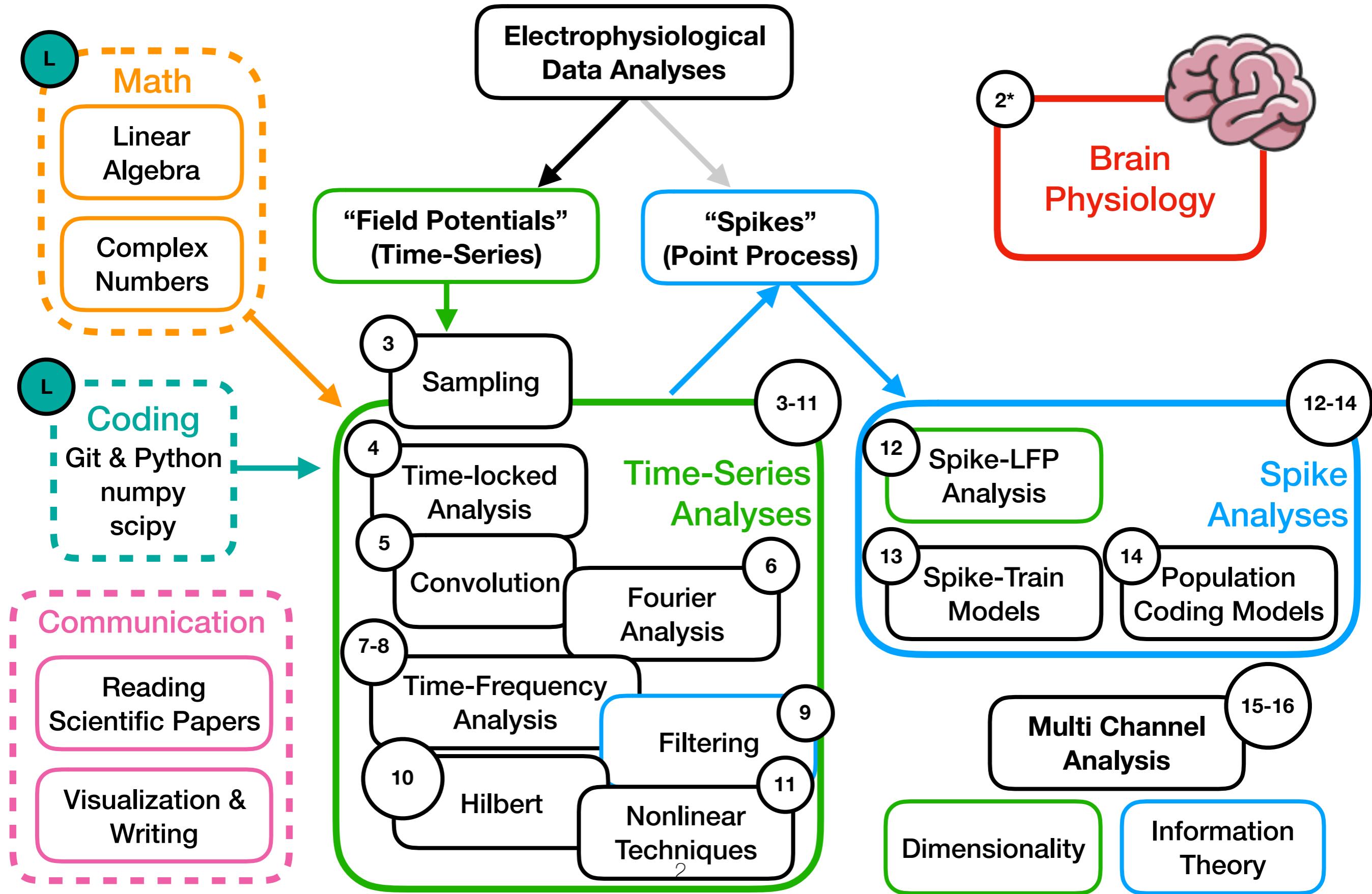


Finale

Lecture 17
August 1, 2019



Course Outline: Road Map

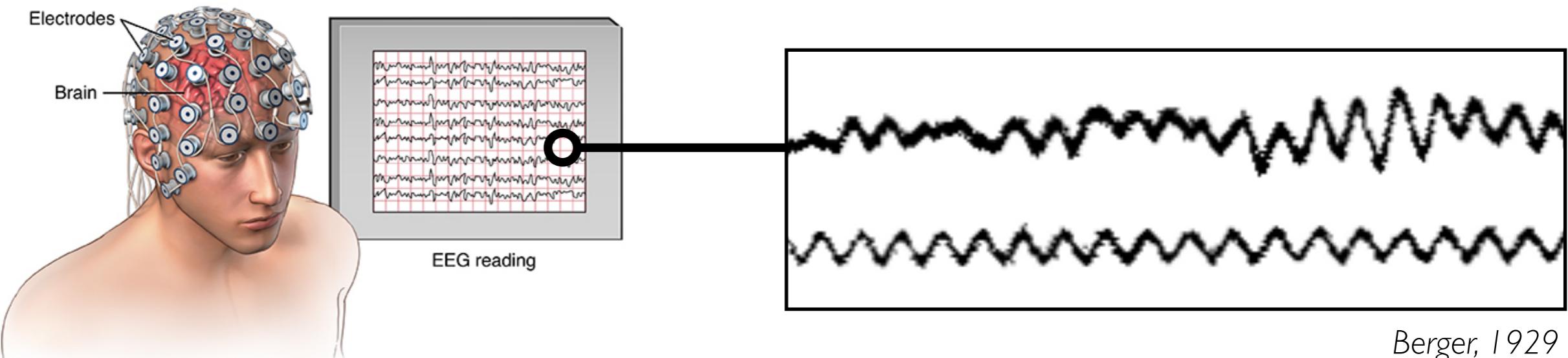


Goals for Today

1. Tell you about my own research
2. Give you examples & practical tips for your project
3. Entertain & motivate your further interest in neural signal processing



Neural Oscillations



Berger, 1929

 ELSEVIER

Opinion *TRENDS in Cognitive Sciences* Vol.9 No.10 October 2005 Full text provided by www.sciencedirect.com

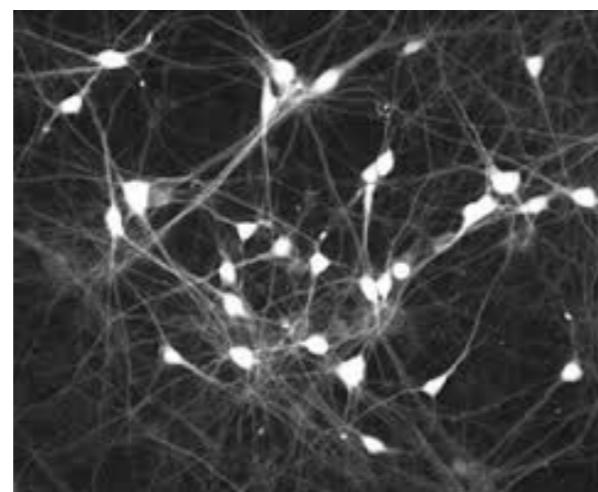
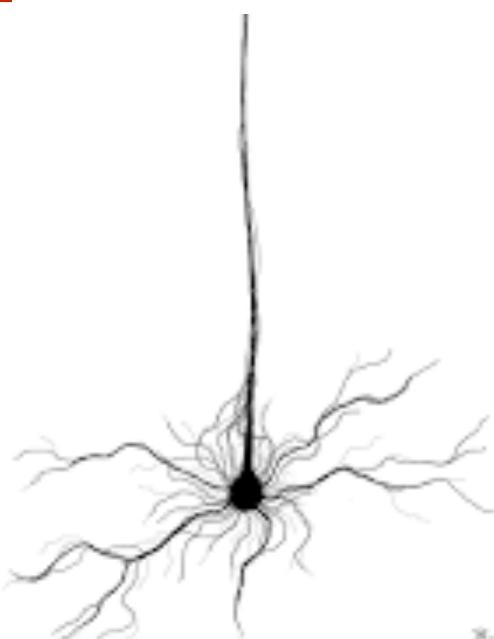
SCIENCE @ DIRECT[®]

A mechanism for cognitive dynamics: neuronal communication through neuronal coherence

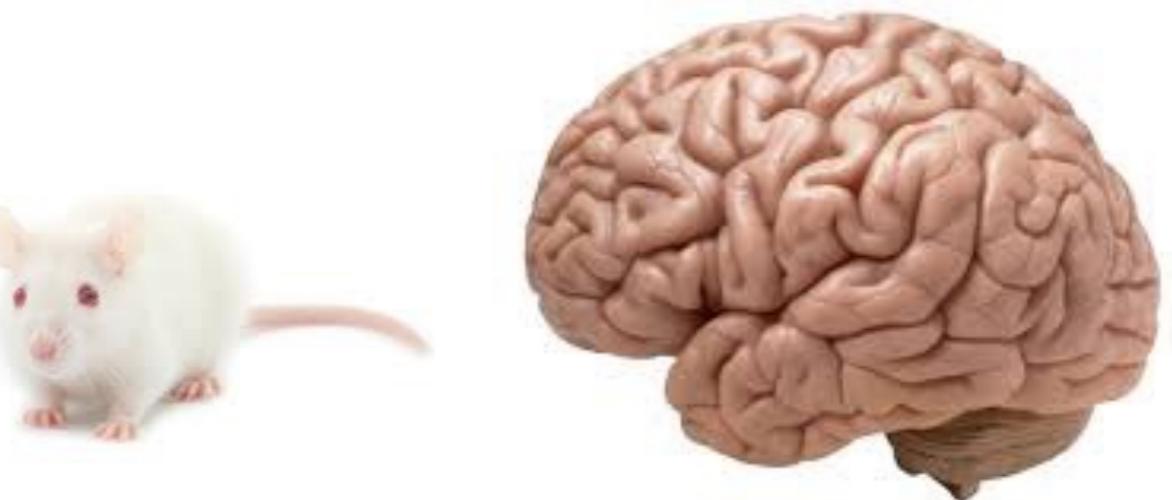
Pascal Fries^{1,2}

Synchronous neural oscillations are **ubiquitous** and tightly linked to **behavior, cognition, and disease**.





...



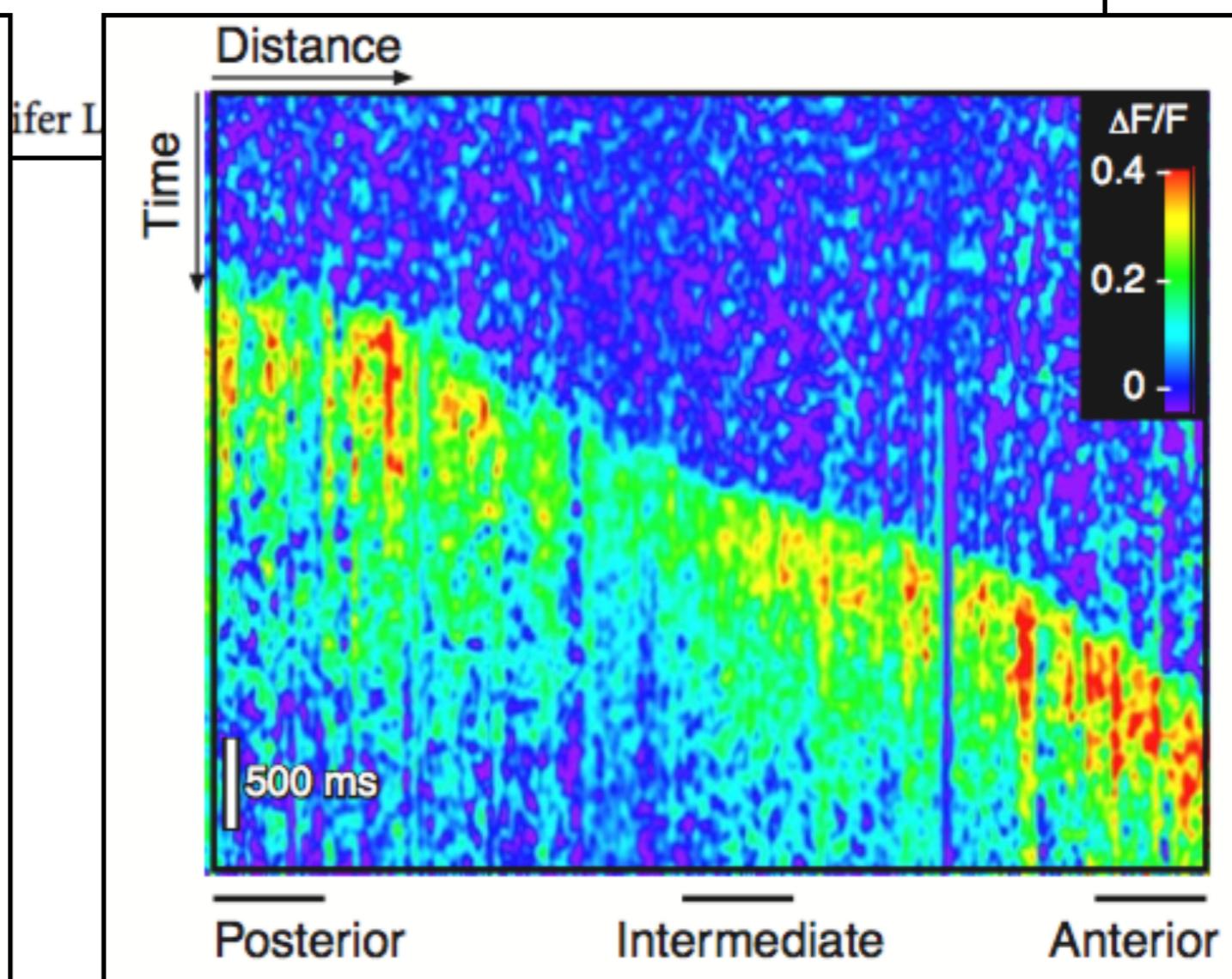
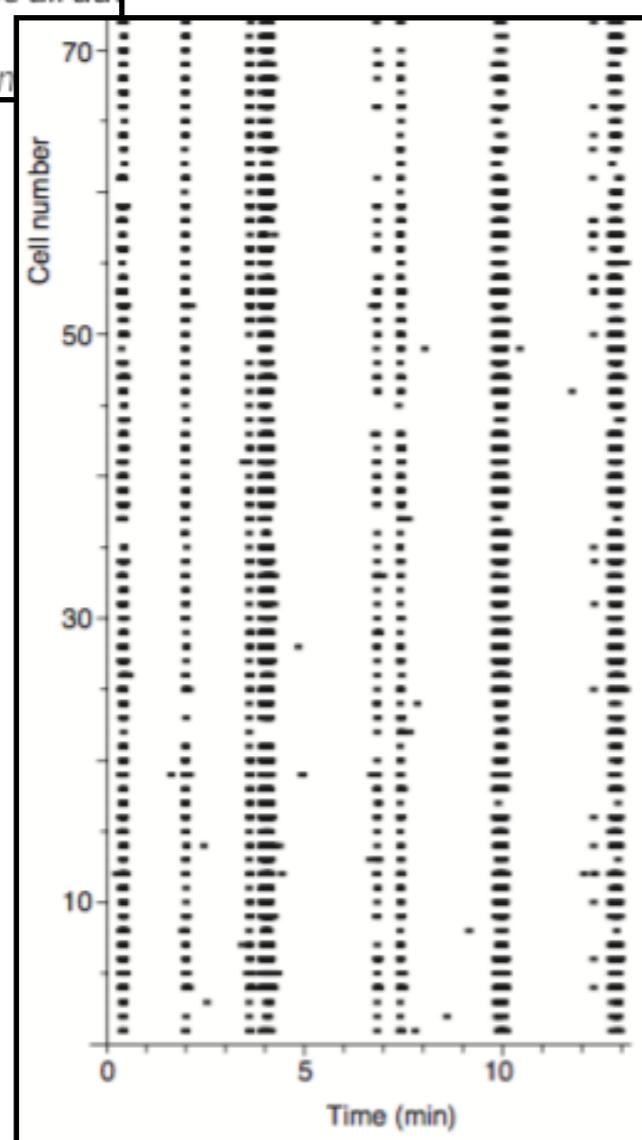
Where does **complex & organized neural activity** begin?



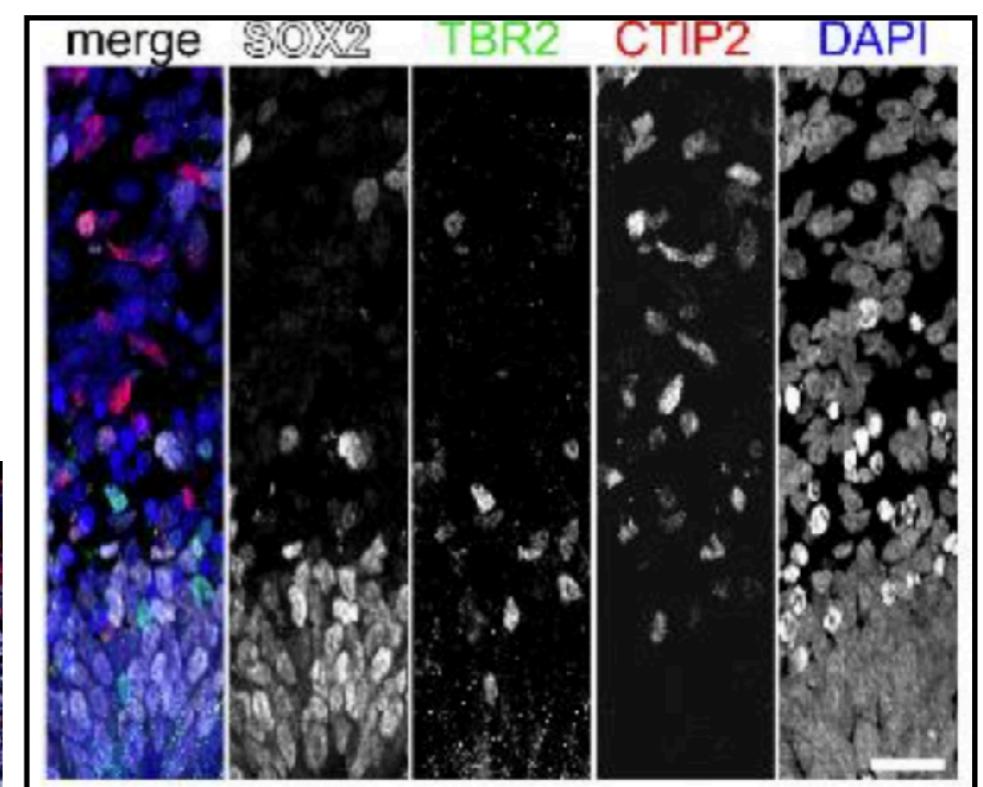
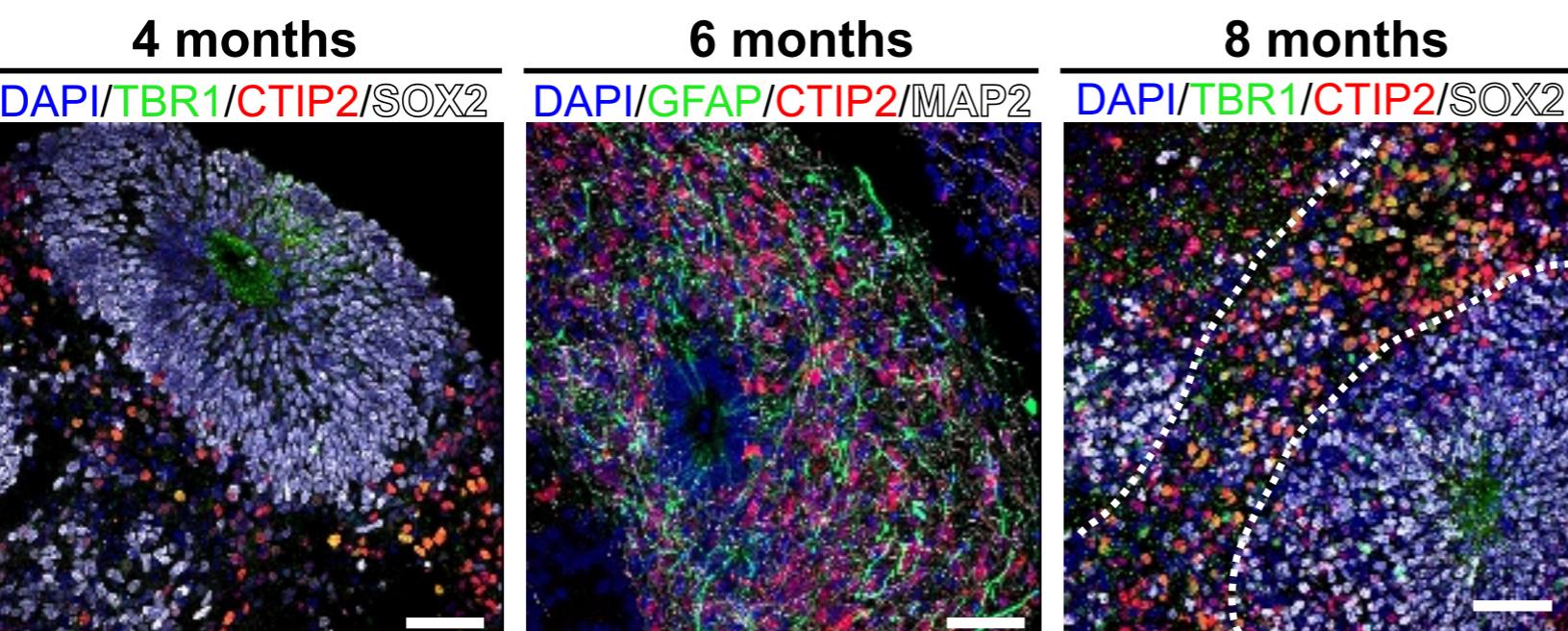
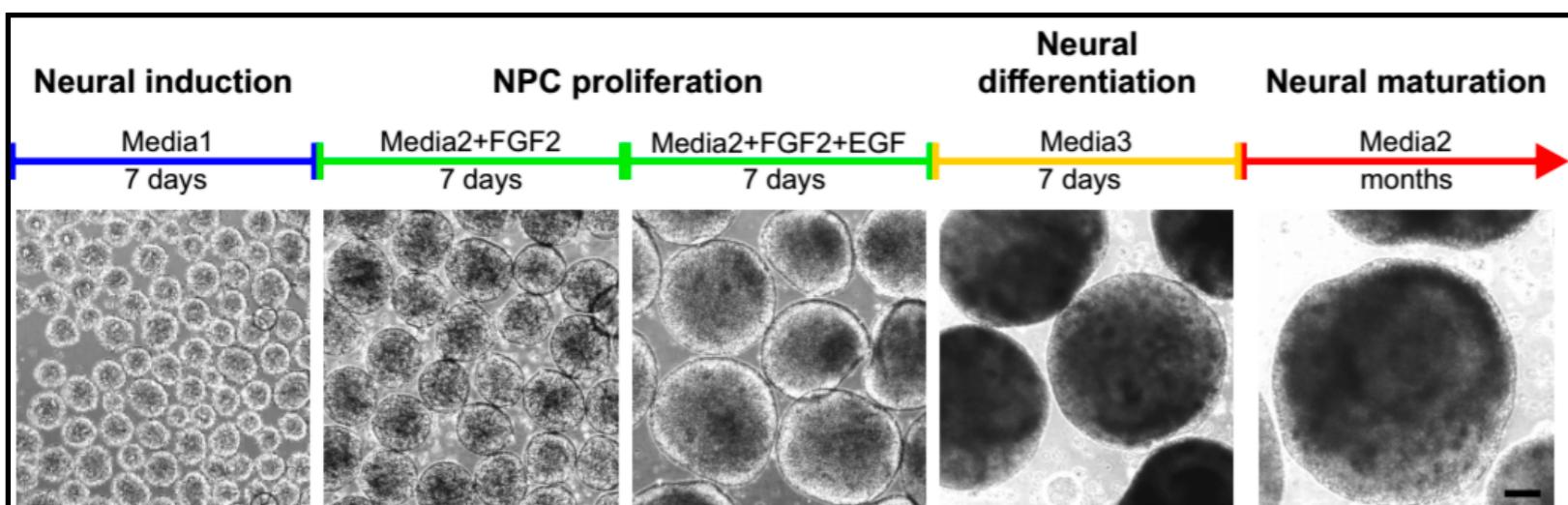
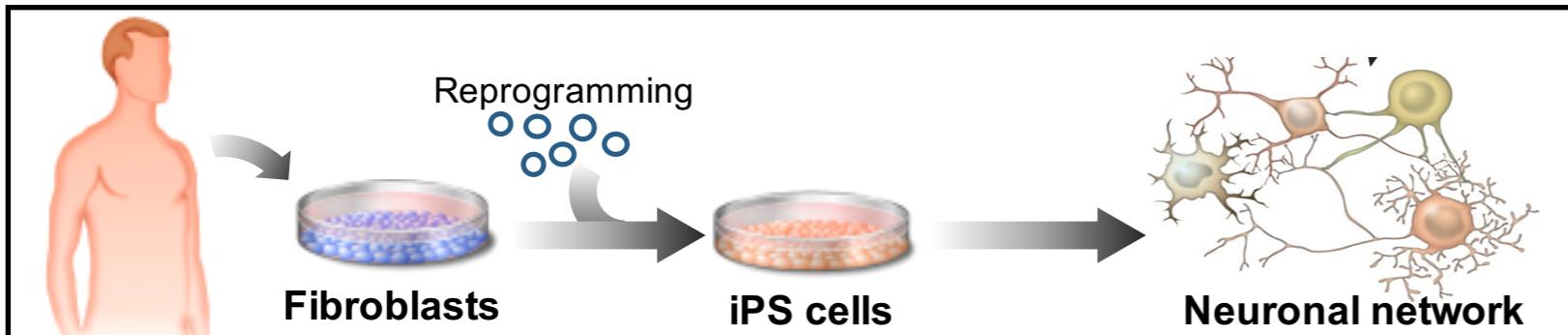
Neural Synchrony & Development

Cortical travelling waves: mechanisms
and applications
Lyle M. Meister, et al.
Synchronous bursts of action potentials in ganglion cells

