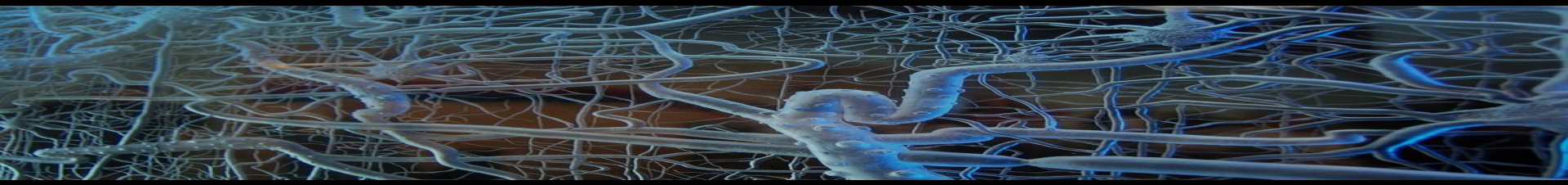
Network Physiology & the Human Physiolome: Implications for Aging and Resilience

Plamen Ch. Ivanov

Relevant Financial Relationships:

- salaried full professor, Department of Physics at Boston University.
- research funded by the W.M. Keck Foundation and Office of Naval Research.
- receives honoraria for courses and seminars on complex systems and network physiology besides place of employment, including at the International Summer Institute on Network Physiology, Lake Como School for Advance Studies.
- Receives financial compensation for reviews of grants from the NIH and other agencies.



Relevant Nonfinancial Relationships:

- non-salaried faculty member at the Center for Systems Neural Science, Boston University
- serves as Field Chief Editor, Frontiers in Network Physiology
- serves on Editorial Boards: New Journal of Physics, Journal of Biological Physics,
- serves as reviewer for several peer-reviewed journals

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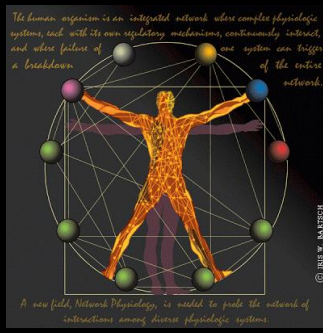
Keck Laboratory for Network Physiology

Physics Department

Boston University



BOSTON UNIVERSITY

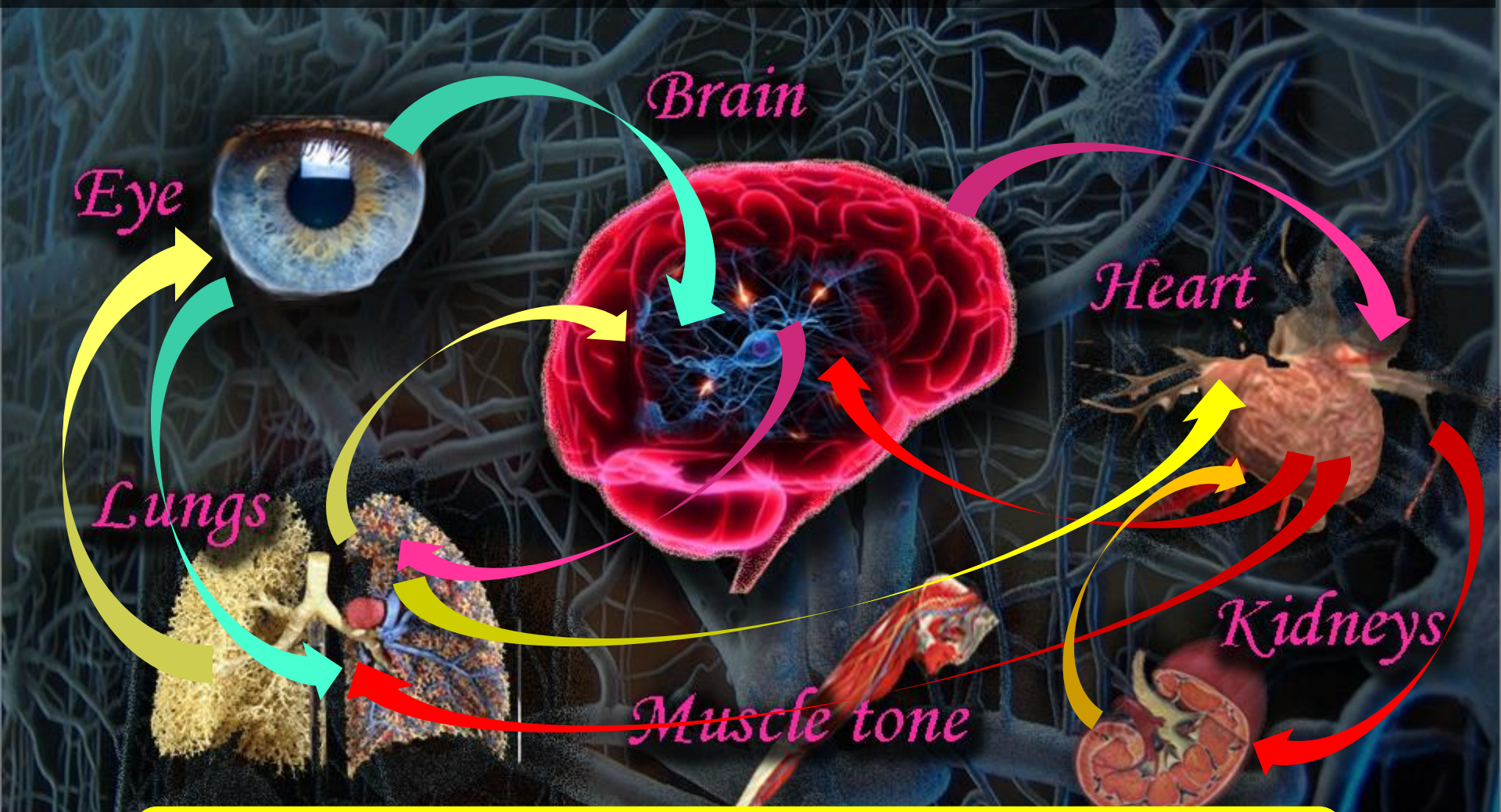
HARVARD MEDICAL SCHOOL

3-4 March 2024

NIH Aging

NIH National Institutes of Health

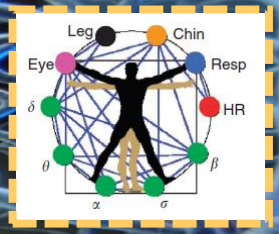
Human Organism – Integrated Network
Coordinated Interactions of Organ Systems

