

A saturation model for impaired learning with enhanced plasticity

based on work in preparation by: T.D. Barbara Nguyen-Vu, Grace Q. Zhao, Han-Mi Lee, SL, Surya Ganguli, Carla J. Shatz, Jennifer L. Raymond

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1. Acknowledge Barbara and Grace

└ Introduction

Expect enhanced plasticity → enhance learning.
But often: → impairment.

Claim: due to basal activity → biased synaptic population
→ fewer synapses available for learning.

Analysis of models of complex synapses:
motor learning of enhanced LTD mice → constrain synaptic structure.

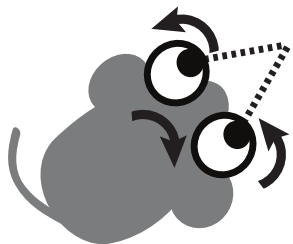
Expect enhanced plasticity → enhance learning.

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1. It does help in some cases



Eye movements compensate for head movements to maintain fixation.

Requires control of VOR gain = $\frac{\text{eye velocity}}{\text{head velocity}}$.

Needs to be adjusted as eye muscles age, etc.

└ Vestibulo-Occular Reflex



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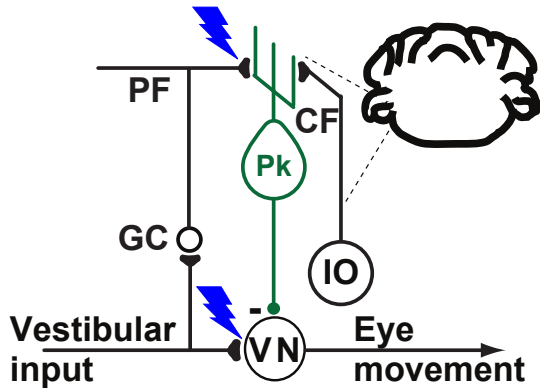
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VOR training

VOR Increase Training



VOR Decrease Training



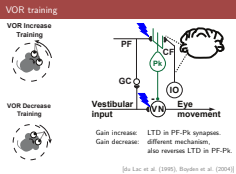
Gain increase: LTD in PF-Pk synapses.
Gain decrease: different mechanism, also reverses LTD in PF-Pk.

[du Lac et al. (1995), Boyden et al. (2004)]

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Saturation by enh. plasticity impairs learning

└ VOR training



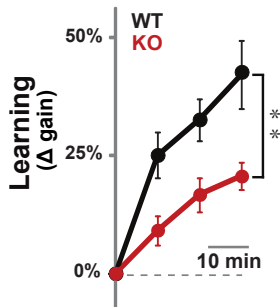
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulus
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Different mechs for different freq, head angle, gain up/down.

MHC-I D^bK^b — / — knockout

Knockout of molecules lowers threshold for LTD in PF-Pk synapses.

[McConnell et al. (2009)]

Gain increase at 1.0 Hz



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└ MHC-I D^bK^b — / — knockout

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MHC-I D^bK^b — / — knockout

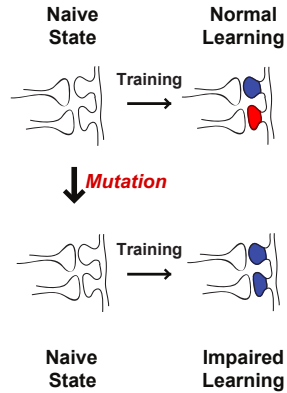
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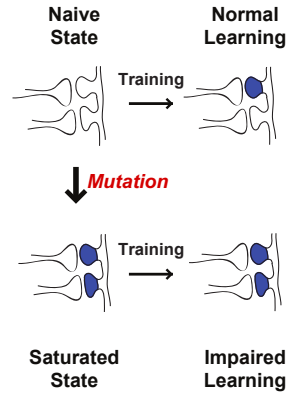
1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD → expect better learning
3. Impairment of learning
4. Looking at change of VOR gain during gain-up training

Saturation hypothesis

Error model



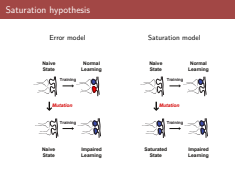
Saturation model



Saturation by enh. plasticity impairs learning

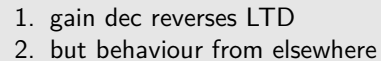
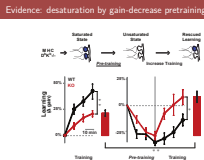
Saturation hypothesis

1. Older explanation: error model
2. Our model: baseline activity \rightarrow saturation \rightarrow less depression possible
3. Saturation has to compete with enhanced plasticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

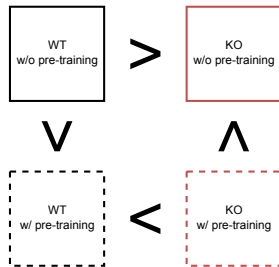
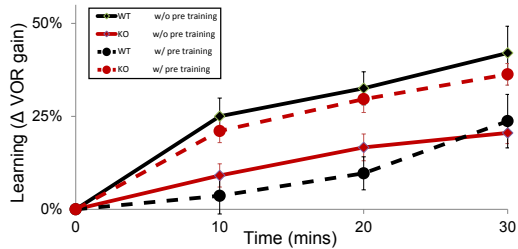


Saturation by enh. plasticity impairs learning

- └ Evidence: desaturation by gain-decrease pretraining



Summary of training results



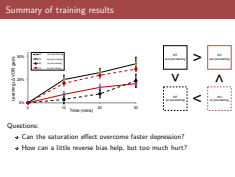
Questions:

- Can the saturation effect overcome faster depression?
- How can a little reverse bias help, but too much hurt?

