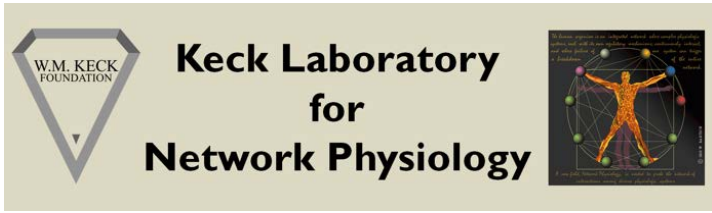
First International Summer Institute on Network Physiology (ISINP)

Lake Como School of Advanced Studies – July 24-29, 2017

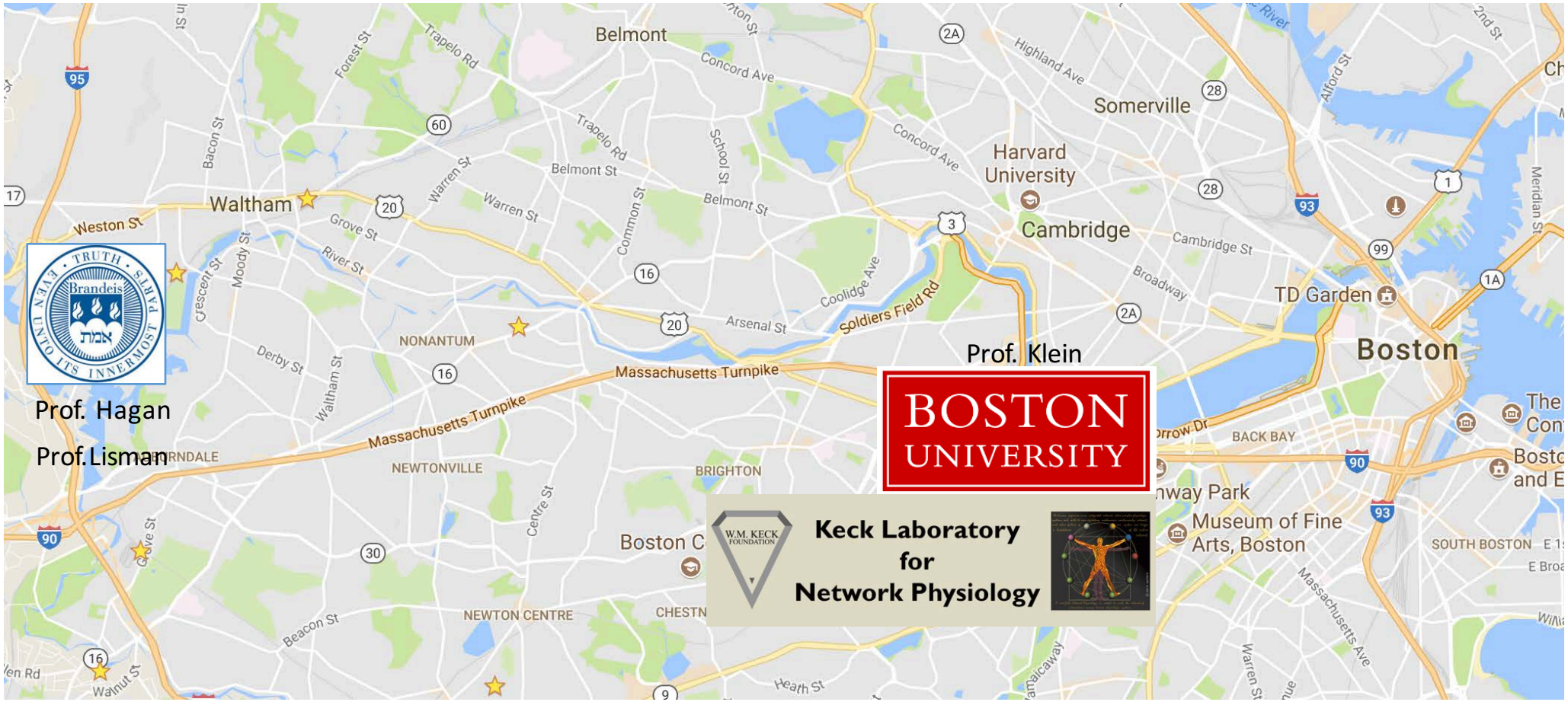
Emergent Coordination Among Physiologic Systems: New Network Signatures for Physiologic State and Function

Kang Liu, PhD

Brandeis University, USA



Self Introduction



Outline

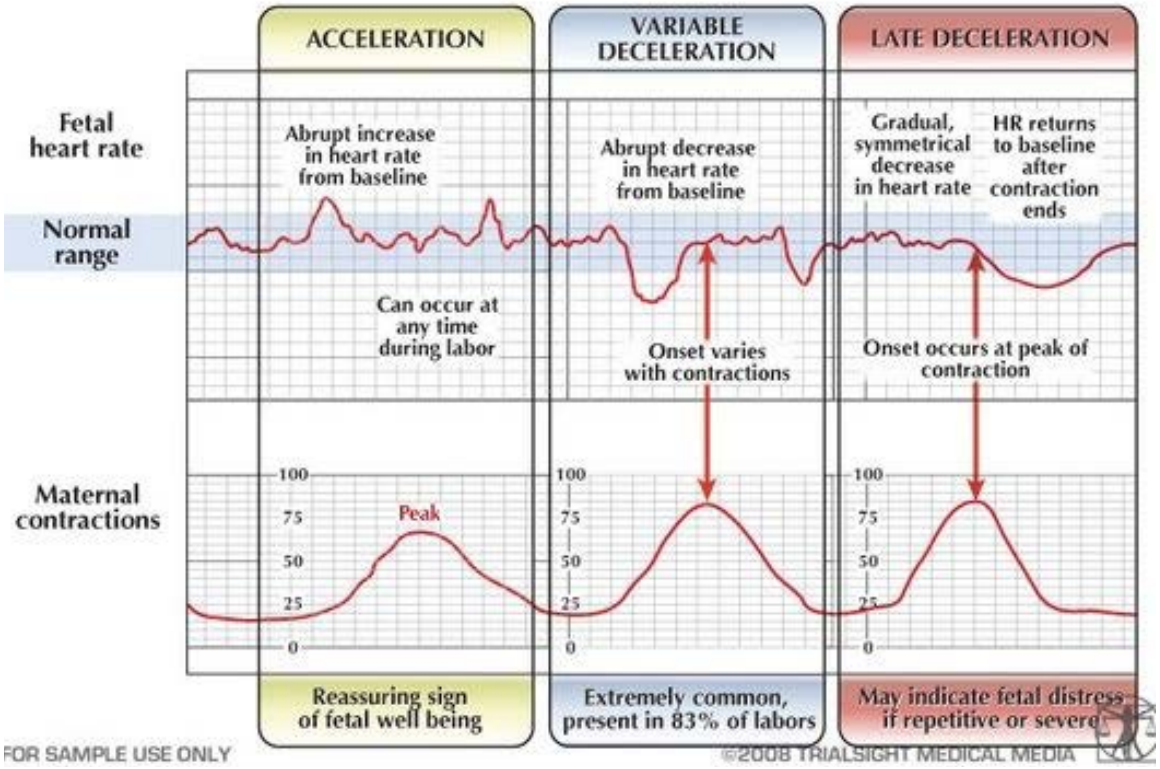
- Personal story → fundamental question
- Strategy to approach the problem
- Example: Brain-heart interaction
- Example: Functional network of brain wave interaction
- Perspective on Network Physiology

Thanks for inviting me!

Photo of Kang's daughter

DOB xx/xx/2017

Fetal Heart Rate – Uterine Contraction



1. Coordination between outputs carry important information
2. Human limitation
3. Teach the computer to monitor these for us?

Strategy

- Step 1: “Pick the right problem”

→ Quantify ***functional connectivity (emergent coordination)*** at the output signal level and explore its relation with physiologic state/function

- Step 2: “Inspect the data”

→ What are the common characteristics shared in physiological signals?

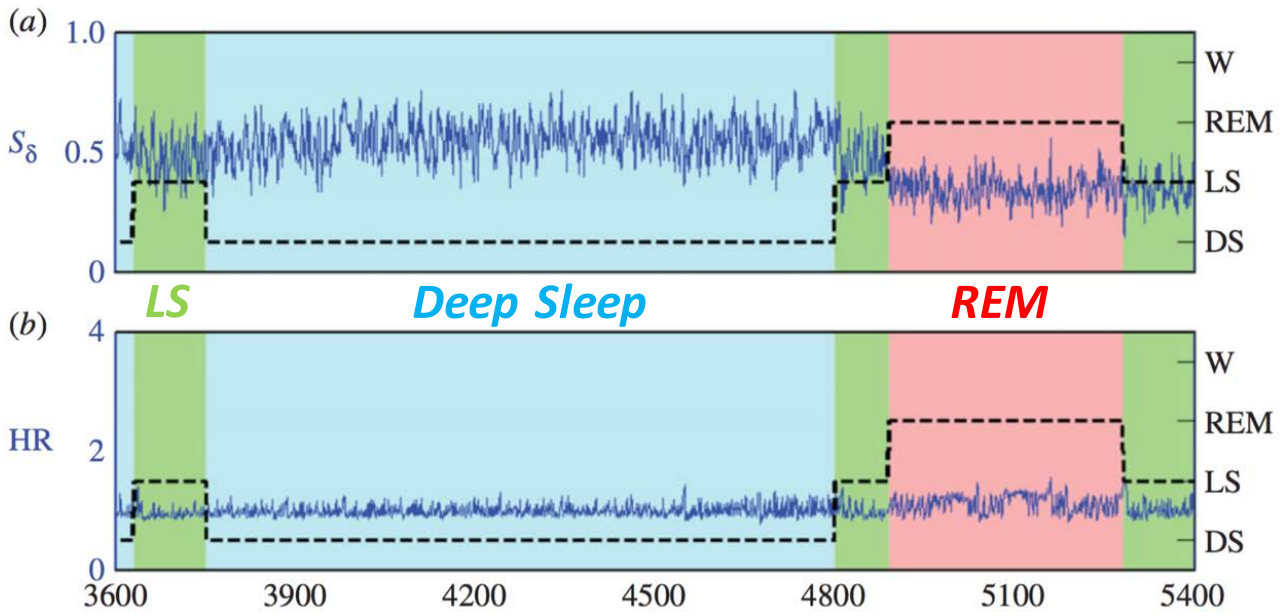
- Step 3: “Assume 0”