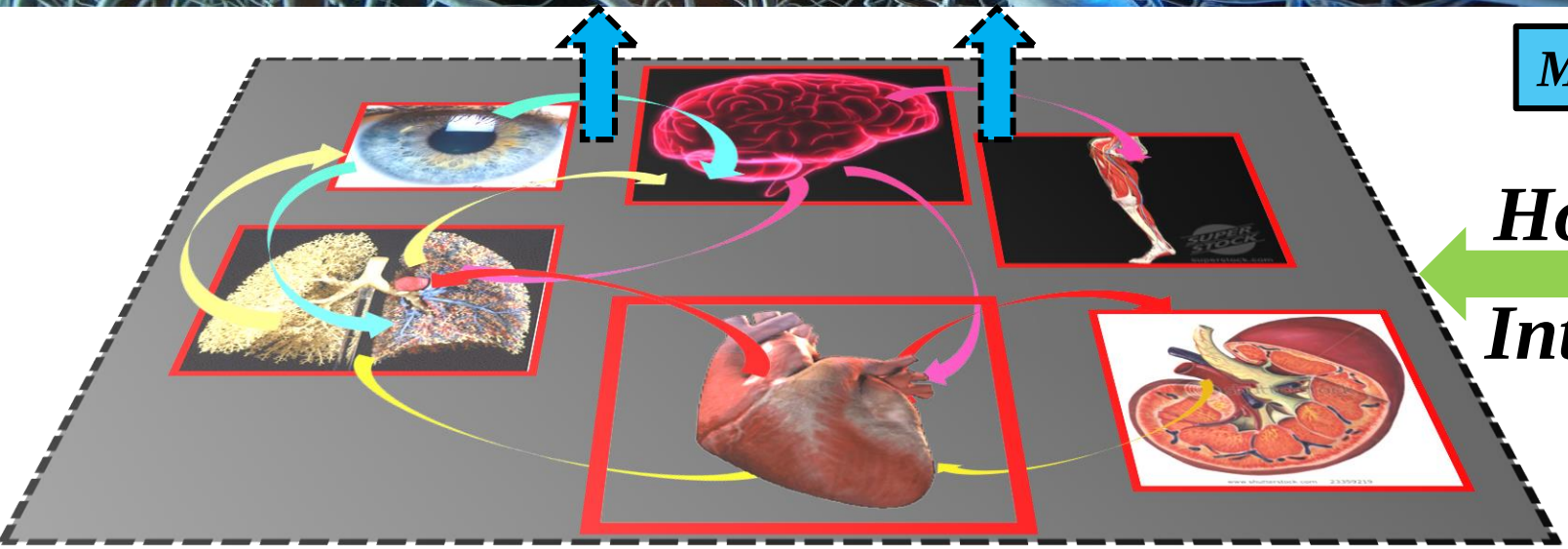


Essential to: **Maintain Health**
Generate distinct physiological states

Fundamental Question:

How Physiologic States and Functions *Emerge* out of Organ Network Interactions ?





