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

- UH Biocomputation group journal club -

Ankur Sinha

University of Hertfordshire - Biocomputation group

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Outline

Context

Biology

Paper 1 - layer 5 pyramidal neurons

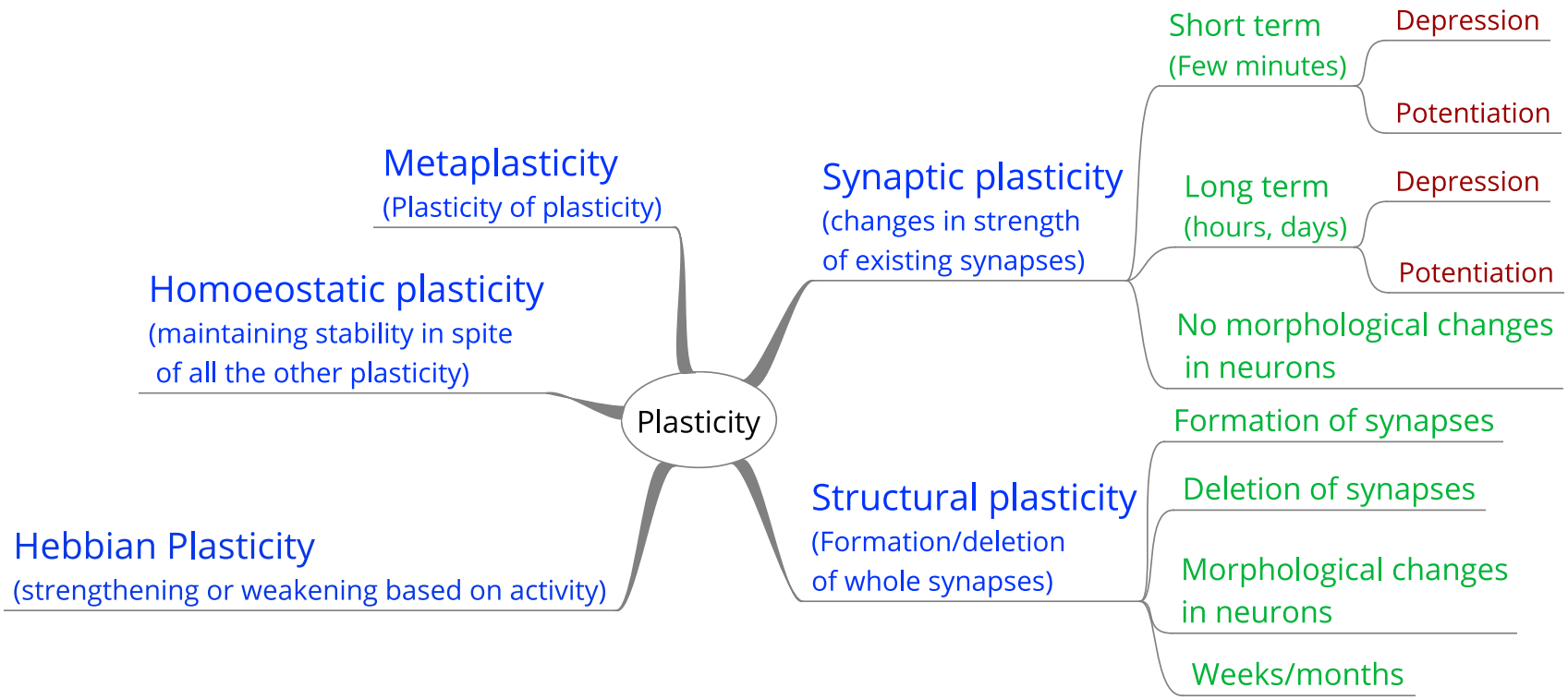
Paper 2 - inhibitory neurons

My work - modelling

I’m looking at:

the functional effects of cortical rewiring following loss of input.

