# 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 15, 2013





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1. Acknowledge Barbara and Grace

# Introduction

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

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

By analysing several models of complex synapses, we see that the behaviour of enhanced LTD mice in a motor learning task can constrain the synaptic structure.





Introduction

Expect enhanced plasticity $\to$ enhance learning.
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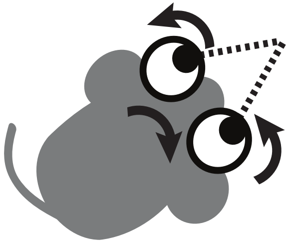
$\to$ fewer synapses available for learning.

By analysing several models of complex synapses, we see that the behaviour of enhanced LTD mice in a motor learning task can constrain the 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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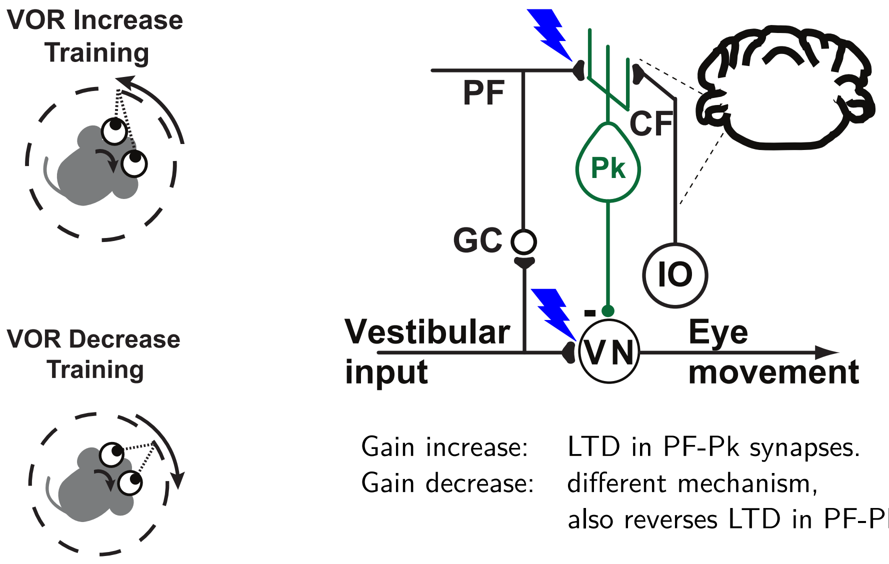
# VOR training

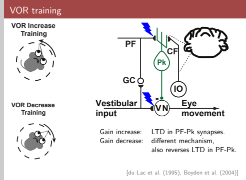



| | |
|---|---|
| Gain increase: | LTD in PF-Pk synapses. |
| Gain decrease: | different mechanism, |
| | also reverses LTD in PF-Pk. |

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







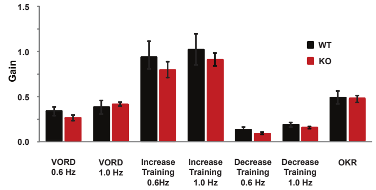
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Marr-Albus-Ito: Pf-Pk synapses
6. Lisberger-Miles: Vestibular input-VN synapses
7. Different mechs for different freq, head angle, gain up/down.
8. Different Pk cells have different tunings.
9. PF-Pk:PF+CF → LTD, PF+~~CF~~ → LTP.

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

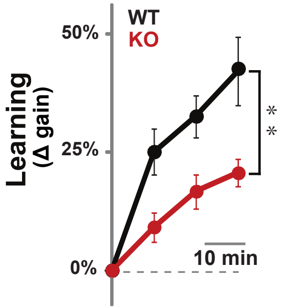
Knockout of molecules lowers threshold for LTD in PF-Pk synapses.

