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

Subhaneil Lahiri

Stanford University, Applied Physics

July 16, 2013

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Saturation by enh. plasticity impairs learning

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1. Acknowledge Barbara and Grace

Introduction

Expect enhanced plasticity $\rightarrow$ enhance learning.
But often: $\rightarrow$ impairment.

Claim: due to basal activity $\rightarrow$ biased synaptic population
$\rightarrow$ fewer synapses available for learning.

Analysis of models of complex synapses:
motor learning of enhanced LTD mice $\rightarrow$ constrain synaptic structure.

Introduction

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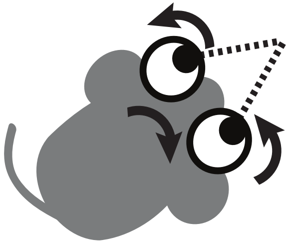
Analysis of models of complex synapses:
motor learning of enhanced LTD mice $\rightarrow$ constrain synaptic structure.

1. It does help in some cases

Vestibulo-Occular Reflex



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.

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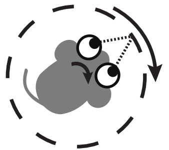
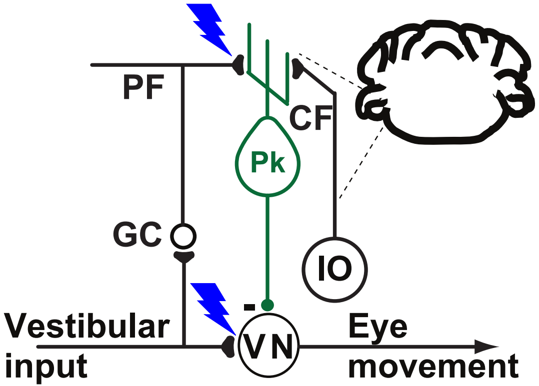
VOR training

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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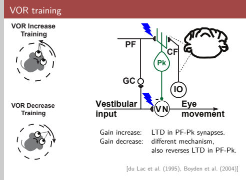
└VOR training



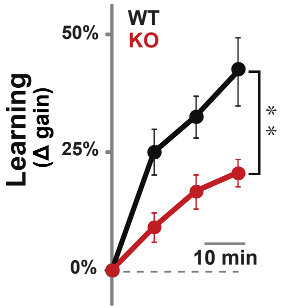
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Different mechs for different freq, head angle, gain up/down.

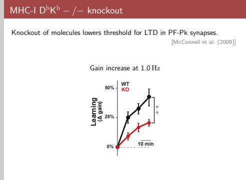
MHC-I $D^bK^b - /-$ knockout

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

[McConnell et al. (2009)]

Gain increase at 1.0 Hz

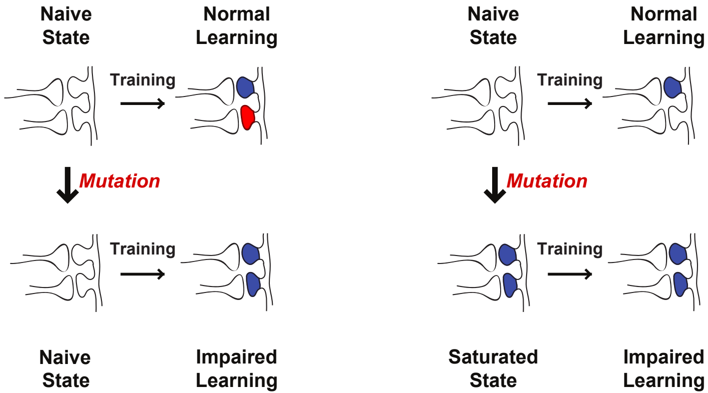


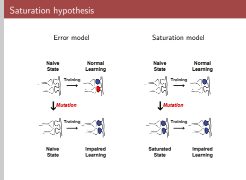


1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD $\rightarrow$ expect better learning
3. Impairment of learning
4. Looking at change of VOR gain during gain-up training

