

Physiologic Network Interactions: Novel Hallmark for Physiologic State and Function

Plamen Ch. Ivanov

Keck Laboratory for Network Physiology, Boston University

and

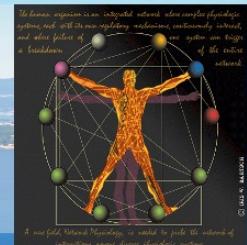
Division of Sleep Medicine

Brigham and Women's Hospital & Harvard Medical School



**Third International Summer Institute
on Network Physiology (ISINP)**

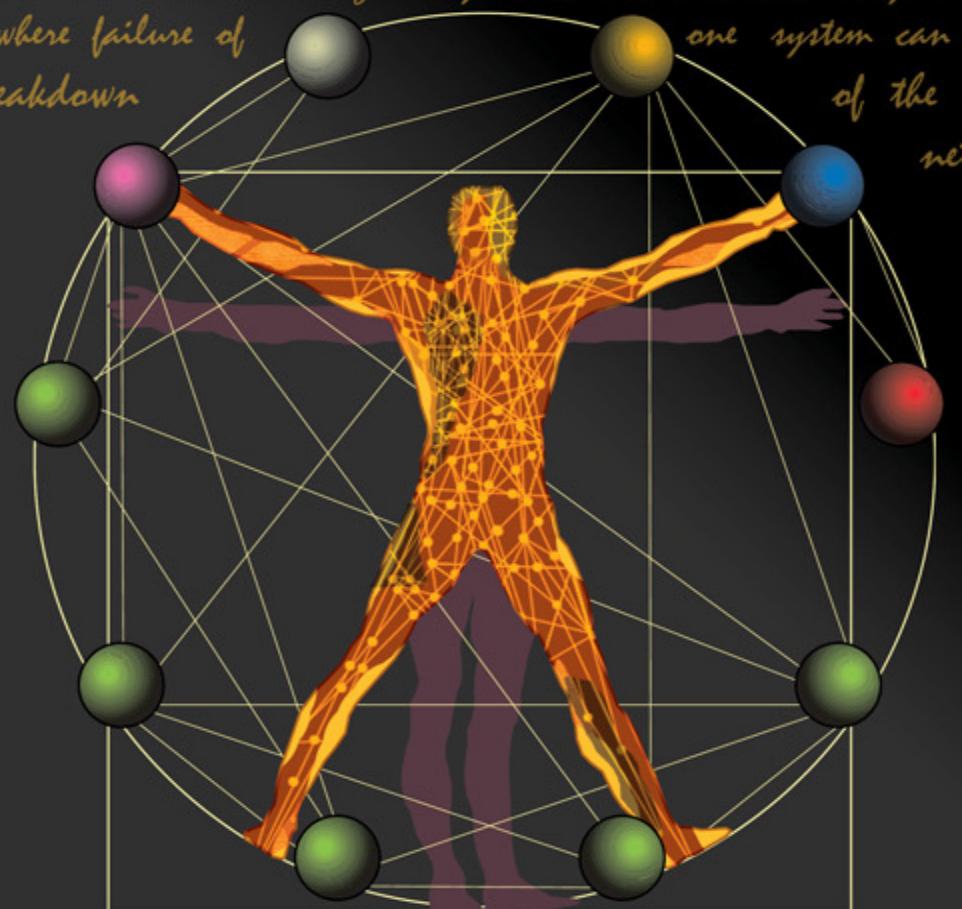
Lake Como School of Advanced Studies, 24 - 29 July 2022



Our Research Program

New Research Direction: Shifting the focus from single organ systems to the network of organ interactions

The human organism is an integrated network where complex physiologic systems, each with its own regulatory mechanisms, continuously interact, and where failure of one system can trigger a breakdown of the entire network.



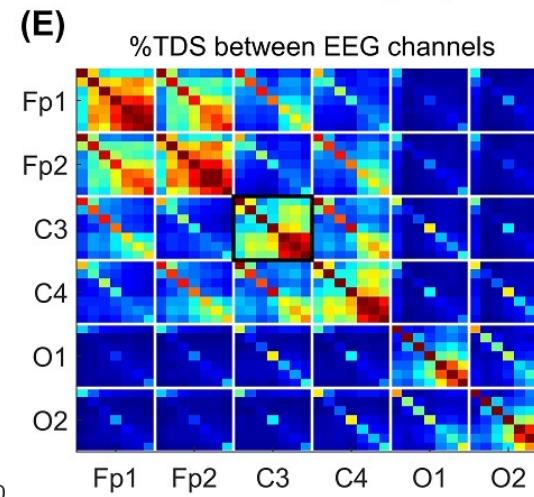
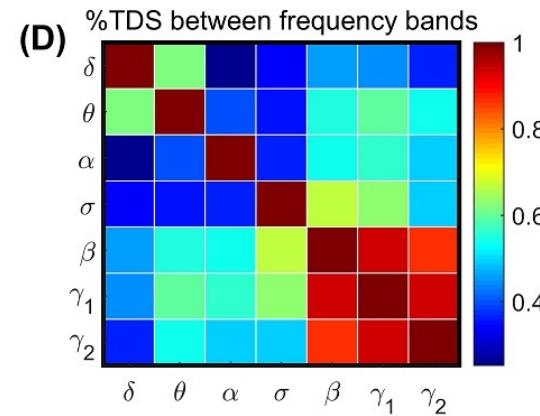
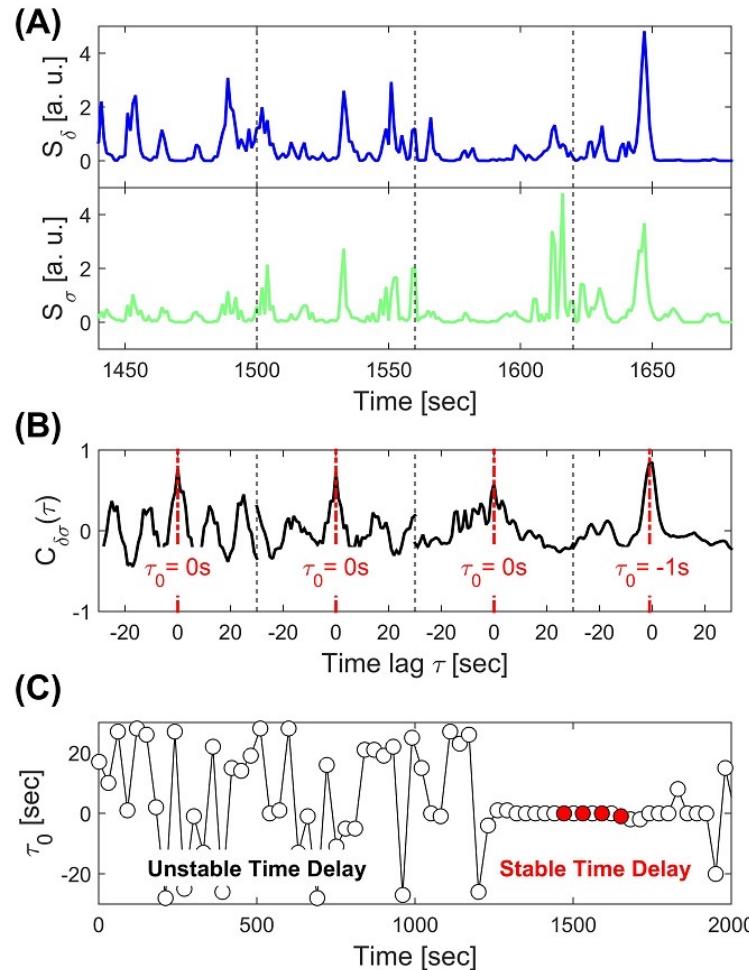
A new field, Network Physiology, is needed to probe the network of interactions among diverse physiologic systems.

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*A new field
Network Physiology
needed to probe
interactions
among diverse
physiologic systems.*

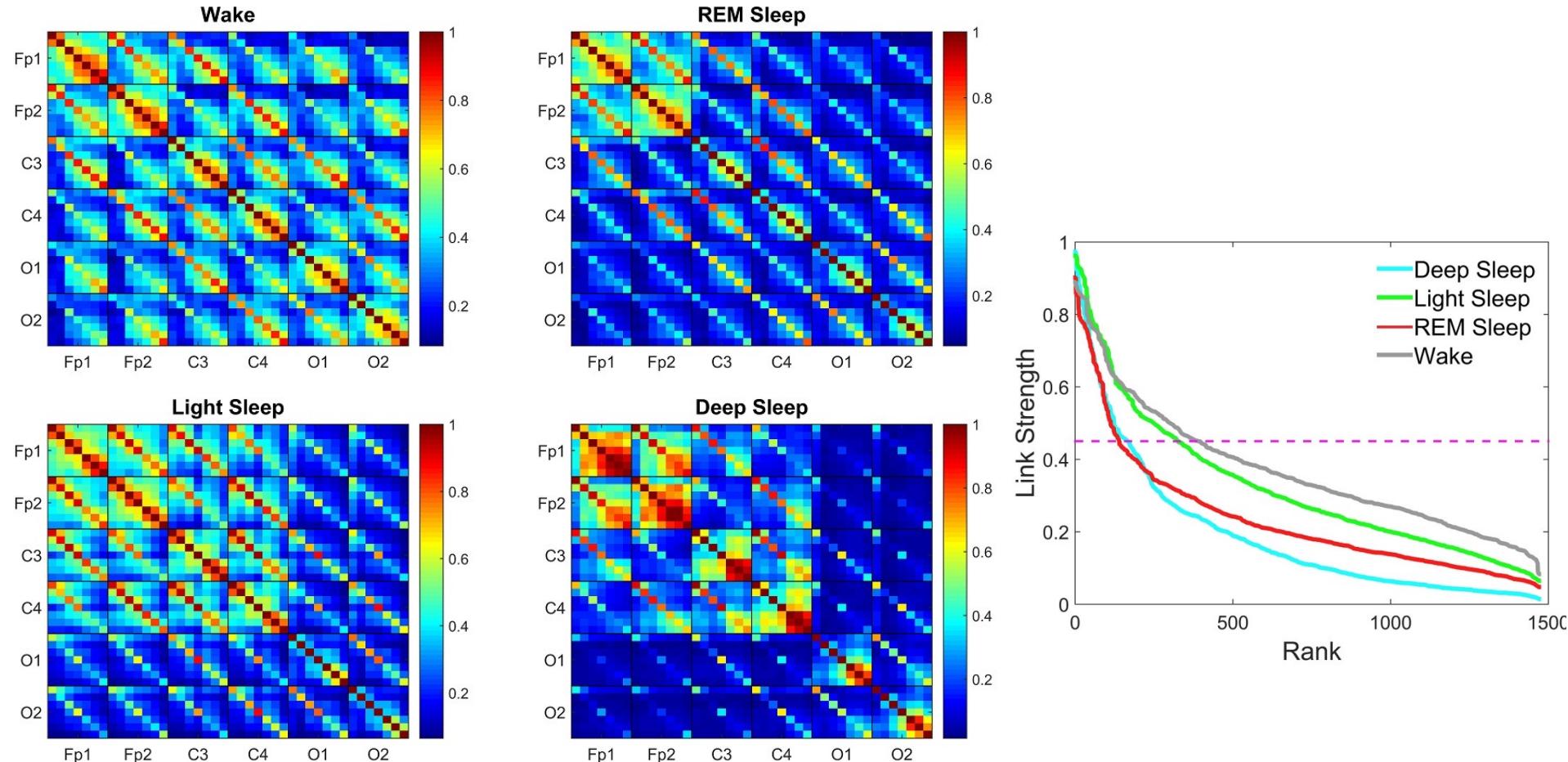
Network Physiology: Implications for brain dynamics and neural plasticity

Key question: How brain rhythms dynamically communicate to facilitate physiologic states and functions?



**Level 3:
Networked
Interactions**

Network Physiology: Networks of brain activity across sleep stages

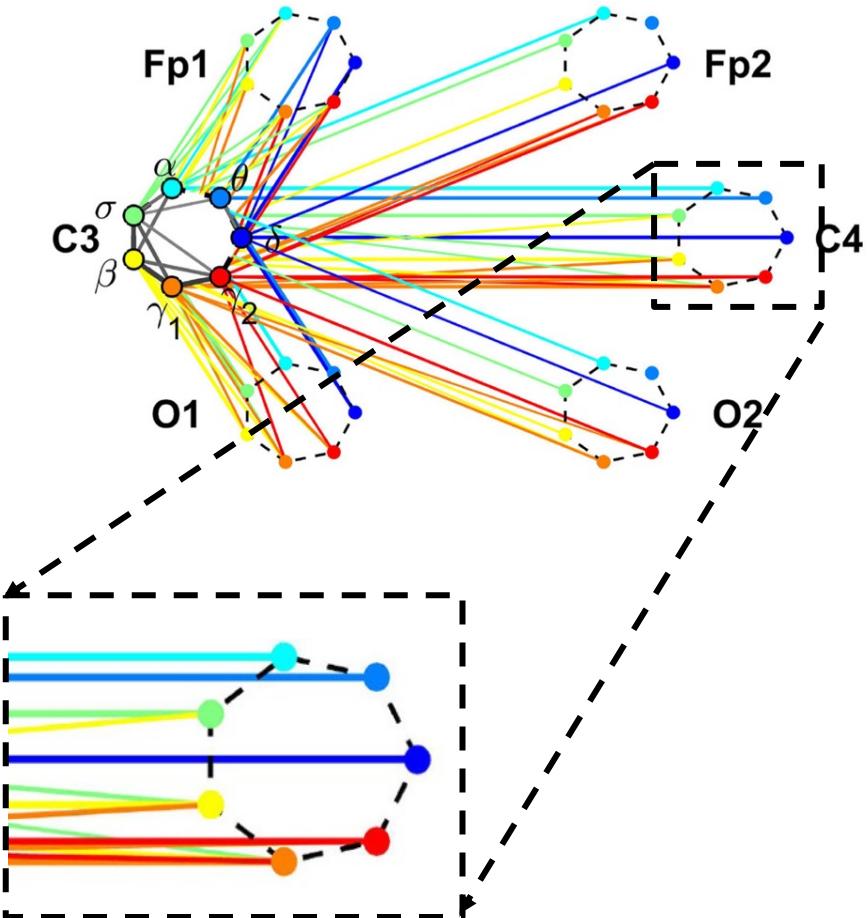
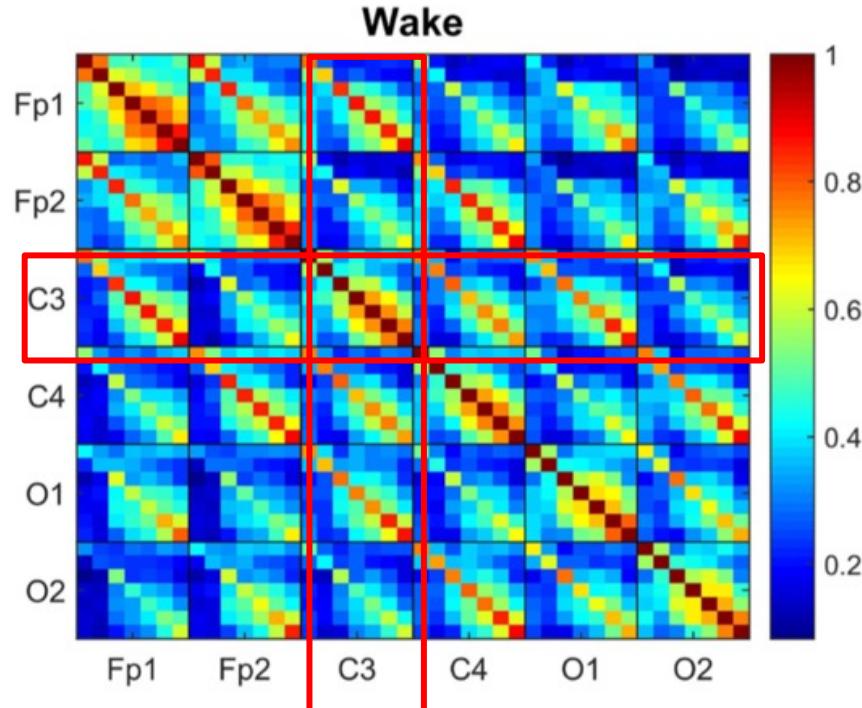


Liu KKL, Bartsch RP, Lin A, Mantegna RN and Ivanov PCh (2015)

Plasticity of brain wave network interactions and evolution across physiologic states. *Front. Neural Circuits* 9:62.

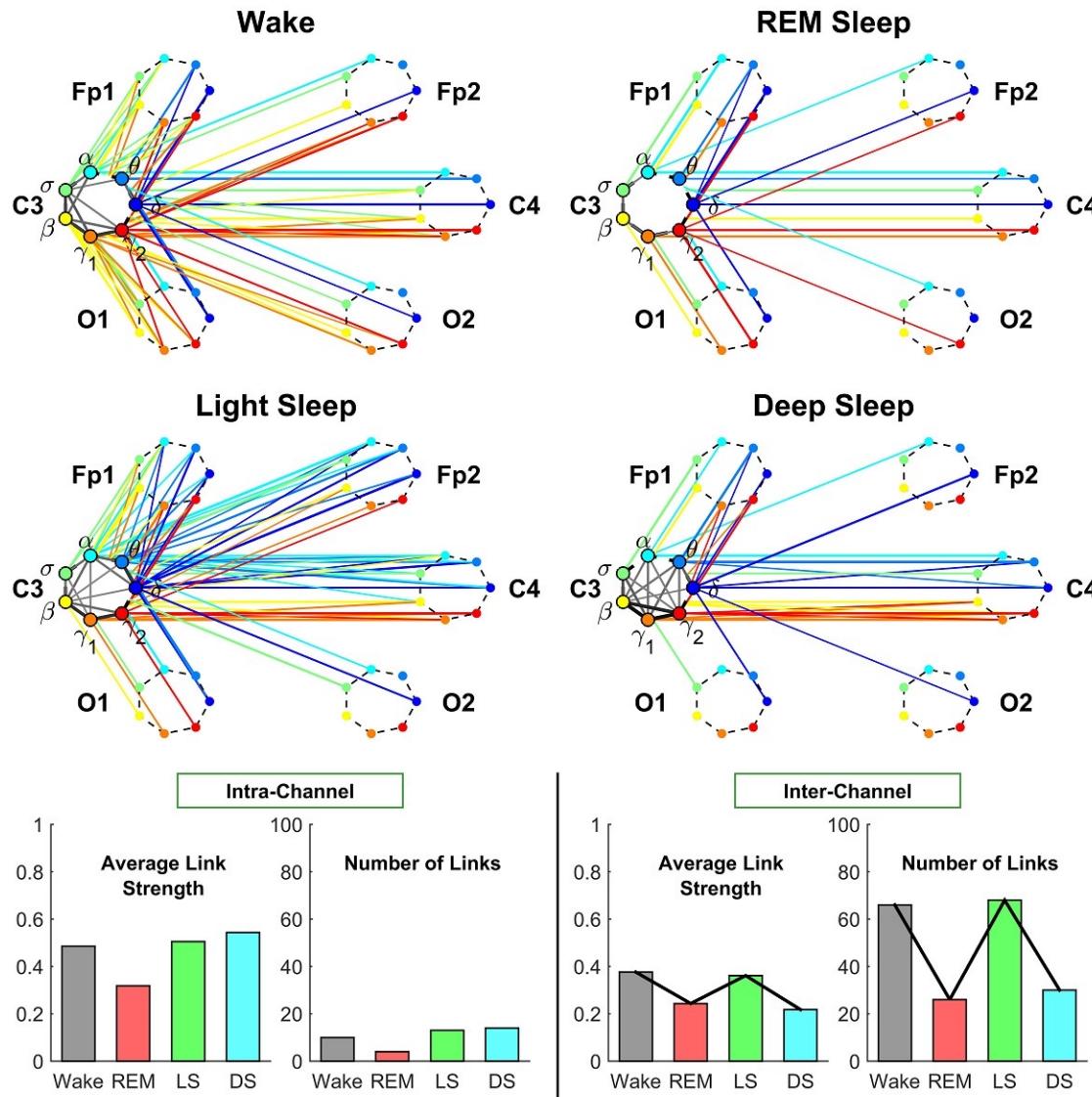
Network Physiology: Implications for brain dynamics and neural plasticity

Visualization of channel specific sub-network

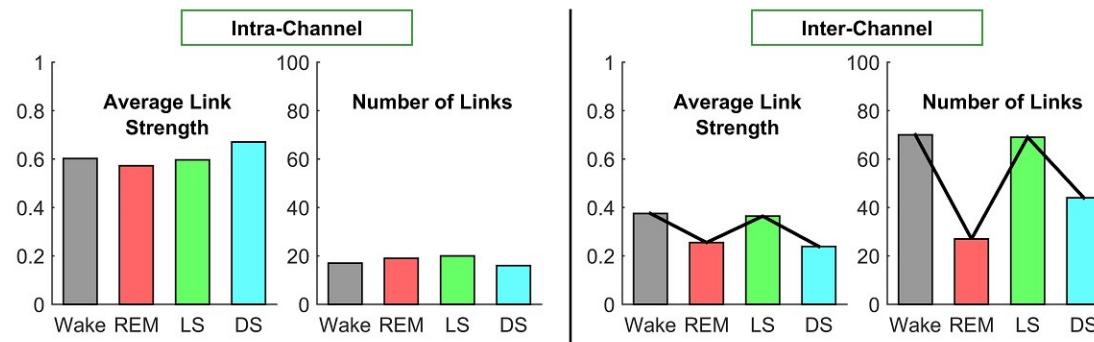
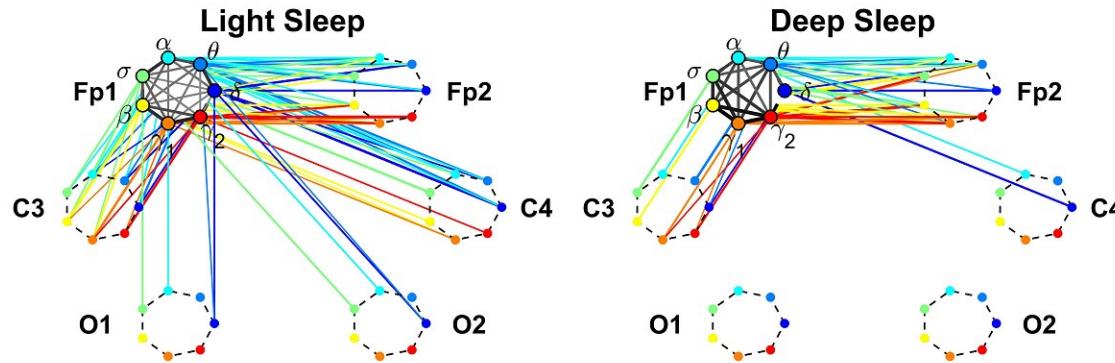
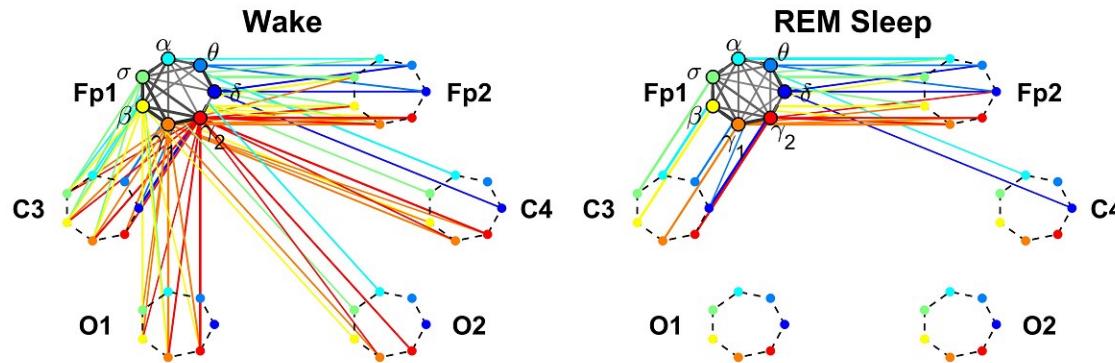


Liu KKL, et al (2015) Plasticity of brain wave network interactions
and evolution across physiologic states. *Front. Neural Circuits* 9:62.

