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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Introduction

Learning requires synaptic plasticity.

Expect enhanced plasticity $\rightarrow$ enhance learning.

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

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But often: $\rightarrow$ impairment.

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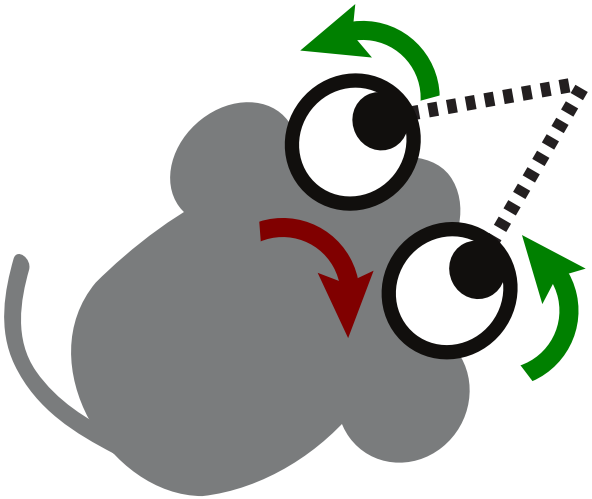
Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Simple synapses cannot explain behaviour.
$\rightarrow$ Necessary & sufficient conditions on complex synapses to replicate this.

Outline

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

Vestibulo-Occular Reflex



Eye movements compensate for head movements to maintain fixation.

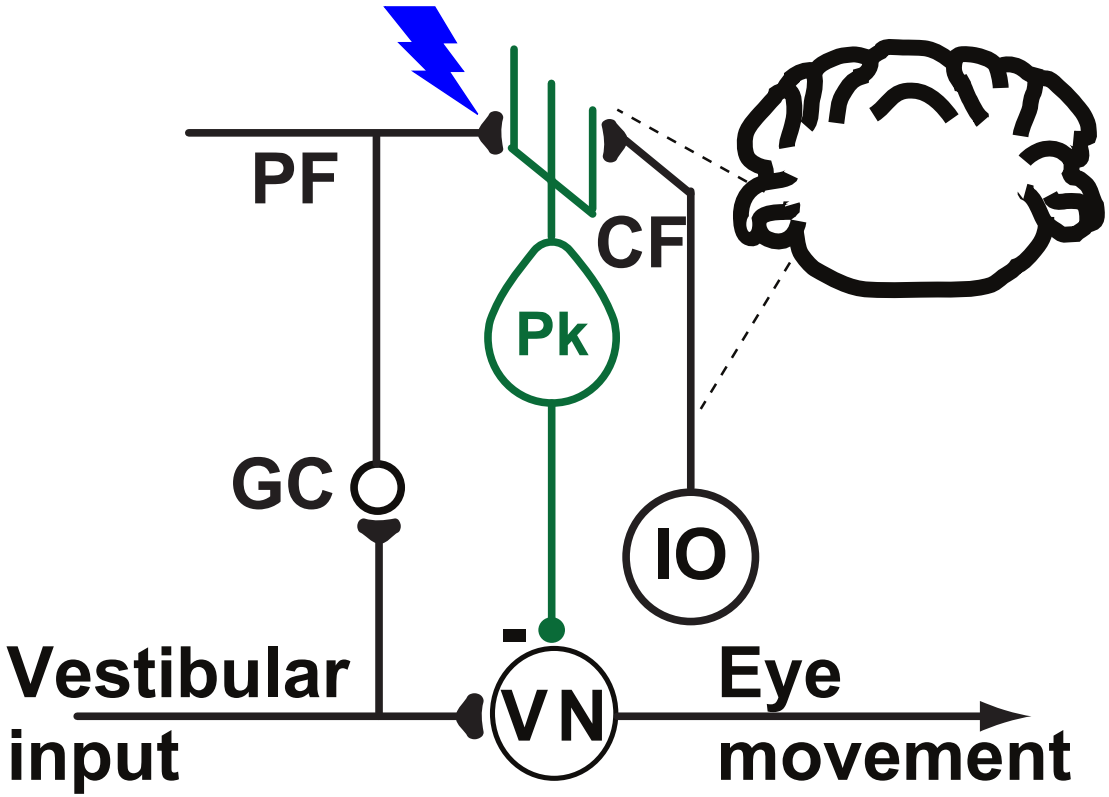
Requires control of VOR gain $= \frac{\text{eye velocity}}{\text{head velocity}}$.

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)]

Enhanced plasticity impairs learning

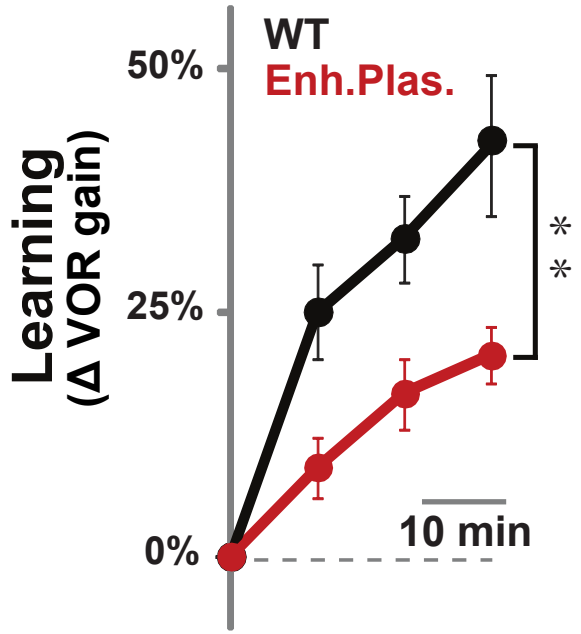
Knockout of MHC-I D^bK^b molecules in PF-Pk synapses

[McConnell et al. (2009)]

$\rightarrow$ lower threshold for LTD $\rightarrow$ enhanced plasticity

$\downarrow$

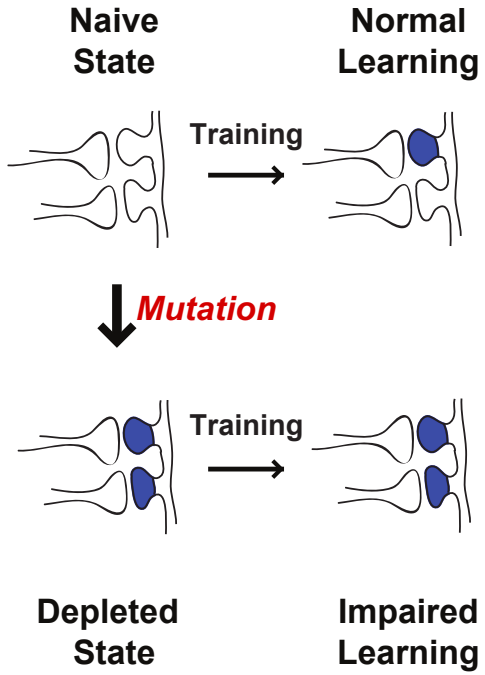
Hypothesis: enhanced learning.



Experiment: enhanced plasticity $\rightarrow$ impaired learning.

