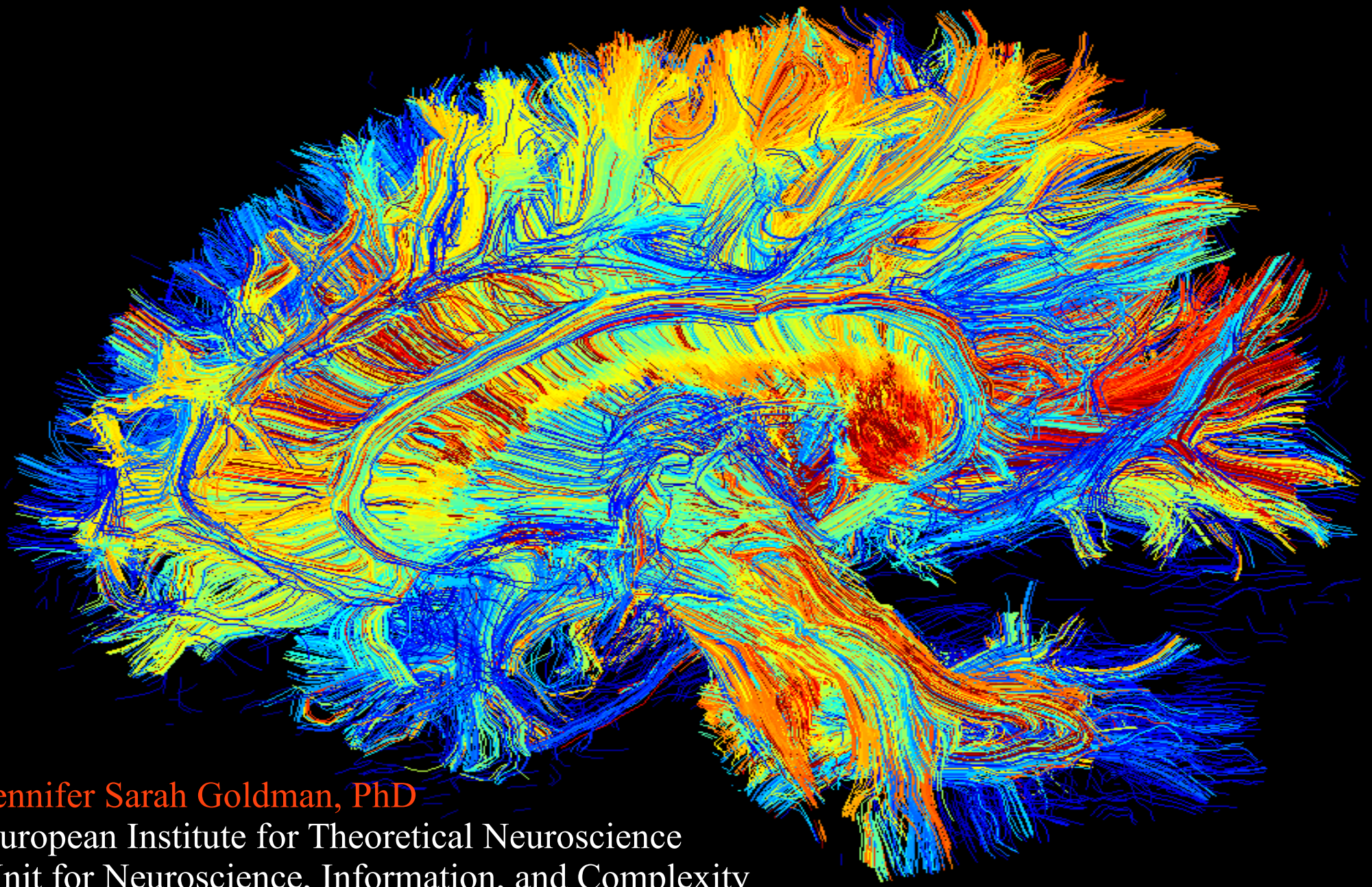
Systems science for medicine;
Synergy at the boundary between biology and physics



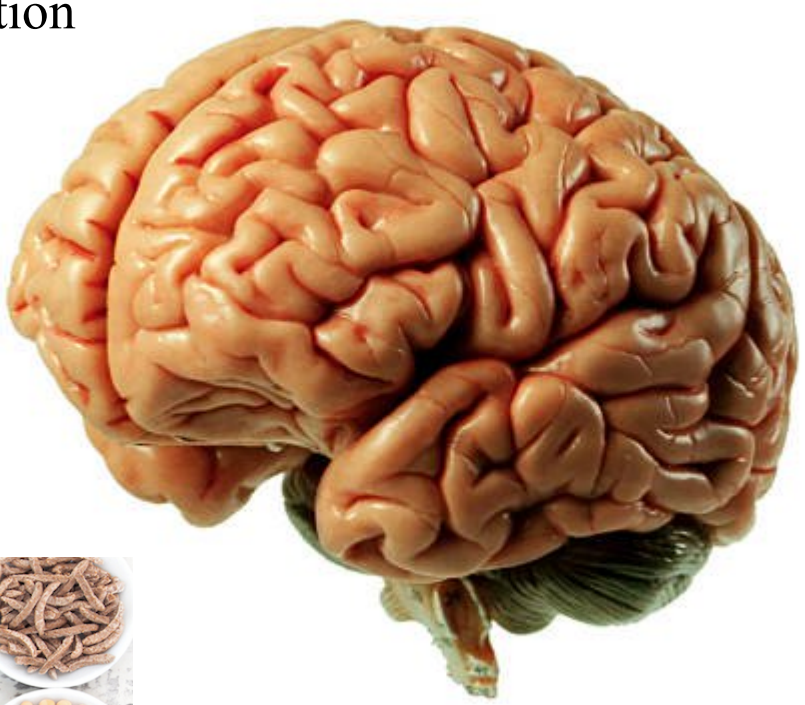
Jennifer Sarah Goldman, PhD
European Institute for Theoretical Neuroscience
Unit for Neuroscience, Information, and Complexity
CNRS, France

”If we could give every individual the right amount of nourishment and exercise, we would have found the safest way to health.”

Hippocrates

Part I Current neurobiology for preventative medicine

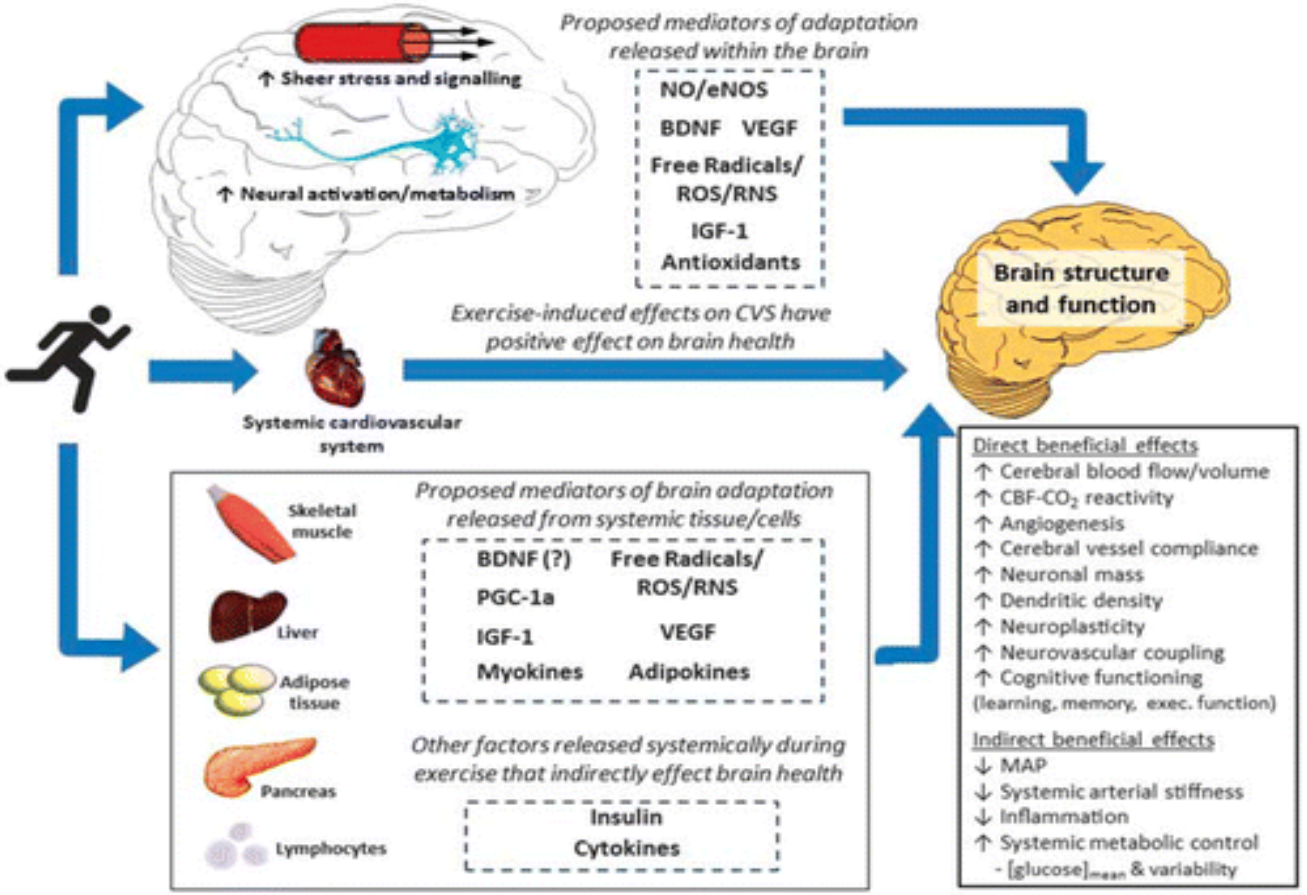
- Exercise
- Nutrition
- Sleep



Neurobiology of Exercise

”A strong body makes the mind strong.” Thomas Jefferson

Exercise enhances synaptic plasticity, cerebral angiogenesis, and neurogenesis (Dishman et al. 2006, Lucas et al., 2015), enhancing cognitive function across the lifespan (Hillman et al., 2008).