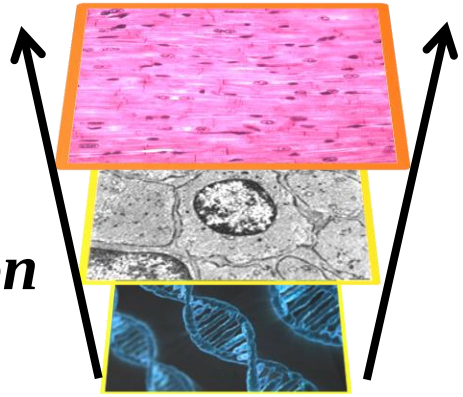
Macroscopic

Horizontal Integration

Integrative Physiology

Systems Biology

Vertical Integration



organs

tissue

cell

sub-cellular

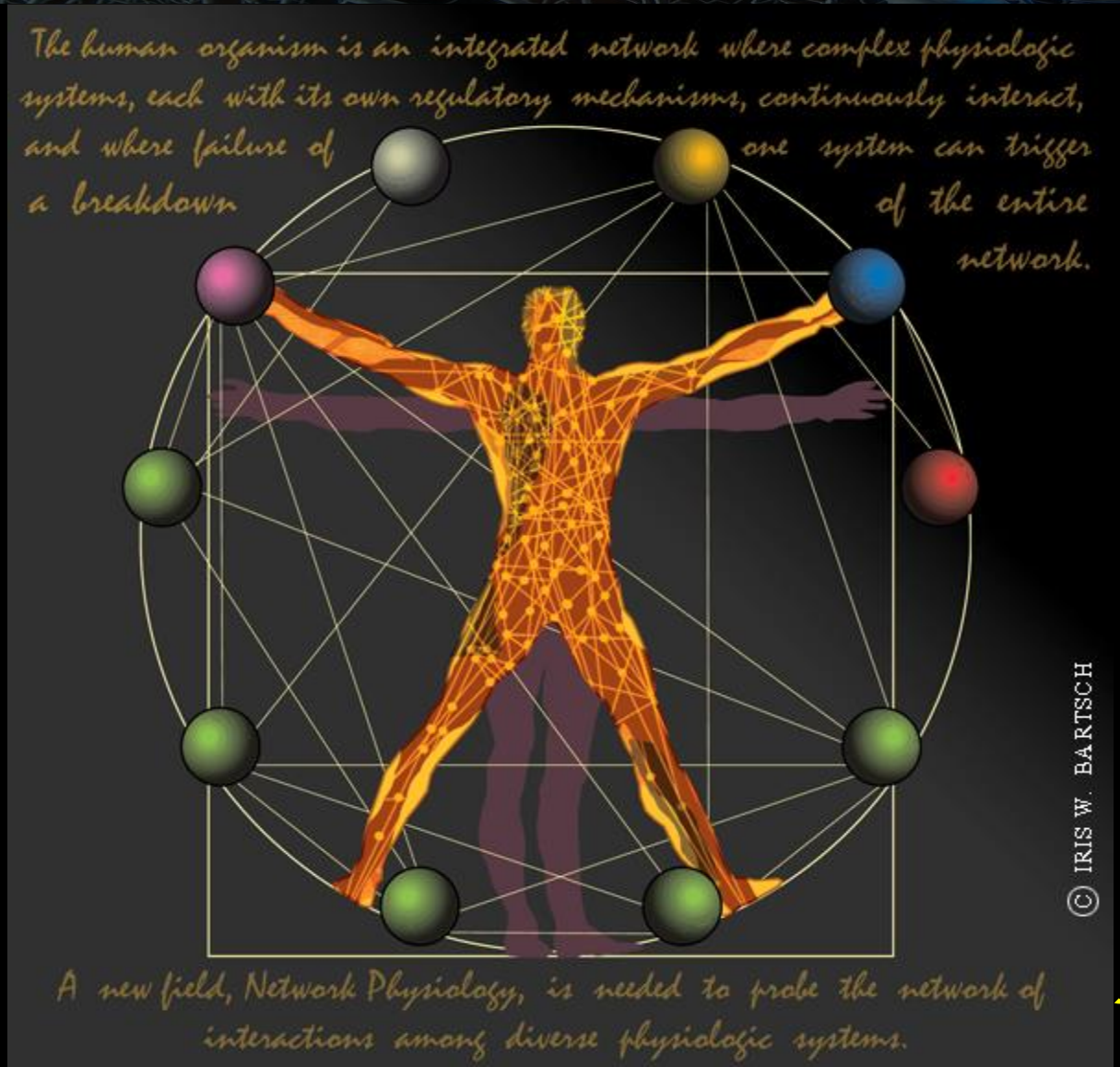
Mesoscopic

Microscopic

Our Research Program

New Research Direction:

Shifting the focus from single organ systems to the network of organ interactions



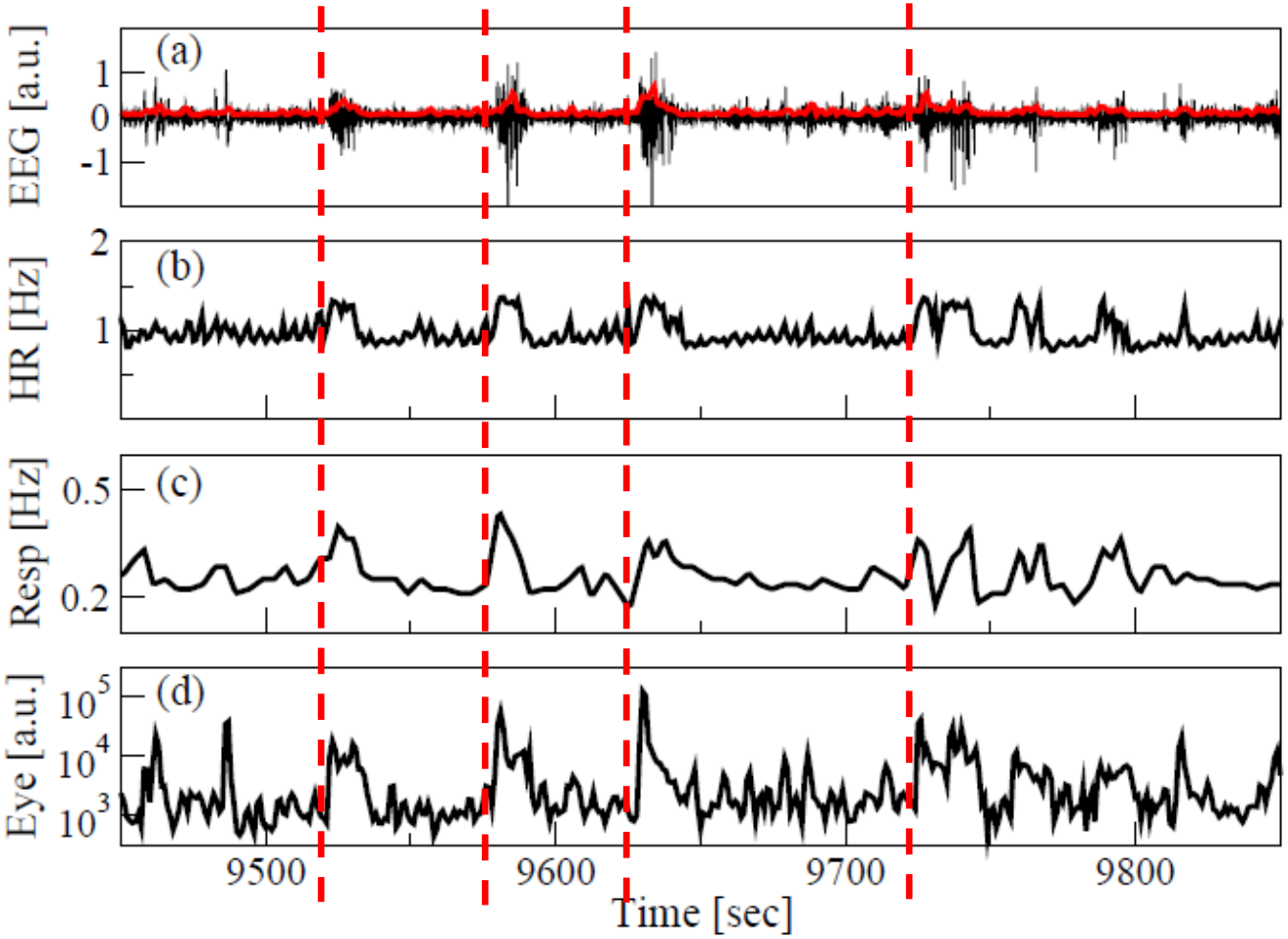
A new field

Network Physiology

needed to probe interactions among diverse physiologic systems.