Depletion hypothesis

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



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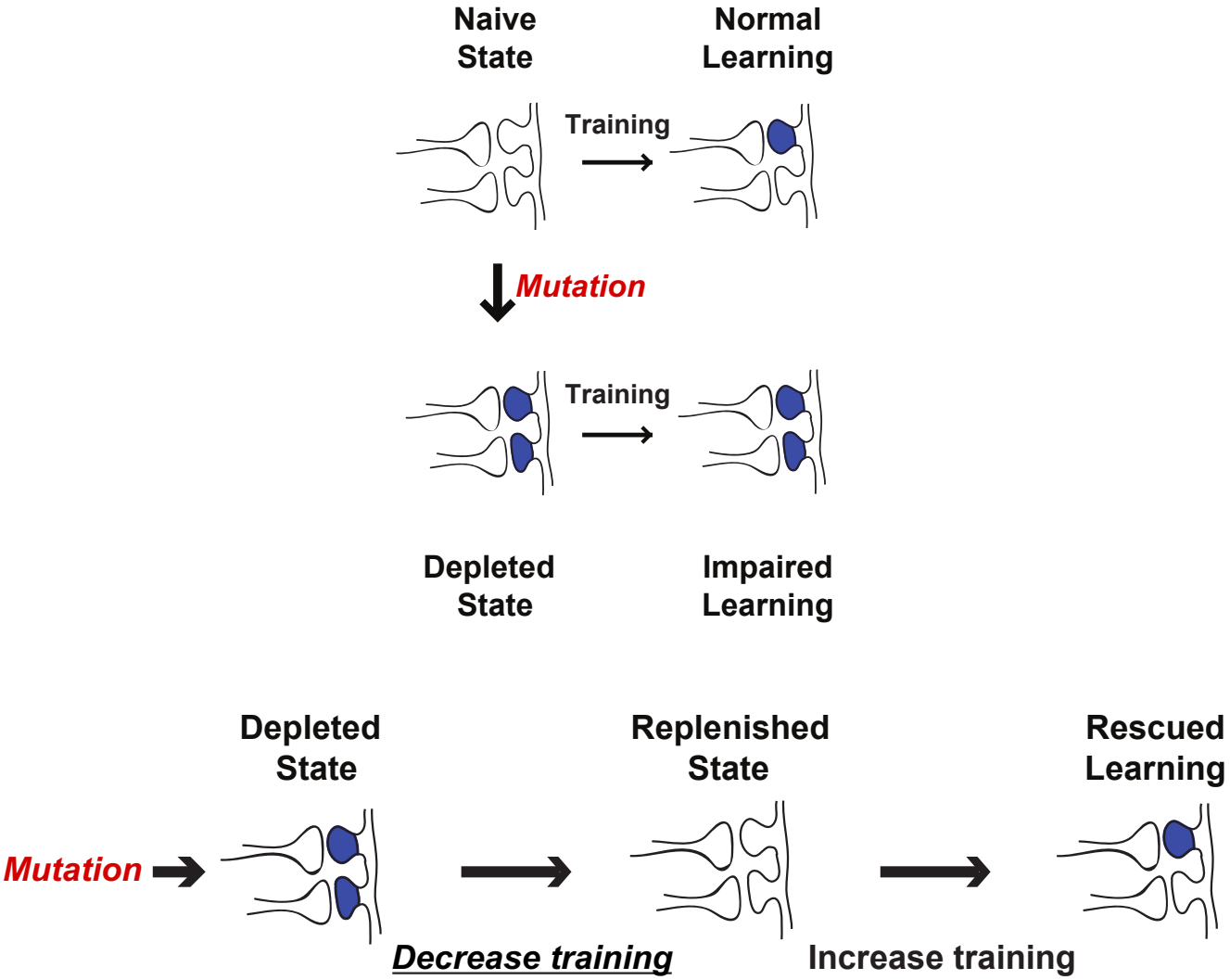
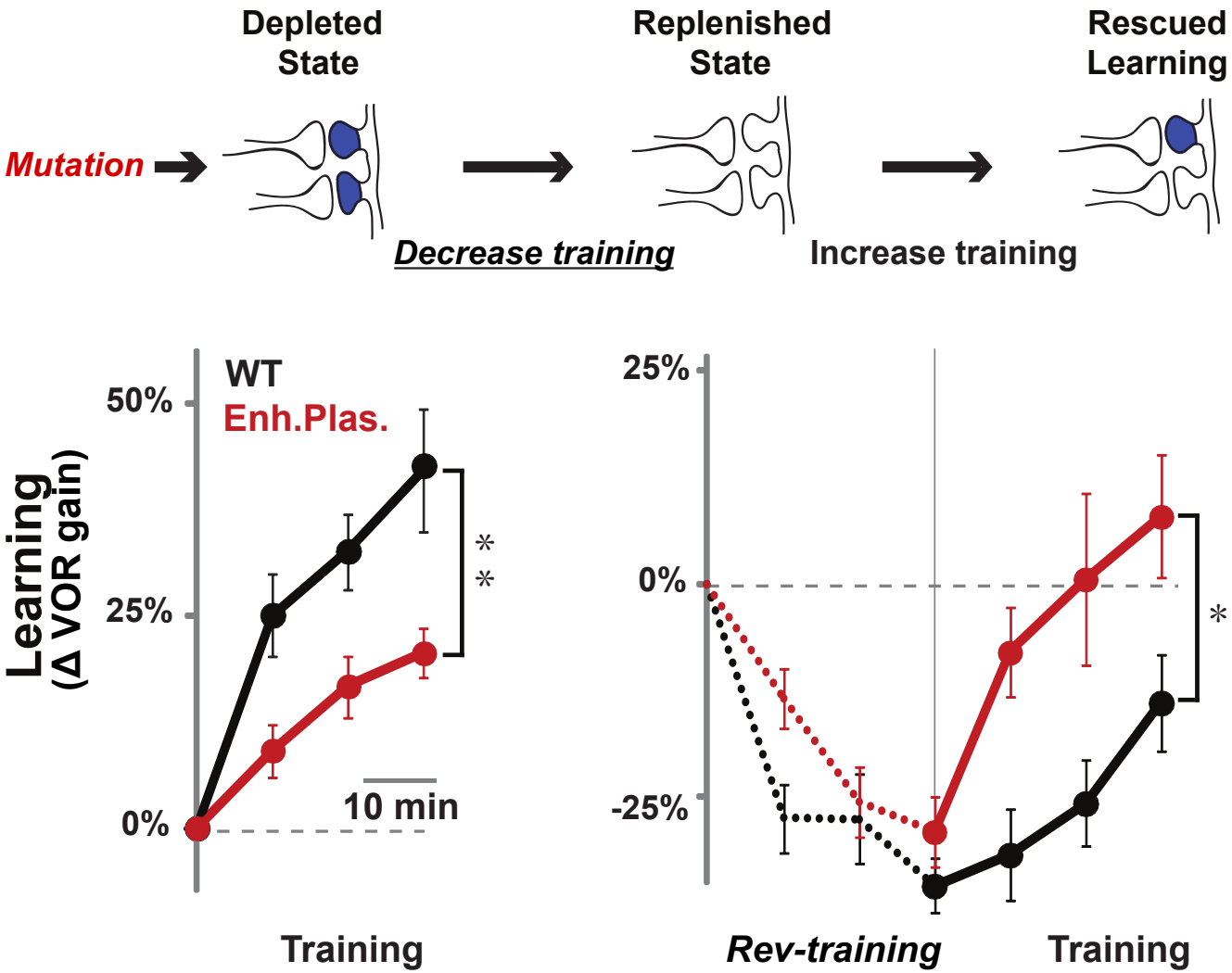
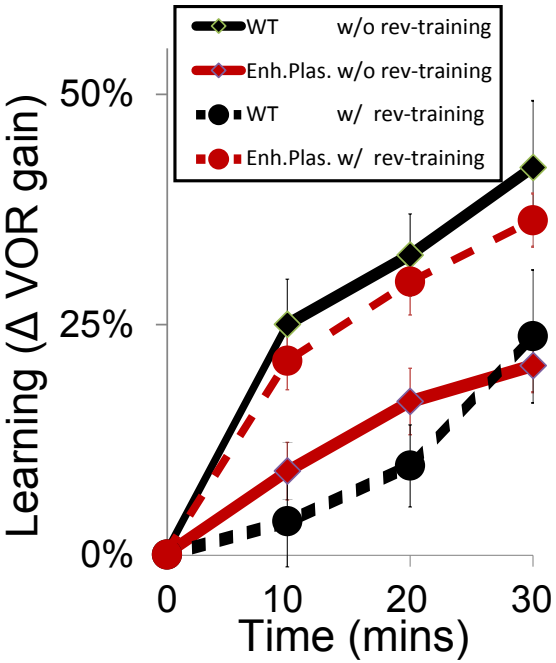
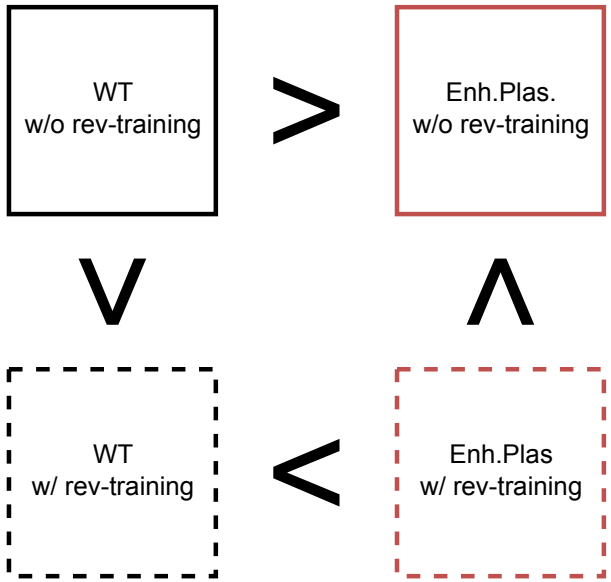


