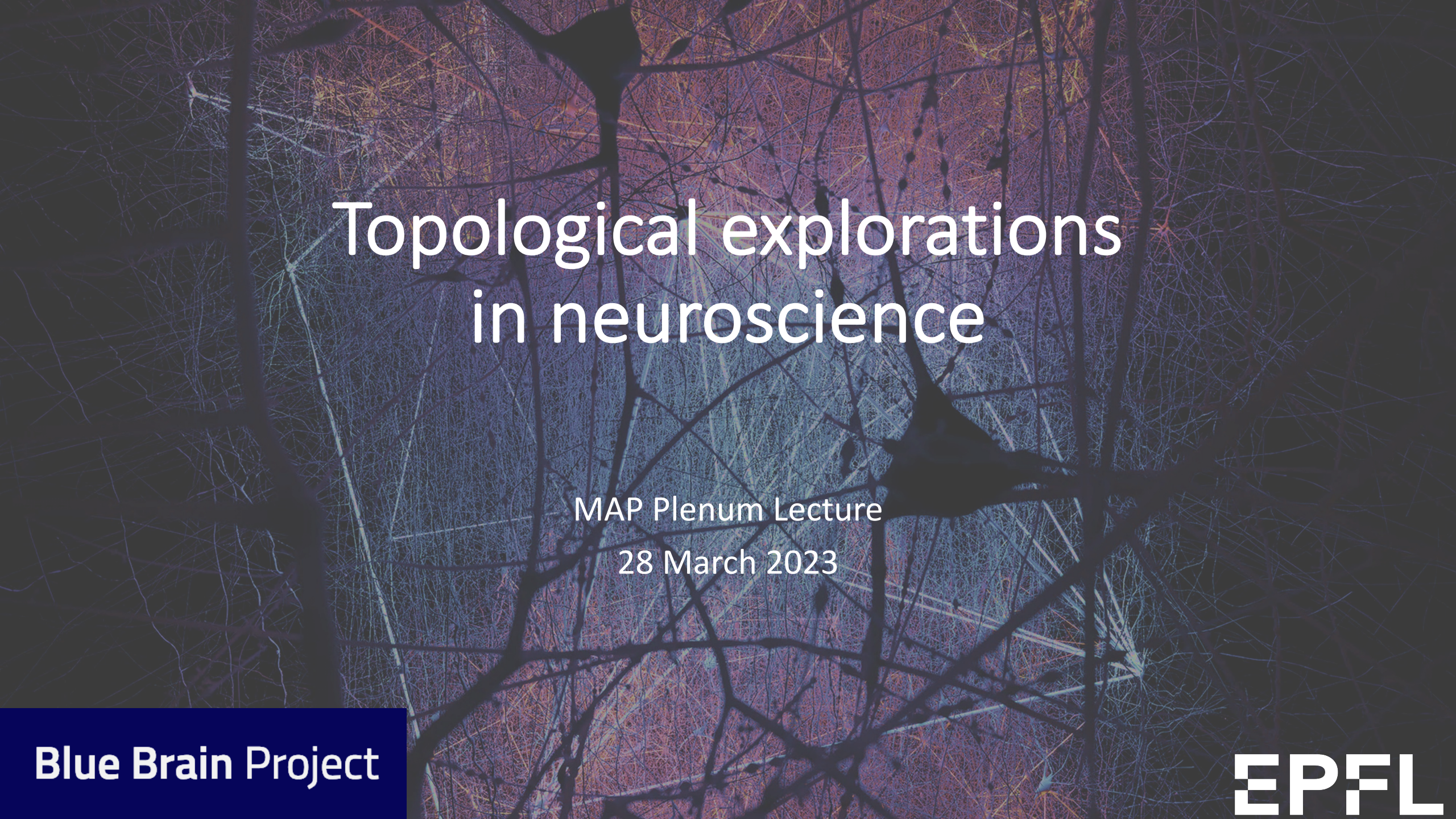


Topological explorations in neuroscience

MAP Plenum Lecture

28 March 2023

Blue Brain Project

EPFL

$\to$ Bimod

$M \tilde{\otimes} N$

$\downarrow$

$P \otimes Q$

$\to O_P$

$F_P(V) \tilde{\otimes} F_Q(W)$

$\| 2$

$F_{P\otimes Q}(V \square W)$

$$(P \circ V \circ P) \square (Q \circ W \circ Q) \xrightarrow{\tau_{V,W}} (P \otimes Q) \circ (V \square W) \circ (\quad$$

$$((p; v_1, \dots, v_k; p_1, \dots, p_m), (q; w_1, \dots, w_l; q_1, \dots q_n)) \mapsto (p \otimes q; (v_i w_j)_{i,j}; (p_r \otimes q_s)_{r,s})$$

$$\forall\, a : F_P V \longrightarrow F_P V' \qquad b : F_Q W \longrightarrow F_Q W'$$

$$a^\# : V \longrightarrow P \circ V' \circ P \qquad b^\# : W \longrightarrow Q \circ W' \circ Q$$

$$\exists\, V \square W \xrightarrow{a^\# \square b^\#} (P \circ V' \circ P) \square (Q \circ W' \circ Q) \xrightarrow{\tau_{V',W'}} (P \otimes Q) \circ (\quad$$

$$\underbrace{\left(\tau_{V',W'} \circ (a^\# \square b^\#)\right)^\flat}_{=: a \tilde{\otimes} b} : F_{P\otimes Q}(V \square W) \longrightarrow F_{P\otimes Q}(V' \square W')$$

$$\tau_{V,W} : (P \otimes Q) \circ (V \square W) \circ (P \otimes Q) \to (P \otimes Q) \circ (V \square W) \circ (P \otimes Q)$$

$$\downarrow (P\otimes Q) \circ (a^\# \square b^\#) \circ (P \otimes Q)$$

$$(P \otimes Q) \circ \big((P \circ V' \circ P) \square (Q \circ W' \circ Q)\big) \circ (P \otimes Q)$$

$$\downarrow (P \otimes Q) \circ \tau_{V',W'} \circ (P \otimes Q)$$

$$(P \otimes Q)^{\circ 2} \circ (V' \square W') \circ (P \otimes Q)^{\circ 2}$$

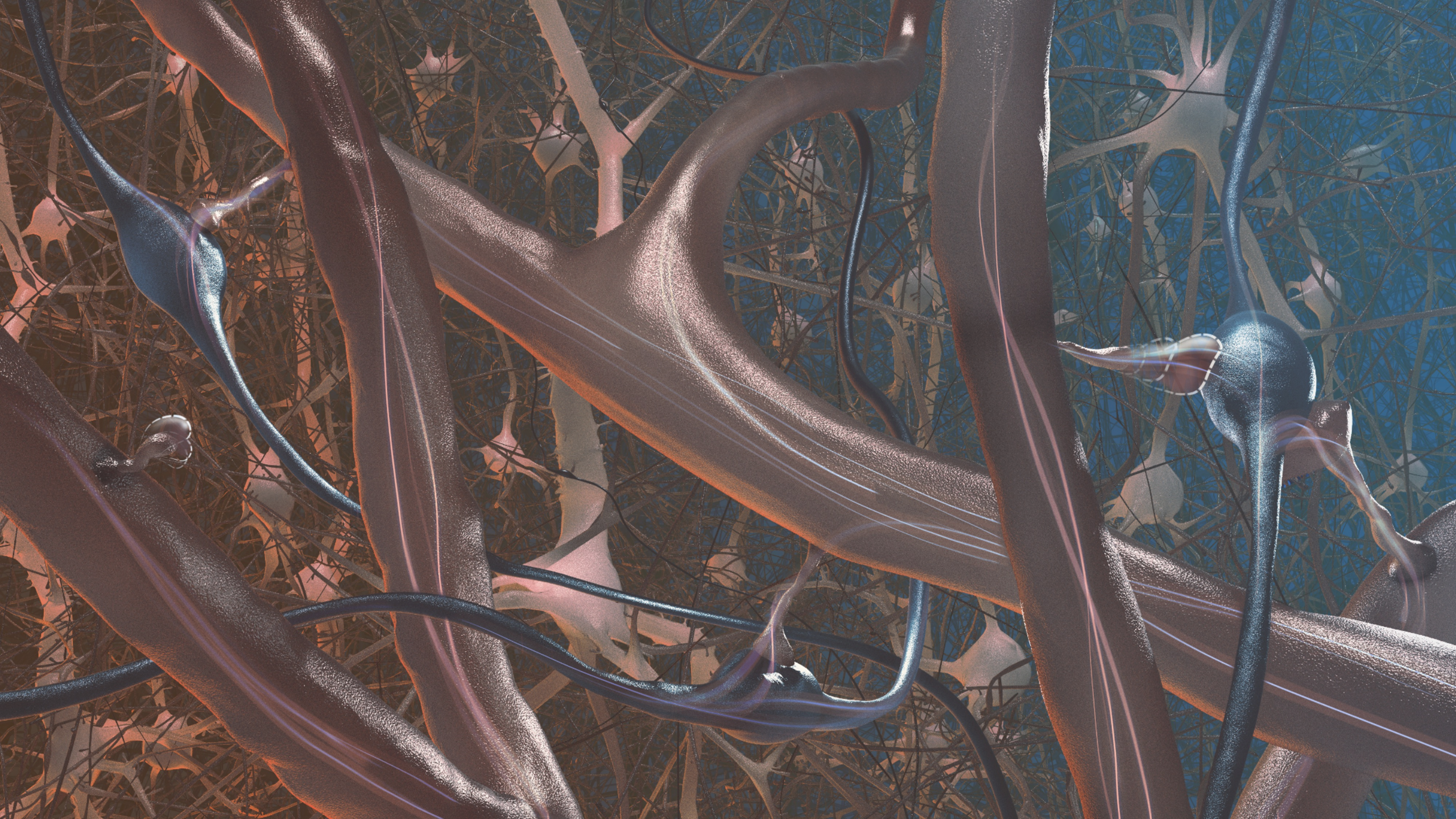
$$\downarrow \mu_{P\otimes Q} \circ (V' \square W') \circ \mu_{P\otimes Q}$$

