Investigating the activity dependent dynamics of synaptic structures using biologically realistic modelling of peripheral lesion experiments

Discussion of my Ph.D. research

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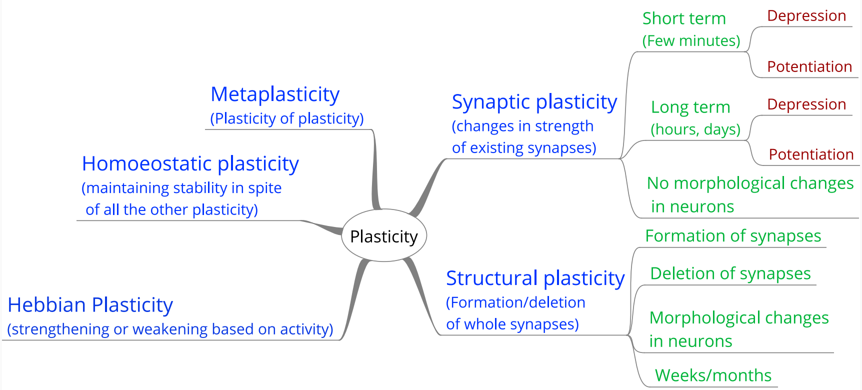
Context

Plasticity while maintaining stability



Synaptic structures are dynamic in the adult brain

1. Chen, J. L. *et al.* Structural basis for the role of inhibition in facilitating adult brain plasticity. *Nature neuroscience* **14,** 587–594 (2011)
2. Marik, S. A. *et al.* Axonal dynamics of excitatory and inhibitory neurons in somatosensory cortex. *PLoS Biology* **8,** e1000395 (2010)
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4. Stettler, D. D. *et al.* Axons and Synaptic Boutons Are Highly Dynamic in Adult Visual Cortex. *Neuron* **49,** 877–887. ISSN: 0896-6273 (2006)
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7. Chen, J. L. *et al.* Clustered dynamics of inhibitory synapses and dendritic spines in the adult neocortex. *Neuron* **74,** 361–373 (2012)
8. Trachtenberg, J. T. *et al.* Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature* **420,** 788–794 (2002)
9. 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 Feb. 2016)

Evidence of homeostatic structural plasticity: lesion studies

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5. Allard, T. *et al.* Reorganization of somatosensory area 3b representations in adult owl monkeys after digital syndactyly. *Journal of neurophysiology* **66,** 1048–1058 (1991)
6. 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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8. Florence, S. L. *et al.* Large-scale sprouting of cortical connections after peripheral injury in adult macaque monkeys. *Science* **282,** 1117–1121 (1998)
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Detailed lesion experiments to study synaptic structures

1. Chen, J. L. *et al.* Structural basis for the role of inhibition in facilitating adult brain plasticity. *Nature neuroscience* **14,** 587–594 (2011)
2. Marik, S. A. *et al.* Axonal dynamics of excitatory and inhibitory neurons in somatosensory cortex. *PLoS Biology* **8,** e1000395 (2010)
3. Yamahachi, H. *et al.* Rapid axonal sprouting and pruning accompany functional reorganization in primary visual cortex. *Neuron* **64,** 719–729 (2009)
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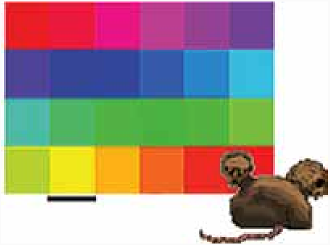
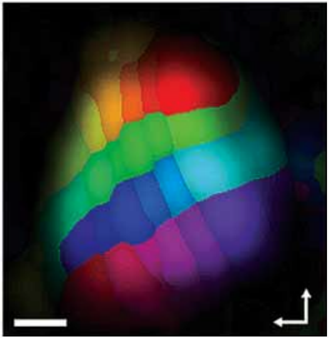
6. Keck, T. *et al.* Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex. *Neuron* **71,** 869–882. ISSN: 0896-6273 (2011)
7. Trachtenberg, J. T. *et al.* Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature* **420,** 788–794 (2002)

