Investigating structural plasticity in brain networks using computational modelling

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Context: what and why?

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What underlies large scale reorganisation?

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Also confirms structural plasticity in the unlesioned adult brain

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- A computational model allows us to:
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Methods: How?

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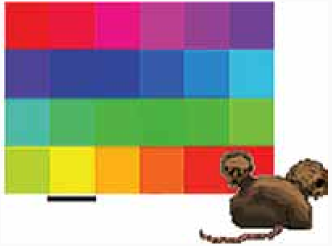
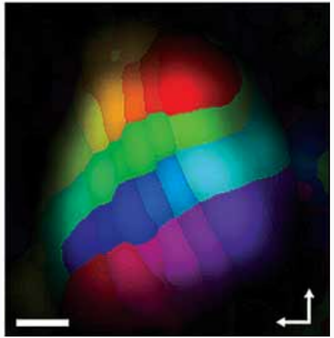
Peripheral lesion protocol I: topographic mapping





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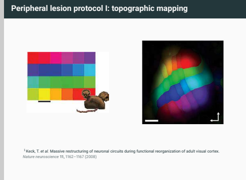
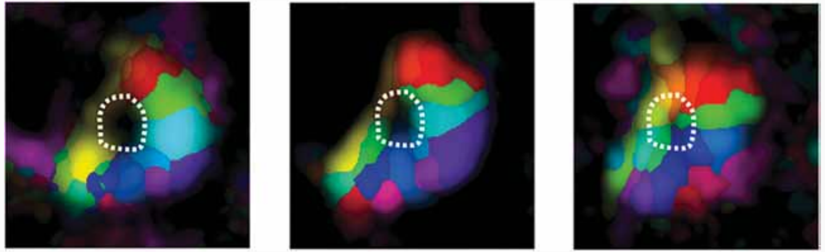


1. The protocol is pretty standard. Here, for a study in the visual cortex, the retinal field of a rat or a mouse is mapped.

Peripheral lesion protocol II: after peripheral lesion



- Dotted region encloses the Lesion Projection Zone (LPZ)
- Inward “repair”.

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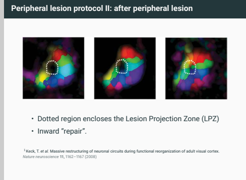
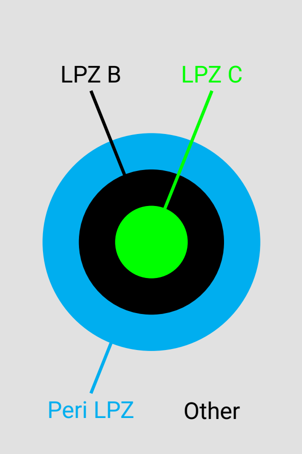
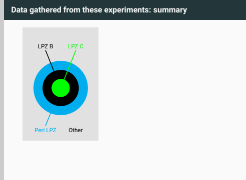


1. Then, a part of the retina is lesioned. This cuts off inputs to a part of the visual cortex, as shown in the first figure. This forms the Lesion Projection Zone (LPZ). By repeated imaging of the region over months, the reorganisation of the network is tracked.
2. Other lesion studies use similar methods: digit removal, whisker trimming, and so on—anything that cuts off projecting activity on to a set of neurons.

Data gathered from these experiments: summary





1. So, if this a simple schematic, of the regions around the LPZ, this is what we know from these studies.

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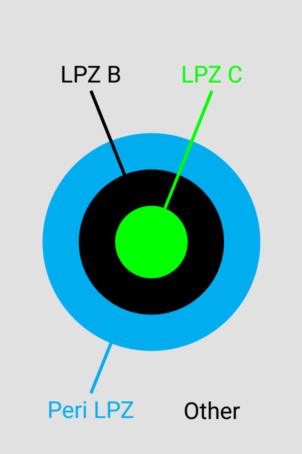
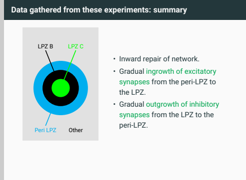


- Inward repair of network.
- Gradual ingrowth of excitatory synapses from the peri-LPZ to the LPZ.
- Gradual outgrowth of inhibitory synapses from the LPZ to the peri-LPZ.



