Theory/modelling club!

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

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02/06/2020

Context: what and why?

Peripheral lesions: large scale reorganisation in the brain

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

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- 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)
- Merzenich, M. M. *et al.* Somatosensory cortical map changes following digit amputation in adult monkeys. *Journal of Comparative Neurology* **224,** 591–605 (1984)
- Calford, M. B. & Tweedale, R. Immediate and chronic changes in responses of somatosensory cortex in adult flying-fox after digit amputation. *Nature* **332,** 446–448 (1988)
- Heinen, S. J. & Skavenski, A. A. Recovery of visual responses in foveal V1 neurons following bilateral foveal lesions in adult monkey. *Experimental Brain Research* **83,** 670–674 (1991)
- Rajan, R. *et al.* Effect of unilateral partial cochlear lesions in adult cats on the representation of lesioned and unlesioned cochleas in primary auditory cortex. *Journal of Comparative Neurology* **338,** 17–49 (1993)

Imaging confirms structural plasticity in these experiments

- Darian-Smith, C. & Gilbert, C. D. Axonal sprouting accompanies functional reorganization in adult cat striate cortex. *Nature* **368,** 737–740 (1994)

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- Florence, S. L. *et al.* Large-scale sprouting of cortical connections after peripheral injury in adult macaque monkeys. *Science* **282,** 1117–1121 (1998)
- Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)
- Keck, T. *et al.* Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex. *Neuron* **71,** 869–882. ISSN: 0896-6273. `http://www.sciencedirect.com/science/article/pii/S0896627311005642` (2011)
- Marik, S. A. *et al.* Large-scale axonal reorganization of inhibitory neurons following retinal lesions. *Journal of Neuroscience* **34,** 1625–1632 (2014)

Also confirms structural plasticity in the unlesioned adult brain

- Holtmaat, A. J. G. D. *et al.* Transient and Persistent Dendritic Spines in the Neocortex In Vivo. *Neuron* **45,** 279–291. ISSN: 0896-6273. `http://www.sciencedirect.com/science/article/pii/S0896627305000048` (2005)

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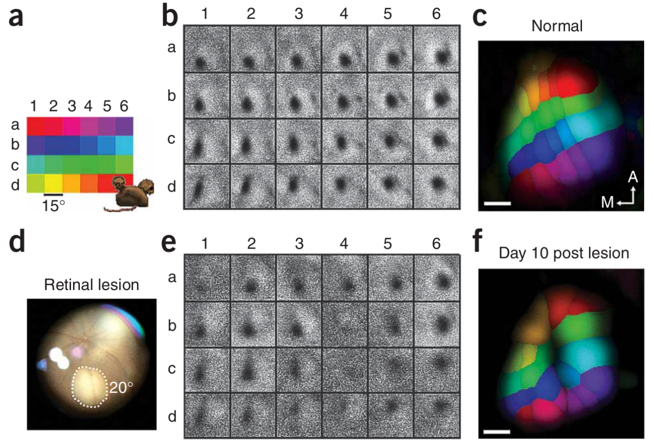
- Stettler, D. D. *et al.* Axons and Synaptic Boutons Are Highly Dynamic in Adult Visual Cortex. *Neuron* **49,** 877–887. ISSN: 0896-6273. http://www.sciencedirect.com/science/article/pii/S0896627306001358 (2006)
- Marik, S. A. *et al.* Axonal dynamics of excitatory and inhibitory neurons in somatosensory cortex. *PLoS Biology* **8,** e1000395 (2010)
- Chen, J. L. *et al.* Clustered dynamics of inhibitory synapses and dendritic spines in the adult neocortex. *Neuron* **74,** 361–373 (2012)
- Villa, K. L. *et al.* Inhibitory Synapses Are Repeatedly Assembled and Removed at Persistent Sites In Vivo. *Neuron* **89,** 756–769. ISSN: 1097-4199 (4 2016)

Example: Keck et al. 2008



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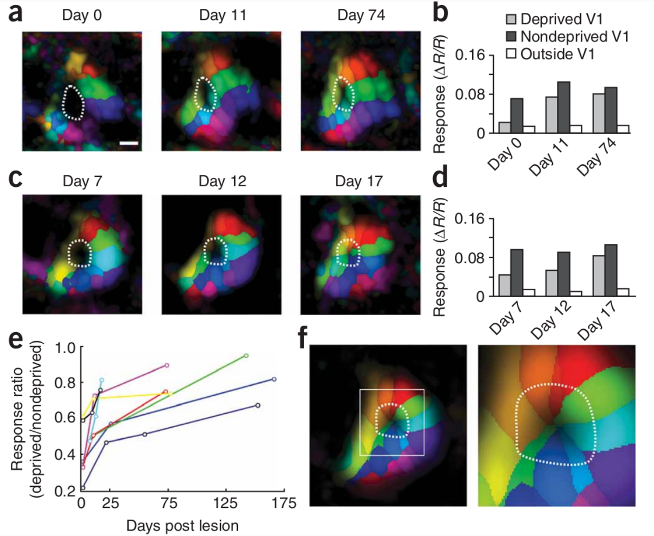
Example: Keck et al. 2008: II