Plasticity - refresher



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

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- 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

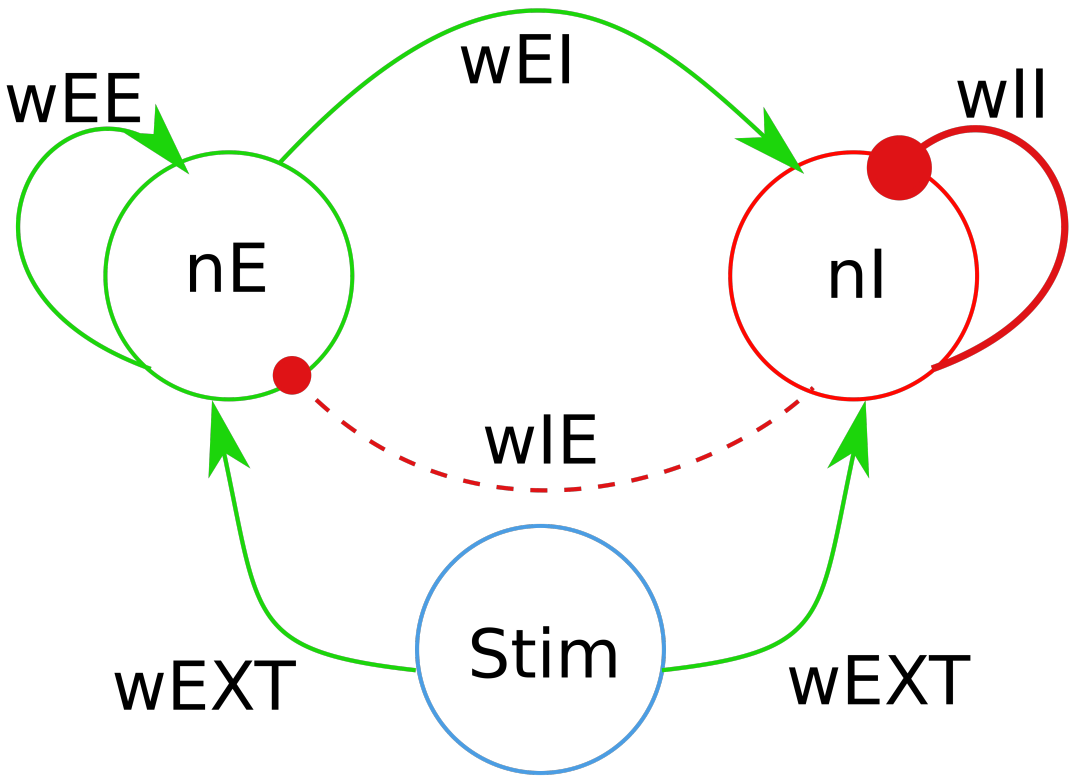

Figure: Model schematic

General observations

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

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- 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

