

Investigating activity dependent dynamics of synaptic structures using biologically plausible models of post-deafferentation network repair

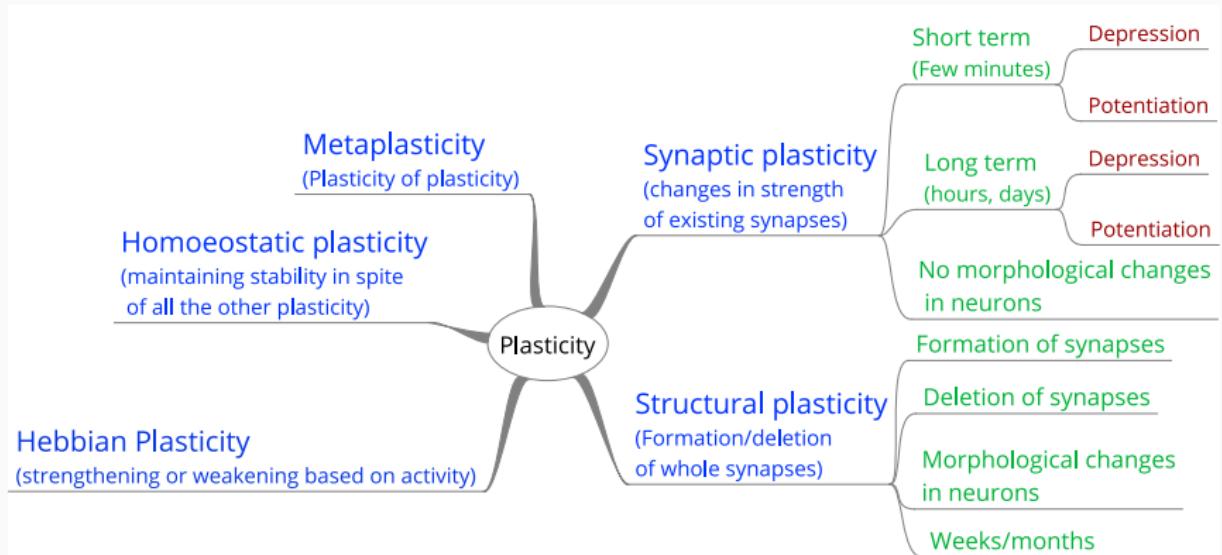
Engineering and Computer Science Conference, 2019

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29/03/2019

Context

Plasticity while maintaining stability



Synaptic structures are dynamic in the adult brain

1. **Chen2011**
2. **Marik2010**
3. **Marik2014**
4. **Stettler2006**
5. **Gogolla2007**
6. **Holtmaat2005**
7. **Chen2012**
8. **Trachtenberg2002**
9. **Villa2016**

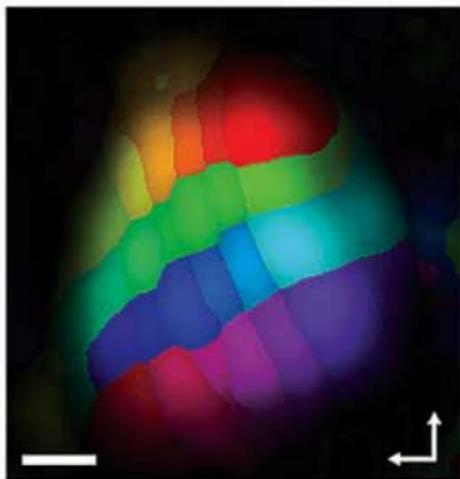
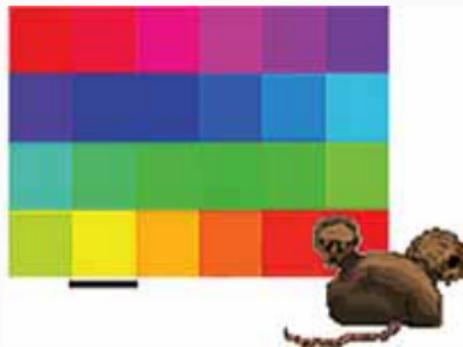
Evidence of homeostatic structural plasticity: lesion studies

1. **Wall1984**
2. **Rasmusson1982**
3. **Rajan1993**
4. **Pons1991**
5. **Allard1991**
6. **Darian-Smith1994**
7. **Darian-Smith1995**
8. **Florence1998**
9. **Heinen1991**

