Theory/modelling club!

Structural plasticity and associative memory in balanced neural networks with spike-time dependent inhibitory plasticity

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Ankur Sinha

02/06/2020

Context: what and why?

Peripheral lesions: large scale reorganisation in the brain

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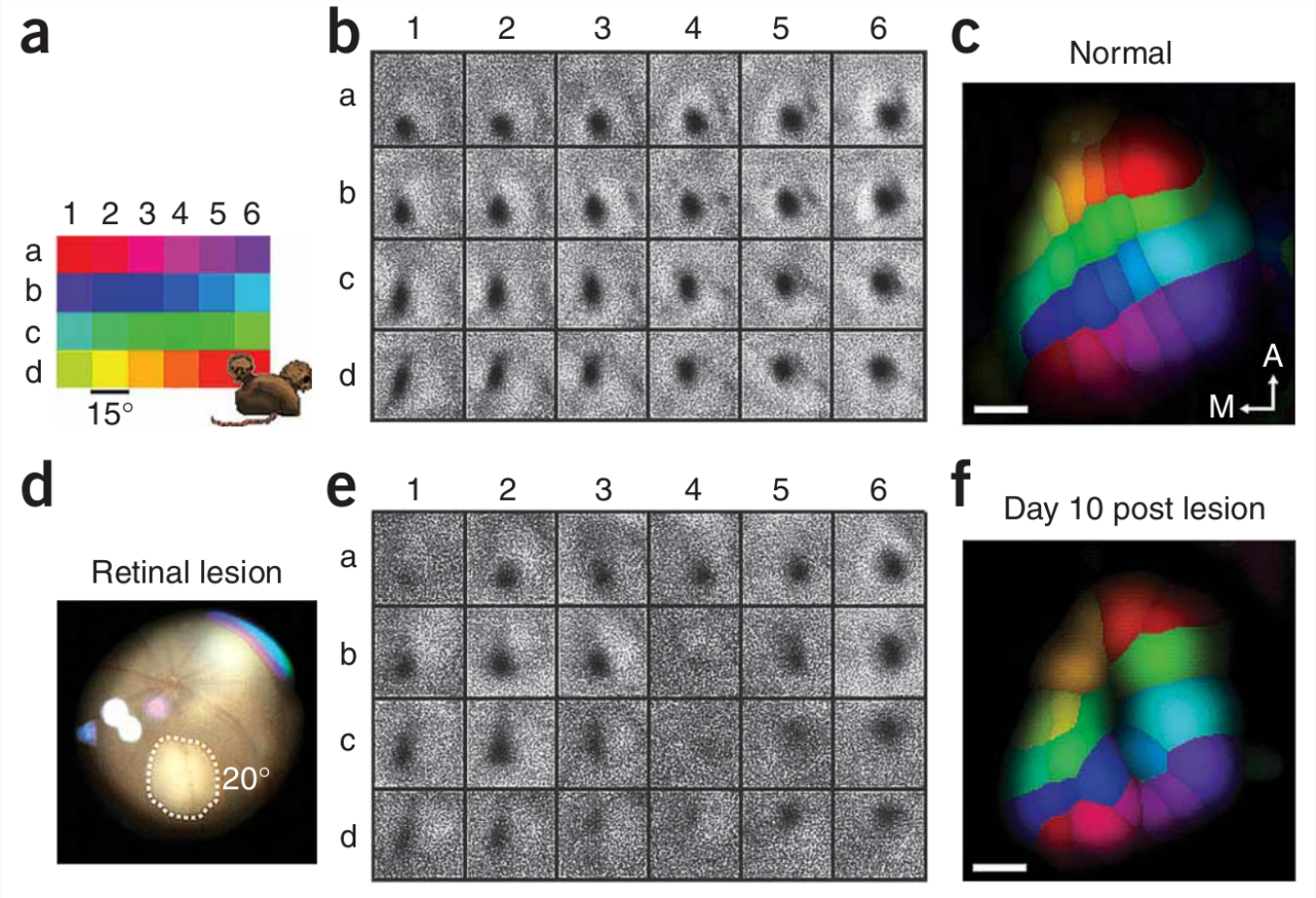
Example: Keck et al. 2008



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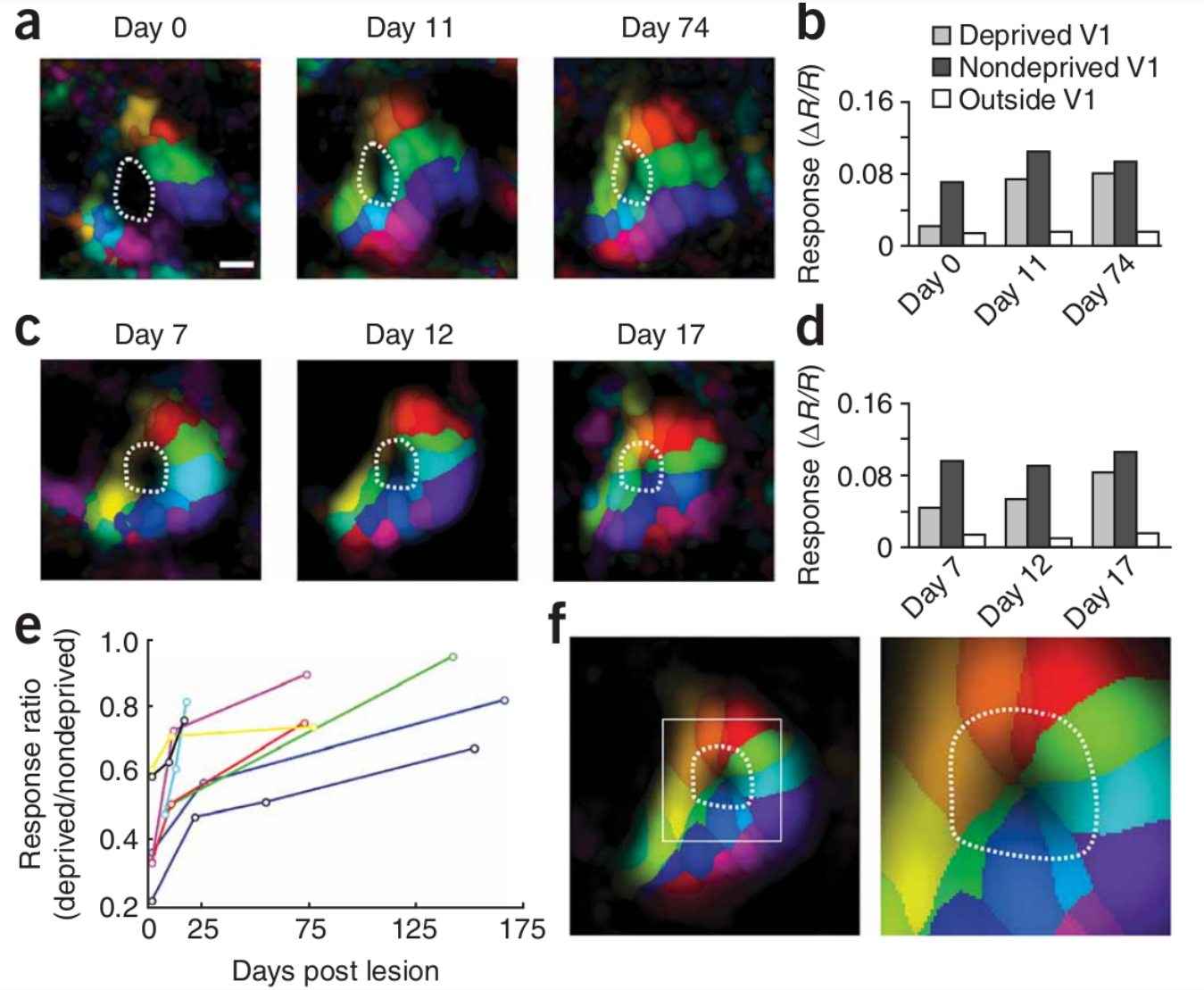
Example: Keck et al. 2008: II



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Features of repair

Table 1: Summary of review of literature on peripheral lesion experiments.