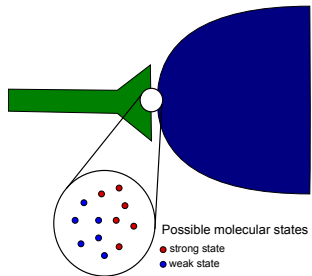
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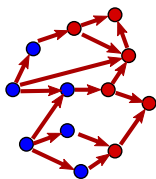
Summary of training results



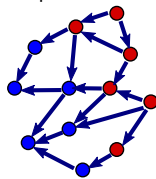
1. Restricted to gain inc for comparison
2. Black: WT. Red: KO
3. Solid: no pre. Dashed: with pre
4. Horz and vert comparisons: conceptual
5. KO hurts w/o, but helps w/
6. pre helps KO but hurts WT
7. Diagonal comparisons: parameter fitting. Depend on size of KO vs. pretraining



Potentiation



Depression



Simplifying assumptions:

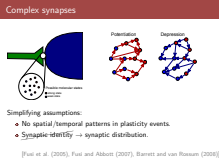
- No spatial/temporal patterns in plasticity events.
- ~~Synaptic identity~~ → synaptic distribution.

[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]

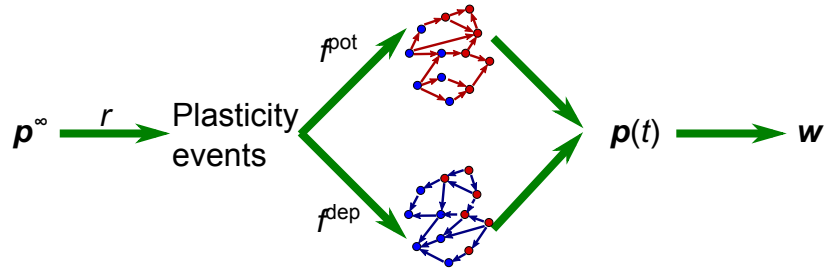
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Saturation by enh. plasticity impairs learning

Complex synapses



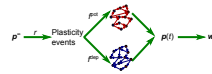
1. functional states, not molecules
2. synaptic weight depends on state
3. many states can have same weight
4. stochastic transitions
5. allows us to concentrate on synapse, not neuron/network
6. This is a question about synaptic populations after all.



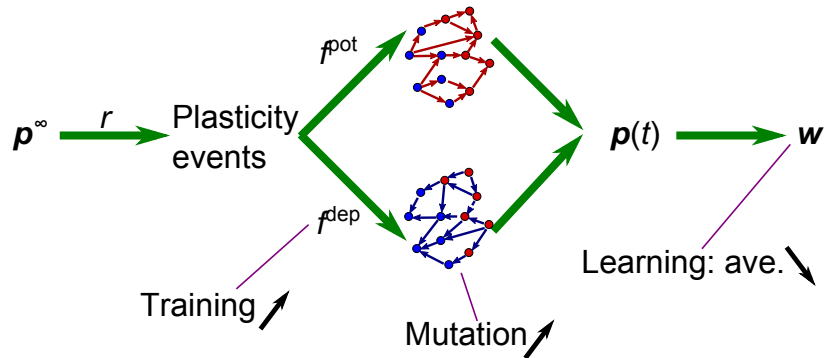
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Saturation by enh. plasticity impairs learning

└ Synaptic dynamics



1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \rightarrow j$
6. Readout: synaptic weight vec when in each state.



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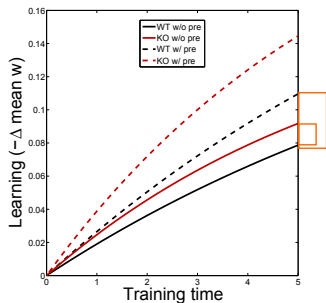
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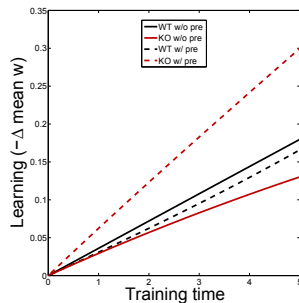
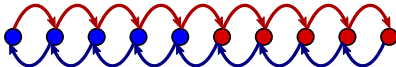


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5. probs changed by Markov matrices, prob $i \rightarrow j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold \rightarrow increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r .
9. Learning: Only output we have. Don't keep track of synaptic identity.
10. Same PF+CF input \rightarrow same $r, f^{\text{pot}}, f^{\text{dep}}$ in each case.
11. Input to P_k , some linear combination of w 's.

