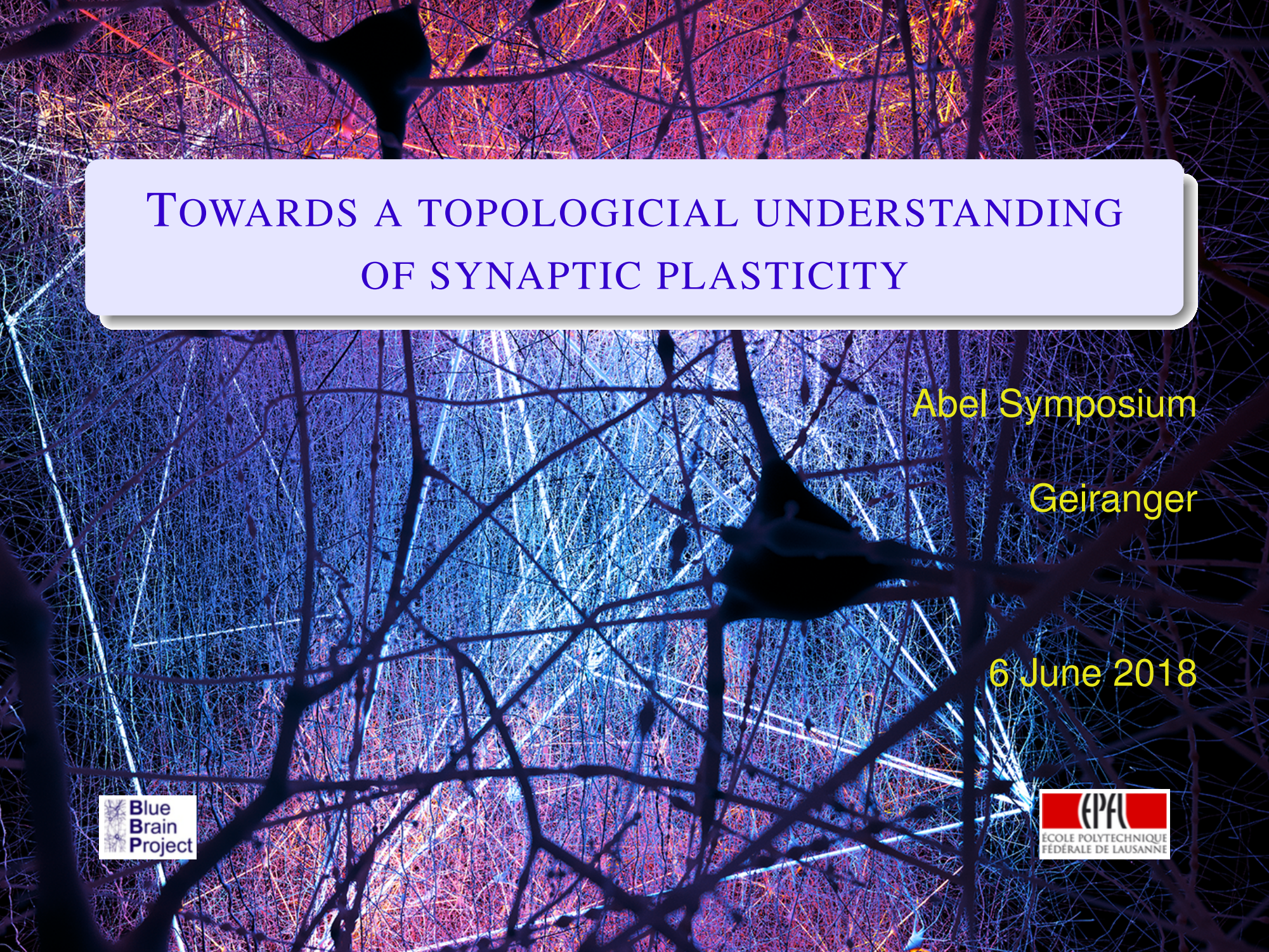


TOWARDS A TOPOLOGICIAL UNDERSTANDING OF SYNAPTIC PLASTICITY

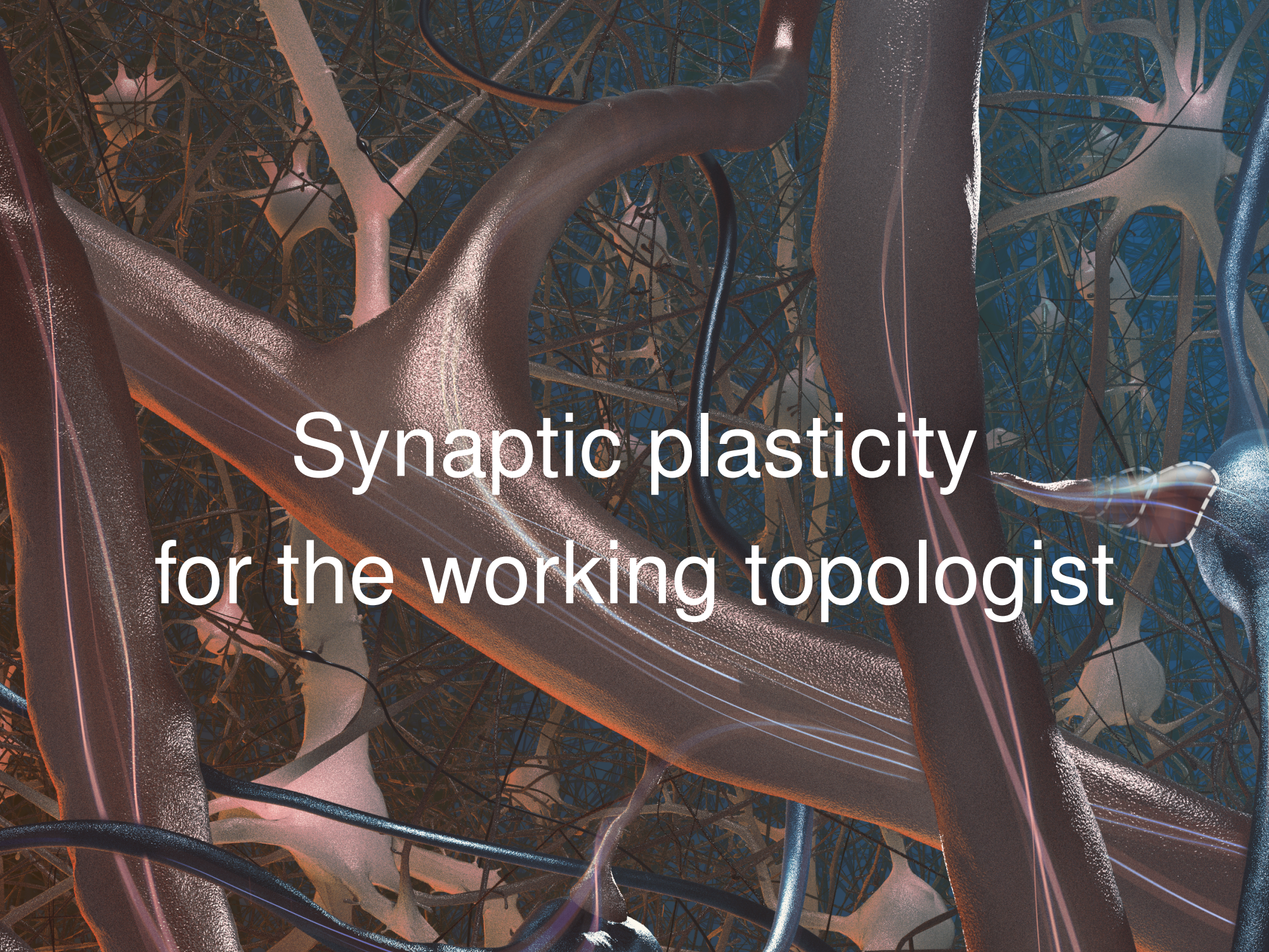
Abel Symposium

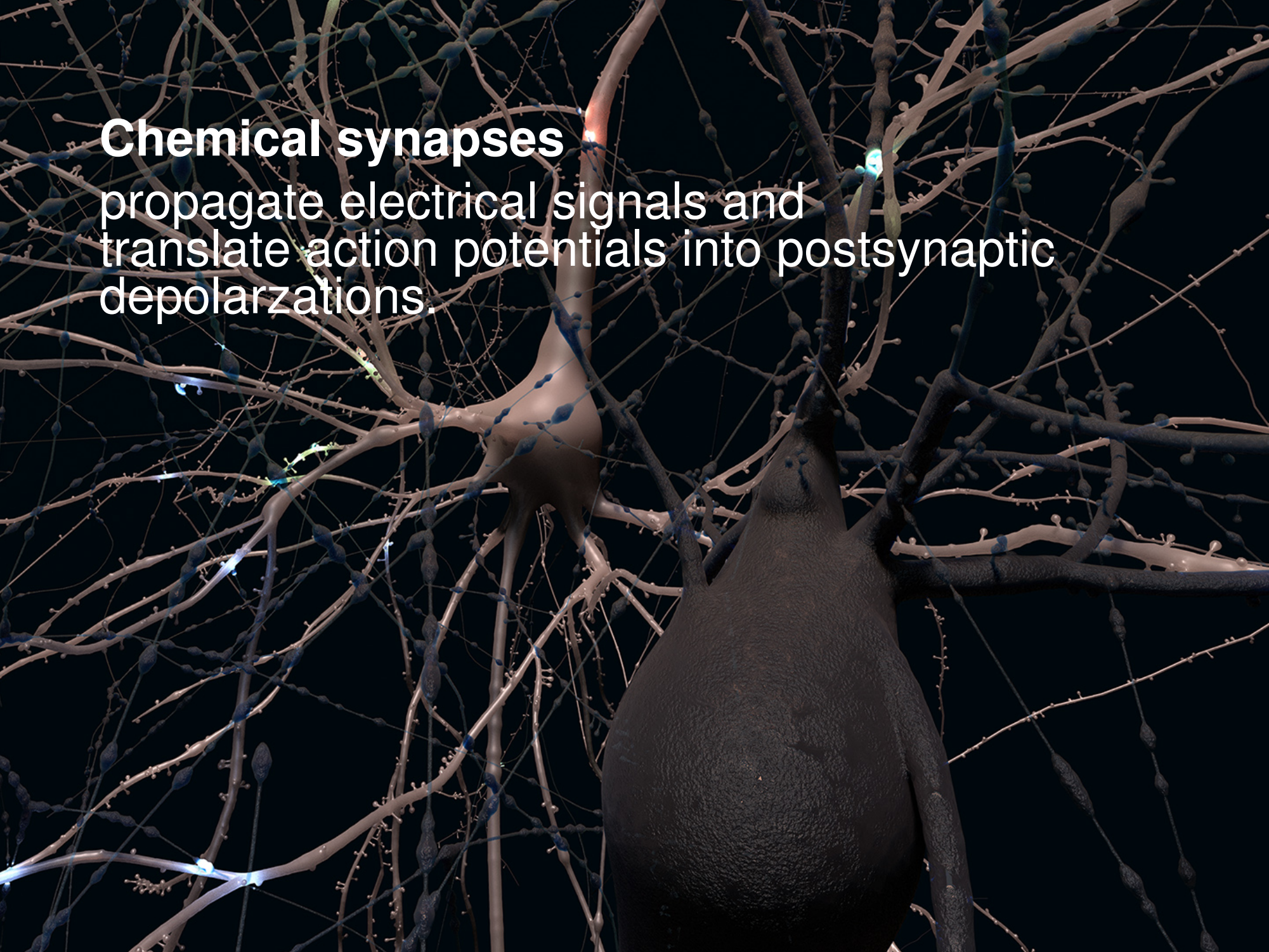
Geiranger

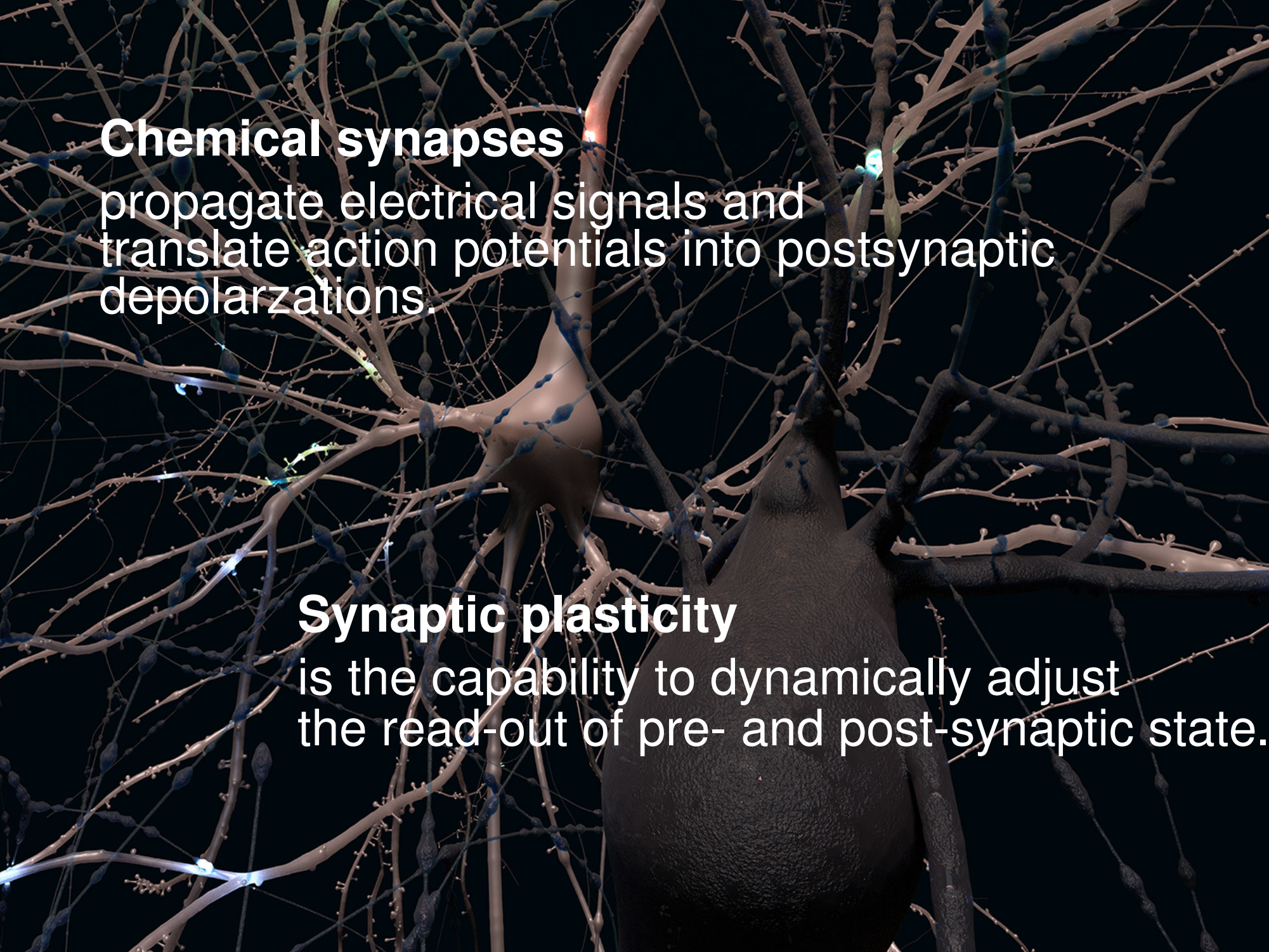
6 June 2018

Blue Brain Project

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE


Synaptic plasticity
for the working topologist


Chemical synapses