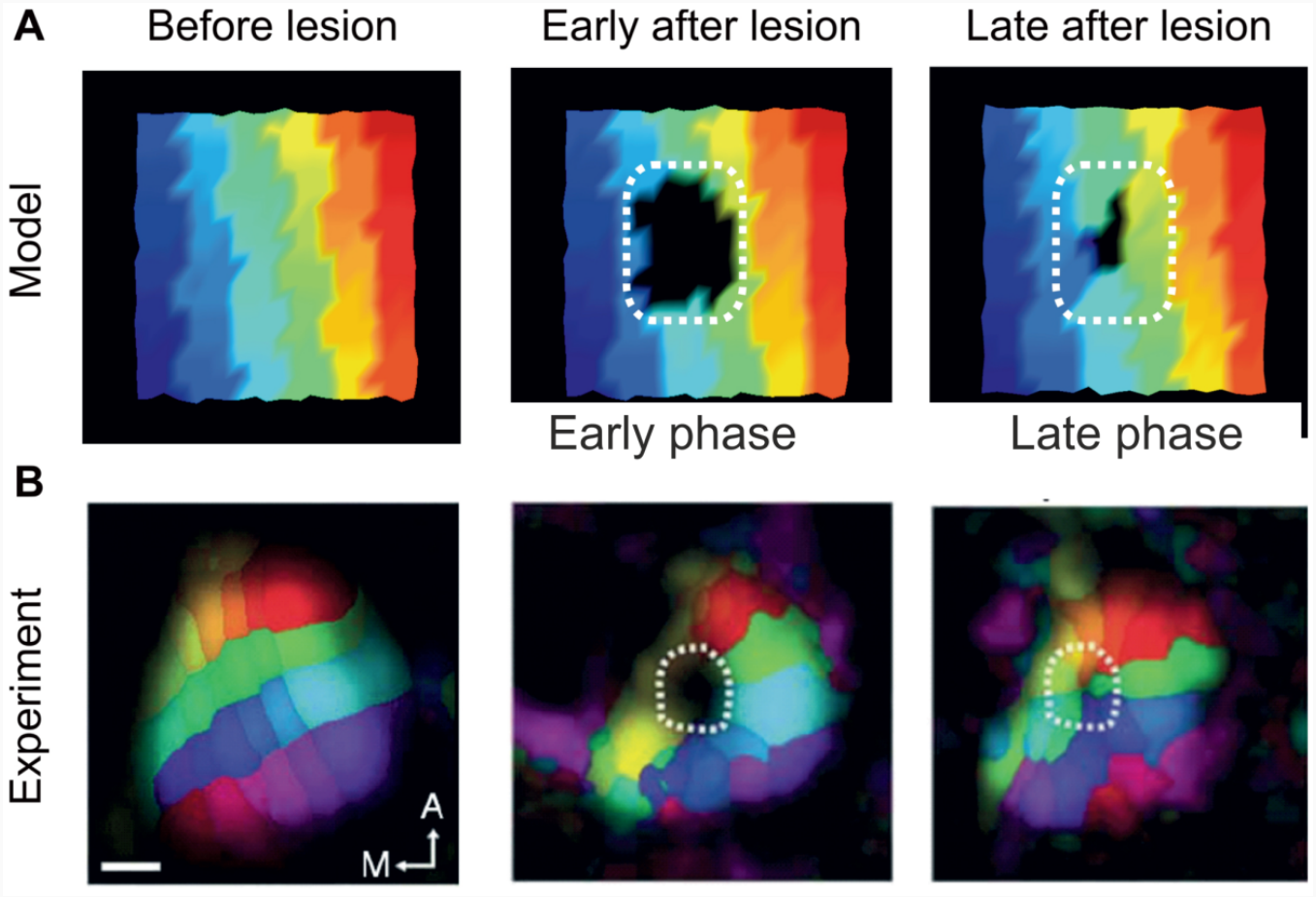
Observation	References
Recovery of neural response in deafferented regions. Inward restoration of activity in LPZ.	Rasmusson [1], Merzenich *et al.* [3], Calford & Tweedale [4], Heinen & Skavenski [5], Rajan *et al.* [6], Florence *et al.* [8], Gilbert & Wiesel [17], and Pons *et al.* [18].
Sprouting of axons into the LPZ.	Darian-Smith & Gilbert [7, 19].
Increase in density of dendritic spines on pyramidal cells in the LPZ.	Keck *et al.* [9].
Ingrowth of excitatory axonal terminals to the LPZ, resulting in increase in density of axonal terminals in the region.	Yamahachi *et al.* [20].
Loss in dendritic spines on inhibitory neurons receiving glutamatergic inputs in LPZ.	Keck *et al.* [10].
Reduction in inhibitory boutons in LPZ.	Keck *et al.* [10].
Disinhibition in LPZ after deafferentation.	Keck *et al.* [10] and Chen *et al.* [21].
Outgrowth of inhibitory axons from the LPZ.	Marik *et al.* [11, 14].

Research question

How does repair by structural plasticity affect the function of the brain network?

How?

Network dynamics during repair: Butz et al.



[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)

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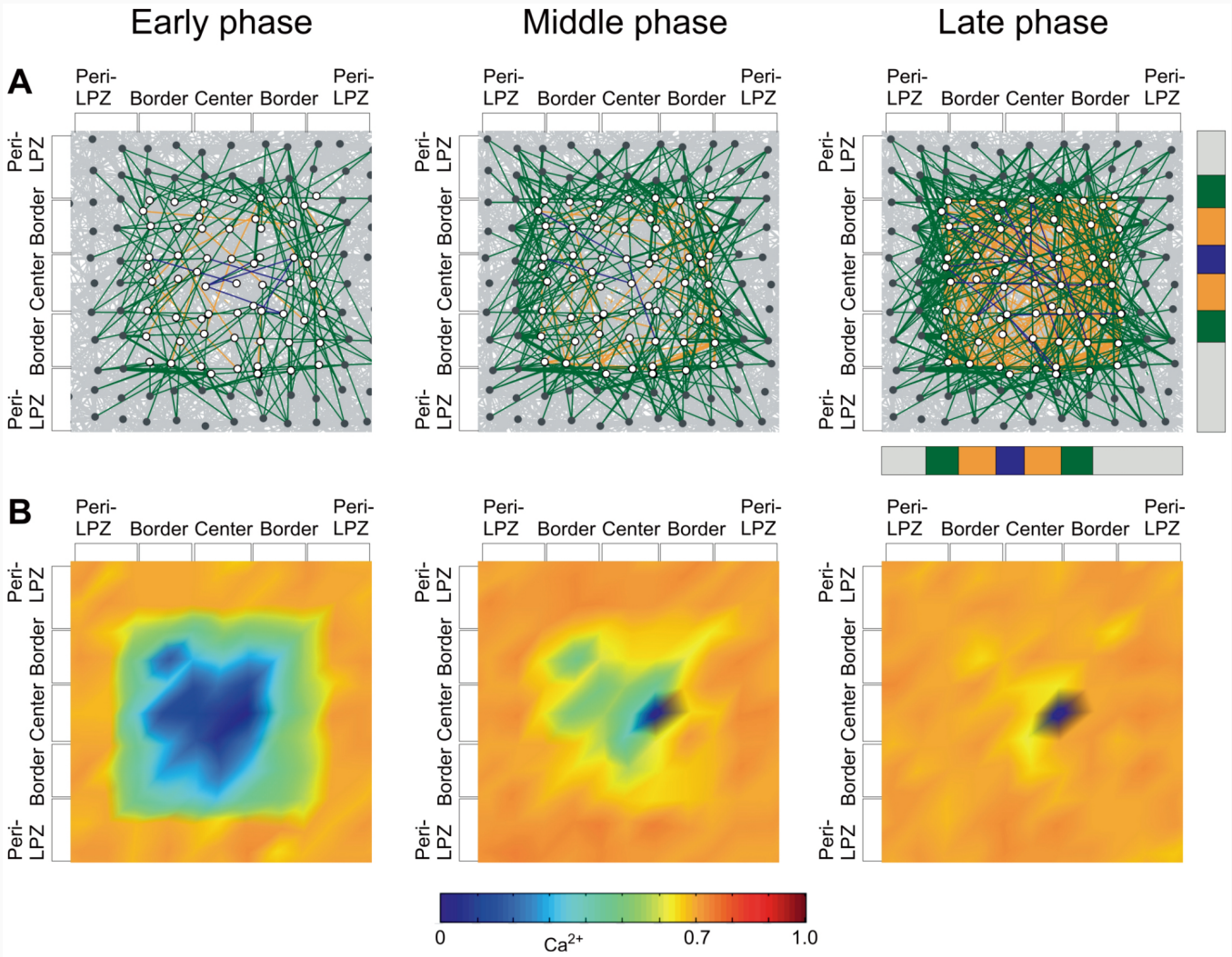