[McConnell et al. (2009)]

Baseline

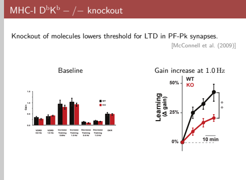



Gain increase at 1.0 Hz





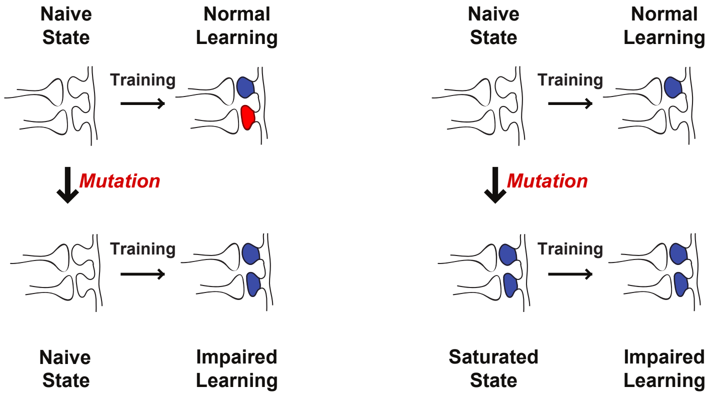


1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD $\rightarrow$ expect better learning
3. No difference in baseline occulomotor performance
4. Impairment of learning
5. Looking at change of VOR gain during gain-up training

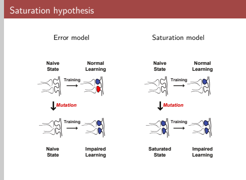
# Saturation hypothesis

**Error model** | **Saturation model**



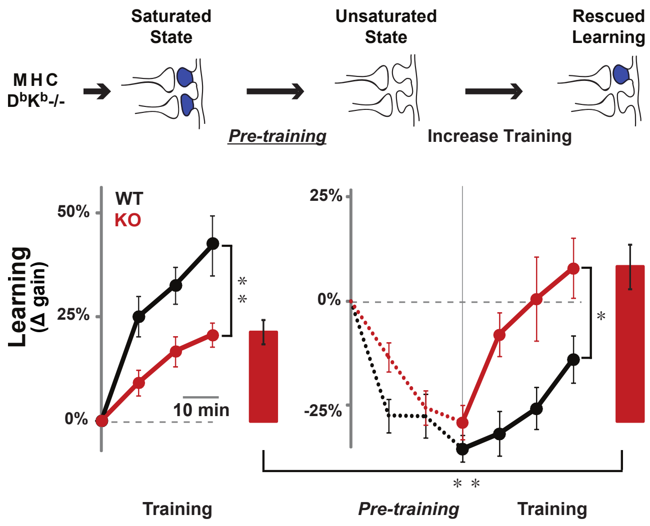




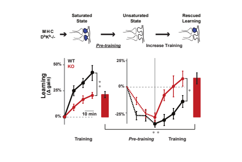
1. Older explanation: error model
2. Our model: baseline activity → saturation → less depression possible
3. Saturation has to compete with enhanced plsaticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

# Evidence: desaturation by gain-decrease pretraining



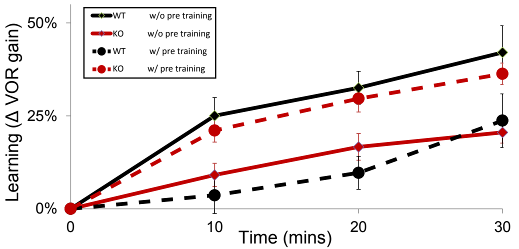


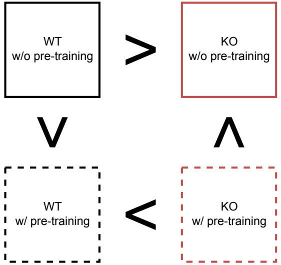


1. gain dec reverses LTD
2. but behaviour from elsewhere

# Summary of training results



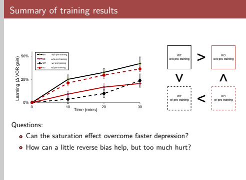




Questions:

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

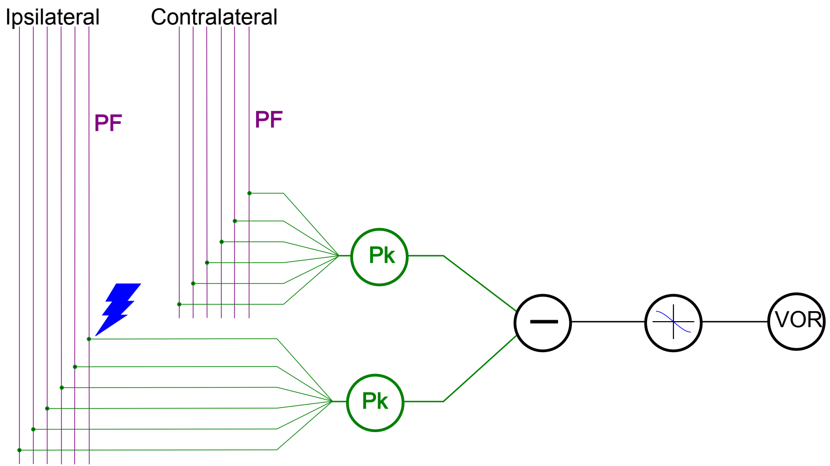






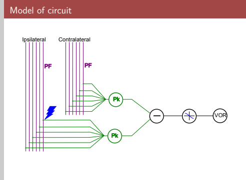
1. Restricted to gain inc for comparison
2. Black: WT. Red: KO
3. Solid: no pre. Dashed: with pre
4. Horz and vert comparisons: conceptual
5. Diagonal comparisons: paramter fitting. Depend on size of KO vs. pretraining
6. KO hurts w/o, but helps w/
7. pre helps KO but hurts WT
8. top and left most restrictive
9. Pay attention to solid: black above red
10. Pay attention to black: solid above dashed
11. Concentrate on initial slope
12. in competition
13. first makes sense, but second?
14. This is a question about synaptic populations after all.

# Model of circuit



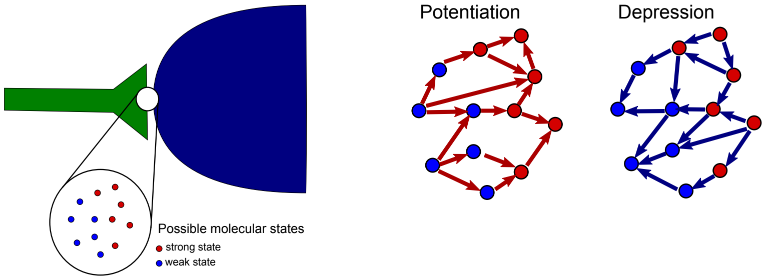





1. Contralateral baseline shift compensates for Our baseline shift
2. Gain increase due to LTD at lightning
3. Gain decease due to plasticity elsewhere, but also reverses LTD at lightning
4. Nonlinearity here won't affect our questions, as long as it doesn't change
5. Nonlinearity before compensation could change things

# Complex synapses



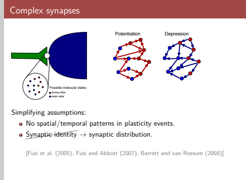

Simplifying assumptions:

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

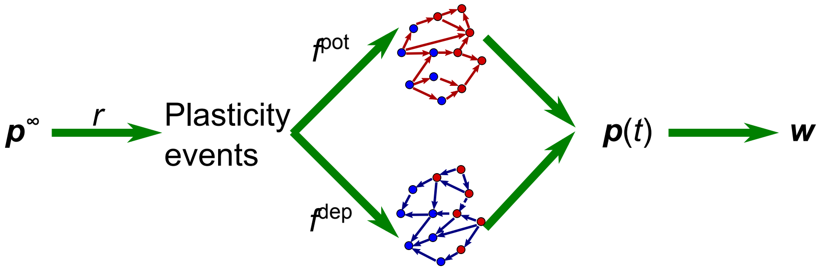
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]