propagate electrical signals and translate action potentials into postsynaptic depolarzations.



Chemical synapses
propagate electrical signals and translate action potentials into postsynaptic depolarzations.

Synaptic plasticity
is the capability to dynamically adjust the read-out of pre- and post-synaptic state.

SIGNAL TRANSMISSION

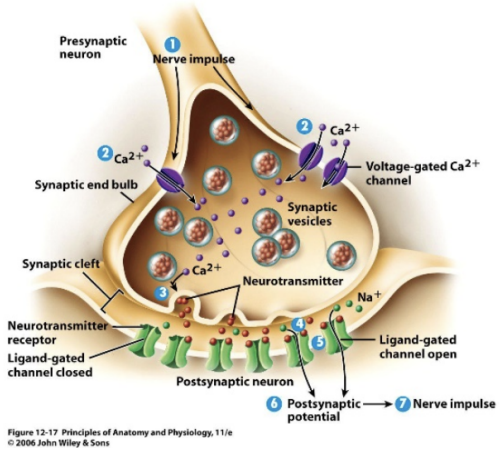
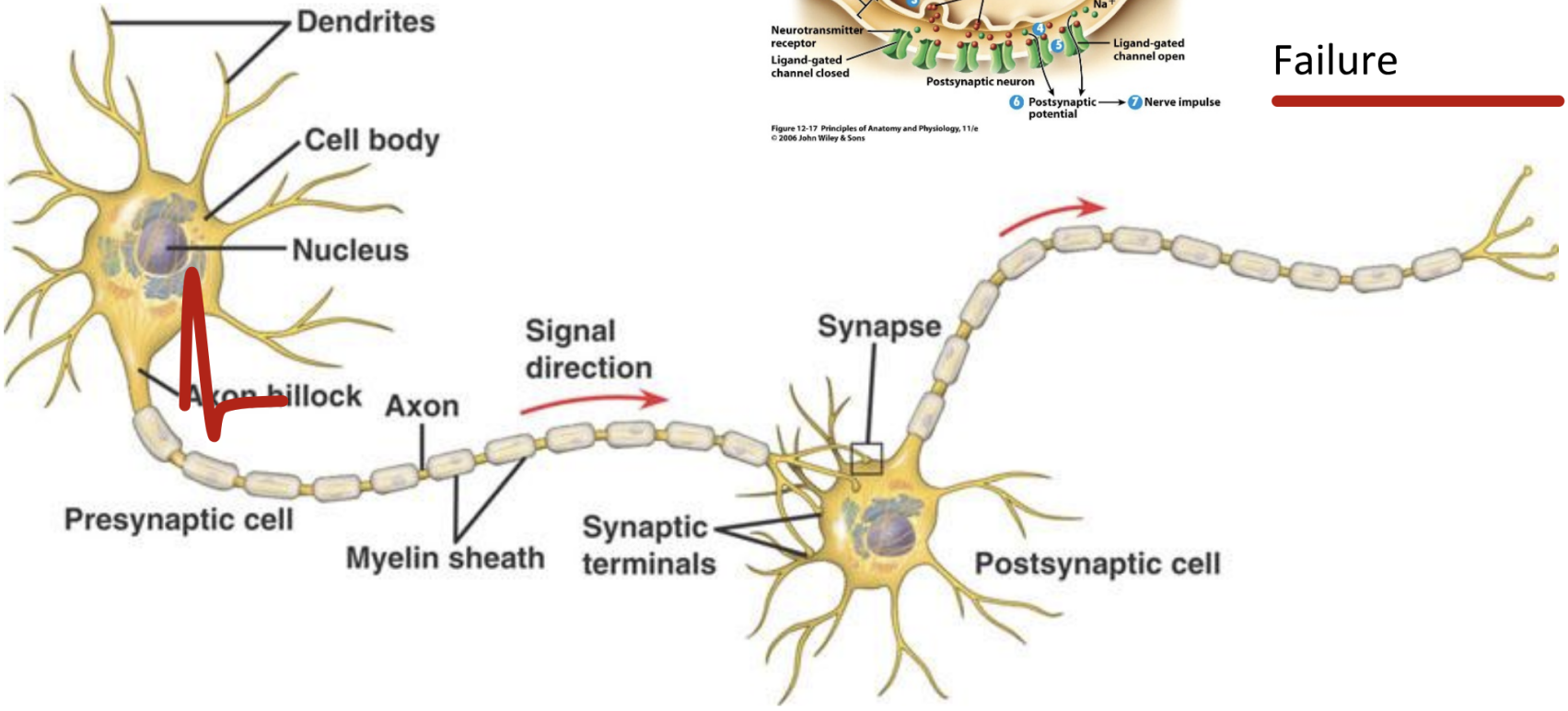