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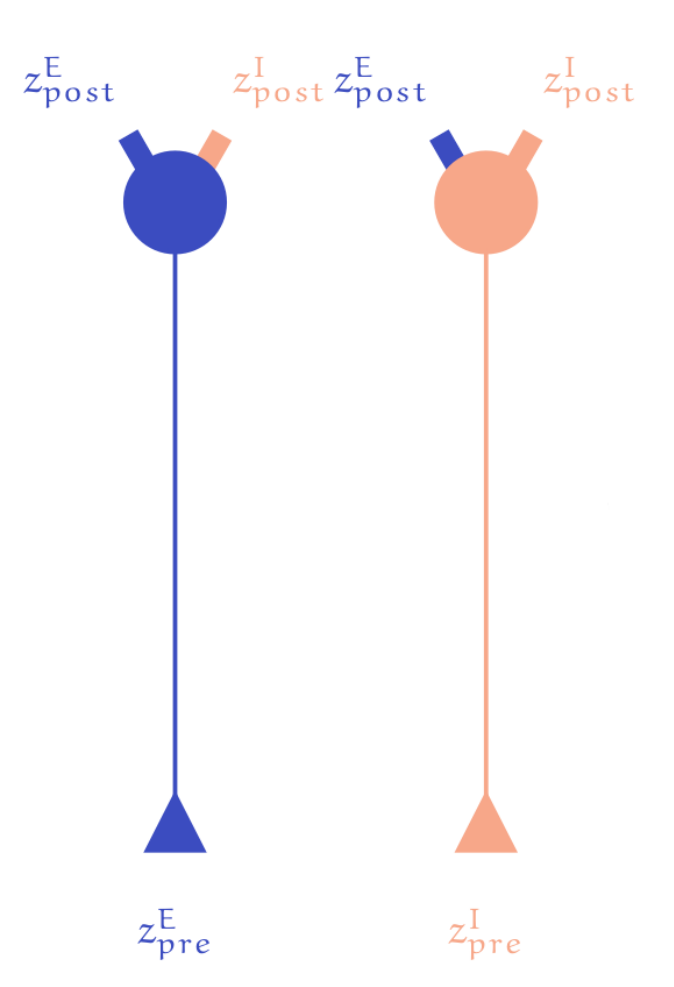
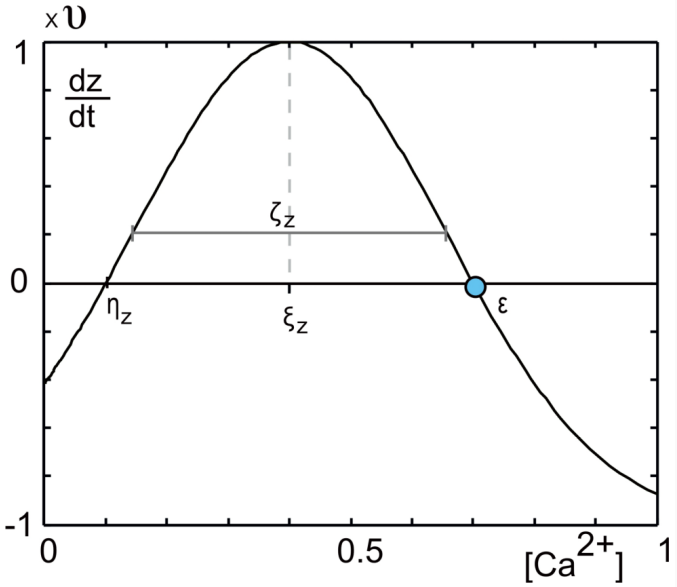
Butz2013: activity dependent homeostatic structural plasticity





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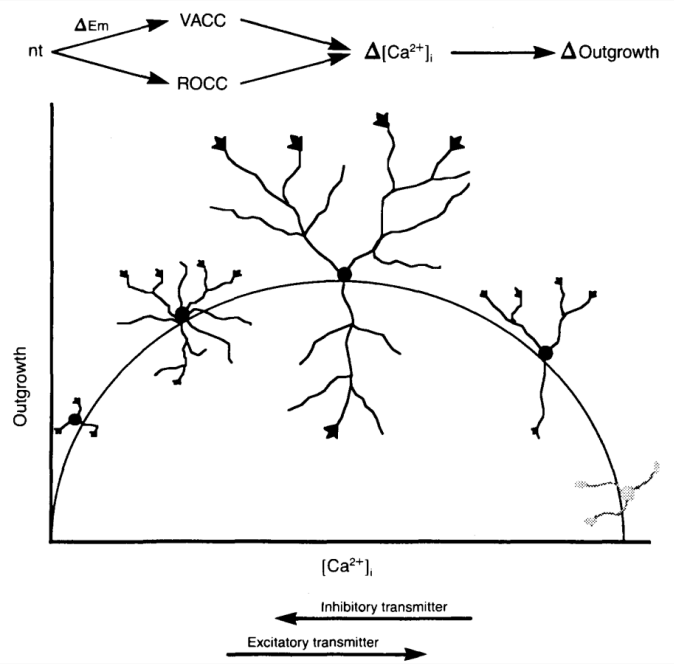