→ Extended cross-correlation measure

- Step 4: “Randomize”

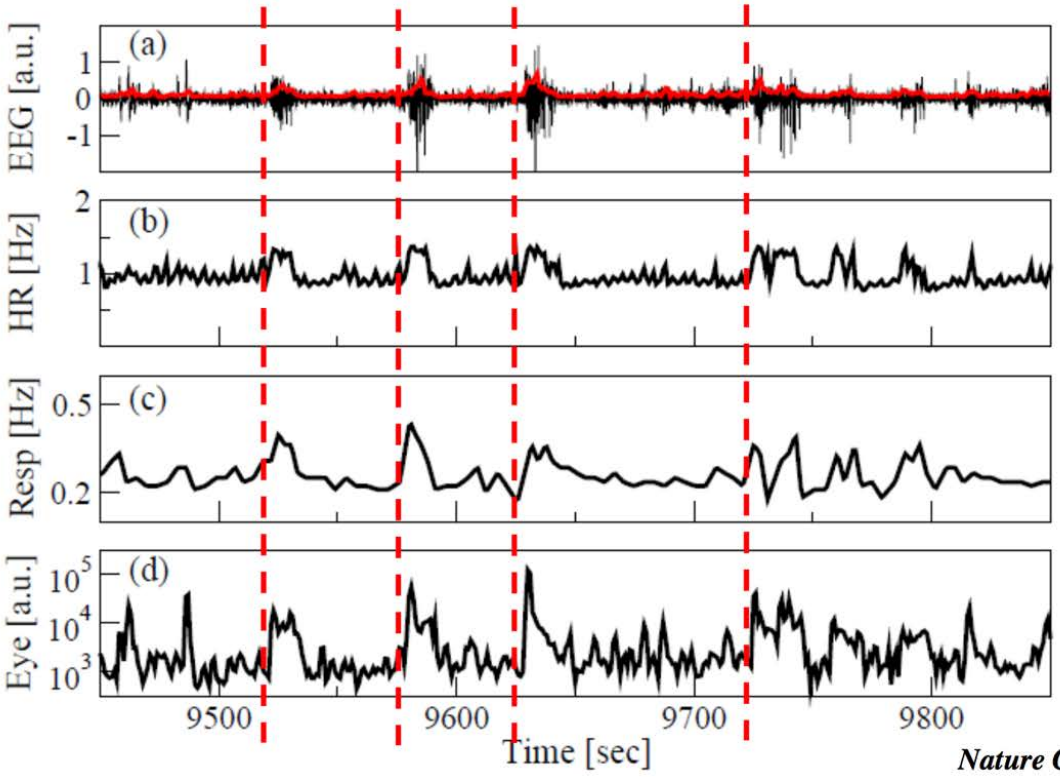
→ Surrogate test and robustness across subjects

Emergent coordination at the signal level



- Focus on the dynamics of physiologic systems, not on homeostasis
- Exploratory investigation without hypothesis
- Focus on functional connectivity, not on coupling functions

Coordinated busting activities



EEG-σ band: sleep spindles

Heart rate

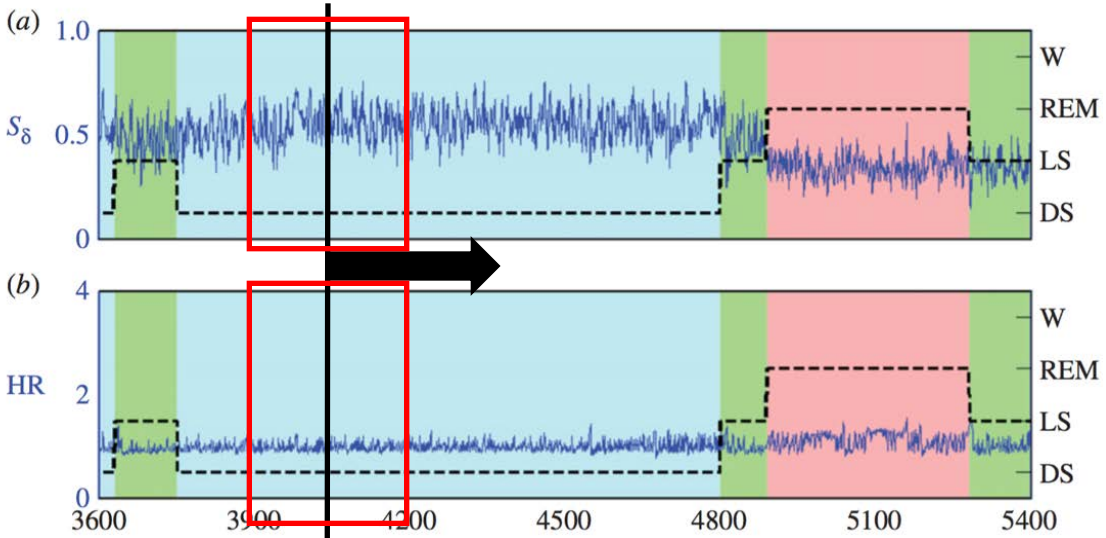
Respiratory rate

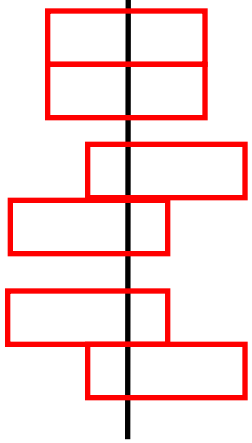
Eye movements

Nature Communications vol. 3:702 (2012)

- Coordination is commonly observed across diverse systems
- Busting activity is important

Extend traditional cross-correlation

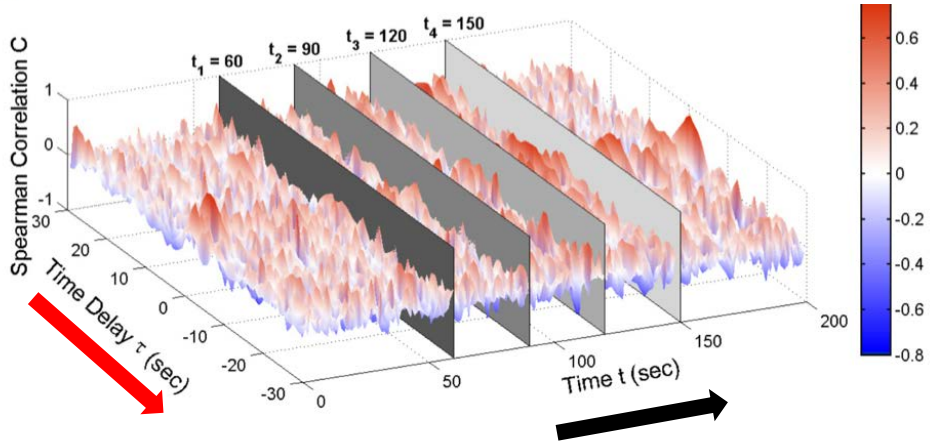




$\tau = 0$

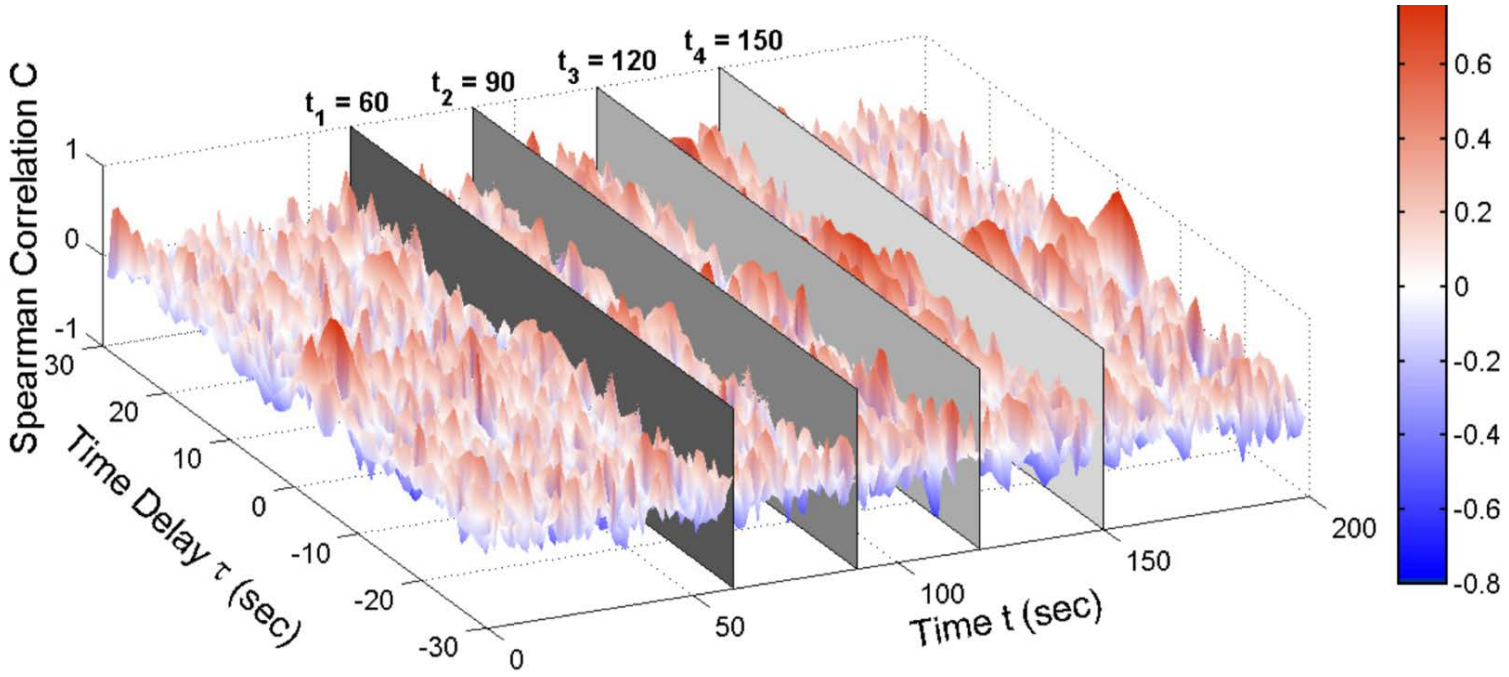
$\tau > 0$

$\tau < 0$



Lin A, et al. 2016 *Phil. Trans. R. Soc. A* **374**: 20150182.