Large-scale oscillatory calcium waves in the immature cortex



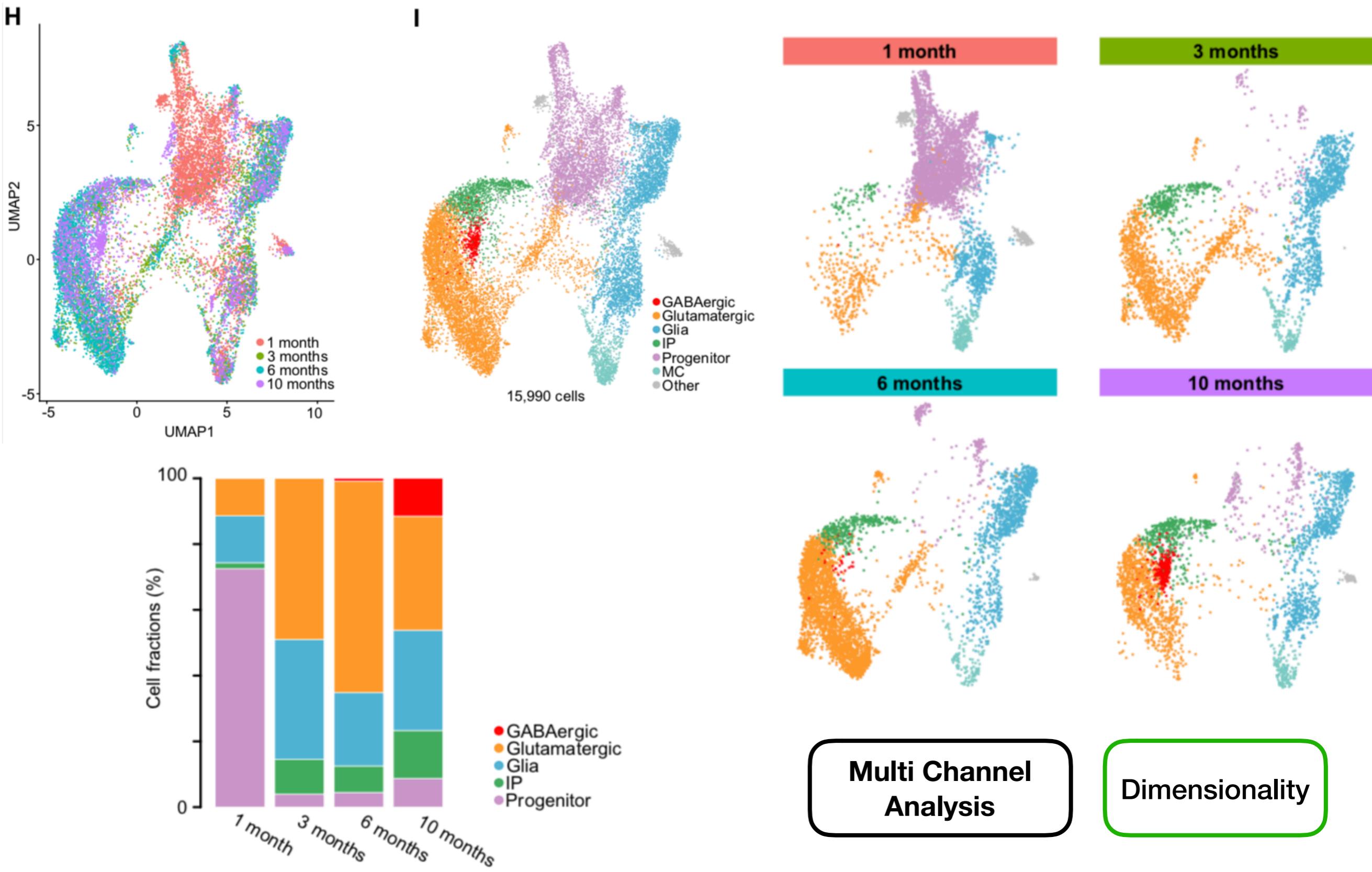
Cerebral Organoids & iPSC



Pluripotency Developing L5/6 Projecting Nuclei

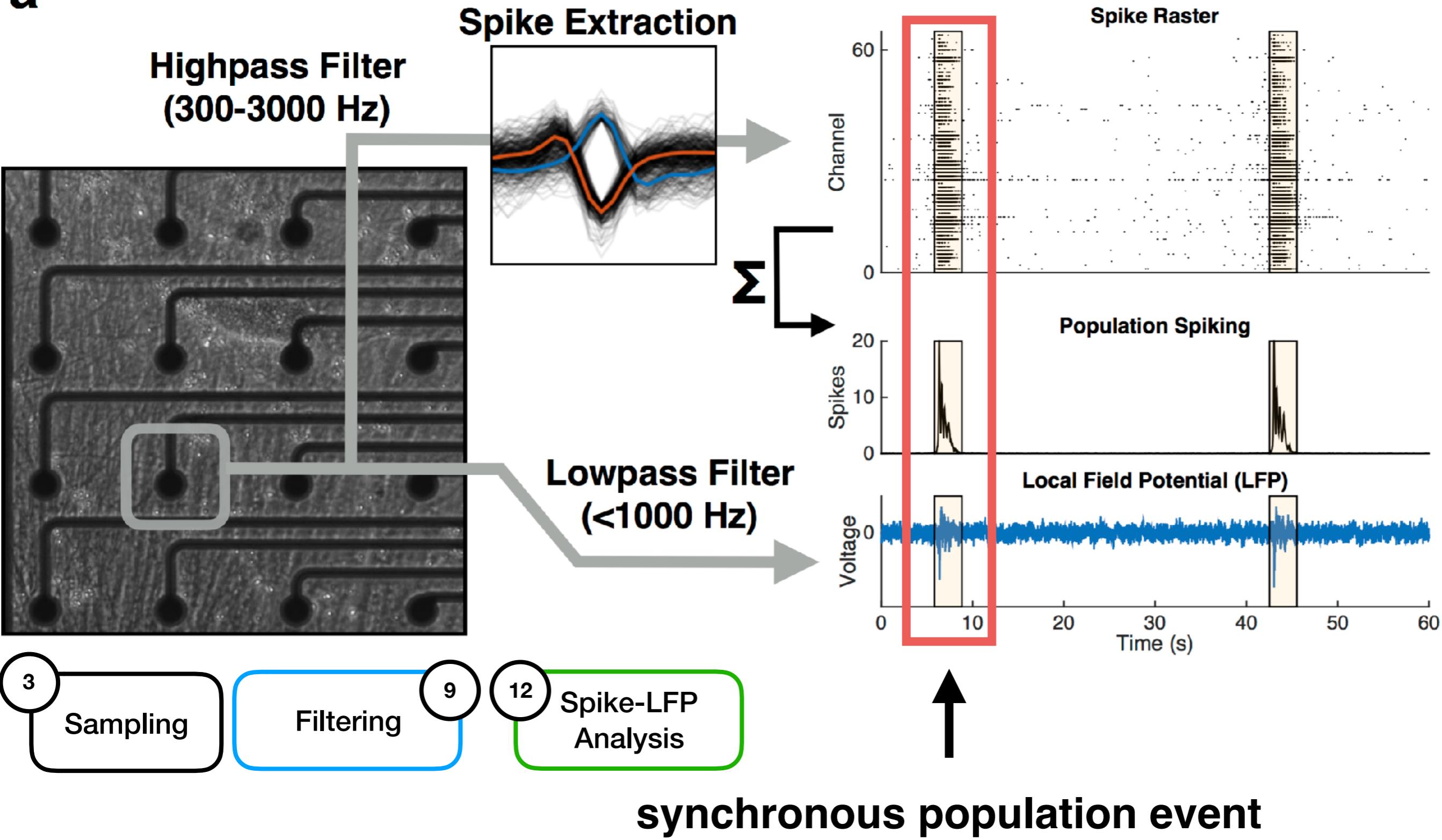


Single Cell RNA Sequencing



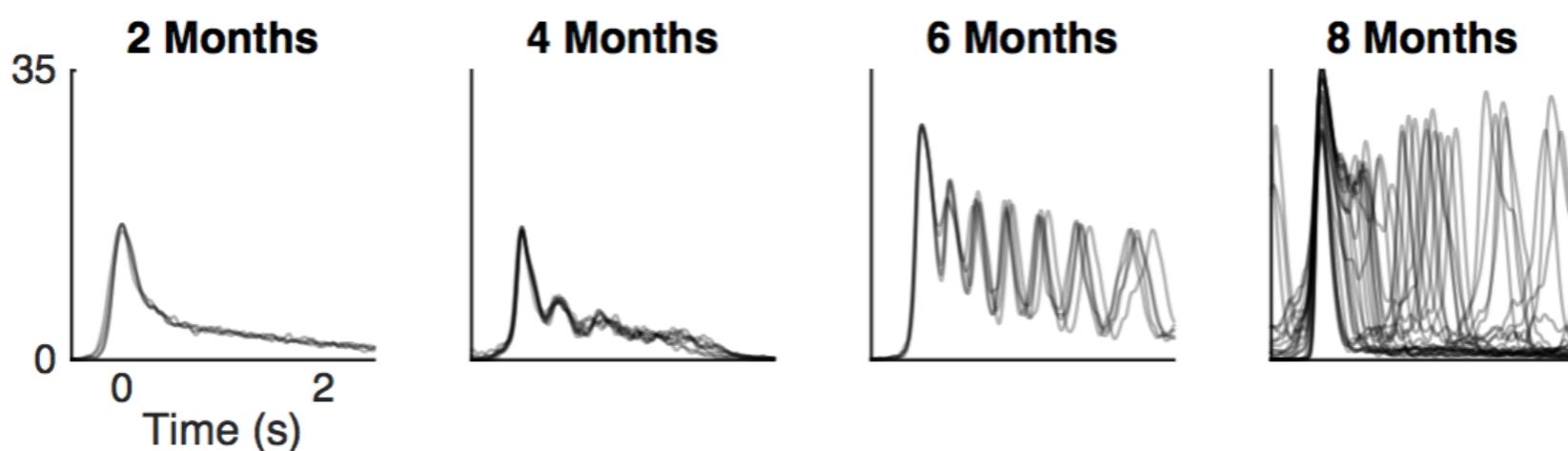
Organoid Electrophysiology

a

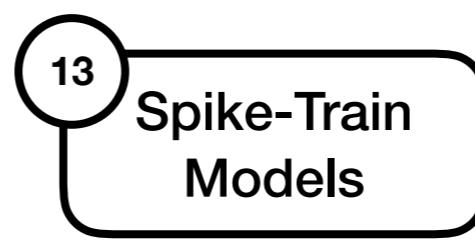
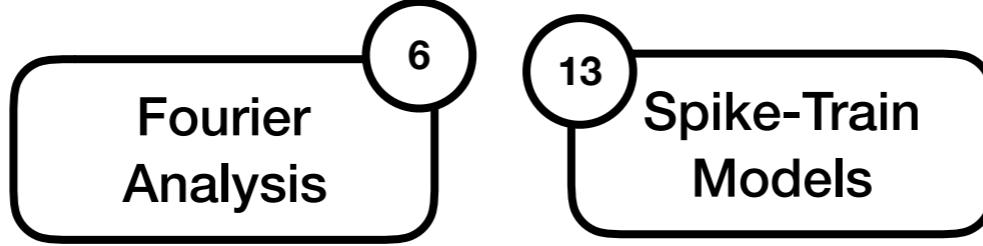
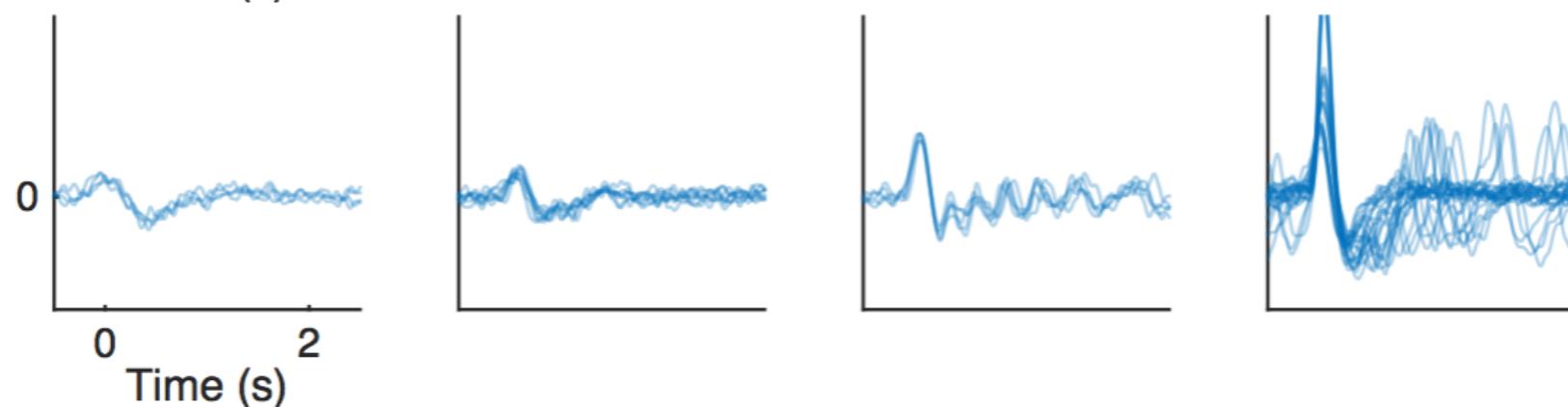


Oscillatory Network Dynamics

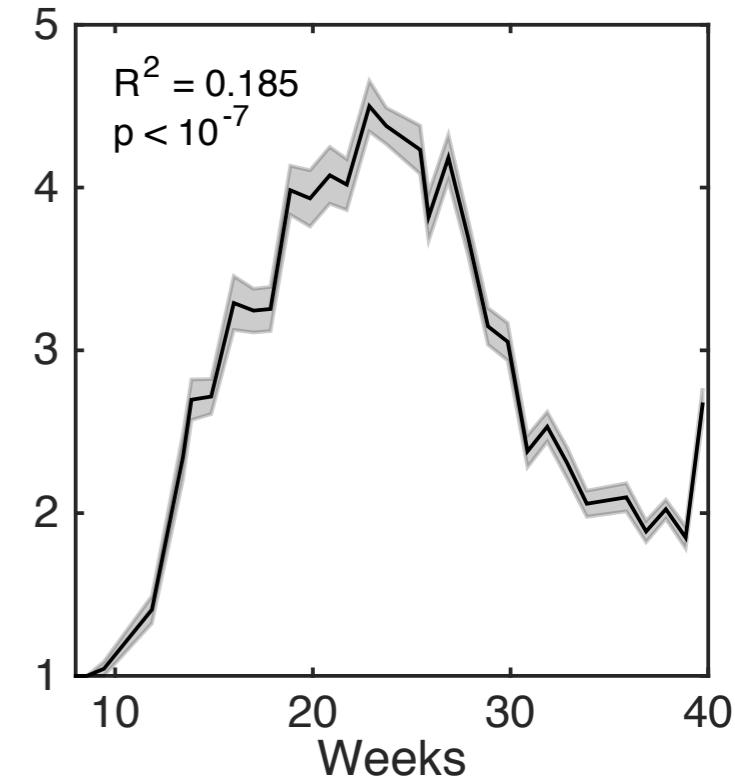
Pop. Firing



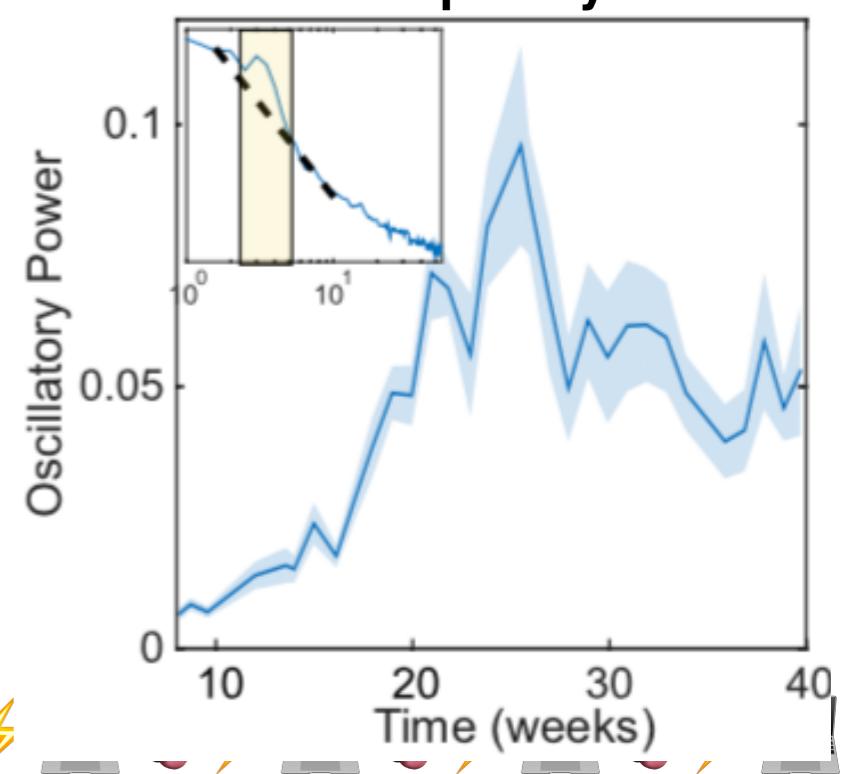
LFP



Number of Sub-Peaks

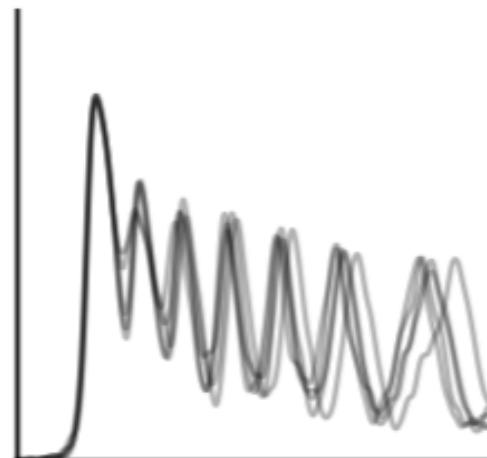


Low-Frequency Power



Oscillatory Network Dynamics

6 Months

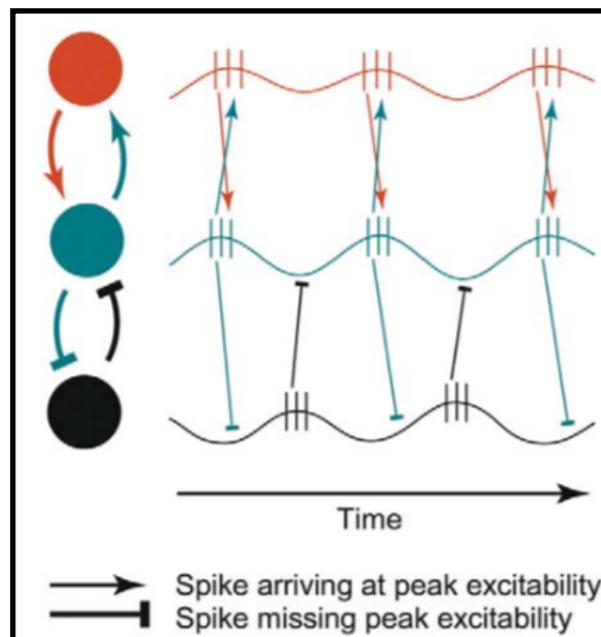


3Hz Rhythmic Population Firing

(5 seconds)



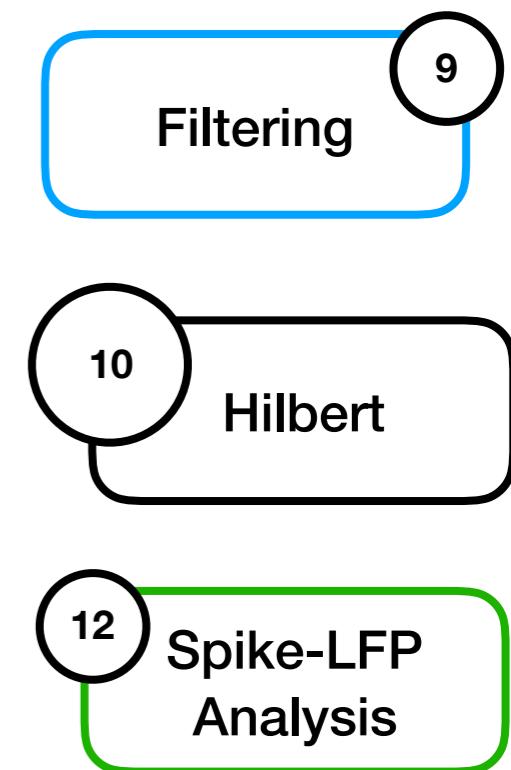
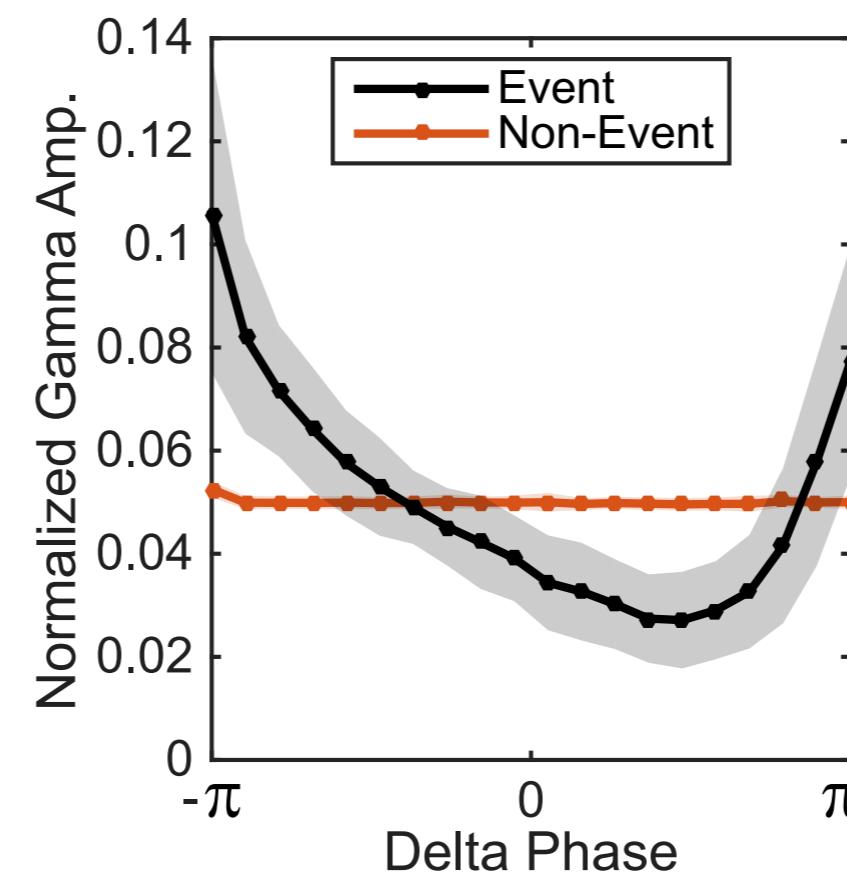
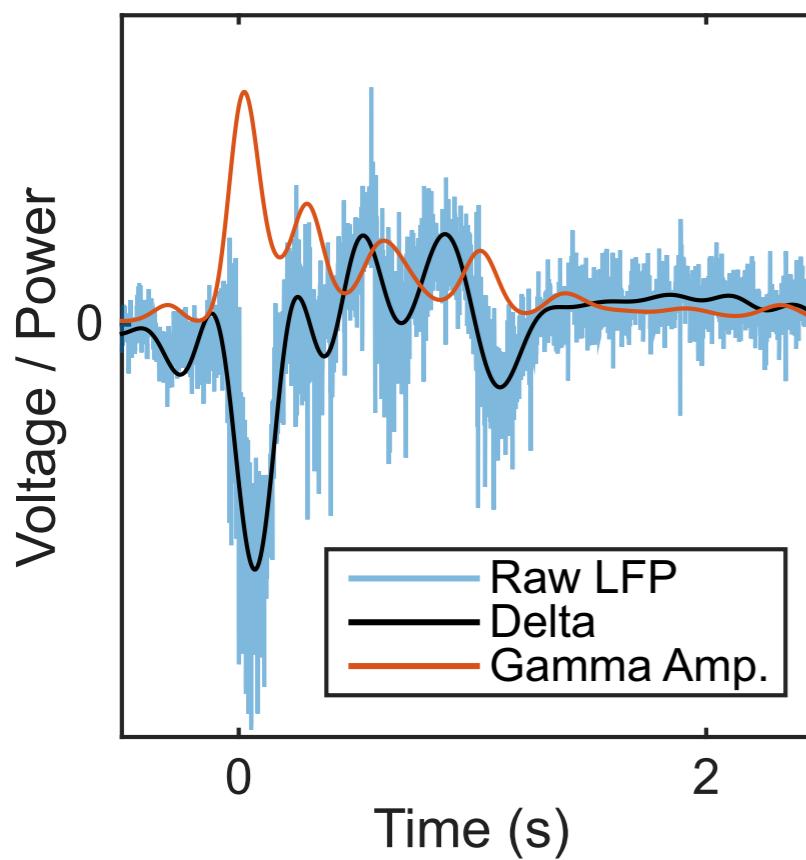
Oscillatory Coordination



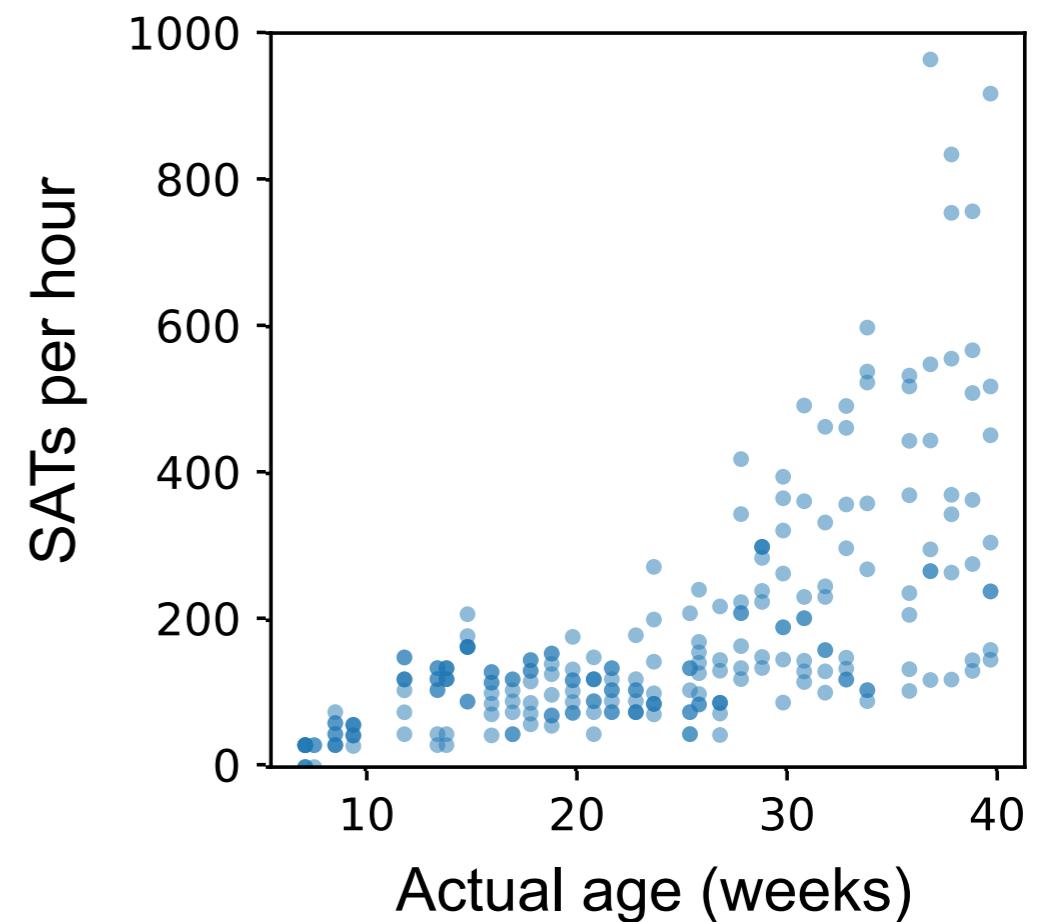
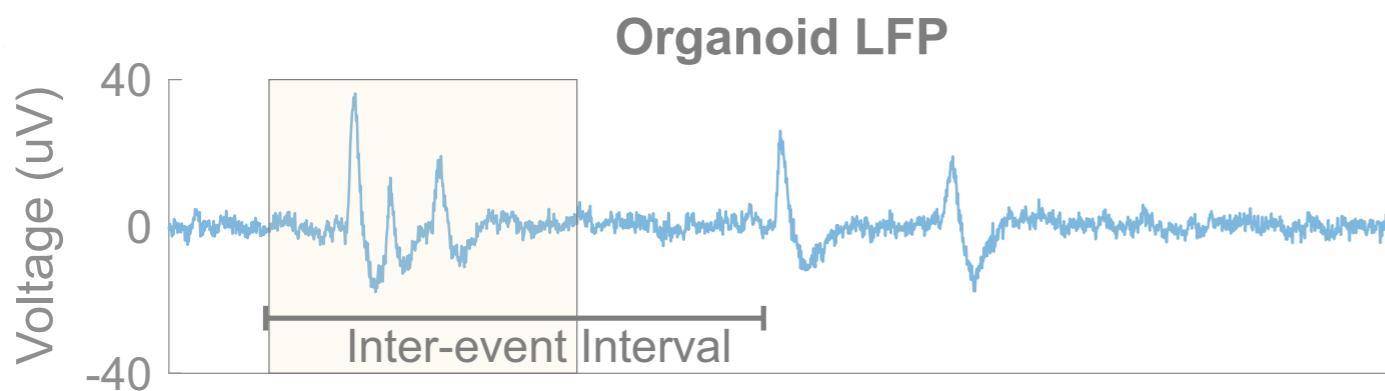
Fries, 2005

Communication Through Coherence

Oscillations are thought to temporally organize spikes, as evidenced by spike-field (SFC) or **phase-amplitude coupling (PAC)**.



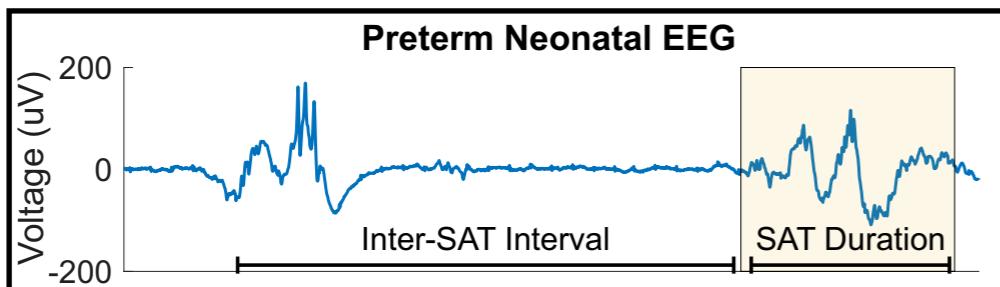
Comparing to Human Electrophysiology



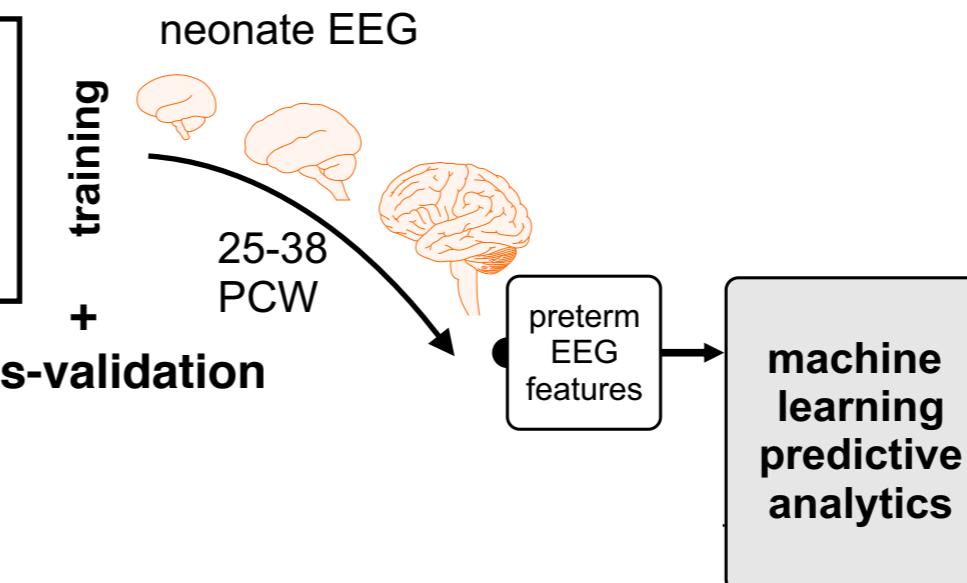
Data: Stevenson et al., 2018.