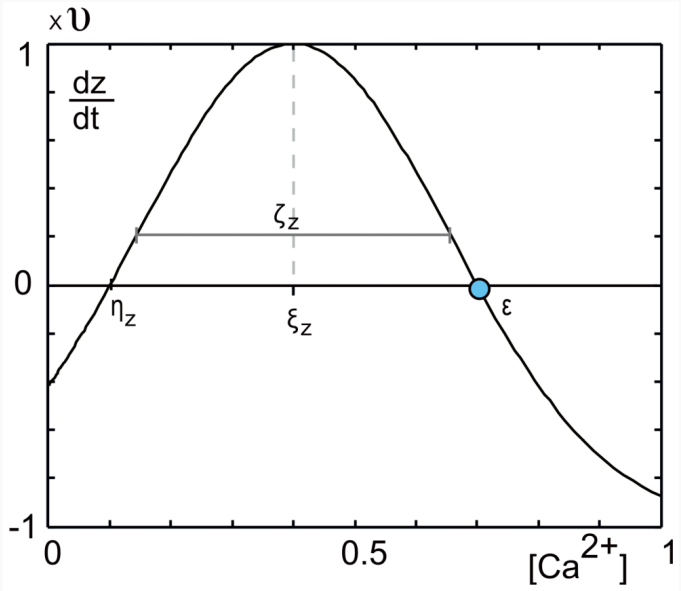

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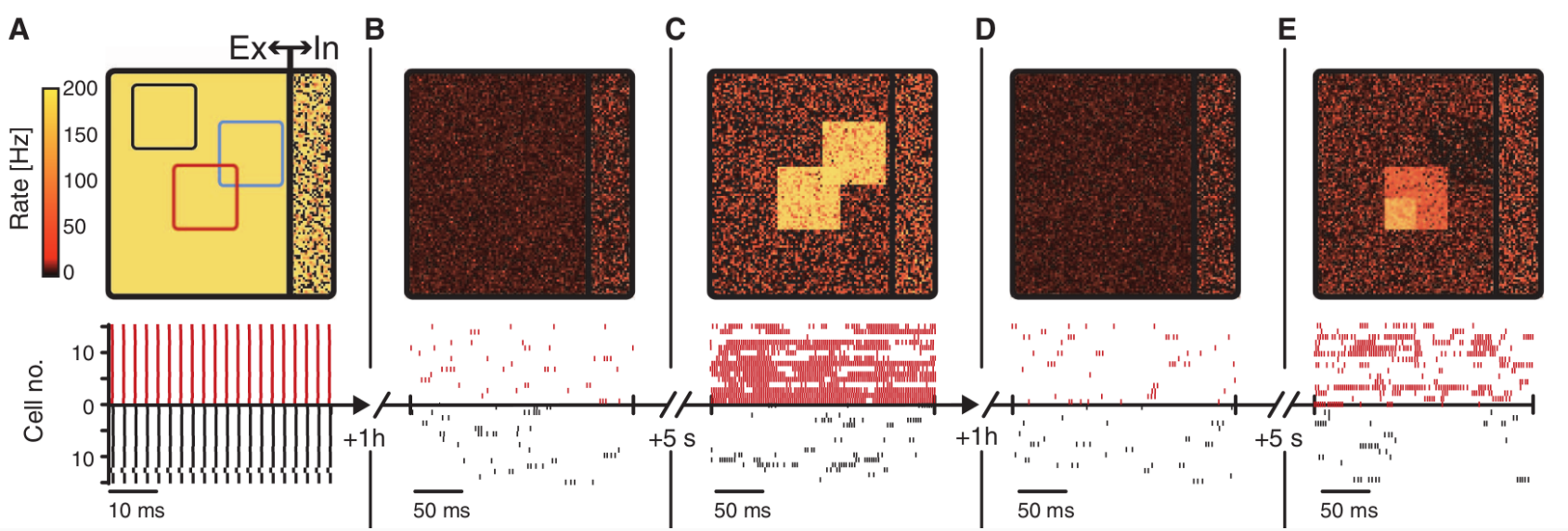
[3] Lipton, S. A. & Kater, S. B. Neurotransmitter regulation of neuronal outgrowth, plasticity and survival. *Trends in neurosciences* **12,** 265–270. ISSN: 0166-2236. http://www.sciencedirect.com/science/article/pii/016622368990026X (1989)

Re-implementation/investigation of Butz et al.'s model

Table 2: Summary of experimental observations reproduced in the model proposed by Butz & van Ooyen [22].

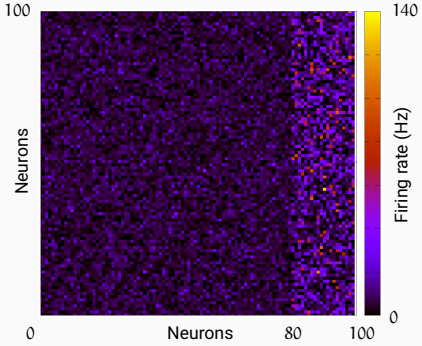
Experimental observation	Reproduced
Gradual inward restoration of activity in LPZ.	Yes.
Sprouting of axons into the LPZ.	Yes.
Increase in density of dendritic spines on pyramidal cells in the LPZ.	Yes.
Ingrowth of excitatory axonal terminals to the LPZ, resulting in increase in density of axonal terminals in the region.	Yes.
Loss in dendritic spines on inhibitory neurons receiving glutamatergic inputs in LPZ.	No—increase of all synaptic elements in neurons of LPZ.
Reduction in inhibitory boutons in LPZ.	No—increase in inhibitory axonal contacts also.
Disinhibition in LPZ after deafferentation.	No.
Outgrowth of inhibitory axons from the LPZ.	No—ingrowth of inhibitory axons also.

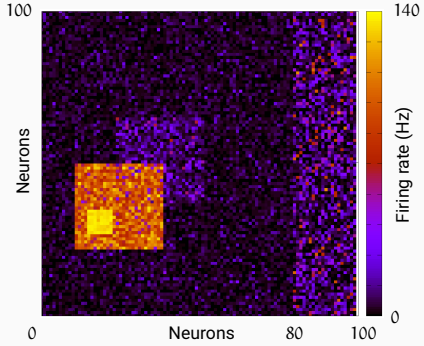
Proxy for network function: associative memory storage

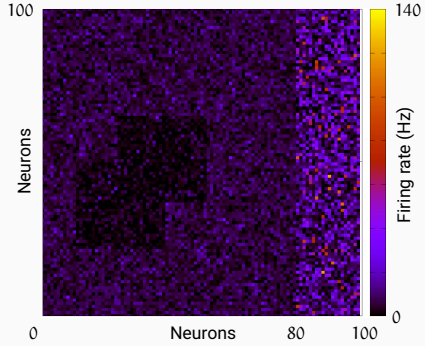


[4] Vogels, T. P. *et al.* Inhibitory plasticity balances excitation and inhibition in sensory pathways and memory networks. *Science* **334,** 1569–1573. http://www.sciencemag.org/content/334/6062/1569.short (2011)