Figure 12-17 Principles of Anatomy and Physiology, 11/e
© 2006 John Wiley & Sons

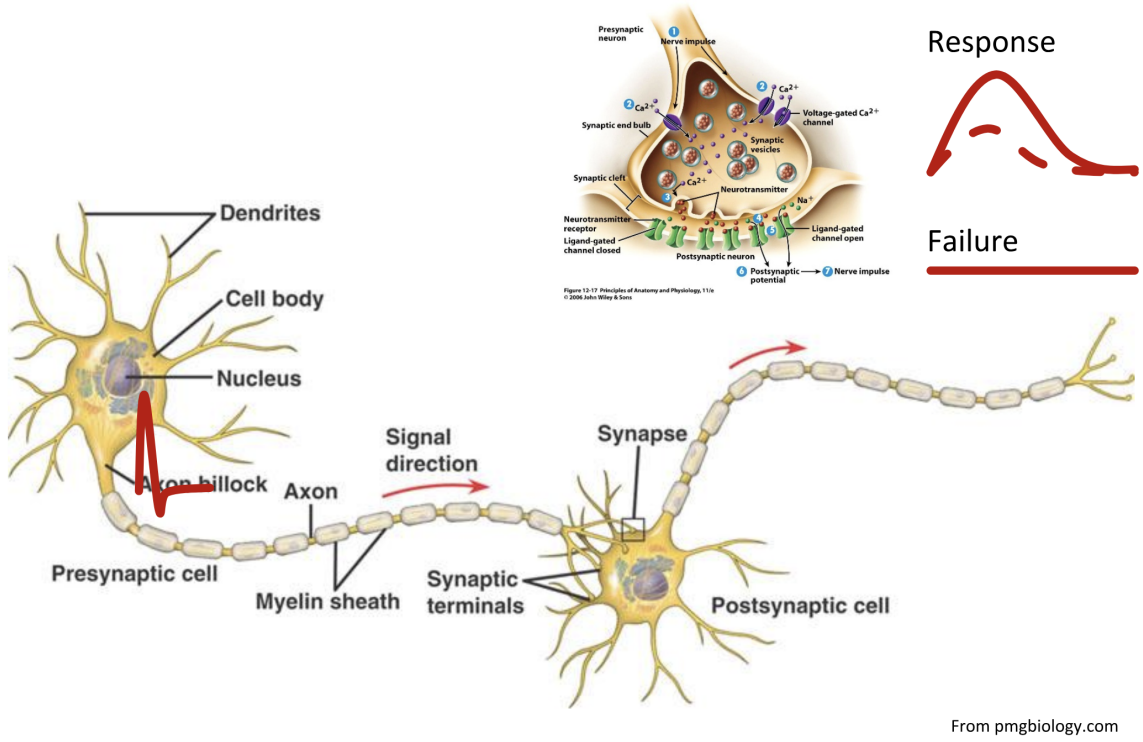
Response

Failure



From pmgbiology.com

Signal transmission



From pmgbiology.com

- Vesicle release is stochastic.
- Plasticity leads to creation and removal of post-synaptic receptors.
- NMDA receptors act as “coincidence detectors” for pre- and post-synaptic activity.

Blue Brain Project

FORMS OF SYNAPTIC PLASTICITY

- Depression: decrease in synaptic “weight” caused by depletion of neurotransmitters at the axon terminal of a pre-synaptic neuron, associated with suppression of synapses
- Potentiation: increase in synaptic “weight” caused by influx of calcium into the axon terminal after spike generation, increasing the release probability of neurotransmitters, associated with creation of synapses

Blue Brain Project

FORMS OF SYNAPTIC PLASTICITY

- Depression: decrease in synaptic “weight” caused by depletion of neurotransmitters at the axon terminal of a pre-synaptic neuron, associated with suppression of synapses
- Potentiation: increase in synaptic “weight” caused by influx of calcium into the axon terminal after spike generation, increasing the release probability of neurotransmitters, associated with creation of synapses

Expands the range of dynamical behaviors and thus information-processing capacities beyond static connections:

- prolongs neural responses to transient inputs,
- modulates network responses to external input,
- induces network state mobility.

The substrate of learning and memory??

Source: Tsodyks & Wu, Scholarpedia.

Blue Brain Project

PHENOMENOLOGICAL MODEL

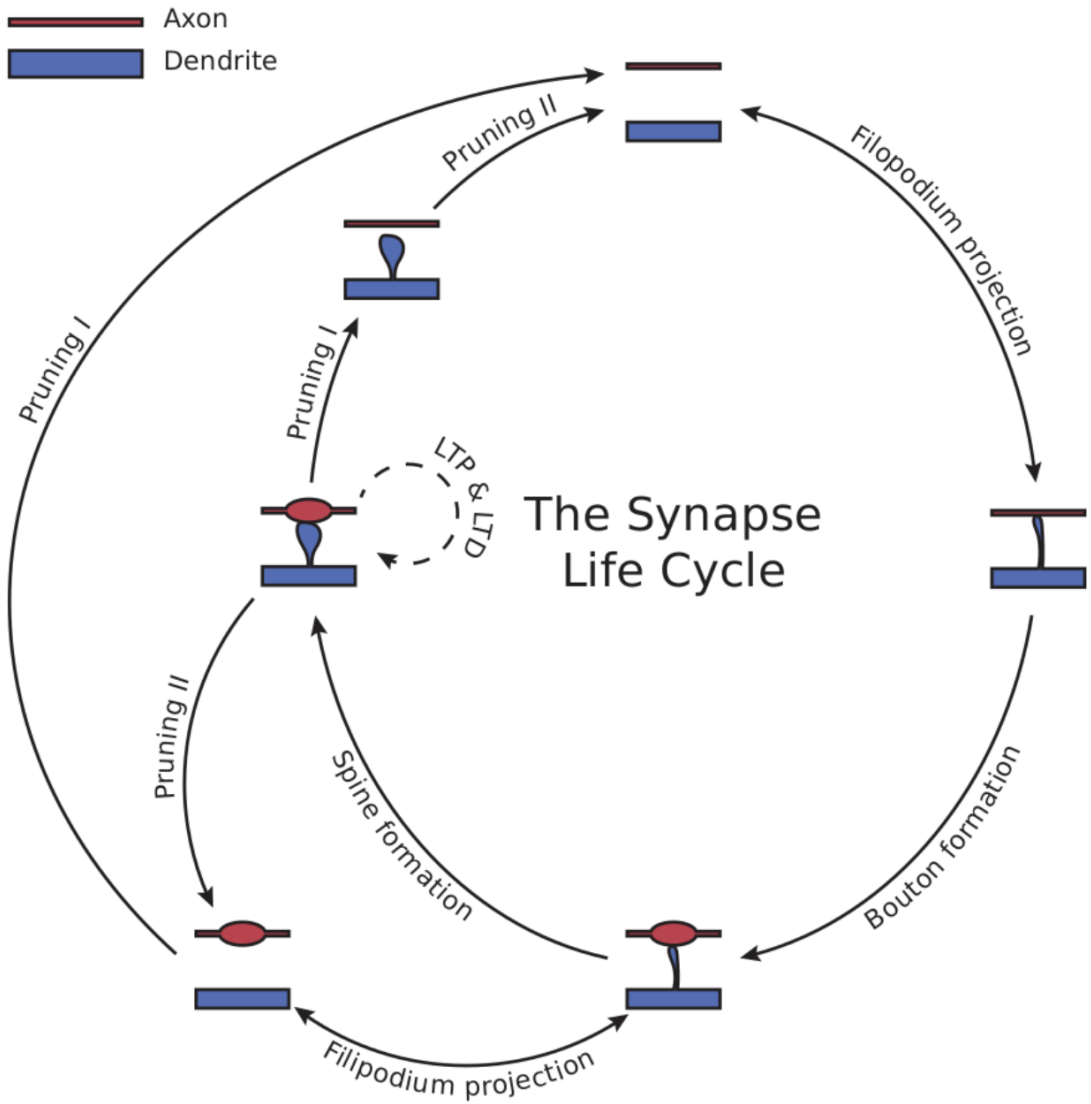
For each synapse and each time t, we consider

- $A =$ absolute synaptic efficacy = maximum excitatory postsynaptic current produced by that synapse,
- $x(t) \in [0, 1]$: the fraction of available resources after neurotransmitter depletion,
- $u(t) \in [0, 1]$: the release probability.

$A \cdot u(t) \cdot x(t) =$ the synaptic current generated at the synapse by a spike arriving at time t

[Tsodyks-Markram, PNAS 1997]

