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

2013-07-15

Saturation by enh. plasticity impairs learning

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

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

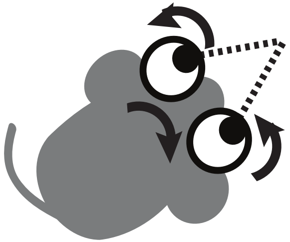
Expect enhanced plasticity $\rightarrow$ enhance learning.
But often: $\rightarrow$ impairment.

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

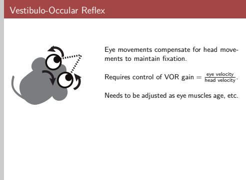
Vestibulo-Occular Reflex



Eye movements compensate for head movements to maintain fixation.

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

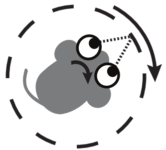
Needs to be adjusted as eye muscles age, etc.

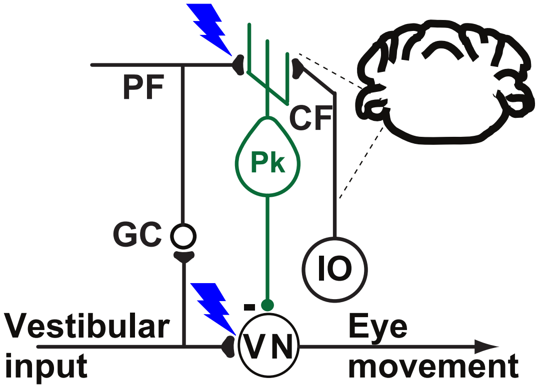


VOR training

VOR Increase Training

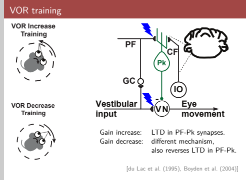
VOR Decrease Training





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)]



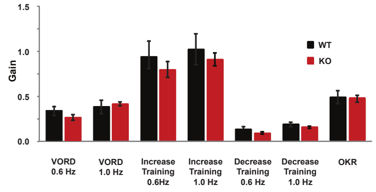
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. Different mechs for different freq, head angle, gain up/down.

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

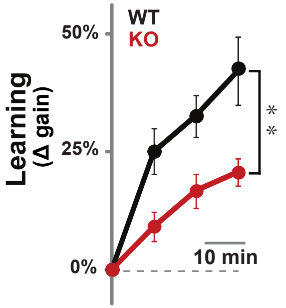
Knockout of molecules lowers threshold for LTD in PF-Pk synapses.

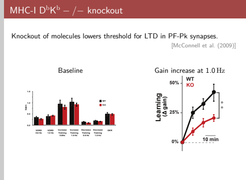
[McConnell et al. (2009)]

Baseline



Gain increase at 1.0 Hz



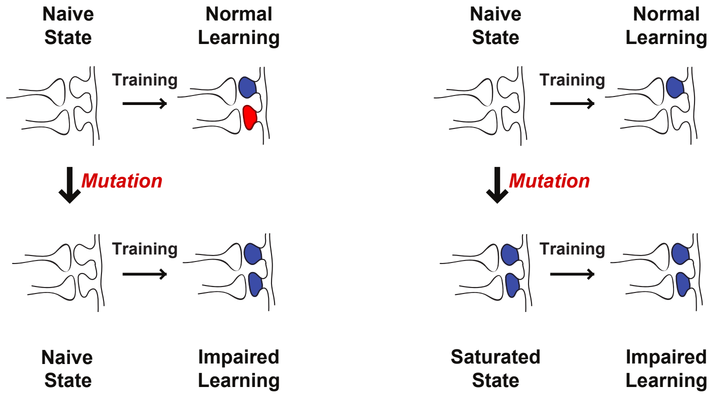


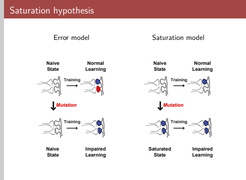
1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD → expect better learning
3. No difference in baseline occulomotor performance
4. Impairment of learning
5. Looking at change of VOR gain during gain-up training