Delay-Correlation Landscape



Time delays between physiologic systems

Maximum Coordination

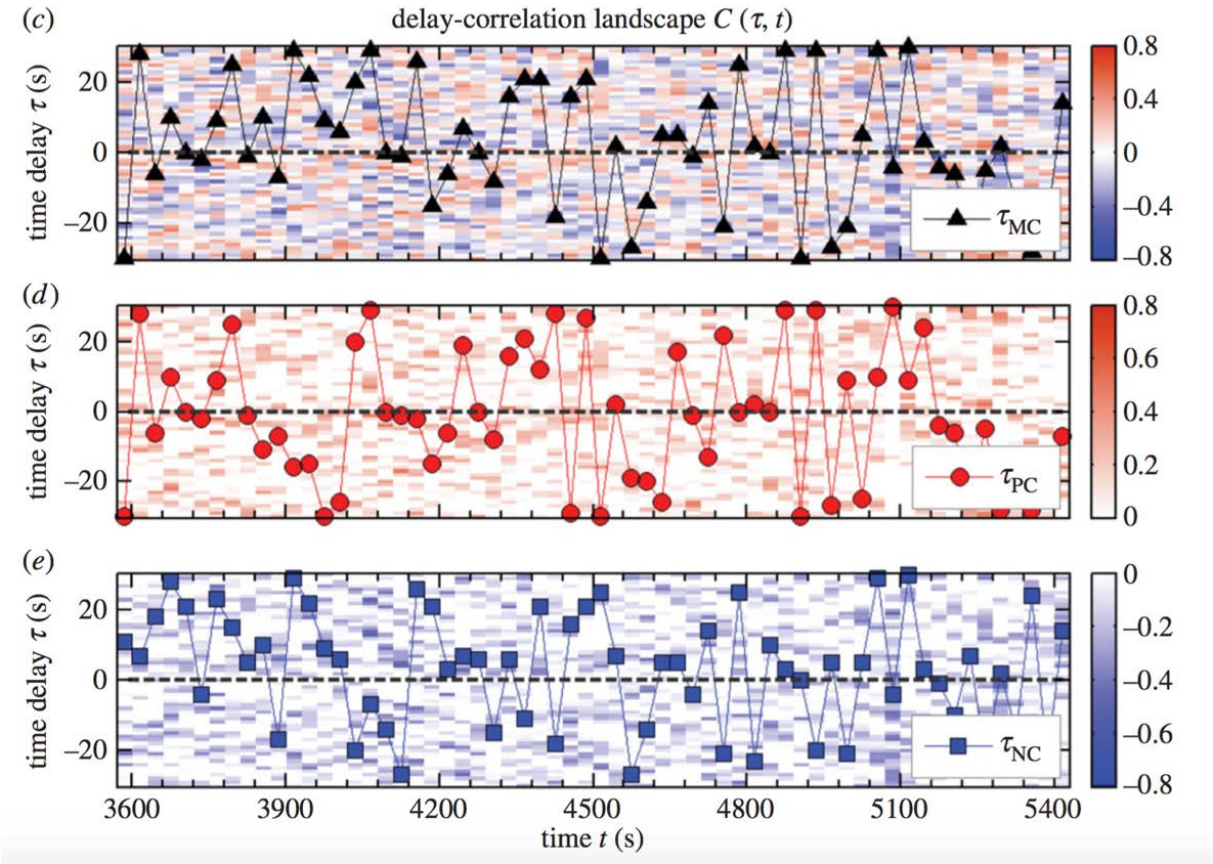
$C(\tau_{MC}, t) = \max|C(\tau, t)|$

Positive Correlation

$C(\tau_{PC}, t) = \max C(\tau, t)$

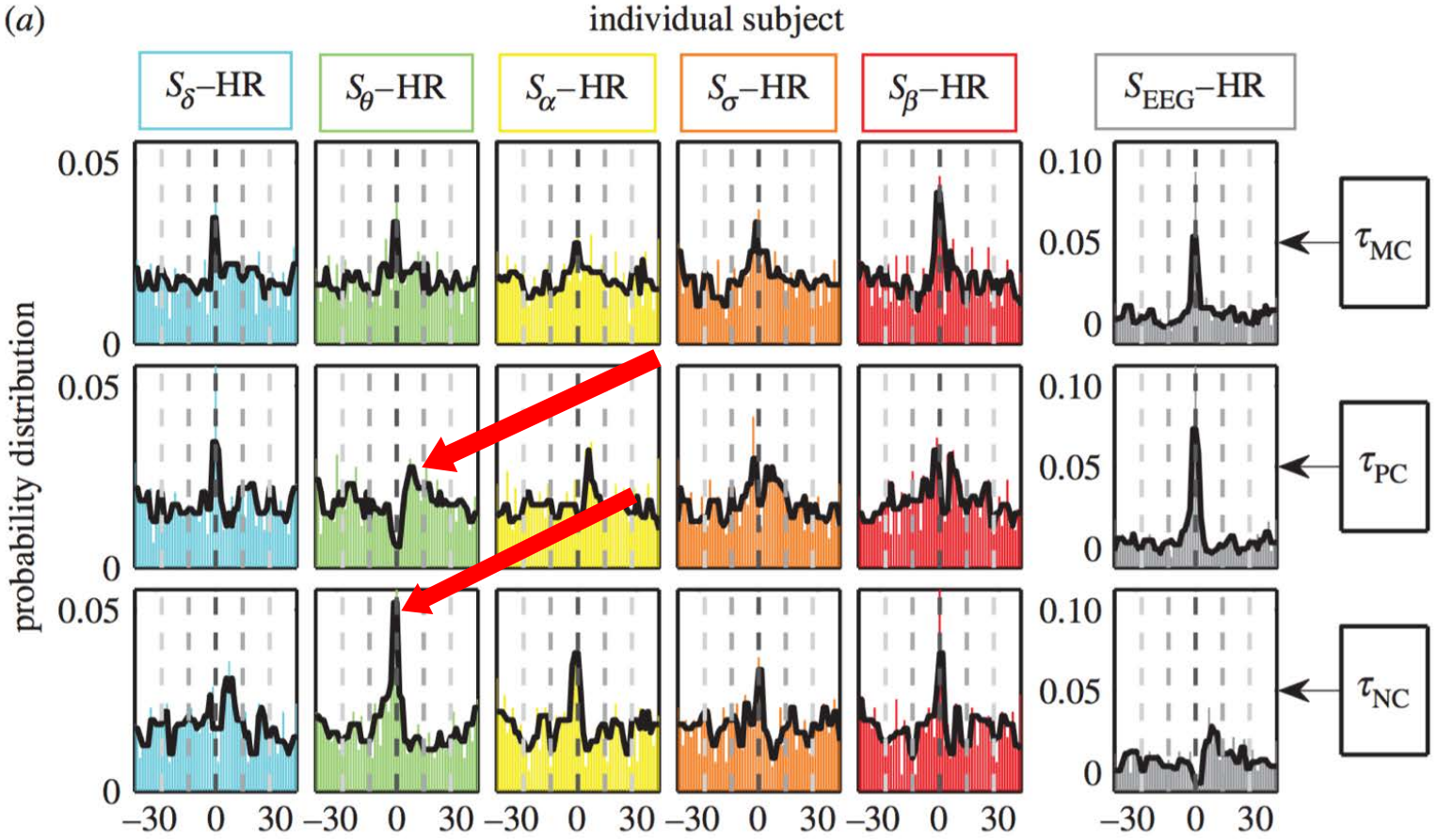
Negative Correlation

$C(\tau_{NC}, t) = \min C(\tau, t)$