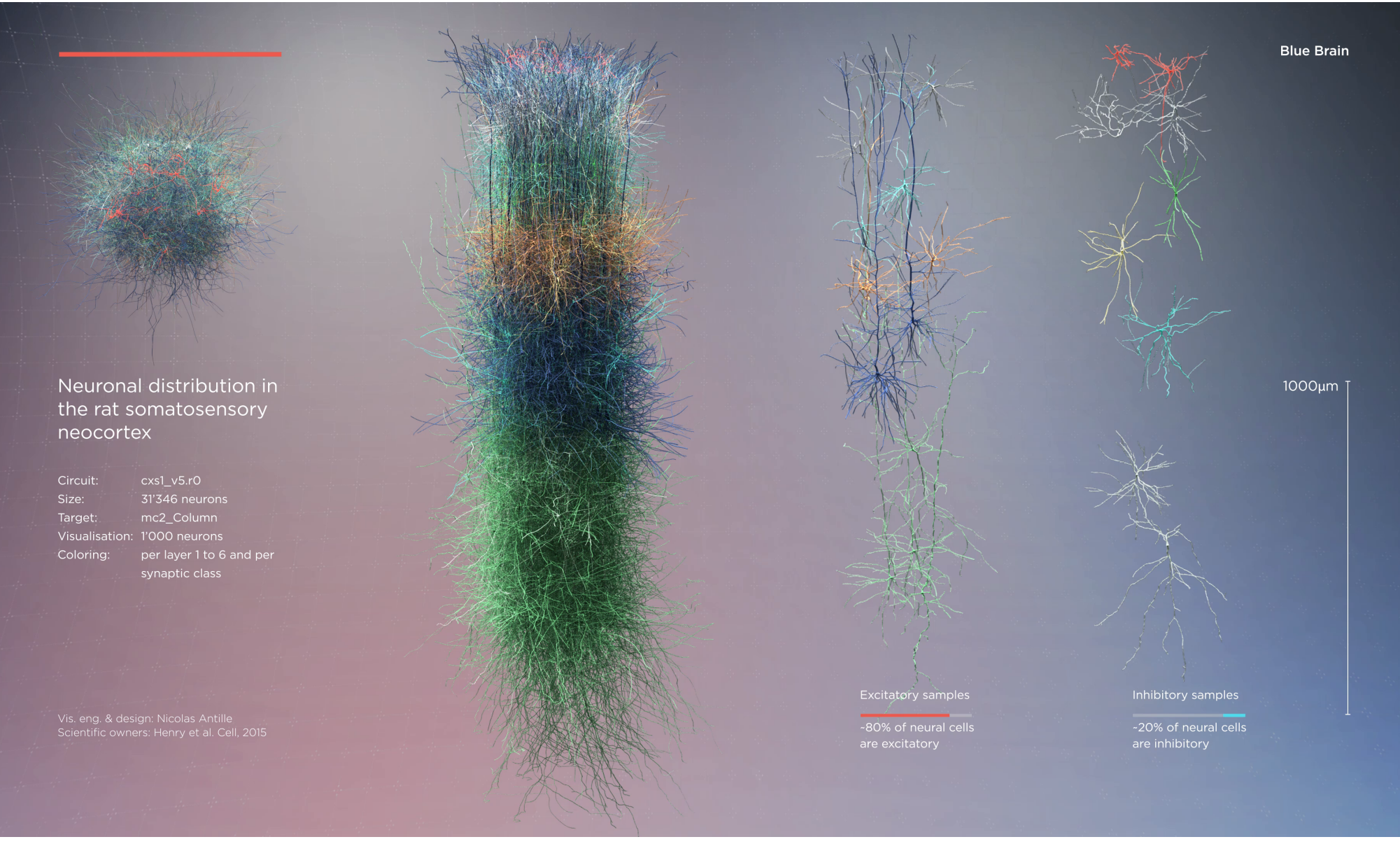
THE SYNAPSE LIFECYCLE



Plasticity of only a few pathways has been experimentally characterized!

Blue Brain Project

THE BLUE BRAIN MICROCIRCUIT



Neuronal distribution in the rat somatosensory neocortex

Circuit:	cxs1_v5.r0
Size:	31'346 neurons
Target:	mc2_Column
Visualisation:	1'000 neurons
Coloring:	per layer 1 to 6 and per synaptic class

Vis. eng. & design: Nicolas Antille
Scientific owners: Henry et al. Cell, 2015

Blue Brain Project

THE INCITE EXPERIMENT

[Chindemi, PhD thesis 2018]: Built and implemented a mathematical model of plasticity

- parametrizing all excitatory-to-excitatory synapses in the Blue Brain microcircuit (4 billion in total, 80% of all synapses),
- restricting to pre-synaptic changes as these seem to be the predominant plastic variables,
- assuming that innervation profile and morphology are the determining elements of plasticity.

Blue Brain Project

THE INCITE EXPERIMENT

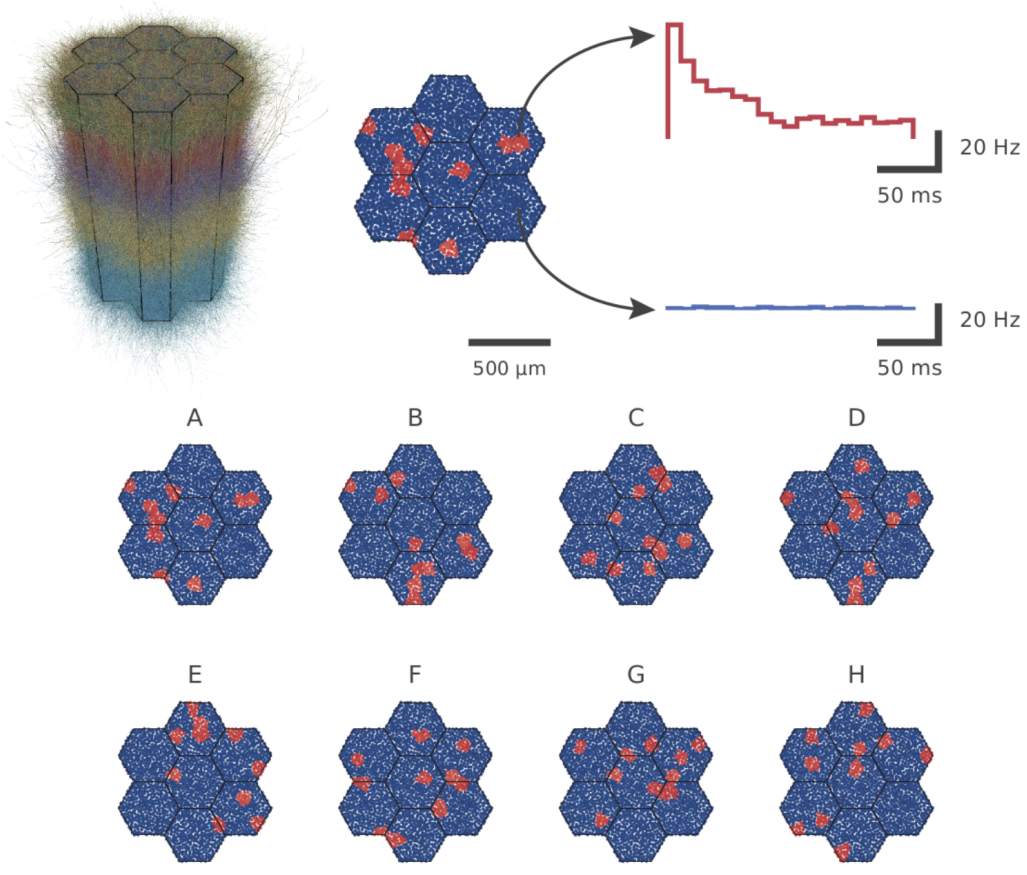
[Chindemi, PhD thesis 2018]: Built and implemented a mathematical model of plasticity

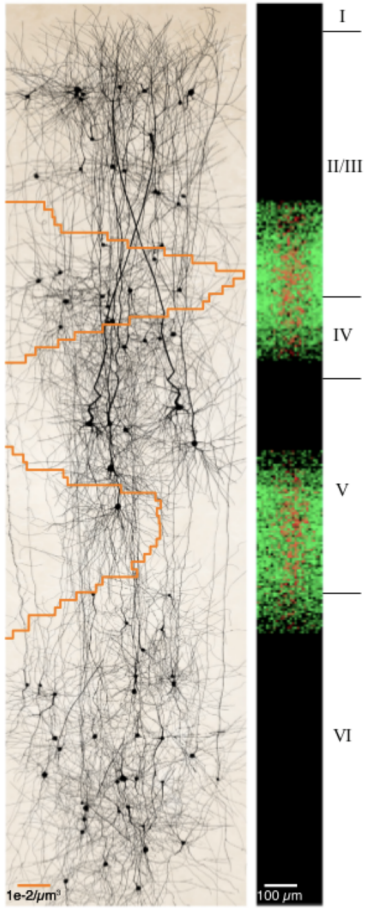
- parametrizing all excitatory-to-excitatory synapses in the Blue Brain microcircuit (4 billion in total, 80% of all synapses),
- restricting to pre-synaptic changes as these seem to be the predominant plastic variables,
- assuming that innervation profile and morphology are the determining elements of plasticity.

Experiment: record and analyze variations in synaptic weights over roughly 22 minutes of simulated biological time during

- spontaneous activity, and
- stimulated activity.

THE INCITE STIMULUS PROTOCOL



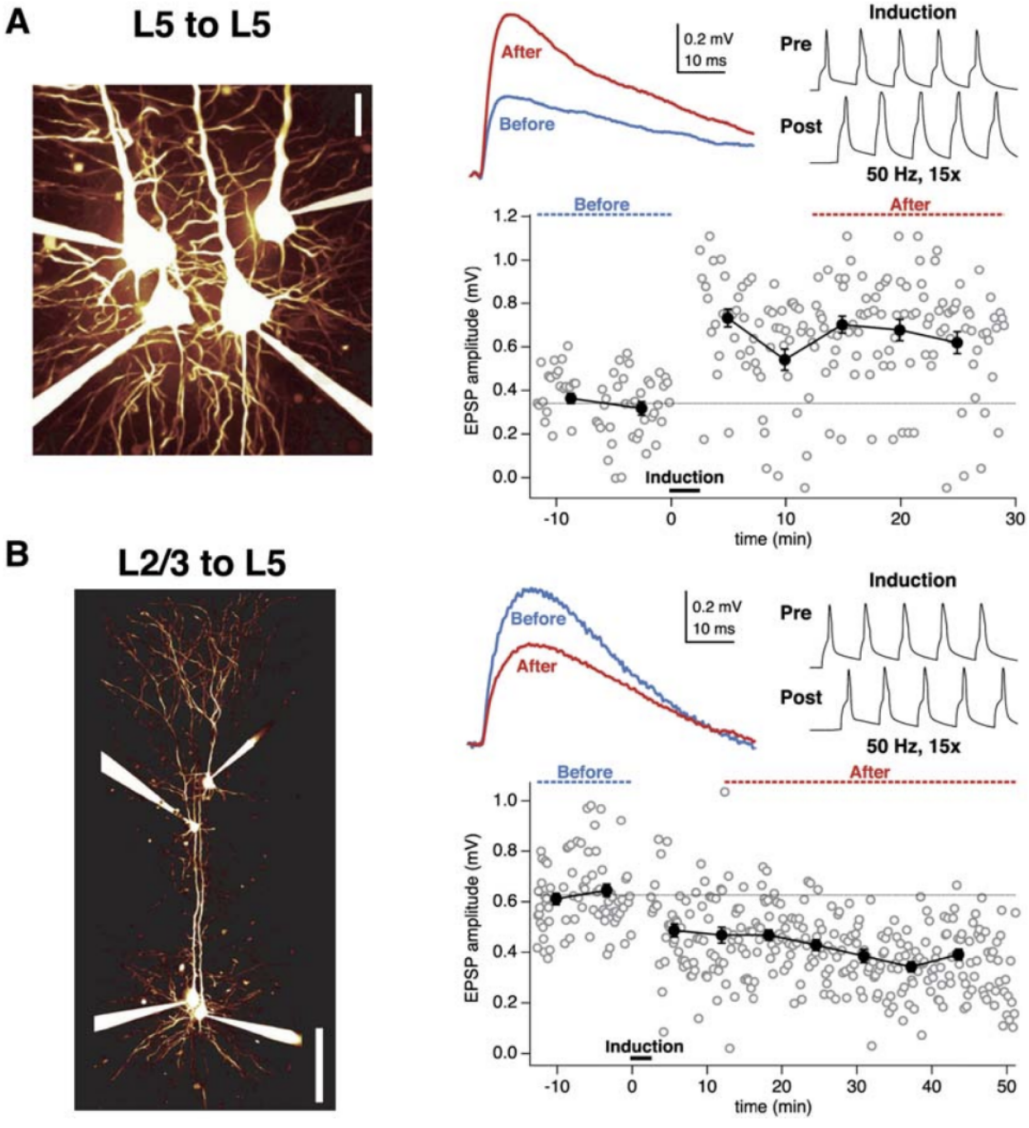


Adapted from Markram et al. 2015

All stimuli have identical statistical properties and are presented in a random order every 200 ms.