Re-implementation/verification of associative memory model



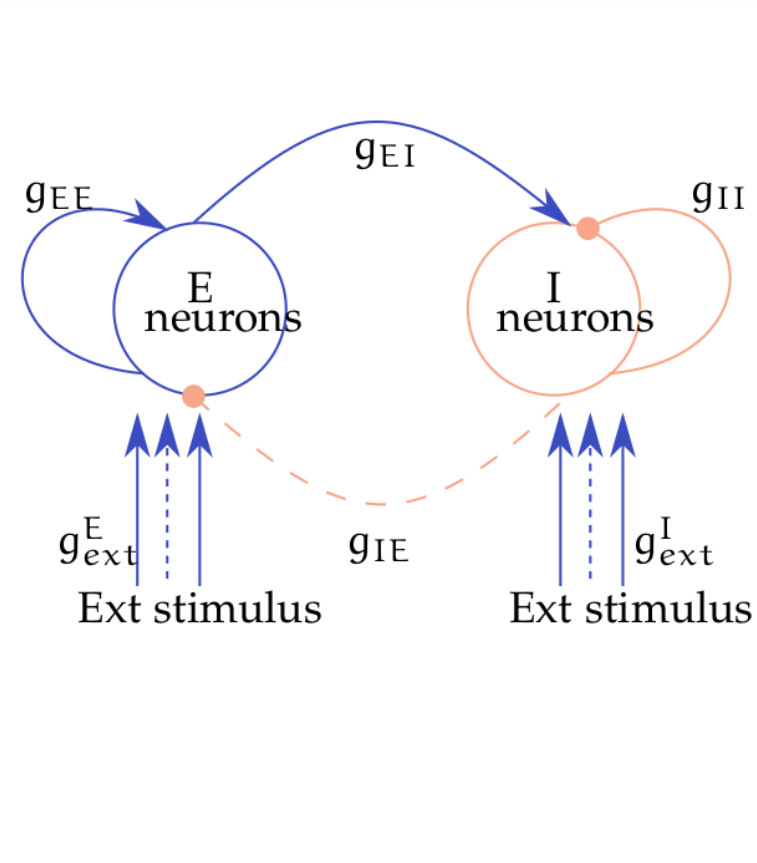


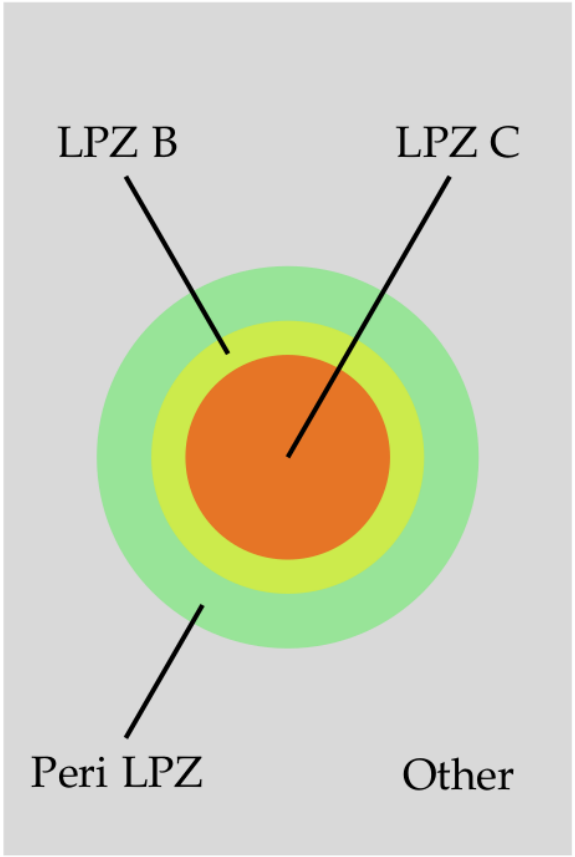


Expected research path

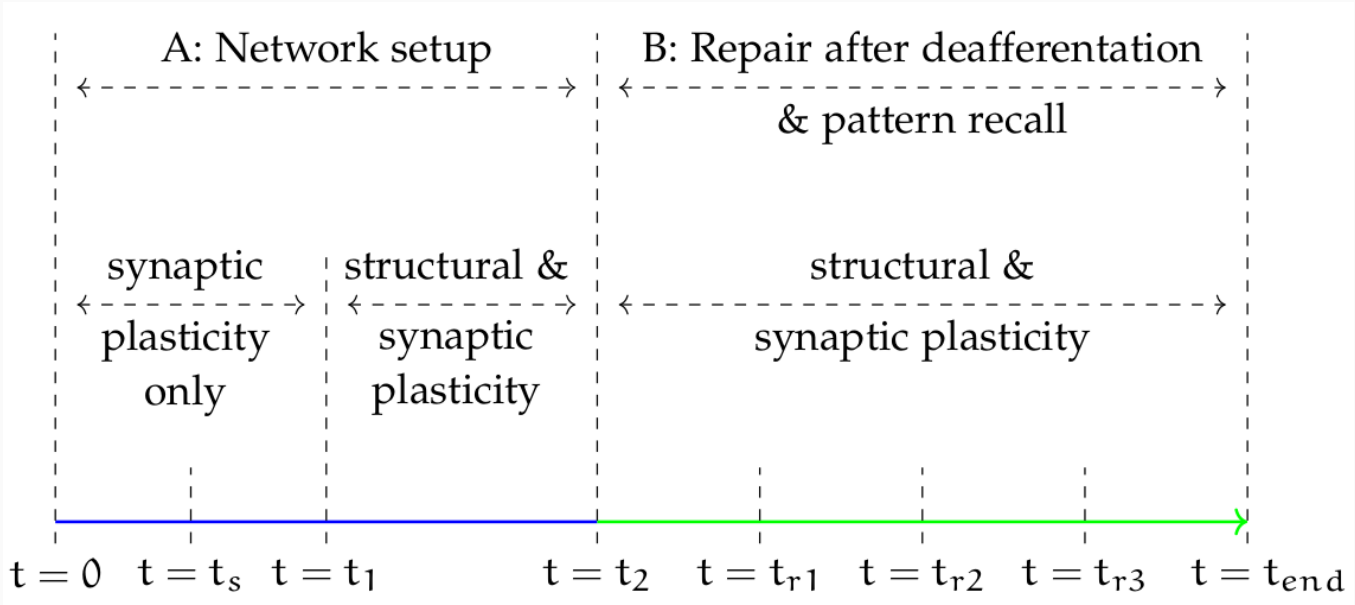
Apply Butz et al.'s model of structural plasticity to the Vogels-Sprekeler's cortical model, store associative memories, measure performance before, during, after repair.

