



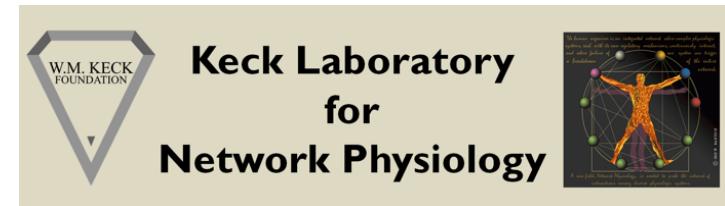
First International Summer Institute on Network Physiology (ISINP)

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

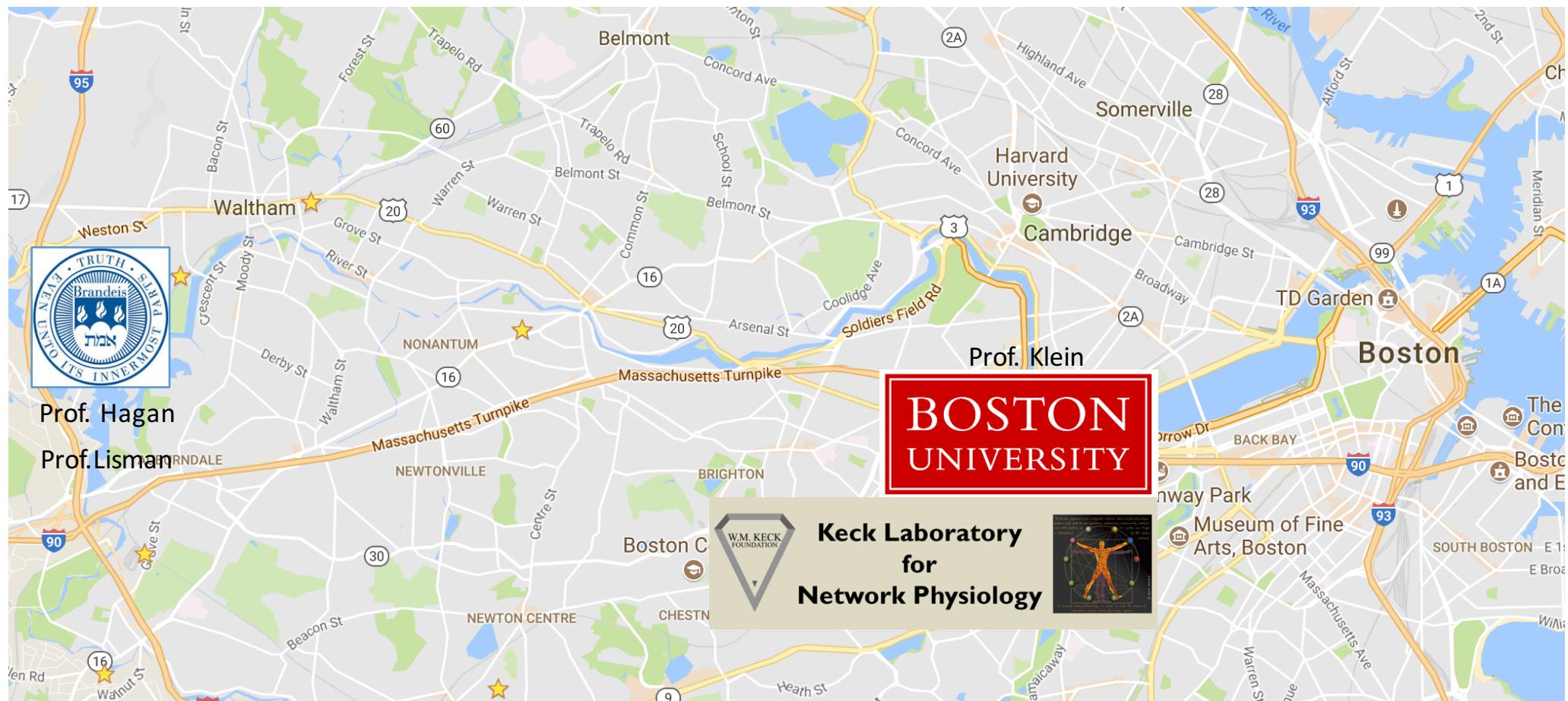
Emergent Coordination Among Physiologic Systems: New Network Signatures for Physiologic State and Function

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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

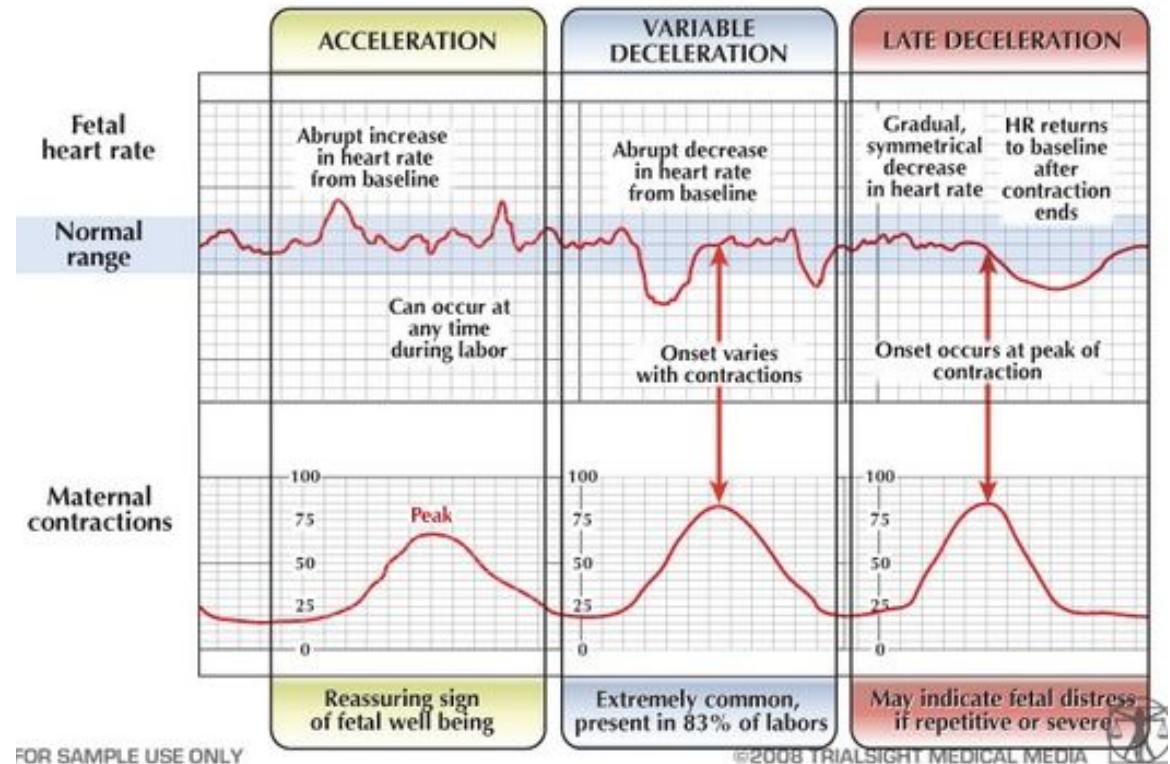
Thanks for inviting me!



Photo of
Kang's
daughter

DOB xx/xx/2017

Fetal Heart Rate – Uterine Contraction

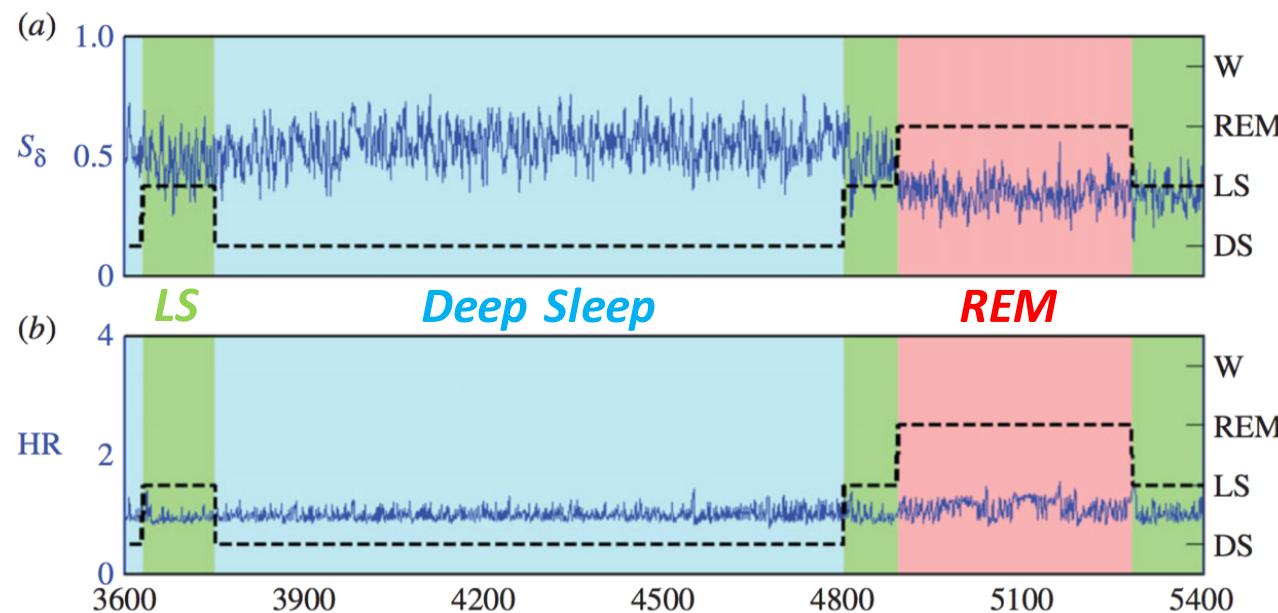


1. Coordination between outputs carry important information
2. Human limitation
3. Teach the computer to monitor these for us?

