Integrating neural morphology in studying neural plasticity with computer simulations: reality, approaches, and challenges

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27/03/2023 | HBP Summit| Marseille

Q1: the key question in studying plasticity?

Flexibility and plasticity

Happy Harvest Mouse
by Charlie Marshall

Flexibility and plasticity

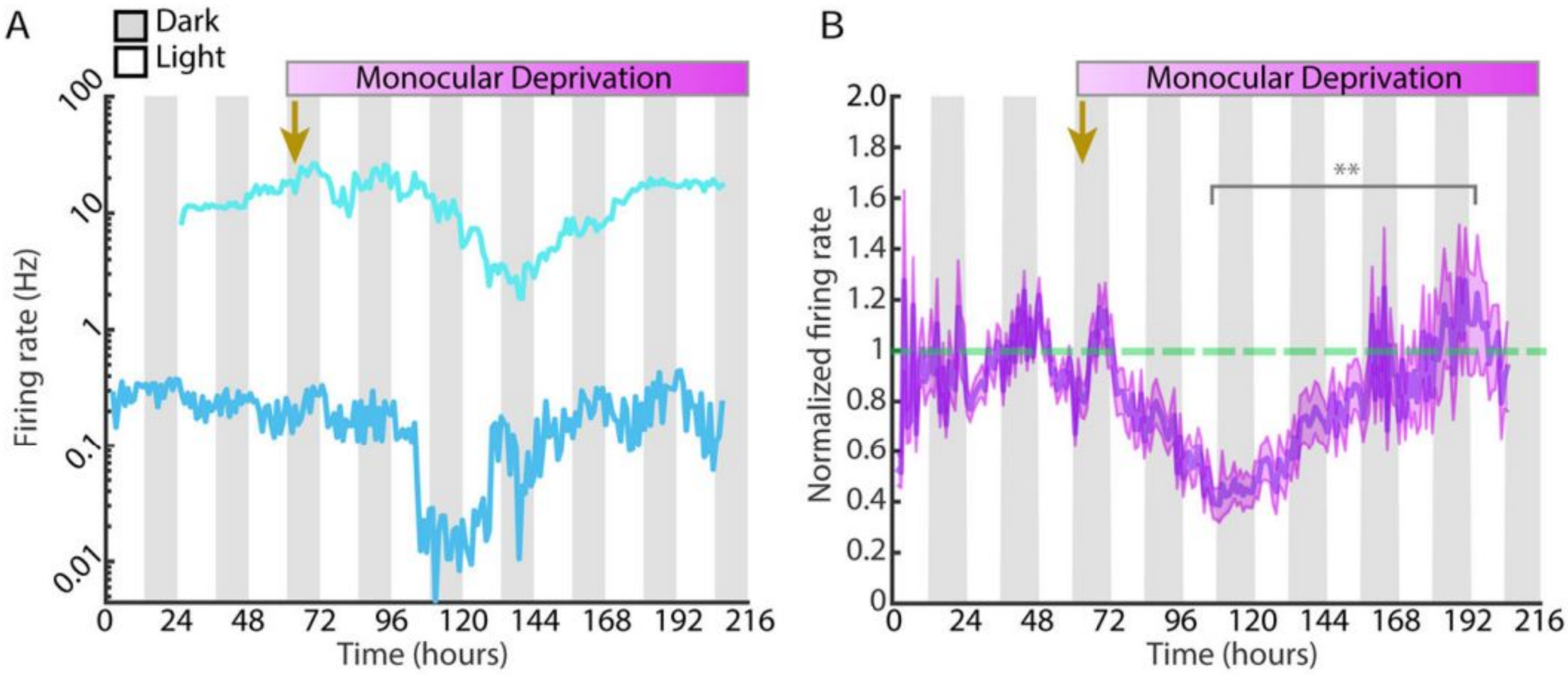
Unknown sounds, smells, and objects…

Critical status of network activity

Cues of pre-encountered predators or food…

Hebbian plasticity (learning & memory)

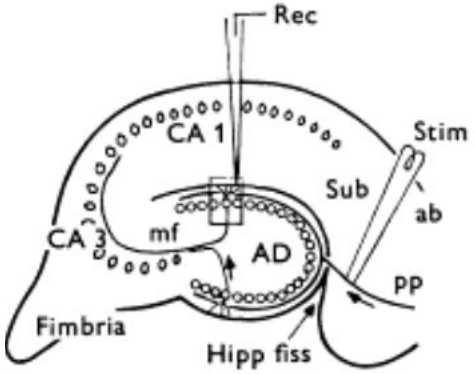
Firing rate homeostasis

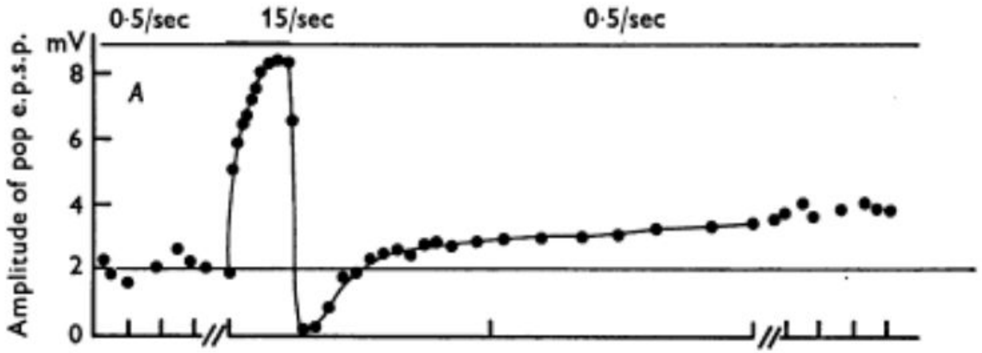


(Hengen et al., Cell, 2016)

LTP & Functional plasticity

LTP: long-term potentiation





(Bliss & Lømo, J Physiol, 1973)