Data-Driven Observation

Coordinated activity across diverse systems



EEG-σ band: sleep spindles

Heart rate

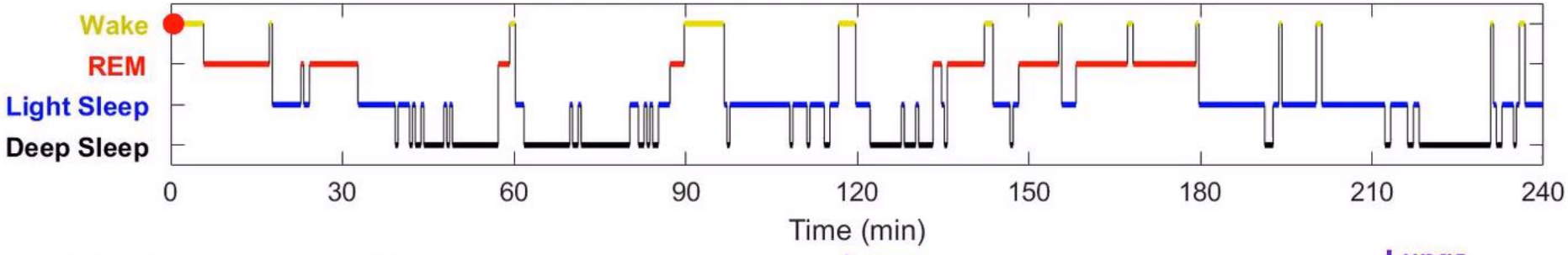
Respiratory rate

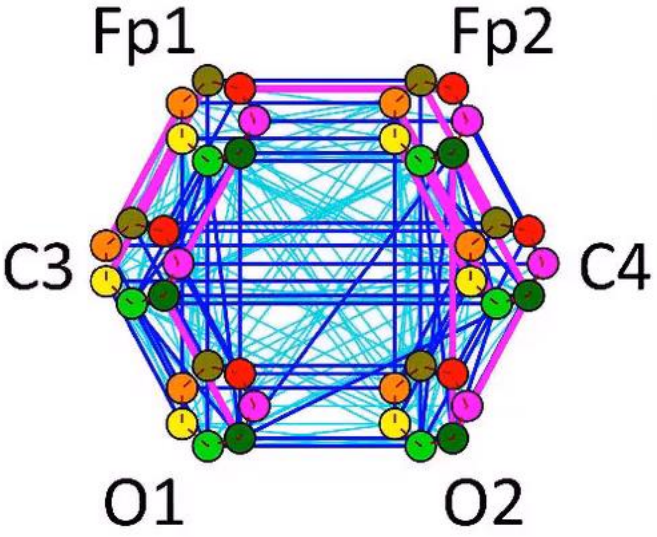
Eye movements

→ Bursts in the dynamics of one system are coordinated with bursts in other systems with stable time delay

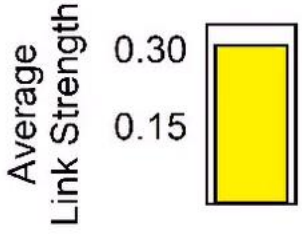
Level 3: Networked Interactions

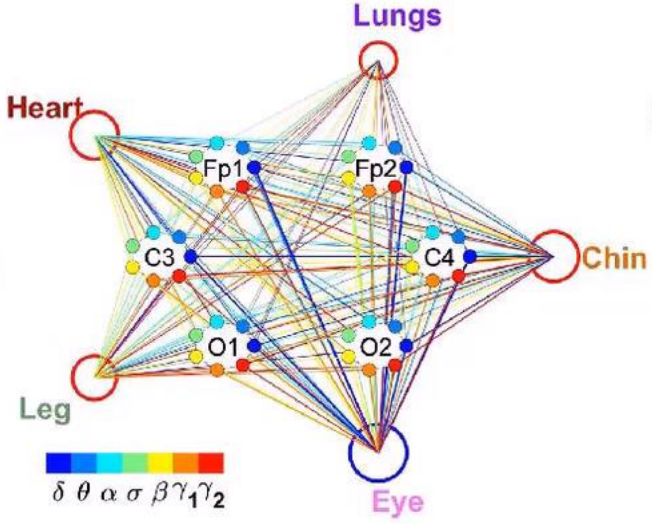
Network Physiology: Networks of brain activity and other physiologic systems across sleep stages