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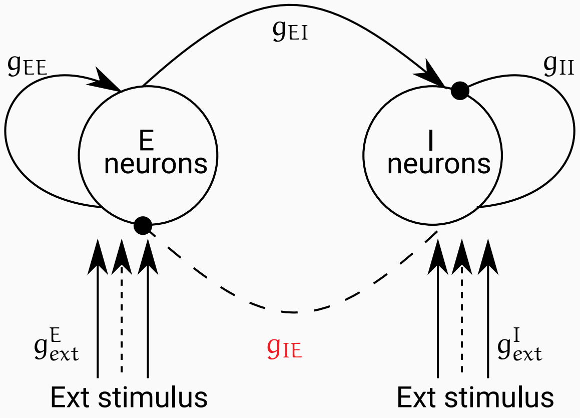
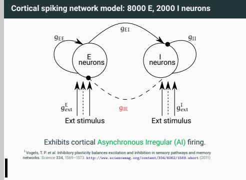
Cortical spiking network model: 8000 E, 2000 I neurons



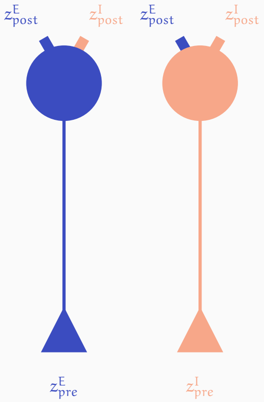
Exhibits cortical Asynchronous Irregular (AI) firing.

[1] Vogels, T. P. *et al.* Inhibitory plasticity balances excitation and inhibition in sensory pathways and memory networks. *Science* **334,** 1569–1573. `http://www.sciencemag.org/content/334/6062/1569.short` (2011)

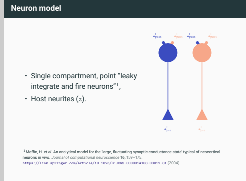


Neuron model

- Single compartment, point "leaky integrate and fire neurons"[1],
- Host neurites (z).

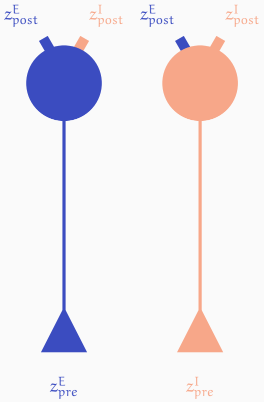


[1] Meffin, H. *et al.* An analytical model for the 'large, fluctuating synaptic conductance state' typical of neocortical neurons in vivo. *Journal of computational neuroscience* **16,** 159–175. `https://link.springer.com/article/10.1023/B:JCNS.0000014108.03012.81` (2004)



Modelling synapse formation and removal

- $z^{E}_{\mathrm{post}} + z^{E}_{\mathrm{pre}}$
- $z^{I}_{\mathrm{post}} + z^{I}_{\mathrm{pre}}$
- New synapses form when free partner neurites are available.
- Synapses are deleted if neurites are retracted by the neuron.



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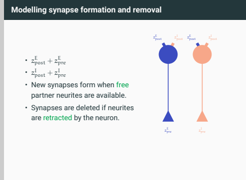
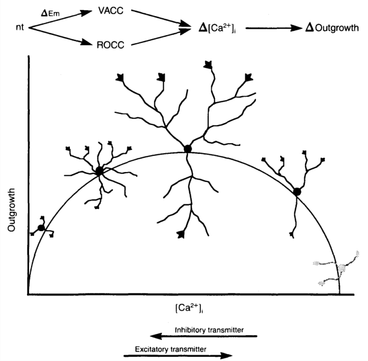
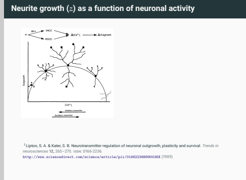
└Methods: How?
└Modelling synapse formation and removal