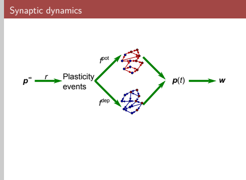



1. functional states, not molecules
2. synaptic weight depends on state
3. many states can have same weight
4. stochastic transitions
5. allows us to concentrate on synapse, not neuron/network



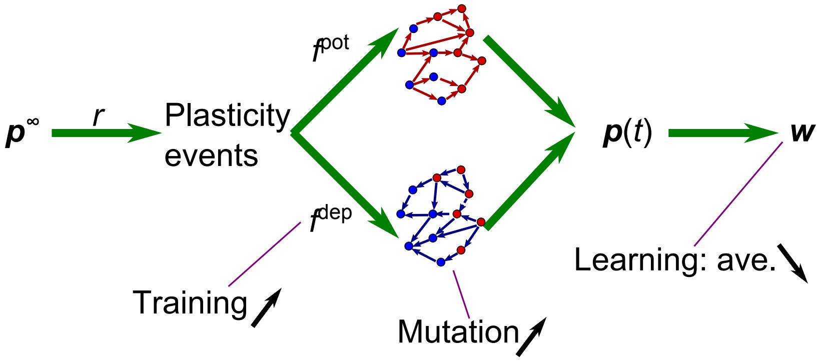




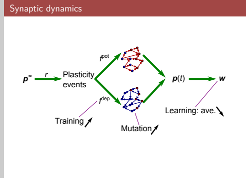
1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

# Synaptic dynamics





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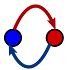
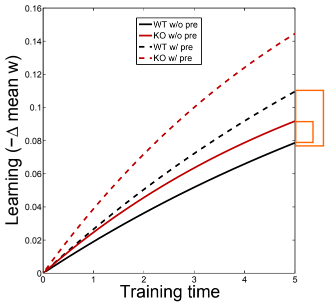
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold → increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about $r$.
9. Learning: Only output we have. Don't keep track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