Saturation hypothesis

Error model

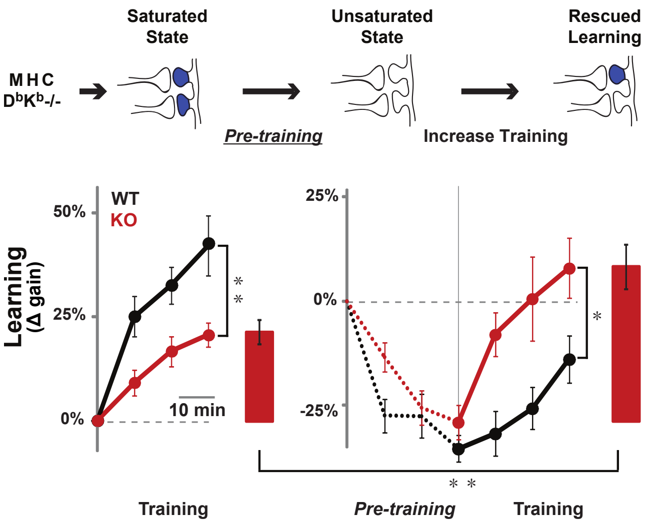
Saturation model

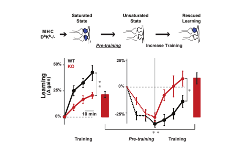




1. Older explanation: error model
2. Our model: baseline activity → saturation → less depression possible
3. Saturation has to compete with enhanced plsaticity. Which will win?
4. Many expt checks of this, but we'll focus on one...

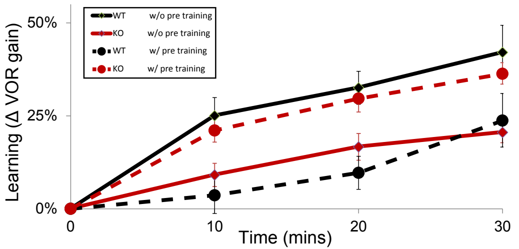
Evidence: desaturation by gain-decrease pretraining

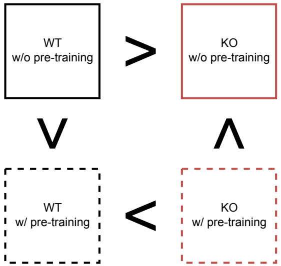




1. gain dec reverses LTD
2. but behaviour from elsewhere

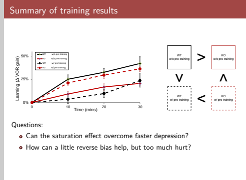
Summary of training results





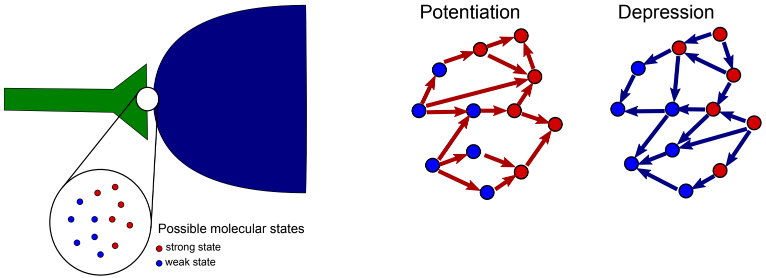
Questions:

- 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. 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

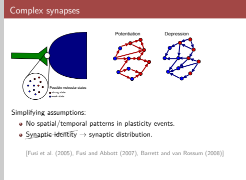
Complex synapses



Simplifying assumptions:

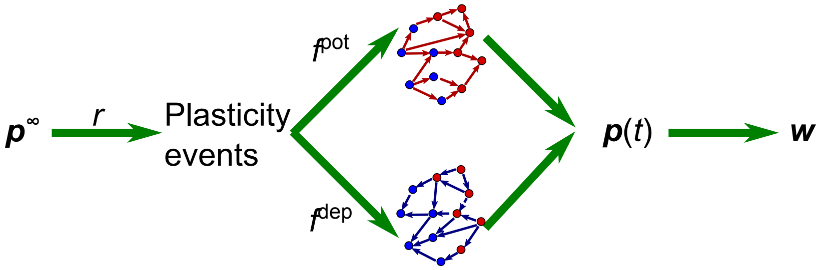
- No spatial/temporal patterns in plasticity events.
- ~~Synaptic identity~~ → synaptic distribution.