Detailed lesion experiments to study synaptic structures

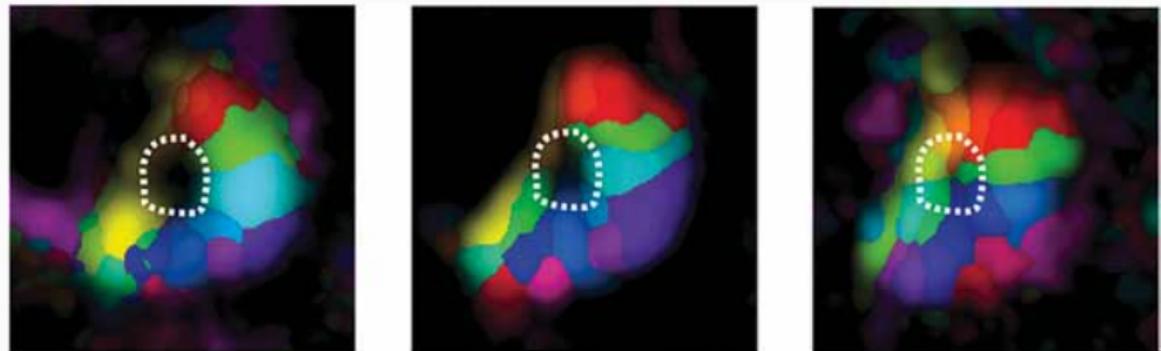
1. **Chen2011**
2. **Marik2010**
3. **Yamahachi2009**
4. **Hickmott2005**
5. **Keck2008**
6. **Keck2011**
7. **Trachtenberg2002**

Experimental protocol I



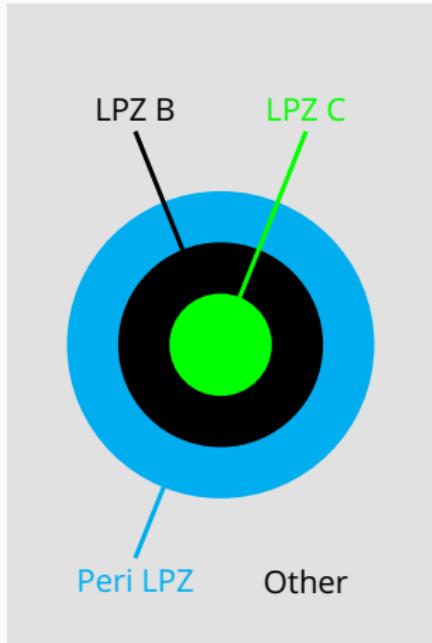
¹ Keck2008

Experimental protocol II: after peripheral lesion

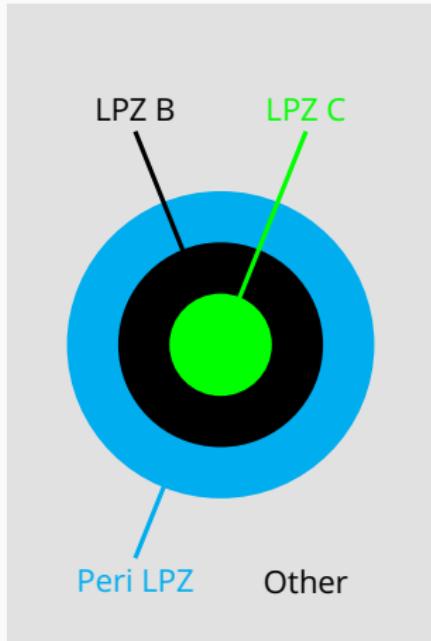


¹ Keck2008

What we know from these experiments

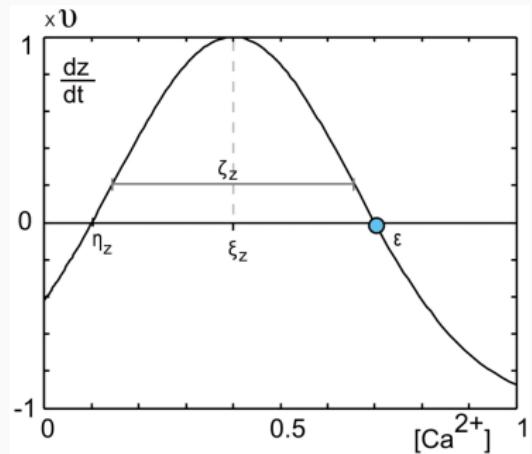
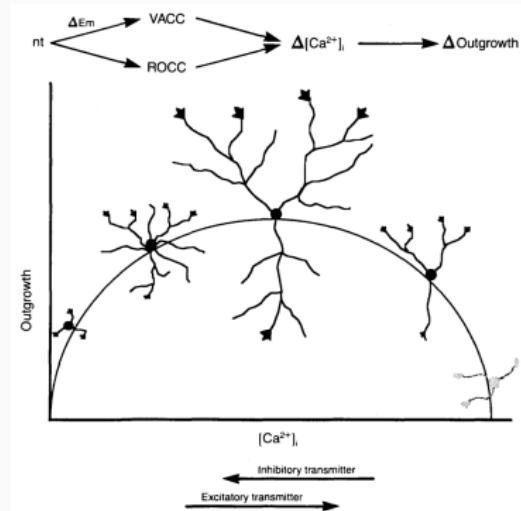