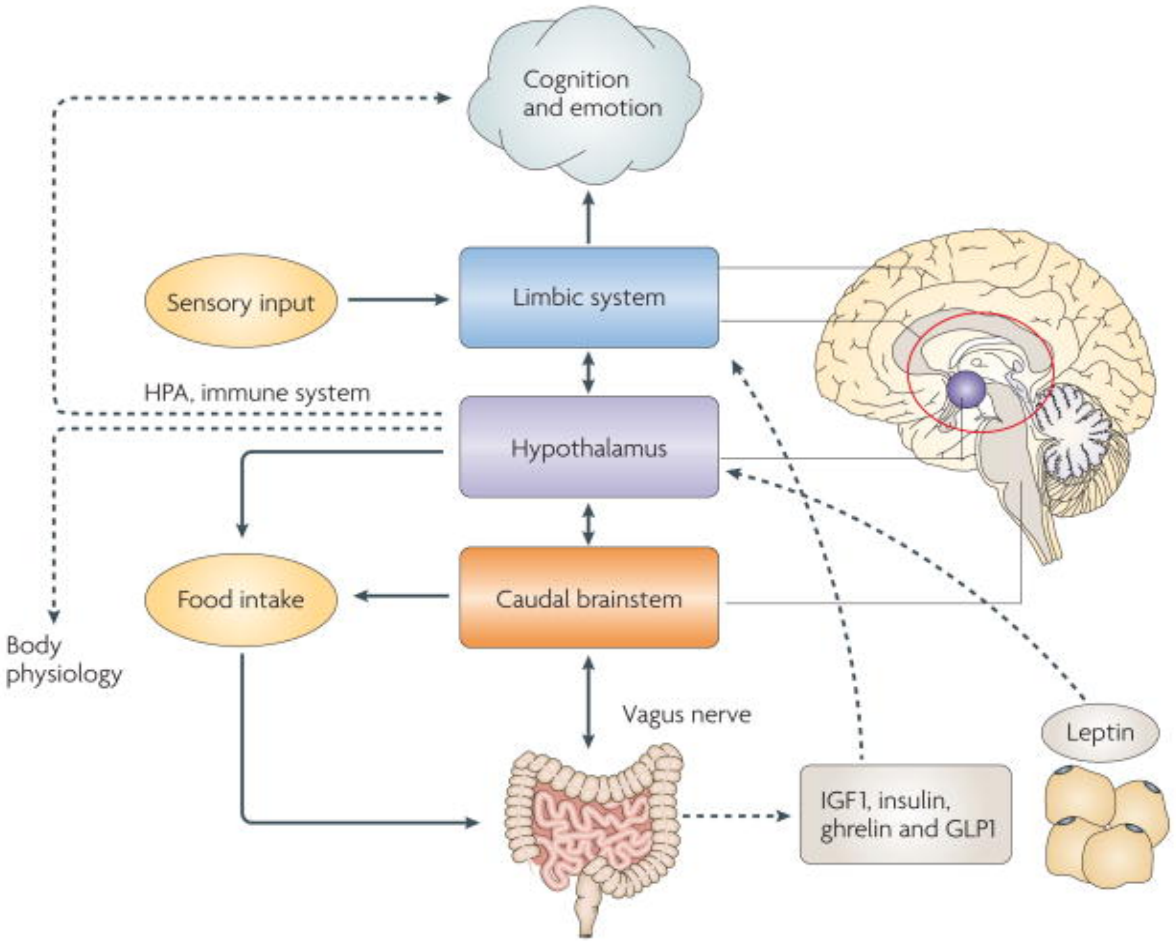


BDNF, brain-derived neurotrophic factor; CBF, cerebral blood flow; CO2, carbon dioxide; eNOS, endothelial nitric oxide synthase; IGF-1, insulin-like growth factor 1; MAP, mean arterial blood pressure; NO, nitric oxide; PGC-1α, peroxisome proliferator-activated receptor-γ coactivator; ROS, reactive oxygen species; RNS, reactive nitrogen species; VEGF, vascular endothelial growth factor.

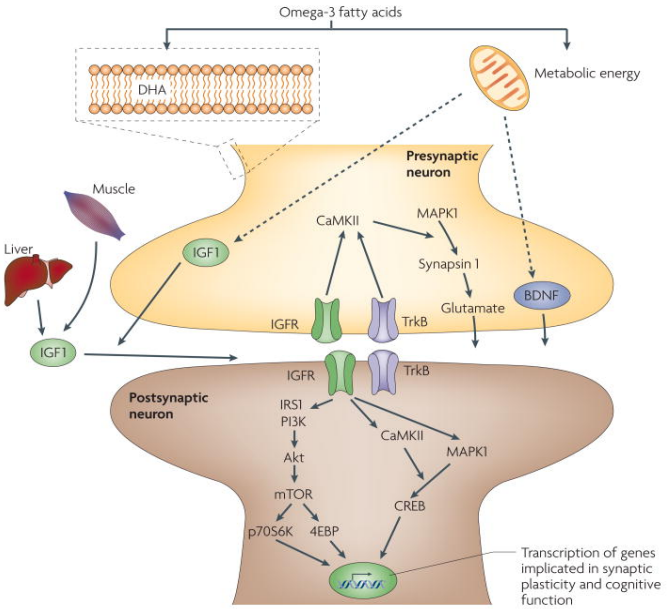
Neurobiology of Nutrition

Classically:

- Means to provide energy for high metabolic demands of the brain
- Building material for constantly remodeling networks

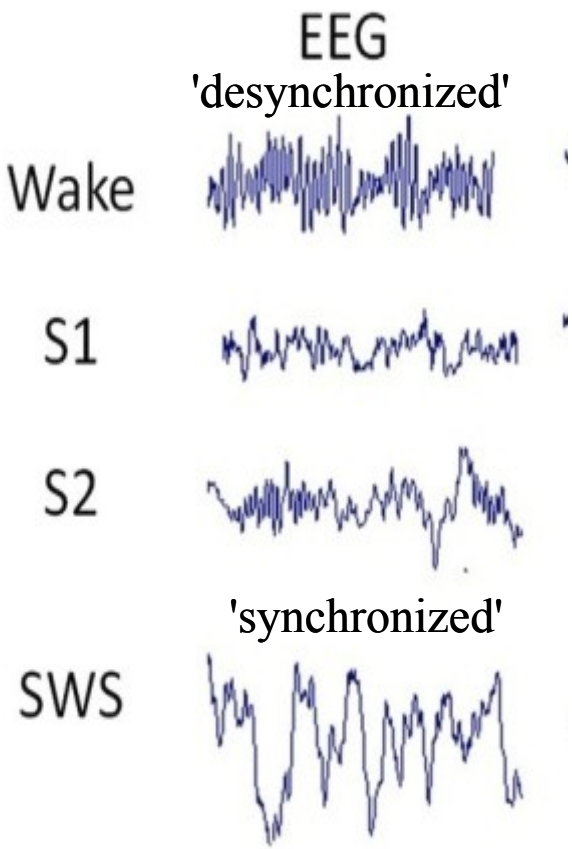


Now widely recognized that diet importantly modulates neural function through many central and peripheral signals (Gomez-Pinilla, 2008)



