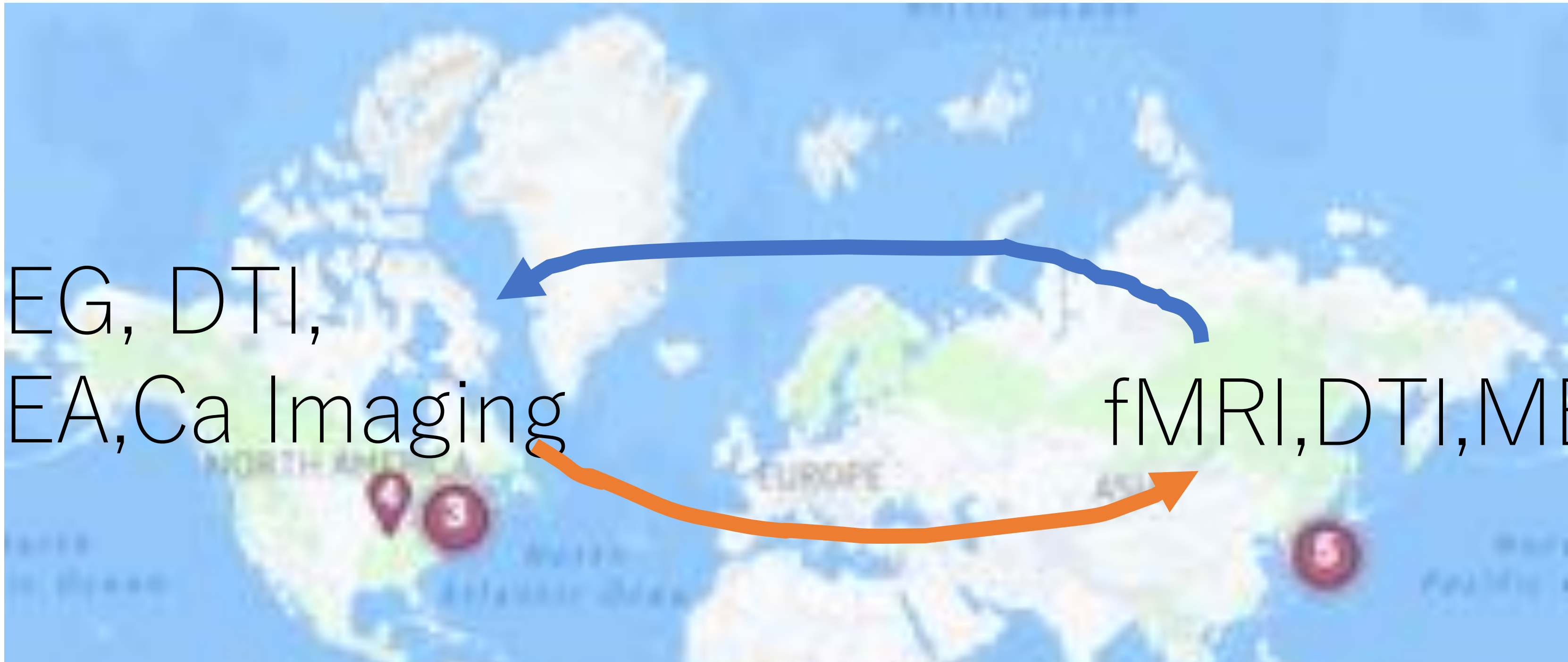
# Bridging multiple scales in neuronal connectivity

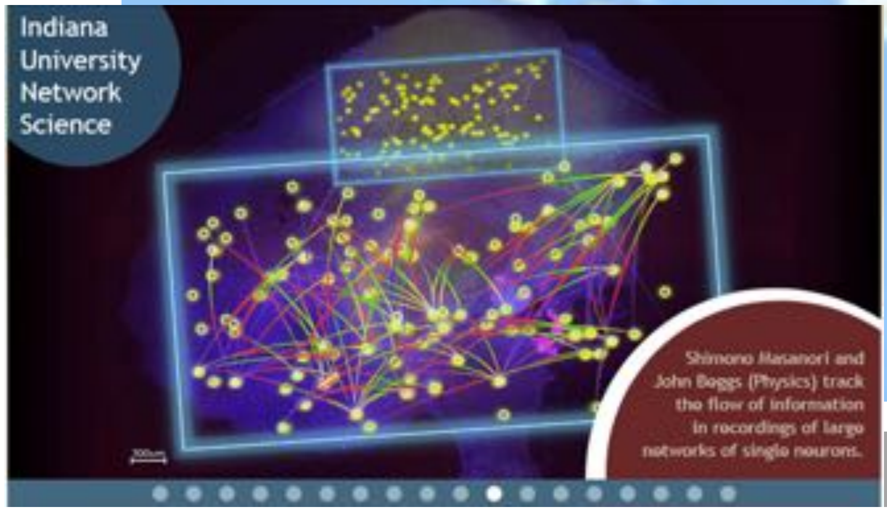
Masanori Shimono
Faculty of Medicine, Kyoto University
Hakubi/LEADER researcher