$$\tau_{V',W'} : (P \otimes Q) \circ (V' \square W') \circ (P \otimes Q) \to (P \otimes Q) \circ (V' \square W') \circ (P \otimes Q)$$

$$\mathcal{L}_P(P) \tilde{\otimes} Q \cup P \tilde{\otimes} \mathcal{L}_Q(Q) \to \mathcal{L}_P(P) \tilde{\otimes} \mathcal{L}_Q(Q) \to P \otimes Q \xrightarrow{1^h} \mathcal{L}_{P\otimes Q}(P \otimes Q)$$

$$(a' \tilde{\otimes} b') \circ (a \tilde{\otimes} b) \overset{?}{=} (a' \circ a) \tilde{\otimes} (b' \circ b)$$

$$V \xrightarrow{a^\#} F_P V' \xrightarrow{a'} F_P V'' \qquad (a'a)^\#$$



A glimpse of neuroscience

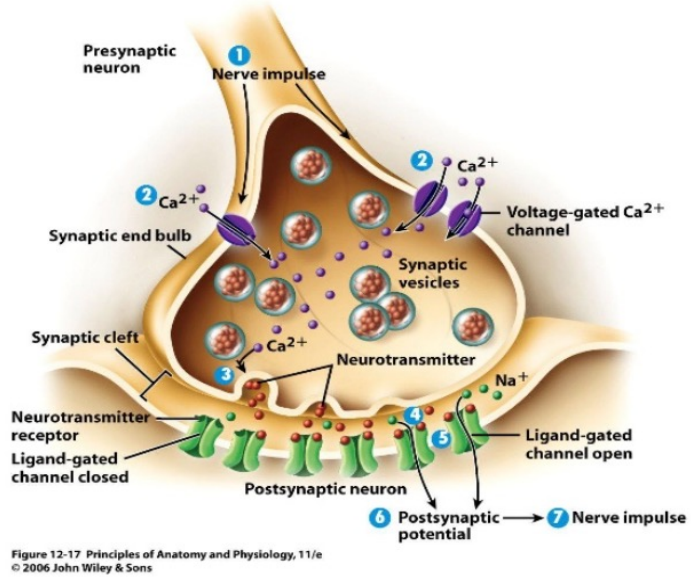
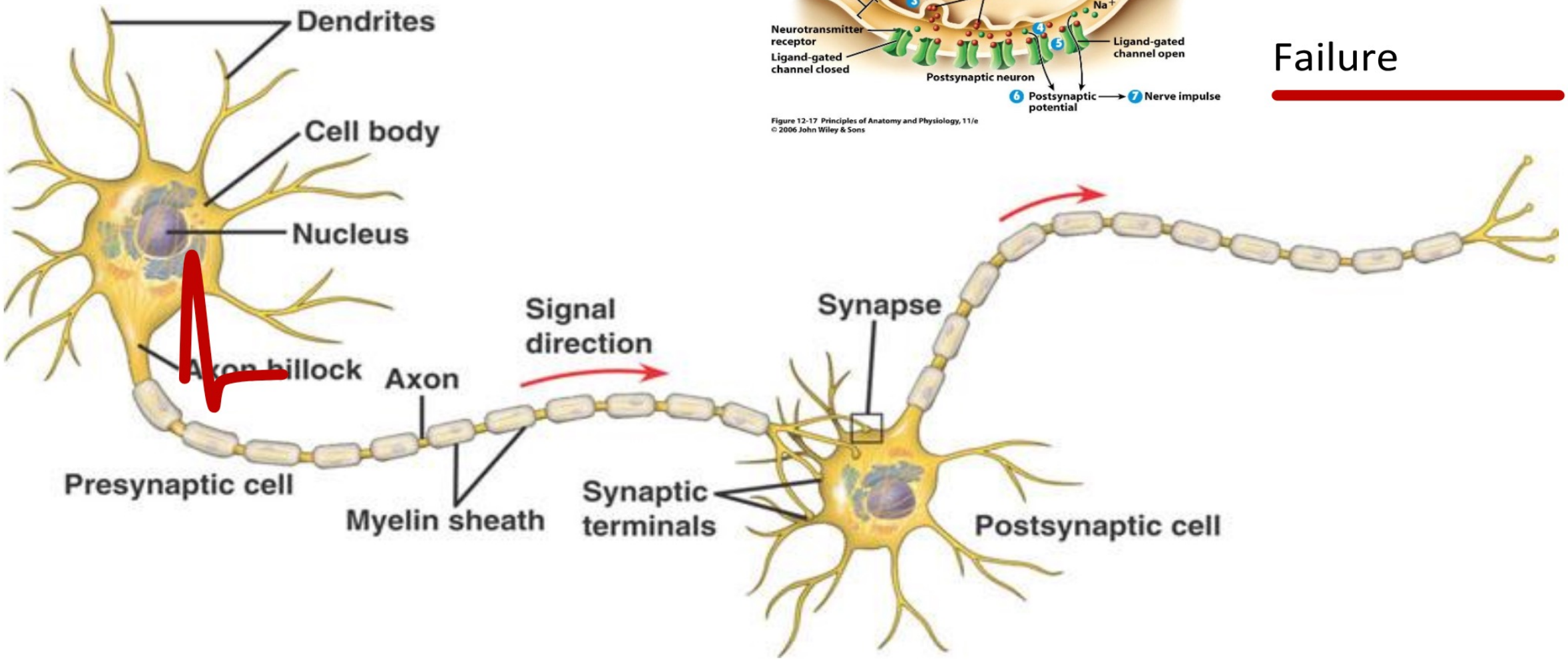


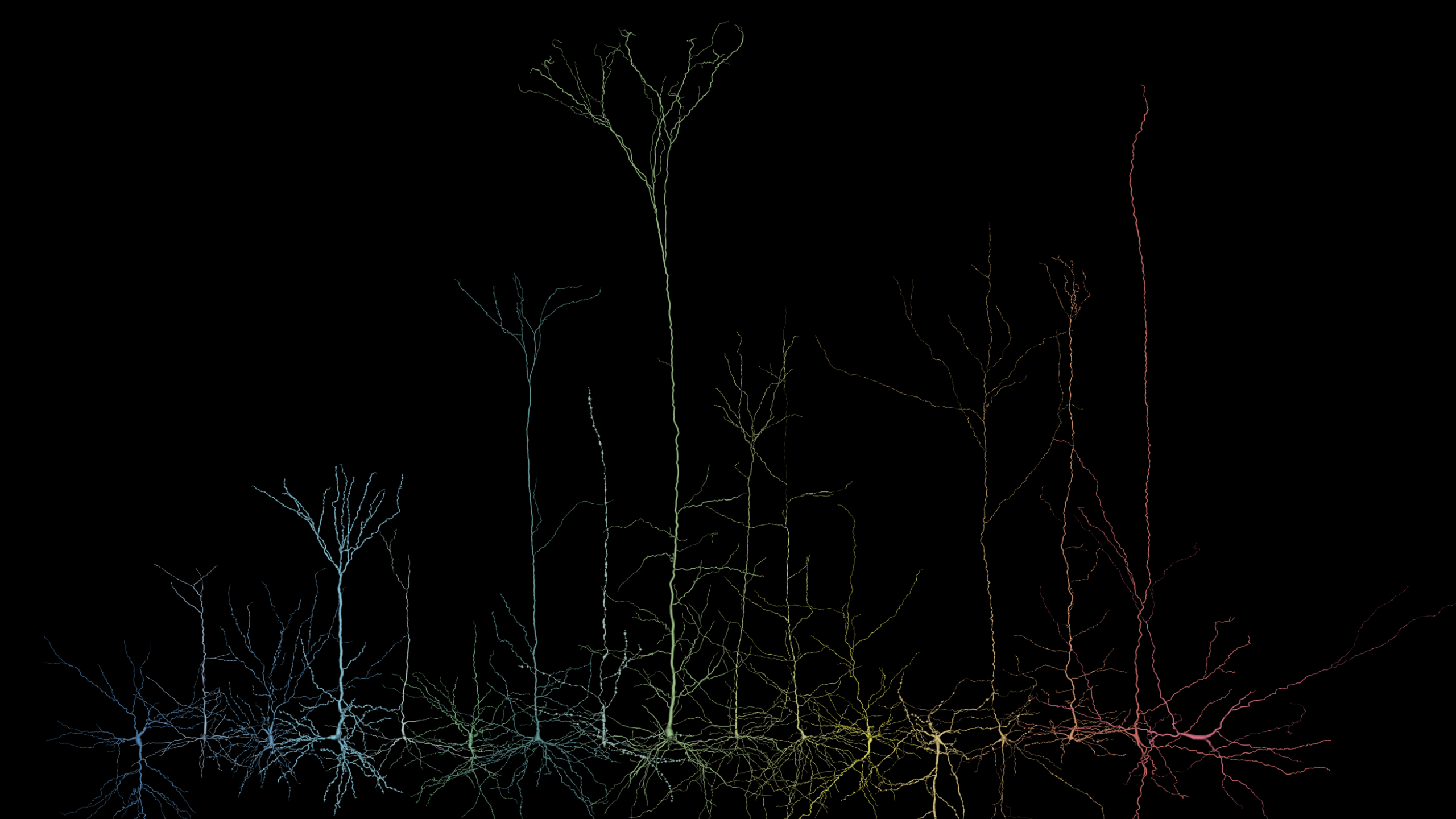
Figure 12-17 Principles of Anatomy and Physiology, 11/e
© 2006 John Wiley & Sons