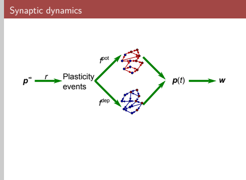
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]



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.

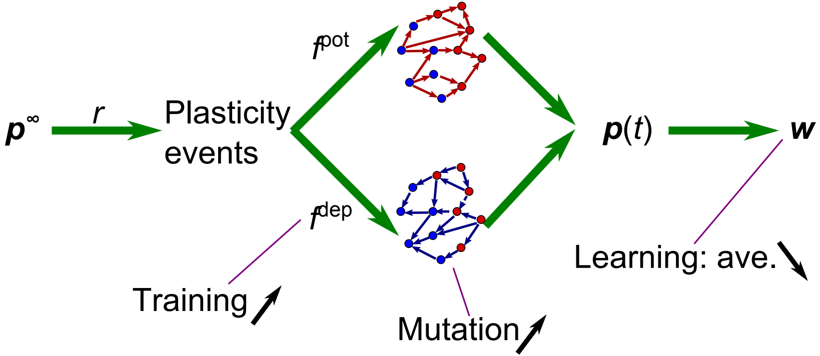
Synaptic dynamics

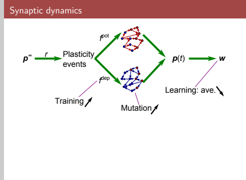




1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

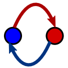
Synaptic dynamics



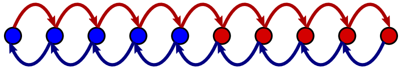


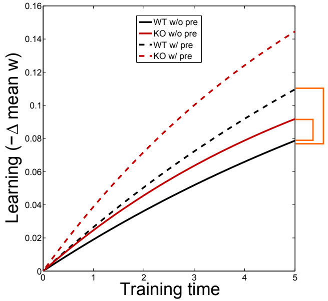
1. stoch process has steady state.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold → increase transition probs
8. Training: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

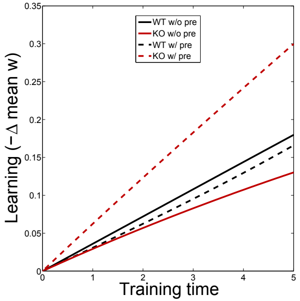
Binary model



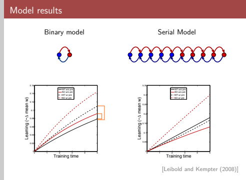
Serial Model





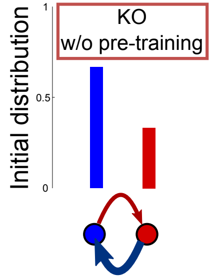


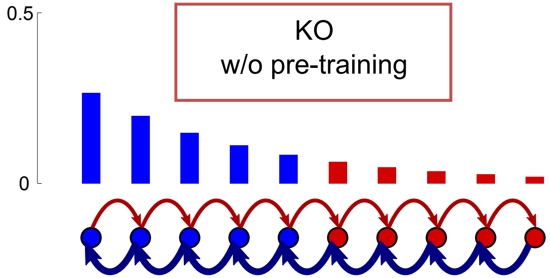
[Leibold and Kempter (2008)]