# Direct experience

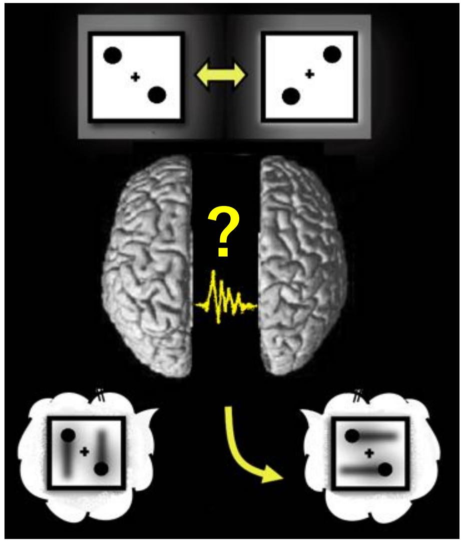
MEG, DTI,
MEA,Ca Imaging

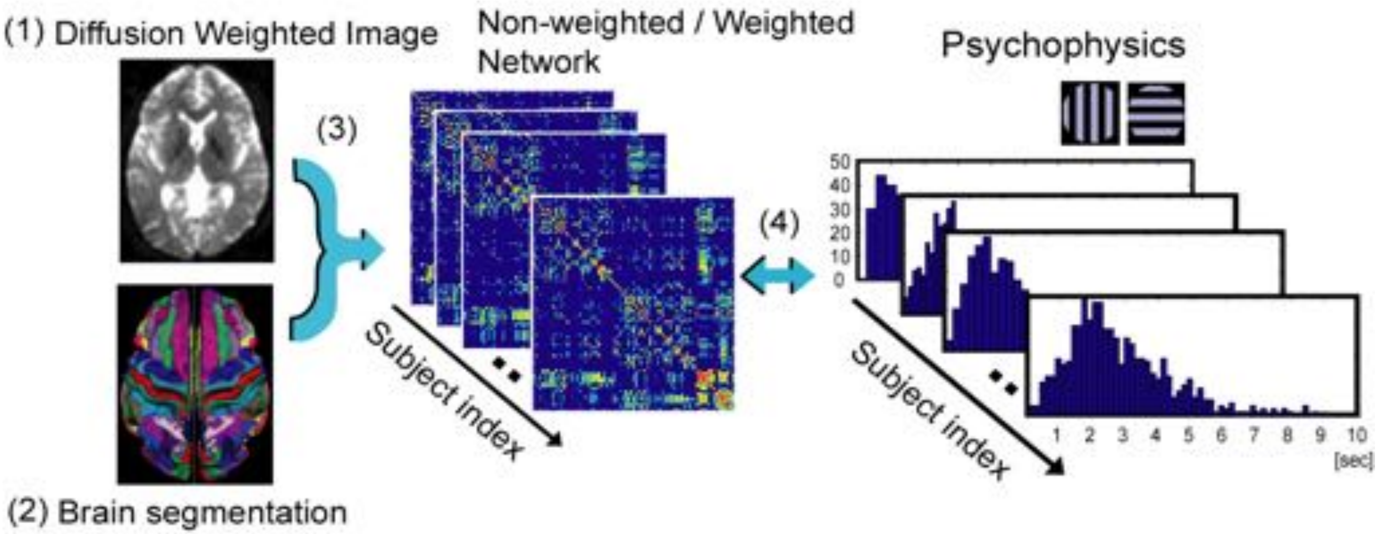
fMRI,DTI,MEG

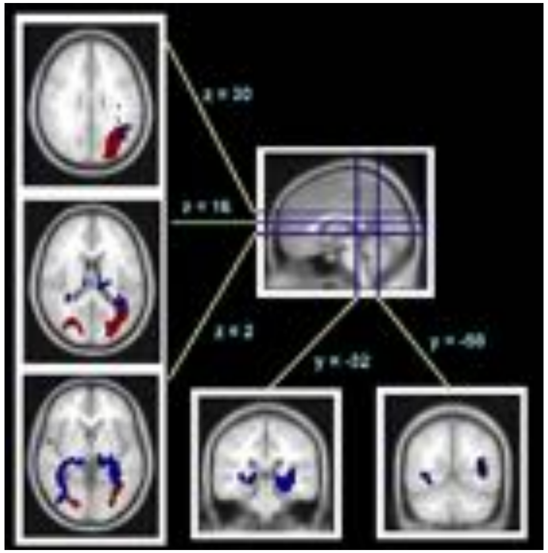


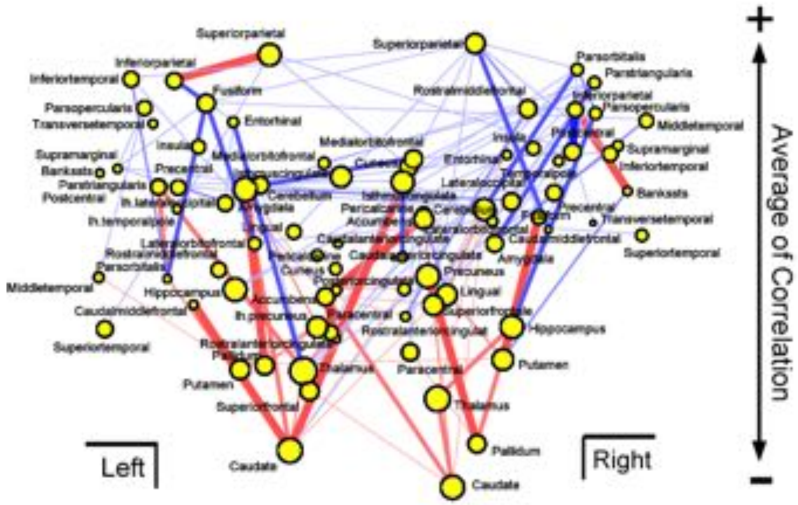




# Perception and connection (2009-)



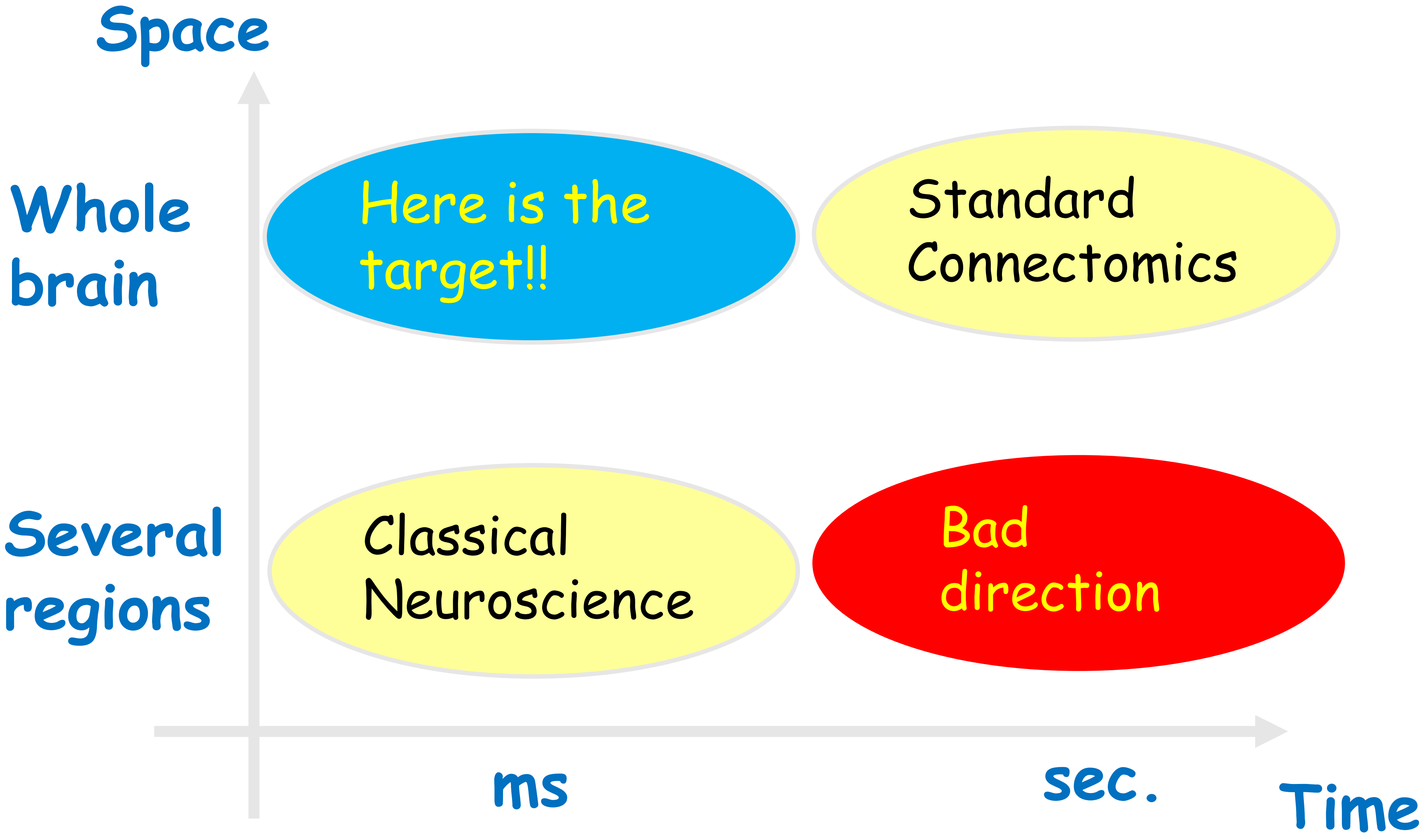



Shimono, Mano, Niki (2011) Cerebral Cortex

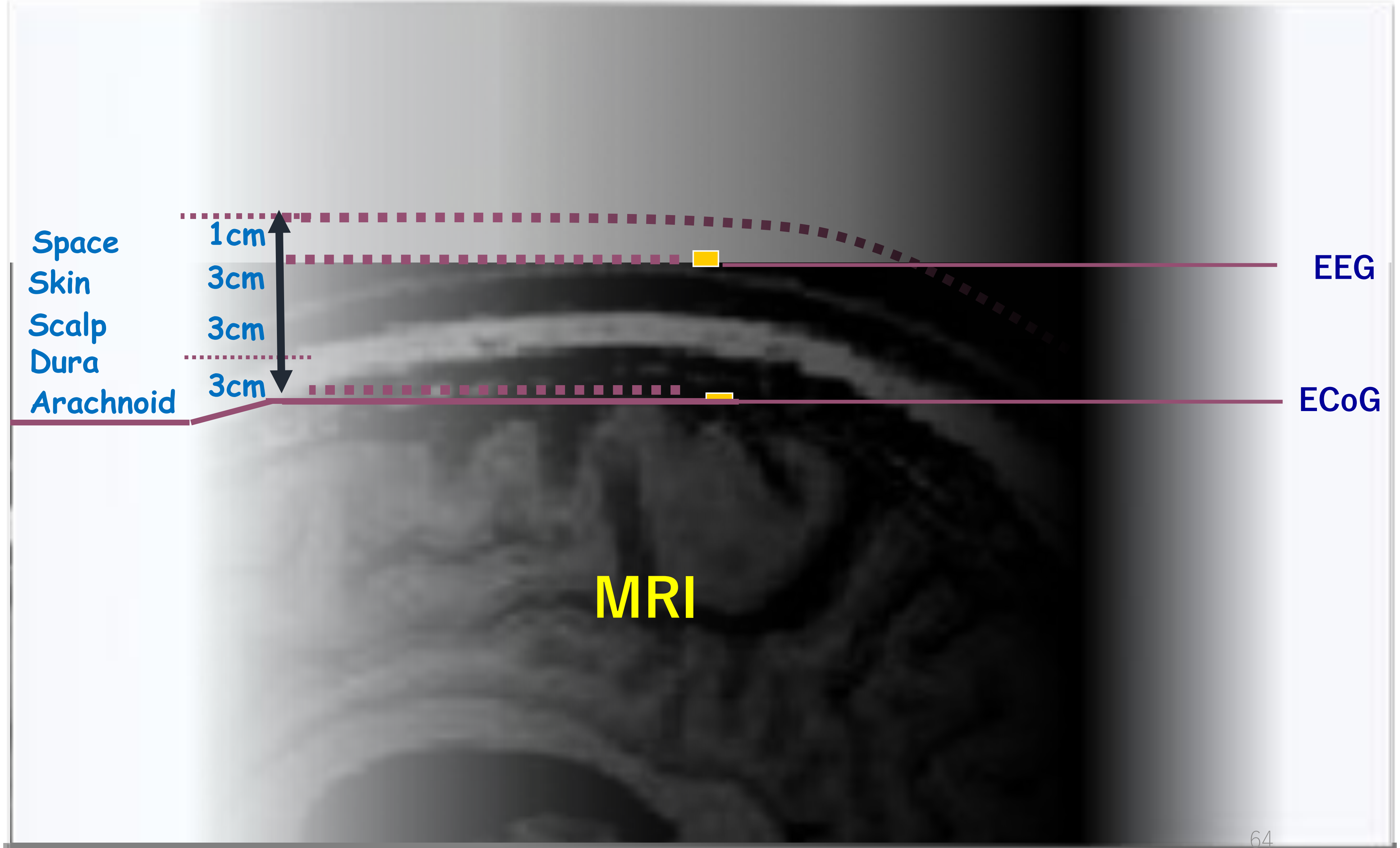
Shimono, Niki (2012) Brain Connectivity

# From recent studies

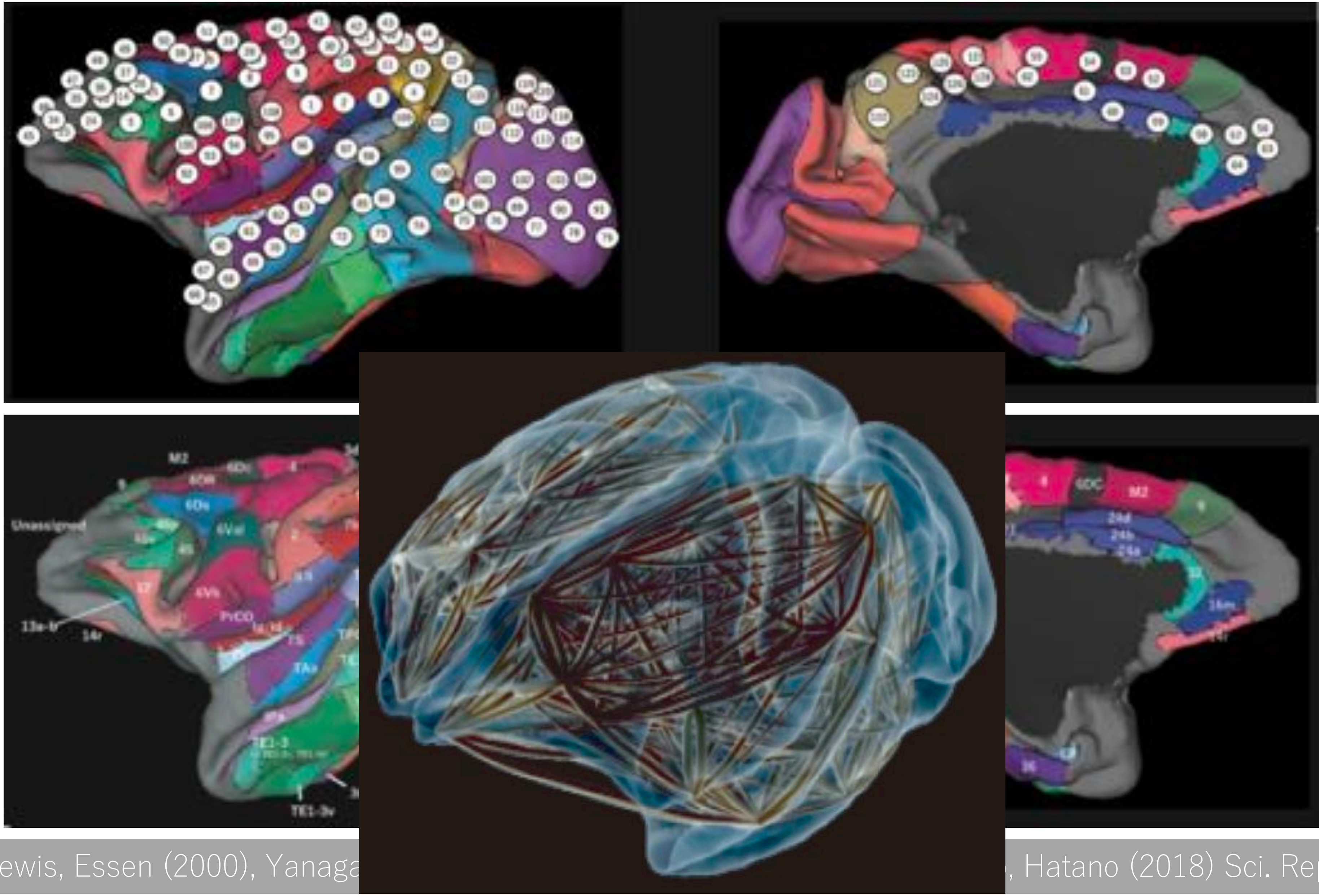
# The open field



# Various brain-recording technologies

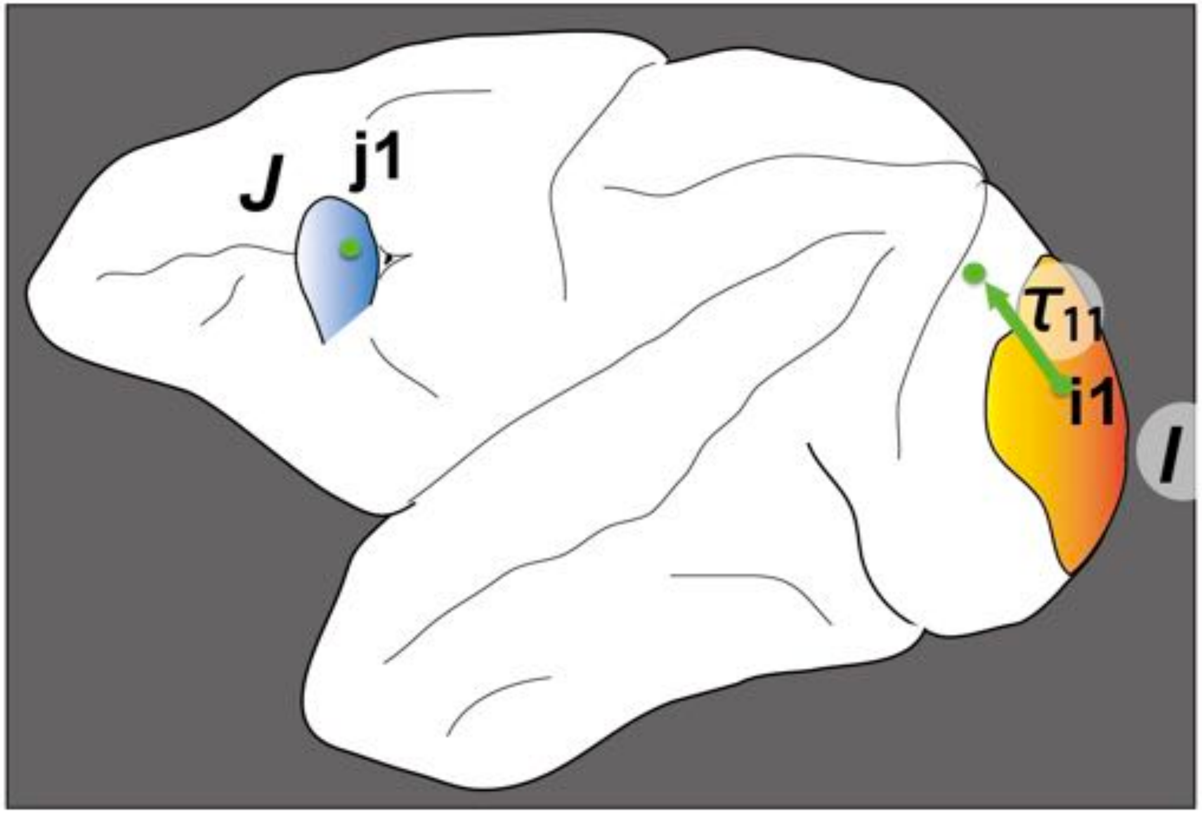


# A recent study



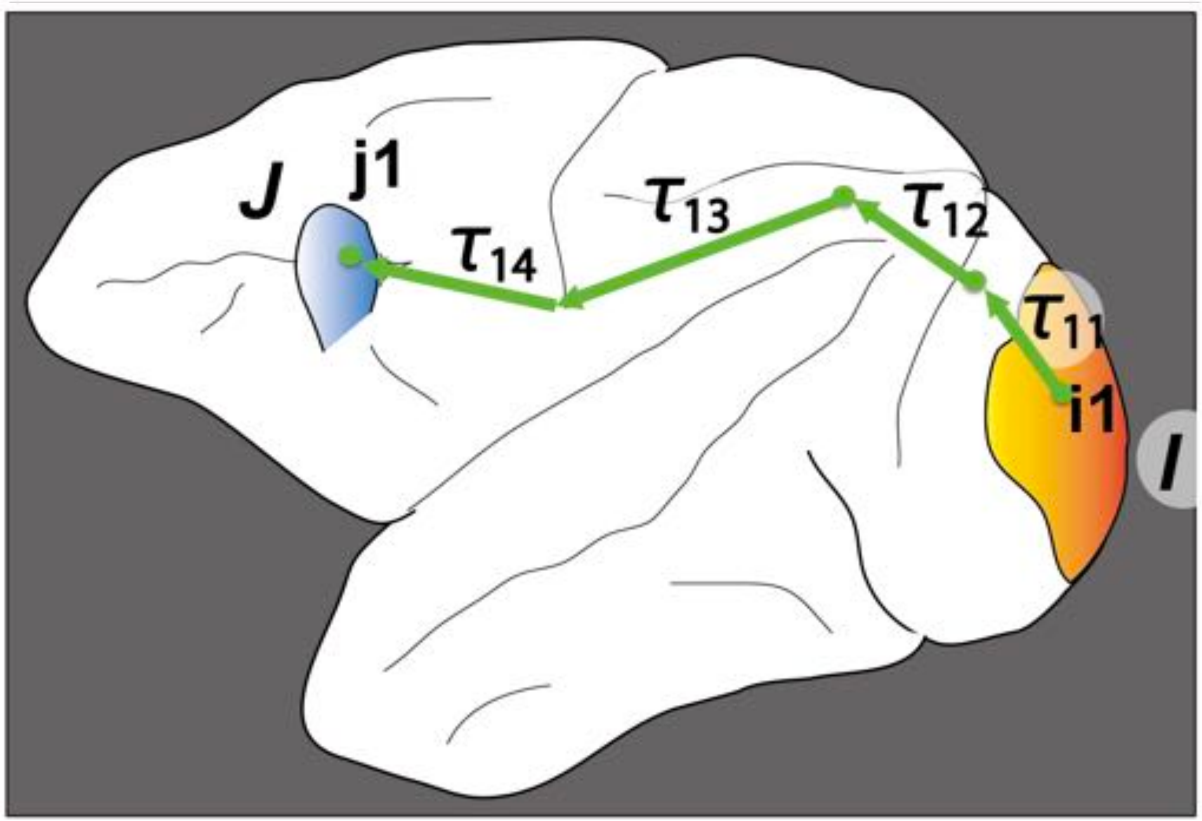

Lewis, Essen (2000), Yanaga … , Hatano (2018) Sci. Rep.

# ECoG (Spontaneous) vs. Spikes



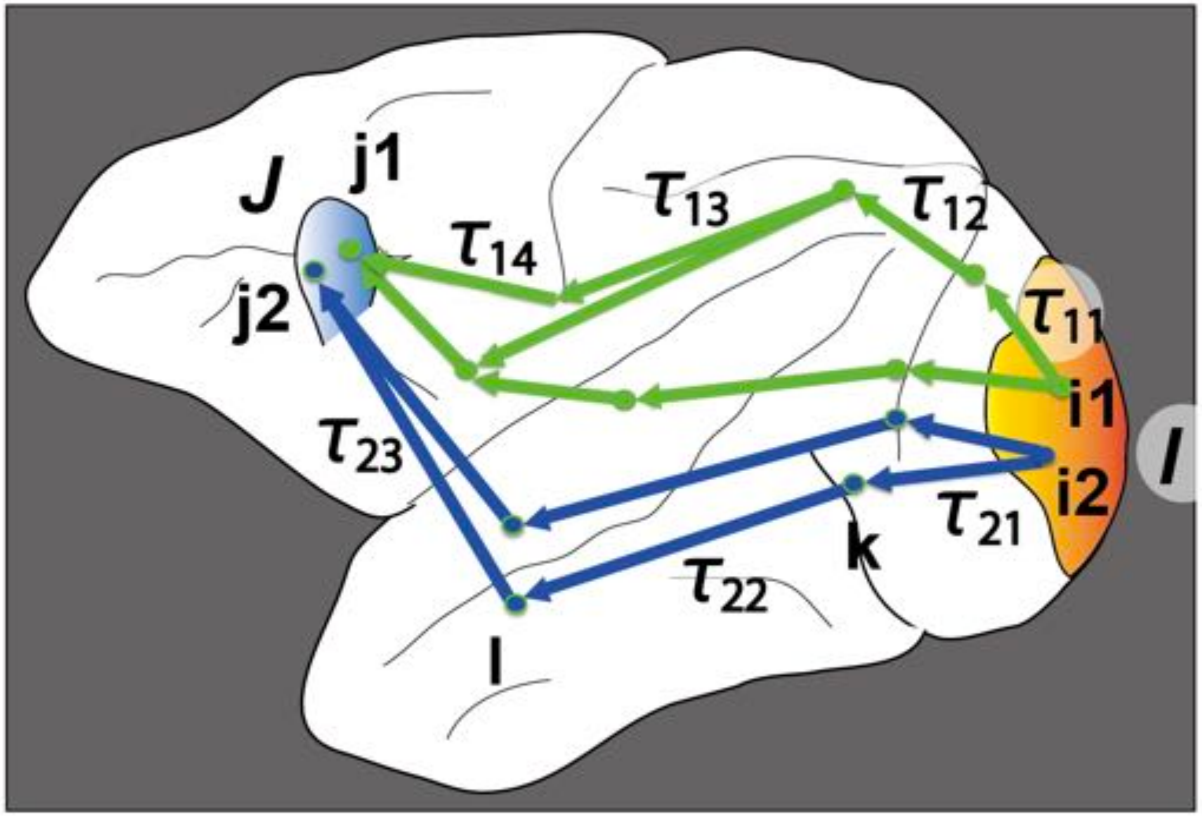

$\tau_{\text{(path index)(walk step)}}$

# ECoG (Spontaneous) vs. Spikes



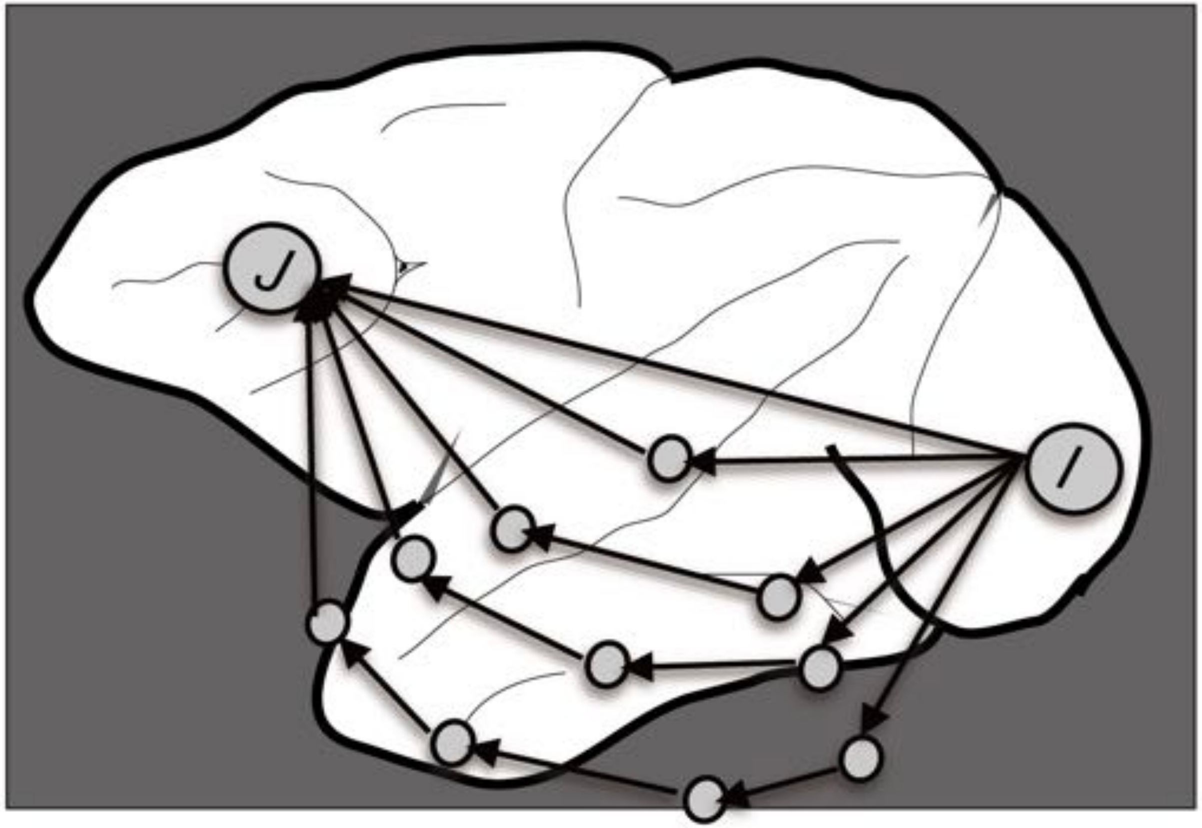

$\tau_{11}$

# ECoG (Spontaneous) vs. Spikes




**~100,000 routes (walks) for 5 path steps**

# ECoG (Spontaneous) vs. Spikes



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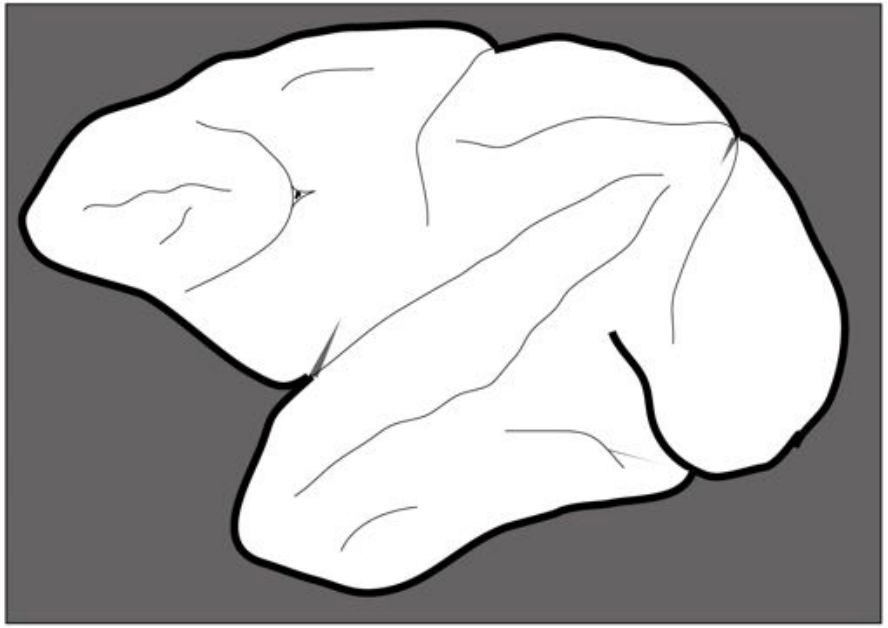

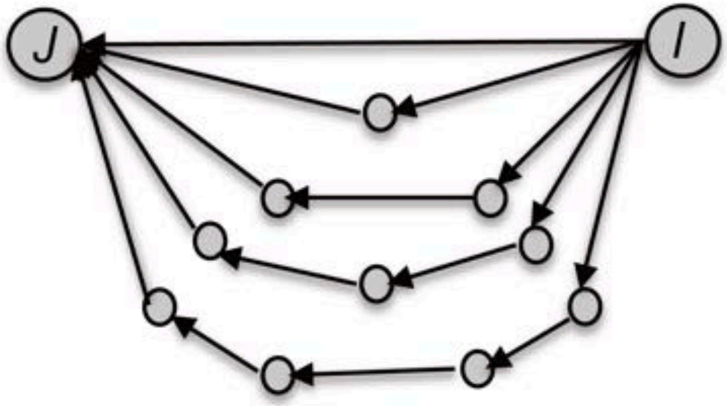

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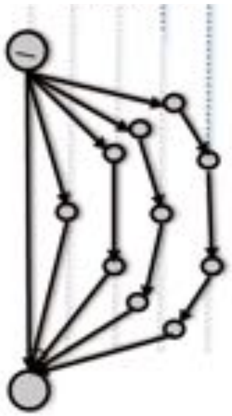

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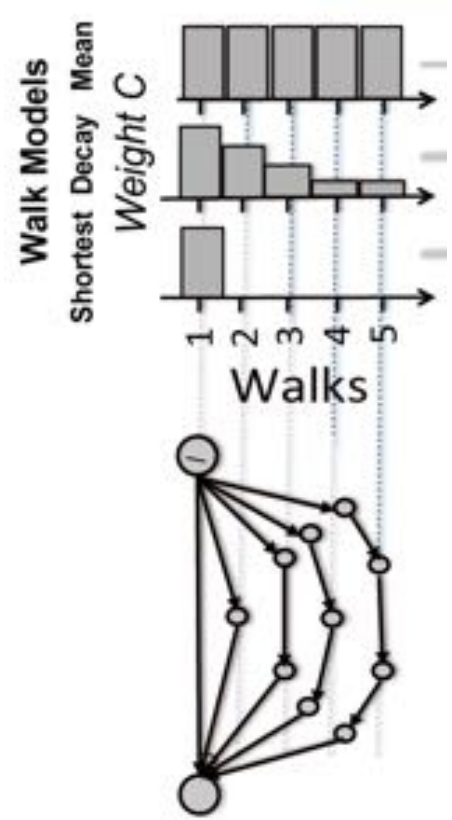