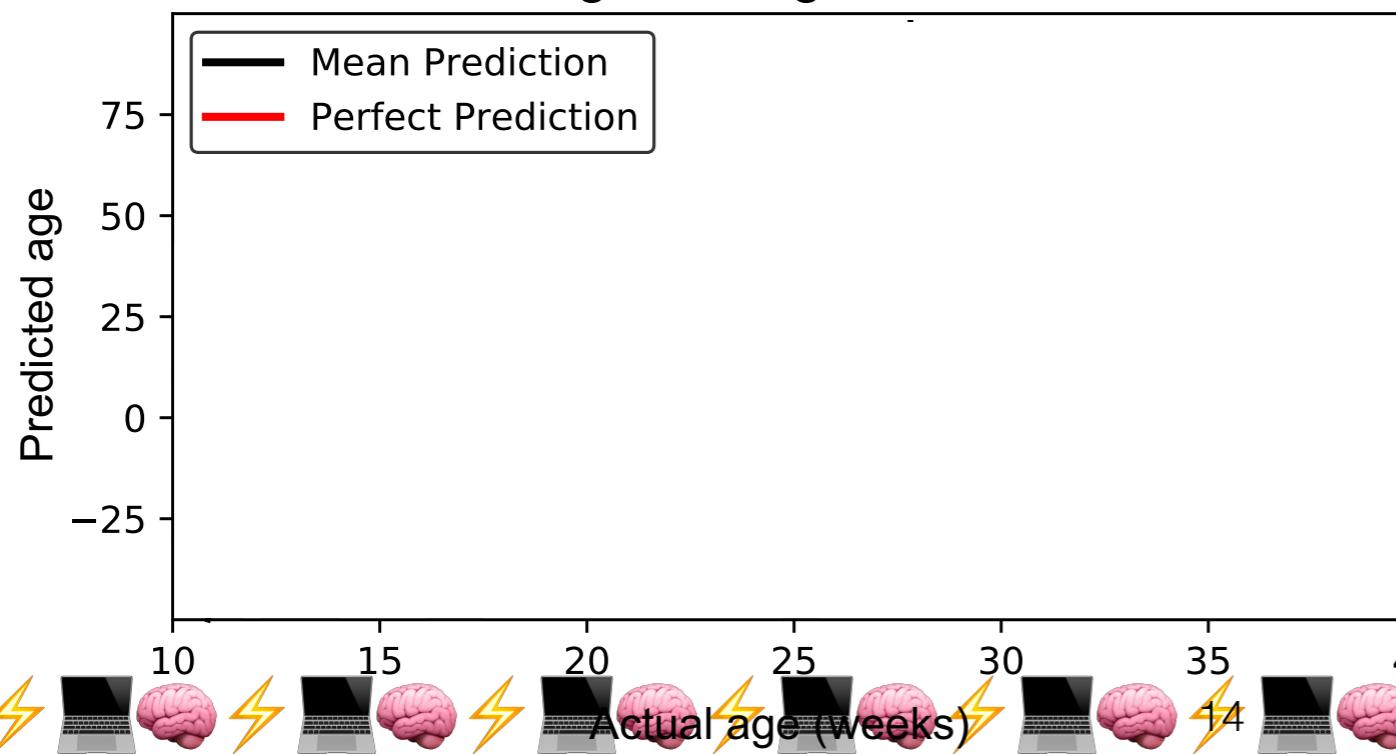
Predicting Organoid “Brain Age”



Data: Stevenson et al., 2018.



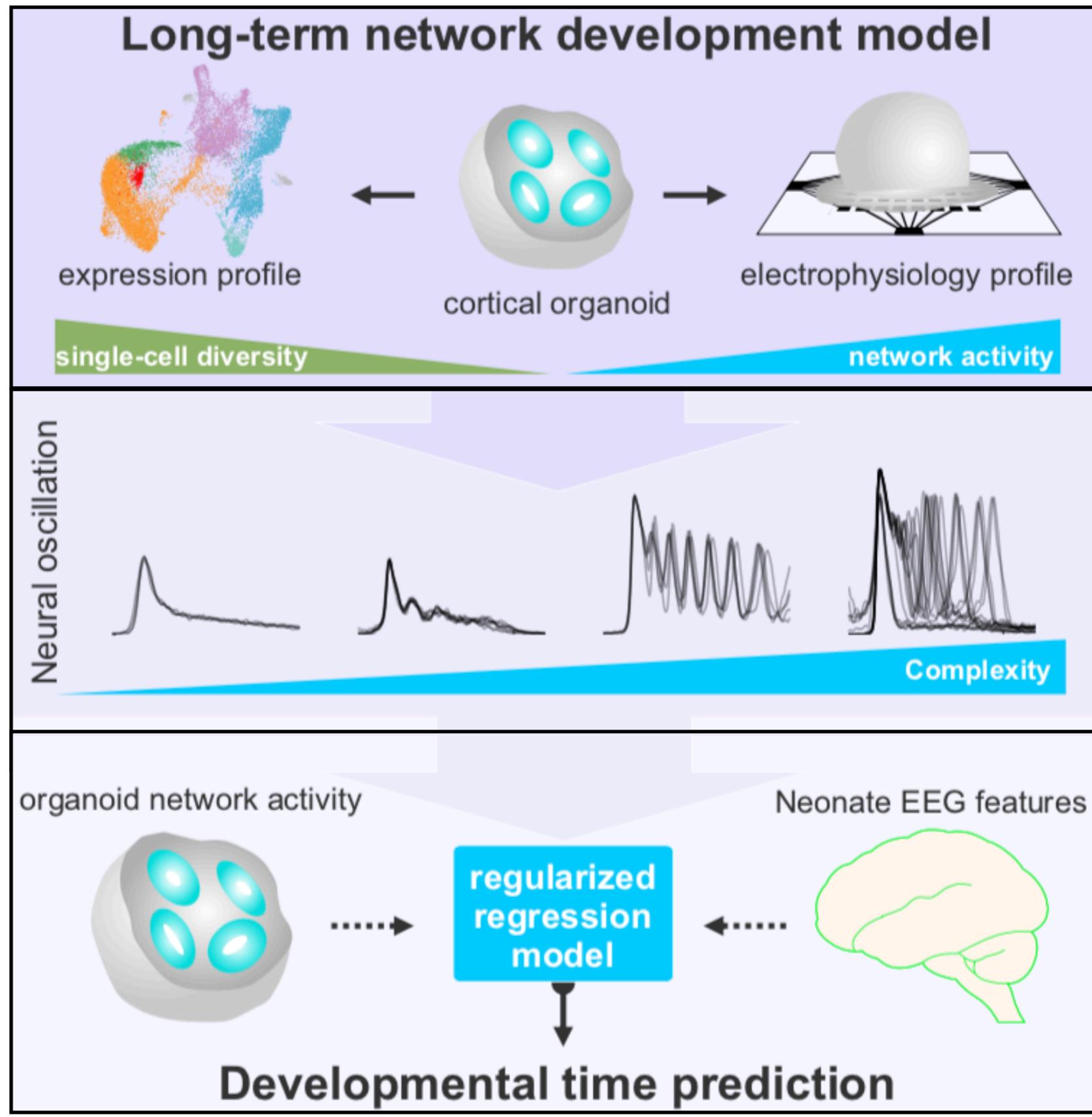
Predicted organoid age from neonate data



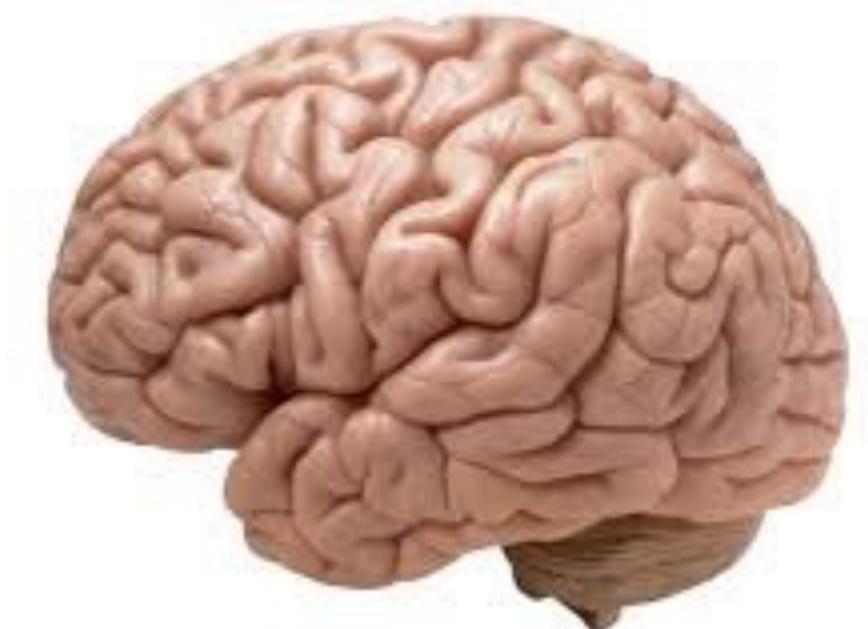
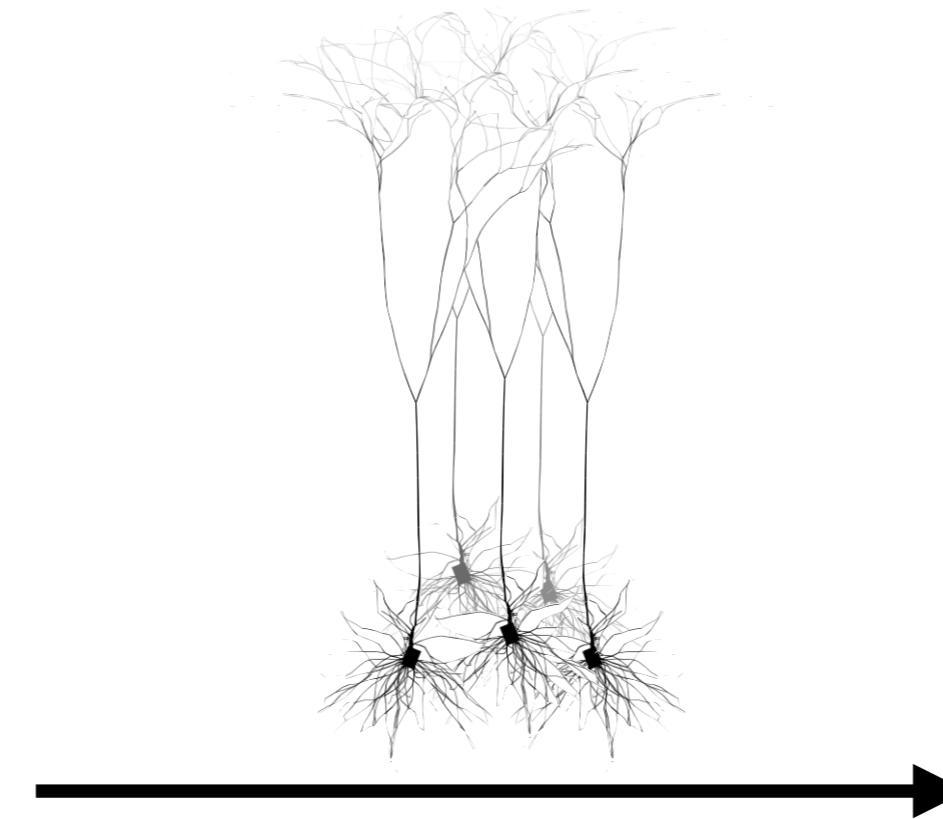
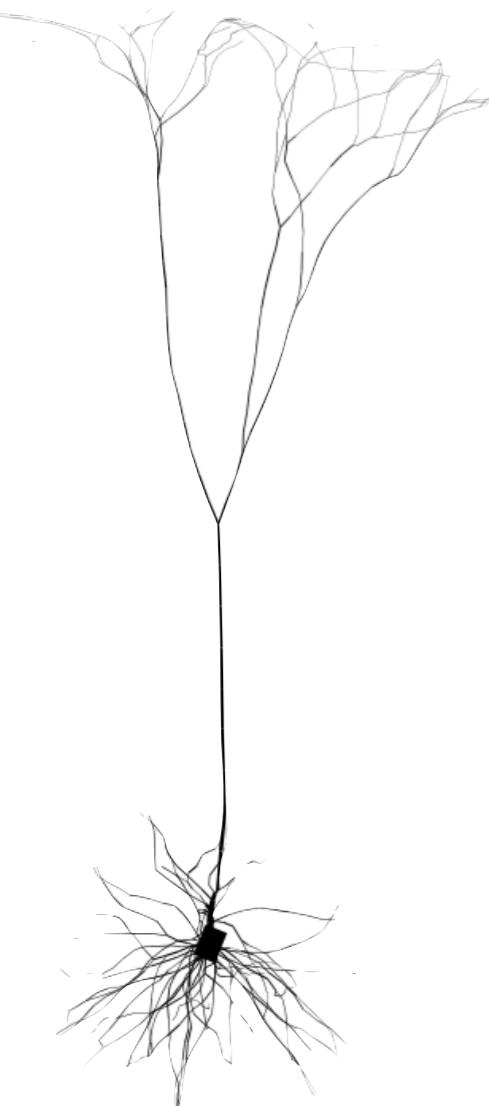
Organoid partially recapitulates the development of electrophysiological features in-vivo.



Developmental Model of Electrophysiology



Complex Dynamical System

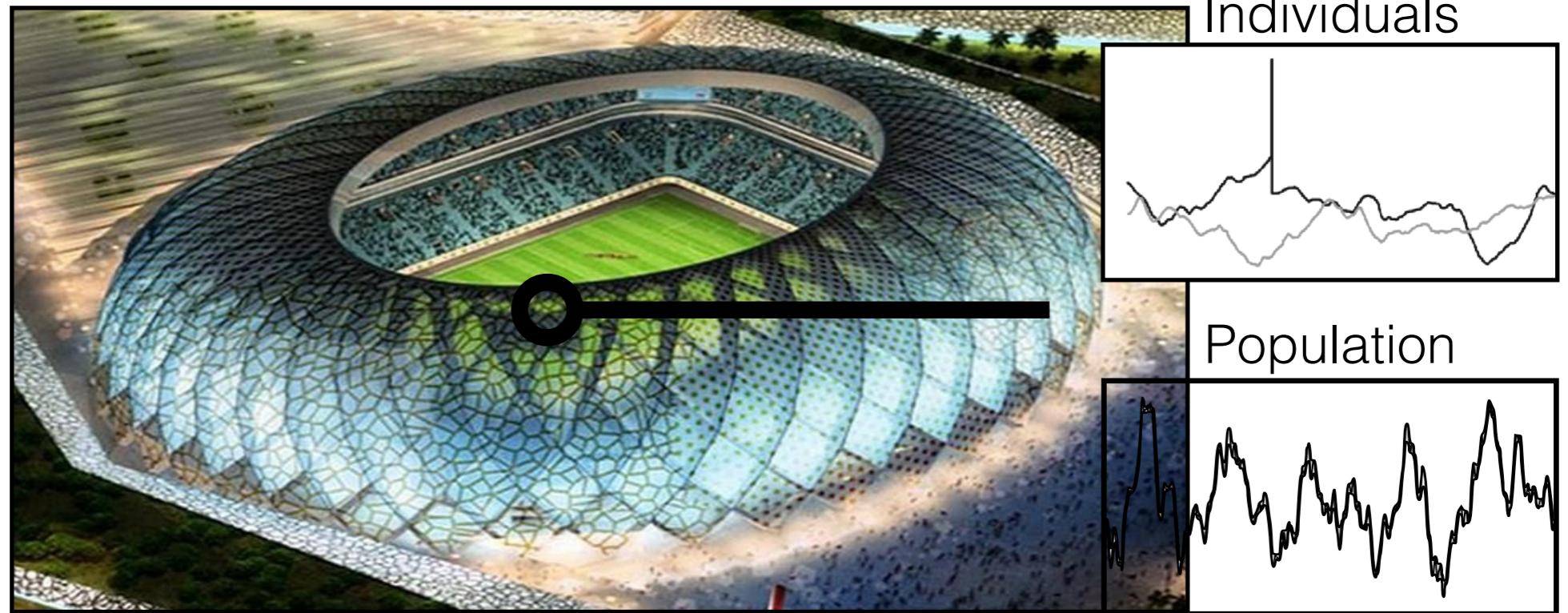


$$\tau_m \frac{dv}{dt} = -v(t) + RI(t)$$

Are we screwed (10 billion ways)?



Complex Dynamical System



“asynchronous”



“oscillatory”



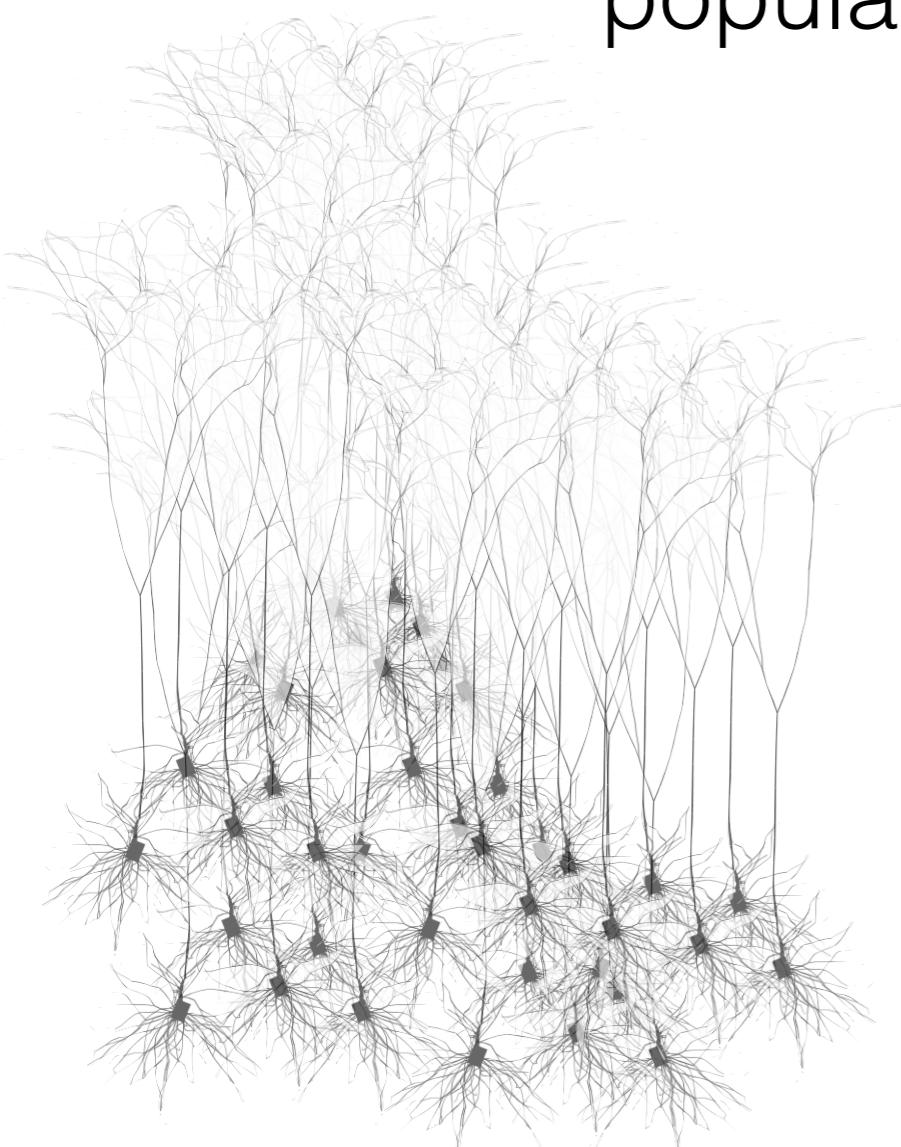
“synchronous”



Low-Dimensional Activity in the Brain

Can we meaningfully study a 10 billion-dimensional system?

Are there low-dimensional attractors in the phase space
populated by our ~10 billion neurons?



(Probabaly) Yes!

1. Experiential Argument
 2. Single Neuron Attractors
 3. Neural Population

Low-Dimensional Activity in the Brain

1. **Experiential Argument**
2. Single Neuron Attractors
3. Neural Population

We have:

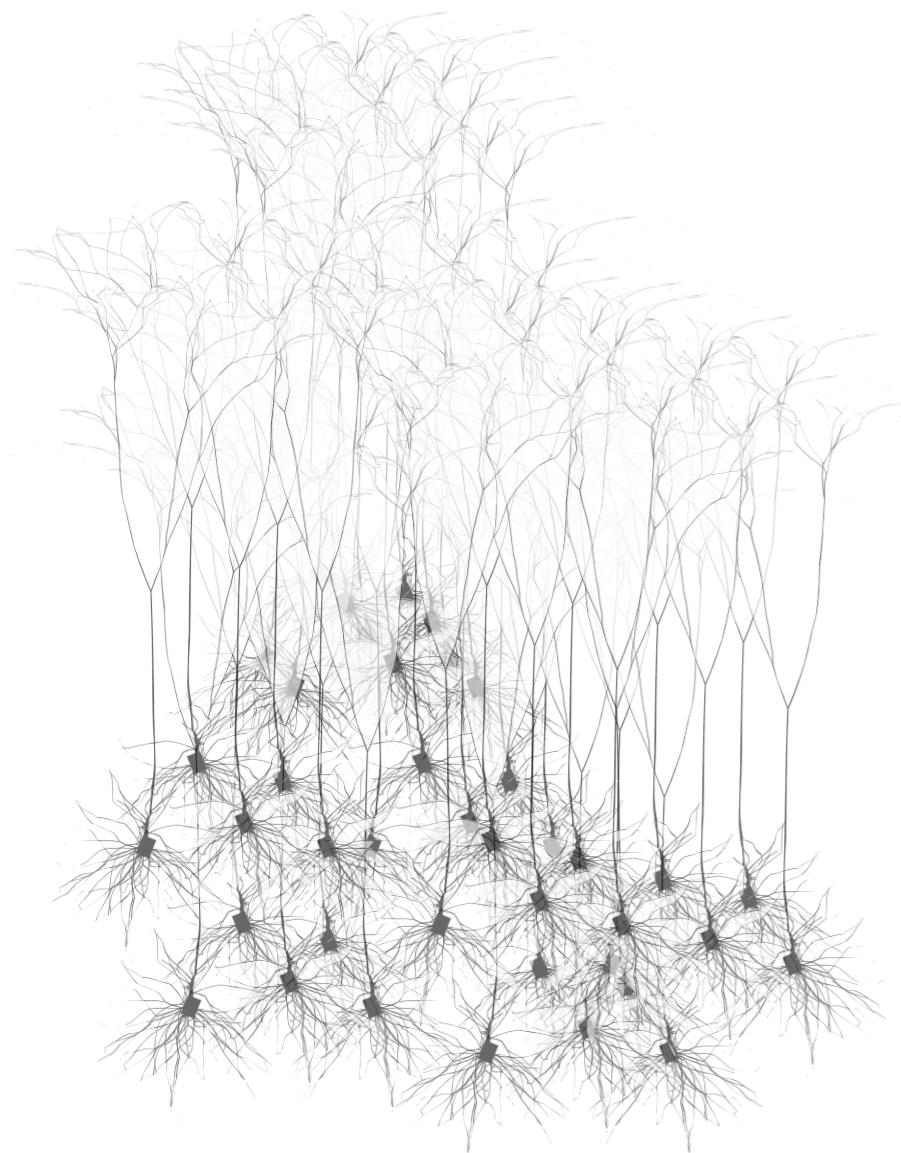
memories

repeatable skills

songs that get stuck in our heads

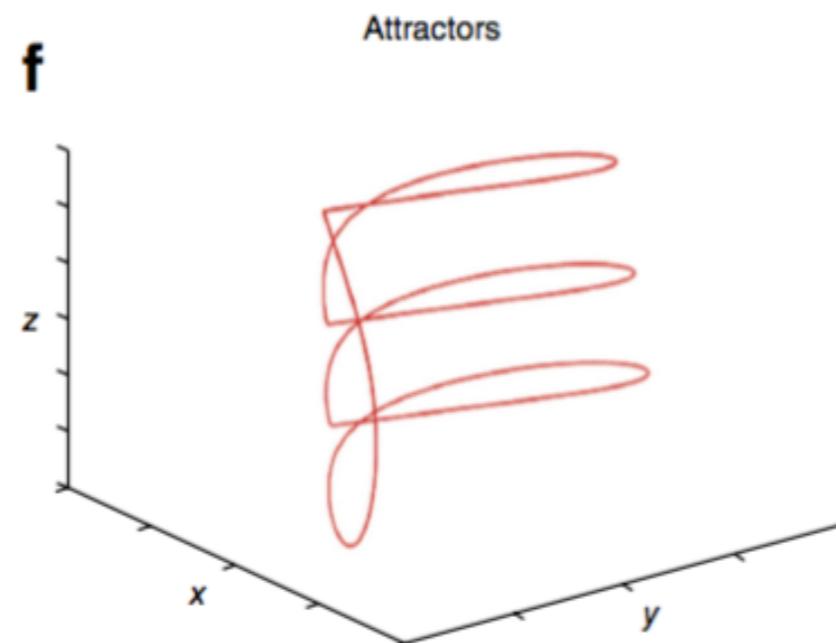
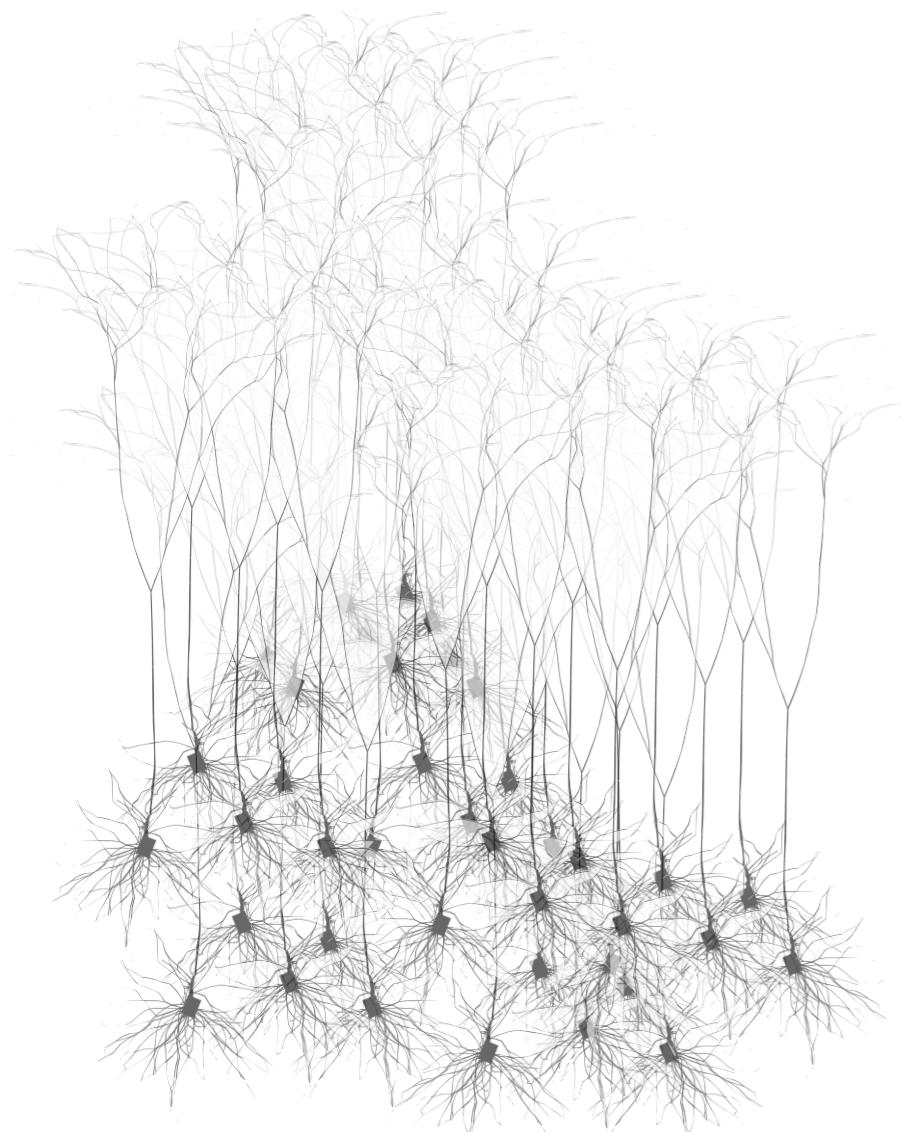
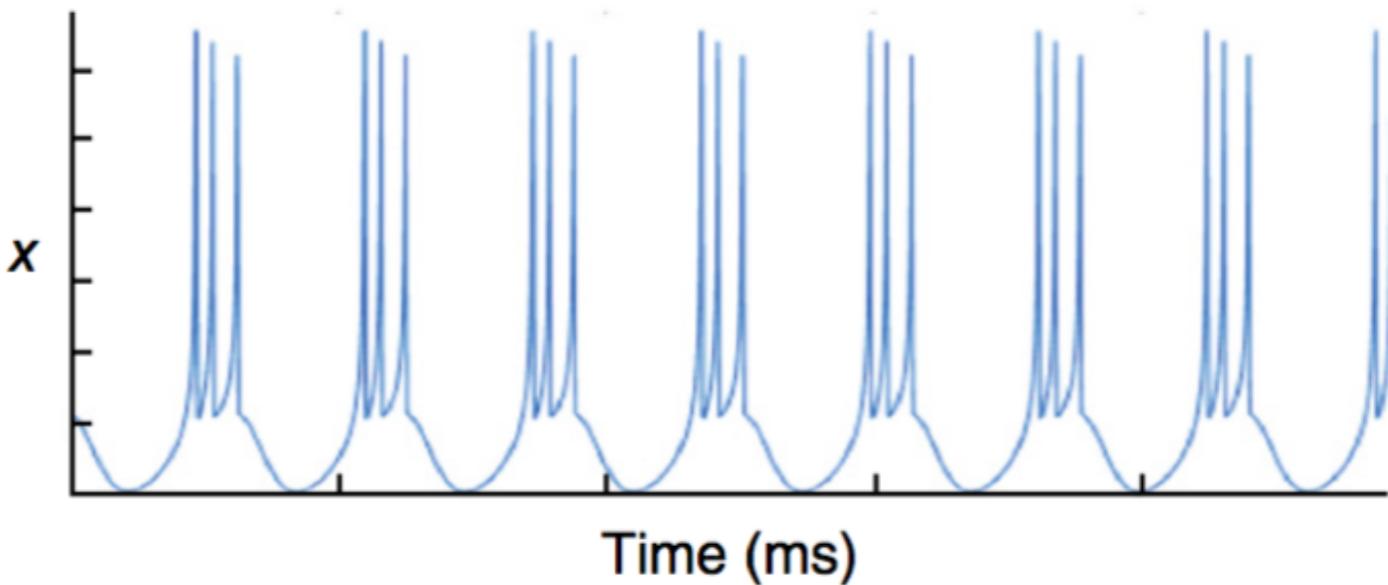
...

Our experiences (probably) do not span an infinite dimensional space, “limited” by our brains.