What we know from these experiments



- Massive disinhibition in the LPZ.
- Gradual ingrowth of excitatory synapses from the peri-LPZ to the LPZ.
- Gradual outgrowth of inhibitory synapses from the LPZ to the peri-LPZ.

Computational modelling: MSP: growth curve

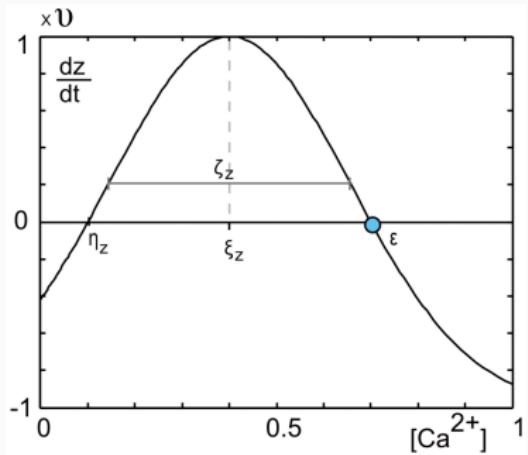


² Lipton 1989

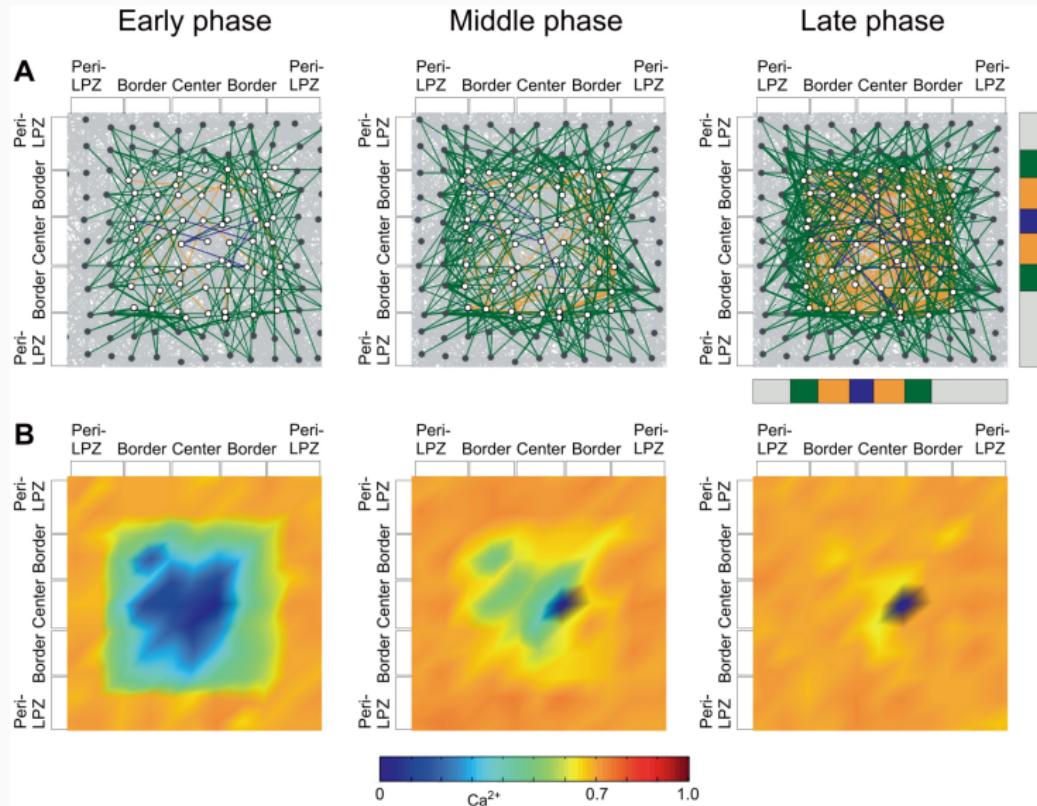
³ Butz 2013

Computational modelling: MSP: turnover

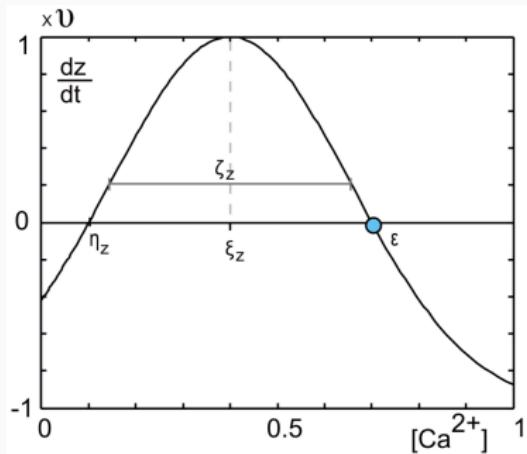
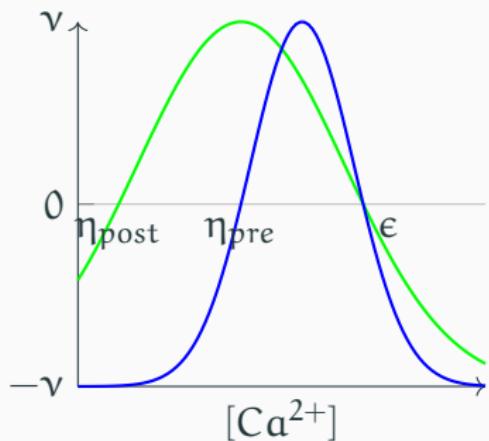
- Synaptic structures (z): excitatory **and** inhibitory post-synaptic, excitatory **or** inhibitory pre-synaptic elements.
- New synapses form when **free** plugs are available: ($z > z_{\text{conn}}$)
- Synapses are deleted if: ($z < z_{\text{conn}}$)