Model schematic

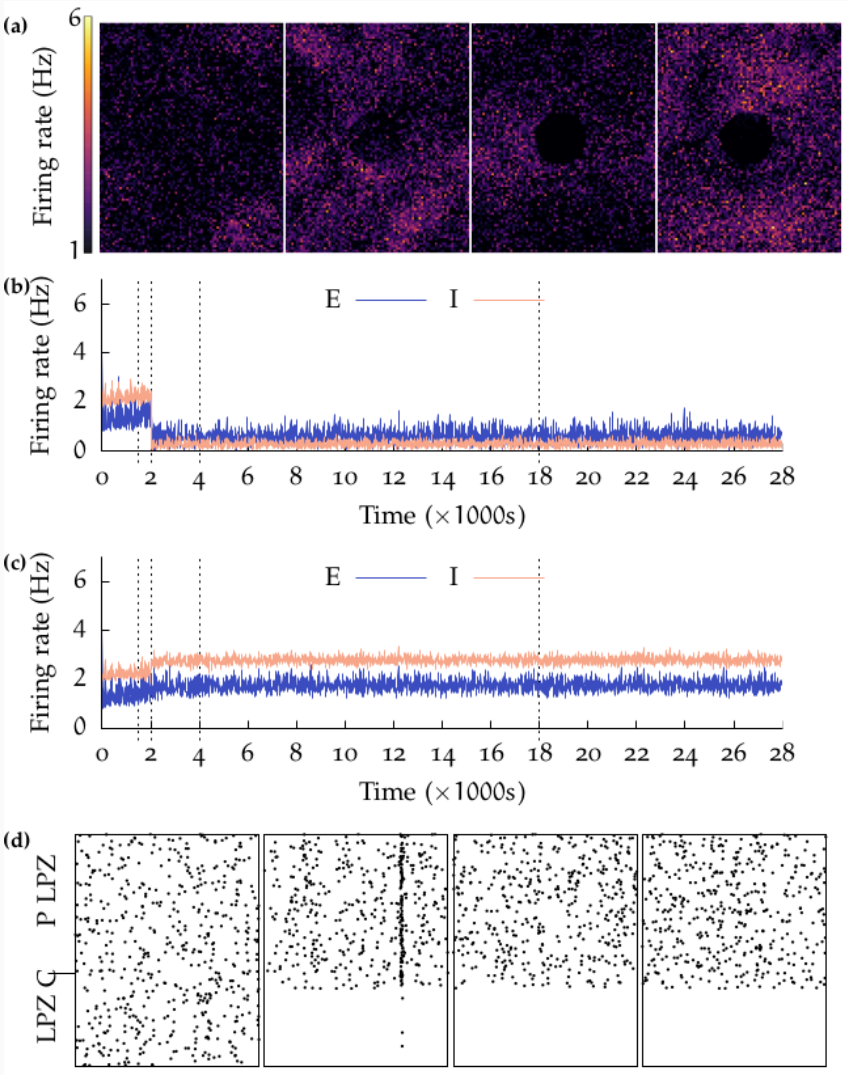




Simulation protocol



Effect of deafferentation on cortical model



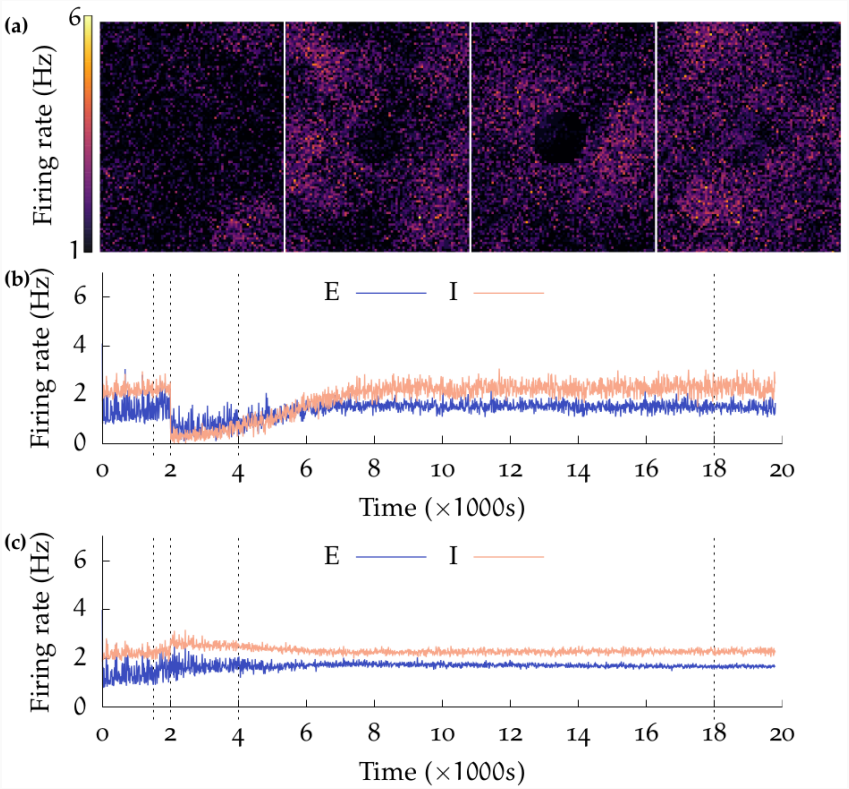
Rejection of Butz et al.'s growth curve hypothesis

If Butz et al.'s single growth curve for all neurites is correct, the increase in activity outside the LPZ as a result of deafferentation will cause:

- retraction of excitatory pre-synaptic elements outside the LPZ,
- retraction of inhibitory post-synaptic elements outside the LPZ.

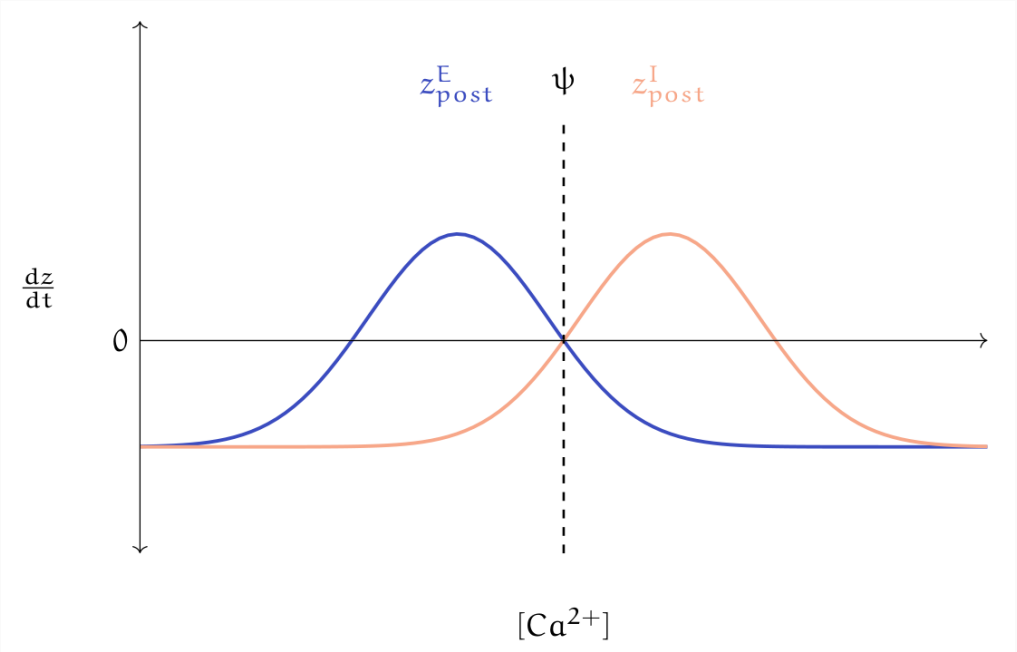
Results

New model of peripheral lesioning and repair in cortical network

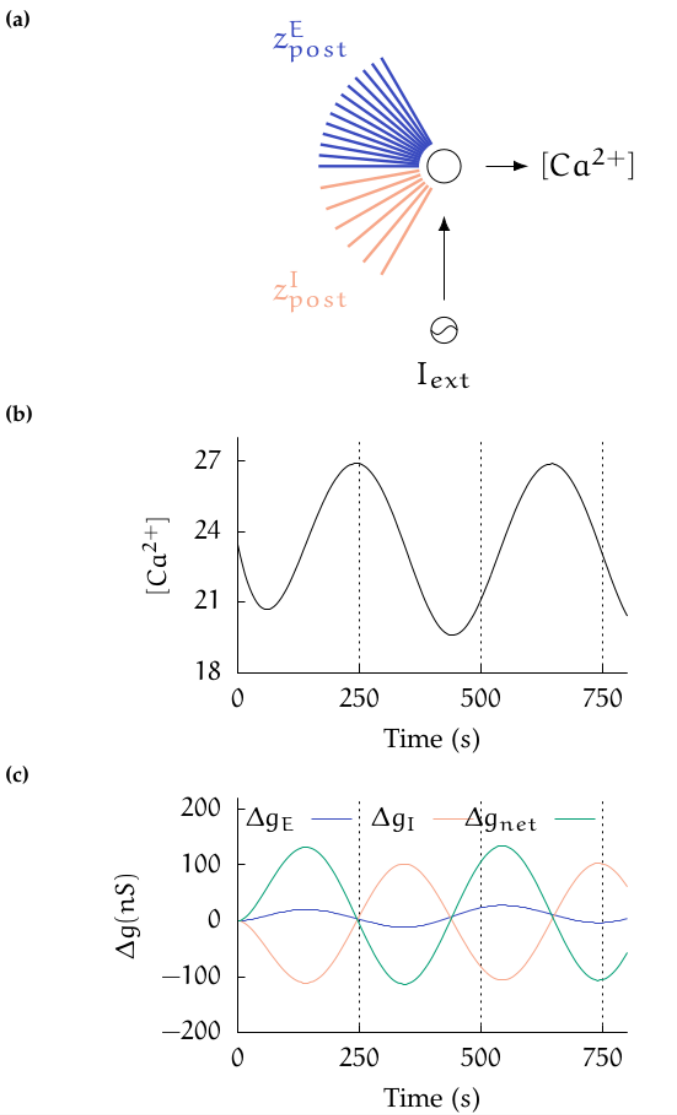


[5] Sinha, A. *et al.* Growth Rules for the Repair of Asynchronous Irregular Neuronal Networks after Peripheral Lesions. *bioRxiv*. eprint: https://www.biorxiv.org/content/early/2019/10/21/810846.full.pdf. https://www.biorxiv.org/content/early/2019/10/21/810846 (2019)

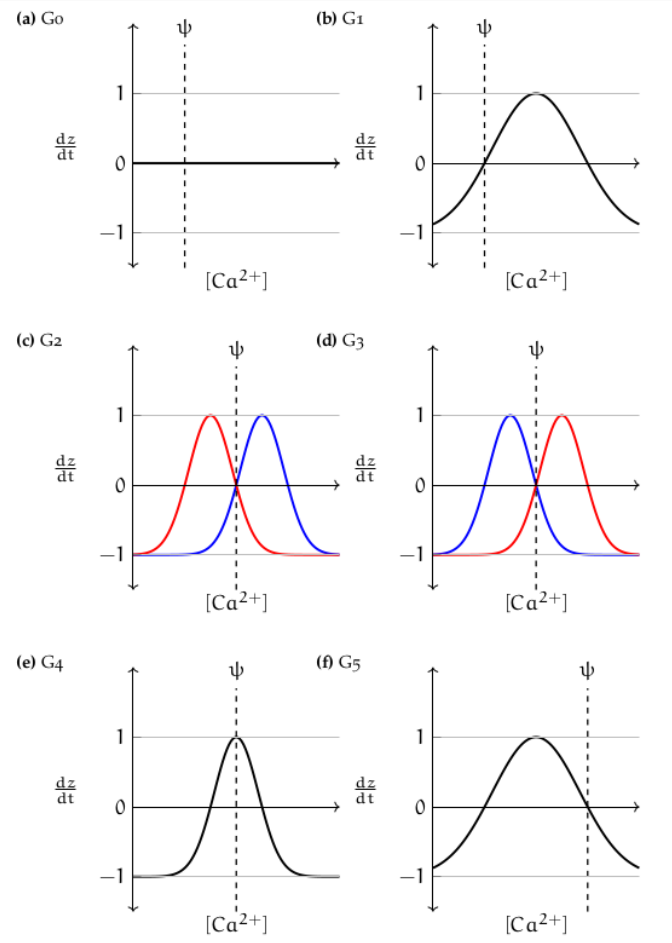
New growth curves for post-synaptic neurites