Blue Brain Project

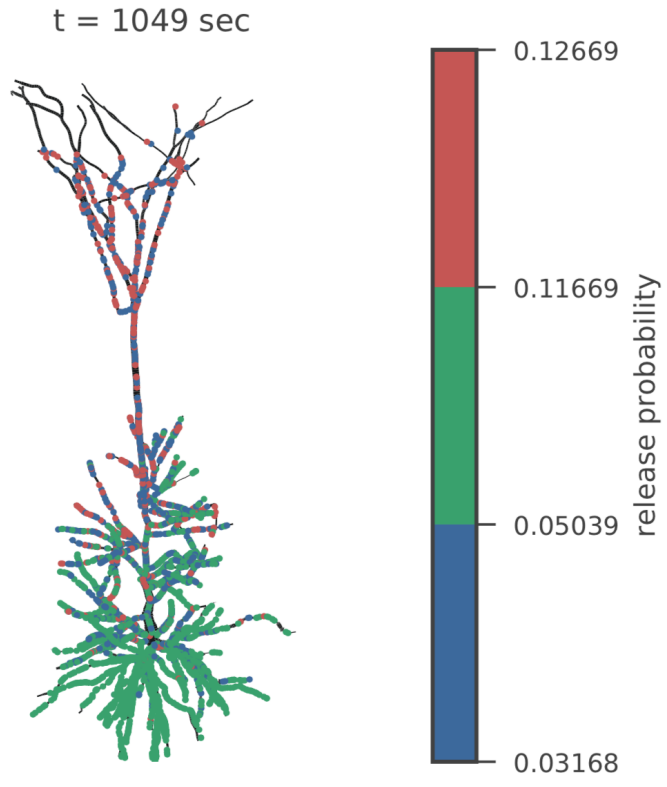
VALIDATION



Sjostrom and Hausser 2006

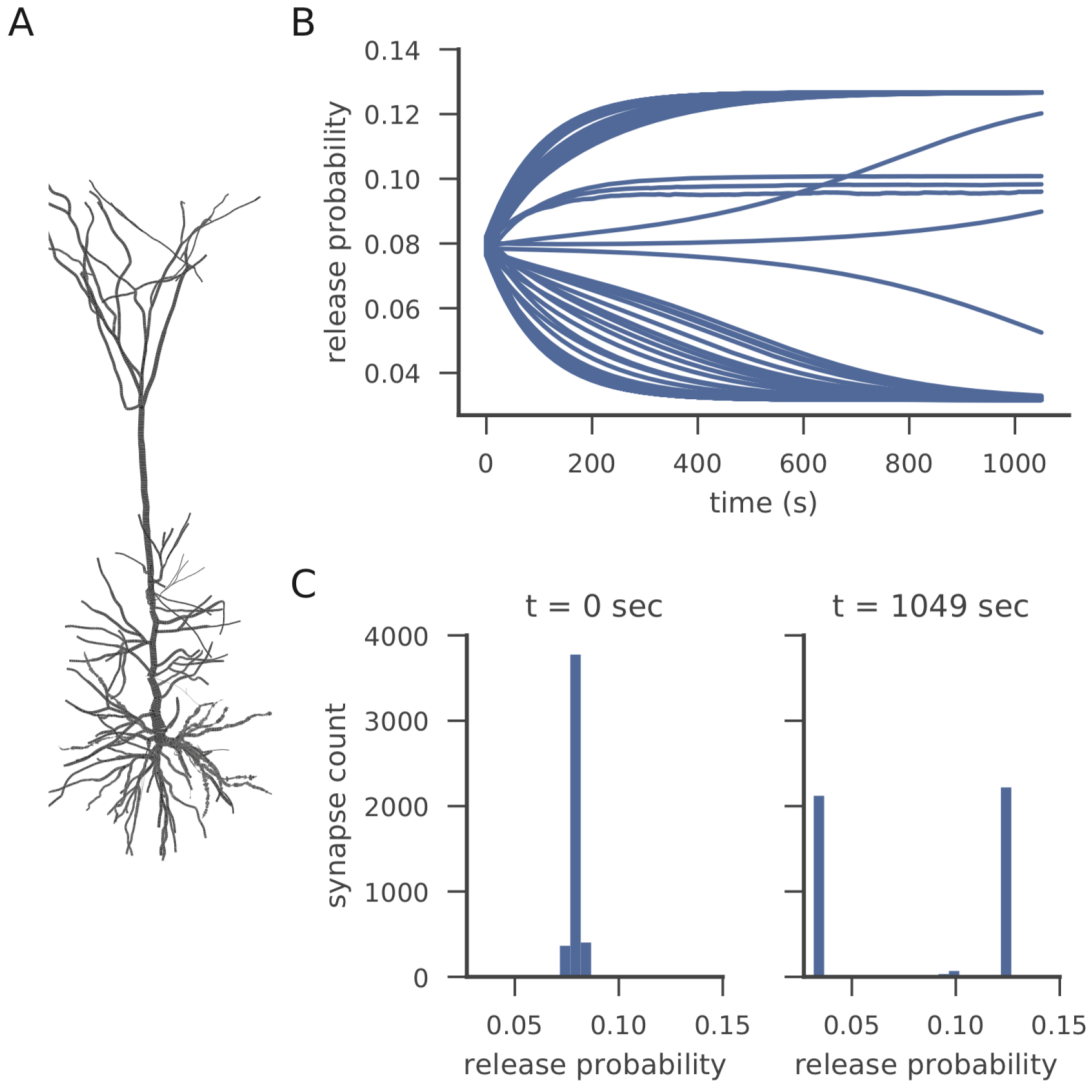
In silico 2017

SYNAPSE WEIGHT AS A FUNCTION OF POSITION



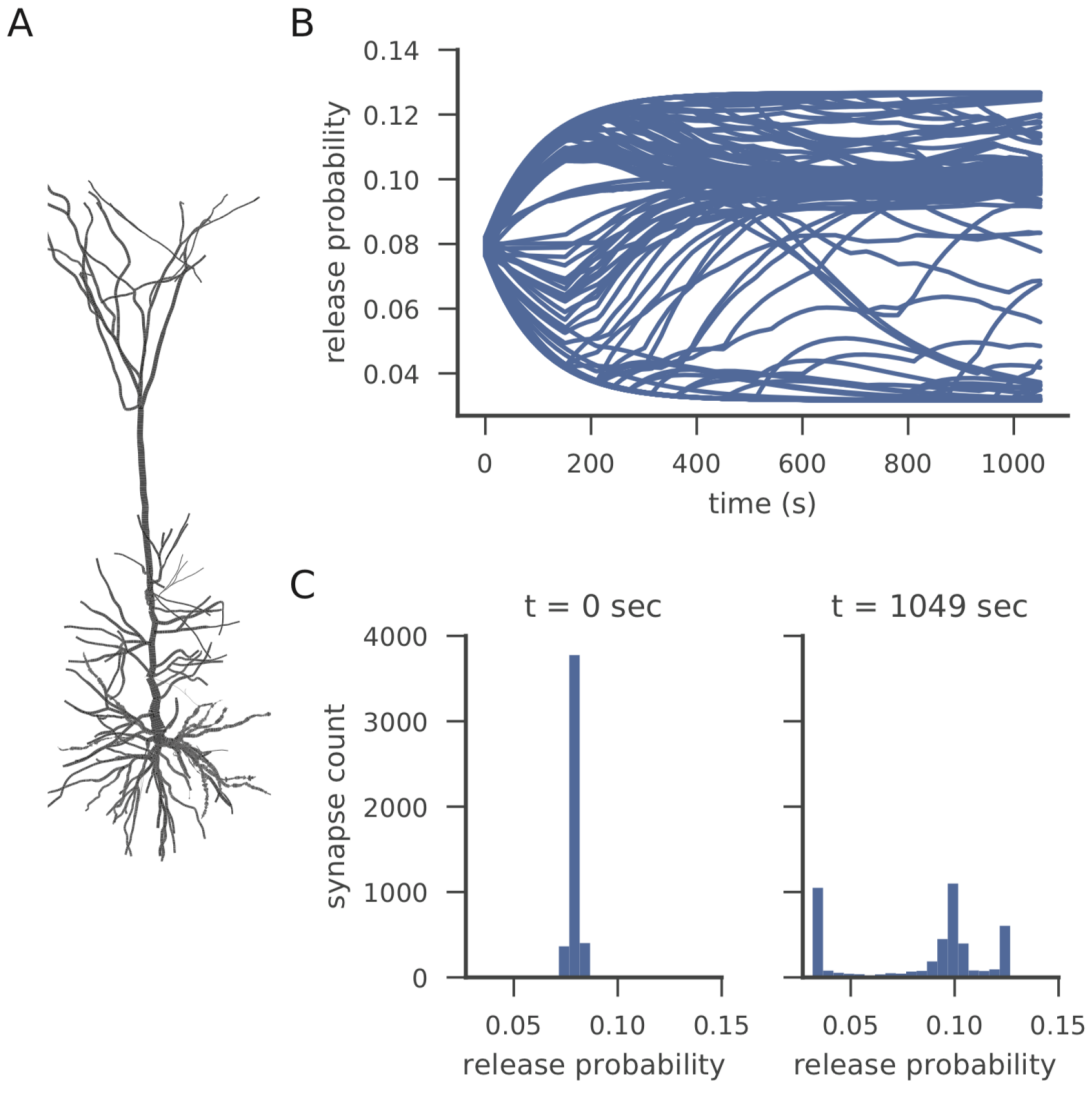
G. Chindemi, PhD Thesis 2018

RESPONSE TO SPONTANEOUS ACTIVITY



