

Understanding impaired learning with enhanced plasticity

based on work in preparation with: T.D. Barbara Nguyen-Vu, Grace Q. Zhao,
Han-Mi Lee, Surya Ganguli, Carla J. Shatz, Jennifer L. Raymond

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1. Acknowledge Barbara and Grace

Learning requires synaptic plasticity.
Expect enhanced plasticity → enhance learning.

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



2013-07-24

Impaired learning with 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



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But often: → impairment.

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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 this.

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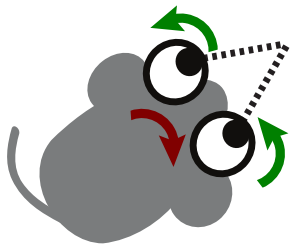
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- Motor learning
 - Cerebellar learning of mice with enhanced plasticity
 - Complex synaptic models
- (Memory capacity of complex synapses)

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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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Impaired learning with enhanced plasticity

└ Vestibulo-Occular Reflex



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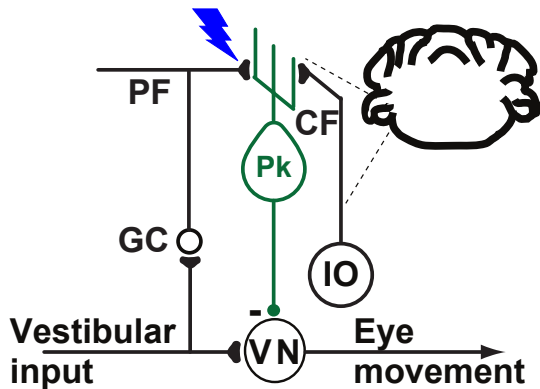
Needs to be adjusted as eye muscles age, etc.

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.

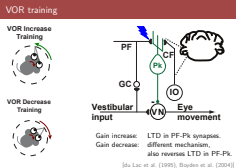
[du Lac et al. (1995), Boyden et al. (2004)]

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Impaired learning with enhanced plasticity

└ VOR training

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



Enhanced plasticity impairs learning

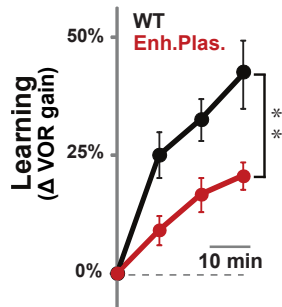
Knockout of MHC-I D^bK^b molecules in PF-Pk synapses

[McConnell et al. (2009)]

→ lower threshold for LTD → enhanced plasticity

Hypothesis: enhanced learning.

VOR Increase Training

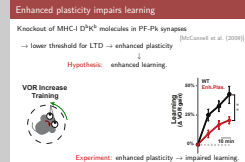


Experiment: enhanced plasticity → impaired learning.

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Impaired learning with enhanced plasticity

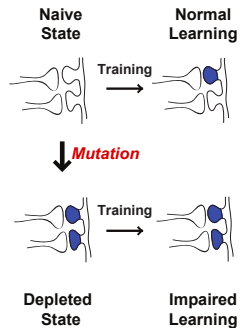
Enhanced plasticity impairs learning



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.



Impaired learning with 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?

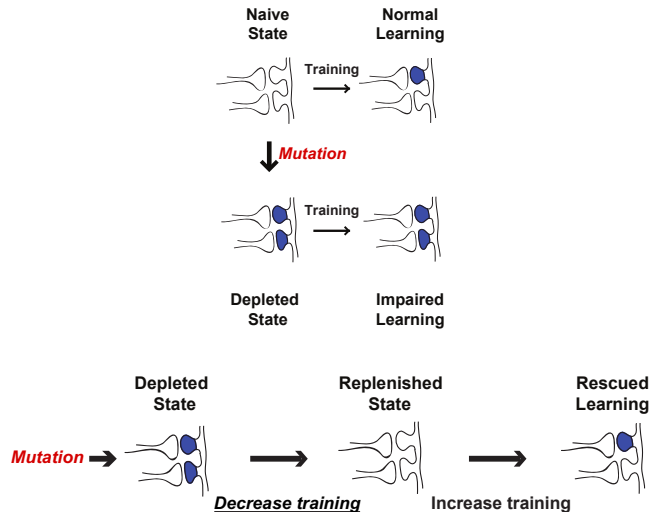
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Depletion hypothesis