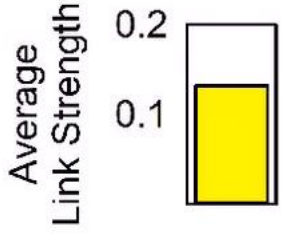


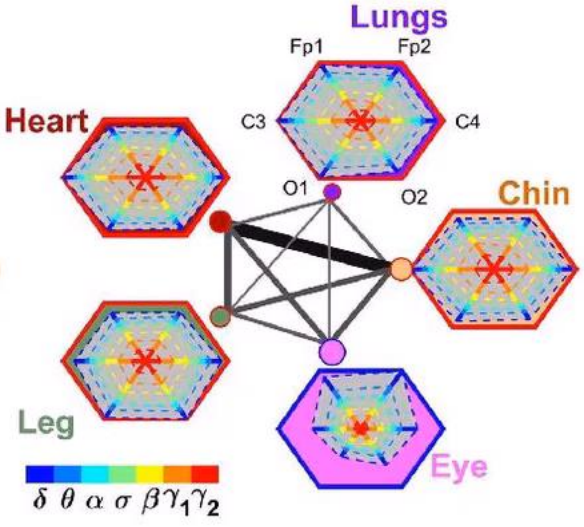
Brain-Brain



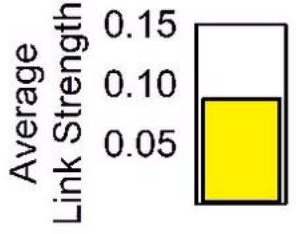


Brain-Organ



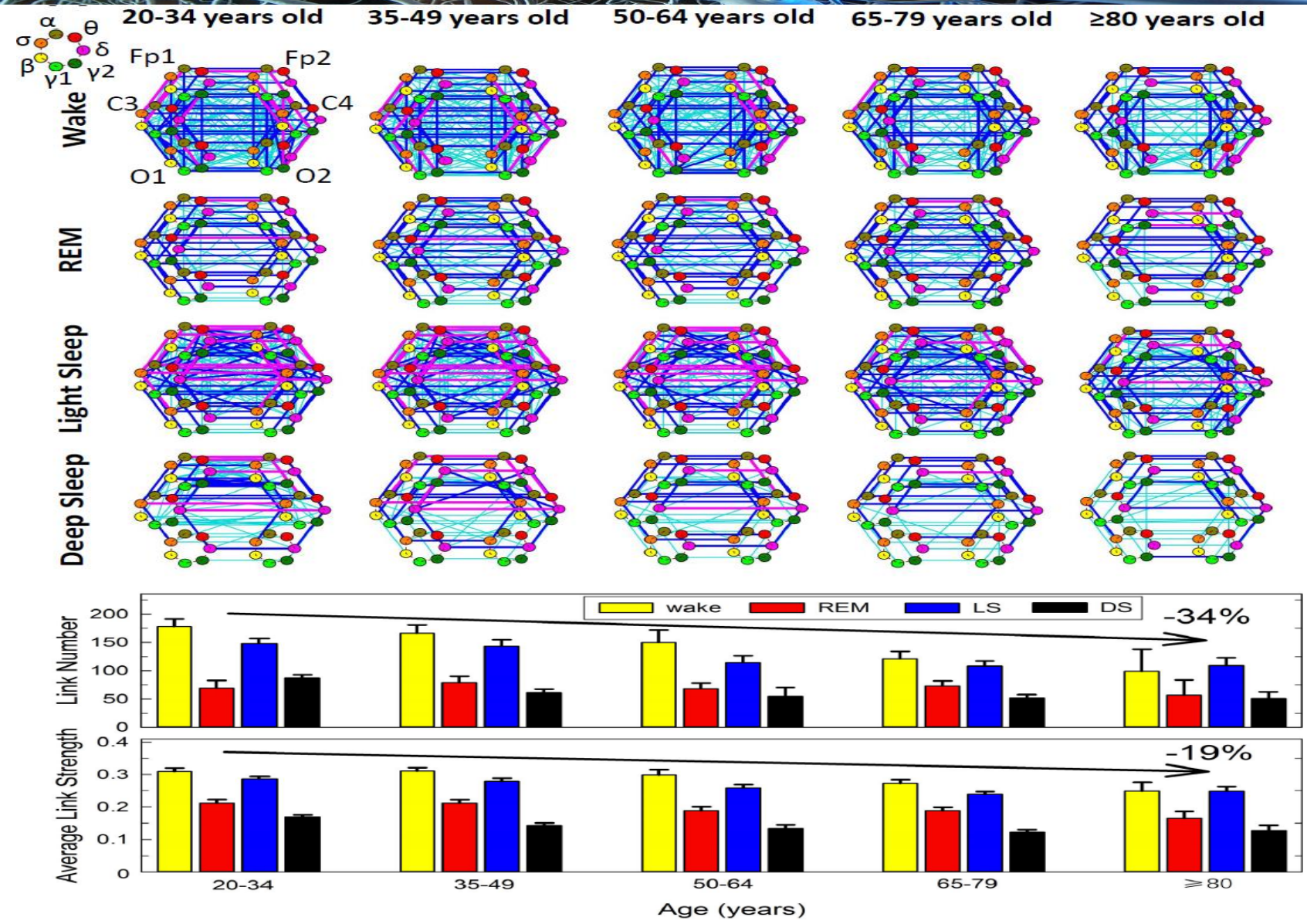


Organ-Organ



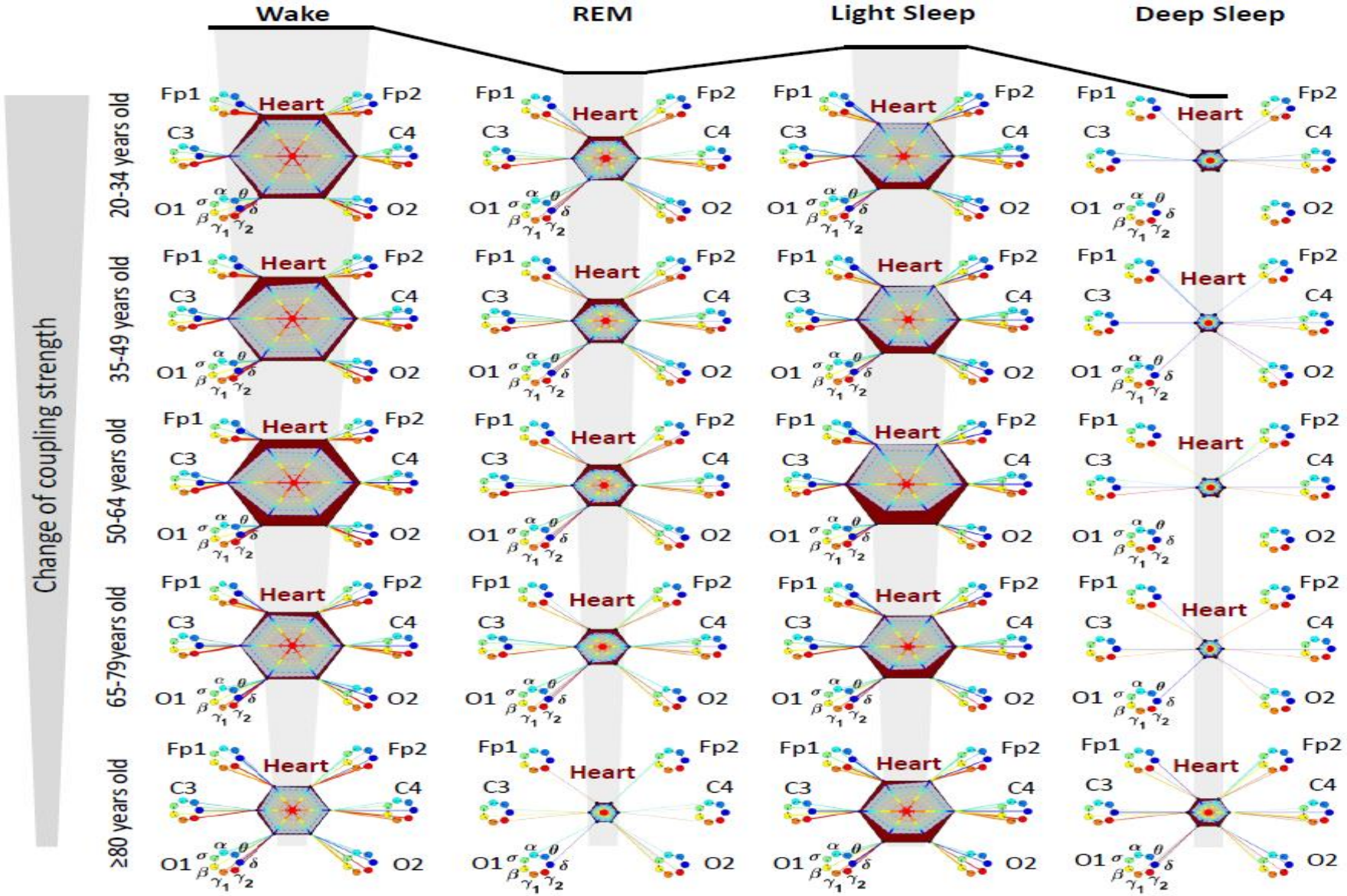
Level 3: Networked Interactions

Network Physiology: Implications for brain dynamics and neural plasticity



Level 3: Networked Interactions

Visualization: brain-organ interactions different physiologic states and age groups