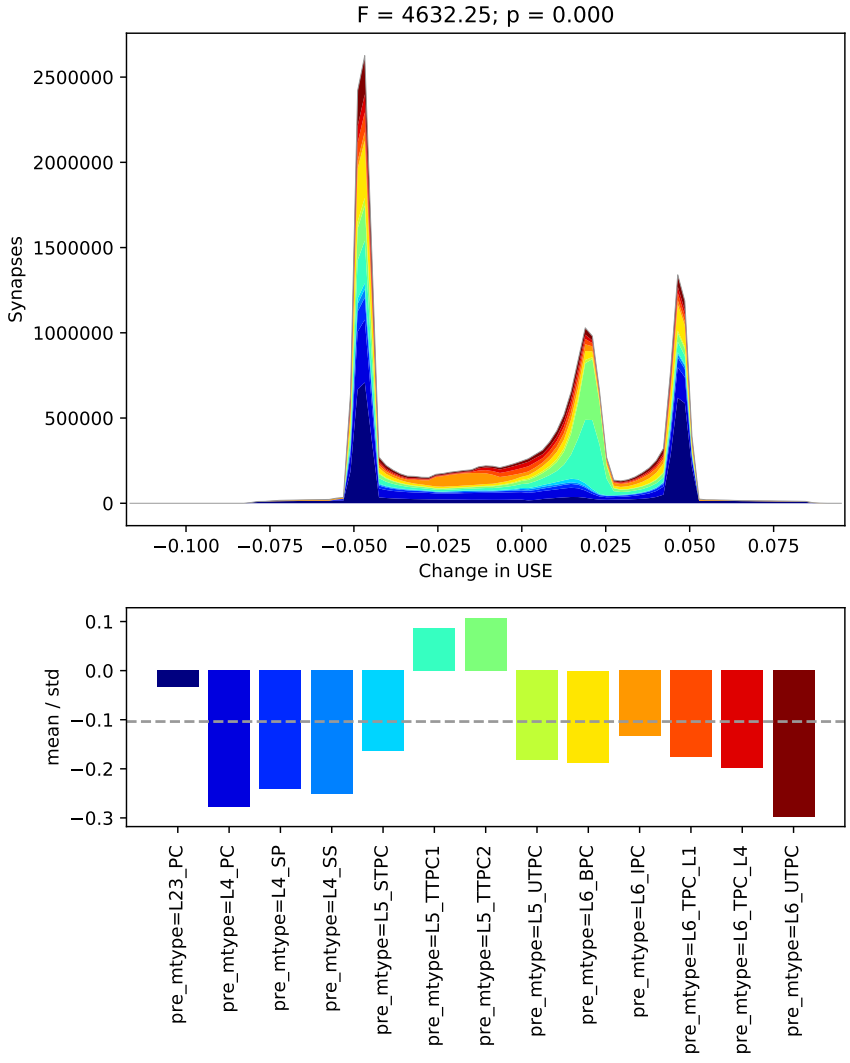
G. Chindemi, PhD Thesis 2018

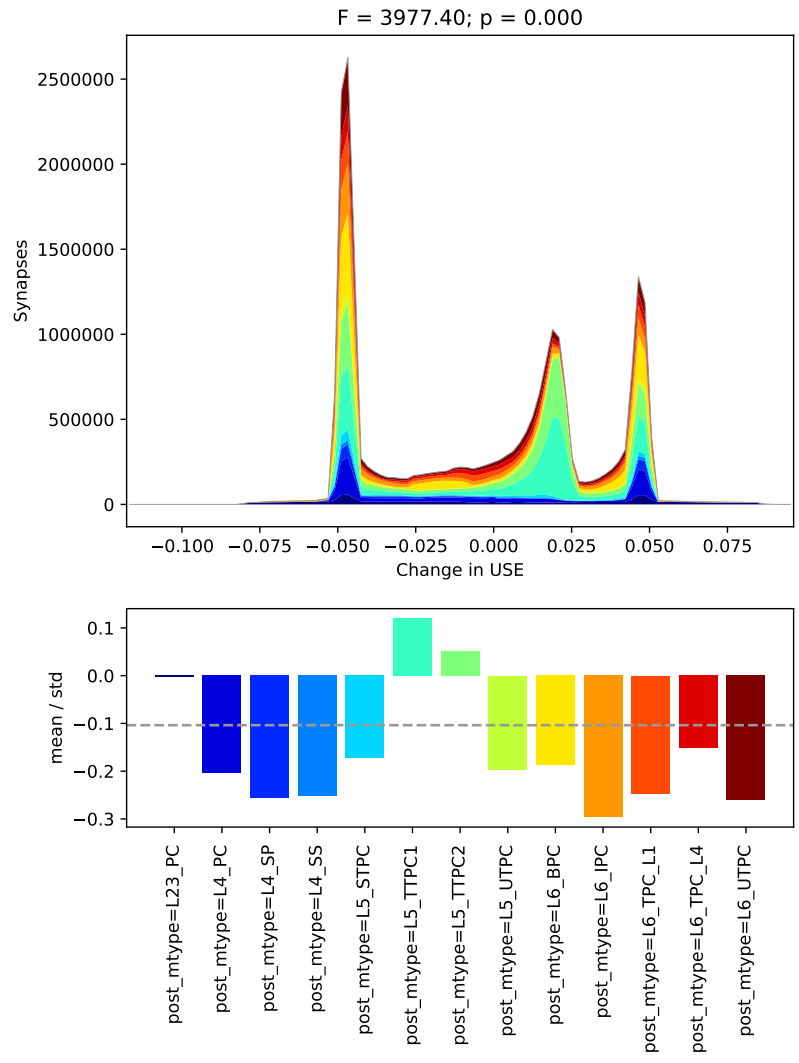
RESPONSE TO STIMULATED ACTIVITY



G. Chindemi, PhD Thesis 2018

CHANGE IN WEIGHT, BY PATHWAY



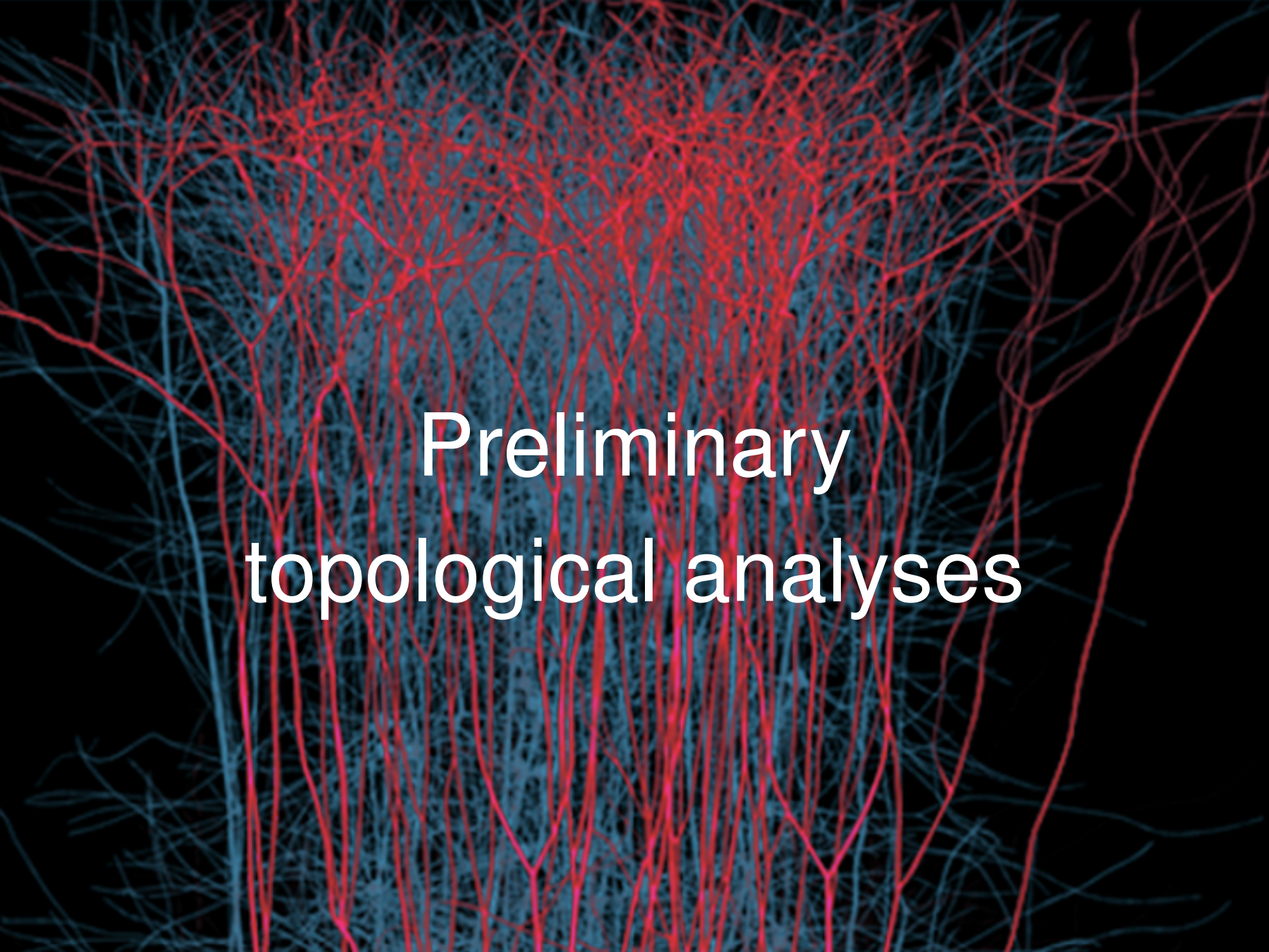


Blue Brain Project

A FEW QUESTIONS

From detailed to general...