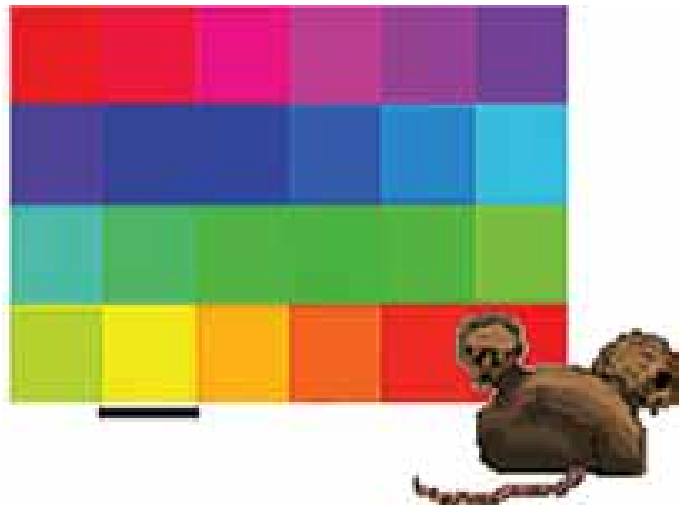

Figure: Drifting grating stimuli

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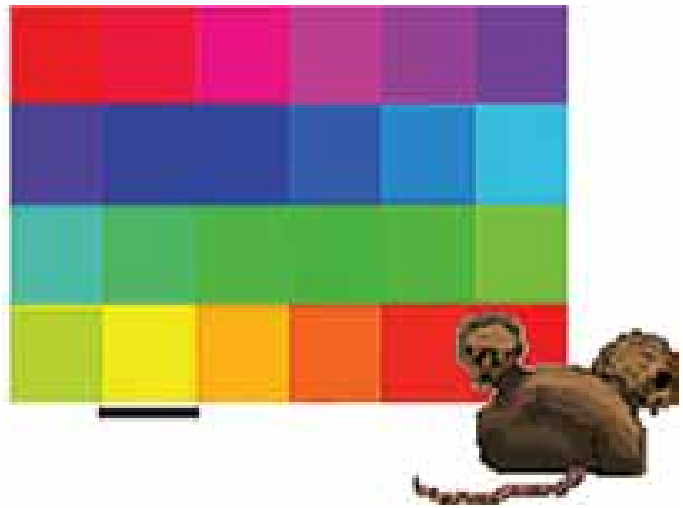

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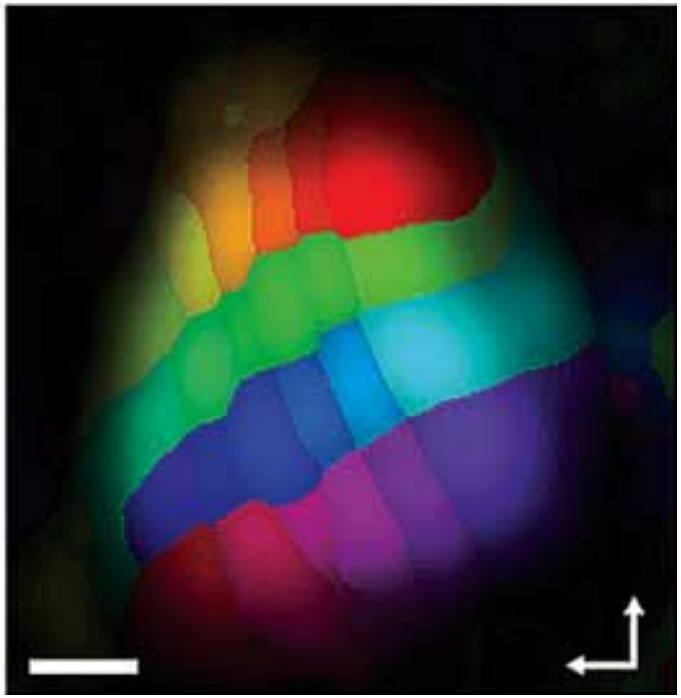