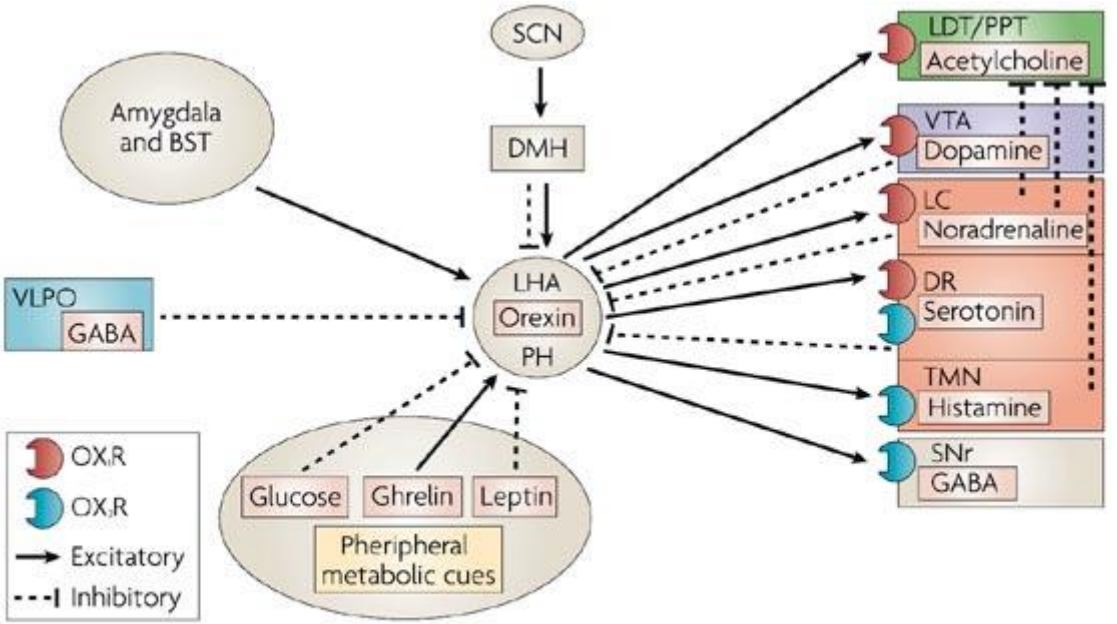
Neurobiology of Sleep

Sleep is an important modulator of homeostasis throughout the body



At lower levels of consciousness, neural EM signals become
larger in magnitude and less complex

Sleep deprivation
Modulates endocrine, metabolic, and immune function
Increases plasma norepinephrine, evening cortisol, and inflammatory markers
Impairs glucose tolerance
Ultimately results in death

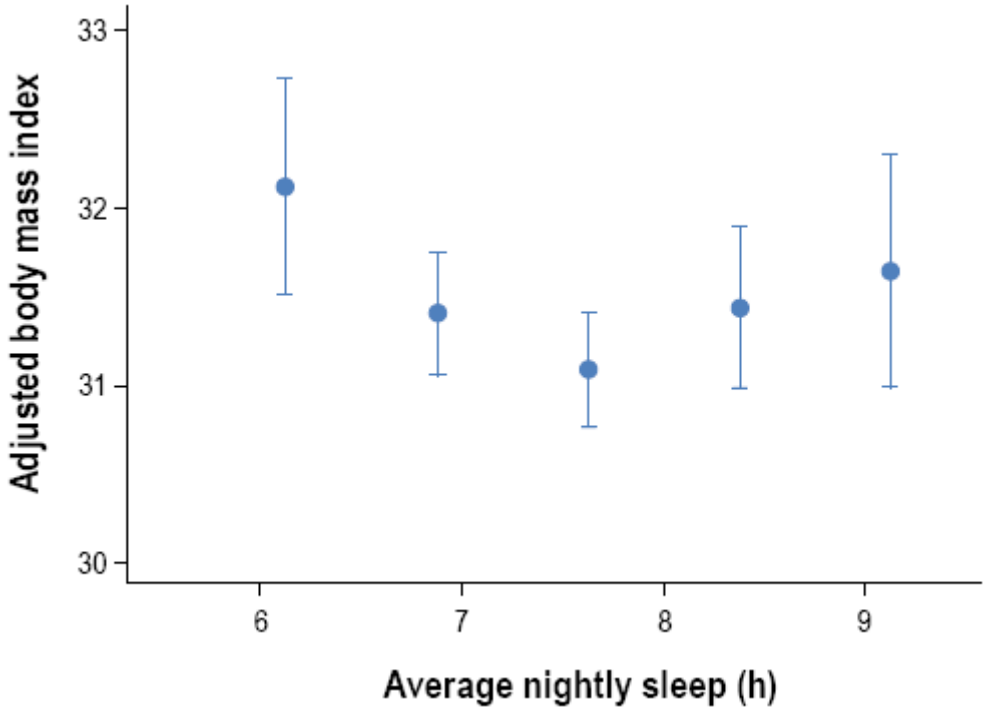


Part II

Formalizing knowledge?

Nonlinearities!

Excess exercise, nutrition, or sleep can be unhealthy



Luyster, et al. 2012

Functional interaction between exercise, nutrition, and sleep

Incorporating and indexing evidence

How can we understand the wealth of existent data??

Can we formalize this knowledge?

Can models make new predictions for patients and inform new empirical analyses?

Incorporating and indexing evidence;

a possible formal description of health-promoting factors?

$$\left.\begin{array}{l} A_e \\ A_s \\ A_n \end{array}\right\}$$ Magnitude of exercise, sleep, and nutrition

$$\left.\begin{array}{l} G_e \\ G_s \\ G_n \end{array}\right\}$$ Fitness resulting from exercise, sleep, and nutrition

$$\begin{aligned} G_e &= \alpha_{ee}A_e + \alpha_{es}A_s + \alpha_{en}A_n \\ G_s &= \alpha_{se}A_e + \alpha_{ss}A_s + \alpha_{sn}A_n \\ G_n &= \alpha_{ne}A_e + \alpha_{ns}A_s + \alpha_{nn}A_n \end{aligned}$$ Interactions between exercise, sleep, and nutrition

$$H = \sum_{i=e,s,n} \beta_i G_i$$ Health as a function of exercise, sleep, and nutrition

$$H = H_{max} \iff \frac{\partial H}{\partial A_i} = 0 \qquad \forall i \in \{e, s, n\}$$ Find values of exercise, sleep, and nutrition that maximize health

Thank you: Michelle Rudolf-Lillith, Matteo di Volo, Trang-Anh Nghiem

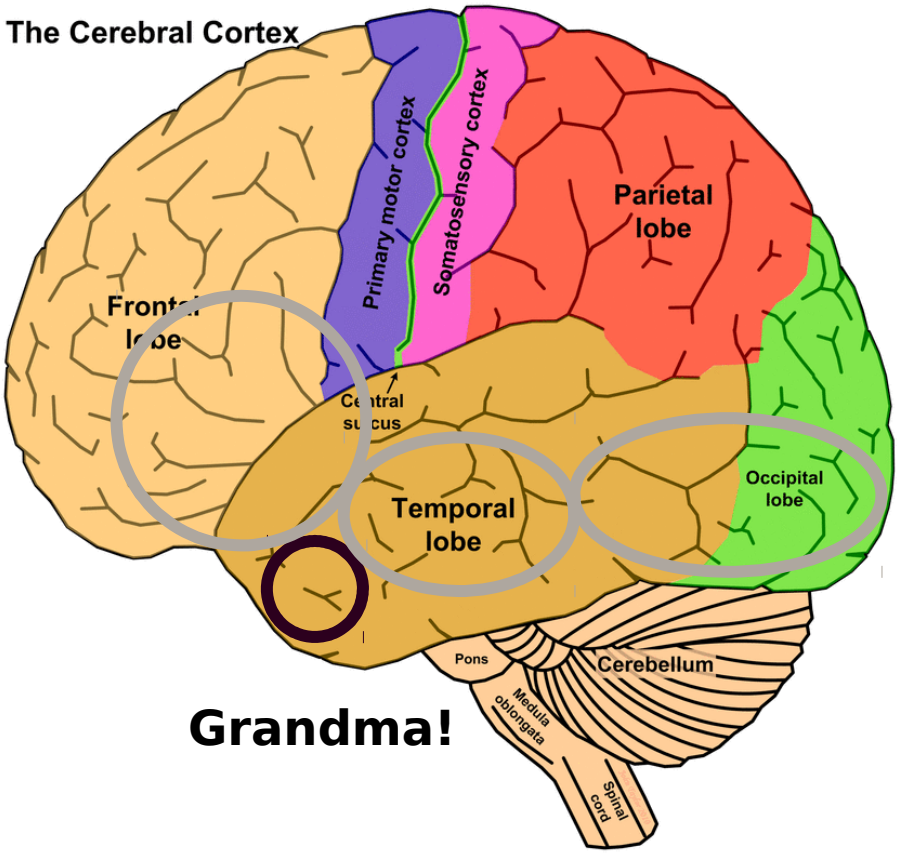
Part III

Current work

Understanding brain function

Persistence or repetition of a reverberatory activity - or trace

Hebb, D.O. (1949). The Organization of Behavior. New York: Wiley & Sons.