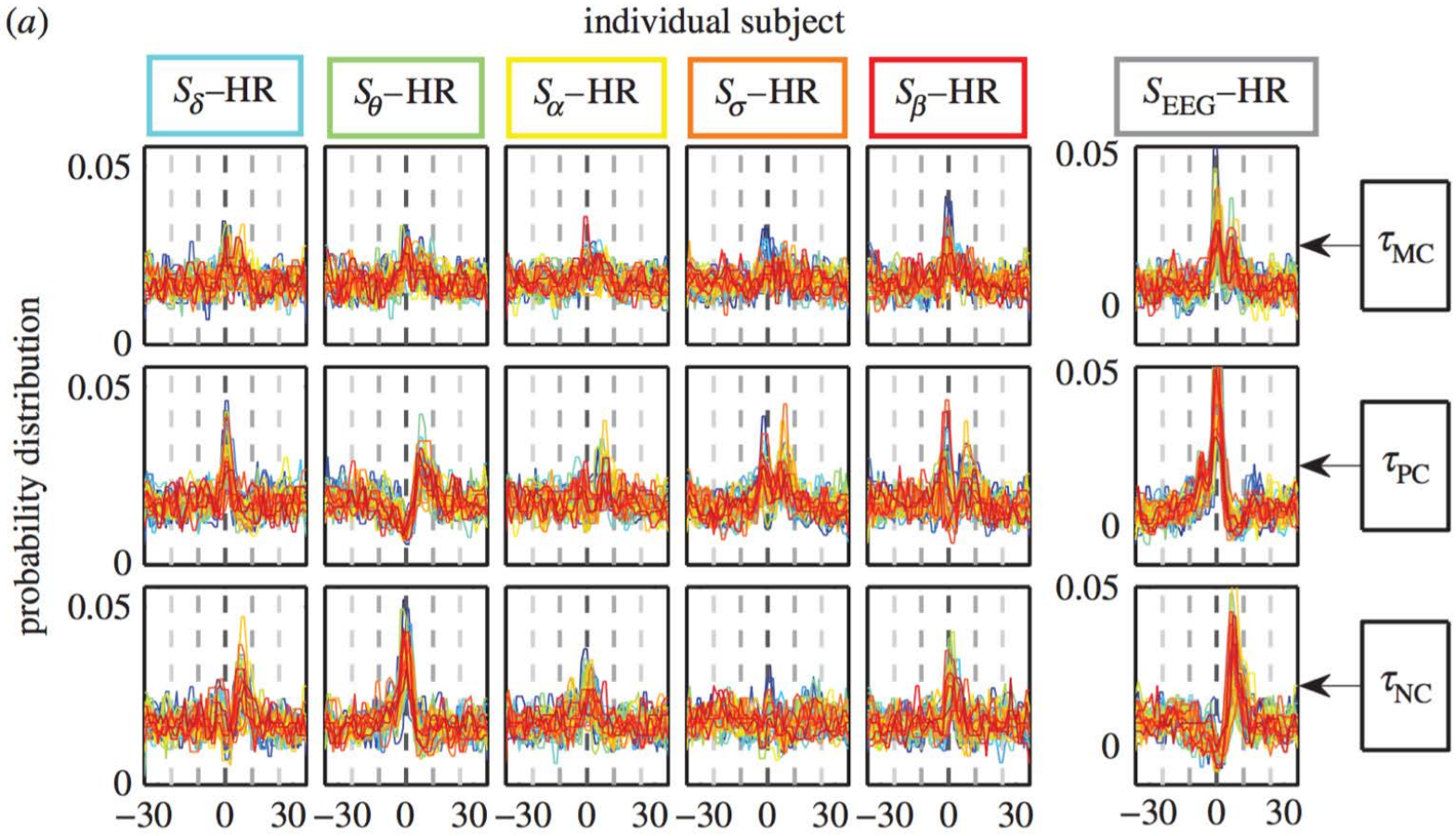


Lin A, et al. 2016 Delay-correlation landscape reveals characteristic time delays of brain rhythms and heart interactions. *Phil. Trans. R. Soc. A* **374**: 20150182.

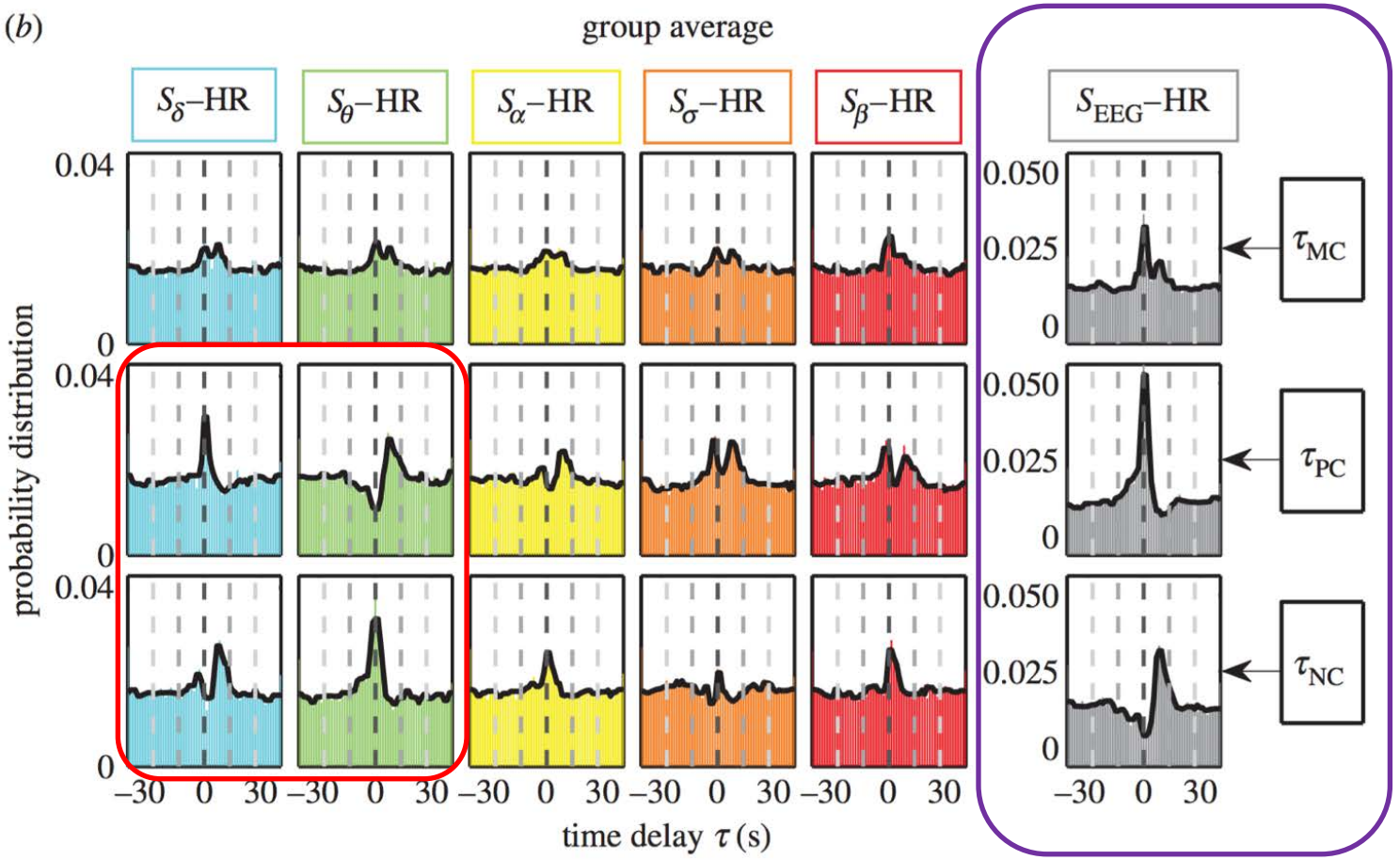
Characteristic time delays of brain-heart interaction