Figure: Pre lesion mapping

Recovery - remapping

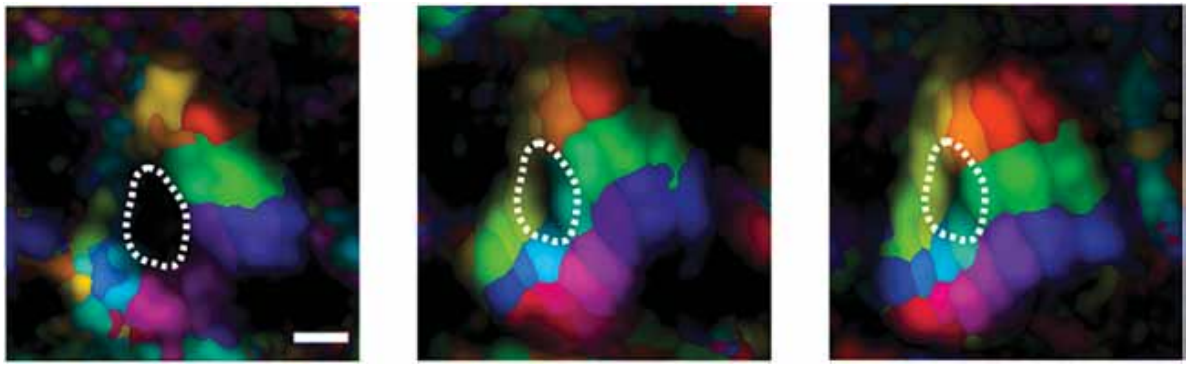

Figure: Time lapse for a particular mouse - days 0, 11, 74

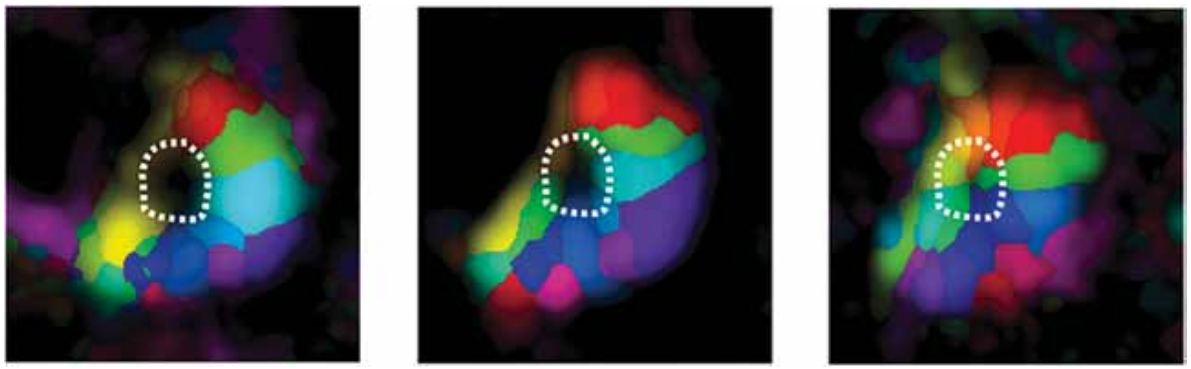

Figure: Time lapse for a particular mouse - days 7, 12, 17

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)

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- 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.

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.

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

Study

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- A subset of inhibitory neurons have dendritic spines with excitatory synapses - which is what they study

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- 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.

Results - summary

- Similar to excitatory neurons, in control animals, the inhibitory neurons show a stable spine density, and axonal bouton density over time.

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- 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

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- 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