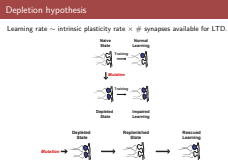
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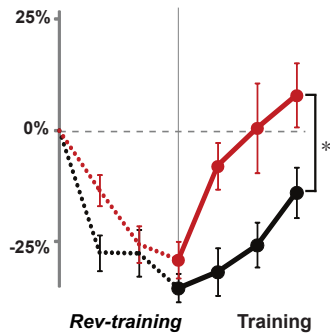
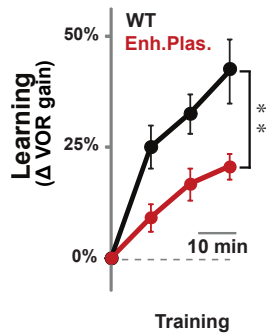
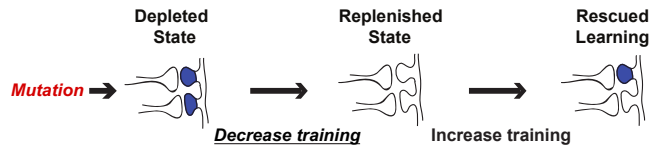
Impaired learning with enhanced plasticity

└ 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

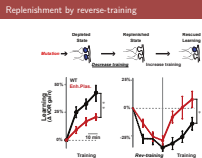
Replenishment by reverse-training



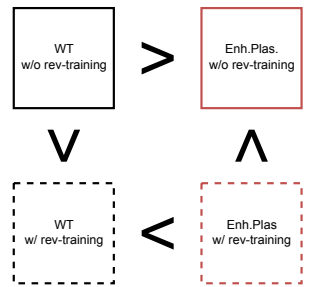
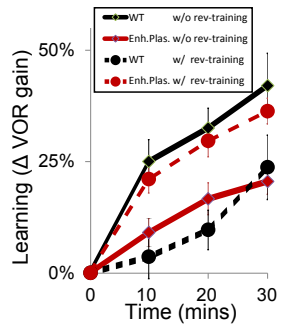
Impaired learning with enhanced plasticity

Replenishment by reverse-training

1. precede gain inc training w/ gain dec rev-training: reverses LTD
2. but behaviour from elsewhere → not modelled
3. Focus on gain inc part



Summary of training results



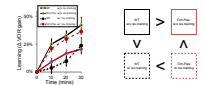
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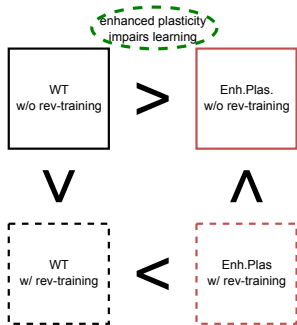
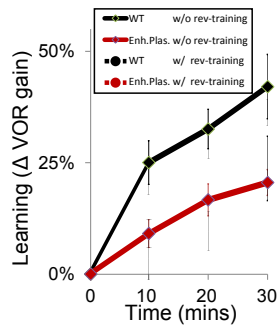
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Summary of training results



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Questions:

- Can the depletion effect overcome intrinsic plasticity?

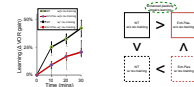
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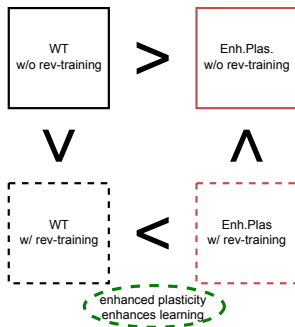
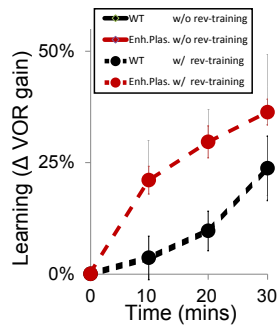
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Summary of training results