Replenishment by reverse-training



Summary of training results





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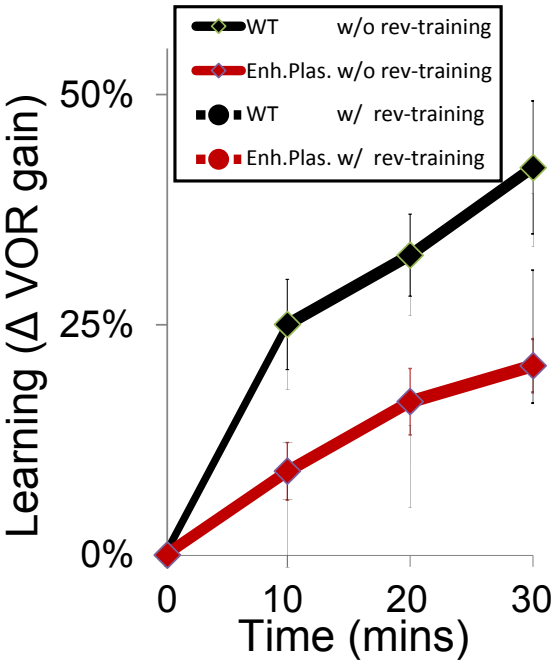

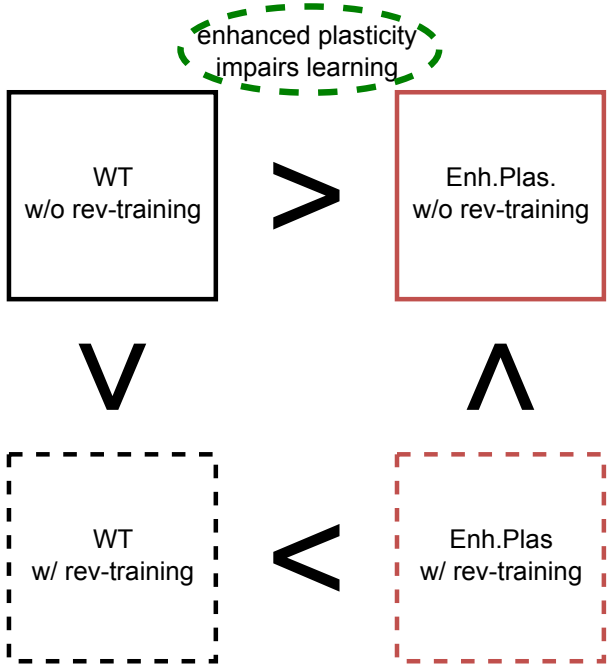

Questions:

- Can the depletion effect overcome intrinsic plasticity?

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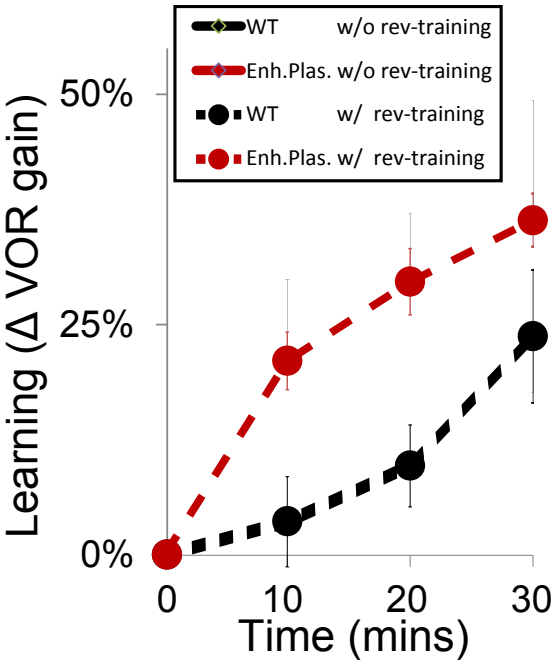