Strategy

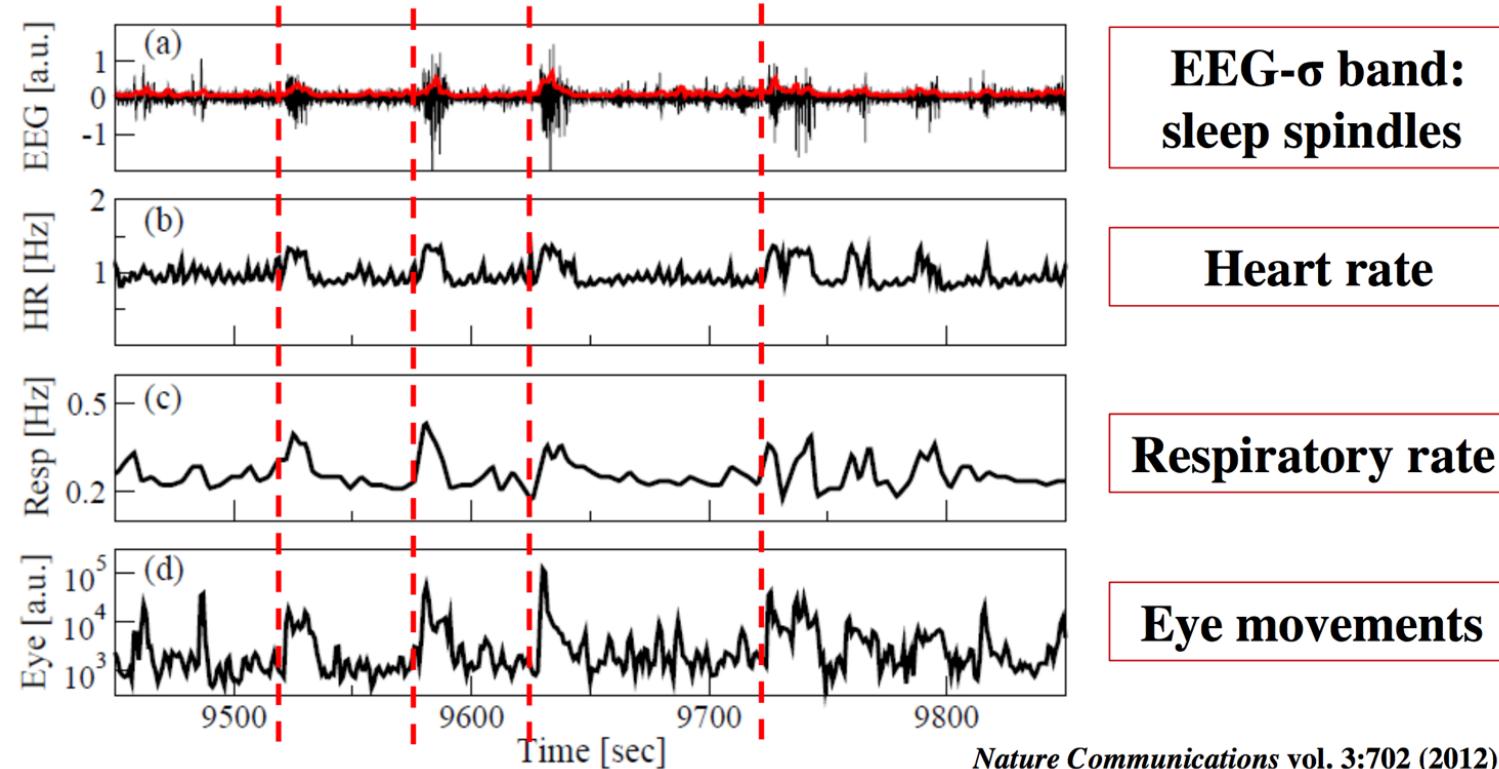
- Step 1: “Pick the right problem”
→ Quantify ***functional connectivity (emergent coordination)*** at the output signal level and explore its relation with physiologic state/function
- Step 2: “Inspect the data”
→ What are the common characteristics shared in physiological signals?
- Step 3: “Assume 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 bursting activities



**EEG- σ band:
sleep spindles**

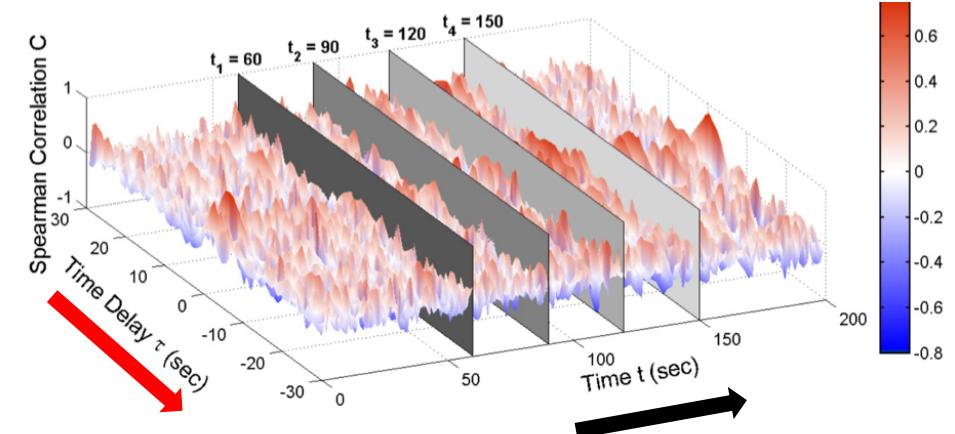
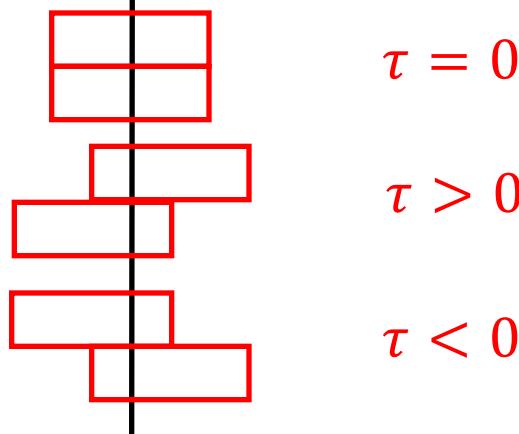
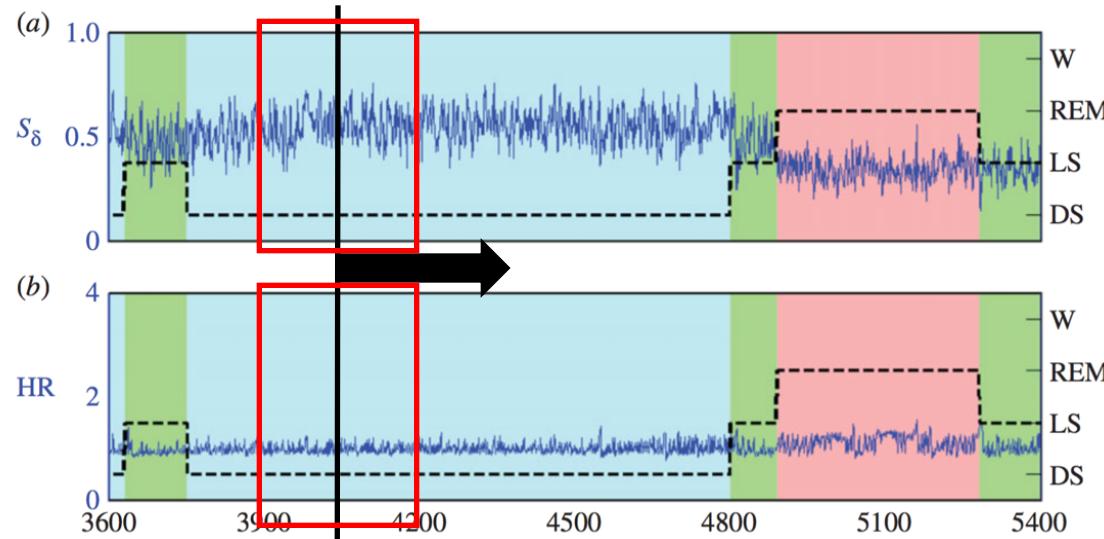
Heart rate

Respiratory rate

Eye movements

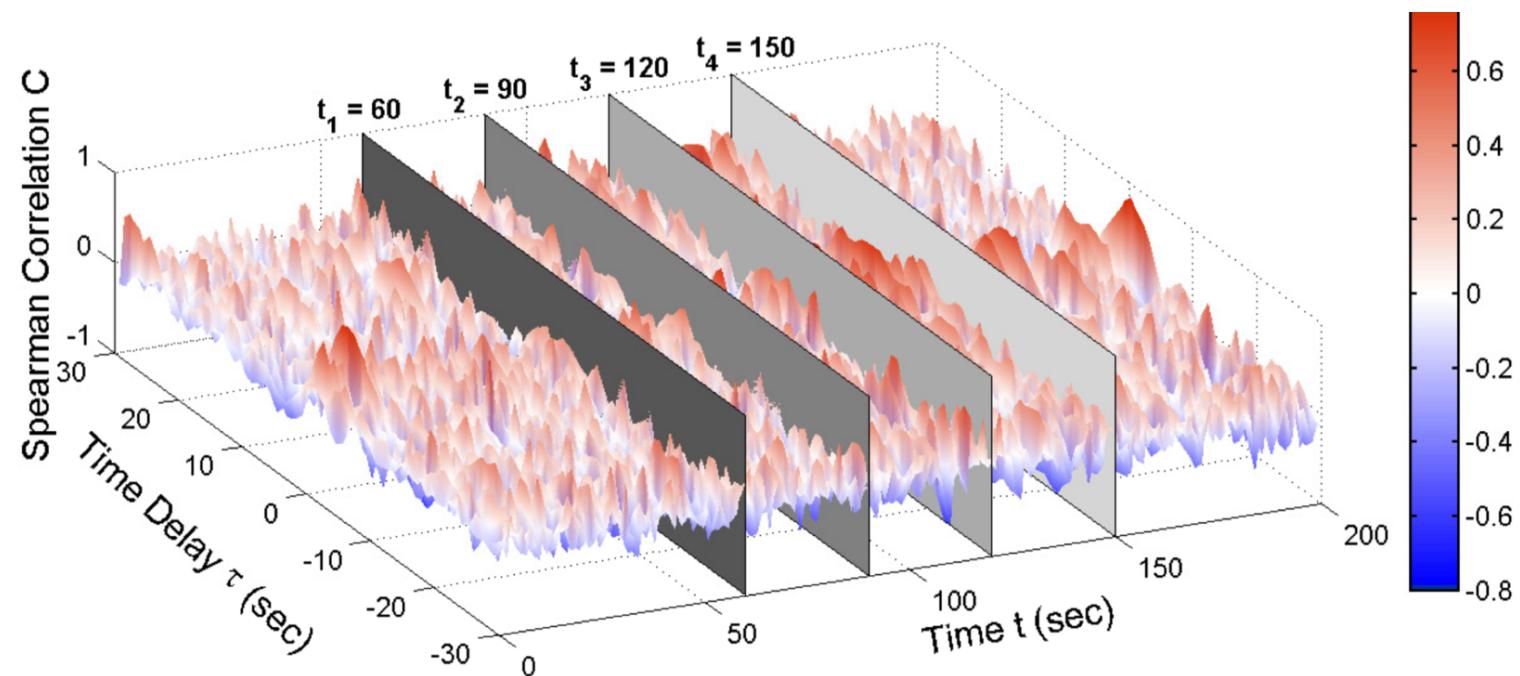
- Coordination is commonly observed across diverse systems
- Busting activity is important