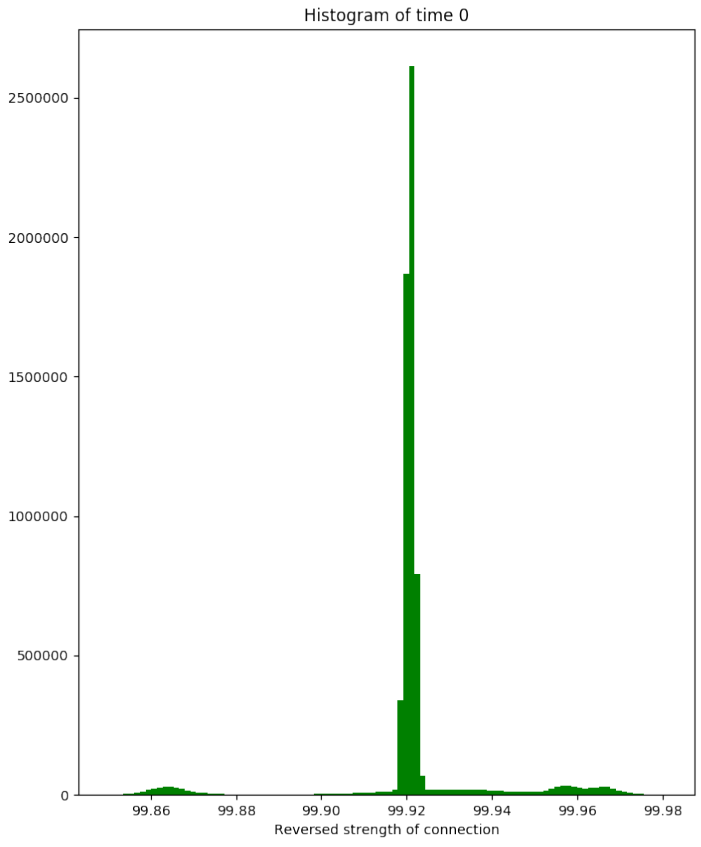
- Is the space of synaptic weights quantal?
- How to define an appropriate weight for a connection between two neurons in terms of the weights of the synapses?
- How to quantify the effect of plasticity on the network?
- What is the role of plasticity in learning and memory?


Preliminary
topological analyses

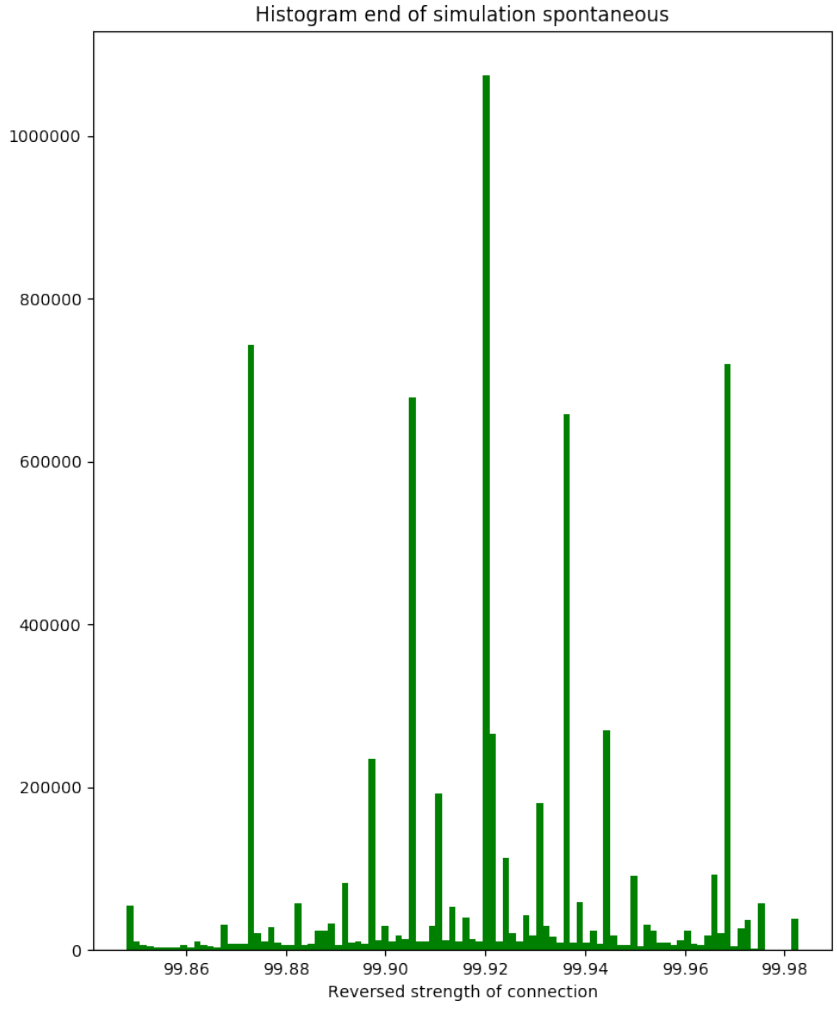
Blue Brain Project

WEIGHT DISTRIBUTIONS: TIME 0

Using the average weight of the synapses in a connection as the weight of the connection...