LTP & Functional plasticity

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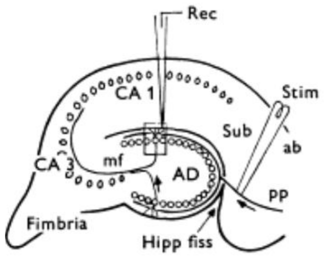
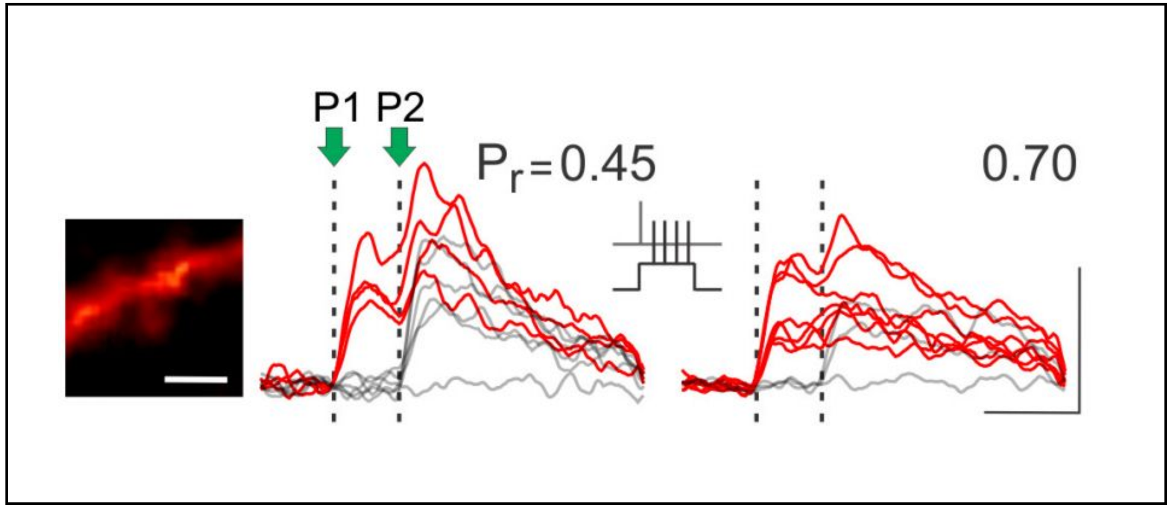
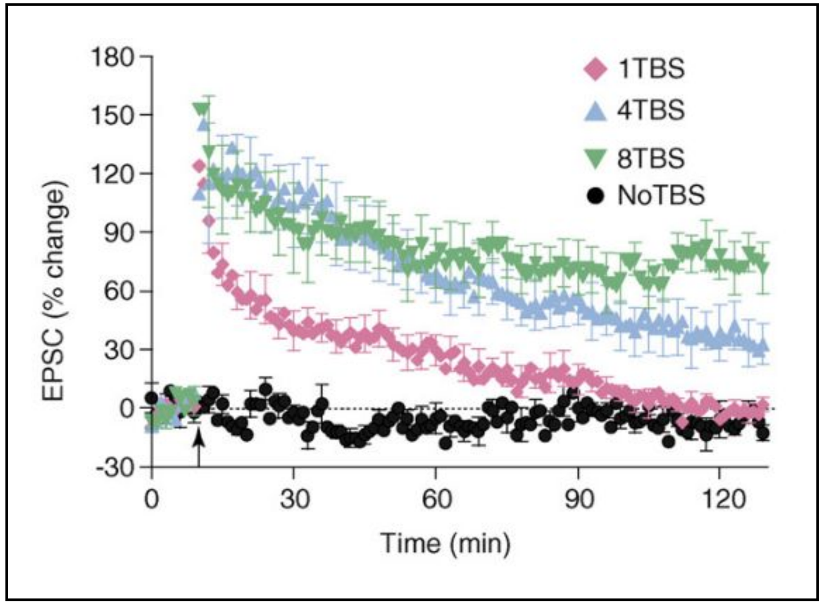
- changes in synaptic transmission
- glutamate release probability × postsynaptic receptor number





Presynaptic



postsynaptic

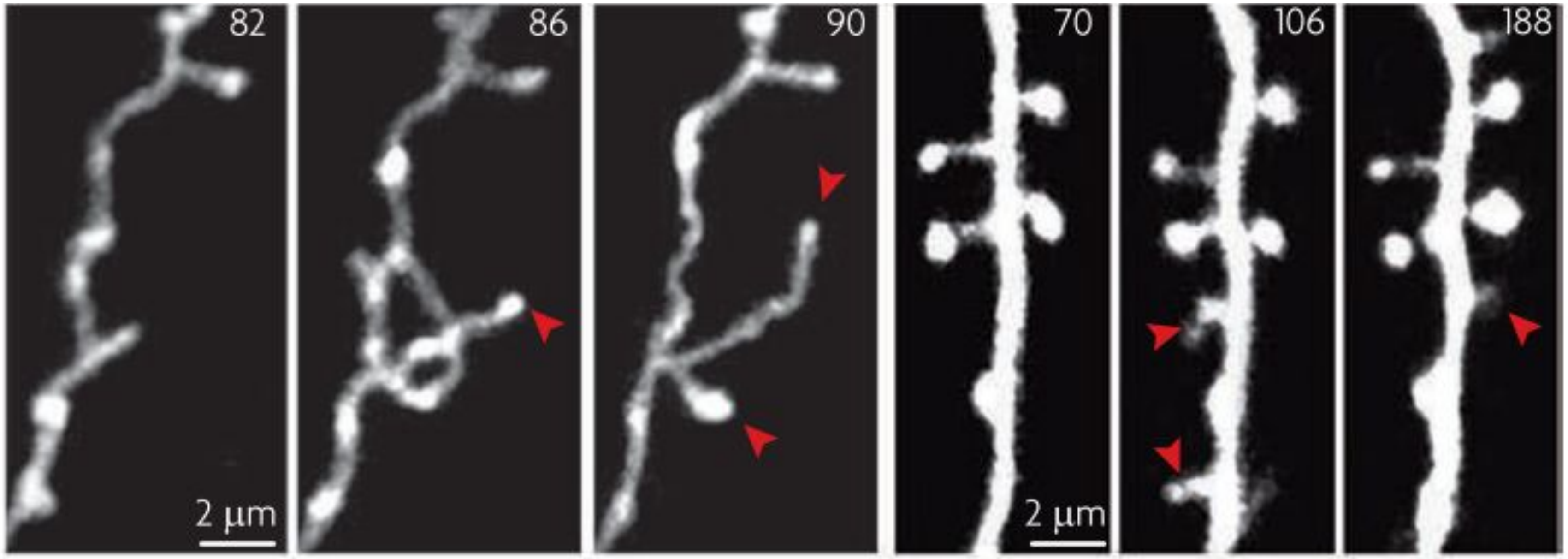
(Bliss & Lømo, J Physiol, 1973; Padamsey et al., elife, 2017; Raymond, Trends in Neurosciences, 2007)