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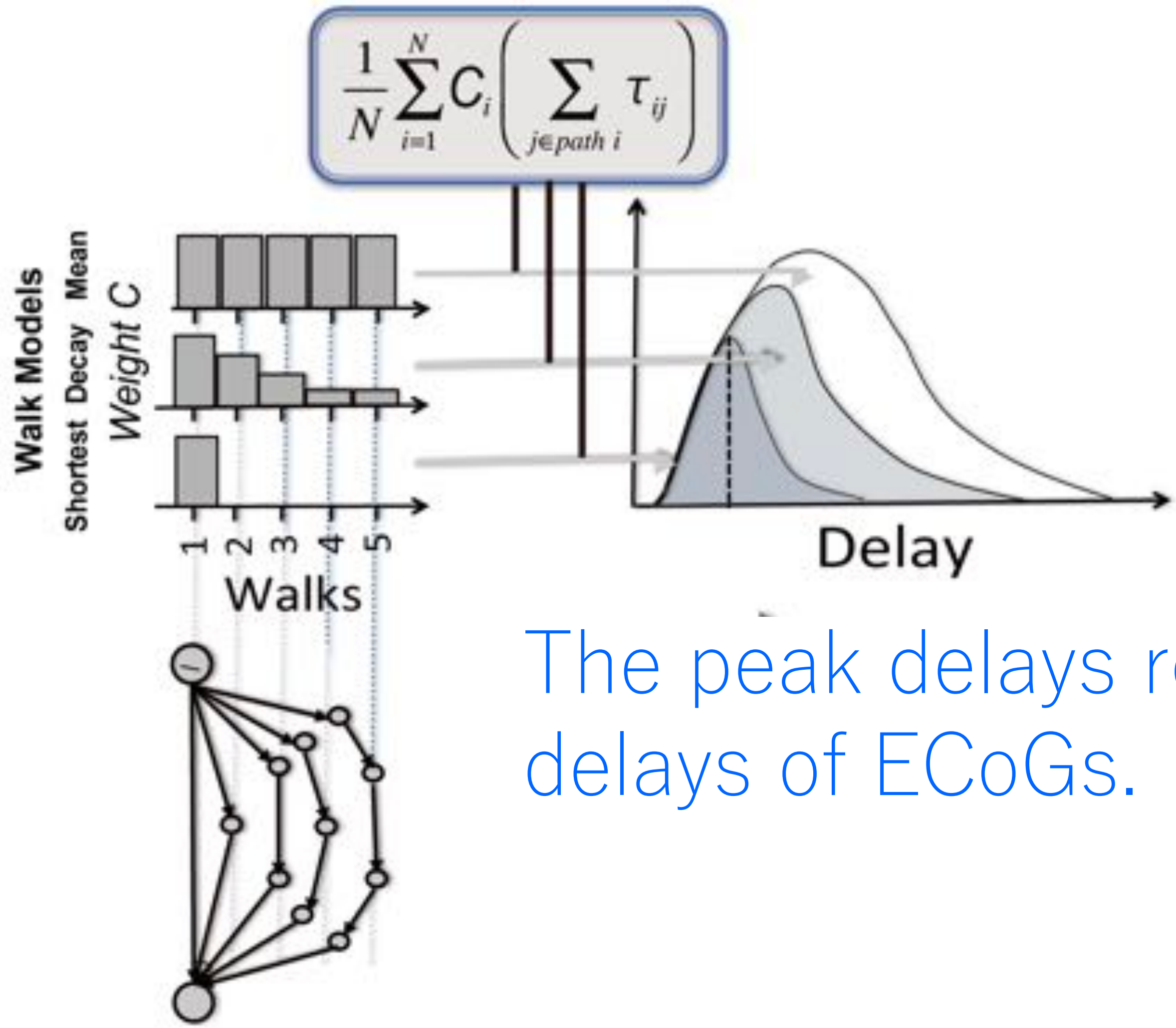
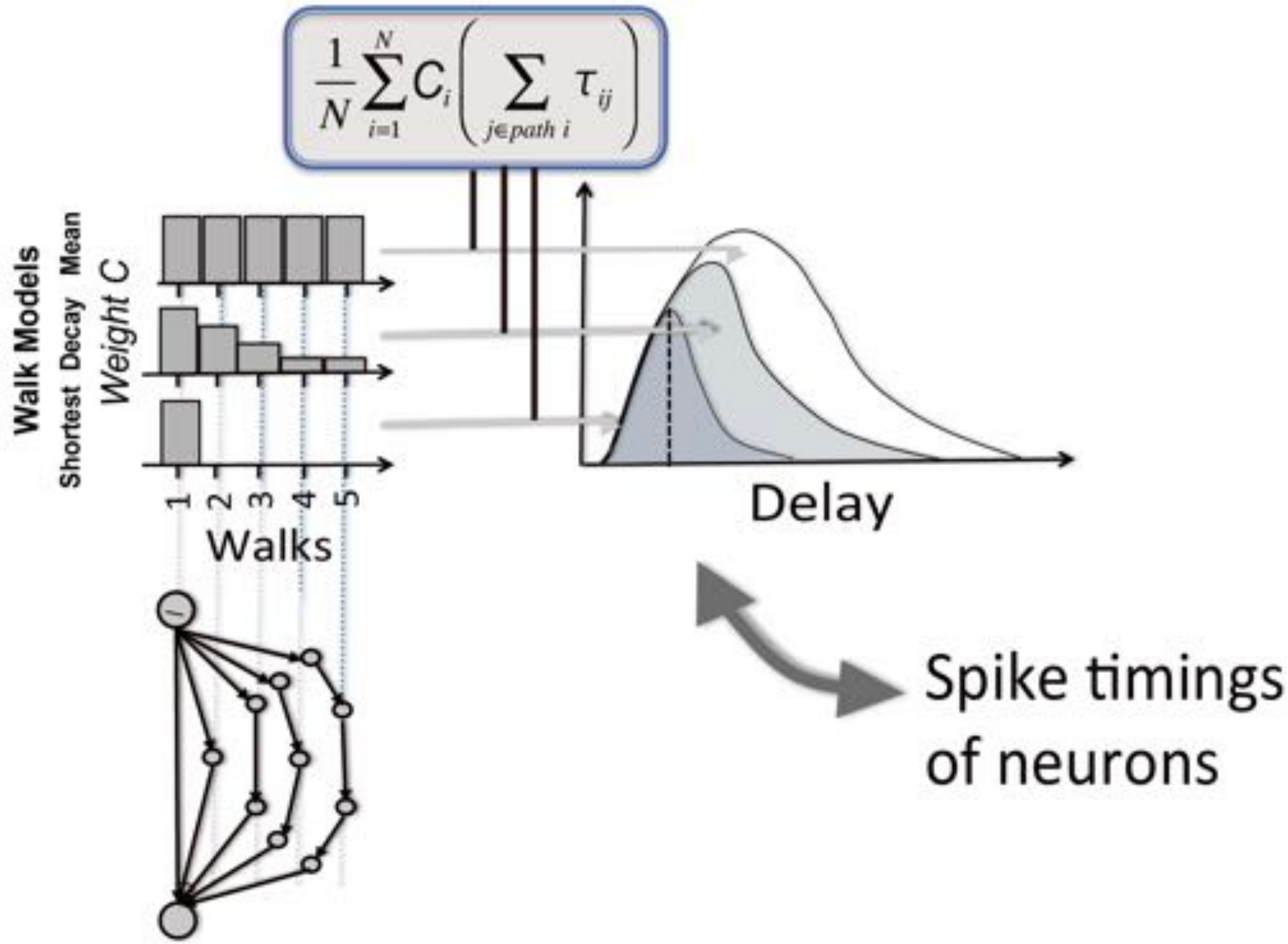
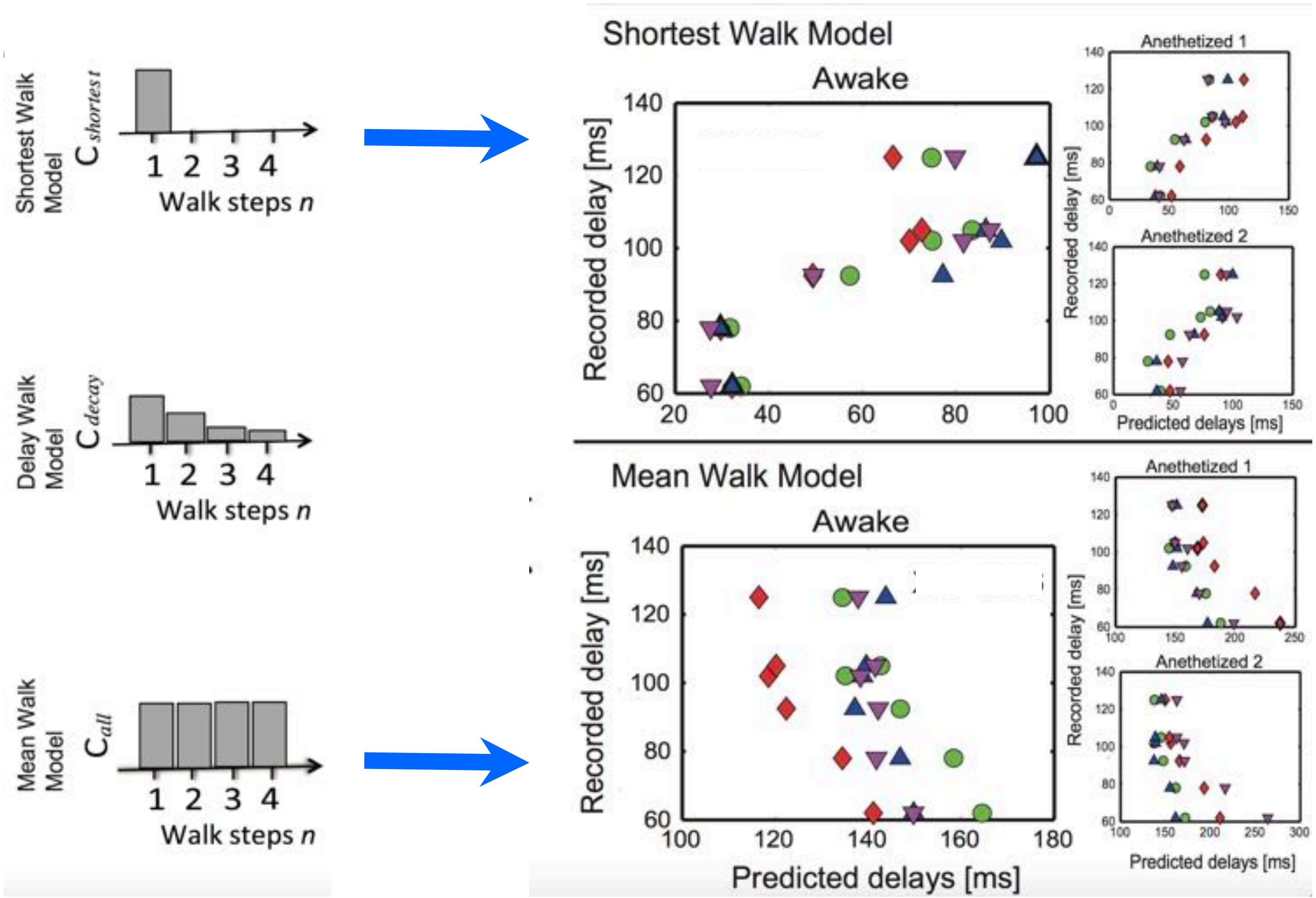



The peak delays represent delays of ECoGs.

# ECoG (Spontaneous) vs. Spikes



# Contribution of indirect connections



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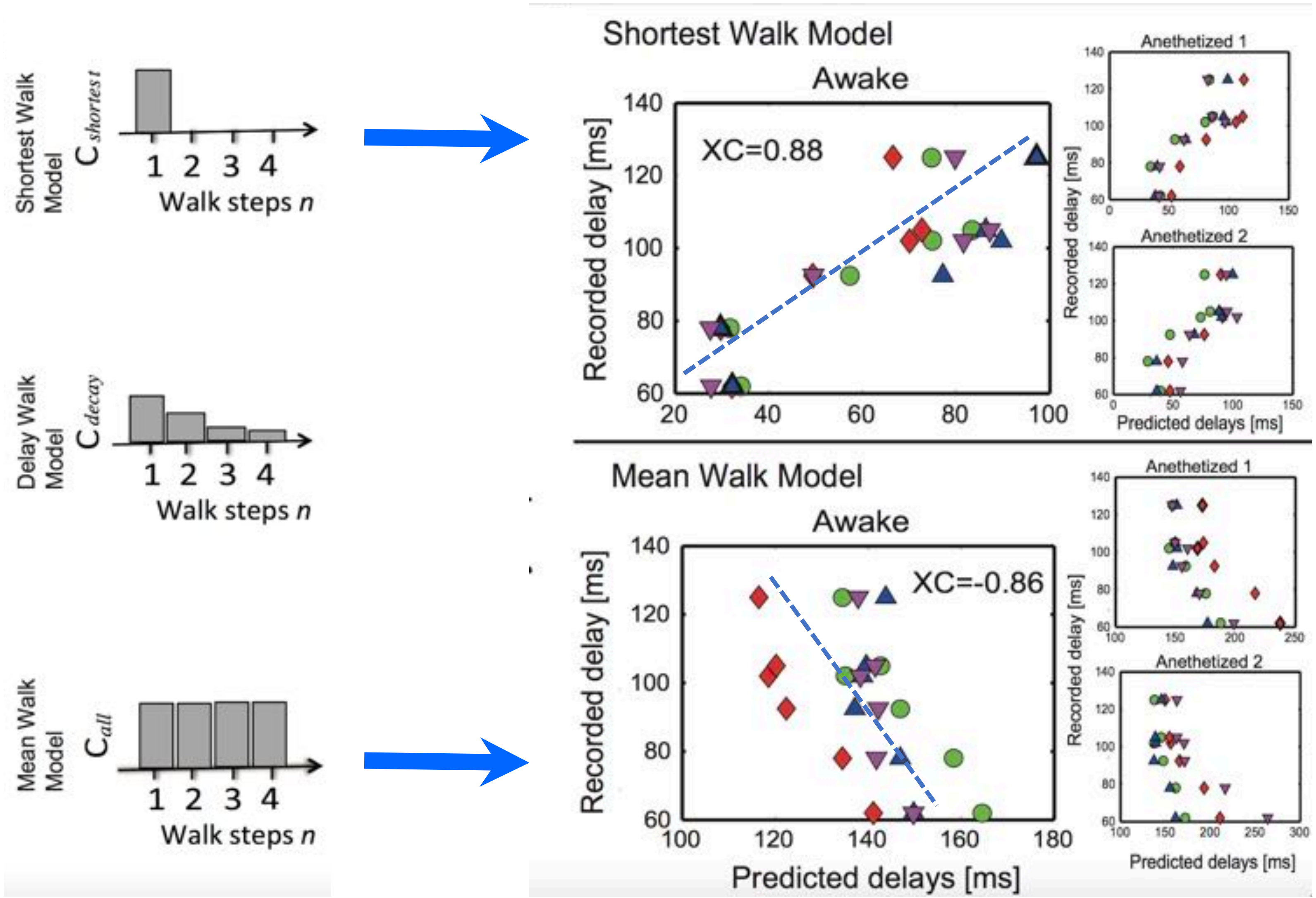
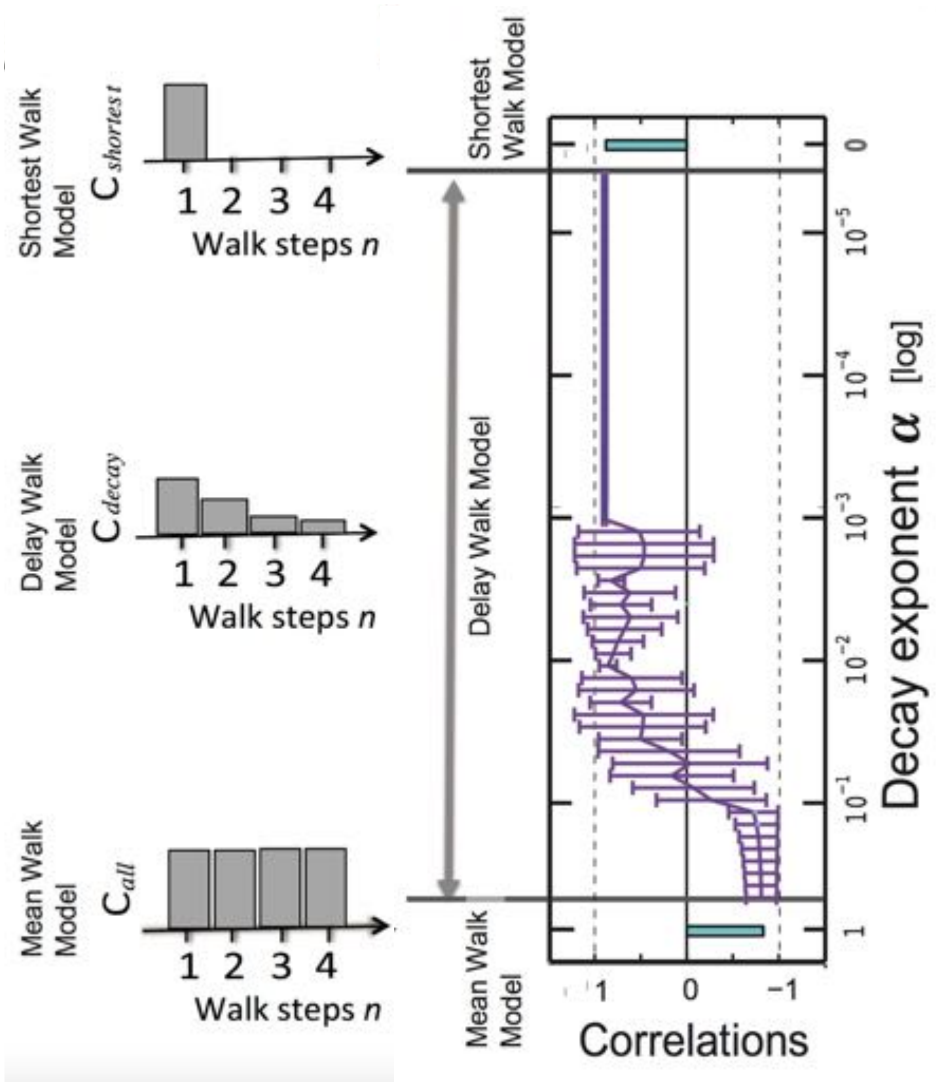


# Contribution of indirect connections




$$c_{delay}(n) = \alpha^n$$

(n : walk steps)

# Communicability G score

(Communicability)=(Weight) × (Walk length)

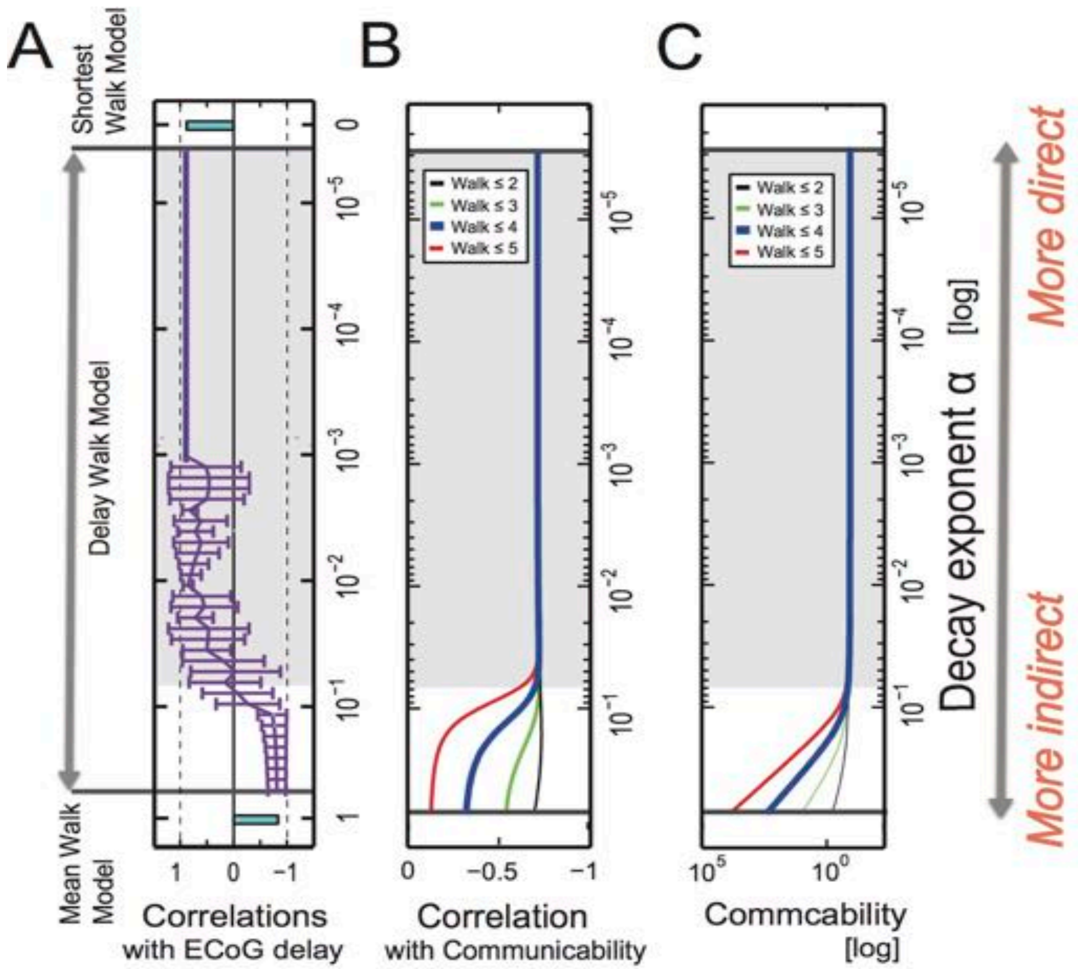
$$G = \sum_{n=0}^{\infty} c(n)A^n = \sum_{n=0}^{\infty} (\alpha A)^n \qquad (c(n)=\alpha^n)$$

$$= \frac{1}{1 - \alpha A}$$

e.g.) $A^3 = \sum_{k,l} A_{ik}A_{kl}A_{lj}$

Communicability can systematically quantify how longer walks contribute to the spread of information in network systems.