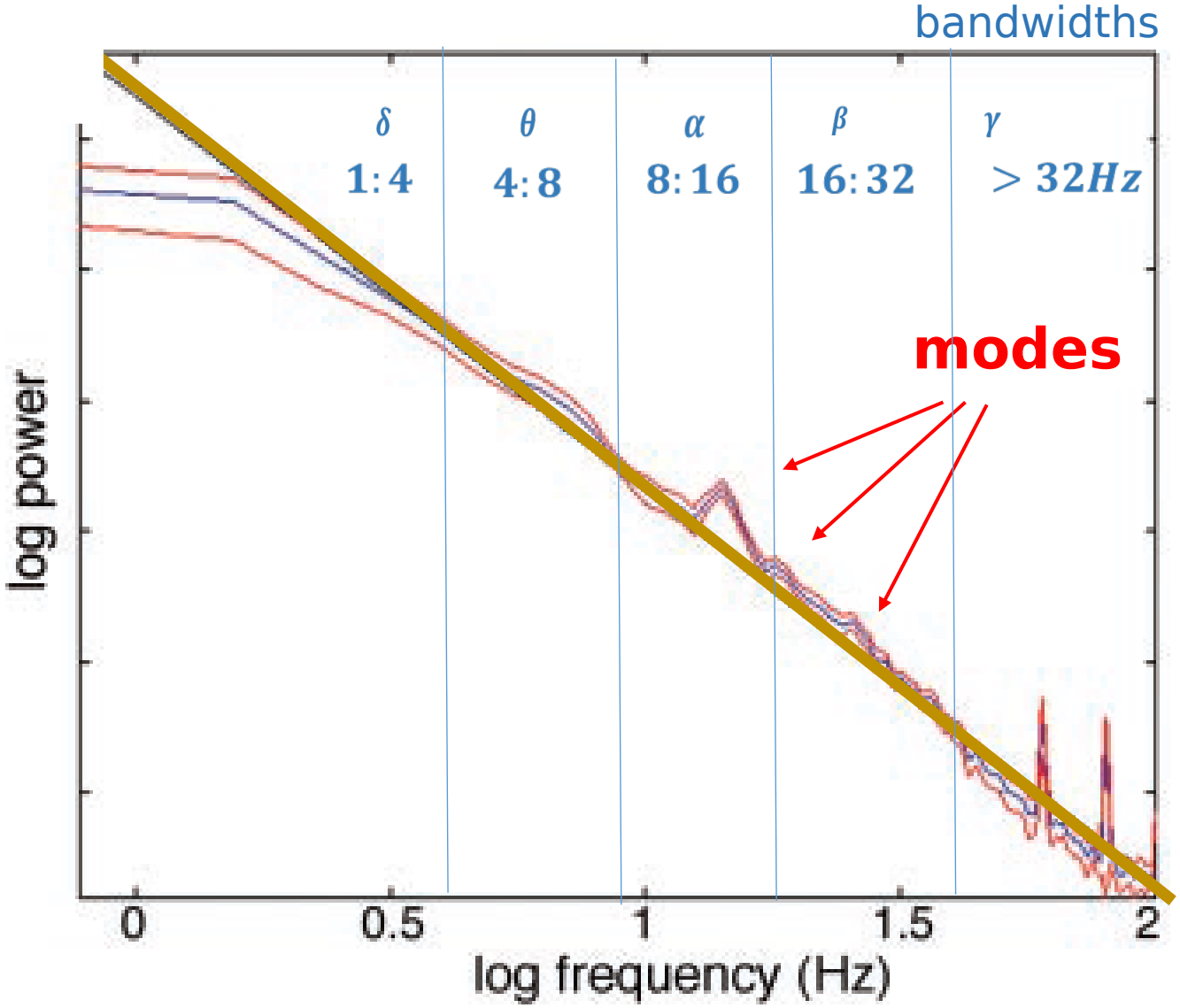
Power Spectra; Neural EM signals

$P=1/f^{\beta}$

Spectral power at every frequency

Modes:
Some frequencies are more represented;

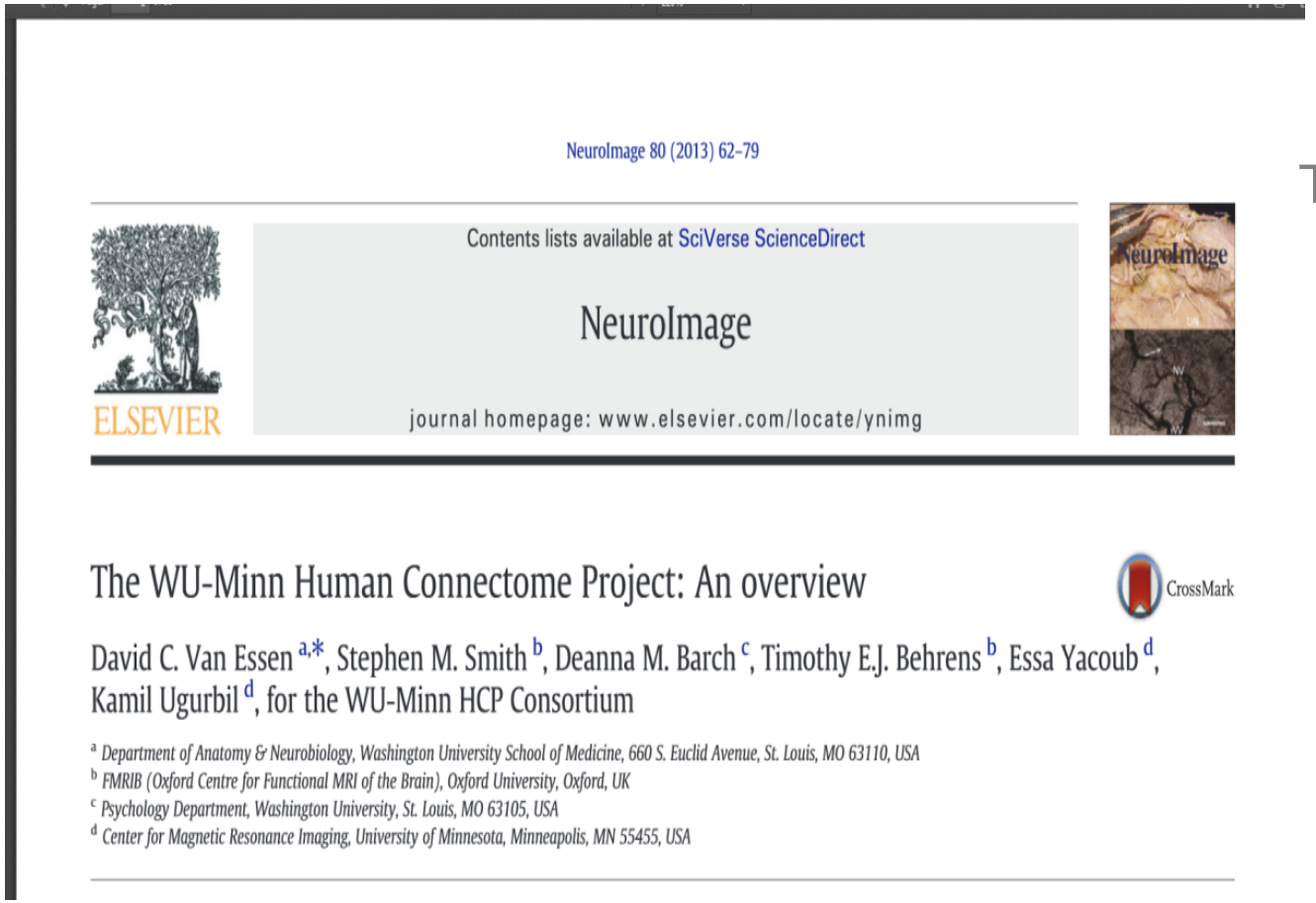
reverberations



Buzsaki and Draguhn 2004

Can we find a more formal description of the organization of modes?

Data



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ELSEVIER

The WU-Minn Human Connectome Project: An overview

David C. Van Essen [a,*], Stephen M. Smith [b], Deanna M. Barch [c], Timothy E.J. Behrens [b], Essa Yacoub [d], Kamil Ugurbil [d], for the WU-Minn HCP Consortium

[a] Department of Anatomy & Neurobiology, Washington University School of Medicine, 660 S. Euclid Avenue, St. Louis, MO 63110, USA
[b] FMRIB (Oxford Centre for Functional MRI of the Brain), Oxford University, Oxford, UK
[c] Psychology Department, Washington University, St. Louis, MO 63105, USA
[d] Center for Magnetic Resonance Imaging, University of Minnesota, Minneapolis, MN 55455, USA

http://www.humanconnectome.org/data/

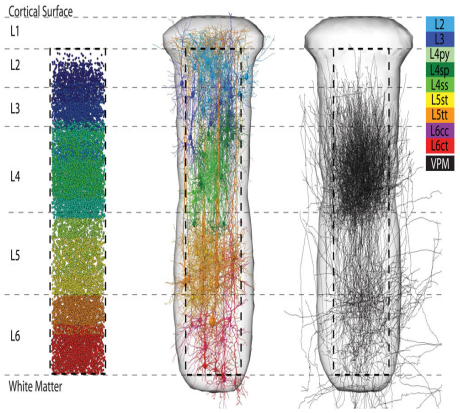
Subjects
1200 healthy adults
22-35yrs old
Twin and non-twin siblings