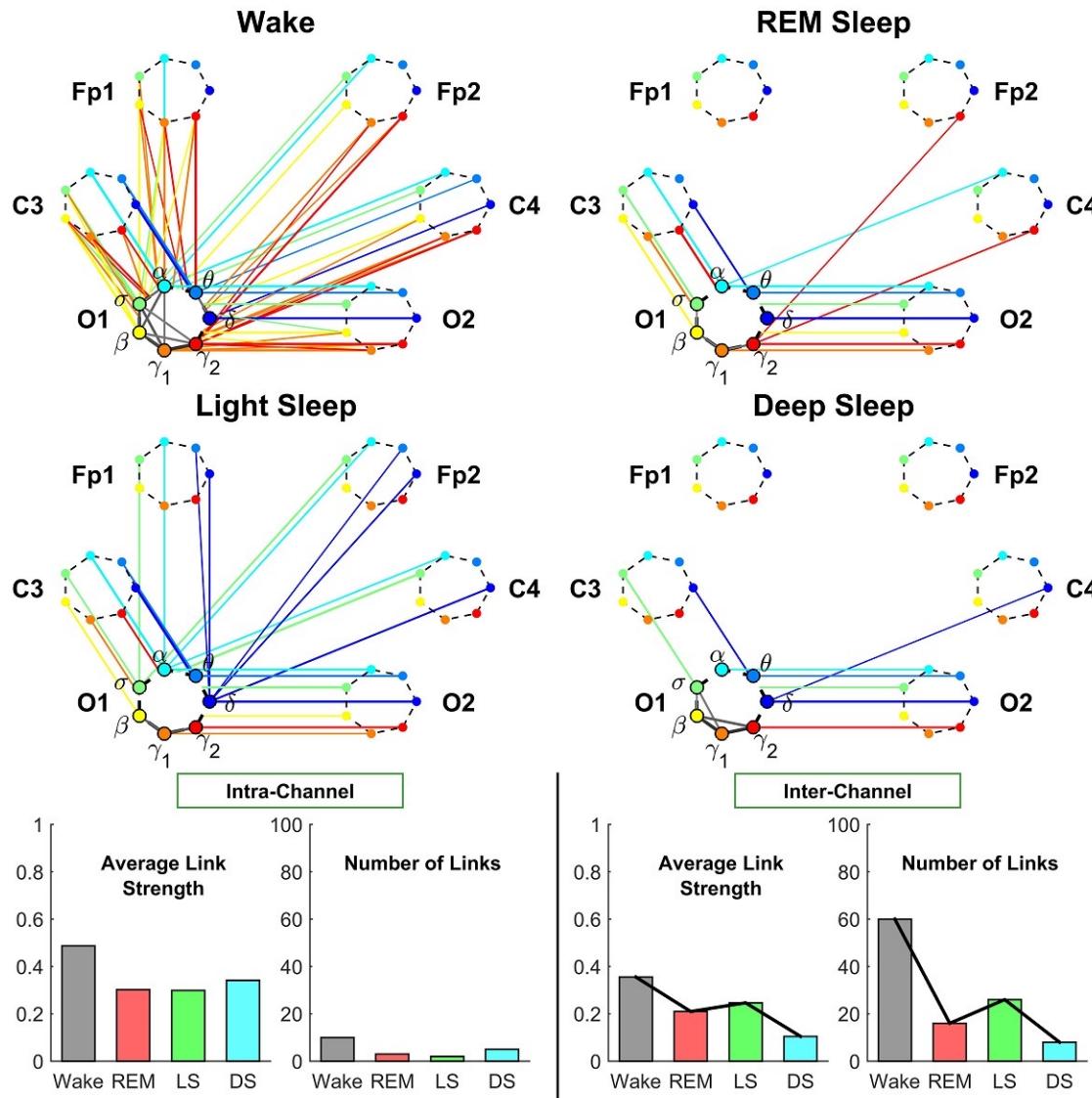
Neural Plasticity of Individual Brain Areas: Central Channel C3



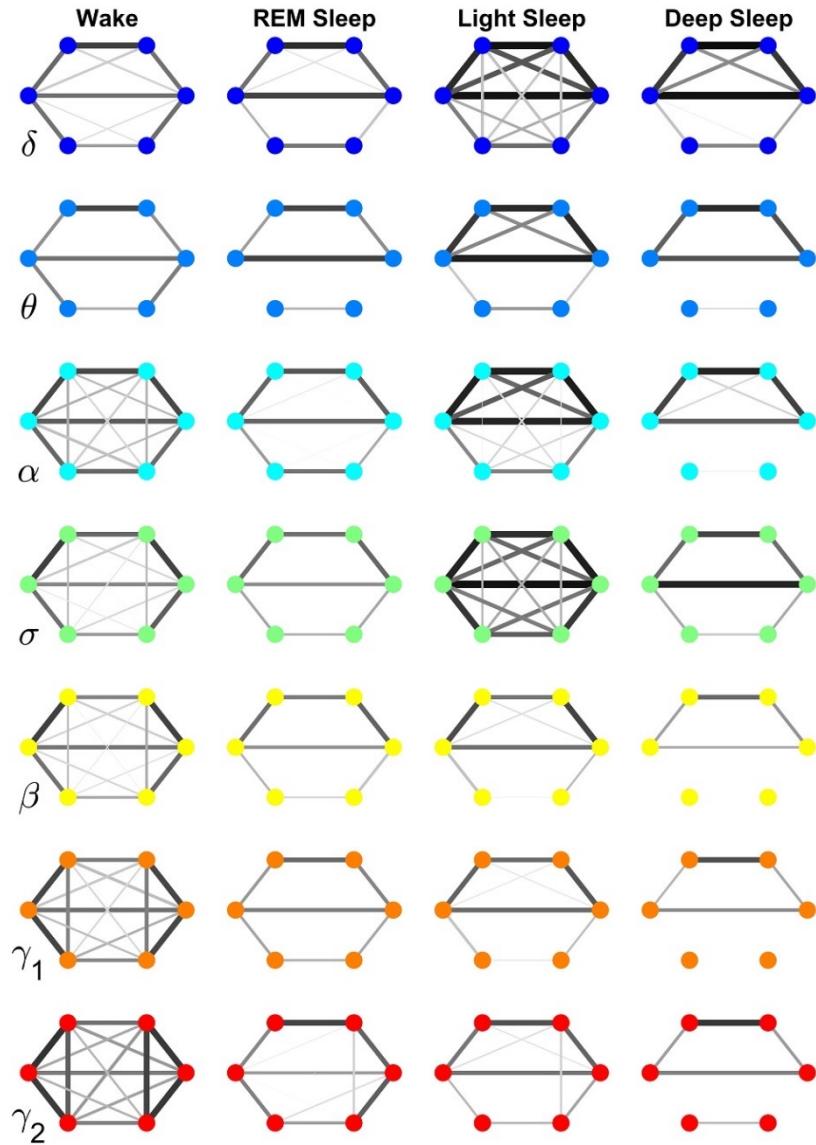
Neural Plasticity of Individual Brain Areas: Frontal Channel Fp1



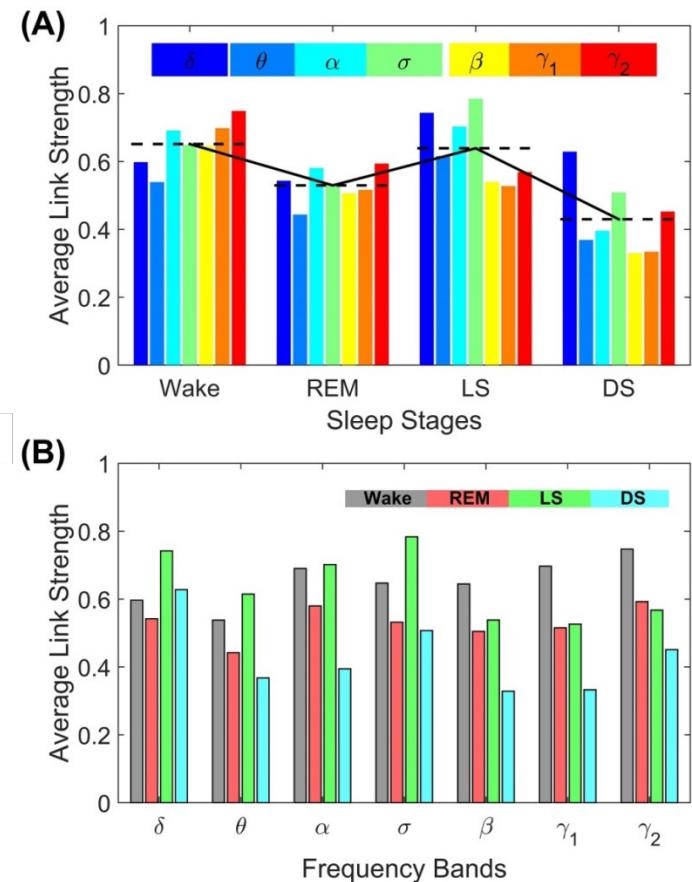
Neural Plasticity of Individual Brain Areas: Occipital Channel O1



Brain-Wave Network Interactions: Frequency Specific Networks



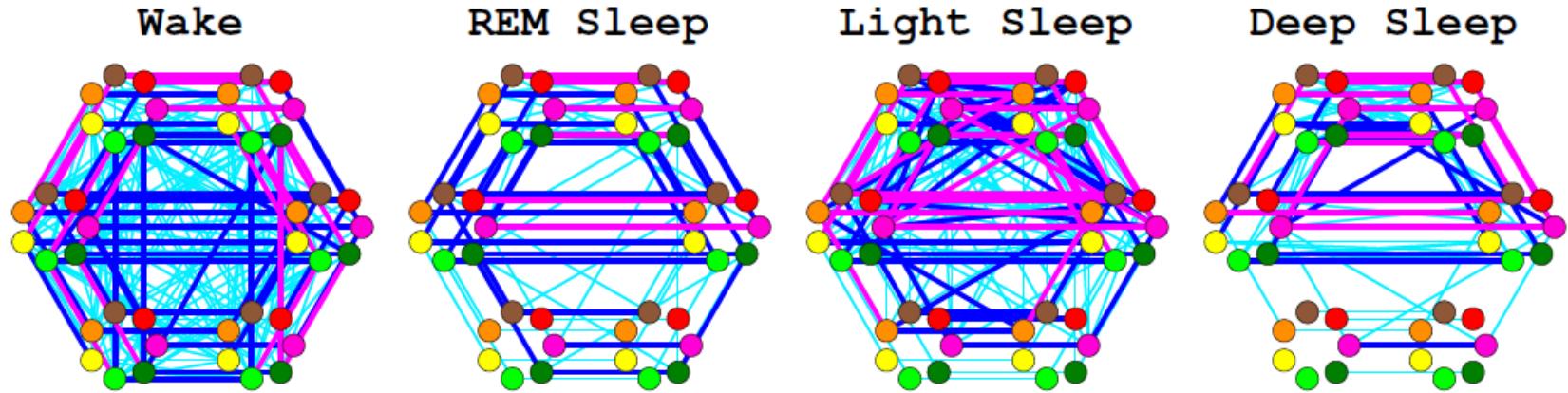
Functional network of brain waves coordination



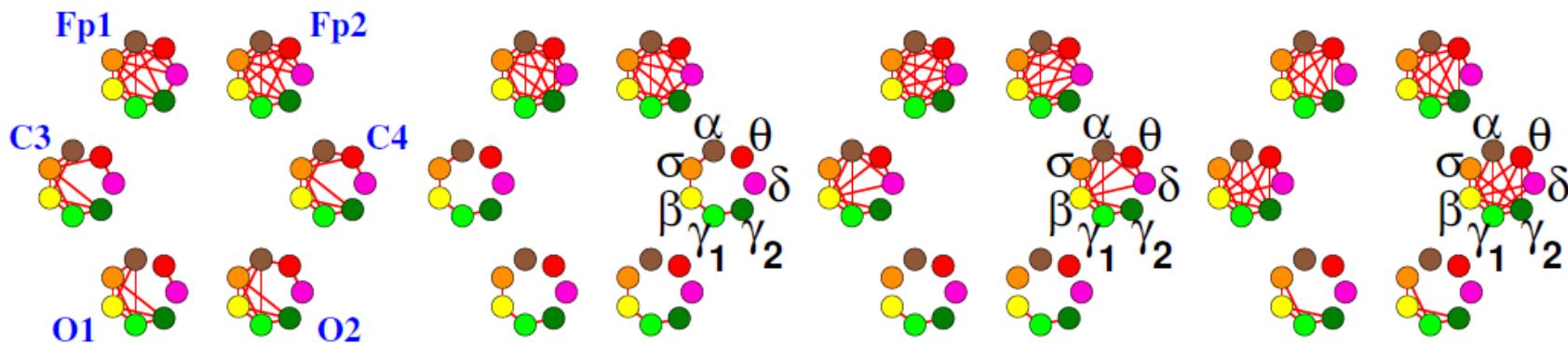
Plasticity of individual brain rhythms:
complex transitions in frequency-specific
networks across physiologic states

Network Physiology: Implications for brain dynamics and neural plasticity

Inter-Channel Networks



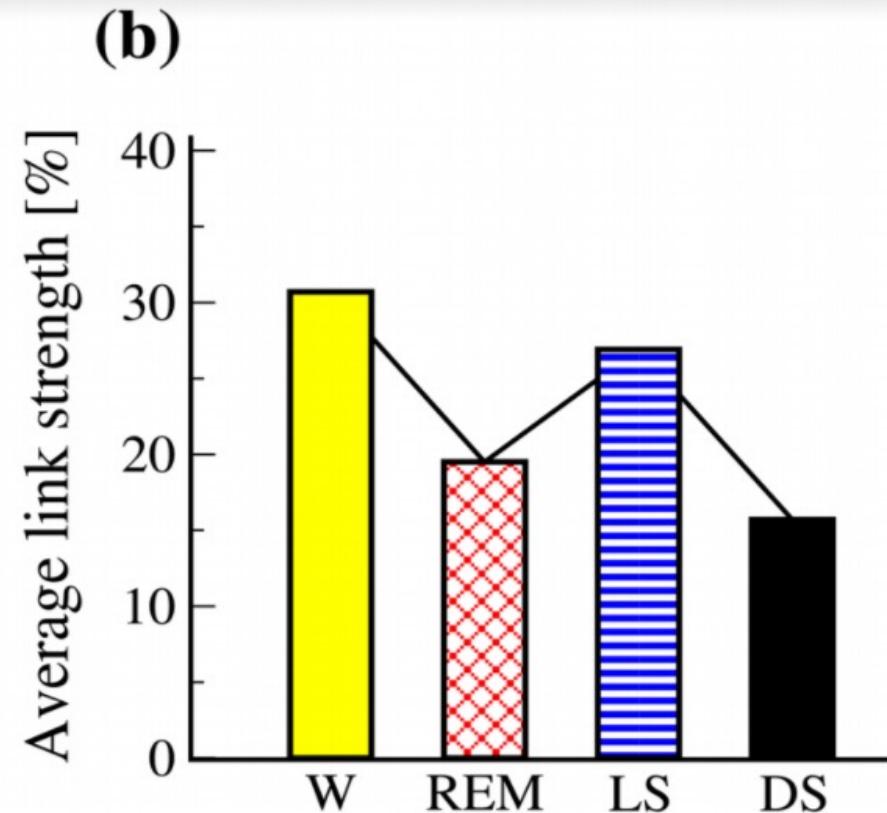
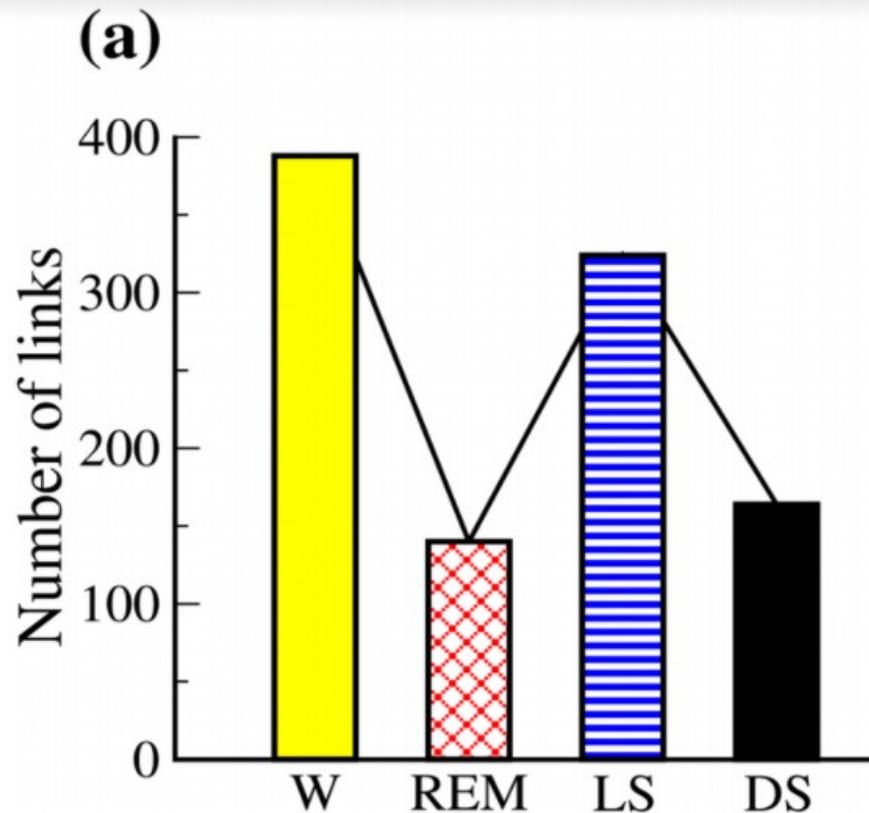
Intra-Channel Networks