Response

Failure



From pmgbiology.com



A glimpse of topology


deformation
shape
connectivity
continuous
path
cavity
invariants
geometry
connected
donut
classification
simplex
open
topology
proximity
mug
homology
algebra
equivalence
closed
continuity
complex

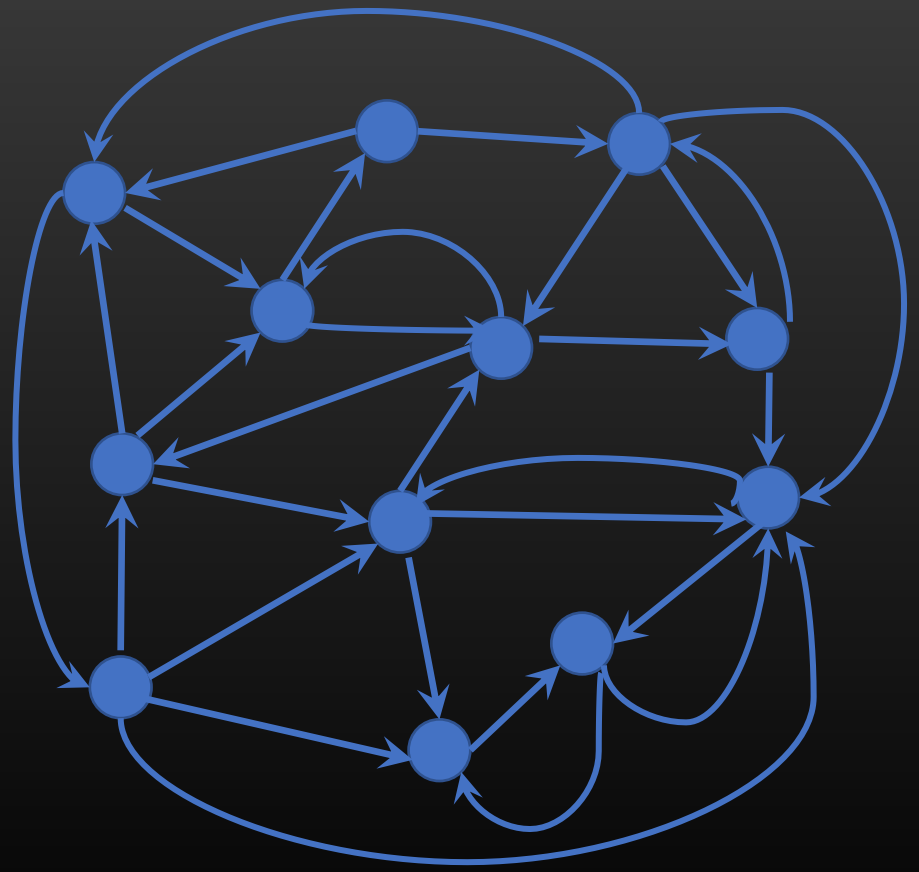
Topology is…

- the mathematics of shape;

Wikipedia, no license

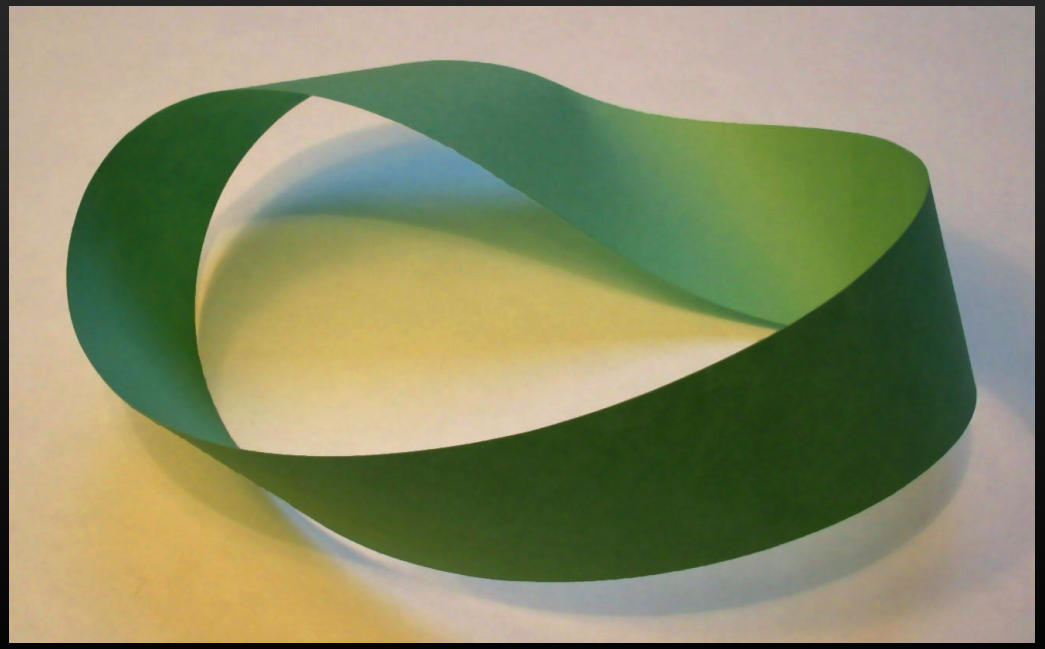
Topology is…

- the mathematics of shape;
- the mathematics of connectivity;



Topology is…

- the mathematics of shape;
- the mathematics of connectivity;
- the mathematics of emergence of global structure from local constraints.



Application to data analysis (TDA)

The shape of a data set,

described by a topological signature

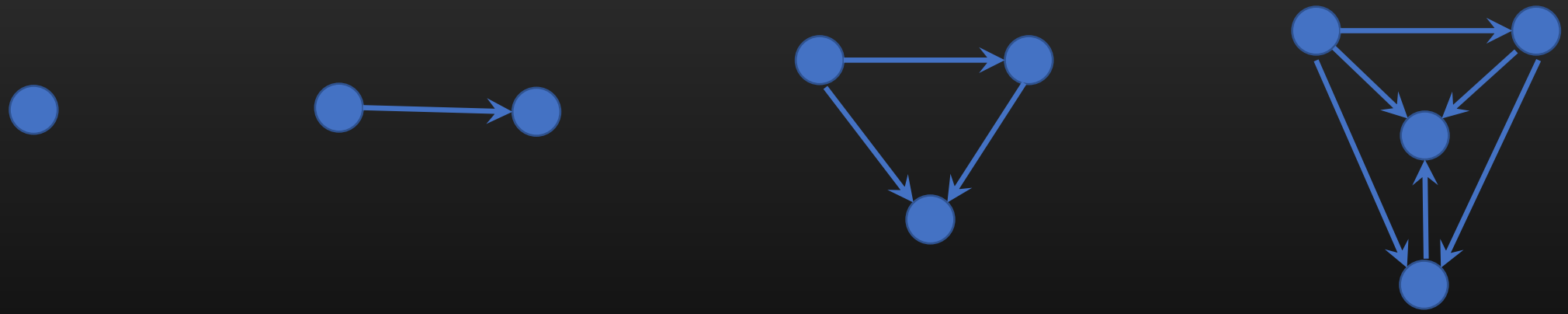
encoding its multi-scale structure,

can reveal important relations among the data points,

with the help of machine learning.

Application to network analysis

- For each type of network (undirected/directed/weighted…), choose an appropriate family of significant subnetworks (e.g., motifs, graphlets) to study.



Directed simplices of dimensions 0, 1, 2, and 3

Application to network analysis

- For each type of network (undirected/directed/weighted…), choose an appropriate family of significant subnetworks (e.g., motifs, graphlets) to study.

- The numbers of different types of significant subnetworks in a given network provide important local information about the network.

- Quantify how the significant subnetworks overlap in the network to obtain important global information.