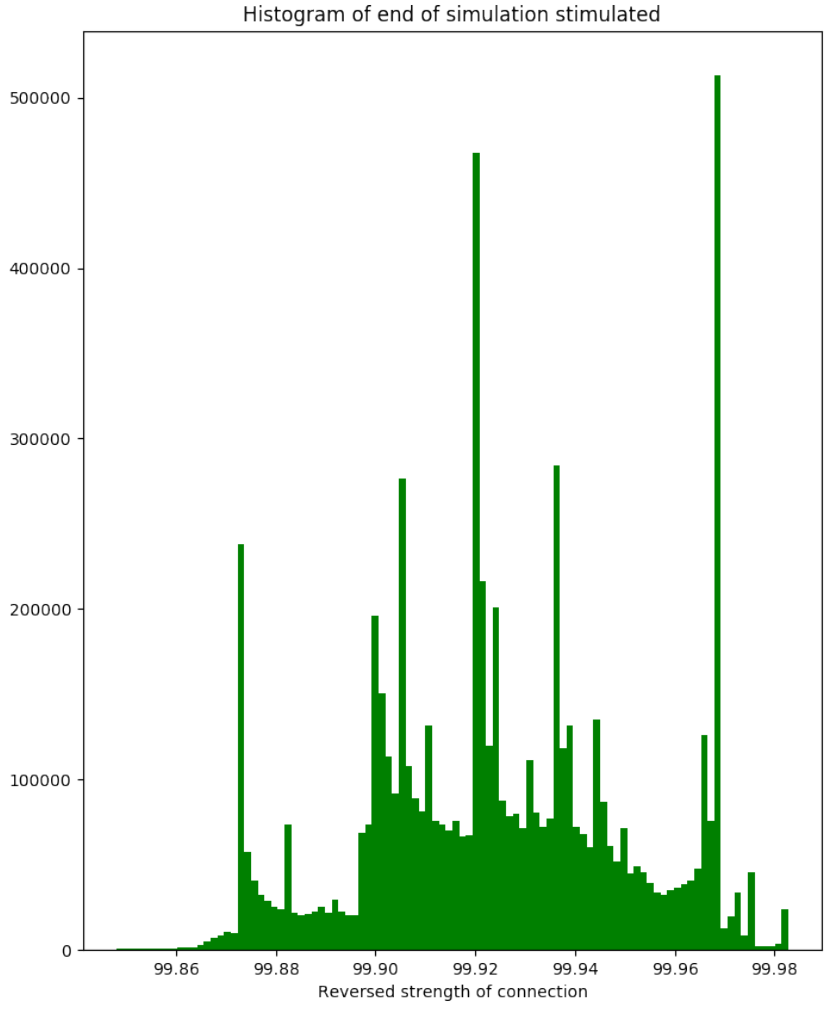


WEIGHT DISTRIBUTIONS: SPONTANEOUS



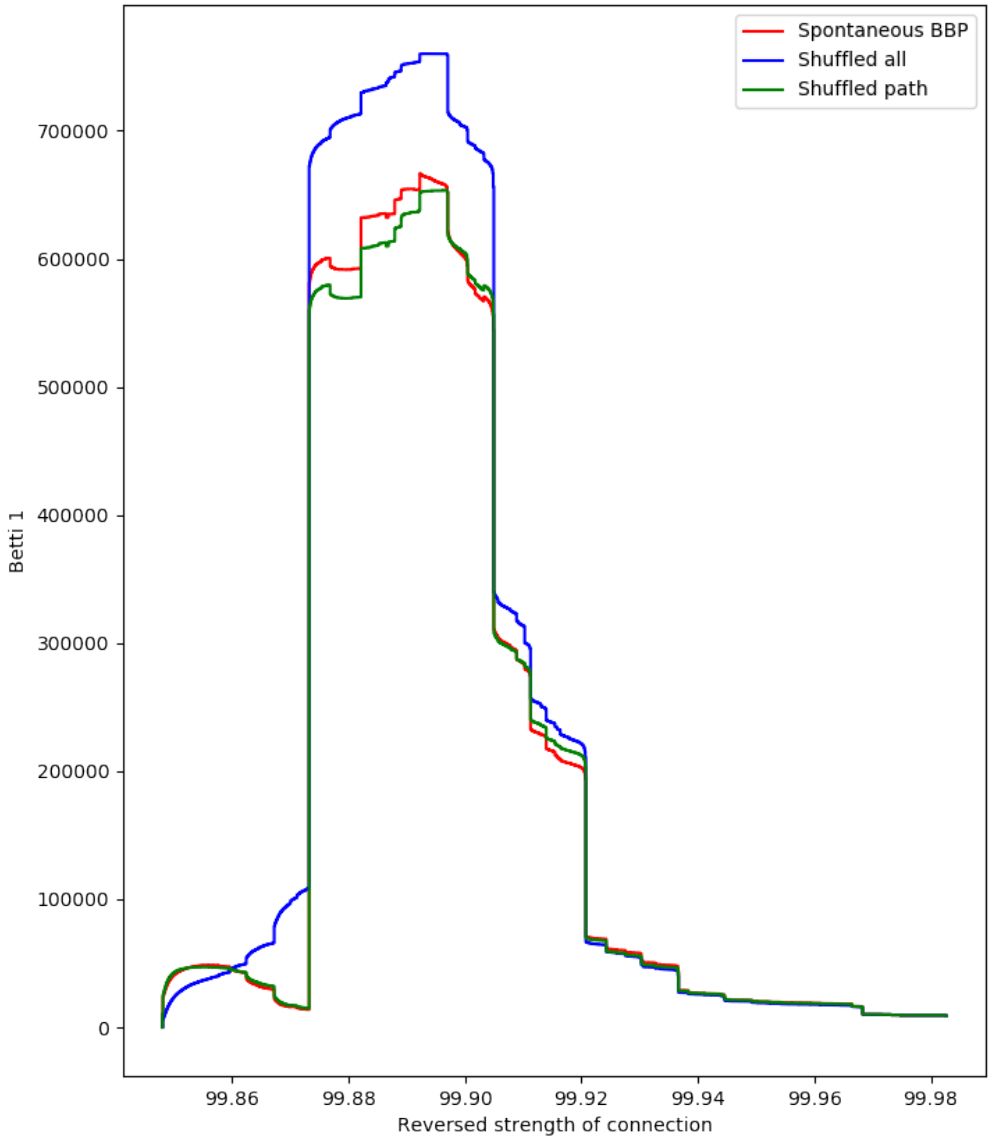
Blue Brain Project

WEIGHT DISTRIBUTIONS: STIMULATED



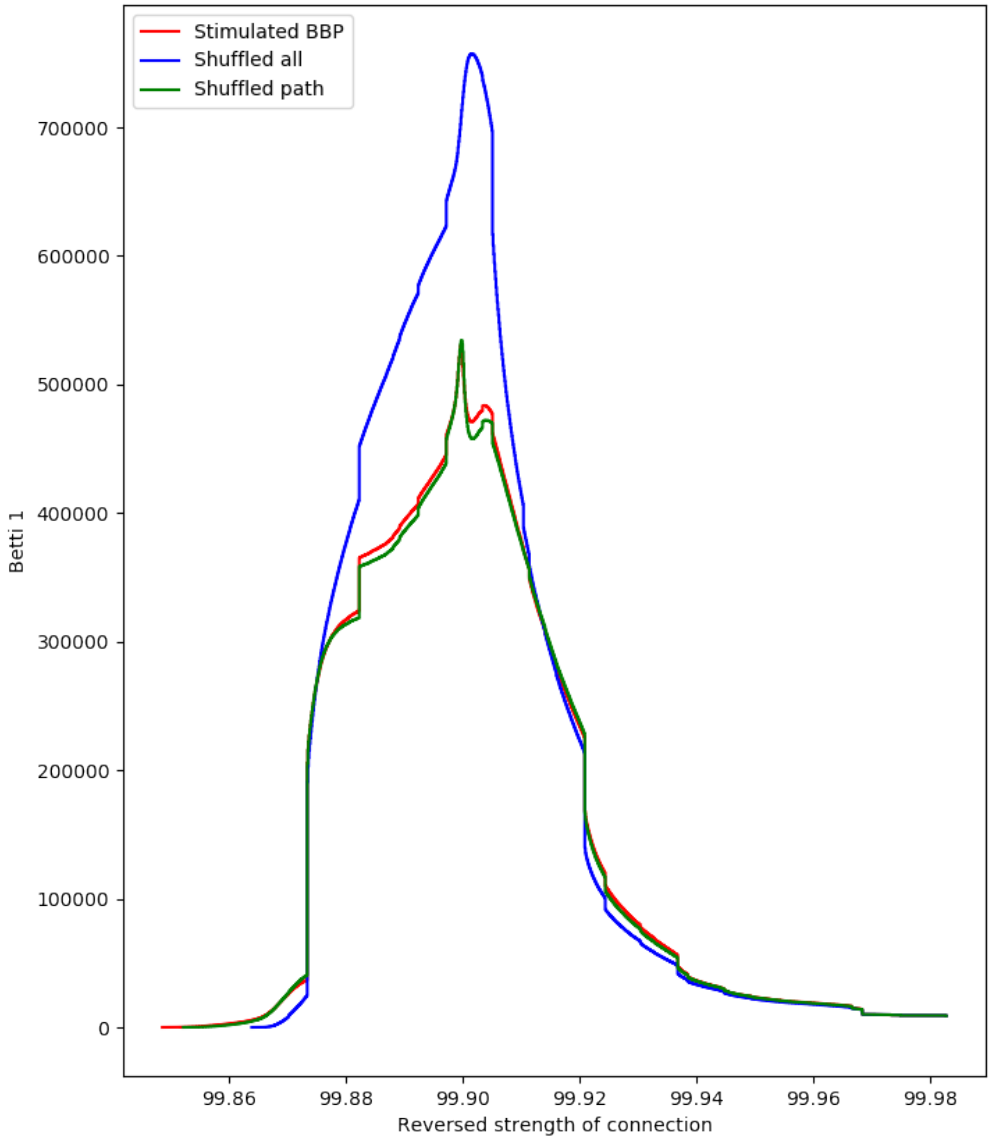
BETTI-1 CURVES: SPONTANEOUS ACTIVITY

Betti curves end of simulation sponanteous activity

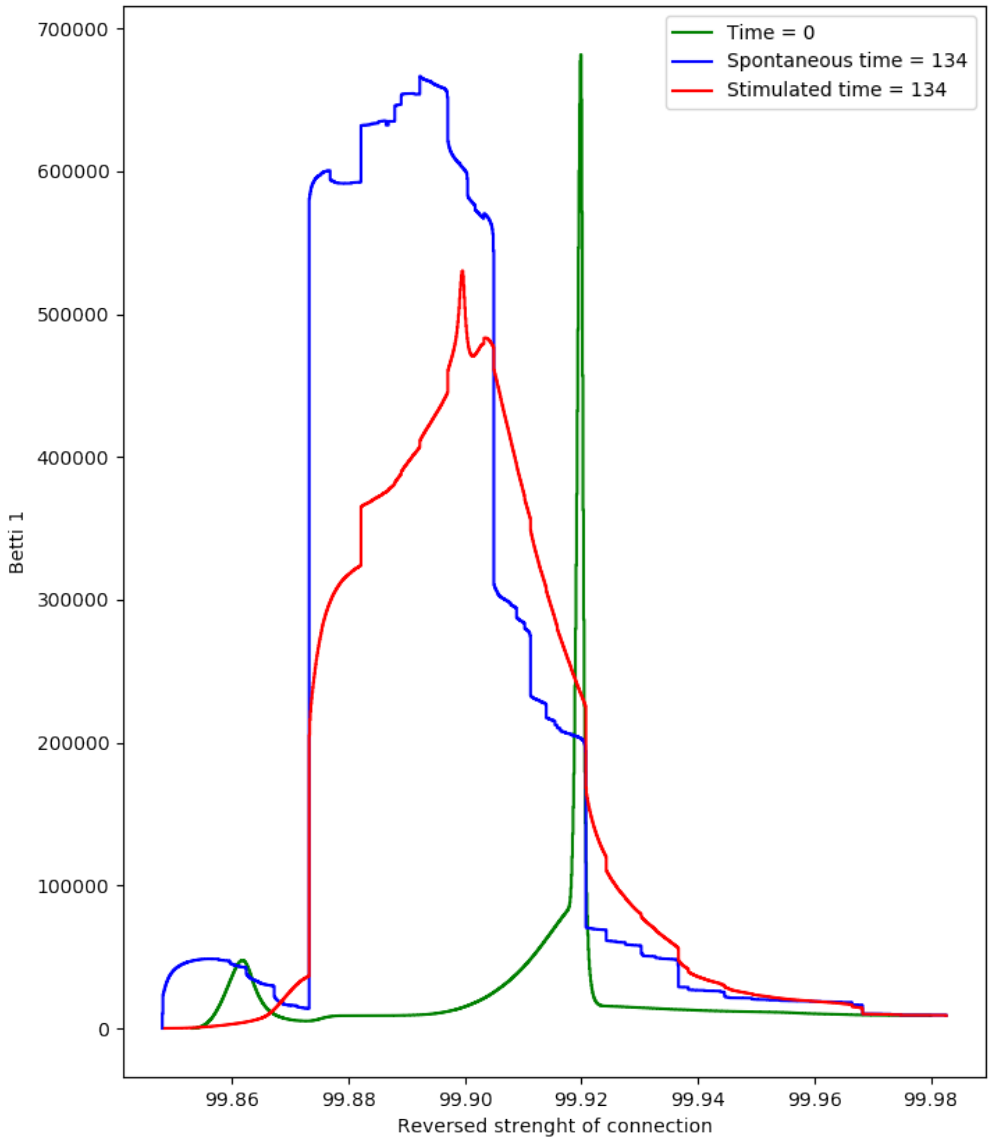


BETTI-1 CURVES: STIMULATED ACTIVITY

Betti curves end of simulation stimulated activity



BETTI-1 CURVES: STIMULATED VS SPONTANEOUS



Blue Brain Project

EVOLUTION OF PLASTICITY: AVERAGE U

Evolution of the network: stimulation vs spontaneous activity

Blue Brain Project

EVOLUTION OF PLASTICITY: AVERAGE U

Evolution of the L23PC-L23PC pathway

Blue Brain Project

EVOLUTION OF PLASTICITY: AVERAGE U

Evolution of the L5TTPC1-L5TTPC1 pathway

Blue Brain Project

EVOLUTION OF PLASTICITY: AVERAGE U

Evolution of the L6BPC-L6BPC pathway

Blue Brain Project

EVOLUTION OF PLASTICITY: AVERAGE U

Recall: stimulation vs spontaneous activity

Blue Brain Project

EVOLUTION OF PLASTICITY: SUMMING U'S

A comparison, with a different connection weight

Blue Brain Project

RAN'S PERSISTENCE MOVIES

Blue Brain Project

RAN'S PERSISTENCE MOVIES

Blue Brain Project

WORK IN PROGRESS

- Determine what is the correct (i.e., most biologically meaningful) weighting to use on connections. Perhaps a "filtered" version of the sum of u's?
- Perform topological analyses of activity, in terms of weighted transmission-response graphs, at different stages of the plasticity simulation.
- Determine the biological meaning (if any!) of the structure of these time series of PD. Correlation of some sort with learning?
- Carry out similar analyses for structural plasticity (elimination/creation of synapses, in addition to weight changes).

Blue Brain Project

COLLABORATORS

- Stefania Ebli, Daniela Egas Santander, Nicolas Ninin, Martina Scolamiero, Gard Spreemann, and Dimitri Zaganidis (Laboratory for Topology and Neuroscience, EPFL)
- Nicolas Antille (visualization), Giuseppe Chindemi, Henry Markram, Eilif Muller, Max Nolte, and Michael Reimann (Blue Brain Project, EPFL)
- Dejan Govc, Ran Levi, and Daniel Lütgehetmann (Aberdeen)


Tusen takk!

Blue Brain Project

COMING ATTRACTIONS...

Workshop on topology and neuroscience

28–30 November 2018

EPFL

Lecture series by Carina Curto and Olaf Sporns

Talks by 12 other invited speakers

Poster session