Neurite growth (z) as a function of neuronal activity



[1] Lipton, S. A. & Kater, S. B. Neurotransmitter regulation of neuronal outgrowth, plasticity and survival. *Trends in neurosciences* **12**, 265–270. ISSN: 0166-2236. http://www.sciencedirect.com/science/article/pii/016622368990026X (1989)



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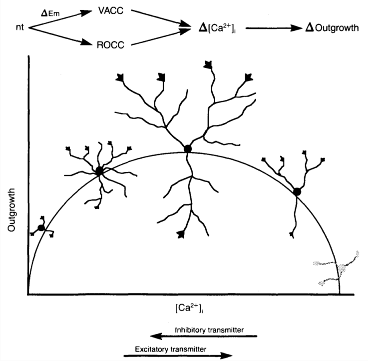

- $[\mathrm{Ca}^{2+}]$ correlates with neuronal activity,
- serves a homeostatic function.

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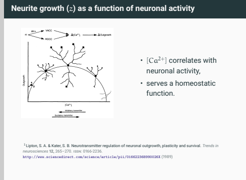
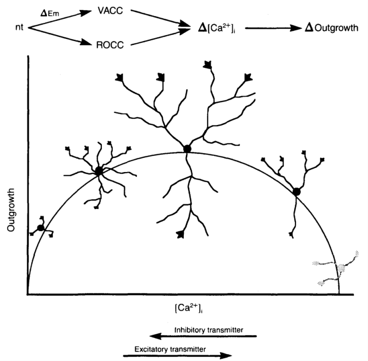
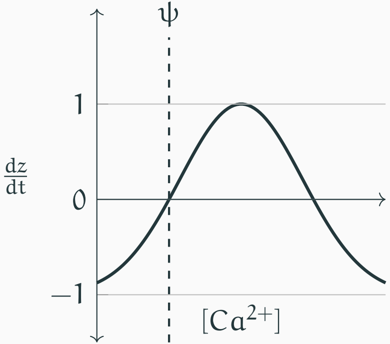


Neurite growth (z) modelled as a Guassian function of activity





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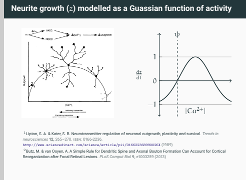
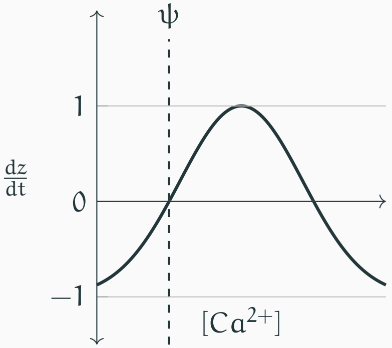
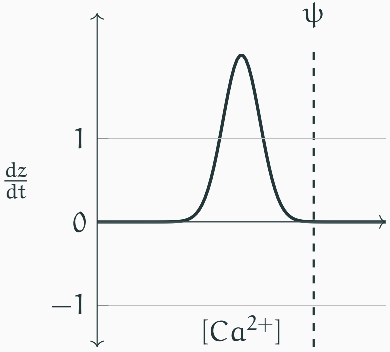
[2] Butz, M. & van Ooyen, A. A Simple Rule for Dendritic Spine and Axonal Bouton Formation Can Account for Cortical Reorganization after Focal Retinal Lesions. *PLoS Comput Biol* **9,** e1003259 (2013)