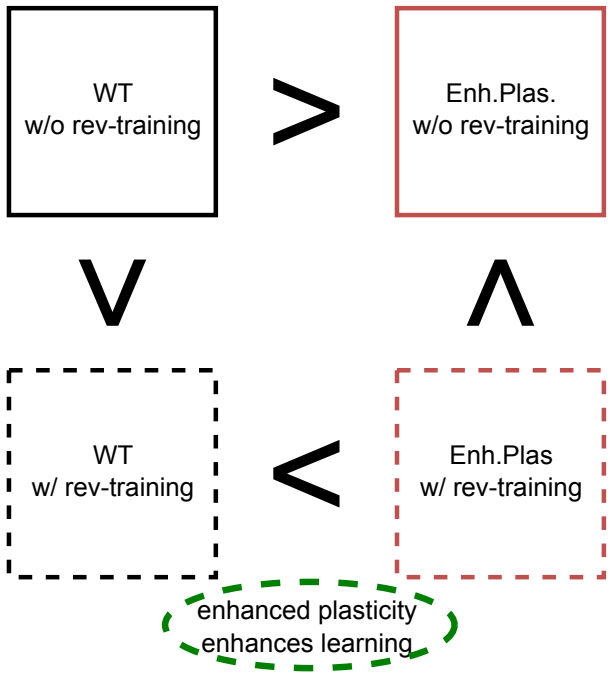

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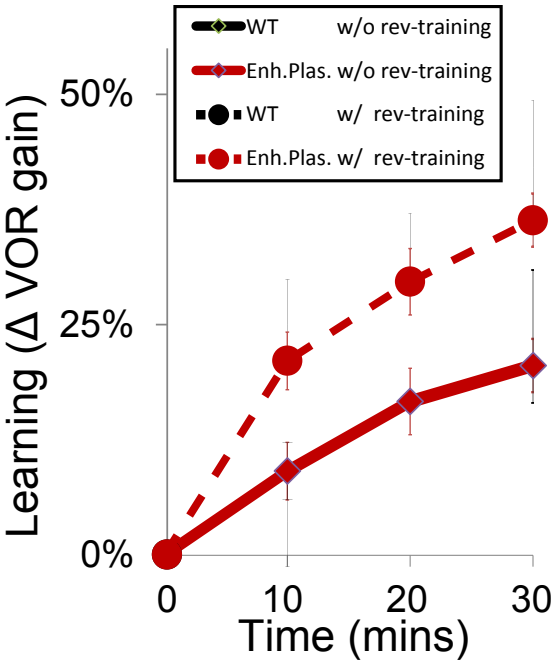

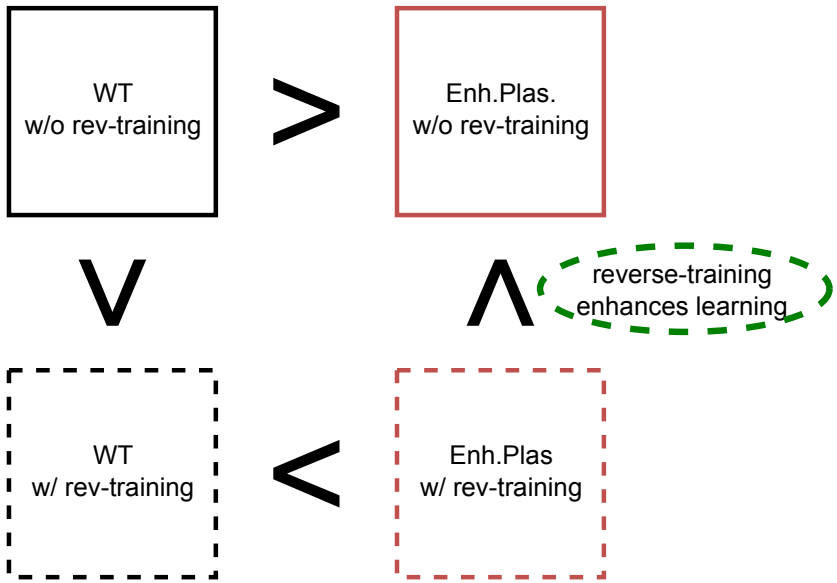

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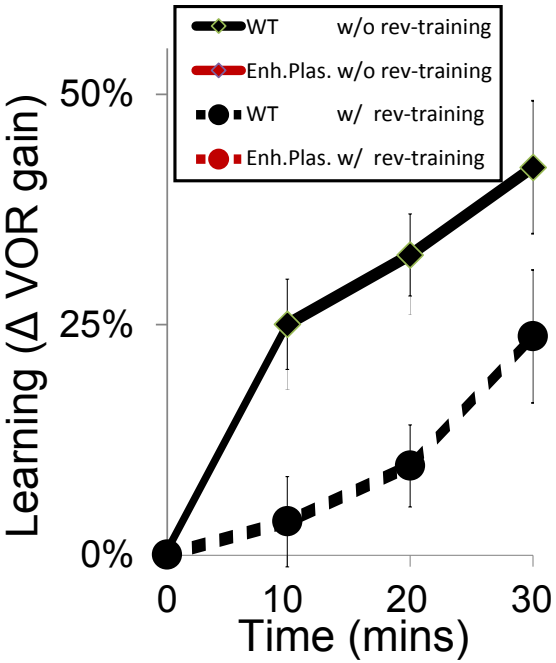

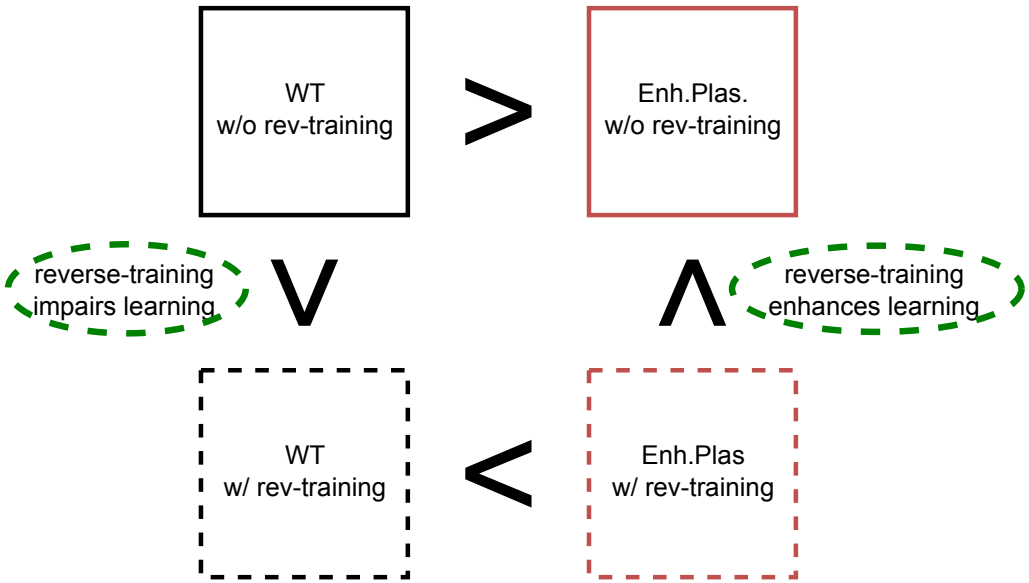

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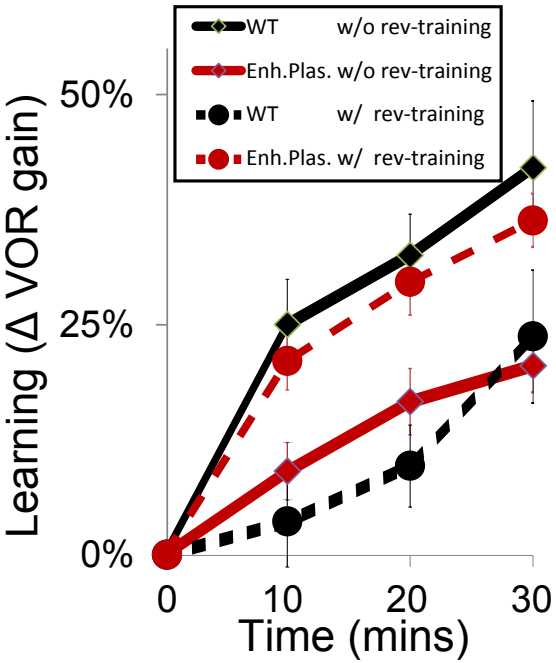

