

# Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex

- UH Biocomputation group journal club -

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## Outline

Context

Biology

Paper 1 - layer 5 pyramidal neurons

Paper 2 - inhibitory neurons

My work - modelling

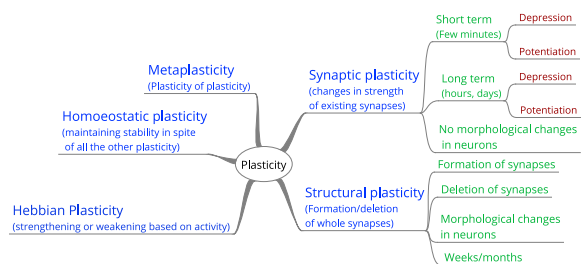


## I'm looking at:

the **functional effects** of cortical rewiring following loss of input.



## Plasticity - refresher



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## Three papers

- ▶ Massive restructuring of neuronal circuits during functional reorganisation of adult visual cortex (Keck et al., 2008)
- ▶ Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex (Keck et al., 2011).
- ▶ Adult plasticity and cortical reorganisation after peripheral lesions (Sammons and Keck, 2015).

## Model

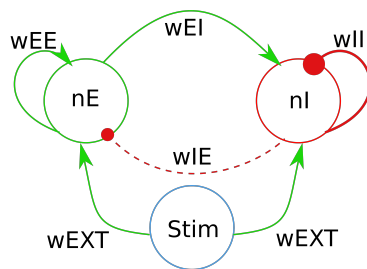


Figure: Model schematic

## General observations

- ▶ Peripheral lesion - retinal, for example
- ▶ Observe the cortex over time
  - ▶ receive feed-forward input from the lesioned peripheral area
- ▶ Loss of input is observed initially after the lesion
- ▶ Gradually, remapping occurs, with activity returning to pre-lesion levels
  - ▶ Receptive fields of deprived neurons become similar to receptive fields of cells that are spatially adjacent in the spared cortical regions
  - ▶ Intra-cortical plasticity, as little or no reorganisation has been observed in the LGN

## Mapping



Figure: Drifting grating stimuli



Figure: Pre lesion mapping

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## Recovery - remapping

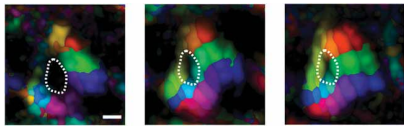


Figure: Time lapse for a particular mouse - days 0, 11, 74

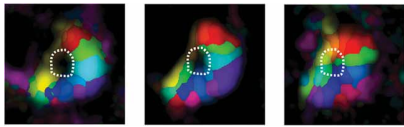


Figure: Time lapse for a particular mouse - days 7, 12, 17

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## Results summary

- ▶ Marked increases in turnover of of dendritic spines during functional reorganisation.
- ▶ Almost complete replacement of set of spines on apical dendrites (91% vs 38% in control mice)
- ▶ Turnover was as a result of an equal amount of spine loss and gain (evidenced by stable spine density)
- ▶ Spine dynamics remained elevated for the first month, and returned to baseline levels after 2 months.

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## Results summary

- ▶ Peri-LPZ, turnover was slightly elevated w.r.t. controls, but significantly lower than LPZ centre.
- ▶ Spine survival but not addition rates for peri-LPZ cells were lower than centre, thus, reorganisation progresses fastest in the centre.
- ▶ No correlation between spine turnover and cortical depth.
- ▶ No change in dendritic architecture

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## Study

- ▶ Dendrites on inhibitory neurons are typically smooth - dendritic spines conventionally believed to be absent
- ▶ A subset of inhibitory neurons have dendritic spines with excitatory synapses - which is what they study
- ▶ Confirmed that the majority of spines on the dendrites of inhibitory neurons carry synapses, and that most of these are from excitatory but not inhibitory, presynaptic neurons
- ▶ Also confirmed that dendritic spines of inhibitory neurons carry functional glutamatergic (excitatory) receptors.

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## Results - summary

- ▶ Similar to excitatory neurons, in control animals, the inhibitory neurons show a stable spine density, and axonal bouton density over time.
- ▶ Following lesions, a long lasting loss of excitatory spines on inhibitory neurons, and axonal boutons is observed in the LPZ.
  - ▶ Initial rapid spine and bouton loss and no recovery of density 1 and 2 months after retinal lesion.



## Results - summary

- ▶ Even inhibitory neurons whose cell body and dendrites were located outside the LPZ showed substantial decrease in spine and bouton density.
  - ▶ For both, correlation between density and distance of cell body from border of LPZ
  - ▶ Cells nearer to LPZ had similar densities, away from LPZ had densities similar to control animals



## Justification

- ▶ changes reflect competition between lost and preserved visual inputs in the LPZ during functional reorganisation
- ▶ simply reflect the overall reduction in cortical activity
- ▶ can be distinguished by observing dynamics after **complete** input removal
- ▶ For excitatory neurons, structural dynamics of **spines** increased after **complete** input removal, but to a much lesser extent than during reorganisation following focal retinal lesions
  - ▶ So, not simply due to reduction in activity, but also because of competition between deprived and non-deprived inputs.



## Justification

- ▶ For both spines and boutons, density and survival fraction decreased to same degree after **complete** input removal
  - ▶ Suggesting that changes in density are largely driven by decrease in cortical activity



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Take away

- Because the changes in inhibitory structures precede increases in excitatory spine turnover, these data suggest that inhibitory structural plasticity may be the first step in the cortical reorganisation after sensory deprivation



Model

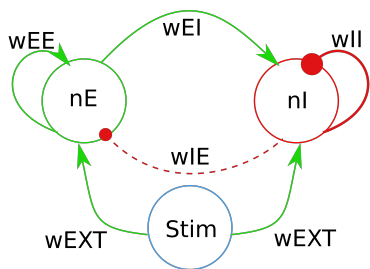


Figure: Model schematic



Without repair - firing rates

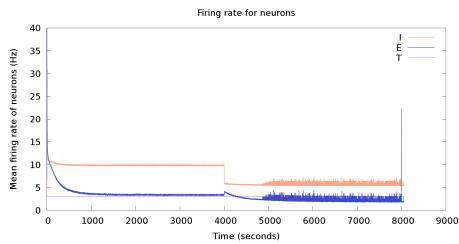


Figure: Firing rates after lesion, without structural plasticity repair



Without repair - conductances

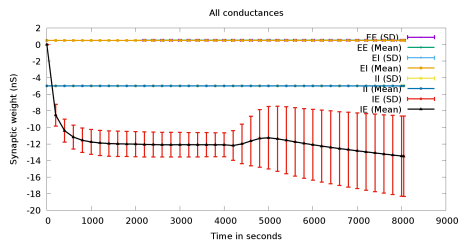


Figure: Conductances, without structural plasticity repair (negative conductance implies inhibitory)



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References I



Keck T, Mrcic-Flogel TD, Afonso MV, Eysel UT, Bonhoeffer T, Hübener M (2008)  
**Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex.**  
*nature neuroscience* 11:1162–1167.



Keck T, Scheuss V, Jacobsen R, Wierenga C, Eysel U, Bonhoeffer T, Hübener M (2011)  
**Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex.**  
*Neuron* 71:869 – 882.



Sammons RP, Keck T (2015)  
**Adult plasticity and cortical reorganization after peripheral lesions.**  
*Current Opinion in Neurobiology* 35:136 – 141  
Circuit plasticity and memory.

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