

Modelling impaired and enhanced learning with enhanced plasticity

based on work with: Barbara Nguyen-Vu, Grace Zhao, Aparna Suvrathan, Han-Mi Lee, Surya Ganguli, Carla Shatz and Jennifer Raymond

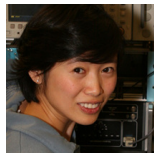
Subhaneil Lahiri

Stanford University, Applied Physics

March 1, 2014



Barbara Nguyen-Vu



Grace Zhao

2014-02-11

Impaired/enhanced learning w/ enhanced plasticity

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1. Acknowledge Barbara and Grace

Learning requires synaptic plasticity.

Expect: enhanced plasticity \rightarrow enhanced learning.

[Tang et al. (1999), Malleret et al. (2001), Guan et al. (2009)]



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Impaired/enhanced learning w/ enhanced plasticity

└ Introduction

1. It does help in some cases
2. Want to understand when and why
3. Depends on circumstance. Rich pattern of behaviour
4. Develop understanding of when and why learning is enhanced/impaired



Learning requires synaptic plasticity.

Expect: enhanced plasticity → enhanced learning.

[Tang et al. (1999), Malleret et al. (2001), Guan et al. (2009)]



But often: enhanced plasticity → impaired learning.

[Migaud et al. (1998), Uetani et al. (2000), Hayashi et al. (2004)]

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Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Simple synapses cannot explain behaviour.

→ Necessary & sufficient conditions on complex synapses to replicate it.



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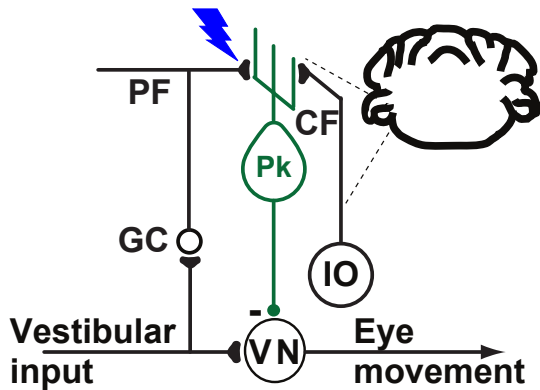


Vestibulo-Occular Reflex training

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)]

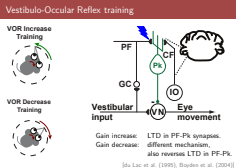
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Impaired/enhanced learning w/ enhanced plasticity

Vestibulo-Occular Reflex training

1. Explain what VOR gain is
2. trick brain into thinking VOR gain needs adjusting by moving visual stimulus
3. anti-phase → increase gain
4. in phase → decrease gain
5. Gain change involves cerebellum
6. If we enhanced plasticity here: expect enhanced learning



Enhanced plasticity impairs learning

Knockout of MHC-I D^bK^b molecules in PF-Pk synapses

[McConnell et al. (2009)]

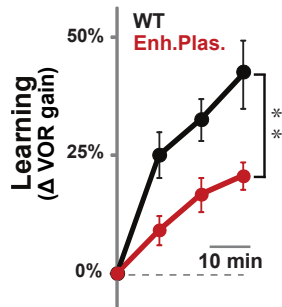
→ lower threshold for LTD → enhanced plasticity

Hypothesis: enhanced learning.

VOR Increase Training



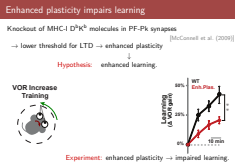
Experiment: enhanced plasticity → impaired learning.



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Impaired/enhanced learning w/ enhanced plasticity

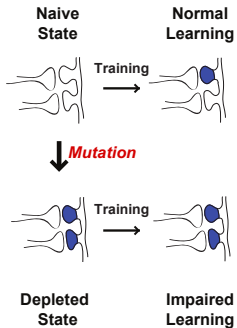
Enhanced plasticity impairs learning



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

Depletion hypothesis

Learning rate \sim intrinsic plasticity rate \times # synapses available for LTD.

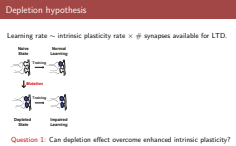


Question 1: Can depletion effect overcome enhanced intrinsic plasticity?

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Impaired/enhanced learning w/ enhanced plasticity

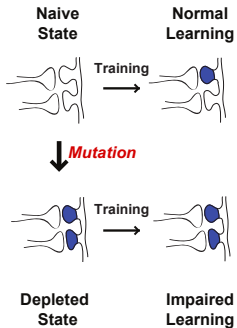
└ Depletion hypothesis



1. Our model: baseline activity \rightarrow saturation \rightarrow less depression possible
2. Saturation has to compete with enhanced plasticity. Which will win?