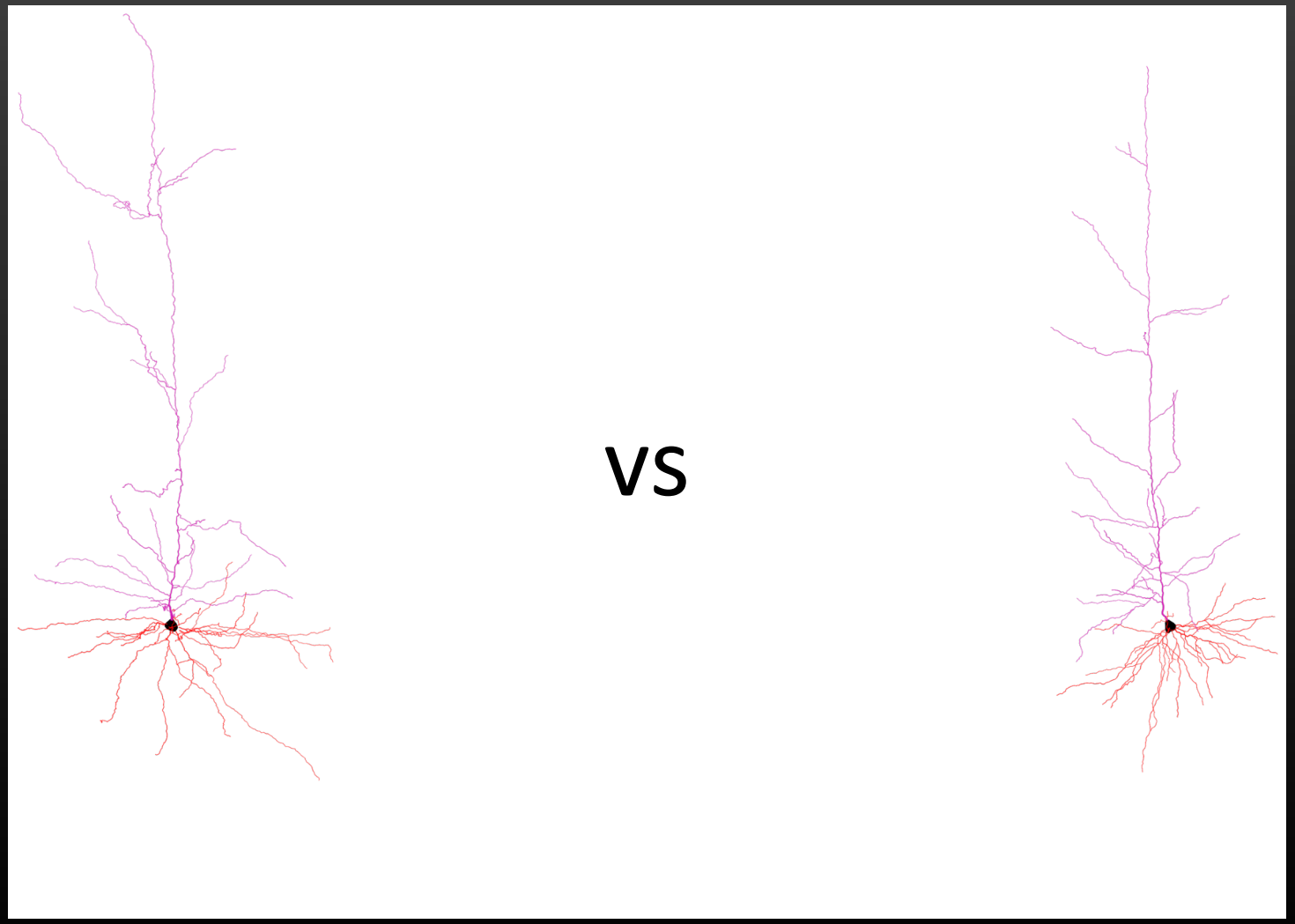
Classification of neuron morphologies

Y. Deitcher et al, Cerebral Cortex, 2017.

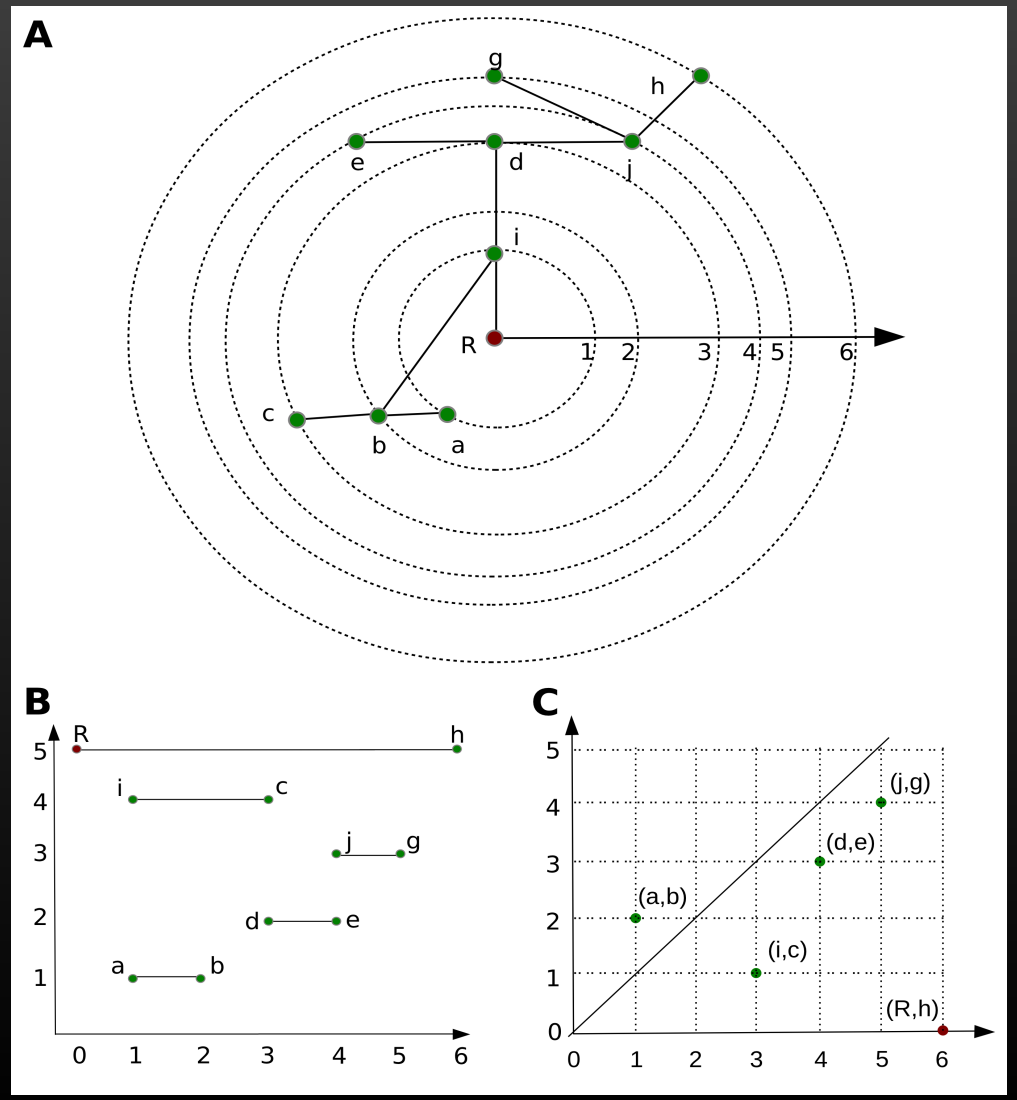
L. Kanari et al, Neuroinformatics, 2018.

L. Kanari et al, Cerebral Cortex, 2019.

How to classify neuron morphologies?

