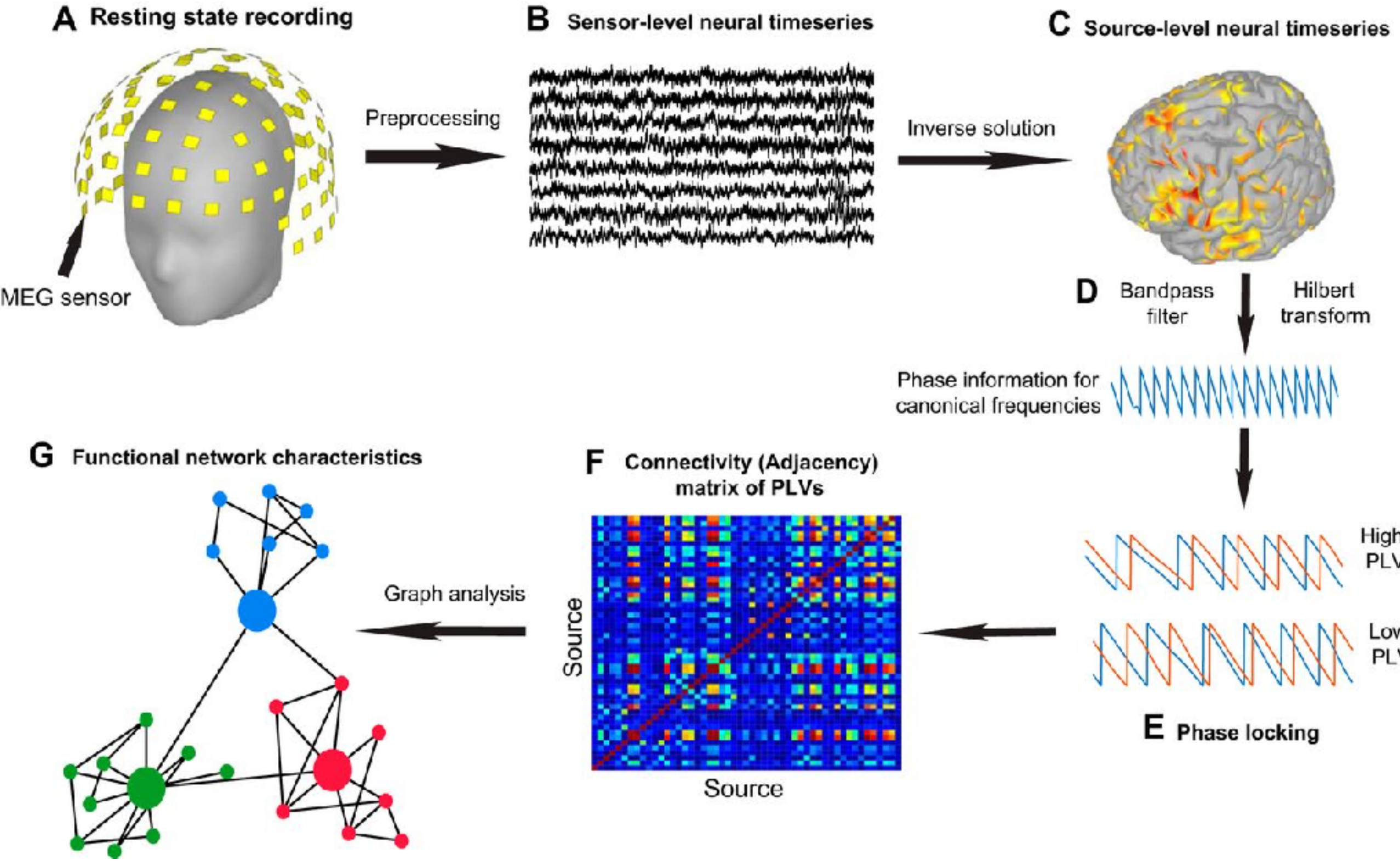
[sylvain.baillet@mcgill.ca]

Google it! 'MEG MNI '

MEG/EEG temporal resolution vs. fMRI:
a curse and many opportunities for connectivity analysis



Connectivity estimation: typical data flow



Alhourani et al., *J Neurophysiology* (2016)

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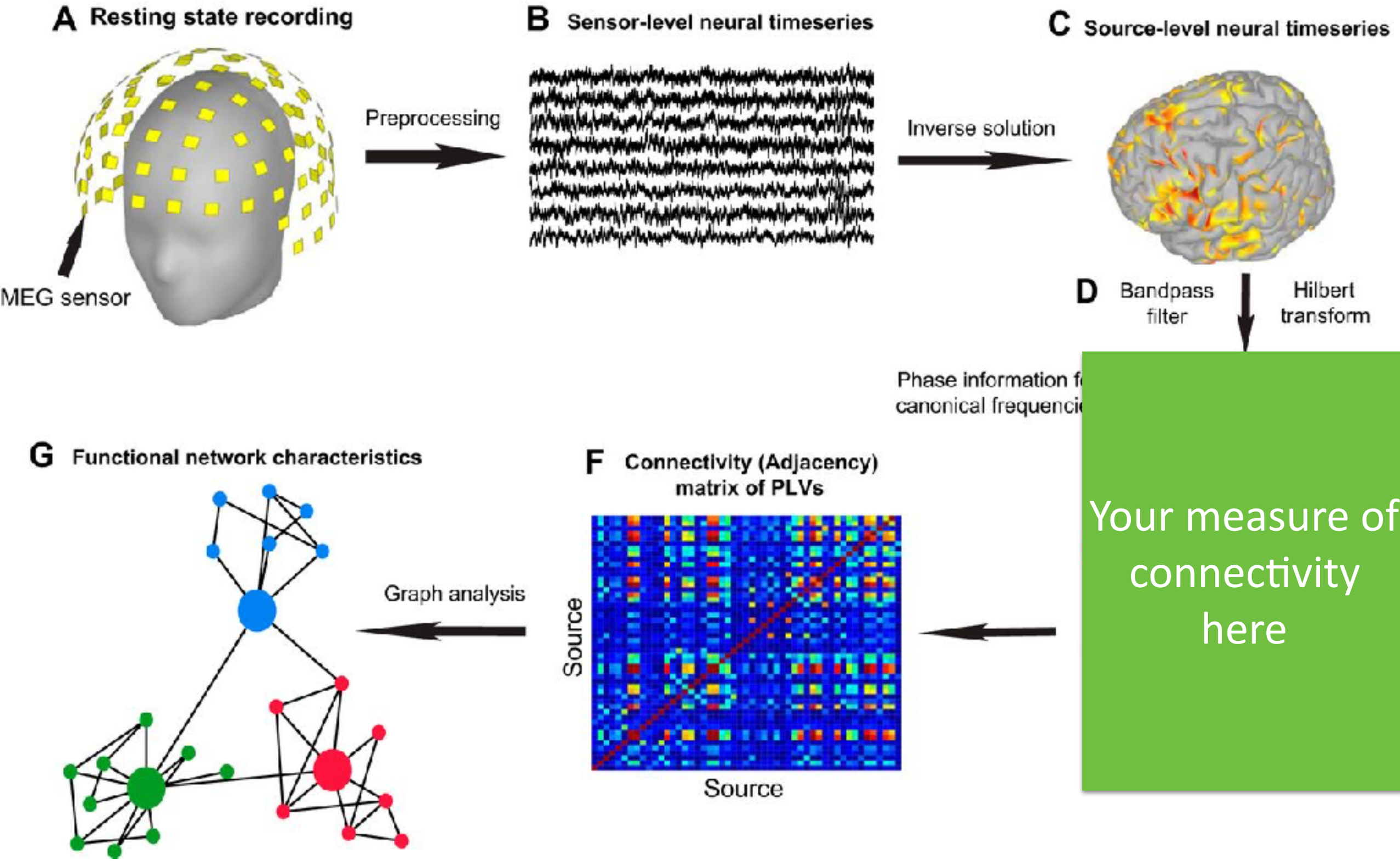

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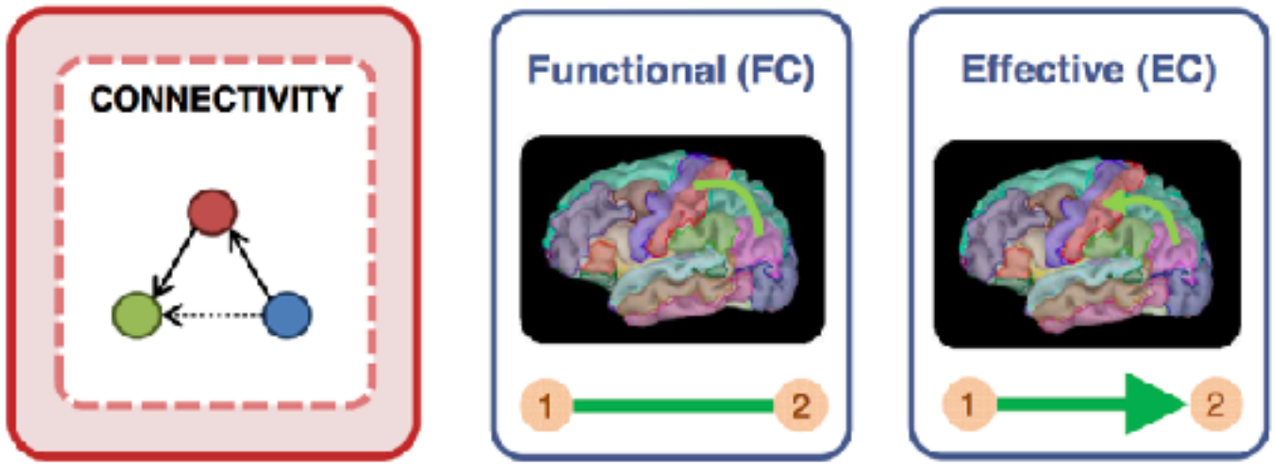
Elements of Connectivity



adapted from Niso et al., *Neuroinformatics* (2013)

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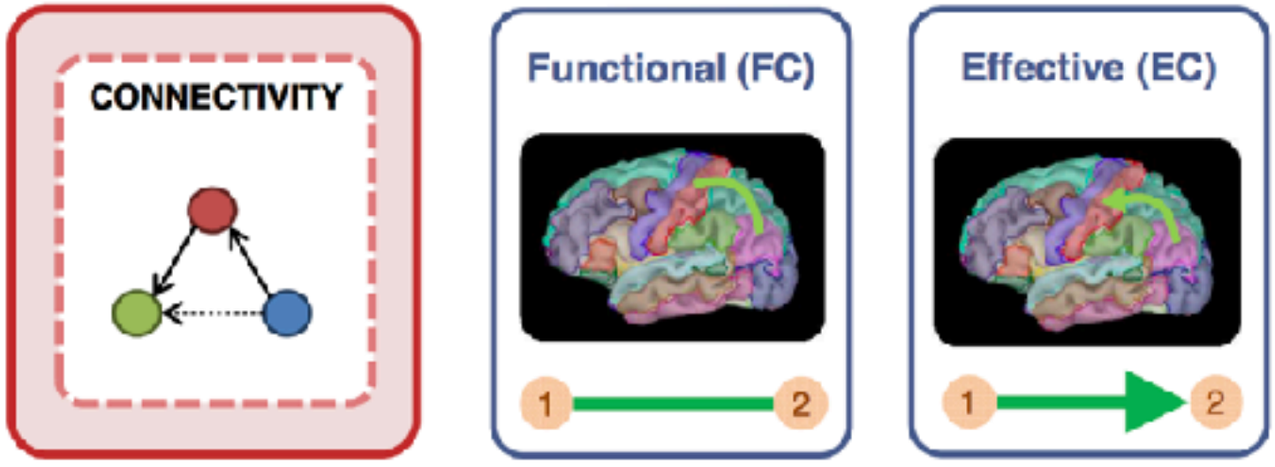
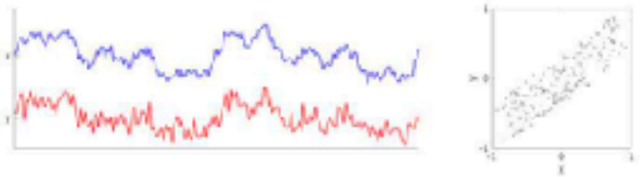
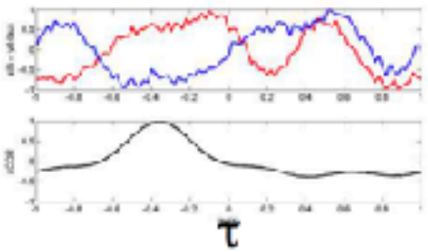


- Pearson's correlation (t)

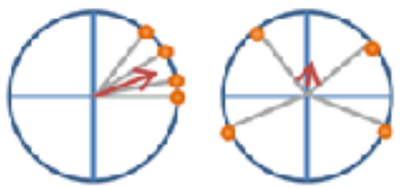


- Cross-Correlation (t)



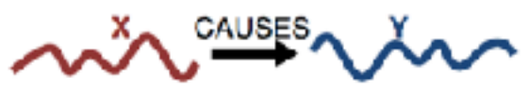
- Coherence (f)

- Phase Loking Value (f)



- Mutual information (t)

- Granger causality (t)



→ For a comprehensive review on these and other functional and effective connectivity metrics: **(Niso et al. Neuroinformatics, 2013)**

adapted from Niso et al., *Neuroinformatics* (2013)

Elements of Connectivity

1. **Classical Methods (CM)**
   - Correlation (COR)
   - CrossCorrelation (xCOR)
   - Coherence (COH)
   - Imaginary Coherence (iCOH)
   - Phase Slope Index (PSI)

2. **Phase Synchronization (PS)**
   - Phase Locking Value (PLV)
   - Phase Lag Index (PLI)
   - Weigthed Phase Lag Index (wPLI)
   - ρ index (RHO)
   - Directionality Phase Index (DPI)

3. **Generalized Synchronization (GS)**
   - S index
   - H index
   - N index
   - M index
   - L index
   - Synchronization Likelihood (SL)

4. **Granger Causality (GC)**
   - Granger Causality (GC)
   - Partial Directed Coherence (PDC)
   - Direct Transfer Function (DTF)

5. **Information Thoretic (IT)**
   - Mutual Information (MI)
   - Transfer Entropy (TE)
   - Partial Mutual Information (PMI)
   - Partial Transfer Entropy (PTE

H.E.R.M.E.S.

http://hermes.ctb.upm.es

(Niso et al. Neuroinformatics, 2013)

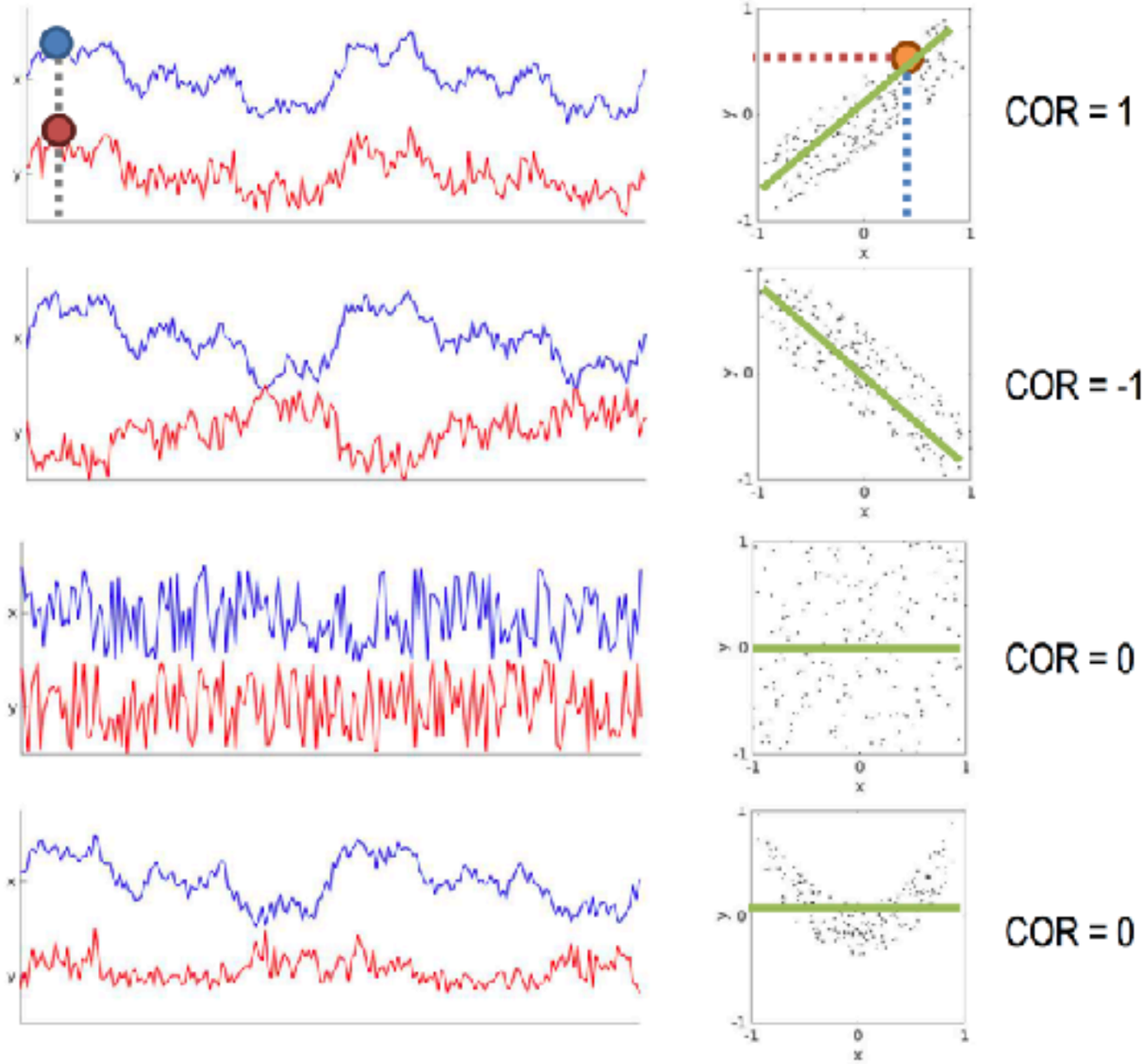
neuro MEG @McGill

Classical measures of interactions

Pearson's correlation (COR)

- Linear correlation in time domain between x(t) and y(t) at zero lag
- **$-1 \leq R_{xy} \leq 1$**

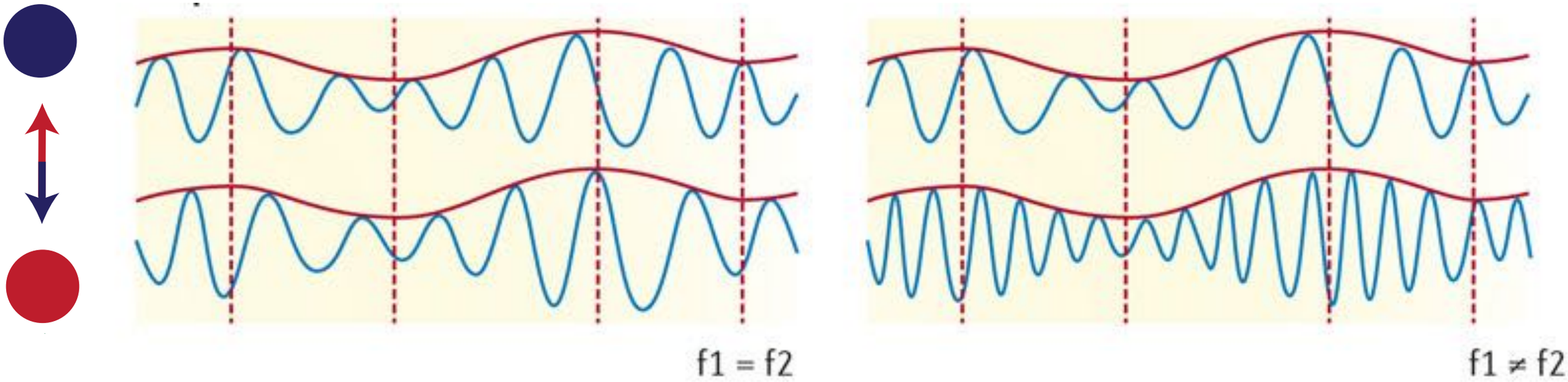
$$R_{xy} = \frac{1}{N} \sum_{k=1}^{N} x(k)\, y(k)$$



adapted from Niso et al., *Neuroinformatics* (2013)

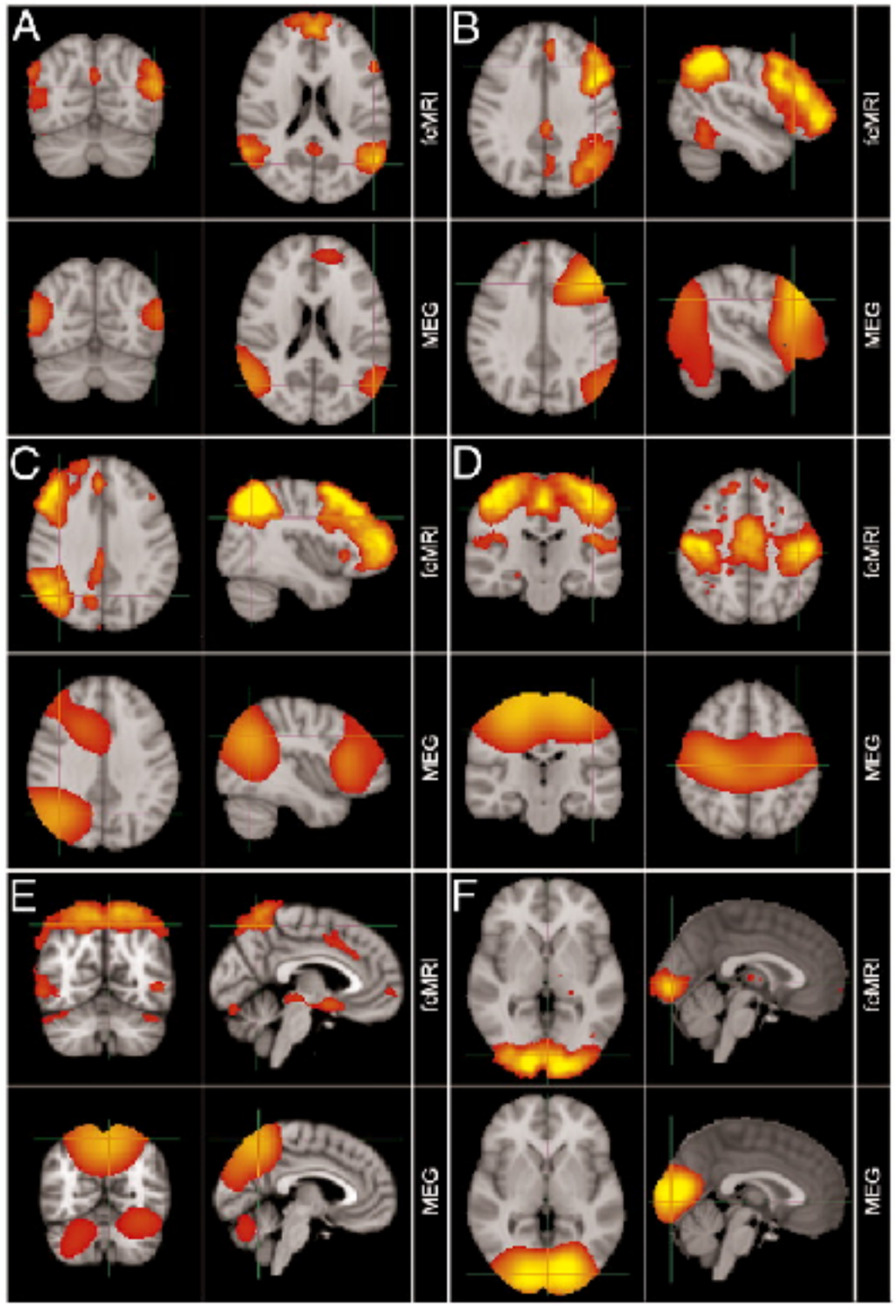
Classical measures of interactions

Narrow-band amplitude correlation



Siegel et al., *Nat Rev Neurosci* (2012)

Narrow-band amplitude correlation in the resting-state



Brookes et al., *PNAS* (2011)

Classical measures of interactions

Coherence (COH)

Magnitude squared coherence

- Linear correlation between x(t) and y(t) as a function of the frequency
- $0 \leq COH_{xy}(f) \leq 1$

$$COH_{xy}(f) = \left|K_{xy}(f)\right|^2 = \frac{\left|S_{xy}(f)\right|^2}{S_{xx}(f)\,S_{yy}(f)}$$

Coherency function

- How the phases of x(t) and y(t) are coupled to each other

$$C_{xy}(f) = \frac{S_{xy}(f)}{\sqrt{S_{xx}(f)S_{yy}(f)}}$$

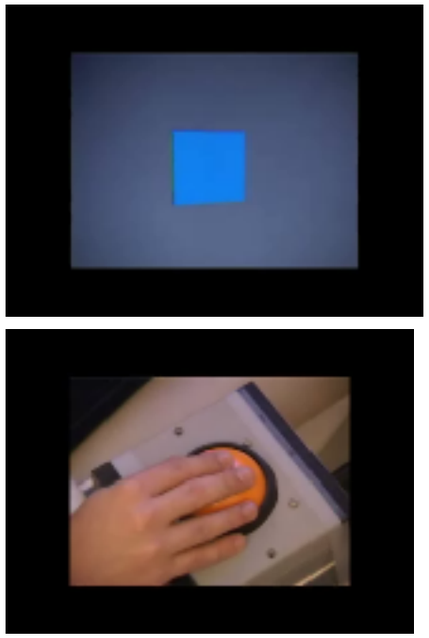
- Normalized cross-spectrum

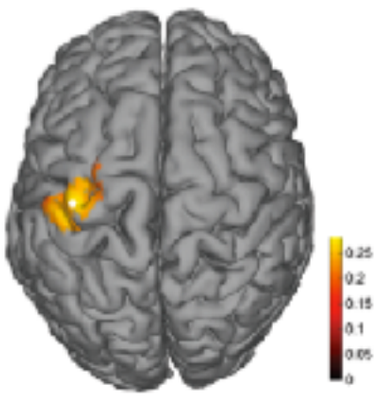
$$S_{xy}(f) = \left\langle X(f) \cdot Y^*(f) \right\rangle$$

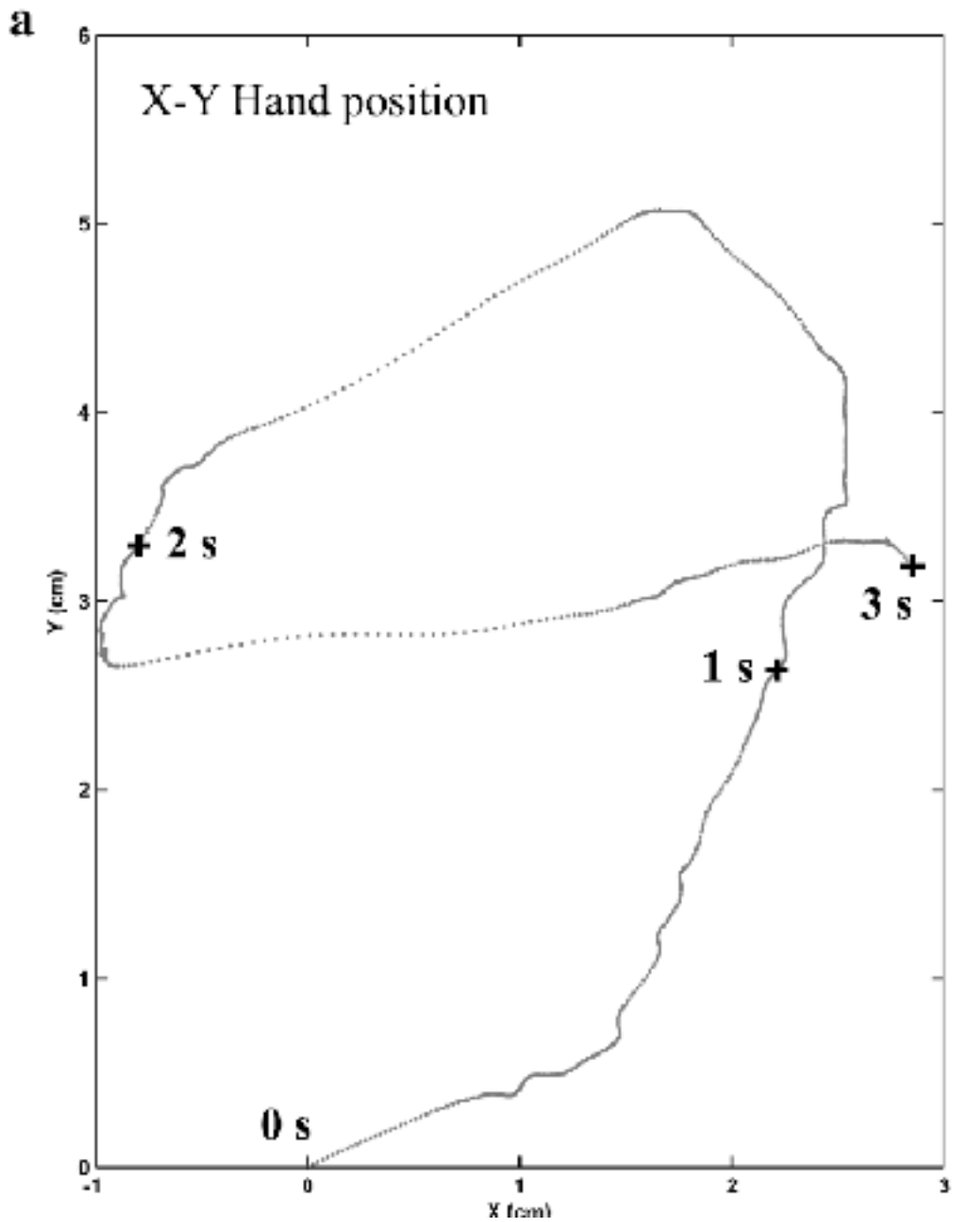
  - Sxy(f): cross spectrum
  - Sxx(f): power spectral density

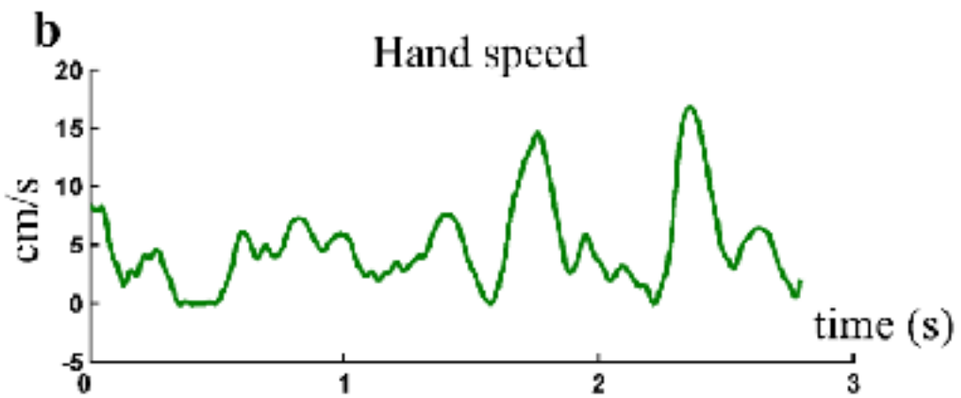
adapted from Niso et al., *Neuroinformatics* (2013)

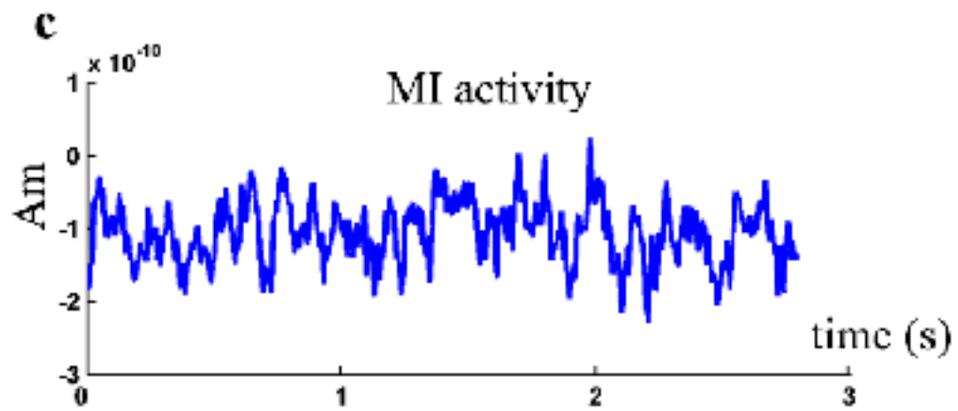
Brain-behaviour coherent activity: velocity of hand movements

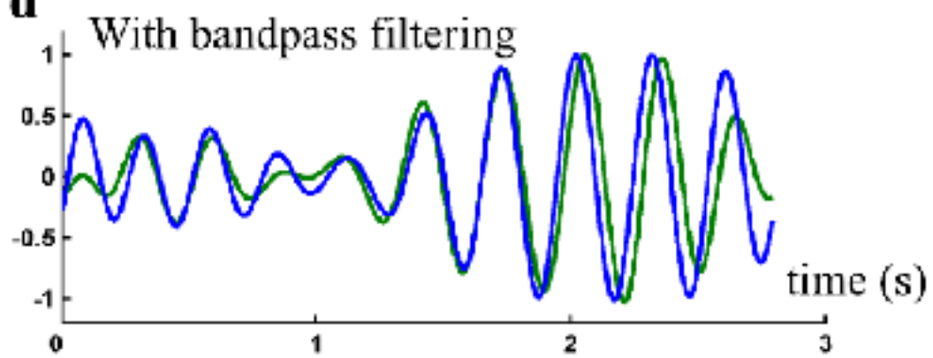












Jerbi et al., *PNAS* (2007)

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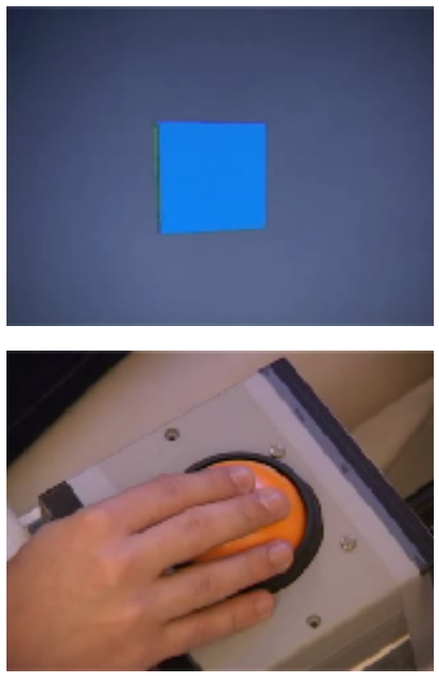

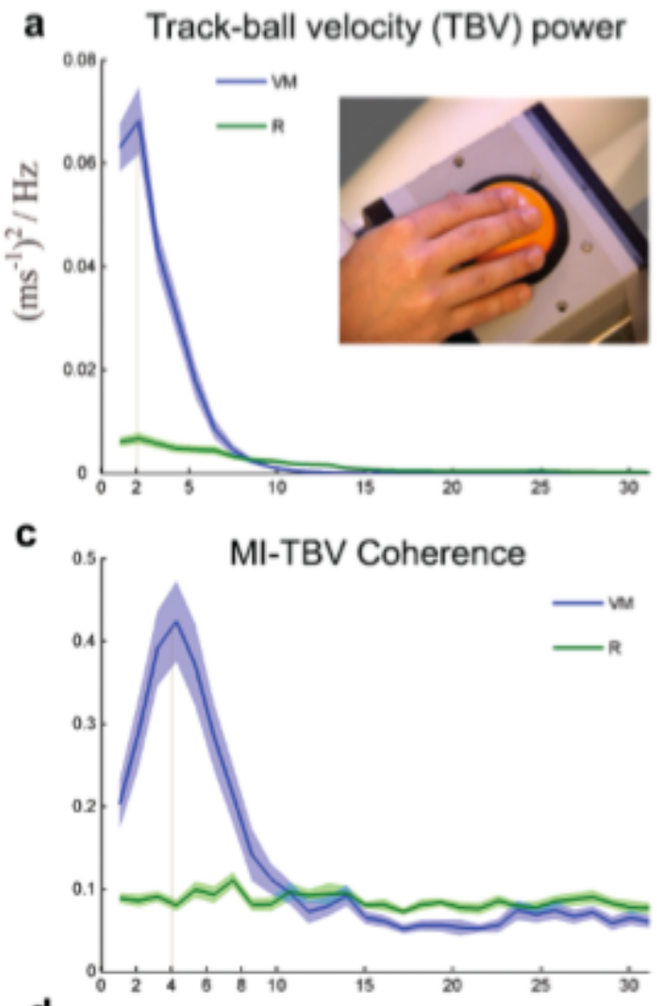

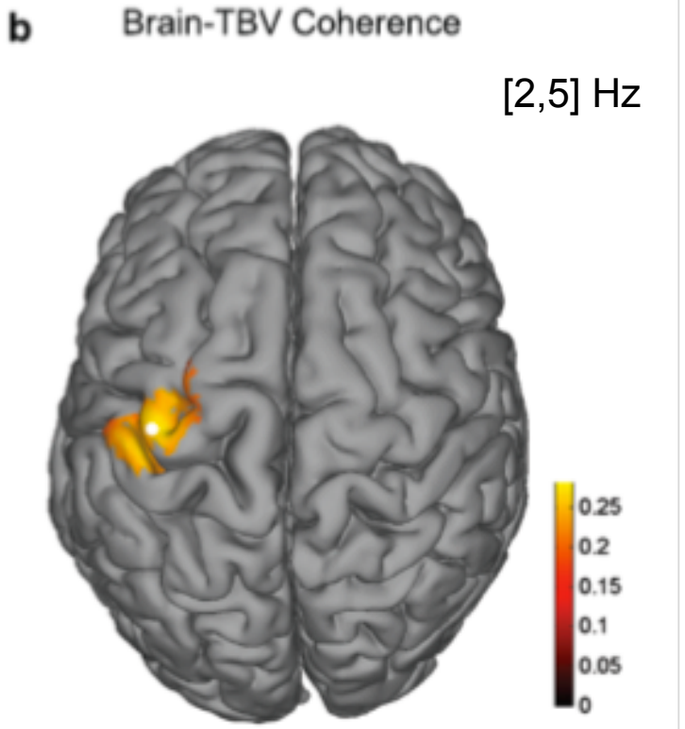

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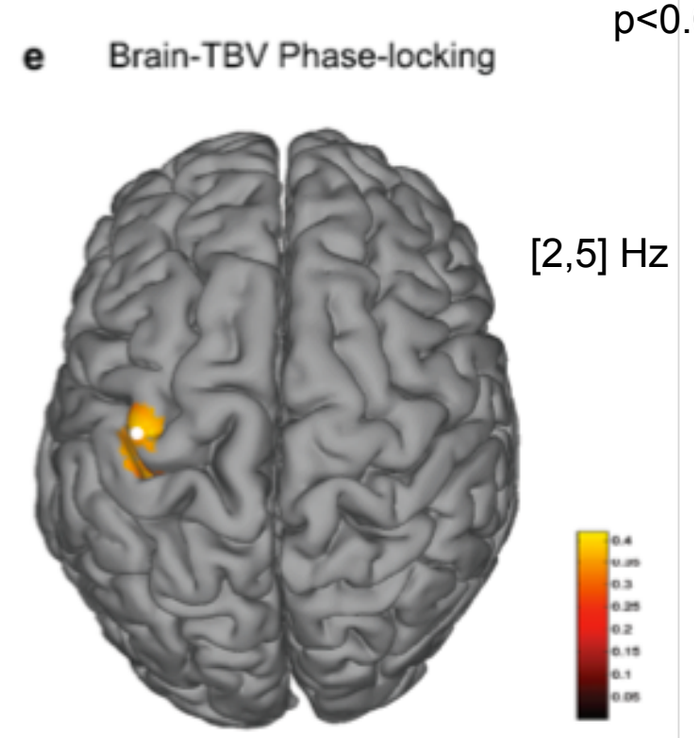

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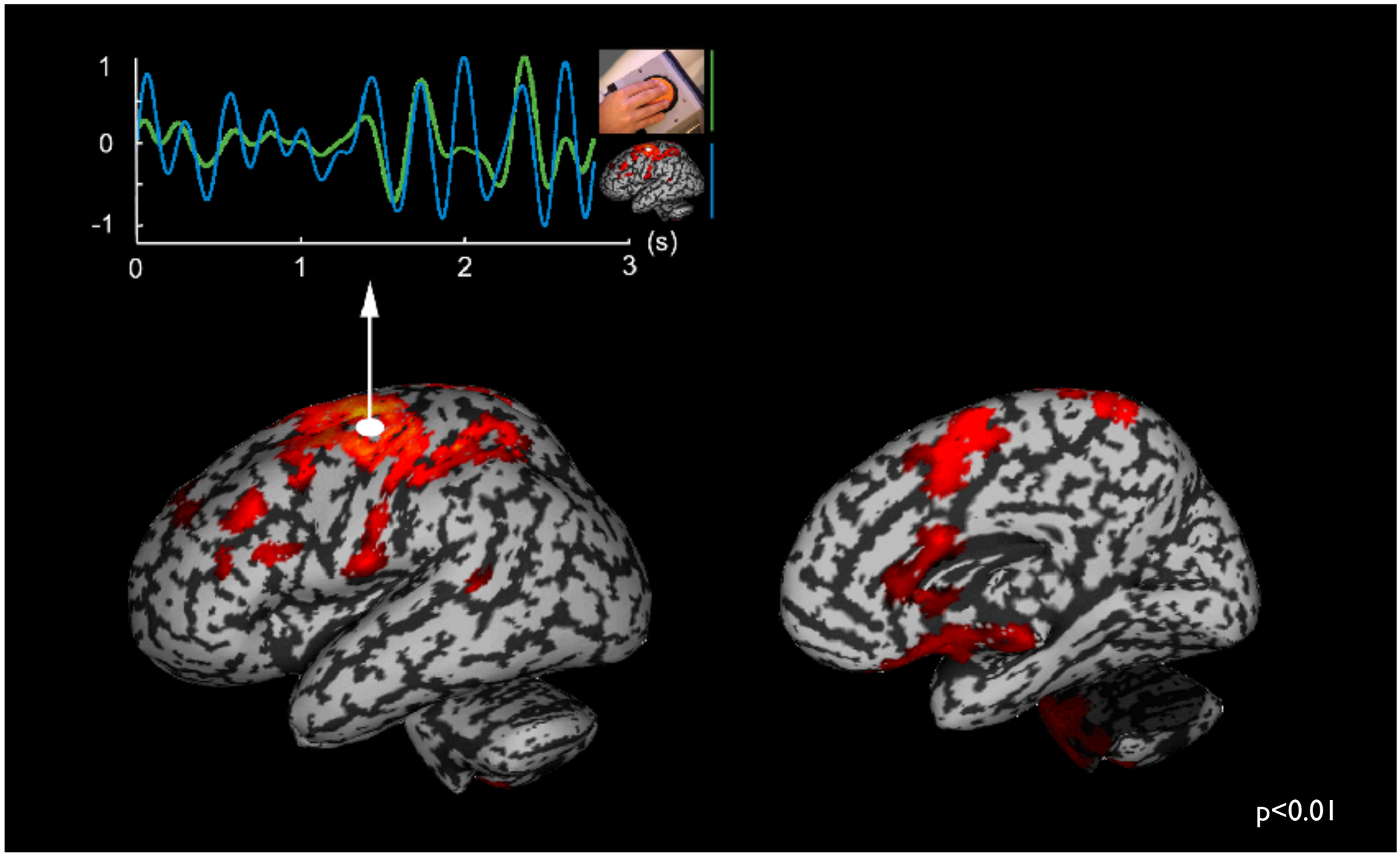
Jerbi et al., *PNAS* (2007)

Cortico-cortical coherence during visuomotor coordination



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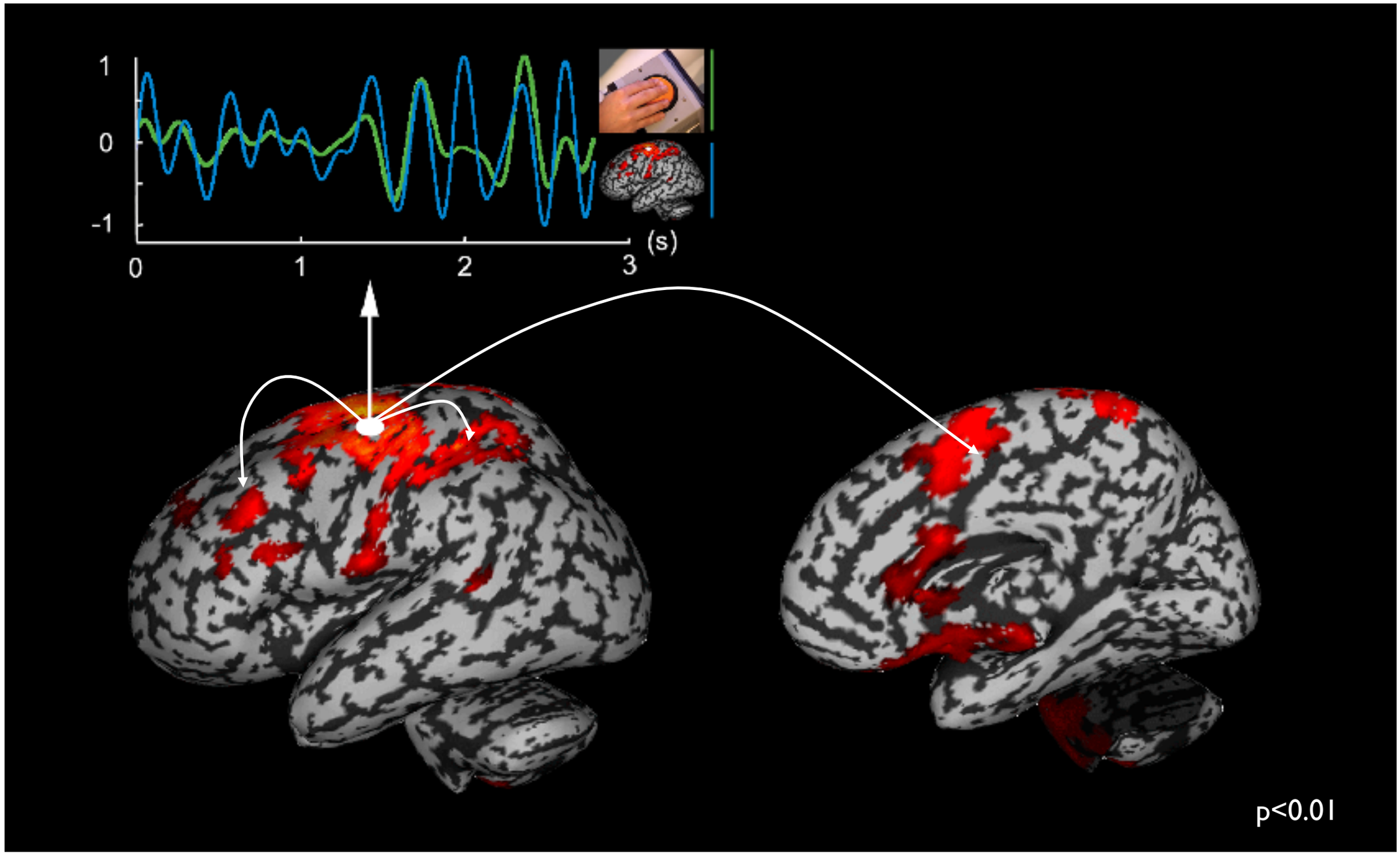

