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

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1. Acknowledge Barbara and Grace

Introduction

One might expect enhanced plasticity to enhance learning. But often it actually causes impairment.

We argue that this impaired learning is due to basal activity biasing the synapses prior to learning, leaving fewer synapses available for further plasticity.

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

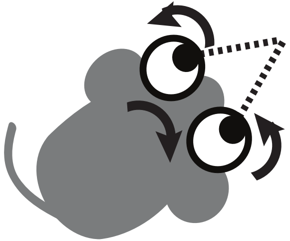
One might expect enhanced plasticity to enhance learning. But often it actually causes impairment.

We argue that this impaired learning is due to basal activity biasing the synapses prior to learning, leaving fewer synapses available for further plasticity.

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

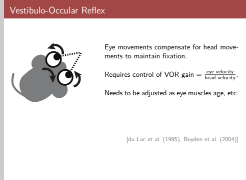


Eye movements compensate for head movements to maintain fixation.

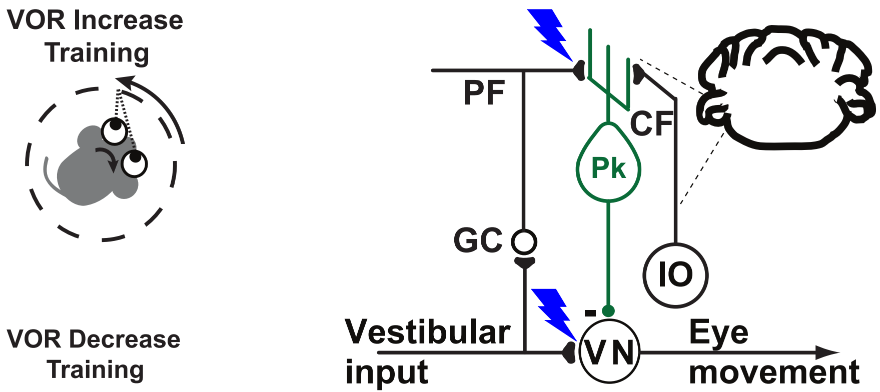
Requires control of VOR gain $= \frac{\text{eye velocity}}{\text{head velocity}}$.

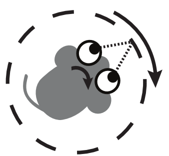
Needs to be adjusted as eye muscles age, etc.

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



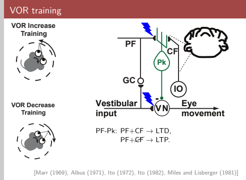
VOR training





PF-Pk: PF+CF → LTD,
PF+~~CF~~ → LTP.

[Marr (1969), Albus (1971), Ito (1972), Ito (1982), Miles and Lisberger (1981)]



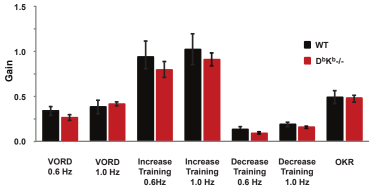
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Marr-Albus-Ito: Pf-Pk synapses
6. Lisberger-Miles: Vestibular input-VN synapses
7. Different mechs for different freq, head angle, gain up/down.
8. Different Pk cells have different tunings.
9. Gain up in case of interest: LTD in Pf-Pk in flocculus
10. Gain down: uses different mech for behaviour, but does reverse LTD in Pf-Pk in flocculus

MHC-I D^bK^b −/− knockout

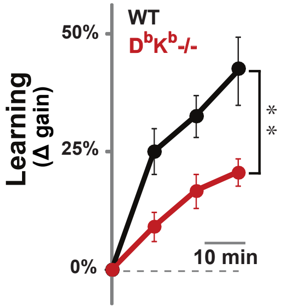
Knockout of molecules lowers threshold for LTD in PF-Pk synapses.