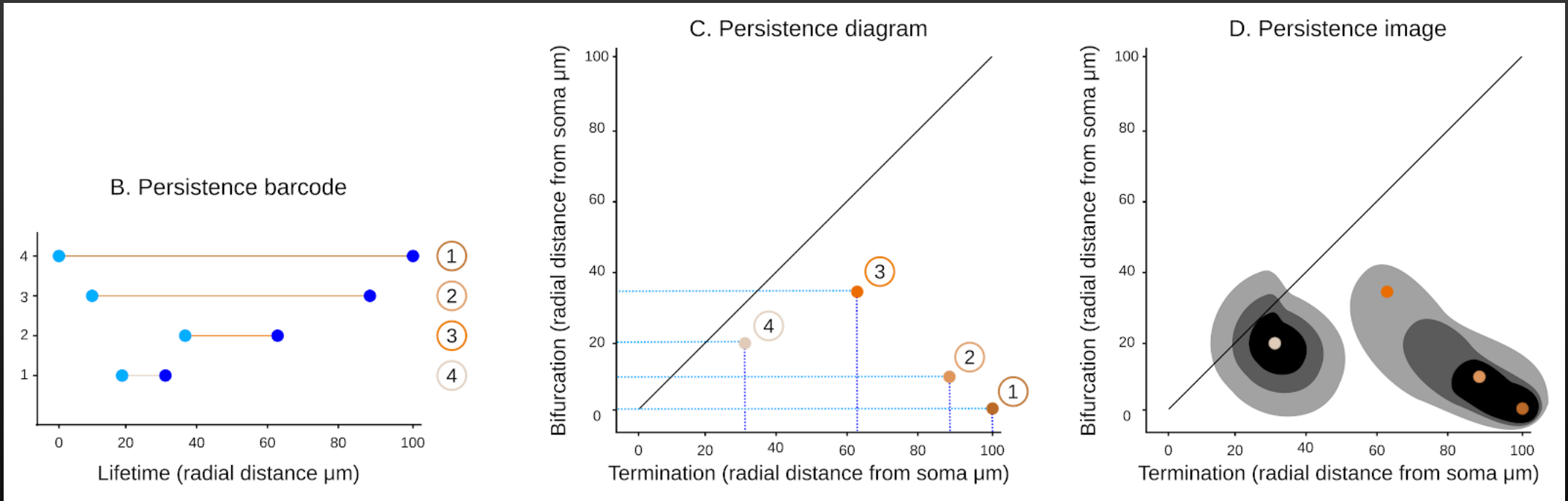


The TMD algorithm

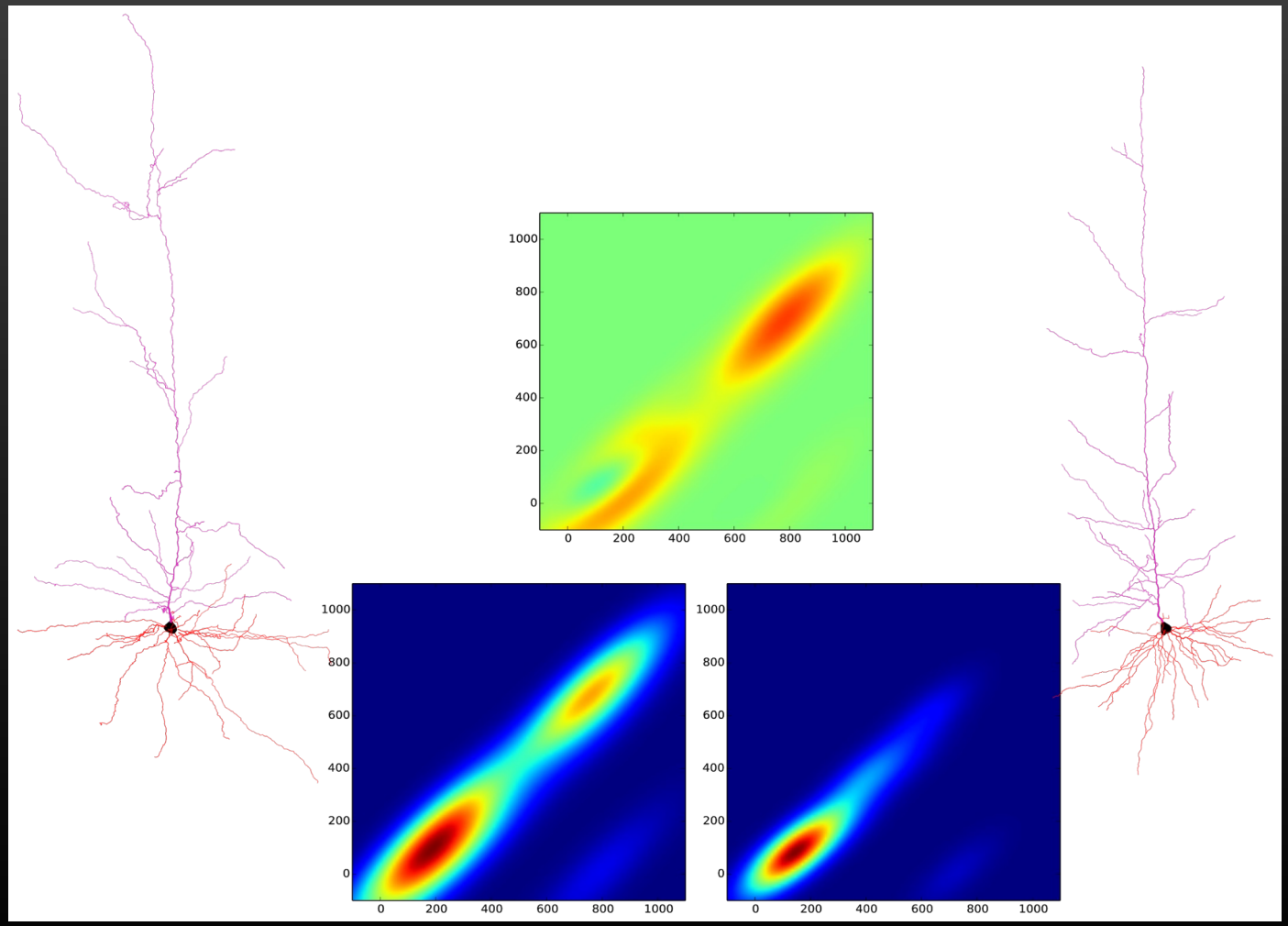


Idea: Starting at the leaves and descending recursively to the root, decompose the tree into branches, while respecting the Elder Rule, i.e., at any bifurcation, the elder (longer) branch survives and the younger branch is broken off.