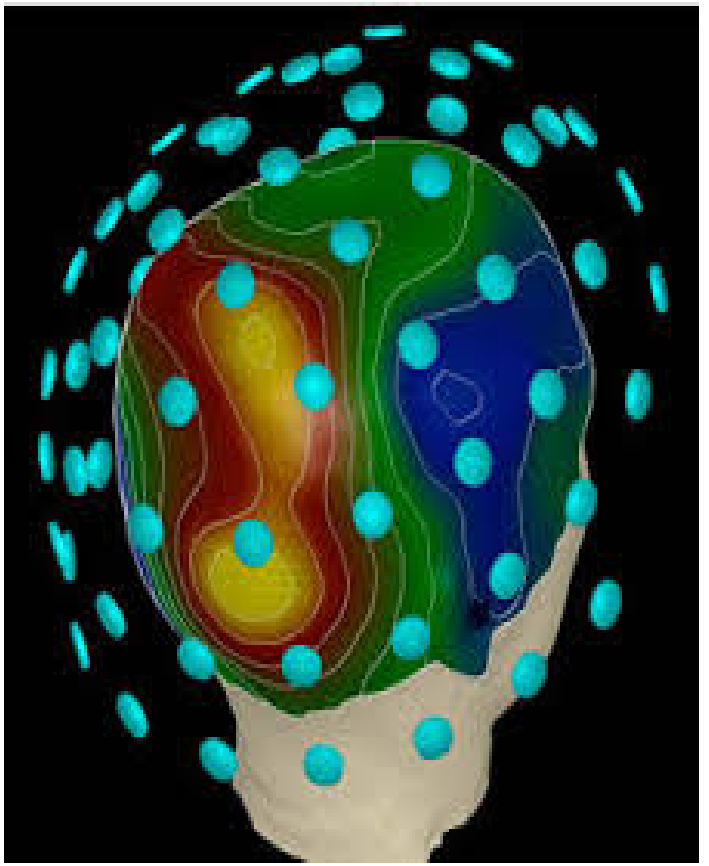
Imaging Data
dMRI
fMRI; rsfMRI & tfMRI
MEG; rsMEG & tMEG

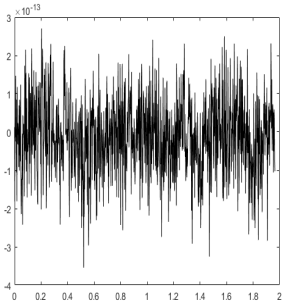
Subject Metadata
Task data scores
Task stimuli
Behavioral data
Physiological data

Magnetoencephalography (MEG)

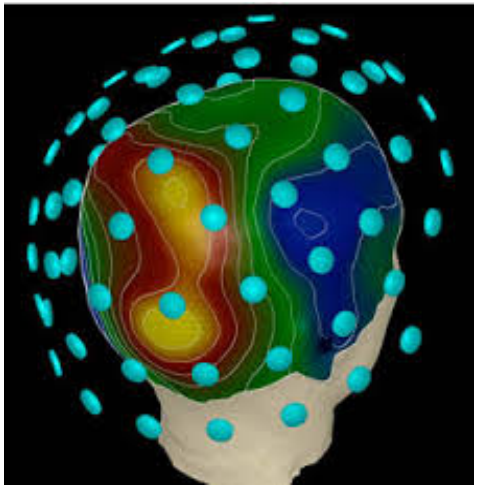
coordinated activity in 1000's of neurons generates magnetic fields measured at each of 248 sensors





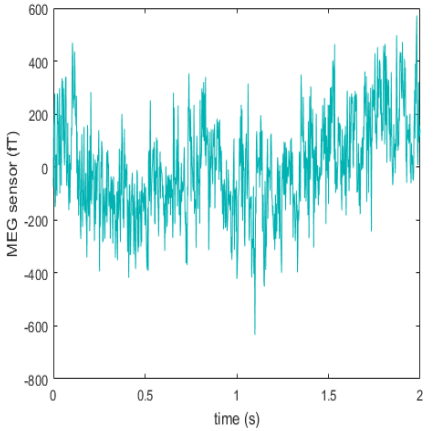


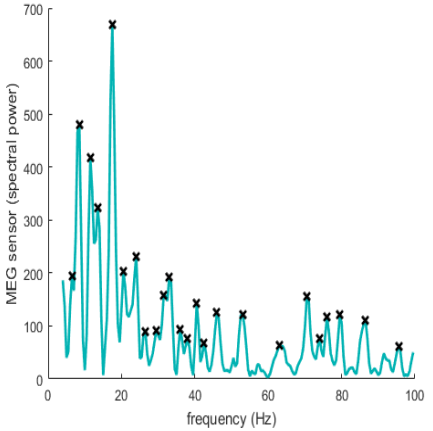
Data



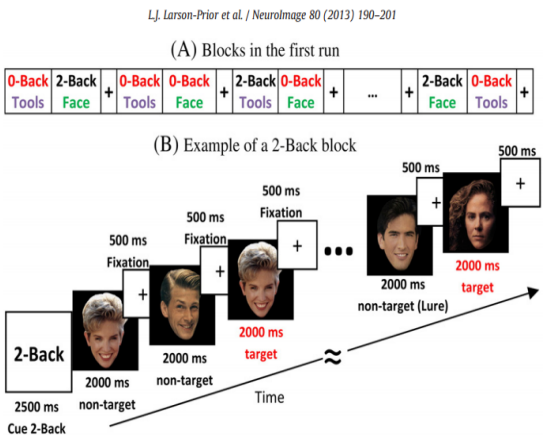
Resting state

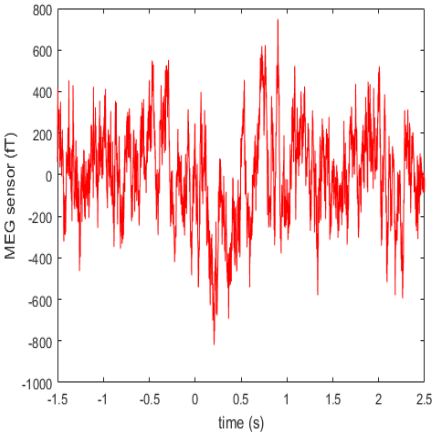
Eyes open, fixated

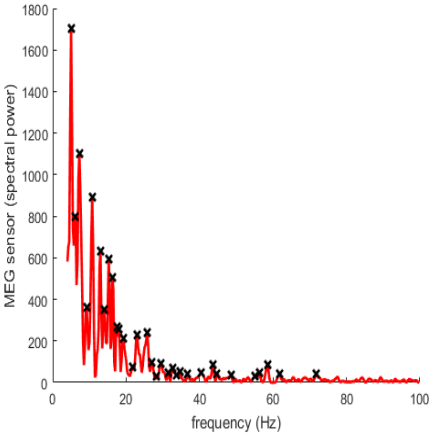




Working Memory (active)



