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

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

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

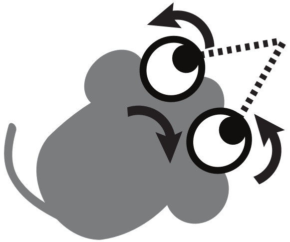
Expect enhanced plasticity $\rightarrow$ enhance learning.
But often: $\rightarrow$ impairment.

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.

1. It does help in some cases

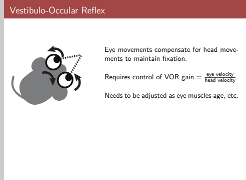
Vestibulo-Occular Reflex

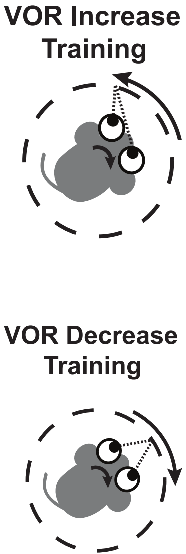


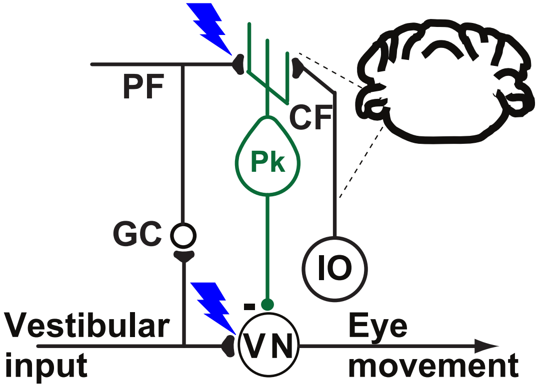
Eye movements compensate for head movements to maintain fixation.

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

Needs to be adjusted as eye muscles age, etc.

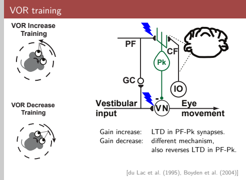






Gain increase: LTD in PF-Pk synapses.
Gain decrease: different mechanism, also reverses LTD in PF-Pk.

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



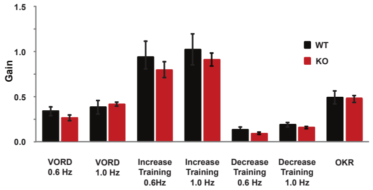
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Marr-Albus-Ito: Pf-Pk synapses
6. Lisberger-Miles: Vestibular input-VN synapses
7. Different mechs for different freq, head angle,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

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

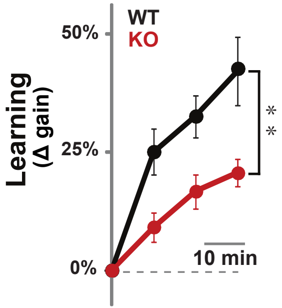
Knockout of molecules lowers threshold for LTD in PF-Pk synapses.

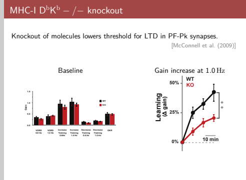
[McConnell et al. (2009)]

Baseline



Gain increase at 1.0 Hz

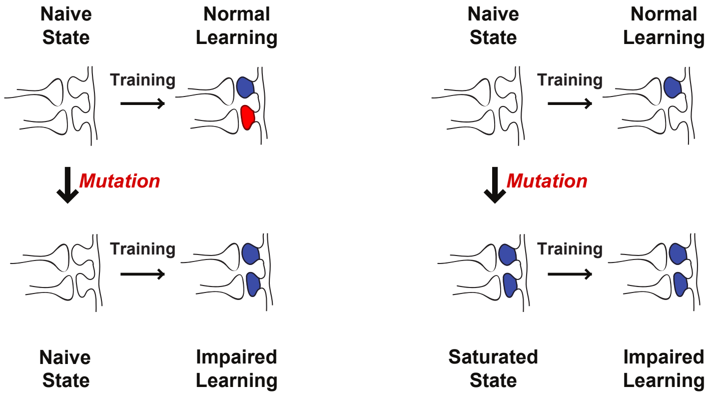


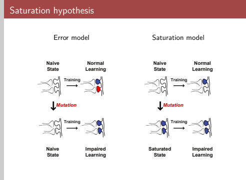


1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD $\rightarrow$ expect better learning
3. No difference in baseline occulomotor performance
4. Impairment of learning
5. Looking at change of VOR gain during gain-up training

