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

Han Lu

Department of Neuroanatomy, Institute of Anatomy and Cell Biology
Faculty of Medicine, University of Freiburg

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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

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

(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

(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

(Ai) Static network
- perturbation
- plasticity-free response

(Aii) Positive feedback
- Hebbian response

(Aiii) Negative feedback
- Homeostatic response

(Lu et al., in submission)
Robustness in complex network system control

(Lu et al., in submission)
Robustness in complex network system control

Ai  Static network
- perturbation
- setpoint
- plasticity-free response

Amplitude vs. Time

Ai  Positive feedback
- Hebbian response

Amplitude vs. Time

Ai  Negative feedback
- Homeostatic response

Amplitude vs. Time

Bi  Hebbian functional plasticity (synaptic weight potentiation)

Before and After images

Bii  Homeostatic functional plasticity (synaptic scaling)

Before and After images

Biii  Homeostatic structural plasticity (spine number)

Before and After images

(Lu et al., in submission)
Robustness in complex network system control

(Ai) Static network
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(Bi) Hebbian functional plasticity (synaptic weight potentiation)

(Bii) Homeostatic functional plasticity (synaptic scaling)

(Biii) Homeostatic structural plasticity (spine number)

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
Connecting functional & structural plasticity with calcium concentration

Ca based plasticity rules

Integral signal
\[ \frac{d}{dt} C(t) = -\frac{1}{\tau_{Ca}} C(t) + \beta_{Ca} S(t) \]

Homeostatic synaptic scaling
\[ \frac{d}{dt} w(t) = \rho w(t) [C(t) - \epsilon] \]

Structural plasticity
outgr.
retra.

(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

- 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

- 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

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

**Example:** synaptic tagging and capture (STC model)

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