# Communicability and latency



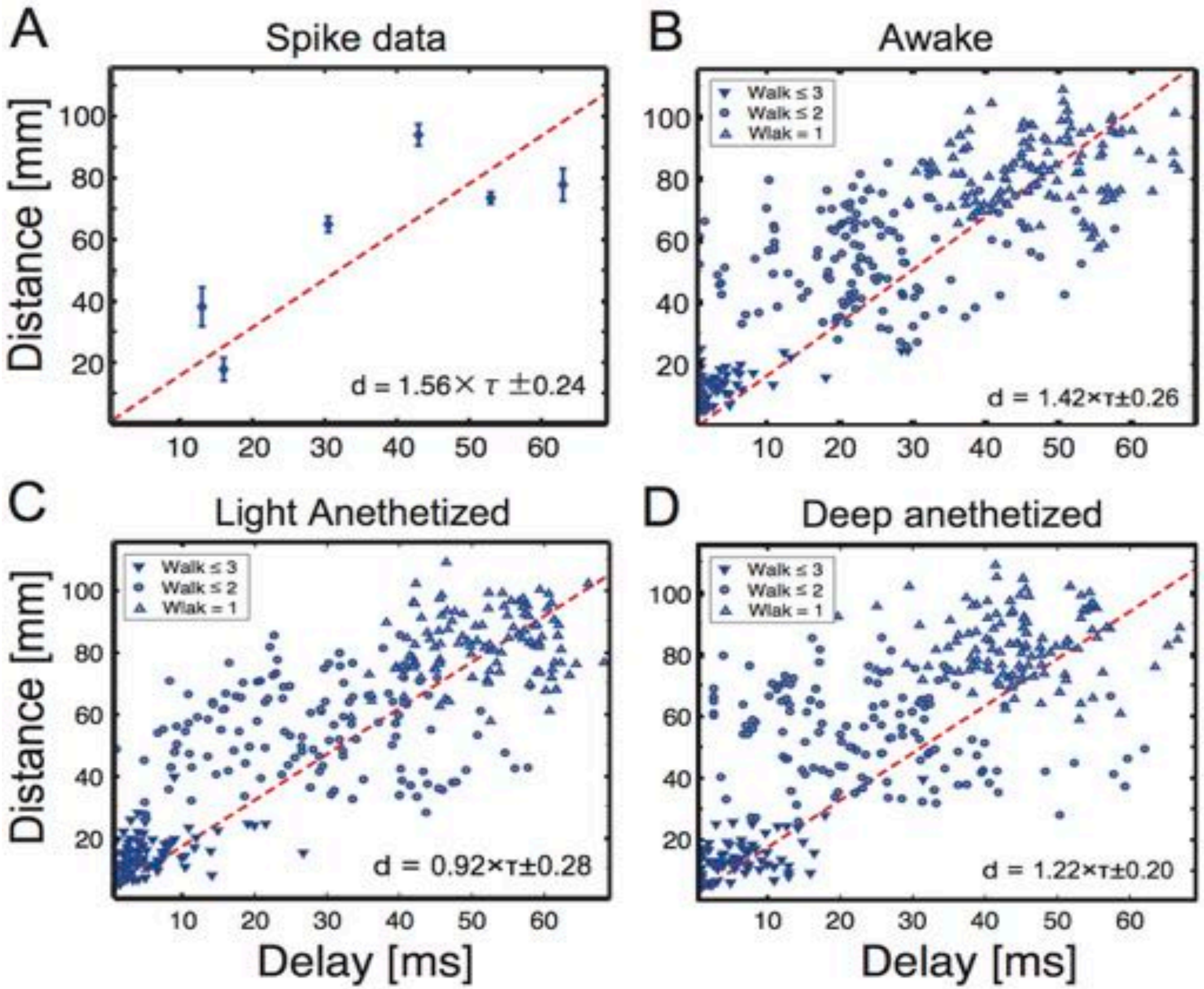

The contribution of indirect connections is …

up to 5%



Shimono, Hatano (2018) Sci. Rep.

# The propagation speed






Shimono, Hatano (2018) Sci. Rep.

# Another relating study

# Is cell density uniform or non-uniform?

## THE BASIC UNIFORMITY IN STRUCTURE OF THE NEOCORTEX

*by* A. J. ROCKEL, R. W. HIORNS *and* T. P. S. POWELL

*(From the Departments of Human Anatomy and Biomathematics, University of Oxford)*

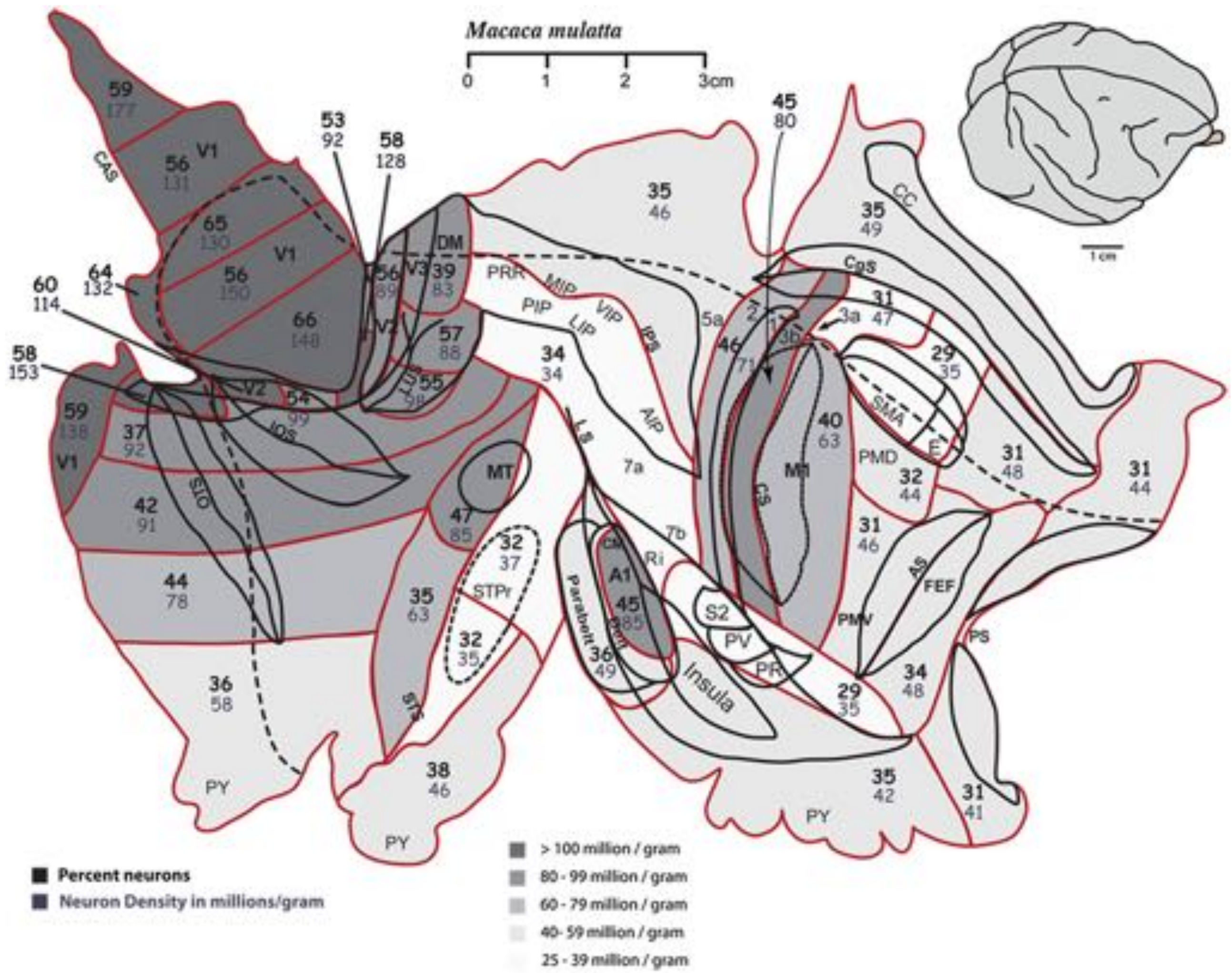
### INTRODUCTION

SEVERAL quantitative studies have shown that the cell density may vary in different laminæ and in different areas of the neocortex in the same brain and between different species (*see* Tower, 1954; Brody, 1955; Cragg, 1967). The cells are usually most closely packed in layer IV, the density is high in the visual cortex and low in the motor and in general the neurons are more widely separated in larger brains. In an electron microscopic study of the motor cortex of area 4 and of area 3b of the somatic sensory area of the monkey (Sloper, 1973; Sloper, Hiorns and Powell, 1979) the number of neuronal cell bodies was counted in a narrow width through the full depth of the cortex from the pia to the white matter. Surprisingly it was found that despite the marked difference in the thickness of the cortex of these two areas, and their different cytoarchitecture and function, the absolute number of neurons through the cortex was the same and the proportions of the two main cell types, the pyramidal and stellate, were similar. A comparison has now been made of the number of cells through the entire thickness of the cortex in most of the major structural and functional areas in the monkey and in several other species, ranging from mouse to man. With the exception of area 17 of the visual cortex of primates the figures are similar for the different areas, and despite the marked differences in the size of the brains the absolute number of cells through the thickness of the cortex has been found to be constant in the brains of different animals. The results may be of relevance to our understanding of the evolution of this part of the brain, and perhaps to the question of the anatomical basis of the functional columnar organization which is a feature of many areas of the cortex (Mountcastle, 1957, 1978; Hubel and Wiesel, 1962, 1977). A preliminary communication of the results has already appeared (Rockel, Hiorns and Powell, 1974).



Rockel et al. (1980)

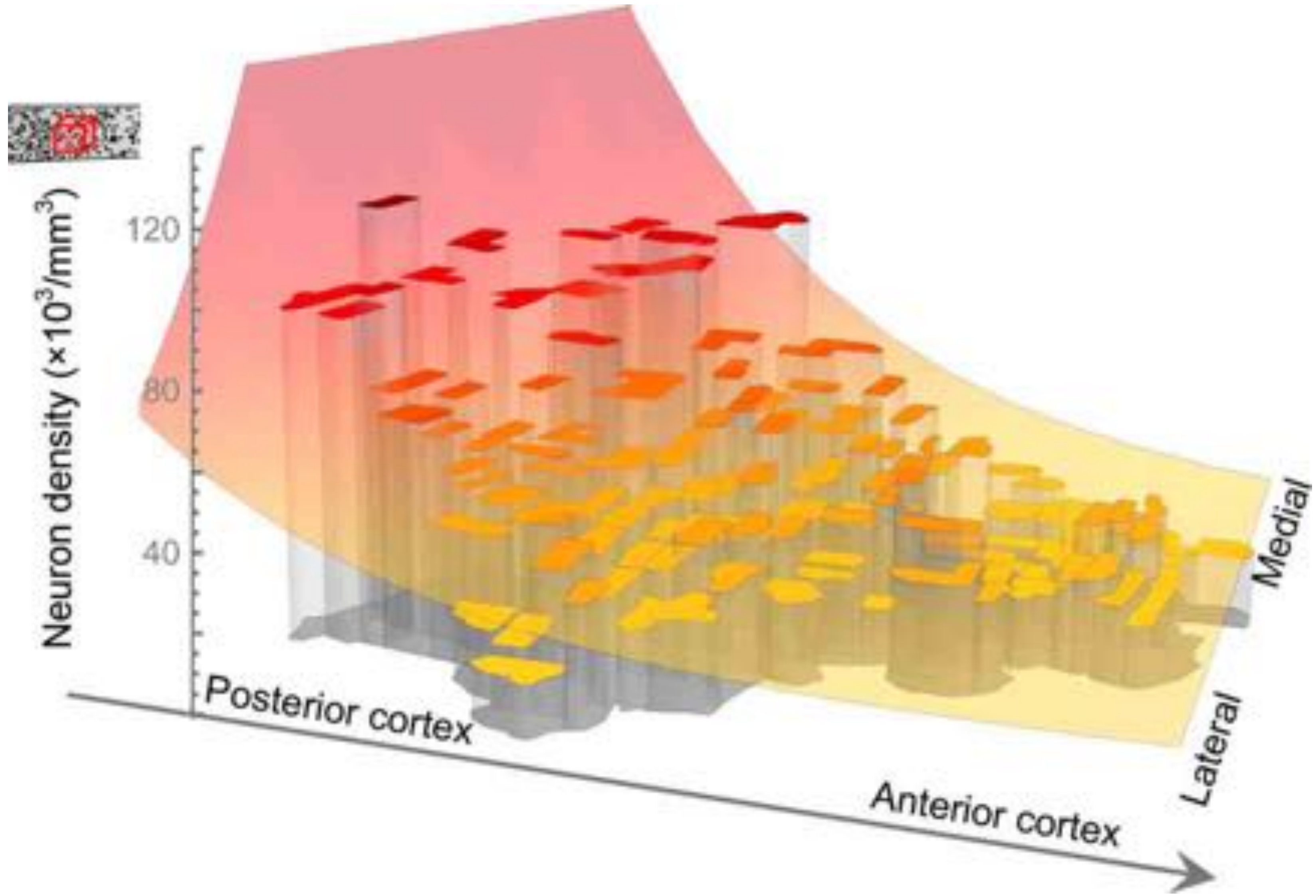
# How cell density is non-uniform?




Evaluations in whole-brains are essential.

Collins et al. (2010) PNAS

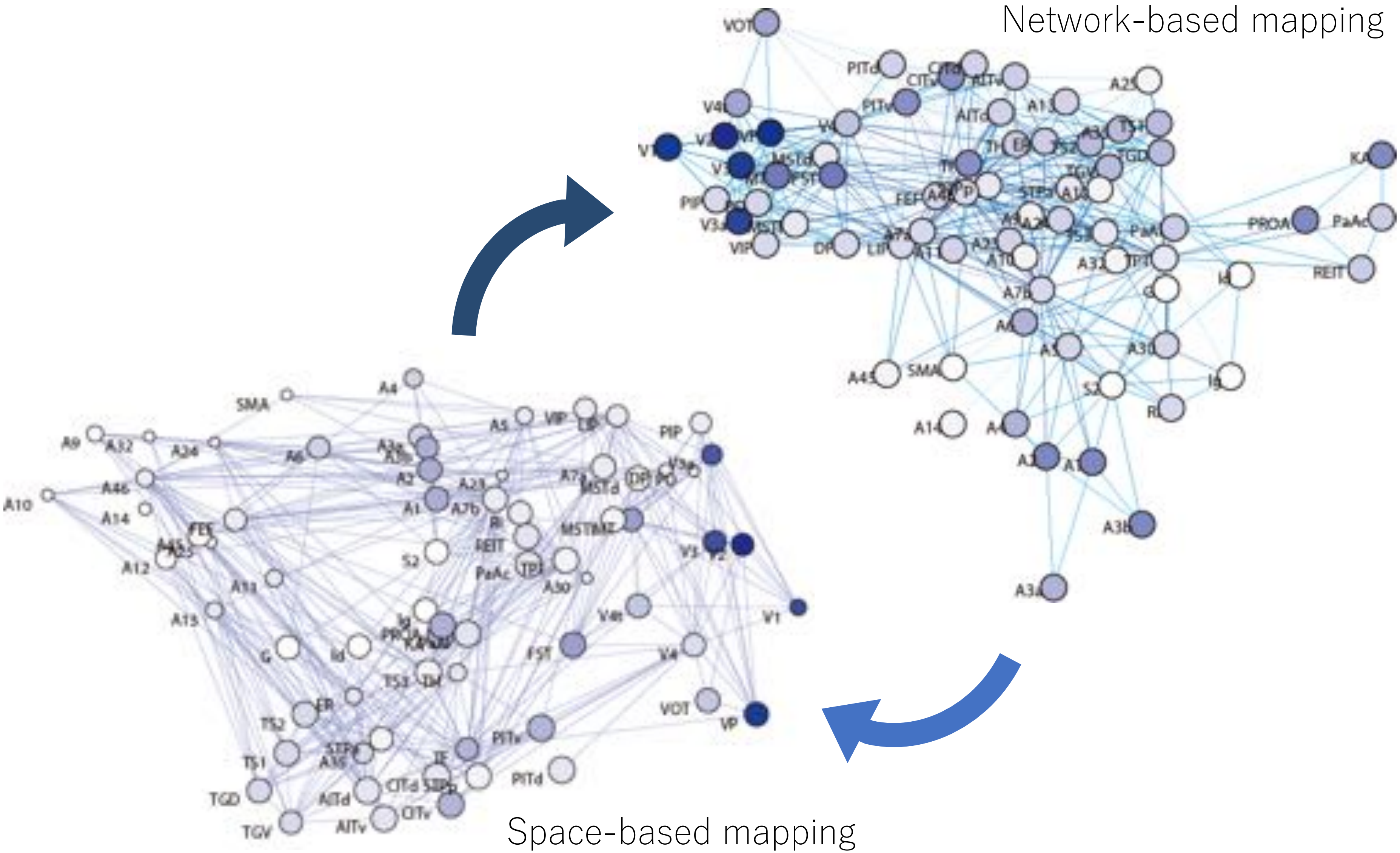
# Spatial decay model






Cahane et al. (2011)