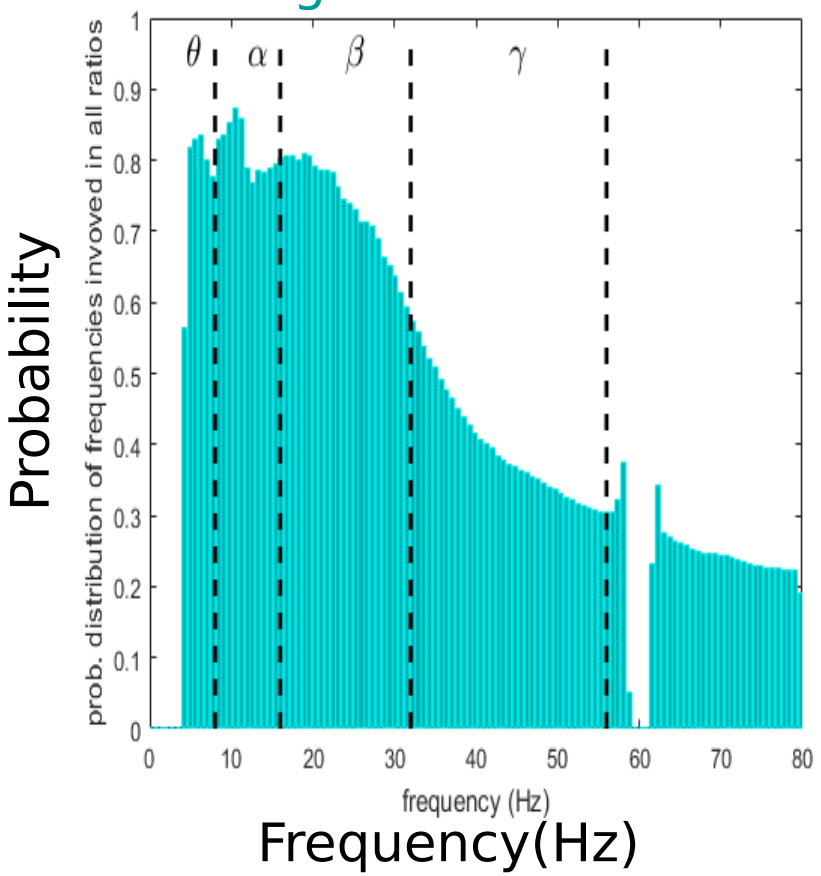




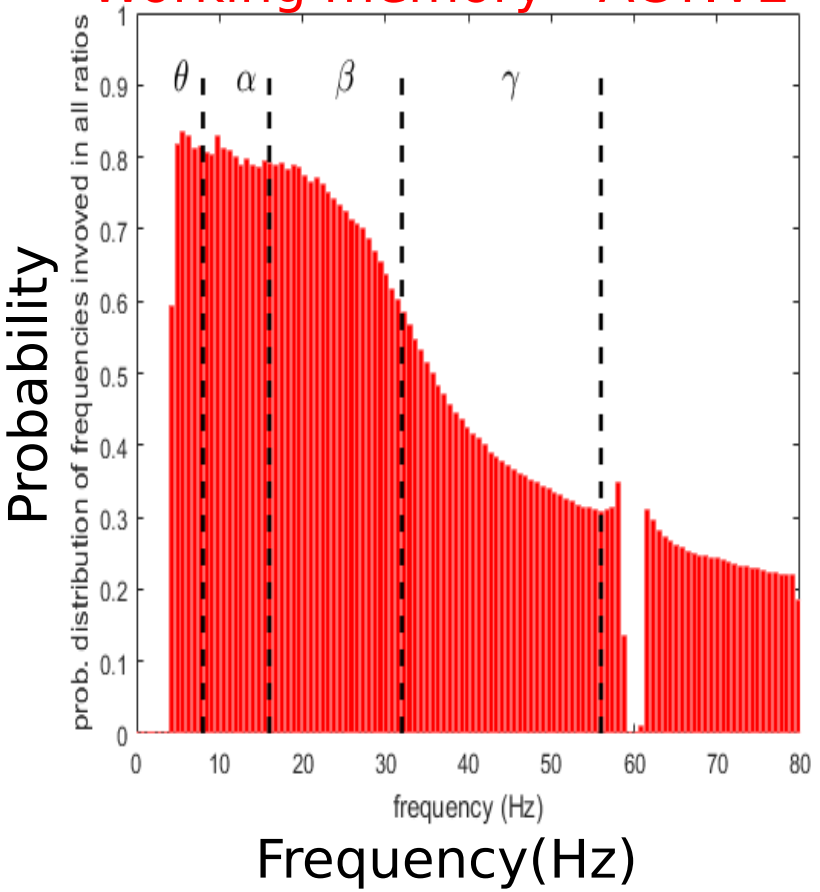
Histogram;

(all subjects, all epochs, all sensors)

Resting state - REST



Working memory - ACTIVE

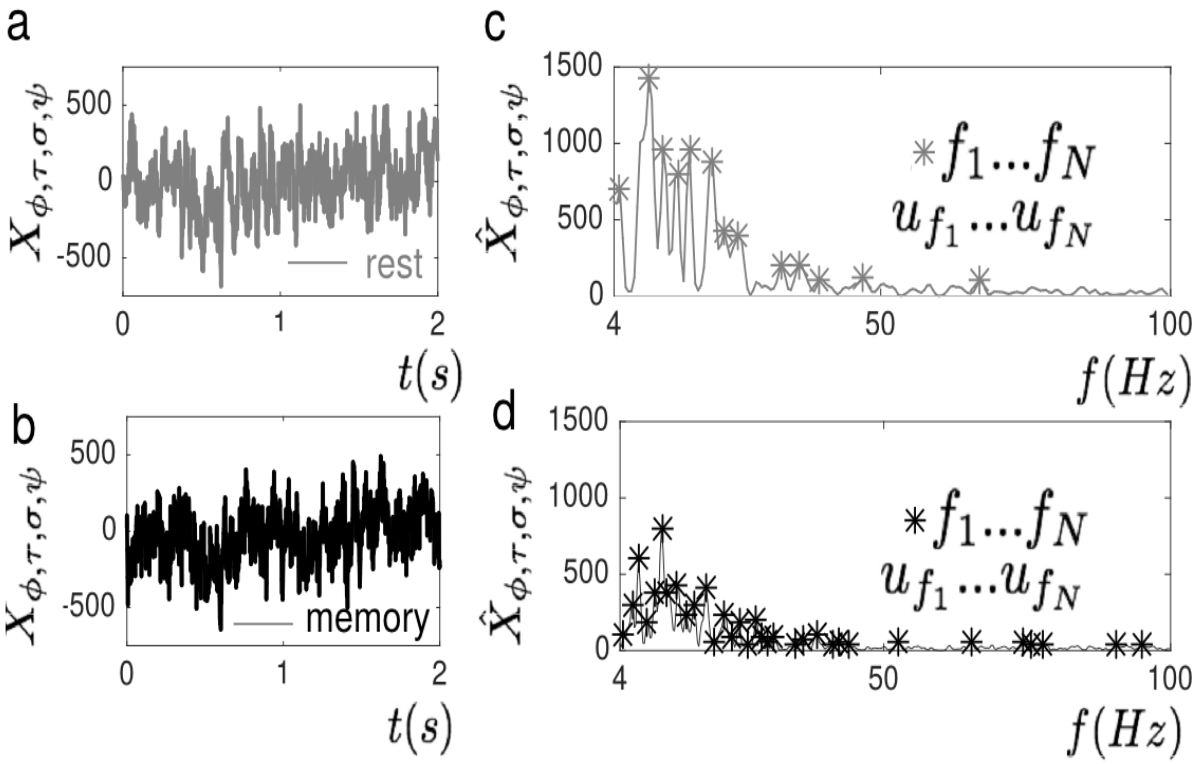


'THERMODYNAMIC' definitions in the frequency domain

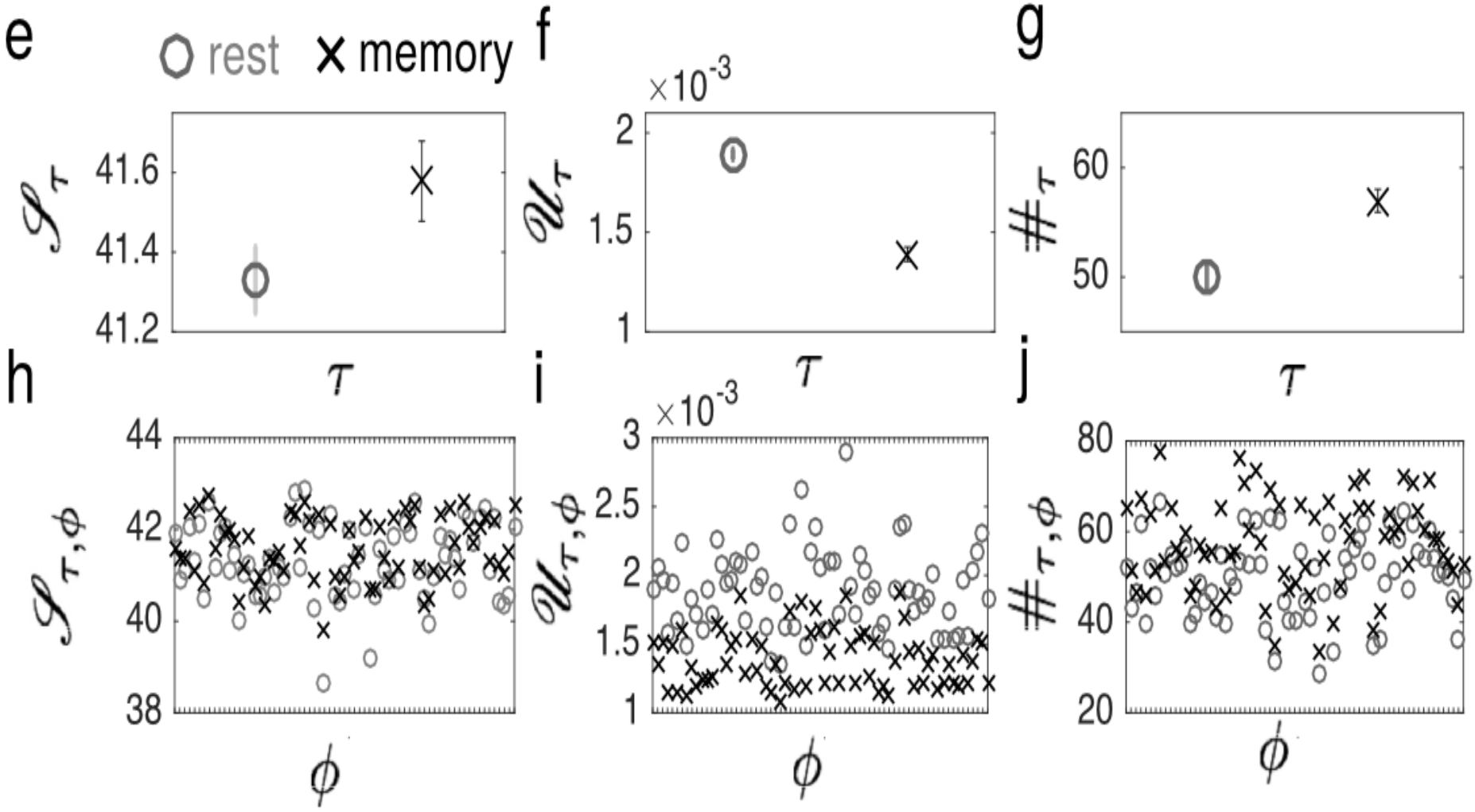
Specifically, we analyze the magnetic field, Xφ,τ,σ,ψ, measured for each subject φ = {1 . . . 69}, brain state τ ={rest, active}, sensor σ = {1 . . . 248}, and time epoch ψ = {1 . . . M} M is the number of epochs.