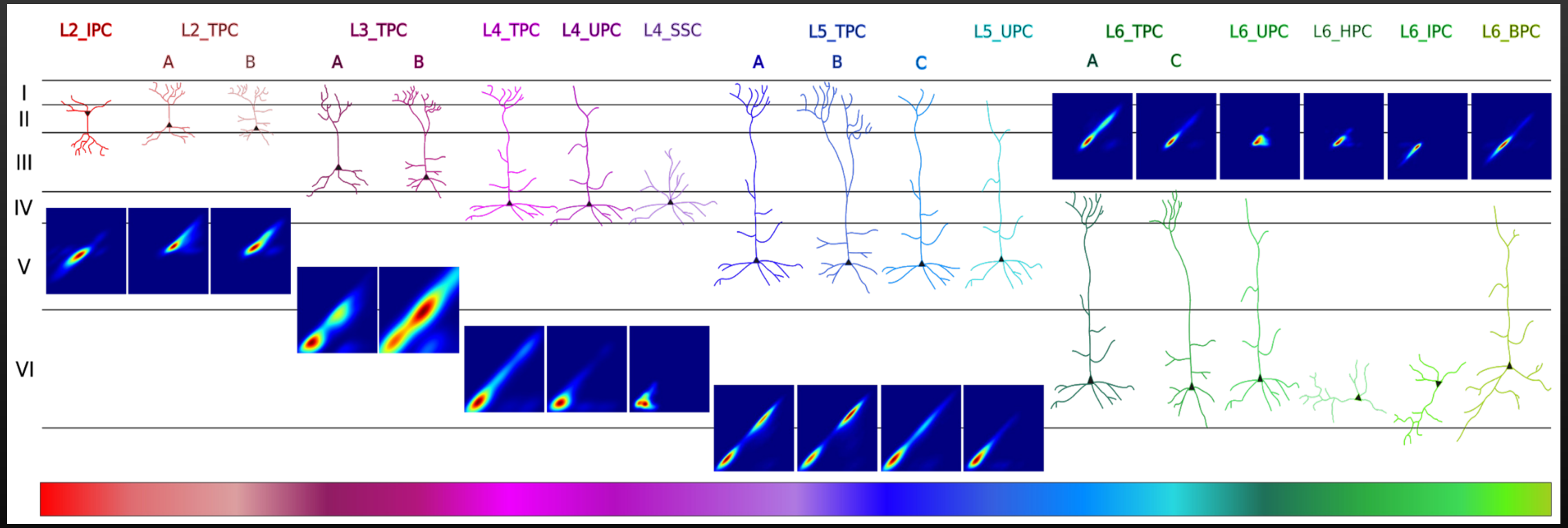
Alternative representations



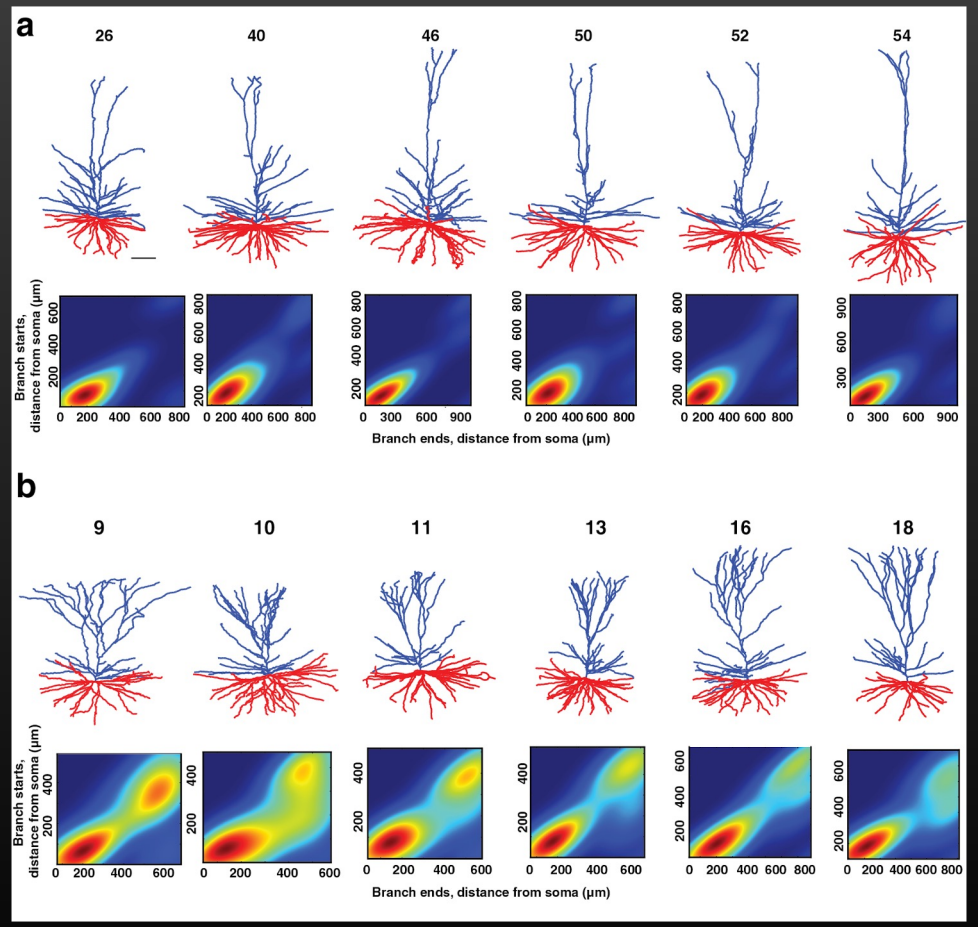
Classification by TMD

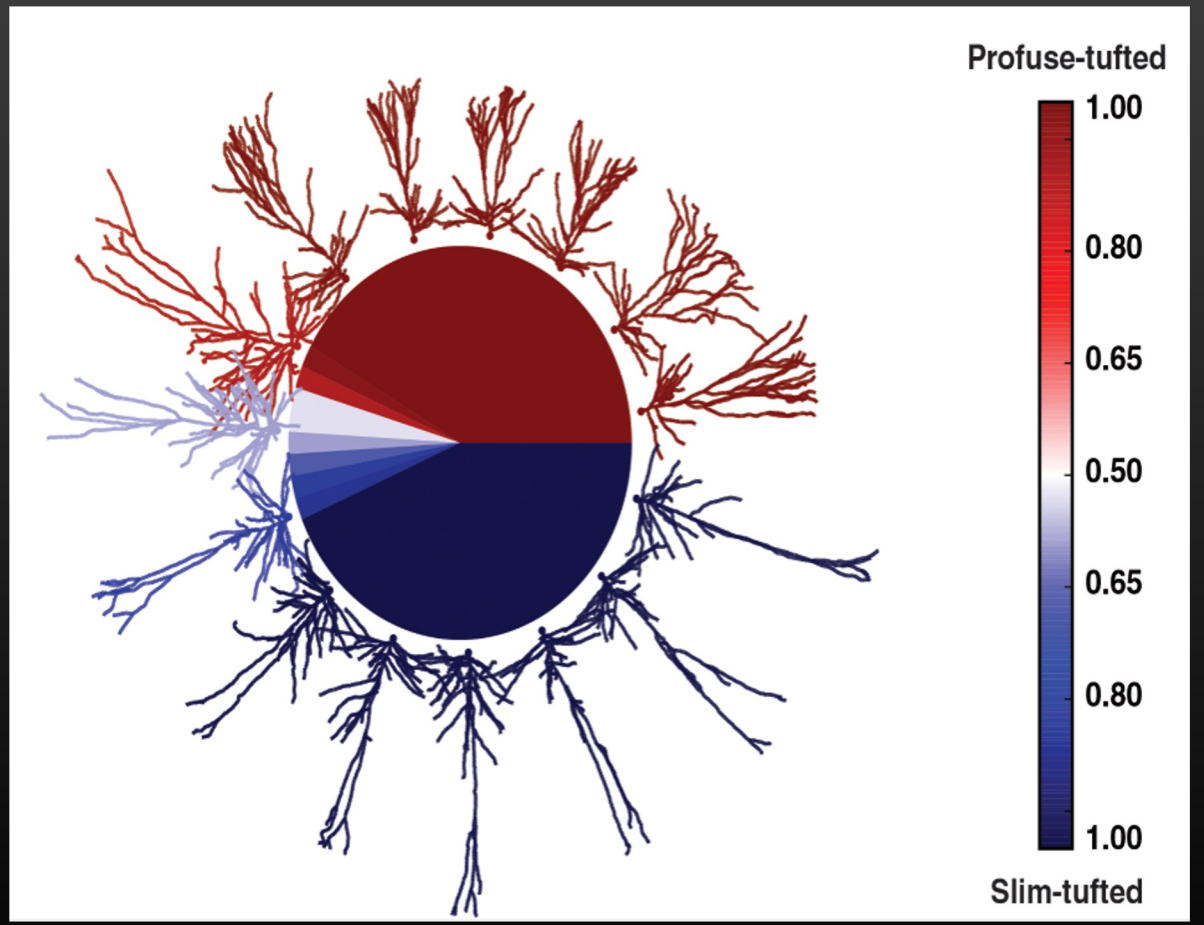


TMD of rat pyramidal cells



Human pyramidal cells





Topological analysis of the microconnectome

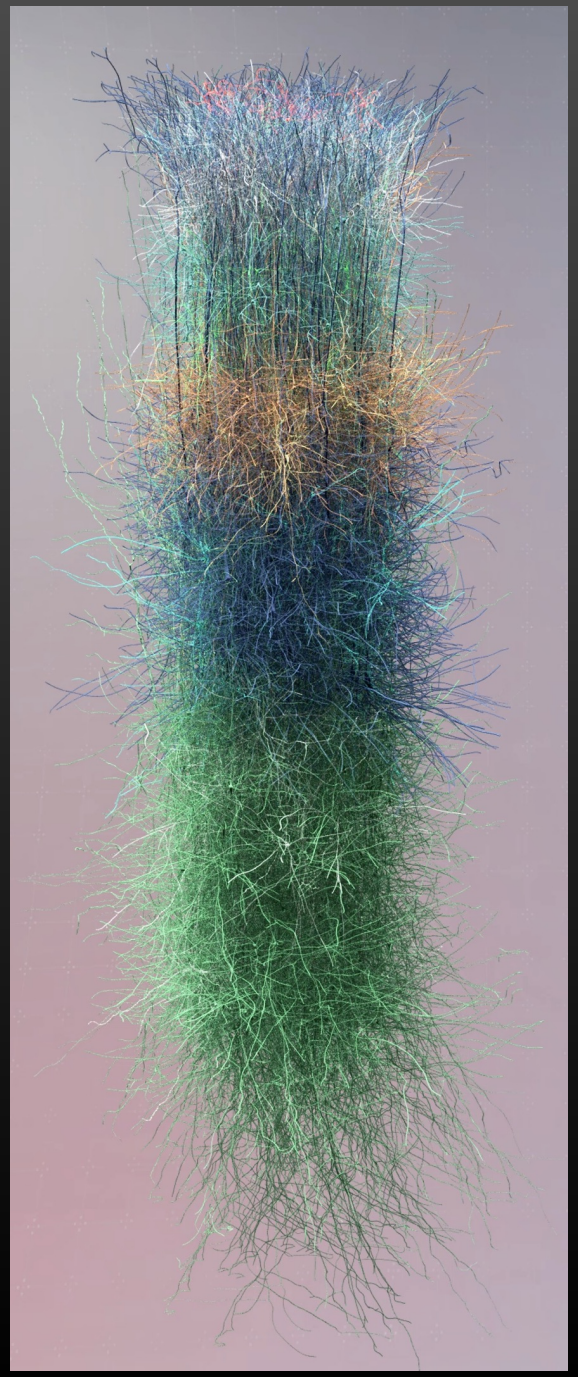
Reimann et al. Frontiers in Computational Neuroscience, 2017.