Structural plasticity

- changes in bouton and spine sizes and numbers, synapse numbers
- changes in network connectivity

terminaux boutons

dendritic spines



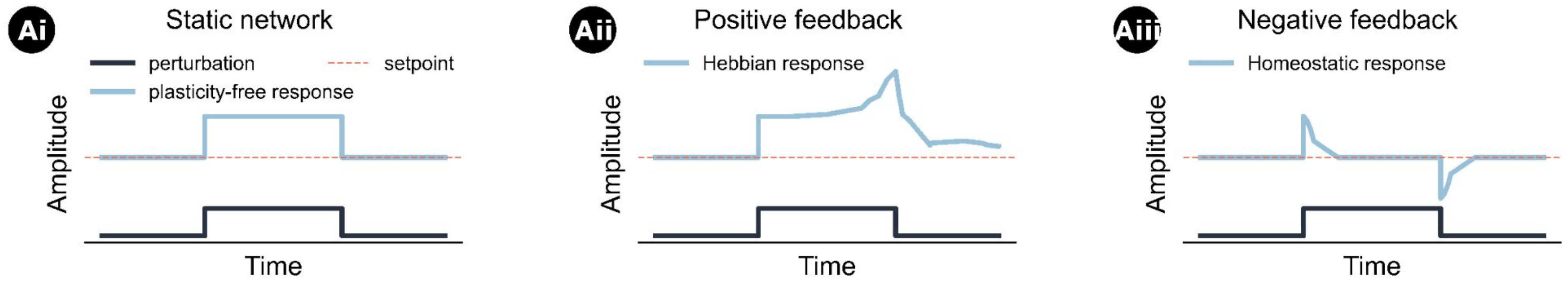
adult mice neocortex
L6 pyramidal cell

adult mice neocortex
L5 pyramidal cell

(De Paola et al., Neuron, 2006; Holtmaat et al., Behavioural Brain Research, 2008; Holtmaat and Svoboda, Nature Reviews Neuroscience, 2009)

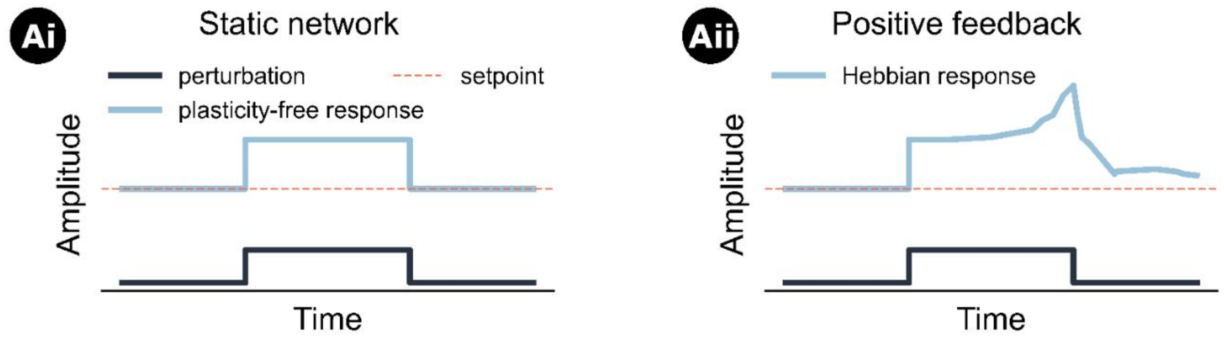
Q2: Reality in matching experiments & theories/models

Robustness in complex network



(Lu et al., in submission)