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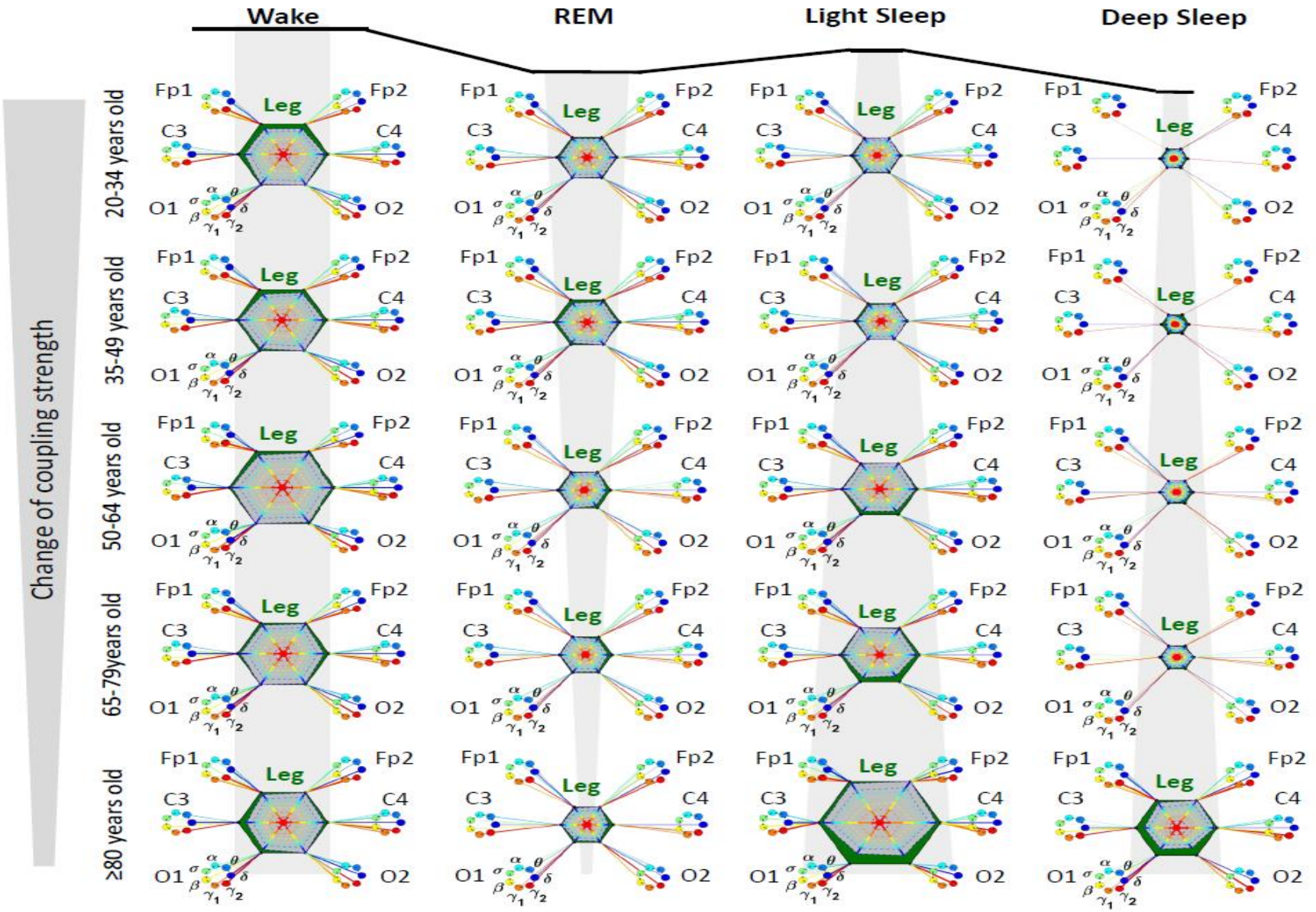
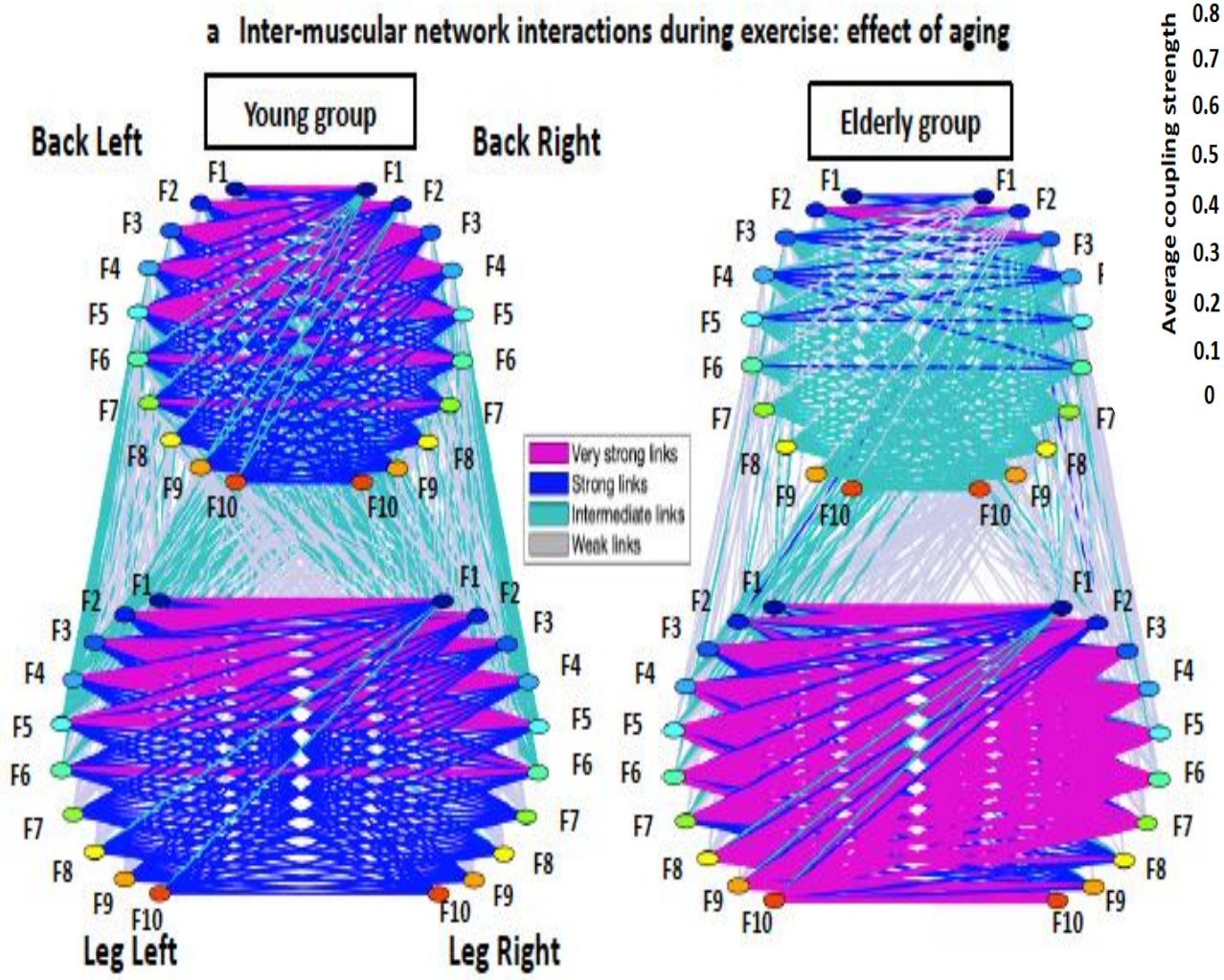
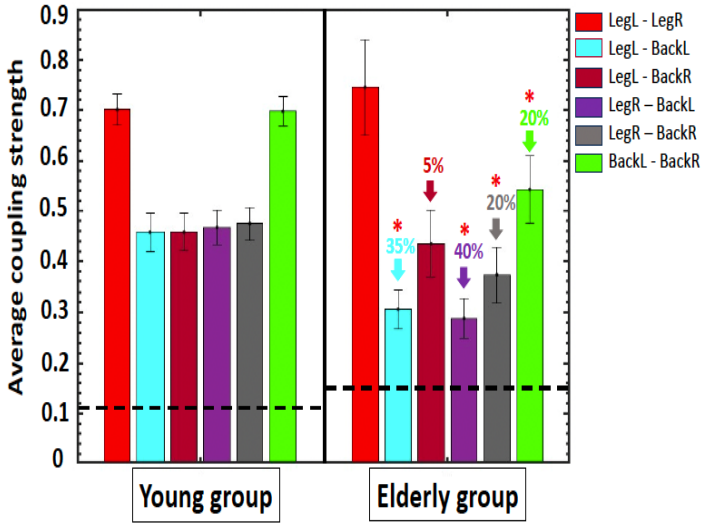


Level 3: Networked Interactions

Reorganization of muscle network interactions during exercise in young and elderly groups