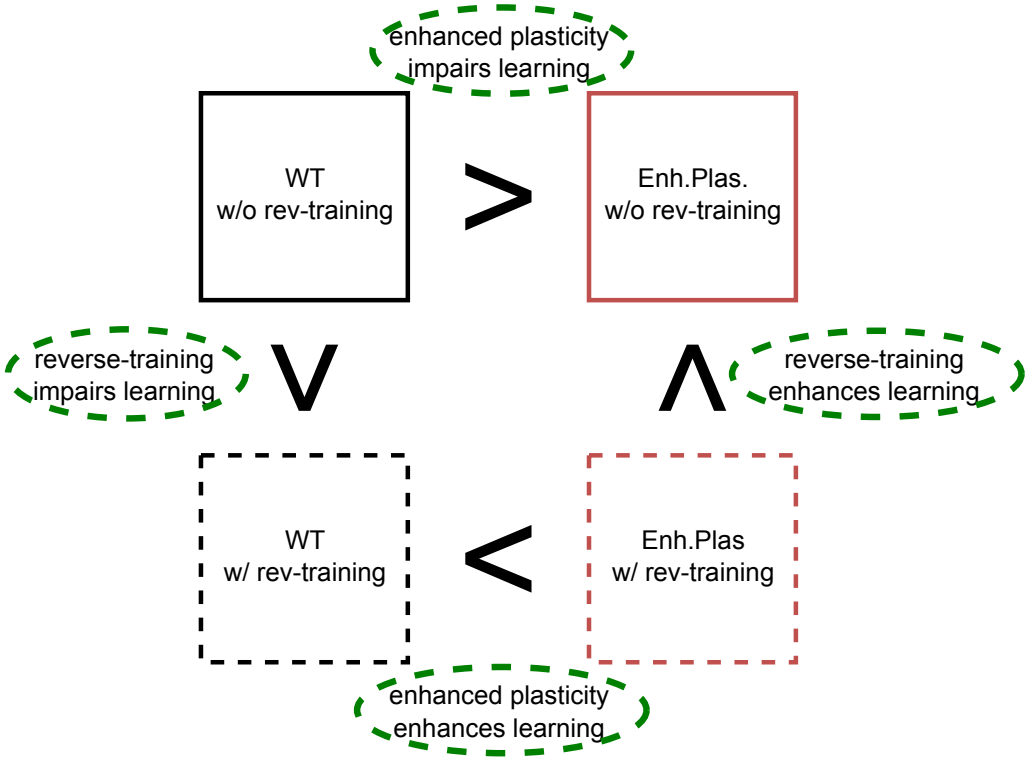

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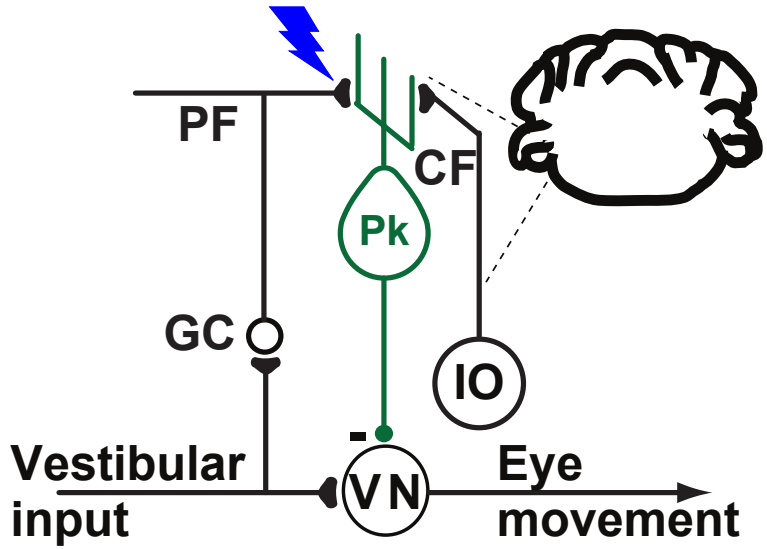
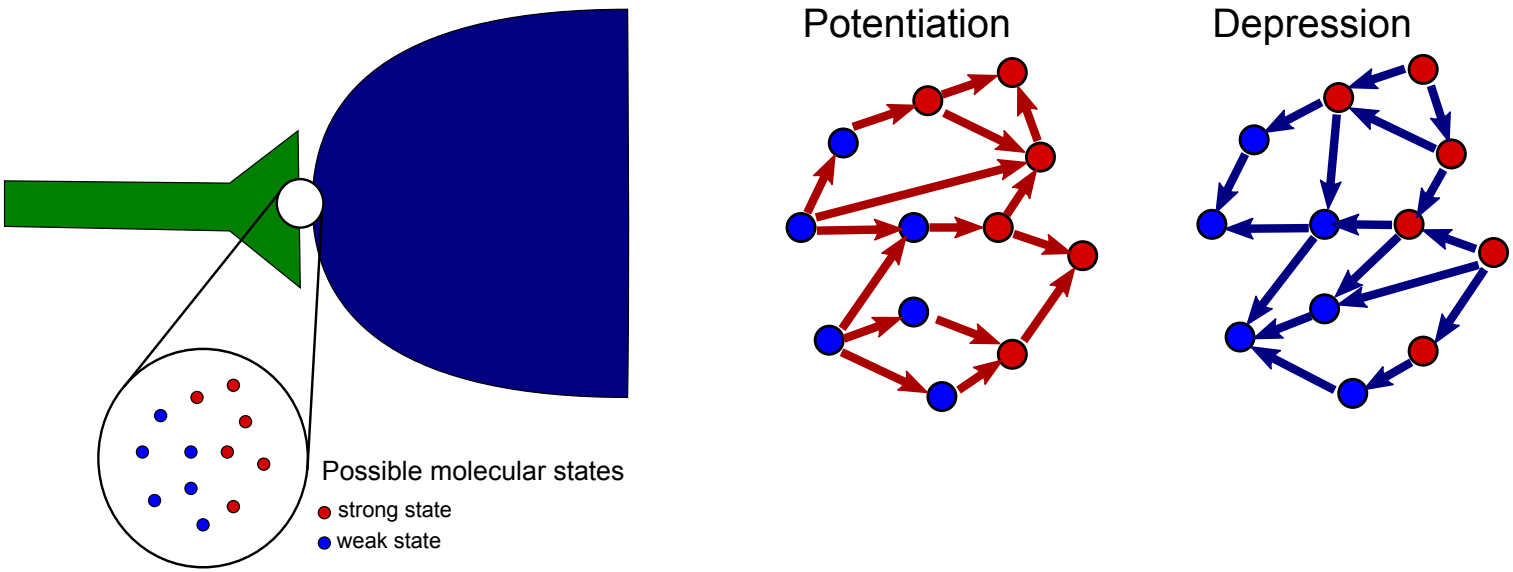
Behaviour to synapses