Phase transition in link strength and network topology

Network Physiology: Implications for brain dynamics and neural plasticity

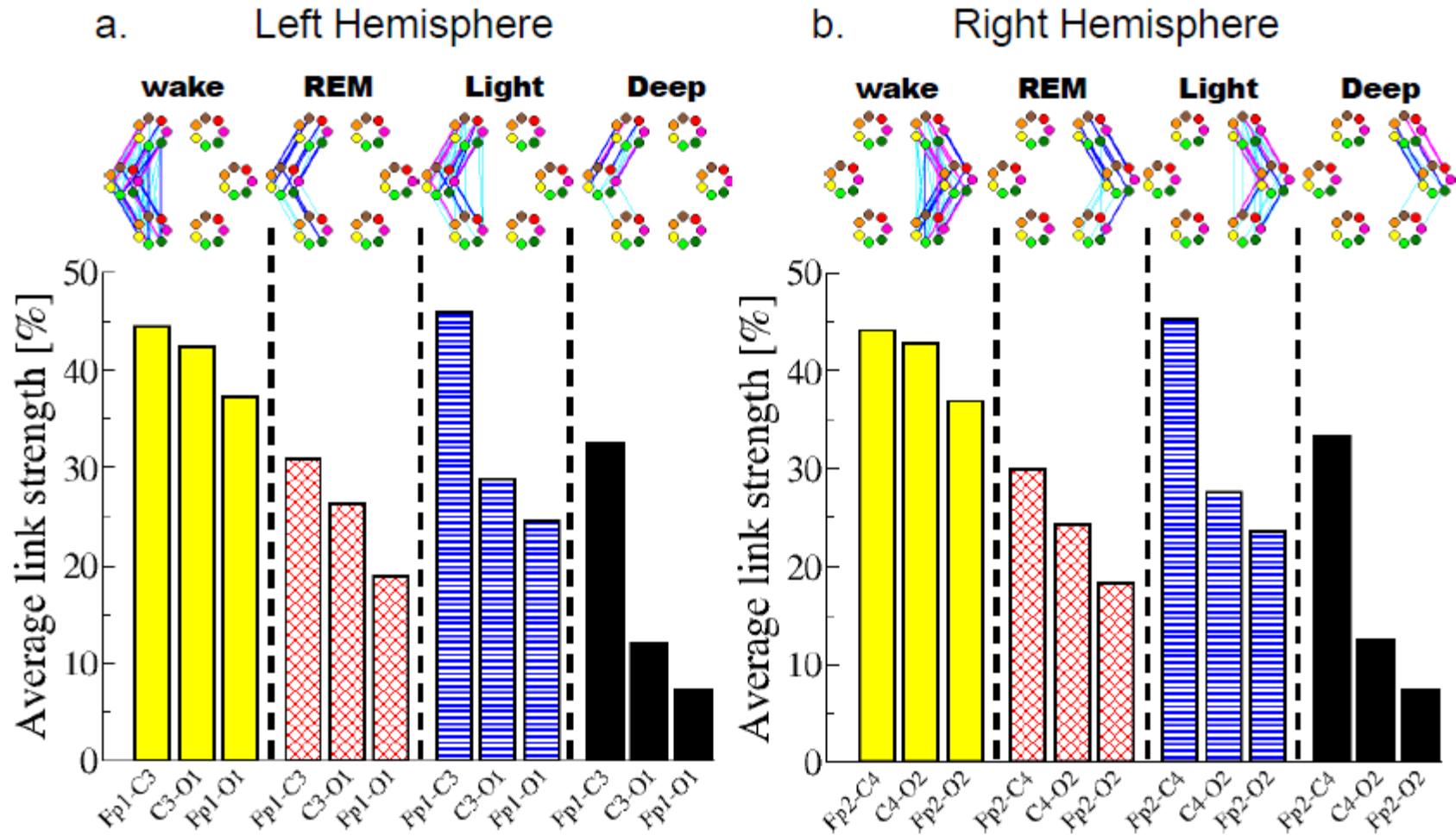
Brain-Brain Interactions



Phase transition in link strength and network topology

Network Physiology: Implications for brain dynamics and neural plasticity

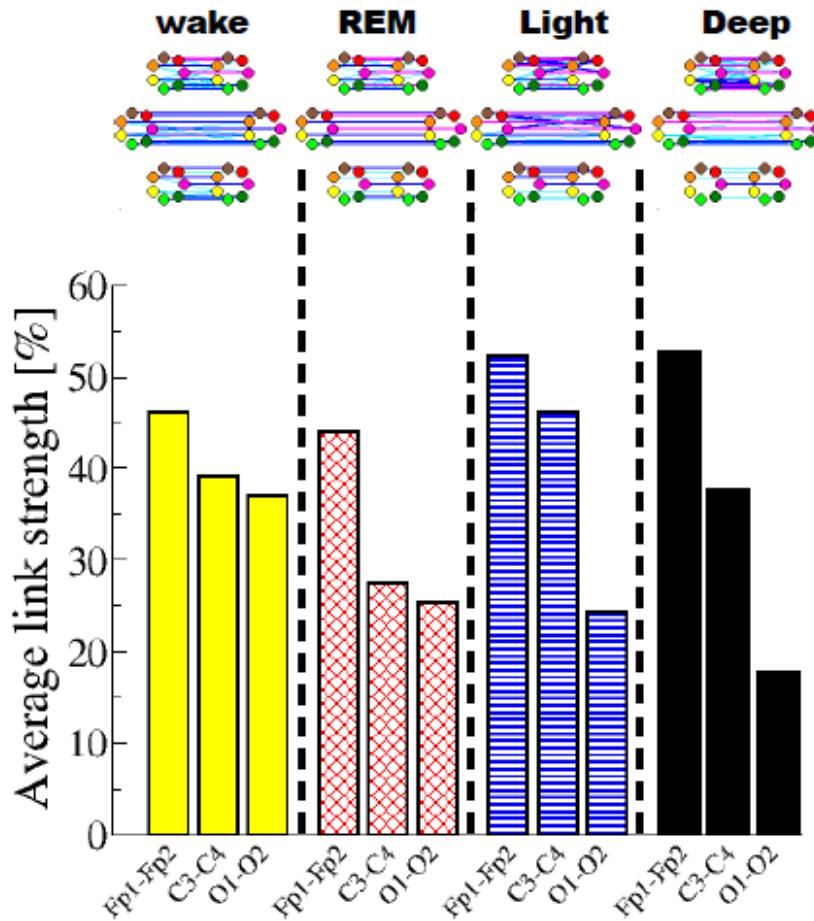
Links within Brain Hemispheres



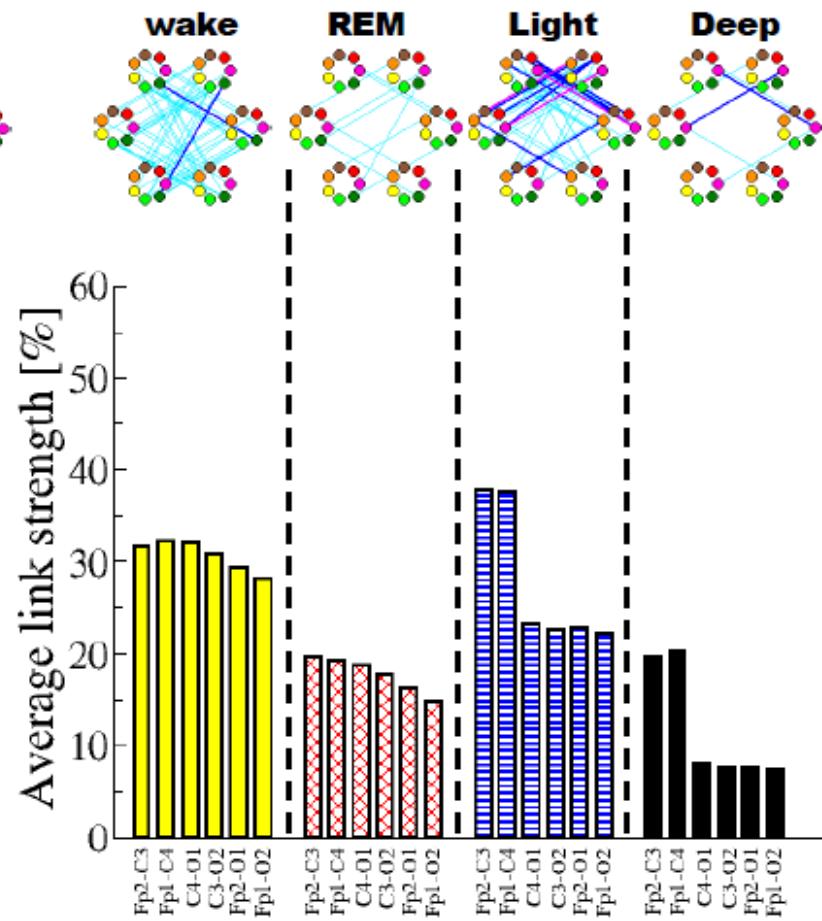
Network Physiology: Implications for brain dynamics and neural plasticity

Links across Brain Hemispheres

a. Horizontal Links

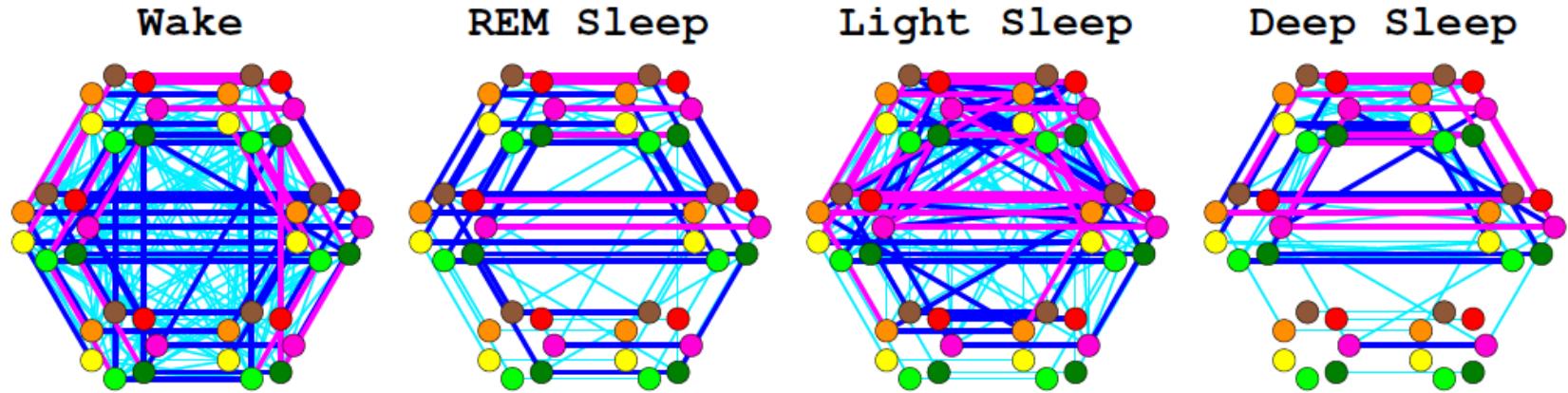


b. Diagonal Links

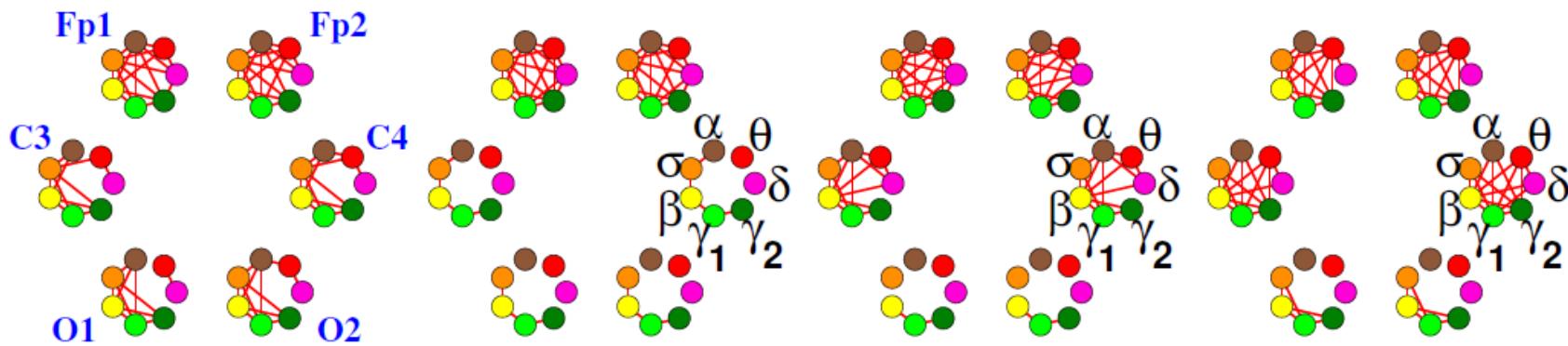


Network Physiology: Implications for brain dynamics and neural plasticity

Inter-Channel Networks

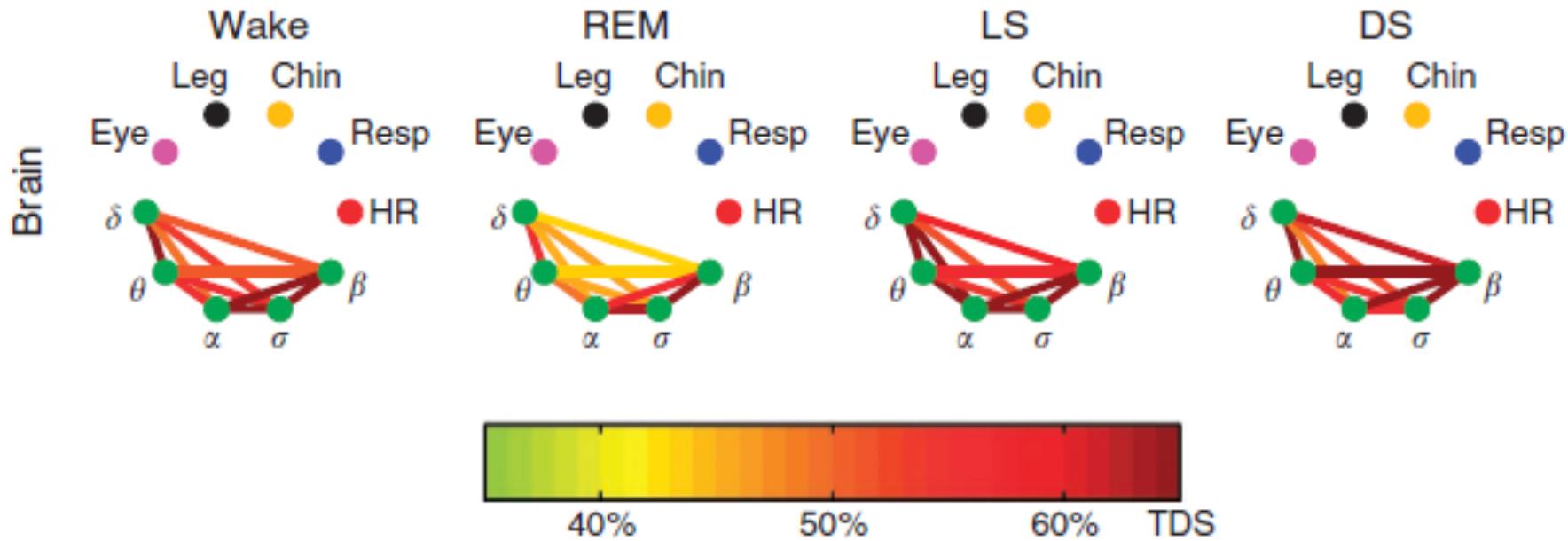


Intra-Channel Networks



Phase transition in link strength and network topology

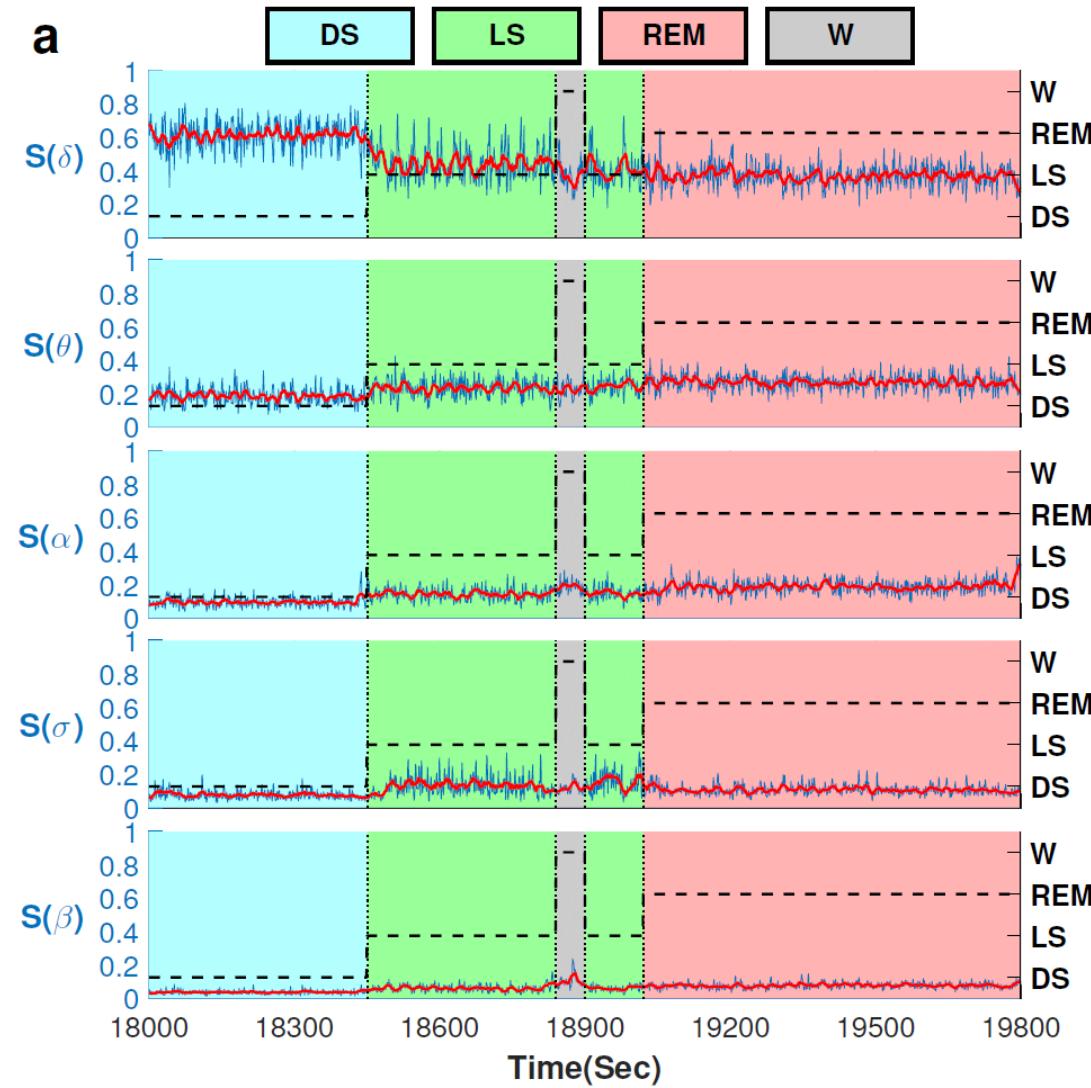
Network connectivity and link strength of the brain–brain sub-network for sleep stages



Topology of brain-brain sub-network → no change
Strength of network links → significant change

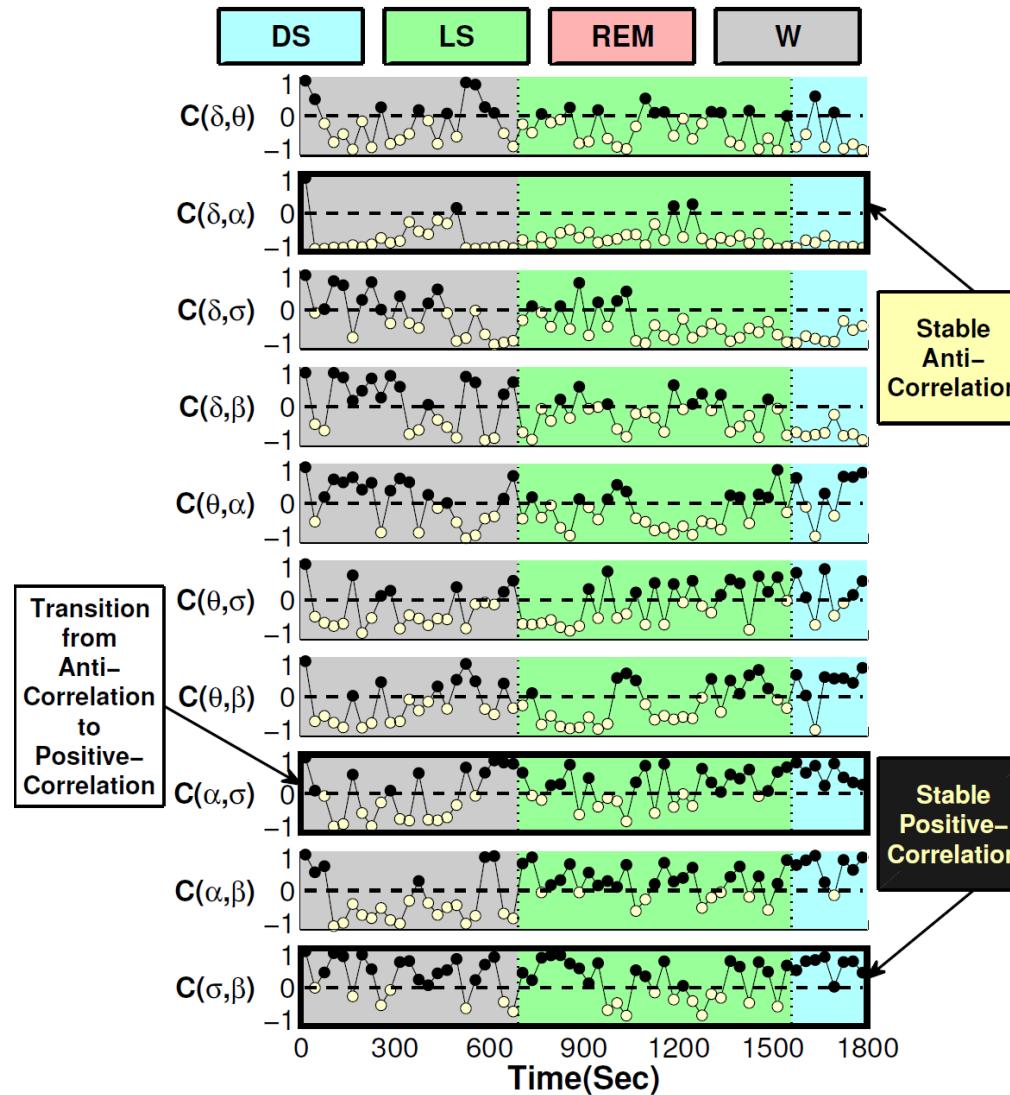
Network Physiology: Implications for brain dynamics and neural plasticity

Complex temporal dynamics and distinct profiles of brain wave interactions.