Robustness in complex network

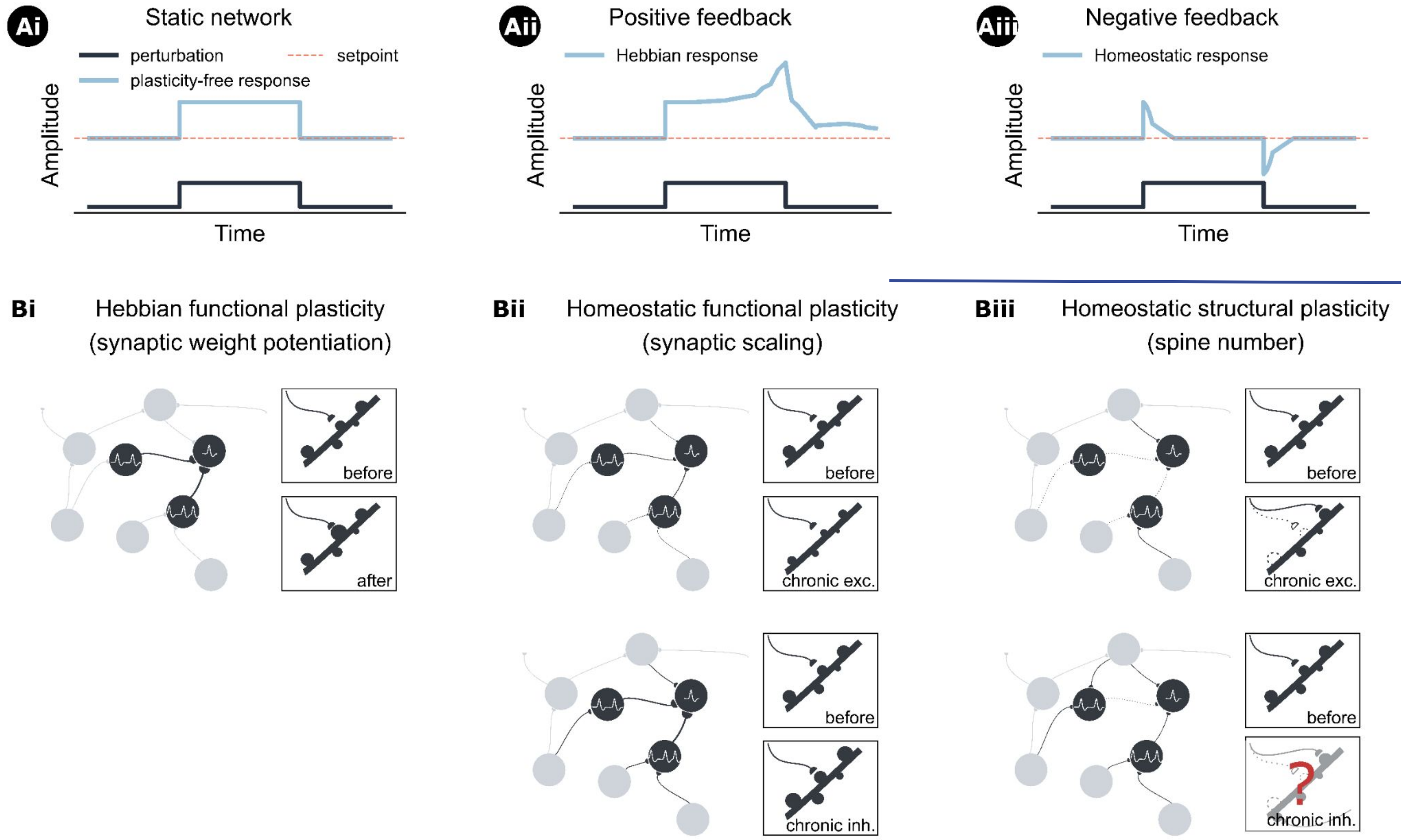


system control

(Lu et al., in submission)

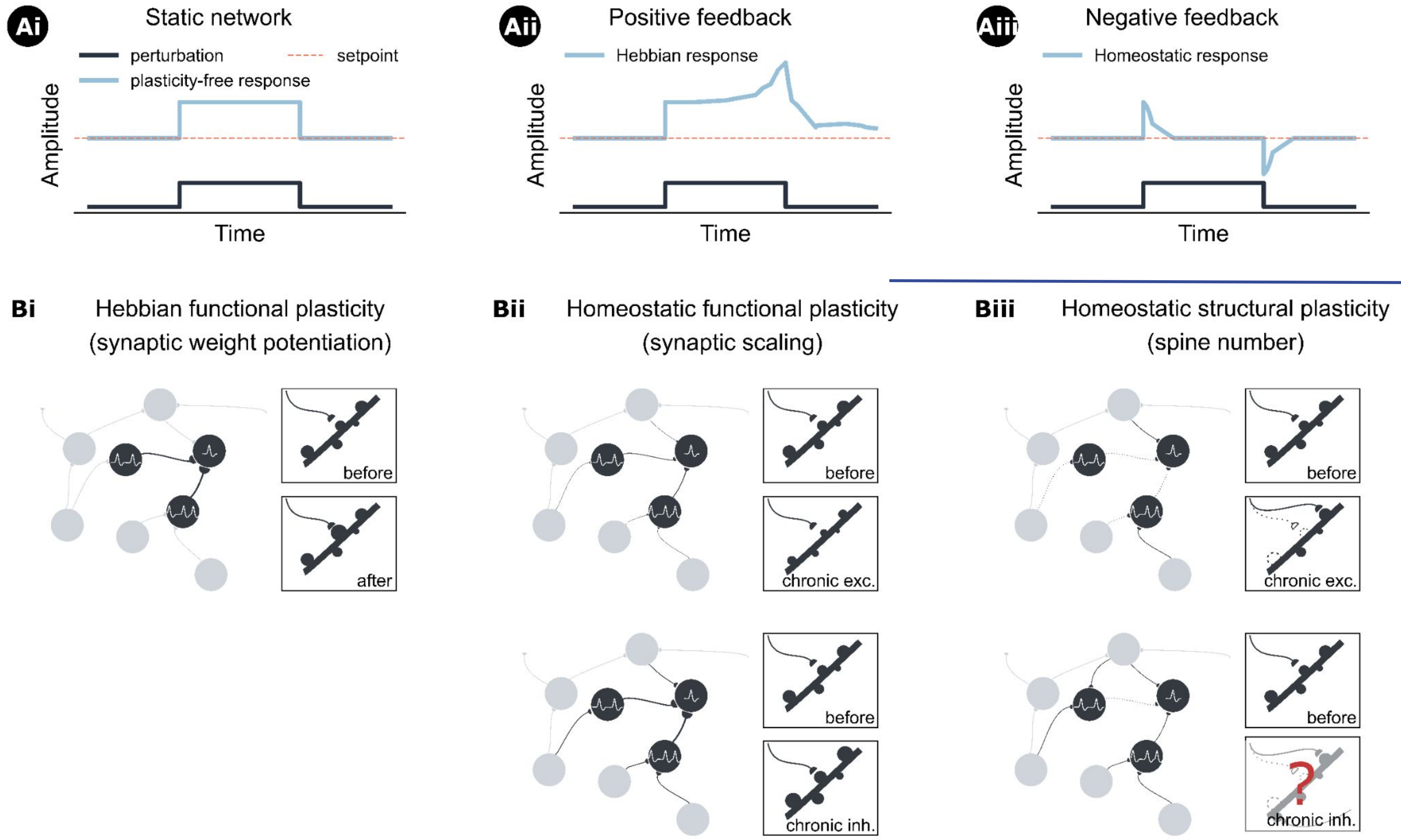
Robustness in complex network

system control



(Lu et al., in submission)