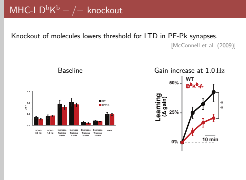
[McConnell et al. (2009)]

Baseline



Gain increase at 1.0 Hz



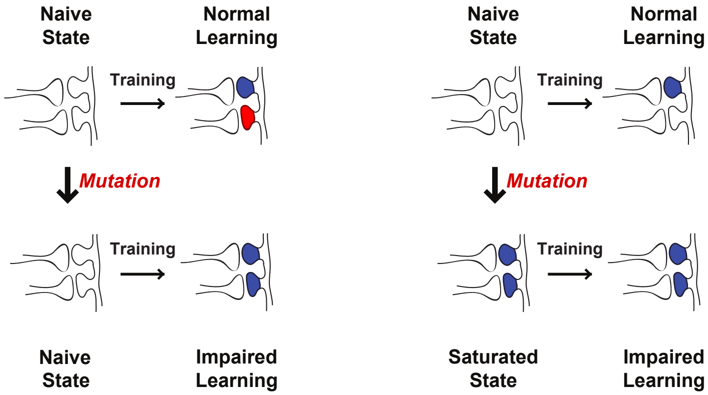


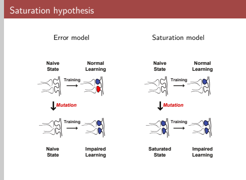
1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD → expect better learning
3. No difference at baseline
4. Impairment of learning
5. Lookng at change of VOR gain during gain-up training

Saturation hypothesis

Error model

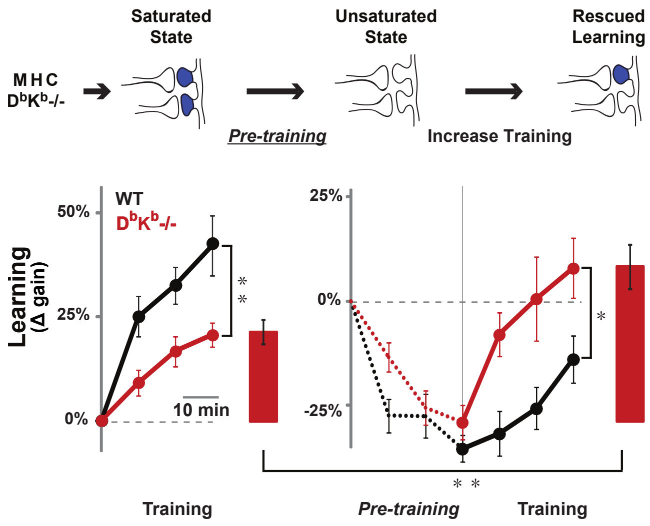
Saturation model





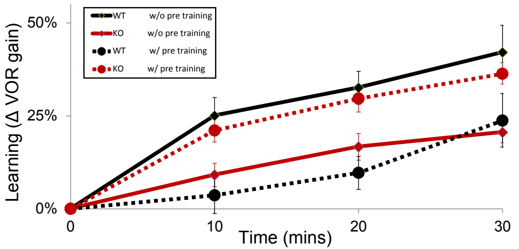
1. Older explanation: error model
2. Our model: baseline activity $\to$ saturation $\to$ less depression possible
3. Saturation has to compete with enhanced plsaticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

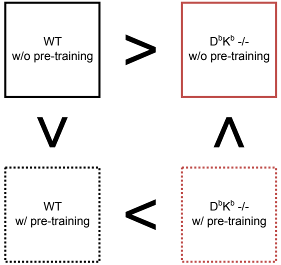
Evidence: desaturation by gain-decrease pretraining