Low-Dimensional Activity in the Brain

1. Experiential Argument
2. **Single Neuron Attractors**
3. Neural Population



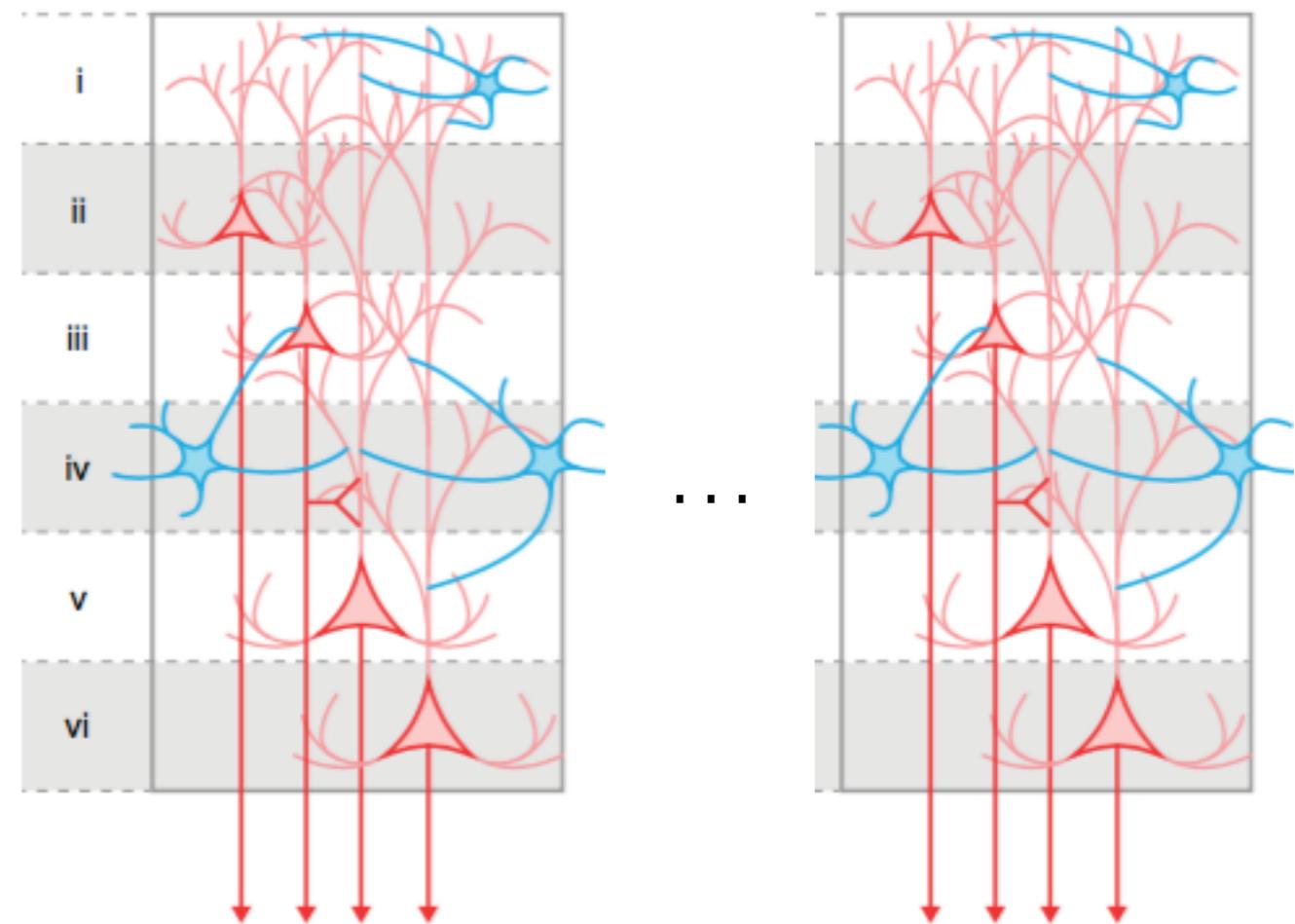
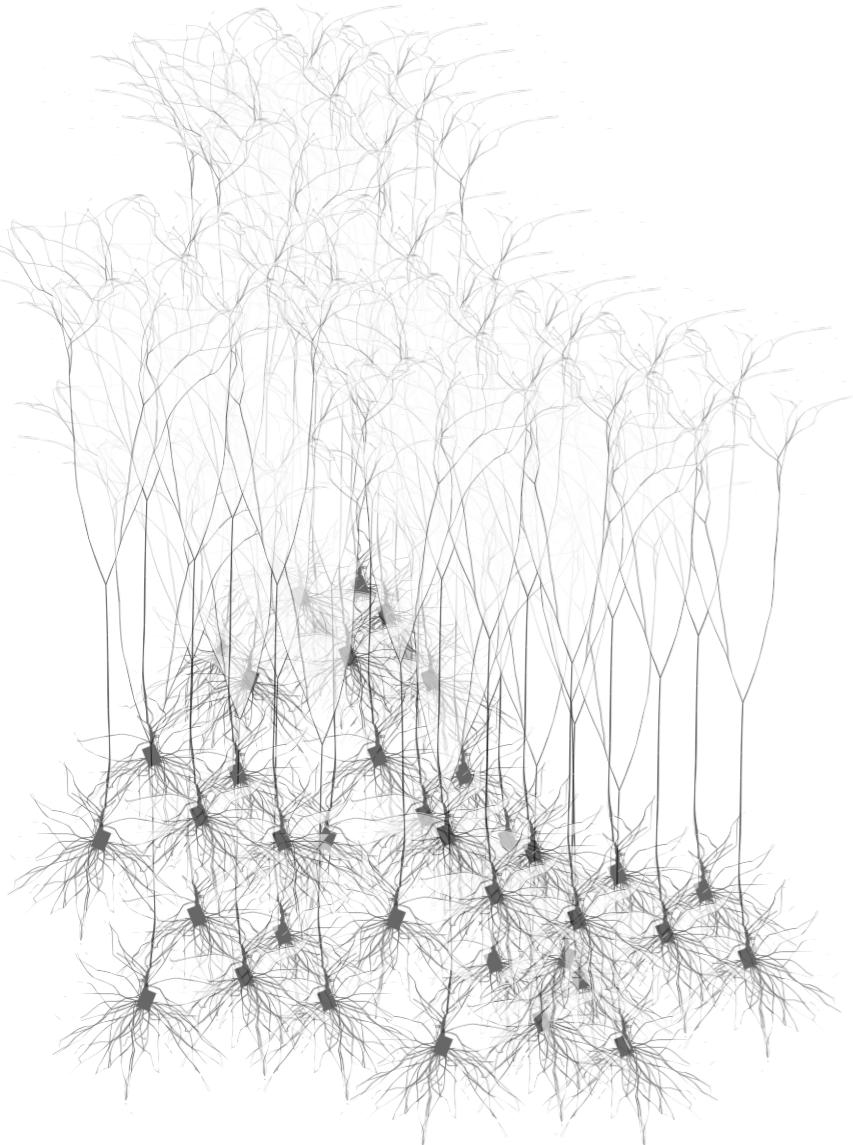
Neurons fire repeated action potentials:
dynamics around a limit cycle

images: Breakspear (2017, Nat Neurosci)



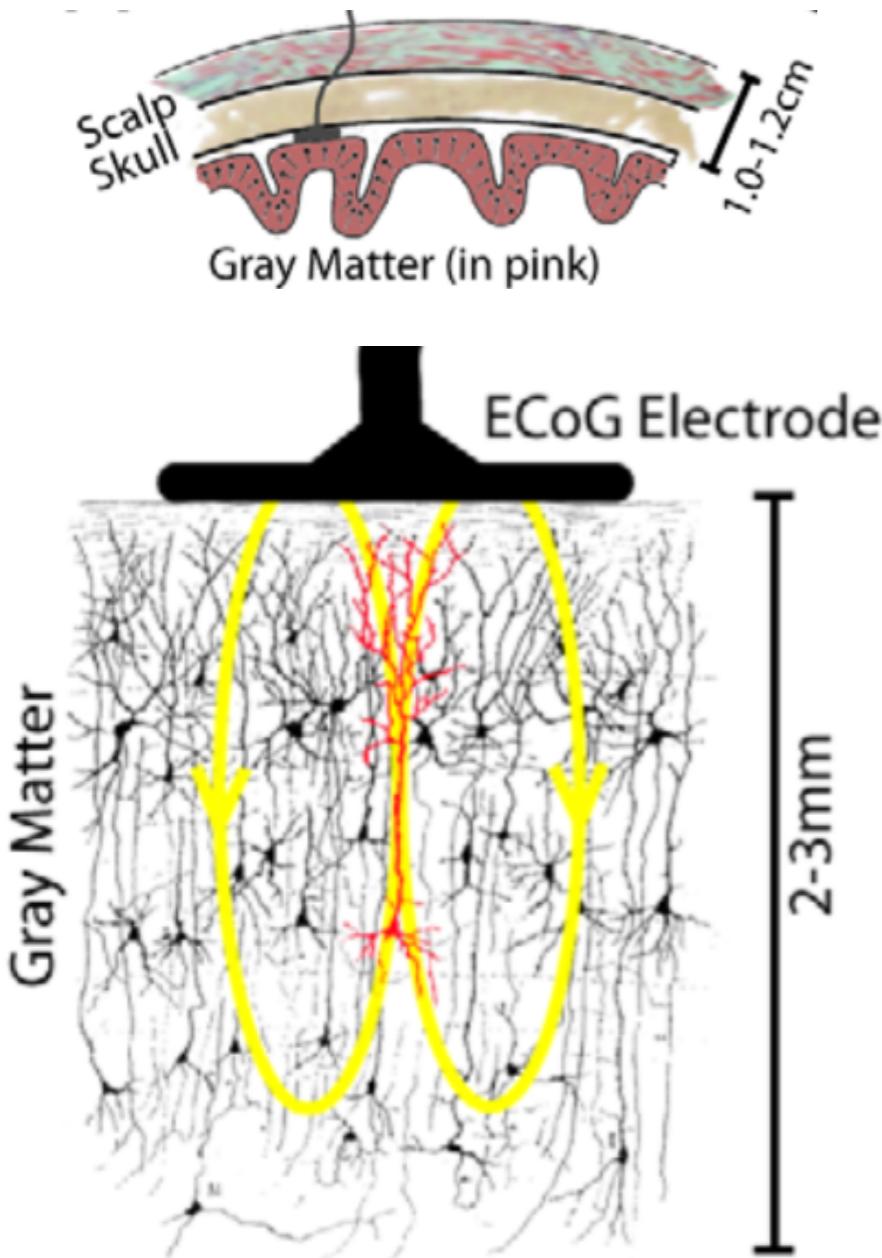
Low-Dimensional Activity in the Brain

1. Experiential Argument
 2. Single Neuron Attractors
 - 3. Neural Population**

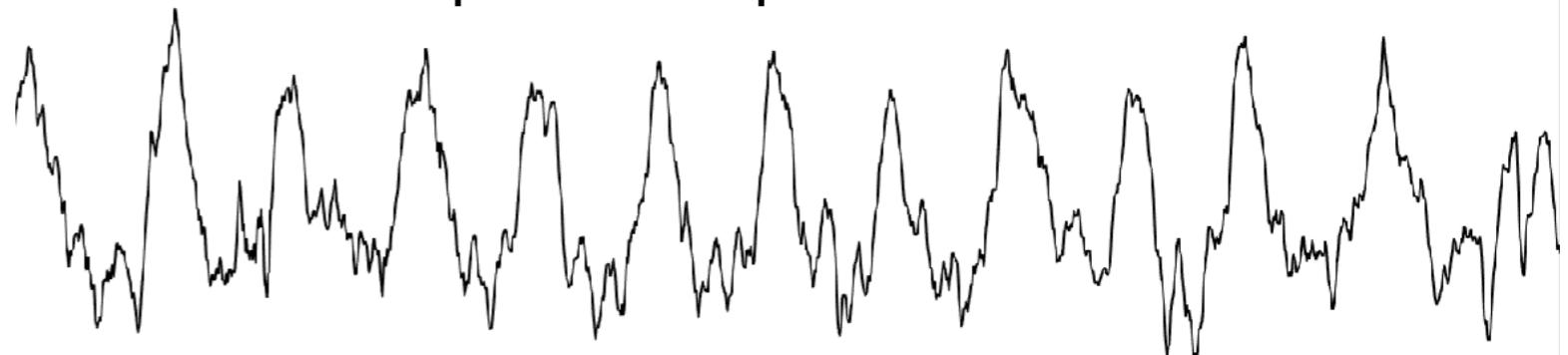


Neurons form ensembles that
behave similarly.
(synchronicity, redundancy)

Synchrony Is Low-Dimensionality



Neural Oscillations (Brain Waves!)
Ubiquitous phenomenon



Not individual action potentials, but
synchronous (synaptic) current
discharges.

Limit Cycles?

images: Miller et al (PLoS CB, 2009)

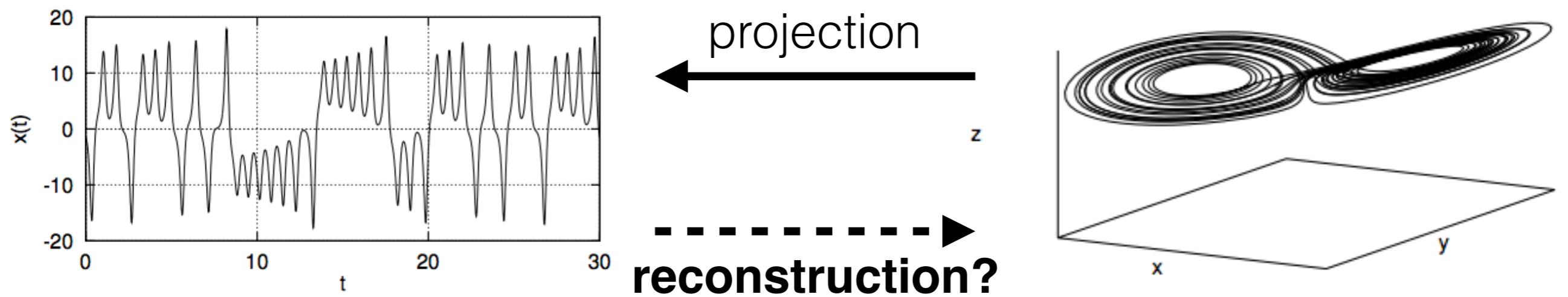


Phase Space Reconstruction

Problem:

There is attractor dynamics in phase space but we only observe data in time projected along a single dimension.

Can we learn anything about the attractor?



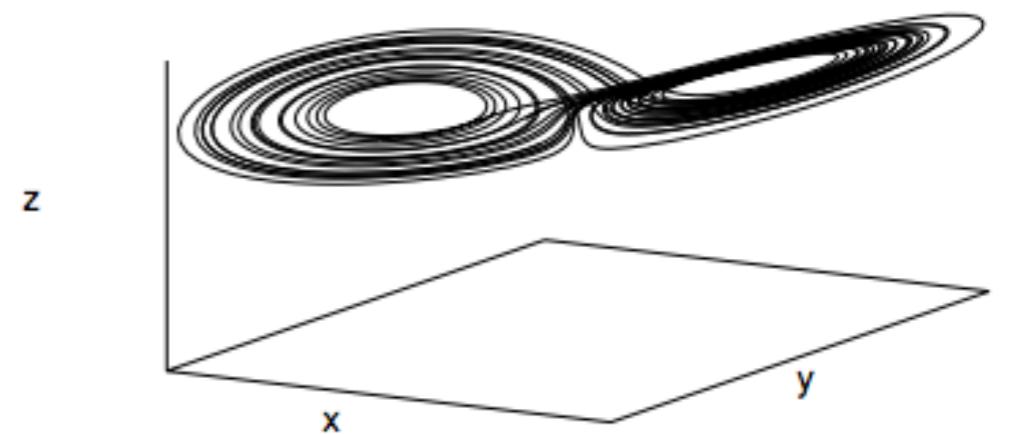
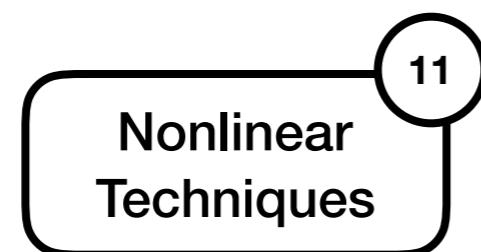
Phase Space Reconstruction

Takens' Theorem

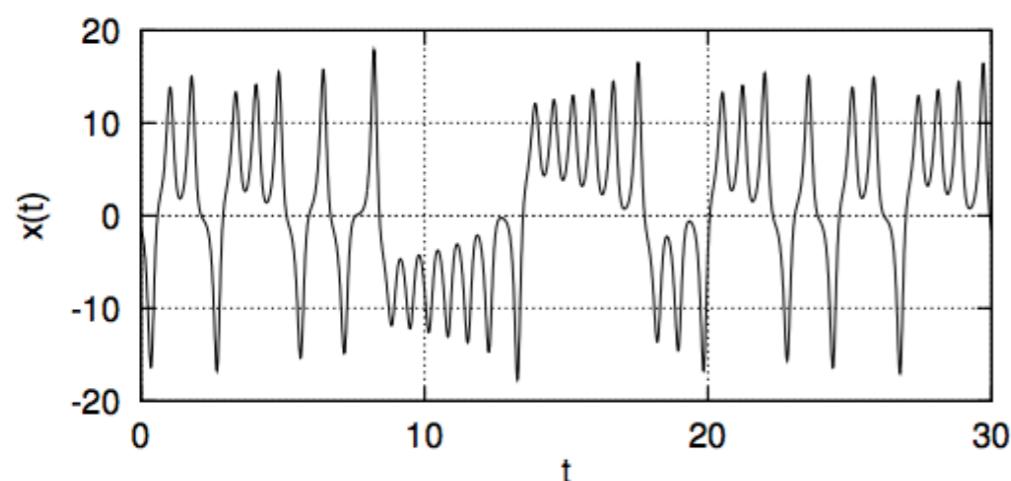
We can reconstruct the attractor dynamics **faithfully** with **delayed** version of the data as “**dimensions**”.

- faithfully: diffeomorphic (warped attractor manifold), preserves topological properties
 - delayed: with optimal* time delay
 - dimensions: $2D+1$ dimensions, D is dimension of **attractor**

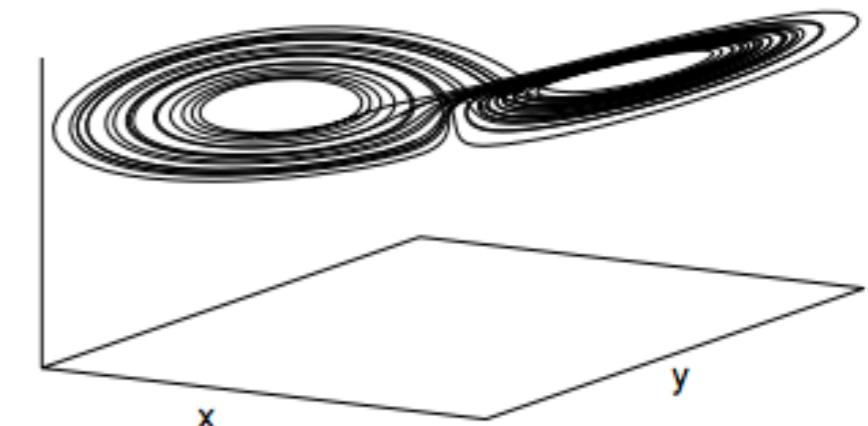
note: cannot recover dimension of phase space, only that of the attractor (hence low-D)



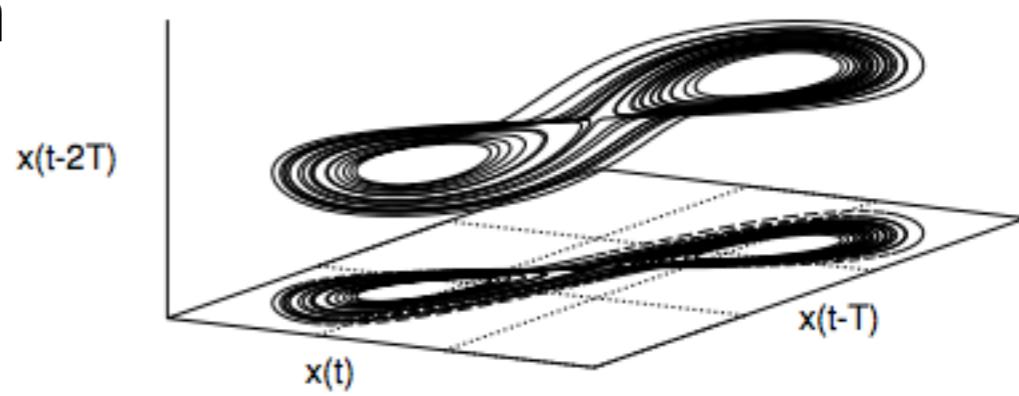
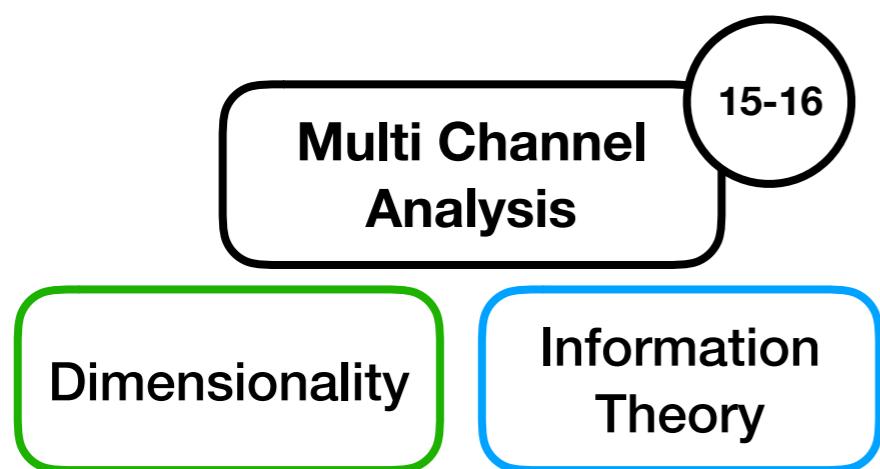
Phase Space Reconstruction



projection



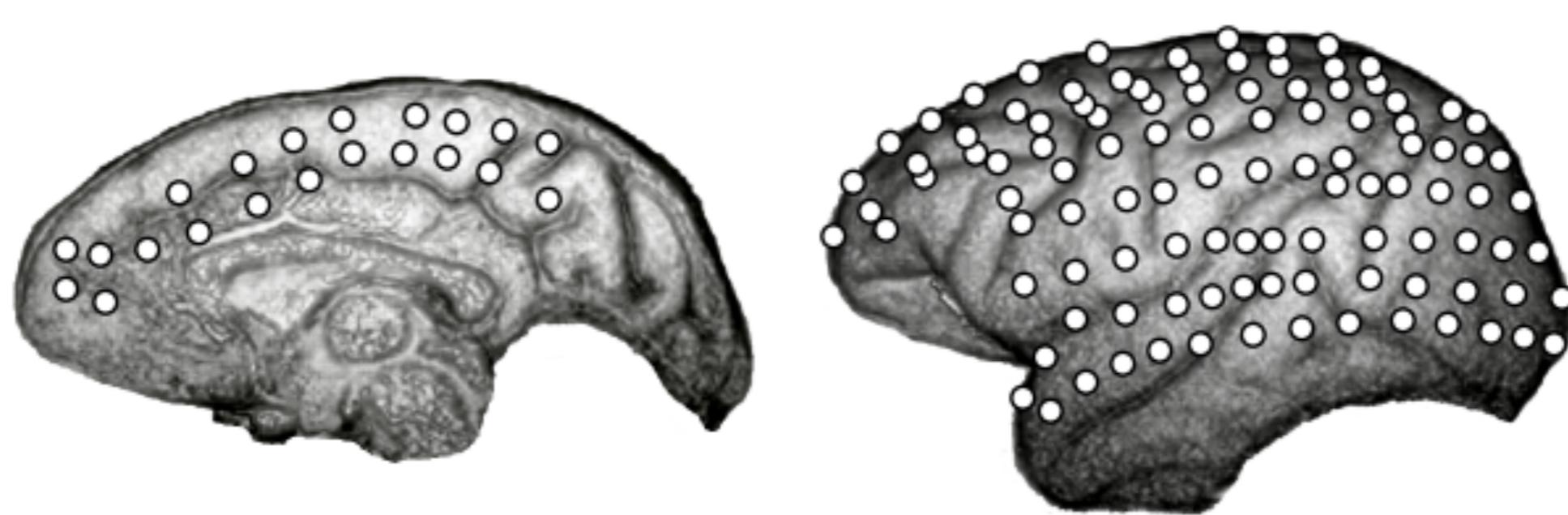
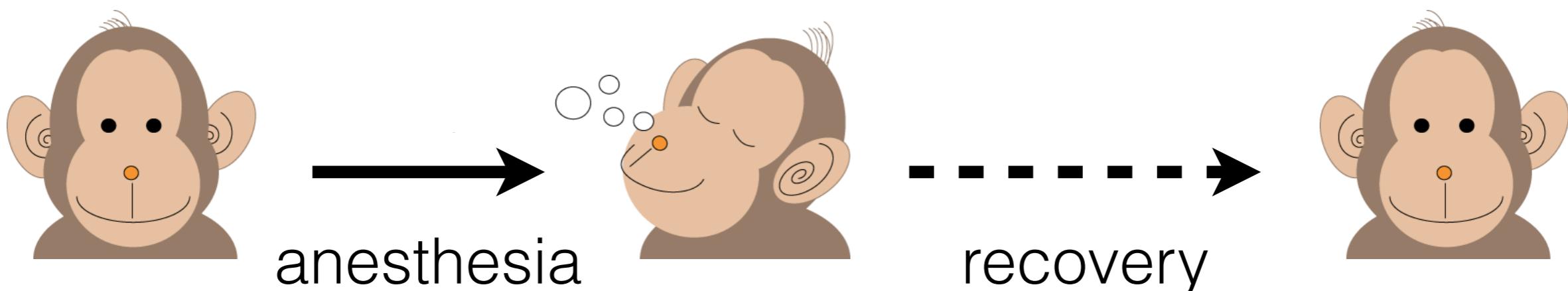
reconstruction



Dimensionality Change in Brain Dynamics

Question:

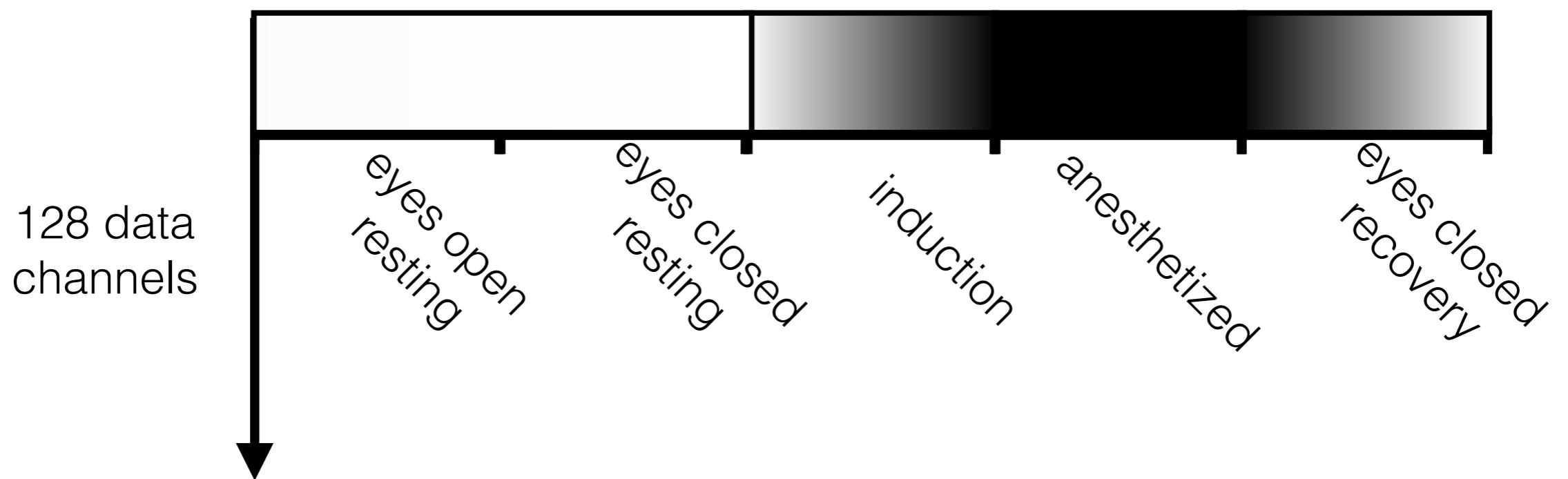
Does attractor dimension, as estimated via delay embedding, change with different brain states?