Stabilisation of individual neurons

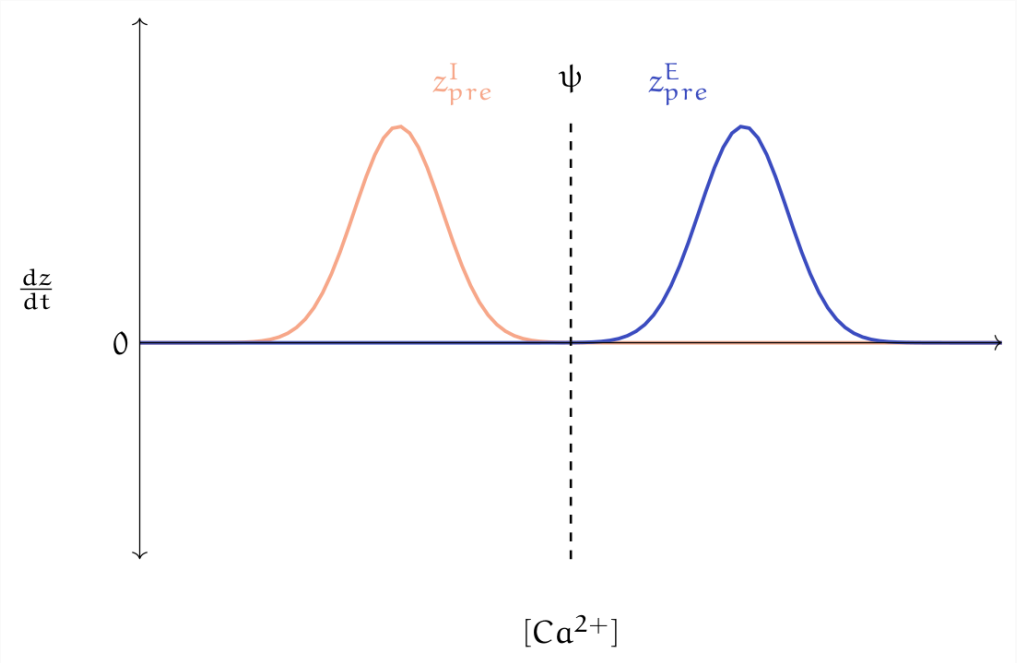


New growth curves for pre-synaptic neurites

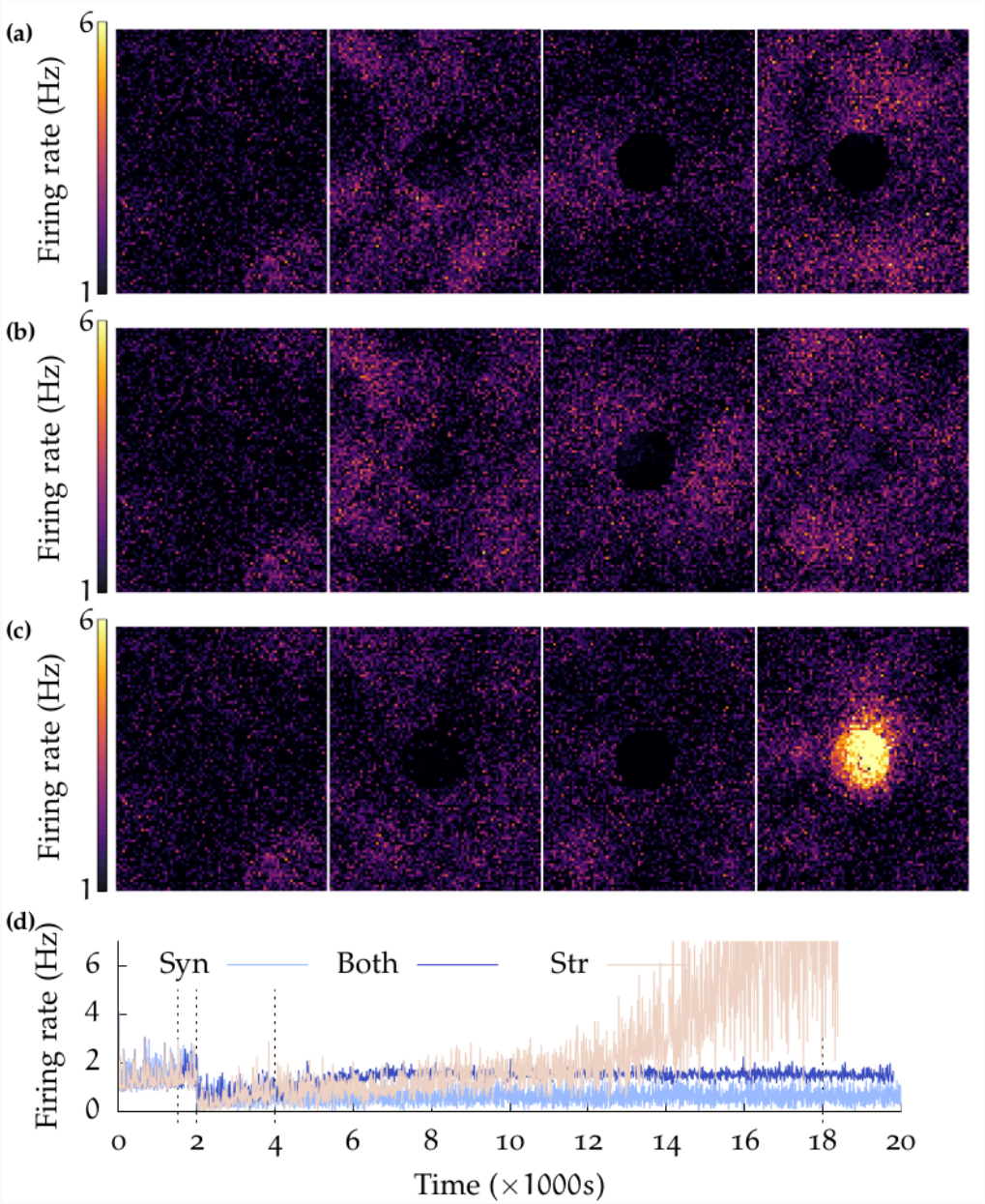


	G0	G1	G2	G3	G4	G5
Initially remains stable	Y	Y	Y	Y	N	Y
LPZ gains activity	Y	Y	Y	N	NA	N
Outside LPZ loses activity	Y	Y	Y	NA	NA	NA
Returns to balanced state	N	N	Y	NA	NA	NA
LPZ B restores before LPZ C	NA	NA	Y	NA	NA	NA
Ingrowth of excitatory projections	NA	NA	Y	NA	NA	NA
Outgrowth of inhibitory projections	NA	NA	Y	NA	NA	NA
Disinhibition in LPZ	NA	NA	Y	NA	NA	NA