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

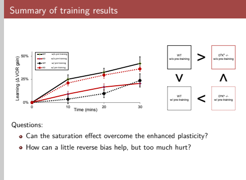
Summary of training results





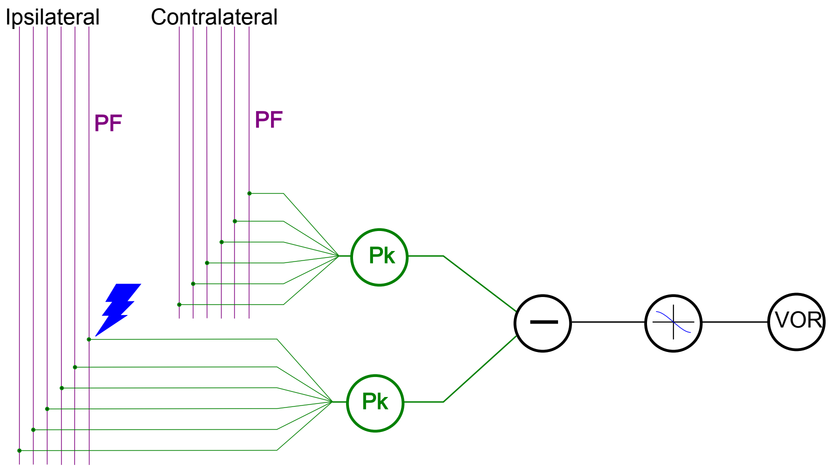
Questions:

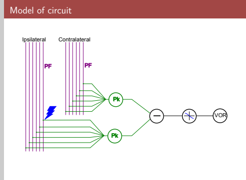
- Can the saturation effect overcome the enhanced plasticity?
- How can a little reverse bias help, but too much hurt?



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.

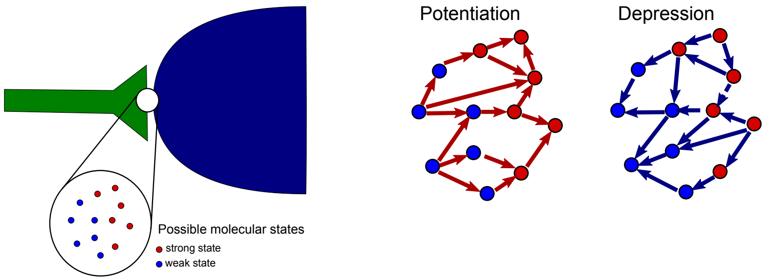
Model of circuit





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

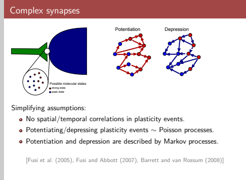
Complex synapses



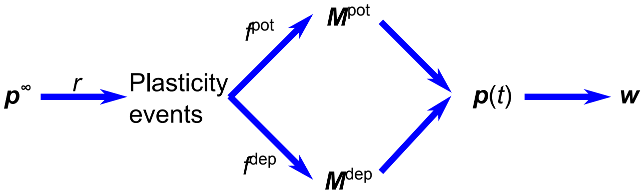
Simplifying assumptions:

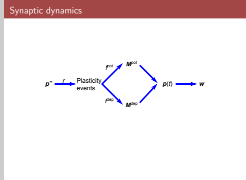
- No spatial/temporal correlations in plasticity events.
- Potentiating/depressing plasticity events $\sim$ Poisson processes.
- Potentiation and depression are described by Markov processes.

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



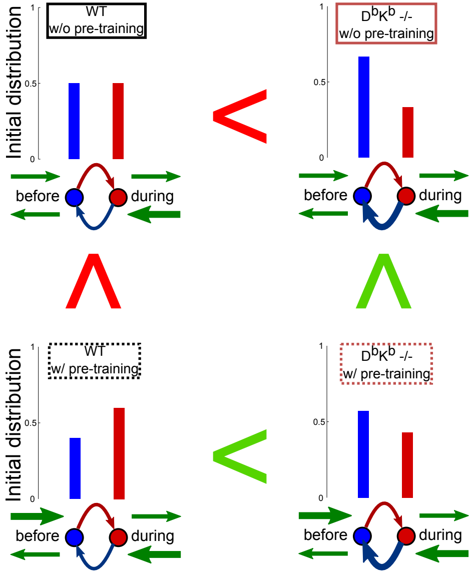
1. functional states, not molecules
2. synaptic weight depends on state
3. many states can have same weight
4. stochastic transitions
5. allows us to concentrate on synapse, not neuron/network
6. don't care if STDP...