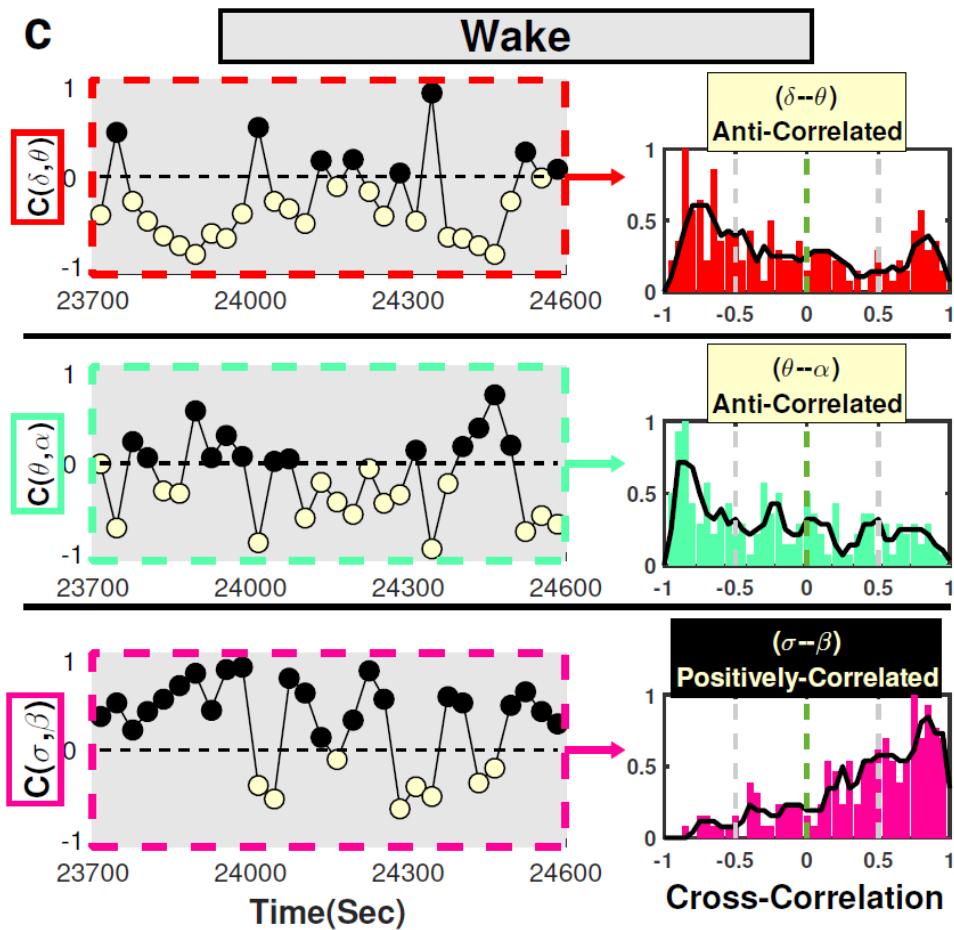
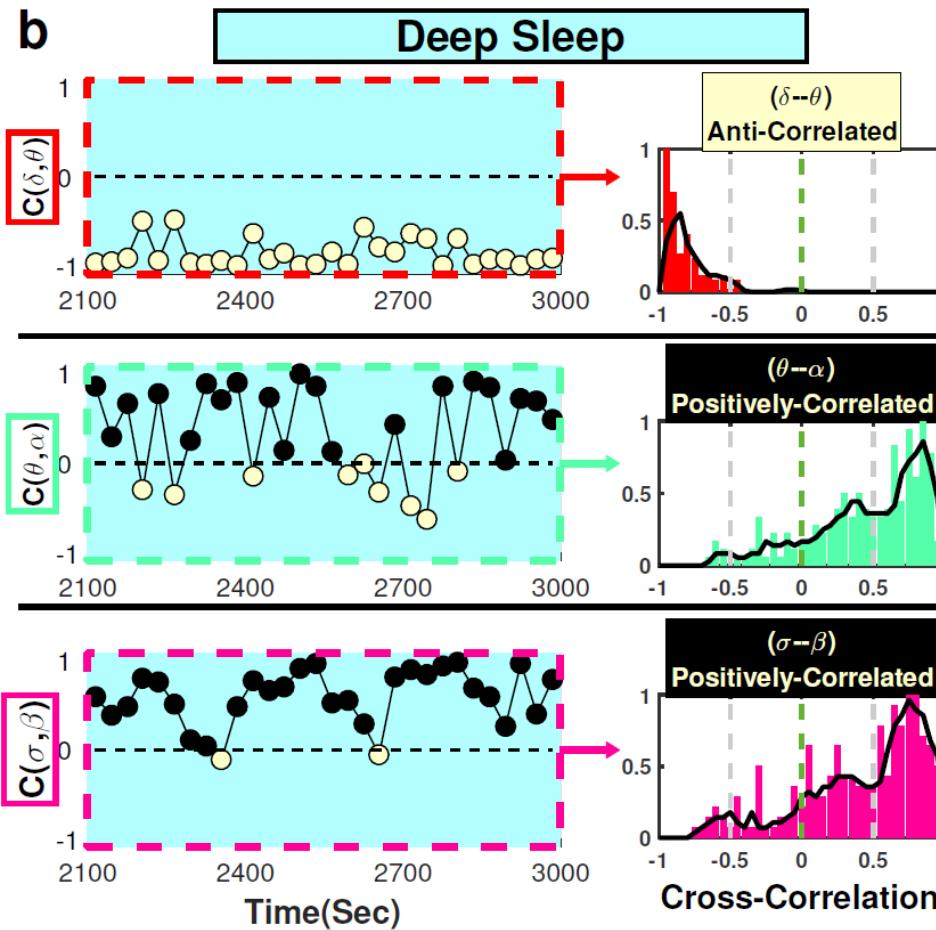
Network Physiology: Implications for brain dynamics and neural plasticity

Temporal dynamics of brain wave interactions and transitions across physiologic states.



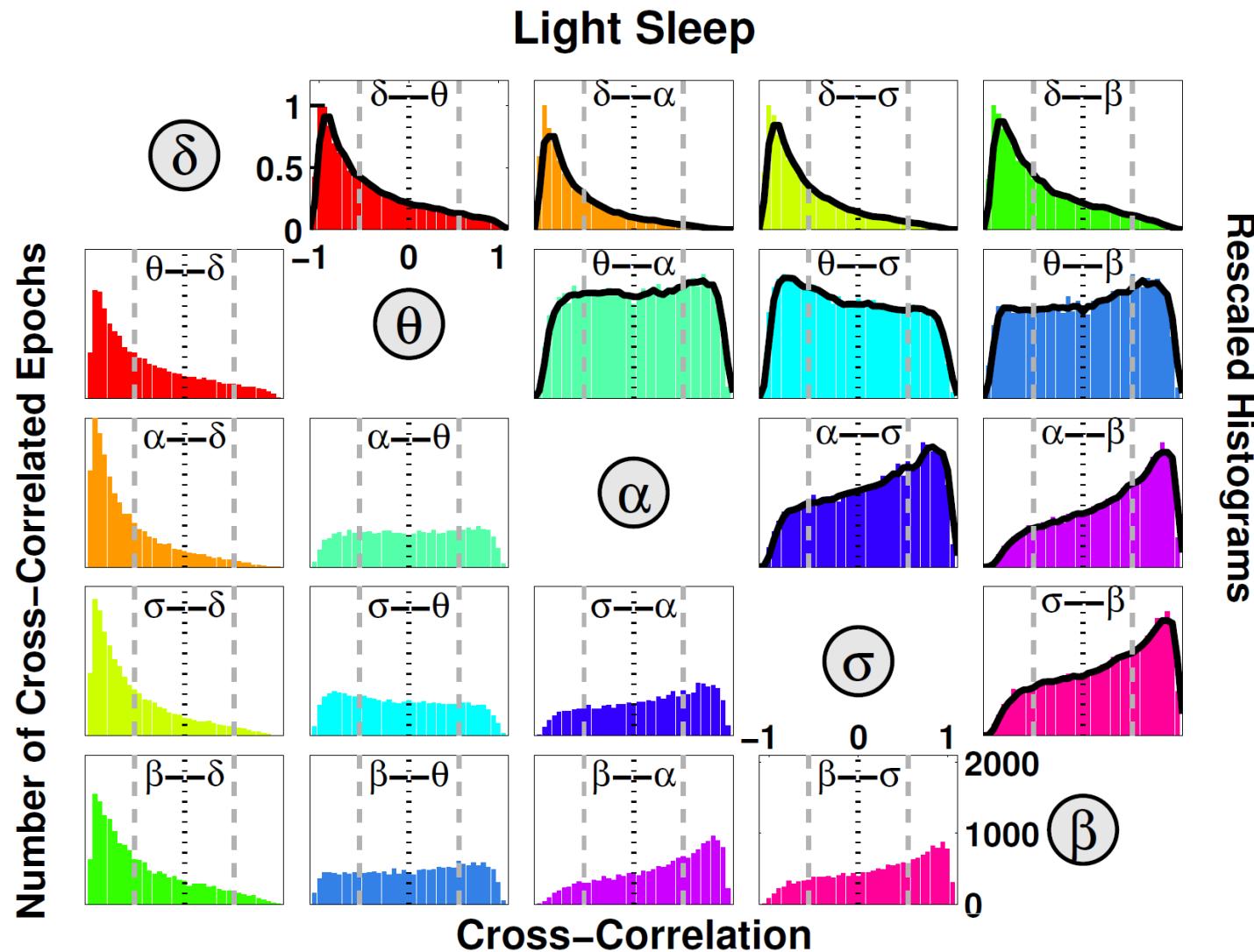
Network Physiology: Implications for brain dynamics and neural plasticity

Complex temporal dynamics and distinct profiles of brain wave interactions.



Network Physiology: Implications for brain dynamics and neural plasticity

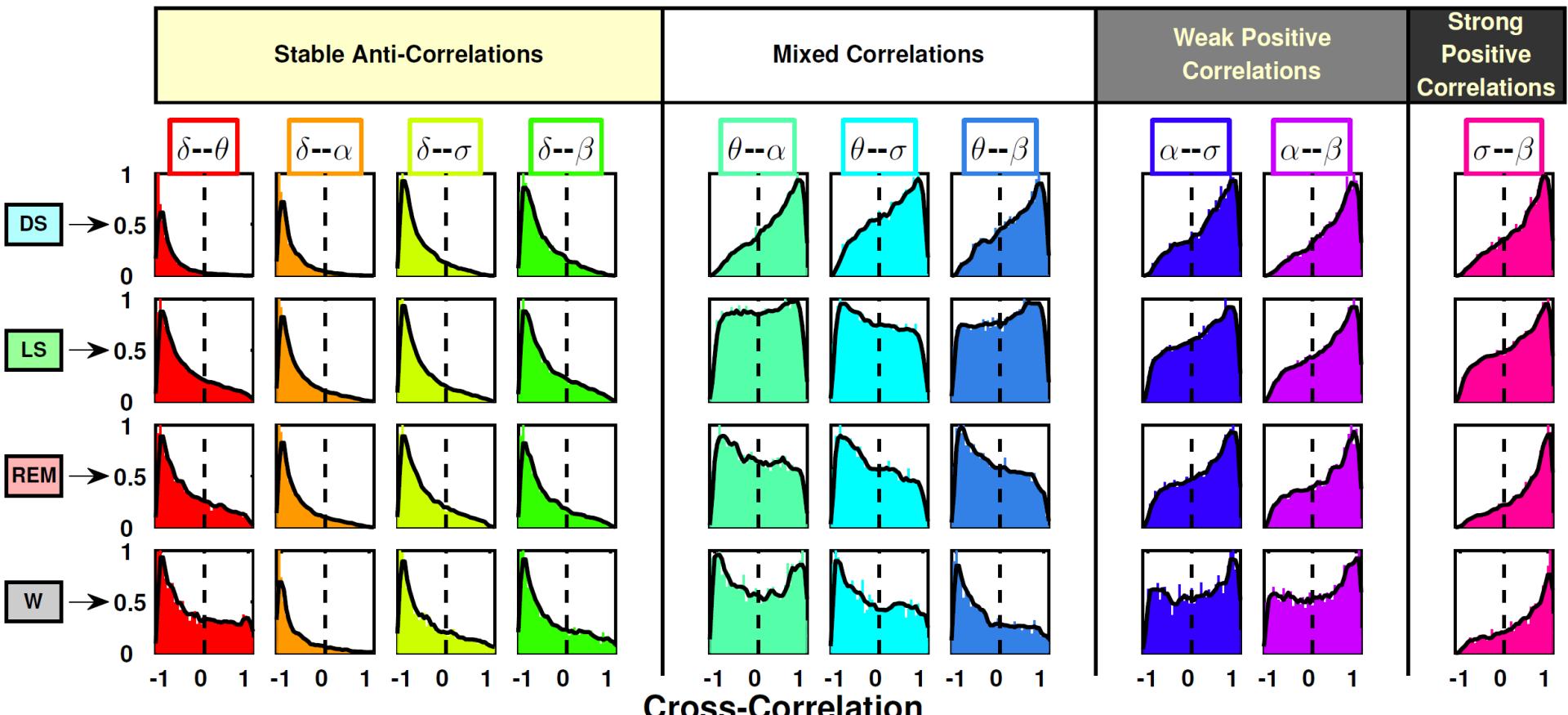
Alphabet of brain-wave interactions as a signature of physiologic state.



Network Physiology: Implications for brain dynamics and neural plasticity

Transitions in brain-wave interactions across physiologic states.

Distinct classes of brain wave interaction patterns



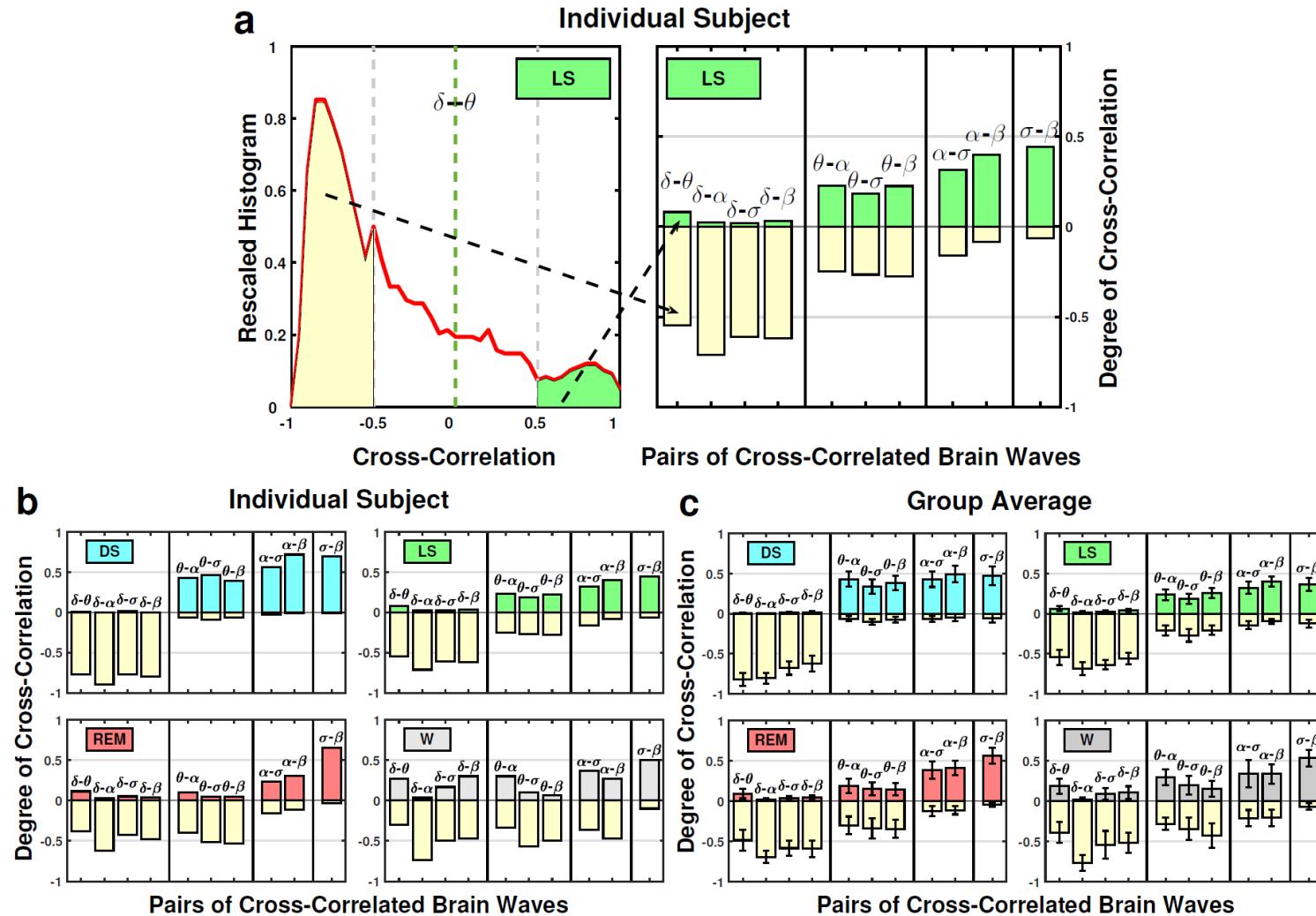
Lin A, Liu KKL, Bartsch RP, and Ivanov PCh.

Dynamic network interactions among distinct brain rhythms as a hallmark of physiologic state and function.

Communications Biology, 2020; 3: 197.

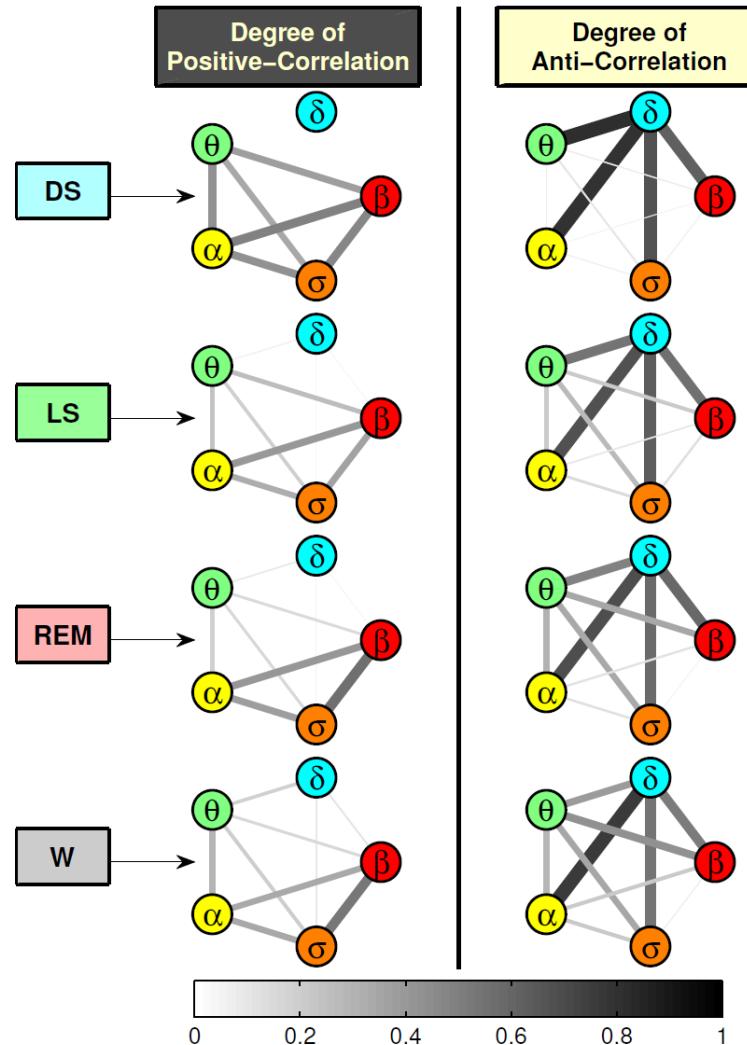
Network Physiology: Implications for brain dynamics and neural plasticity

Robust sleep-stage stratification in the degree of cross-correlation for different pairs of brain rhythms.