[1] Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)

Features of repair

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

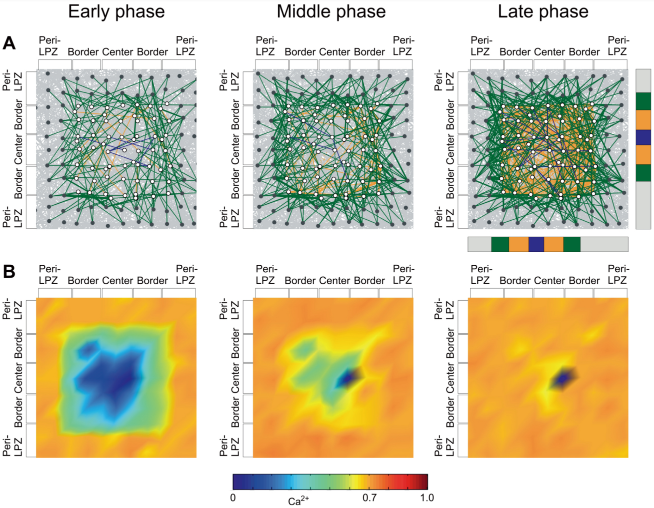
Observation	References
Recovery of neural response in deafferented regions. Inward restoration of activity in LPZ.	Rasmusson [1], Merzenich *et al.* [3], Calford & Tweedale [4], Heinen & Skavenski [5], Rajan *et al.* [6], Florence *et al.* [8], Gilbert & Wiesel [17], and Pons *et al.* [18].
Sprouting 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?

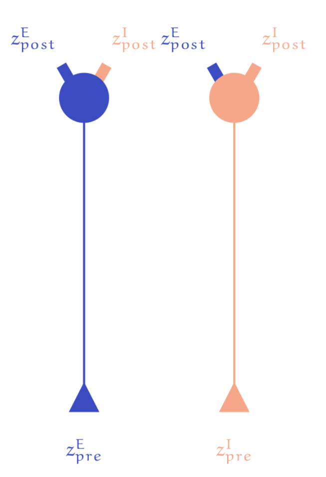
How?

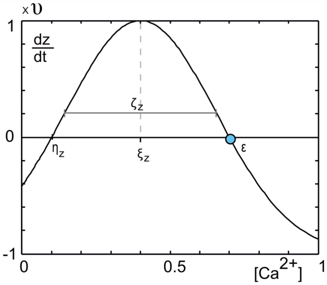
Network dynamics during repair: Butz et al.



[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)

Butz2013: activity dependent homeostatic structural plasticity





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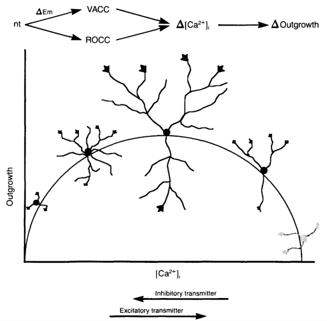

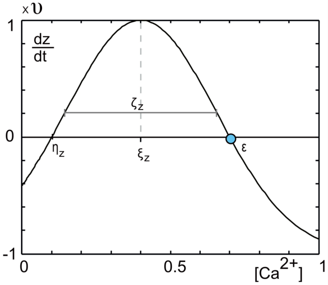

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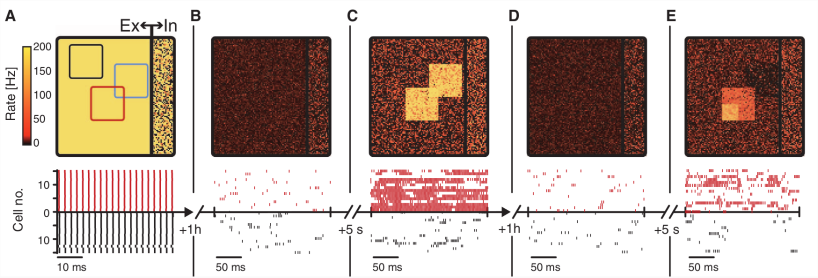
[3] Lipton, S. A. & Kater, S. B. Neurotransmitter regulation of neuronal outgrowth, plasticity and survival. *Trends in neurosciences* **12,** 265–270. ISSN: 0166-2236. http://www.sciencedirect.com/science/article/pii/016622368990026X (1989)

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].