$$\mathcal{S}_{\phi,\tau} = -\sum_f P_{\phi,\tau}(f)\ln(P_{\phi,\tau}(f))$$

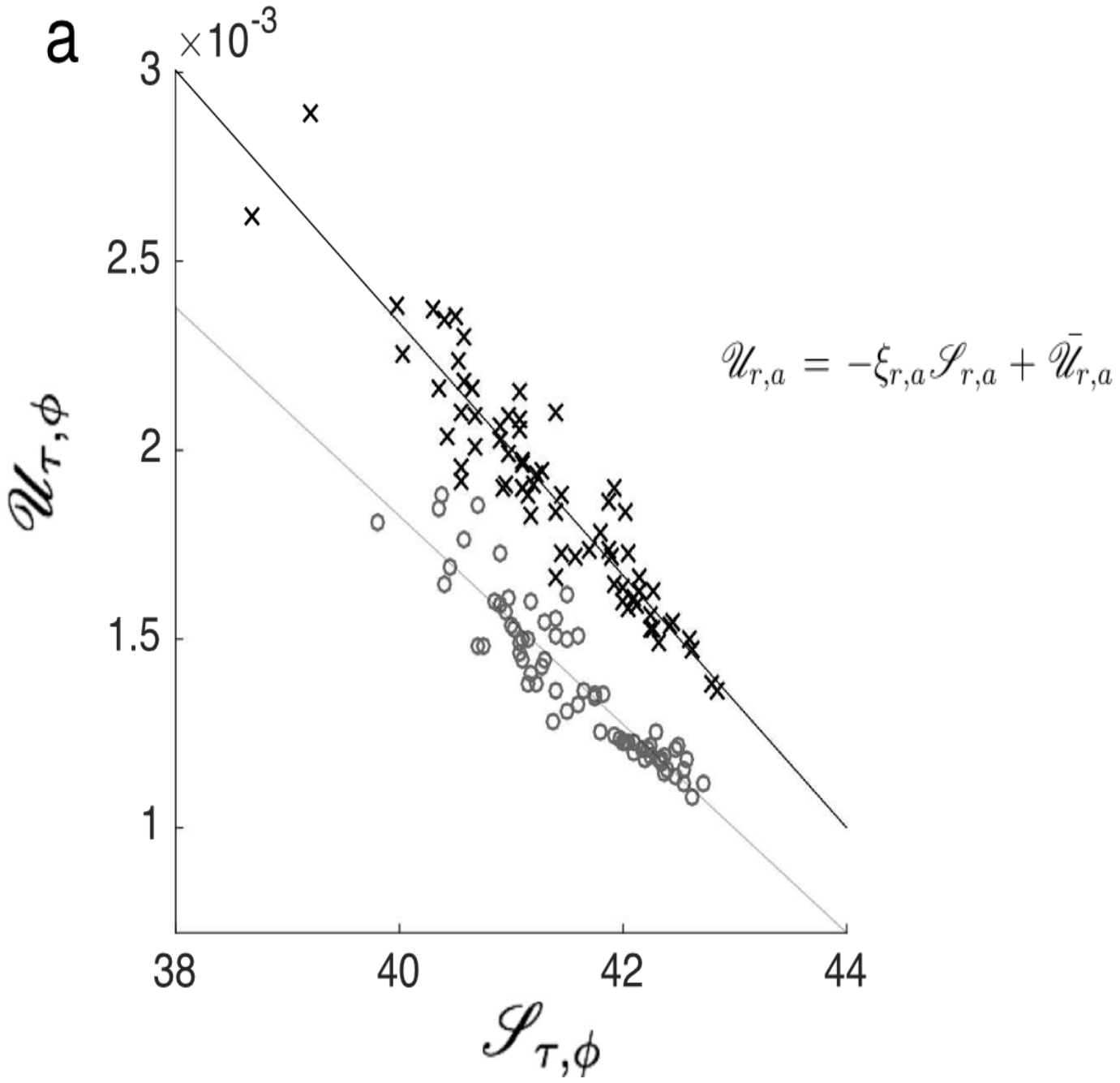
$$\mathcal{U}_{\phi,\tau} = \sum_f u_f$$



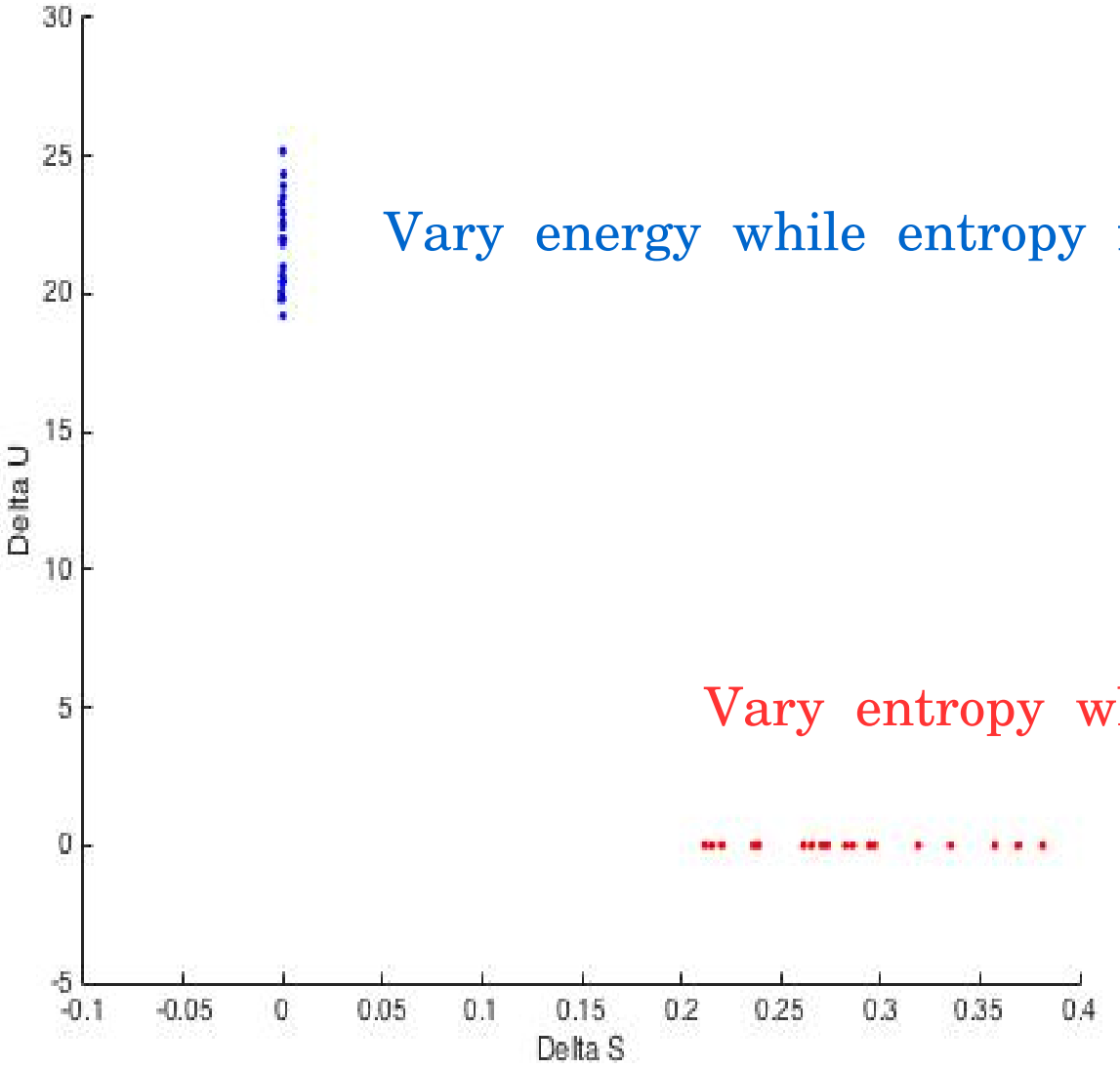
'THERMODYNAMIC' definitions in the frequency domain
Comparison between brain states



