Cortical rewiring

Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex - UH Biocomputation group journal dub -

Ankur Sinha

University of Hersfordshire - Biocomputation grou 28 April 2017

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

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Cortical rewiring

# -Outline

Outline

Cortical rewiring

# I'm looking at:

the functional effects of cortical rewiring following loss of input.



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└─Context

Cortical rewiring

-I'm looking at:

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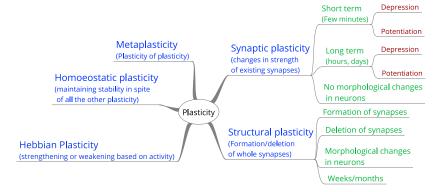








# Plasticity - refresher





Cortical rewiring
Context
Plasticity - refresher

04-28



# Three papers

► Massive restructuring of neuronal circuits during functional reorganisation of adult visual cortex (Keck et al., 2008)

Cortical rewiring -Biology

Three papers

1. This is a short review paper that summaries the two above

Three papers

► Massive restructuring of neuronal circuits during functional







Three papers

 Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex (Kock et al., 2011).

Three papers

#### Three papers

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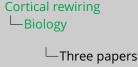
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#### Three papers

- ► 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).





 Massive restructuring of neuronal circuits during functional reorganisation of adult visual cortex (Keck et al., 2008)
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 Adult plasticity and cortical reorganisation after periphera lesions (Sammons and Keck, 2015).

Three papers

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## Cortical rewiring 2017-04-28 └─Biology

└─Model



## Model

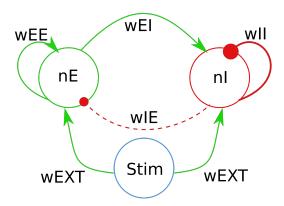


Figure: Model schematic





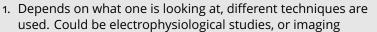


## Cortical rewiring -Biology

#### ► Peripheral lesion - retinal, for example

#### General observations

- ▶ Peripheral lesion retinal, for example
- Observe the cortex over time.
  - receive feed-forward input from the lesioned peripheral area



- 2. Keck et al. use a cranial window technique. There's also a thinning skull technique. Both of which I do not know much about
- 3. Various species, various cortices, but a lot of work has been done on the visual cortex
- 4. Several weeks and months

General observations

5. Michael had asked me this at last week's meeting



# 17-04-28

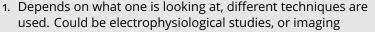
# Cortical rewiring Biology

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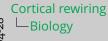
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#### General observations

- ► Peripheral lesion retinal, for example
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- 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
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- 1. Depends on what one is looking at, different techniques are used. Could be electrophysiological studies, or imaging
- 2. Keck et al. use a cranial window technique. There's also a thinning skull technique. Both of which I do not know much about
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# 2017-04-28

## Cortical rewiring └─Biology



Mapping

# Mapping



Figure: Drifting grating stimuli









# Mapping

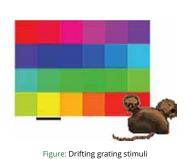


Figure: Pre lesion mapping





#### Recovery - remapping

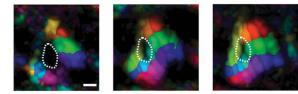


Figure: Time lapse for a particular mouse - days o, 11, 74

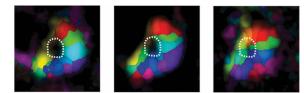


Figure: Time lapse for a particular mouse - days 7, 12, 17

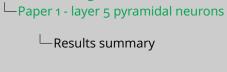




# Cortical rewiring Paper 1 - layer 5 pyramidal neurons Recovery - remapping

#### 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)



Cortical rewiring

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1. Turnover - number of new and lost spines divided by twice the total number of spines



Paper 1 - layer 5 pyramidal neurons

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- ► 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.



1. Turnover - number of new and lost spines divided by twice the total number of spines

Paper 1 - layer 5 pyramidal neurons

#### 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.



# Cortical rewiring Paper 1 - layer 5 pyramidal neurons

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- ► 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



#### Cortical rewiring Paper 1 - layer 5 pyramidal neurons

-Results summary

#### Results summary

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- - ► No change in dendritic architecture

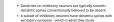
#### Study

- ► 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





└─Study



Study

- It is well established that nearly all dendritic spines of excitatory neurons receive synaptic inputs
- 2. Using immunostaining



Study

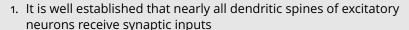
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2. Using immunostaining

#### Results - summary

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Results - summary

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#### Paper 2 - inhibitory neurons

#### 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

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- ► 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



#### Cortical rewiring -Paper 2 - inhibitory neurons

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 changes reflect competition between lost and preserved visual inputs in the LPZ during functional reorganisation





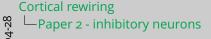
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Justification

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- can be distinguished by observing dynamics after complete input removal



#### Cortical rewiring Paper 2 - inhibitory neurons

**Justification** 

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- 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.



Cortical rewiring Paper 2 - inhibitory neurons

**Justification** 

#### Justification

- visual inputs in the LPZ during functional reorganisation
- · simply reflect the overall reduction in cortical activity · can be distinguished by observing dynamics after
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- . So, not simply due to reduction in activity, but also because
  - of competition between deprived and non-deprived inputs

- ► 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





**Justification** 

#### 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



# Cortical rewiring Paper 2 - inhibitory neurons Take away Take away Take away Take away Take away Take away

#### Cortical rewiring ☐My work - modelling

└─Model

Model

#### Model

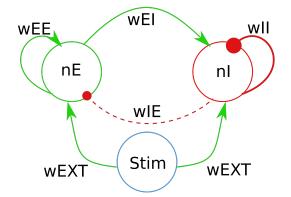


Figure: Model schematic





#### Without repair - firing rates

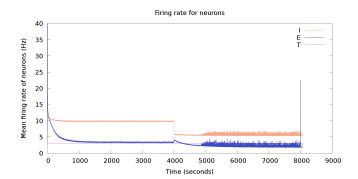
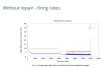


Figure: Firing rates after lesion, without structural plasticity repair







└ My work - modelling

#### Without repair - conductances

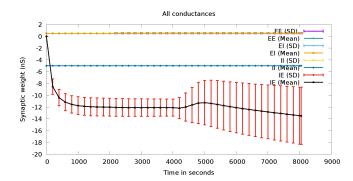


Figure: Conductances, without structural plasticity repair (negative conductance implies inhibitory)







Cortical rewiring -References

-References

References I

#### References I



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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, Hbener M (2011)

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Fin.