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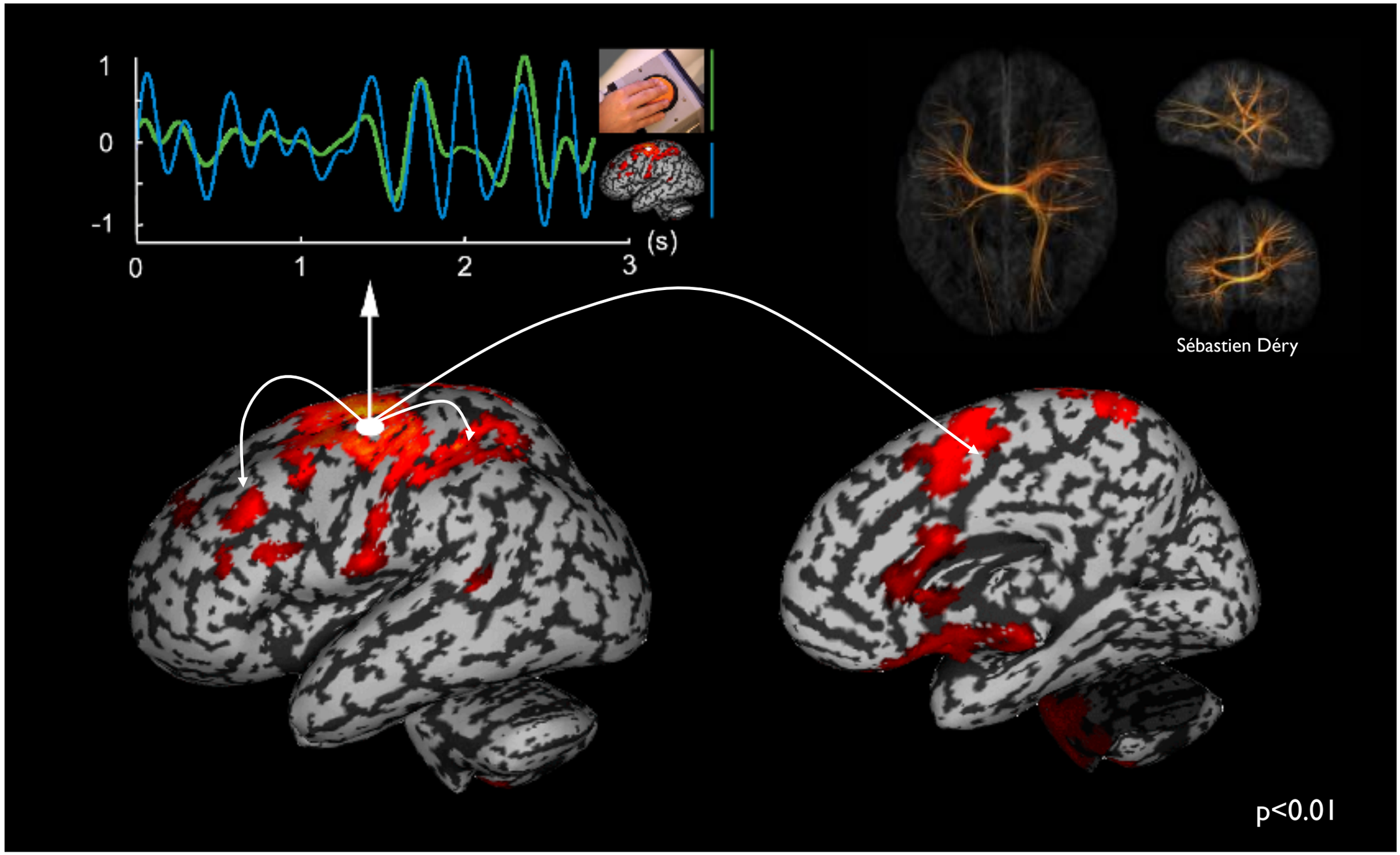
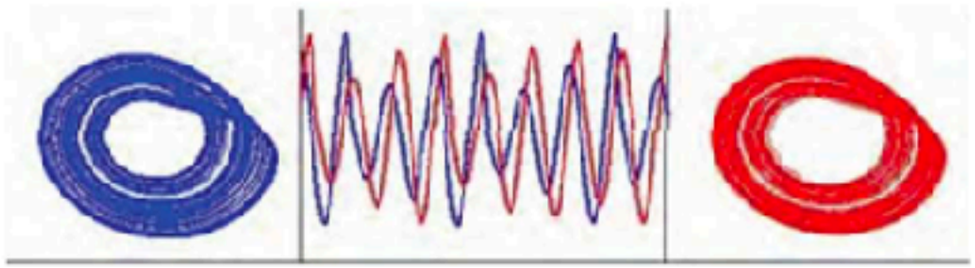


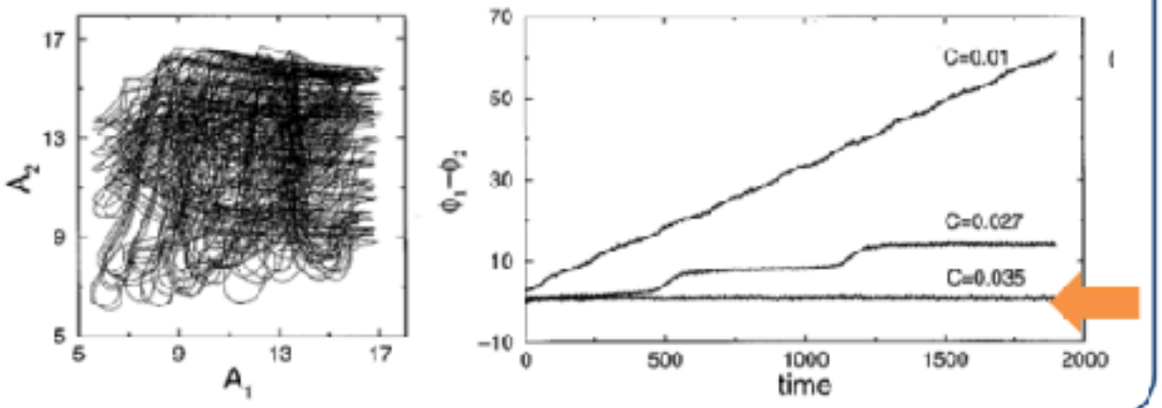
Jerbi et al., *PNAS* (2007)

Measures considering neural activity as oscillations

Phases of coupled oscillators synchronize, even though their amplitudes remain uncorrelated

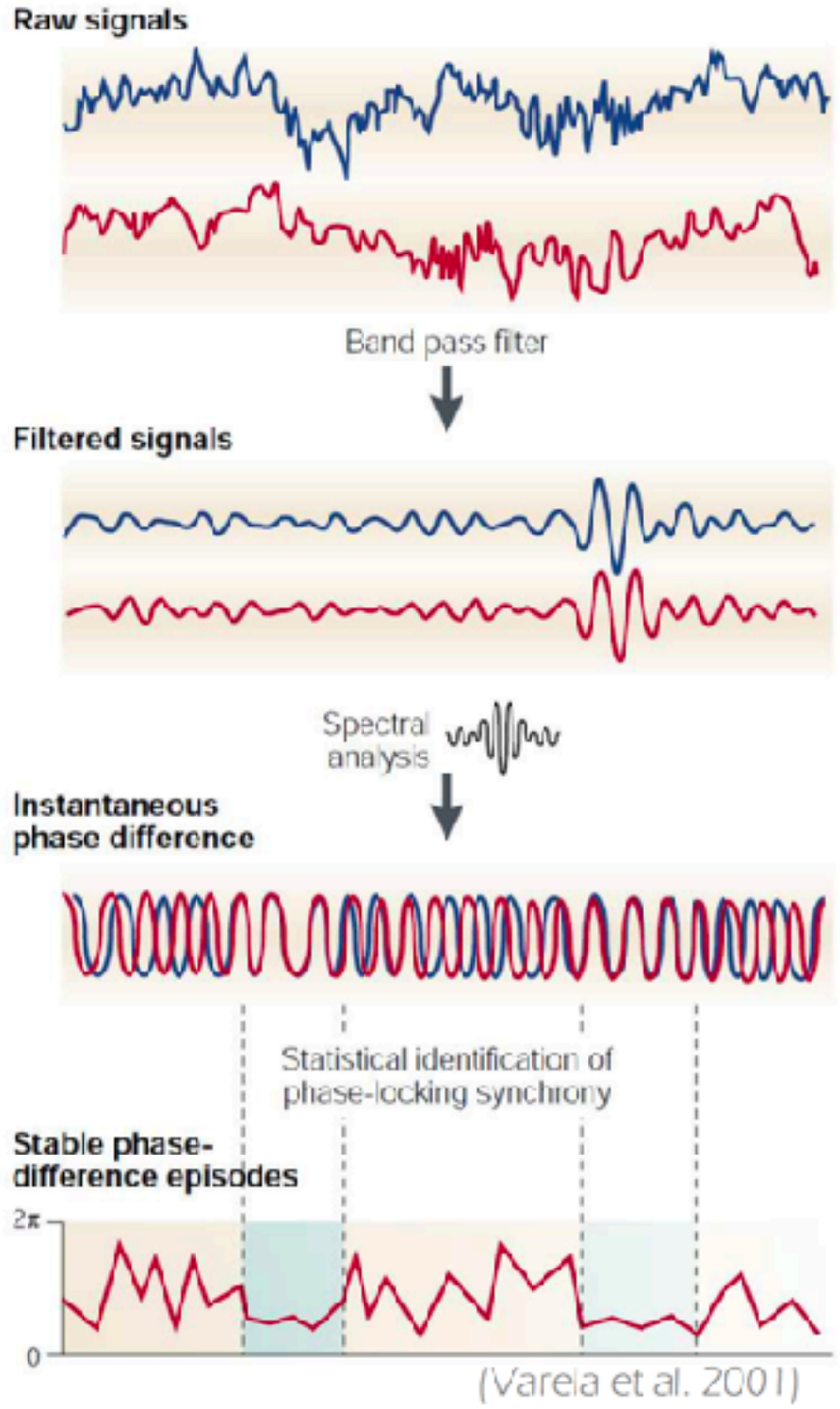


(Rosenblum et al. 1996)



Phase locking condition

$$\Delta\phi(t) = \left|\phi_x(t) - \phi_y(t)\right| \leq cte$$



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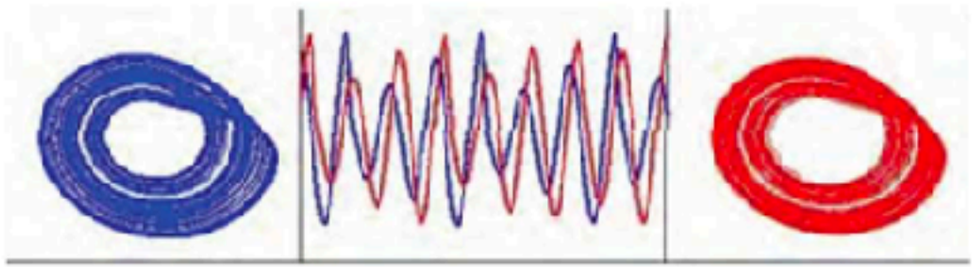

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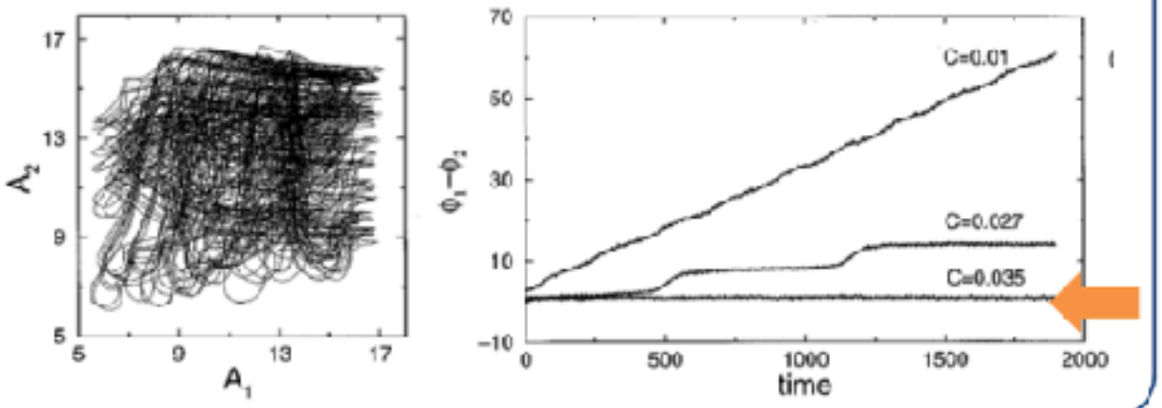

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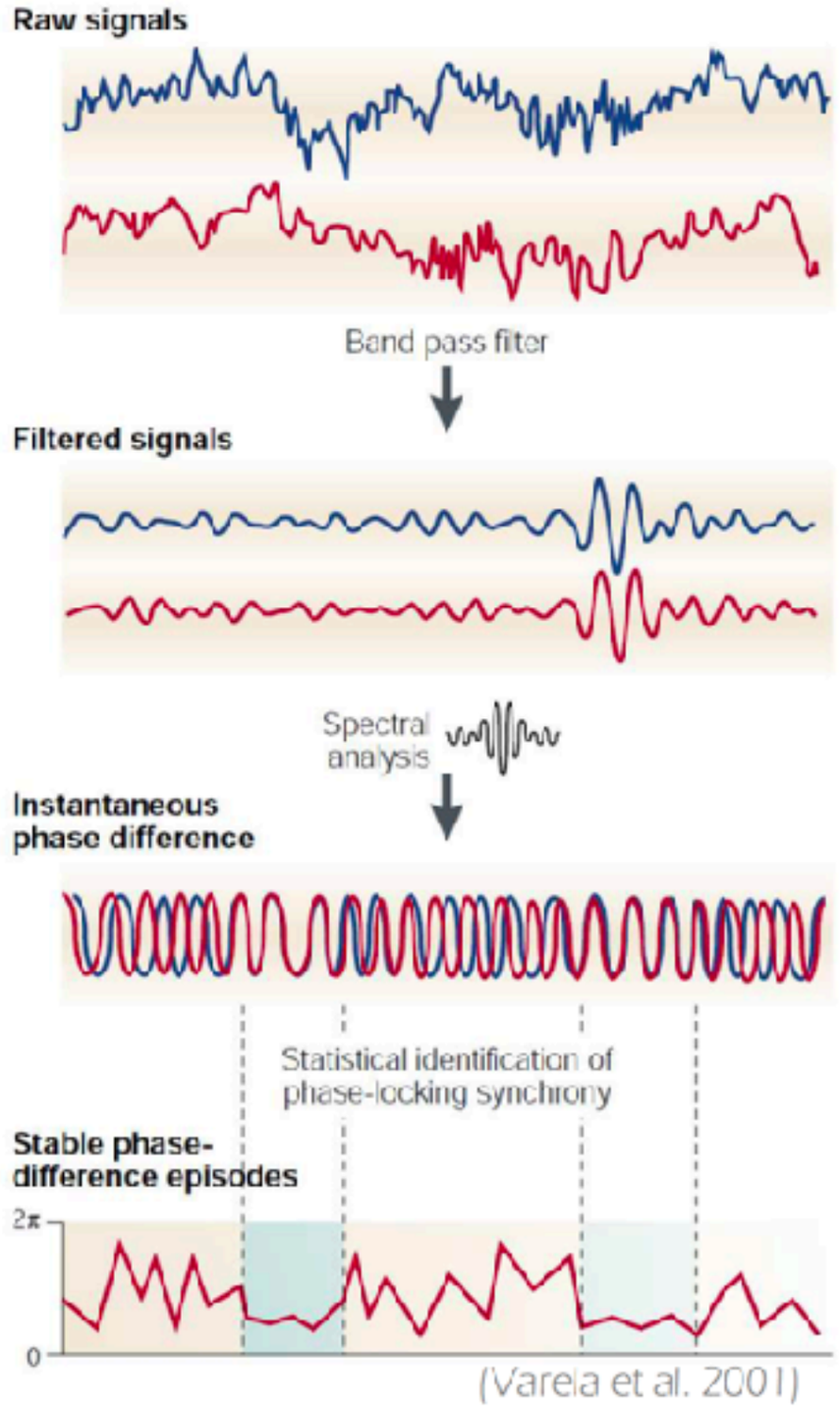


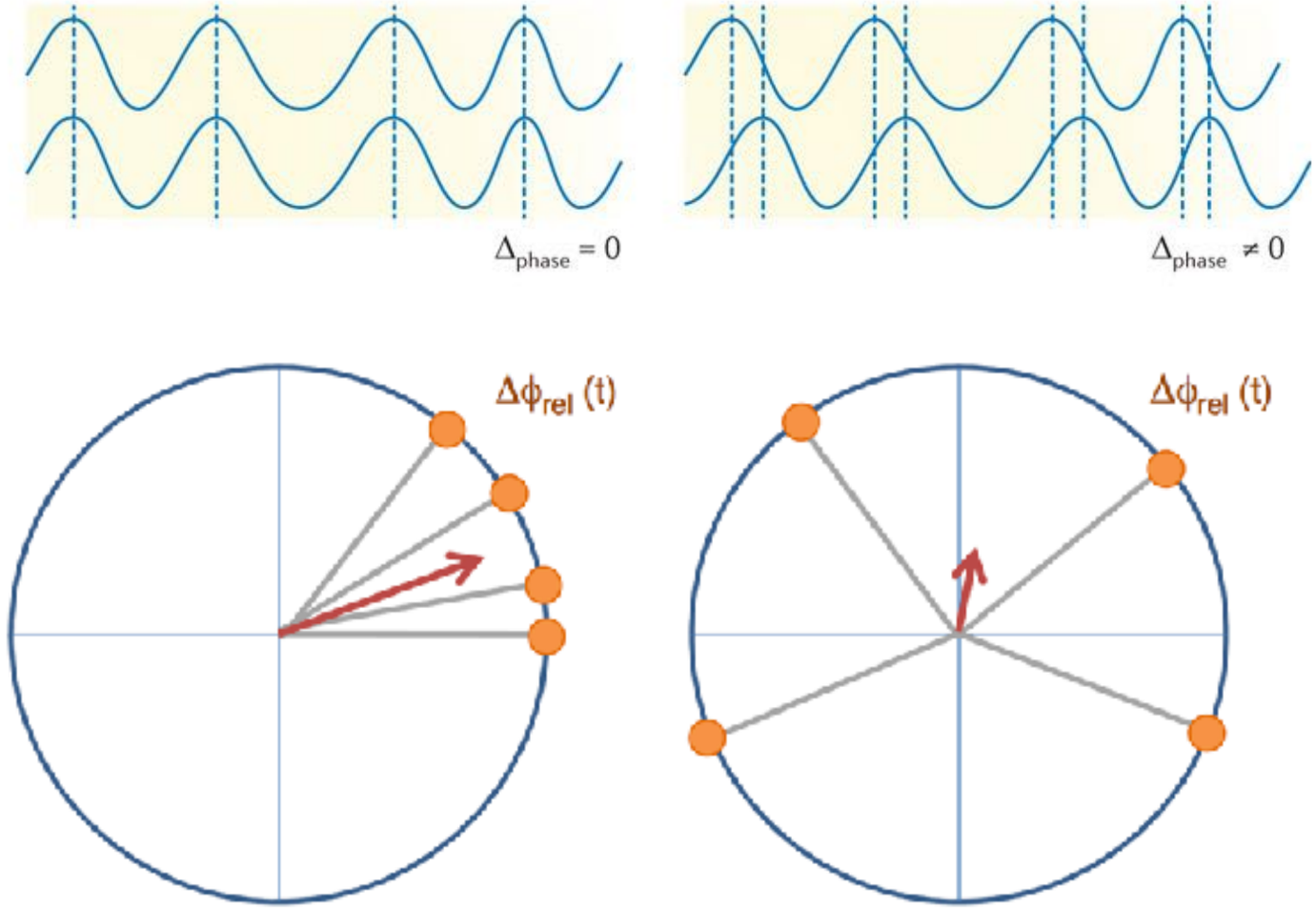
adapted from Niso et al., *Neuroinformatics* (2013)

Measures considering neural activity as oscillations

Phase Locking Value (PLV)

- (Lachaux et al. 1999)
- How relative phase is distributed over the unit circle
- $0 \leq PLV \leq 1$

$$PLV = \left| \left\langle e^{i\Delta\phi_{rel}(t)} \right\rangle \right| = \left| \frac{1}{N} \sum_{n=1}^{N} e^{i\Delta\phi_{rel}(t_n)} \right|$$



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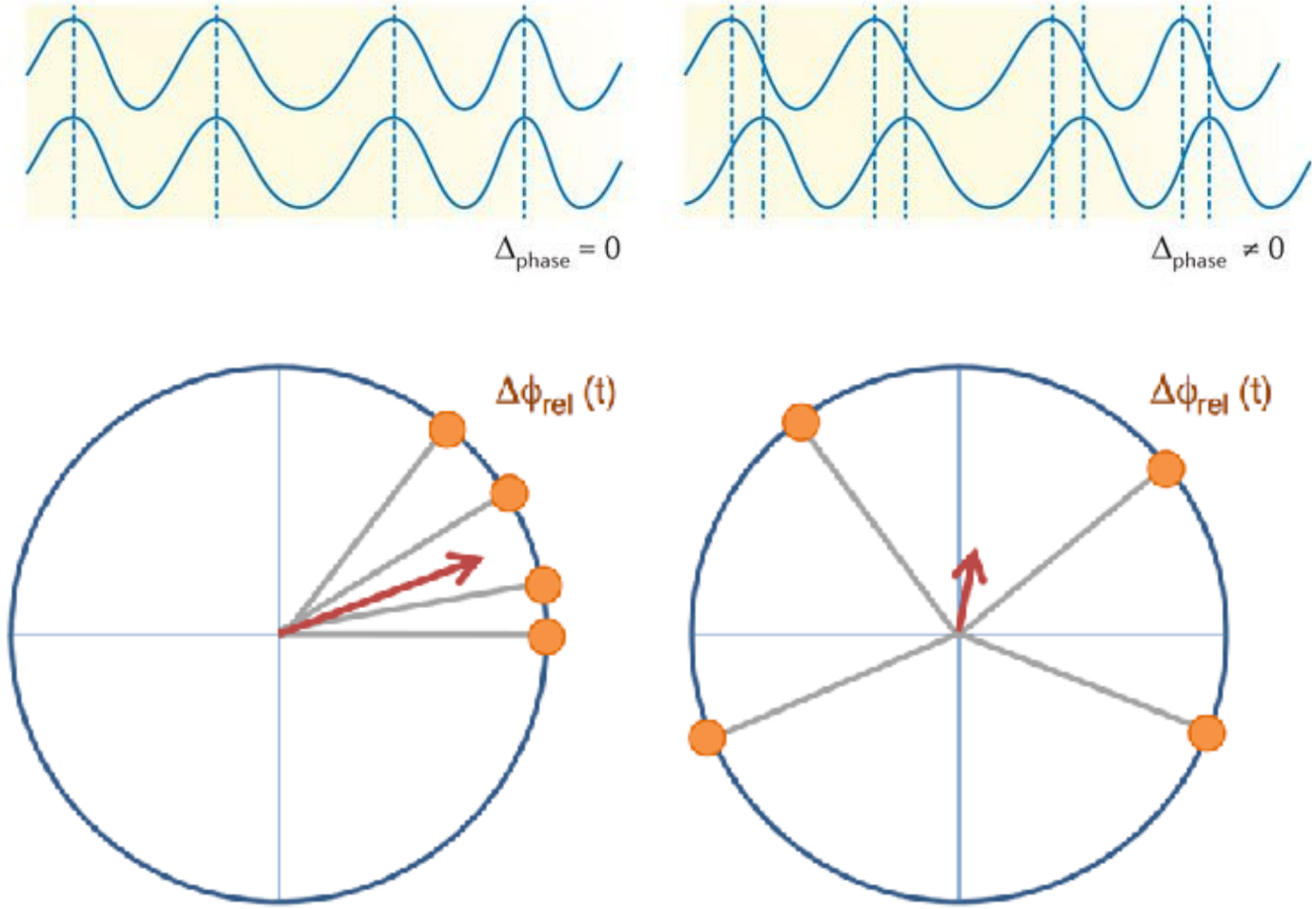

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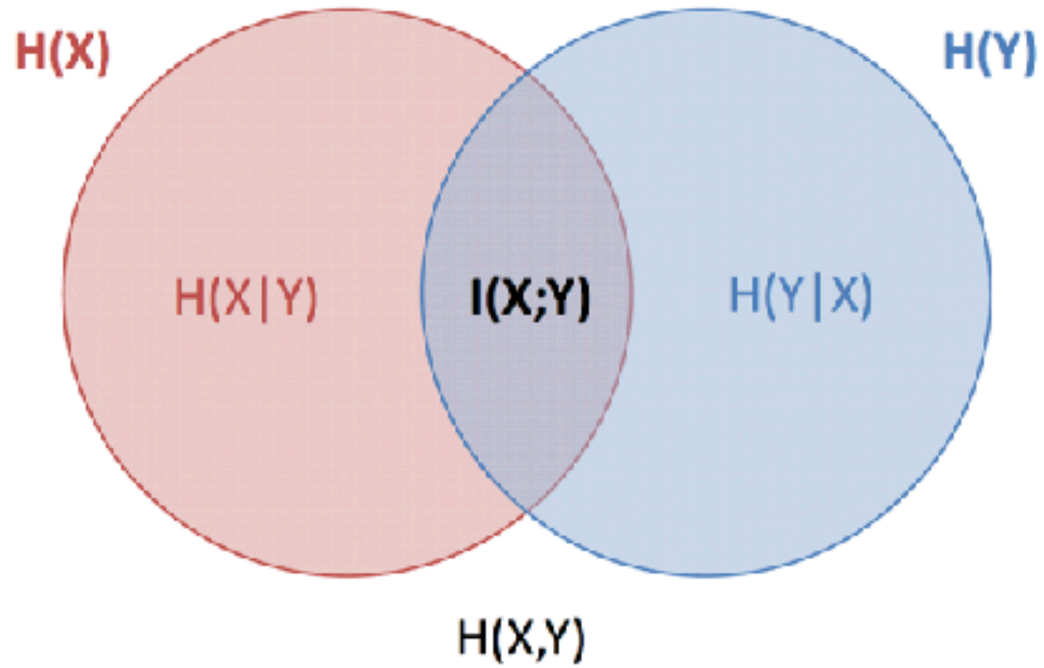
Model-free methods based on information theory

Mutual Information (MI)

- Amount of information that can be obtained about a variable by observing another (**information shared by x and y**)
- $0 \leq MI_{XY} \leq \infty$

$$MI_{xy} = \sum_i p(x,y) \log \frac{p(x,y)}{p(x)\,p(y)}$$

$$MI_{XY} = H(X) + H(Y) - H(X,Y)$$



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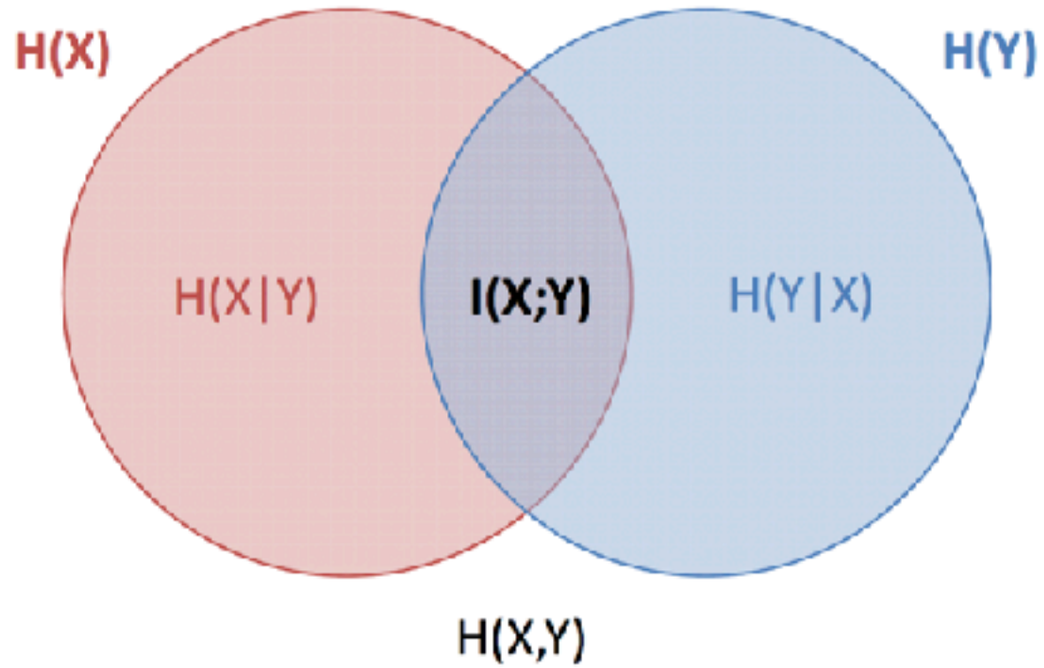

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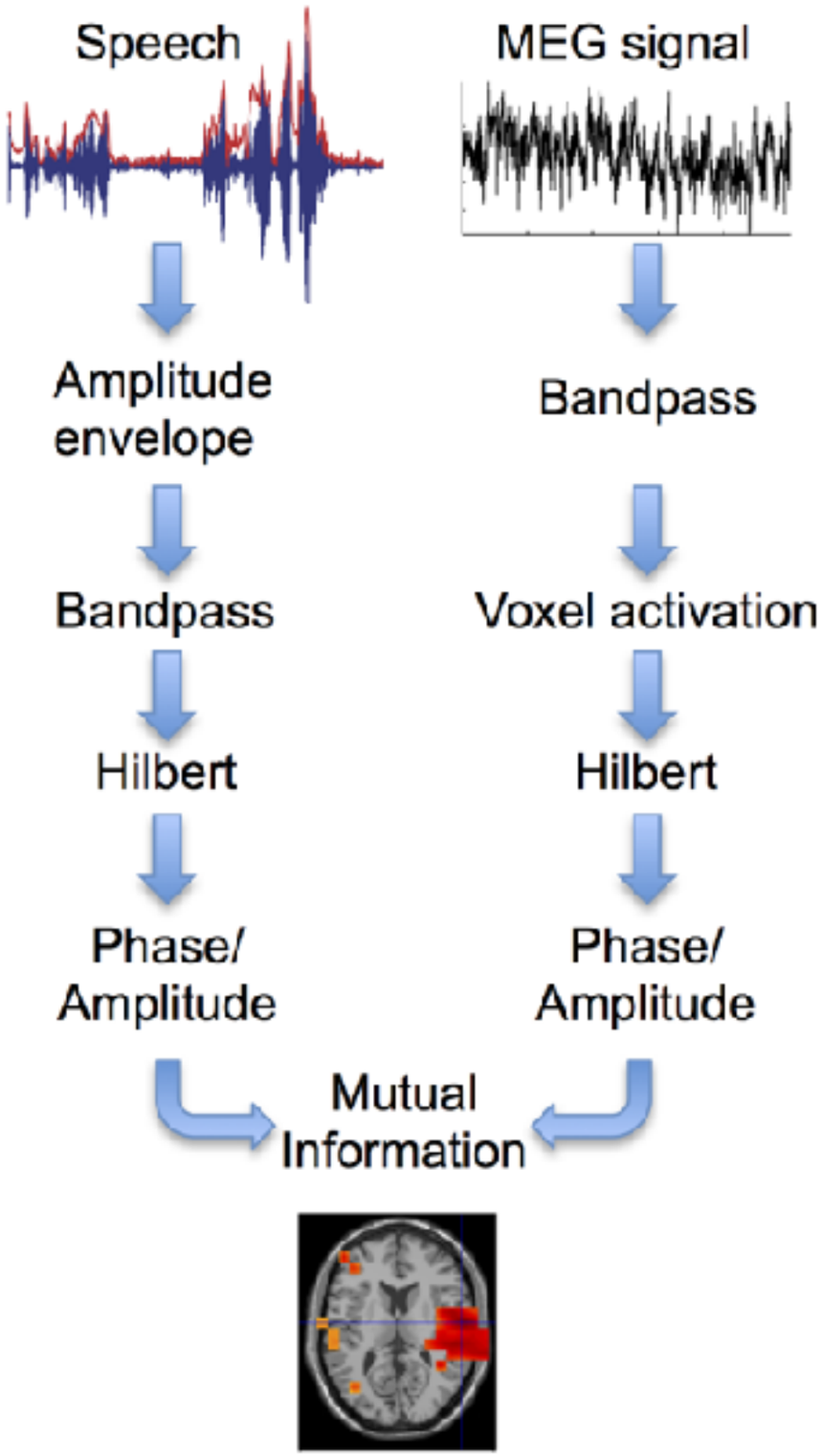

Gross et al., *PLoS Biology* (2013)

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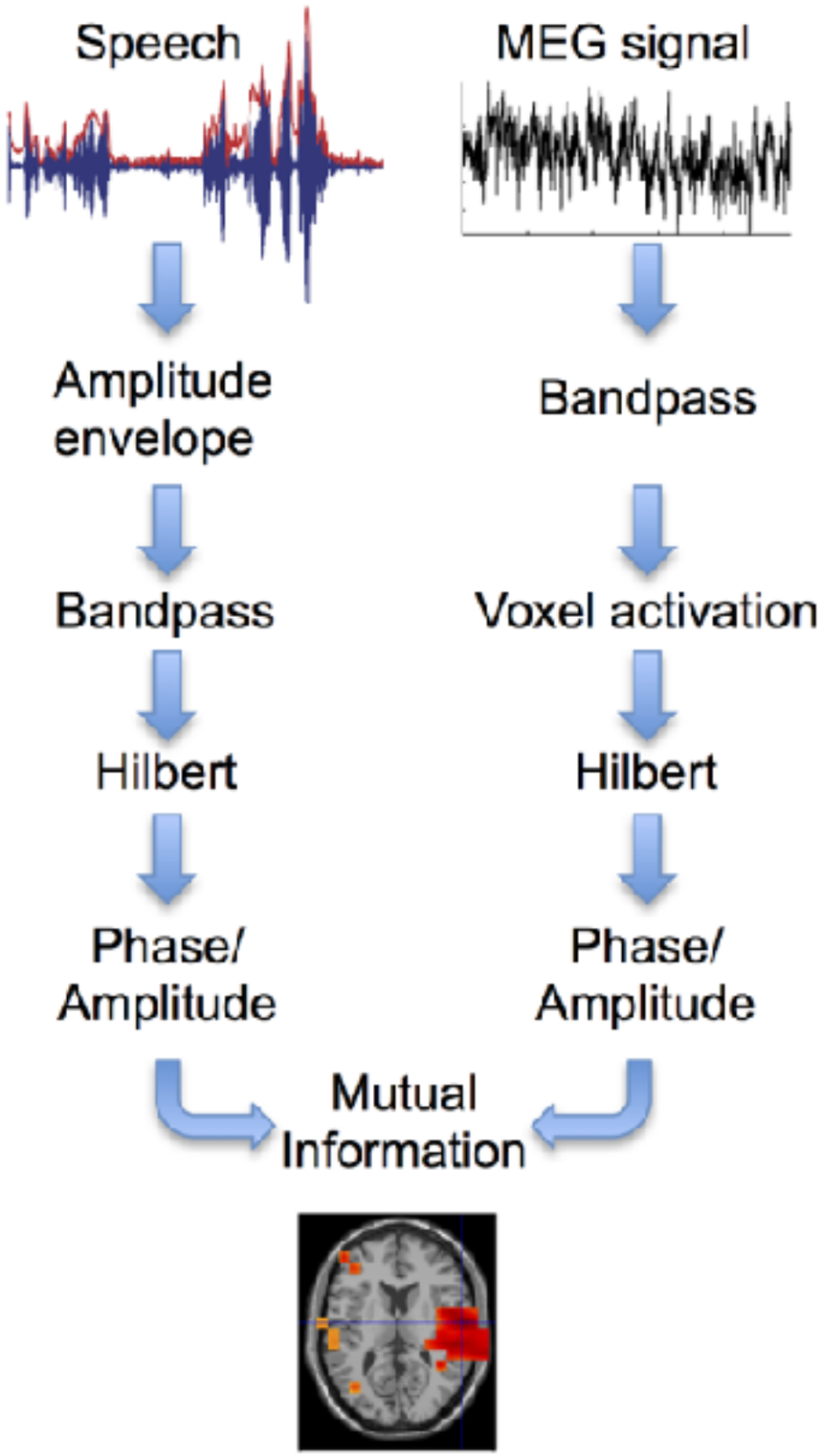

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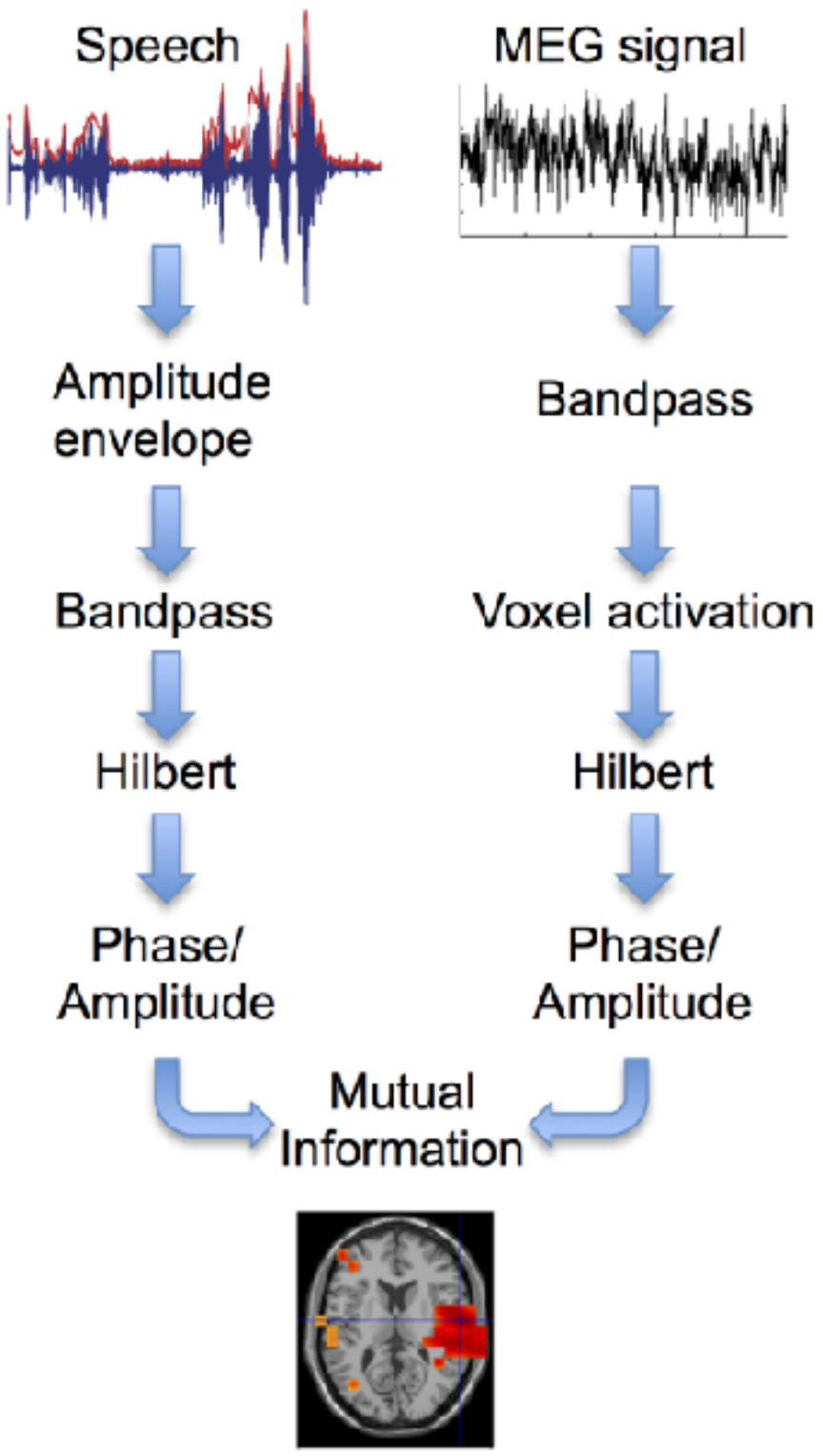