VOR Increase Training



Complex synapses

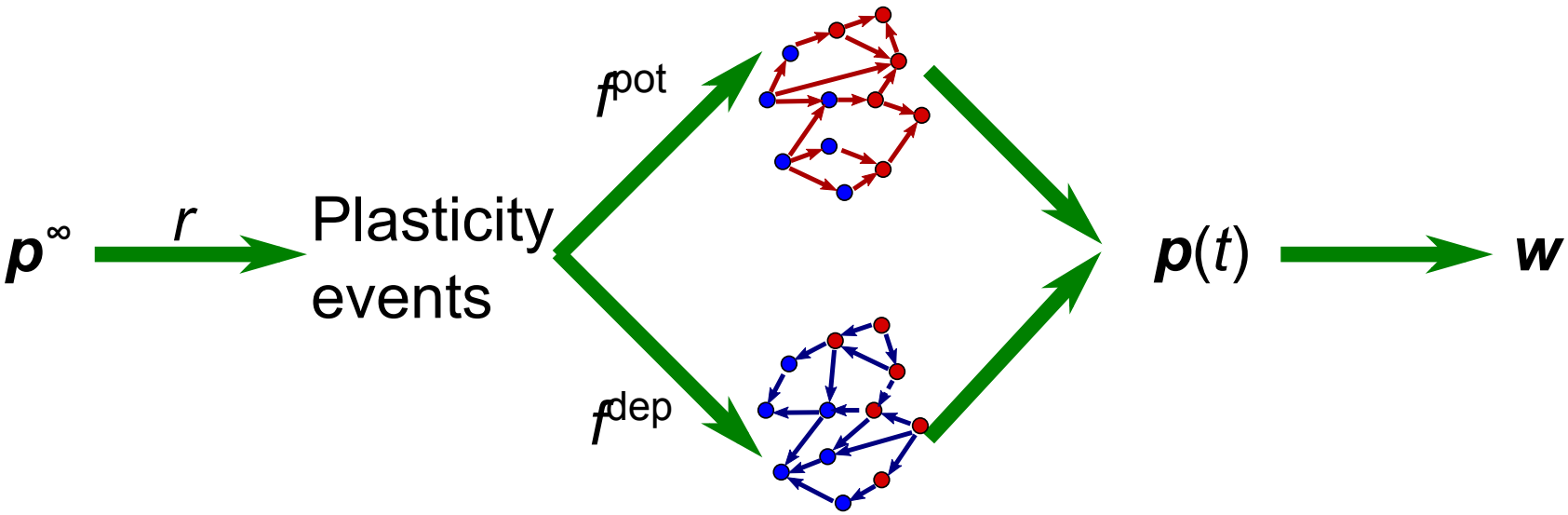


Simplifying assumptions:

- Different synapses are statistically independent of each other.
- Keep track of distribution of synapses across states.

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

Synaptic dynamics



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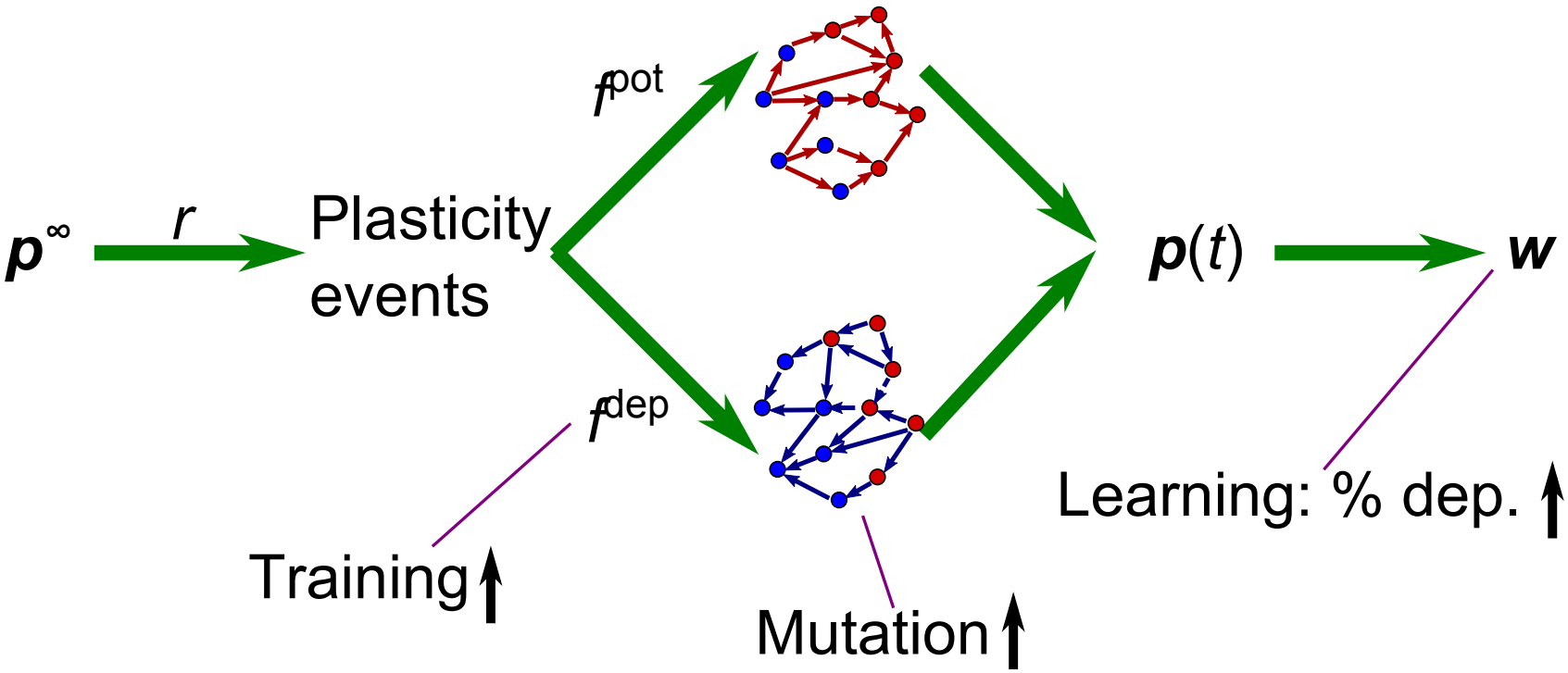


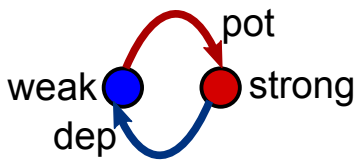
PF+~~CF~~ $\rightarrow$ LTP,
PF+CF $\rightarrow$ LTD.