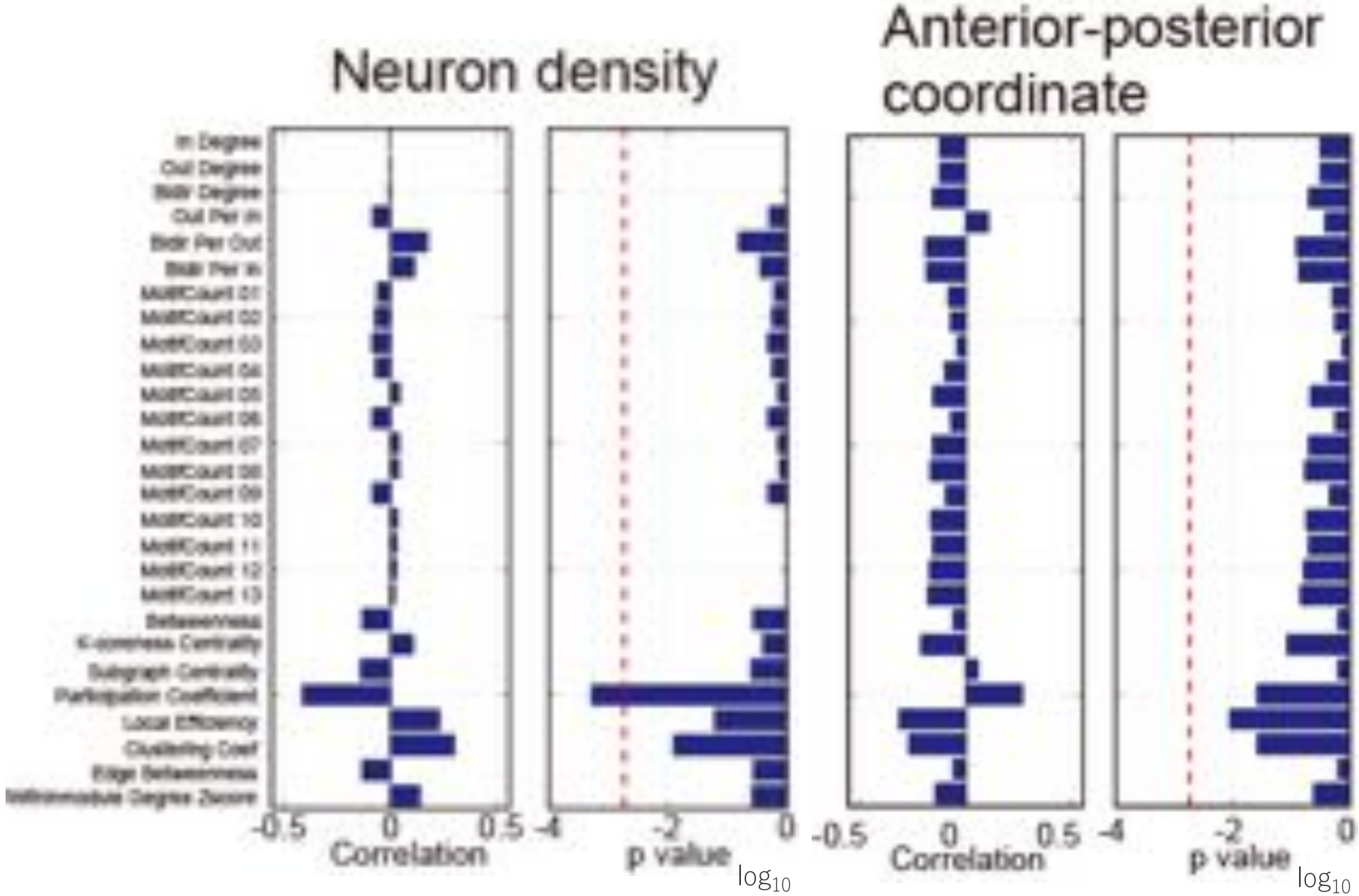
# Network as an other “closeness”




Fruchterman, Reingold (1991)

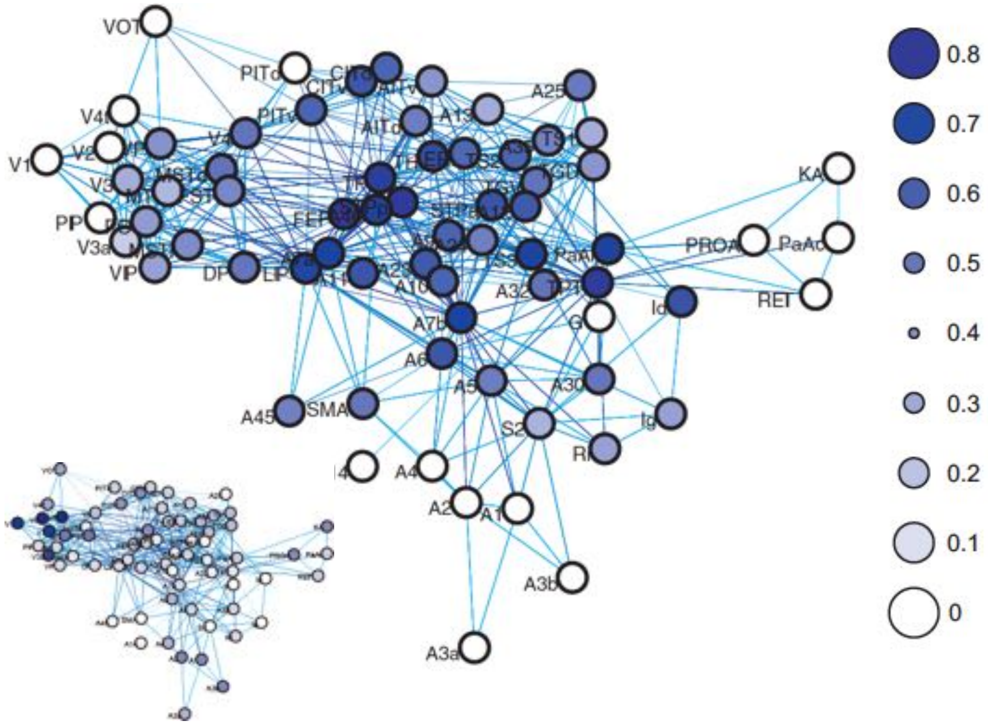
# Cell density and networks

## Various network measures

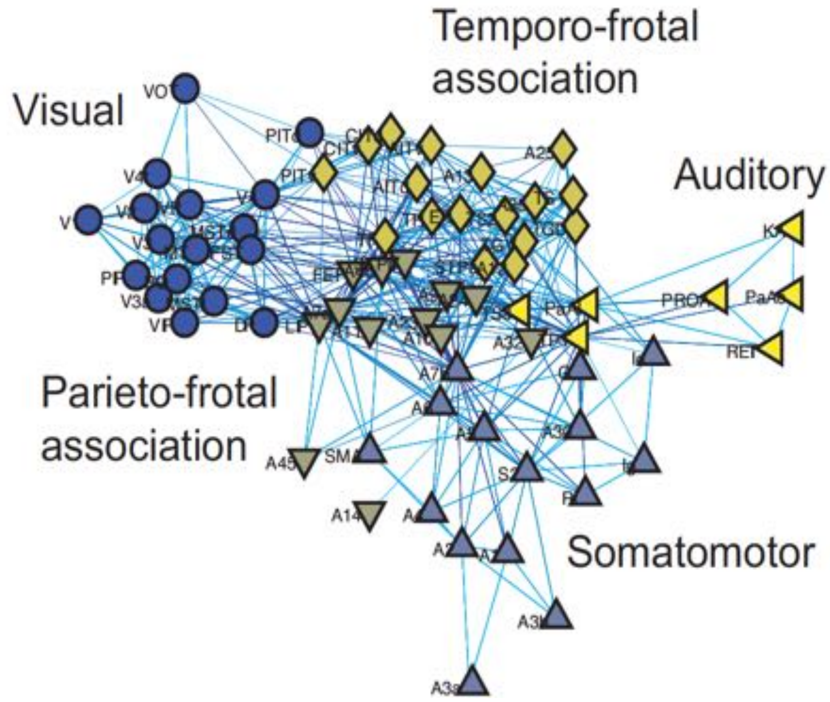


# What is Participation Coefficient?

Participation Coefficient




Modules/Communitie

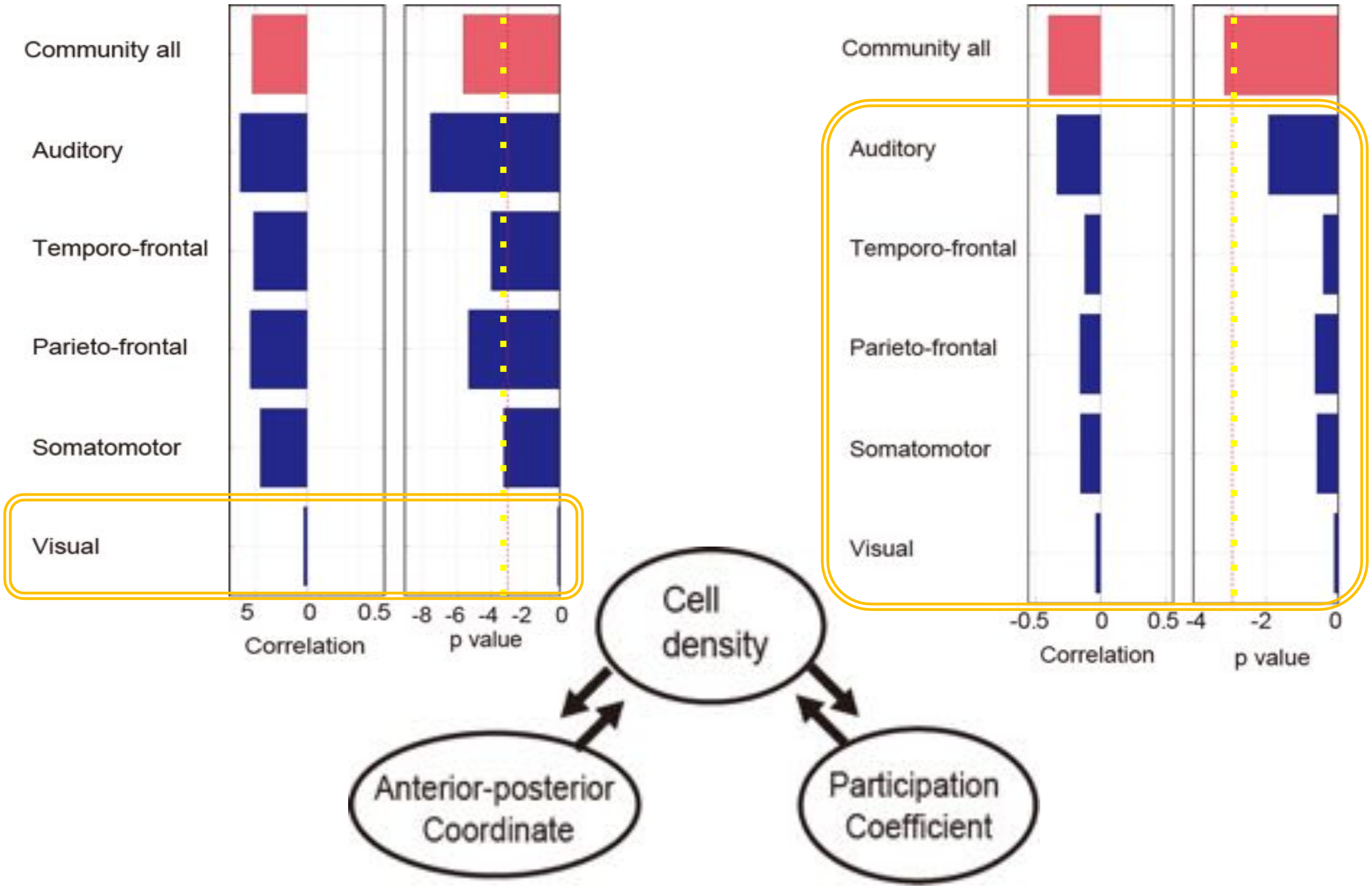



High Participation Coefficient – Information integration - association regions.
Low Participation Coefficient – Information segmentation - primary regions



Gumera, Amaral (2007)

# Global influence of Modules





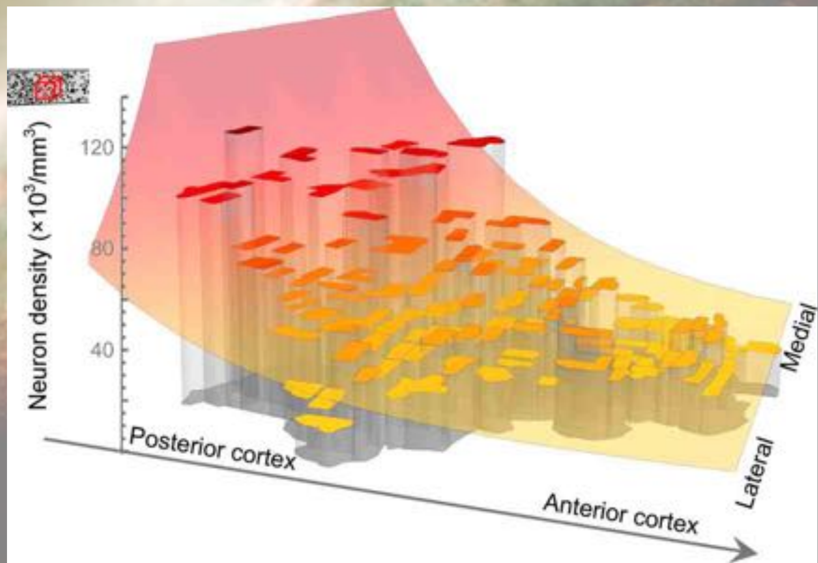

Shimono (2013) Sci.Rep.

# Summary

Non-uniformity of cell density

↑ ↓

Spatial decay



# Summary

Non-uniformity of cell density

↑ ↓

High cell density
at visual module

# Summary

Non-uniformity of cell density

↑ ↓

High cell density
at visual module

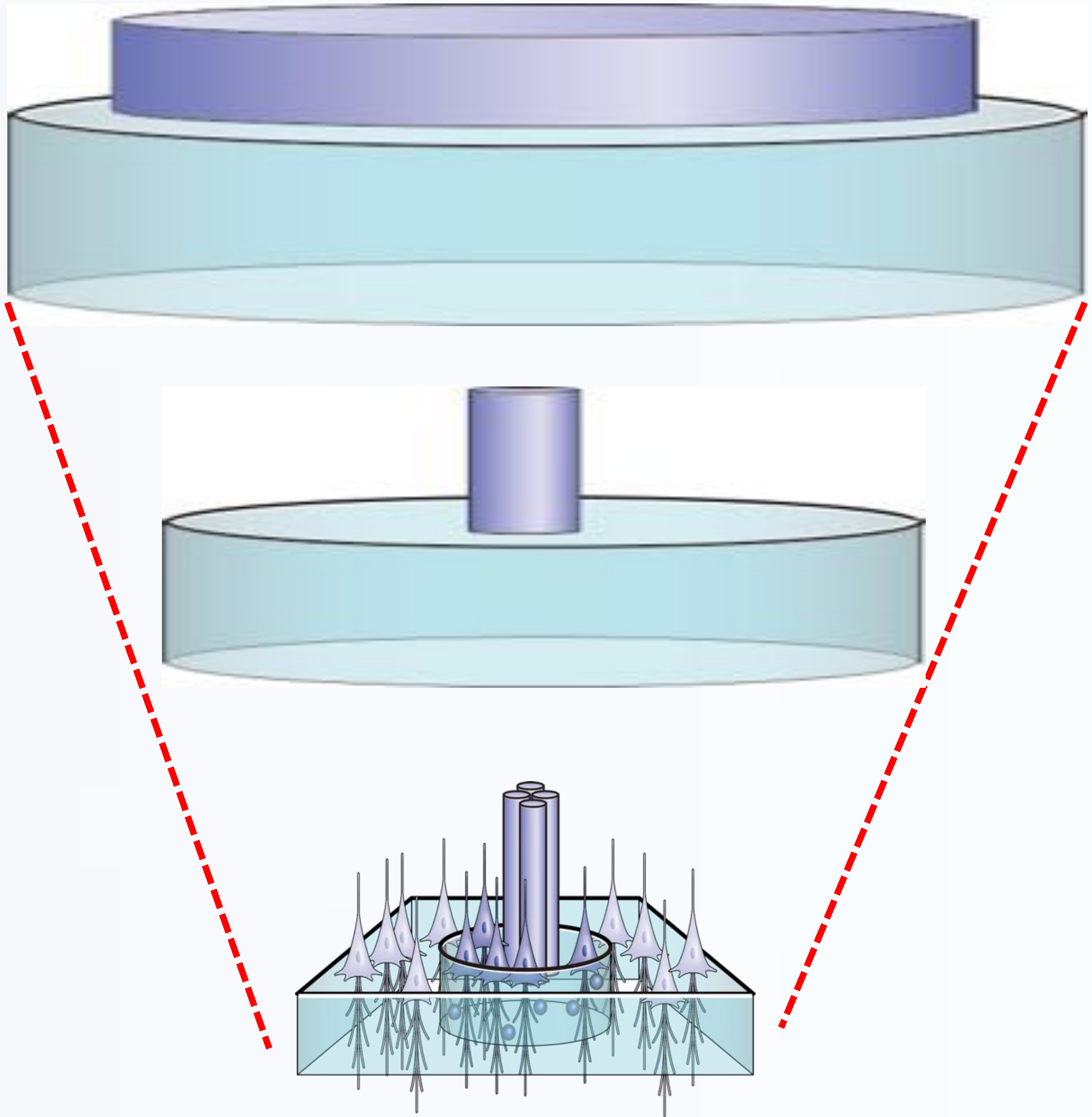
+

Global integration
of all network modules



Shimono (2013) Sci.Rep.