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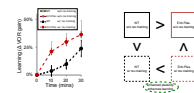
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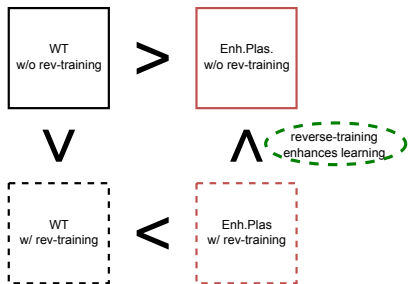
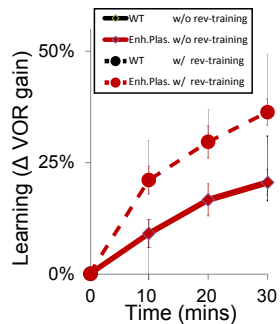
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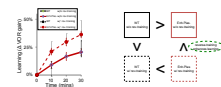
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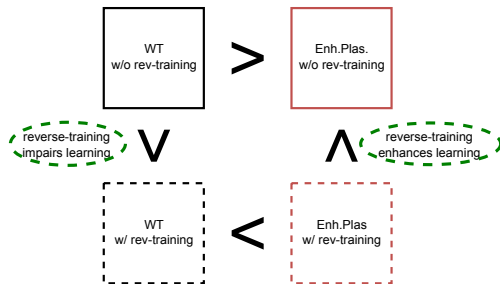
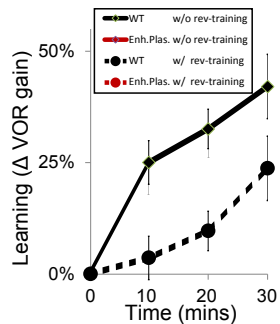
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Summary of training results



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Questions:

- Can the depletion effect overcome intrinsic plasticity?
- How can a little replenishment help, but too much hurt?

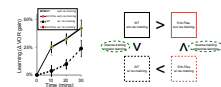
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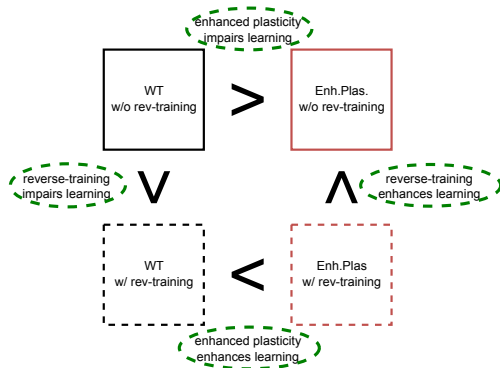
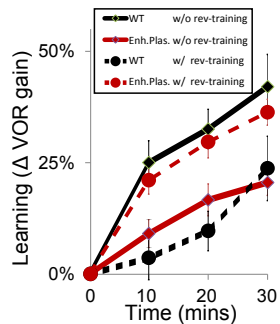
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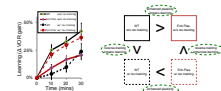
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9. Summarize: Enh.Plas. can impair/enhance. Rev can impair/enhance
10. Diagonal comparisons: parameter fitting. Depend on size of mut vs. rev

Summary of training results

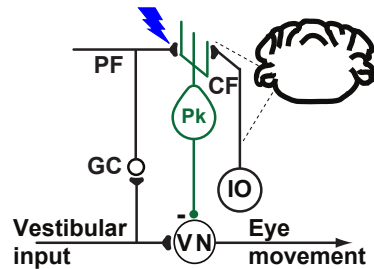


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Behaviour to synapses

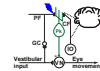
VOR Increase Training



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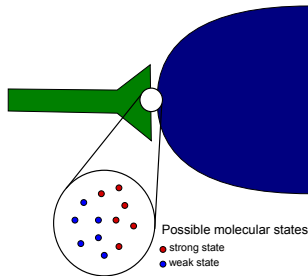
Impaired learning with enhanced plasticity

└ Behaviour to synapses

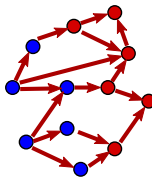


1. Focus on synapses. See if we can understand this behaviour.

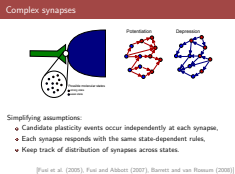
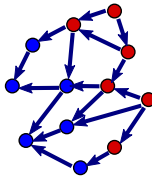
Complex synapses



Potentiation



Depression

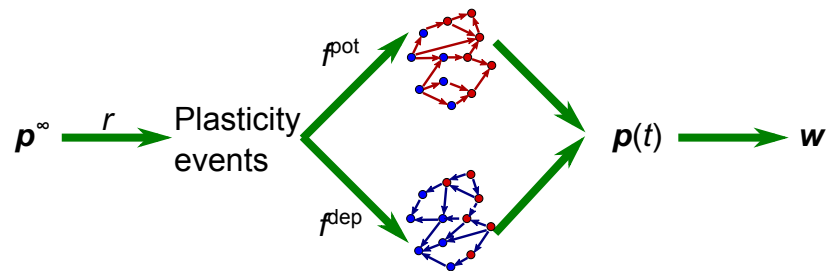


Simplifying assumptions:

- Candidate plasticity events occur independently at each synapse,
- Each synapse responds with the same state-dependent rules,
- Keep track of distribution of synapses across states.