Computational modelling II: Butz2013 replication

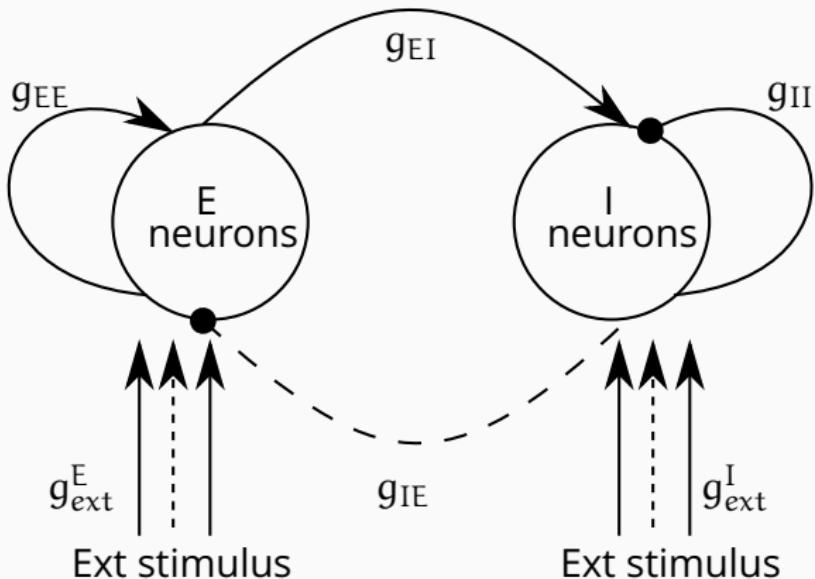


Computational modelling II: Butz2013 results



Methods: our approach

Start with a biologically realistic network model



⁴Vogels2011

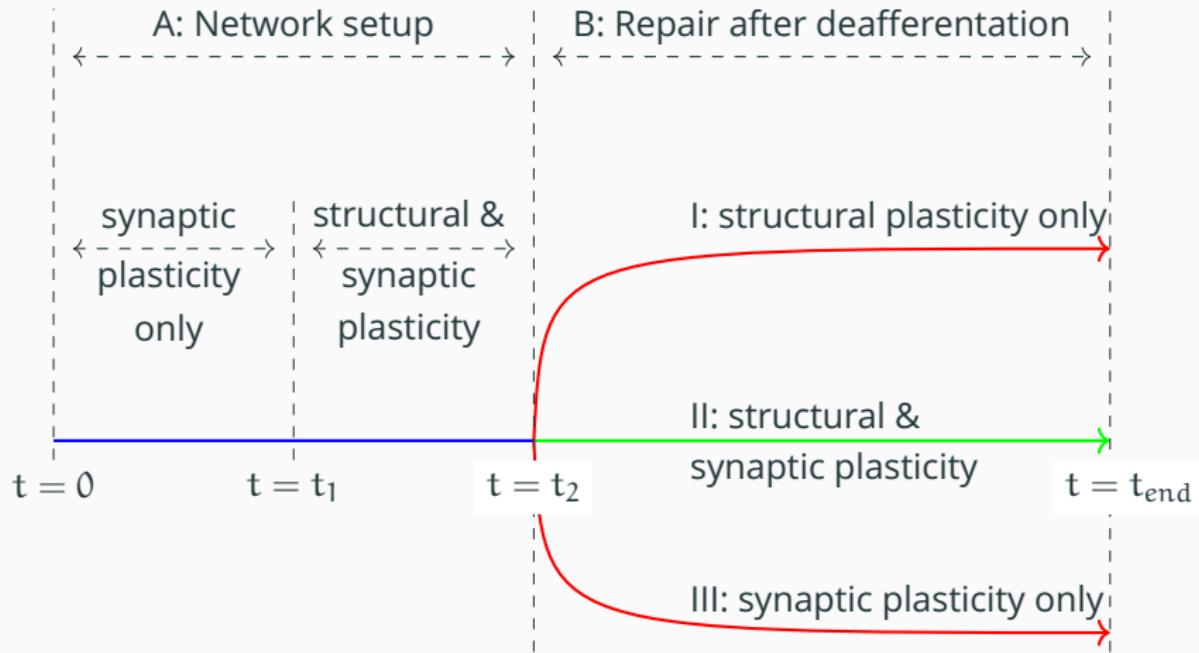
Extensions

- Probabilistic formation of synapses, also: “longer” inhibitory than excitatory connections¹.
- Probabilistic deletion of synapses (incorporating evidence that stronger synapses have less likelihood of removal²).
- Further generalisation of growth curves.

⁵ Citation buried in my lab logs somewhere!