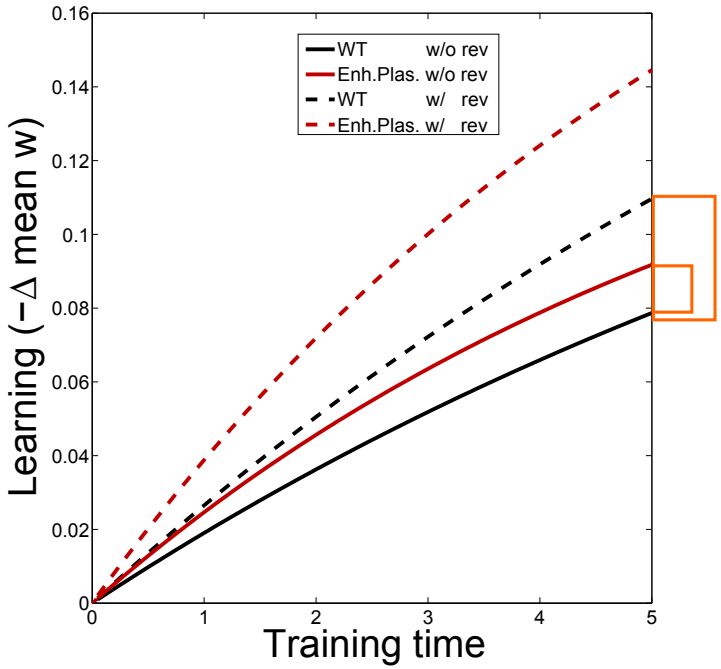
Lower threshold for LTD

VOR gain increase

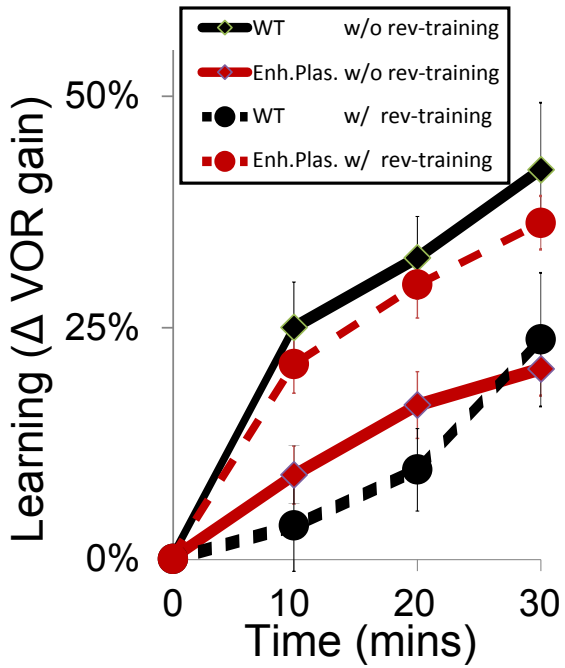
Simple synapses cannot explain the data

Binary synapse



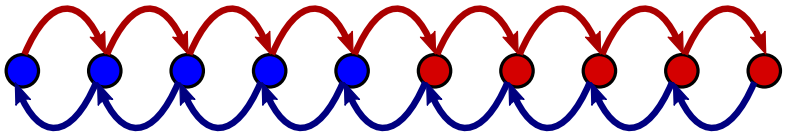


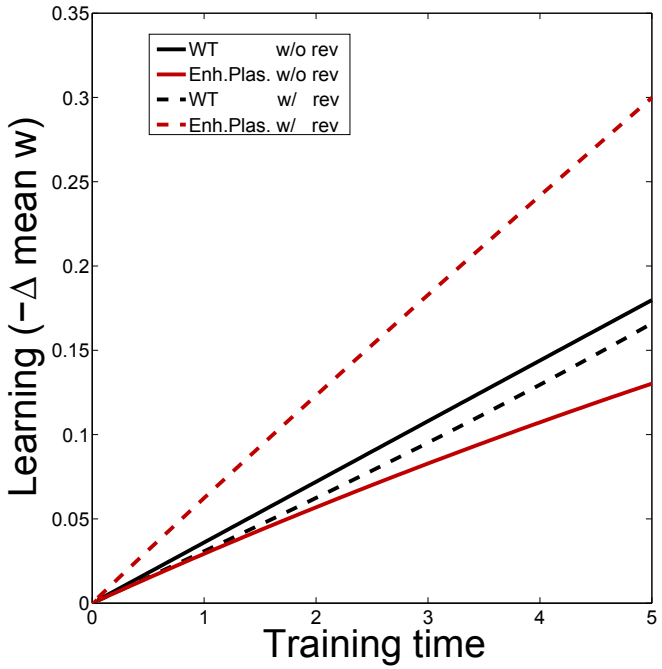
VOR Increase Training



Complex synapses can explain the data

Serial synapse





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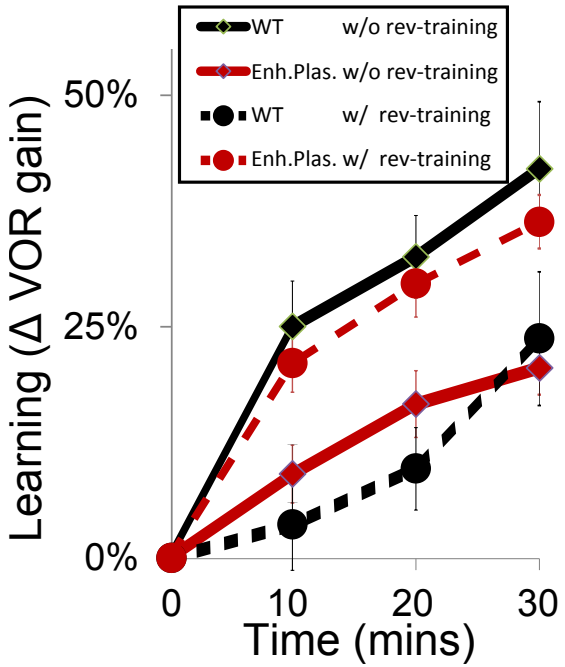
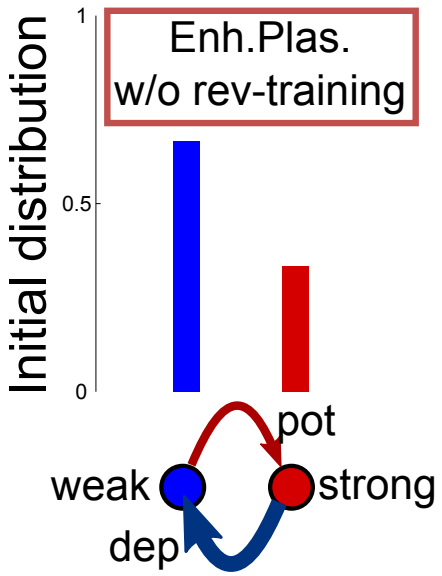
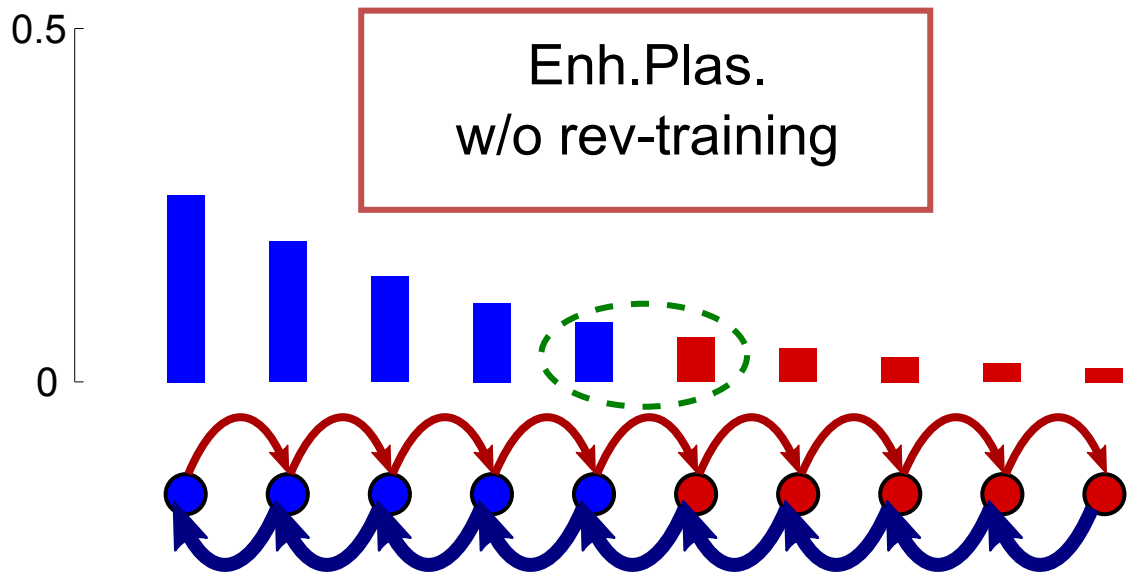


[Leibold and Kempter (2008)]

Enhanced plasticity can enhance or impair learning





Intrinsic plasticity dominates depletion

↓

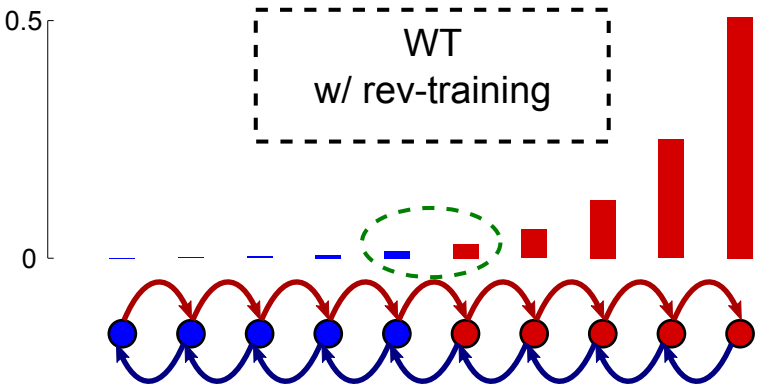
enhanced plasticity enhances learning

Depletion dominates intrinsic plasticity

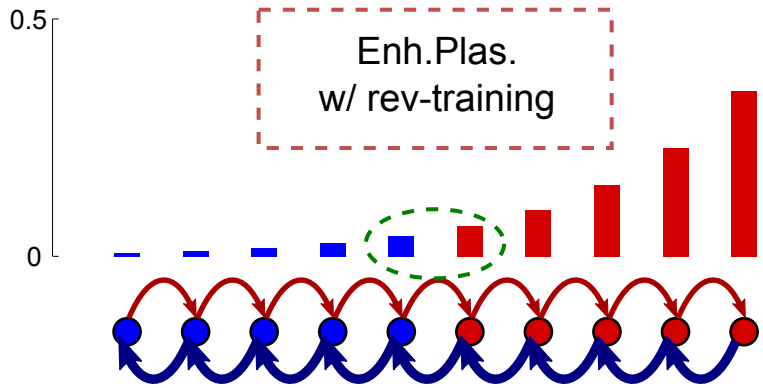
↓

enhanced plasticity impairs learning

Reverse-training can impair or enhance learning



reverse-training
depopulates boundary
↓
impaired learning



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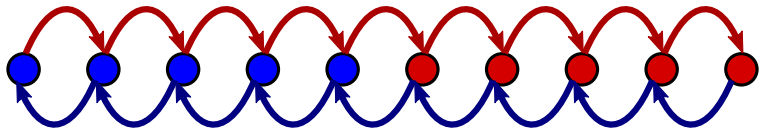
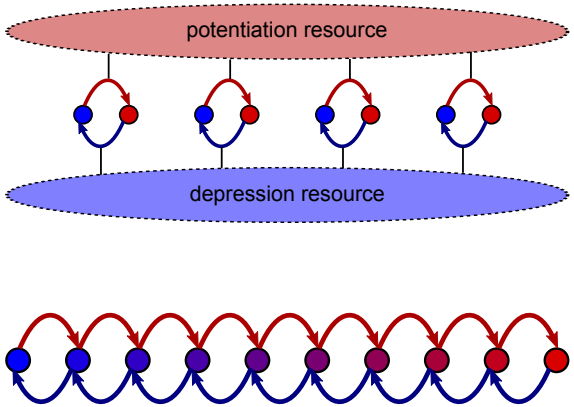