Linear relationship between state variables



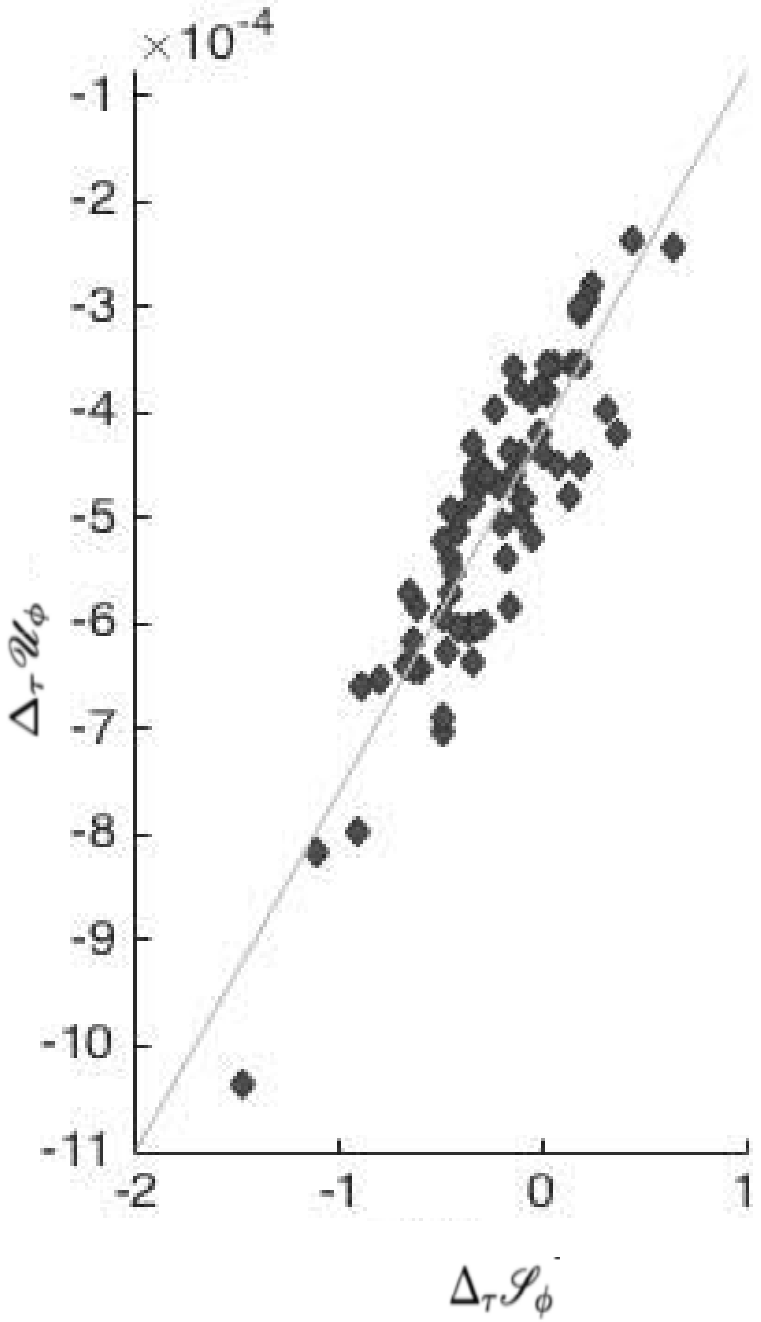
Non-tautological definitions



Vary energy while entropy is unchanged

Vary entropy while energy is unchanged

Conservation between brain states



$$\Delta_\tau \mathscr{U}_\phi = \mathscr{U}_{m,\phi} - \mathscr{U}_{r,\phi}$$

$$\Delta_\tau \mathscr{S}_\phi = \mathscr{S}_{m,\phi} - \mathscr{S}_{r,\phi}$$

$$\Delta U = \psi \Delta S + \Delta W$$

Mechanism?

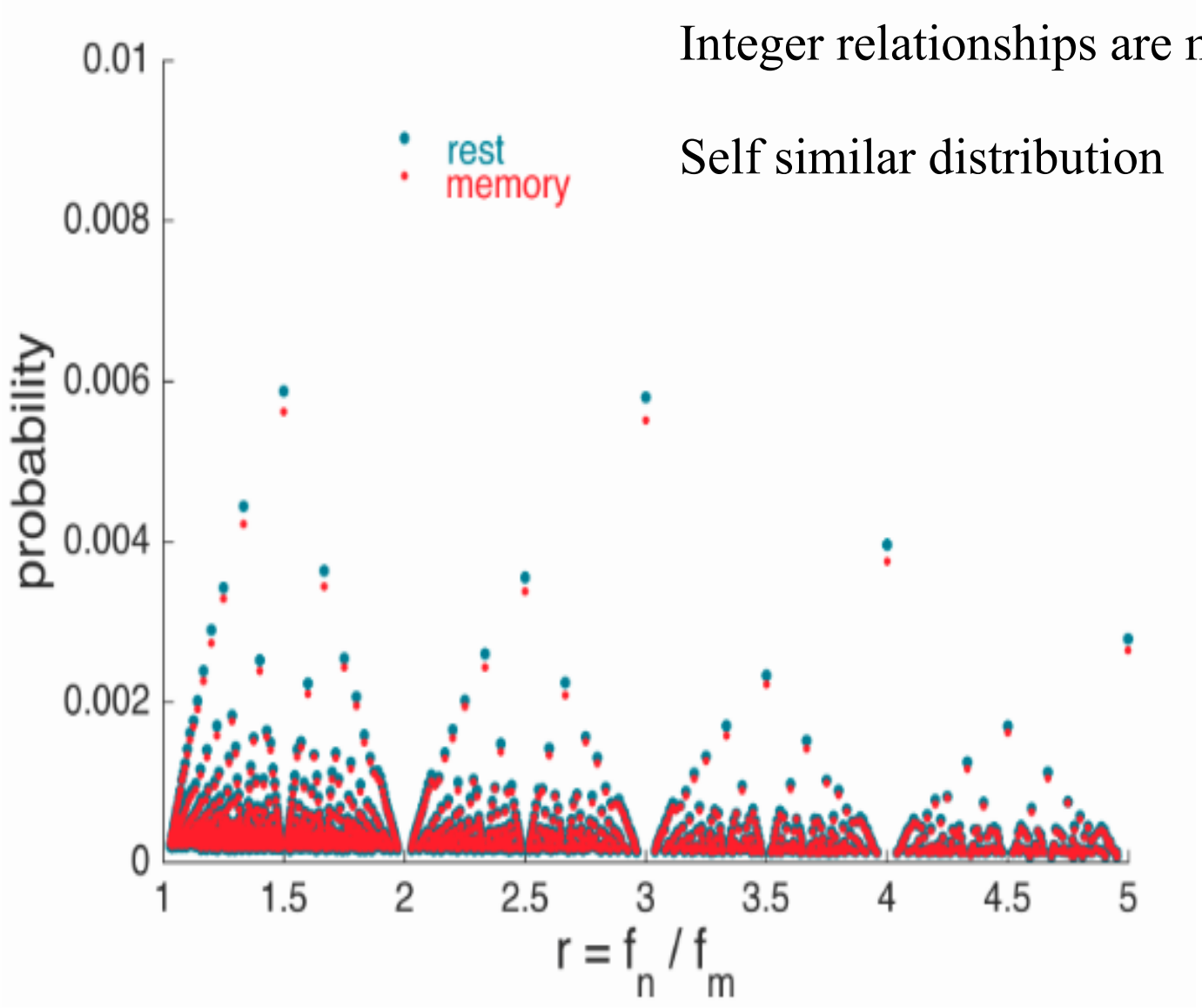
What could cause energy and entropy to vary together between brain states?

Coherence Principle; the orchestra

Harmony (ἁρμονία) and Energy

Harmony and Entropy

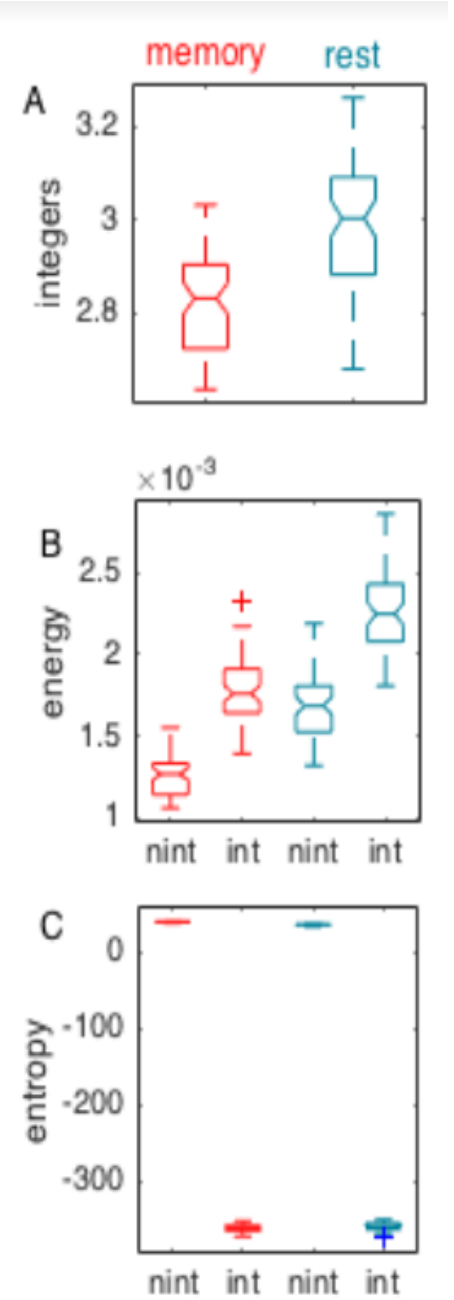
Probability of frequency ratios



Integer relationships are most common

Self similar distribution

Integer relationships between modes are more prevalent in resting than active brain states



Integer related modes are more energetic than non integer modes Especially in the resting state

Integer related modes represent a population with lower entropy than non integer related modes

Biology uses fundamental physics in common with the rest of the universe.

We must seek a more formal understanding of biological phenomena toward informing advances in future medicine.

Thank you






George Kostopoulos, Christian Bénar, Celia Greenwood,
Amir Shmuel, Gleb Bezgin, Stephen Clarke

Alain Destexhe

Jean Marc Lina

Wolf Singer

Alan Evans