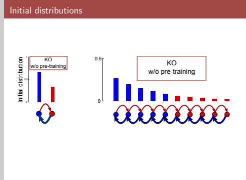


1. Binary fails
2. KO: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training

Initial distributions

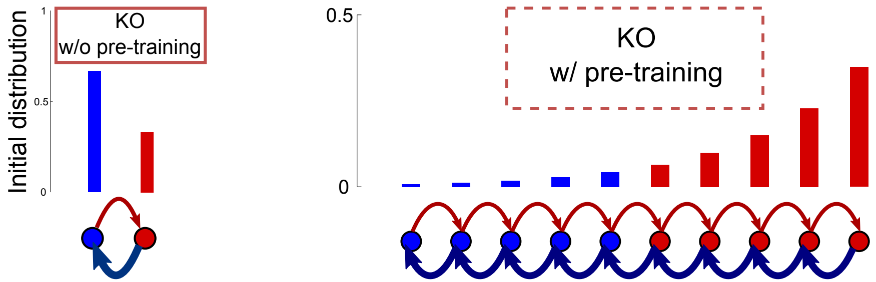


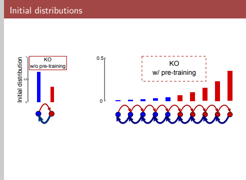




1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias

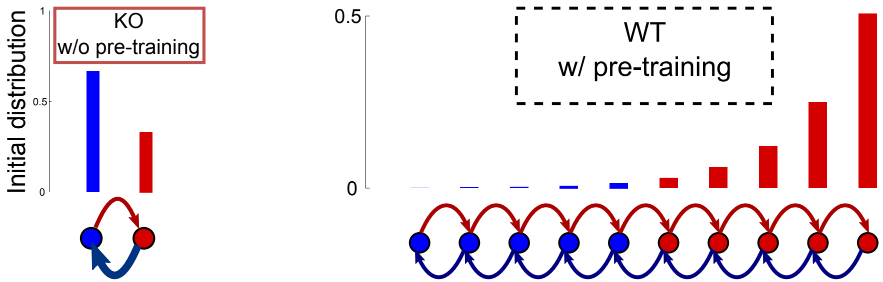
Initial distributions

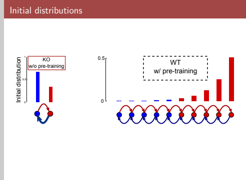




1. Binary: enhanced plasticity $\rightarrow$ bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary

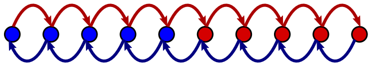
Initial distributions





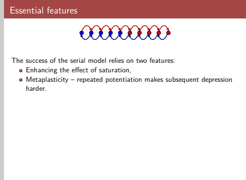
1. Binary: enhanced plasticity $\rightarrow$ bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias
5. Pretraining: little repopulates boundary
6. Too much pushes to other side, depopulates boundary

Essential features



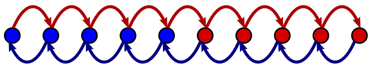
The success of the serial model relies on two features:

- 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

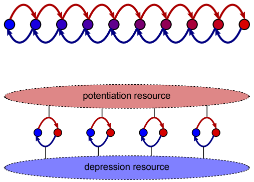
Essential features



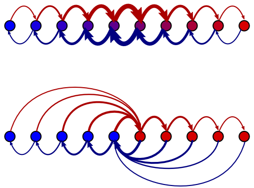
The success of the serial model relies on two features:

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

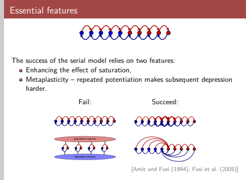
Fail:



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

- 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

- 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?

1. 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

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

Christian Leibold and Richard Kempter.
"Sparseness Constrains the Prolongation of Memory Lifetime via Synaptic Metaplasticity".
Cerebral Cortex, 18(1):67–77, (2008) .
13

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

References III
A. B. Barrett and M. C. van Rossum.
"Optimal learning rules for discrete synapses".
PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .
Christian Leibold and Richard Kempter.
"Sparseness Constrains the Prolongation of Memory Lifetime via Synaptic Metaplasticity".
Cerebral Cortex, 18(1):67–77, (2008) .
D. J. Amit and S. Fusi.
"Learning in neural networks with material synapses".
Neural Computation, 6(5):957–982, (1994) .