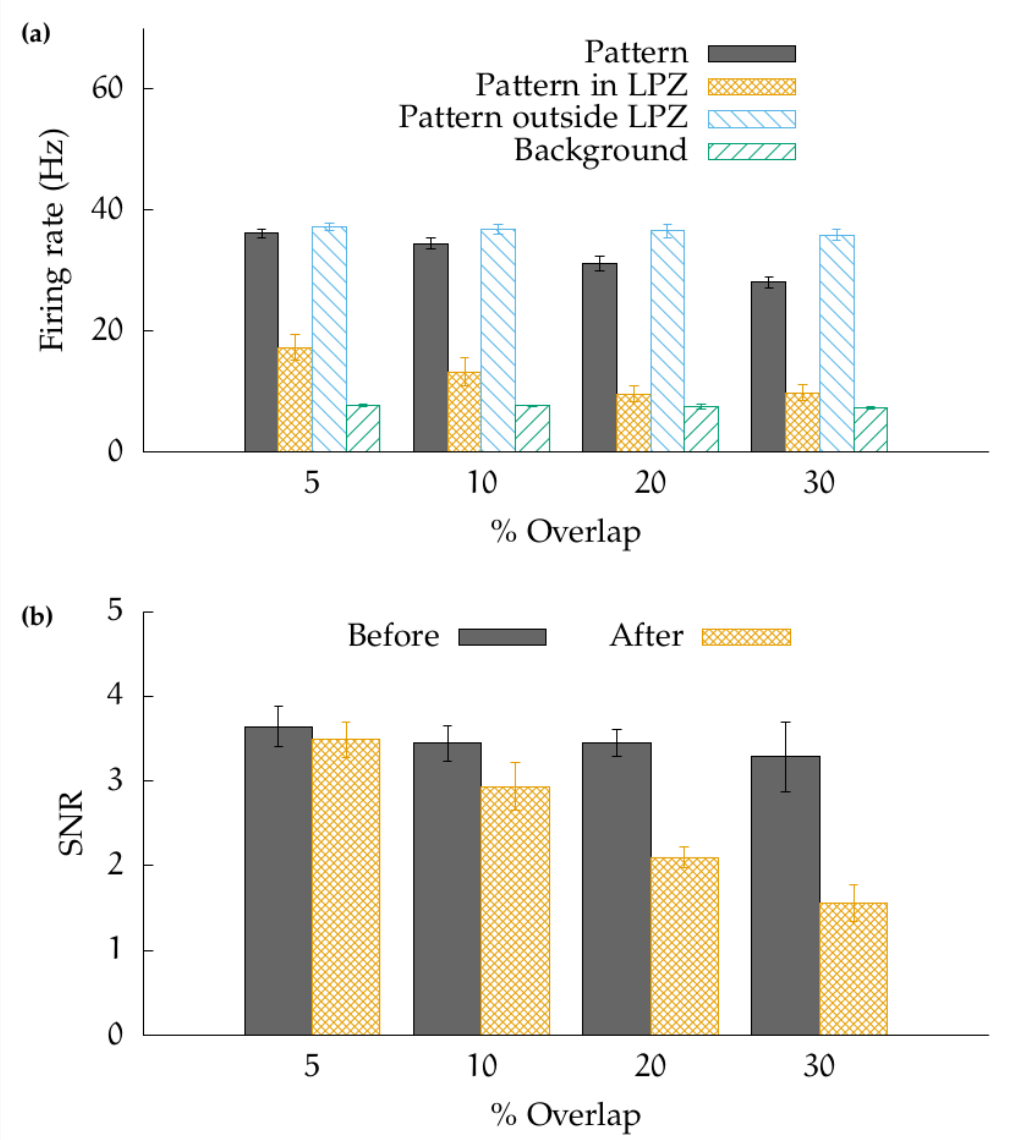
New growth curves for pre-synaptic neurites



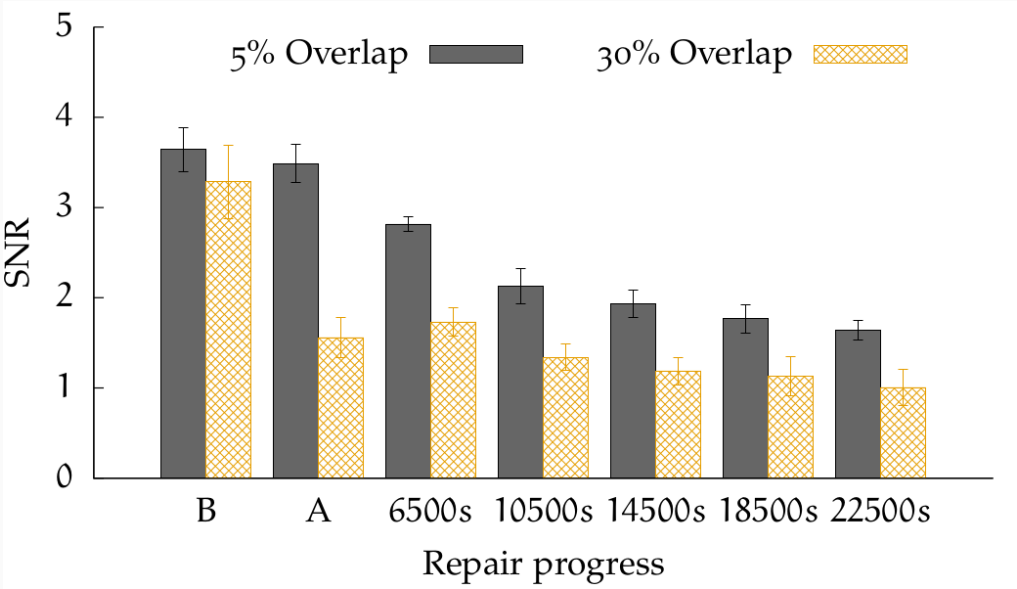
Both synaptic and structural plasticity are necessary for repair



Associative memory performance after deafferentation (no repair)



Associative memory performance during repair



Conclusions

- New model of peripheral lesioning and repair in a balanced cortical network model.
- New activity dependent growth curves for all types of neurites.
- Lack of AI firing characteristics in the LPZ post-repair.
- Deterioration in associative memory recall performance after deafferentation even with deafferentation.

Bibliography i

Rasmusson, D. D. Reorganization of raccoon somatosensory cortex following removal of the fifth digit. *Journal of Comparative Neurology* **205,** 313–326 (1982).

Wall, J. T. & Cusick, C. G. Cutaneous responsiveness in primary somatosensory (SI) hindpaw cortex before and after partial hindpaw deafferentation in adult rats. *The journal of neuroscience* **4,** 1499–1515 (1984).

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Bibliography ii

Florence, S. L., Taub, H. B. & Kaas, J. H. Large-scale sprouting of cortical connections after peripheral injury in adult macaque monkeys. *Science* **282,** 1117–1121 (1998).

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Bibliography iii

Marik, S. A., Yamahachi, H., McManus, J. N. J., Szabo, G. & Gilbert, C. D. Axonal dynamics of excitatory and inhibitory neurons in somatosensory cortex. *PLoS Biology* **8,** e1000395 (2010).

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Gilbert, C. D. & Wiesel, T. N. Receptive field dynamics in adult primary visual cortex. *Nature* **356,** 150–152 (1992).

Pons, T. P. *et al.* Massive cortical reorganization after sensory deafferentation in adult macaques. *Science* **252,** 1857–1860 (1991).

Darian-Smith, C. & Gilbert, C. D. Topographic reorganization in the striate cortex of the adult cat and monkey is cortically mediated. *The journal of neuroscience* **15,** 1631–1647 (1995).

Yamahachi, H., Marik, S. A., McManus, J. N. J., Denk, W. & Gilbert, C. D. Rapid axonal sprouting and pruning accompany functional reorganization in primary visual cortex. *Neuron* **64,** 719–729 (2009).

Bibliography iv

Chen, J. L. *et al.* Structural basis for the role of inhibition in facilitating adult brain plasticity. *Nature neuroscience* **14,** 587–594 (2011).

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).

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