# Various brain-recording technologies

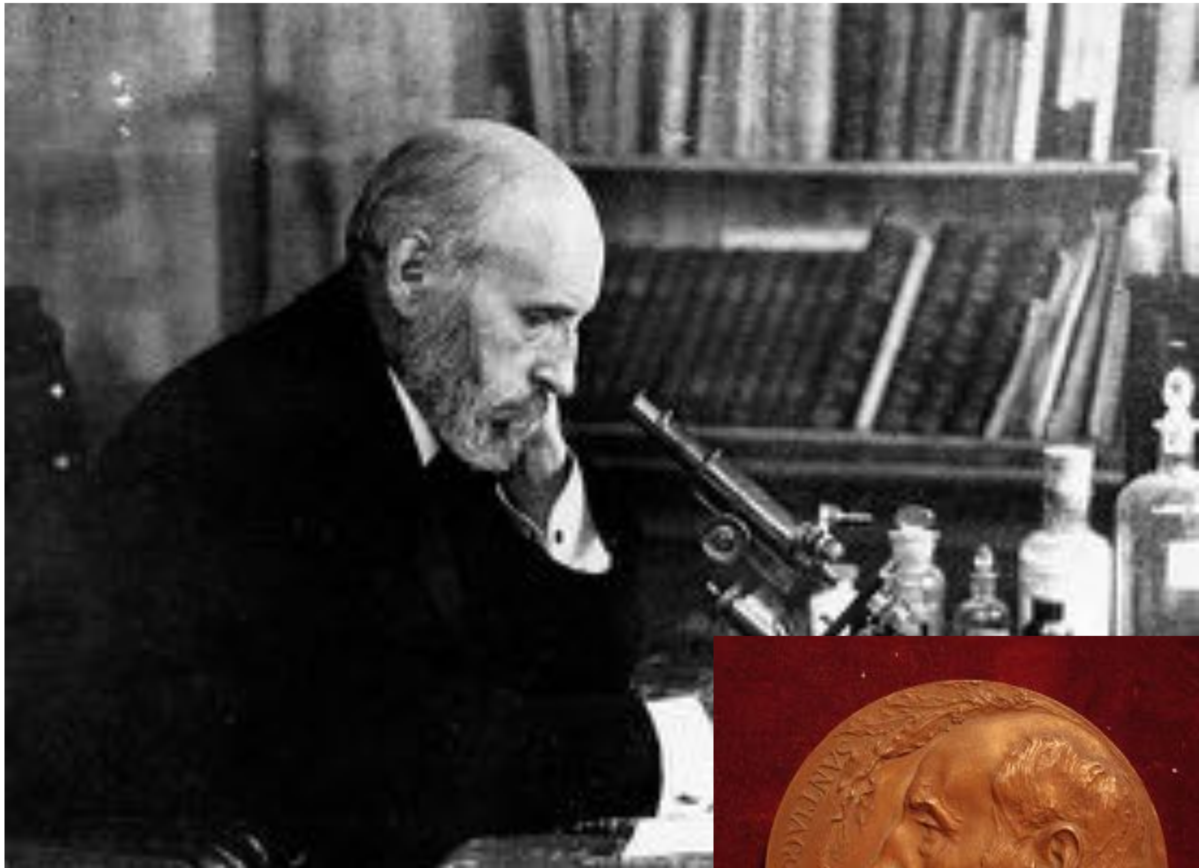


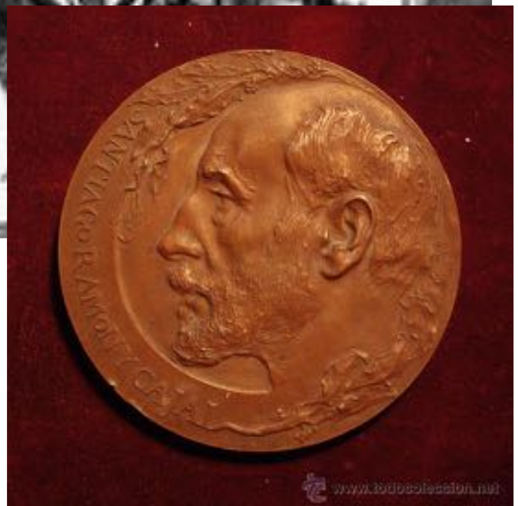
Resolution

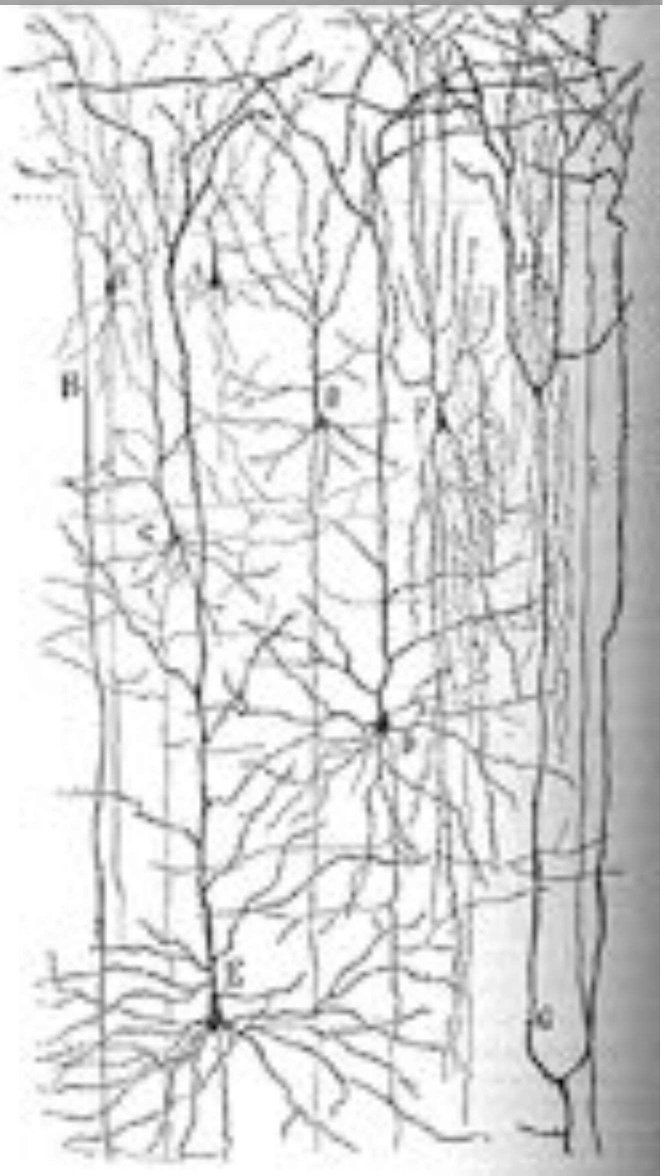
| | | |
|---|---|---|
| ECoG | Region | ~1 cm |
| LFP | | ~1 mm |
| S/MUA | Neuron | ~1 μm |

# Micro: Circuitry level

# Dream of Santiago Ramón y Cajal

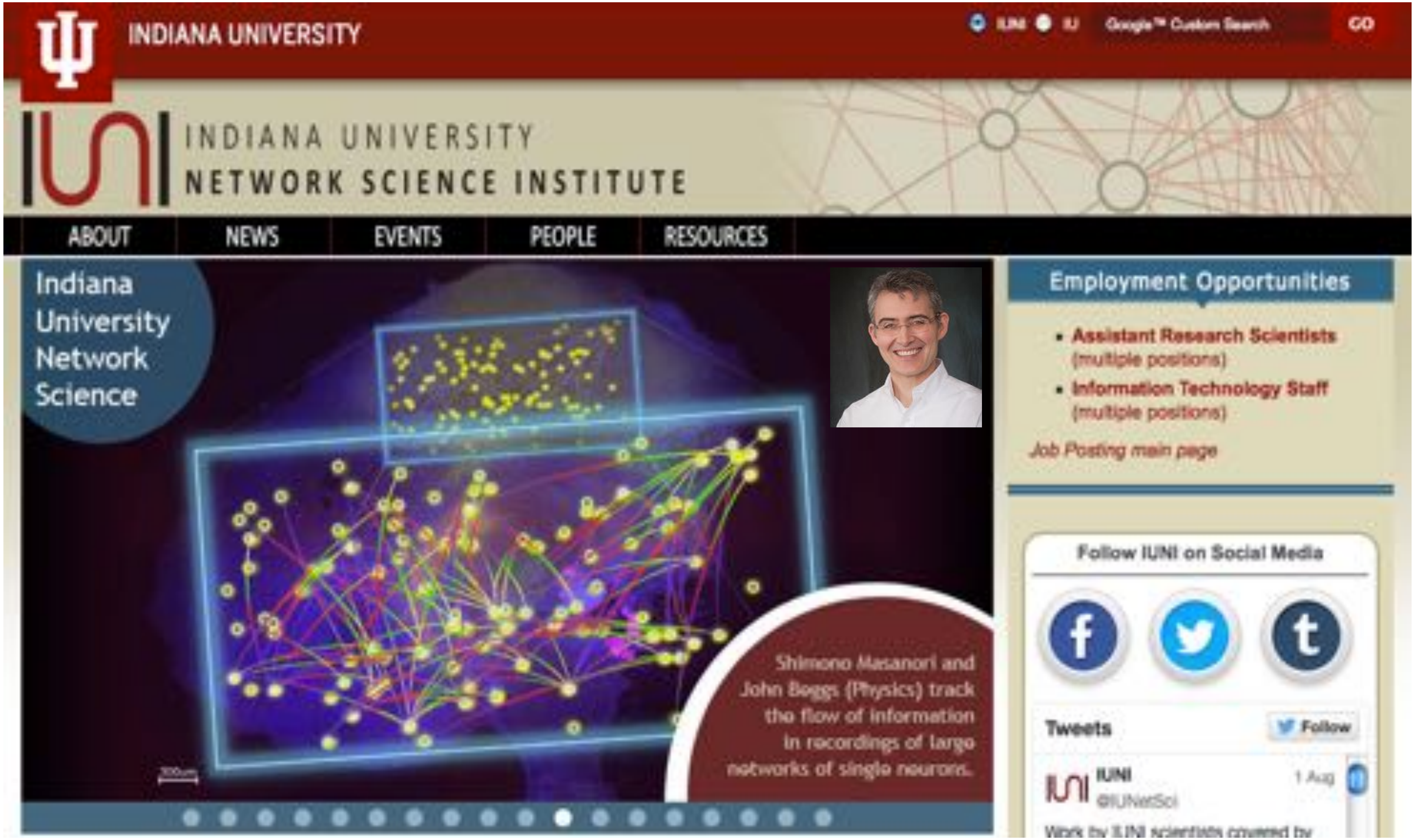




*Nobel prize*
*in physiology or medicine*
*1906*

# Causal interactions among neurons




Shimono, Beggs (2014) *Cerebral Cortex*

# Three types of networks

## ■ Structural networks

A set of physical or structural (anatomical) connections linking neural elements (Cajal, 1905; Fellman and Van Essen, 1991).

## ■ Functional networks

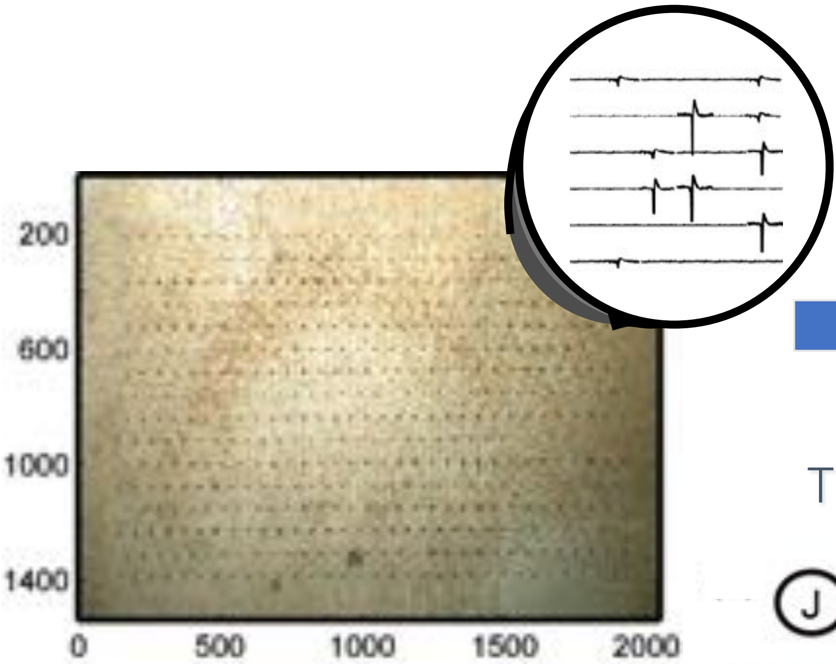
Deviations from statistical independence between distributed and often remote neuronal units (e.g. Gerstein and Perkel, 1969; Singer and Gray, 1995)

## ■ Effective networks

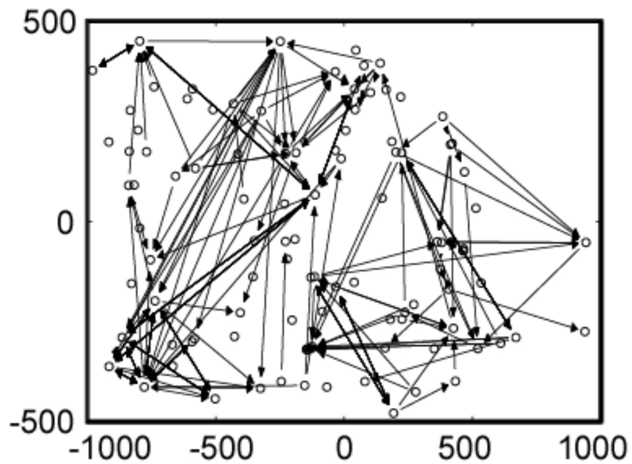
The networks of causal effects between neural elements (Adertsen et al., 1989; Friston, 1994)

# Spikes ~ functional networks

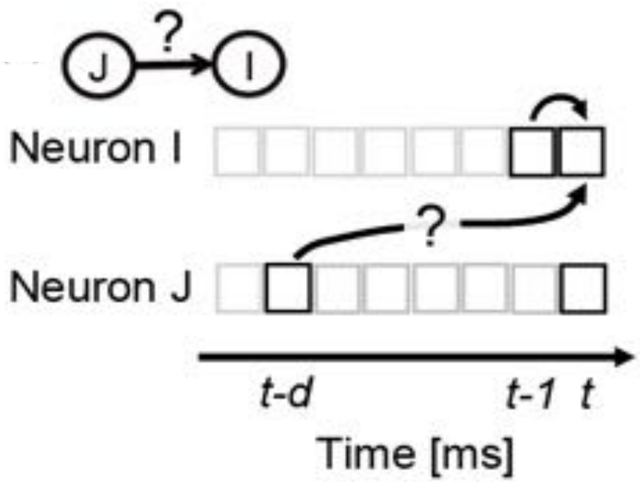
Neuronal spikes




Effective connectivity



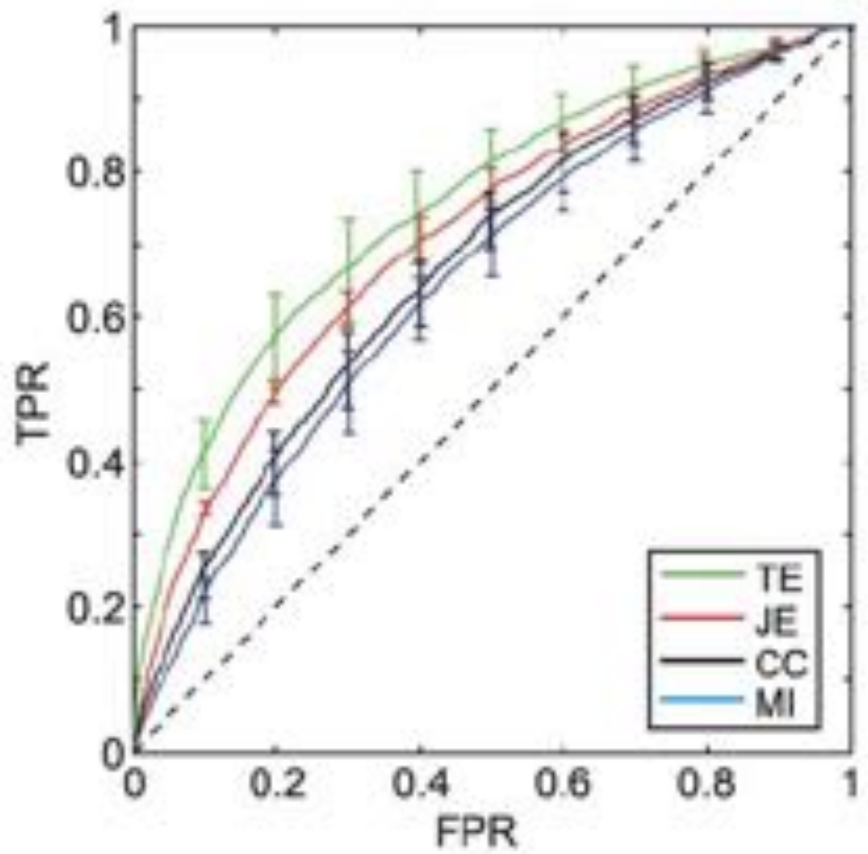

Transfer Entropy




Garofalo et al. (2009), Ito et al. (2011), Liner et al. (2011), Shimono, Beggs (2011)

# Evaluation in computational models

◆ Predicting structural connectivity from effective connectivity

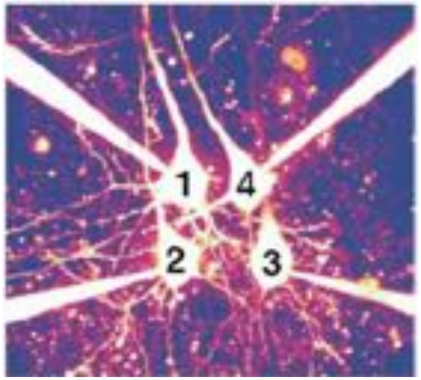






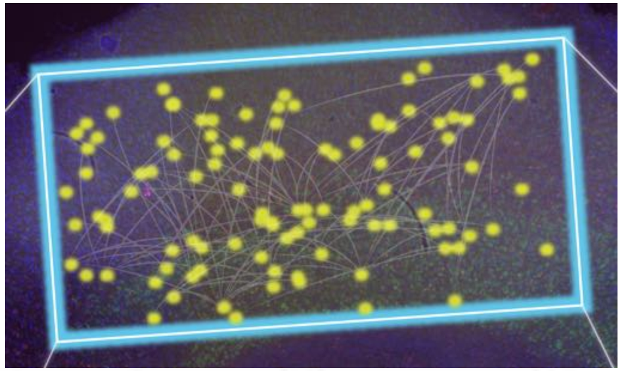
Transfer Entropy is the current champion.

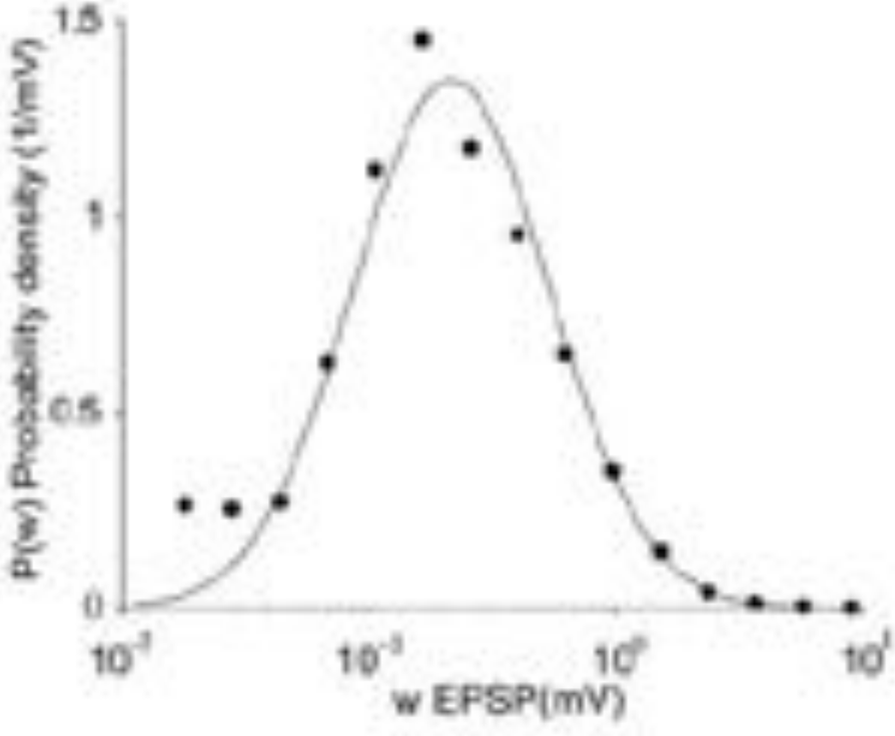
# Complex networks




Patch-clamp method

Multi-electrode recording





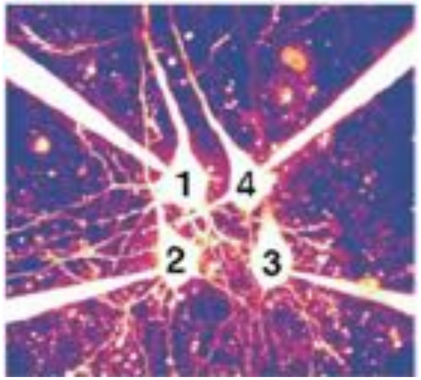


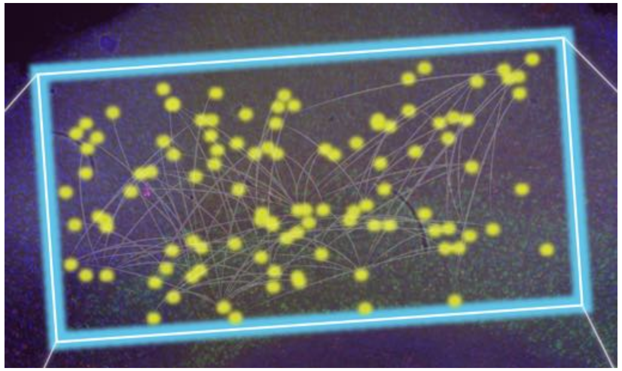


Song et al. (2009) *PLOS Biol.*

Sunny, Shimono,,, Sporns, Beggs (2016) *J.Neurosci.*

# Complex networks



Multi-electrode recording

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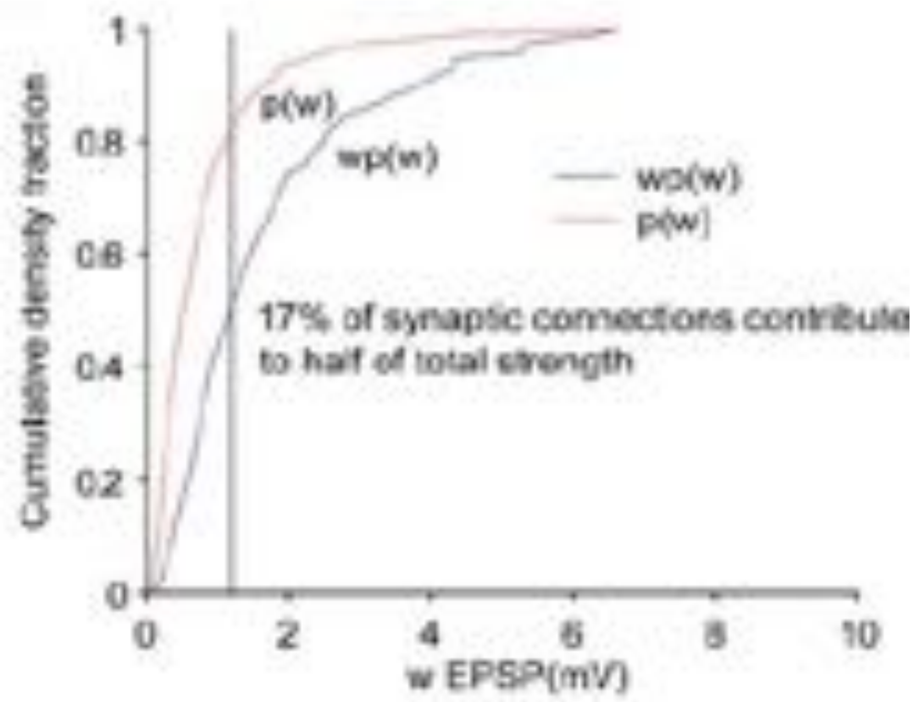