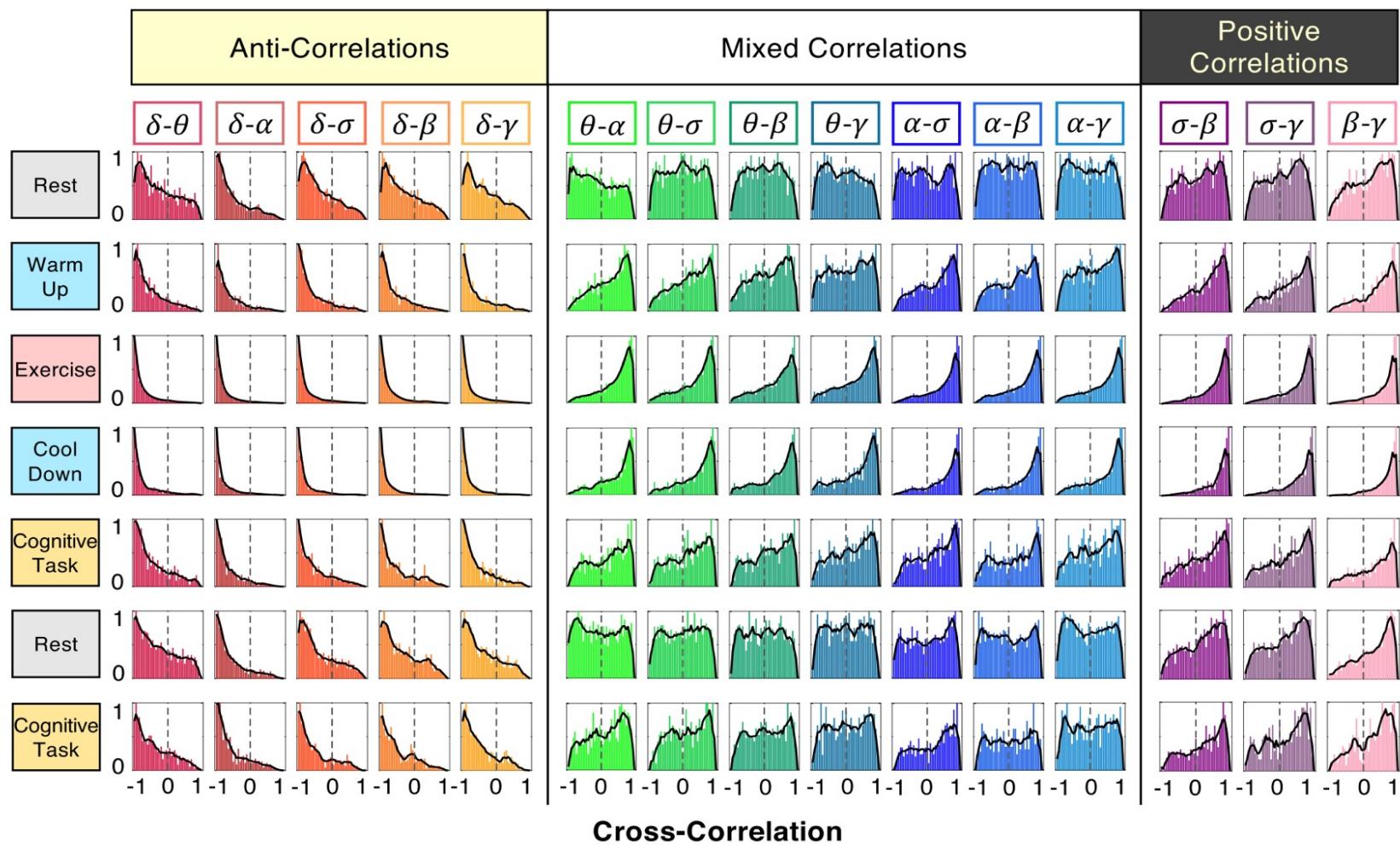
Network Physiology: Implications for brain dynamics and neural plasticity

Network communications and topological clustering of brain rhythms.
Group Average



Lin A, Liu KKL, Bartsch RP, and Ivanov PCh.
Dynamic network interactions among distinct
brain rhythms as a hallmark of physiologic state
and function.
Communications Biology, 2020; 3: 197.

Network Physiology: Implications for brain dynamics and neural plasticity



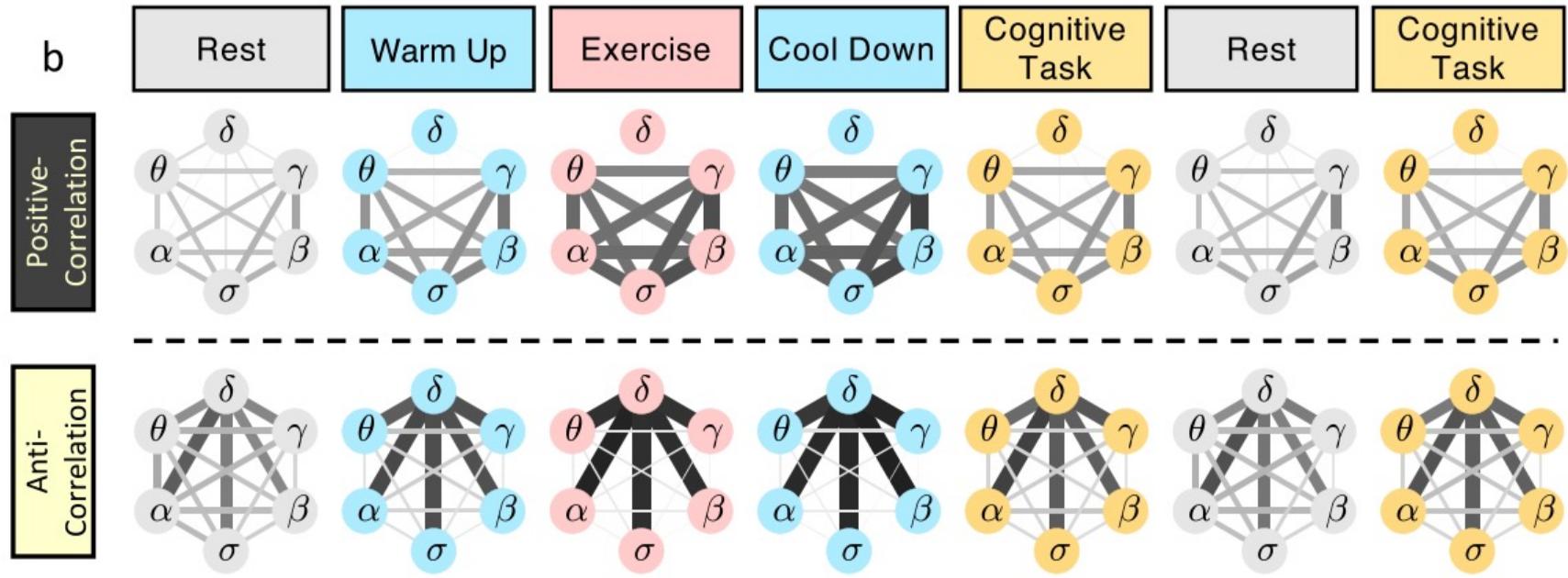
Transitions in brain-wave interactions across physiologic states.

Chen B, Ciria L, Hu C, and Ivanov PCh.

Ensemble of coupling forms and networks among brain rhythms as function of states and cognition.

Communications Biology, 2022;53: 82.

Network Physiology: Implications for brain dynamics and neural plasticity



Network of cortical rhythm interactions and their evolution
across physiological states.

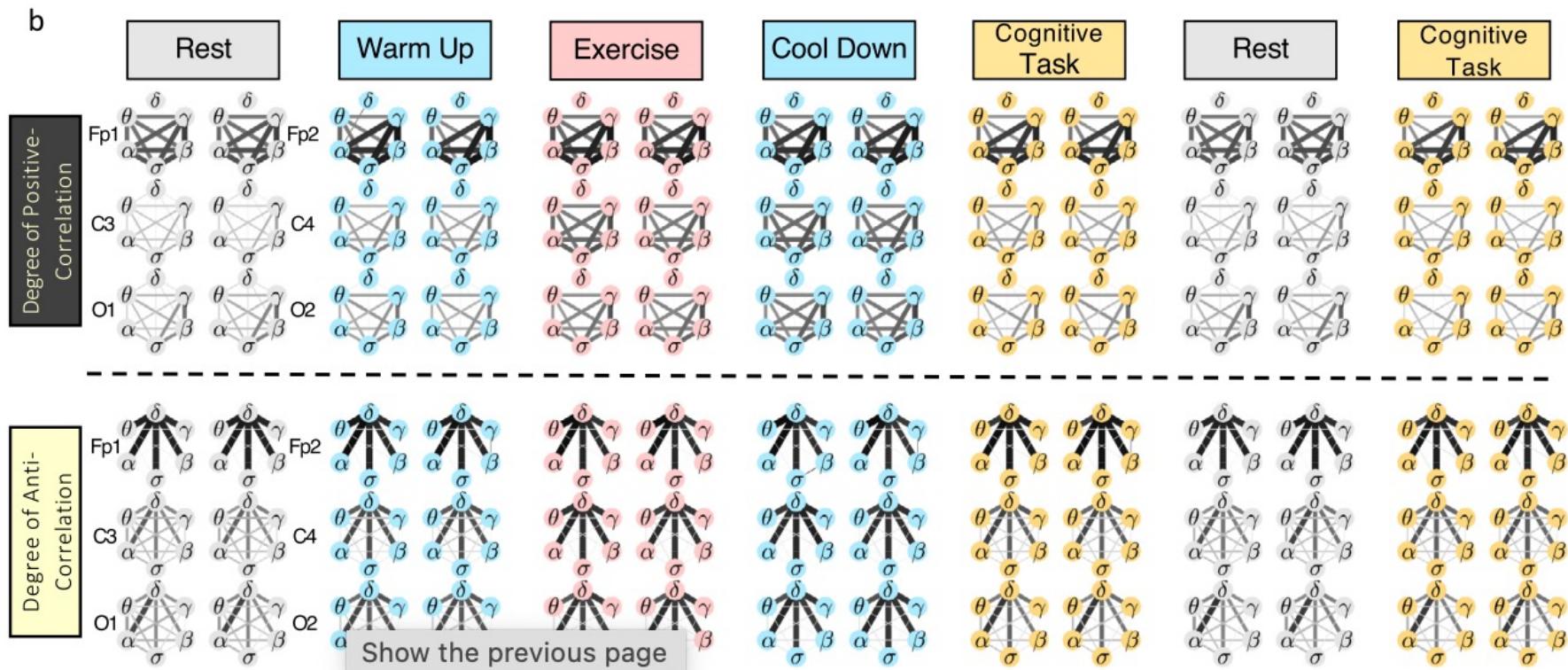
Chen B, Ciria L, Hu C, and Ivanov PCh.

Ensemble of coupling forms and networks among brain rhythms as function of states and cognition.

Communications Biology, 2022;53: 82.

Level 3: Networked Interactions

Network Physiology: Implications for brain dynamics and neural plasticity



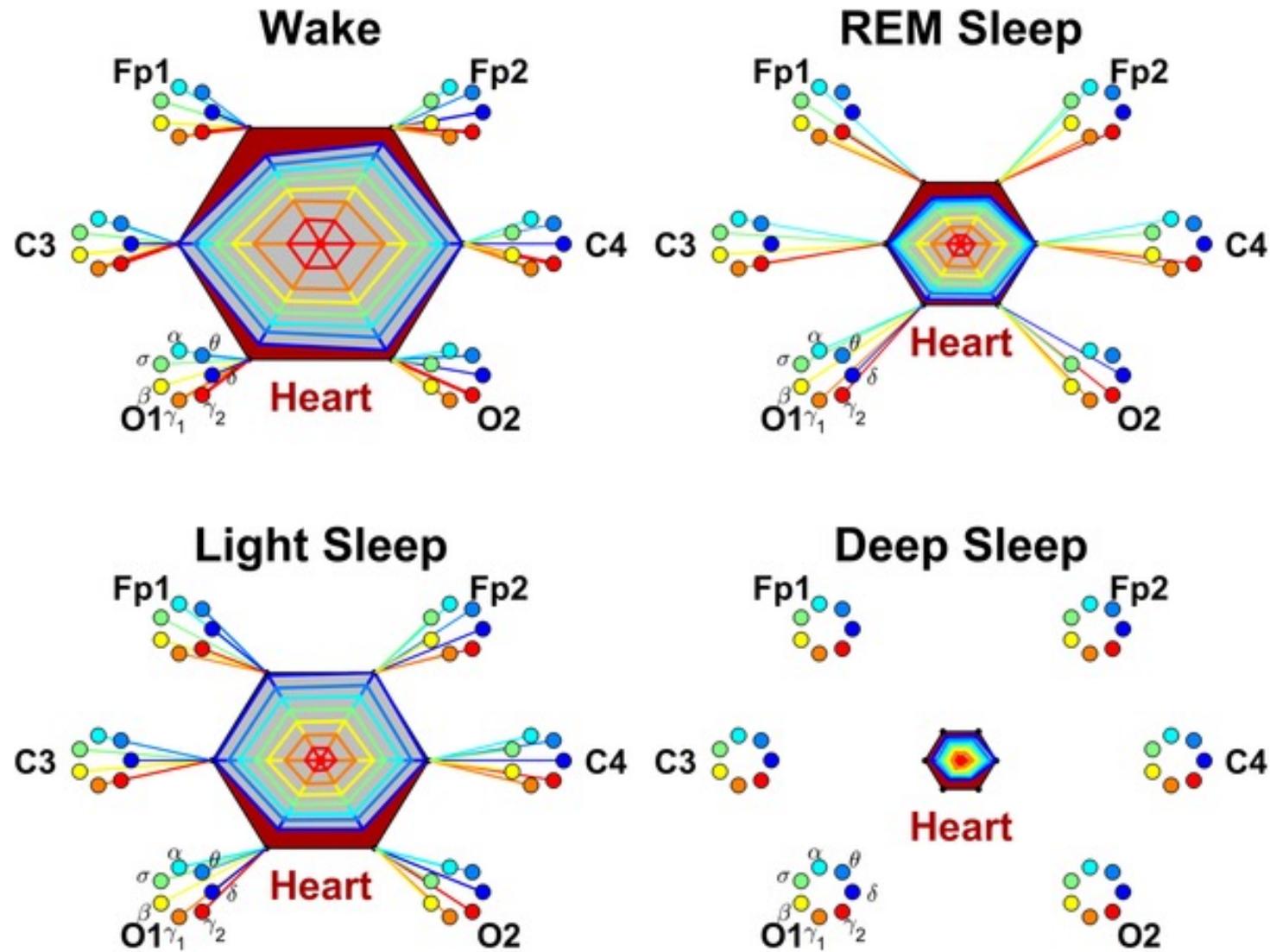
Network communications and topological clustering of brain rhythm interactions at different cortical locations uniquely represent physiological states.

Chen B, Ciria L, Hu C, and Ivanov PCh.

Ensemble of coupling forms and networks among brain rhythms as function of states and cognition.

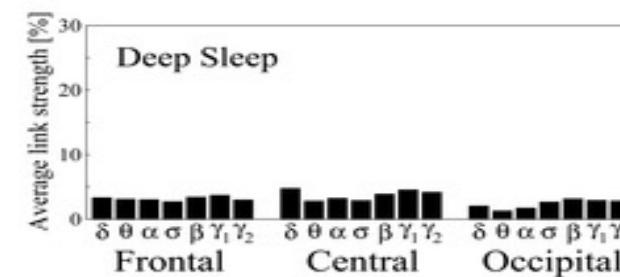
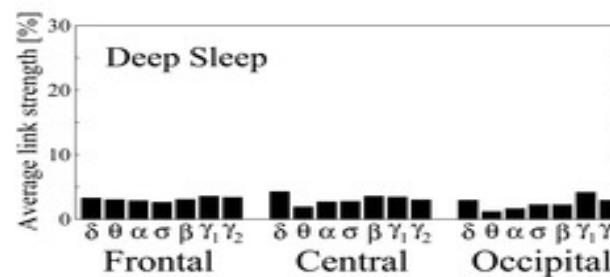
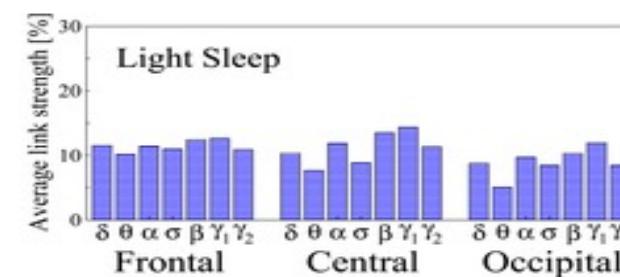
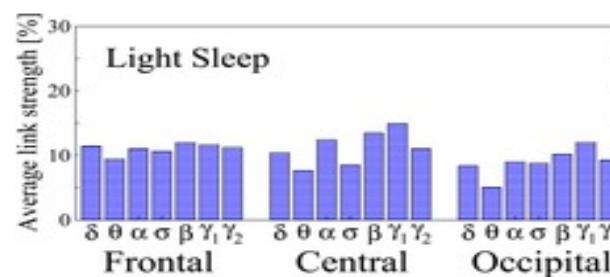
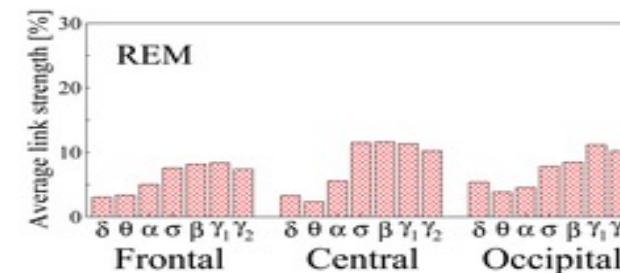
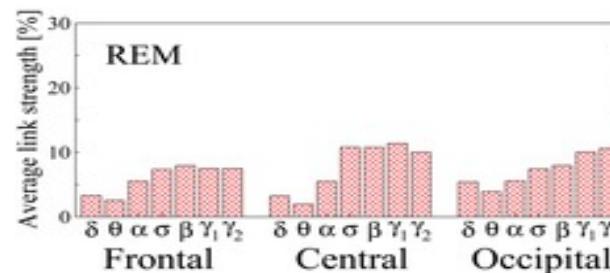
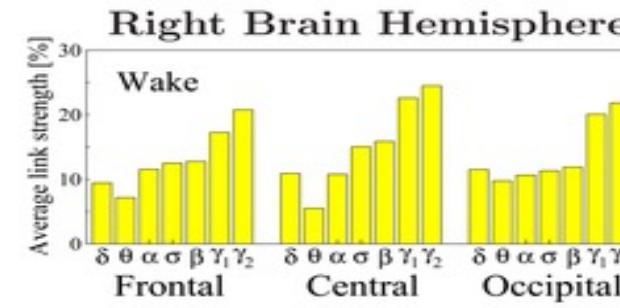
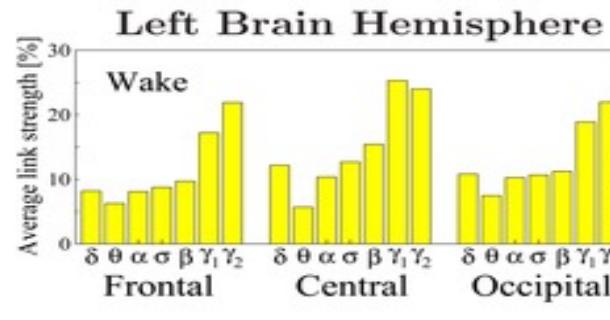
Communications Biology, 2022;53: 82.