Fatigue response & Resilience in muscle networks

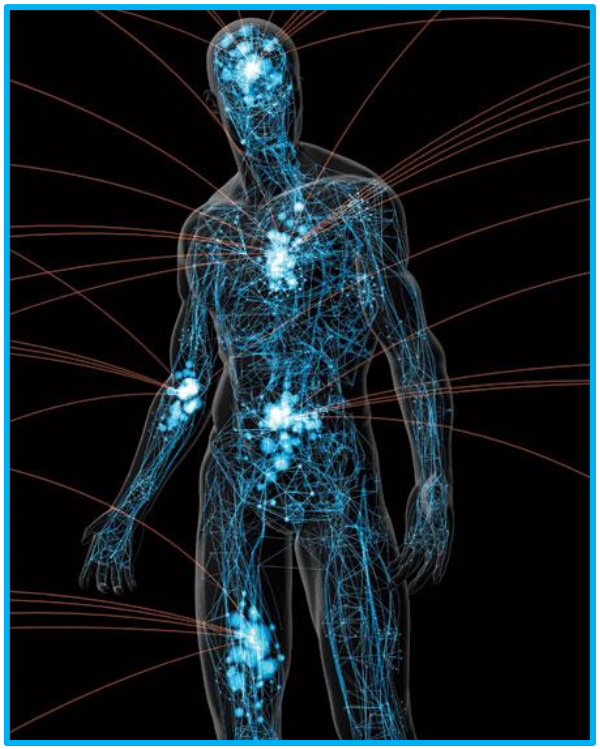




Big Data

Network Physiology and the Human Physiolome

Human body produces gigantic amount of Data & Information
Continuous streams of waveforms and physiologic parameters