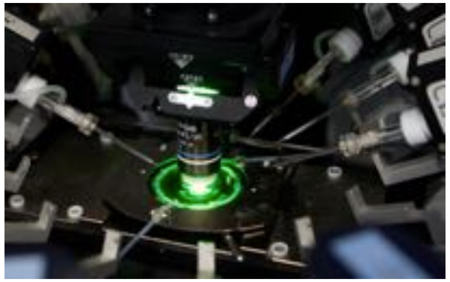
Song et al. (2009) *PLOS Biol.*

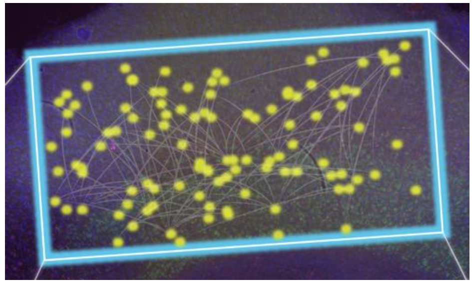
Sunny, Shimono,,, Sporns, Beggs (2016) *J.Neurosci.*

# Microconnectome

- Beyond simple statistical properties
- The detailed design of the network organization
- Nodes are generally neurons
- As one many body problem

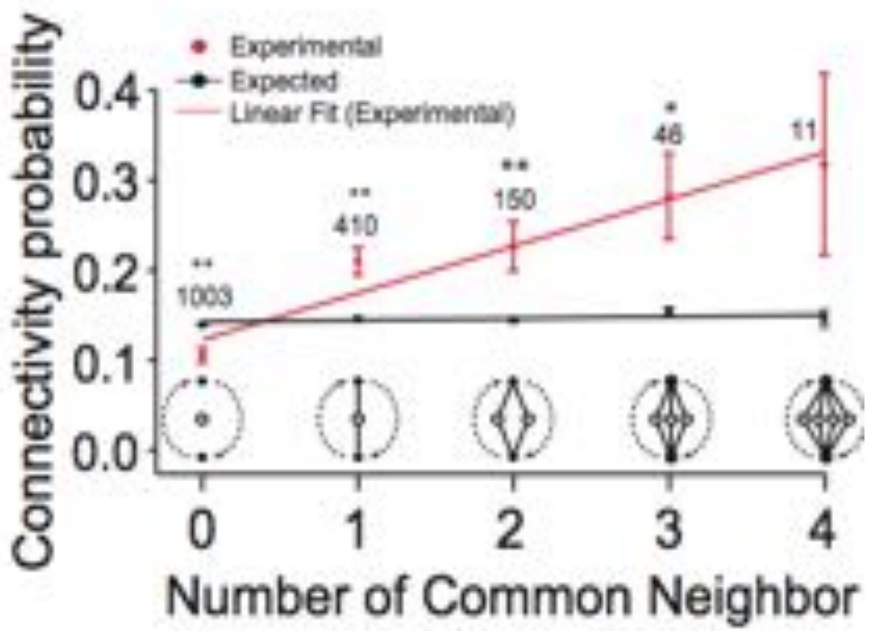
# Common neighbor effect





Patch-clamp experiment

Multi-electrode array





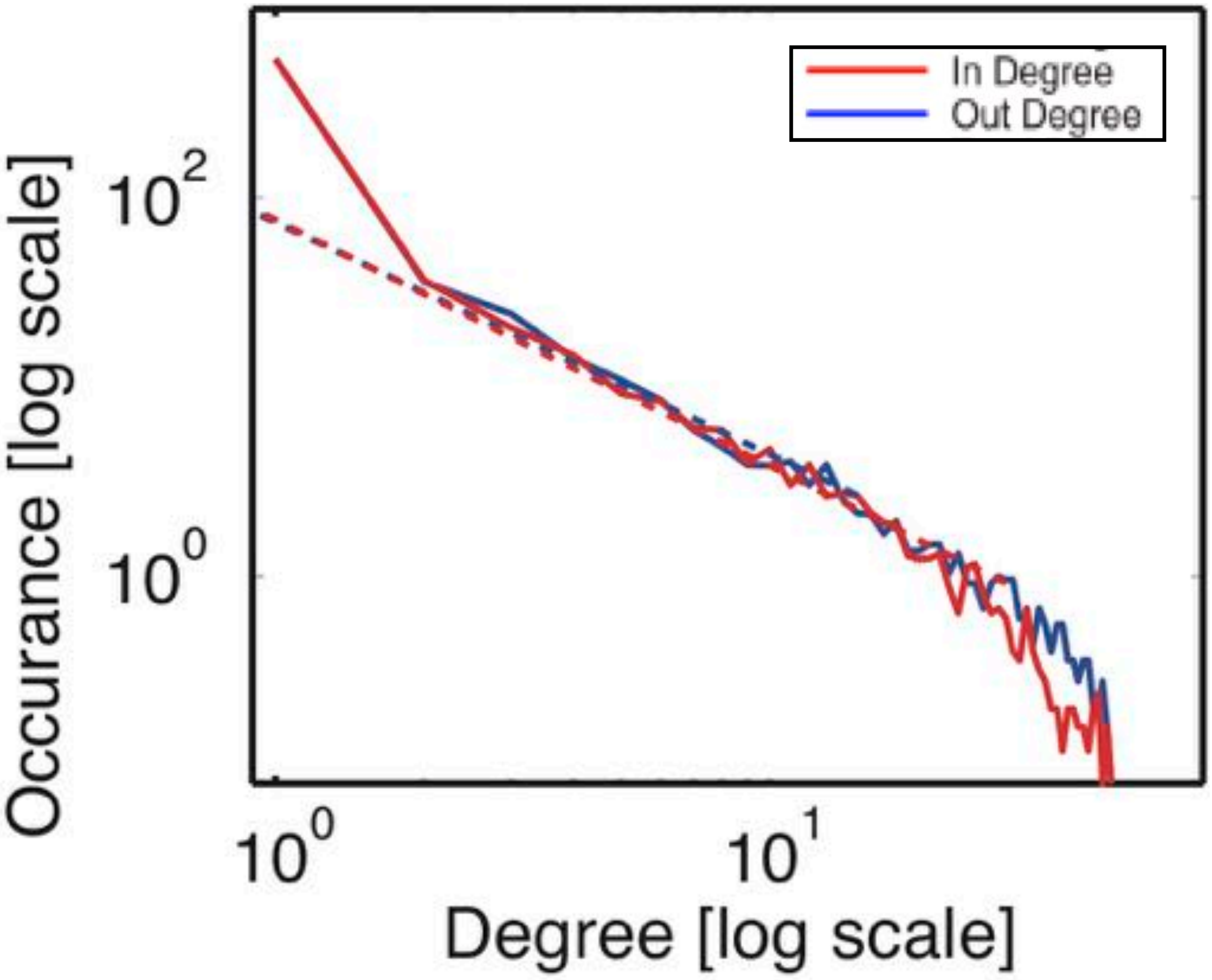




Perin, Berger, Malkram (2009)

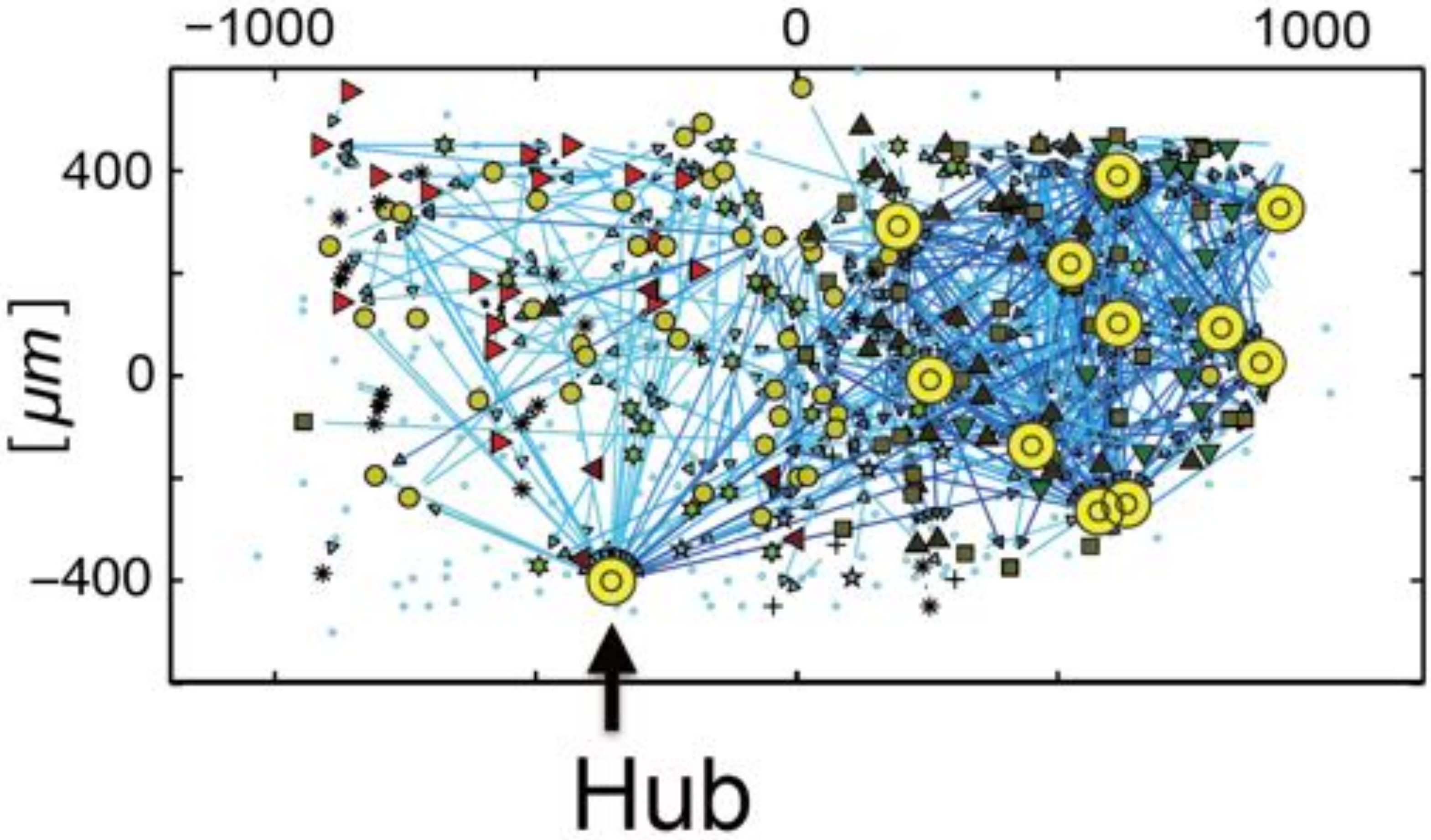
Shimono, Beggs (2011)

# Degree histogram

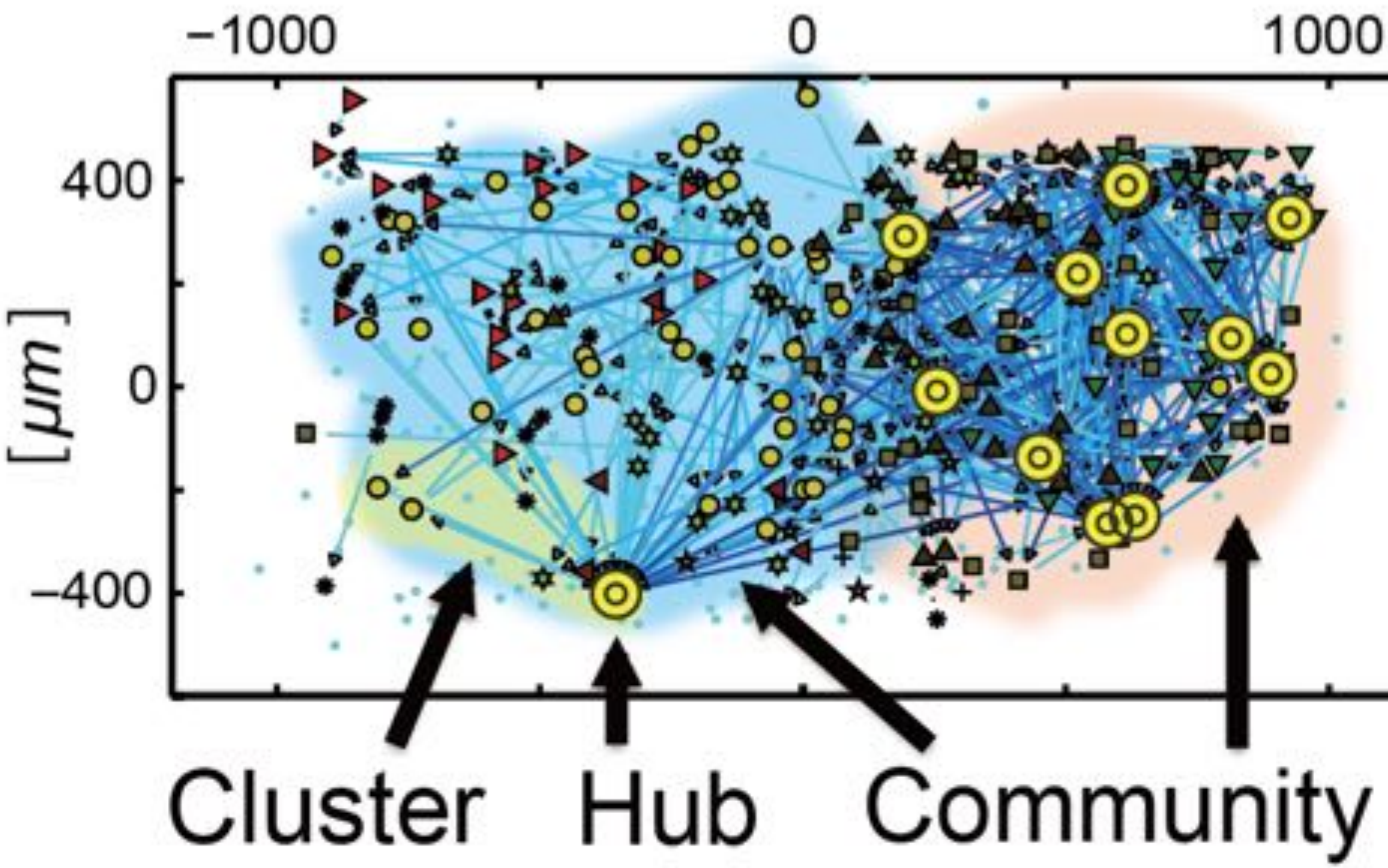



Shimono, Beggs (2014) ***Cerebral Cortex***

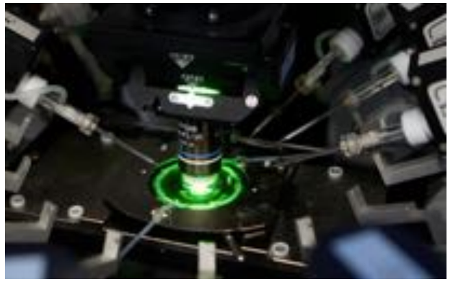
# Hubs



# Communities



# There were opposite opinion before.



## A synaptic organizing principle for cortical neuronal groups

Rodrigo Perin, Thomas K. Berger[1], and Henry Markram[2]

Blue Brain Project, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland

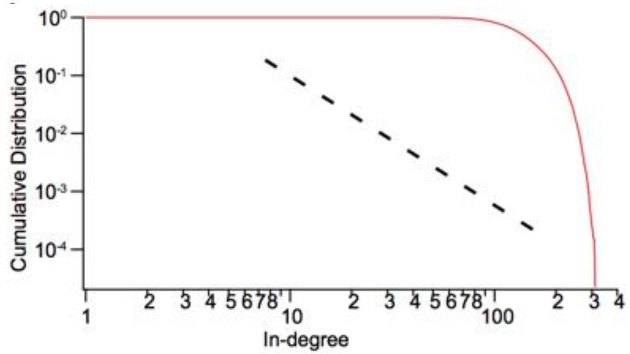
Edited by Roger A. Nicoll, University of California, San Francisco, CA, and approved February 7, 2011 (received for review October 29, 2010)

**Neuronal circuitry is often considered a clean slate that can be dynamically and arbitrarily molded by experience. However, when we investigated synaptic connectivity in groups of pyramidal neurons in the neocortex, we found that both connectivity and synaptic weights were surprisingly predictable. Synaptic weights**

tions. The first is that memory is stored in the configuration of the connectivity of neurons in an assembly and in the set of synaptic weights of the connections; the second is that experience can freely mold the network connectivity and synaptic weights.

What is known about the network topology of cortical micro-

Blue Brain Project

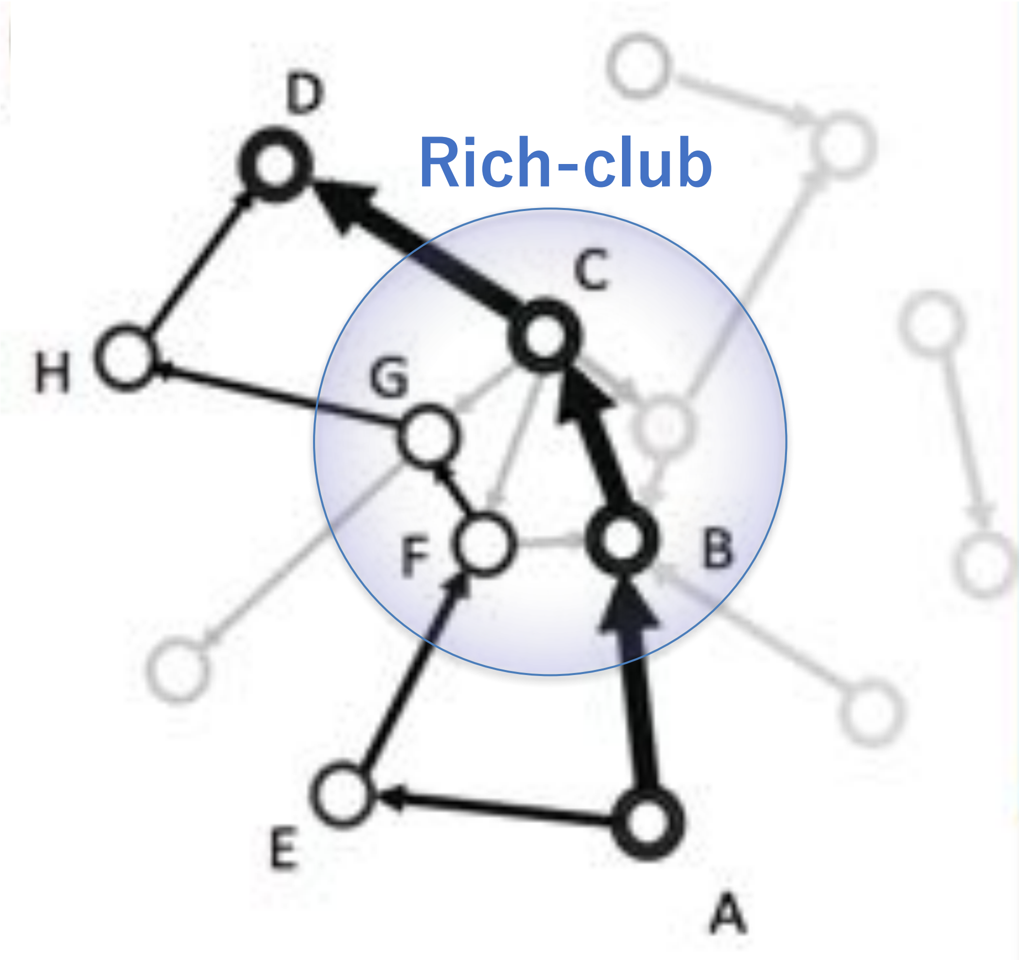




No evidence for hubs or a lattice-like organization of connections was found.