Visualization: different physiologic states



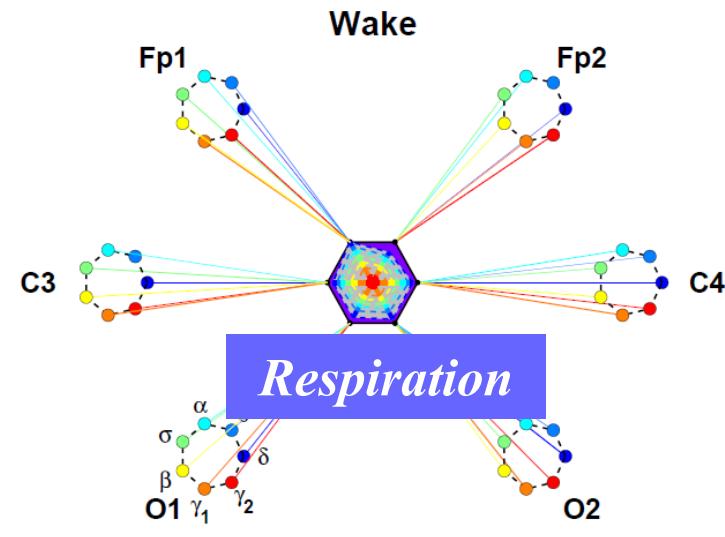
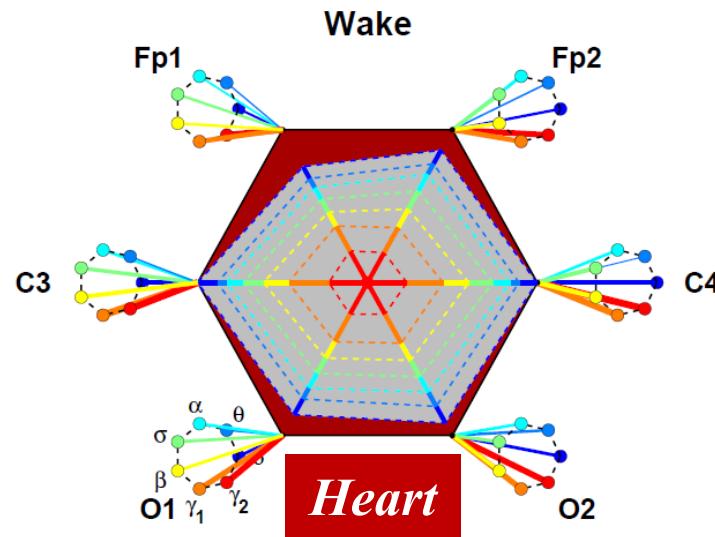
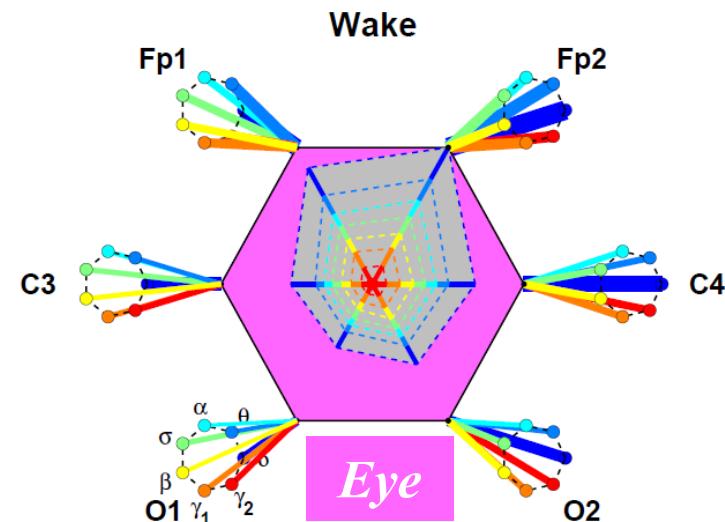
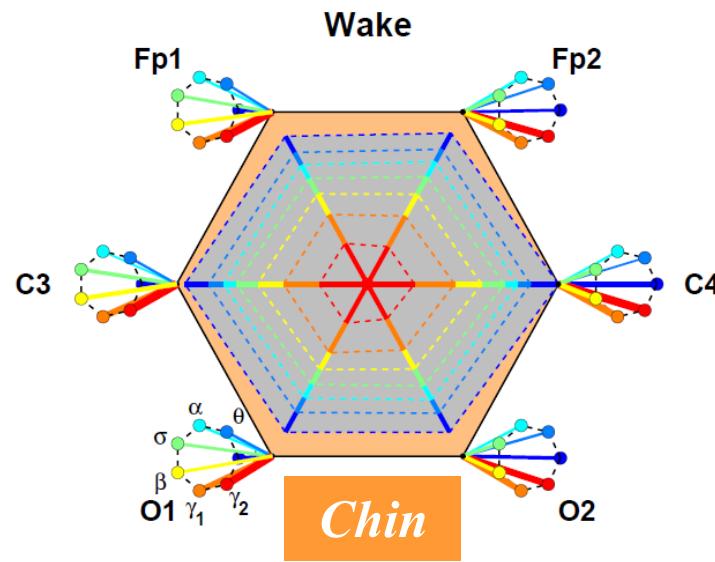
Brain-organ interactions

Brain-Heart Interaction

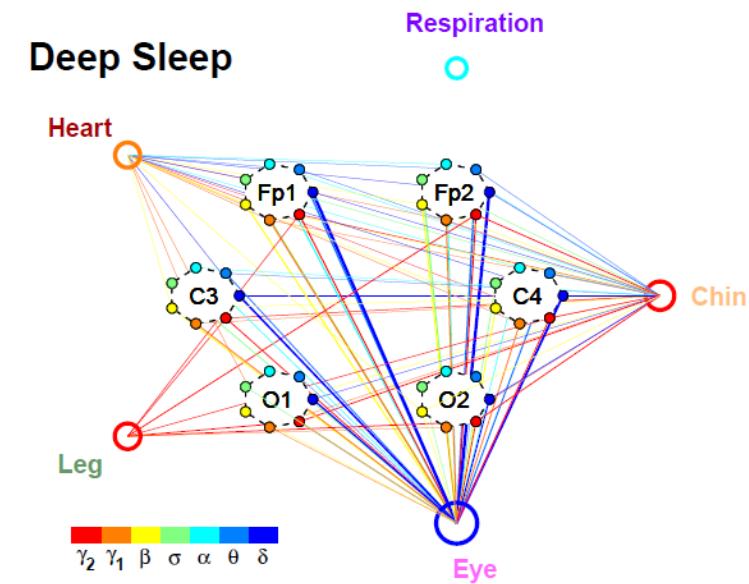
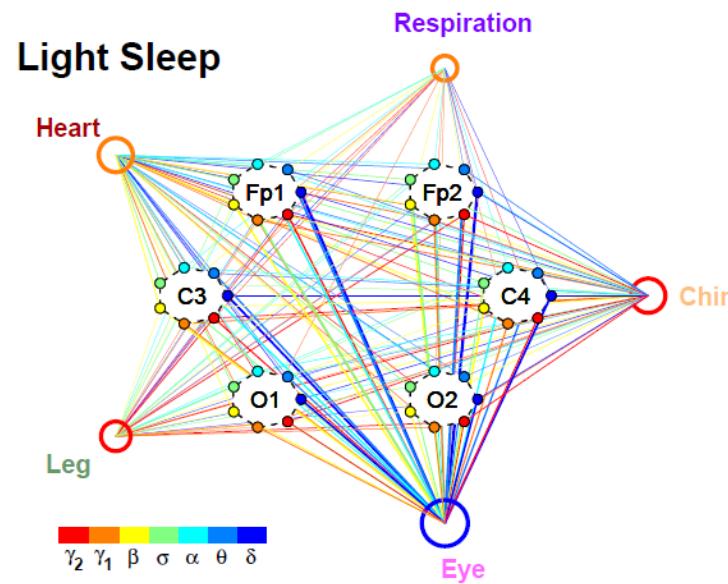
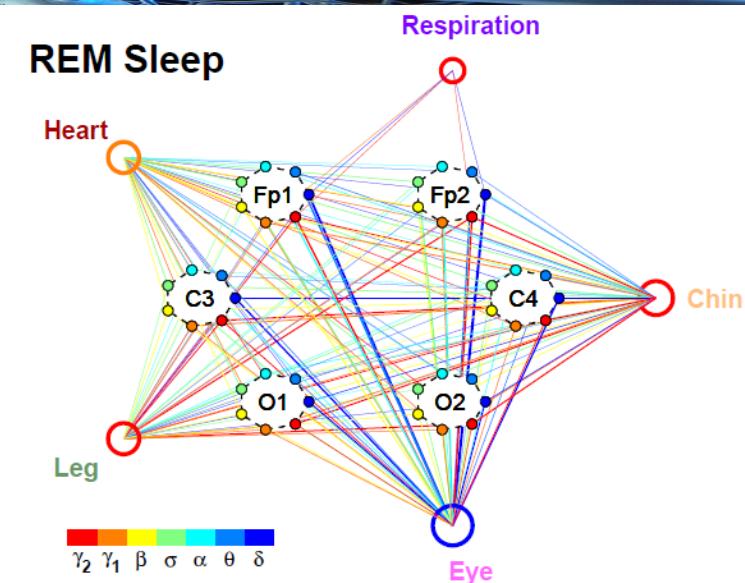
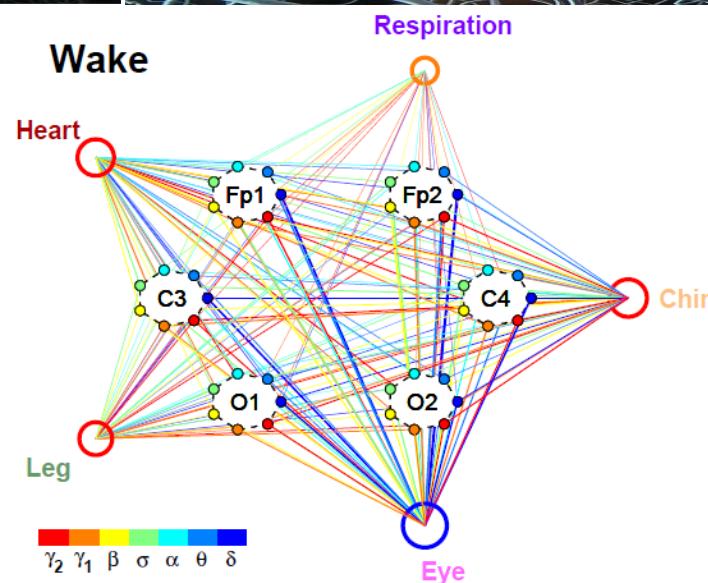


mediated by
different
frequency bands

Maps for different organ systems



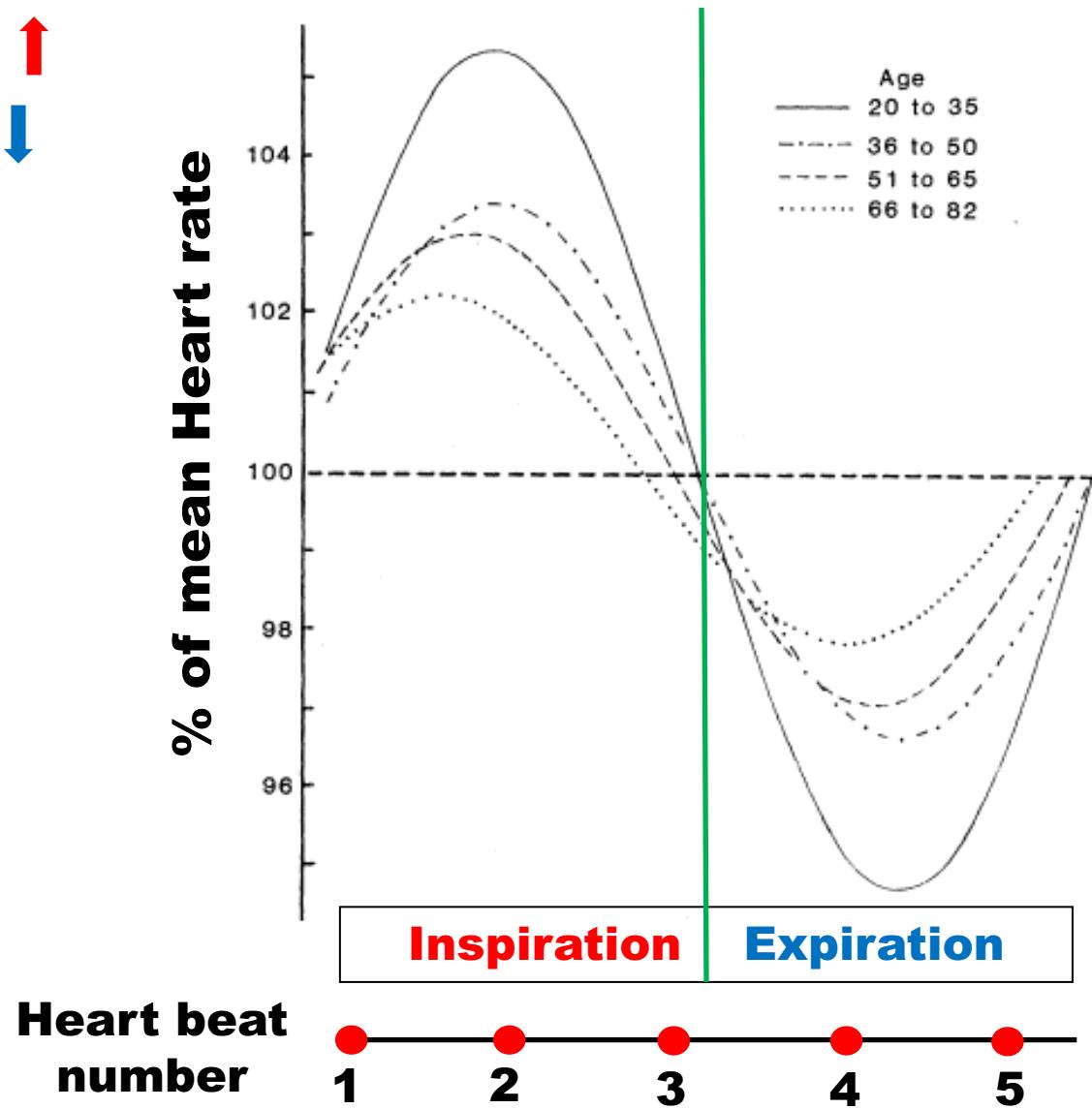
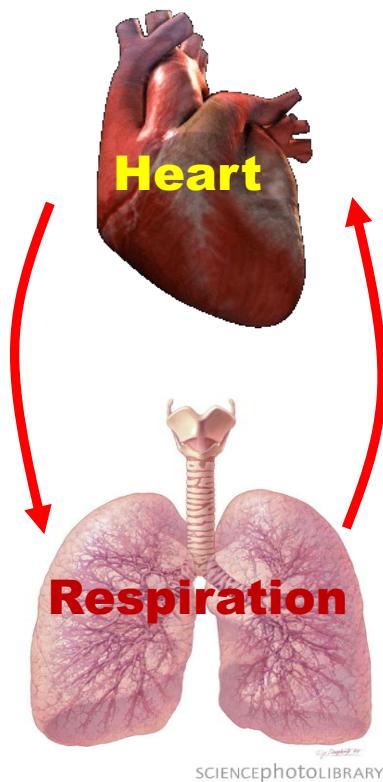
Network Physiology: Networks of brain activity and other physiologic systems across sleep stages



Cardio-respiratory Interaction Respiratory Sinus Arrhythmia (RSA)

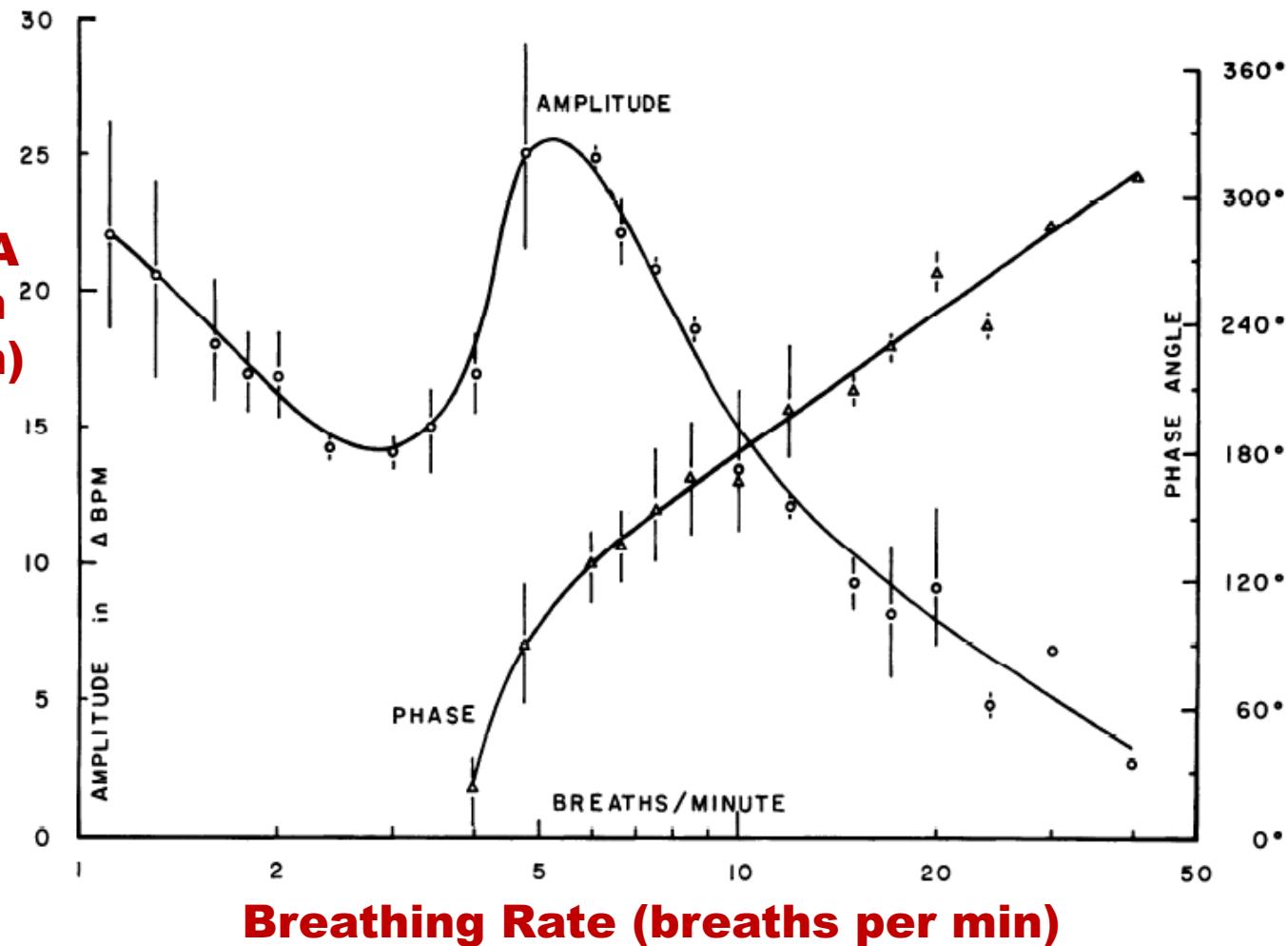
Inspiration → Heart rate ↑

Expiration → Heart rate ↓



Cardio-respiratory Interaction Respiratory Sinus Arrhythmia (RSA)

**Strength of RSA
(deviation from
mean beats/min)**



Angelone & Coulter, *J Appl Physiol* 19, 479 (1964)

How do systems interact? Synchronization: Definition

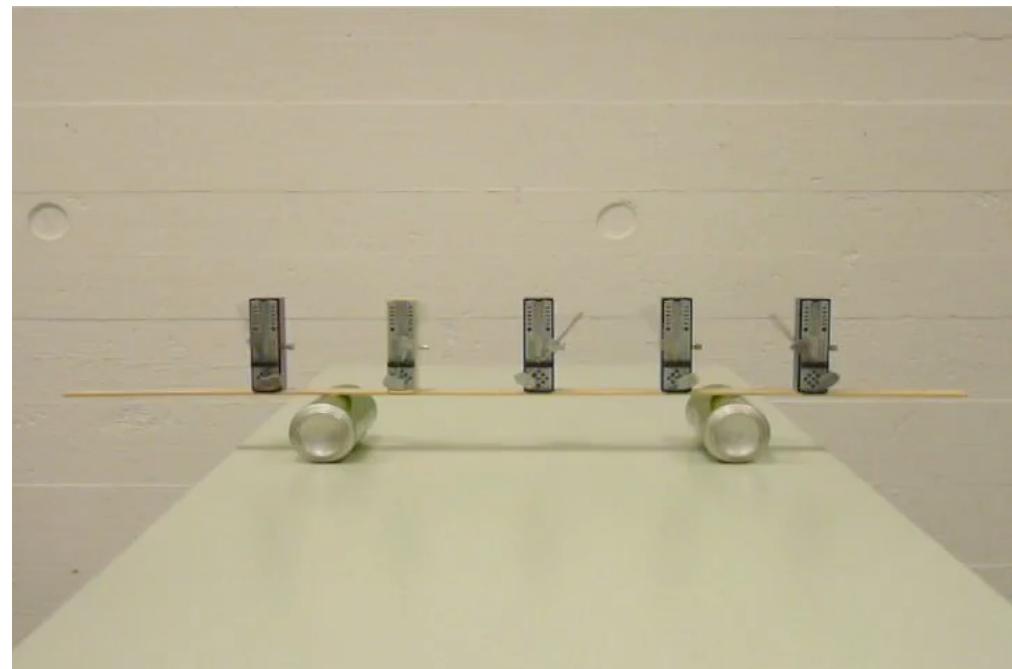
“Synchronization is an adjustment of rhythms of self-sustained oscillators due to their weak interaction.”