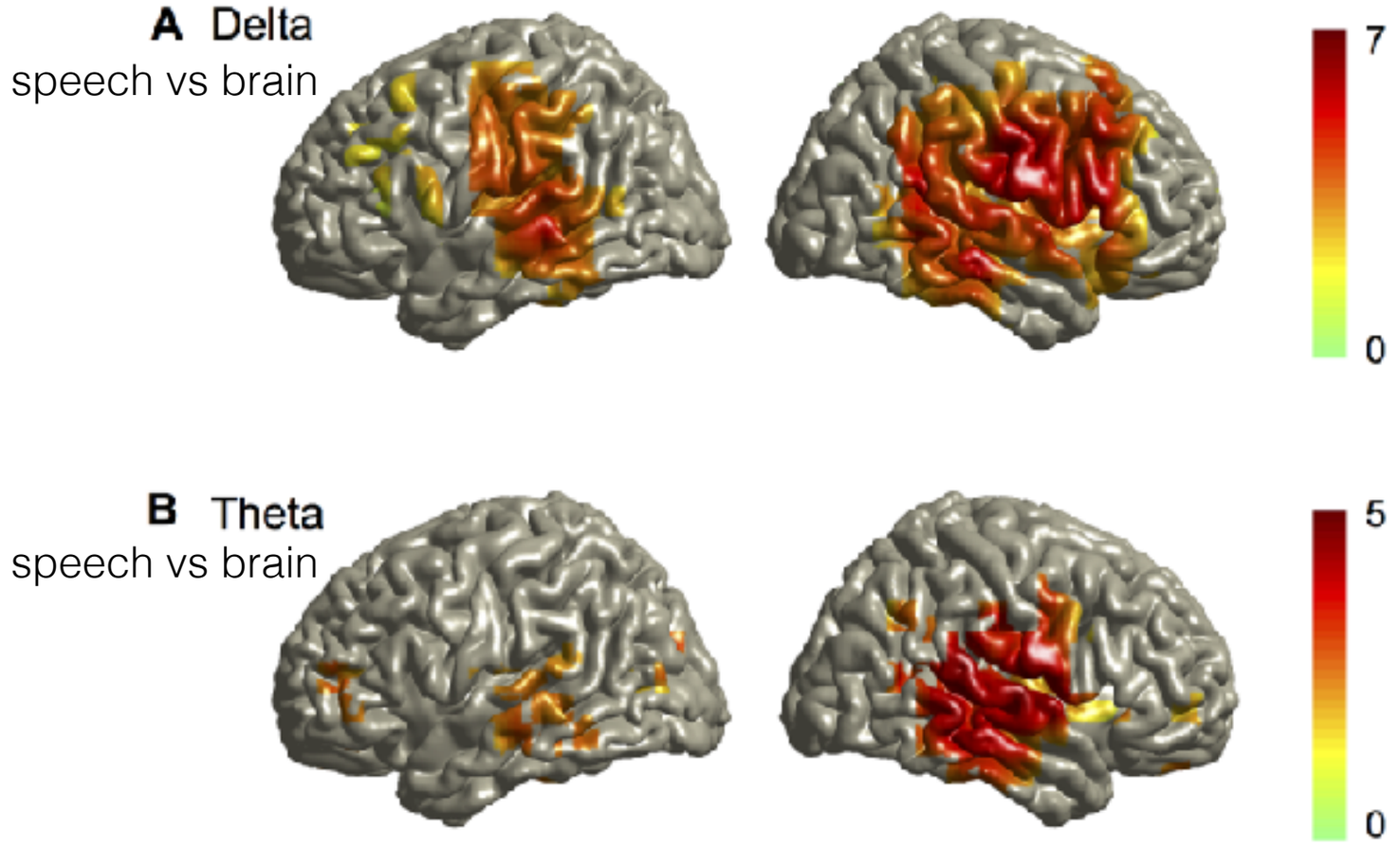

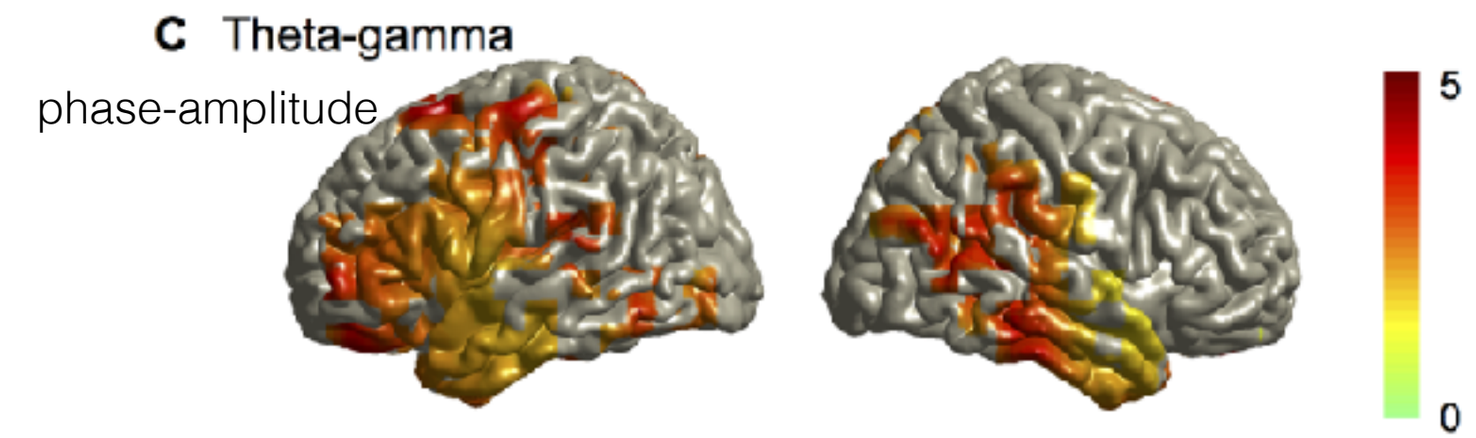

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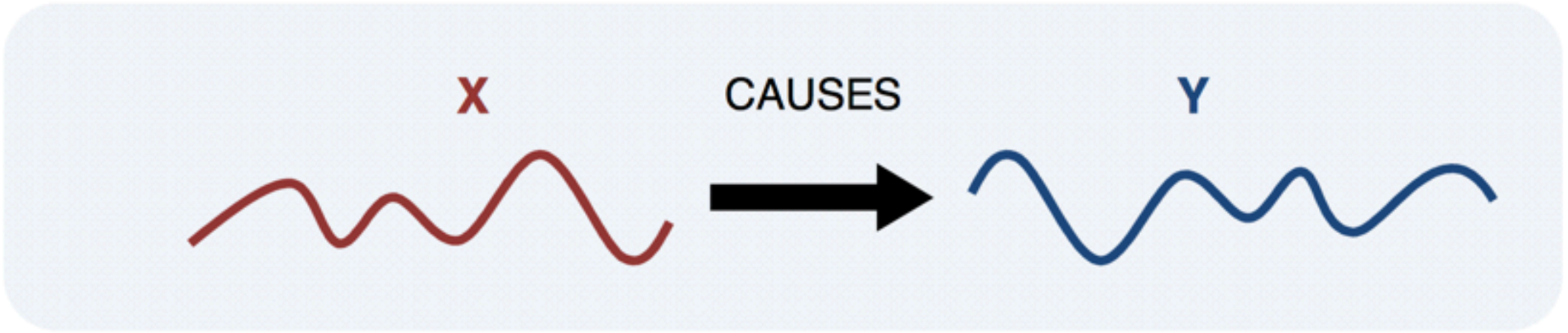
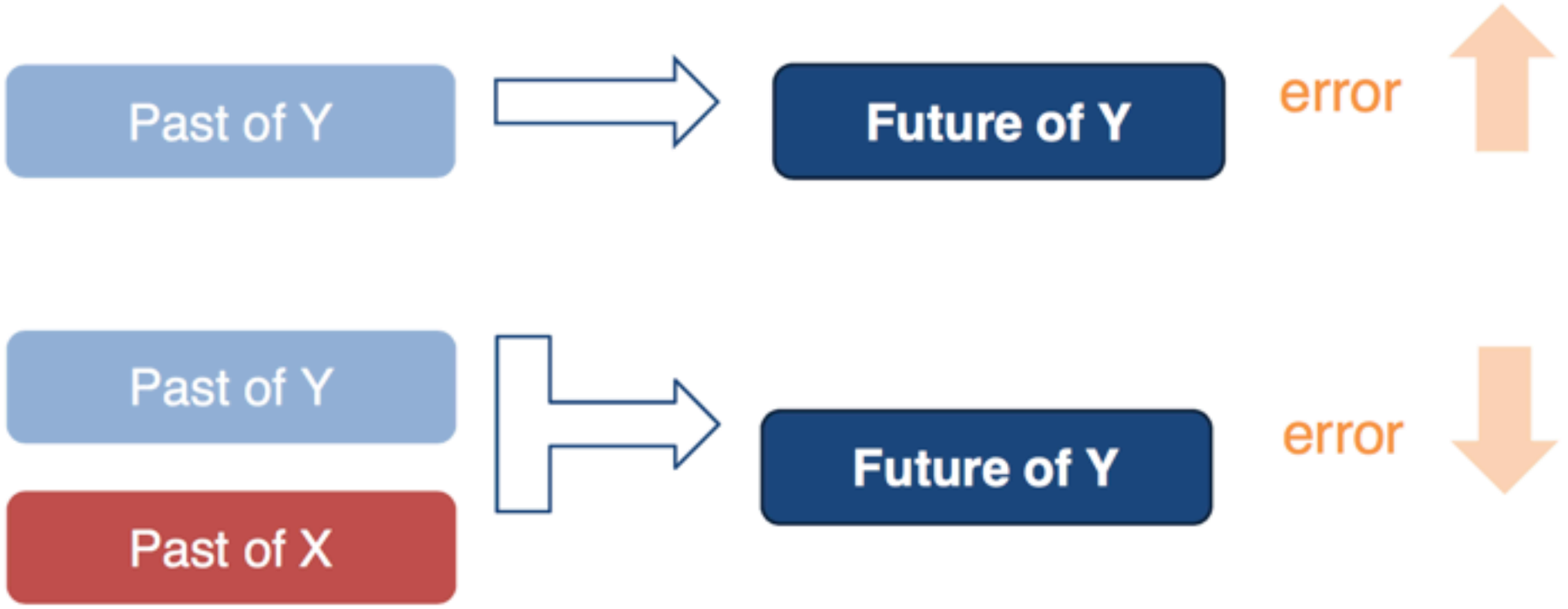
Effective connectivity: Granger causality





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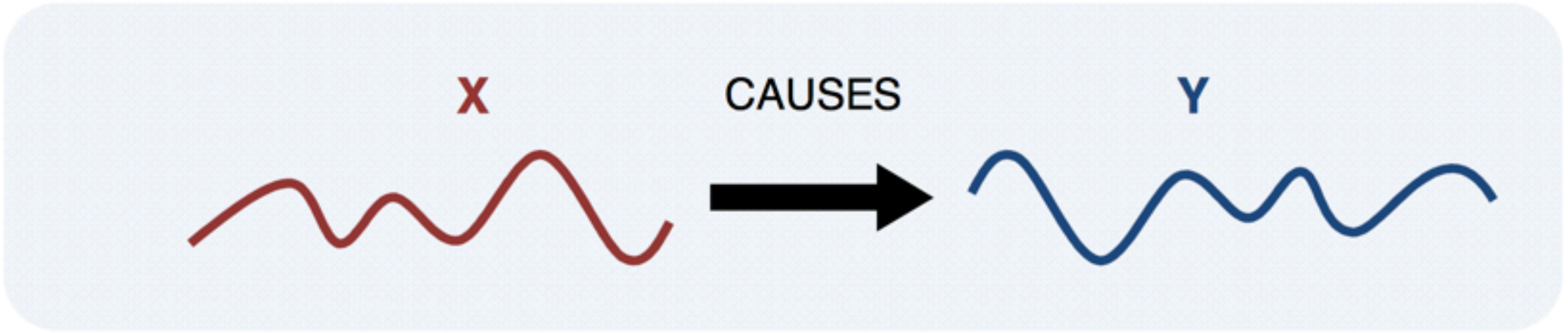
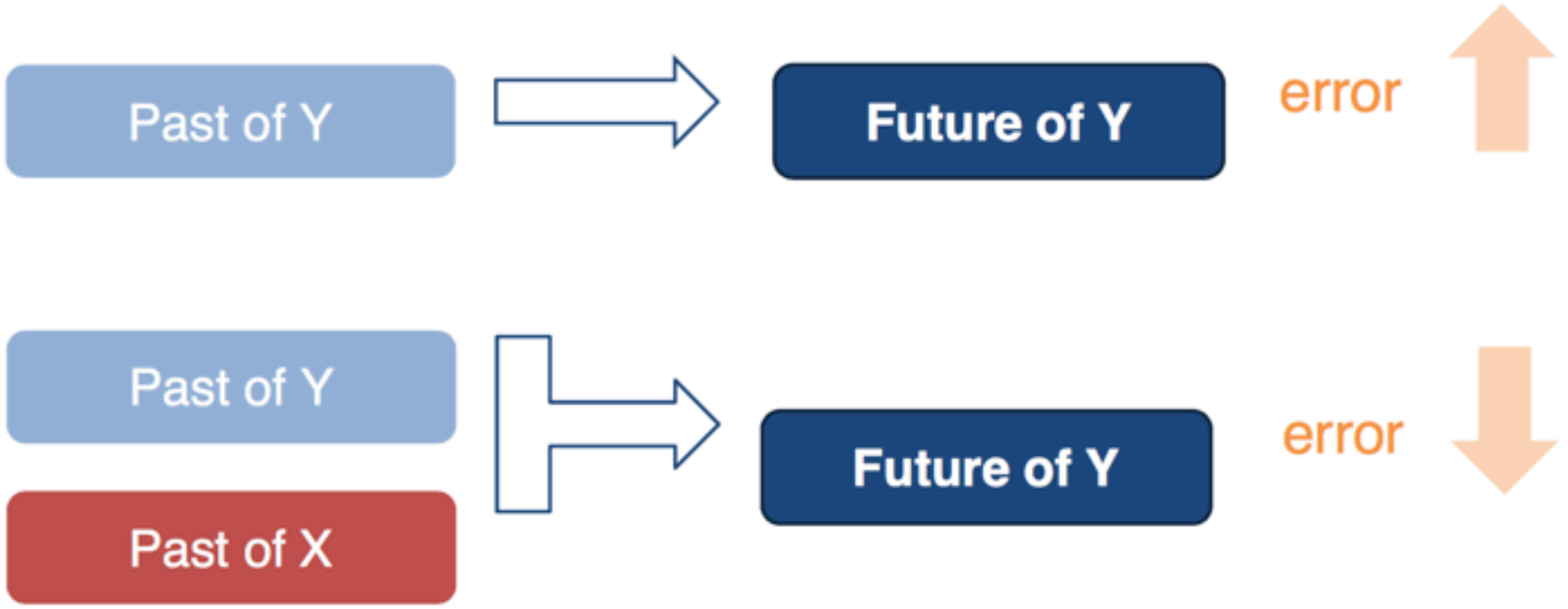




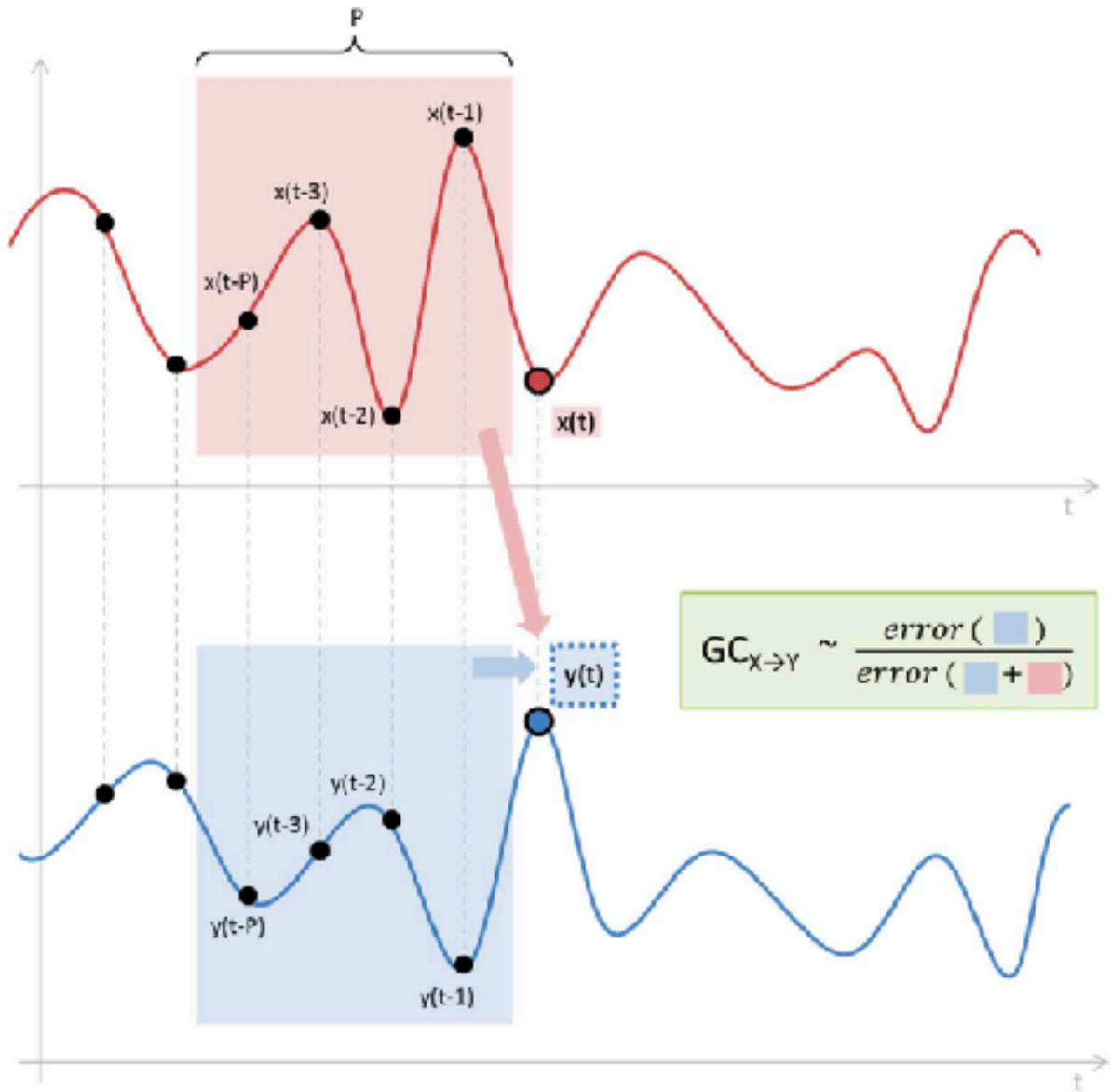
adapted from Niso et al., *Neuroinformatics* (2013)

Effective connectivity: Granger causality

- Wiener (1956) - Granger (1969)
- AR processes on time domain
- $0 \leq GC_{Y \rightarrow X} < \infty$

$$\left.\begin{aligned} x(n) &= \sum_{k=1}^{P} a_{x,k}\, x(n-k) + u_x(n) \\ x(n) &= \sum_{k=1}^{P} a_{x|x,k}\, x(n-k) + \sum_{k=1}^{P} a_{x|y,k}\, y(n-k) + u_{xy}(n) \end{aligned}\right\}$$

$$\left.\begin{aligned} V_{x|\bar{x}} &= \mathrm{var}(u_x) \\ V_{x|\bar{x},\bar{y}} &= \mathrm{var}(u_{xy}) \end{aligned}\right\} \qquad GC_{y \rightarrow x} = \ln\left(\frac{V_{x|\bar{x}}}{V_{x|\bar{x},\bar{y}}}\right)$$



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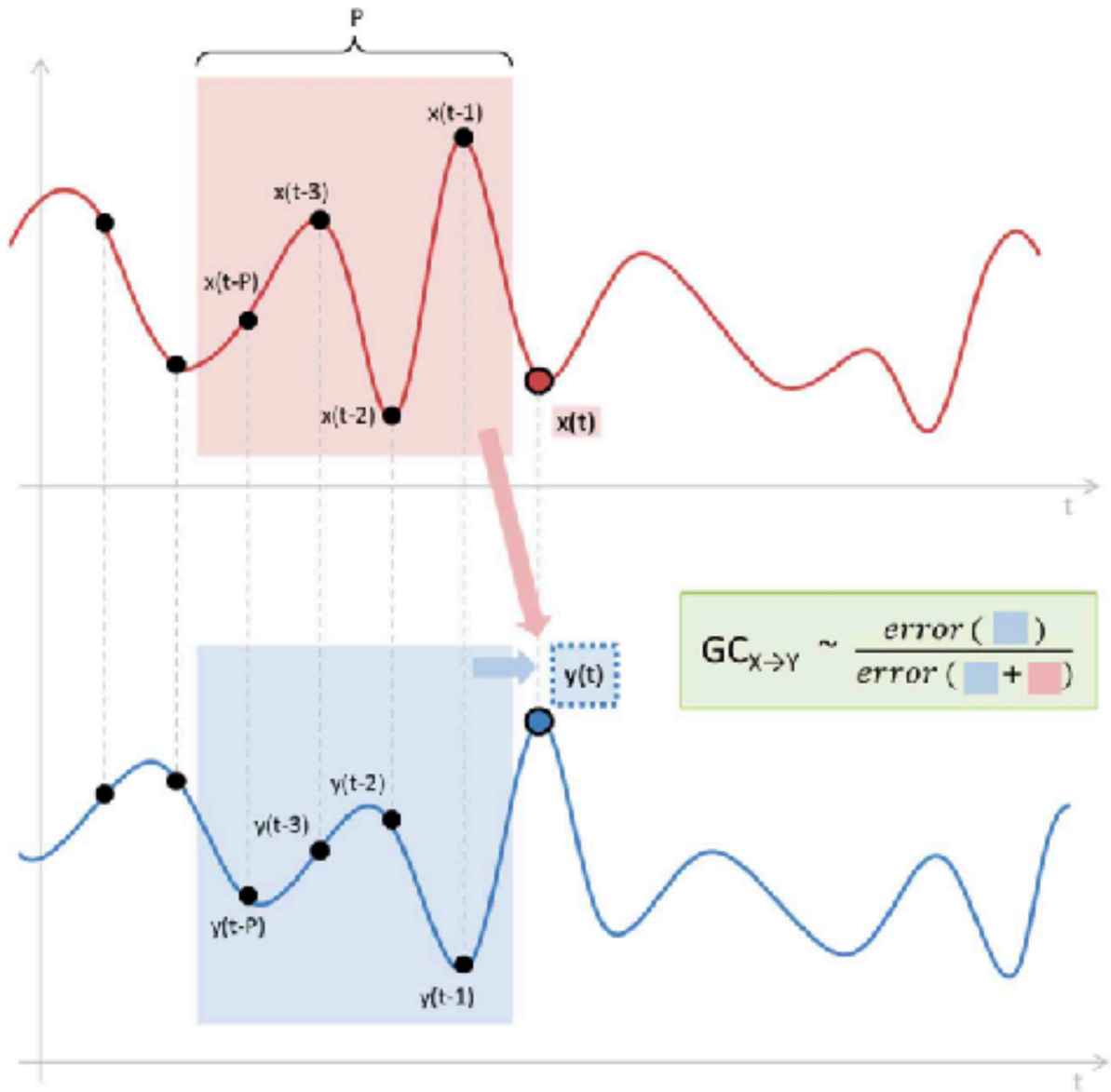
- AR processes on time domain
- $0 \leq GC_{Y \rightarrow X} < \infty$

$$\left.\begin{aligned} x(n) &= \sum_{k=1}^{P} a_{x,k}\, x(n-k) + u_x(n) \\ x(n) &= \sum_{k=1}^{P} a_{x|x,k}\, x(n-k) + \sum_{k=1}^{P} a_{x|y,k}\, y(n-k) + u_{xy}(n) \end{aligned}\right\}$$

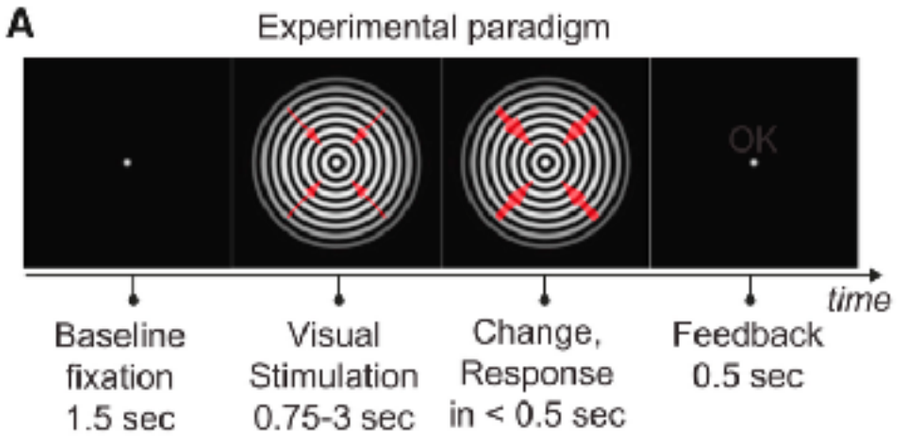
$$\left.\begin{aligned} V_{x|\bar{x}} &= \mathrm{var}(u_x) \\ V_{x|\bar{x},\bar{y}} &= \mathrm{var}(u_{xy}) \end{aligned}\right\} \qquad GC_{y \rightarrow x} = \ln\left(\frac{V_{x|\bar{x}}}{V_{x|\bar{x},\bar{y}}}\right)$$



(Niso et al. 2014)

adapted from Niso et al., *Neuroinformatics* (2013)

Effective connectivity: Granger causality



Michalareas et al., *Neuron* (2016)

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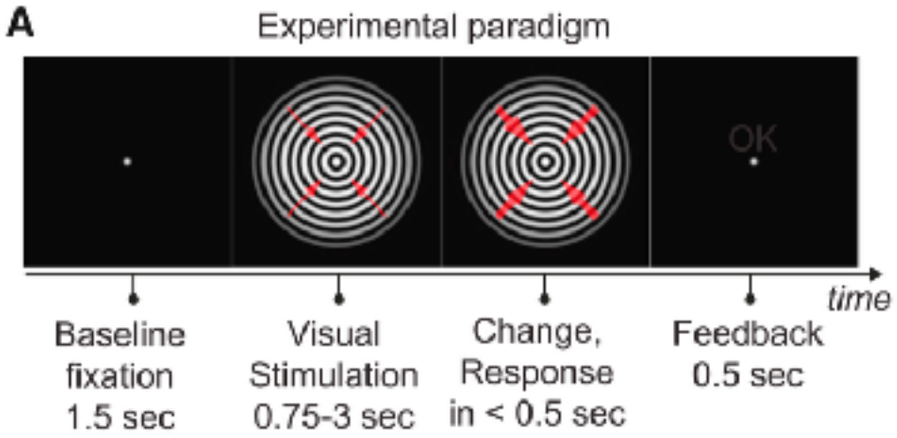

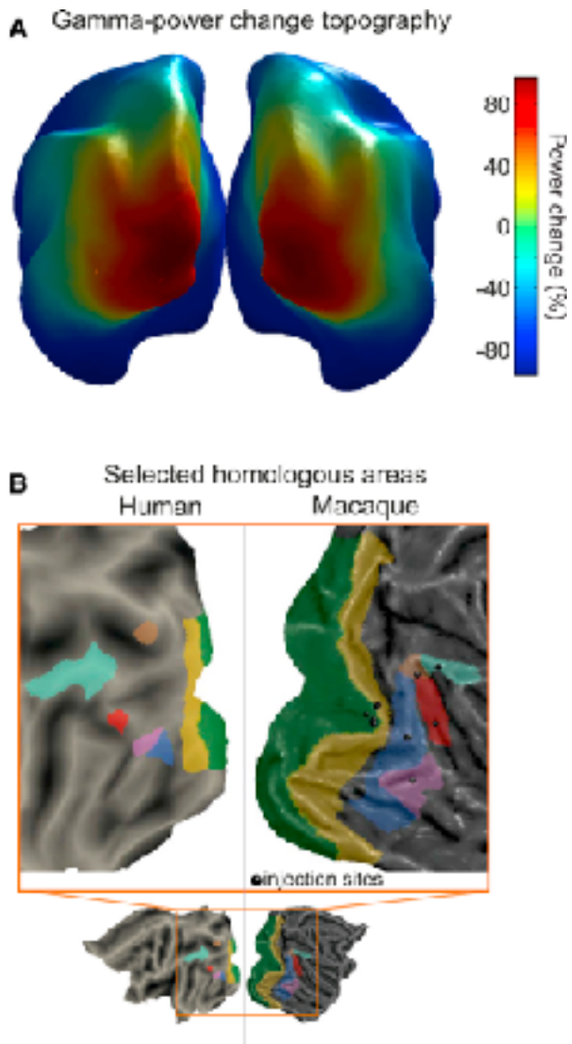

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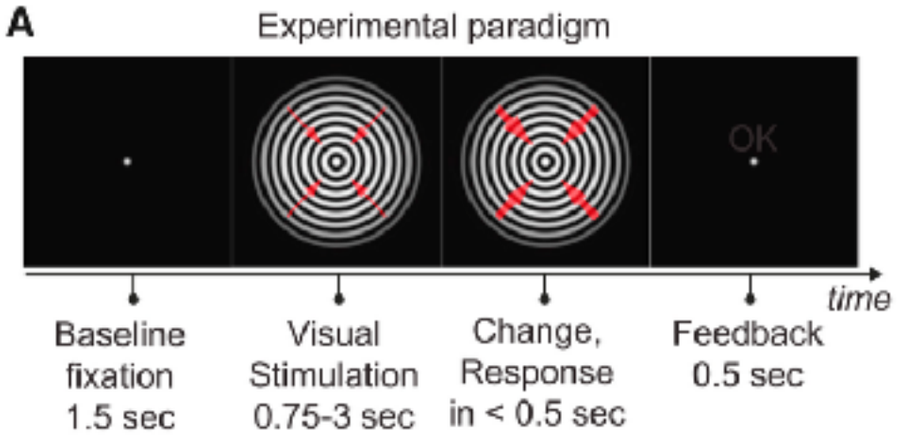

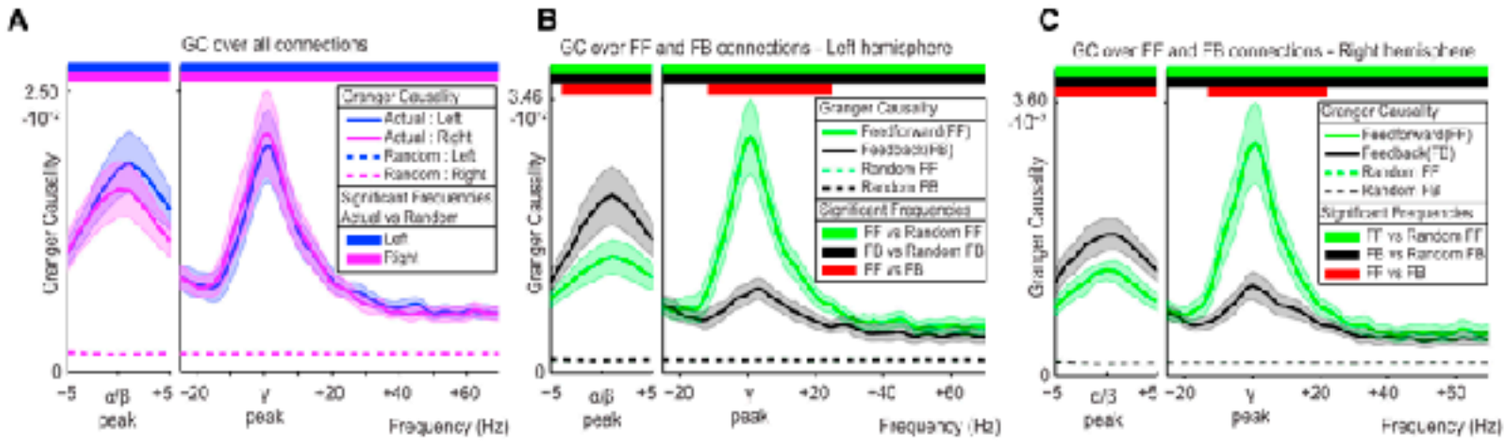

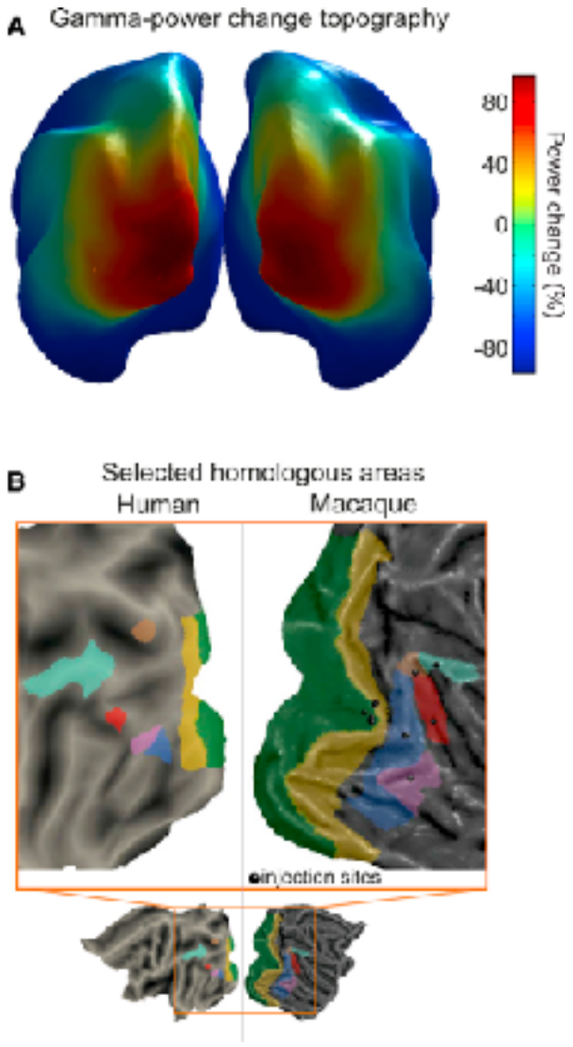

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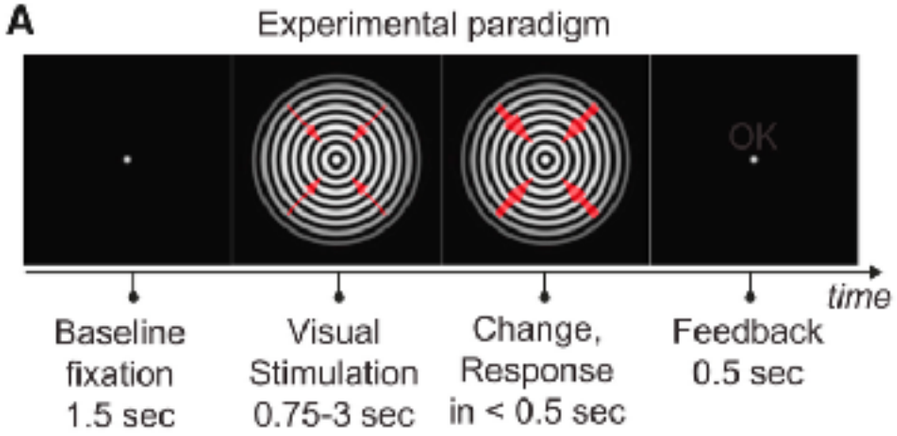

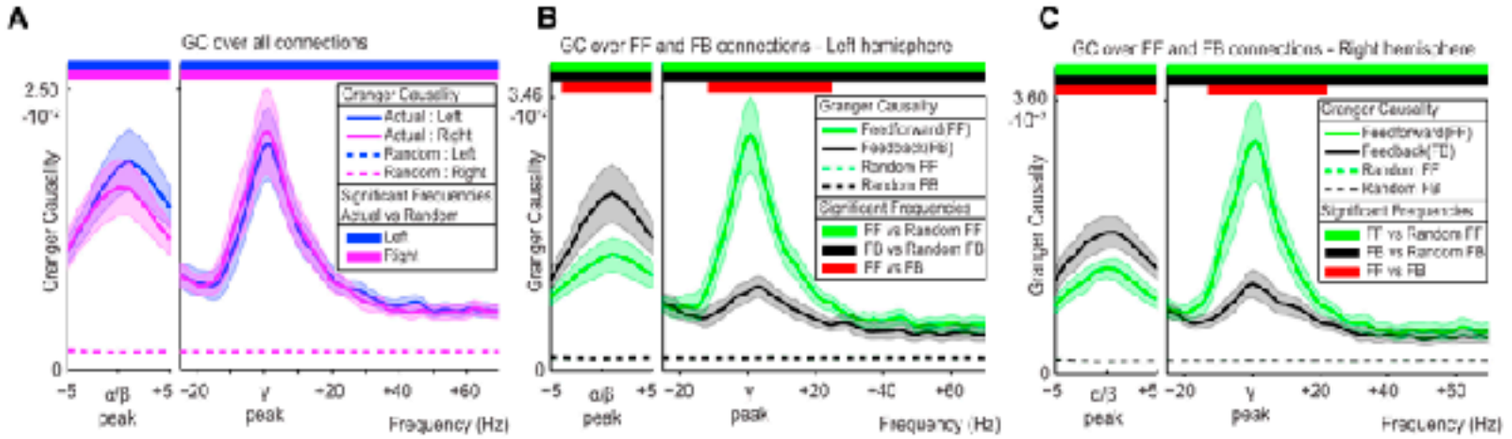

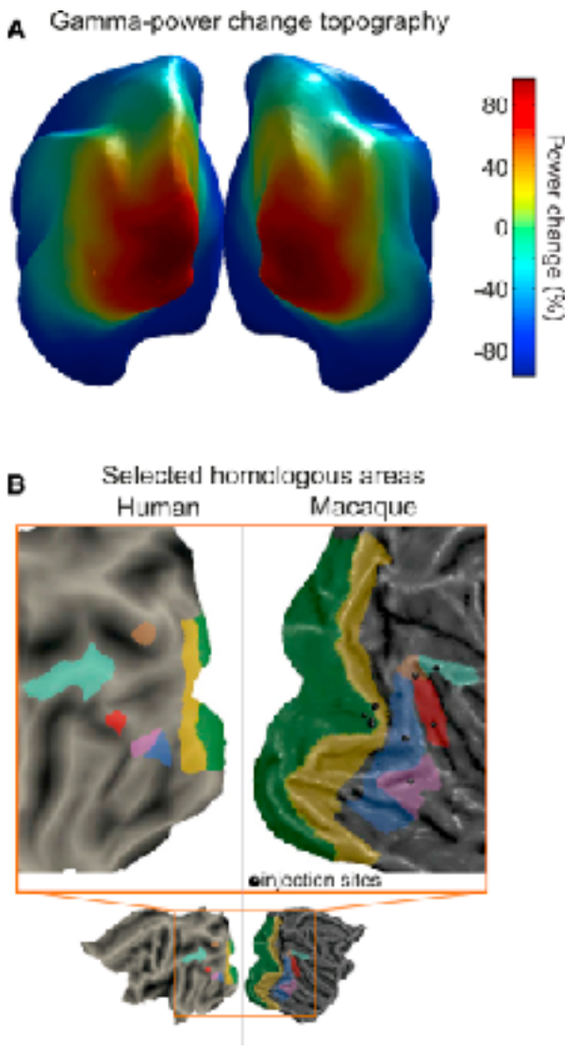

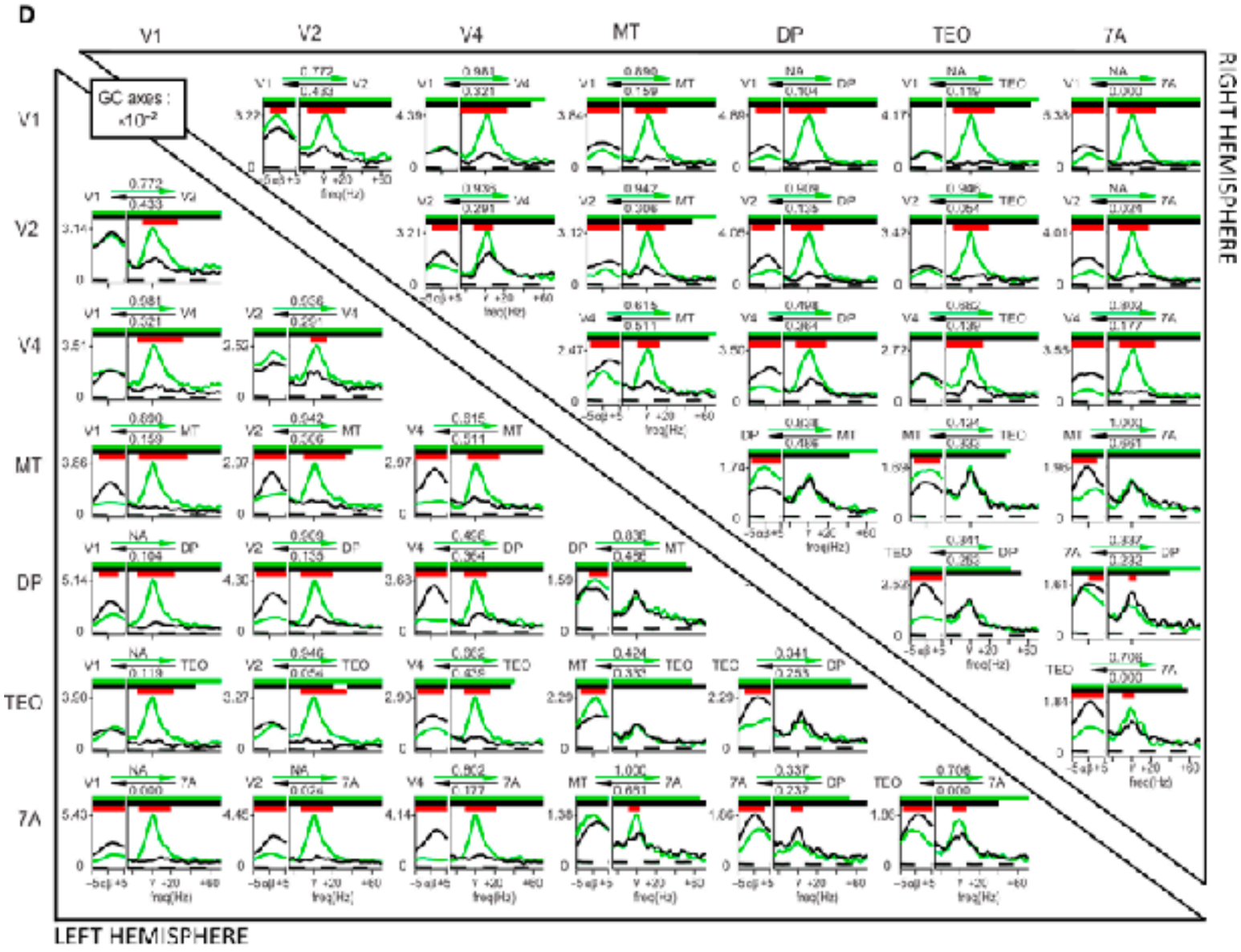

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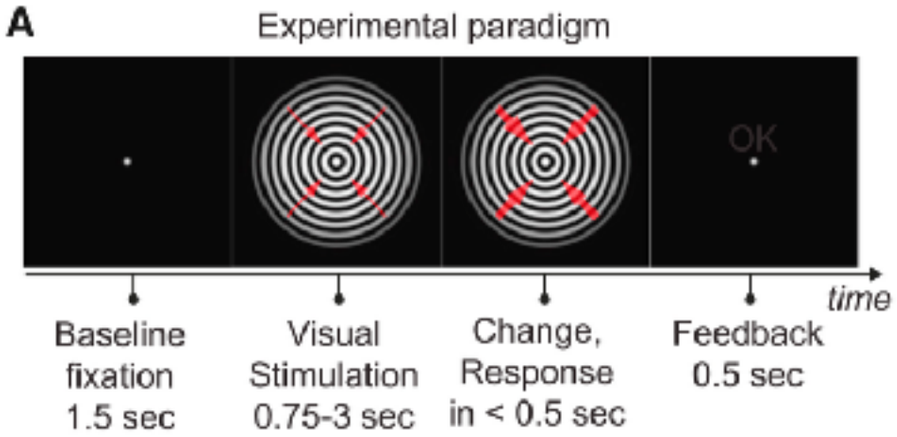
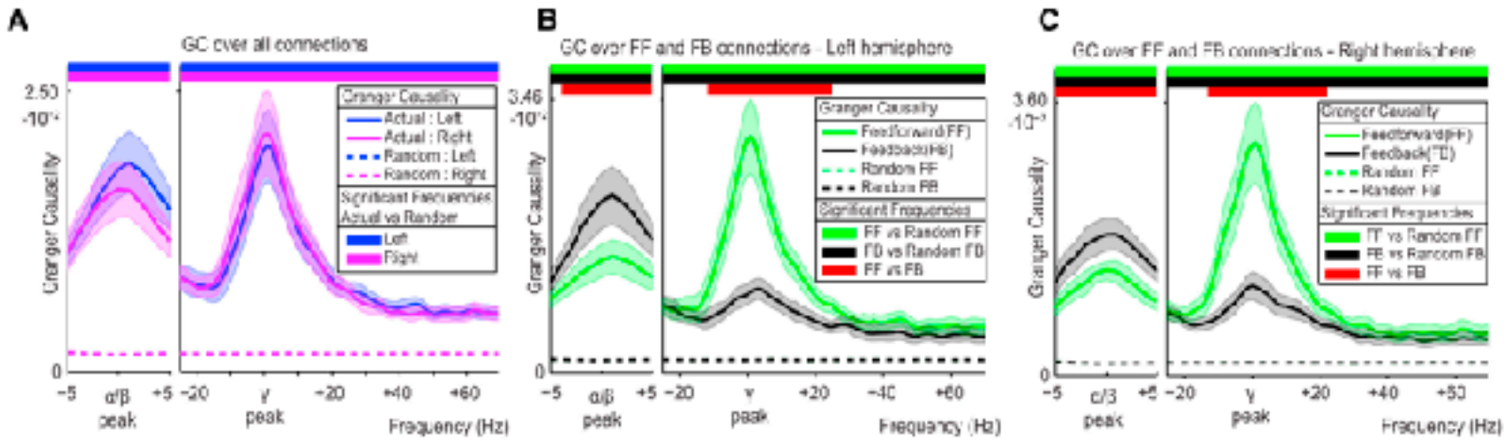
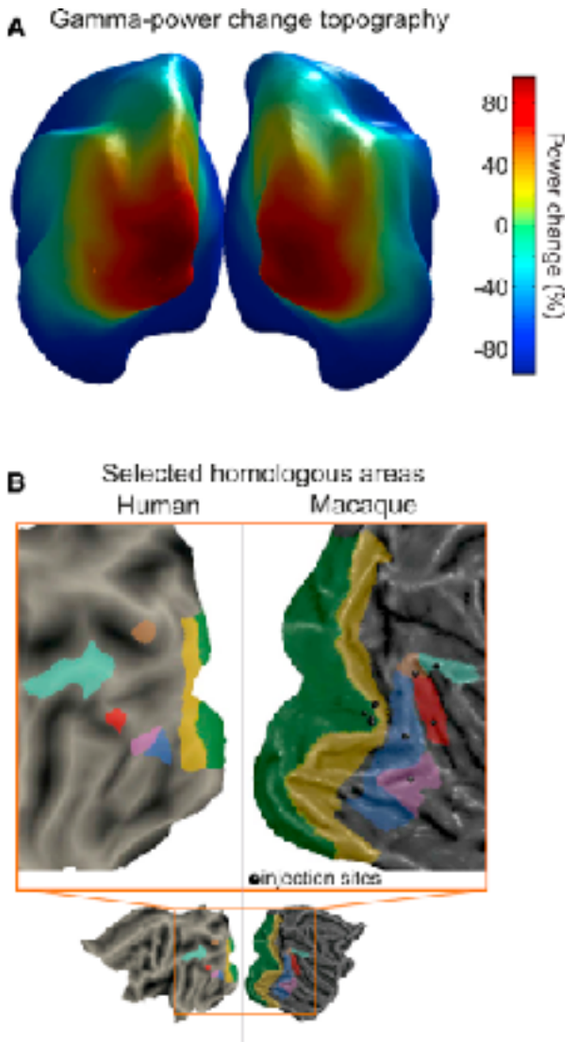
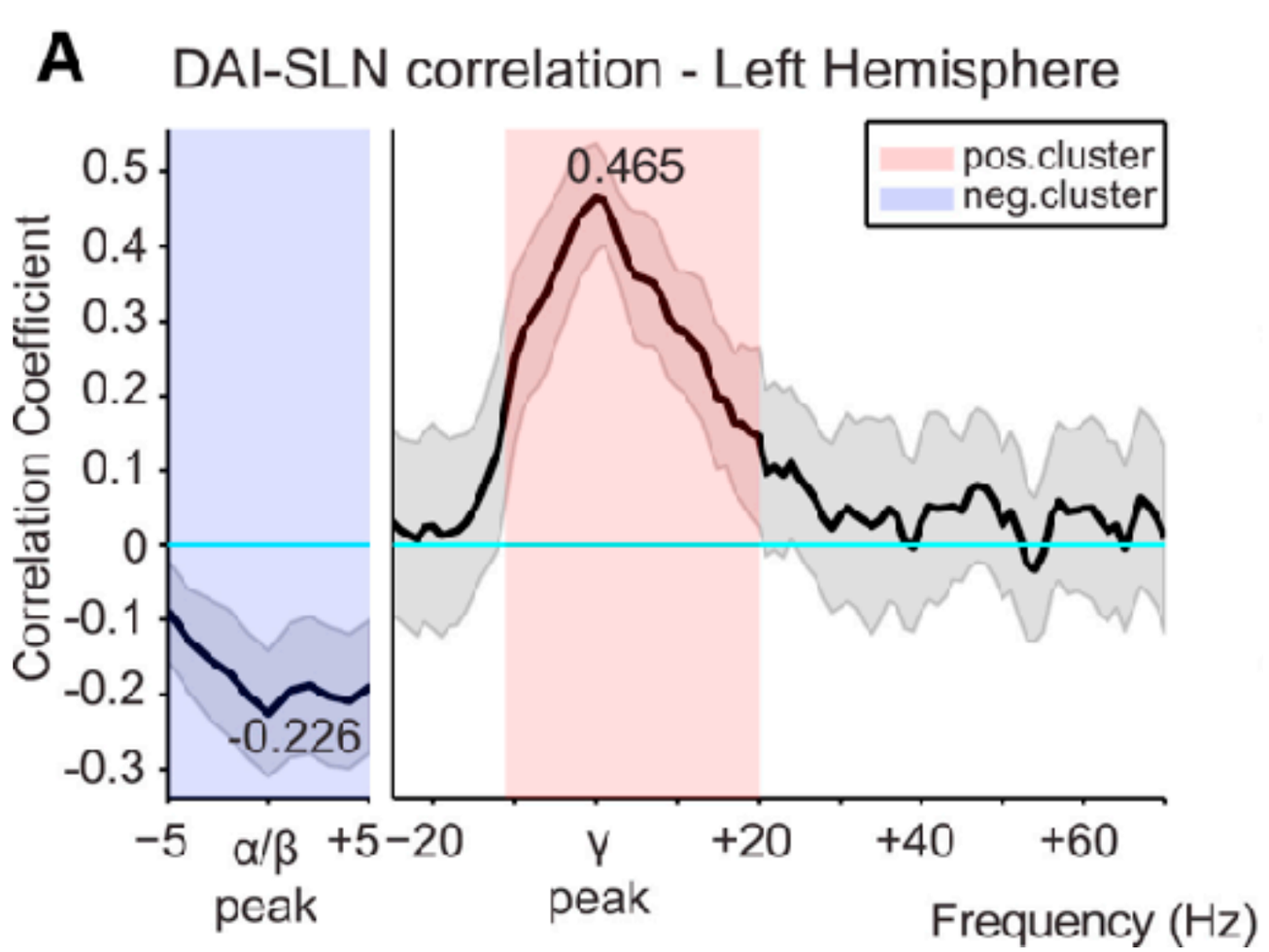