Robustness in complex network



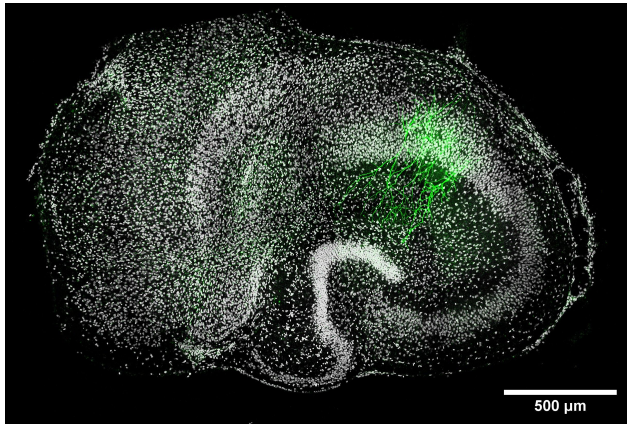
system control

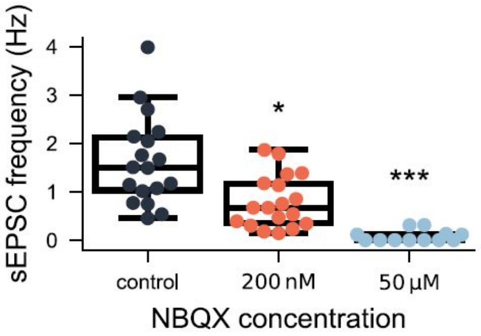
Redundancy & heterogeneity

(Lu et al., in submission)

Interpreting experimental results with plasticity rules

Functional plasticity

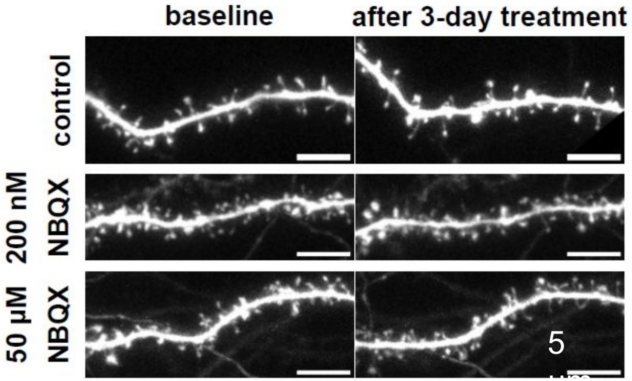


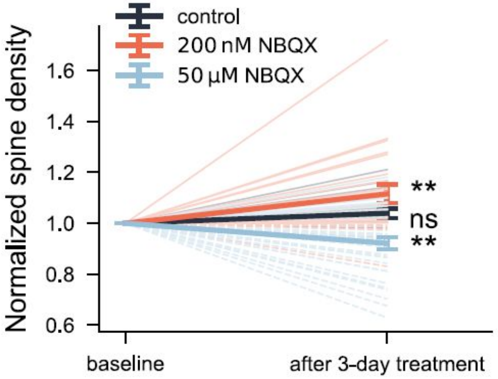


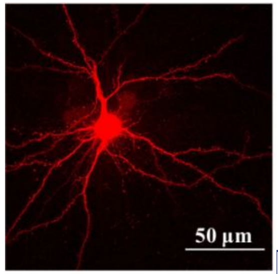
Whole-cell patch-clamp recordings

Point neural models are optimal!

Structural plasticity







Time-lapse imaging or
filling neurons with fluorescent dye

Point neural models are not optimal but a working solution for simulating plasticity rules in large neural network

(Lu et al., Cereb Cortex, 2022; Lu et al., in submission)

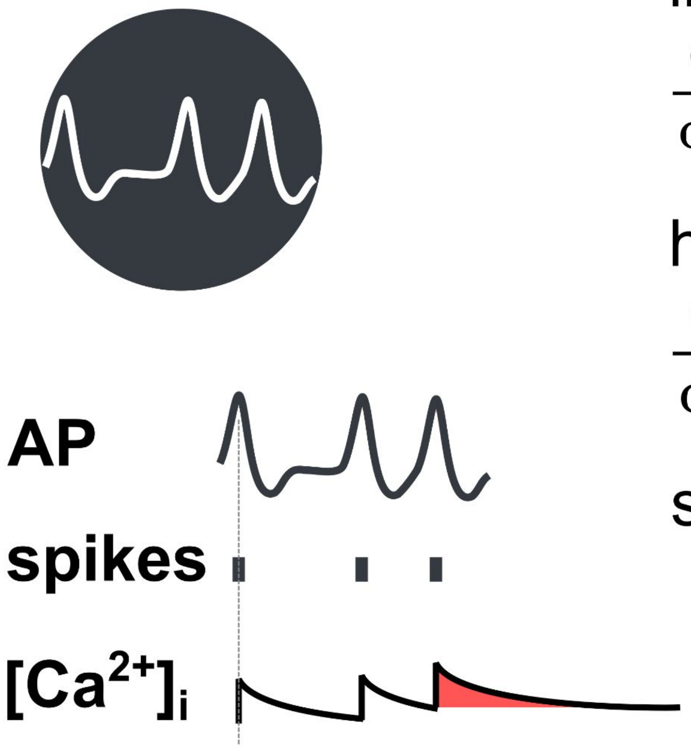
Q3: challenges and approaches: using NEST, prepared for Arbor