Saturation hypothesis

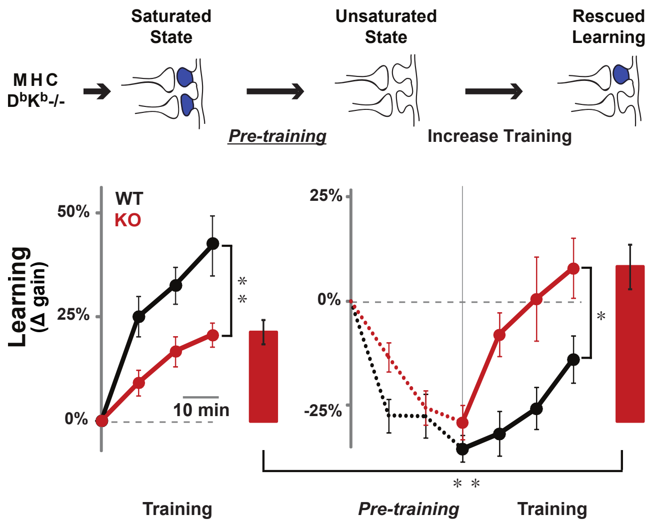
Error model | Saturation model





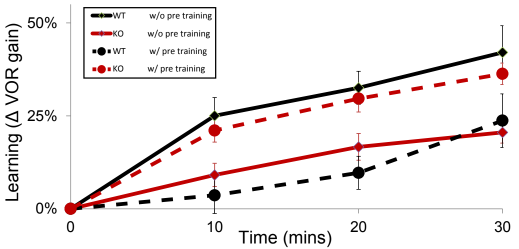
1. Older explanation: error model
2. Our model: baseline activity → saturation → less depression possible
3. Saturation has to compete with enhanced plsaticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

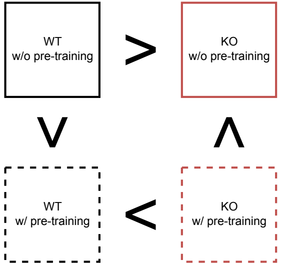
Evidence: desaturation by gain-decrease pretraining



1. gain dec reverses LTD
2. but behaviour from elsewhere

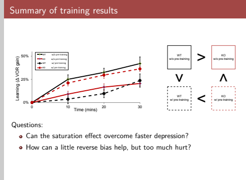
Summary of training results





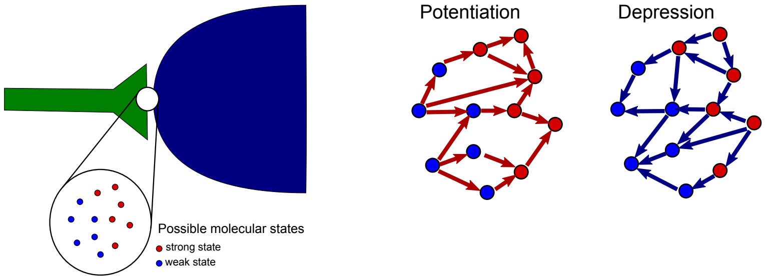
Questions:

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



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

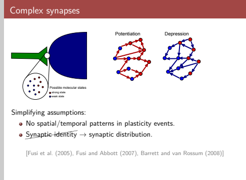
Complex synapses



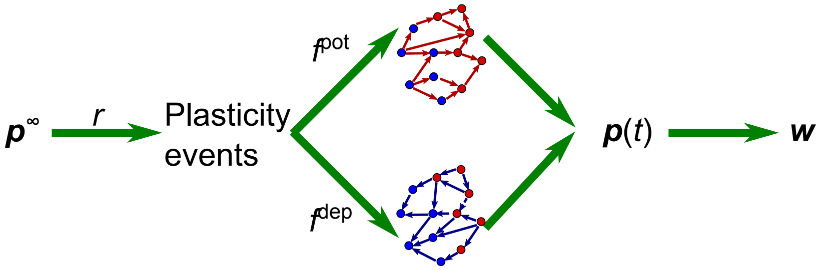
Simplifying assumptions:

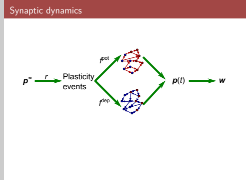
- No spatial/temporal patterns in plasticity events.
- ~~Synaptic identity~~ $\rightarrow$ synaptic distribution.

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



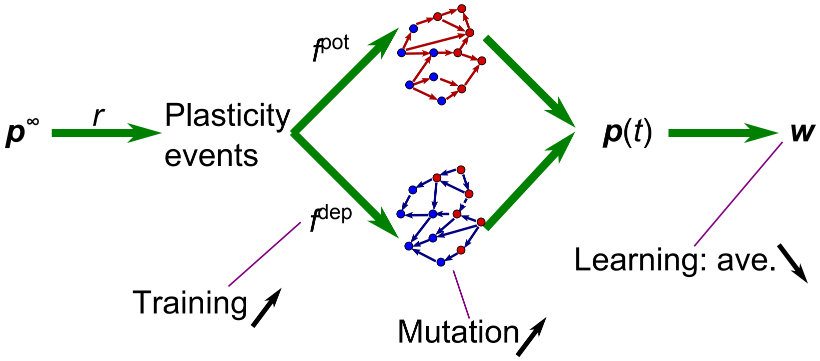
1. functional states, not molecules
2. synaptic weight depends on state
3. many states can have same weight
4. stochastic transitions
5. allows us to concentrate on synapse, not neuron/network
6. This is a question about synaptic populations after all.