Extend traditional cross-correlation



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

Delay-Correlation Landscape

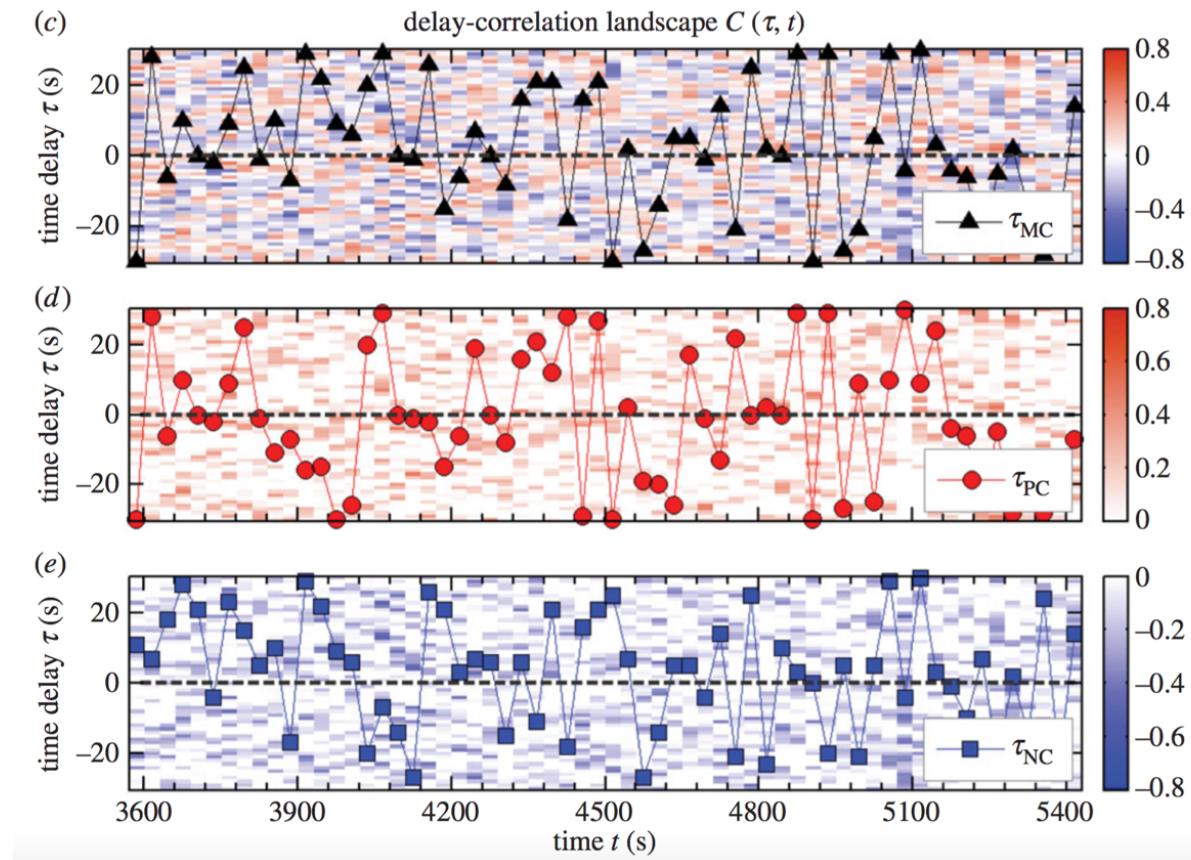


Time delays between physiologic systems

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

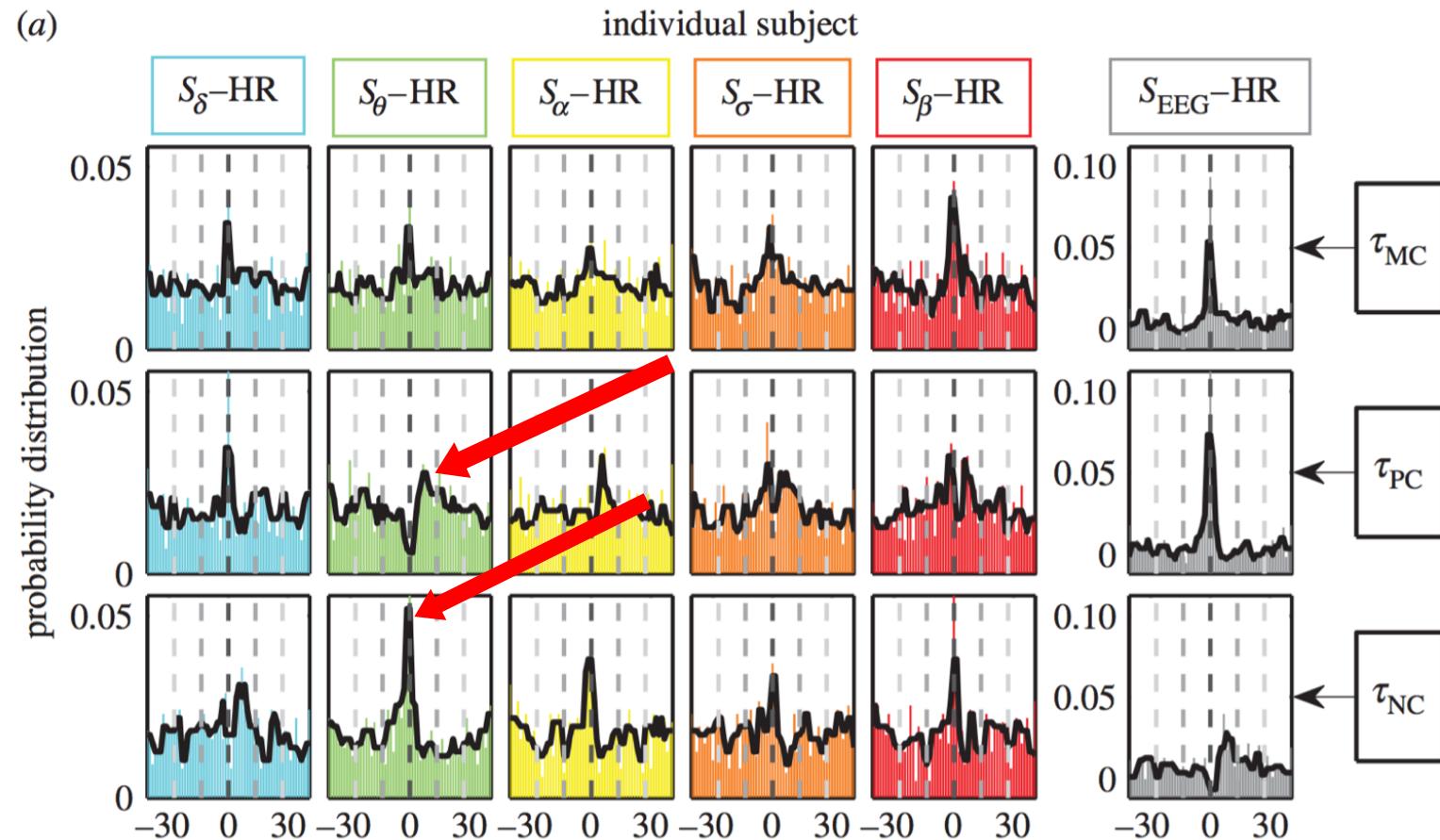
Positive Correlation
 $C(\tau_{PC}, t) = \max C(\tau, t)$