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

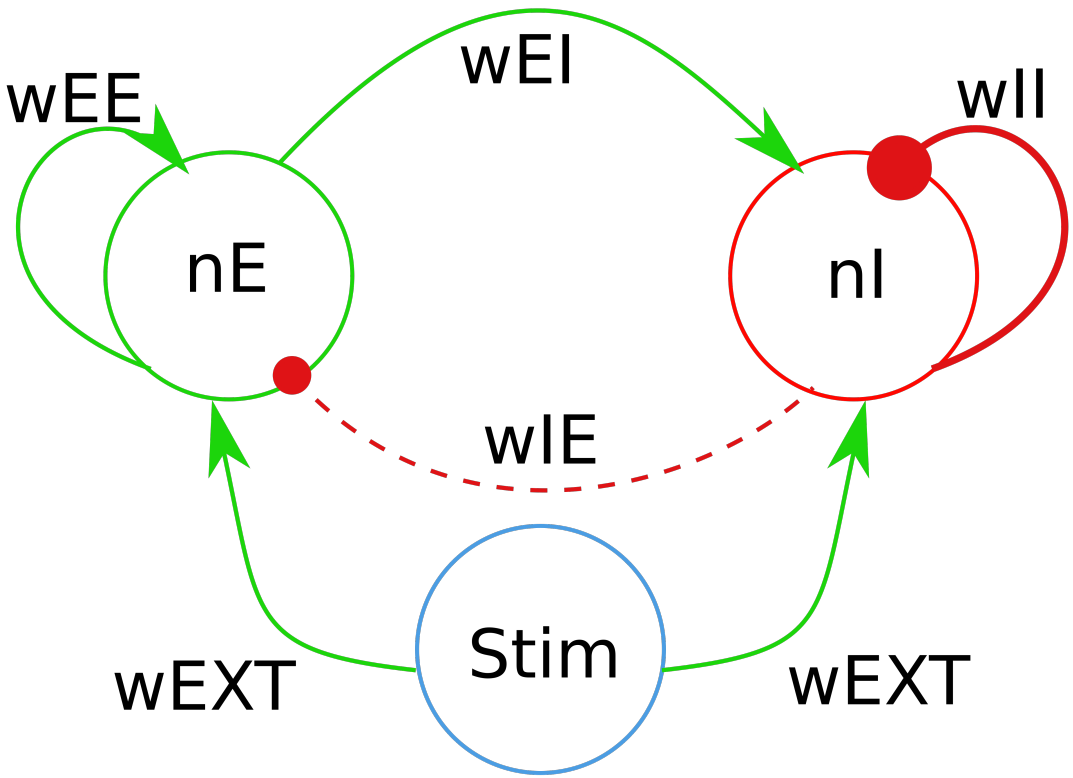

Figure: Model schematic

Without repair - firing rates

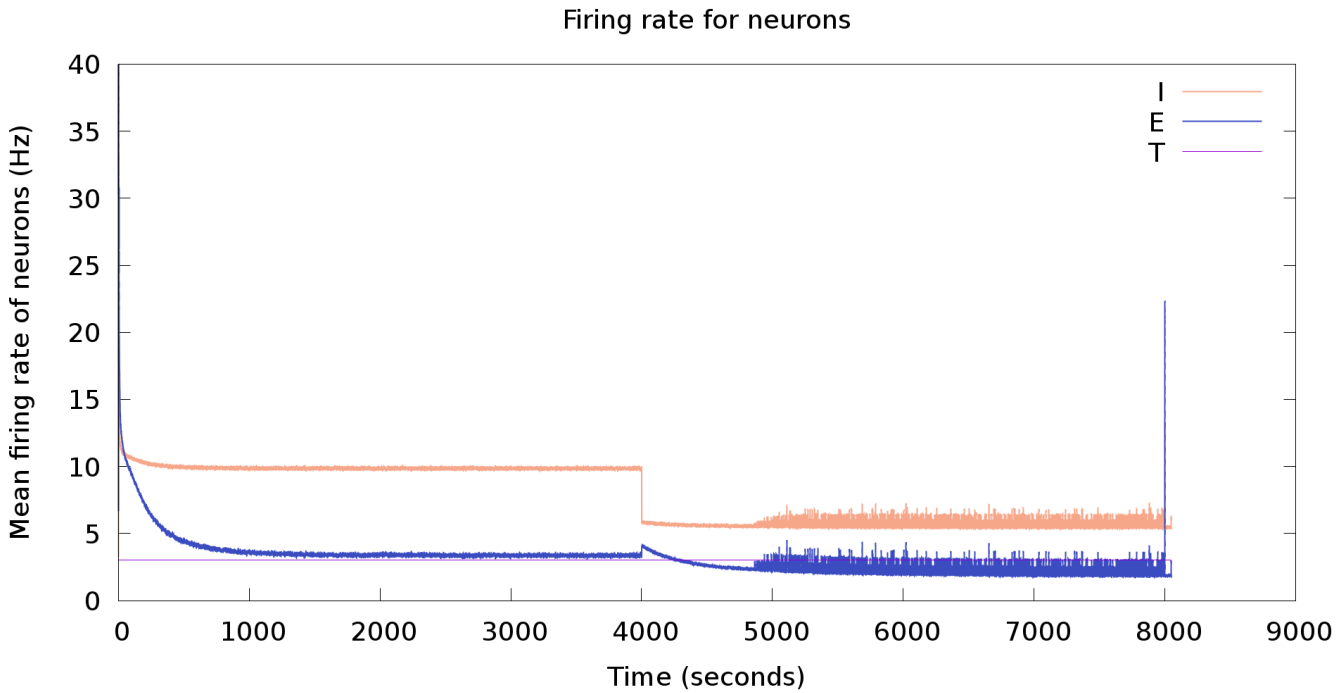

Figure: Firing rates after lesion, without structural plasticity repair

Without repair - conductances