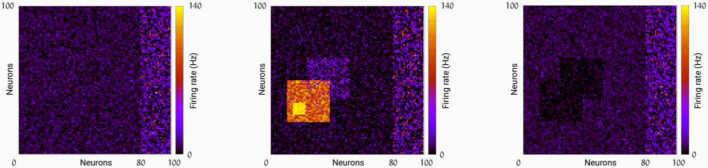
Experimental observation	**Reproduced**
Gradual inward restoration of activity in LPZ.	Yes.
Sprouting of axons into the LPZ.	Yes.
Increase in density of dendritic spines on pyramidal cells in the LPZ.	Yes.
Ingrowth of excitatory axonal terminals to the LPZ, resulting in increase in density of axonal 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)

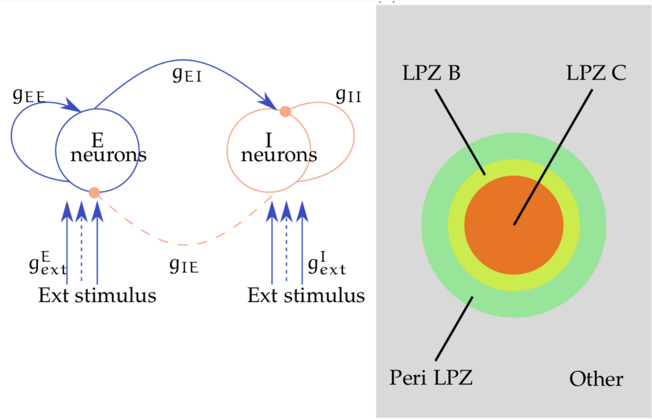
Re-implementation/verification of associative memory model



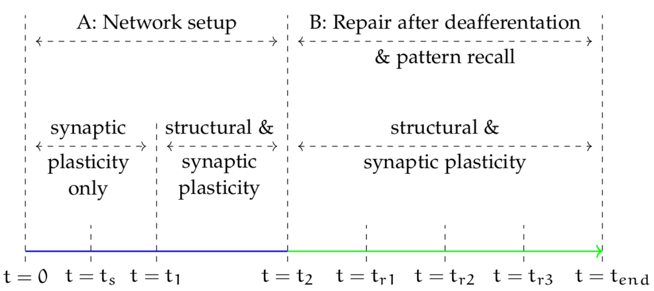
Expected research path

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.

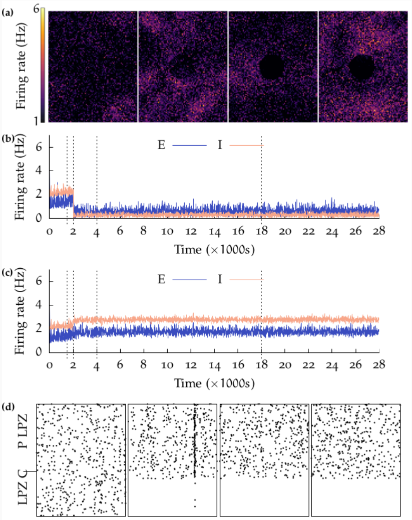
Model schematic



Simulation protocol



Effect of deafferentation on cortical model



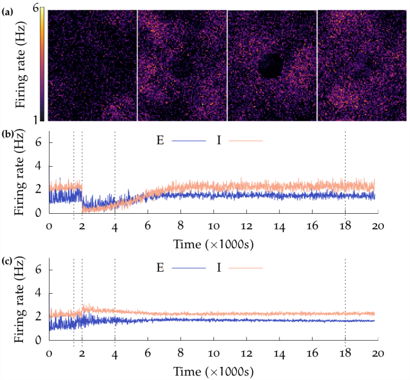
Rejection of Butz et al.'s growth curve hypothesis

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.