Dimensionality Change in Brain Dynamics

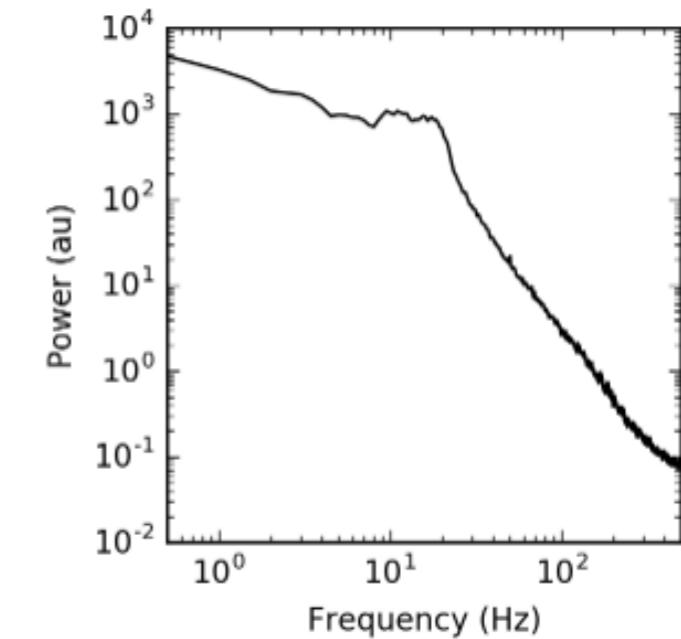
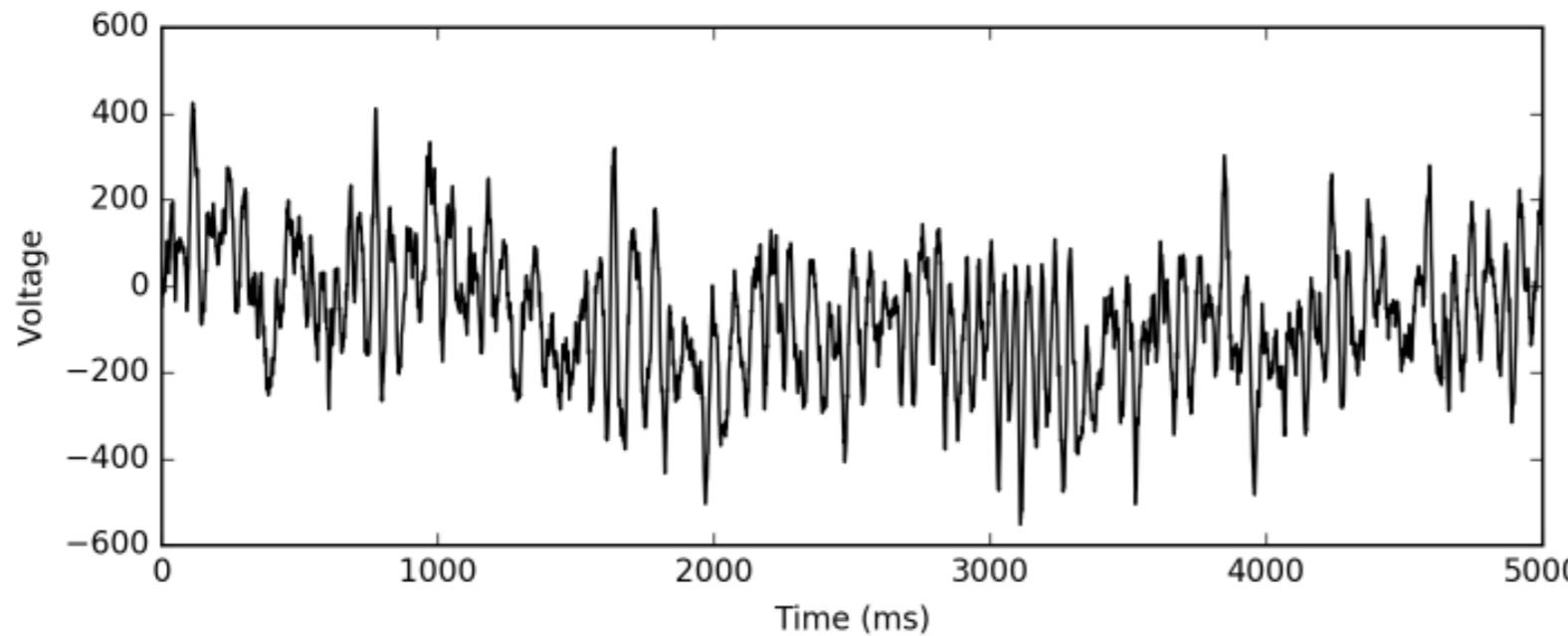
Hypothesis

Anesthetized brain should have attractors of lower dimension due to decreased computational needs.

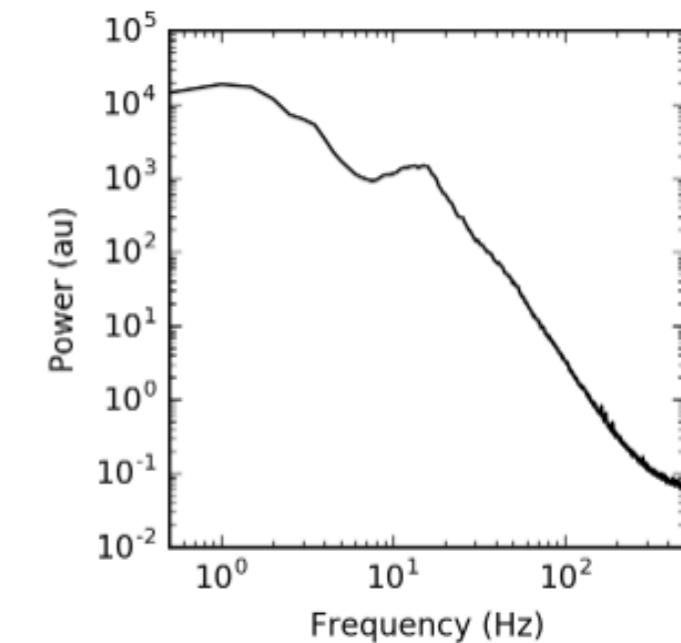
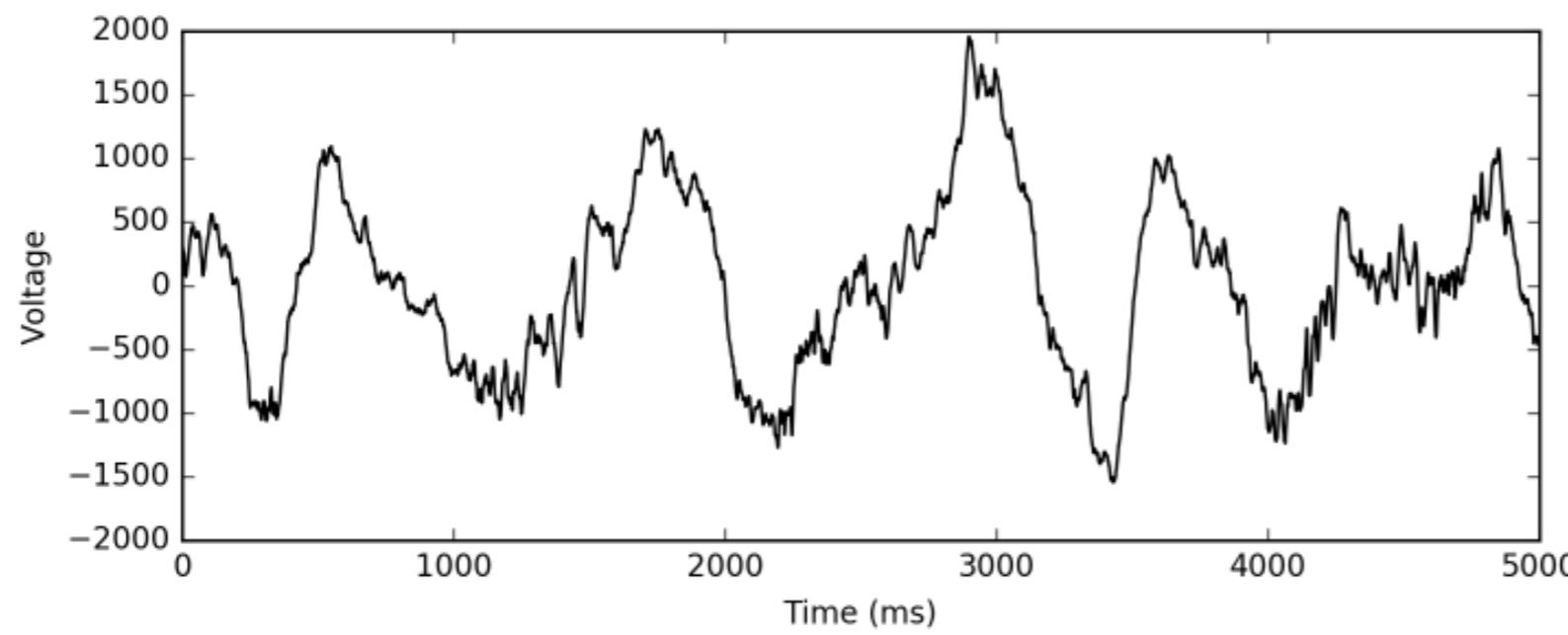


Dimensionality Change in Brain Dynamics

Awake



Anesthetized

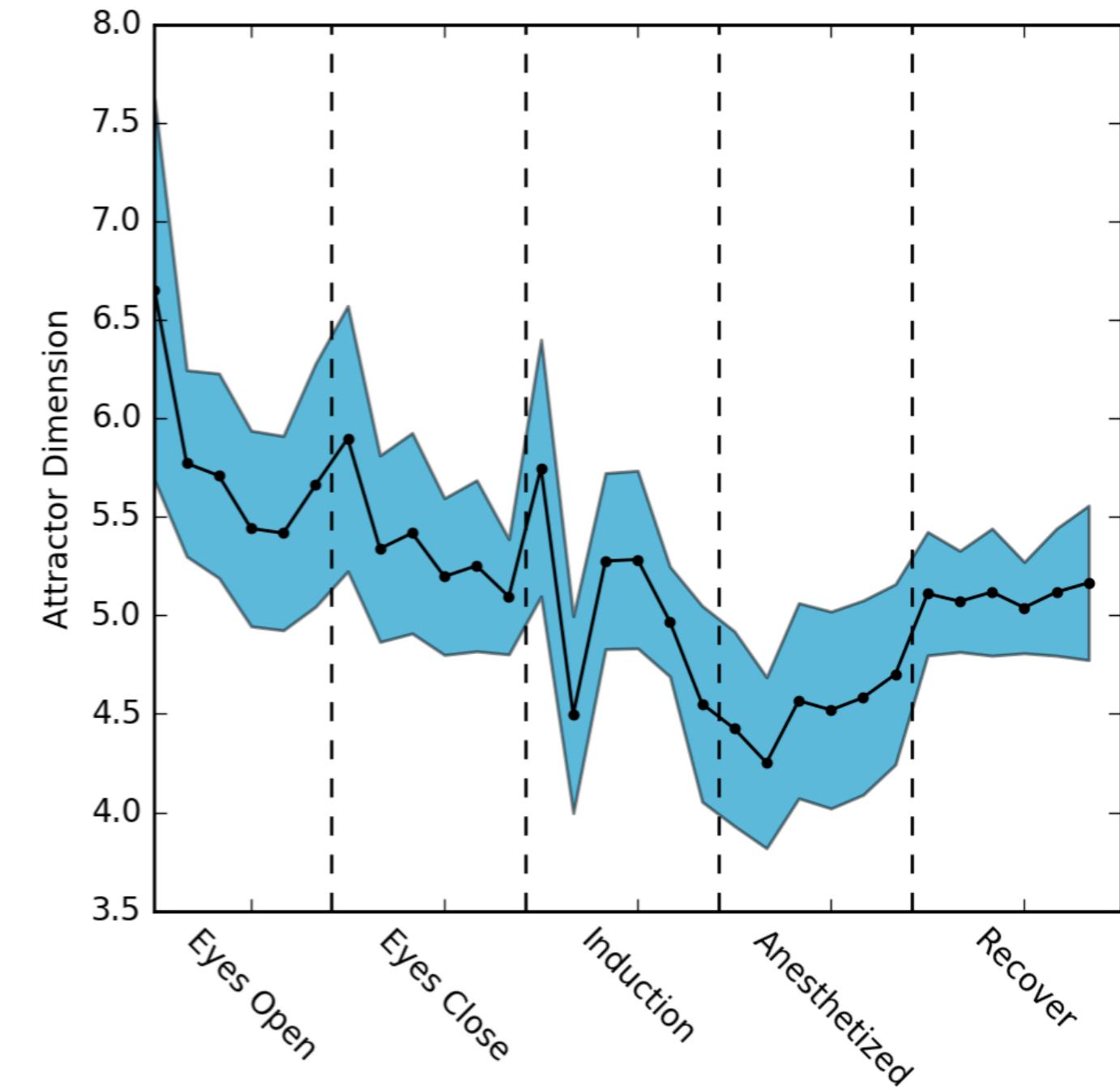
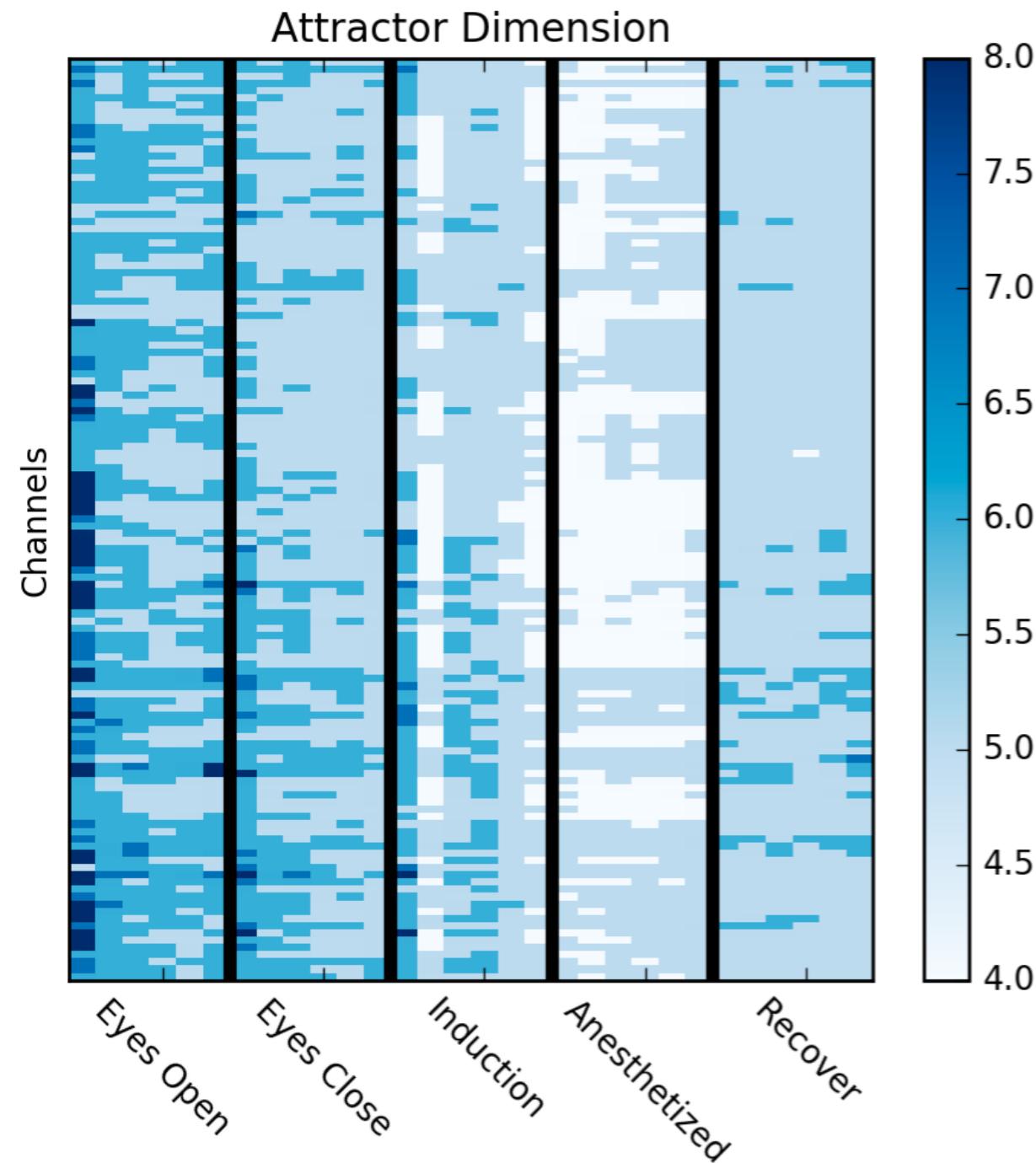


Fourier Analysis

6



Attractor Dimension

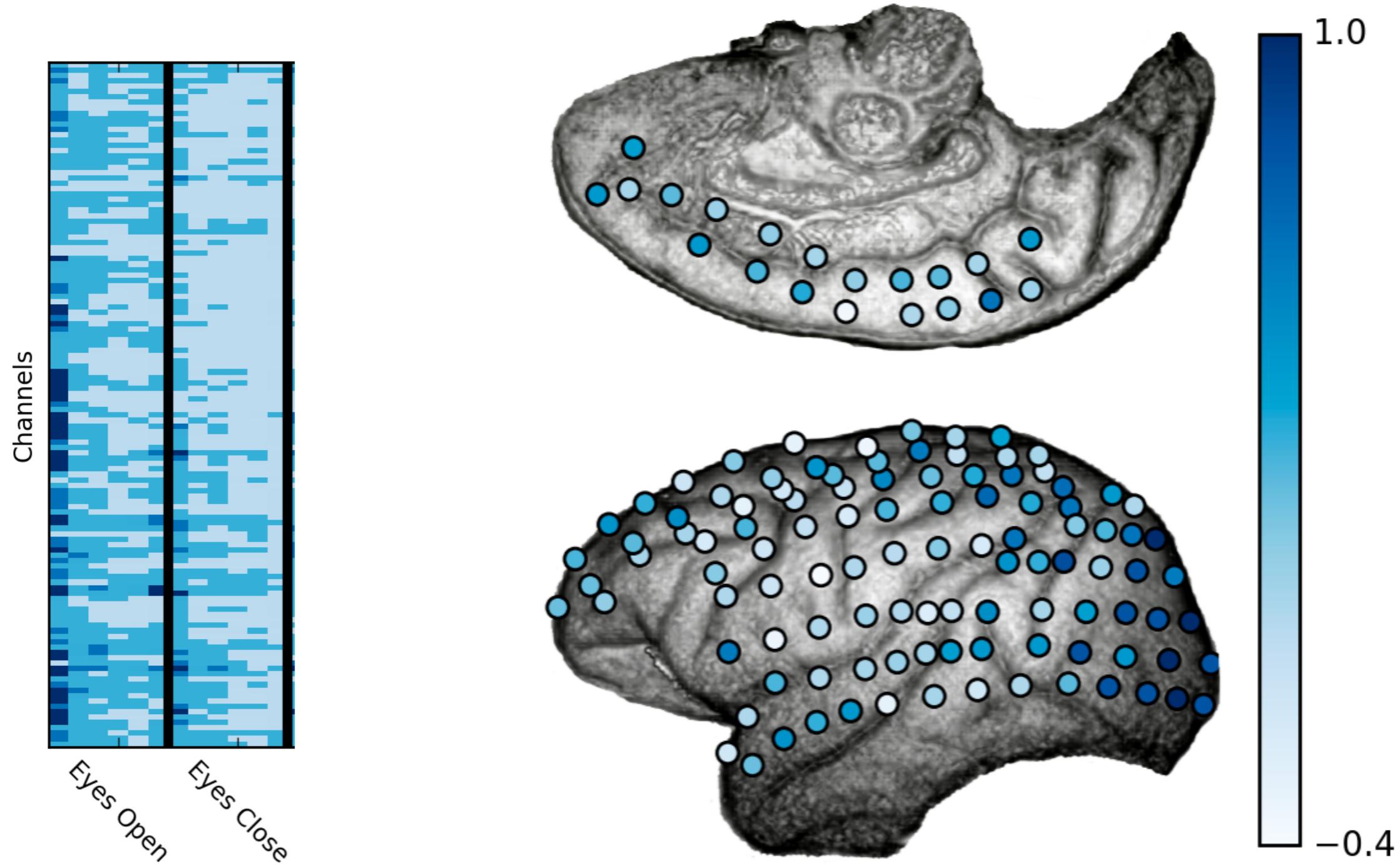


Anesthetized state has lower attractor dimension.



Attractor Dimension

Dimension Difference (EyesOpen-EyesClosed)

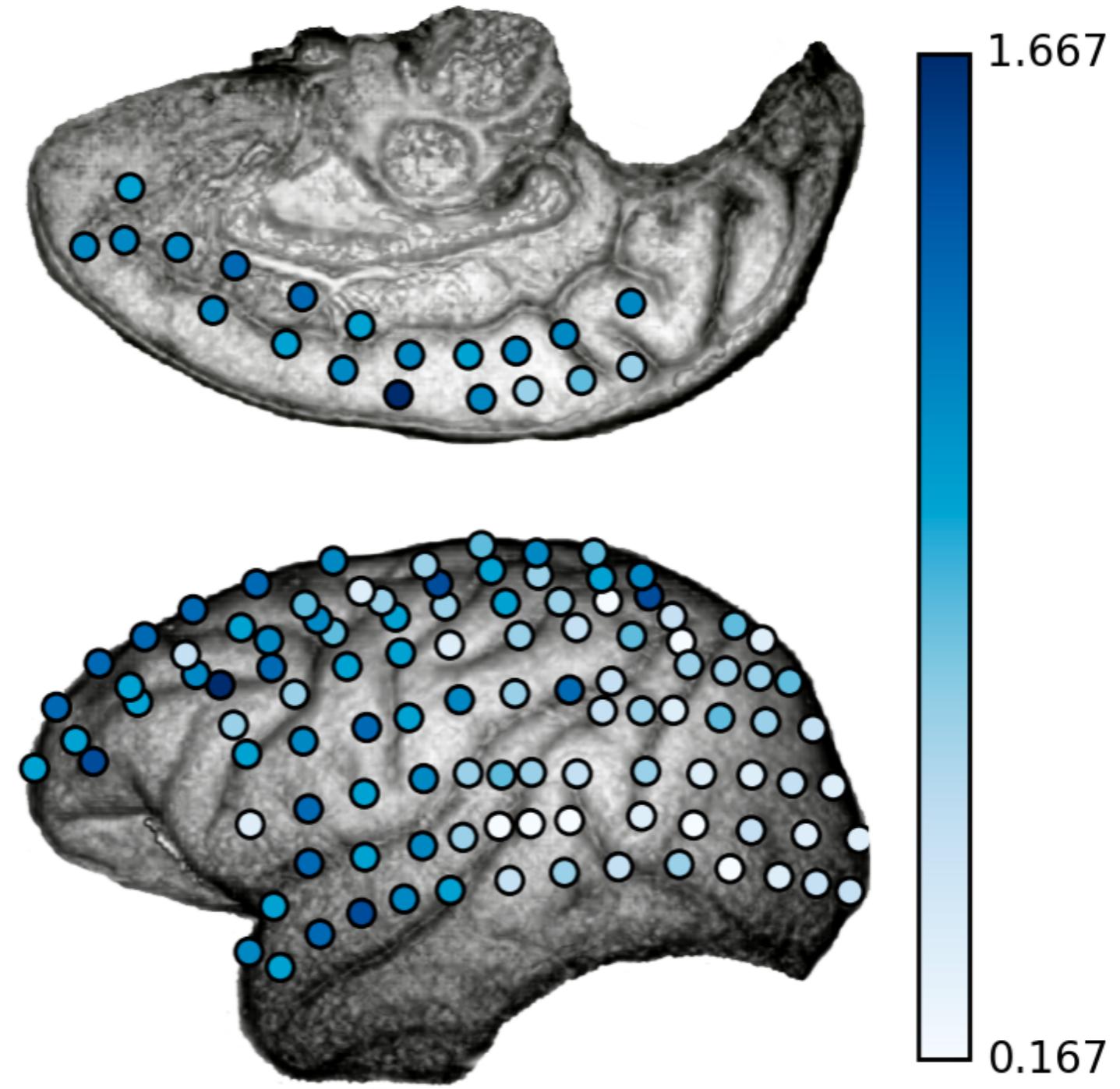
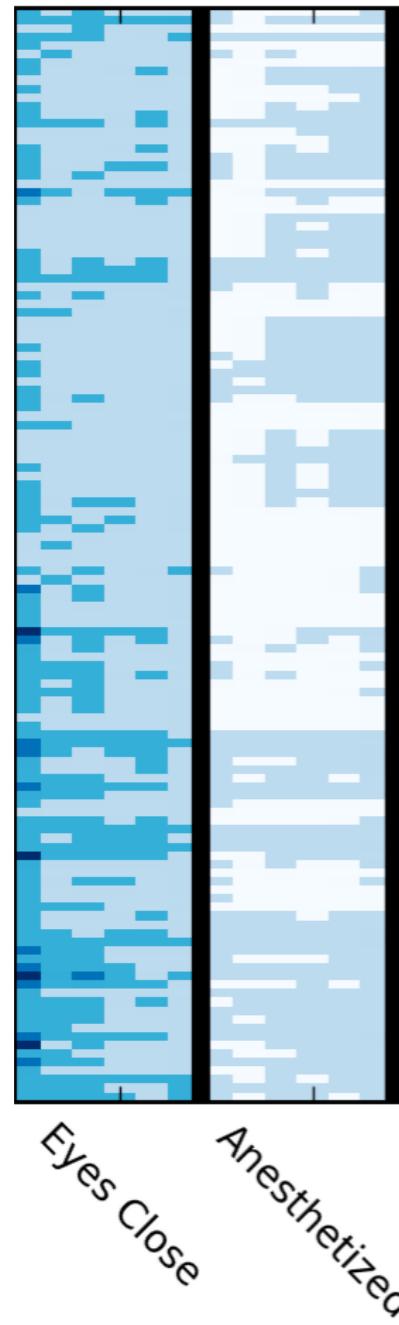


Visual areas have higher dimension when eyes are open.
Some areas actually increase in dimensions.



Attractor Dimension

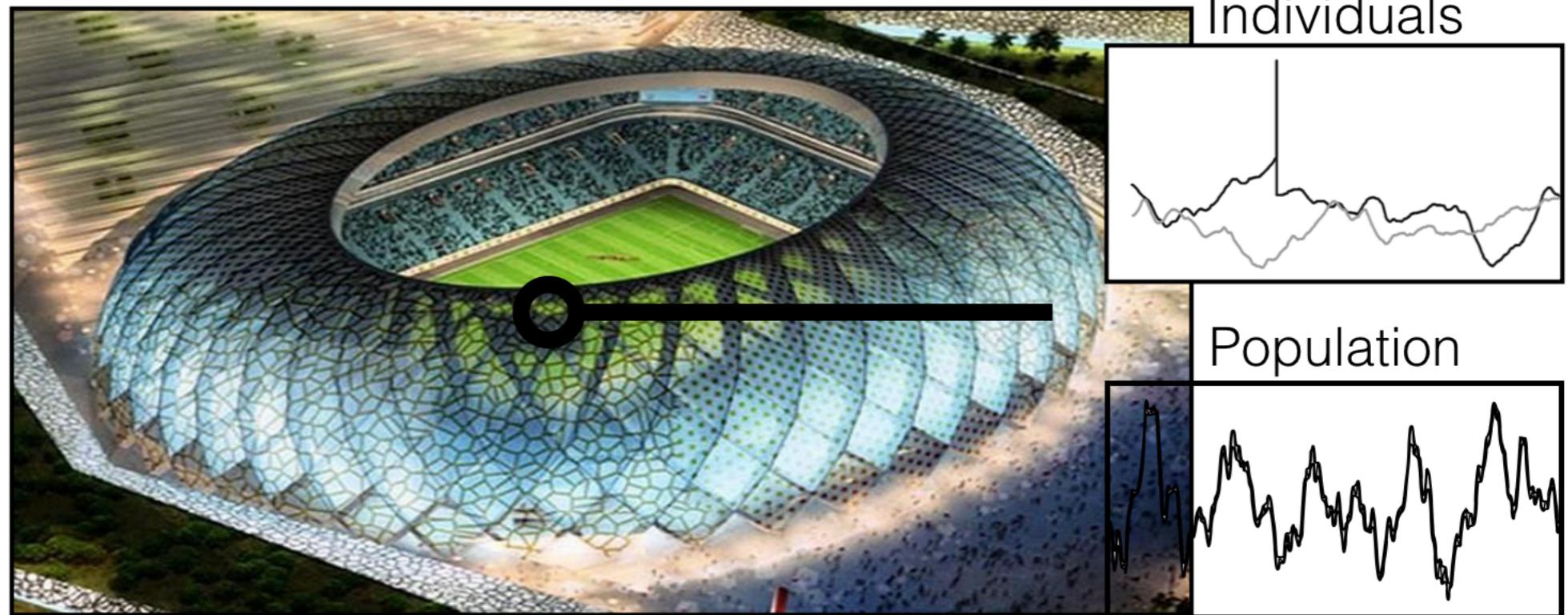
Dimension Difference (EyesClosed-Anesthetized)



Fronto-temporal areas have higher dimension when awake.