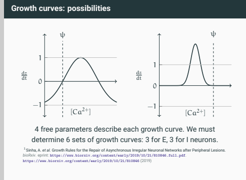
Growth curves: possibilities



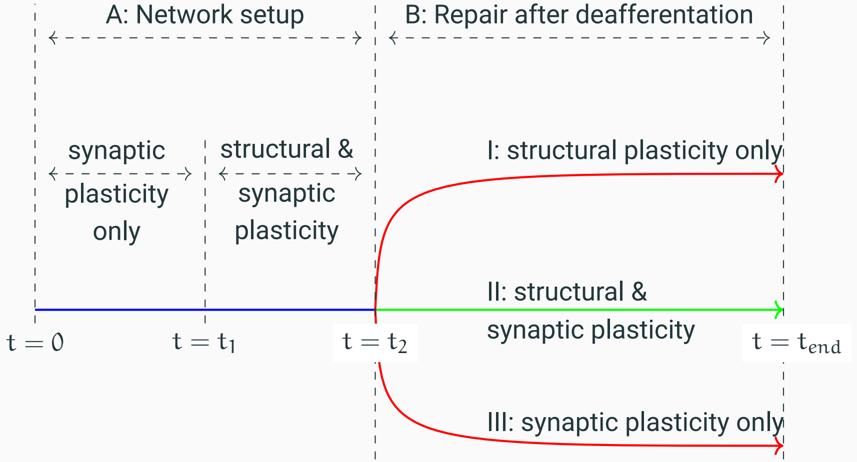


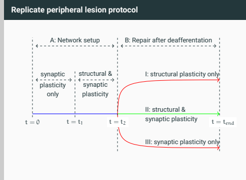
4 free parameters describe each growth curve. We must determine 6 sets of growth curves: 3 for E, 3 for I neurons.

[1] Sinha, A. *et al.* Growth Rules for the Repair of Asynchronous Irregular Neuronal Networks after Peripheral Lesions. *bioRxiv.* eprint: `https://www.biorxiv.org/content/early/2019/10/21/810846.full.pdf`. `https://www.biorxiv.org/content/early/2019/10/21/810846` (2019)



Replicate peripheral lesion protocol





Results: a few years later

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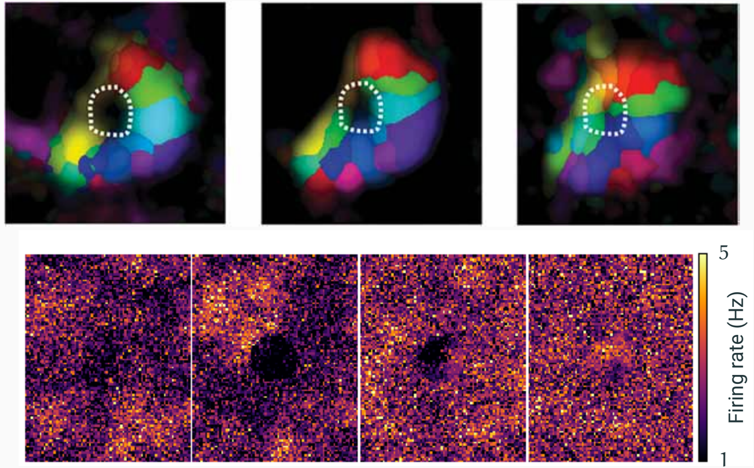
Reproduction of deafferentation and repair



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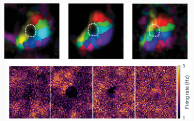
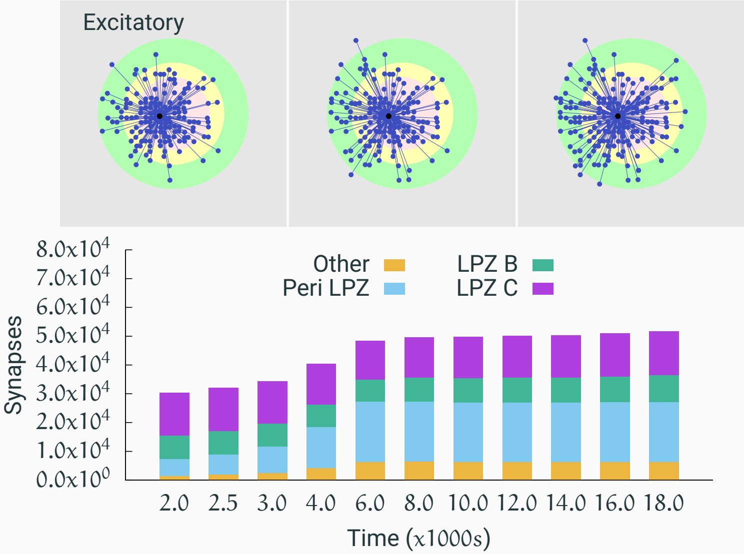