nest :: simulated()

arbor

Connecting functional & structural plasticity with calcium concentration

Ca based plasticity rules



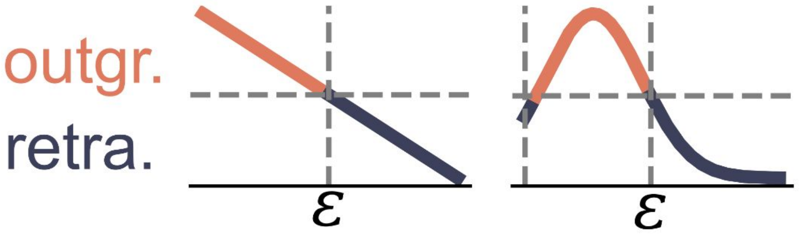
integral signal

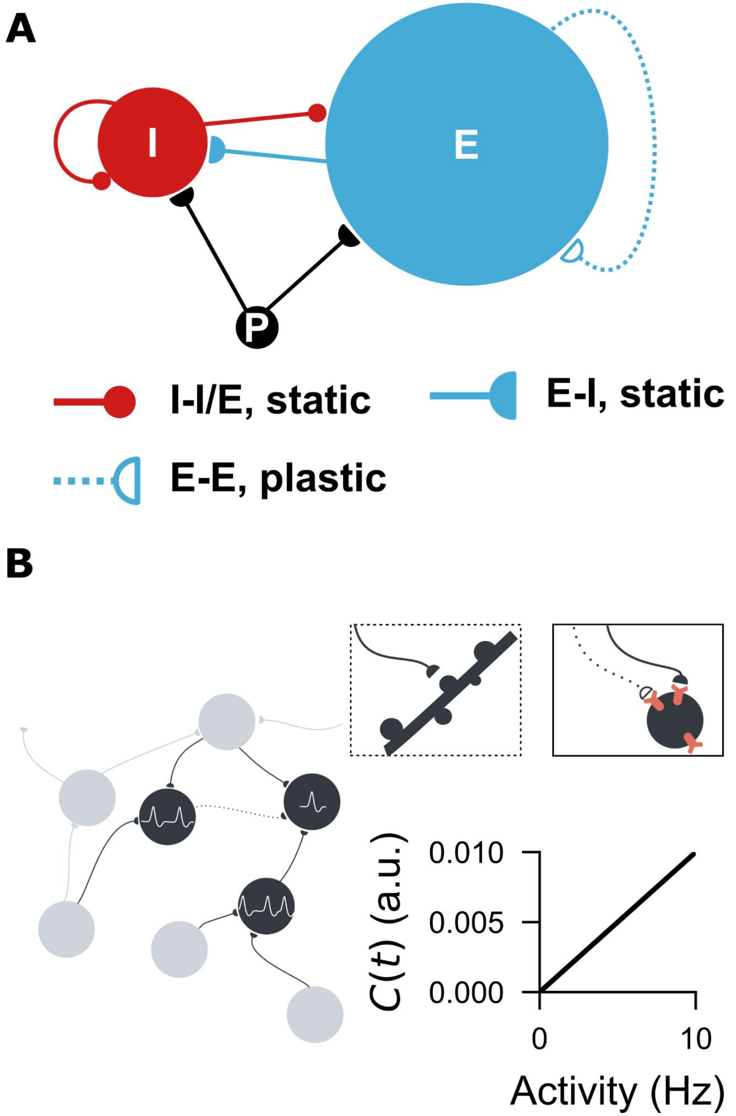
$$\frac{\mathrm{d}}{\mathrm{d}t}C(t) = -\frac{1}{\tau_{\mathrm{Ca}}}C(t) + \beta_{\mathrm{Ca}}S(t)$$

homeostatic synaptic scaling

$$\frac{\mathrm{d}}{\mathrm{d}t}w(t) = \rho w(t)[C(t) - \epsilon]$$

structural plasticity

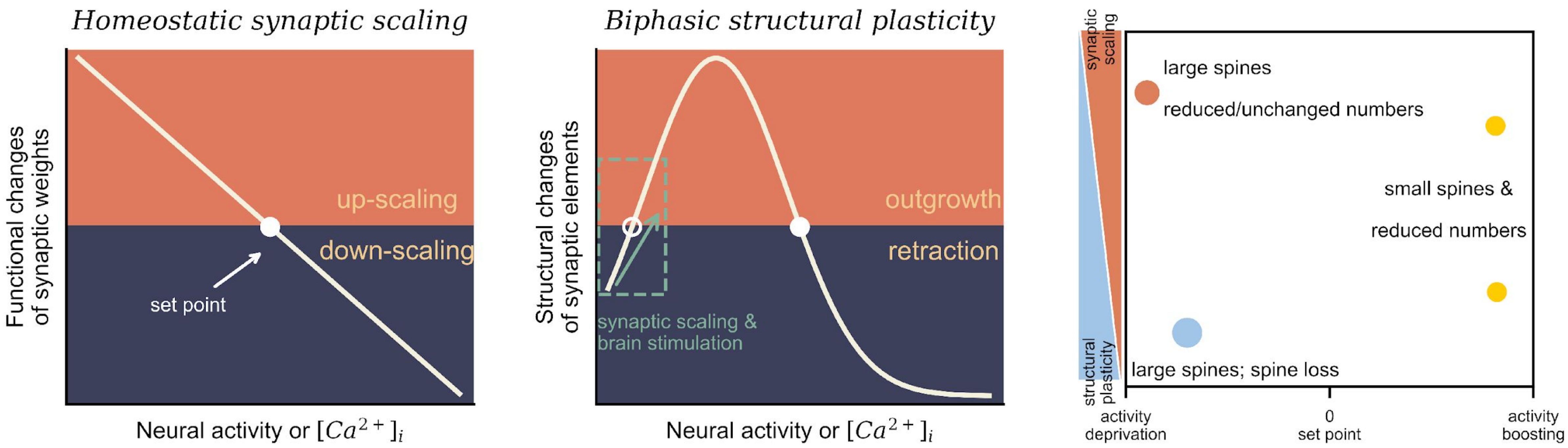




(Lu et al., in submission)