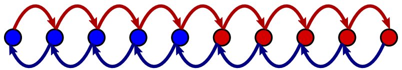
# Model results

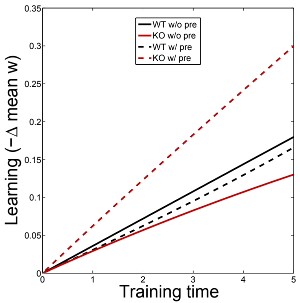
## Binary model





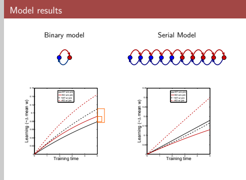

## Serial Model





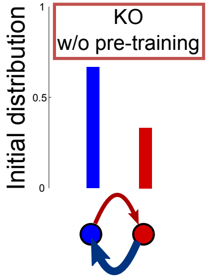


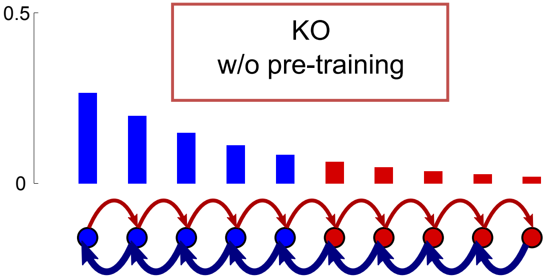


1. Binary fails
2. KO: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training

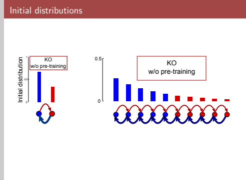
# Initial distributions








1. Binary: enhanced plasticity → 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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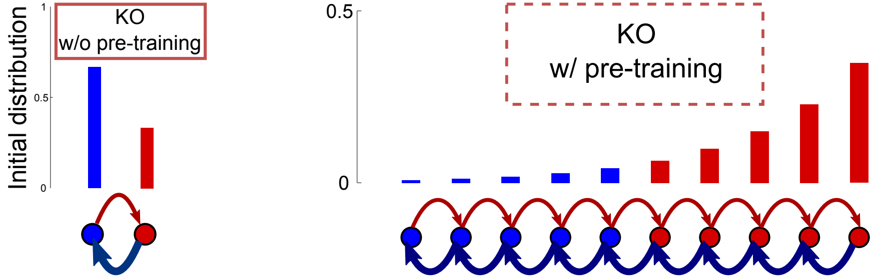






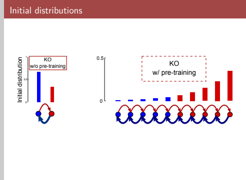

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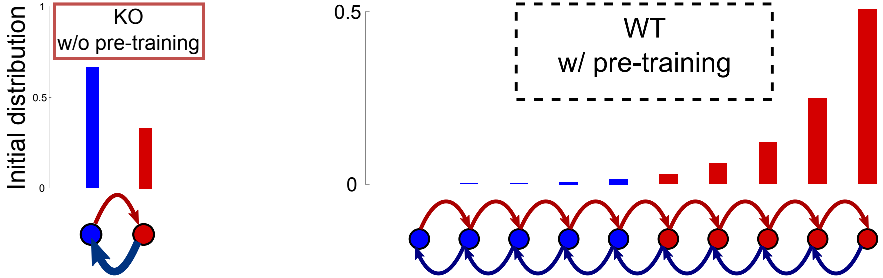






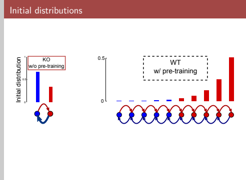


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3. Serial: Only get signal from boundary
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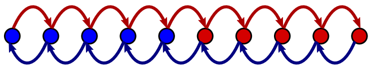
5. Pretraining: little repopulates boundary
6. Too much pushes to other side, depopulates boundary

# Essential features



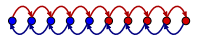
The success of the serial model relies on two features:

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





Essential features



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2. push away from boundary where signal generated
3. borne out by other models that fail/succeed

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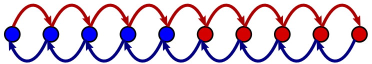

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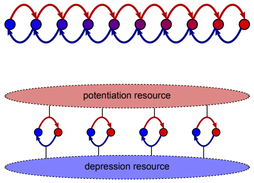
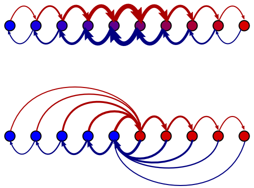
Fail:



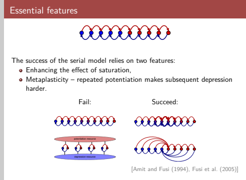

Succeed:



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







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3. borne out by other models that fail/succeed

# Conclusions and further questions

- The saturation effect can overcome faster depression, if it is enhanced. Requires complexity
- A little reverse bias can help, but too much hurts, if repeated potentiation makes depression harder. Requires metaplasticity
- We can find a purely synaptic explanation of VOR behaviour, iff the synapses have these features.
- We used behaviour to constrain molecular structure of synapses!
- Can we constrain it further with more experiments?





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- We used behaviour to constrain molecular structure of synapses!
- Can we constrain it further with more experiments?

1. e.g. exponential deacy, resource depletion,...
2. e.g. moving away from weight boundary, or weaker transitions.
3. Other explanations? Non-linearity in PK cell?

# Acknowledgements


| | | |
|---|---|---|
| **Surya Ganguli** | **Jennifer Raymond** | **Carla Shatz** |
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2013-07-15

Saturation by enh. plasticity impairs learning

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