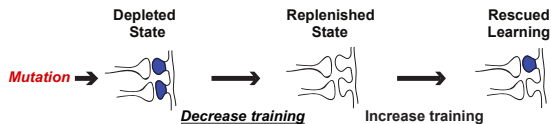
Depletion hypothesis

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Other tests:

- Mimic depletion with ChR2 stim of CF
- Biochemical marker of LTD

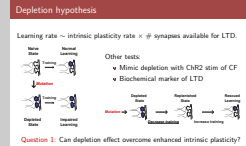


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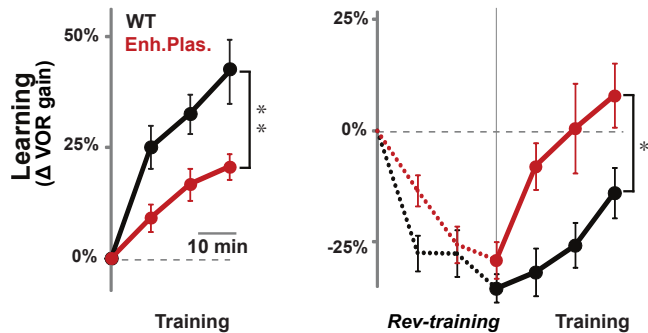
Impaired/enhanced learning w/ enhanced plasticity

└ Depletion hypothesis



1. Our model: baseline activity \rightarrow saturation \rightarrow less depression possible
2. Saturation has to compete with enhanced plasticity. Which will win?
3. Prediction: replenish with rev-training \rightarrow rescue

Replenishment by reverse-training

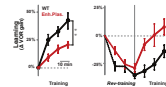


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Impaired/enhanced learning w/ enhanced plasticity

└ Replenishment by reverse-training

Replenishment by reverse-training



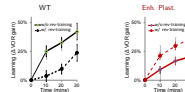
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2. but behaviour from elsewhere \rightarrow not modelled
3. Focus on gain inc part

Replenishment by reverse-training

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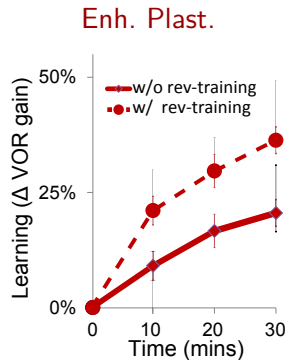
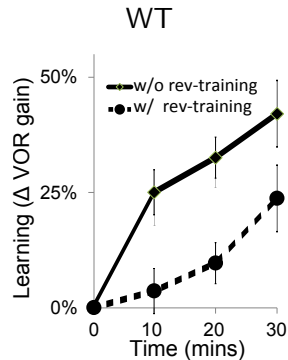
Impaired/enhanced learning w/ enhanced plasticity

└ Replenishment by reverse-training



Question 2: How can too much replenishment impair learning?

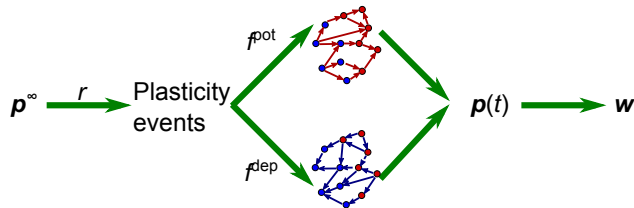
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2. but behaviour from elsewhere → not modelled
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Question 2: How can *too much* replenishment impair learning?

Models of complex synaptic dynamics

- Internal functional state of synapse \rightarrow synaptic weight.
- Candidate plasticity events \rightarrow transitions between states



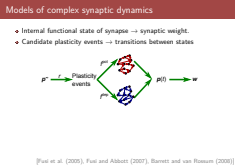
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]

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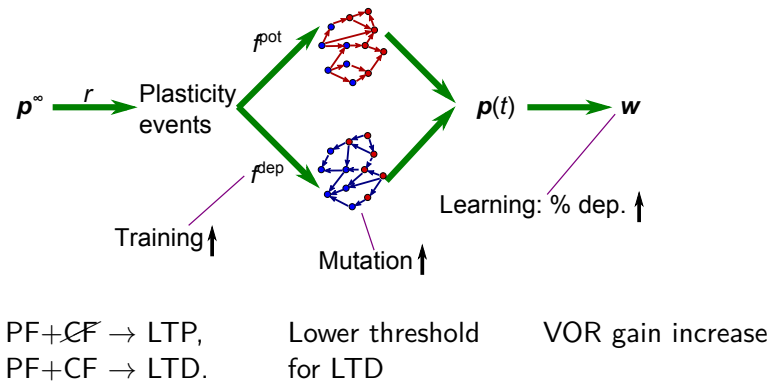
└ Models of complex synaptic dynamics

1. complex synapse: not just synaptic weight. dynamical system
2. important for memory with bounded synapses
3. plasticity events at rate r . indep at each synapse.
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \rightarrow j$
6. Readout: synaptic weight vec when in each state.