Saturation hypothesis

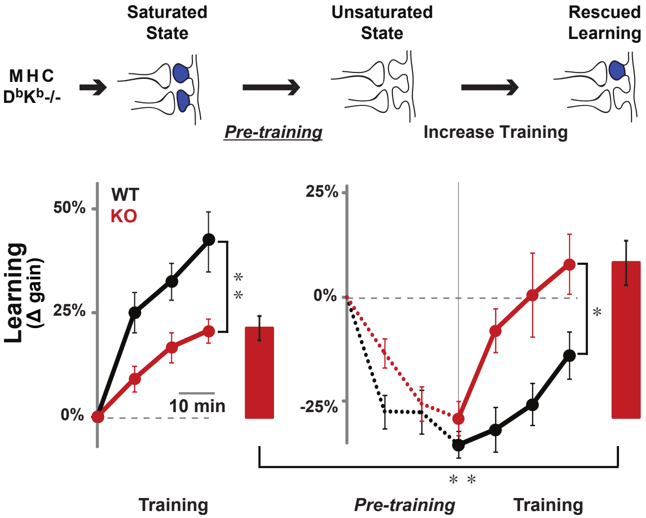
Error model | Saturation model

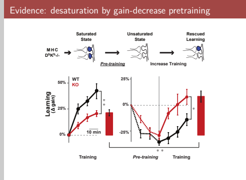




1. Older explanation: error model
2. Our model: baseline activity → saturation → less depression possible
3. Saturation has to compete with enhanced plsaticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

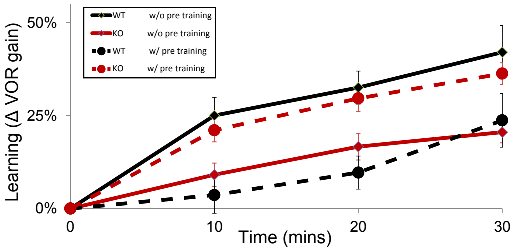
Evidence: desaturation by gain-decrease pretraining

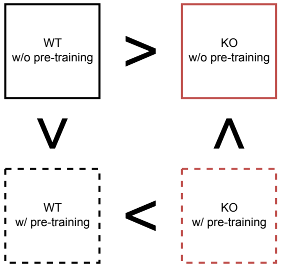




1. gain dec reverses LTD
2. but behaviour from elsewhere

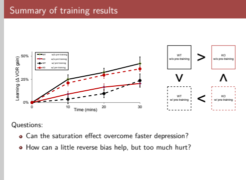
Summary of training results



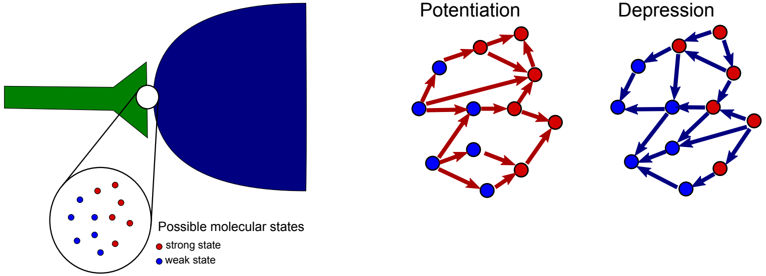


Questions:

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



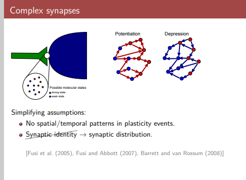
1. Restricted to gain inc for comparison
2. Black: WT. Red: KO
3. Solid: no pre. Dashed: with pre
4. Horz and vert comparisons: conceptual
5. Diagonal comparisons: paramter fitting. Depend on size of KO vs. pretraining
6. KO hurts w/o, but helps w/
7. pre helps KO but hurts WT
8. top and left most restrictive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



Simplifying assumptions:

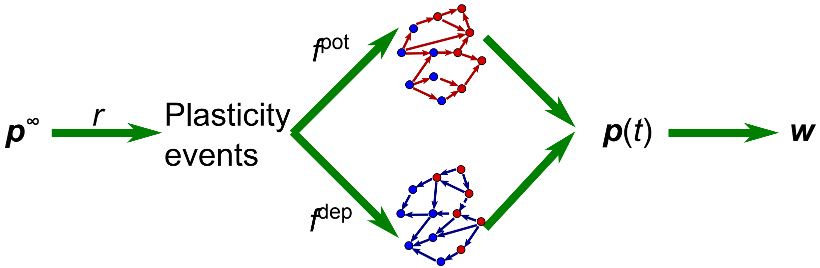
- No spatial/temporal patterns in plasticity events.
- ~~Synaptic identity~~ $\rightarrow$ synaptic distribution.