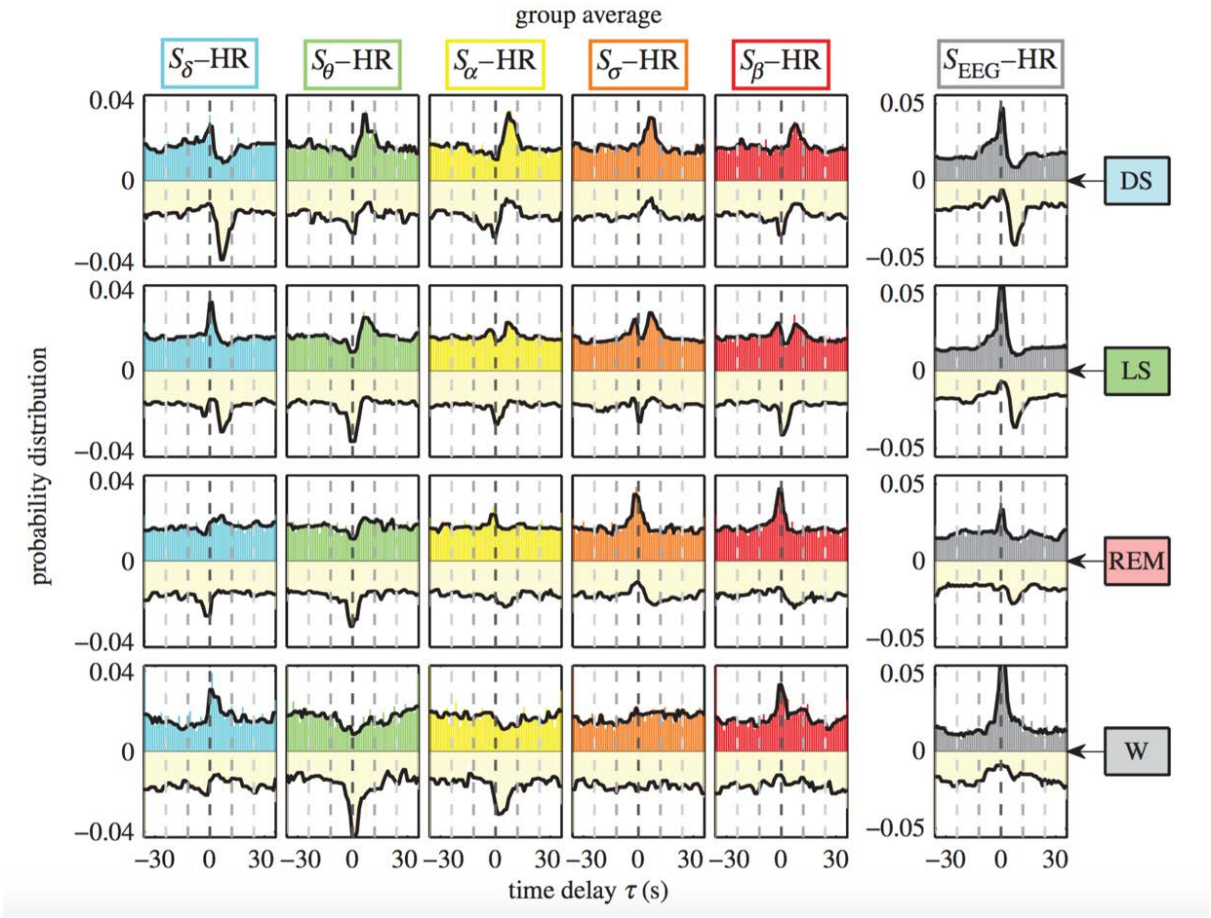
Robust pattern across subjects



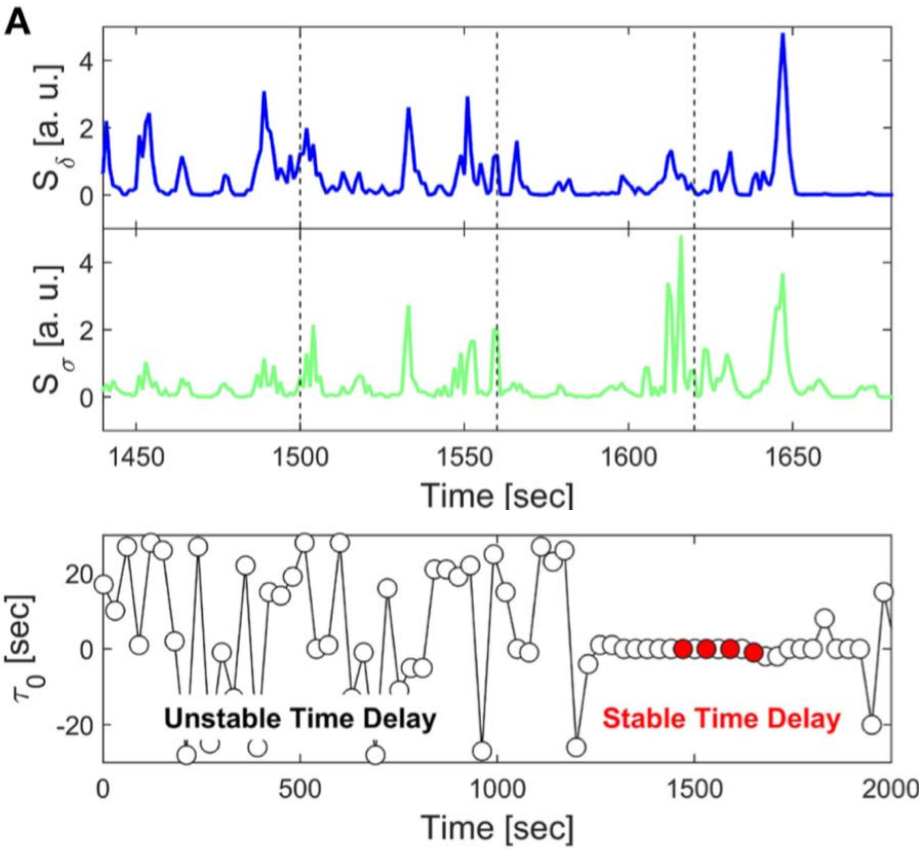
Characteristic time delays of brain-heart interaction



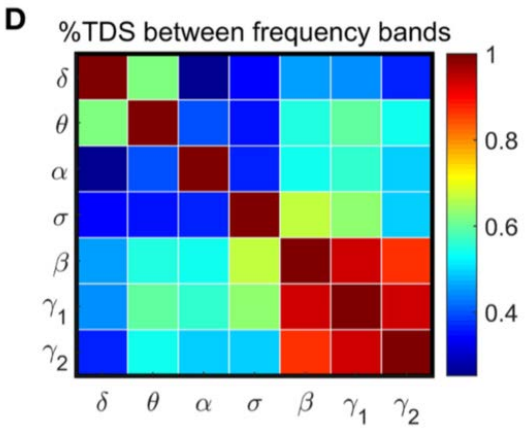
Brain-heart interaction across physiologic states

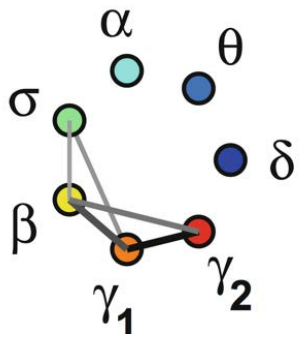


Time-delay stability



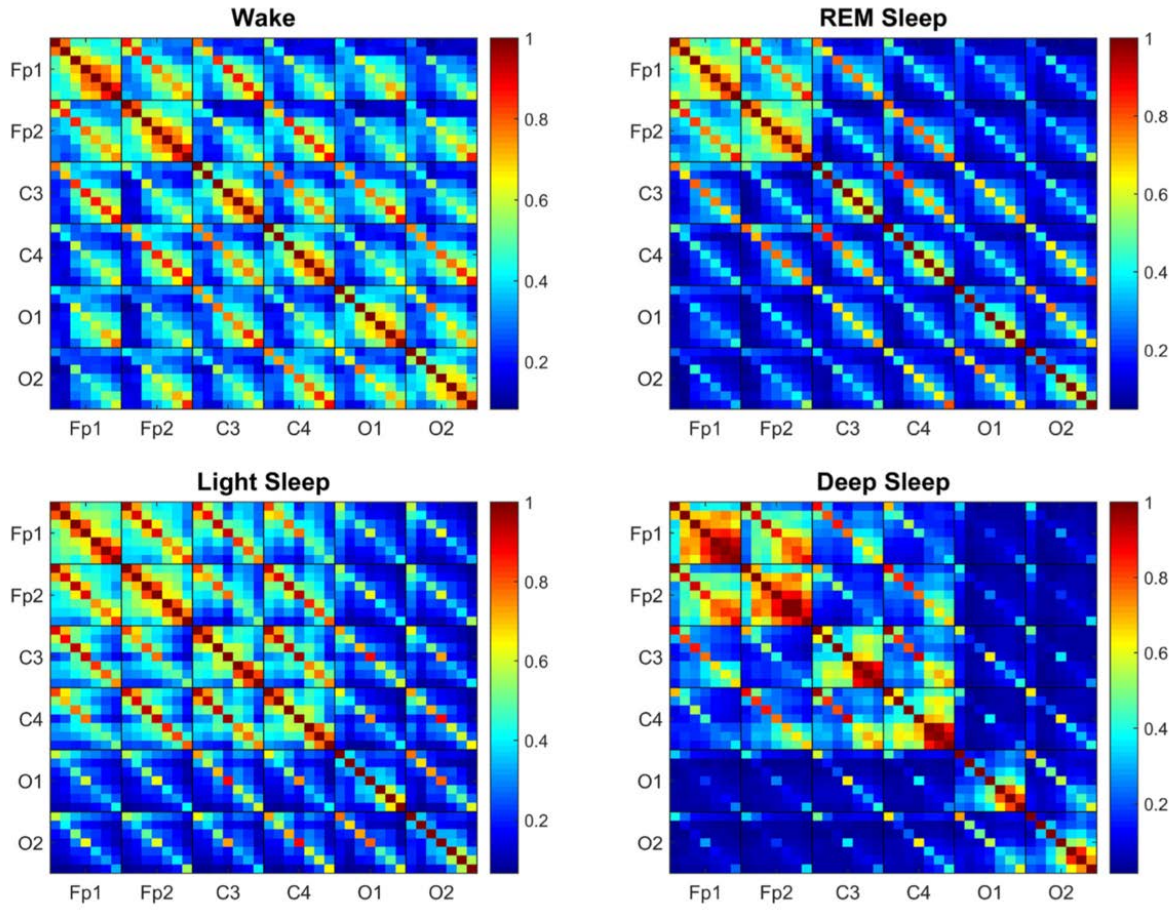
Higher percentage of TDS → stronger interaction

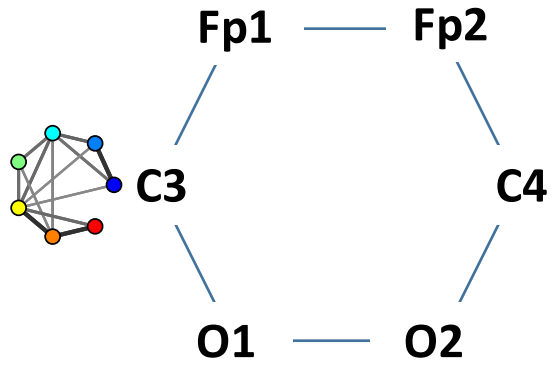


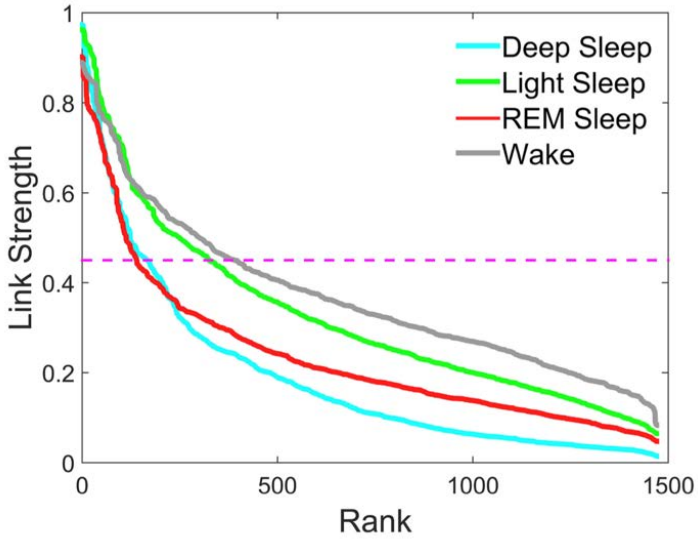


Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits 9:62*.