Models of complex synaptic dynamics

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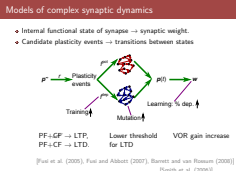
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Models of complex synaptic dynamics



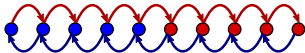
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5. probs changed by Markov matrices, prob $i \rightarrow j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold \rightarrow increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r .
9. Learning: Only output we have. Don't keep track of synaptic identity.

Complex synapses are required to explain behaviour

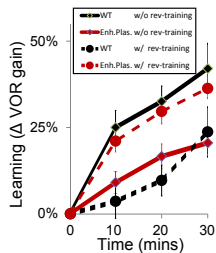
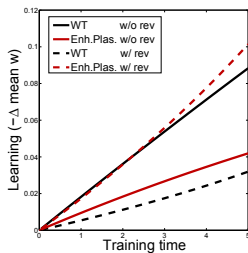
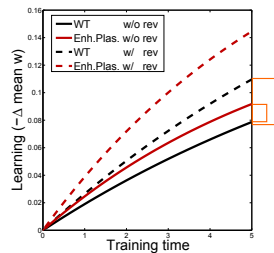
Binary synapse



Serial synapse



VOR Increase Training



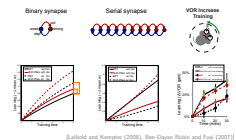
[Leibold and Kempner (2008), Ben-Dayan Rubin and Fusi (2007)]

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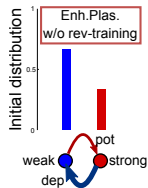
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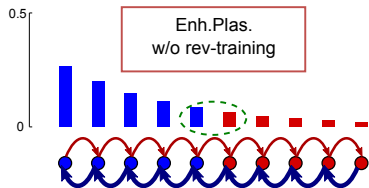
1. Binary fails – mathematical proof for any params
2. Enh.Plas: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.
4. Serial: still only two weights. Works.
5. Understand by looking at distributions before training



Enhanced plasticity can enhance or impair learning



Intrinsic plasticity
dominates depletion
↓
enhanced plasticity
enhances learning



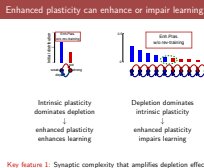
Depletion dominates
intrinsic plasticity
↓
enhanced plasticity
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Key feature 1: Synaptic complexity that amplifies depletion effect.

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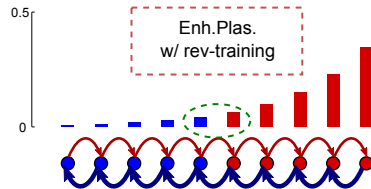
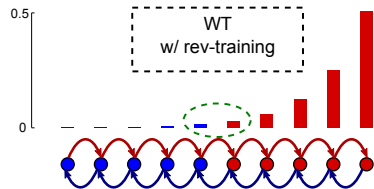
Impaired/enhanced learning w/ enhanced plasticity

Enhanced plasticity can enhance or impair learning



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. borne out by other models

Reverse-training can impair or enhance learning

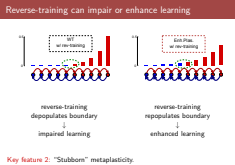


Key feature 2: "Stubborn" metaplasticity.

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Impaired/enhanced learning w/ enhanced plasticity

Reverse-training can impair or enhance learning



1. rev-training: little repopulates boundary
2. Too much pushes to other side, depopulates boundary
3. this effect is absent in any simple synapse
4. repeated potentiation makes subsequent depression harder
5. borne out by other models

- We find diverse behavioural patterns in these mutant mice:
Enhanced plasticity → **enhance/impair** learning depending on prior experience.
Reverse-training → **enhance/impair** learning depending on plasticity rates.
- We can explain these behavioural patterns using synaptic models.
- Key required synaptic properties are:
Synaptic complexity: necessary to amplify depletion.
Synaptic stubbornness: repeated potentiation makes subsequent depression harder.
- We used behaviour to constrain the dynamics of synaptic plasticity