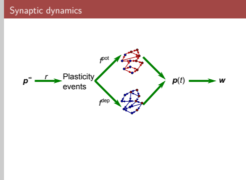
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]



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

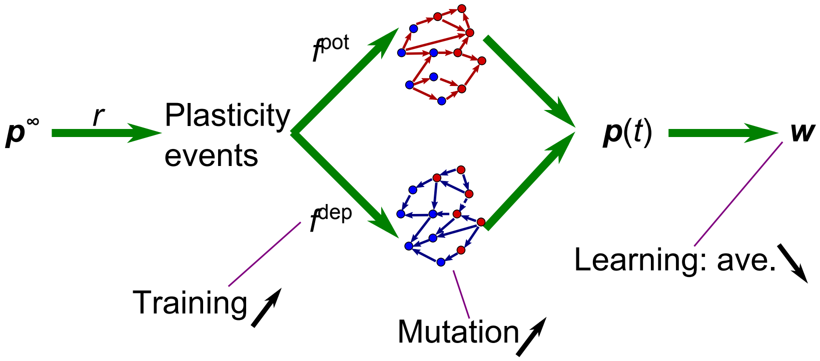
Synaptic dynamics

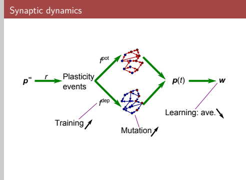




1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

Synaptic dynamics

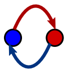


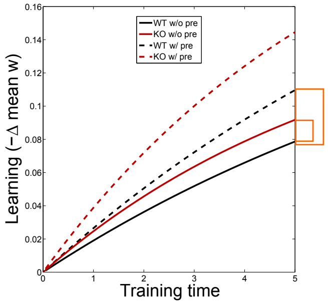


1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold $\to$ increase transition probs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

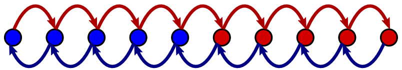
Model results

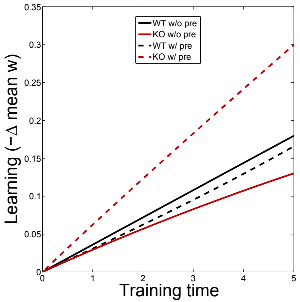
Binary model

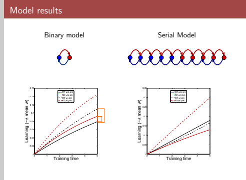




Serial Model

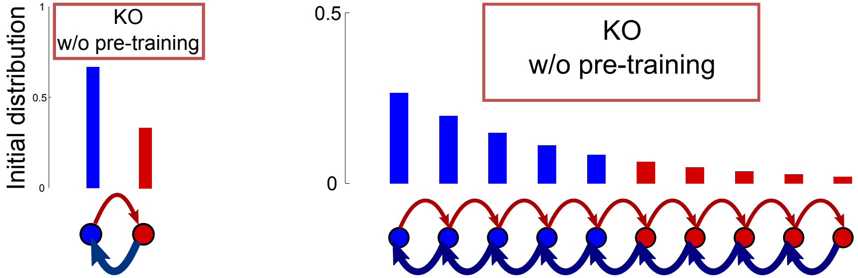


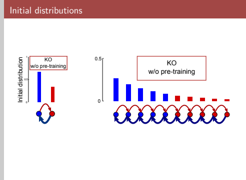




1. Binary fails
2. KO: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training

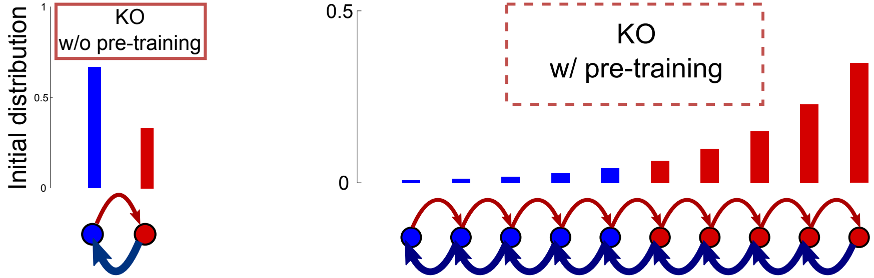
Initial distributions

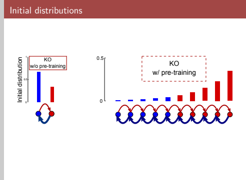




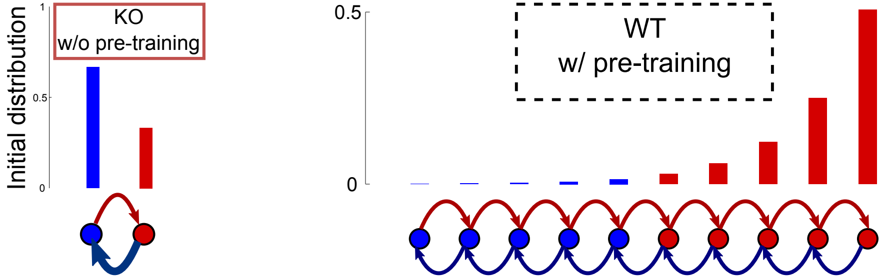
1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias

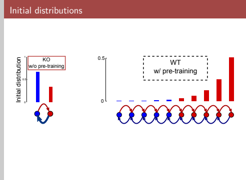
Initial distributions



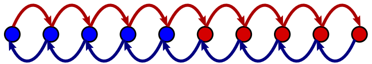


1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary





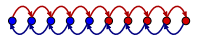
1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary
6. Too much pushes to other side, depopulates boundary



The success of the serial model relies on two features:

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

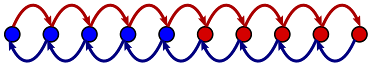
Essential features



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
3. borne out by other models that fail/succeed

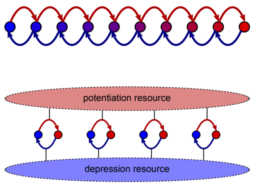
Essential features



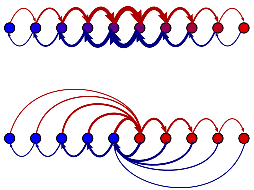
The success of the serial model relies on two features:

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

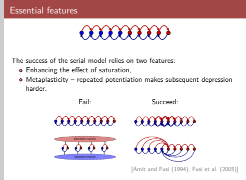
Fail:



Succeed:



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



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 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?

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?

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**
Madhu Advani	Barbara Nguyen-Vu	Han-Mi Lee
Pairan Gao	Grace Zhao	
Niru Maheswaranathan	Aparna Suvrathan	

Funding: Swartz Founsation, Stanford Bio-X Genentech fellowship.

Acknowledgements

Surya Ganguli Jennifer Raymond Carla Shatz
Madhu Advani Barbara Nguyen-Vu Han-Mi Lee
Pairan Gao Grace Zhao
Niru Maheswaranathan Aparna Suvrathan

Funding: Swartz Founsation, Stanford Bio-X Genentech fellowship.

References I

S du Lac, J L Raymond, T J Sejnowski, and S G Lisberger.
"Learning and Memory in the Vestibulo-Ocular Reflex".
Annual Review of Neuroscience, 18(1):409–441, (1995) .
5

Edward S. Boyden, Akira Katoh, and Jennifer L. Raymond.
"CEREBELLUM-DEPENDENT LEARNING: The Role of Multiple Plasticity Mechanisms".
Annual Review of Neuroscience, 27(1):581–609, (2004) .
5

2013-07-15

Saturation by enh. plasticity impairs learning

└References

References I

S du Lac, J L Raymond, T J Sejnowski, and S G Lisberger.
"Learning and Memory in the Vestibulo-Ocular Reflex".
Annual Review of Neuroscience, 18(1):409–441, (1995) .
5

Edward S. Boyden, Akira Katoh, and Jennifer L. Raymond.
"CEREBELLUM-DEPENDENT LEARNING: The Role of Multiple Plasticity Mechanisms".
Annual Review of Neuroscience, 27(1):581–609, (2004) .
5

References II

Michael J. McConnell, Yanhua H. Huang, Akash Datwani, and Carla J. Shatz.
"H2-Kb and H2-Db regulate cerebellar long-term depression and limit motor learning".
Proc. Natl. Acad. Sci. U.S.A., 106(16):6784–6789, (2009) .
6

S. Fusi, P. J. Drew, and L. F. Abbott.
"Cascade models of synaptically stored memories".
Neuron, 45(4):599–611, (Feb, 2005) .
10 17 18

S. Fusi and L. F. Abbott.
"Limits on the memory storage capacity of bounded synapses".
Nat. Neurosci., 10(4):485–493, (Apr, 2007) .
10

References II

Michael J. McConnell, Yanhua H. Huang, Akash Datwani, and Carla J. Shatz.
"H2-Kb and H2-Db regulate cerebellar long-term depression and limit motor learning".
Proc. Natl. Acad. Sci. U.S.A., 106(16):6784–6789, (2009) .

S. Fusi, P. J. Drew, and L. F. Abbott.
"Cascade models of synaptically stored memories".
Neuron, 45(4):599–611, (Feb, 2005) .

S. Fusi and L. F. Abbott.
"Limits on the memory storage capacity of bounded synapses".
Nat. Neurosci., 10(4):485–493, (Apr, 2007) .

References III

A. B. Barrett and M. C. van Rossum.
"Optimal learning rules for discrete synapses".
PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .
10

D. J. Amit and S. Fusi.
"Learning in neural networks with material synapses".
Neural Computation, 6(5):957–982, (1994) .
17 18

└References

References III

A. B. Barrett and M. C. van Rossum.
"Optimal learning rules for discrete synapses".
PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .
10

D. J. Amit and S. Fusi.
"Learning in neural networks with material synapses".
Neural Computation, 6(5):957–982, (1994) .
17 18