Reproduction of ingrowth of excitatory projections



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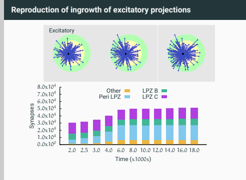
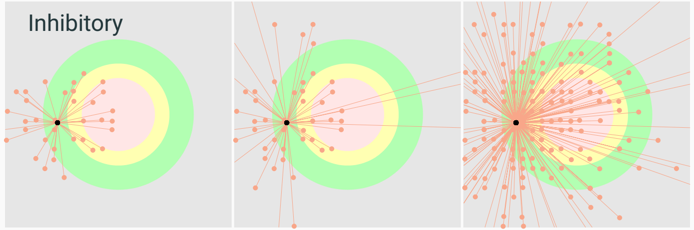
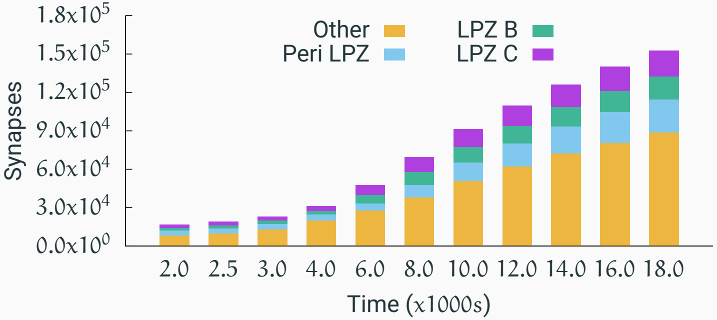


Reproduction of outgrowth of inhibitory projections





2020-06-02

Investigating structural plasticity in brain networks using computational modelling
└ Results: a few years later
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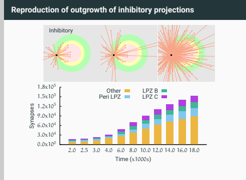
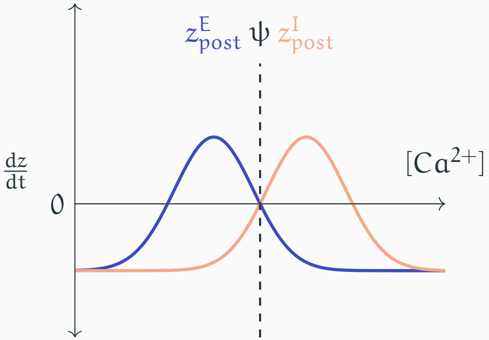


Resultant activity dependent growth rules: post-synaptic



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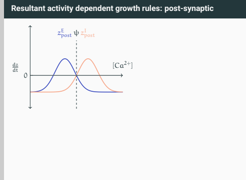

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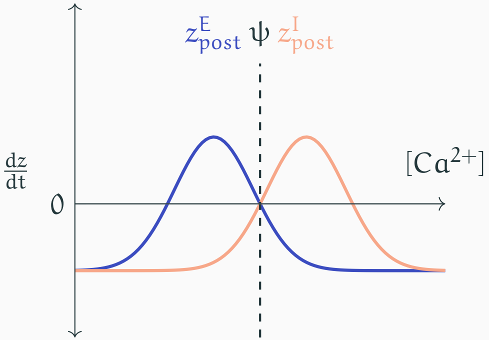

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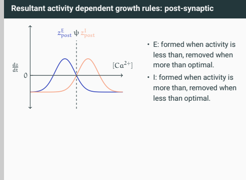

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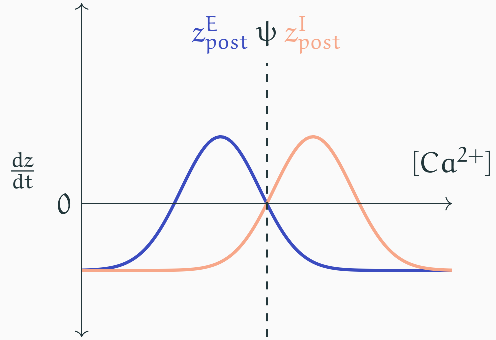