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

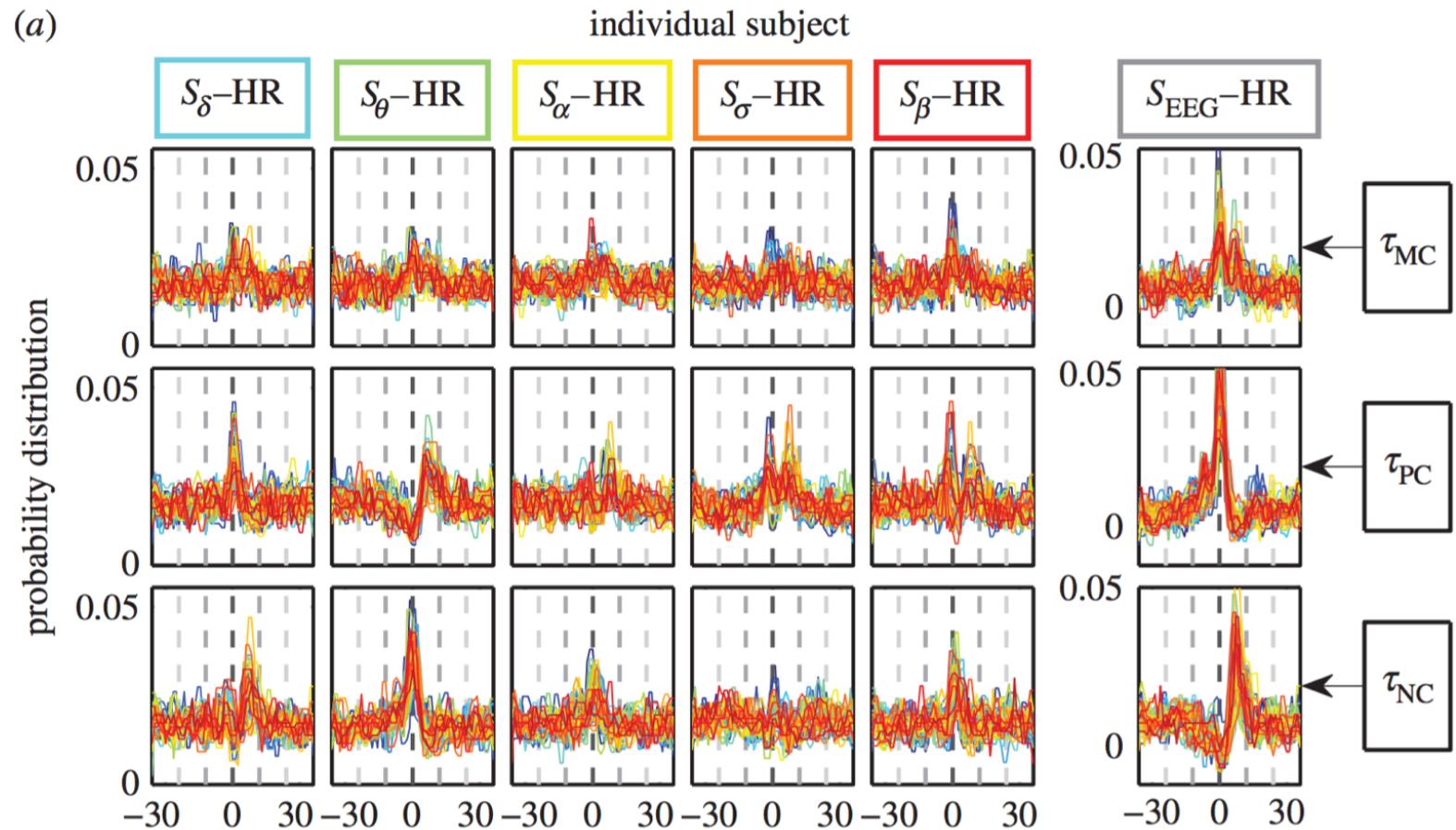


Lin A, et al. 2016 Delay-correlation landscape reveals characteristic time delays of brain rhythms and heart interactions. *Phil. Trans. R. Soc. A* **374**: 20150182.

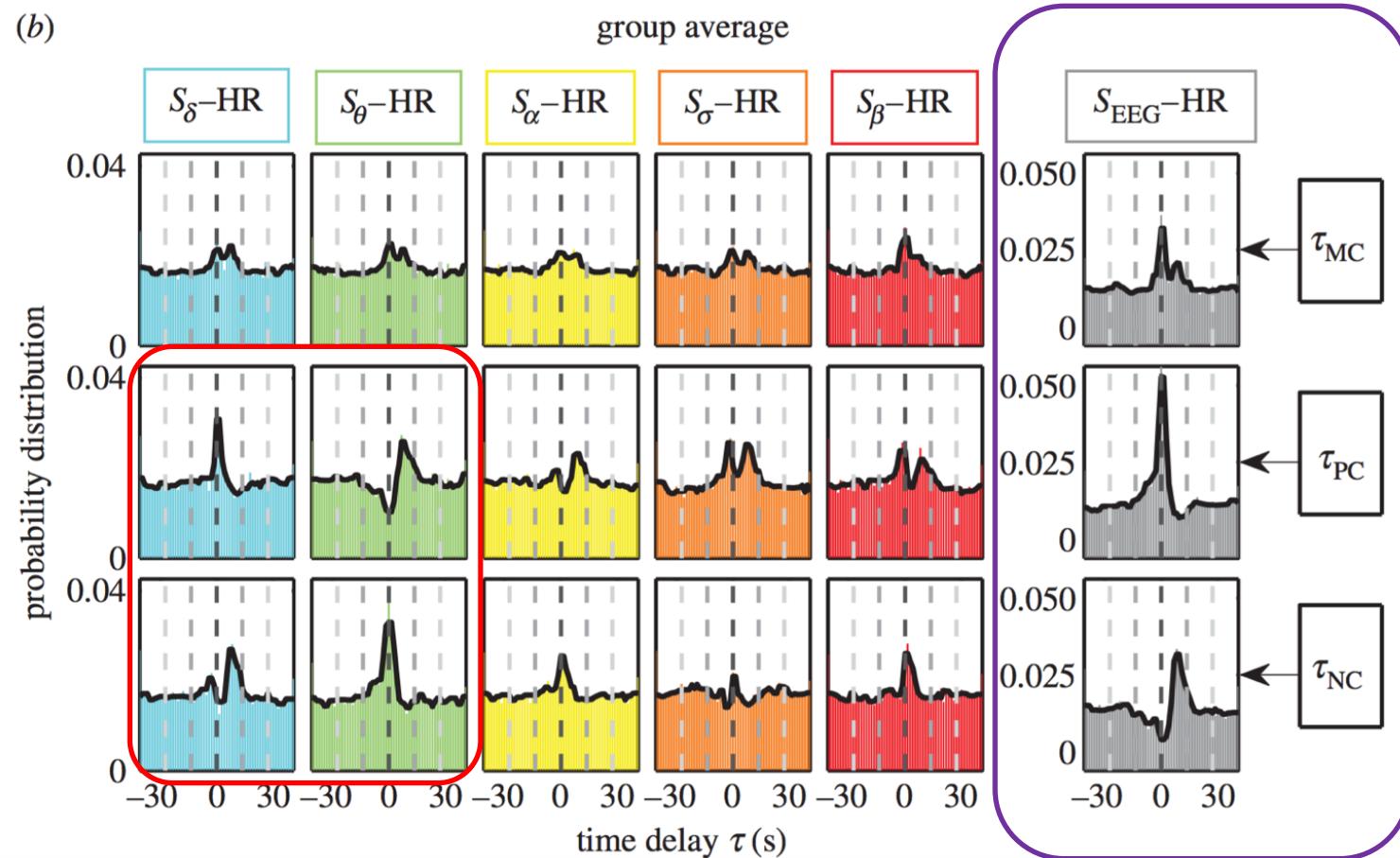
Characteristic time delays of brain-heart interaction