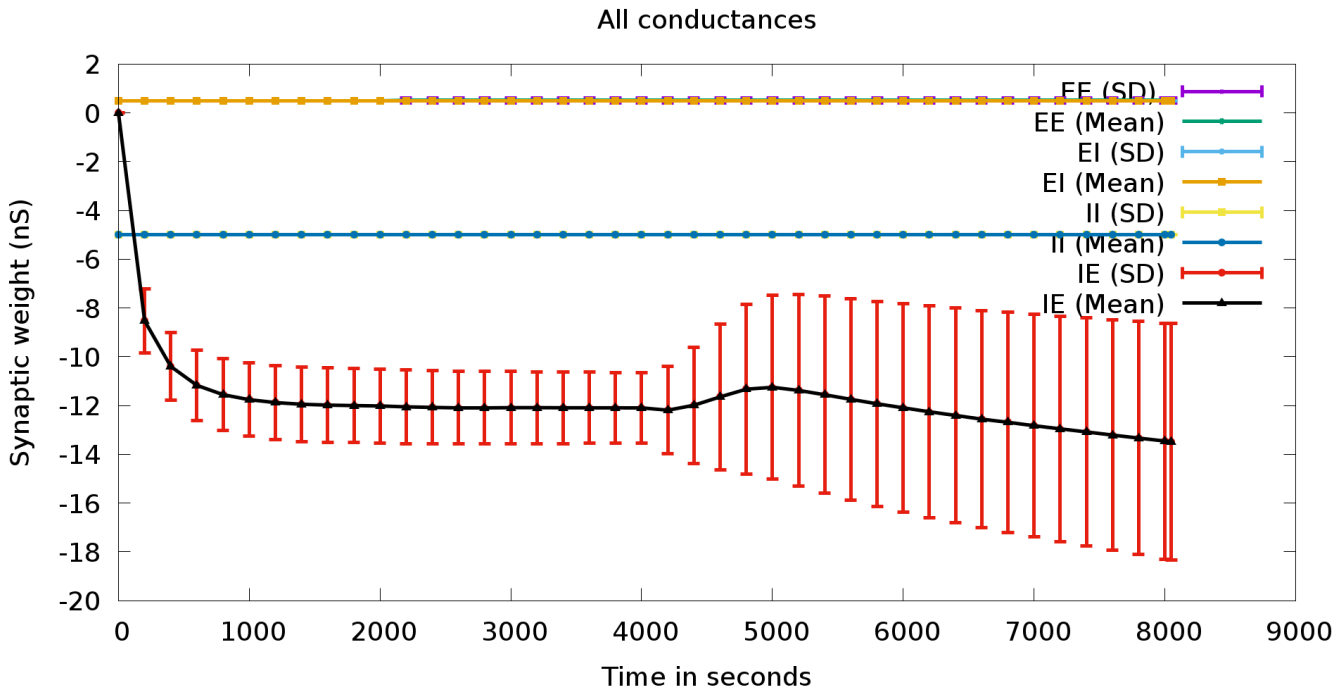

Figure: Conductances, without structural plasticity repair (negative conductance implies inhibitory)

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Neuron 71:869 – 882.

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Circuit plasticity and memory.

Fin.