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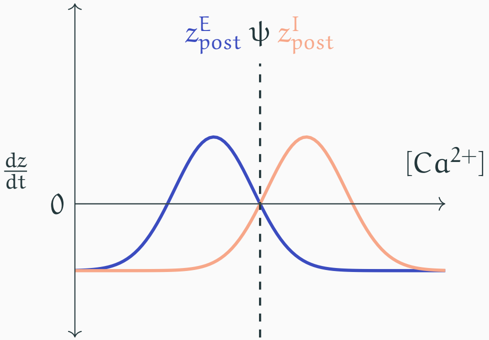

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[2] Knott, G. W. *et al.* Formation of dendritic spines with GABAergic synapses induced by whisker stimulation in adult mice. *Neuron* **34,** 265–273 (2002)

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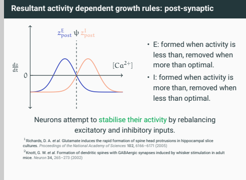

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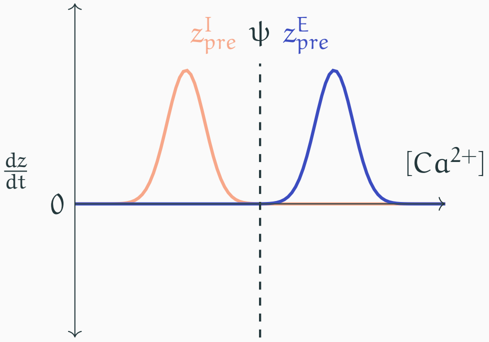

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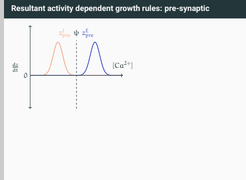

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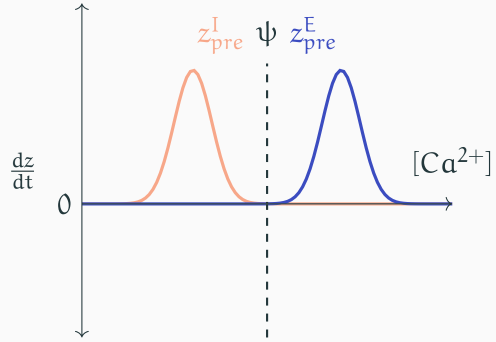

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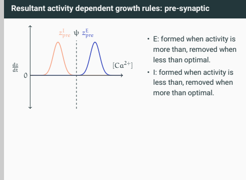

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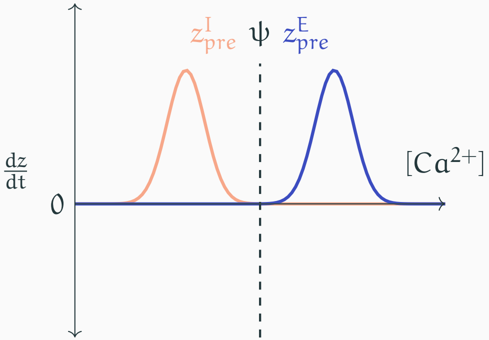

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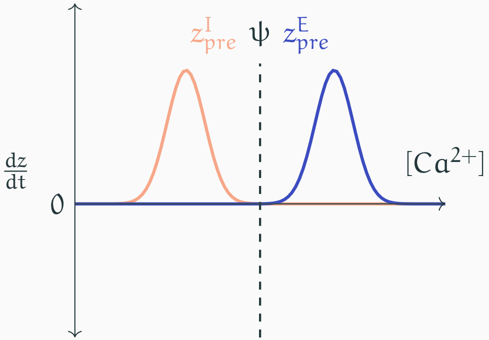

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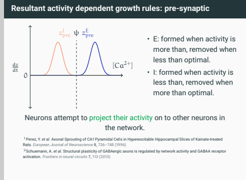

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