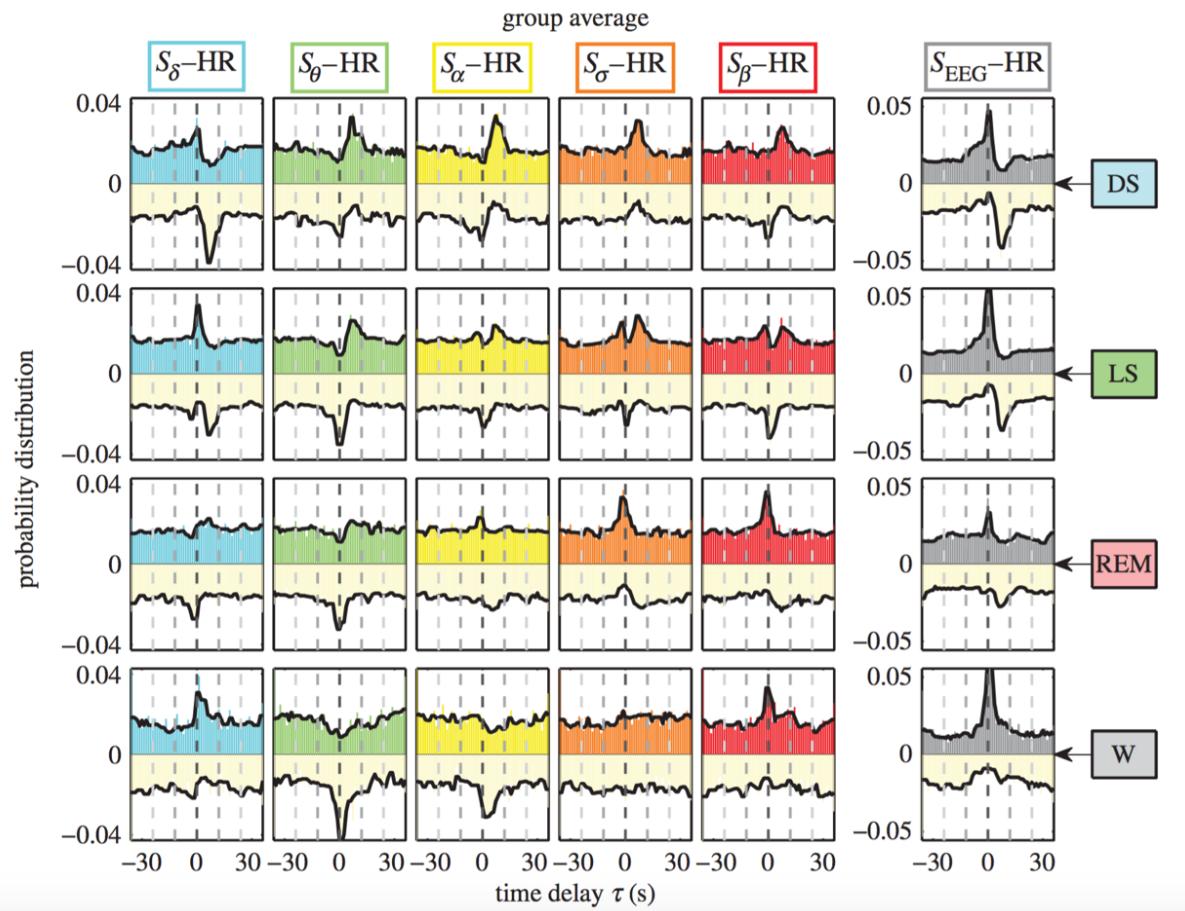
Robust pattern across subjects



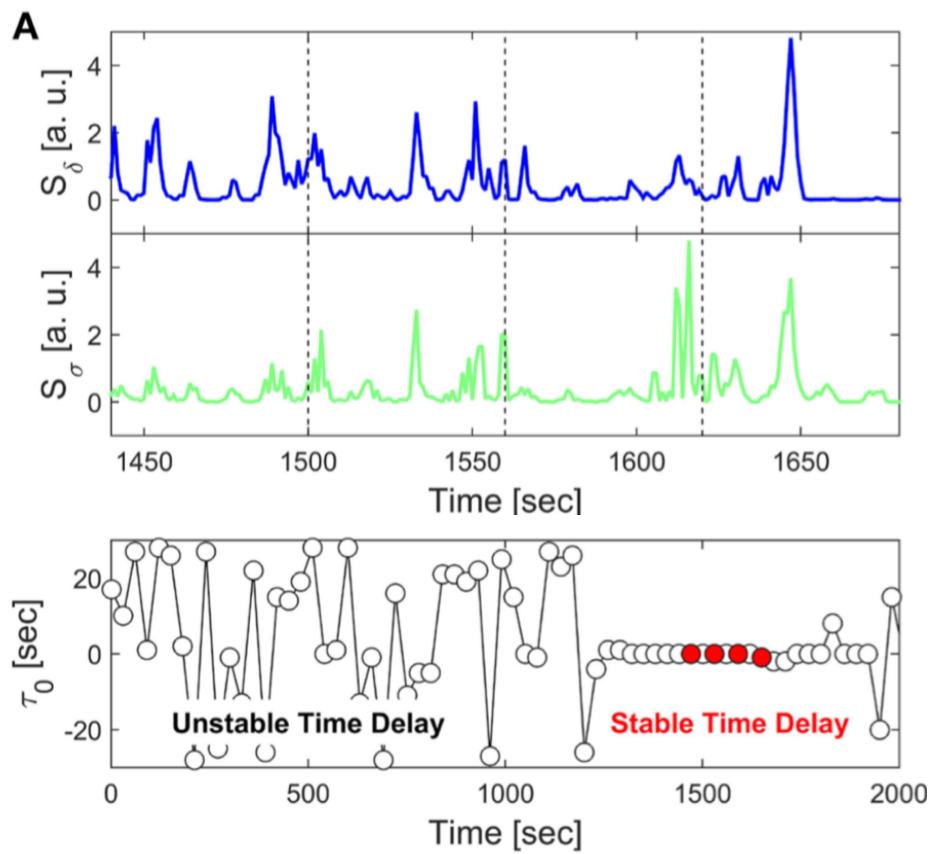
Characteristic time delays of brain-heart interaction



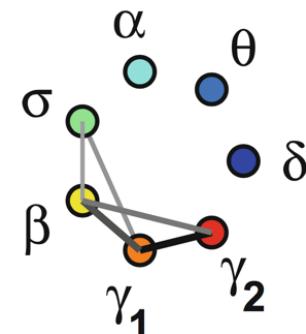
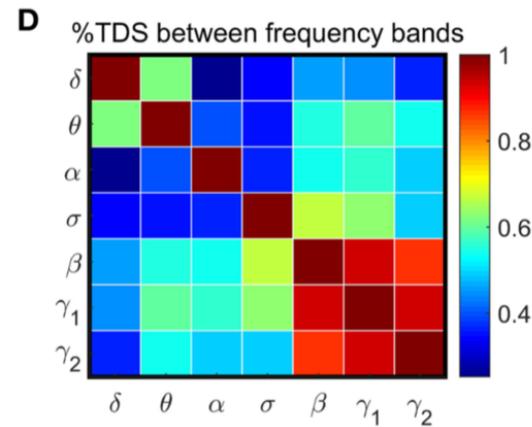
Brain-heart interaction across physiologic states



Time-delay stability

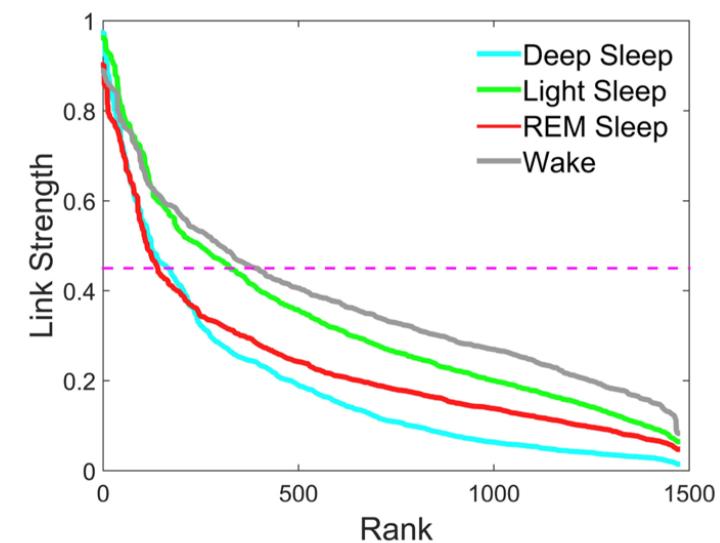
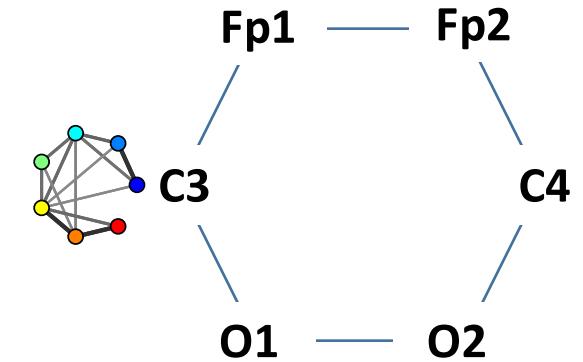
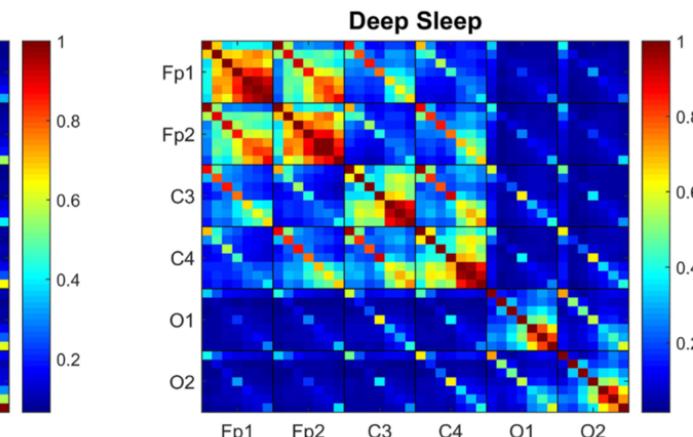
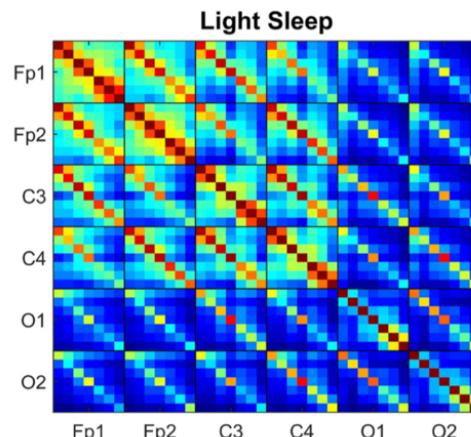
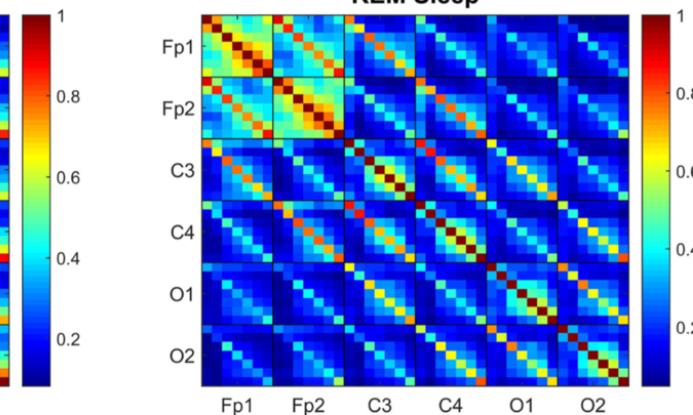
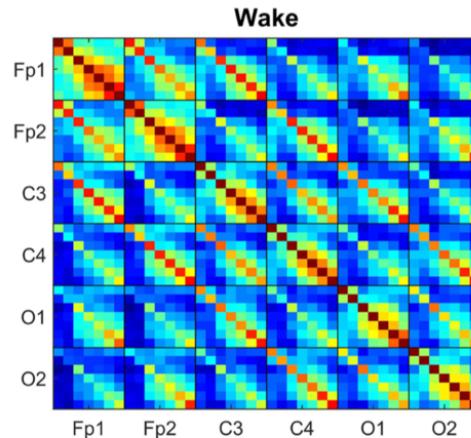