Perin, Berger, Marklam (2011) *PNAS*

# Rich club effect

## How do hubs connect each other?

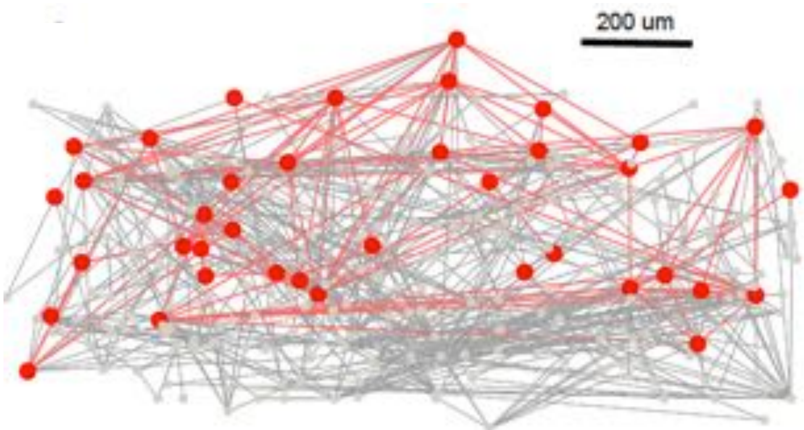


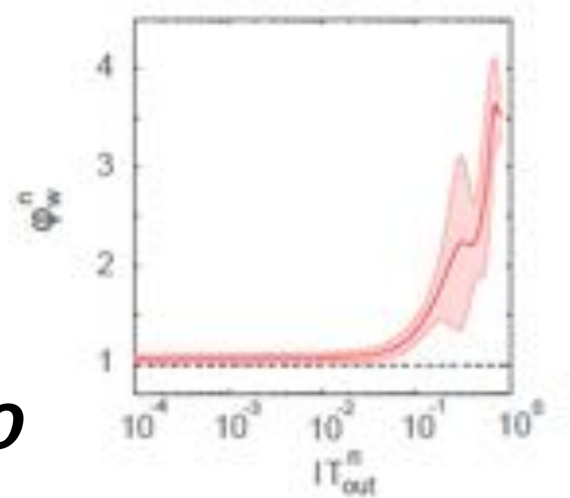



Sunny Shimono,,, Sporns, Beggs (2016) *J.Neurosci.*

# Rich club effect

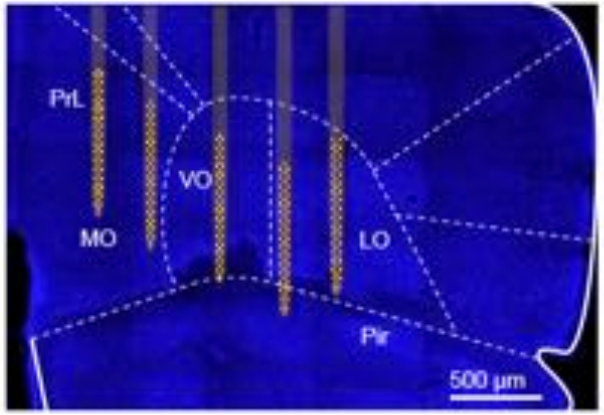
## How do hubs connect each other?

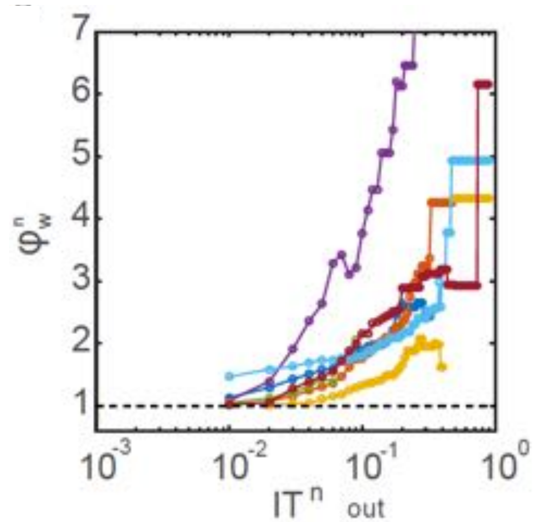



***In vitro***

W. Smith & S. C. Masmanidis




***In vivo***

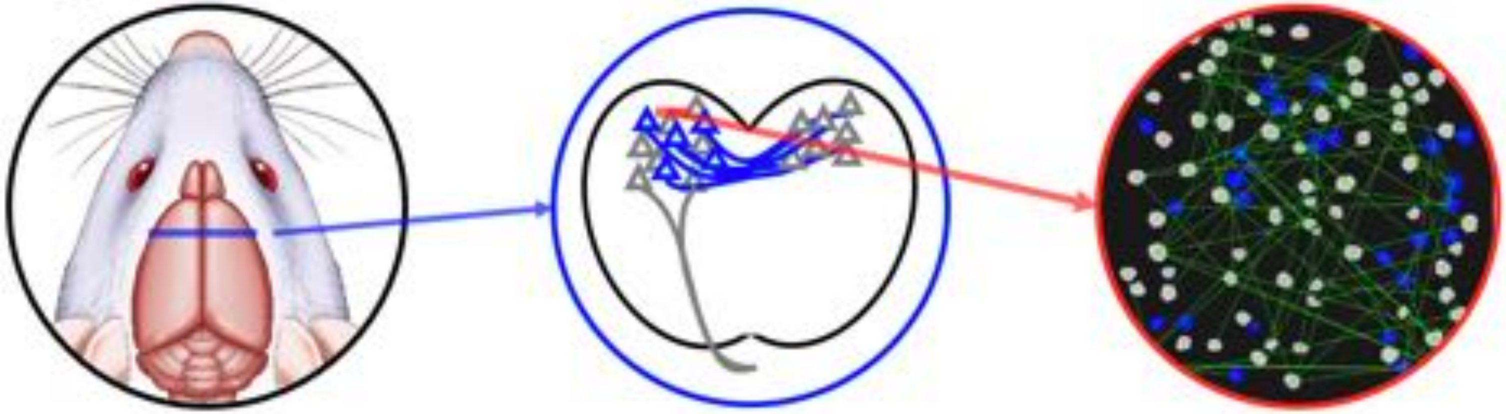


Sunny Shimono,,, Sporns, Beggs (2016) *J.Neurosci.*

# At Osaka University

OSAKA UNIVERSITY

## Microconnectome reflects global bi-hemispheric interactions



Akihiro Nakamura[1], Masanori Shimono[1,2]

1. Osaka University, Toyonaka, Osaka, Japan

2. Riken Brain Science Institute, Saitama, Japan

# Moving to Kyoto



https://twitter.com/i/web/status/797574312056098816

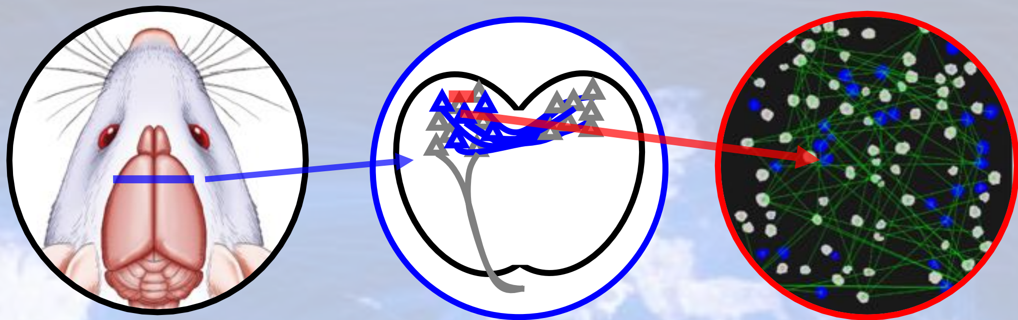
http://studio3264.doorblog.jp/archives/46074095.htm

# ネットワーク神経科学研究室

複合的計測が可能
[イメージング] MRI
(人 & 動物)
[生理] 超多電極計測

***世界最高の細胞数からの同時計測！***

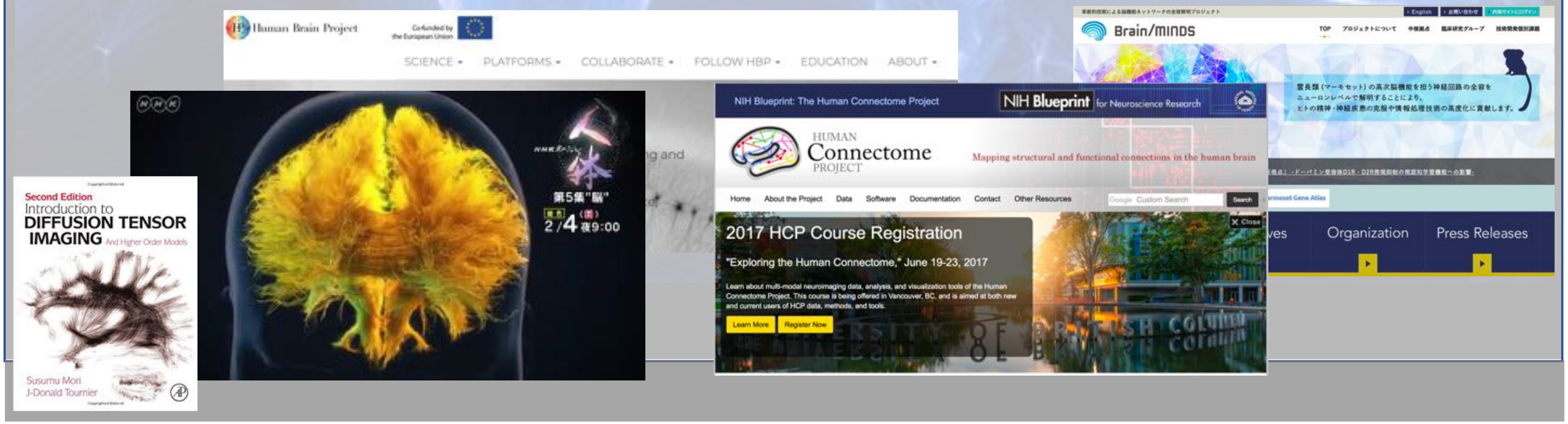
スケール間融合　　ニューラルネットワーク



ビックデータ解析
オミックス解析で
複雑な自己を探求

***多並列マシン使い放題！***

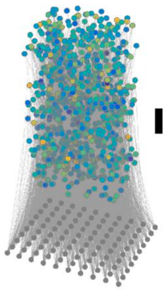
「我々の自己の根幹をなす脳神経」
✖
「”つながり”を解明するネットワーク」



# Now,,,

1F:
コンピューターサーバー

モデリング

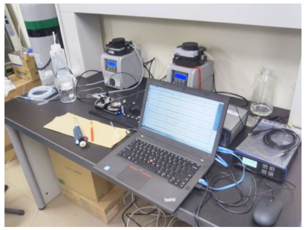


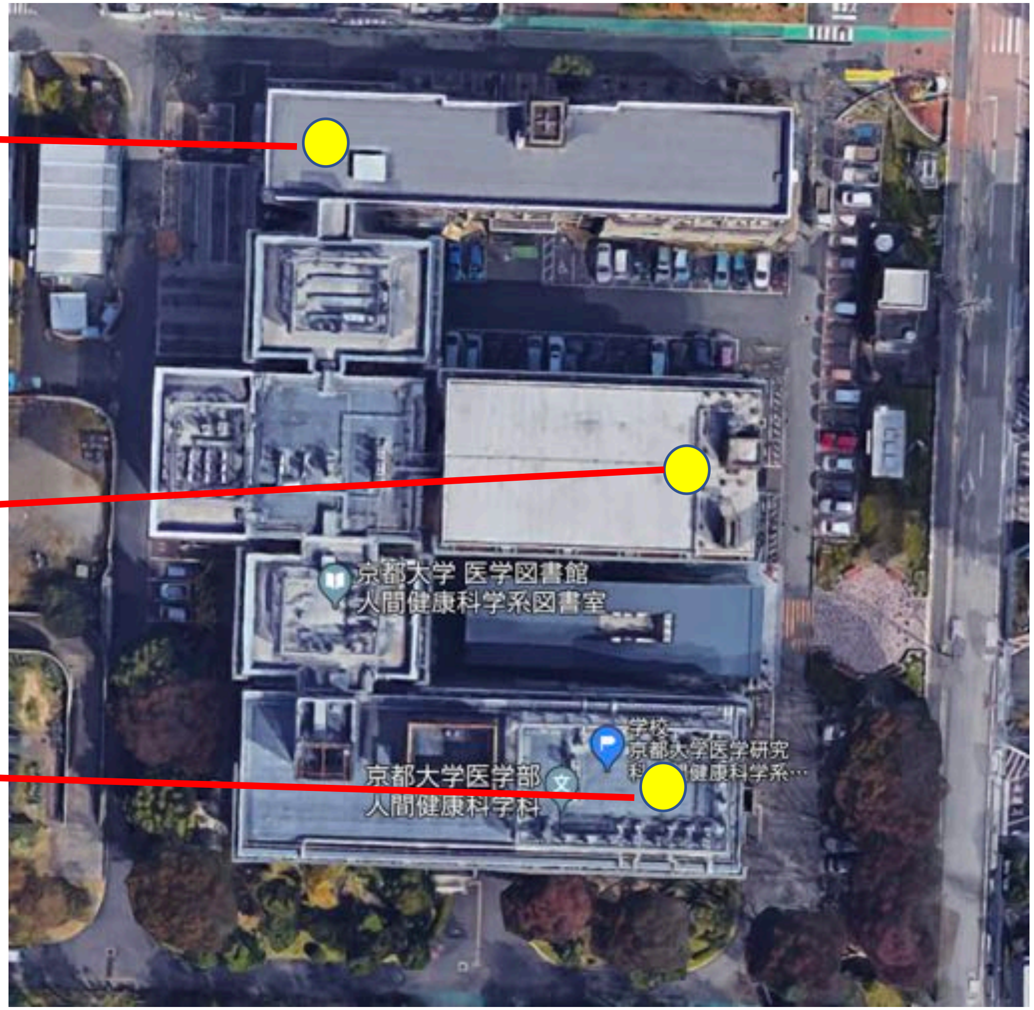
解析


3Dスキャナー

B1F: MRI計測

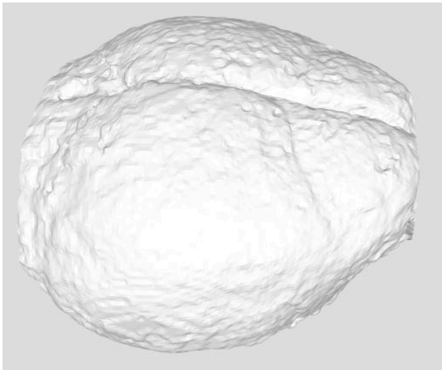
3F: 実験室
電気生理計測





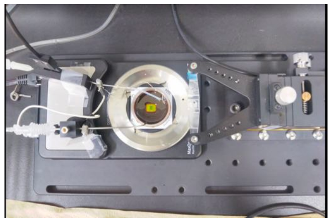
# Connecting micro & macro

## (a) Striped MRI

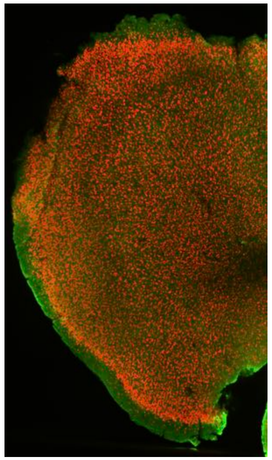


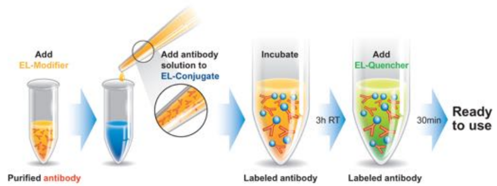
## (b) Connected 3D scan


## (c) Neuronal recording



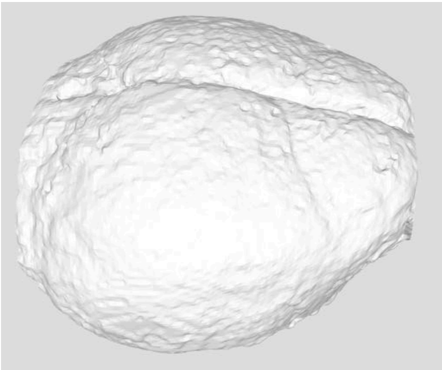
## (d) Staining

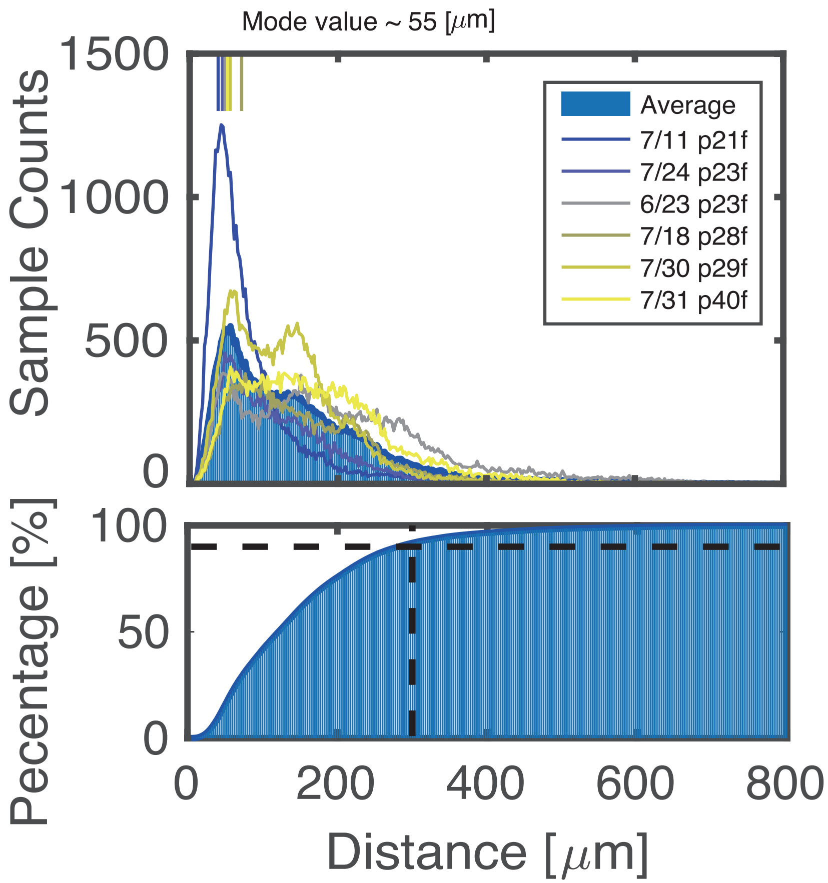




# Connecting micro & macro

MRI






3D scan

END