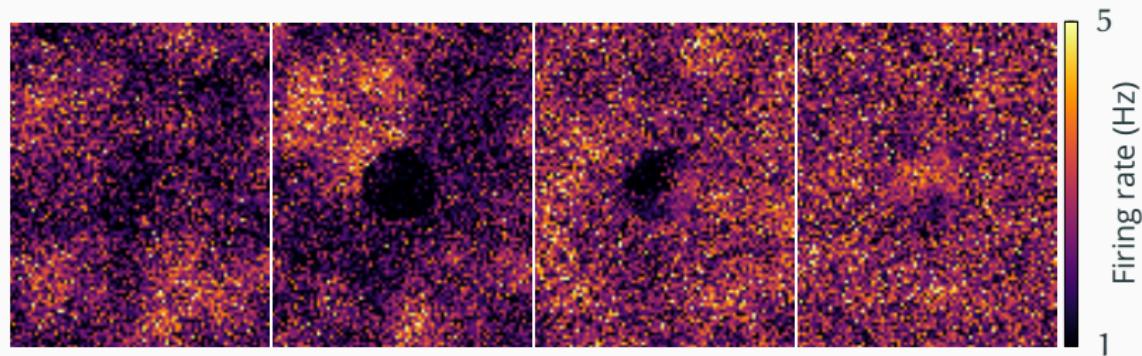
⁶ Knott 2006

Simulation protocol

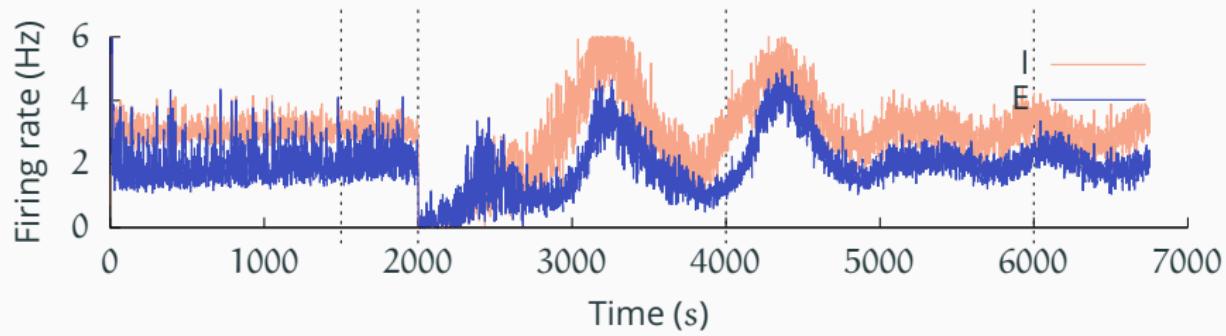


Results and discussion

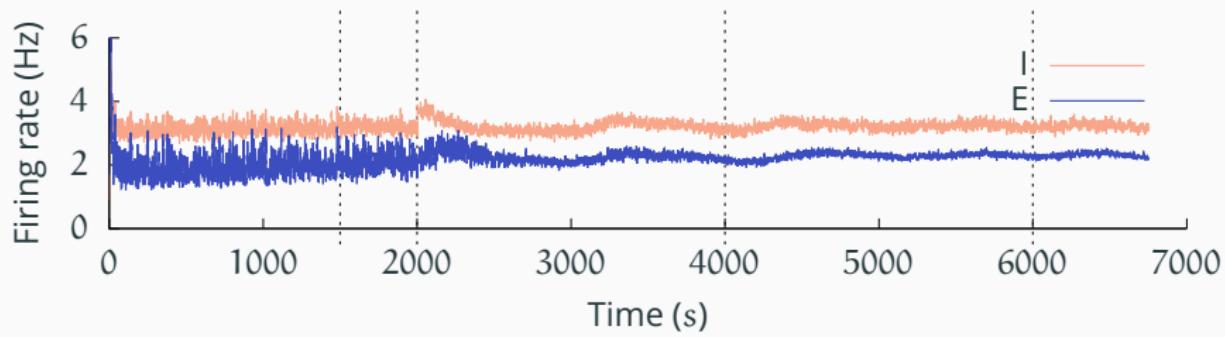
Deafferentation and successful repair



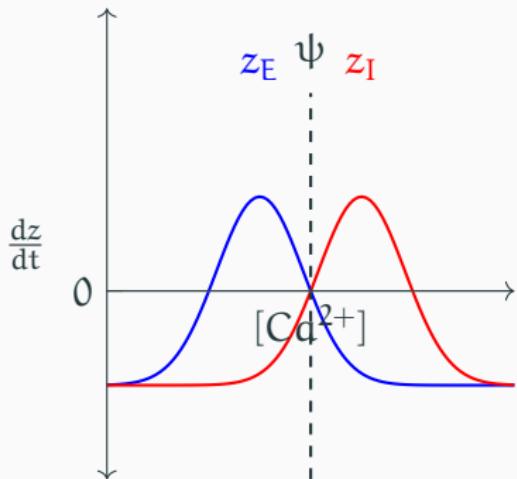
Deafferentation and repair: LPZ



Deafferentation and repair: outside the LPZ

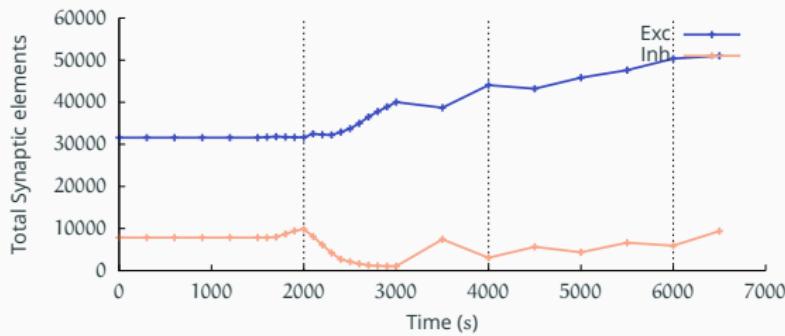
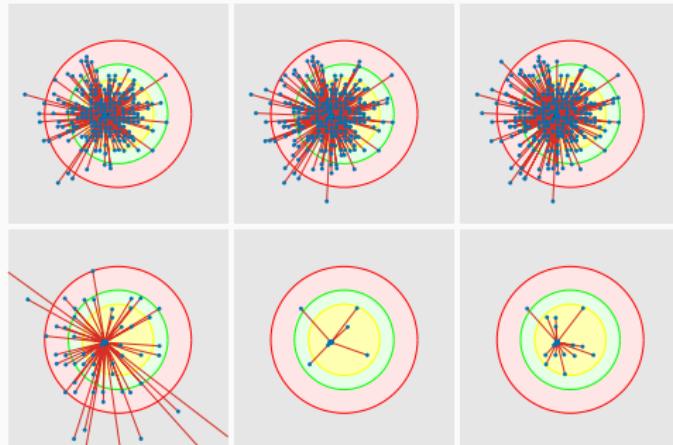