Essential features



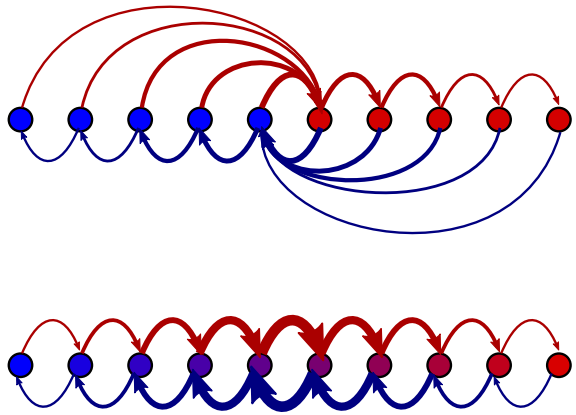
The success of the serial model relies on two features:

- 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)]

Conclusions and further questions

- We find diverse behavioural patterns:
  Enhanced plasticity $\rightarrow$ enhance/impair learning depending on prior experience.
  Reverse-training $\rightarrow$ 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 stubborness: repeated potentiation makes subsequent depression harder.
- We used behaviour to constrain the dynamics of synaptic plasticity

Tradeoff: learning vs. remembering

What about memory?

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

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

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

[Lahiri and Ganguli (submitted)]

The frontiers of complex synaptic memory

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 $\sqrt{N}M$.
- fidelity decay slower than $\sqrt{N}M/rt$.

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

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