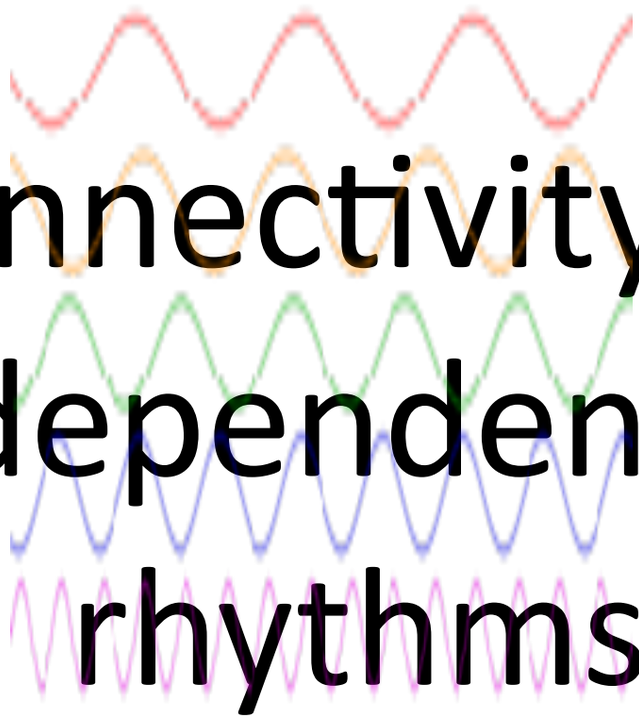






Michalareas et al., *Neuron* (2016)

Connectivity via interdependent brain rhythms



Connectivity via interdependent brain rhythms

State-dependent expressions of neural oscillations

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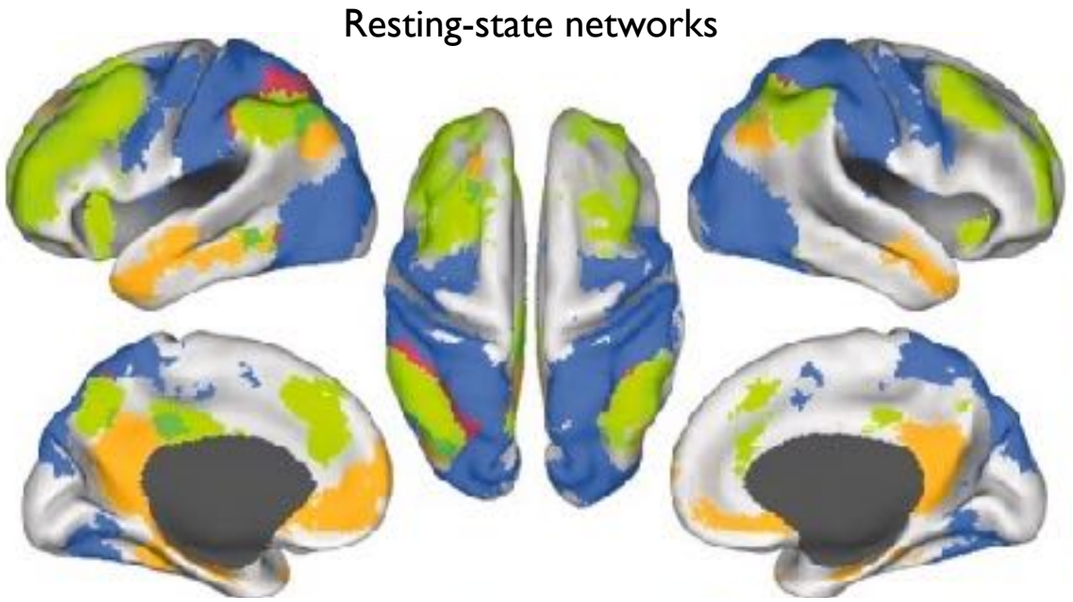
Consider the “resting-state” as a case example

State-dependent expressions of neural oscillations

Consider the “resting-state” as a case example

fMRI - BOLD



Buckner et al. *Ann NY Acad. Sci.* (2008)
Carhart-Harris & Friston, *Brain* (2010)

State-dependent expressions of neural oscillations

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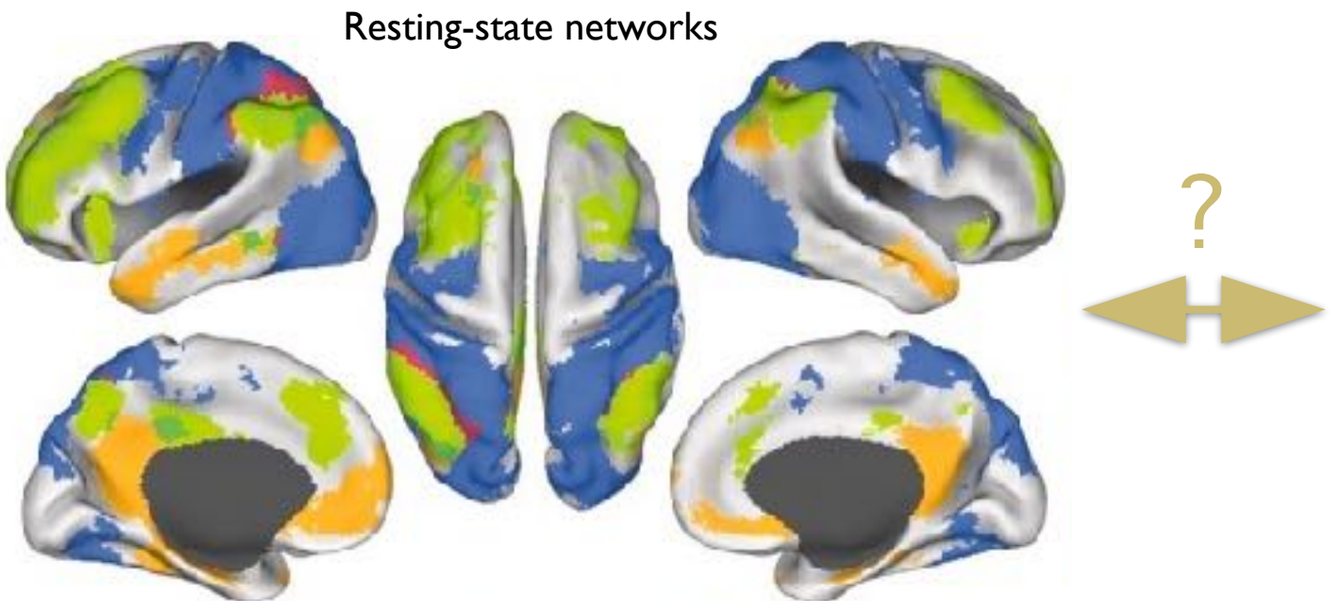

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State-dependent expressions of neural oscillations

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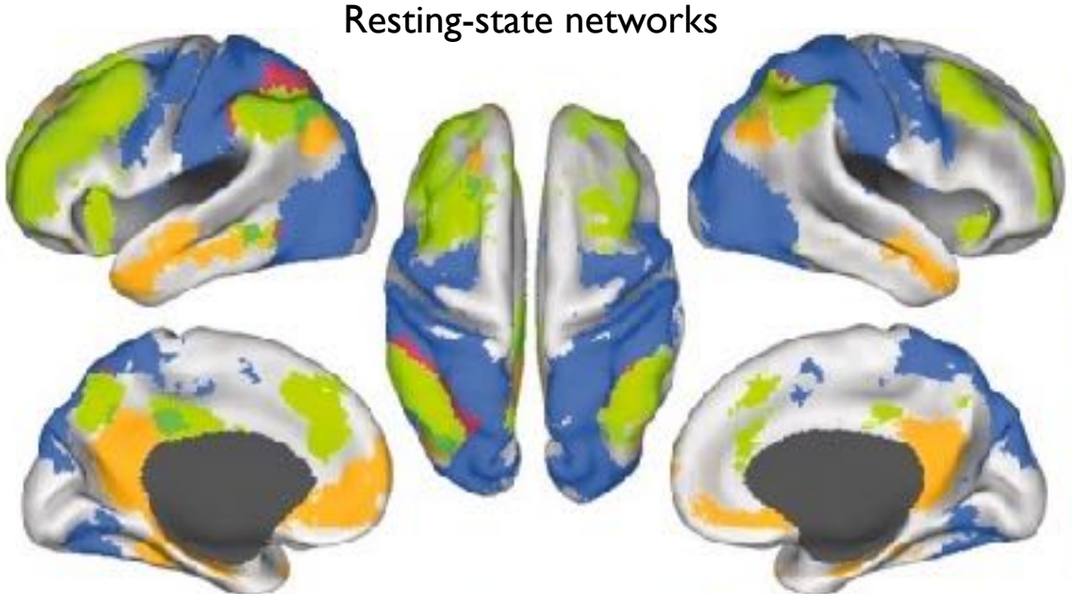

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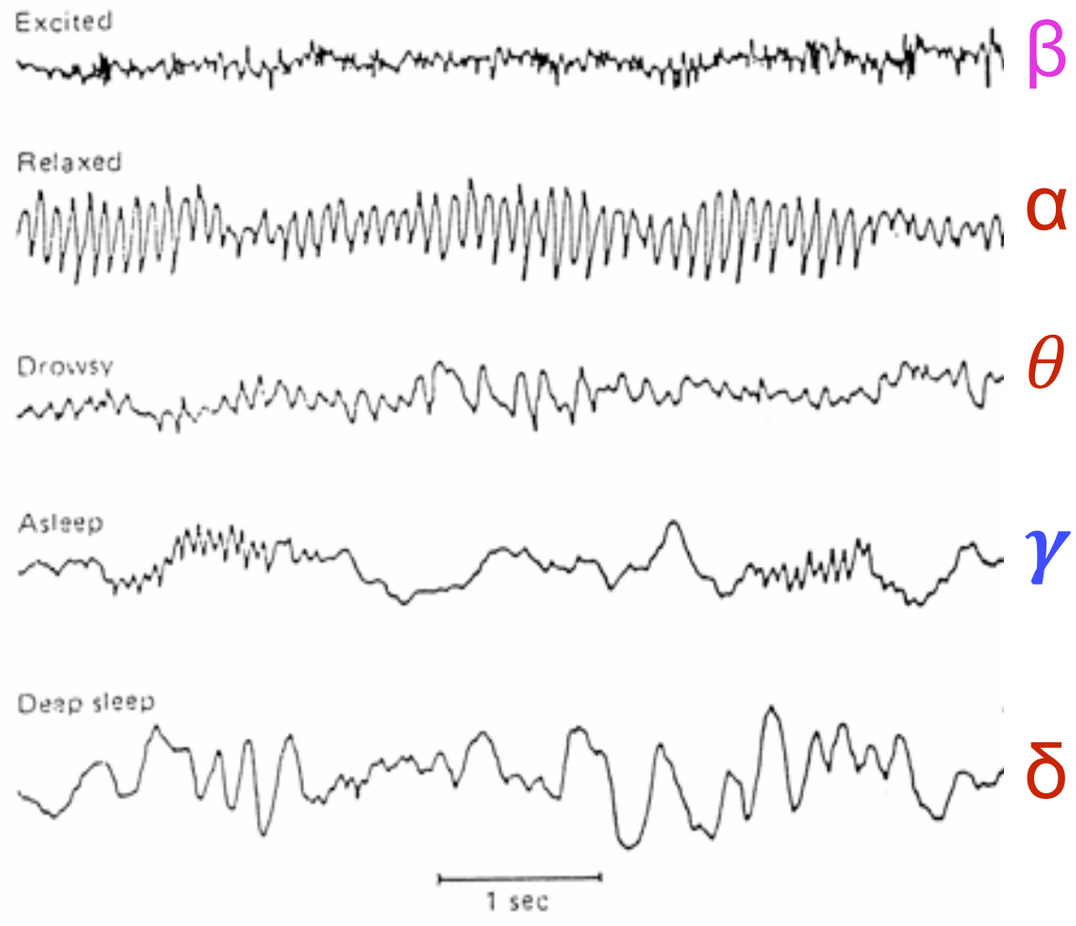
electrophysiology



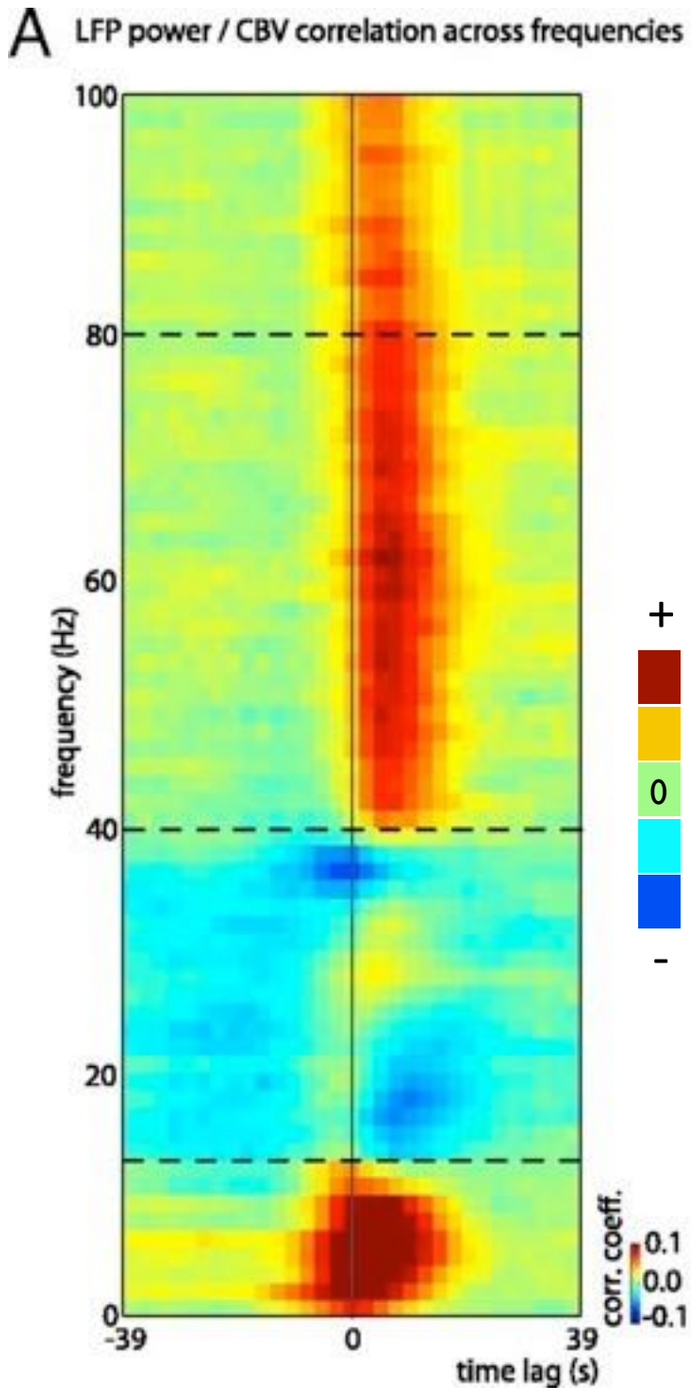
Correlation between ongoing brain rhythms and BOLD

high γ

γ

β

δ θ α



correlation
BOLD
vs.
envelope of oscillatory fluctuations

Schölvinck et al. *PNAS* (2010)
see also Logothetis et al., *Nature* (2001)

Interdependencies in the polyrhythmic activity of the brain?

Baillet, *Nature Neuroscience* (2017)

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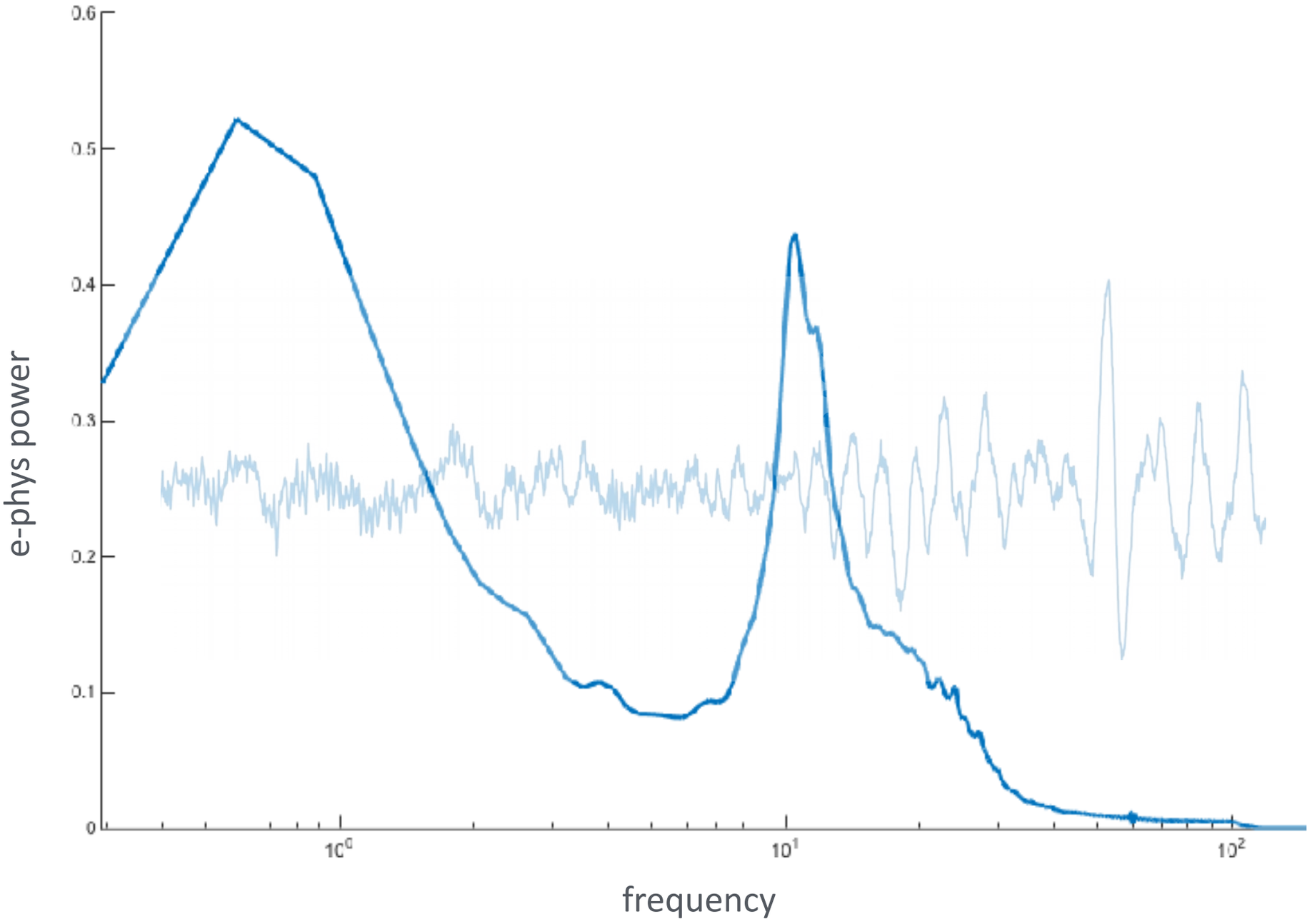

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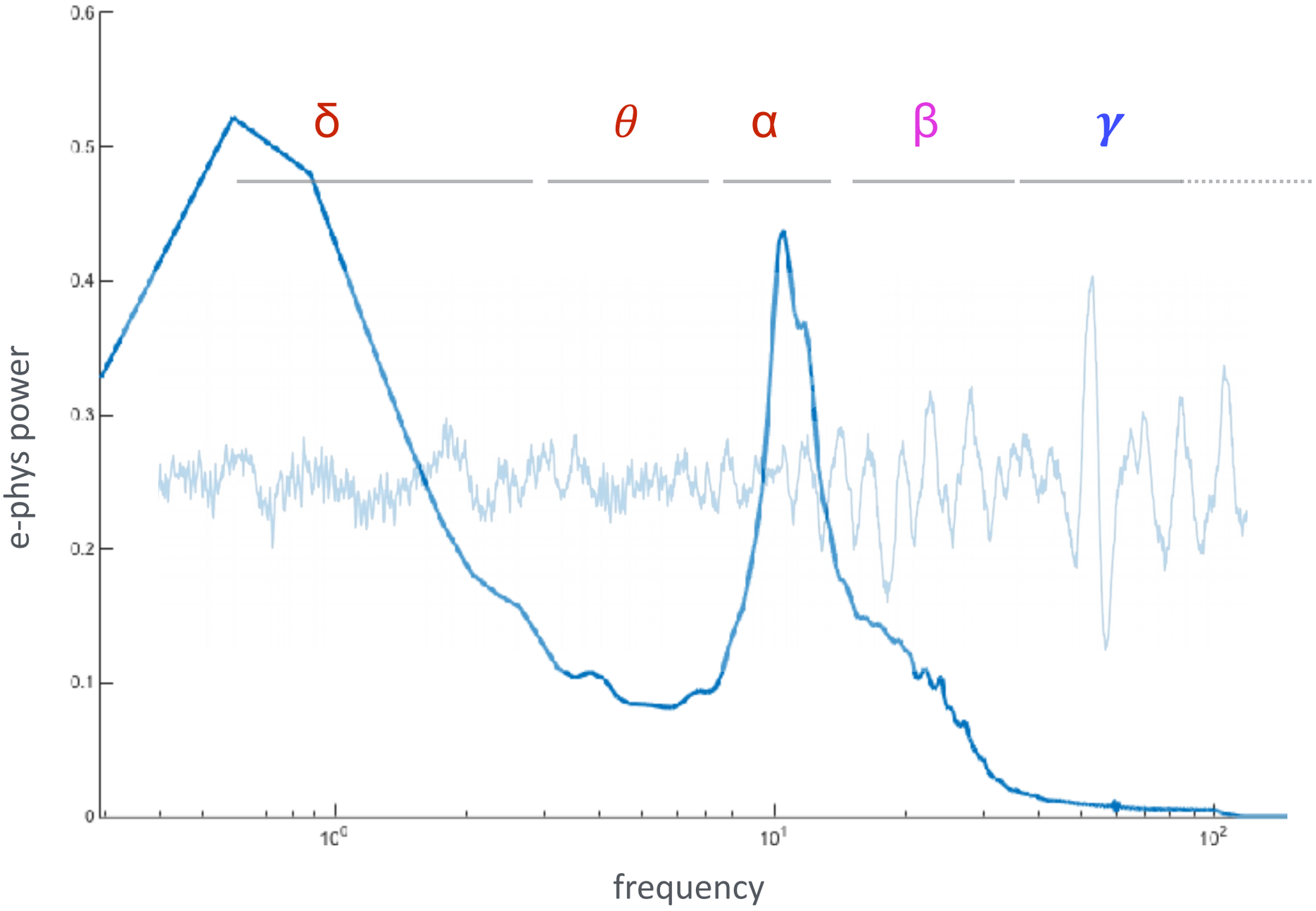

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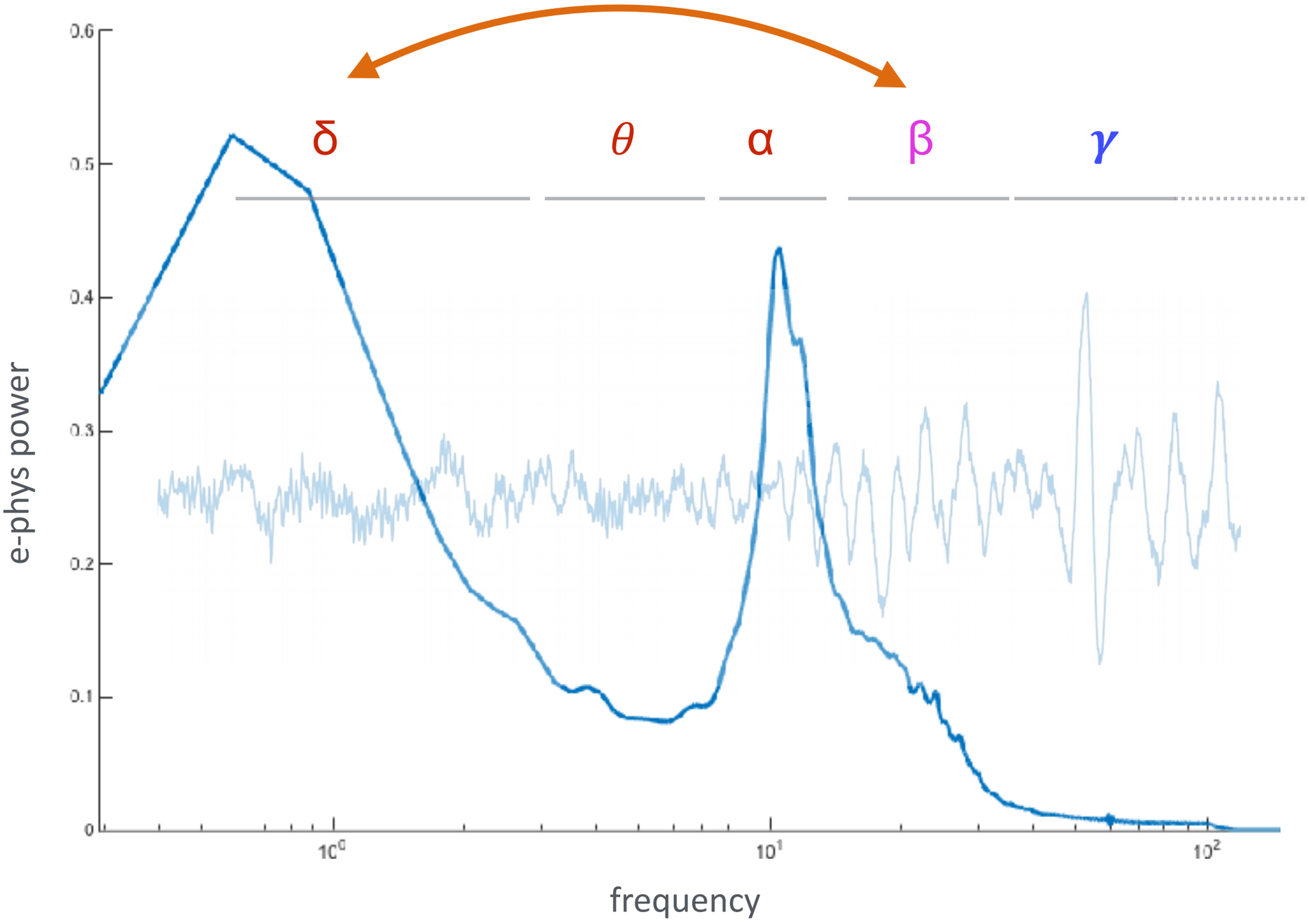

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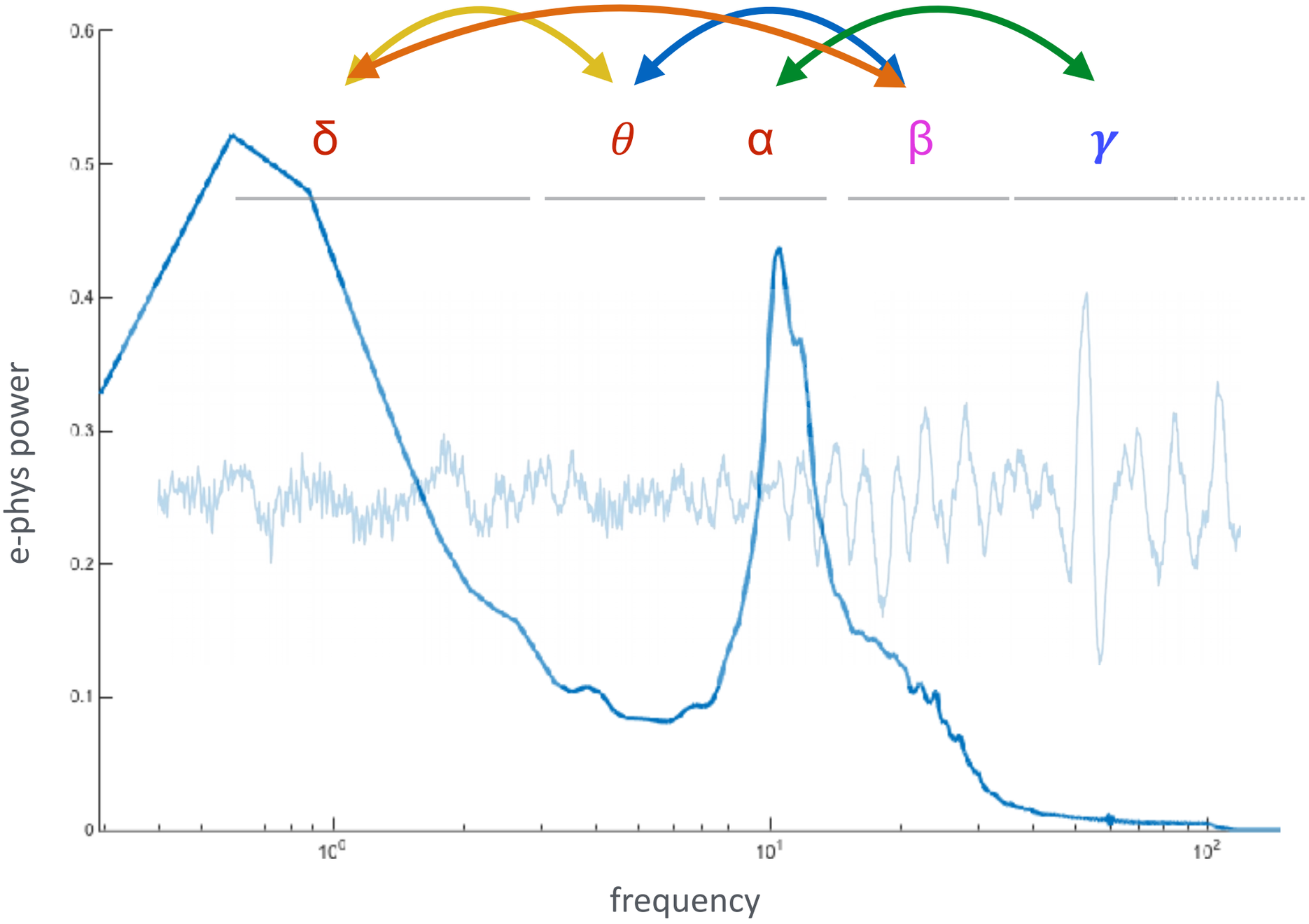

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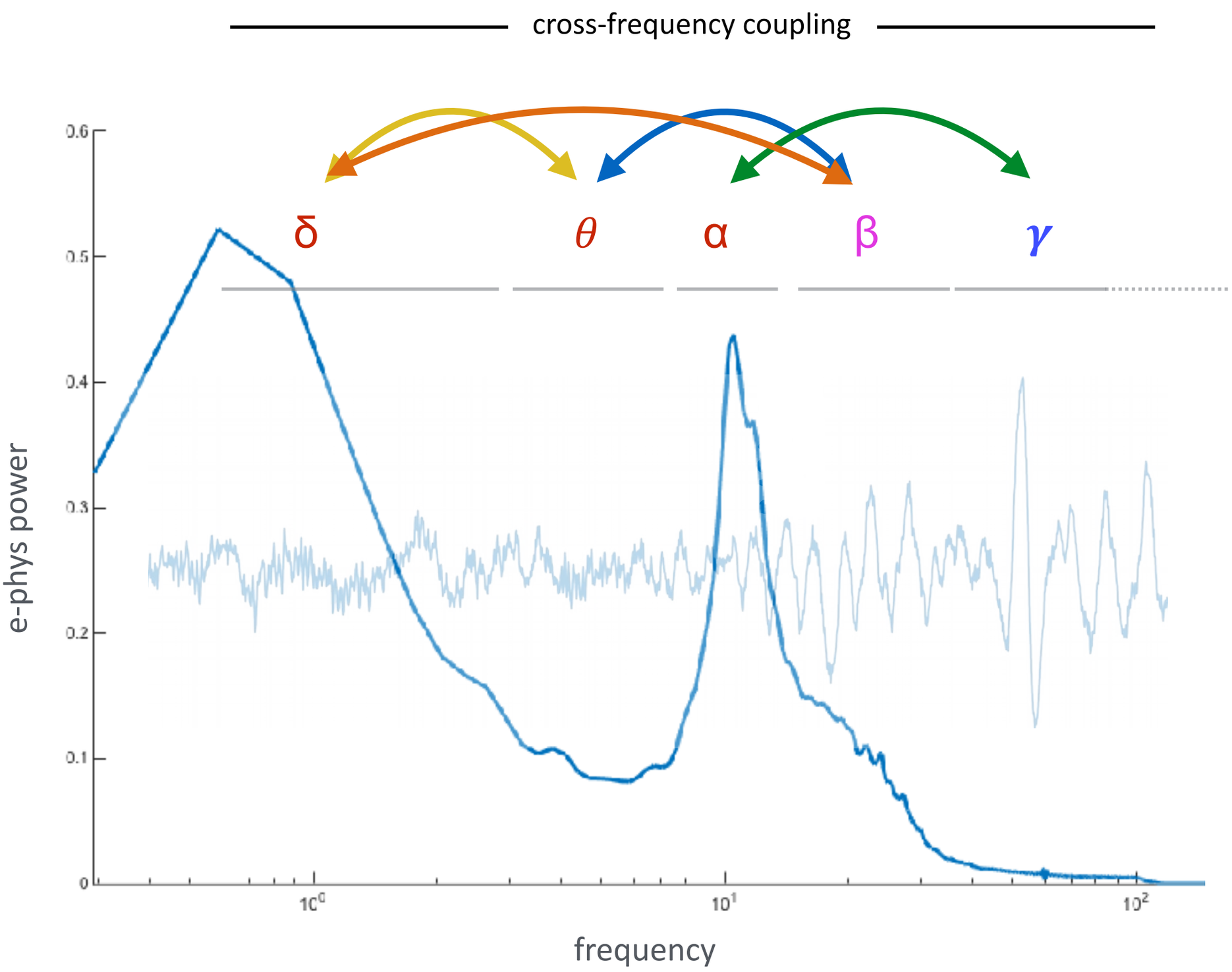

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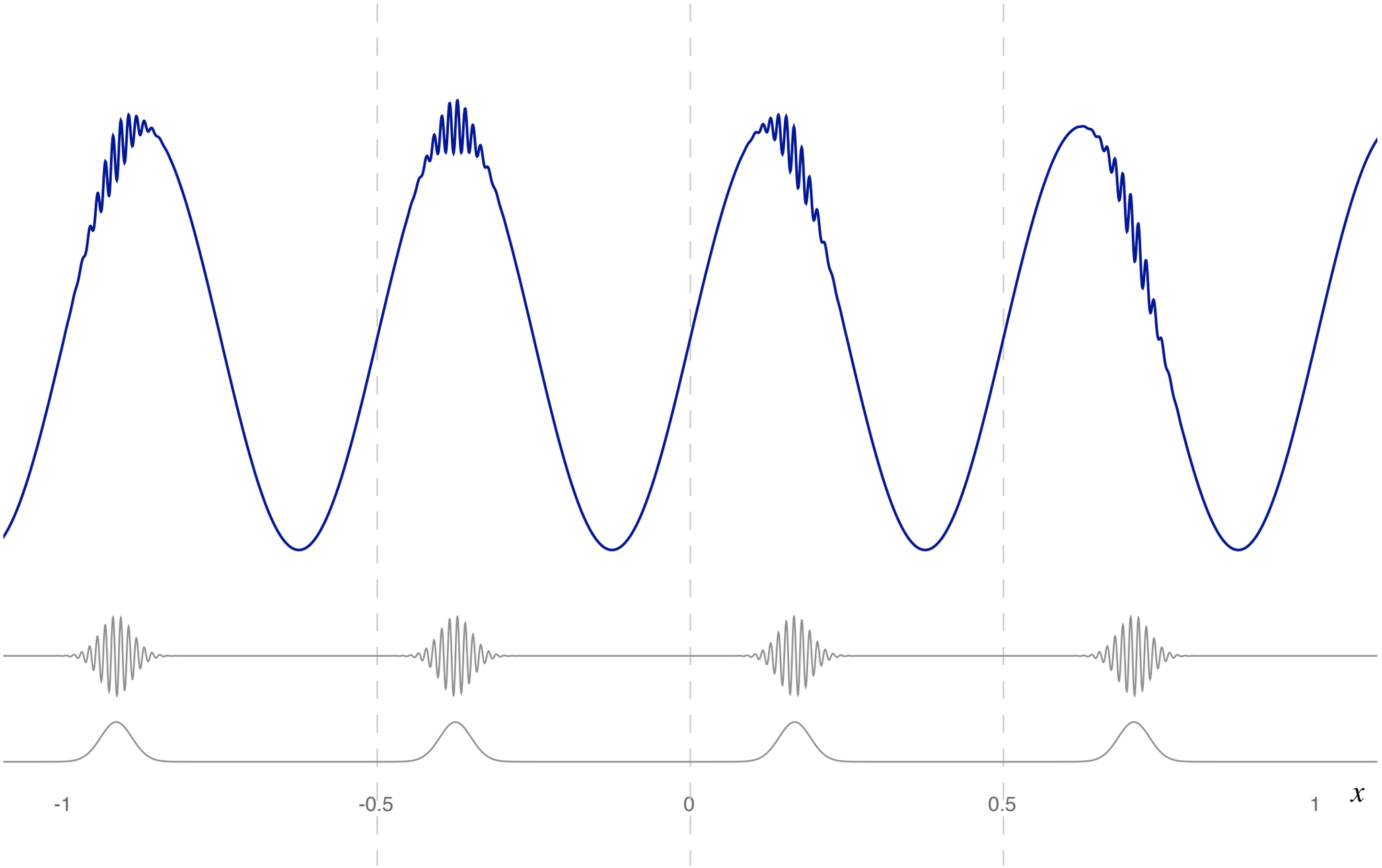
Cross-frequency phase-amplitude coupling (PAC)



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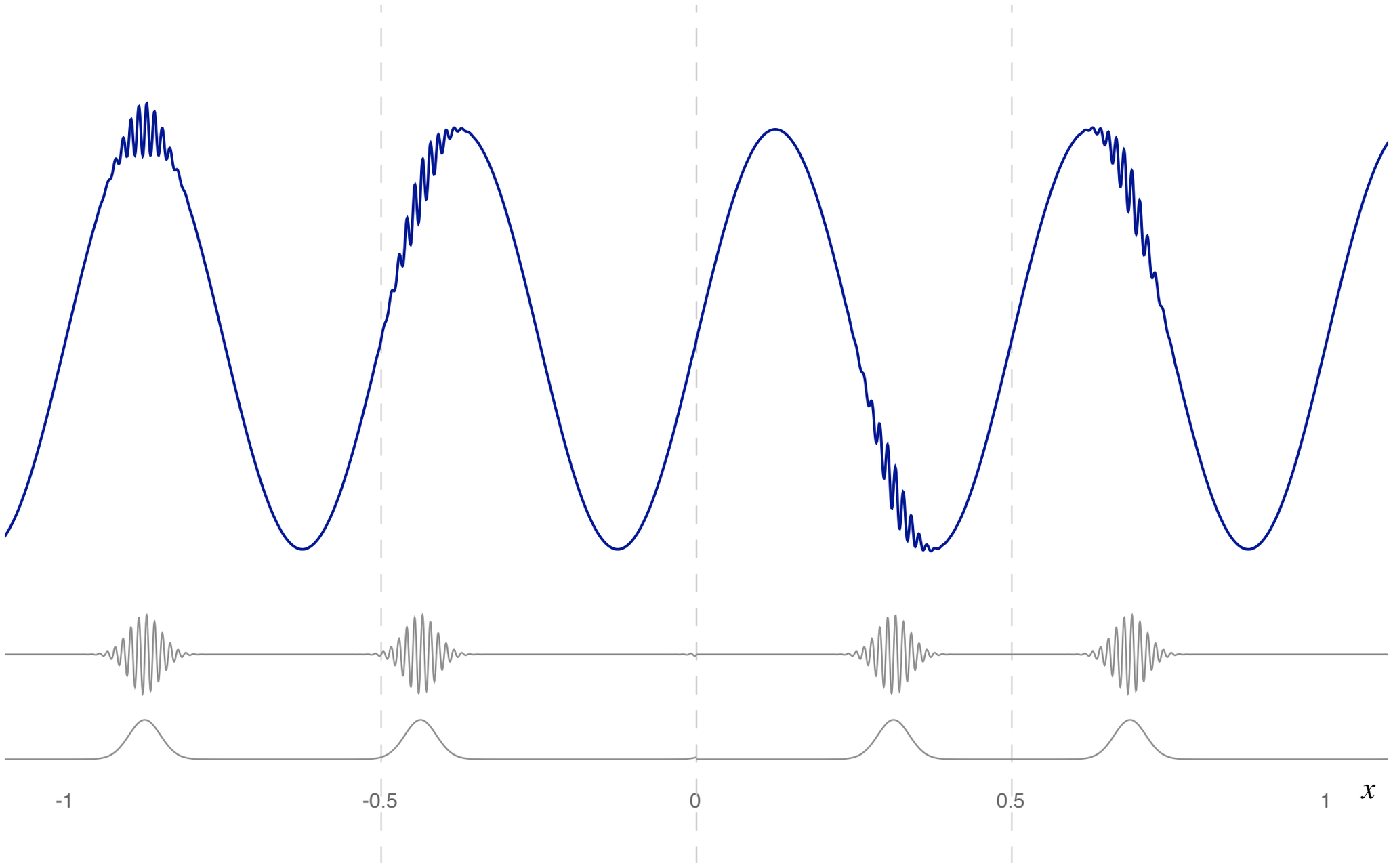

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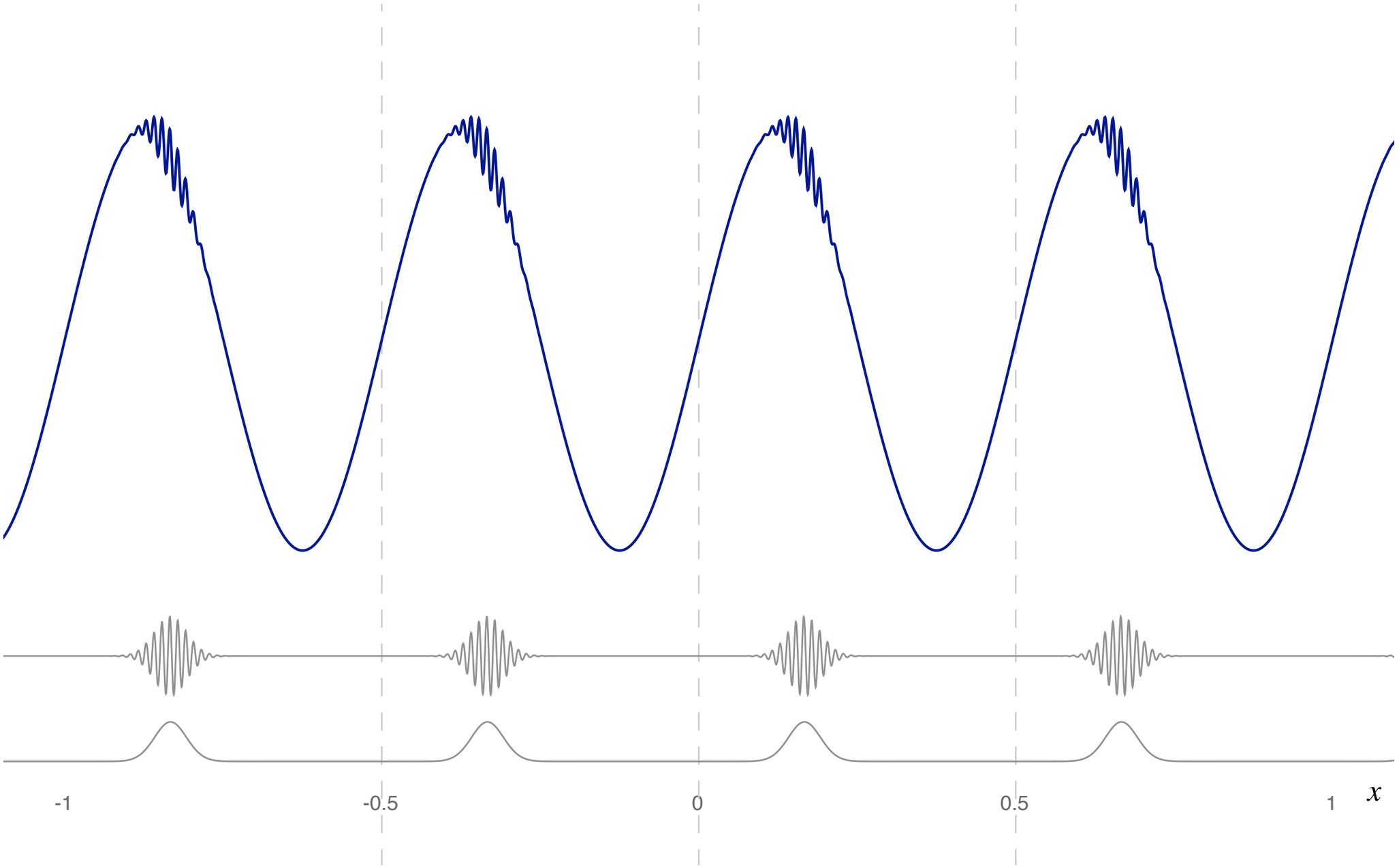