Higher percentage of TDS \rightarrow stronger interaction



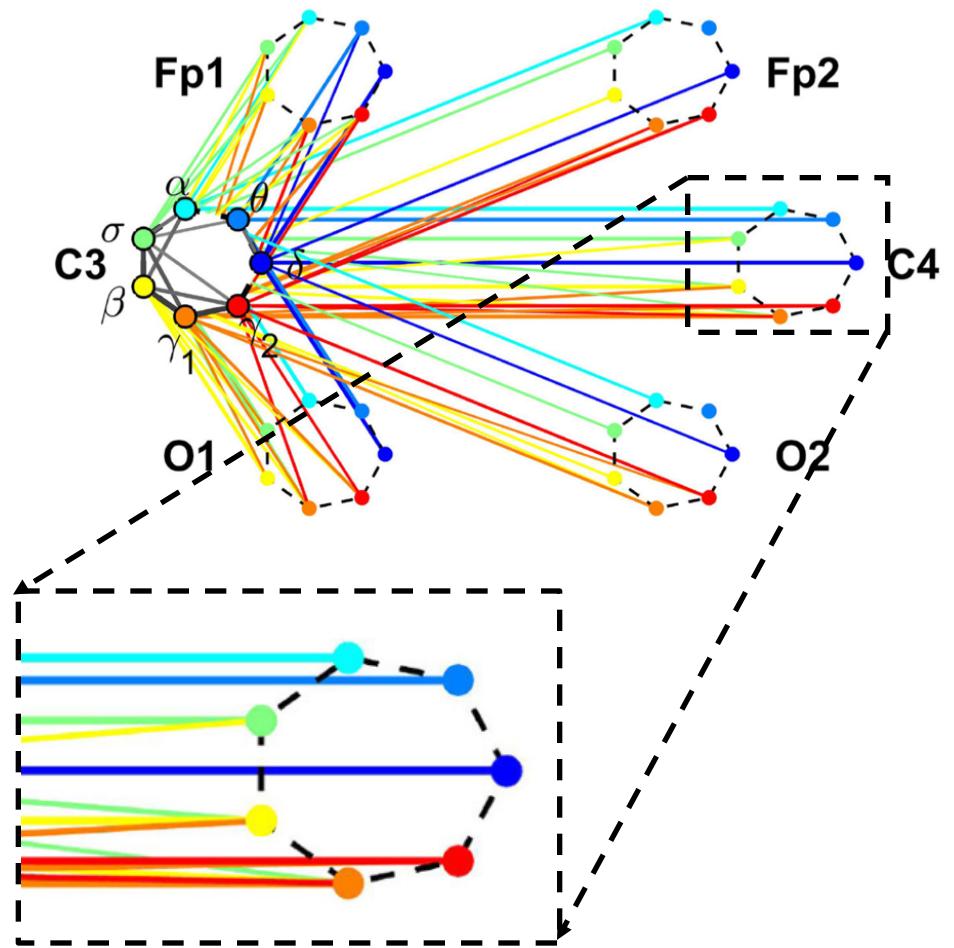
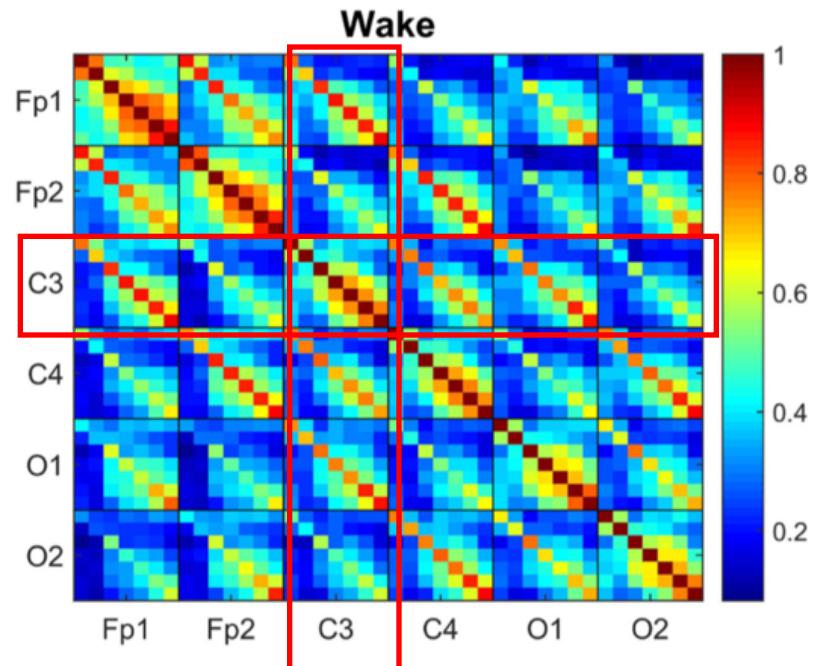
Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits* 9:62.

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.

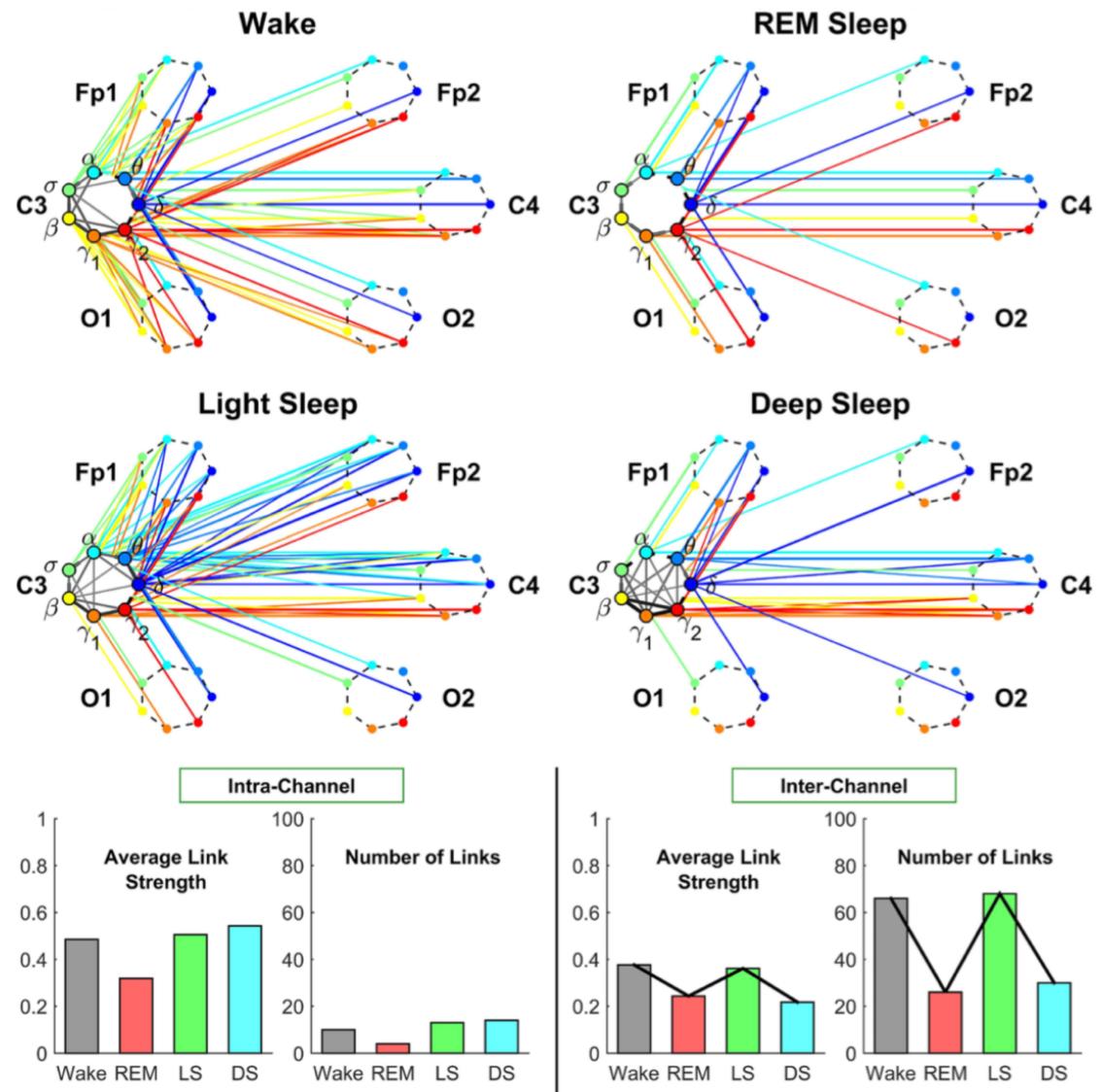
Visualization of channel specific sub-network



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

Central Channel

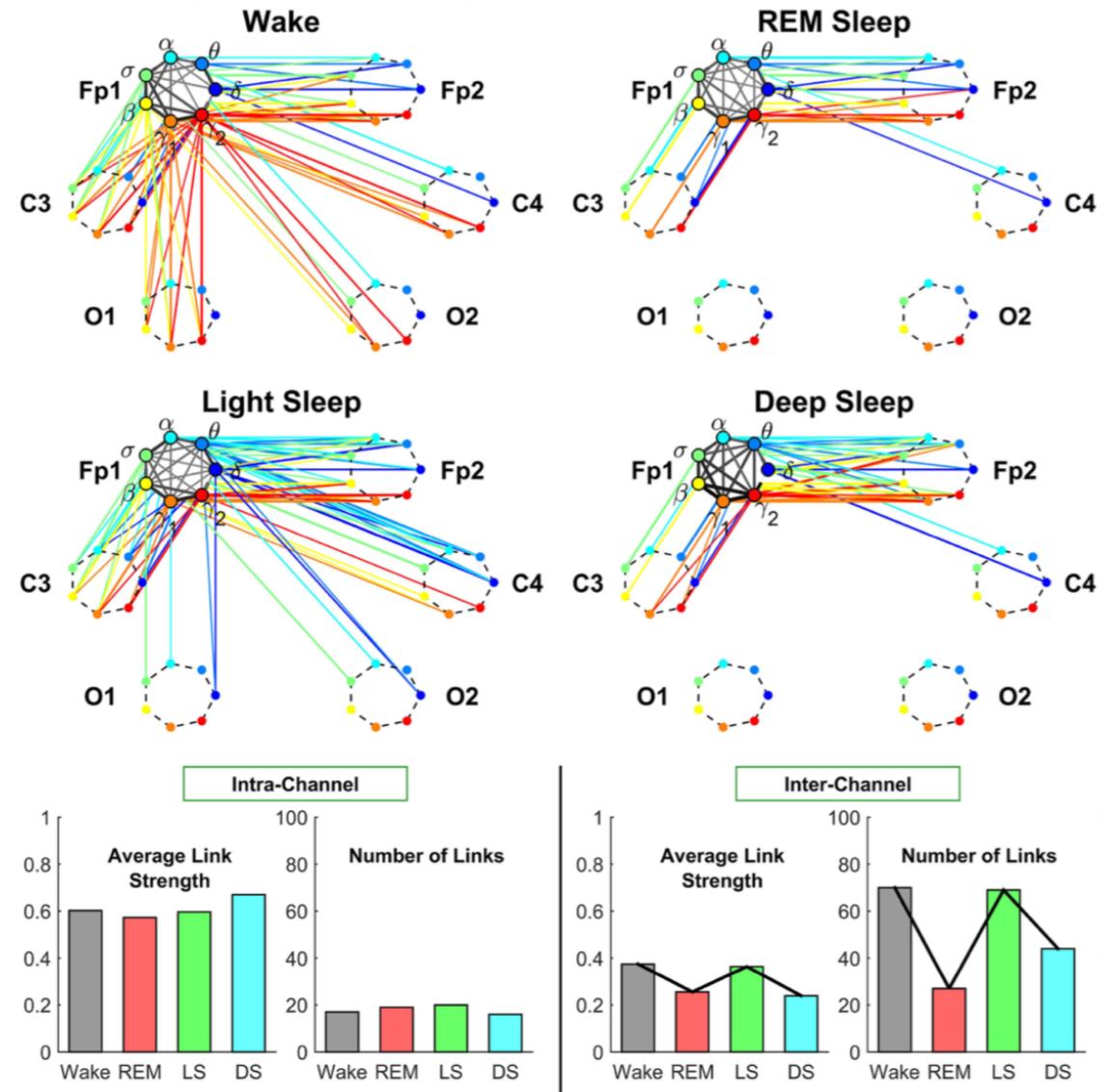
- Parallel links
- Symmetry
- Reorganization
- C3-C4 networks
- C-F > C-O
- Inter-channel Connectivity