Post-synaptic growth dynamics

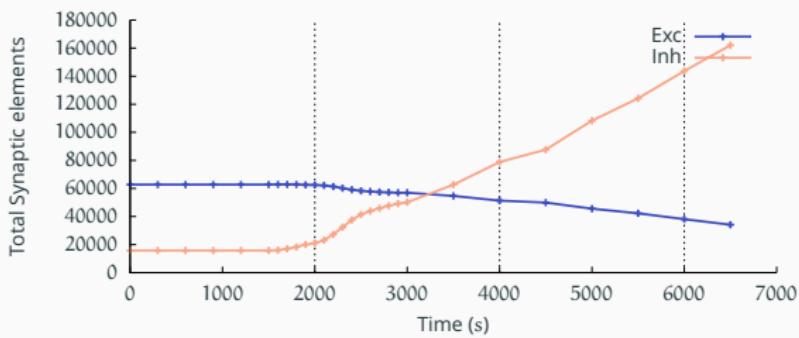
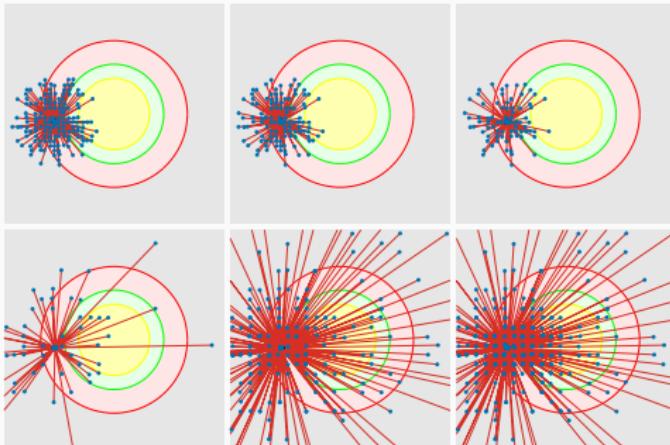


- Loss of activity: sprouting of E, retraction of I
- Extra activity: retraction of E, sprouting of I