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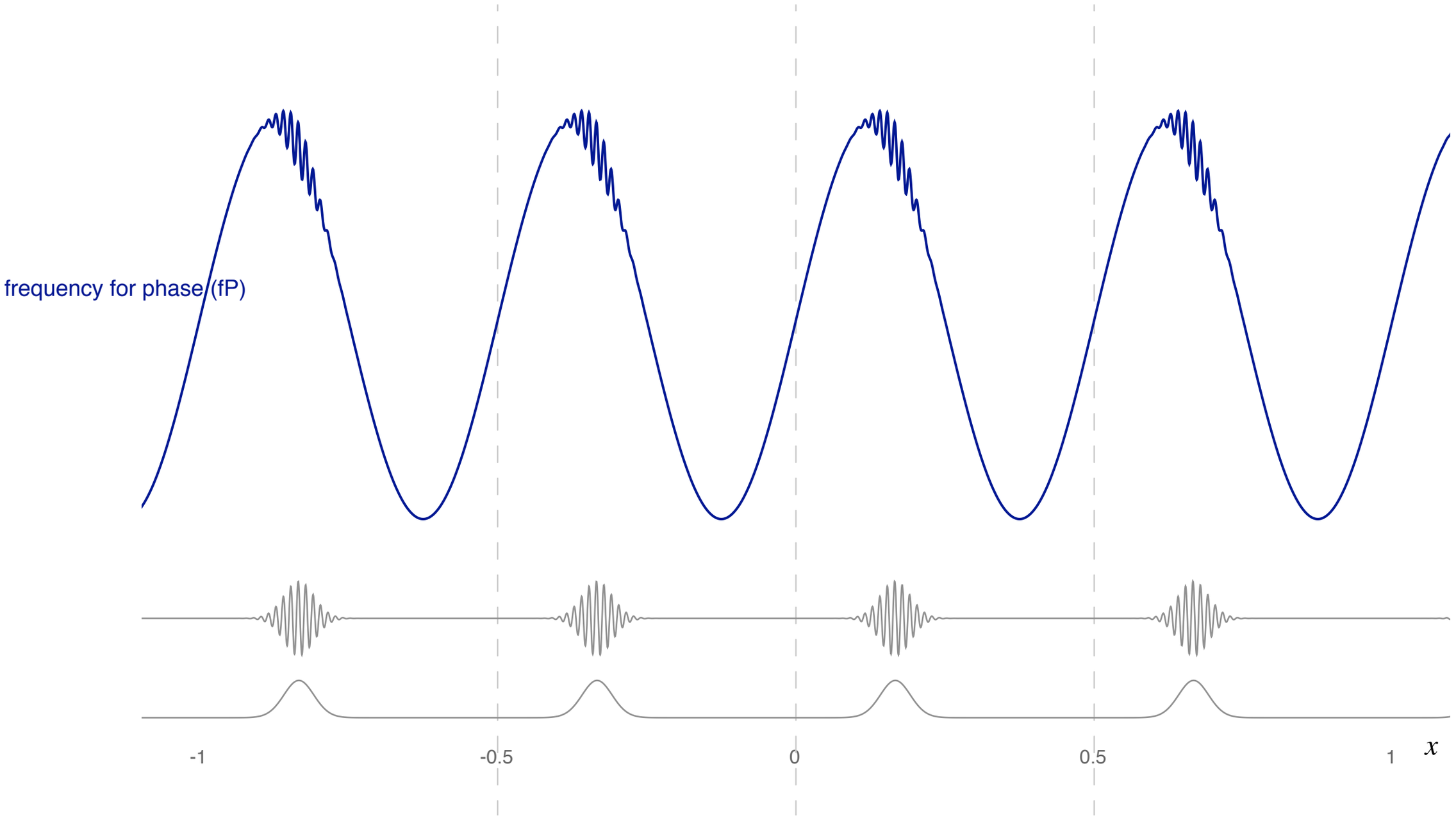

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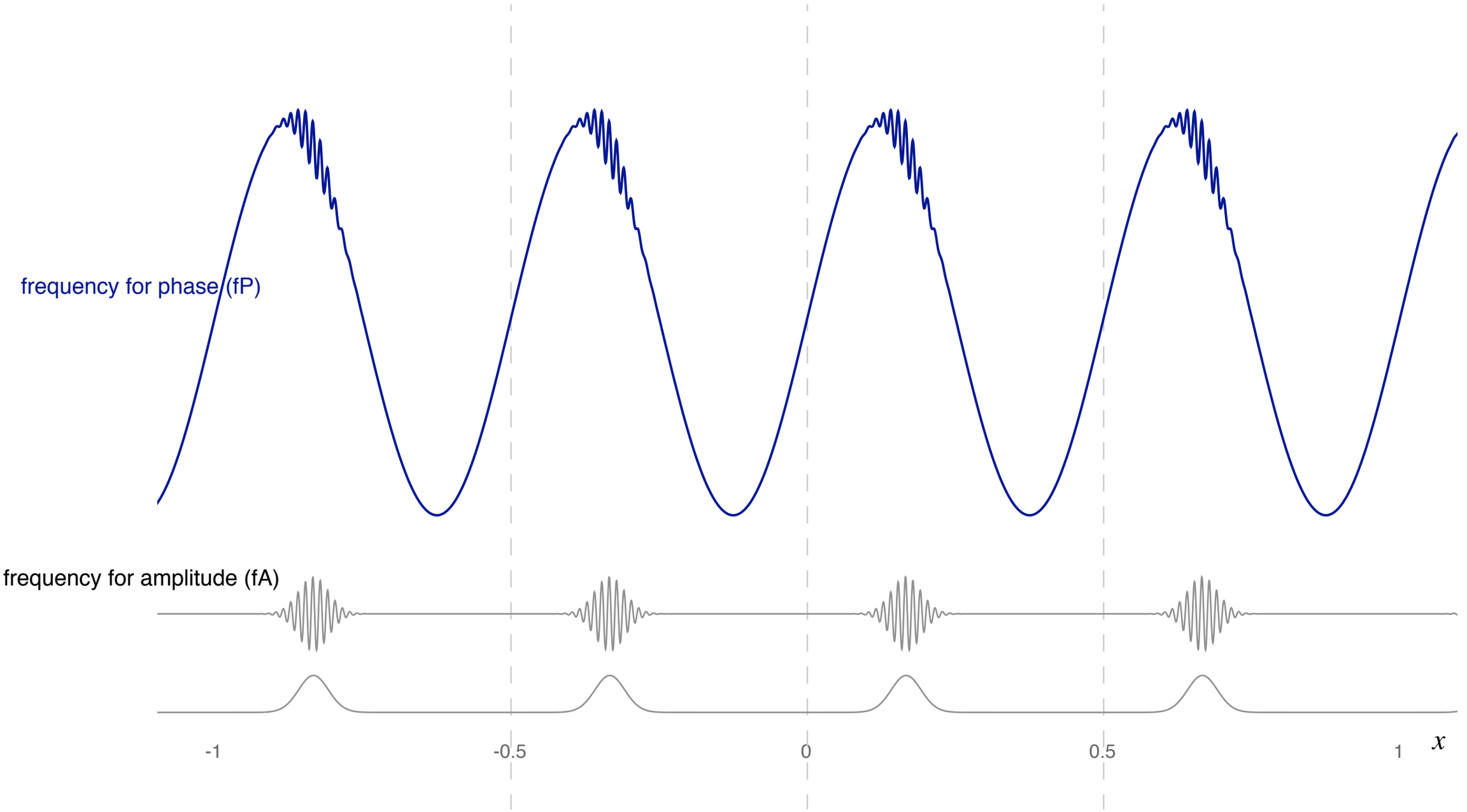

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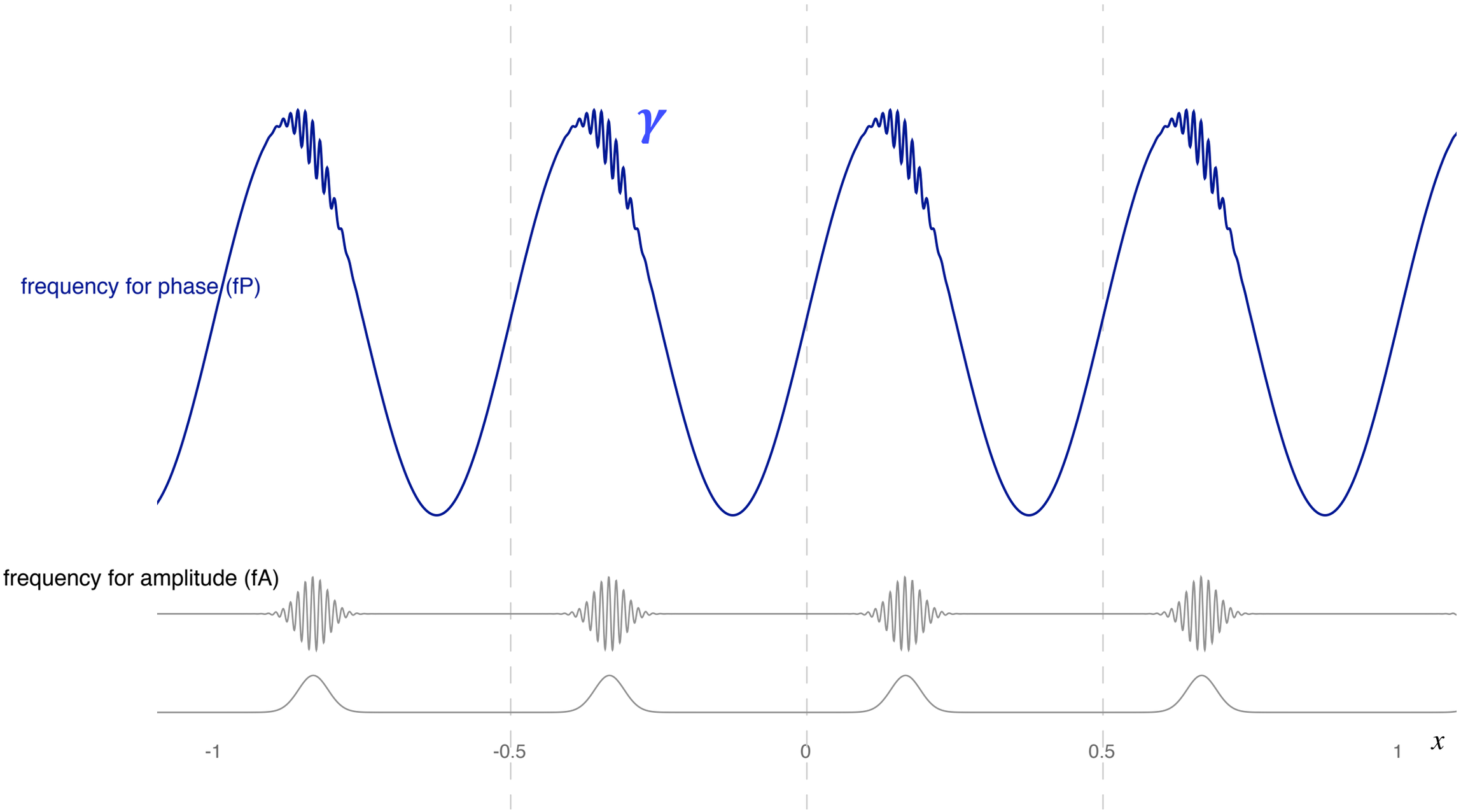

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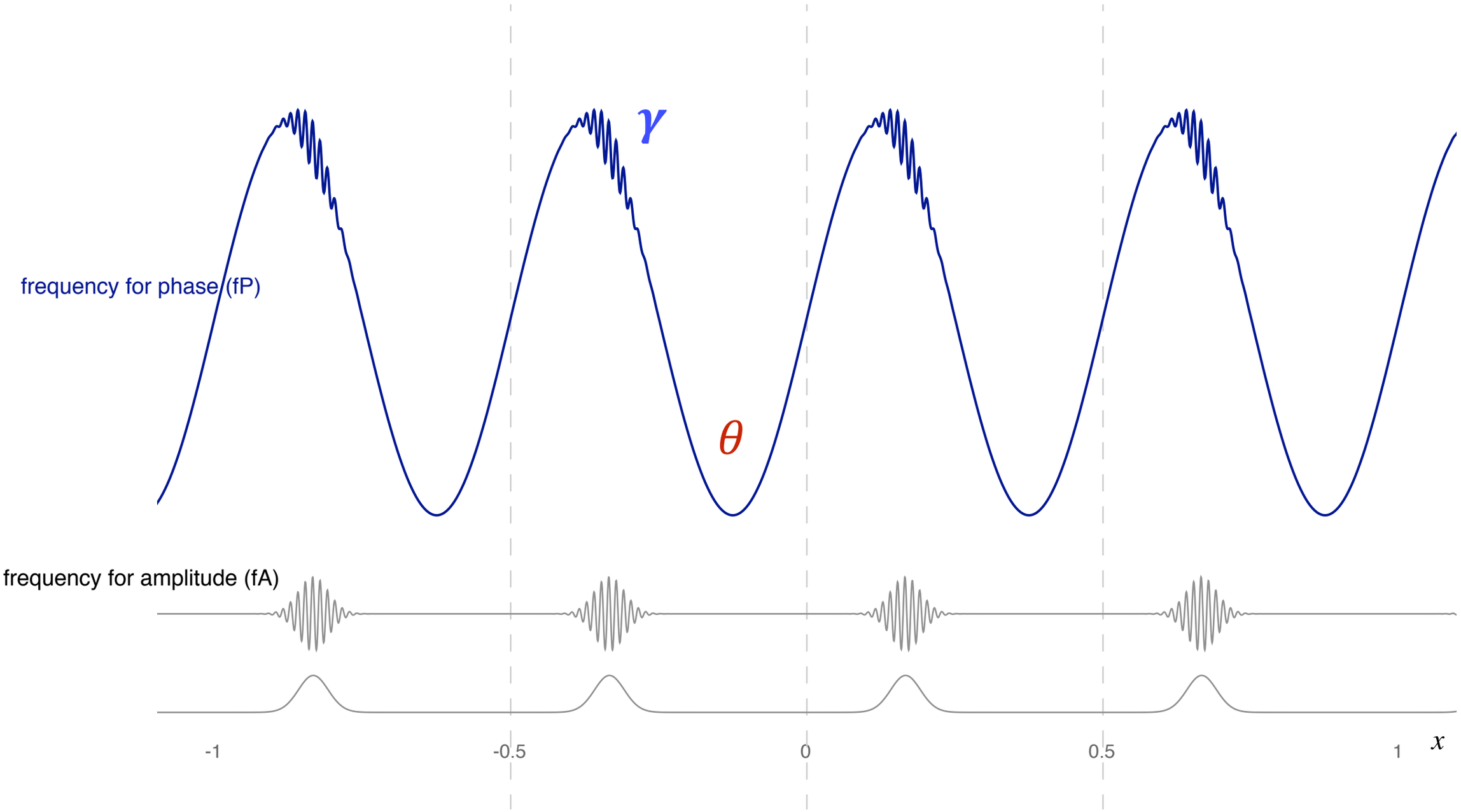

Cross-frequency phase-amplitude coupling (PAC): A generic mechanism regulating local brain dynamics?

Baillet, *Nature Neuroscience* (2017)

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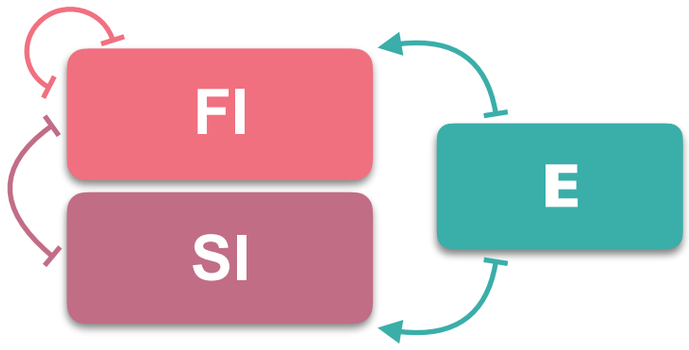
neural cell assembly



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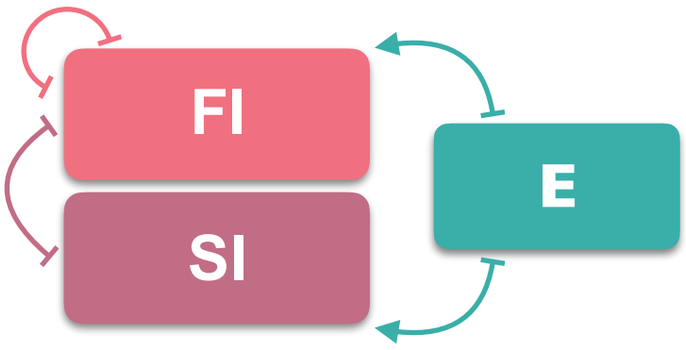

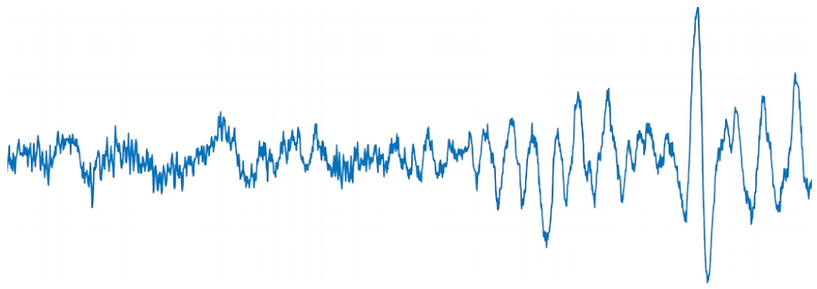

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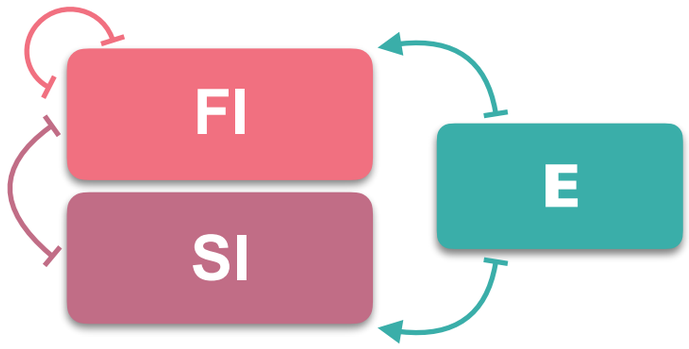
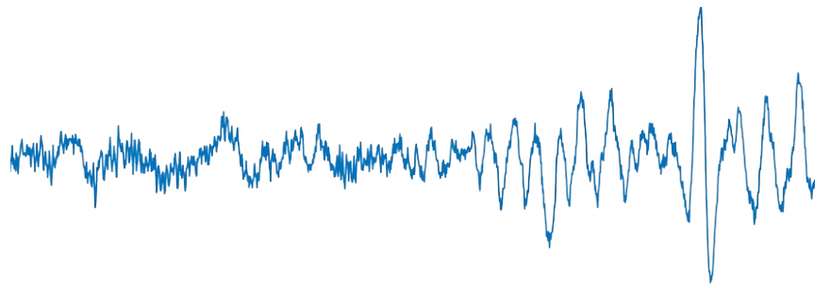
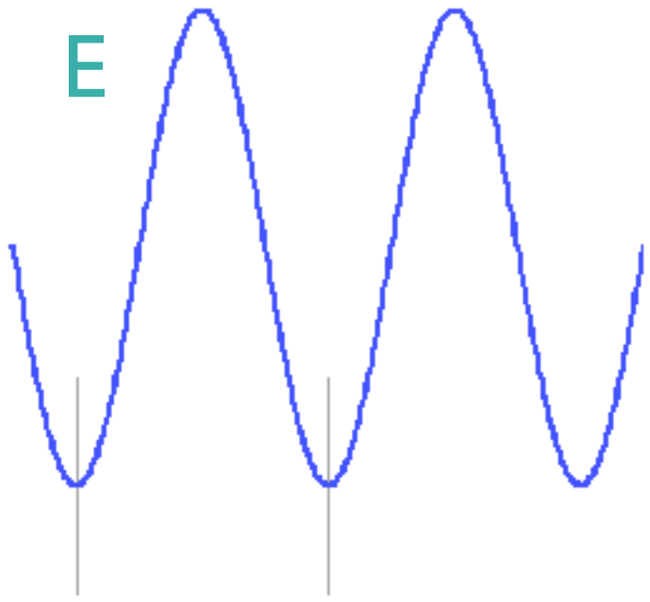




E: net excitability
I: net inhibition



Buszaki & Wang
Ann Rev Neurosc (2012)

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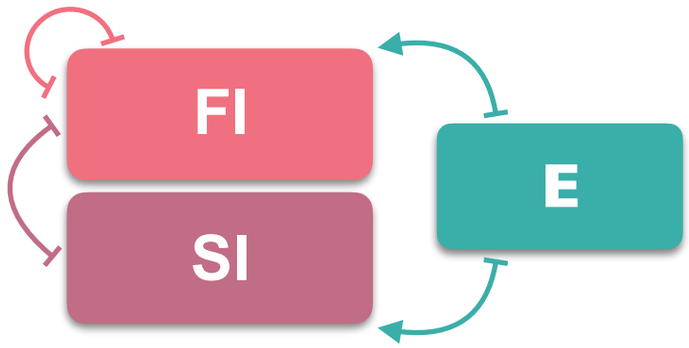

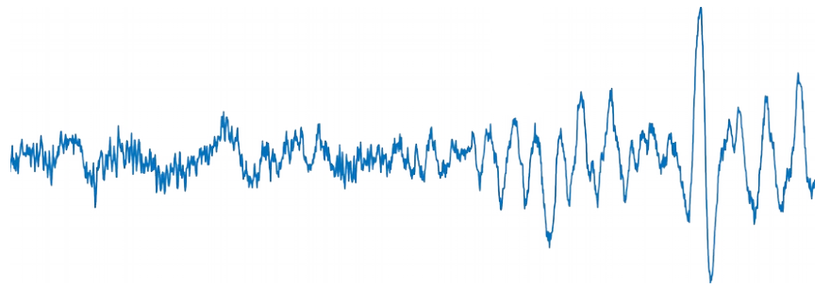

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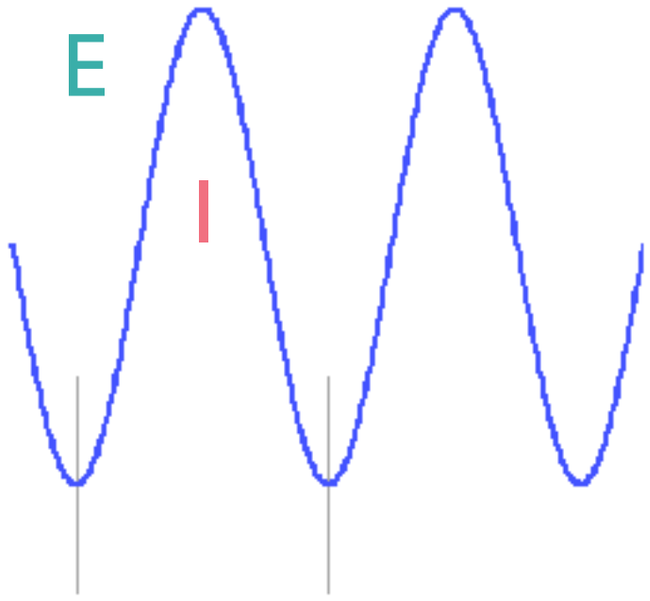

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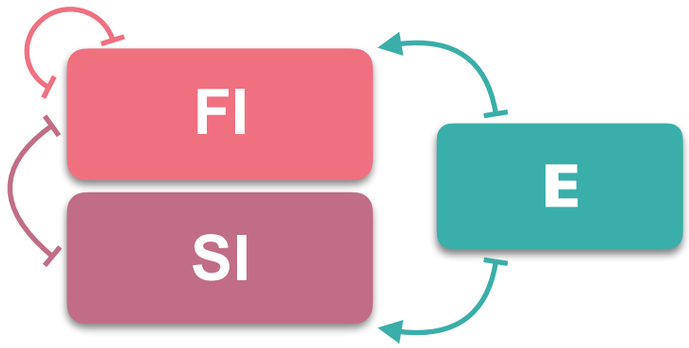

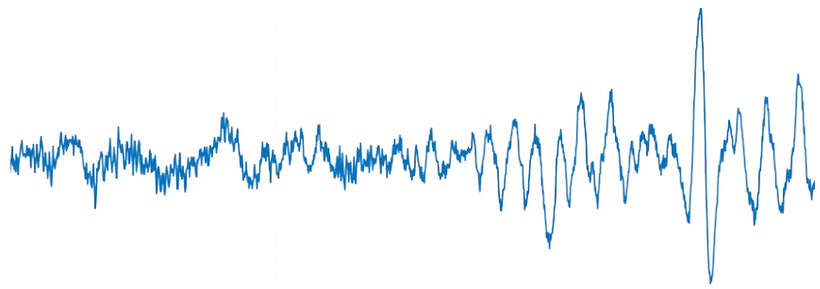

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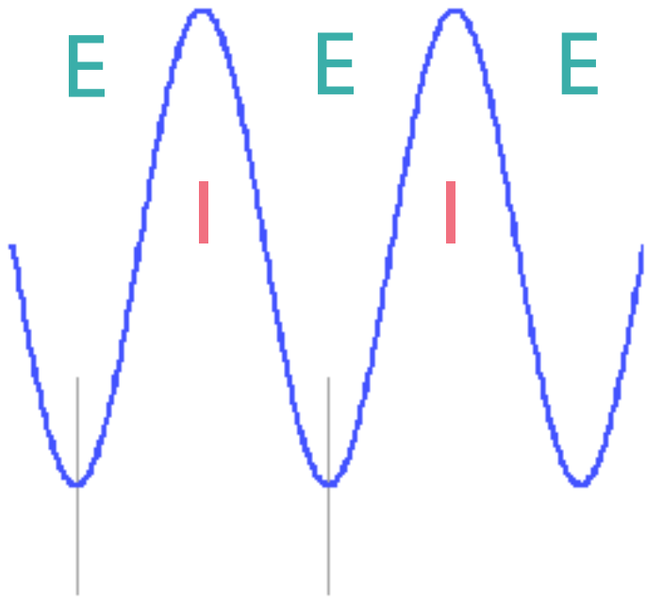

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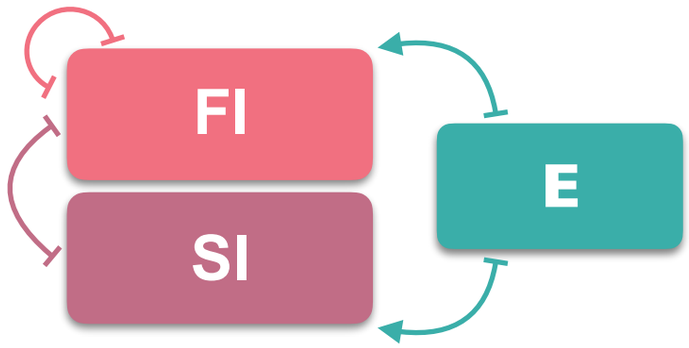

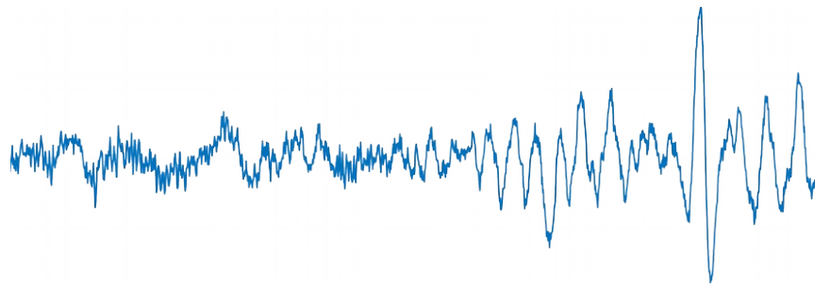

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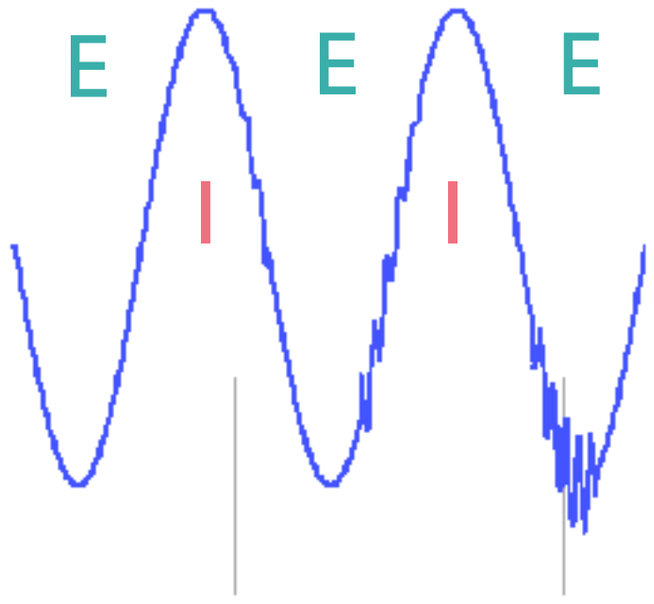

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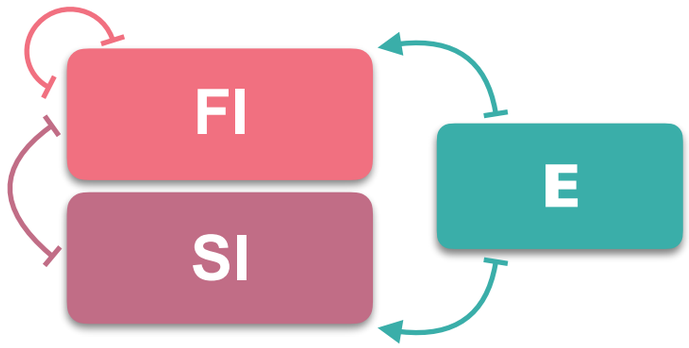

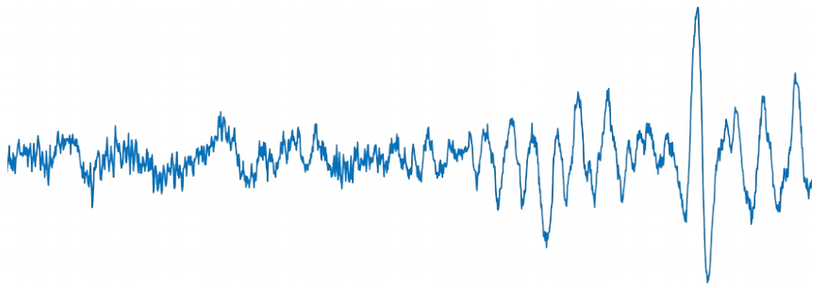

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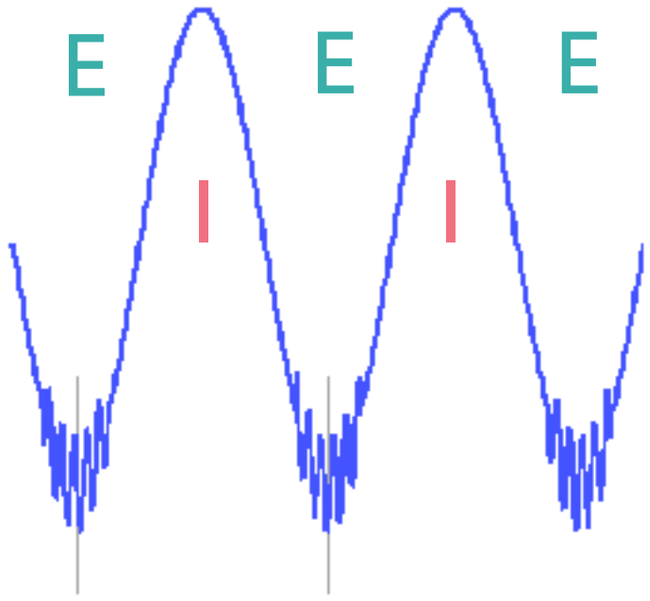

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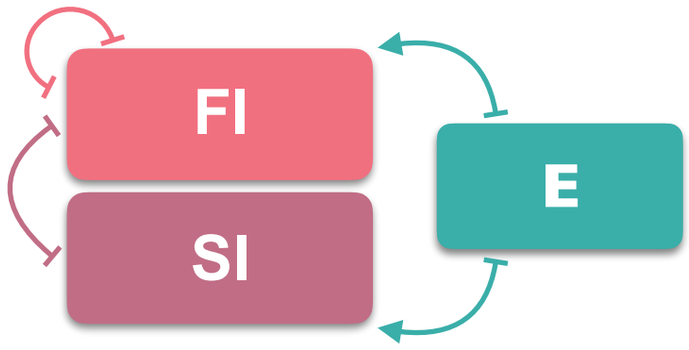

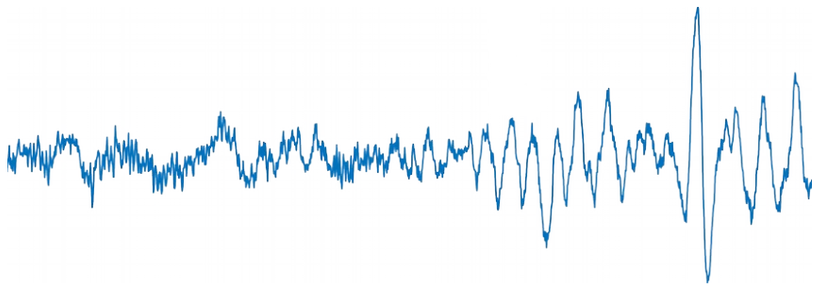

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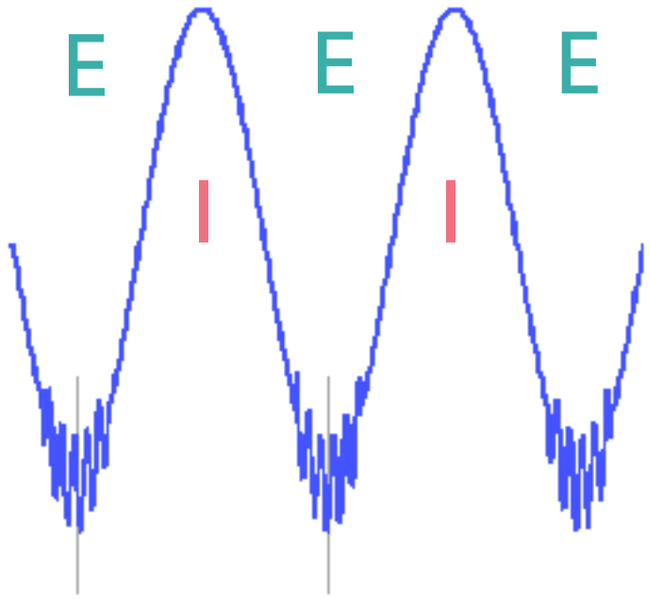
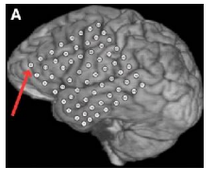
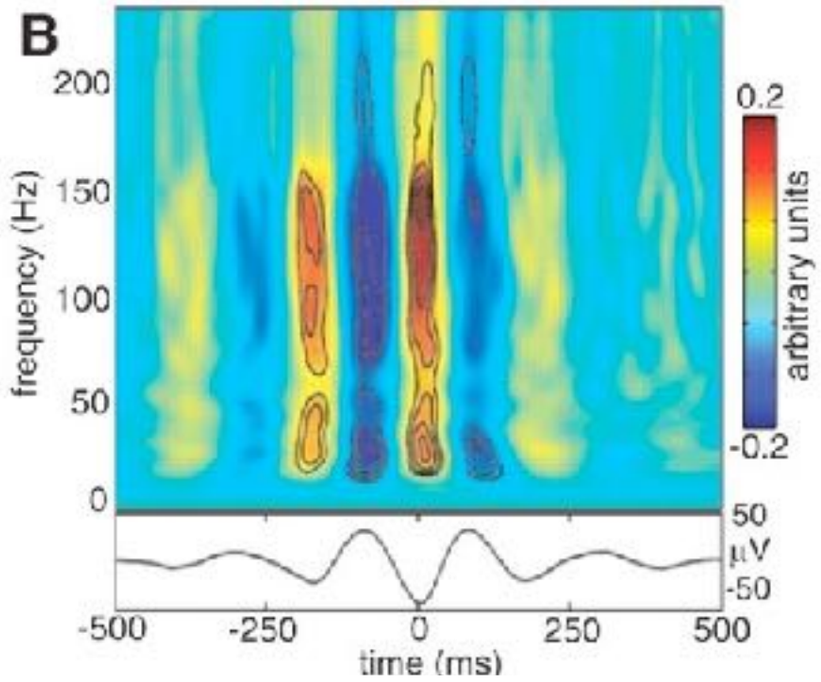


Buszaki & Wang
Ann Rev Neurosc (2012)



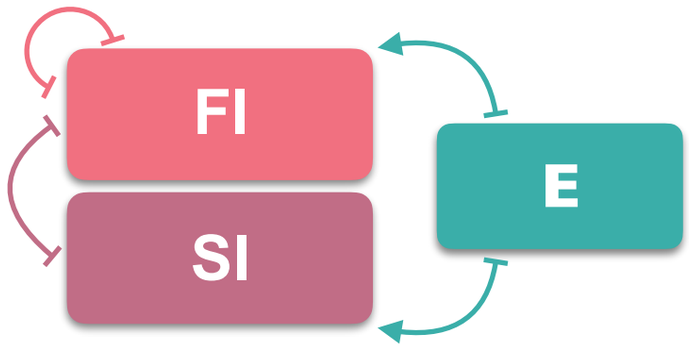
Human LFP
Canolty et al. *Science* (2006)

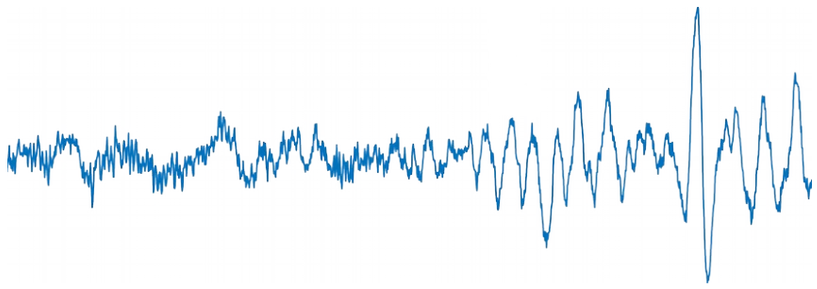


Baillet, *Nature Neuroscience* (2017)

Cross-frequency phase-amplitude coupling (PAC): A generic mechanism regulating local brain dynamics?

neural cell assembly





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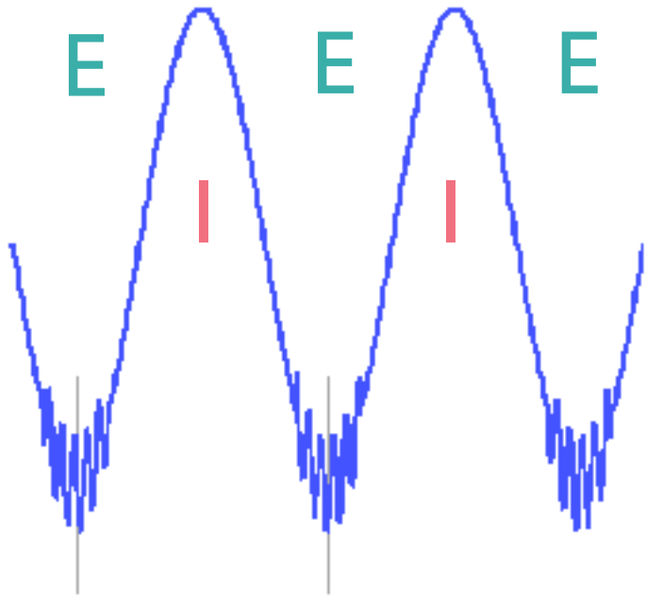

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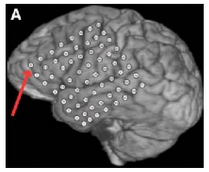

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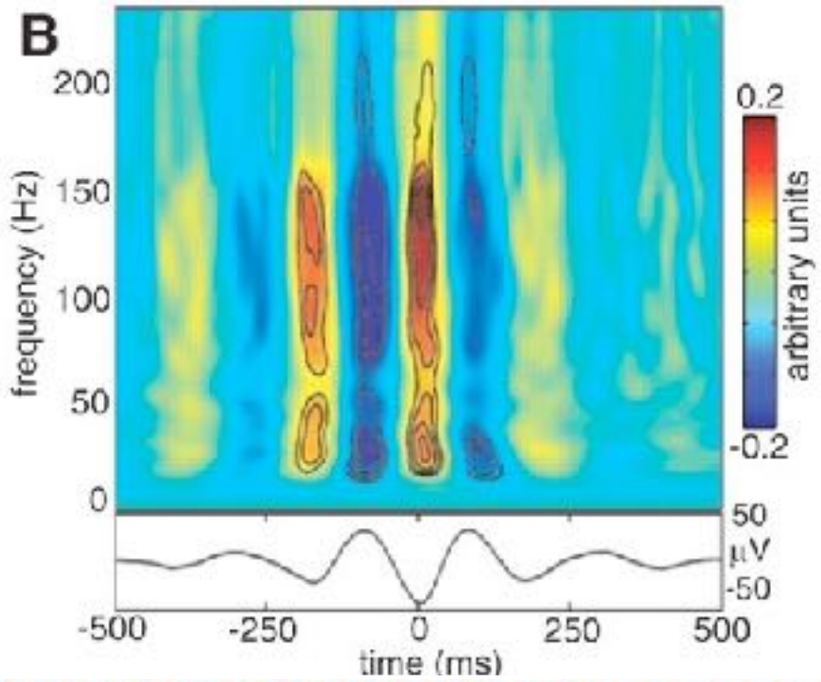

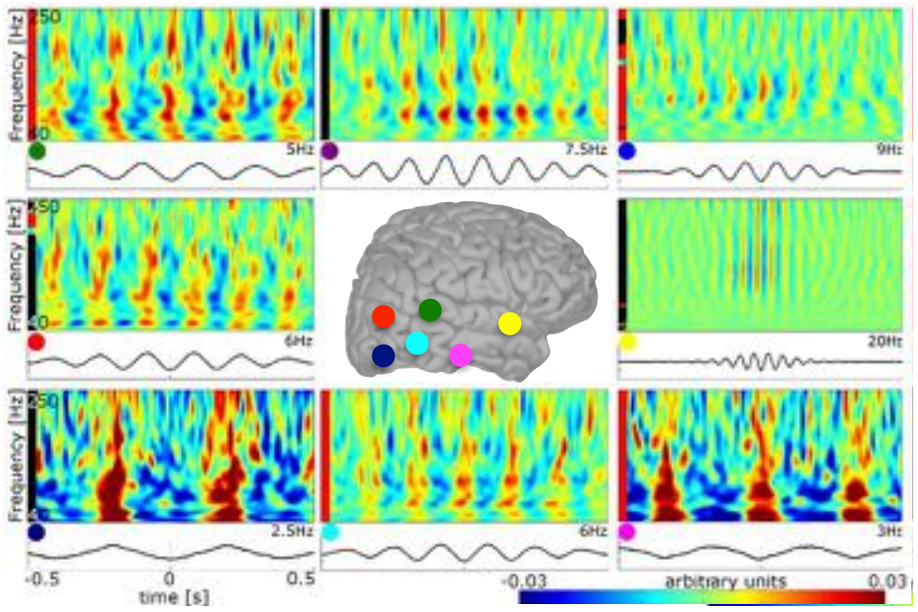

MEG
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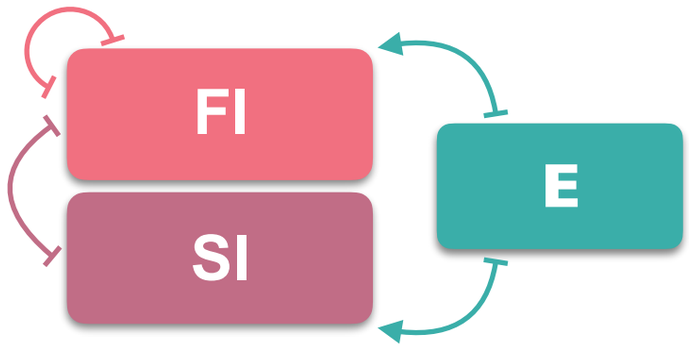