Approach 1: systematically combining different rules in one neuron

- Redundancy and heterogeneity between homeostatic synaptic scaling and structural plasticity



(Lu et al., in submission)

Approach 2: using different parameters of the same rule in one neuron

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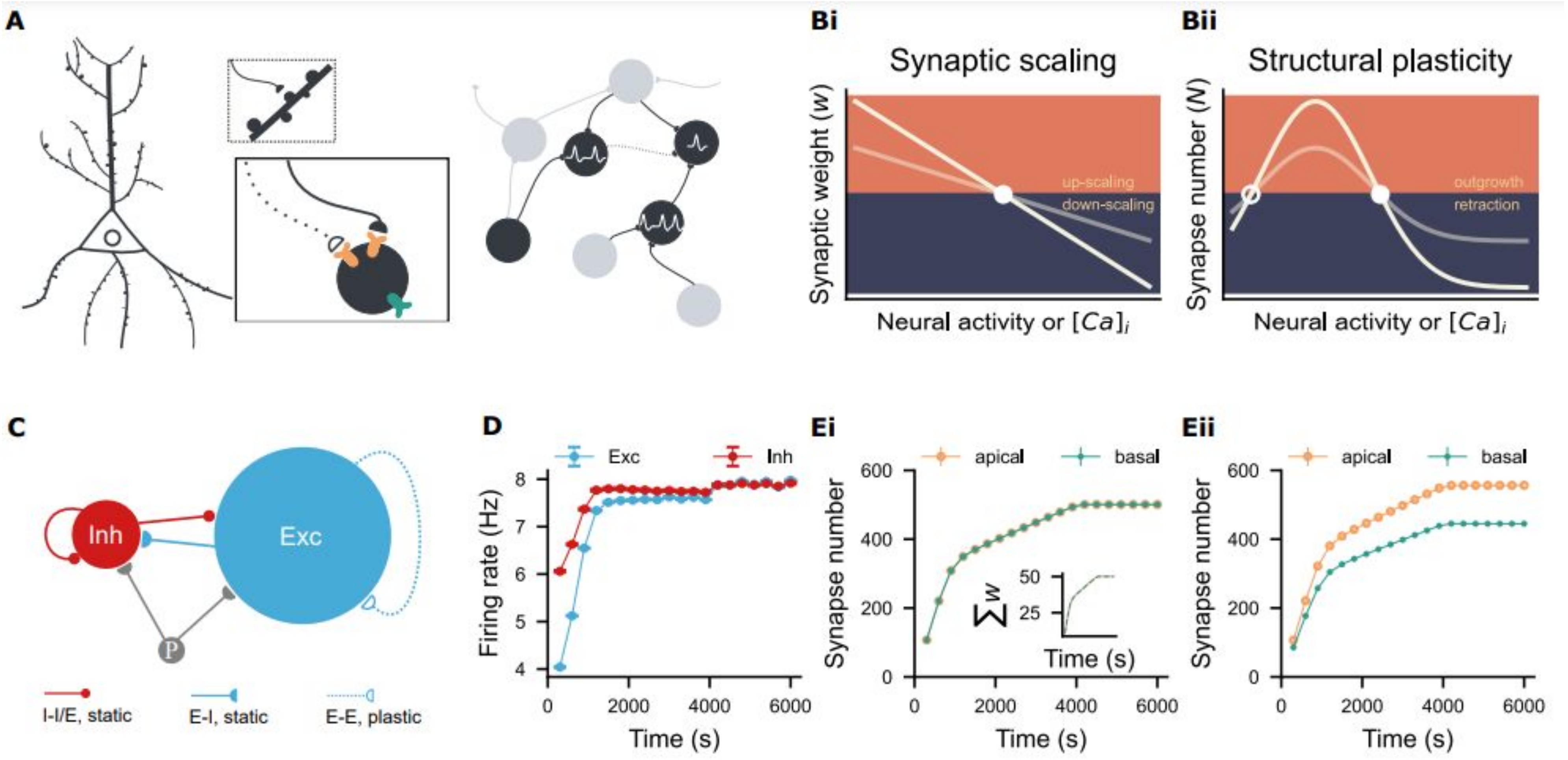
- Heterogeneity between apical and basal dendrites during growth



(Lu et al., in preparation)