- brain: EEG, MEG, fMRI
- heart: Blood Pressure, ECG
- body temperature: Core, Brain, Peripheral
- muscles: EMG
- liver: Albumin, Phosphatase, GGT
- lungs: CO_2, O_2, Tidal Volume
- hormones: Oxytocin, Dopamine, Serotonin
- kidneys: Blood flow, Urinalysis, Creatinine

High frequency recordings (10^2-10^3Hz)
Number of data points per person:
(just for 100 parameters)

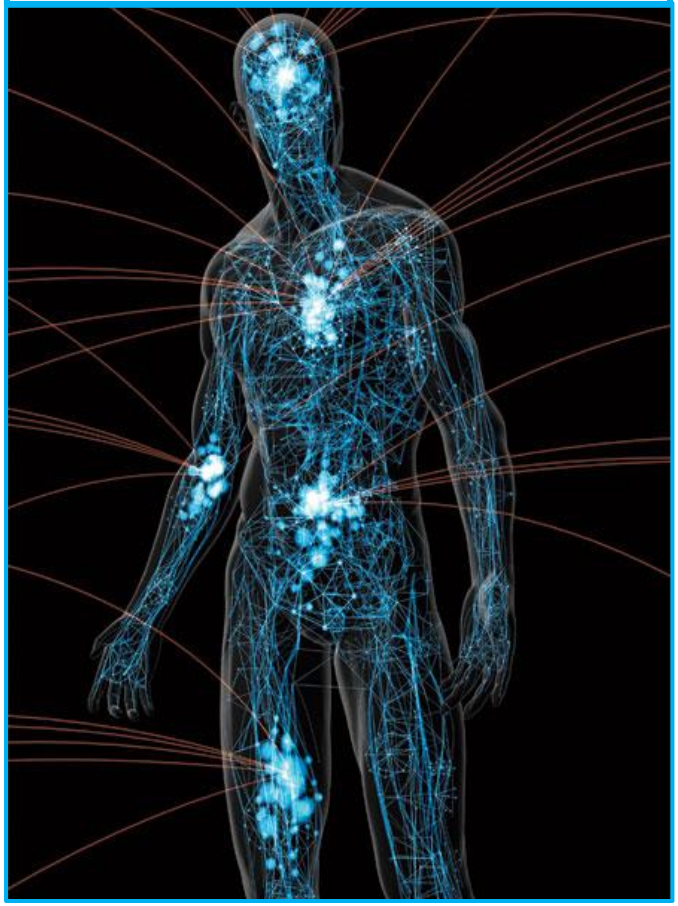
1 Day	1 Year	Life Time
~10^{10}	~10^{12}	~10^{14}

Vision

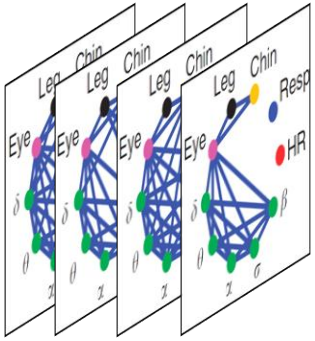
Physiology and Medicine

Such Atlas would contain:

Atlas of Dynamic Interactions of Organ Systems

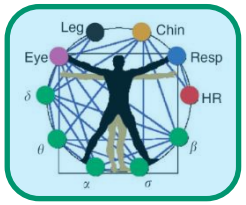


Catalog of reference maps representing dynamical organ interactions under:

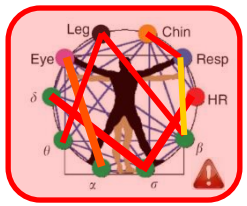


- **healthy conditions**
- **age groups**
- **different physiologic states (rest/exercise, sleep/wake, sleep stages, circadian phases)**
- **pathological conditions (multiple organ failure, coma, heart failure, sleep apnea …)**

Quantitative assessment of variability in coupling strength for each map at a given state or condition

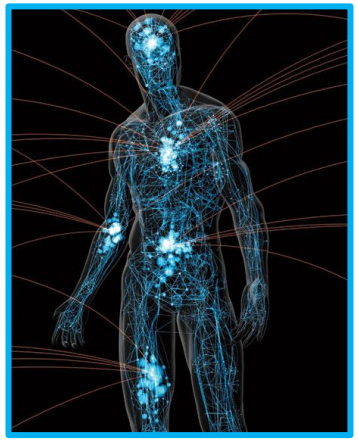


- **Boundaries of coupling variability for normal conditions**



- **Establishing a critical zone for disease development as a function of age and physiologic state**

Network Physiology and the Human Physiolome



Knowledge Gaps

Despite the importance to:

- **understanding basic physiologic functions**
- **clinical relevance**

We <u>do not know</u> how organ systems dynamically interact as a network to coordinate and optimize their functions

Fundamental Question:

What are the "blueprint reference" network maps that uniquely define physiologic states and functions in health, aging and disease?

Research Opportunities

- **Identify *<u>laws of systems cross-communication</u>* from sub-cellular to organism level and their alteration with aging and disease**
- **Establish *<u>regulatory mechanisms</u>* of network integration and re-organization with aging and disease**
- **Develop *<u>new class of network-based dynamic markers</u>* of aging and disease: functional forms and strength of interaction; network connectivity and network modularity**