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

Frontal Channel

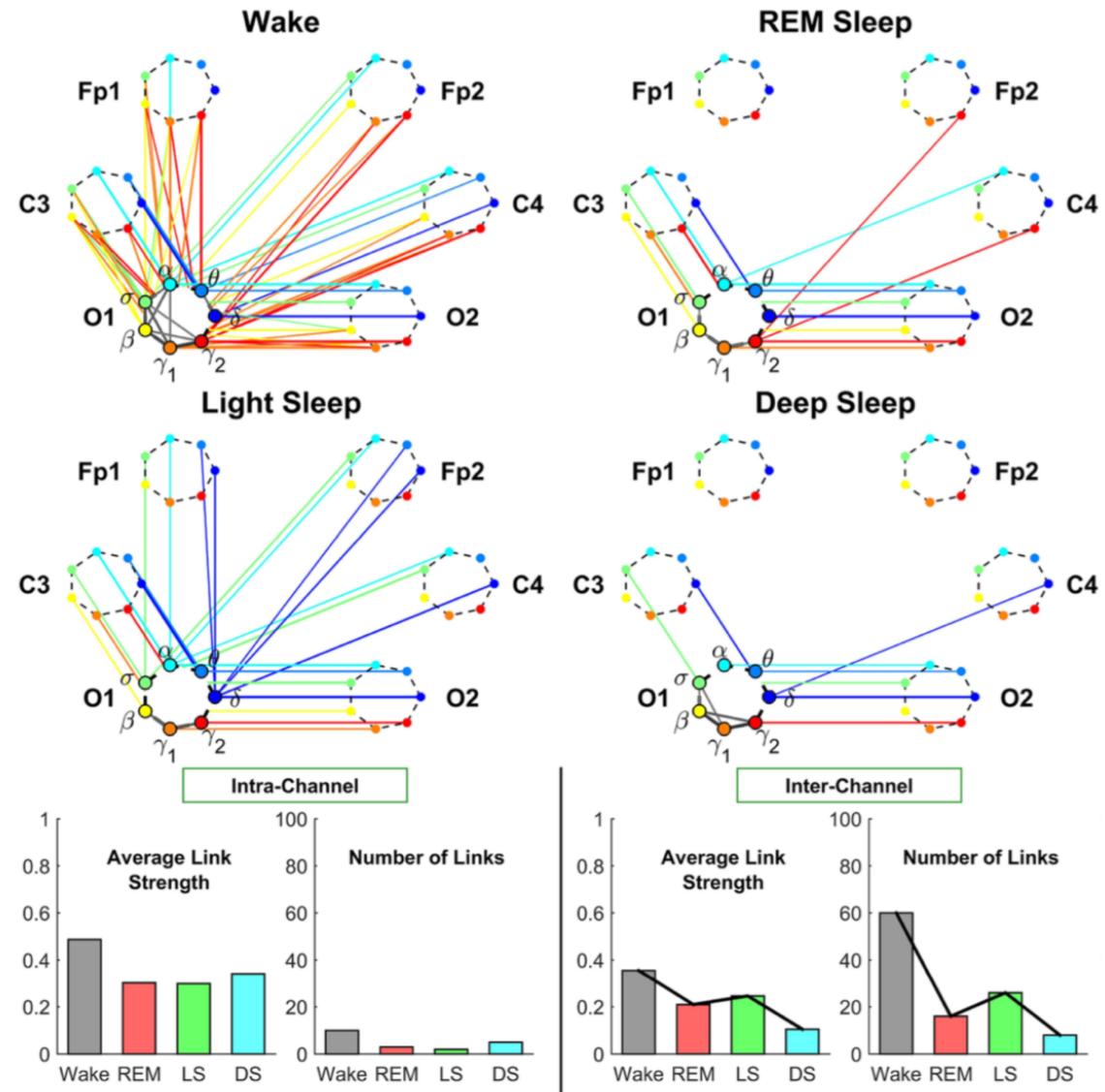
- FP1-FP2 interaction
- Frontal-Central interaction
- Wake – high frequency
- Light Sleep – low frequency
- REM and DS – Disconnected Frontal-Occipital
- Connectivity



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

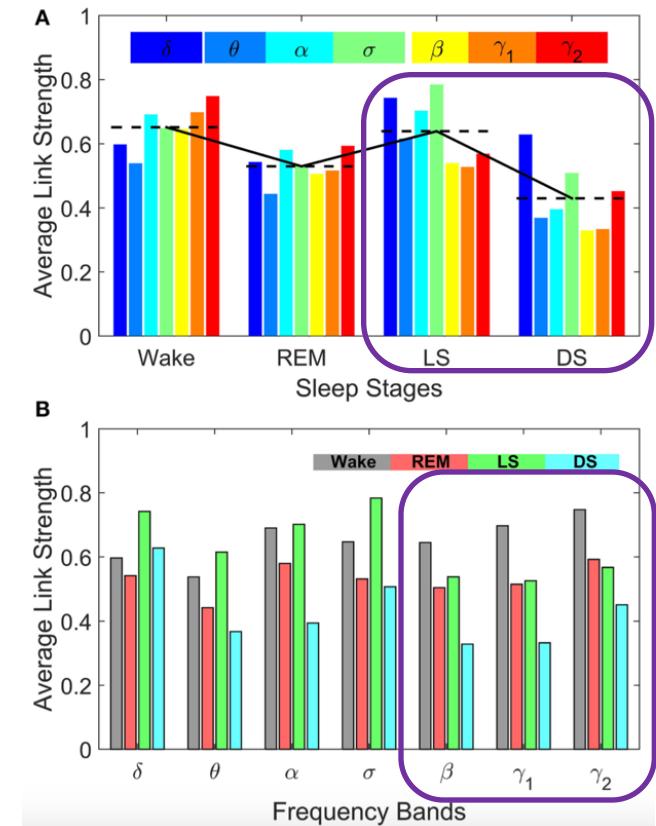
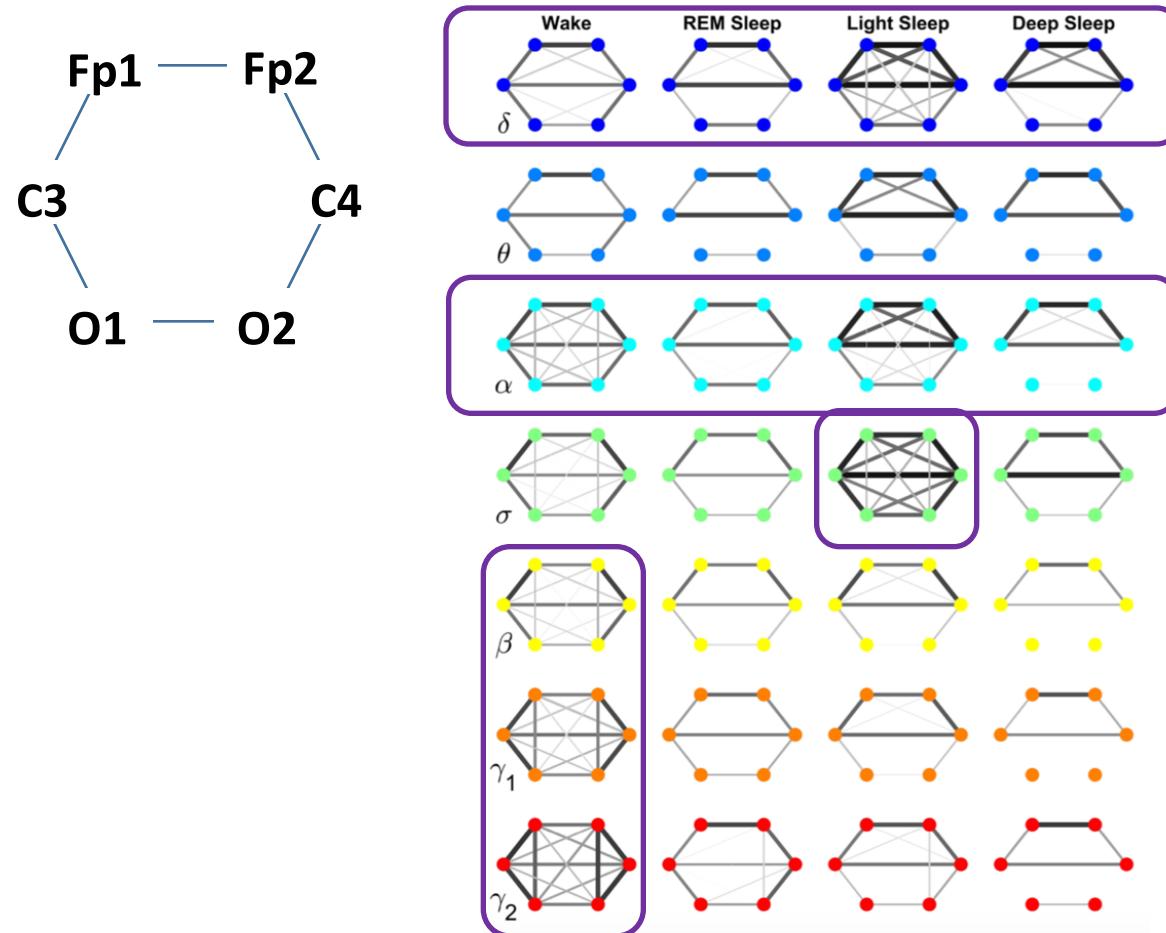
Occipital Channel

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



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

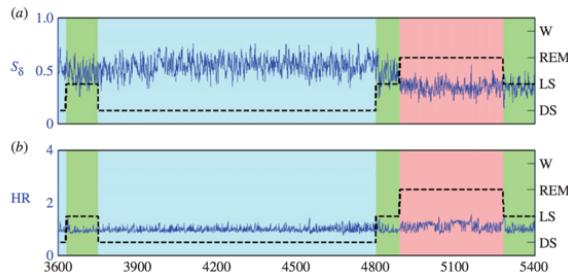
Functional network of brain waves coordination



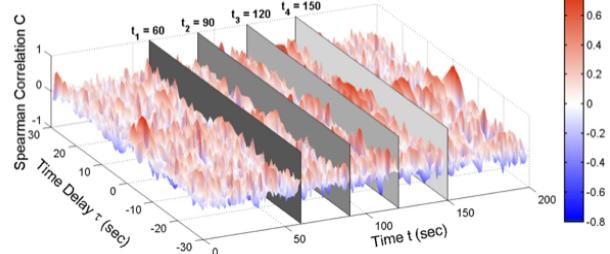
Liu KKL, et al (2015) Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits* 9:62.