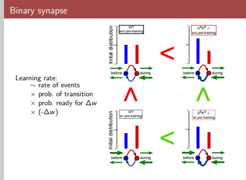




1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

Learning rate:
- $\sim$ rate of events
- $\times$ prob. of transition
- $\times$ prob. ready for Δw
- $\times$ (-Δw)

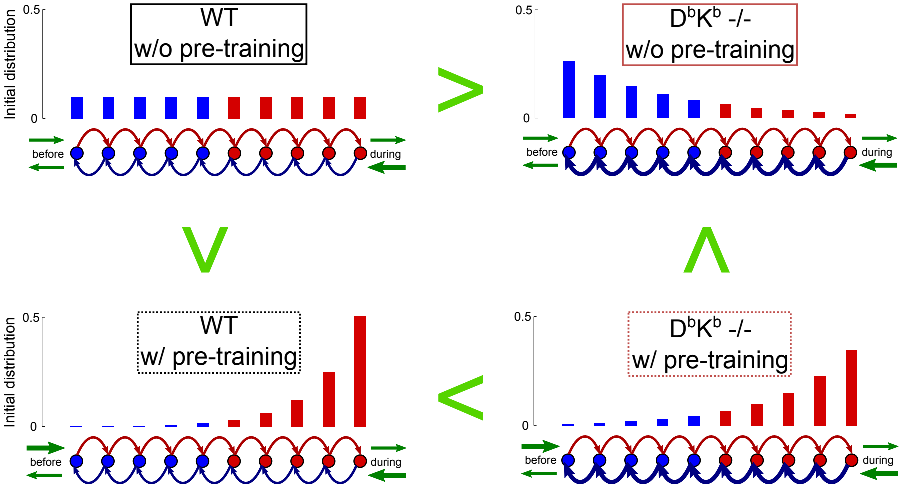


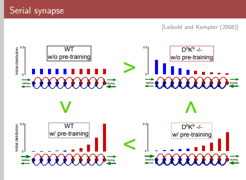


1. WT: start with everything equal – just for illustration, not essential
2. WT: during training, increase f^{dep} (green arrow) $\to$ weakening.
3. KO: inc q^{pot} $\to$ bias
4. KO: competition between inc prob trans & dec prob ready
5. KO: first one wins. see why after next model
6. pre: reduces/reverses bias. always helps.

Serial synapse

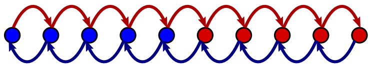
[Leibold and Kempter (2008)]





1. Now only get signal from crossing boundary
2. KO: inc $q^{\text{pot}} \to$ bias, now exponential
3. KO: prob ready wins over prob trans, now exponential
4. pre: reduces/reverses bias.
5. pre: little reverse bias repopulates bndry, helps.
6. pre: too much reverse bias moves away from bndry, hurts.
7. maths next slide

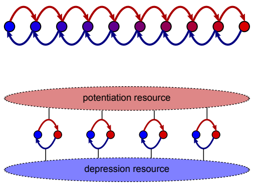
Essential features



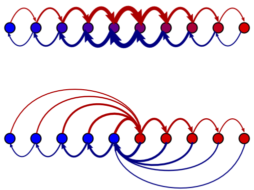
The success of the serial model relies on two features:

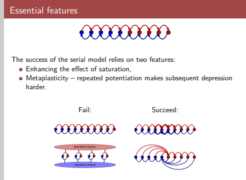
- Enhancing the effect of saturation,
- Metaplasticity – repeated potentiation makes subsequent depression harder.

Fail:



Succeed:





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

- The saturation effect overcome the enhanced plasticity, 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 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?

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?

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David Marr.
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Saturation by enh. plasticity impairs learning

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