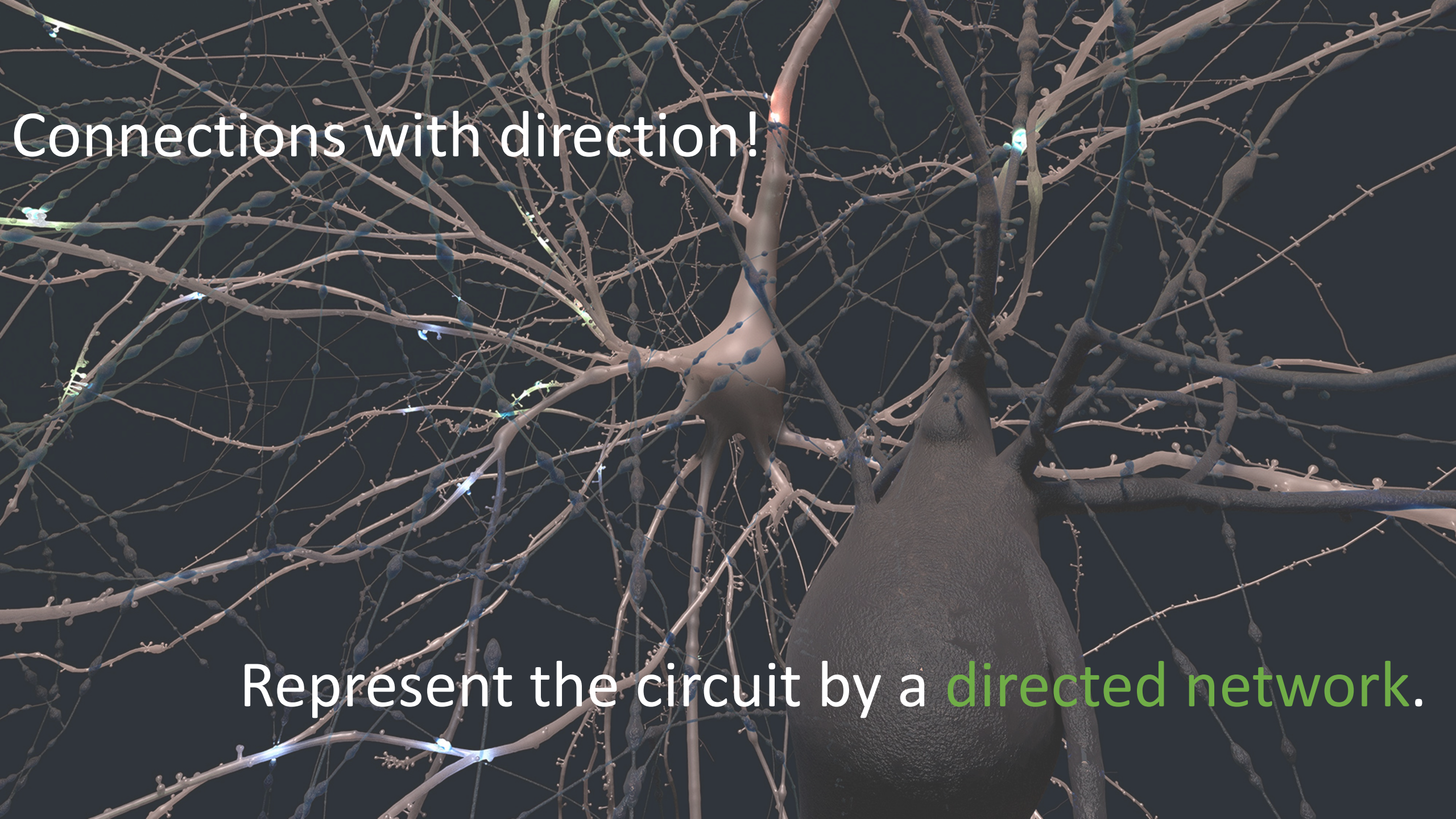
The Blue Brain model

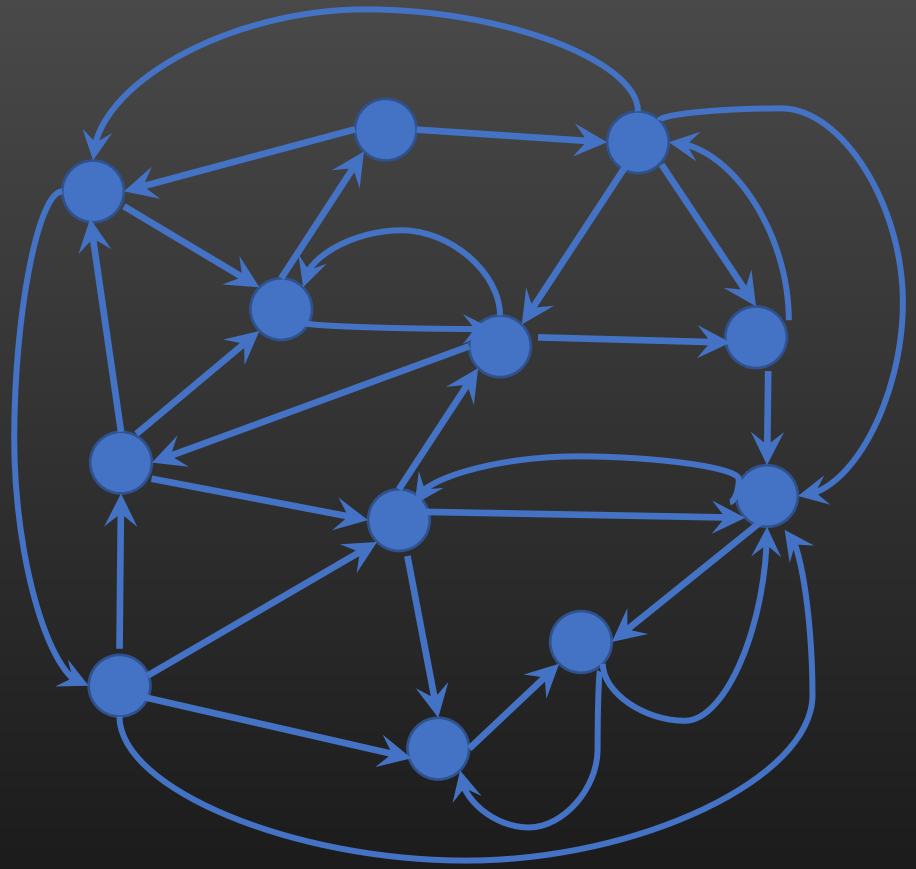
- Digital reconstruction of the microcircuit of layers 1 through 6 of the somatosensory cortex of a 14-day-old rat : 31’000 neurons and 8 million connections

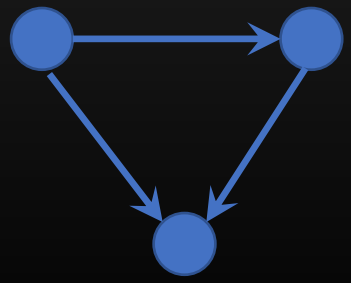
- Simulations of spontaneous and evoked activity

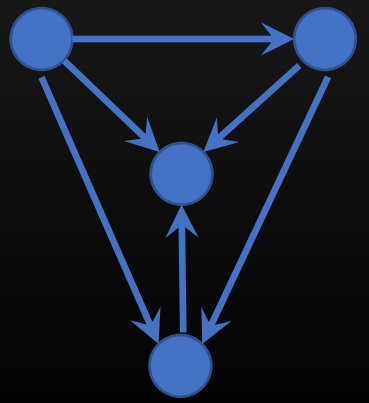
H. Markram et al., Cell, 2015



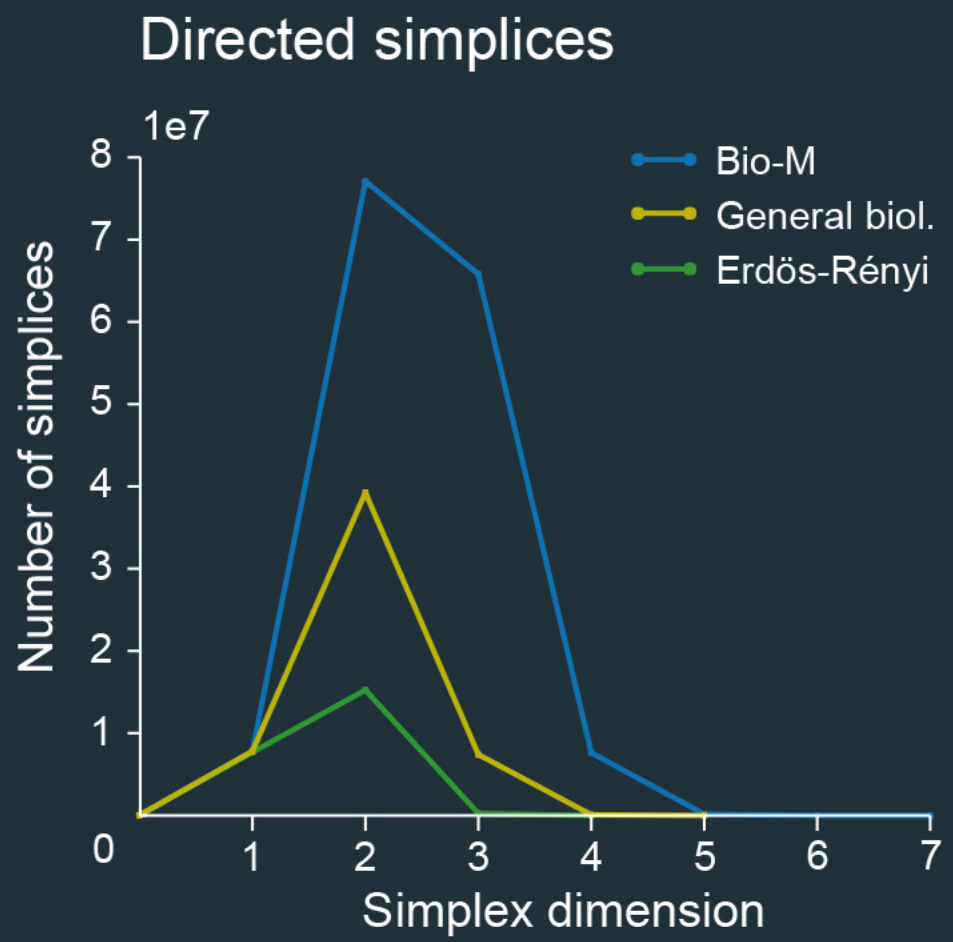

Connections with direction!
Represent the circuit by a directed network.