Approach 2: using different parameters of the same rule in one neuron

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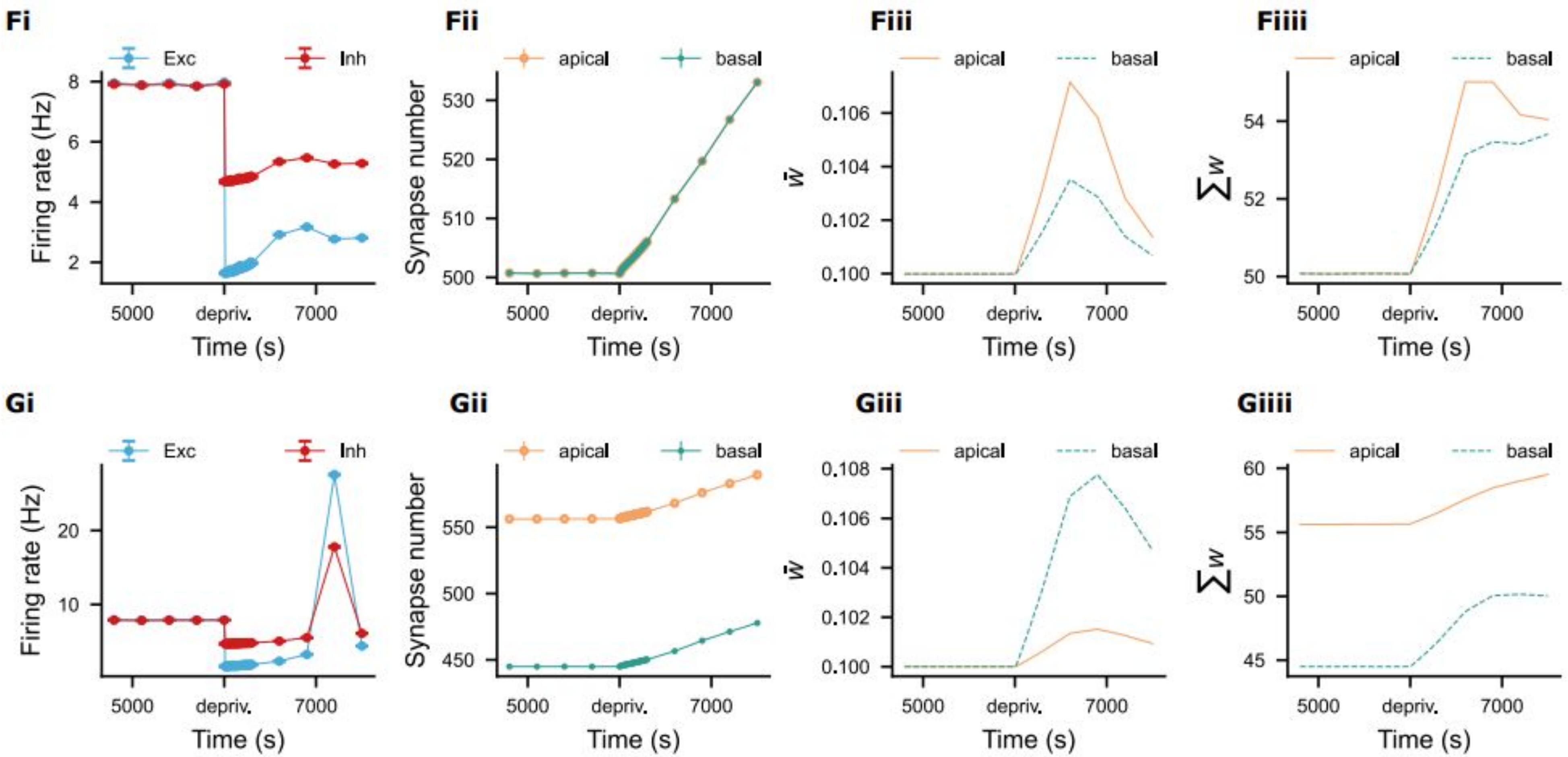
- Heterogeneity between apical and basal dendrites during activity deprivation



(Lu et al., in preparation)

Q4: something to expect in Arbor

Features that are out there in Arbor

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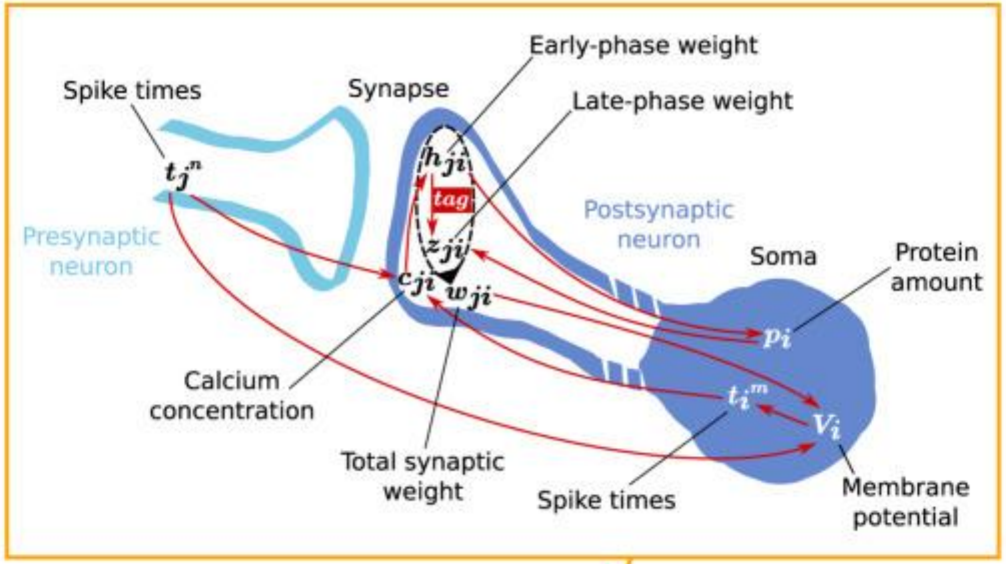
arbor

- Activity dependent calcium update
  - Presynaptic event
  - Postsynaptic event
- Calcium diffusion
- Calcium dependent functional plasticity & structural plasticity

Example: synaptic tagging and capture (STC model)

Schematics of the synaptic model and the network model



(Hater et al., in progress; Luboeinski et al., Communications Biology, 2021)

Acknowledgements

Institute of Anatomy and Cell Biology

University of Freiburg

Prof. Dr. Andreas Vlachos

Dr. Maximilian Lenz

Bernstein Center Freiburg & Biology Faculty

University of Freiburg

Prof. Dr. Stefan Rotter

Dr. Julia V. Gallinaro

Forschungszentrum Jülich

Dr. Sandra Diaz

Dr. Brent Huisman

Dr. Thorsten Hater

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IMBIT //BrainLinks
BrainTools
acting thoughts

nest::
simulated()

arbor

bcf