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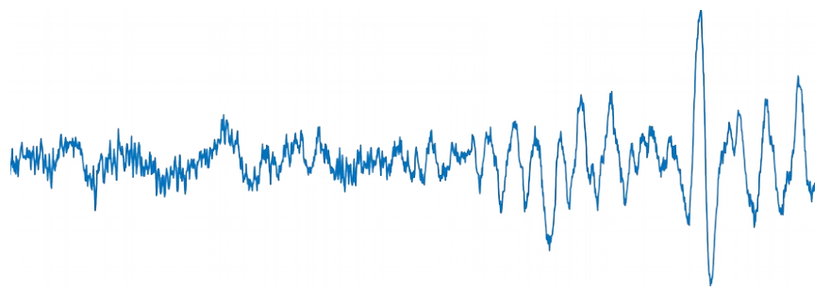

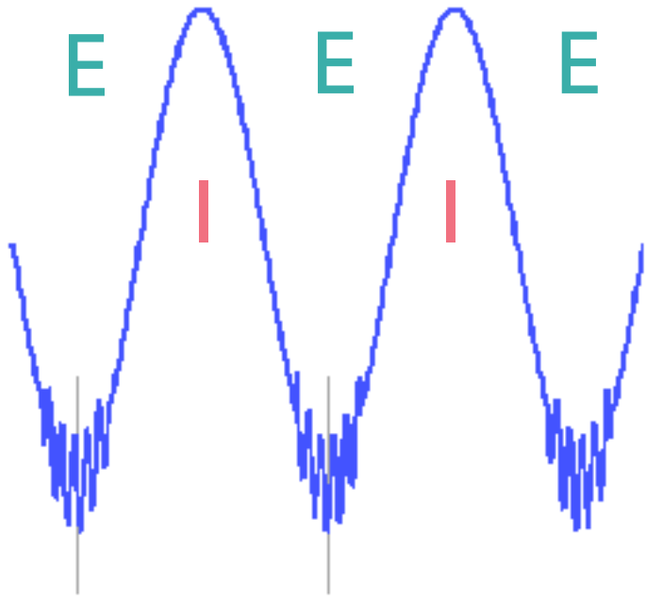

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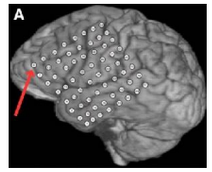

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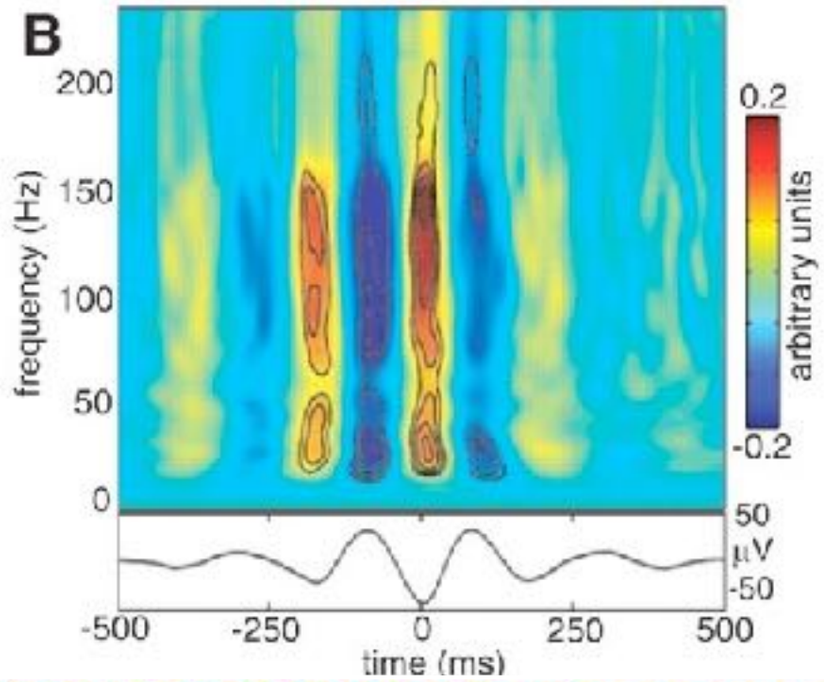

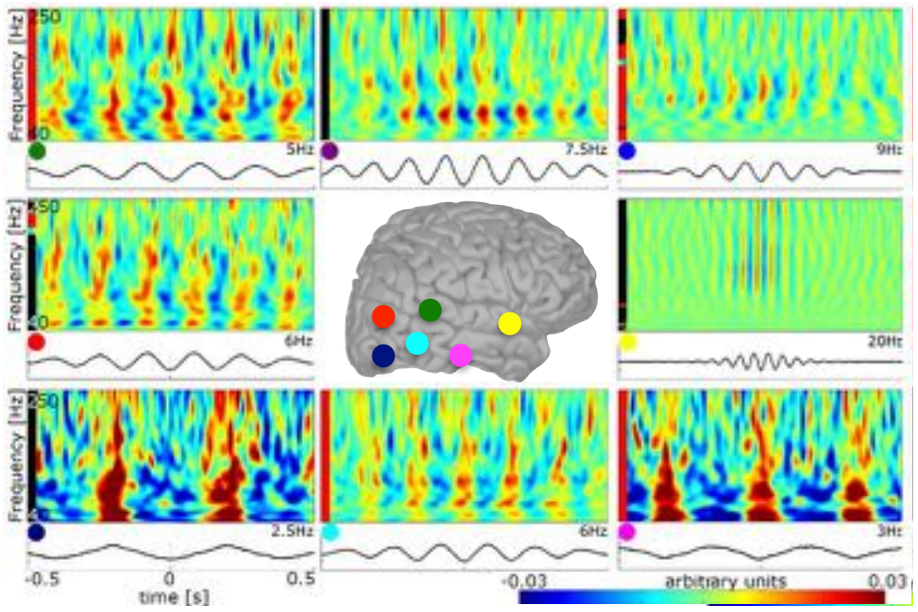

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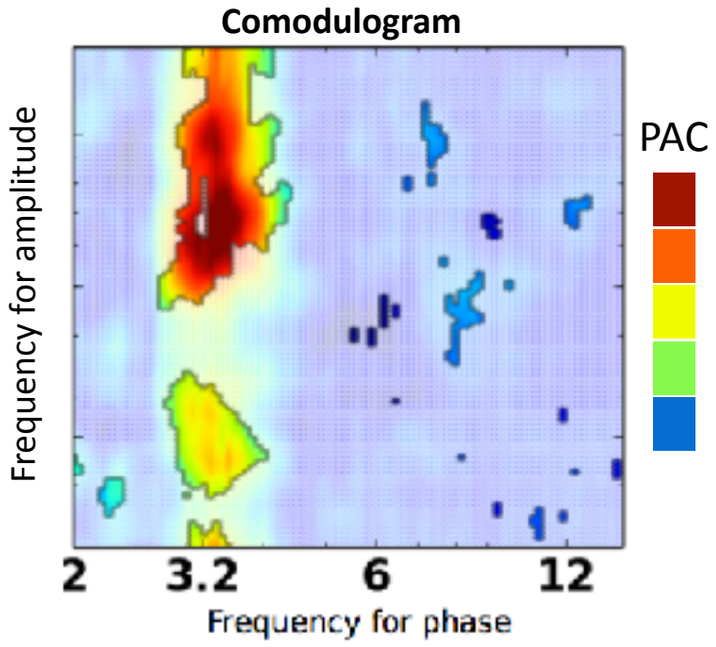

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Cross-frequency coupling:
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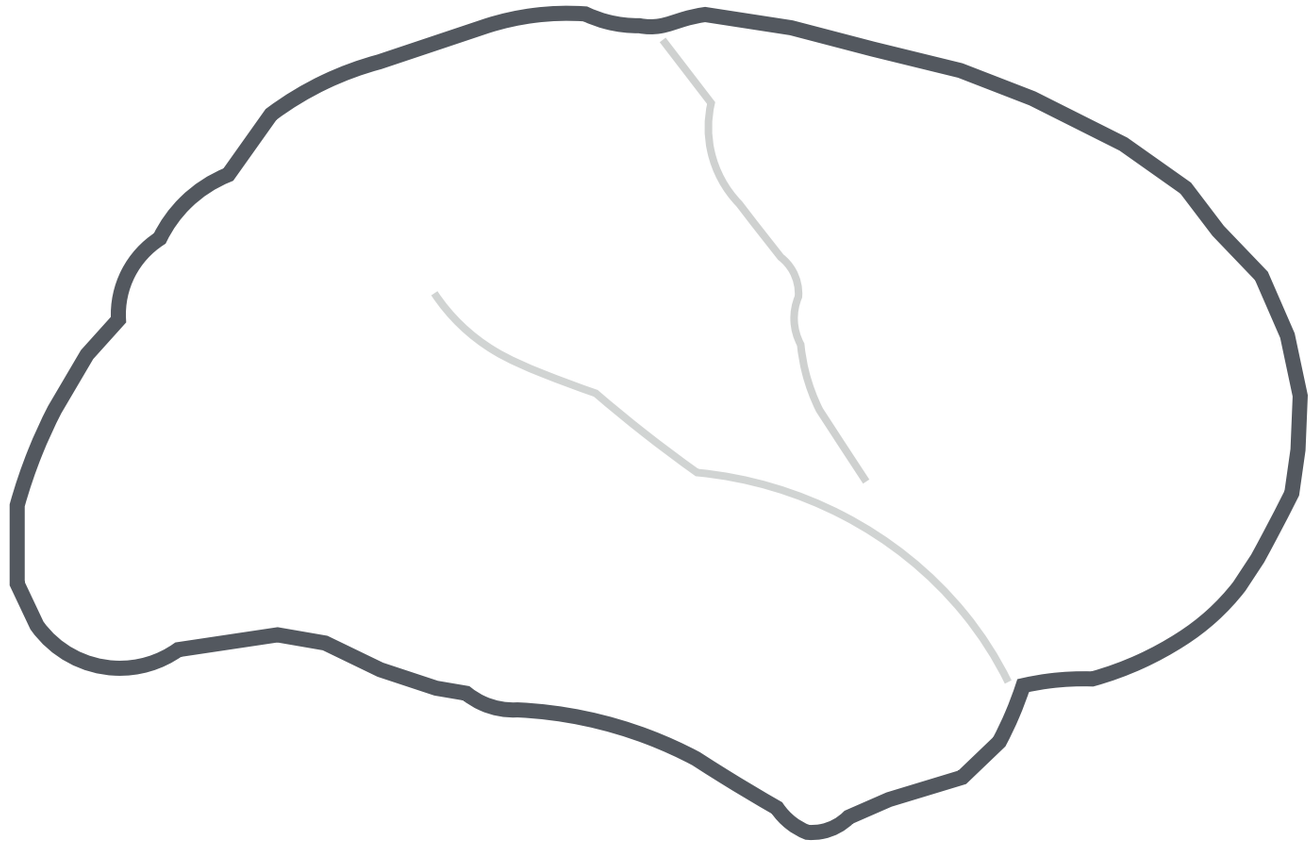

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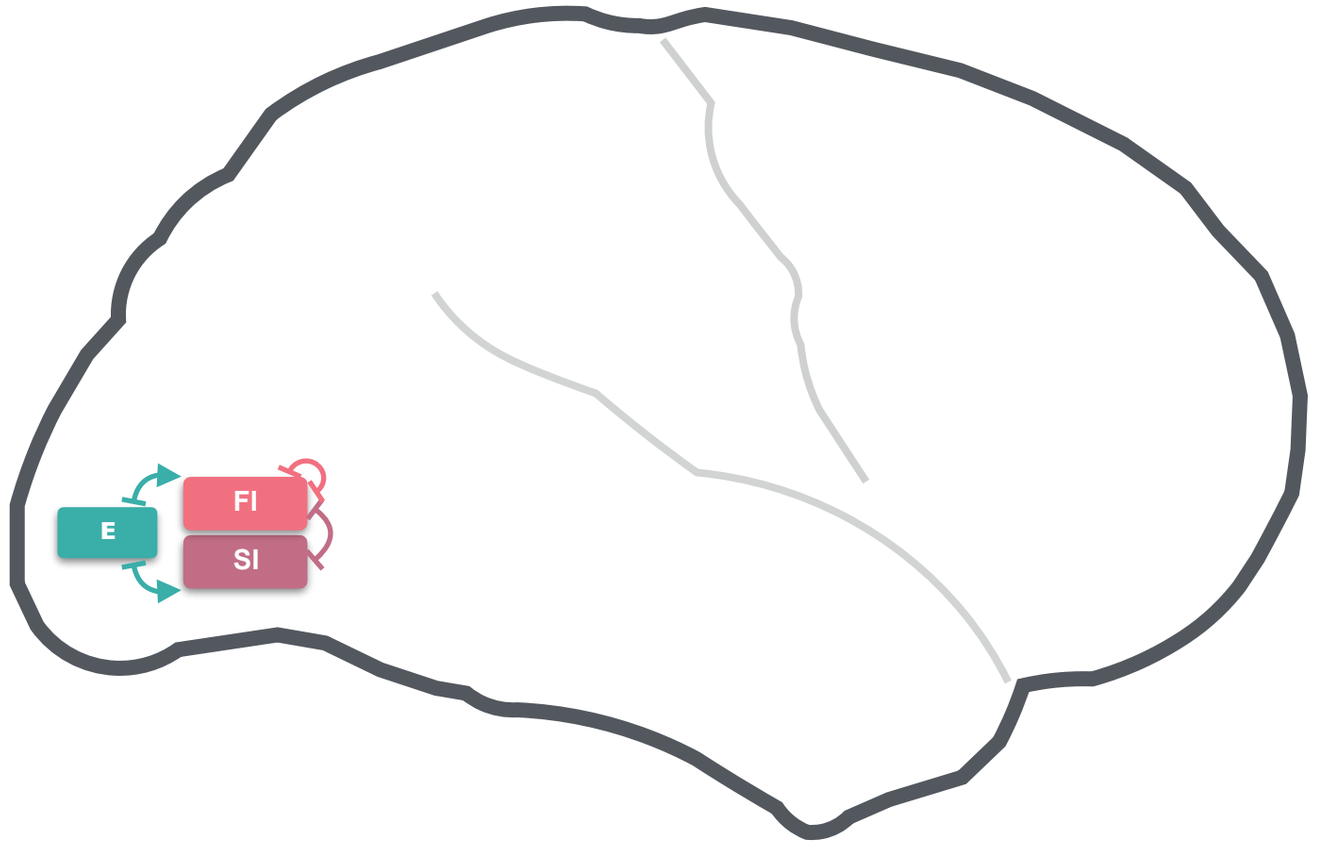

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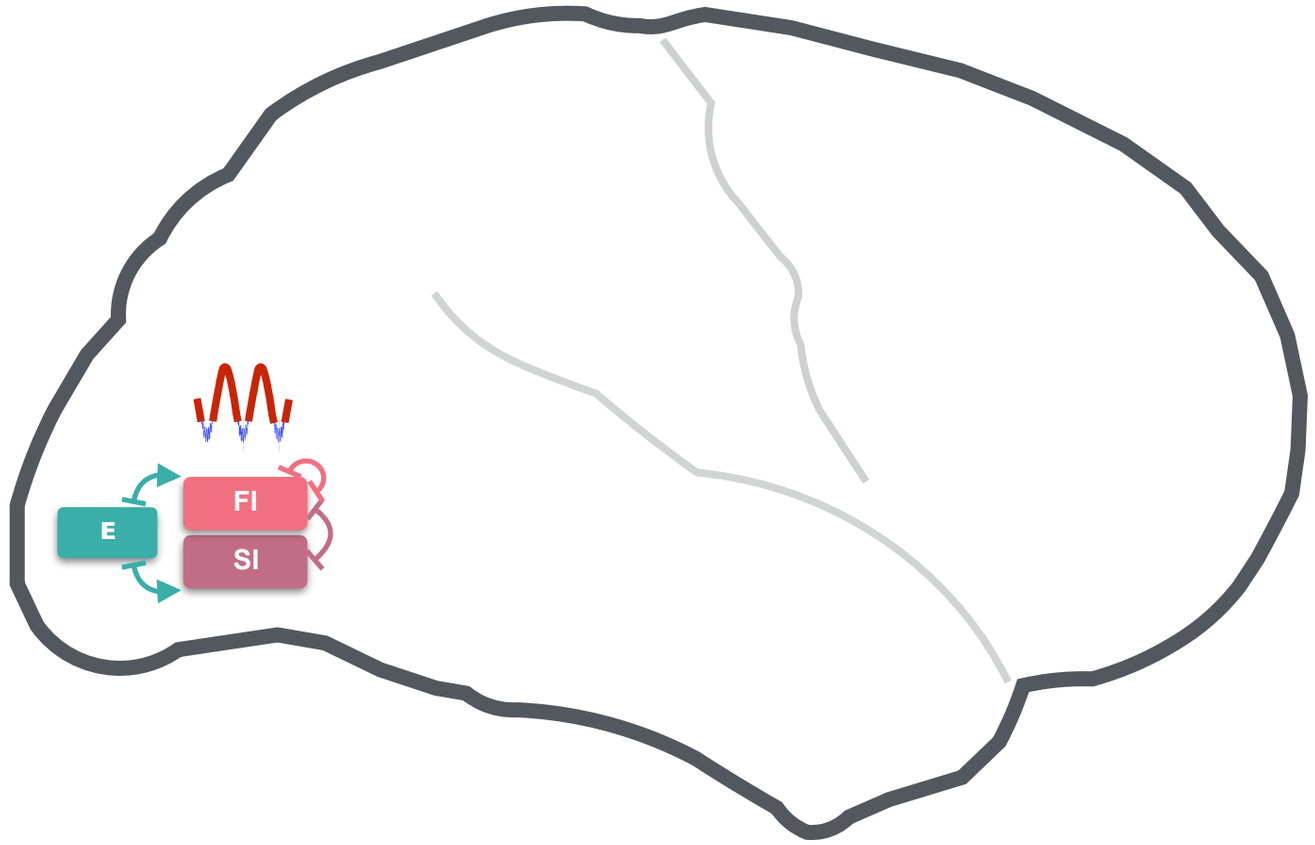

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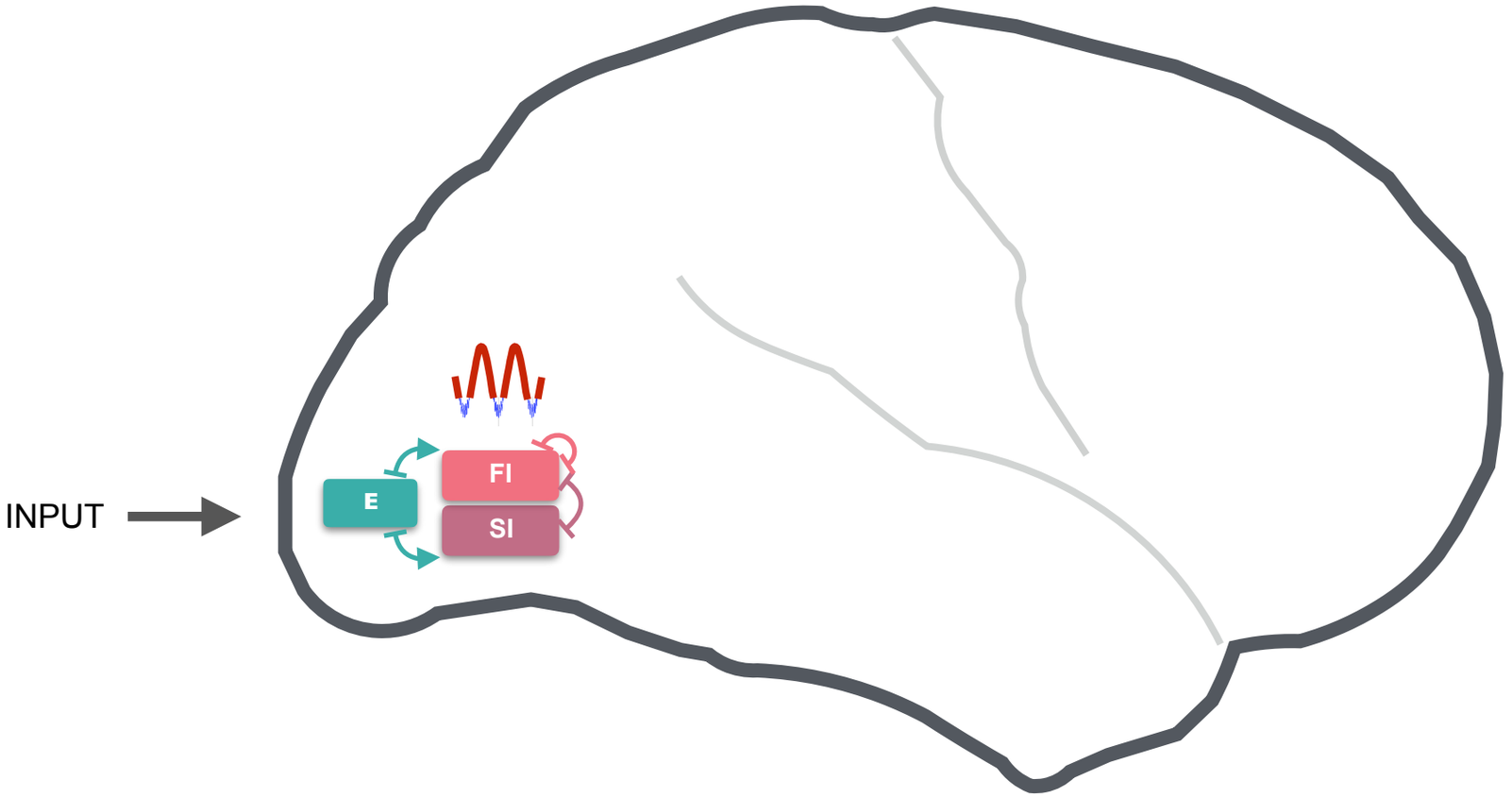

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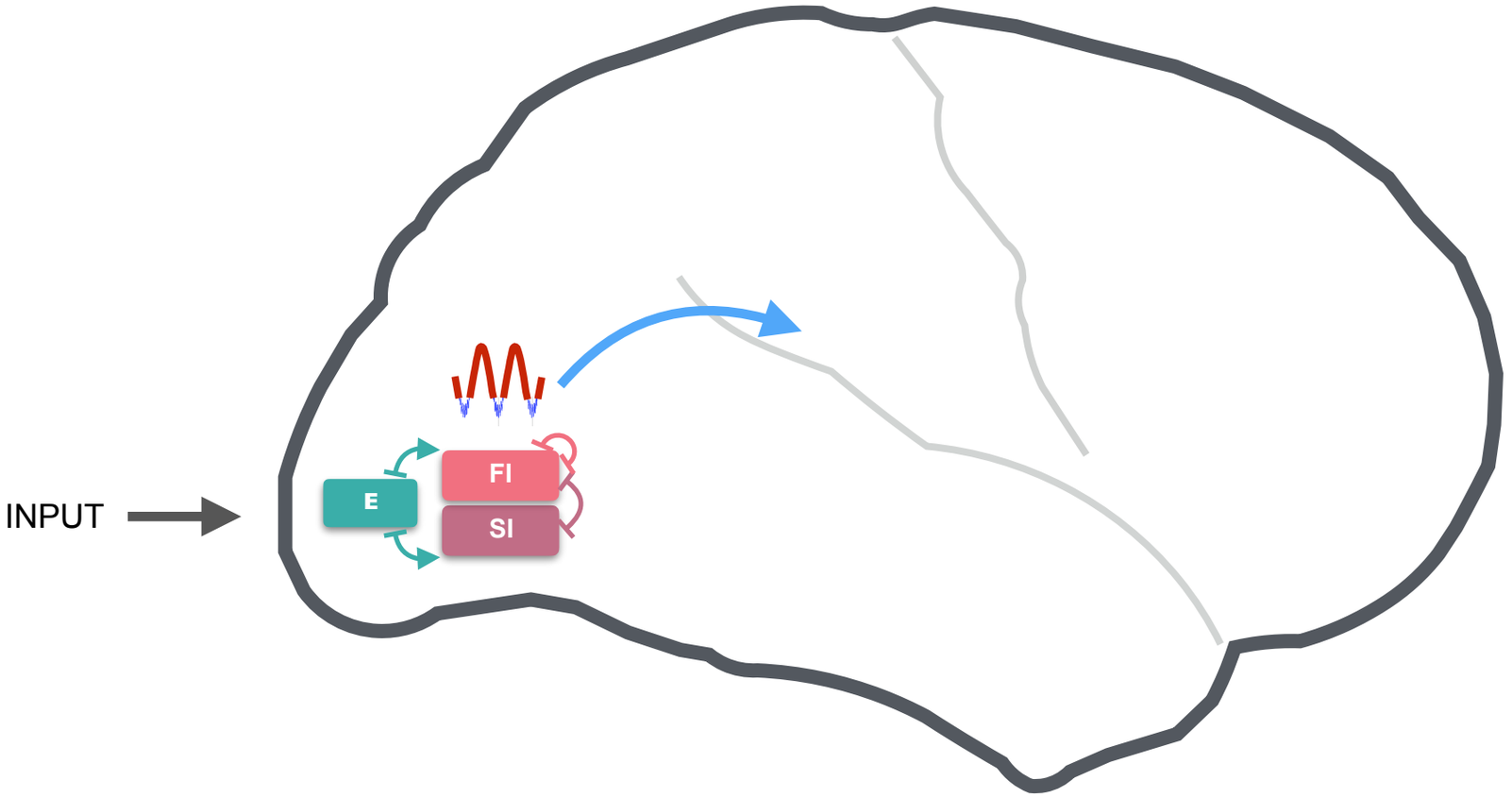

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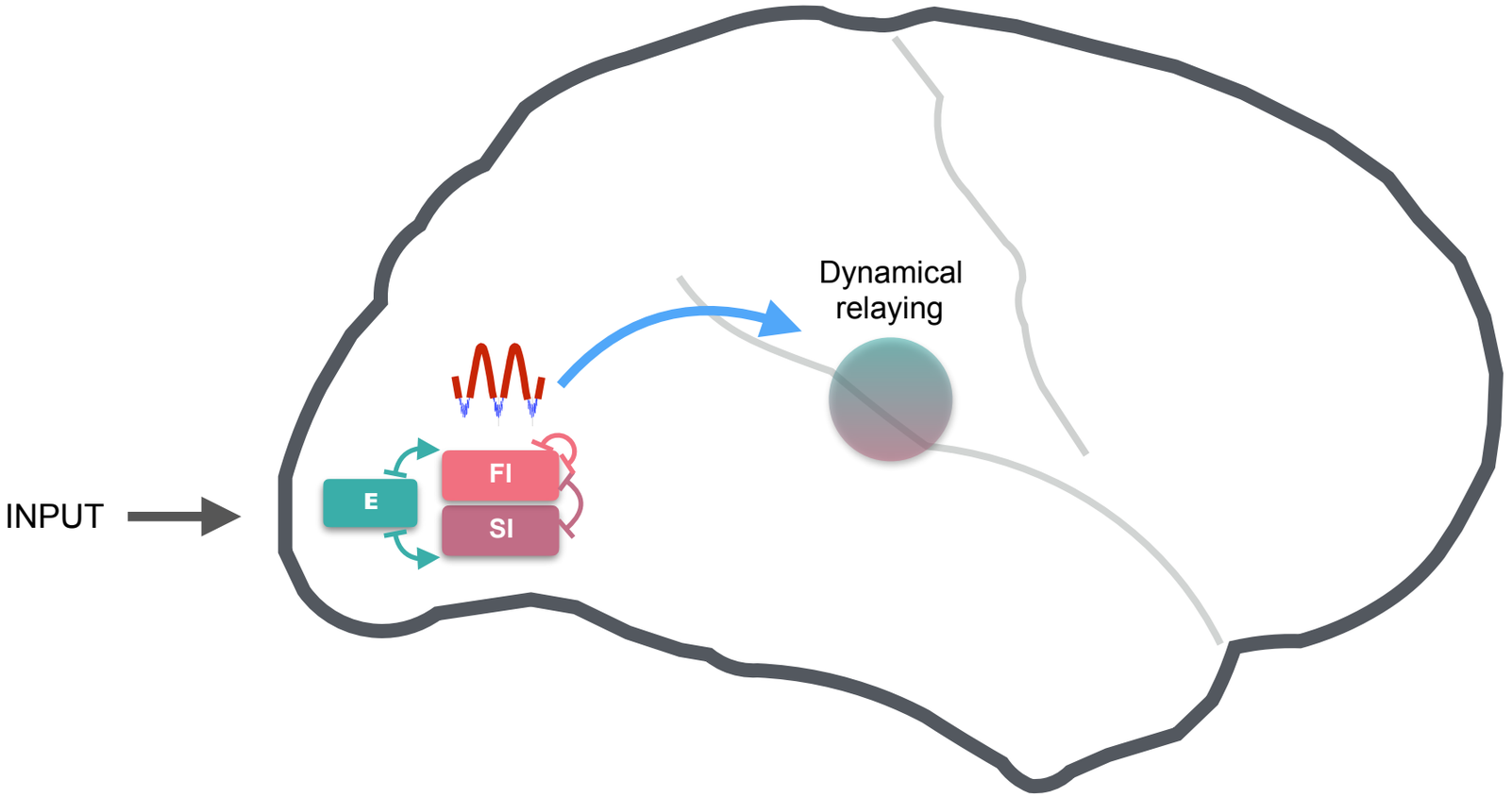

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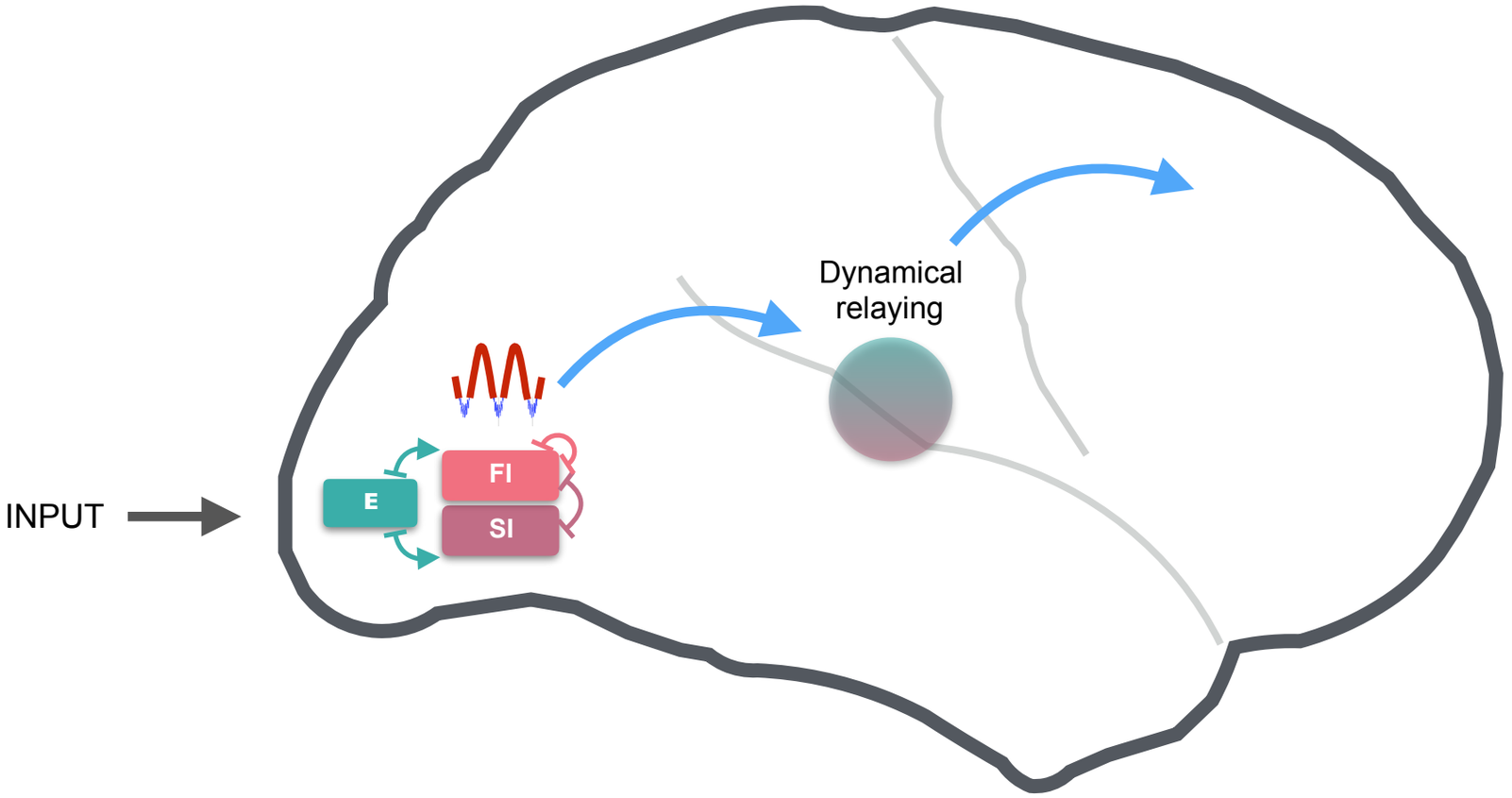

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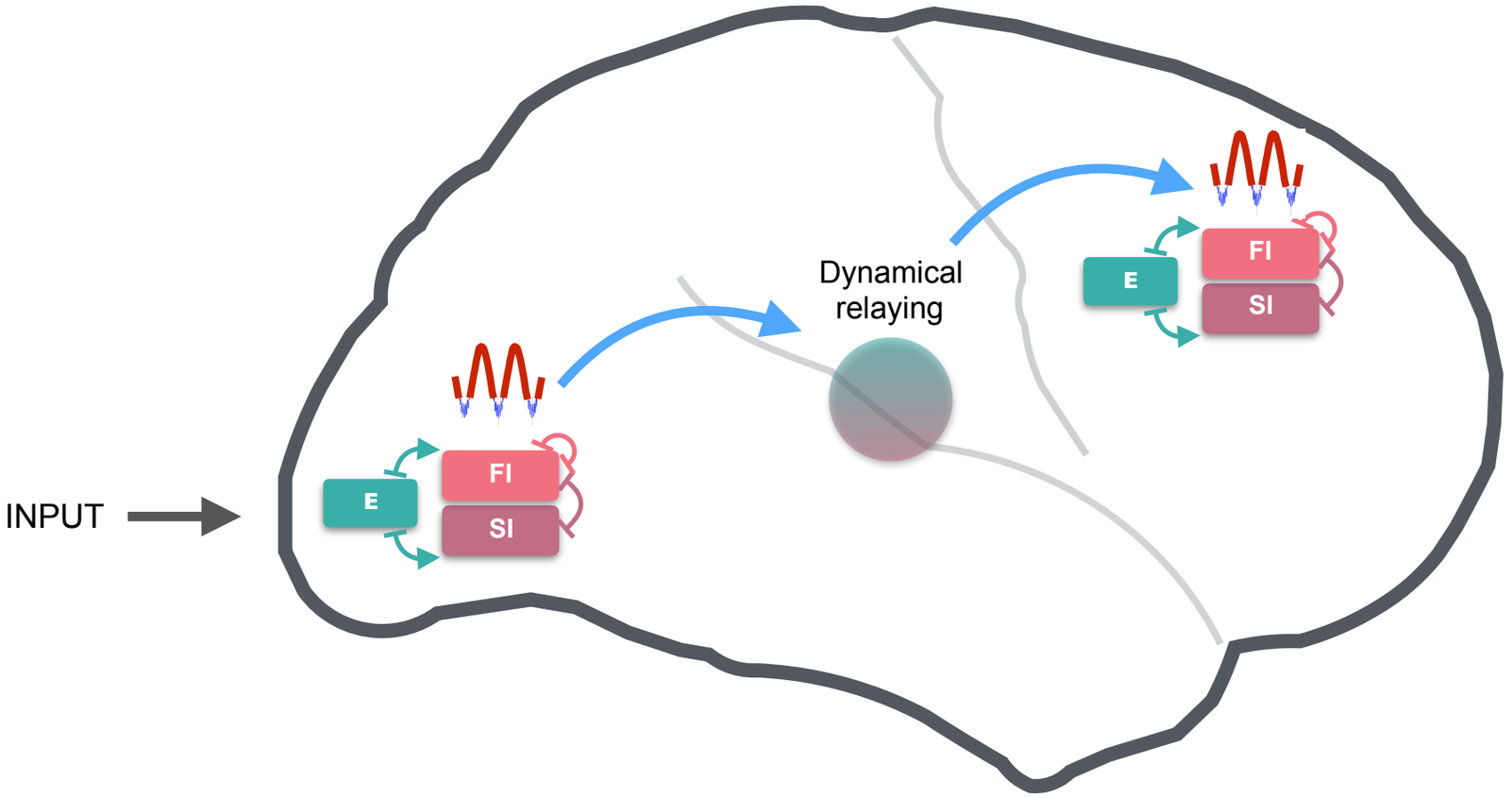

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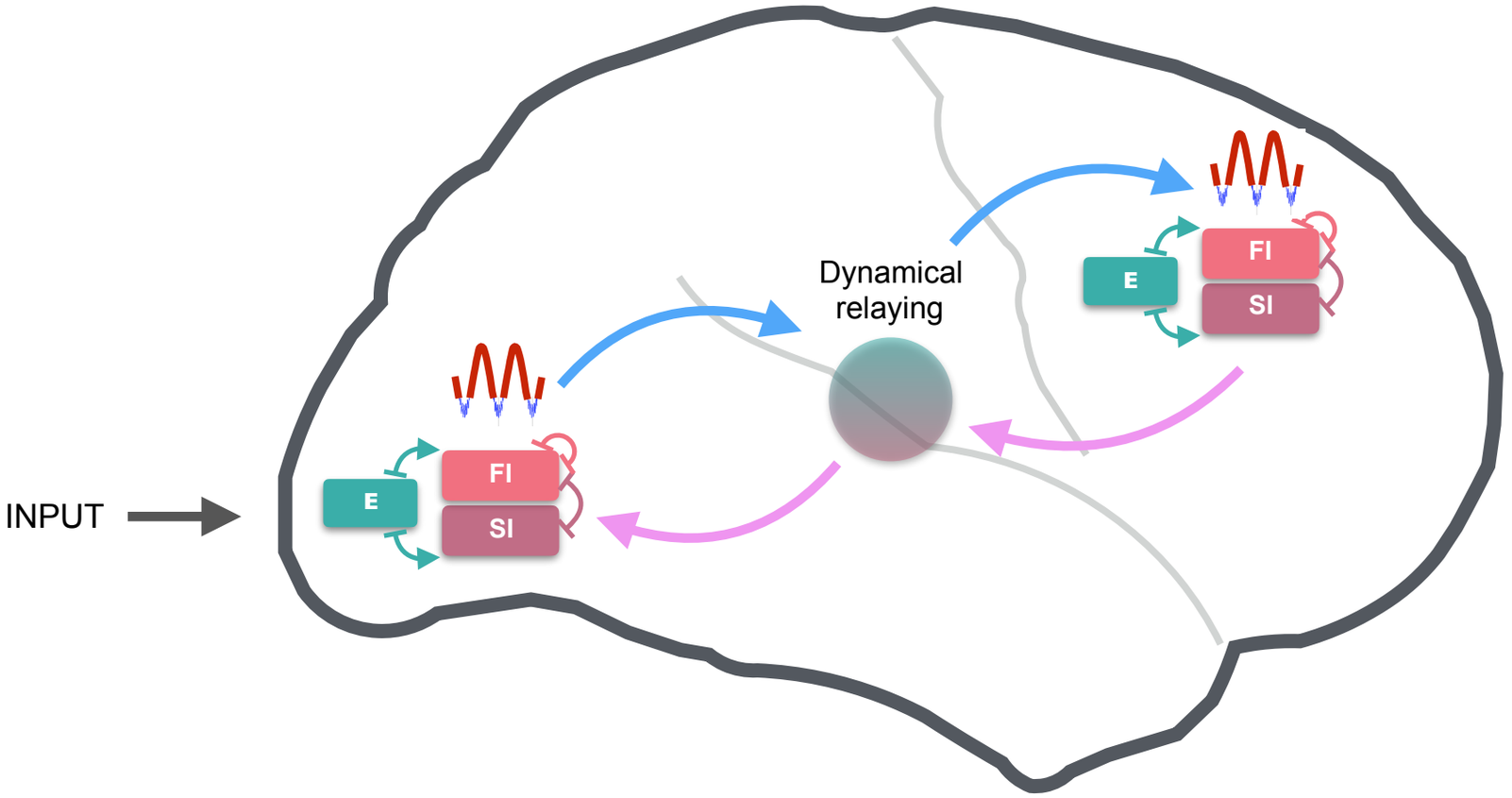

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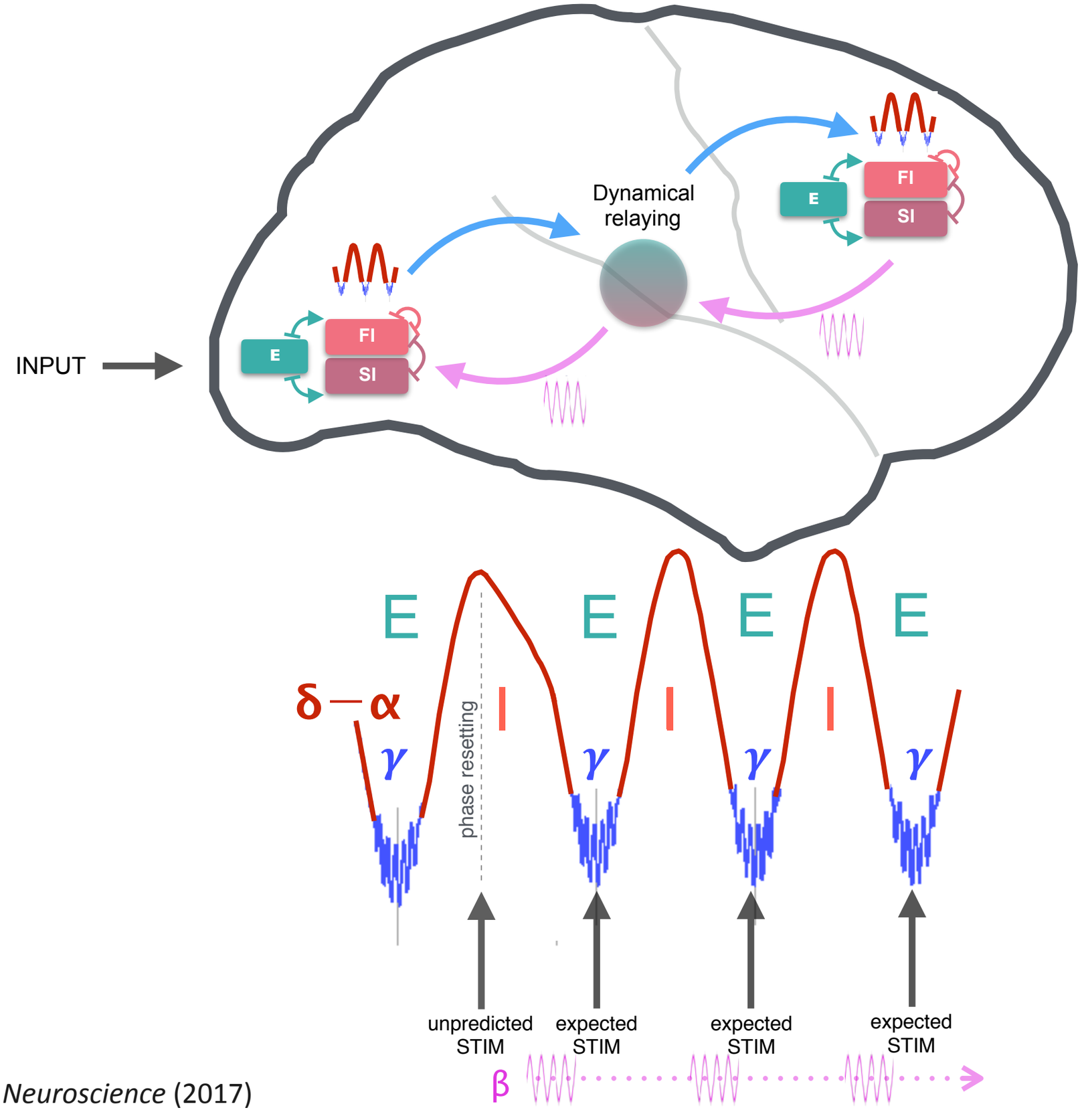

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Wrap-up: distinct roles for distinct frequencies

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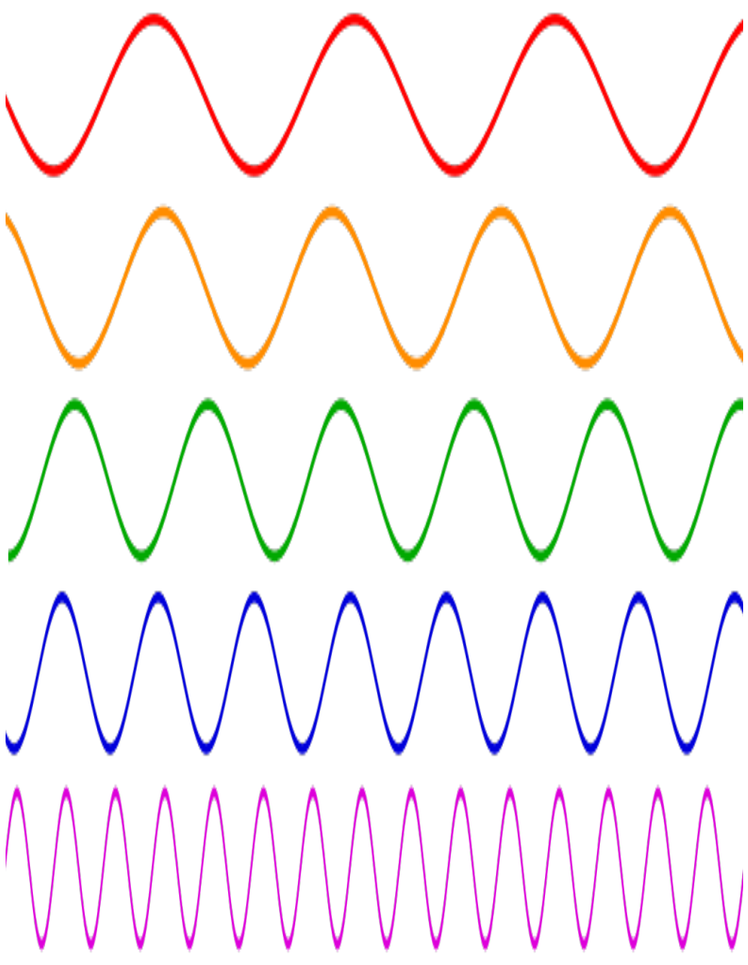