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

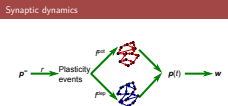
1. Not just synaptic weight, internal dynamical system
2. Important for memory: simple synapses – terrible storage, rescued by complexity
3. Multiple functional states w/ different weights
4. Stochastic transitions between states
5. allows us to concentrate on synapse, not neuron/network
6. This is a question about synaptic populations after all.



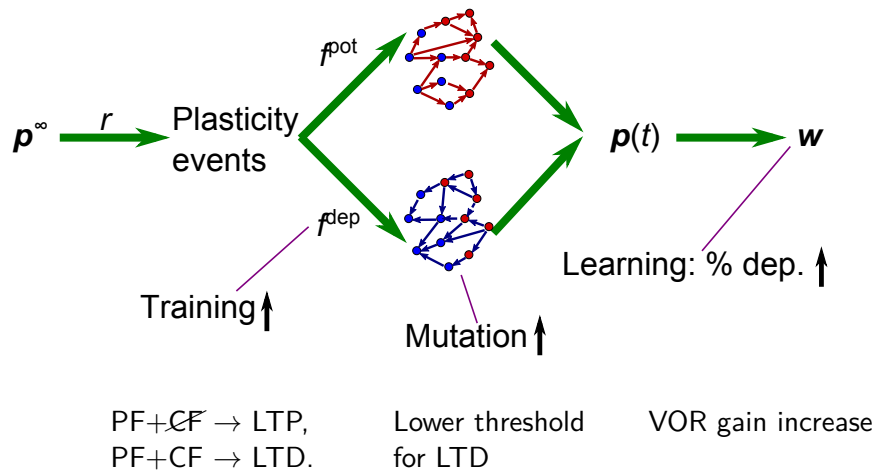
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Impaired learning with enhanced plasticity

└ Synaptic dynamics



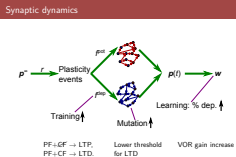
1. stoch process has steady state distribution.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \rightarrow j$
6. Readout: synaptic weight vec when in each state.



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Impaired learning with enhanced plasticity

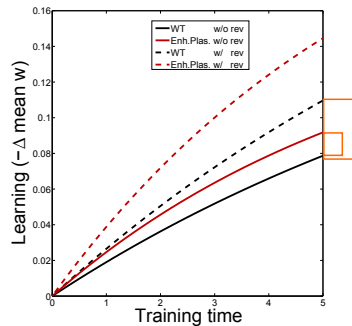
└ Synaptic dynamics



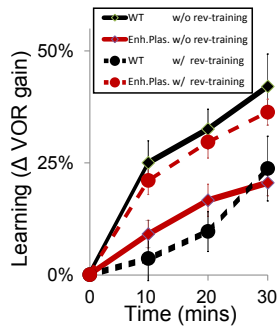
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6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold \rightarrow increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r .
9. Learning: Only output we have. Don't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

Simple synapses cannot explain the data

Binary synapse



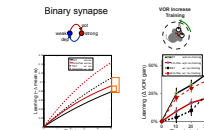
VOR Increase Training



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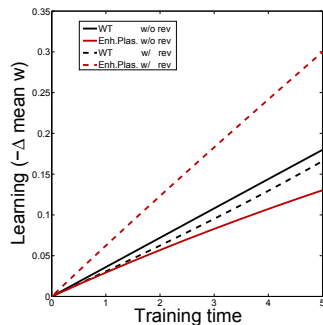
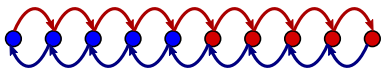
Simple synapses cannot explain the data

1. Binary fails – mathematical proof for any params
2. Enh.Plas: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.

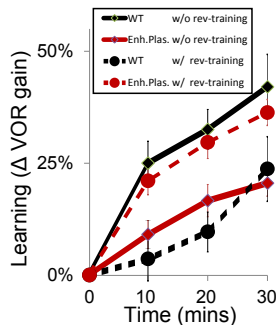


Complex synapses can explain the data

Serial synapse



VOR Increase Training



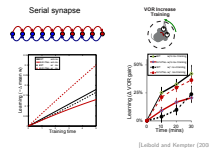
[Leibold and Kempter (2008)]