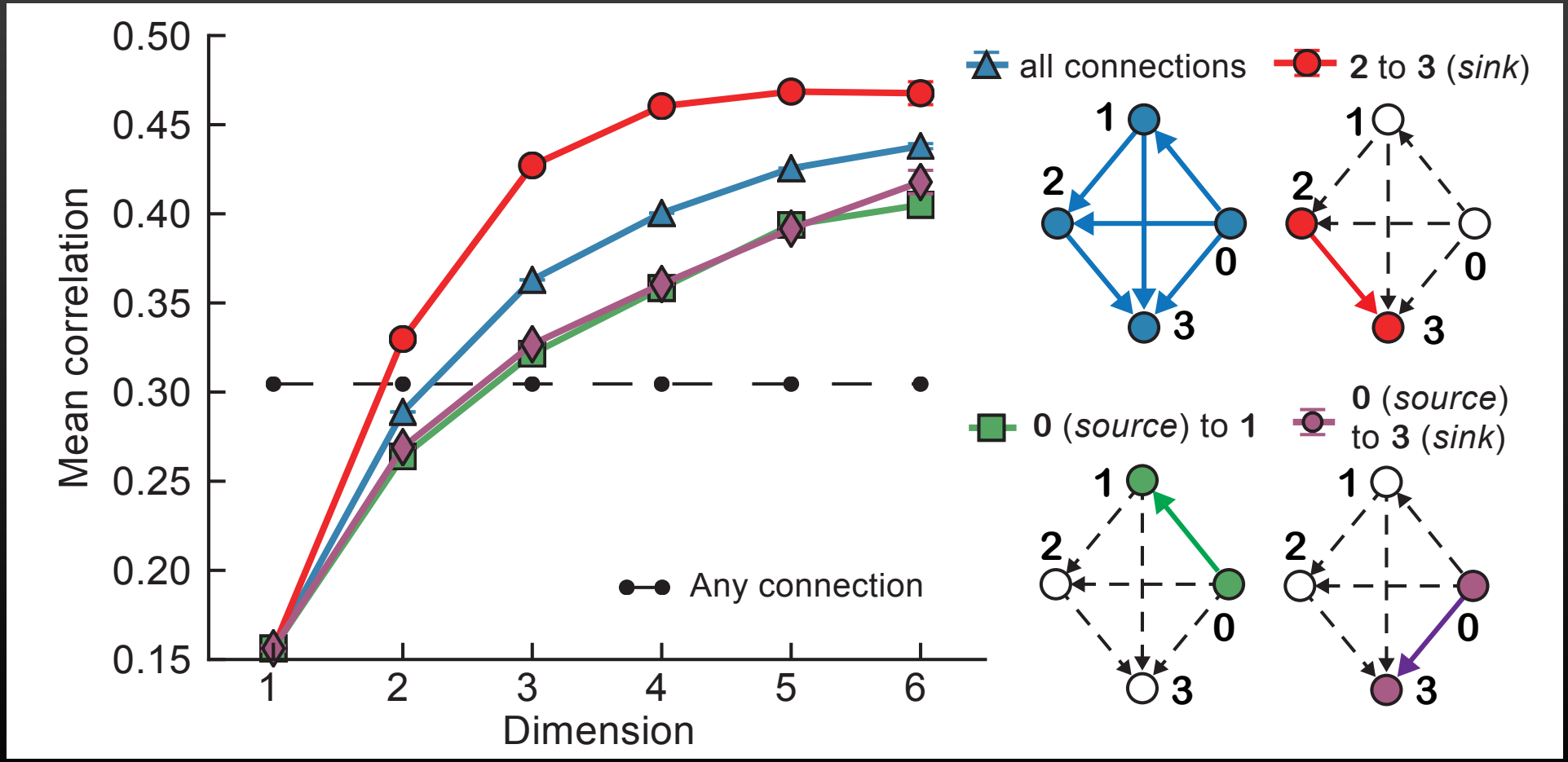




Measuring structure

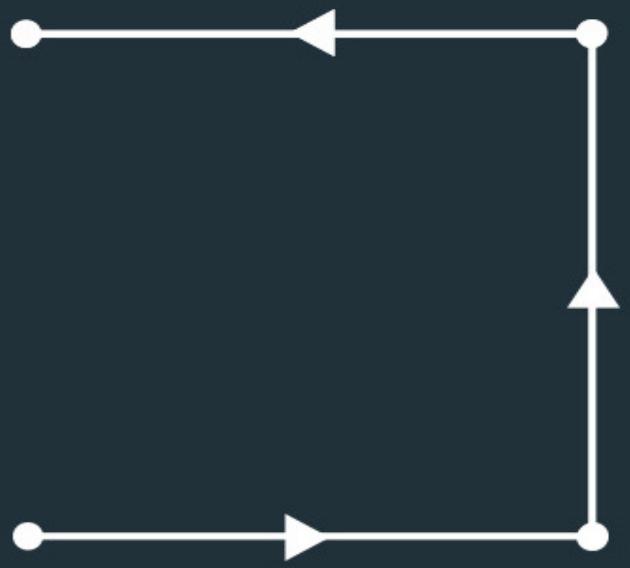


The functional importance of simplices



The idea of a cavity

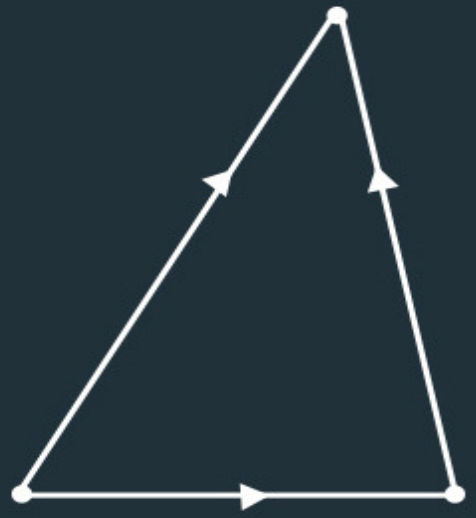
1 simplex



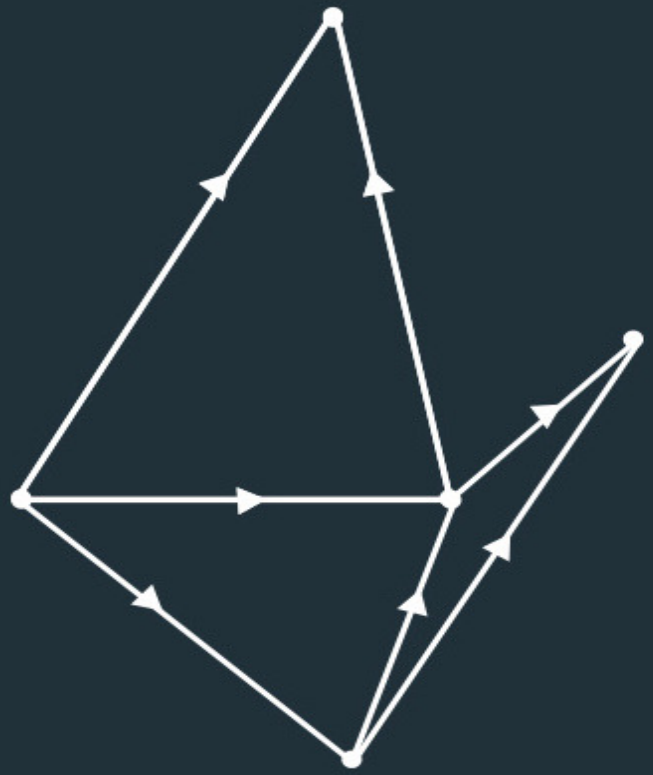
3 simplices...

a cavity made of 4 simplices

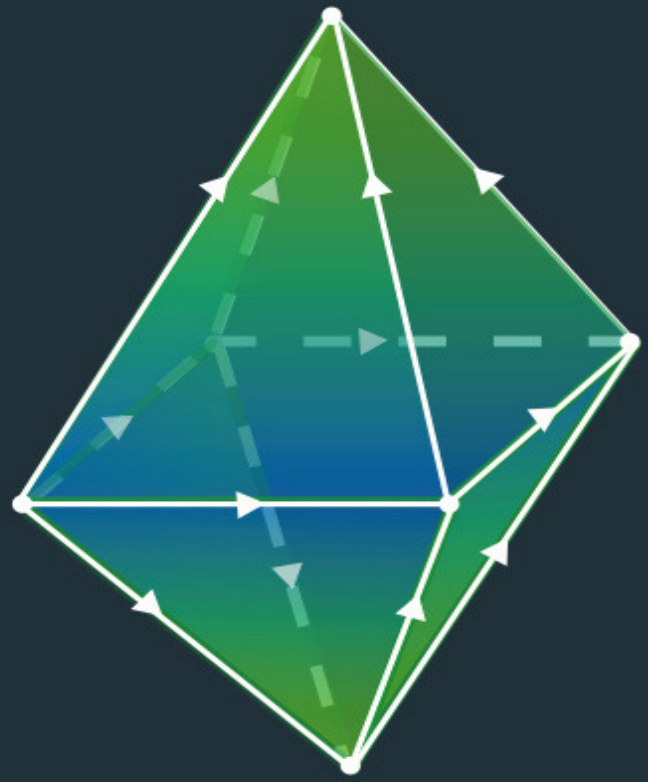
Higher dimensions for a cavity



1 simplex

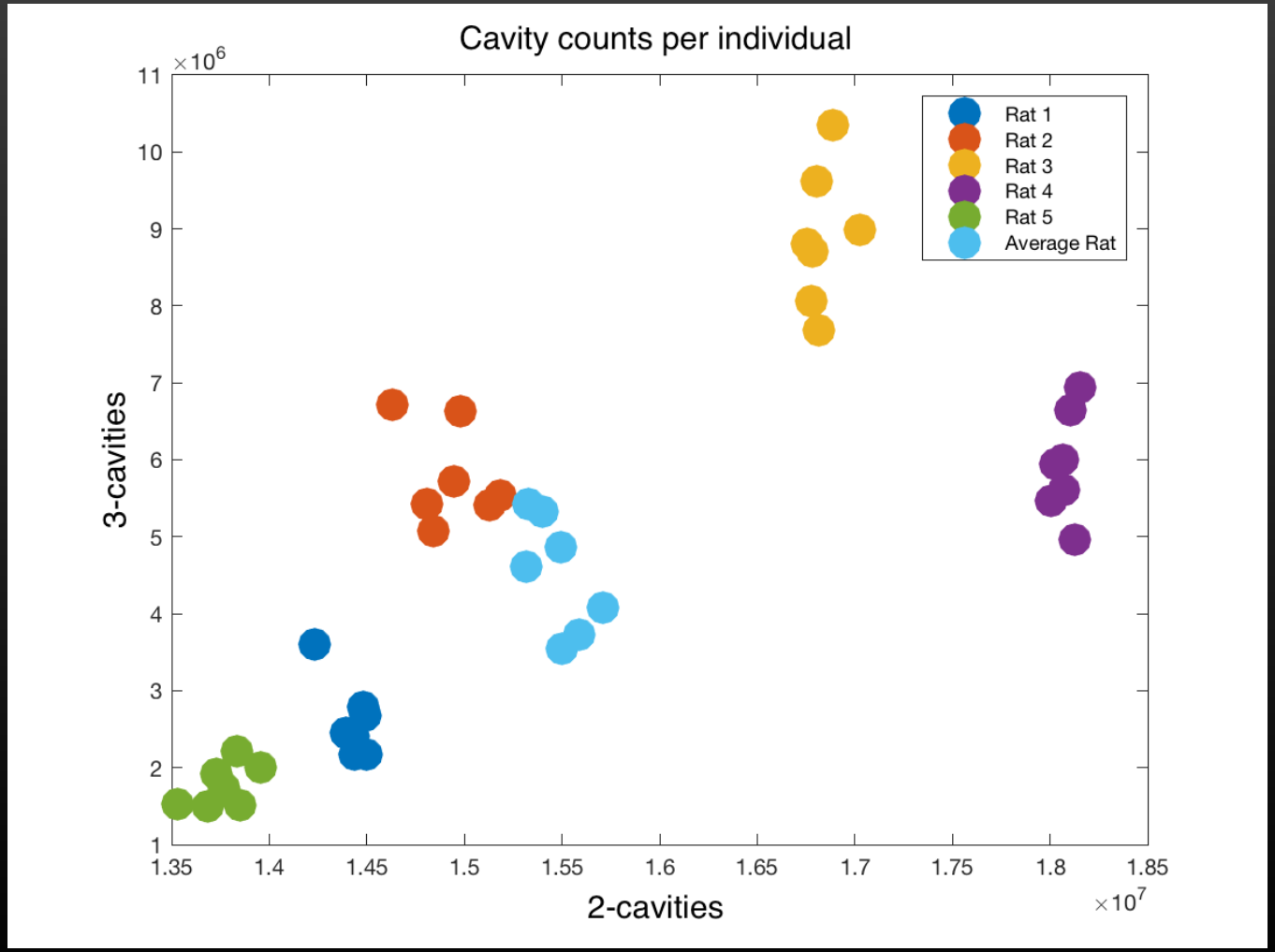


3 simplices...



a cavity made of 8 simplices

Topology faithfully reflects biology



Other topological explorations

- TDA classification of neural dynamics
- A topological biomarker for long-term outcome in schizophrenia
- Reverse engineering of the TMD classification of neuron morphologies to synthesize digital neuron populations
- Topological analysis of larval fruit fly brains, leading to discovery of sexual dimorphism in brain structure
- TMD applied to analysis of microglia structure and evolution

Bardin, et al., Network Neuroscience, 2019.
Fournier, Scolamiero, et al, Molecular Psychiatry, 2020.
L. Kanari et al, Cell Reports, 2022.
Jiao et al, eLife, 2022.
Colombo et al, Nature Neuroscience, 2022.

Ongoing projects

- Topological analysis of synaptic plasticity
- Topological analysis of single-cell gene expression data

Thank you!

Membres du Laboratoire de Topologie et Neurosciences