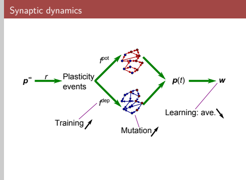




1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

Synaptic dynamics





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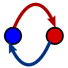
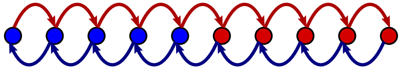
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold $\to$ increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r.
9. Learning: Only output we have. Don't keep track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

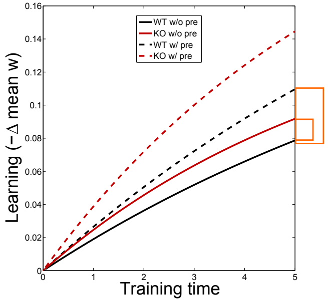
Model results

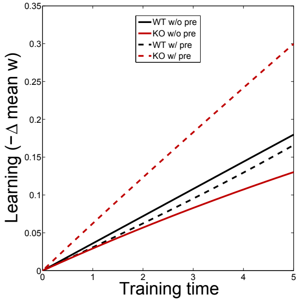
Binary model



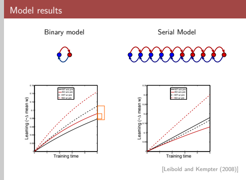
Serial Model





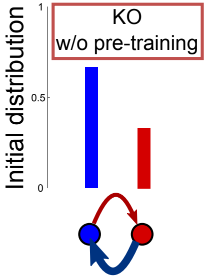


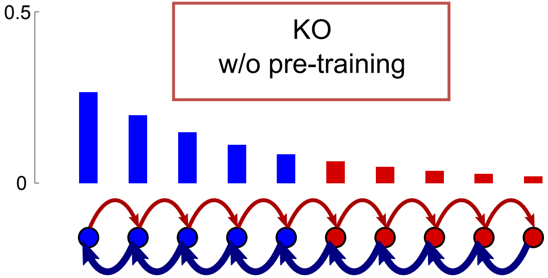
[Leibold and Kempter (2008)]

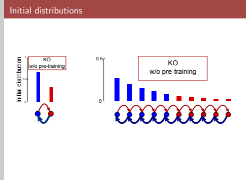


1. Binary fails
2. KO: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training

Initial distributions







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2. Not enough to overcome faster depression
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4. Exponential decay depopulates boundary, enhances effect of bias

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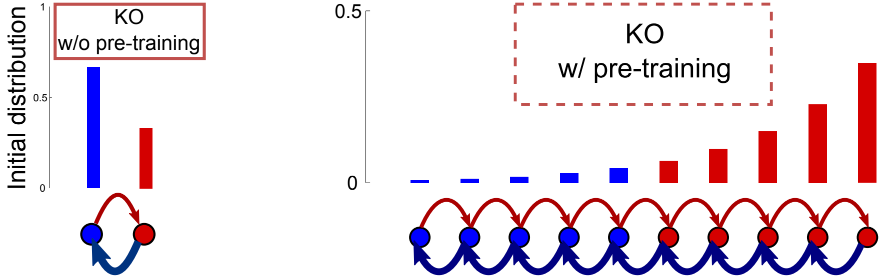

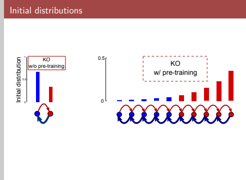

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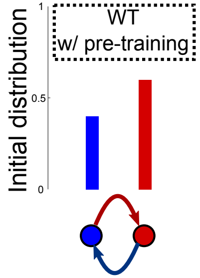
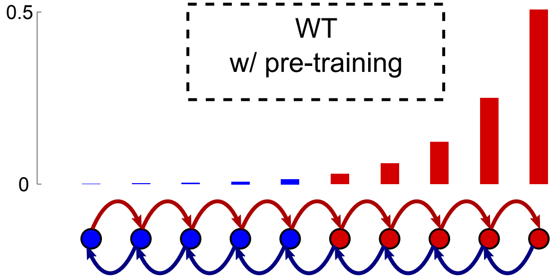
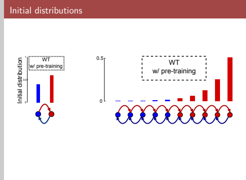
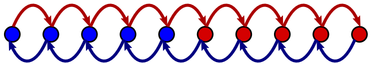






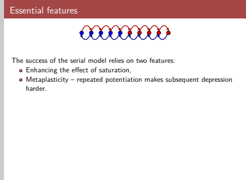
1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary
6. Too much pushes to other side, depopulates boundary

Essential features



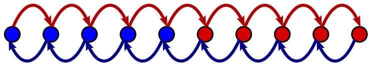
The success of the serial model relies on two features:

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



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

Essential features



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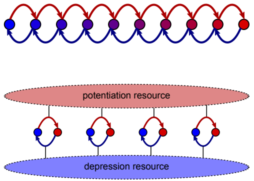
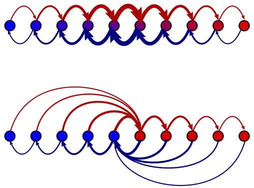
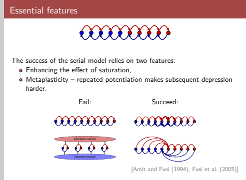
Fail:



Succeed:



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



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

Conclusions and further questions

- 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?

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

Acknowledgements

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