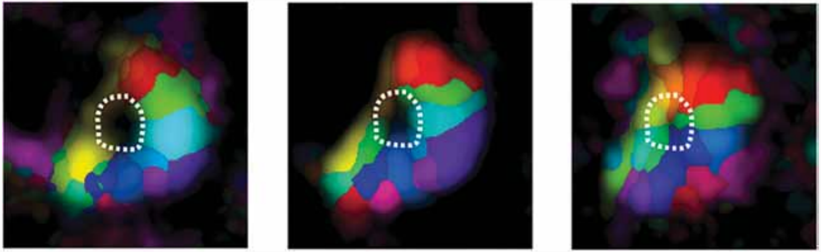
Experimental protocol I





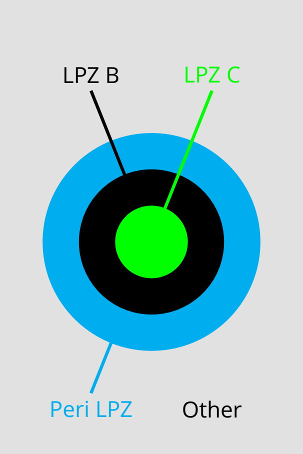
[1] Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)

Experimental protocol II: after peripheral lesion

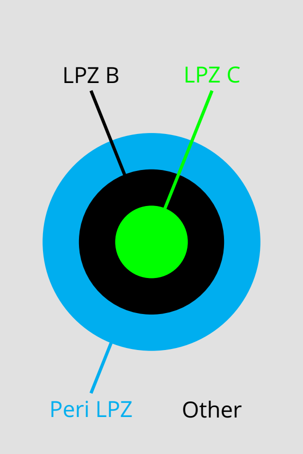


[1] Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)

What we know from these experiments

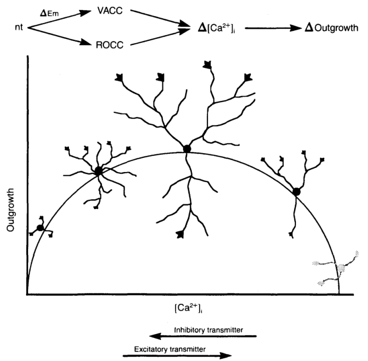


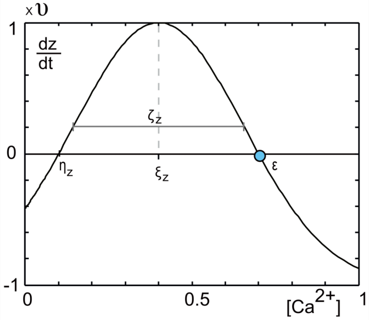
What we know from these experiments



- Massive disinhibition in the LPZ.
- Ingrowth of excitatory synapses from the peri-LPZ to the LPZ.
- Outgrowth of inhibitory synapses from the LPZ to the peri-LPZ.

Computational modelling: MSP I



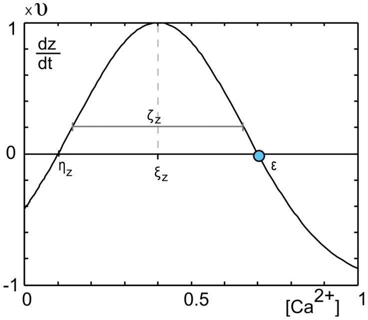


[2] Lipton, S. A. & Kater, S. B. Neurotransmitter regulation of neuronal outgrowth, plasticity and survival. *Trends in neurosciences* **12,** 265–270. ISSN: 0166-2236 (1989)

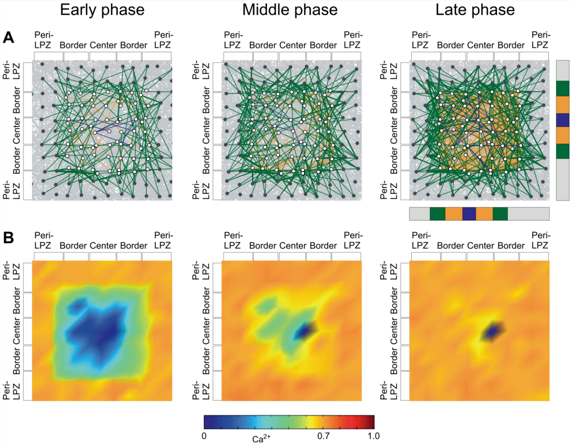
[3] Butz, M. & van Ooyen, A. A Simple Rule for Dendritic Spine and Axonal Bouton Formation Can Account for Cortical Reorganization after Focal Retinal Lesions. *PLoS Comput Biol* **9,** e1003259 (2013)

Computational modelling: MSP II

- Synaptic structures (z): excitatory and inhibitory post-synaptic, excitatory or inhibitory pre-synaptic elements.
- New synapses form when free plugs are available: ($z > z_{\mathrm{conn}}$)
- Synapses are deleted if: ($z < z_{\mathrm{conn}}$)



Computational modelling II



[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)

Methods

Results and discussion