Transition across sleep stages

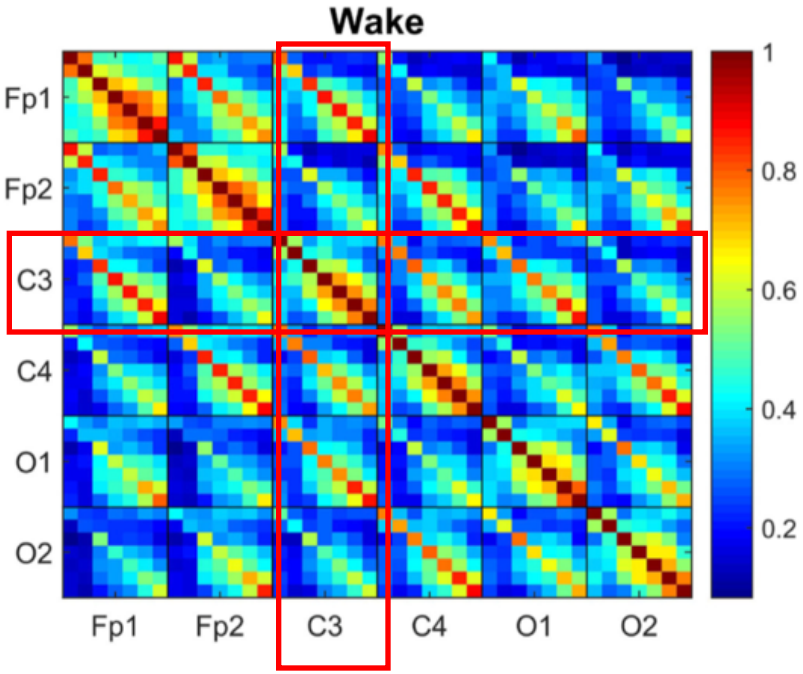


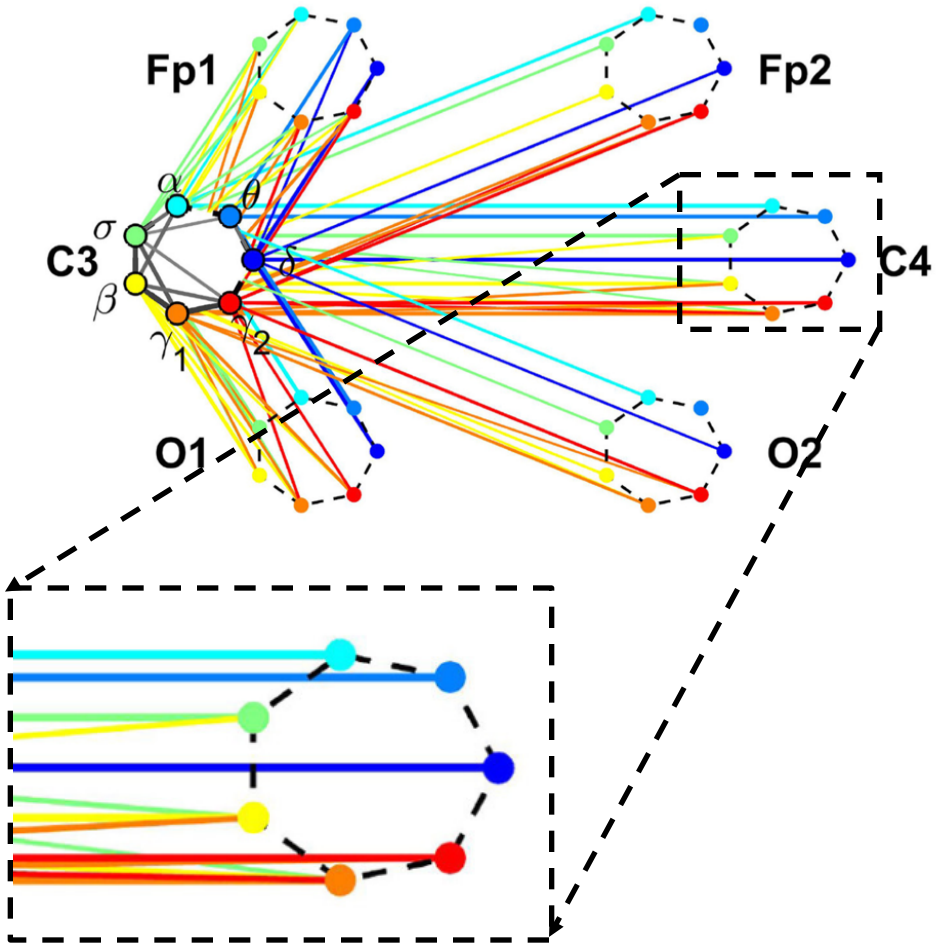




Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits 9:62*.

Visualization of channel specific sub-network

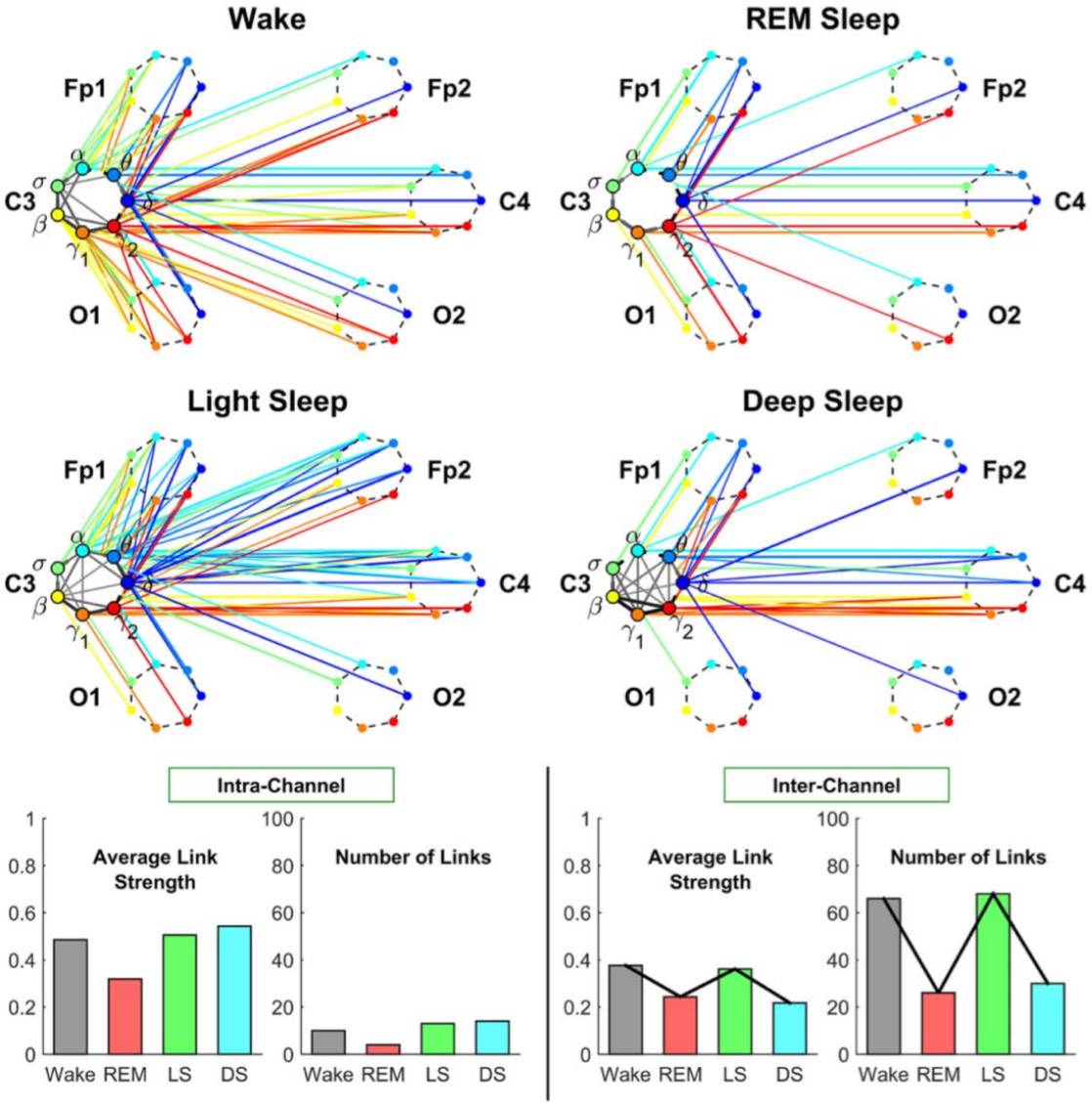




Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits 9:62*.

Central Channel

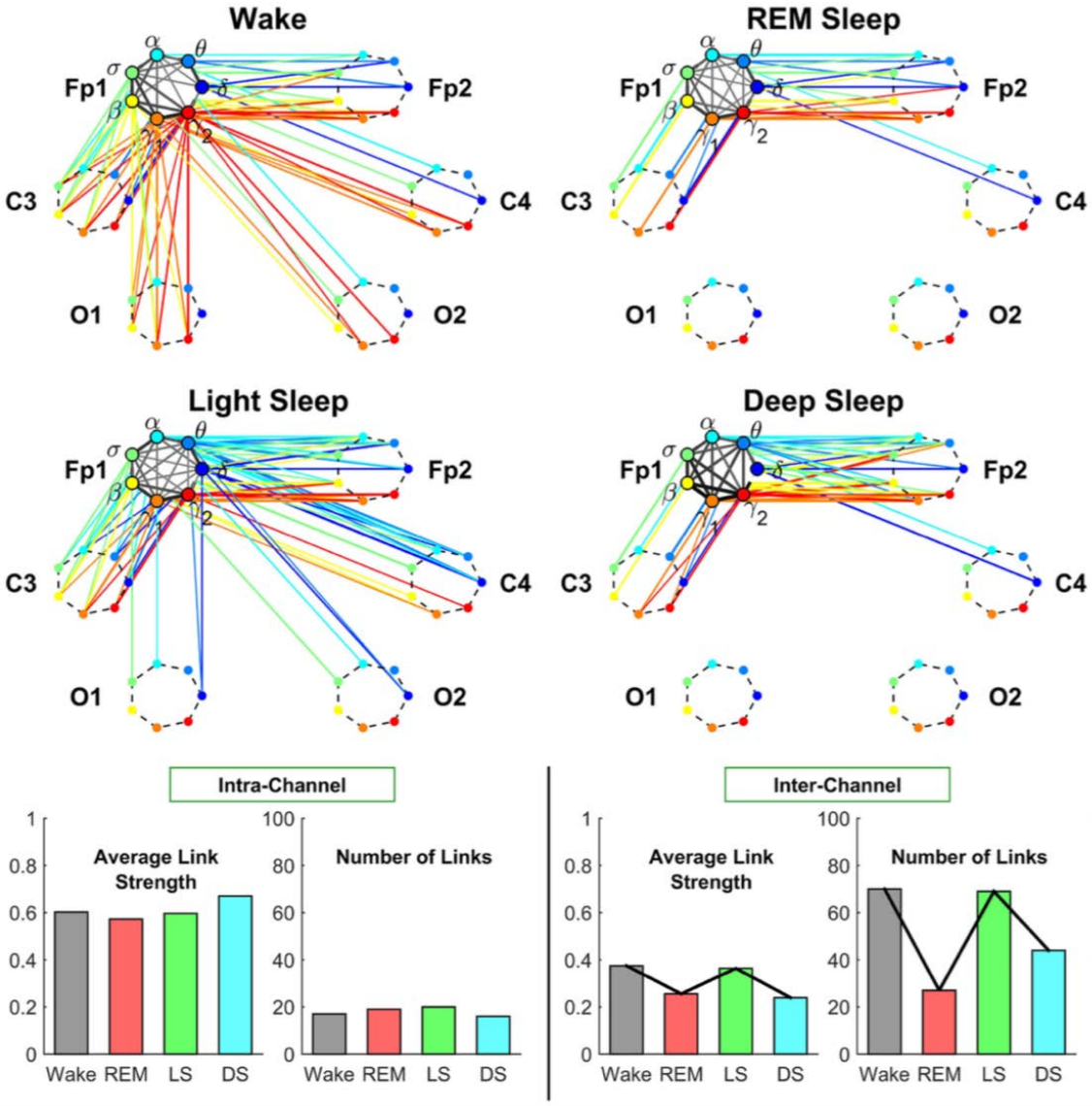
- Parallel links
- Symmetry
- Reorganization
- C3-C4 networks
- C-F > C-O
- Inter-channel Connectivity



Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits 9:62*.

Frontal Channel

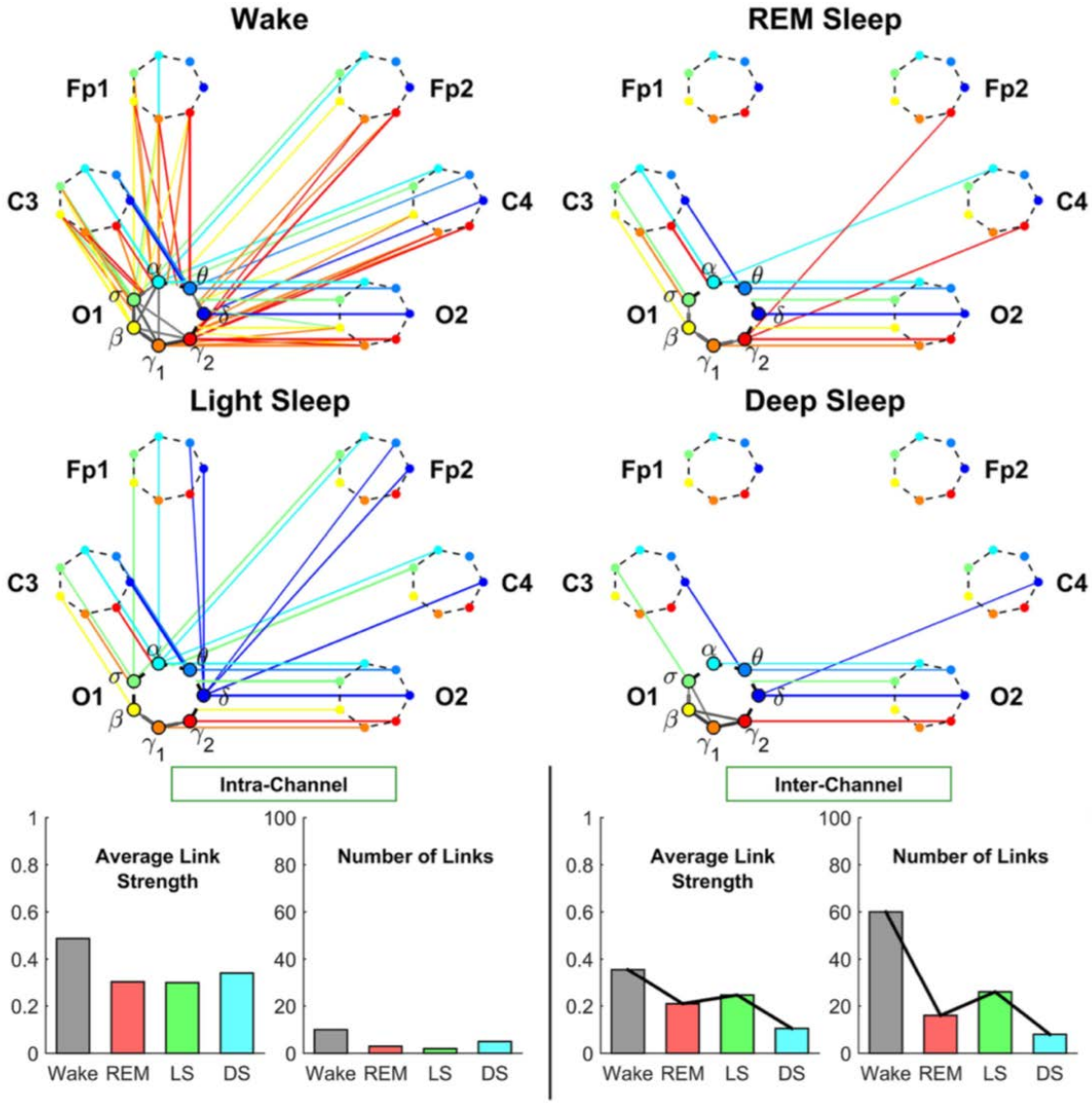
- FP1-FP2 interaction
- Frontal-Central interaction
- Wake – high frequency
- Light Sleep – low frequency
- REM and DS – Disconnected Frontal-Occipital
- Connectivity



Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits 9:62*.

Occipital Channel

- Sparse network
- Wake – High frequency
- REM and DS – Disconnected Frontal-Occipital
- Inter-channel Connectivity



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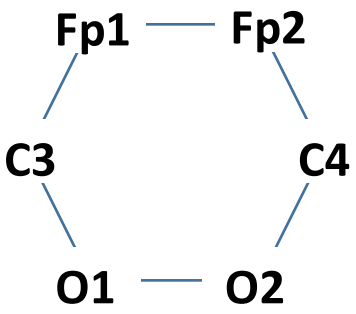
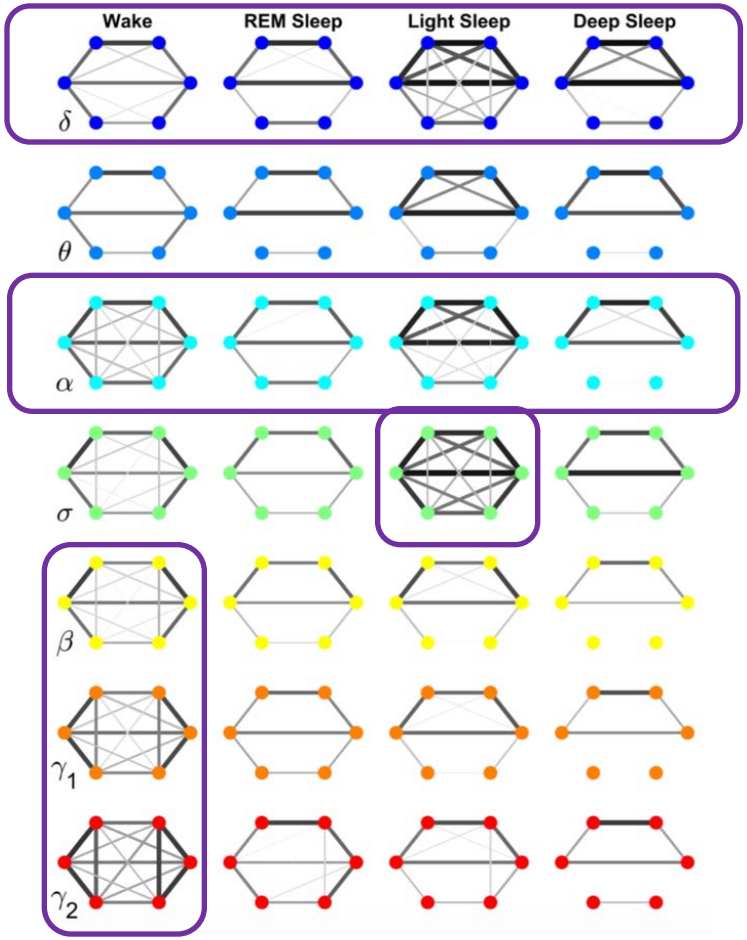
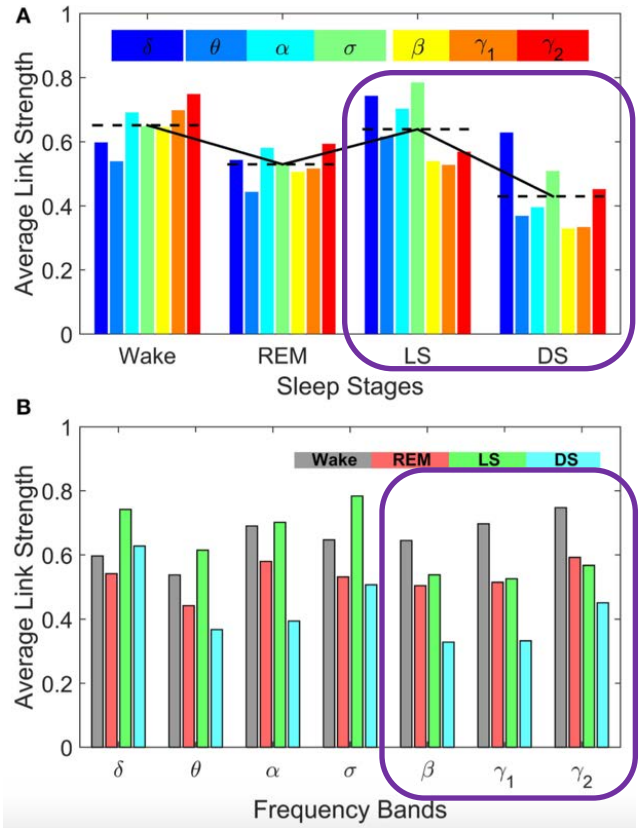
Functional network of brain waves coordination