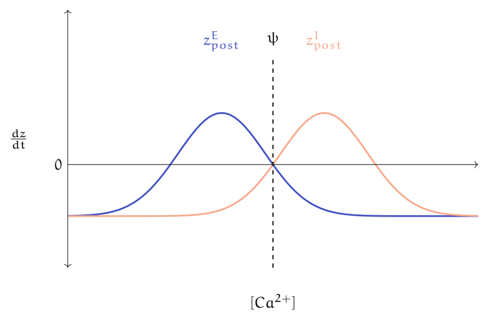
Results

New model of peripheral lesioning and repair in cortical network

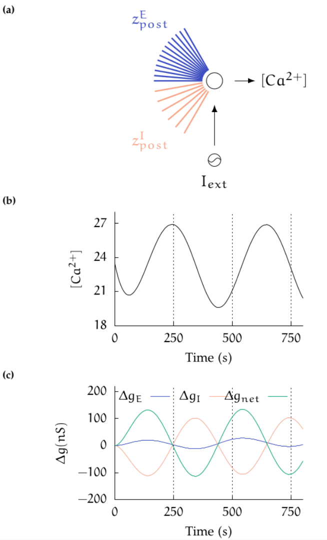


[5] Sinha, A. *et al.* Growth Rules for the Repair of Asynchronous Irregular Neuronal Networks after Peripheral Lesions. *bioRxiv.* eprint: https://www.biorxiv.org/content/early/2019/10/21/810846.full.pdf. https://www.biorxiv.org/content/early/2019/10/21/810846 (2019)

New growth curves for post-synaptic neurites



Stabilisation of individual neurons



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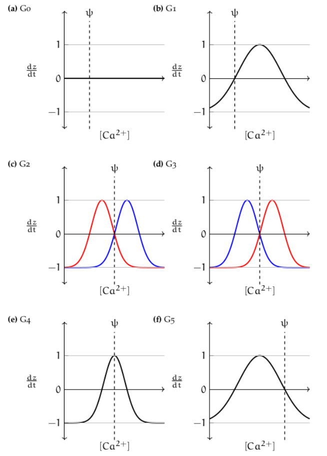
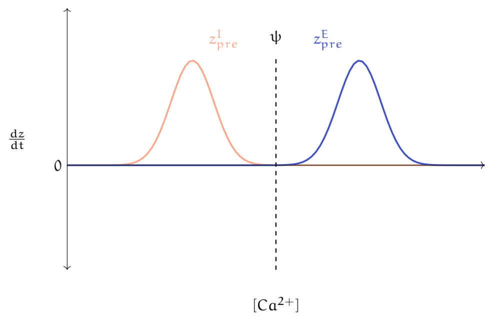
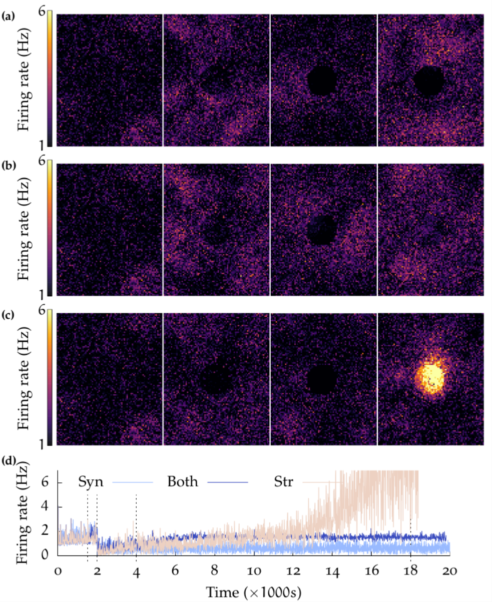


	G0	G1	G2	G3	G4	G5
Initially remains stable	Y	Y	Y	Y	N	Y
LPZ gains activity	Y	Y	Y	N	NA	N
Outside LPZ loses activity	Y	Y	Y	NA	NA	NA
Returns to balanced state	N	N	Y	NA	NA	NA
LPZ B restores before LPZ C	NA	NA	Y	NA	NA	NA
Ingrowth of excitatory projections	NA	NA	Y	NA	NA	NA
Outgrowth of inhibitory projections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

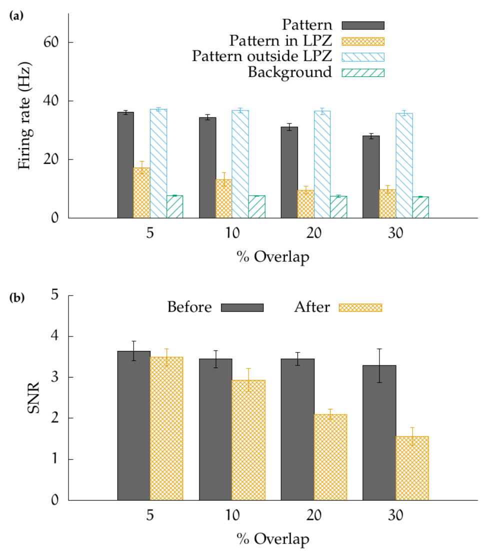
New growth curves for pre-synaptic neurites



Both synaptic and structural plasticity are necessary for repair



Associative memory performance after deafferentation (no repair)



Associative memory performance during repair