Binary model



Serial Model

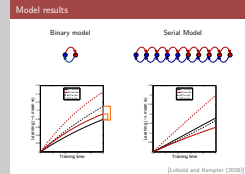


[Leibold and Kempner (2008)]

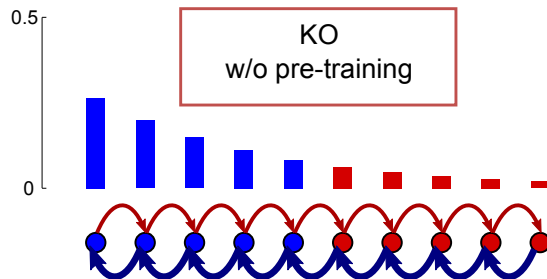
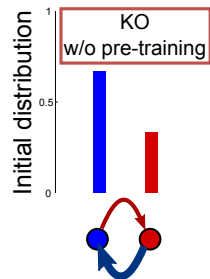
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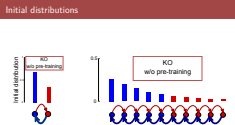
└ Model results



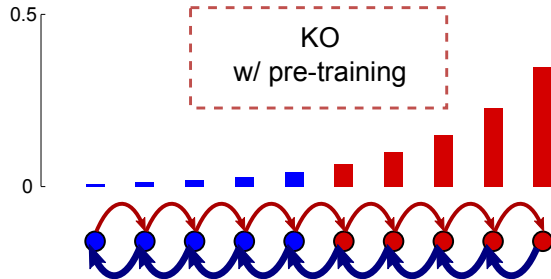
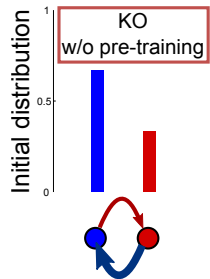
1. Binary fails
2. KO: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training



Initial distributions



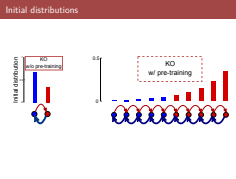
1. Binary: enhanced plasticity \rightarrow bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias



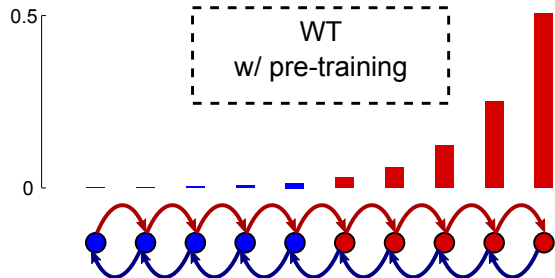
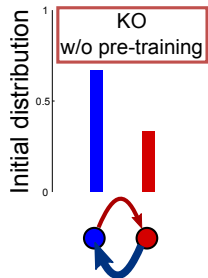
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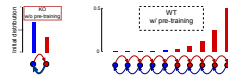
Initial distributions



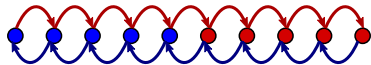
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Initial distributions



1. Binary: enhanced plasticity \rightarrow bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary
6. Too much pushes to other side, depopulates boundary



The success of the serial model relies on two features:

- Enhancing the effect of saturation,
- Metaplasticity – repeated potentiation makes subsequent depression harder.

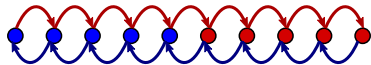
└ Essential features

1. due to exponential decay
2. push away from boundary where signal generated



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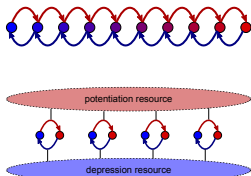
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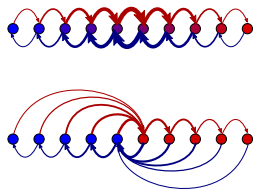
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Fail:



Succeed:



[Amit and Fusi (1994), Fusi et al. (2005)]

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Saturation by enh. plasticity impairs learning

└ Essential features

1. due to exponential decay
2. push away from boundary where signal generated
3. borne out by other models that fail/succeed

Essential features

The success of the serial model relies on two features:

- Enhancing the effect of saturation,
- Metaplasticity – repeated potentiation makes subsequent depression harder.

Fail:

Succeed:

[Amit and Fusi (1994), Fusi et al. (2005)]

- We can find a purely synaptic explanation of impaired learning, iff the synapses have two features.
- We used behaviour to constrain molecular structure of synapses!
- Can we constrain it further with more experiments?

└ Conclusions and further questions

1. Other explanations? Non-linearity in PK cell?

- We can find a purely synaptic explanation of impaired learning, iff the synapses have two features.
- We used behaviour to constrain molecular structure of synapses!
- Can we constrain it further with more experiments?

Acknowledgements

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Saturation by enh. plasticity impairs learning

└ Acknowledgements

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6



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18



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18

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