└ Conclusions

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Enhanced plasticity → enhance/impair learning depending on prior experience.
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Acknowledgements

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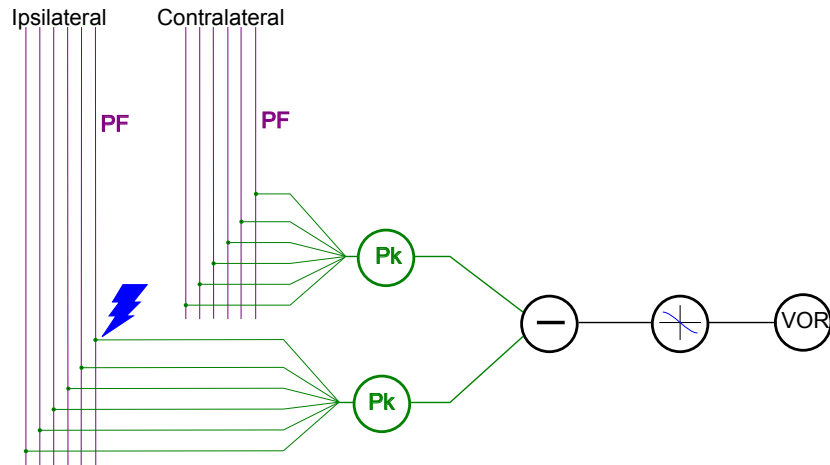
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References

References III

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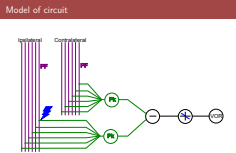
Model of circuit



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Impaired/enhanced learning w/ enhanced plasticity

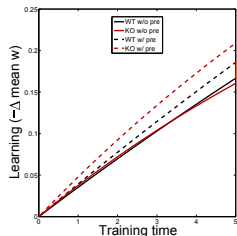
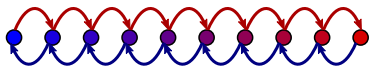
Model of circuit



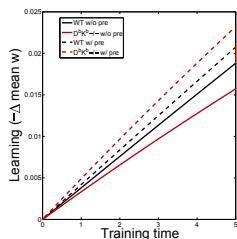
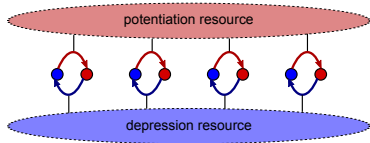
1. Contralateral baseline shift compensates for Our baseline shift
2. Gain increase due to LTD at lightning
3. Gain decrease due to plasticity elsewhere, but also reverses LTD at lightning
4. Nonlinearity here won't affect our questions, as long as it doesn't change
5. Nonlinearity before compensation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

Other models that fail

Multistate model



Pooled resource model

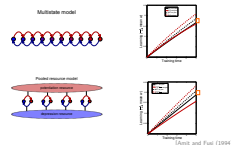


[Amit and Fusi (1994)]

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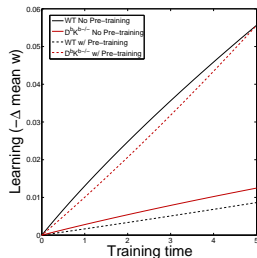
Other models that fail



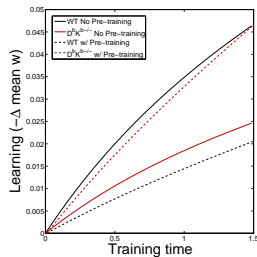
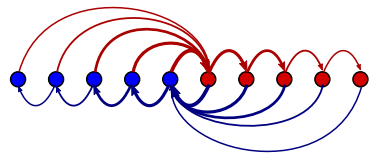
1. MS: linear weights, unlike serial.
2. like bunch of binary synapses in series.
3. solid curves: fails early on, but catches up quickly
4. black curves: fails badly
5. No real enhancement of saturation, no metaplasticity.
6. All transitions contribute: pushing to end has little effect.
7. Pooled: resource depleted by pot/dep. replenished by reverse.
8. solid curves succeed: enhanced saturation
9. black curves fail: opposite metaplasticity, pot makes dep easier

Other models that work

Non-uniform multistate model



Cascade model



[Fusi et al. (2005)]

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Impaired/enhanced learning w/ enhanced plasticity

Other models that work

1. Both models, trans probs decay exponentially from centre.
2. Nonuni: linear weights. Cascade: binary weights.
3. Enhanced saturation and metaplasticity
4. Pushing to end makes pot and dep harder
5. Note: hidden states not necessary