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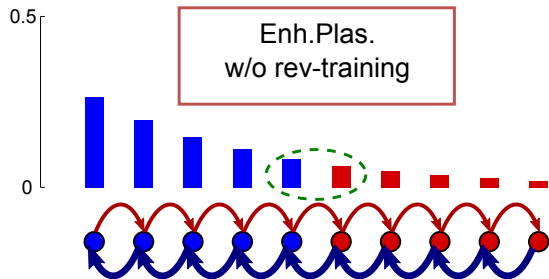
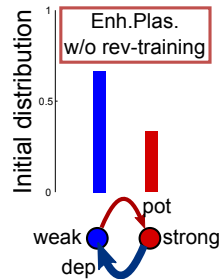
Impaired learning with enhanced plasticity

Complex synapses can explain the data

1. Serial: still only two weights. Works.
2. Understand by looking at distributions before training



Enhanced plasticity can enhance or impair learning



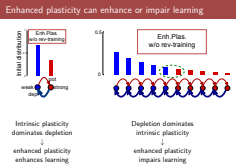
Intrinsic plasticity
dominates depletion
↓
enhanced plasticity
enhances learning

Depletion dominates
intrinsic plasticity
↓
enhanced plasticity
impairs learning

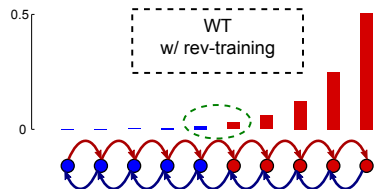
Impaired learning with enhanced plasticity

Enhanced plasticity can enhance or impair learning

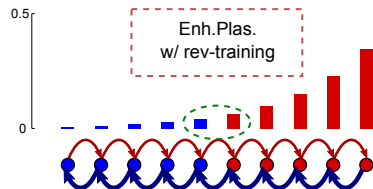
1. Binary: enhanced plasticity → bias
2. Not enough to overcome faster depression
3. Serial: Only get signal from boundary
4. Exponential decay depopulates boundary, enhances effect of bias



Reverse-training can impair or enhance learning



reverse-training
depopulates boundary
↓
impaired learning



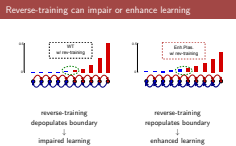
reverse-training
repopulates boundary
↓
enhanced learning

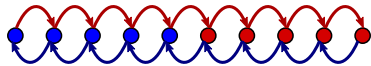
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Impaired learning with enhanced plasticity

└ 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

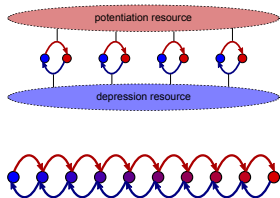




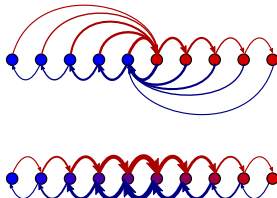
The success of the serial model relies on two features:

- Complexity - needed to amplify the effect of depletion,
- Metaplasticity – repeated potentiation makes subsequent depression harder.

Fail:



Succeed:



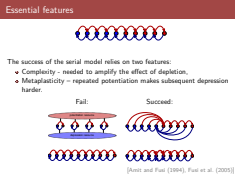
[Amit and Fusi (1994), Fusi et al. (2005)]

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└ Essential features

1. due to exponential decay
2. push away from boundary where signal generated
3. borne out by other models that fail/succeed



- We find diverse behavioural patterns:
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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Tradeoff: learning vs. remembering

What about memory?

- Simple synapses have poor memory storage capacity.
Synaptic complexity is needed for rescue.

[Amit and Fusi (1992), Amit and Fusi (1994)]

- Trade-off between learning and remembering:
Too rigid → difficult to learn new memories.
Too plastic → new memories quickly overwrite old.

- Exploring the *entire* space of complex synaptic models
→ upper bounds on their storage ability
& the models that saturate them.

[Lahiri and Ganguli (submitted)]

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We have N synapses with M internal states each.

We study the decay of one memory over time due to corruption by subsequent memories.

We prove that, no matter what the structure, no synaptic model can have:

- initial fidelity (SNR) greater than \sqrt{N} .
- memory lifetime greater than $\sim \sqrt{NM}$.
- fidelity decay slower than $\sim \sqrt{NM}/t$.

At late times, fidelity is maximised by a model with a simple chain structure.

└ The frontiers of complex synaptic memory

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