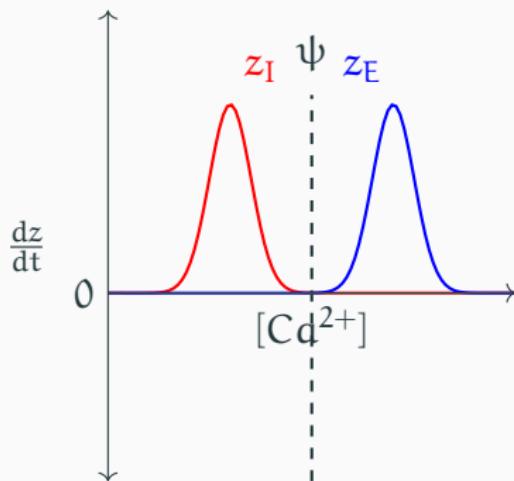
Resultant turnover: LPZ



Resultant turnover: outside LPZ

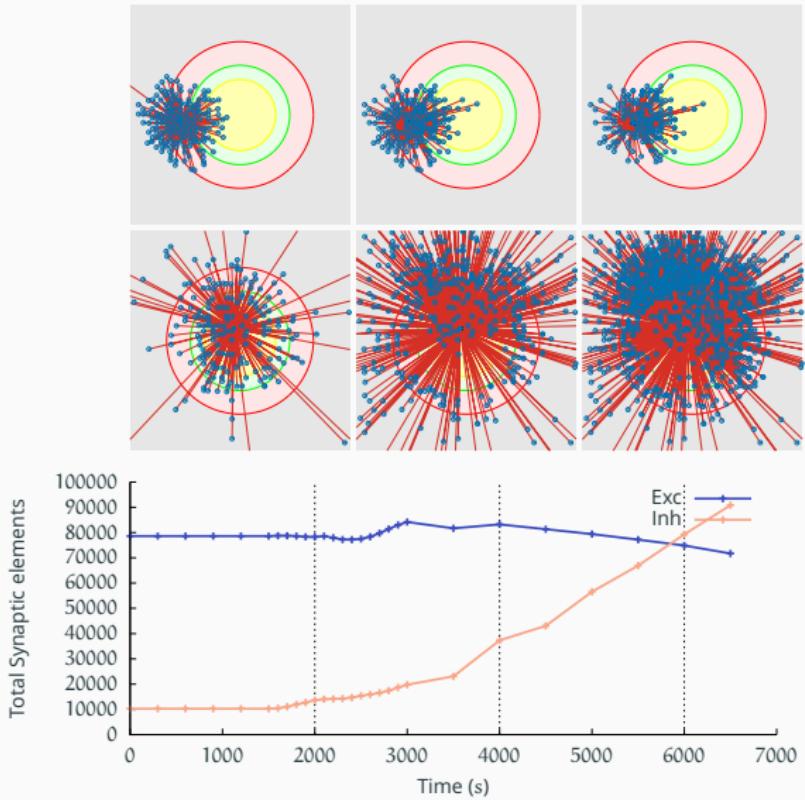


Pre-synaptic growth dynamics

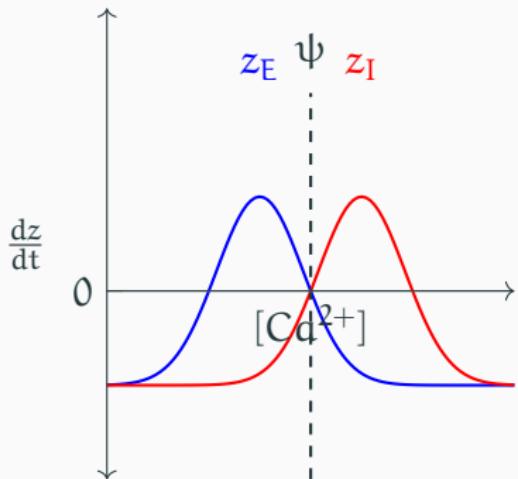


- Extra activity: sprouting of E
- Less activity: sprouting of I

Resultant turnover: pre-synaptic

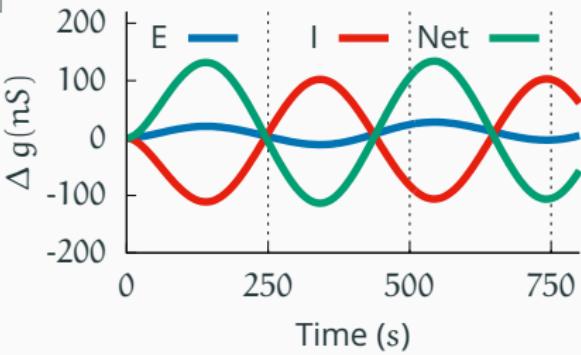
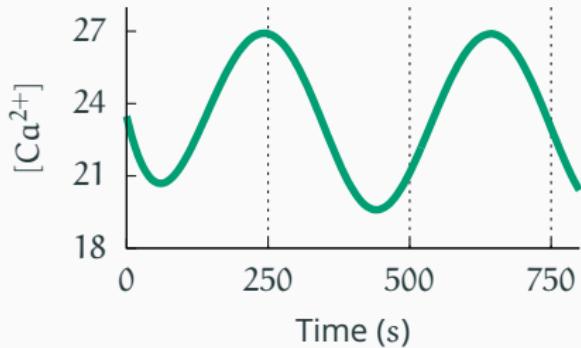
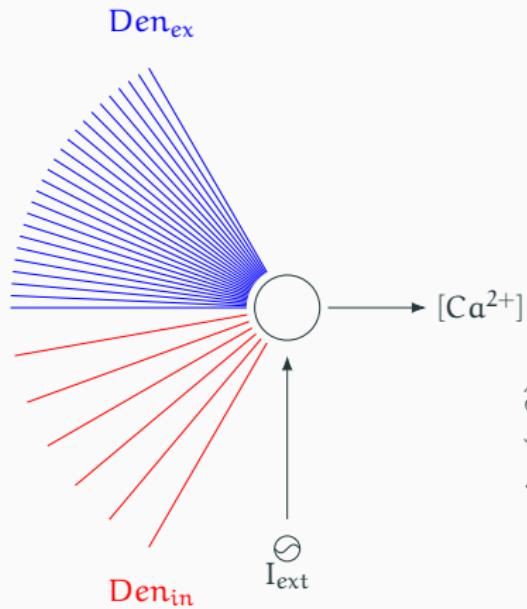


Post-synaptic growth dynamics



- Loss of activity: sprouting of E, retraction of I
- Extra activity: retraction of E, sprouting of I

Post-synaptic dynamics: single neuron stability



Conclusions

- New model: biologically realistic.
- Replicates experimental observations:
 - Ingrowth of excitatory axons to LPZ.
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Conclusions

- New model: biologically realistic.
- Replicates experimental observations:
 - Ingrowth of excitatory axons to LPZ.
 - Outgrowth of inhibitory axons from LPZ.
 - Massive disinhibition in LPZ.
 - Role of inhibition in structural plasticity as a controller of critical time window?
- Suggests:
 - Activity dependent dynamics for synaptic structures.
 - Single neuron stabilisation by structural plasticity.

Now what?

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- Functional implications of structural plasticity? Associative memory?
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- Faithful modelling of cytoskeleton modification (actin)?