Pikovsky, Rosenblum, Kurths. Synchronization: a universal concept in nonlinear sciences (Cambridge University Press 2001)

Start:
different frequencies,
different phases
→ **No synchronization**

End:
same frequencies,
same phase difference
("phase locked")
→ **Synchronization**

Coupled Metronomes



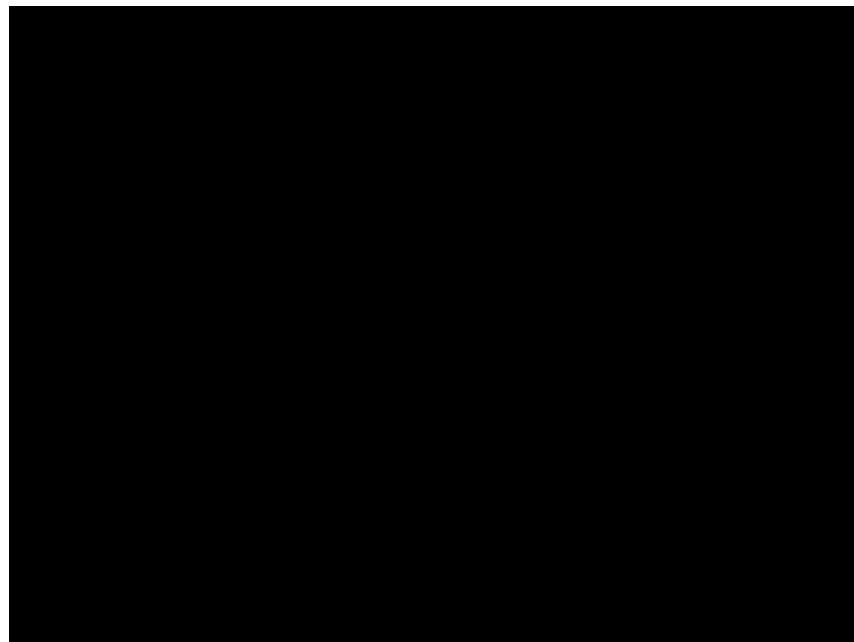
The Synchronization Phenomenon

- **London: Millennium (“Wobbly”) bridge opening day June 10, 2000**



The Synchronization Phenomenon

- **London: Millennium (“Wobbly”) bridge opening day June 10, 2000**

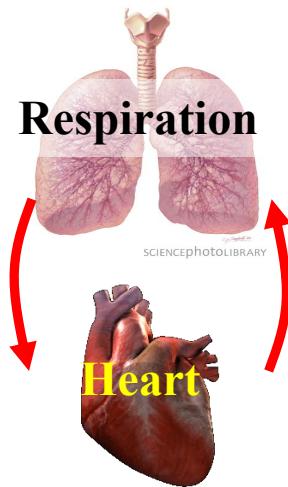


Millenium bridge reopened in February 2002:

- **after 5 Million £ spent on bridge modifications**
- **research based on work by S. Strogatz et al. Nature 438, 43 (2005)**

Level 2:
Pair-wise Coupling

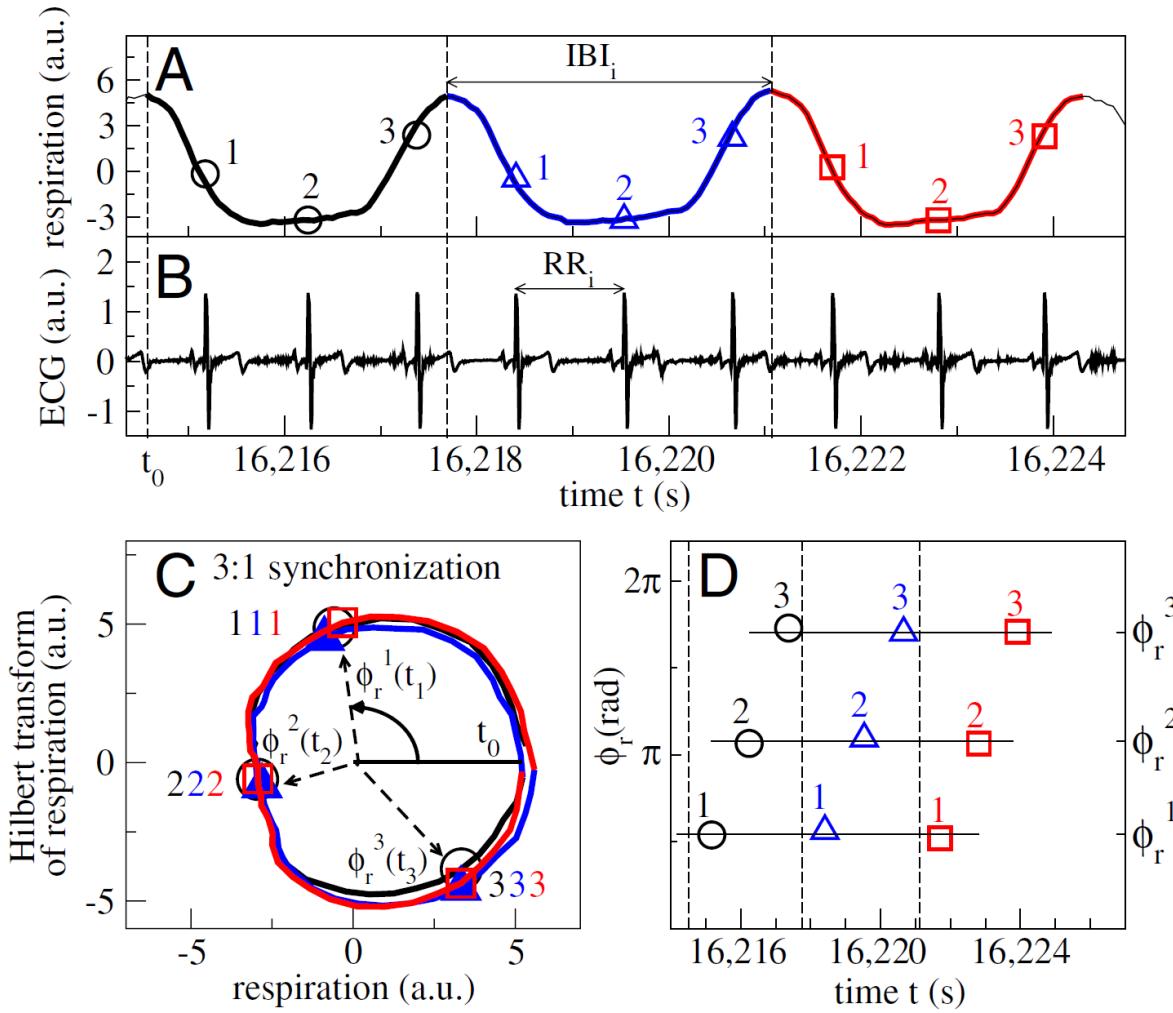
Cardio-respiratory Interaction Phase Synchronization



Phases collapse

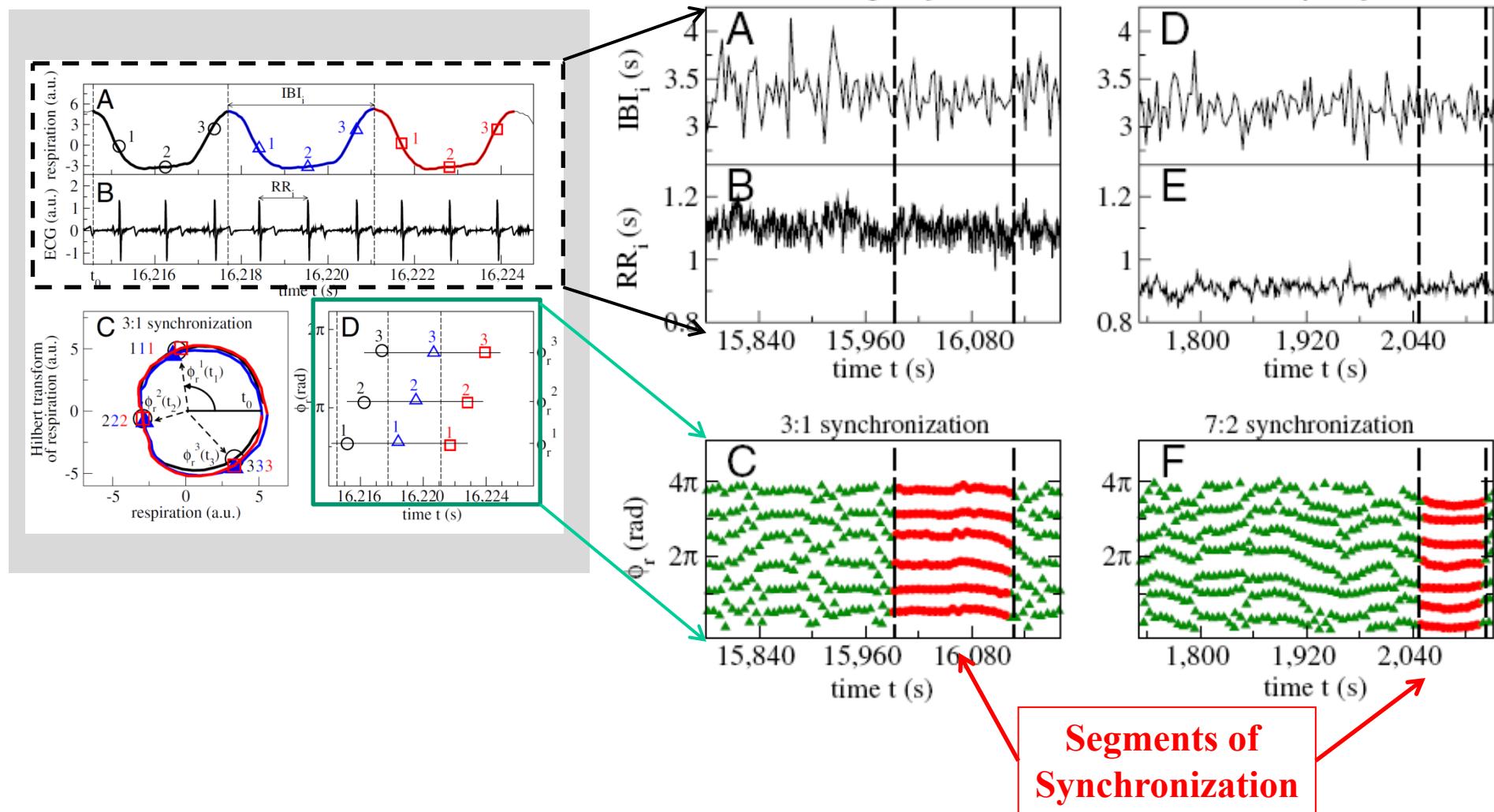


Phase synchronization



Cardio-respiratory Interaction

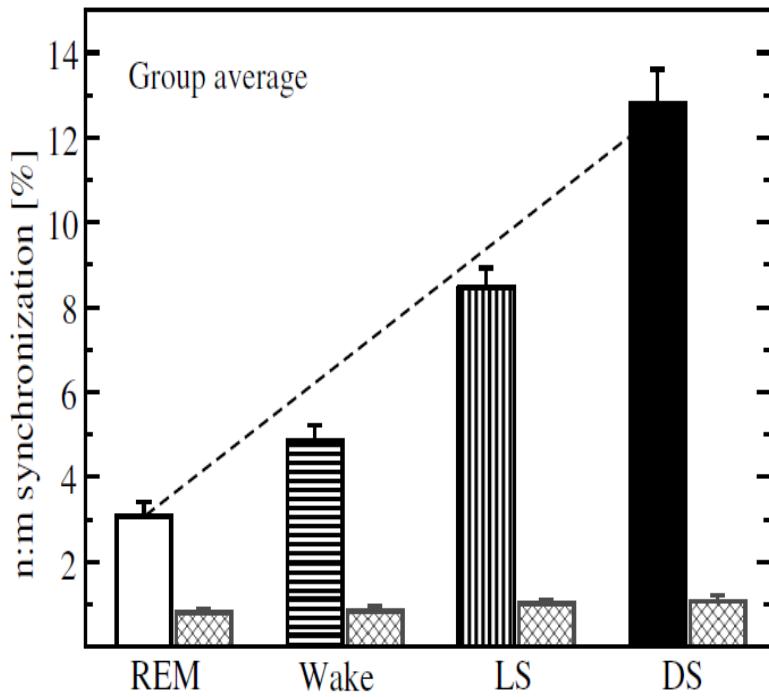
Phase Synchronization despite continuous fluctuations



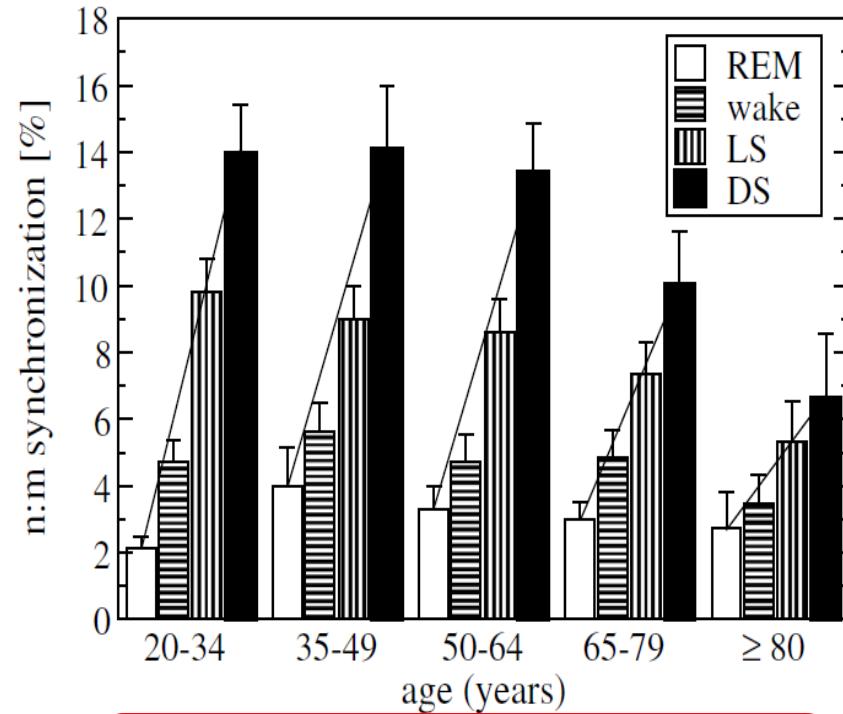
Segments of
Synchronization

Cardio-respiratory Interaction Phase Synchronization

Pronounced stratification of synchronization is stable for all age groups



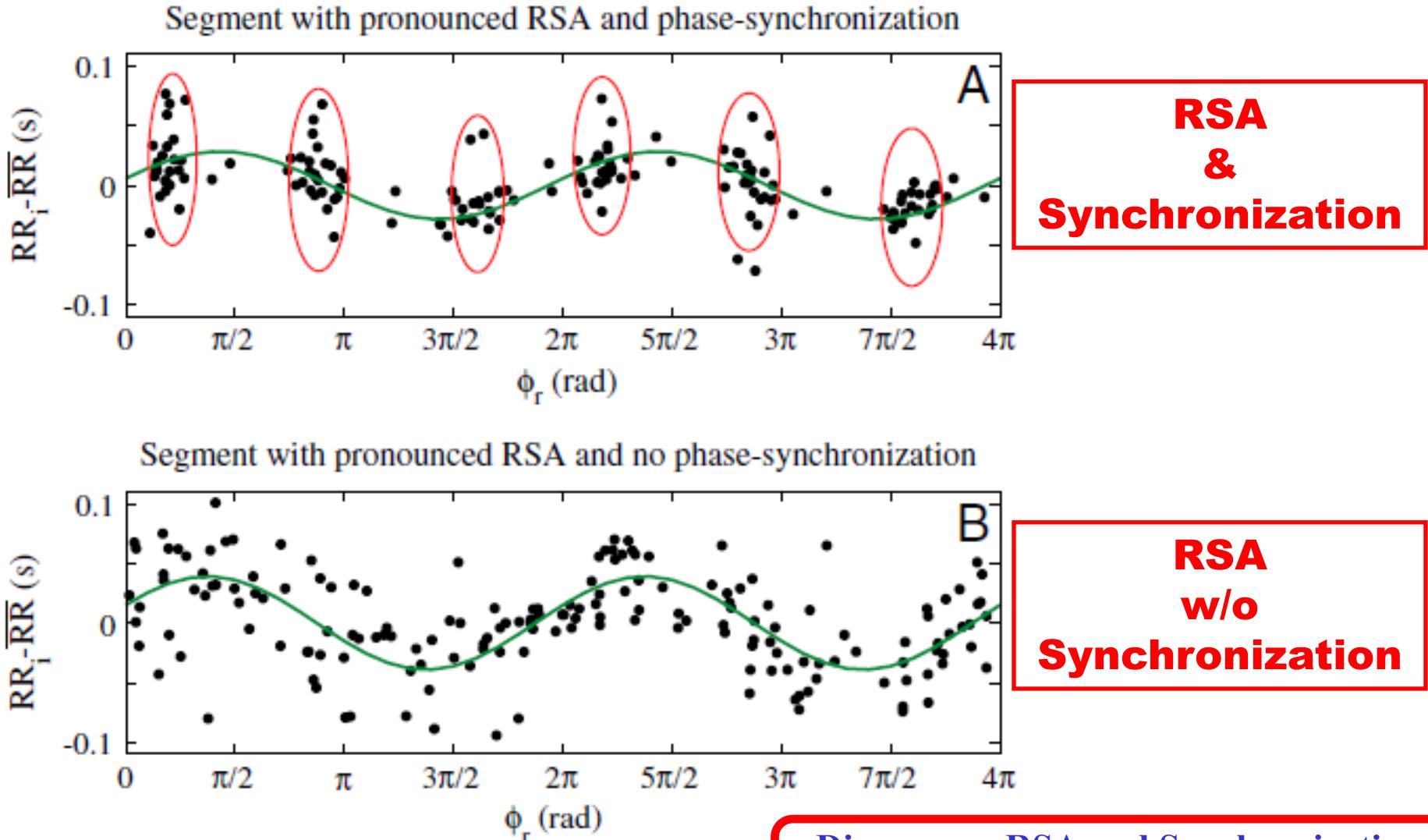
400% increase in
synchronization from
REM to deep sleep



Discovery:
Phase transitions in
cardio-respiratory coupling

Coexisting forms of physiologic coupling

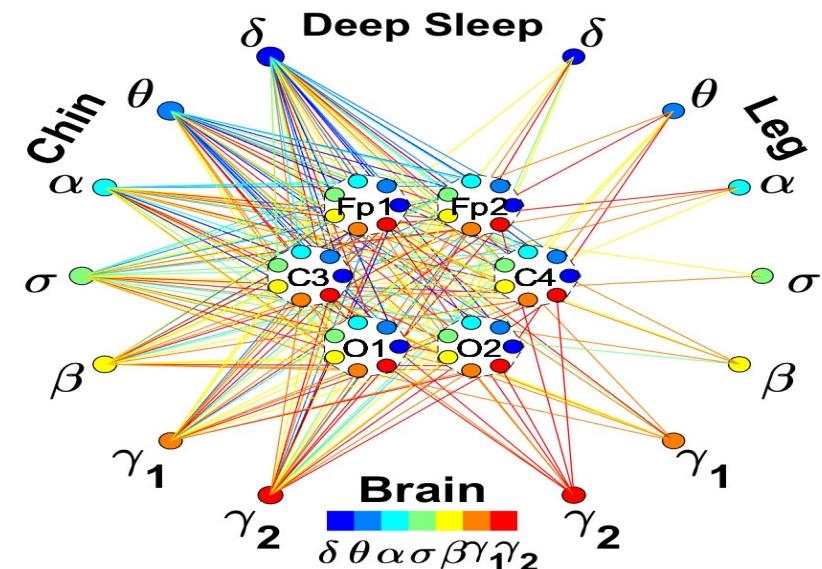
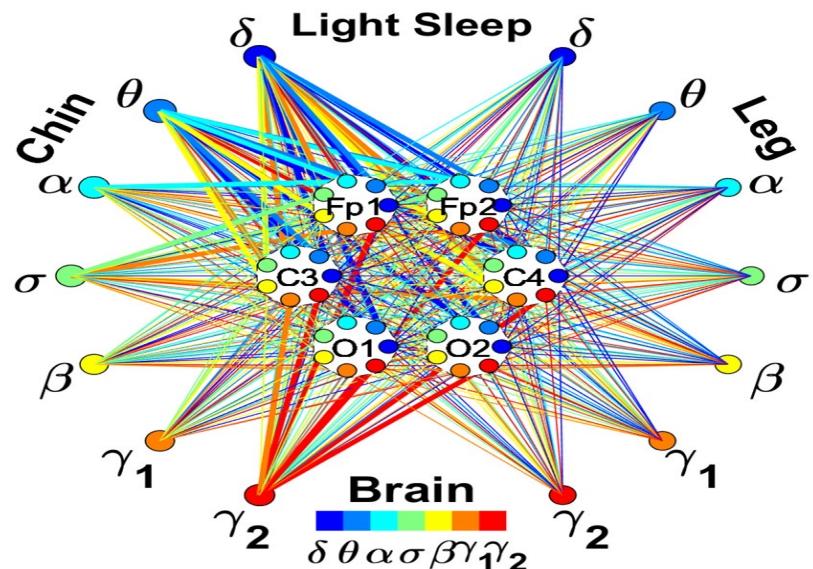
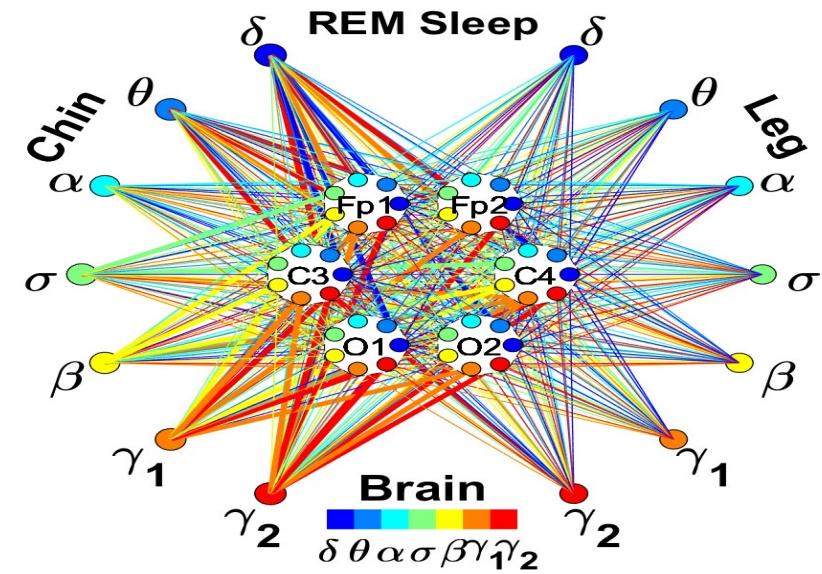
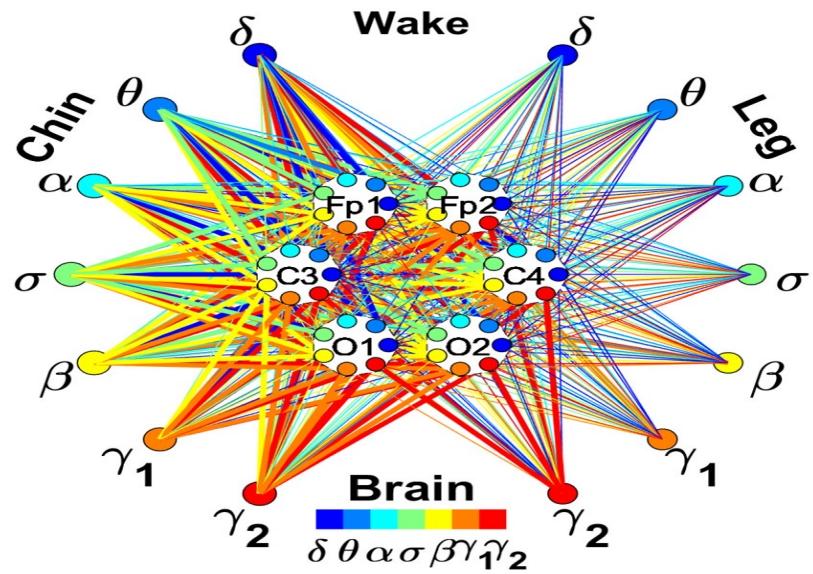
Cardio-Respiratory interaction