Higher Dimensional Dynamics



“asynchronous”



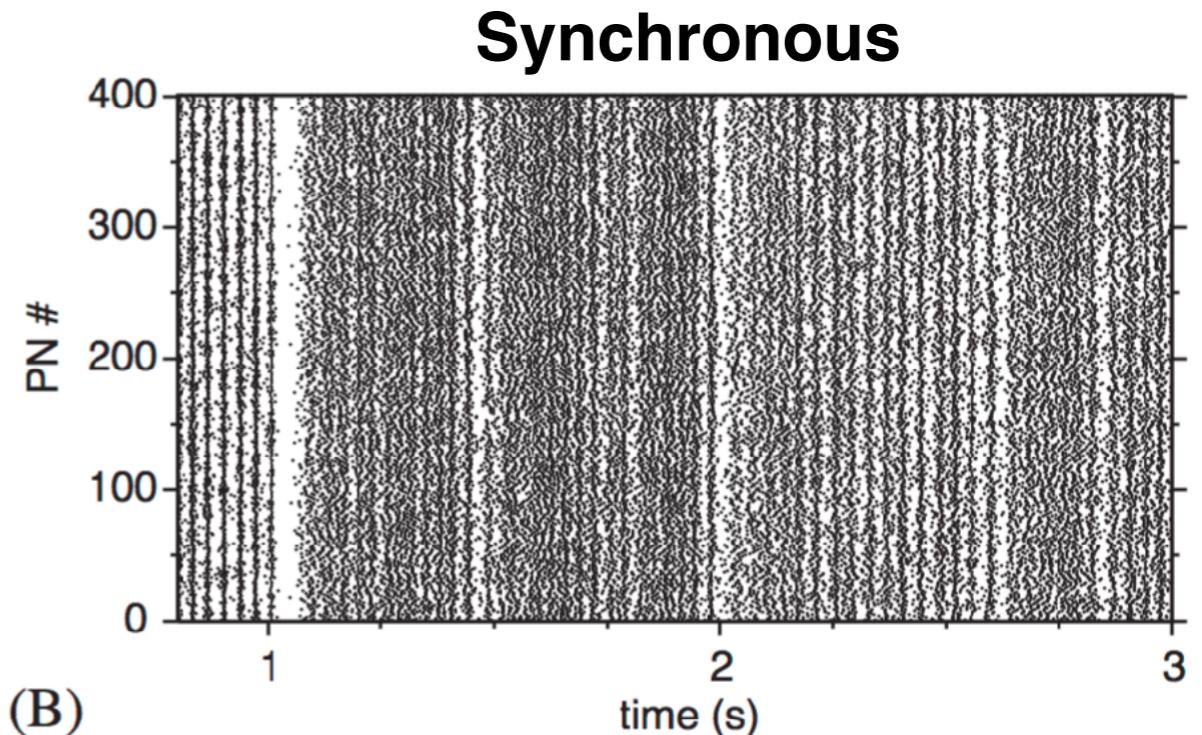
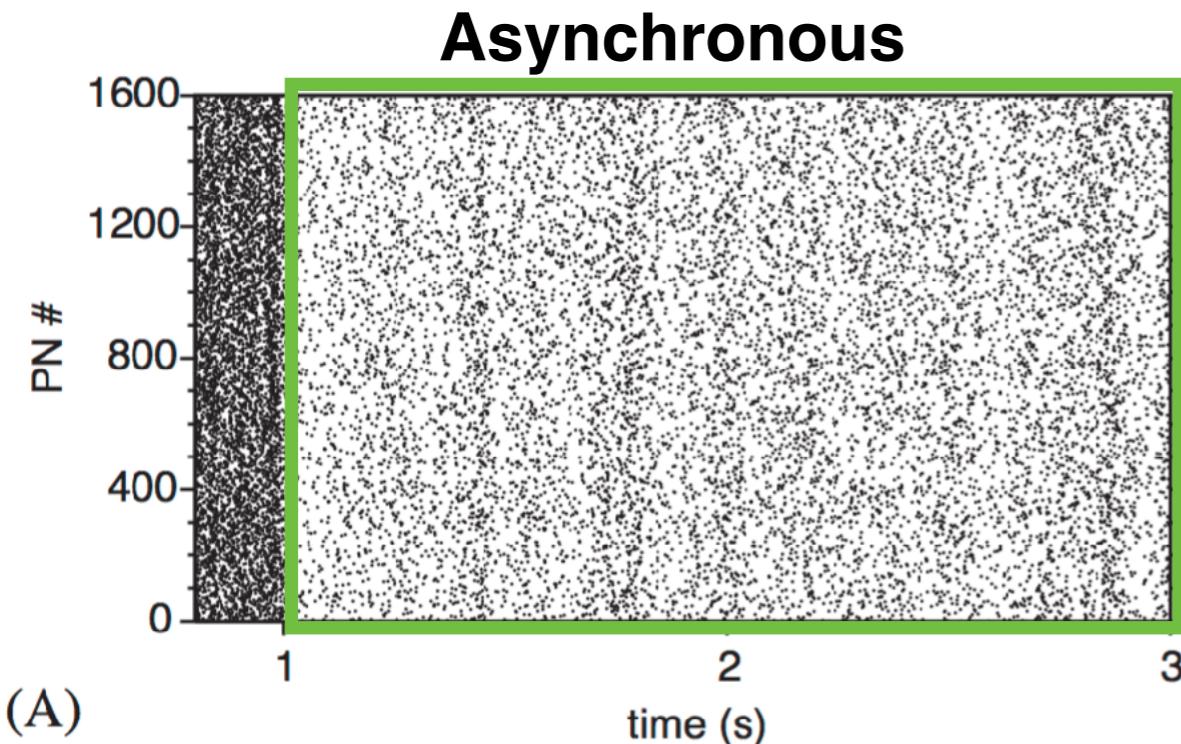
“oscillatory”



“synchronous”



Chaos - Noise - Asynchrony

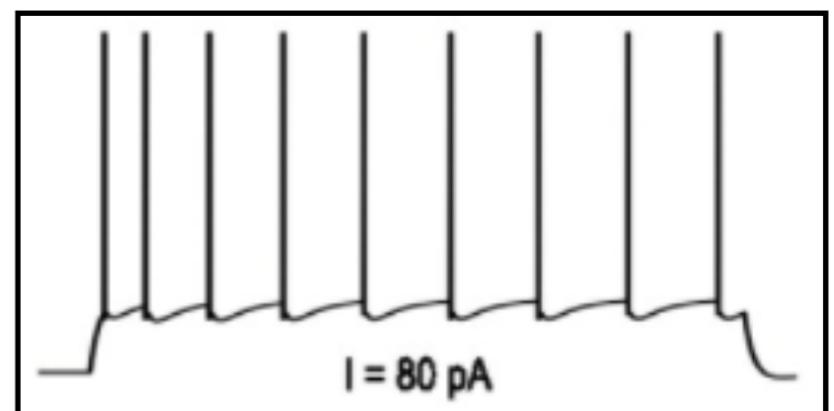


Alvarez & Destexhe, 2004

Also referred to as:

- Asynchronous irregular state
 - Fluctuation-driven regime
 - High conductance state
 - Chaotic regime - sensitive but deterministic

In contrast:



EI Balance



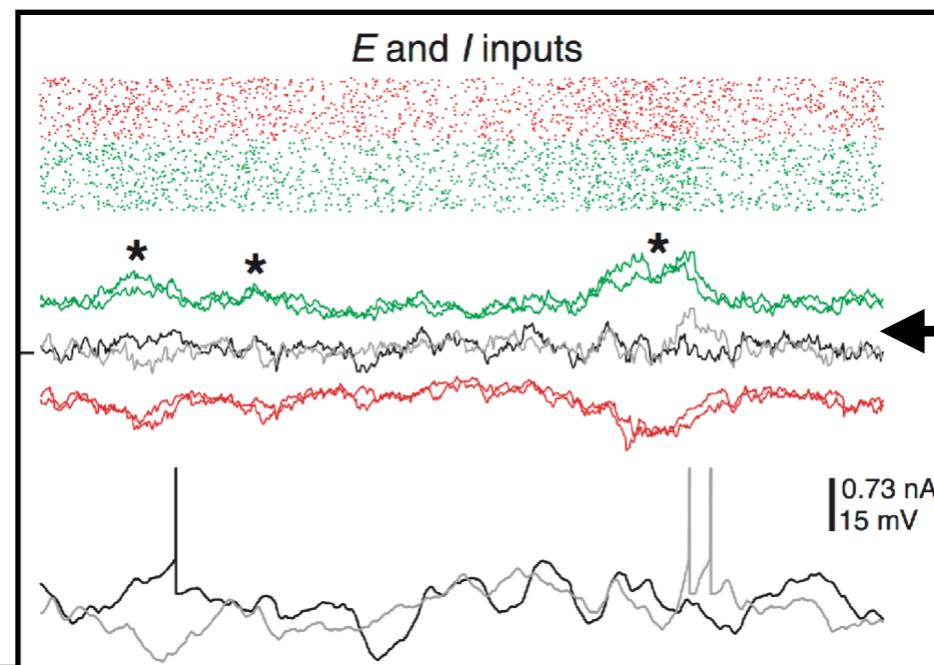
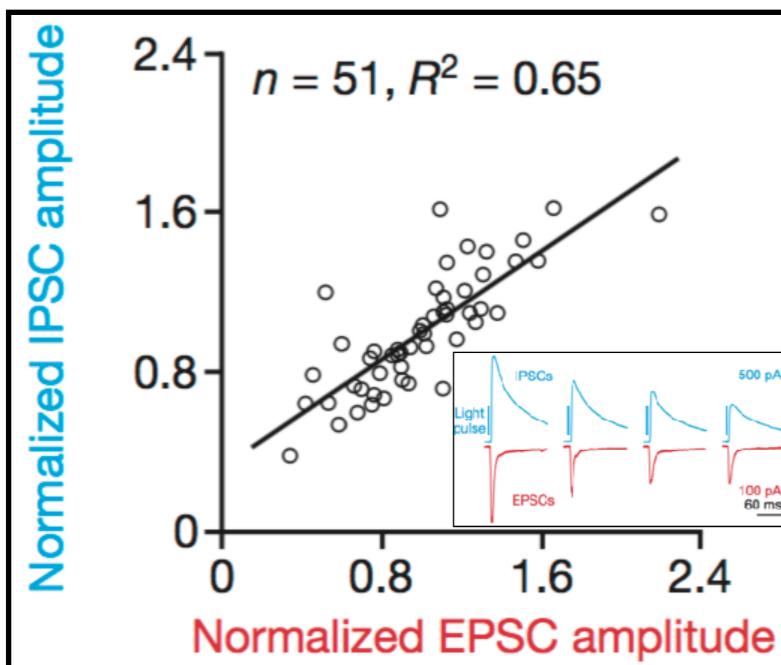
Excitation

- principal cells
- glutamate synapse
- depolarizing
- promote firing



Inhibition

- interneurons
- GABA synapse
- hyperpolarizing
- suppress firing



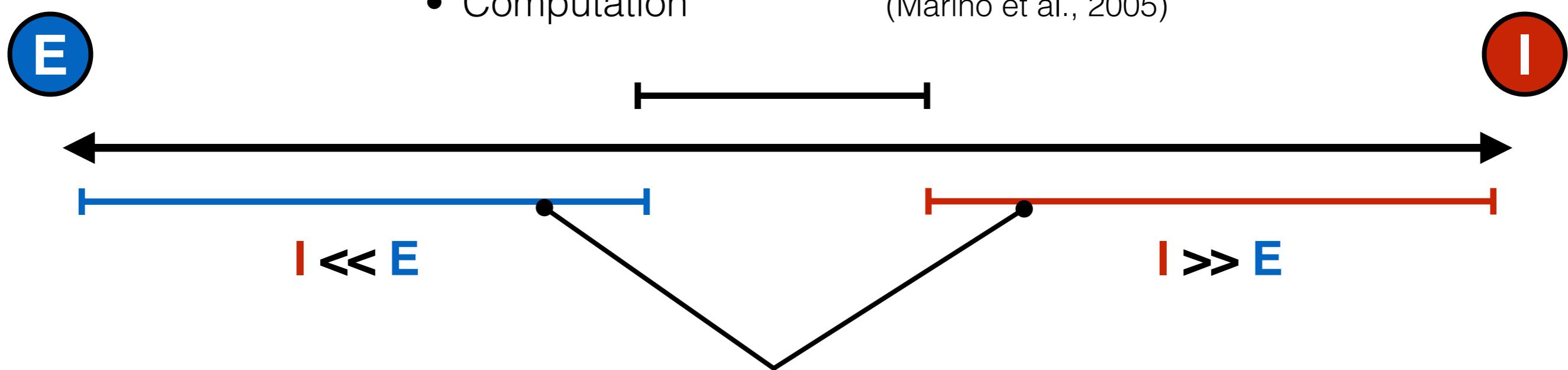
high conductance
fluctuations

Renart et al., 2010
Xue et al., 2014



“Balance”

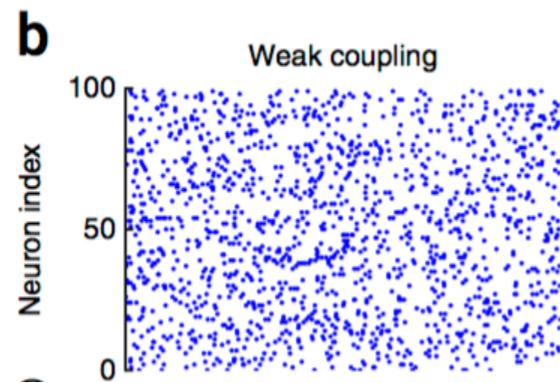
- Spontaneous
- Enable Oscillations (Atallah et al., 2012)
- Information Gating (Vogels & Abbott, 2009)
- Computation (Marino et al., 2005)



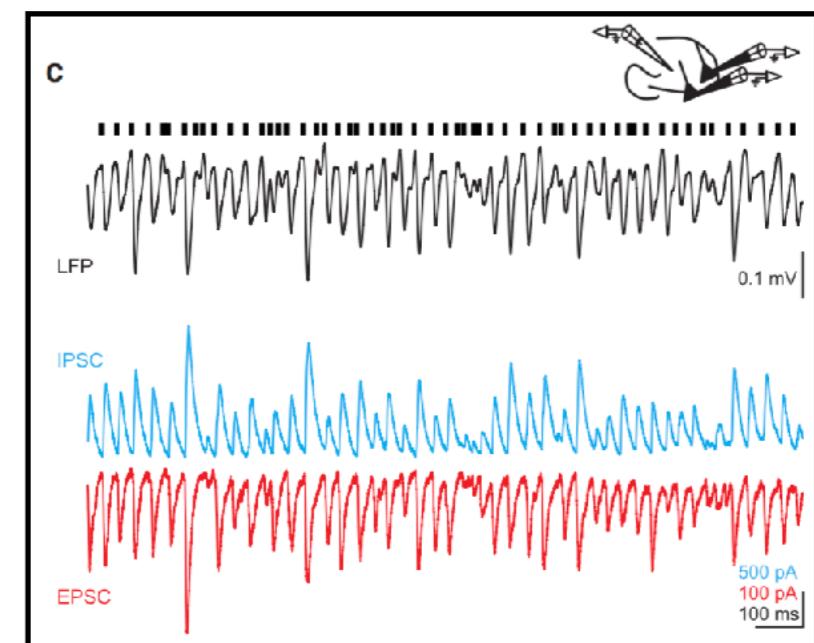
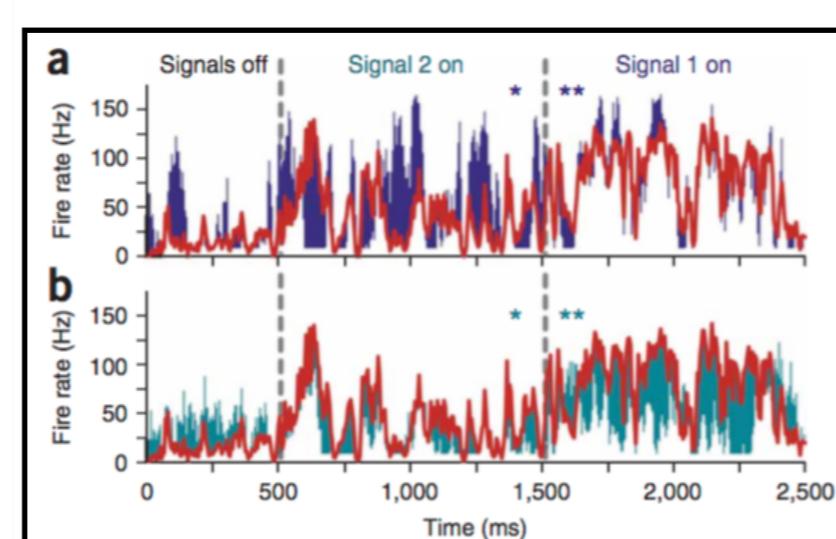
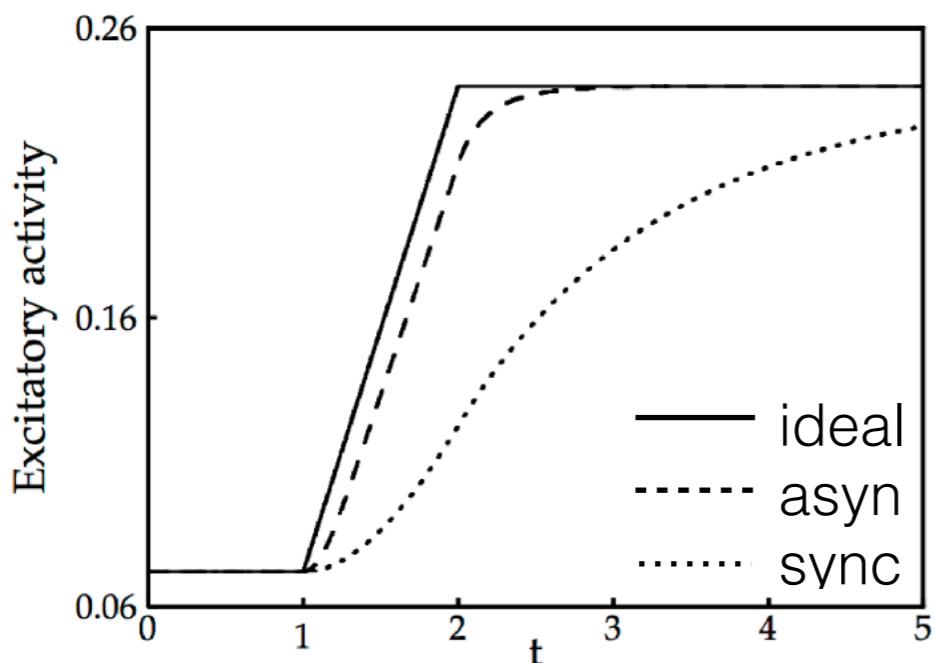
“Imbalance”

- Epilepsy (Symonds, 1959)
- Autism (Rubenstein & Merzenich, 2003)
- Schizophrenia (Uhlhaas & Singer, 2010)
- Social Dysfunction (Yizhar et al., 2011)





Spike-timing Chaos in EI Balanced Circuits



Stimulus Tracking

Van Vreeswijk & Sompolinsky,
1996

Signal Gating & Gain Modulation

Vogels & Abbott, 2009
Chance et al., 2003

Oscillations

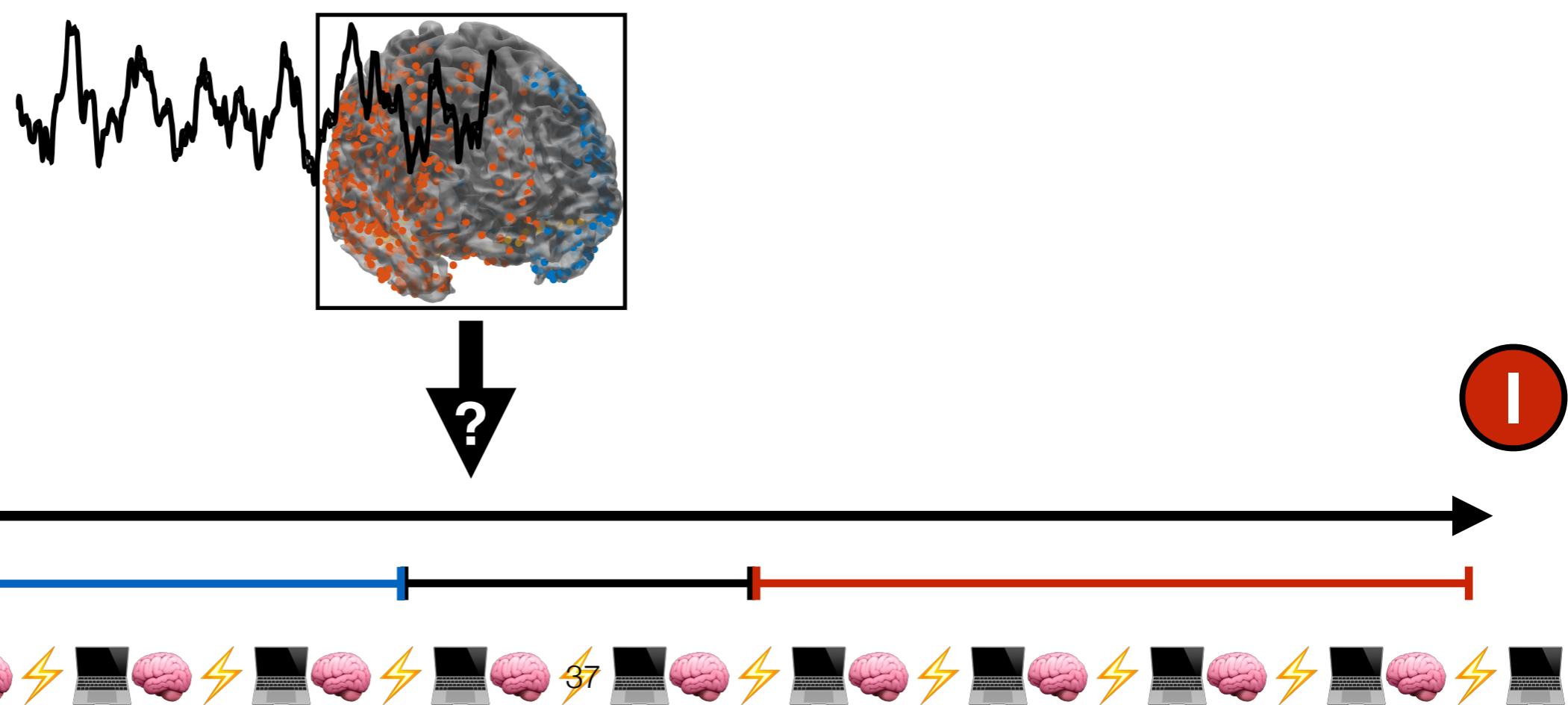
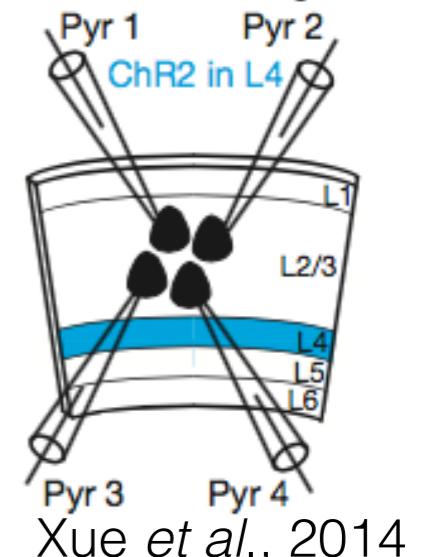
Atallah & Scanziani, 2009



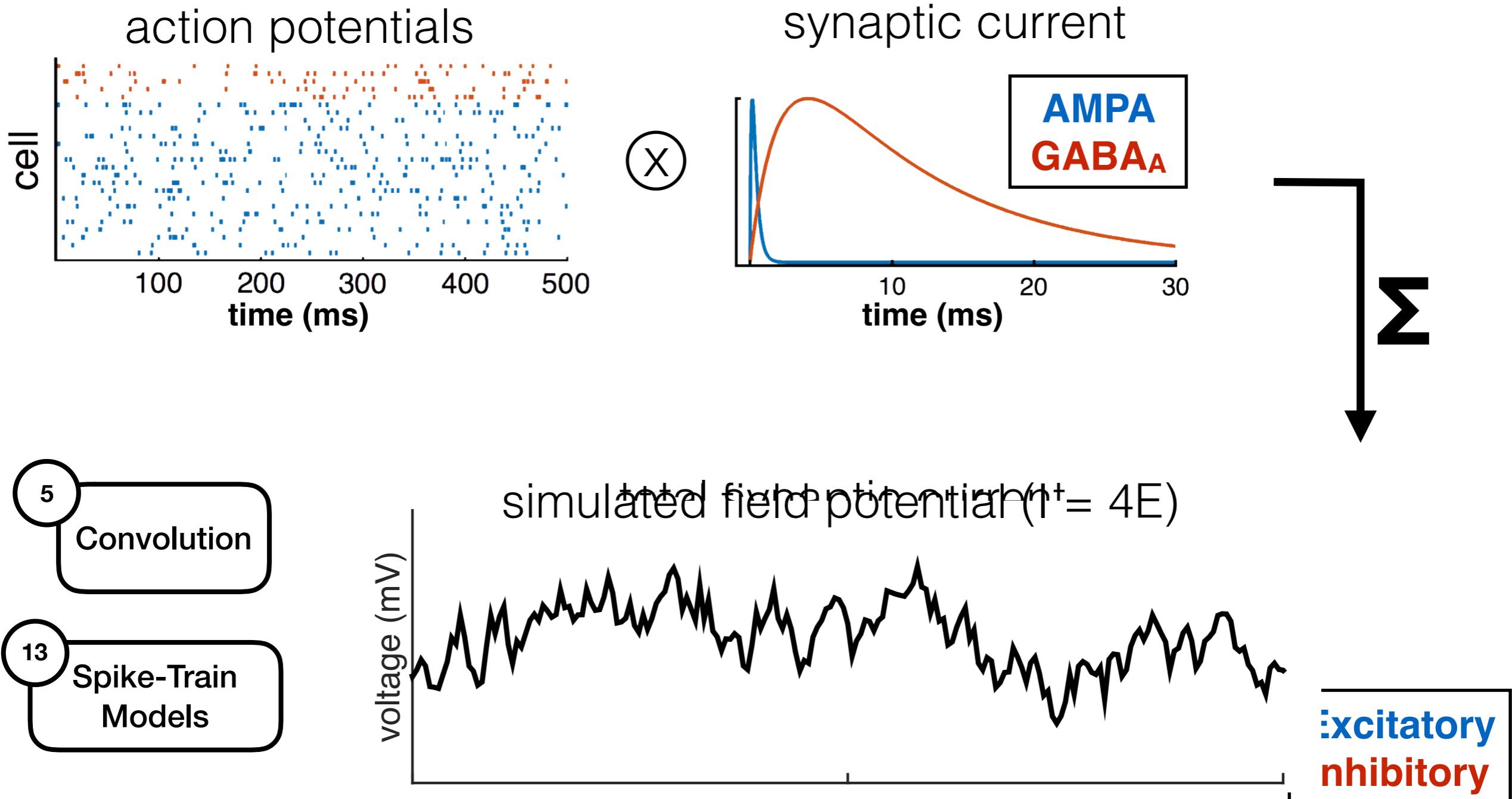
Measuring EI Balance

Motivation

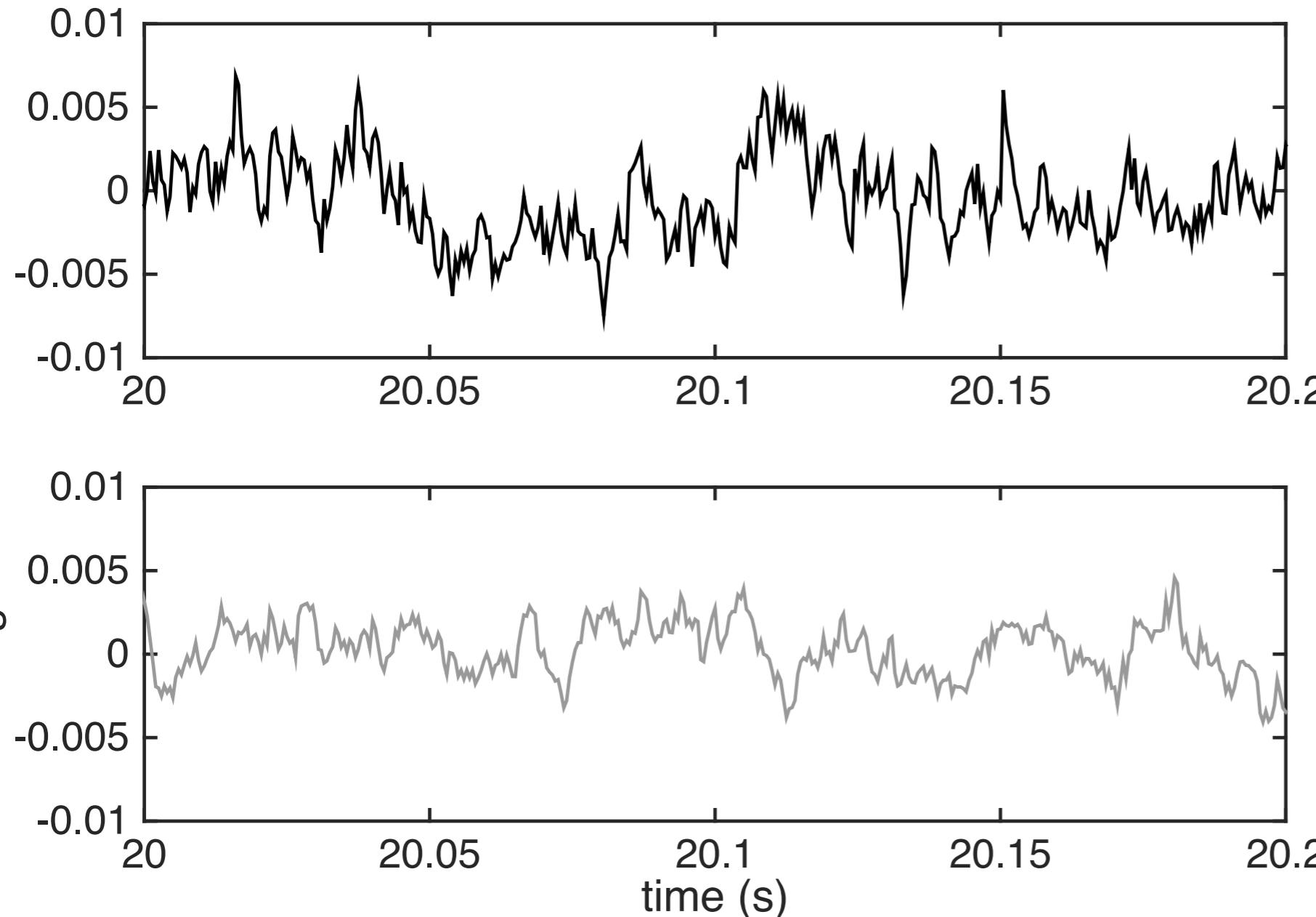
Can we determine E:I ratio without intracellular
and/or active manipulation studies?