Summary

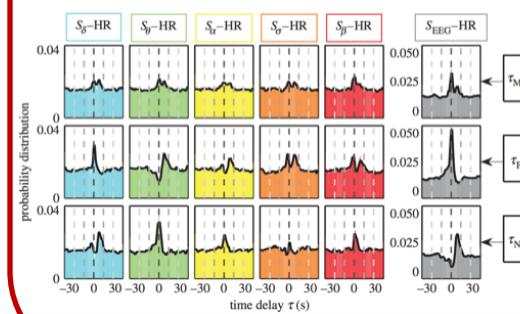
Physiologic signals



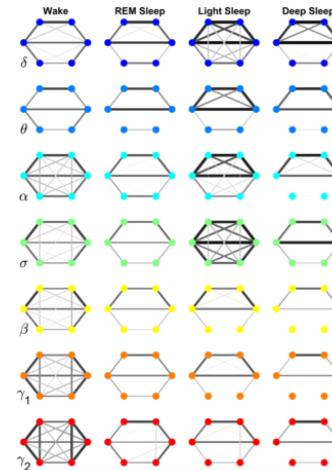
Delay-Correlation Landscape



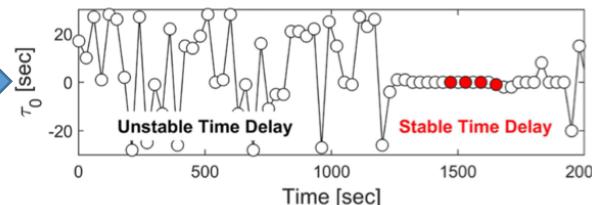
Characteristic Time-Delay



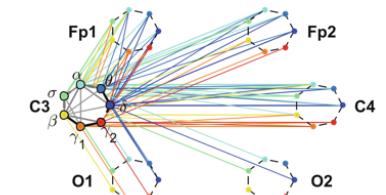
Network Signature



Time-Delay Stability (TDS)



Physiologic Networks



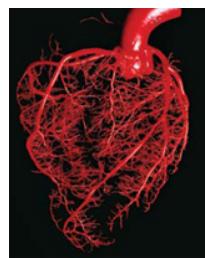
New perspective on Network Physiology



- 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”

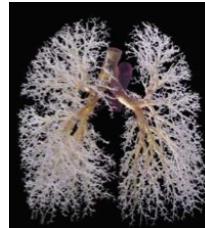
New perspective on Network Physiology

Structural Connectivity
(physical networks)

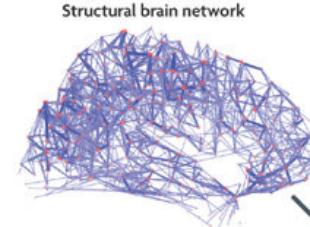


Effective Connectivity
(coupling functions)

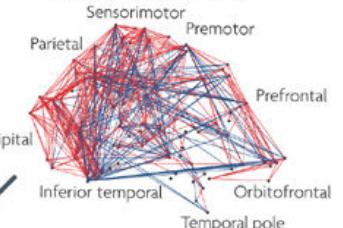
$$\begin{aligned} \dot{x} &= f_1(x) + g_1(x, y) \\ \dot{y} &= f_2(y) + g_2(x, y) \end{aligned}$$



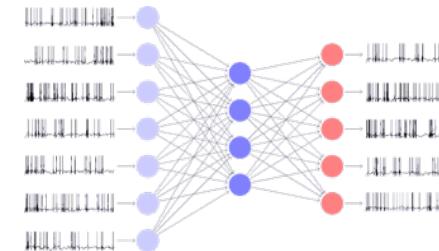
Structural brain network



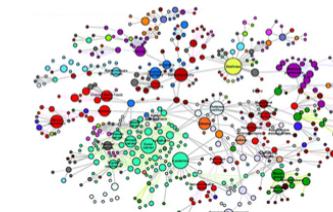
Functional brain network



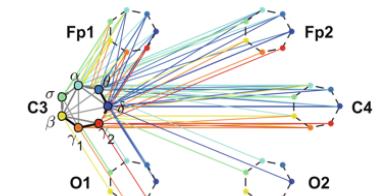
Graph theoretical analysis



Functional Connectivity
(Statistical dependence)

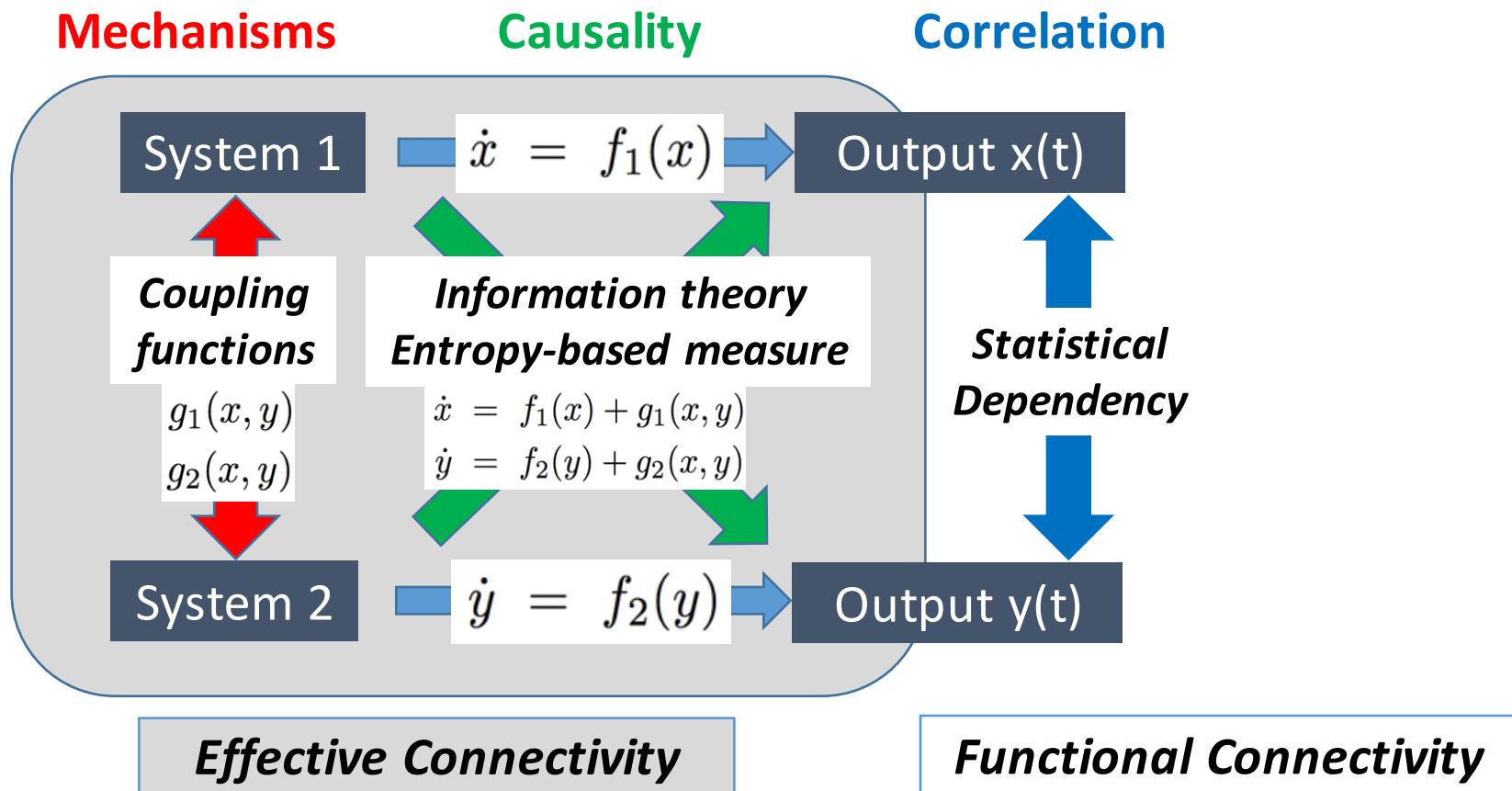


Static indices



Time series

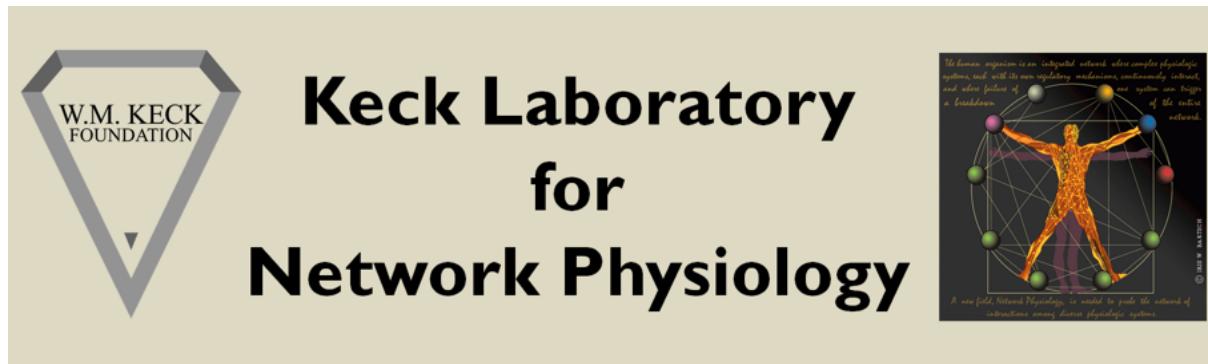
Functional and Effective Connectivity



“Trajectory of the patient” → predictive monitoring

Acknowledgement

- Prof. Plamen Ivanov
- Dr. Ronny Bartsch
- Dr. Aijing Lin and other members from



Questions? Comments?

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