Discovery: RSA and Synchronization
 Two coexisting forms of coupling

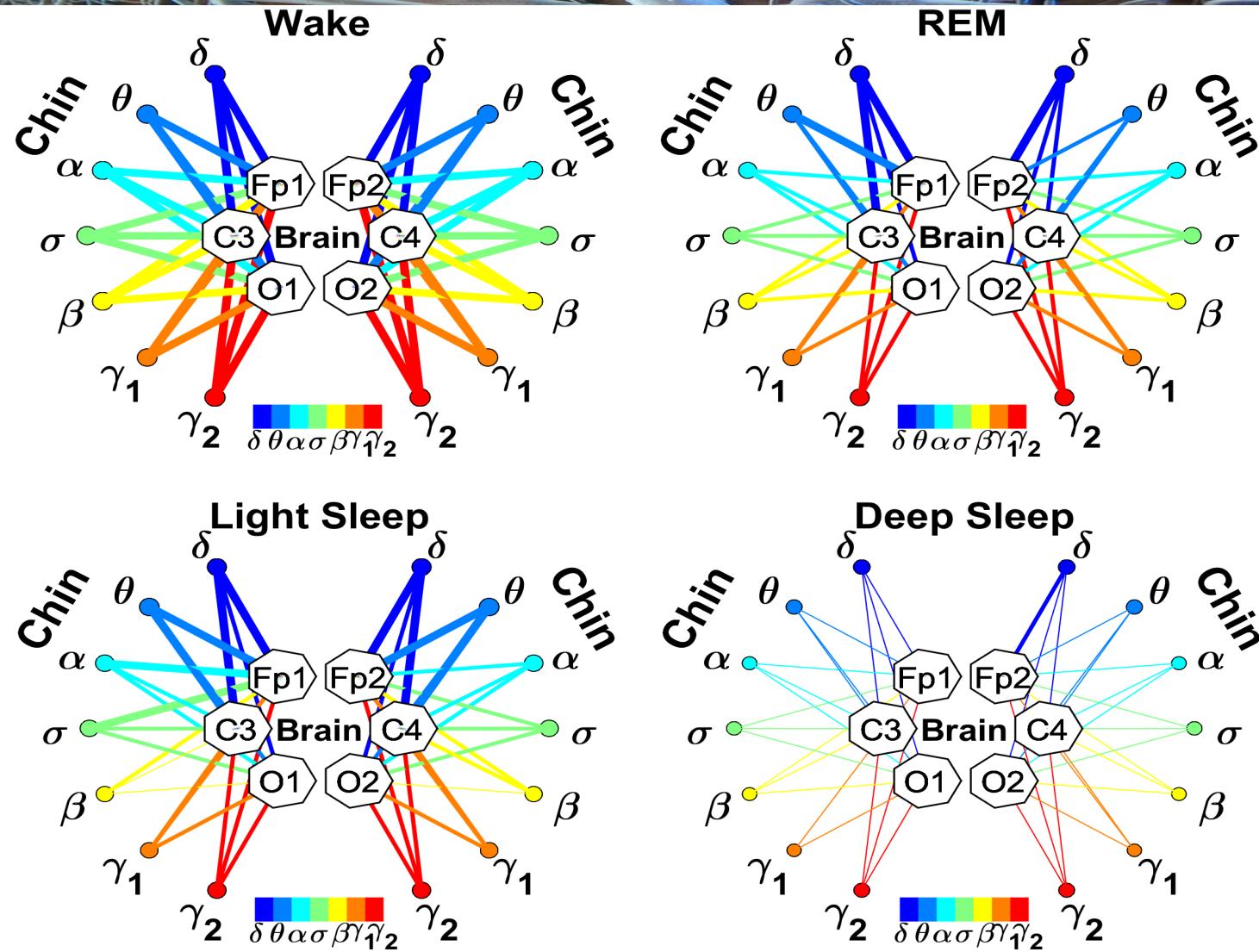
Functional Interaction Networks

Brain waves vs EMG frequency bands



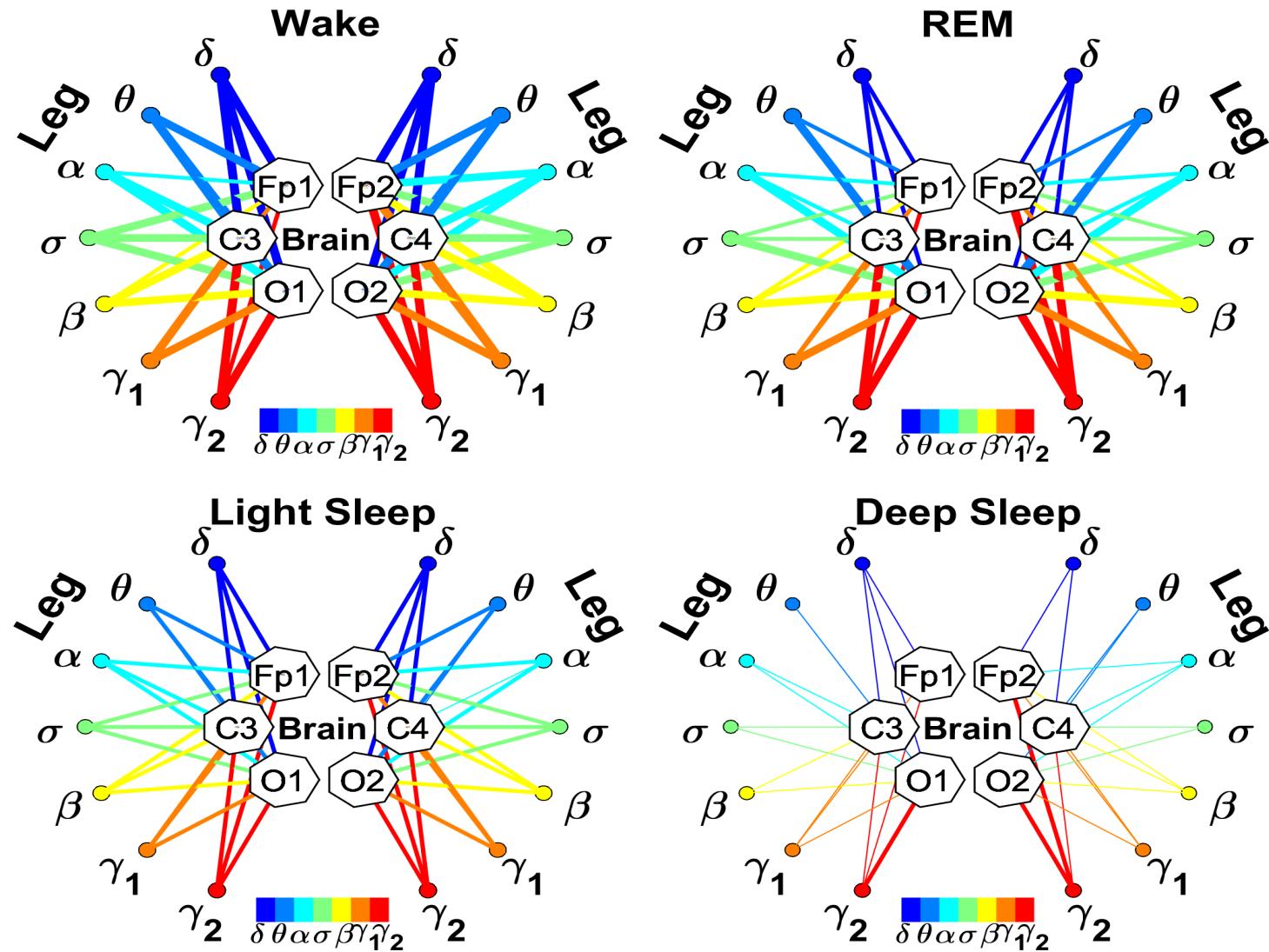
Functional Interaction Networks

Chin EMG Frequency Bands vs Brain Areas

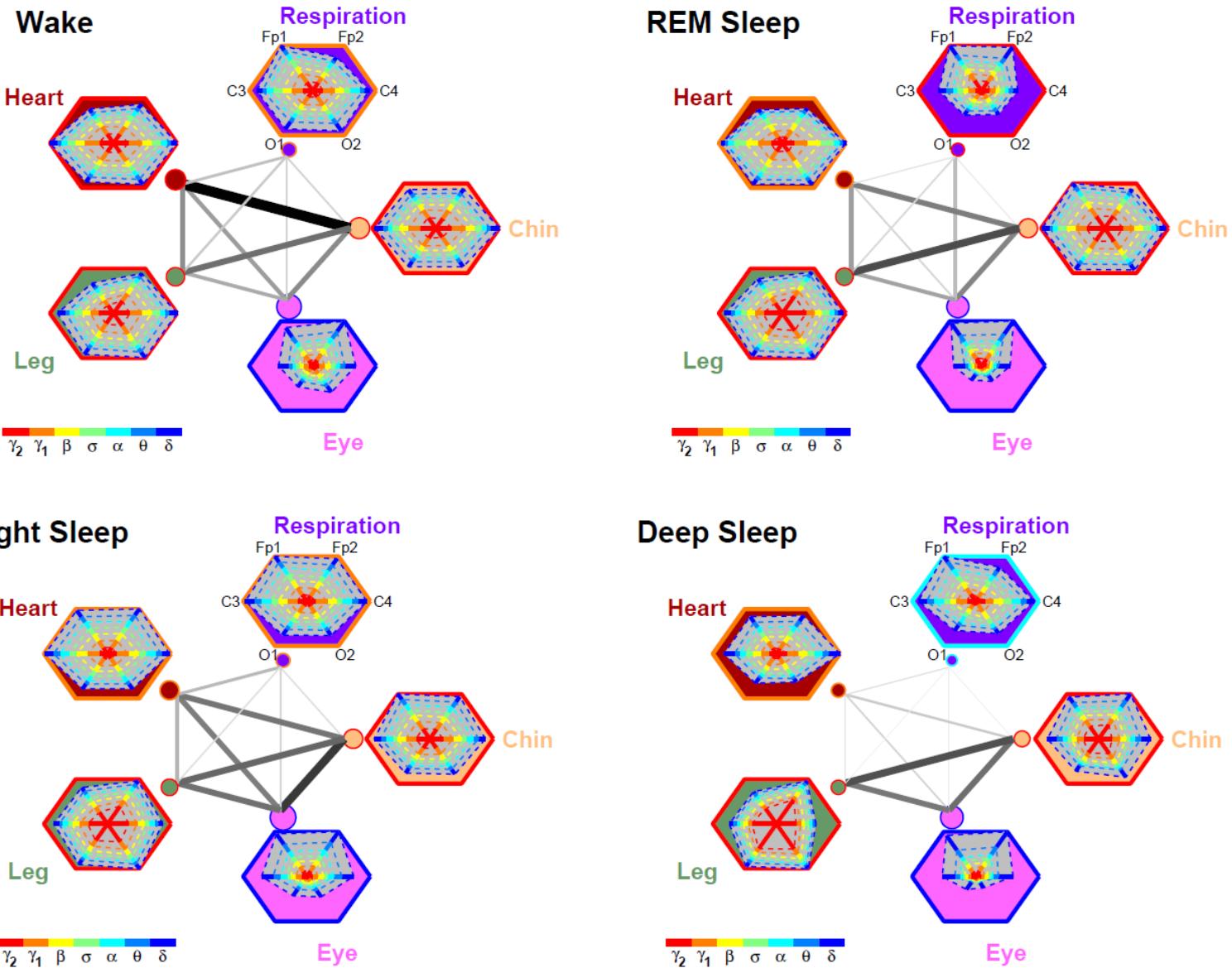


Functional Interaction Networks

Leg EMG Frequency Bands vs Brain Areas

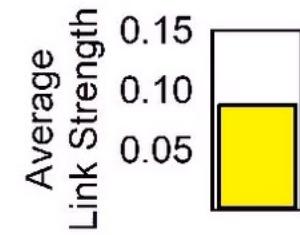
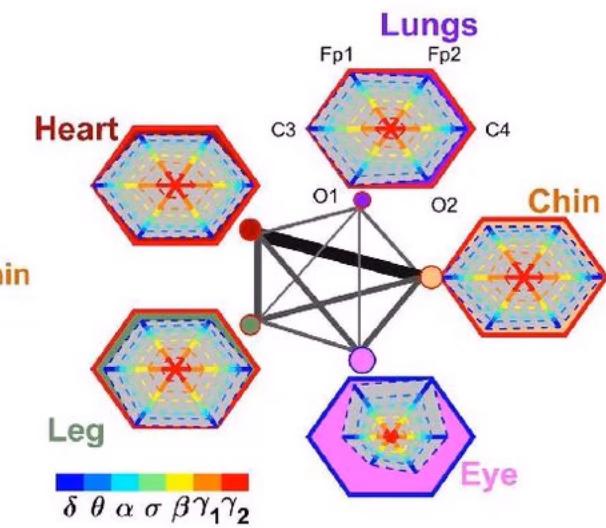
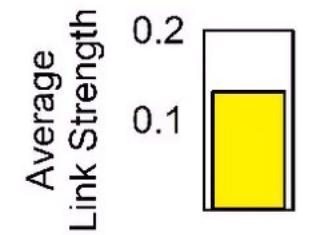
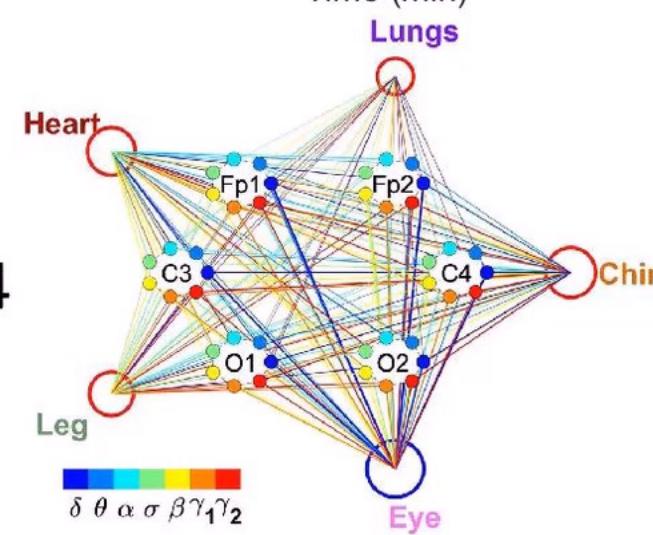
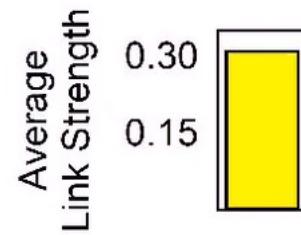
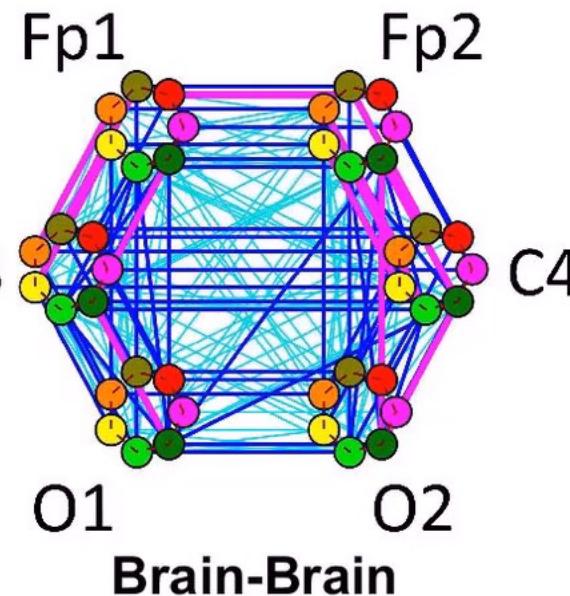
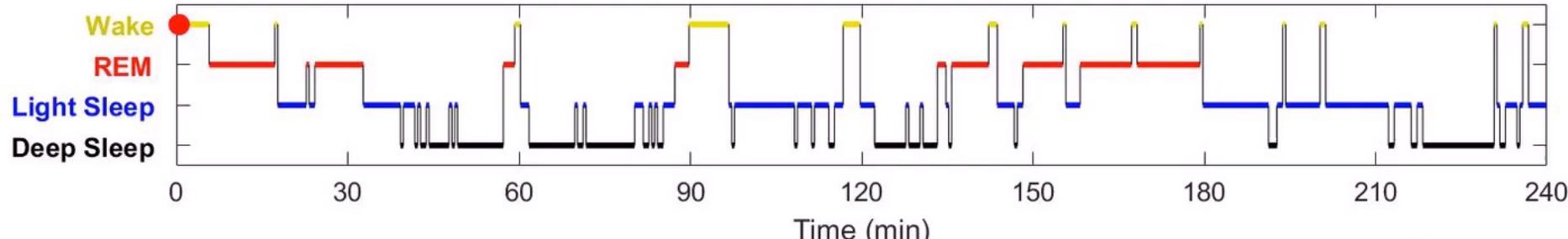


Network Physiology: Networks of brain activity and other physiologic systems across sleep stages



**Level 3:
Networked
Interactions**

Network Physiology: Networks of brain activity and other physiologic systems across sleep stages



Physiology and Medicine

Novel biomarkers



New kind of Physicians



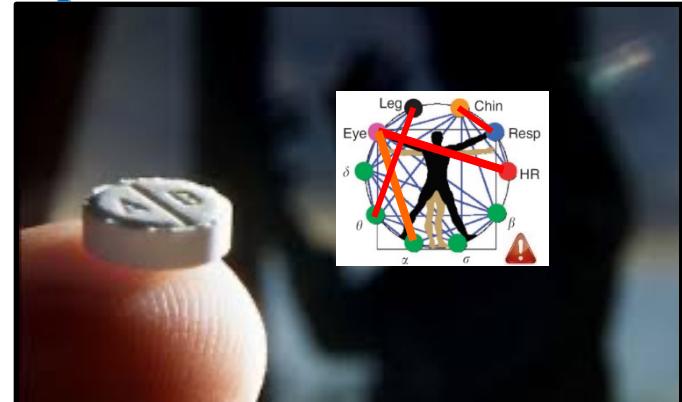
Personalized health monitoring



Next generation ICU monitoring devices and alert system



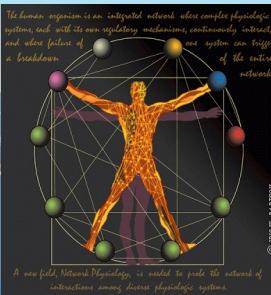
Comprehensive assessment of drugs





Third International Summer Institute on Network Physiology (ISINP)

Lake Como School of Advanced Studies,
25 - 30 July 2022



New Journal: Frontiers in Network Physiology

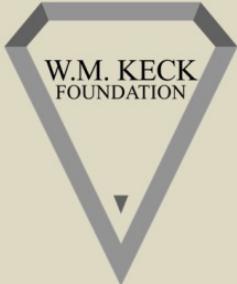


frontiers
in Network Physiology

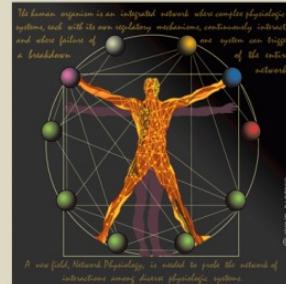
- **Ten journal sections**
- **Multiple focus issues**

Our Group:

<http://physics.bu.edu/labnetworkphysiology>



Keck Laboratory for Network Physiology



Openings:

- Research Scientists
- Visiting Researchers

Support:

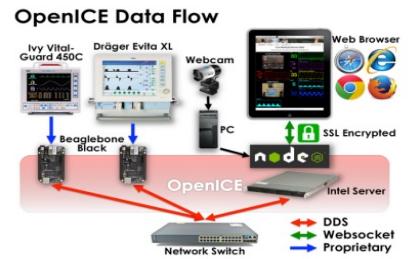
- *Atlas of Dynamic Interactions among Organ Systems*

W. M. KECK FOUNDATION



Collaboration

Ongoing Program: Interdisciplinary Collaboration



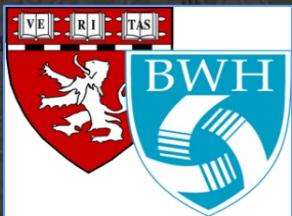
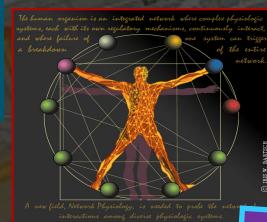
Keck Support: Catalyze a new field,
Network Physiology; Leverage
large-scale available resources



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