Simulating Local Field Potentials



Measuring EI Balance

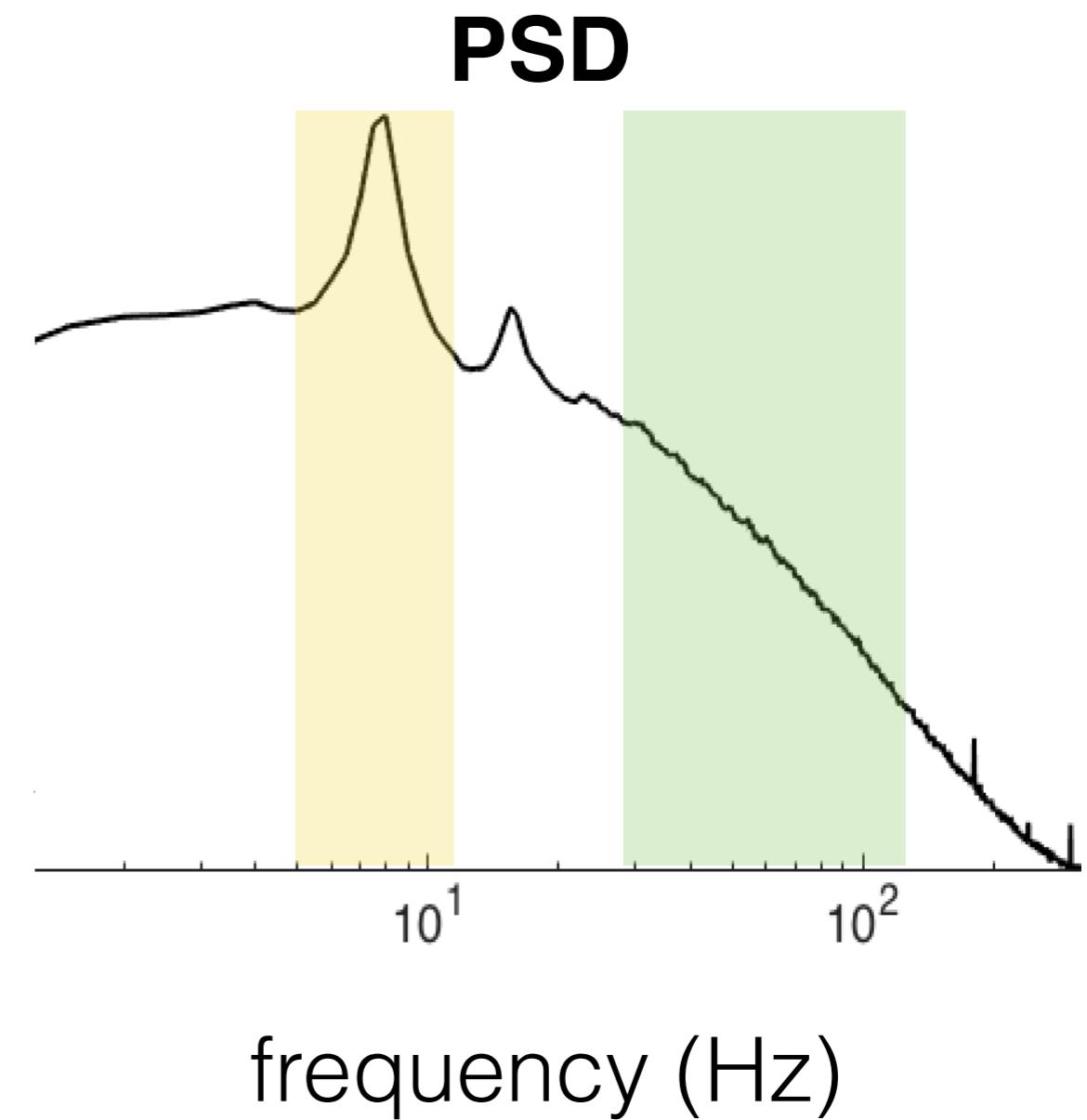
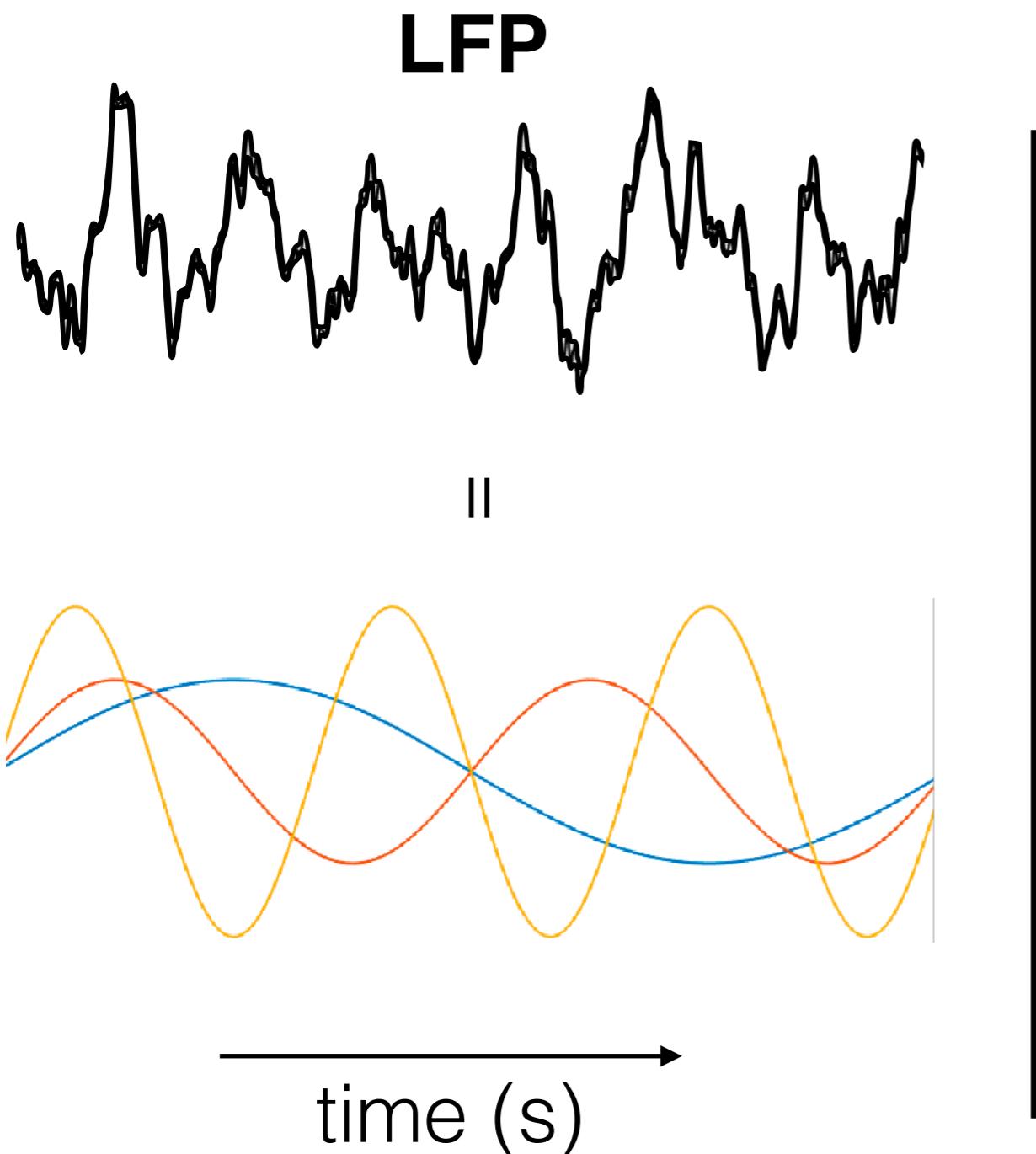


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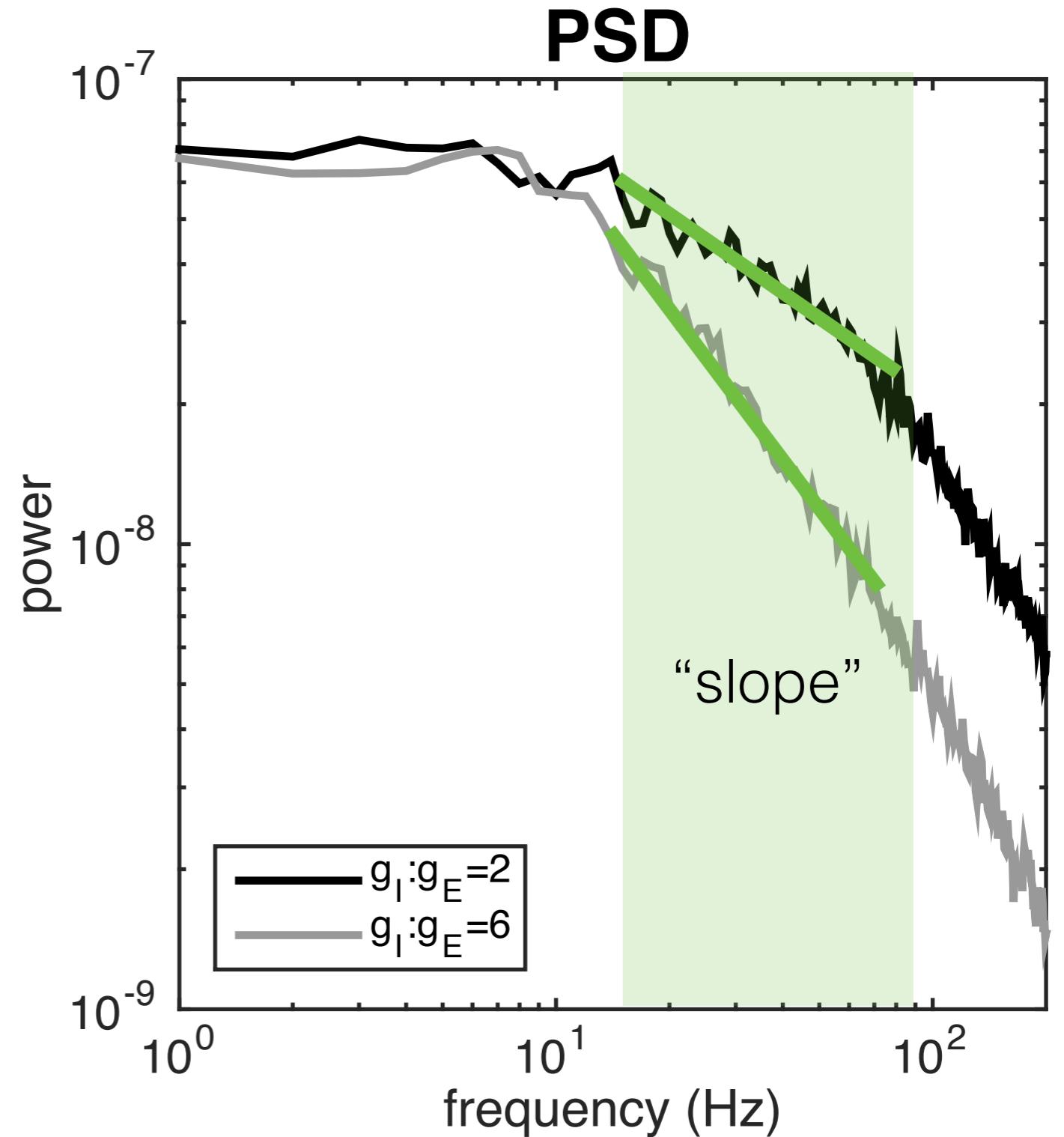
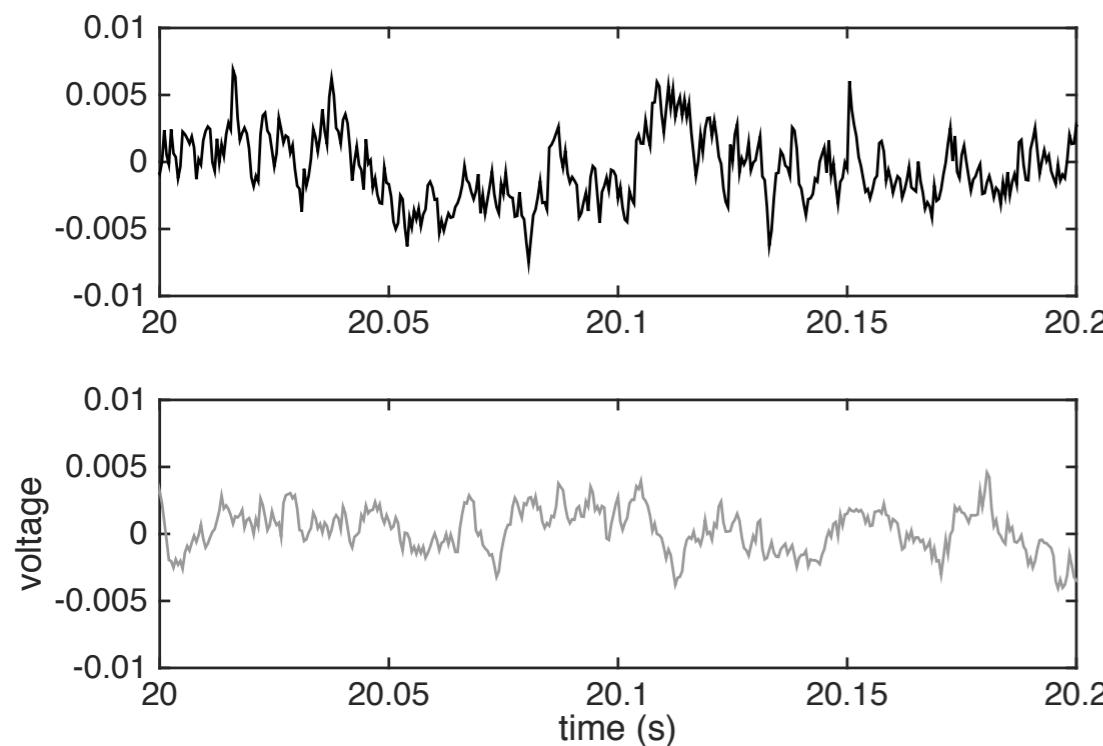
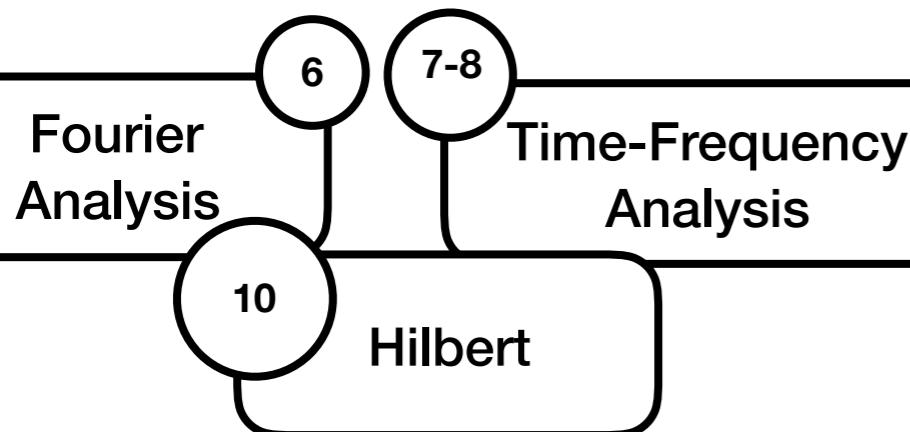
E:I = 1:2 or 1:6



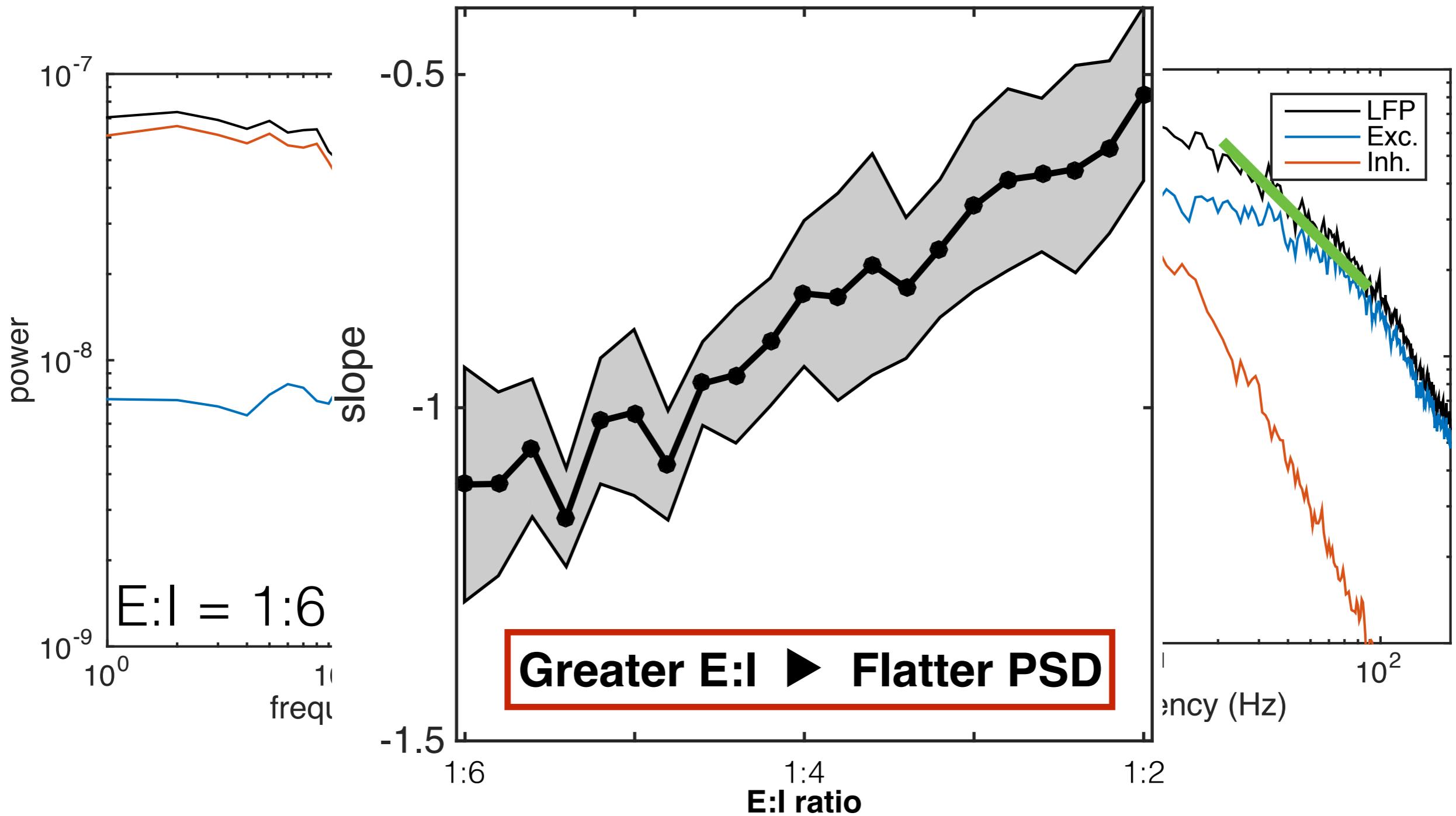
Measuring EI Balance



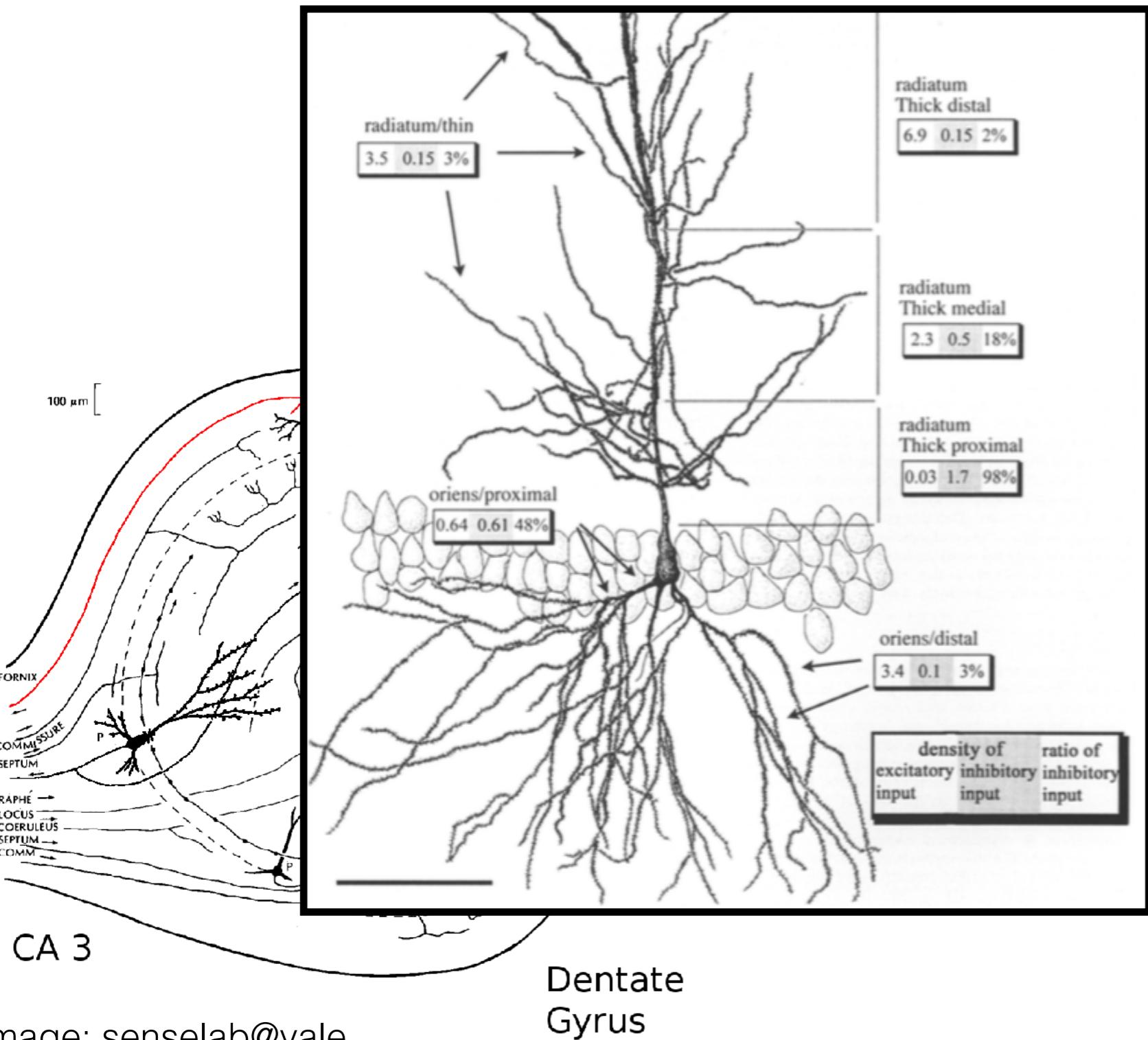
Measuring EI Balance



Measuring EI Balance



Measuring EI Balance



GABA synapse
density (per μm)

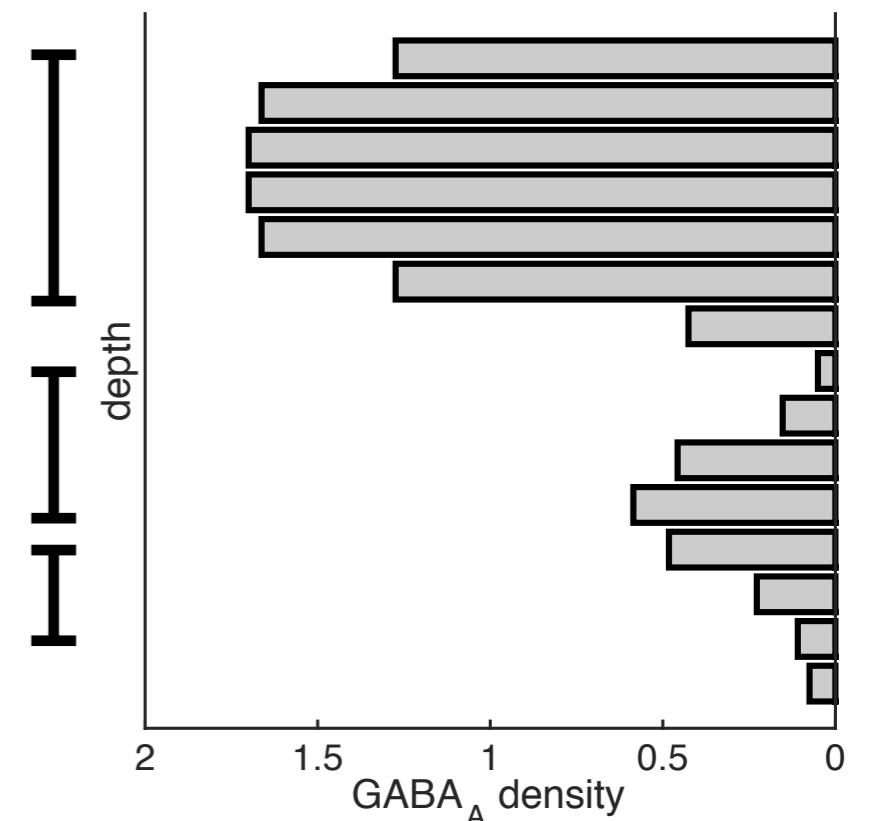
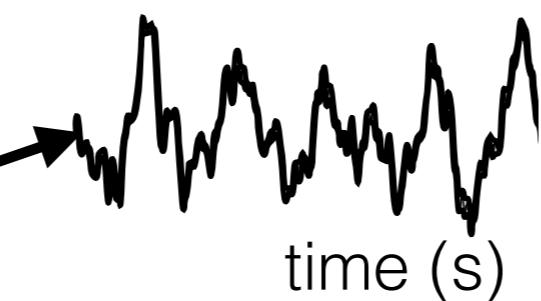
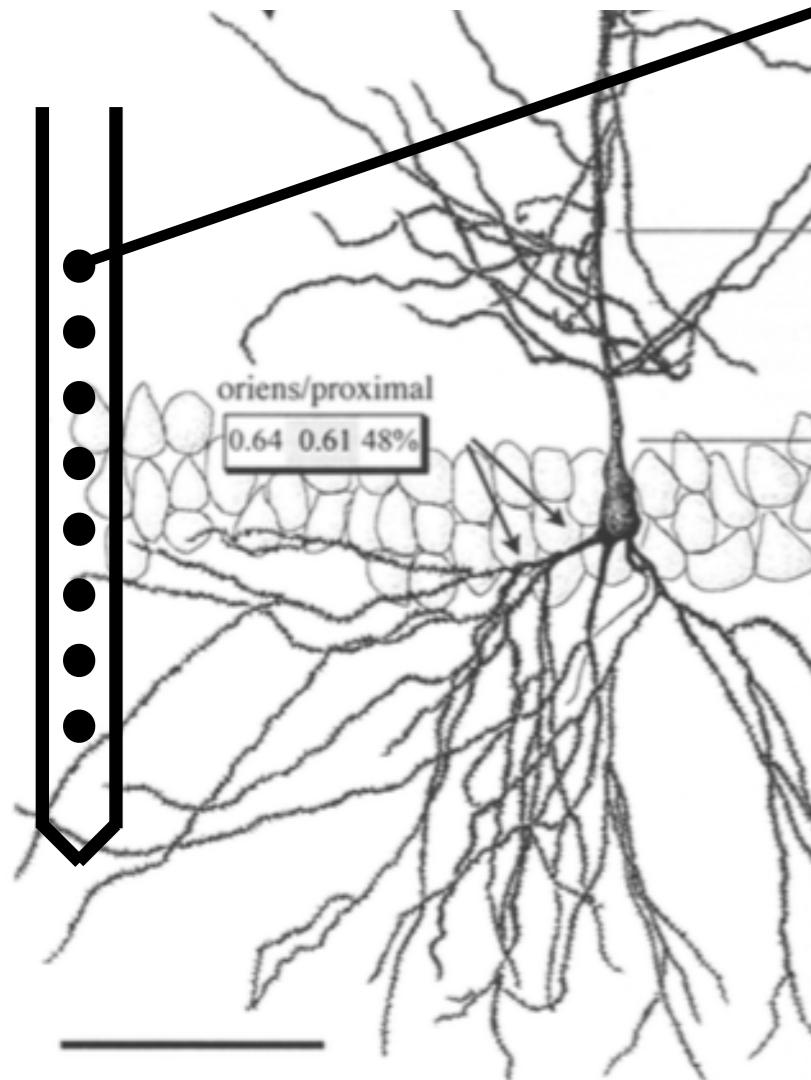


image: senselab@yale

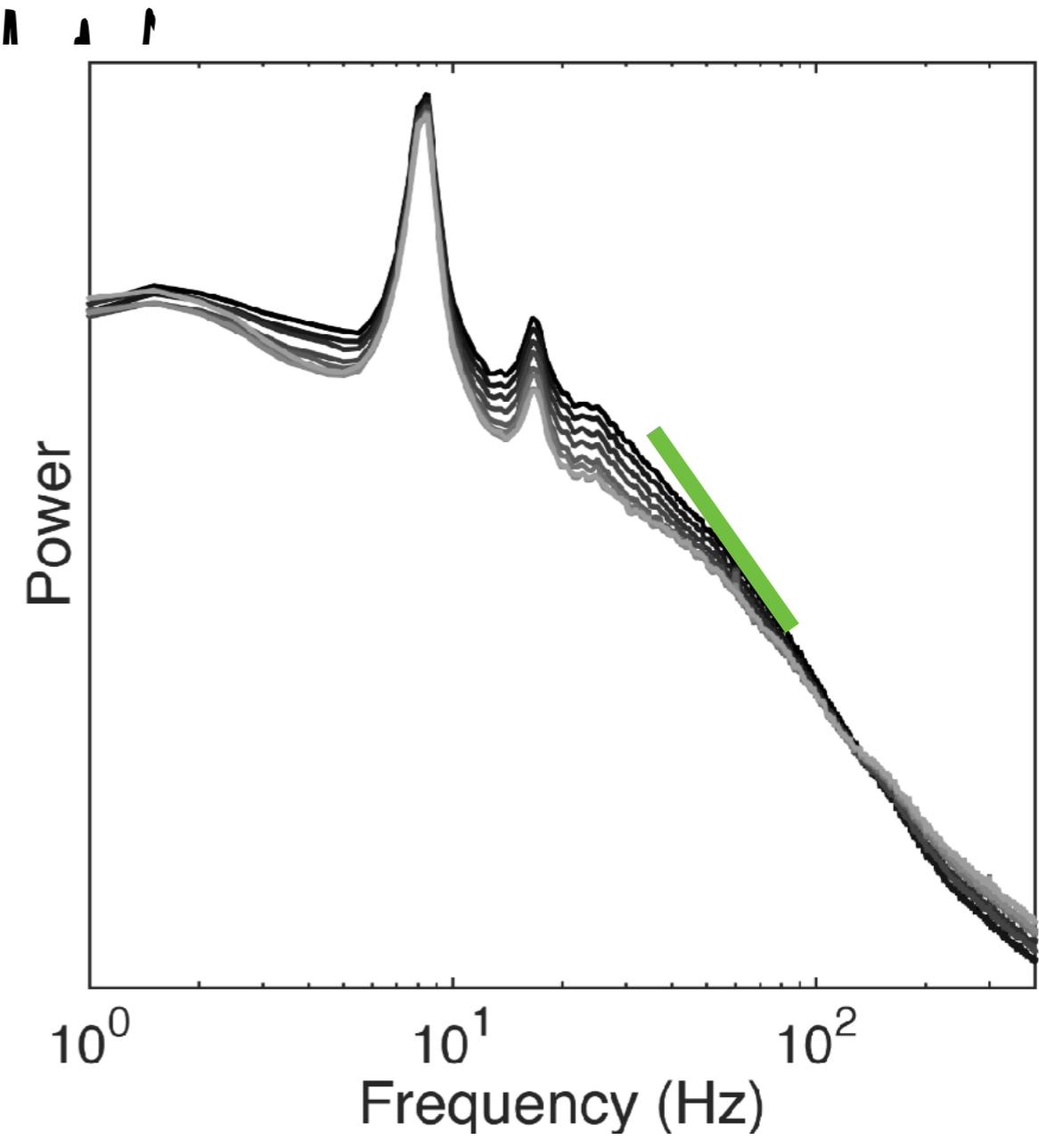


Depth Dependent Inhibition in Hippocampus (CA1)