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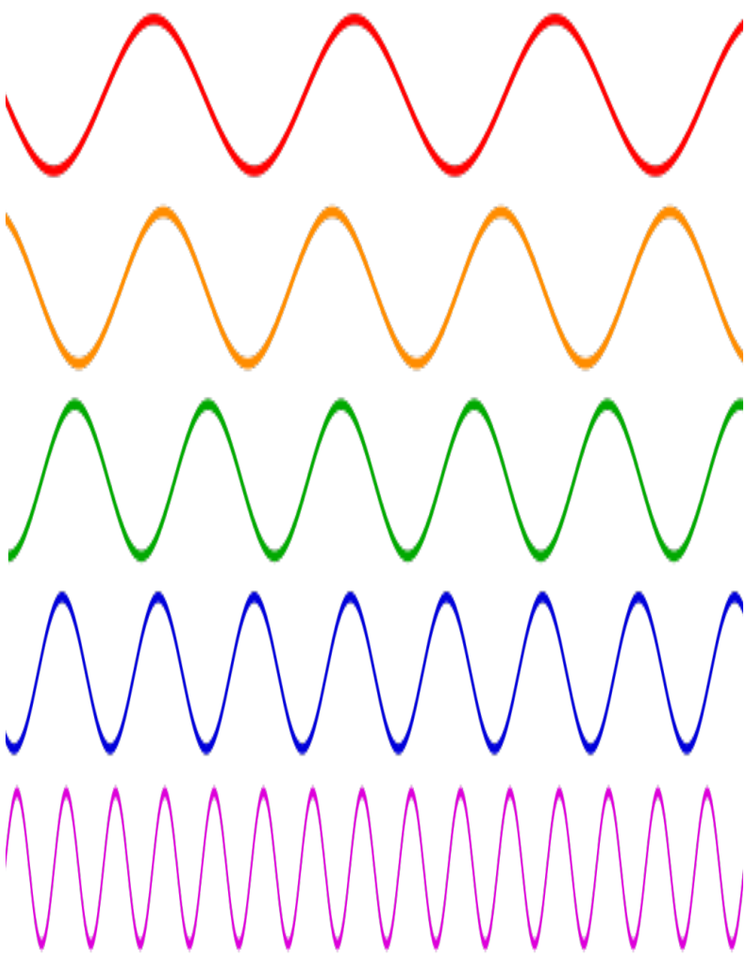

δ−α: cycles of regional excitability

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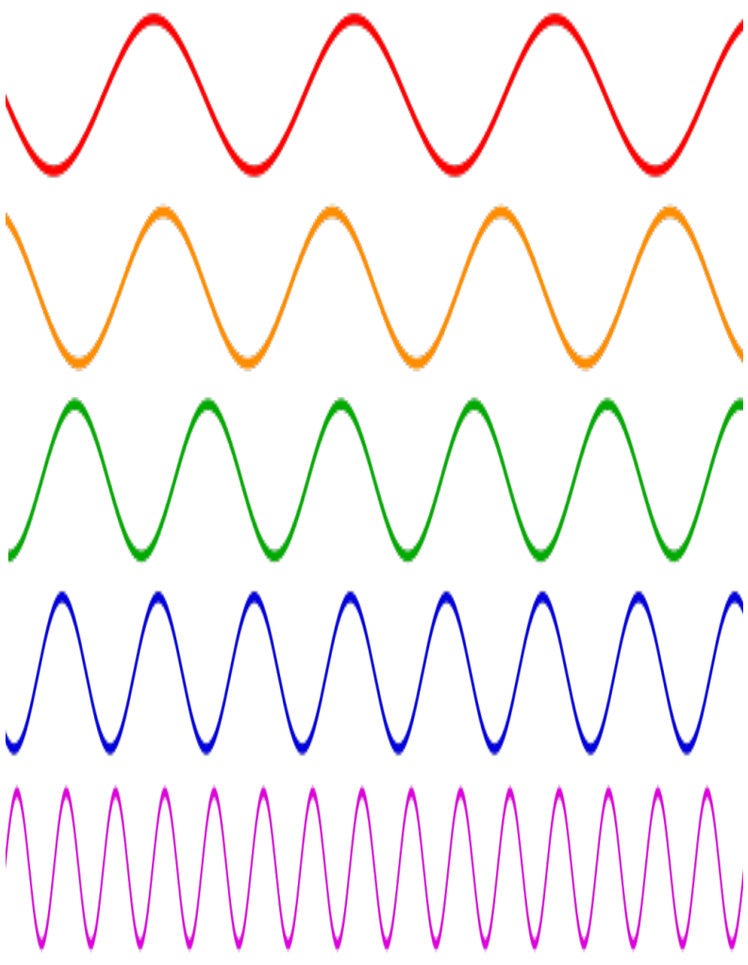

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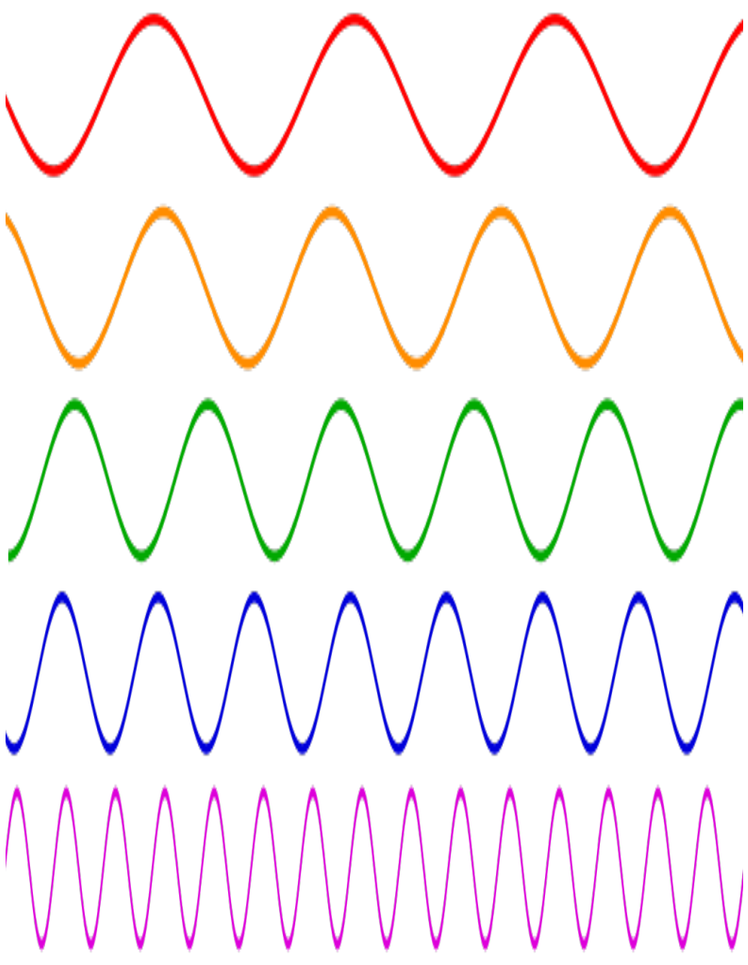

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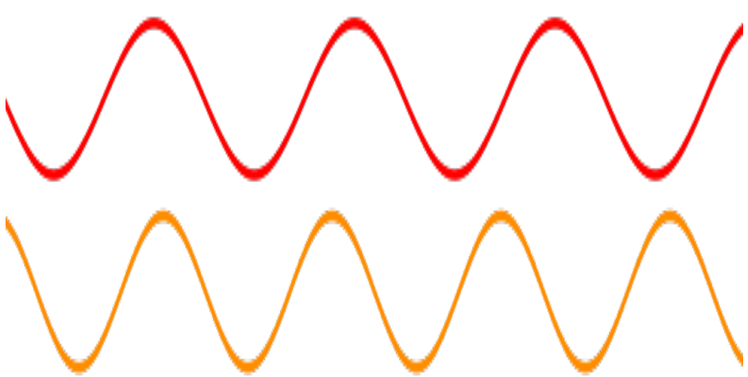

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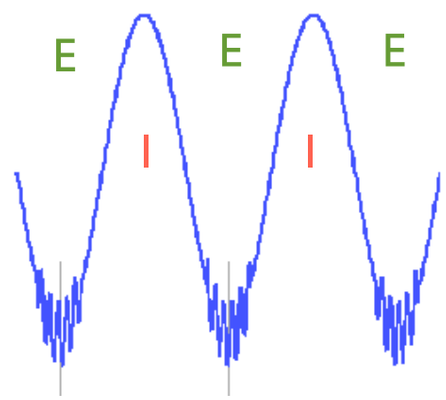

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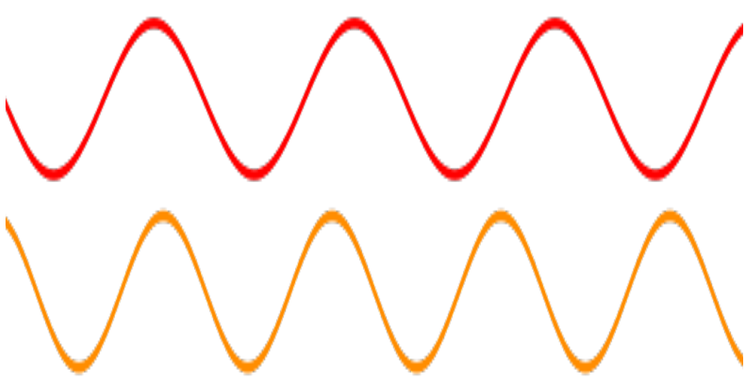

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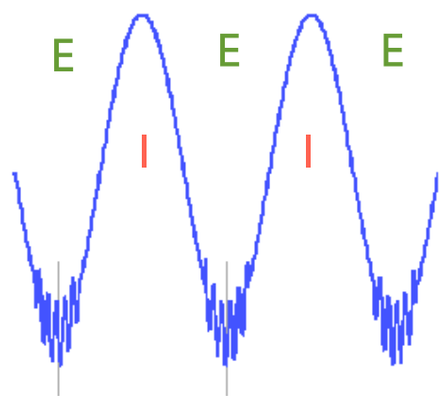

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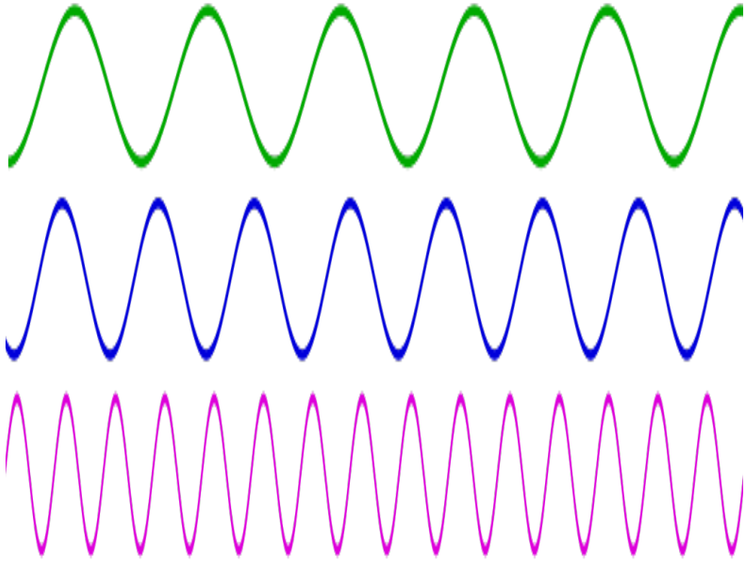

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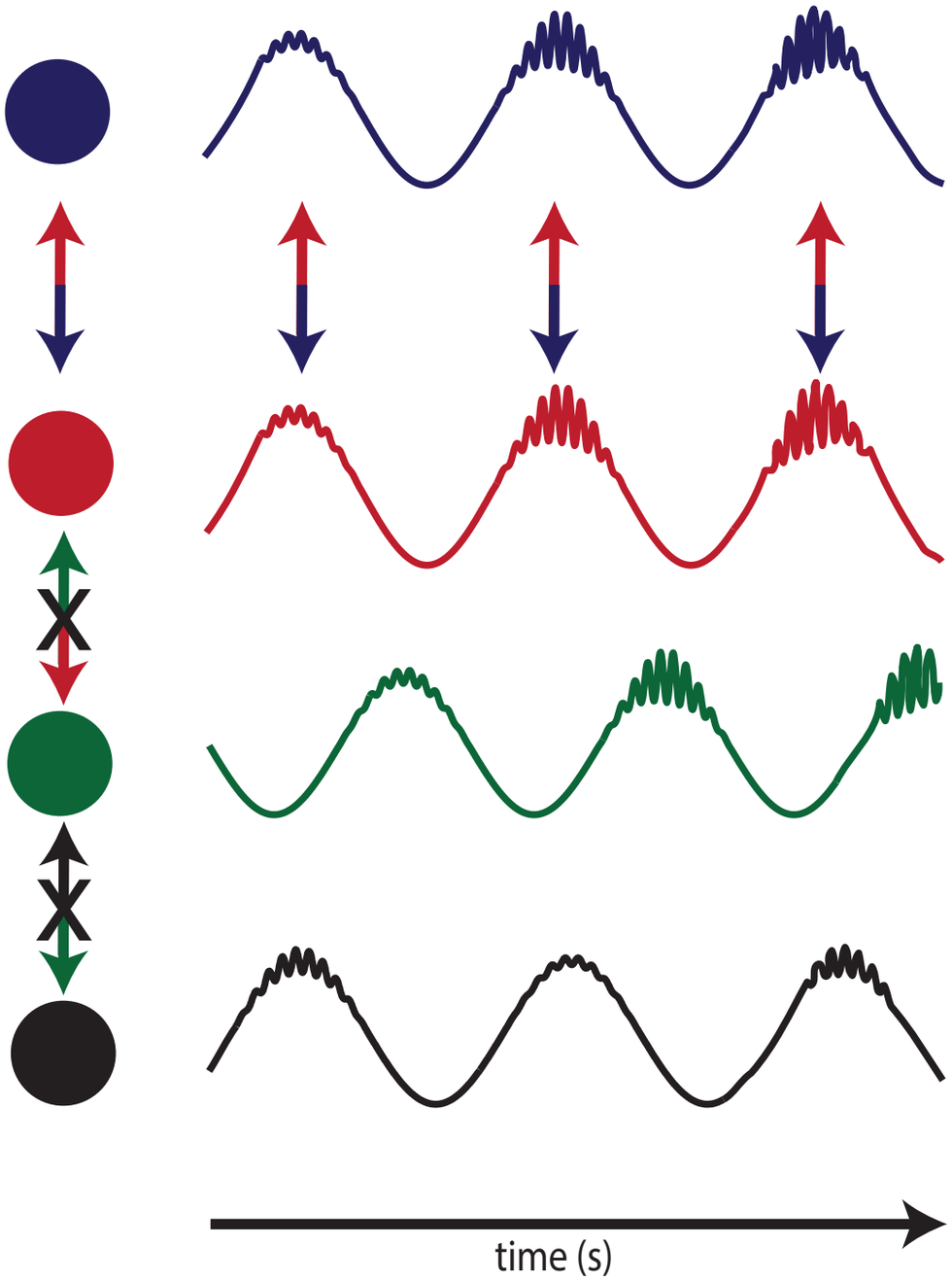
higher γ: PSP/AP spiking ?

Synchronized gating: a possible mechanism enabling functional connectivity @ rest



Florin & Baillet, *NeuroImage* (2015)

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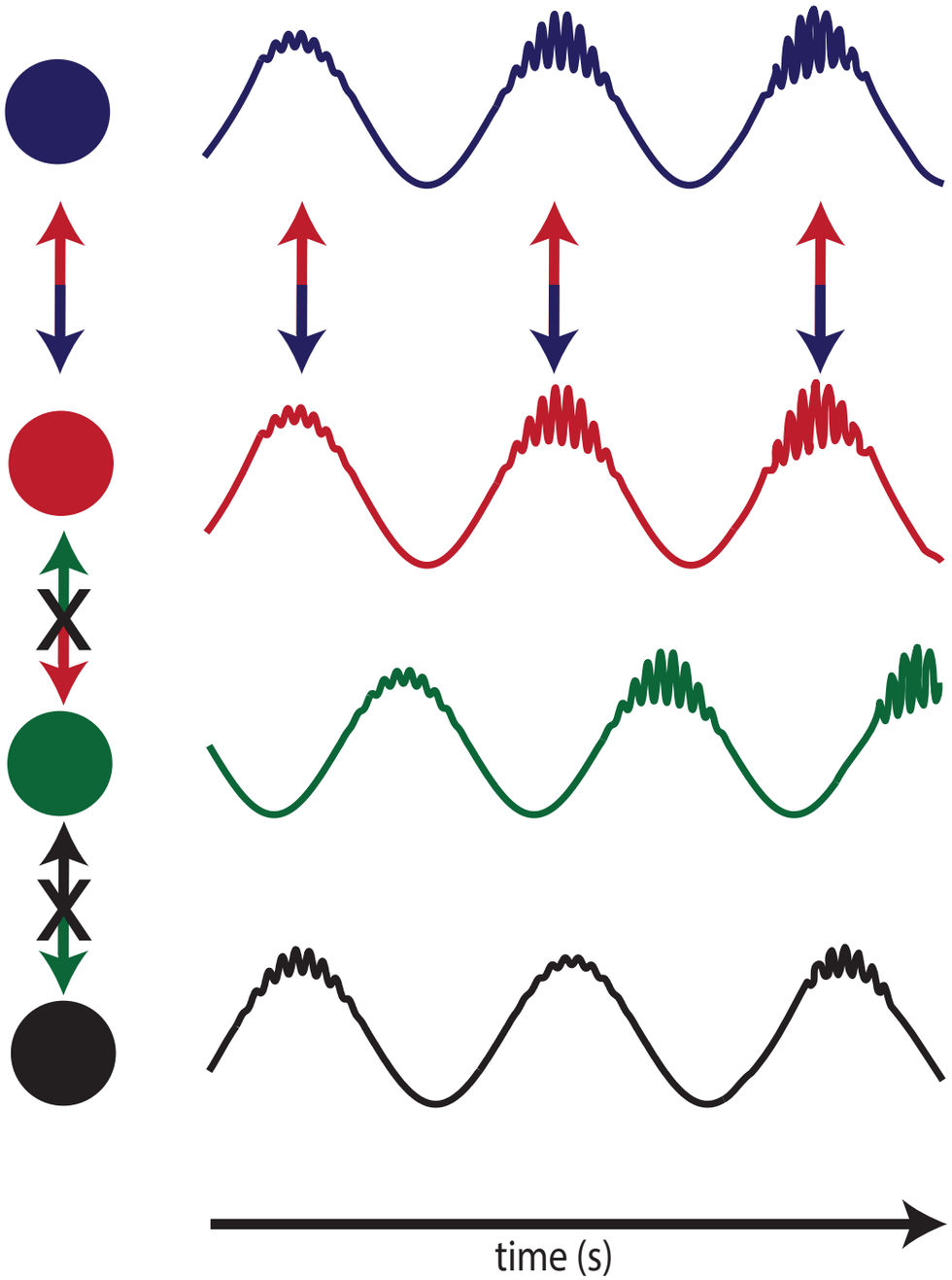

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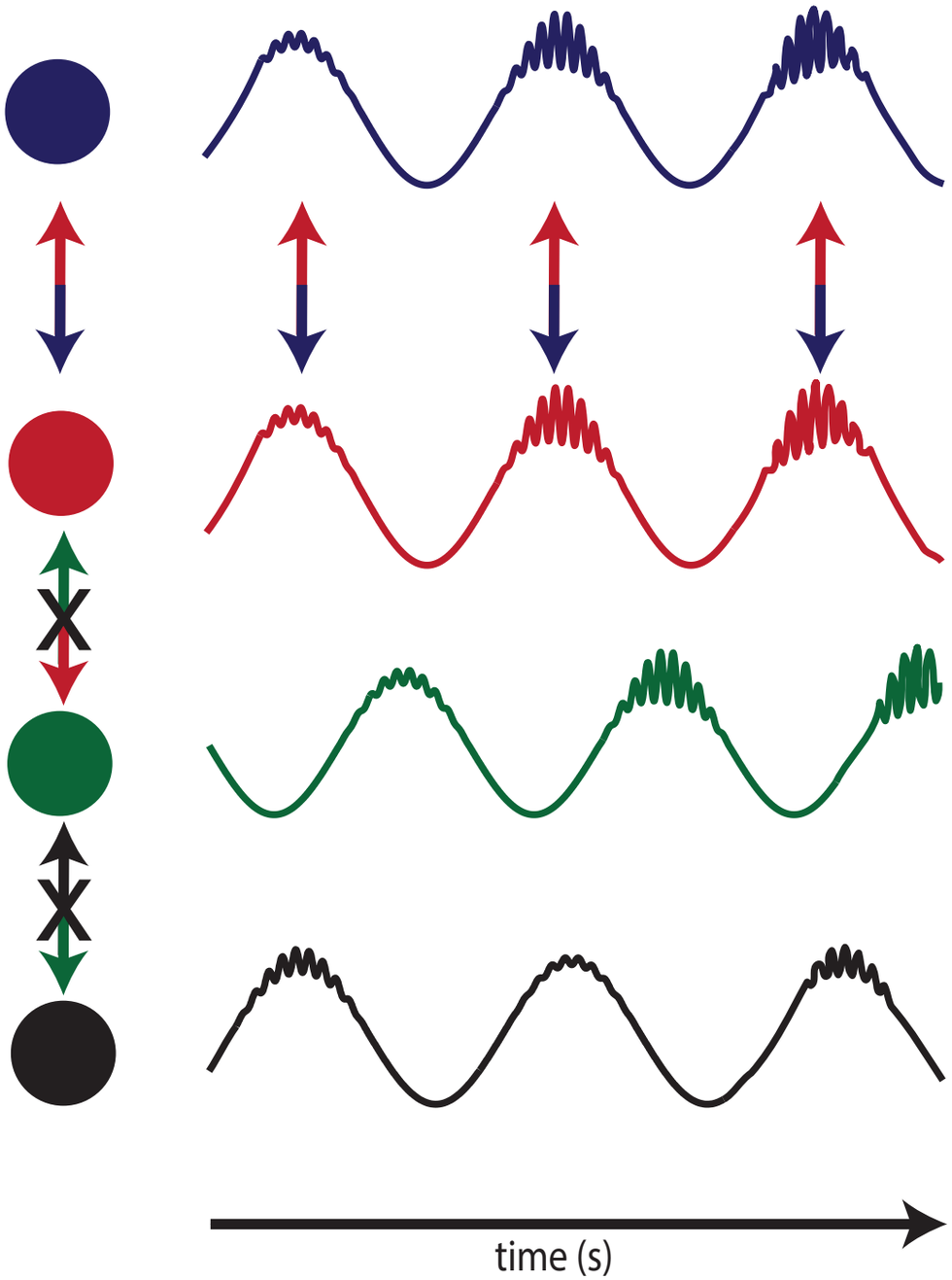

"Resting-state network"

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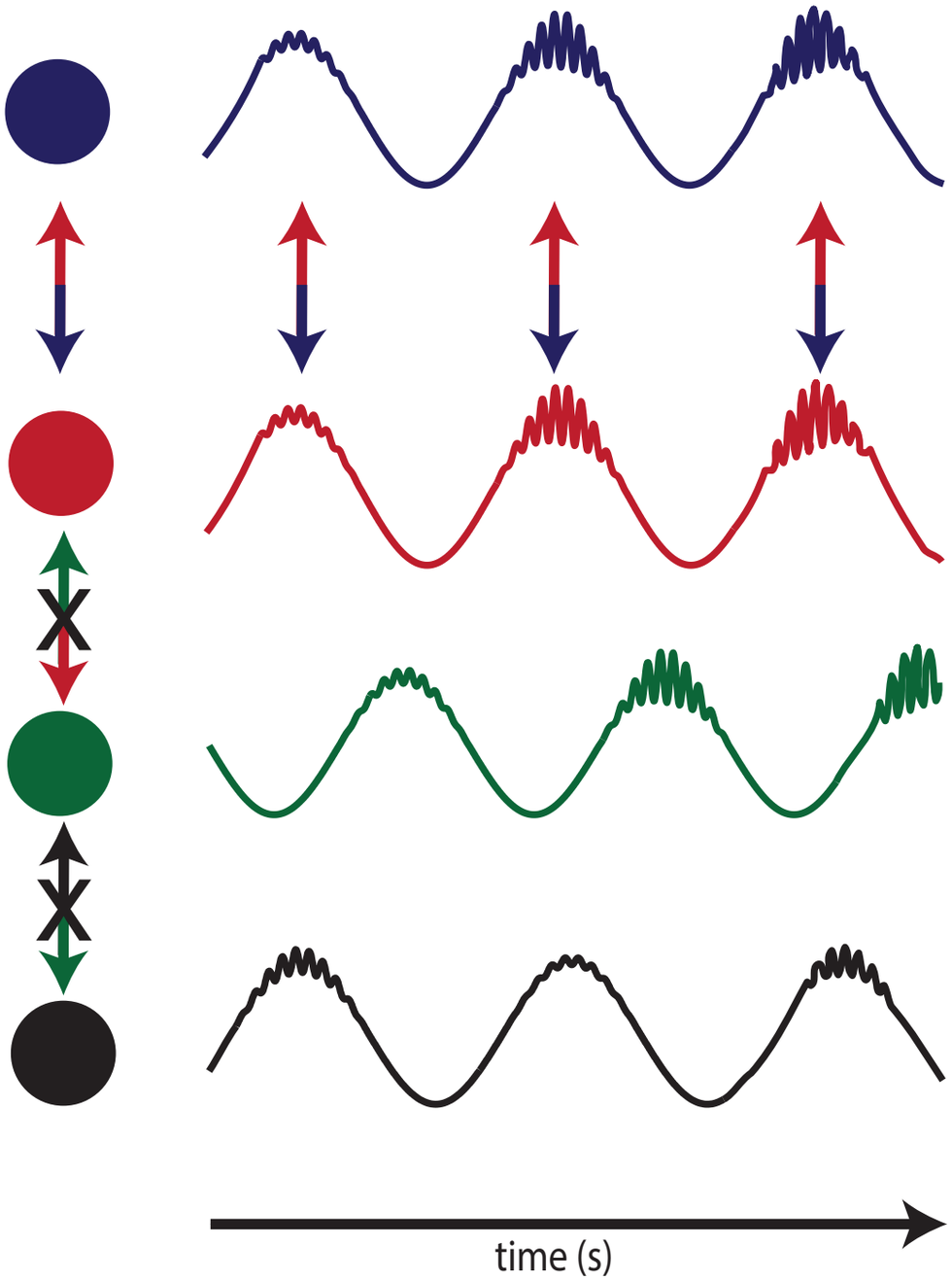

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Set of brain regions/neural populations, which over time:

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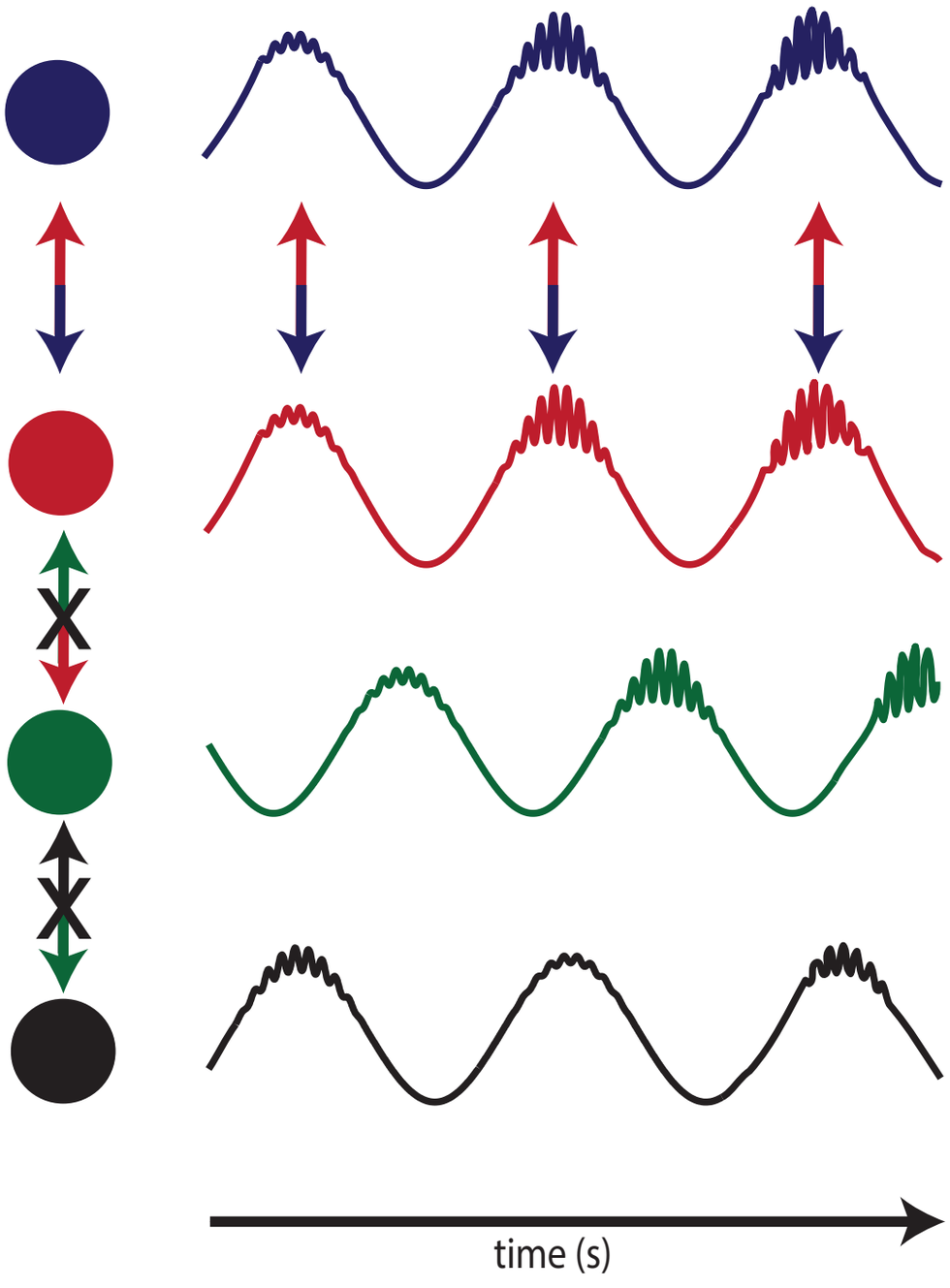

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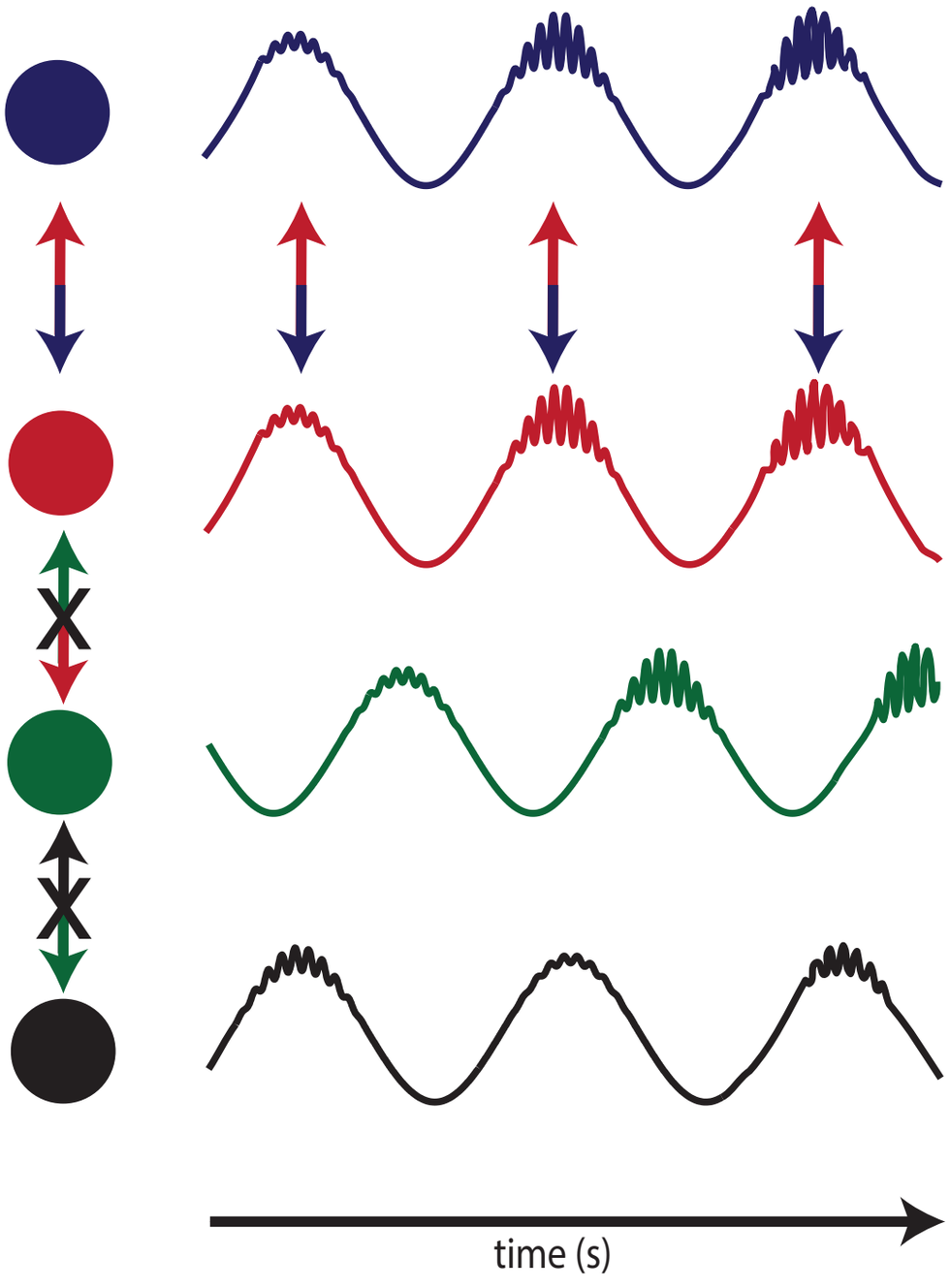

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Set of brain regions/neural populations, which over time:

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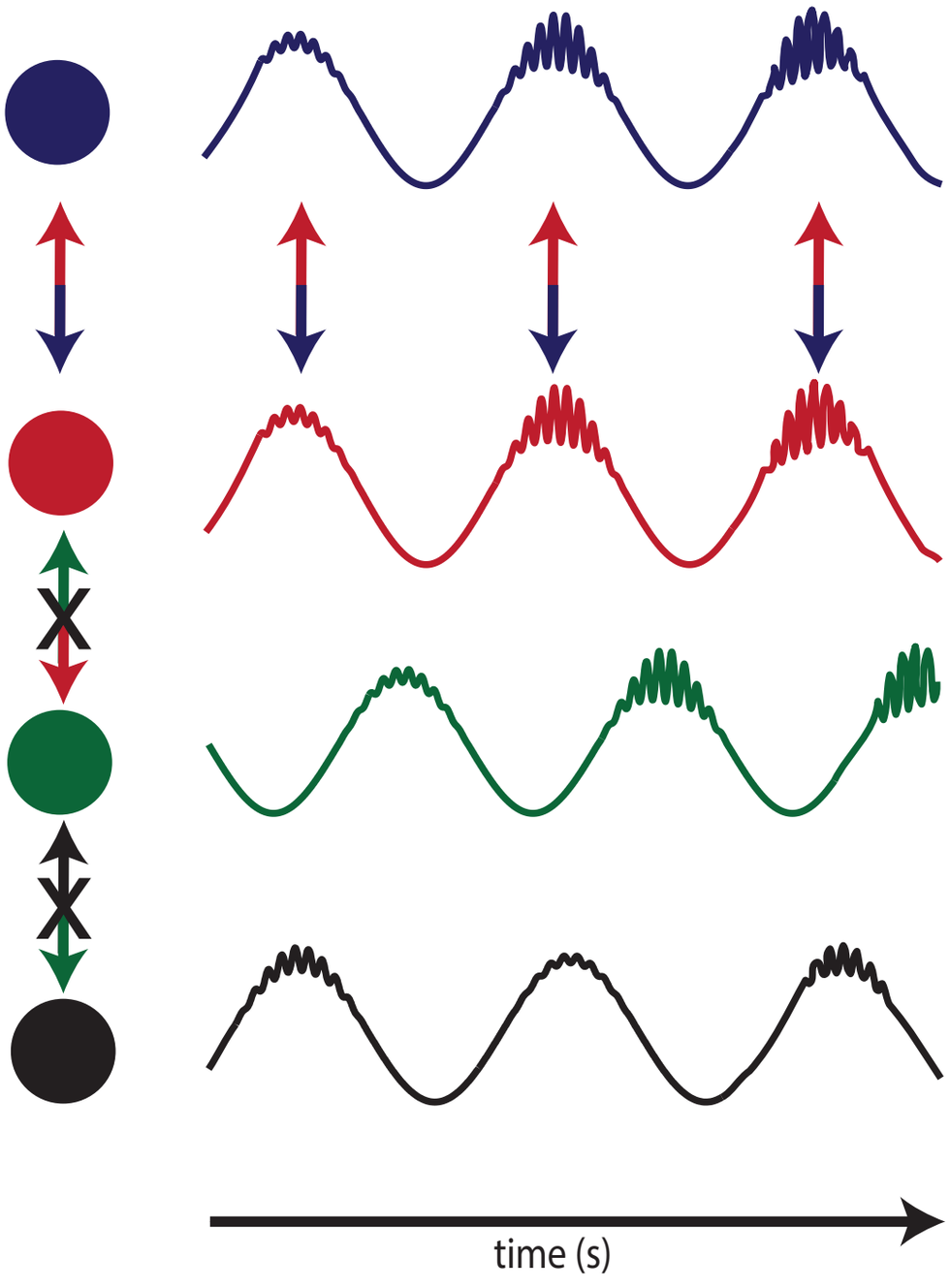

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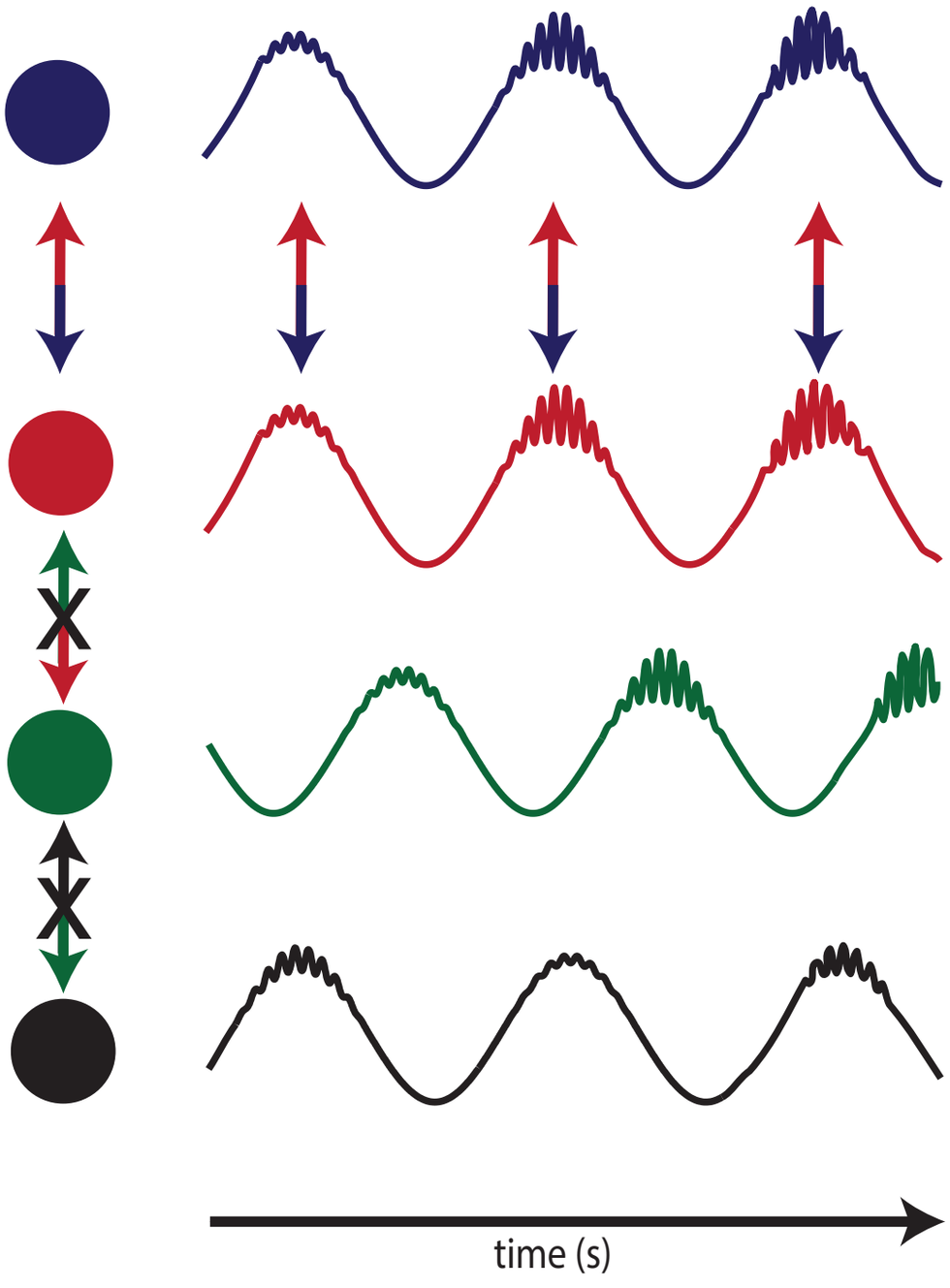

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- ✓ RS-BOLD: hemodynamic changes related to gamma bursts, phase-locked to low-frequency E/I duty cycles

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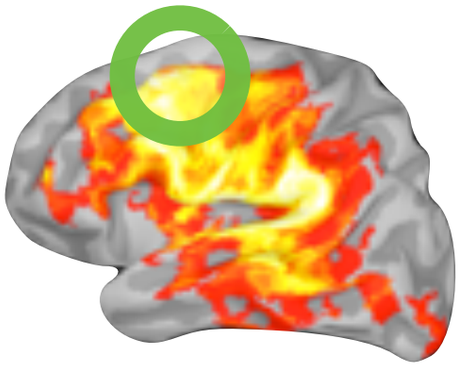
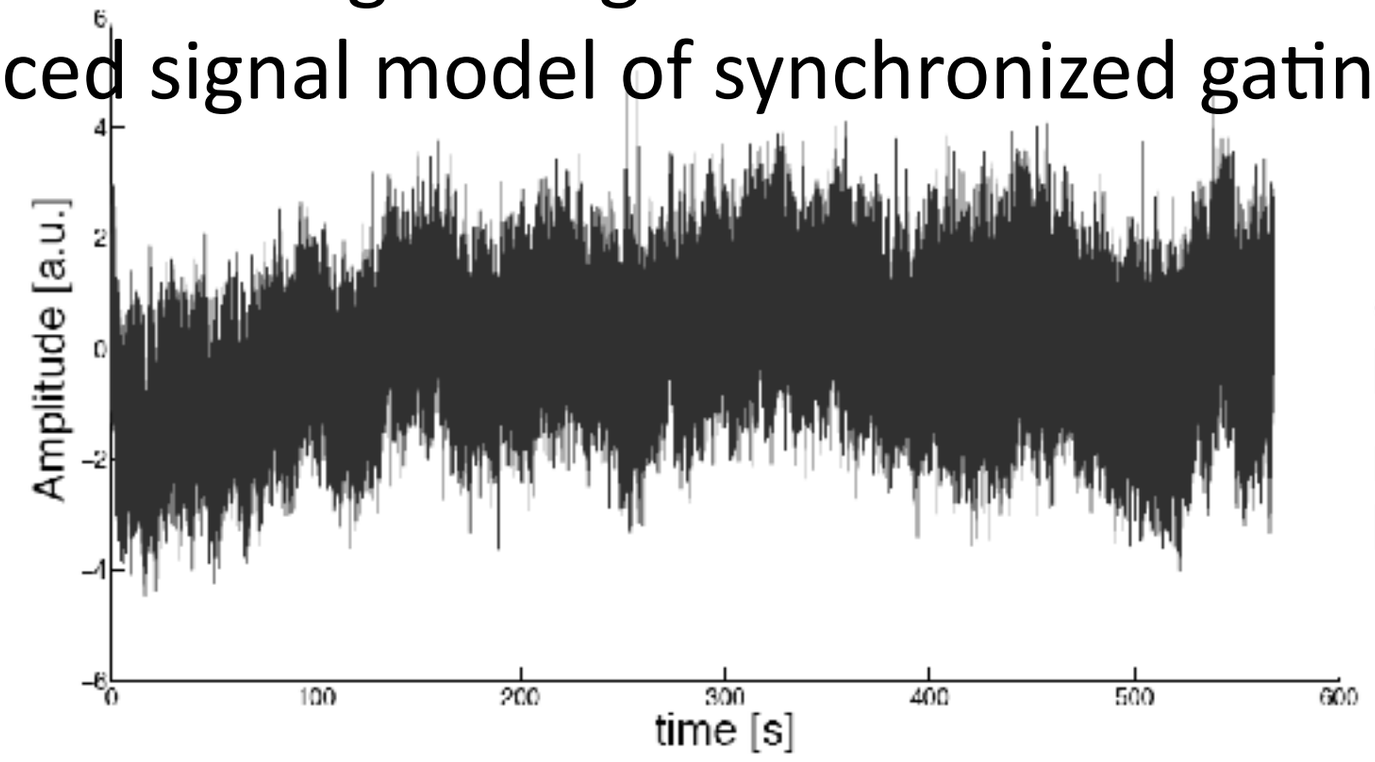
megPAC signal model:
reduced signal model of synchronized gating