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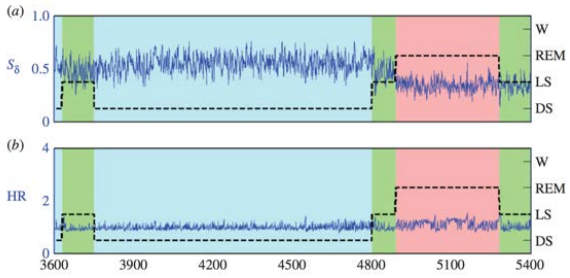
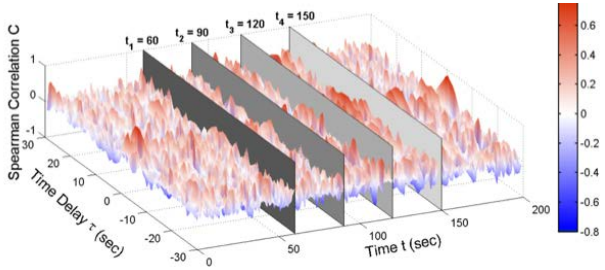
Summary

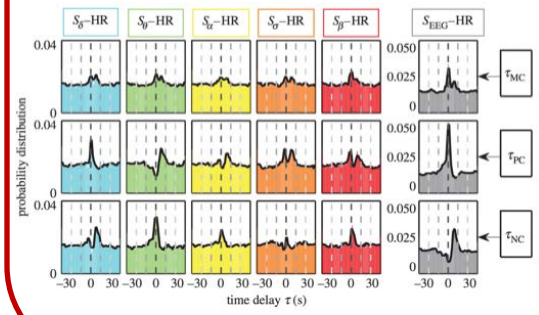
Physiologic signals



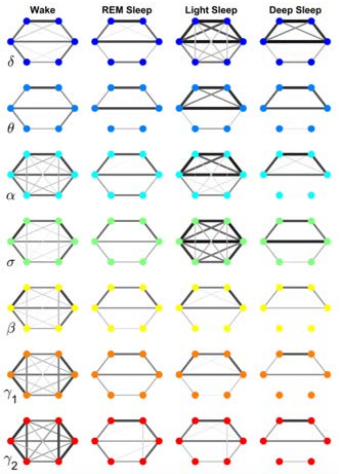
Delay-Correlation Landscape



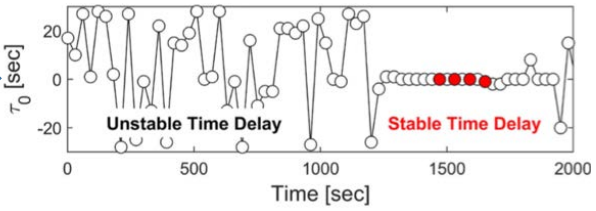
Characteristic Time-Delay



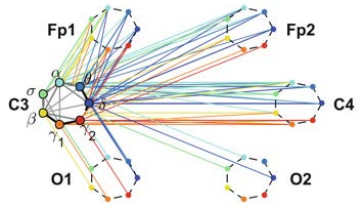
Network Signature



Time-Delay Stability (TDS)



Physiologic Networks



New perspective on Network Physiology

- Structural connectivity:

→ "defined by the existence of a physical link"

- Effective connectivity:

→ "defined as influence one system exerts over another, under a particular model of causal dynamics"

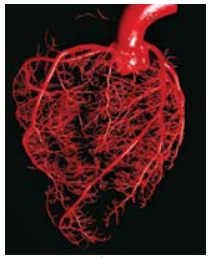
- Functional connectivity:

→ "Referred to statistical dependences between systems"

Stankovski et al, *Coupling functions: Universal insights into dynamical interaction mechanisms* arXiv:1706.01810v1

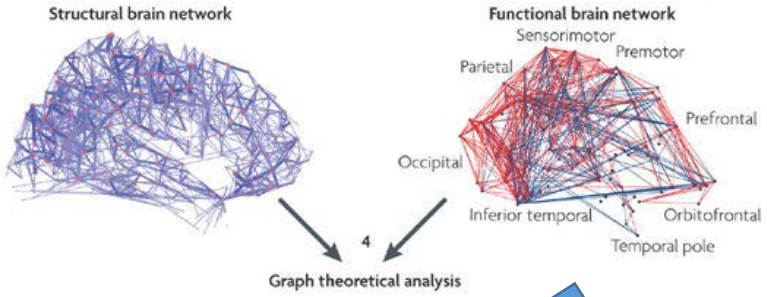
New perspective on Network Physiology

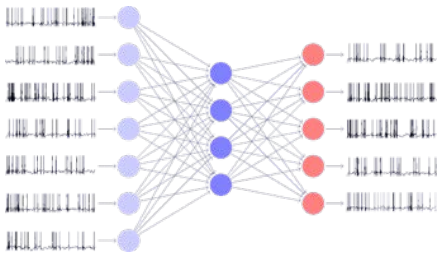
Structural Connectivity
(physical networks)



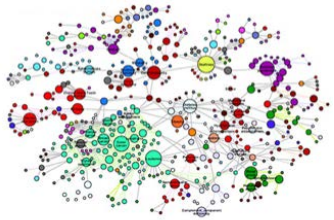
Effective Connectivity
(coupling functions)

$$\dot{x} = f_1(x) + g_1(x, y)$$
$$\dot{y} = f_2(y) + g_2(x, y)$$

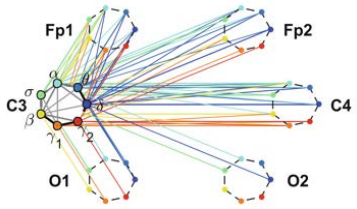




Functional Connectivity
(Statistical dependence)

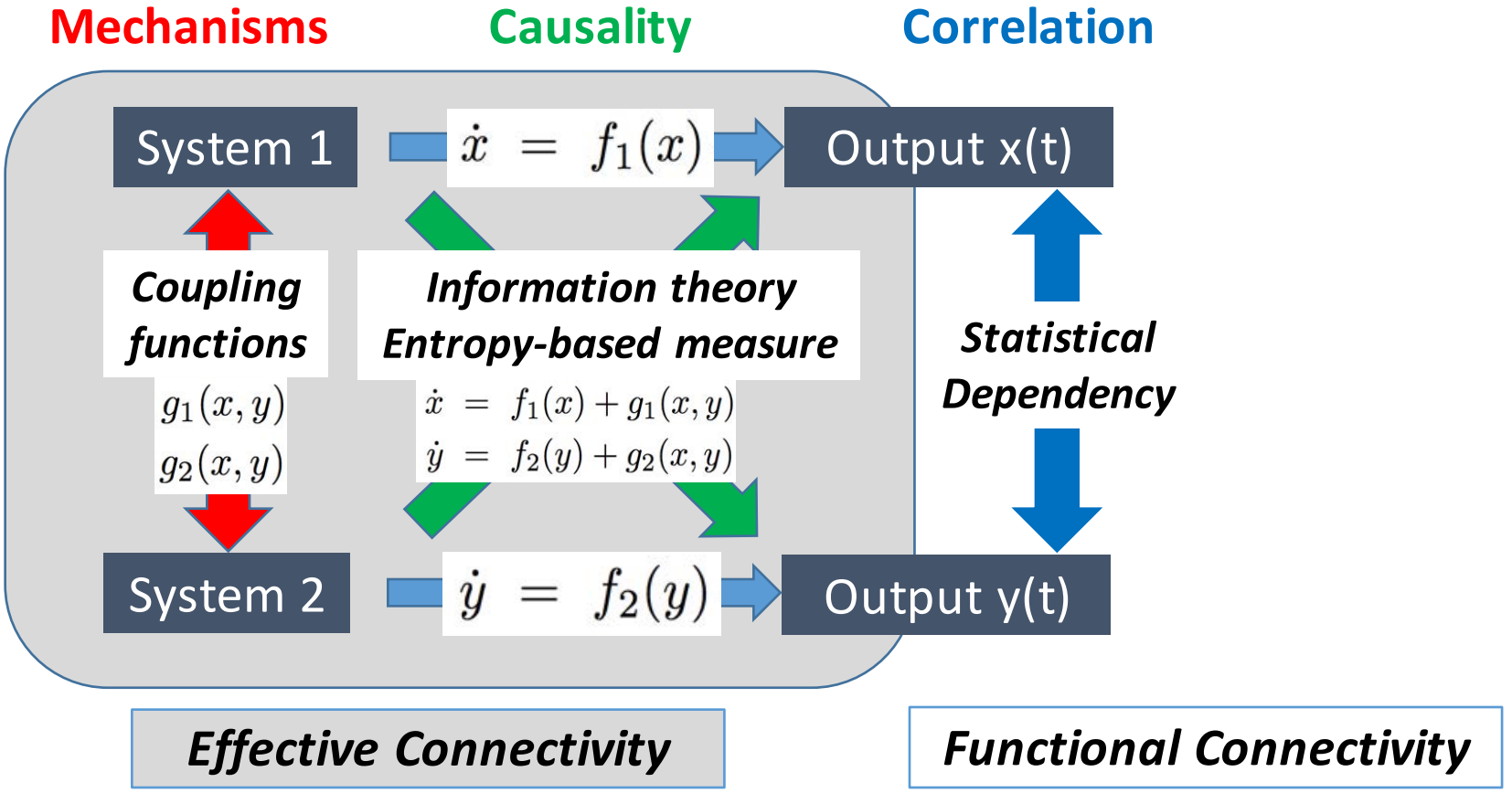


Static indices



Time series

Functional and Effective Connectivity



"Trajectory of the patient" → predictive monitoring

Acknowledgement

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- Dr. Aijing Lin and other members from

W.M. KECK FOUNDATION

Keck Laboratory for Network Physiology

Questions? Comments?

Email: kangliu@brandeis.edu