LFP



280 μ m



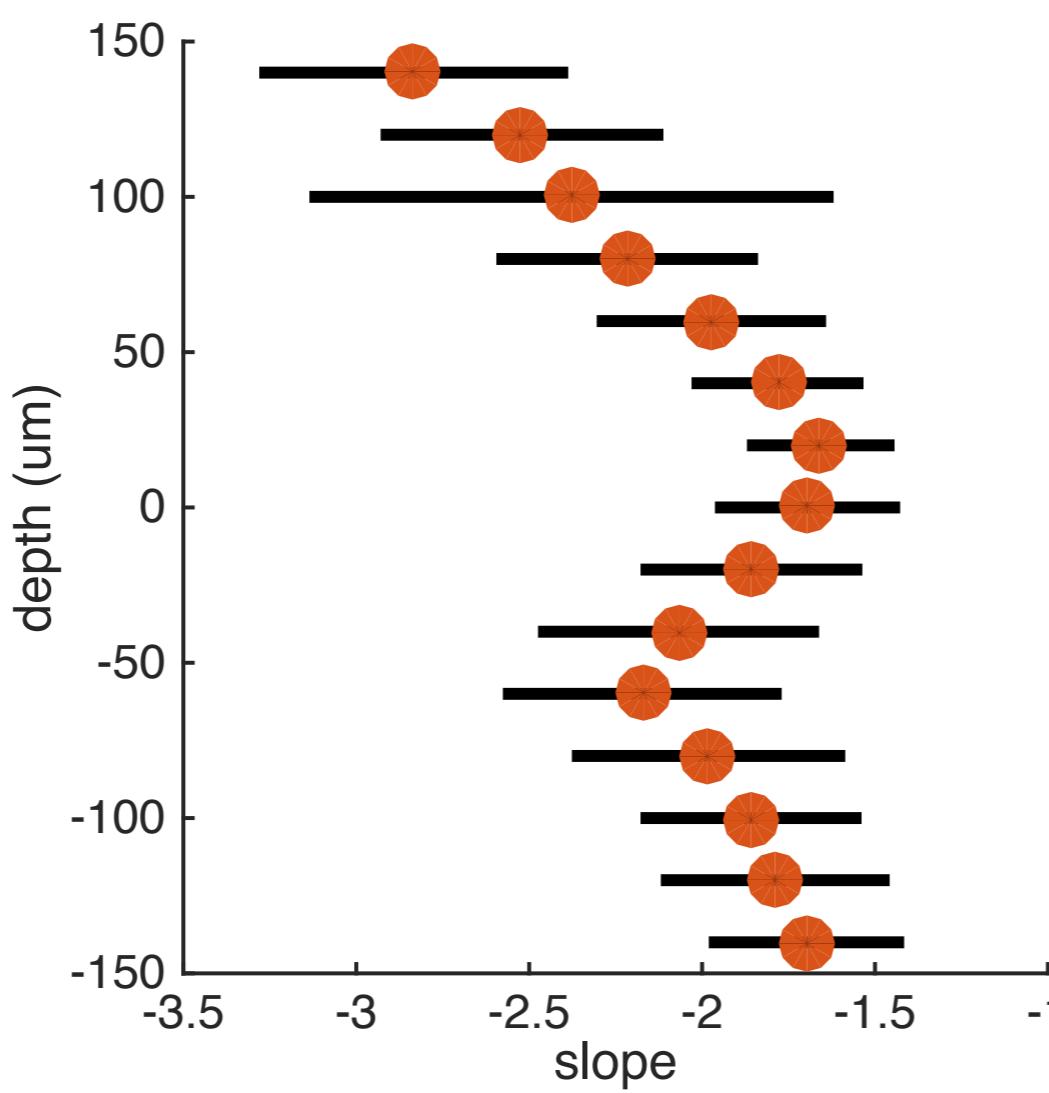
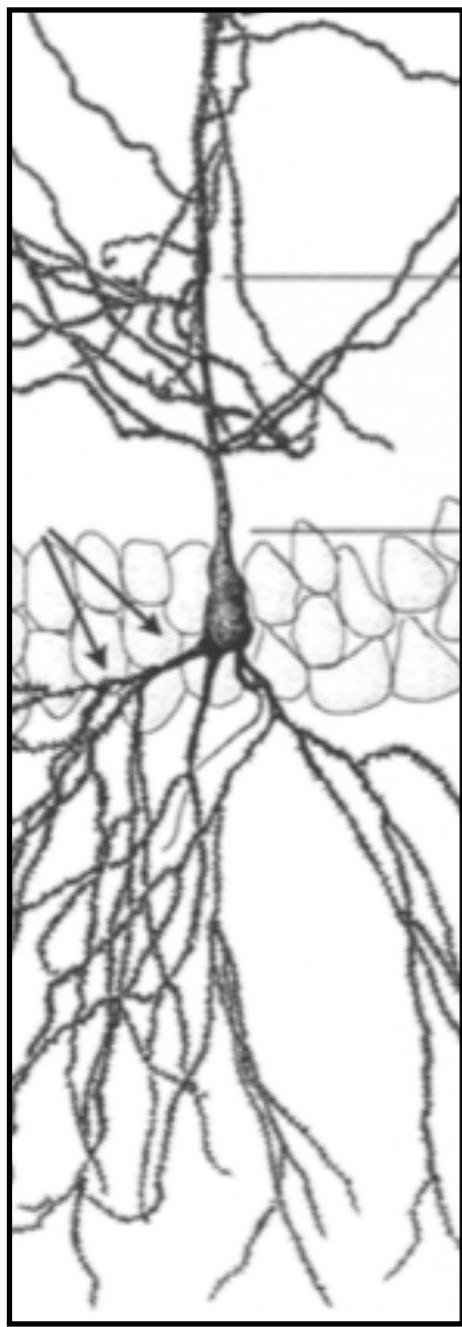
$10^0 \quad 10^1 \quad 10^2$

Frequency (Hz)

data: CRCNS & Buzsaki Lab



Measuring EI Balance

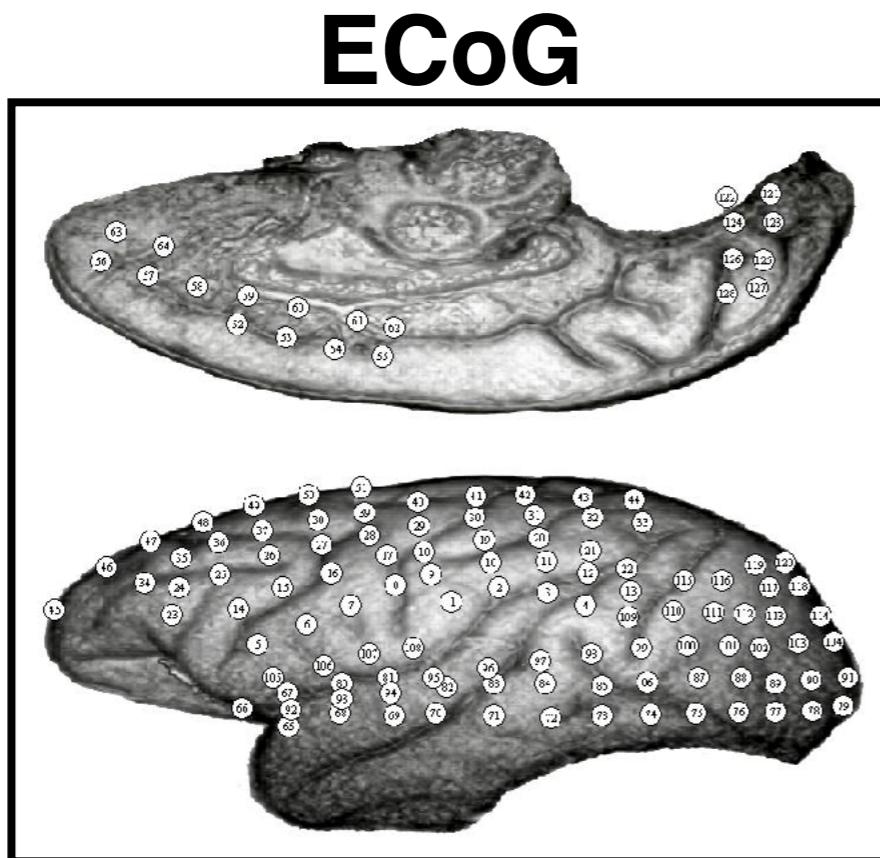
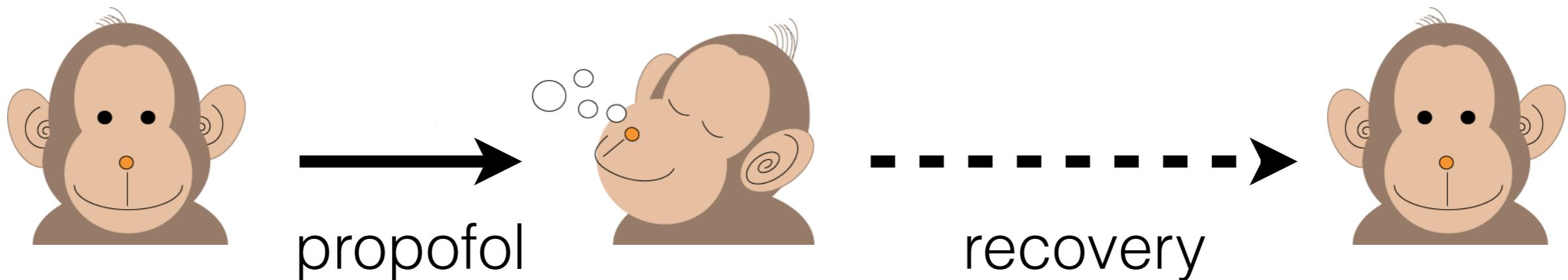


PSD slope across depth reflects density of inhibitory synapses.



Measuring EI Balance

Anesthesia Induced Increase of Inhibition

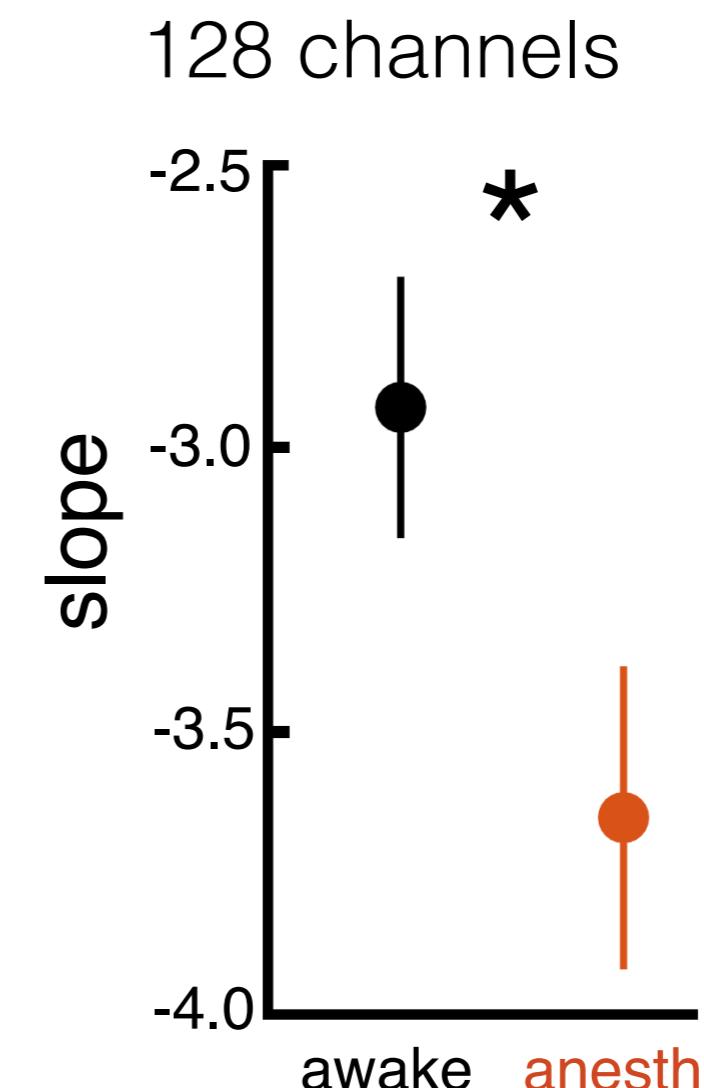
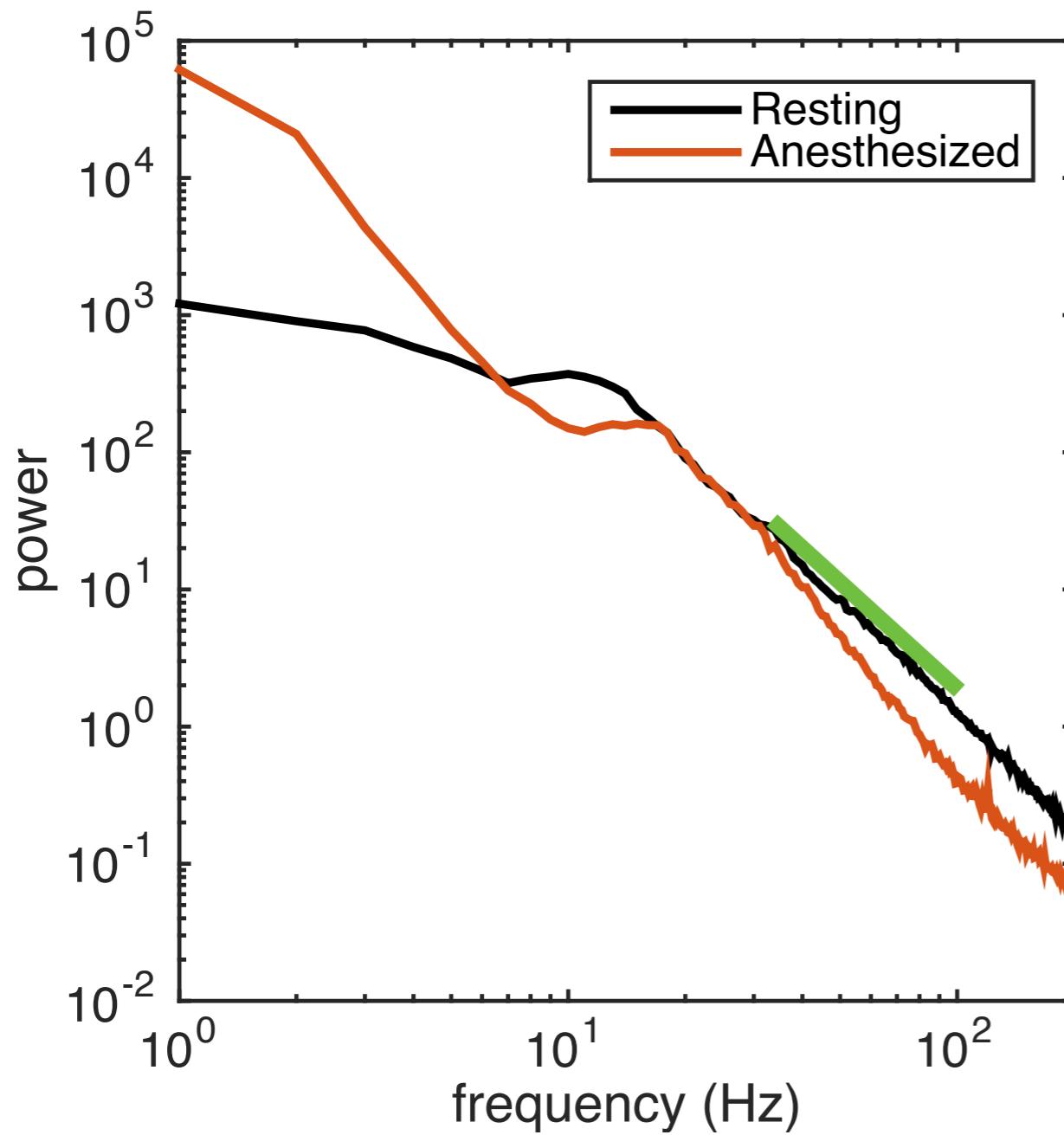


“Propofol significantly increases both the amplitude & frequency of inhibitory post-synaptic potentials.”

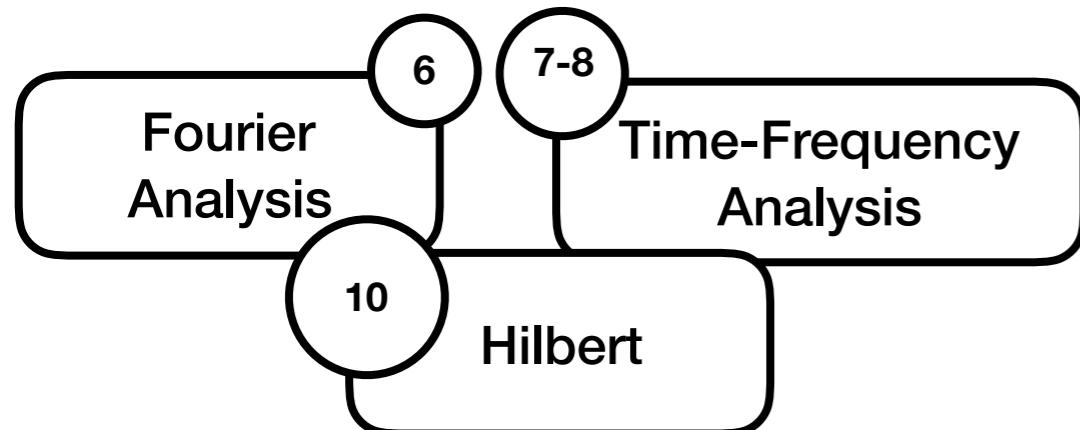
Wakita *et al.* 2013, & others

Measuring EI Balance

Anesthesia Induced Increase of Inhibition

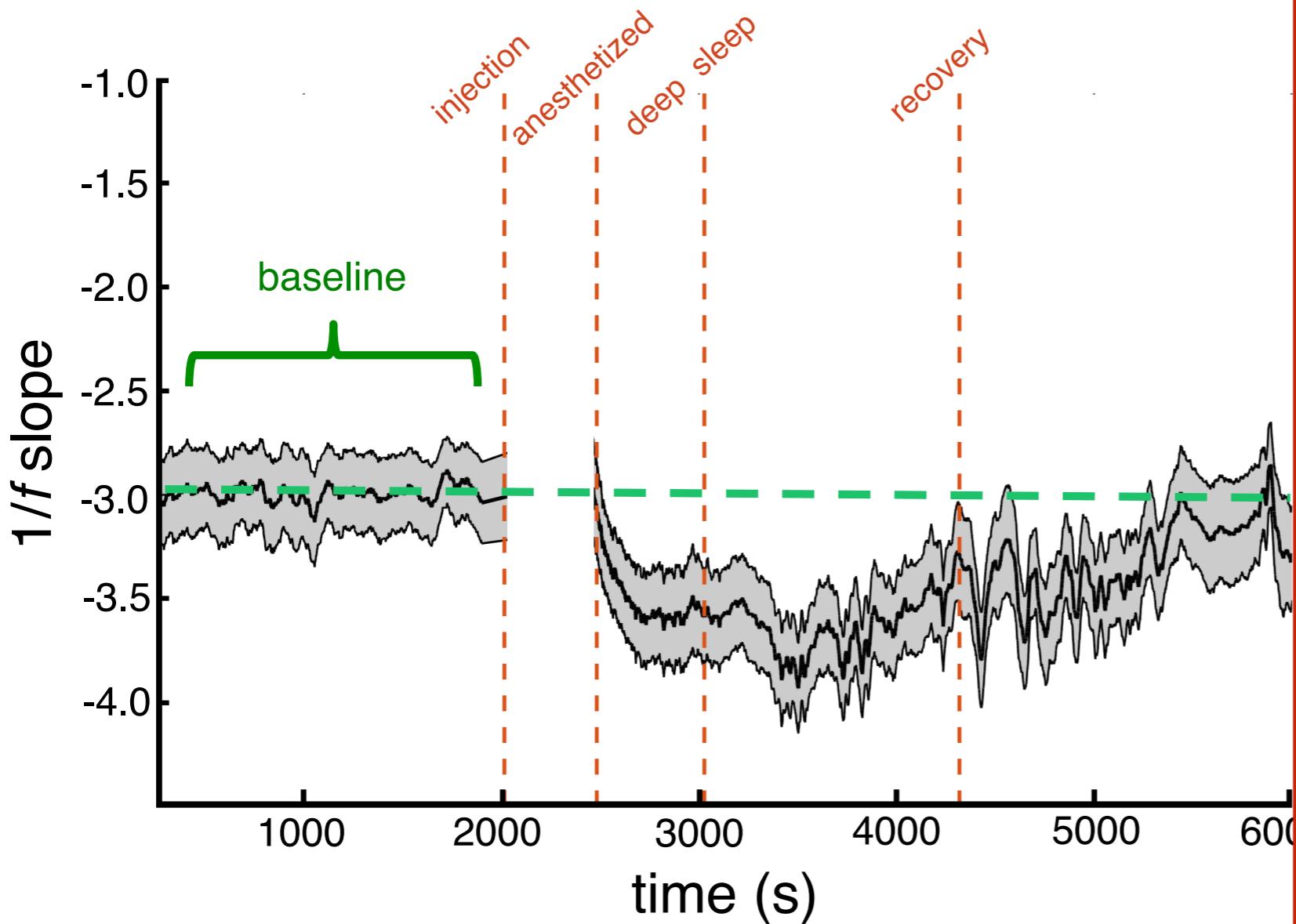


Measuring EI Balance



Time-Resolved Estimate

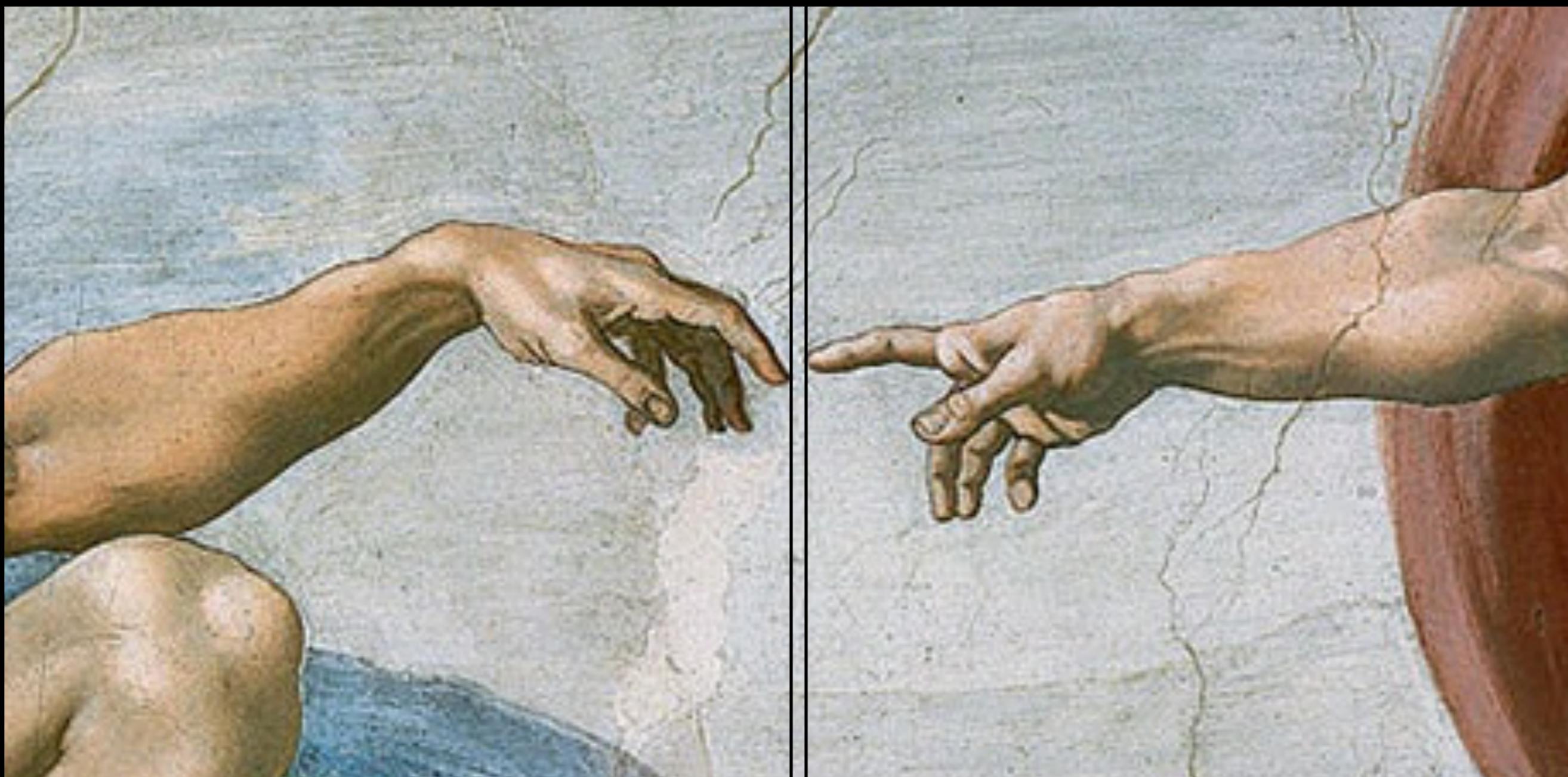
PSD Slope Time Course



PSD slope tracks
anesthesia induced
increase of inhibition
over cortex.

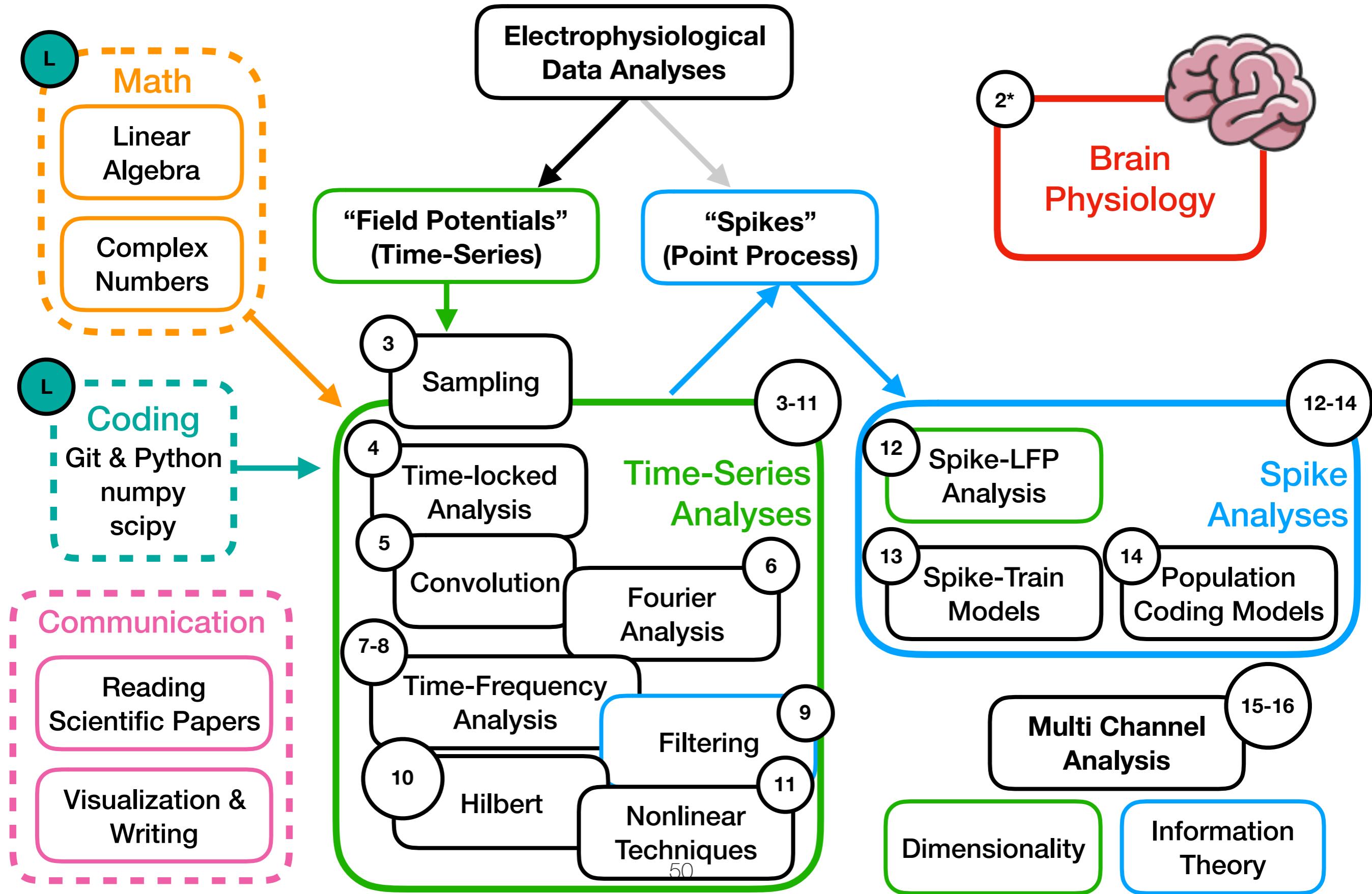
Human Cognitive Neuroscience

Systems Neuroscience



Data Analysis & Computational Modeling

Course Outline: Road Map



**Thank you for a great
session!**

<https://tinyurl.com/cogs118c-att>

<https://cape.ucsd.edu/students/>