Gamma envelope
[80, 150] Hz

Nesting cycles
[2, 48] Hz

Florin & Baillet, *NeuroImage* (2015)

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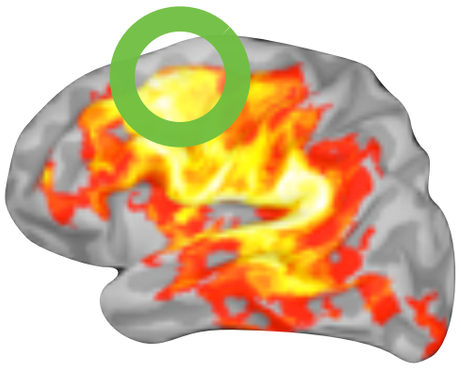

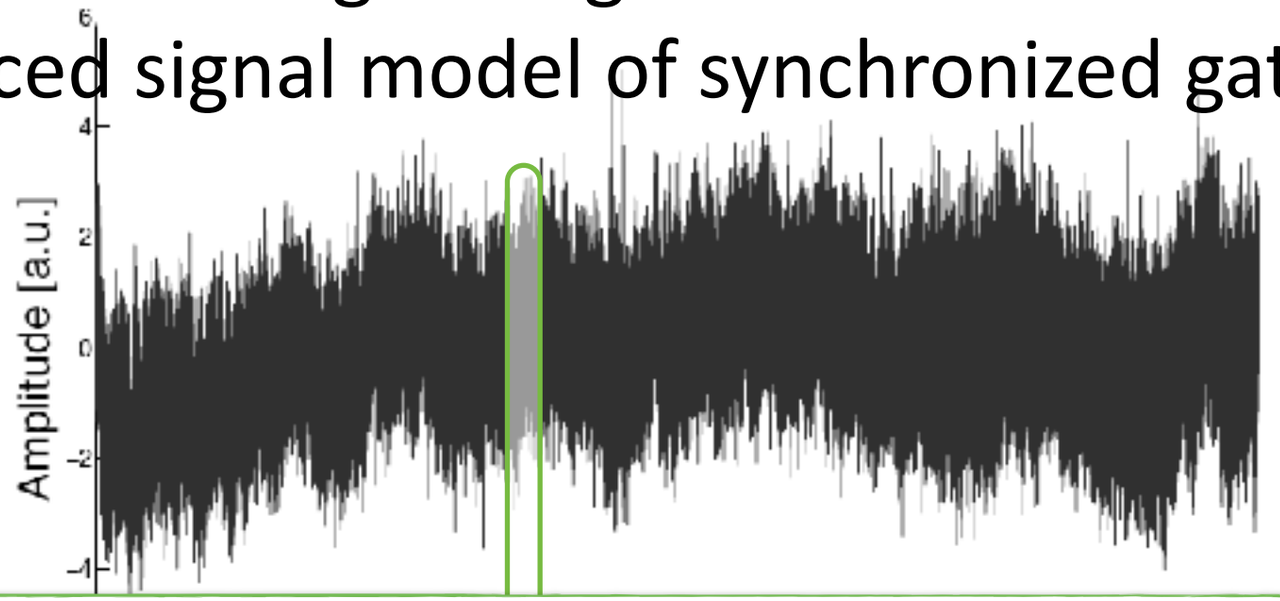

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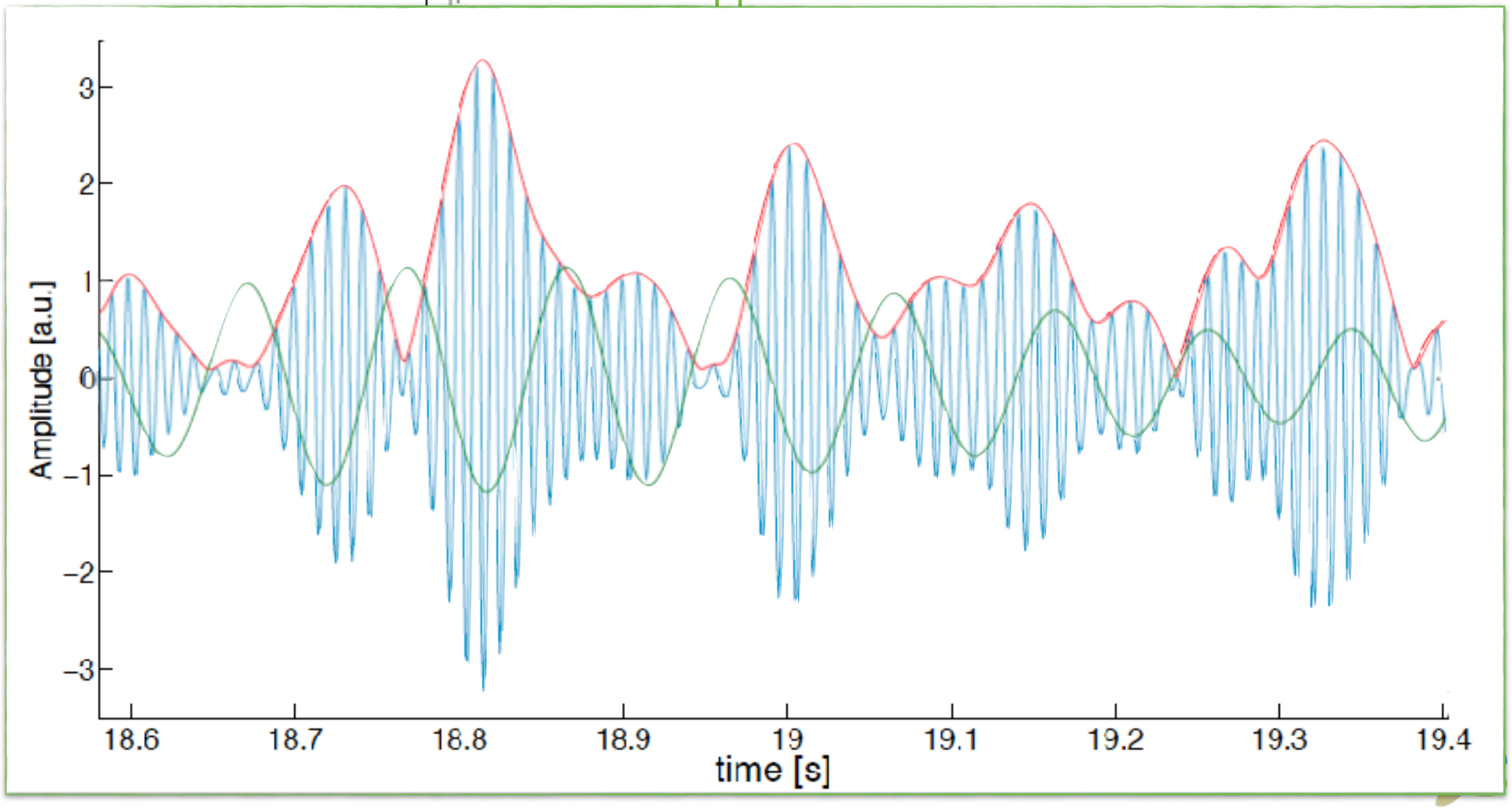

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neuro

MEG McGill

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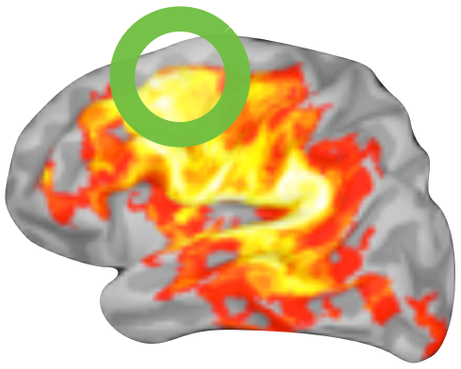

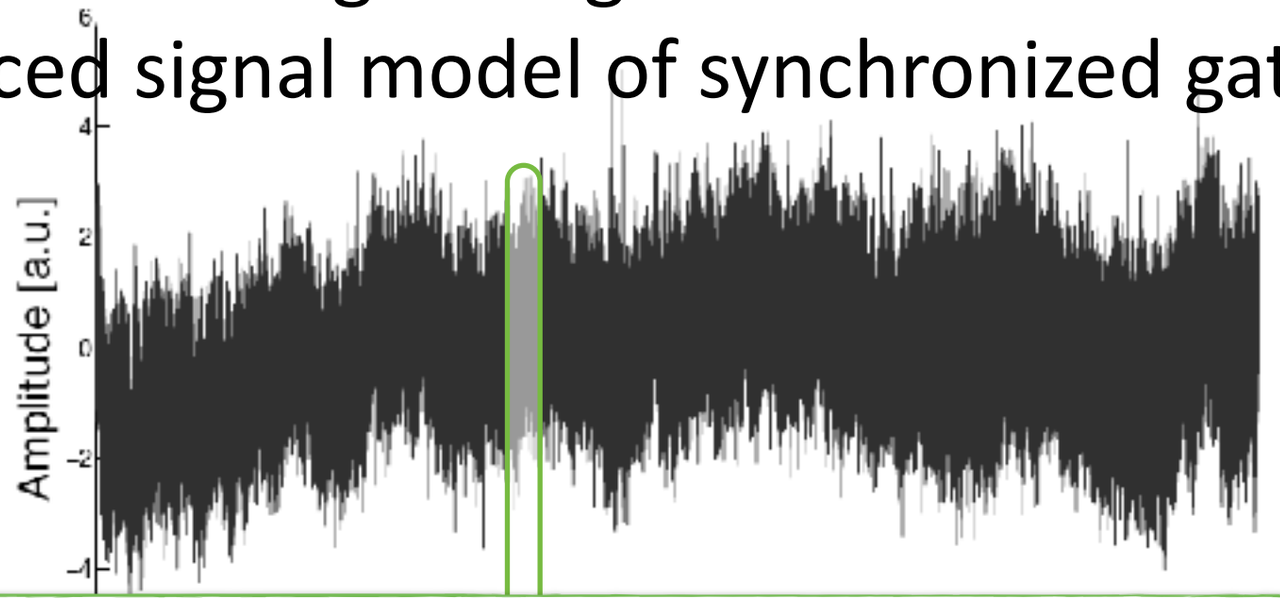

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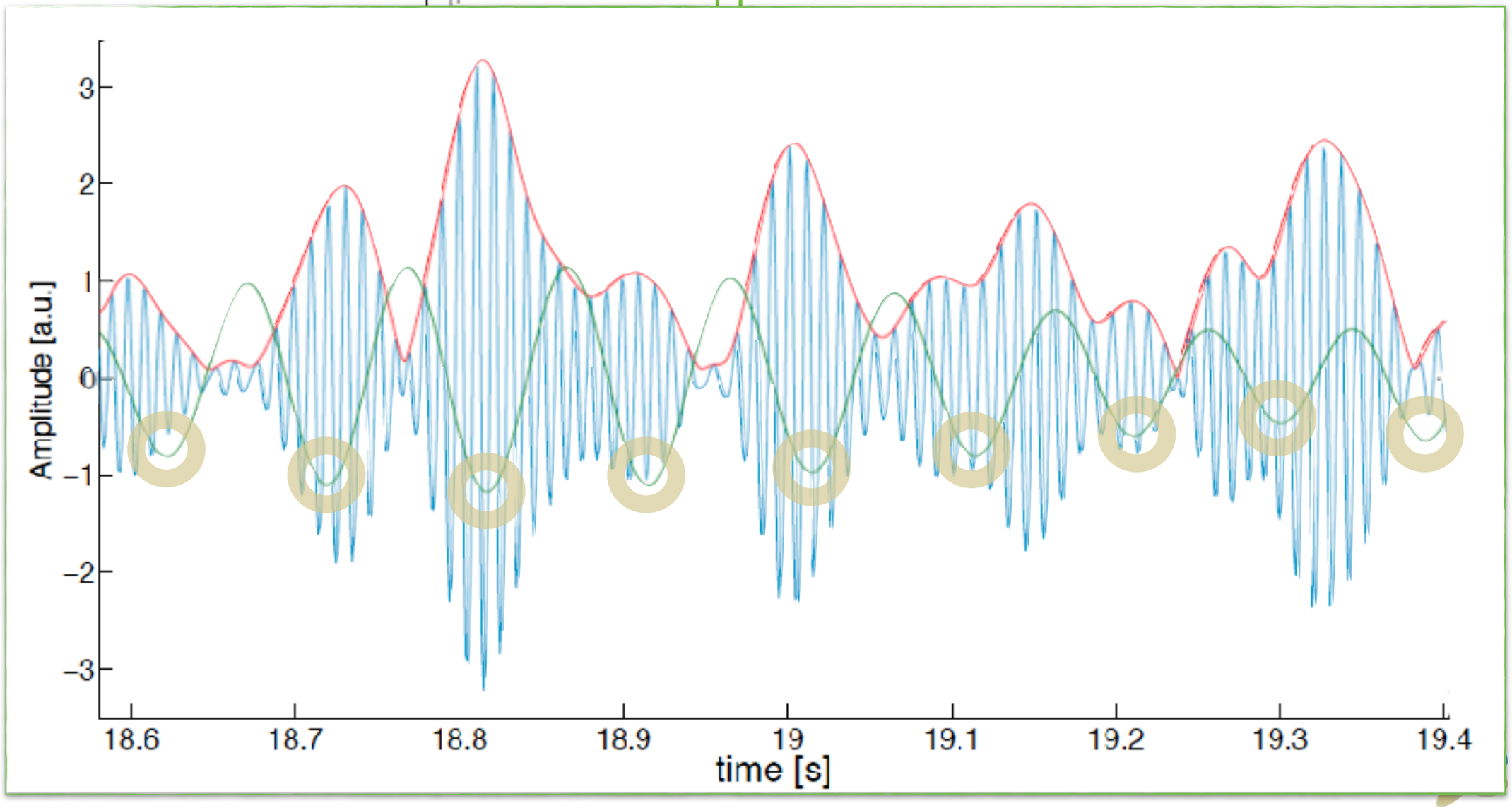
Nesting cycles
[2, 48] Hz

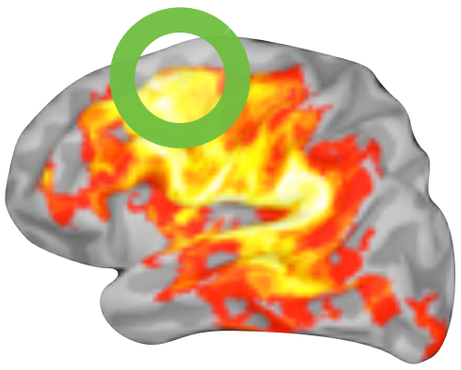


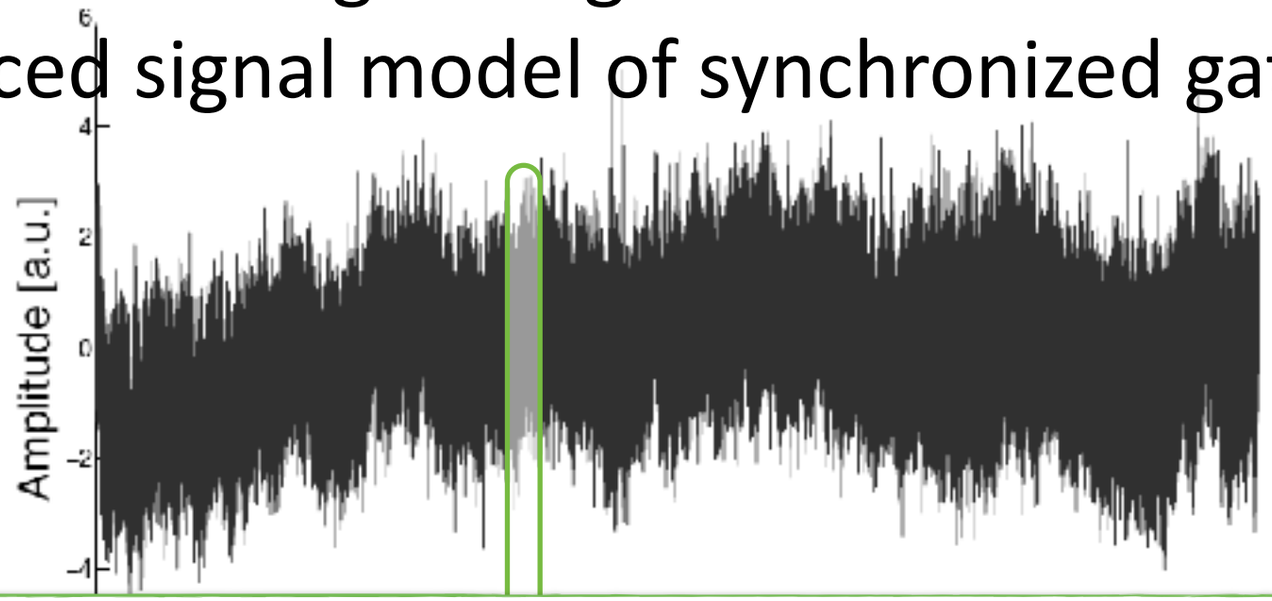
Florin & Baillet, *NeuroImage* (2015)

neuro

MEG McGill

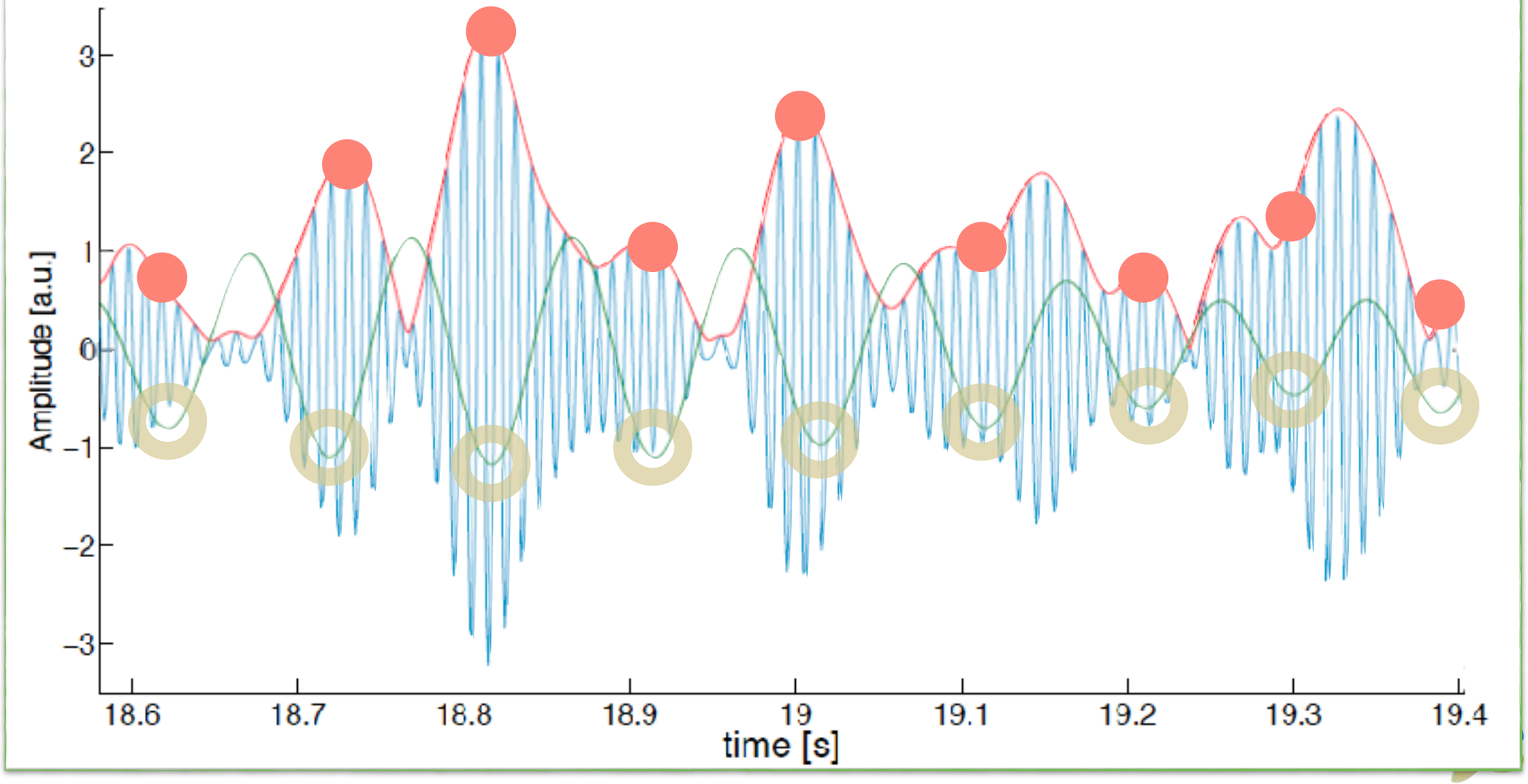
megPAC signal model:
reduced signal model of synchronized gating





Gamma envelope
[80, 150] Hz

Nesting cycles
[2, 48] Hz



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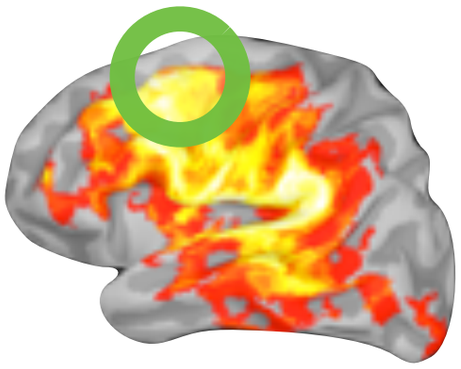

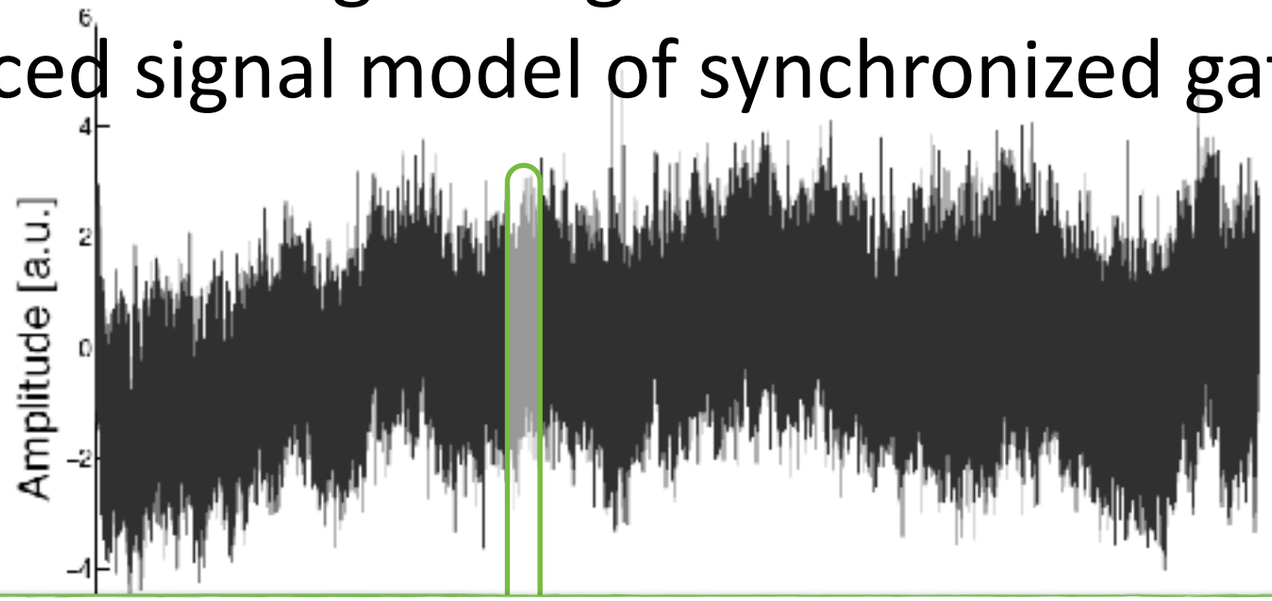

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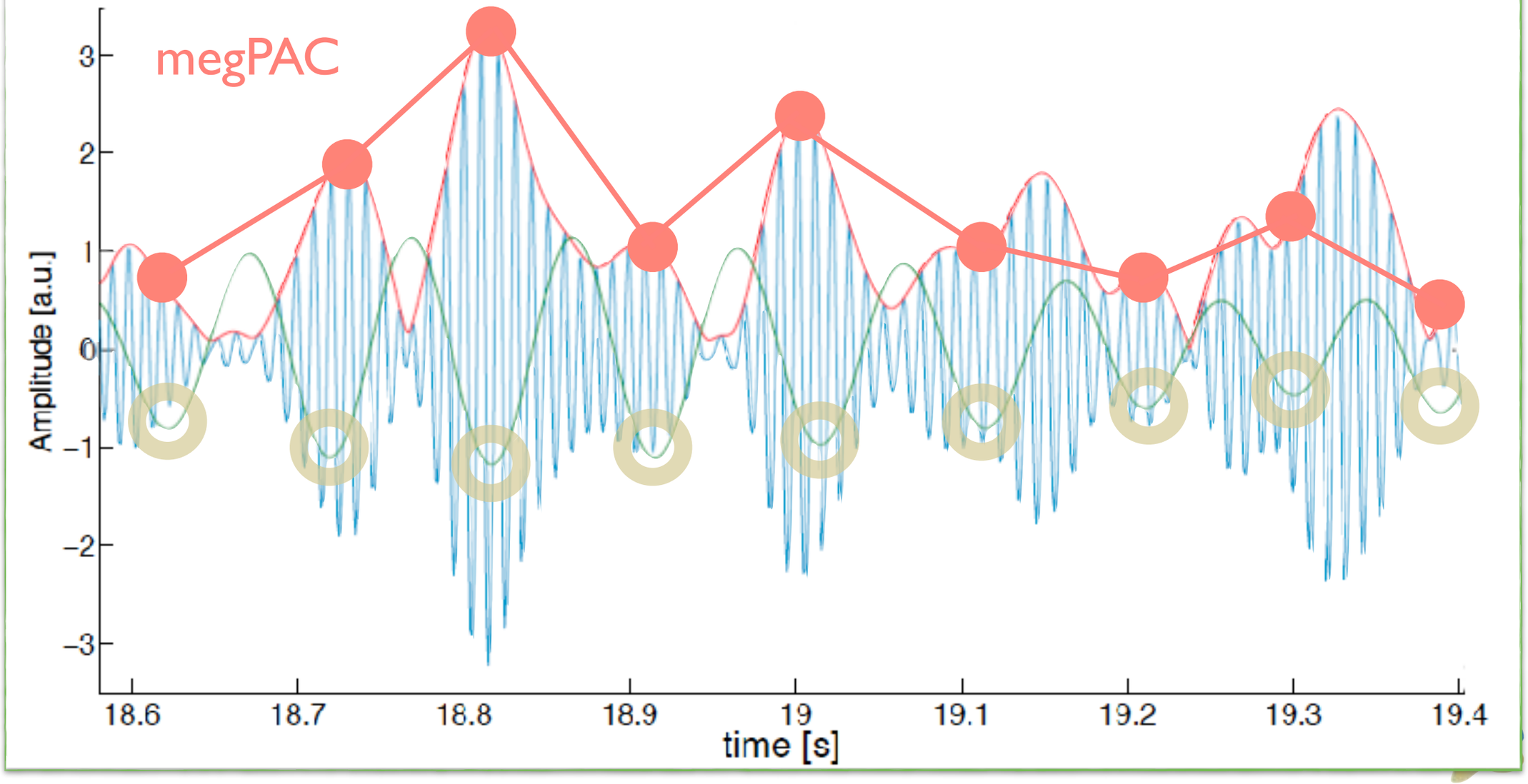

Florin & Baillet, *NeuroImage* (2015)

megPAC signal model:
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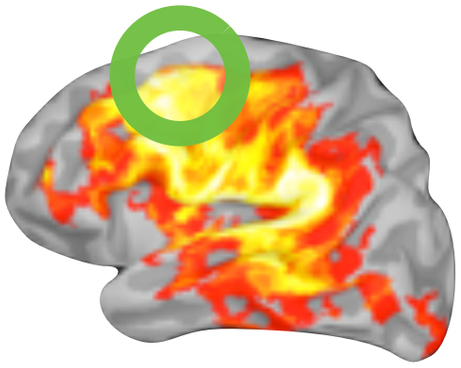
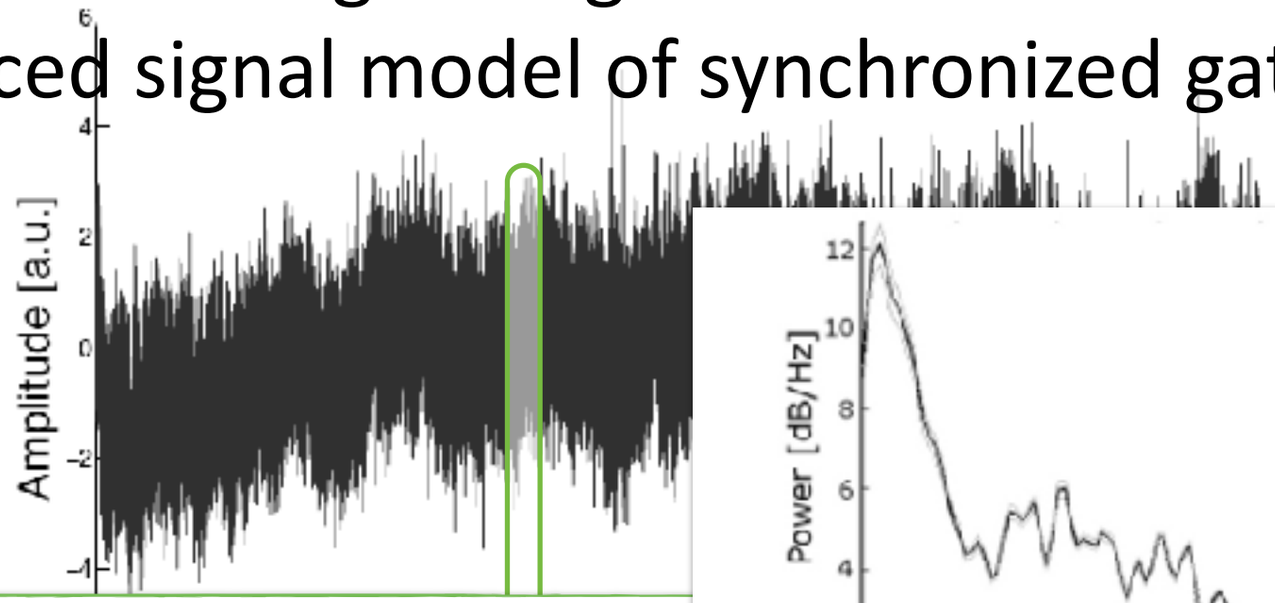
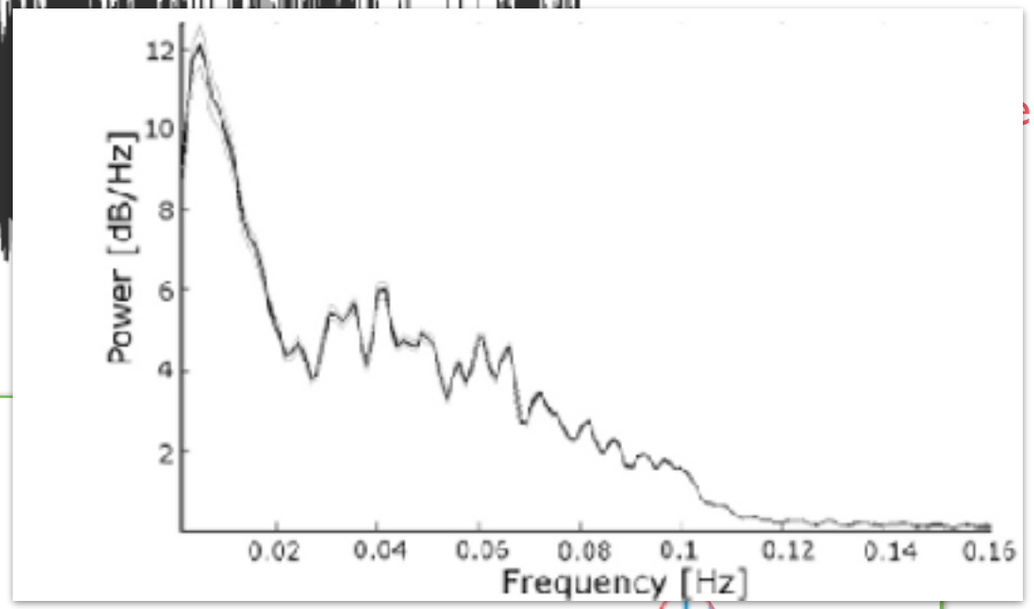
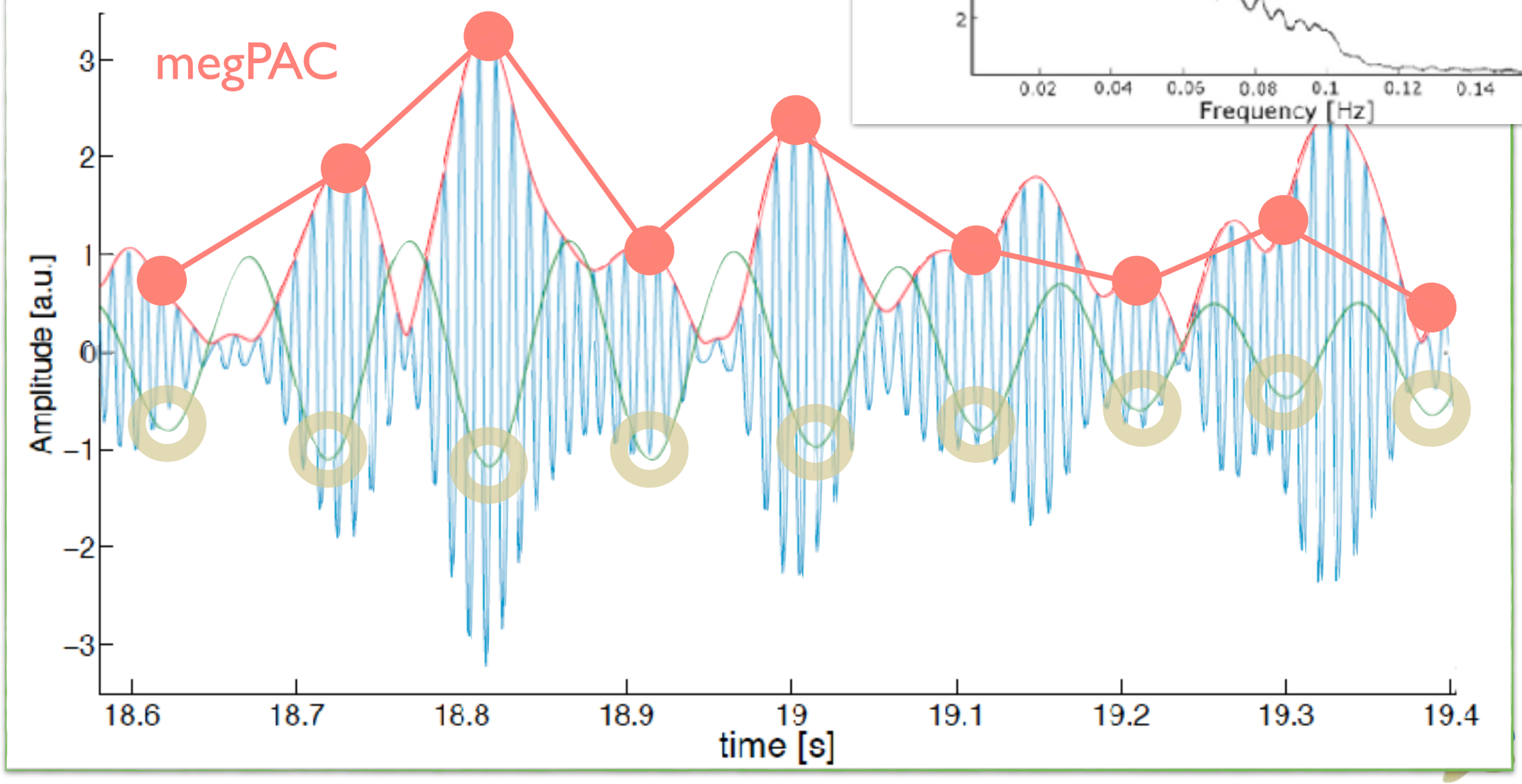




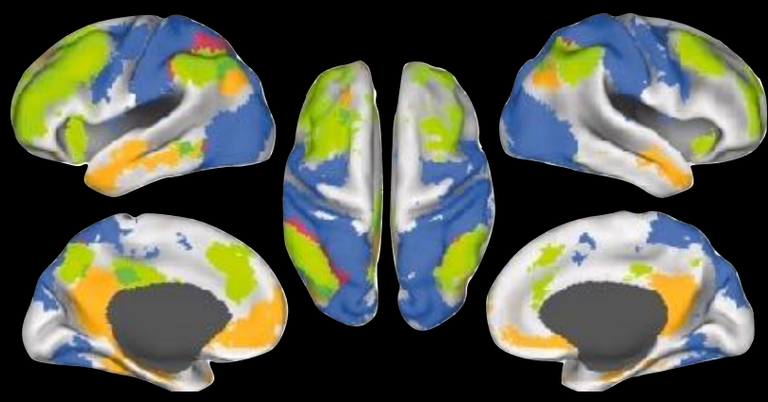




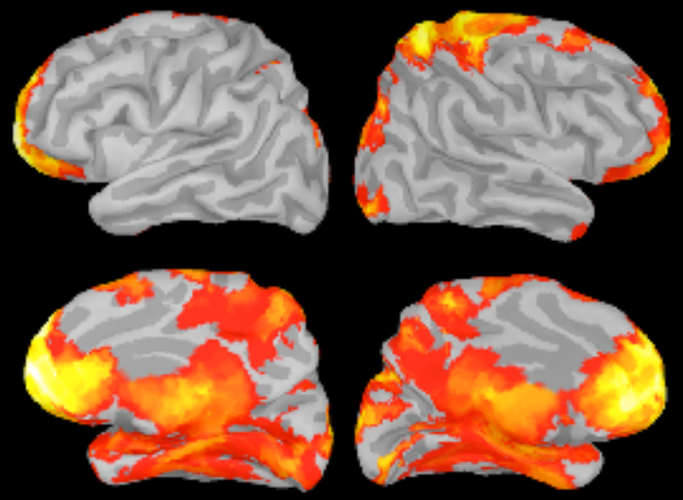
Florin & Baillet, *NeuroImage* (2015)

MEG Resting-State Networks

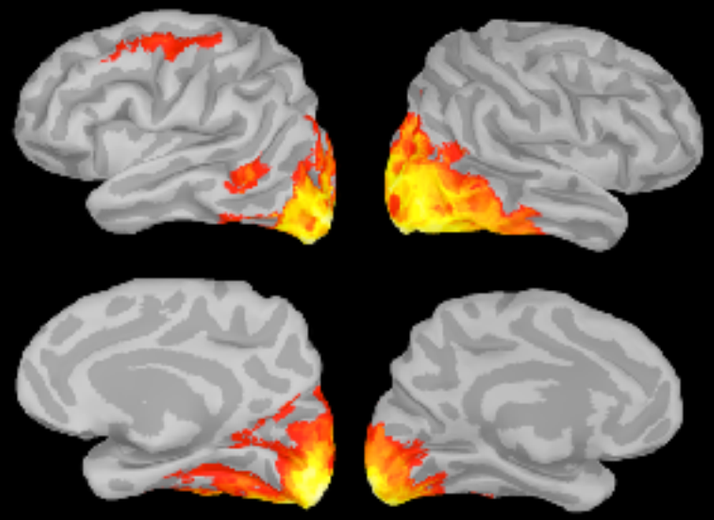
fMRI



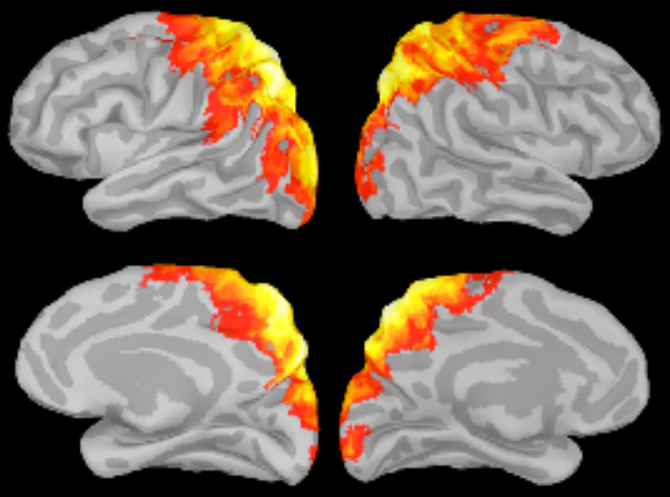
DMN



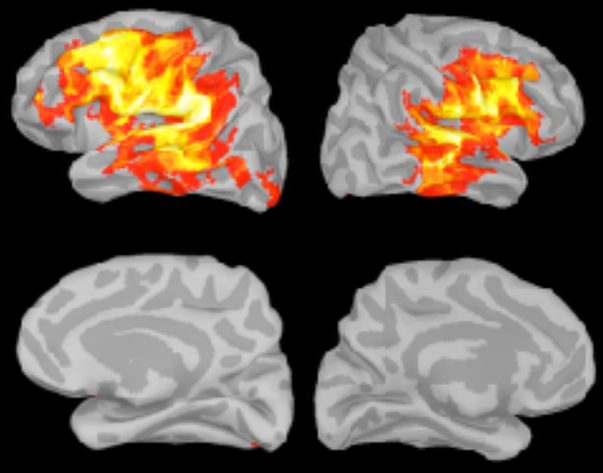
Visual



Dorsal, sensori-motor

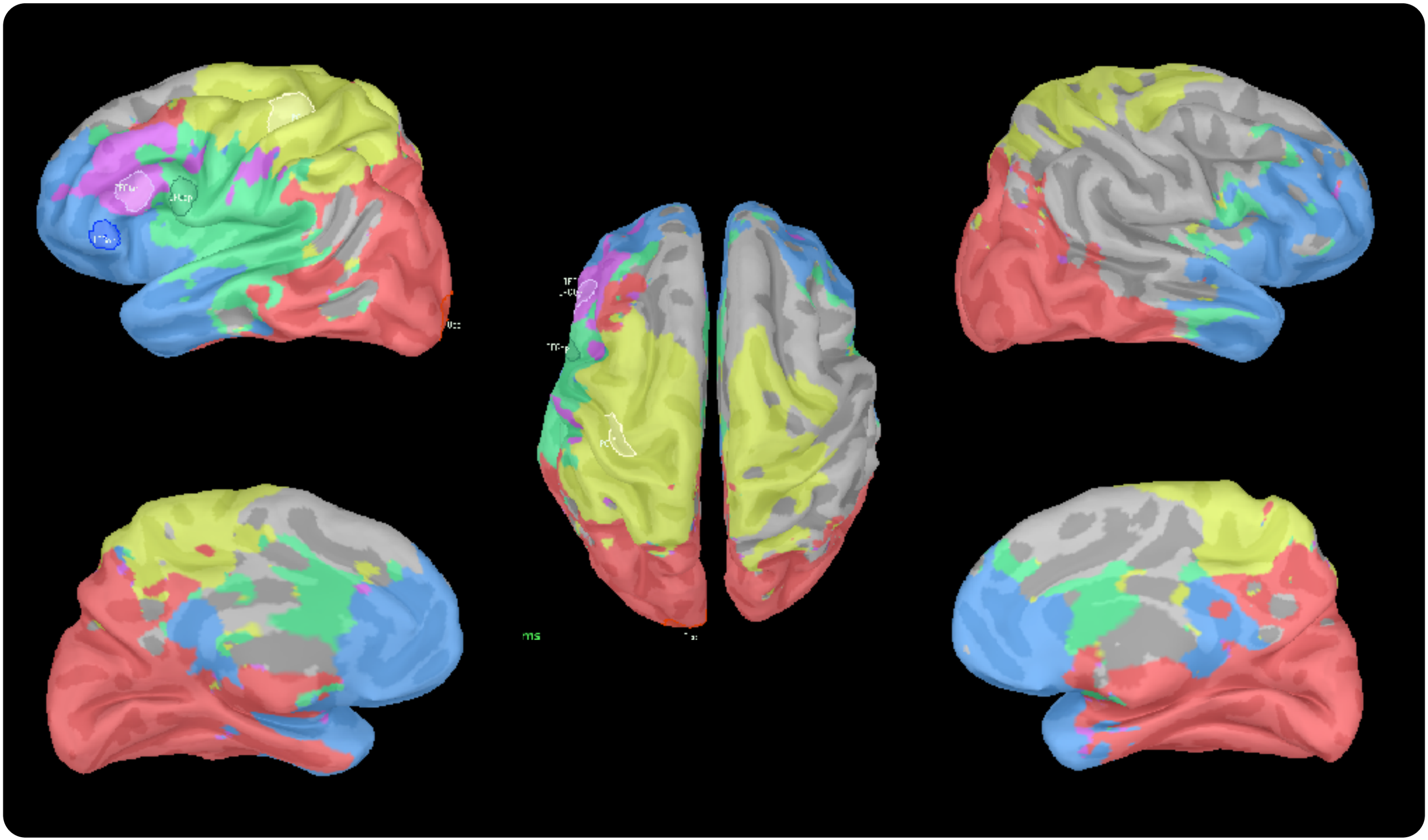


Auditory+



Florin & Baillet, *NeuroImage* (2015)

Seed-based connectivity patterns



Florin & Baillet, *NeuroImage* (2015)

Review

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- Estimation of connectivity

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  - Too many methods

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  - When in doubt, use most reported methods (coherence or phase-locking)

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  - Too many methods
  - When in doubt, use most reported methods (coherence or phase-locking)
- Still a very open field of research
  - Model-free methods (information theoric)
  - Try bottom-up mechanistic models