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

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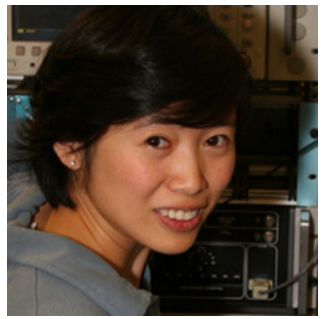
March 1, 2014

Barbara Nguyen-Vu



Grace Zhao

Introduction

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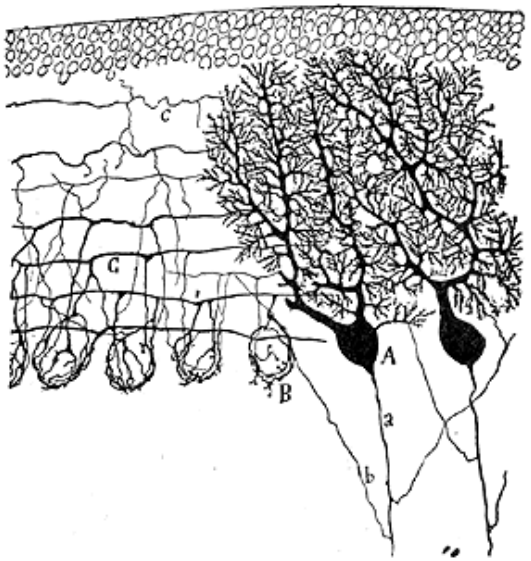
Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Simple synapses cannot explain behaviour. Complex synapses are required.
$\rightarrow$ predictions for synaptic physiology.

Vestibulo-Occular Reflex training

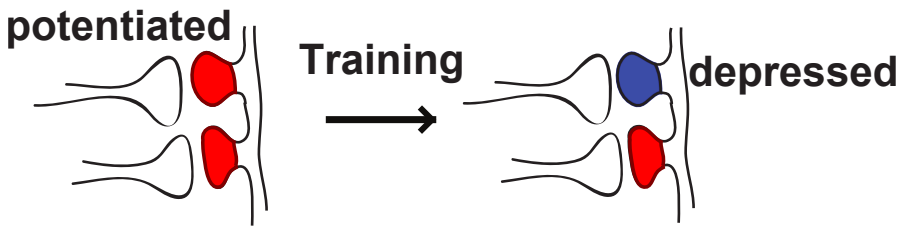
VOR Increase Training

VOR Decrease Training



[Cajal]

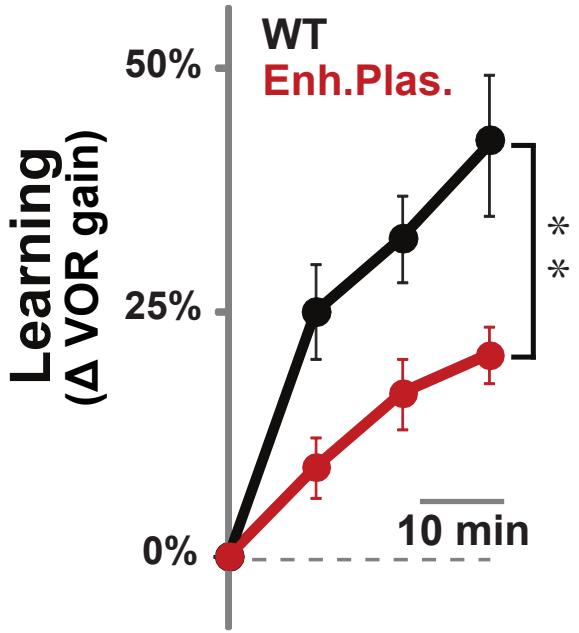
Gain increase: LTD in PF-Pk synapses.



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

Enhanced plasticity impairs learning

Expectaton: enhanced LTD $\rightarrow$ enhanced learning.



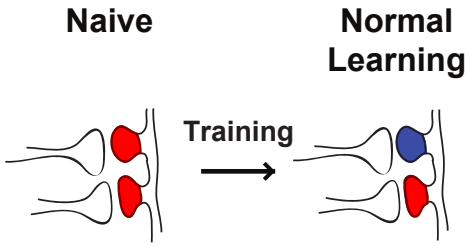
Experiment: enhanced plasticity $\rightarrow$ impaired learning.

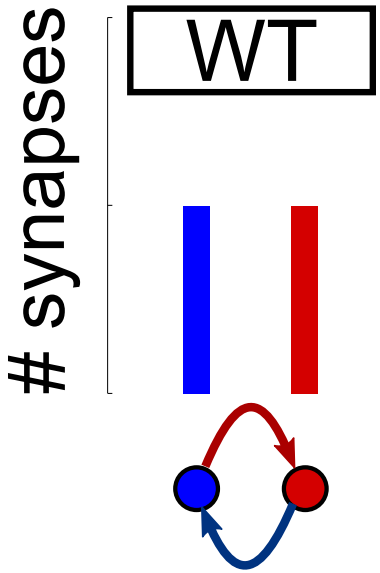
Knockout of MHC-I D^bK^b molecules in PF-Pk synapses
$\rightarrow$ lower threshold for LTD

[McConnell et al. (2009)]

Depletion hypothesis

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





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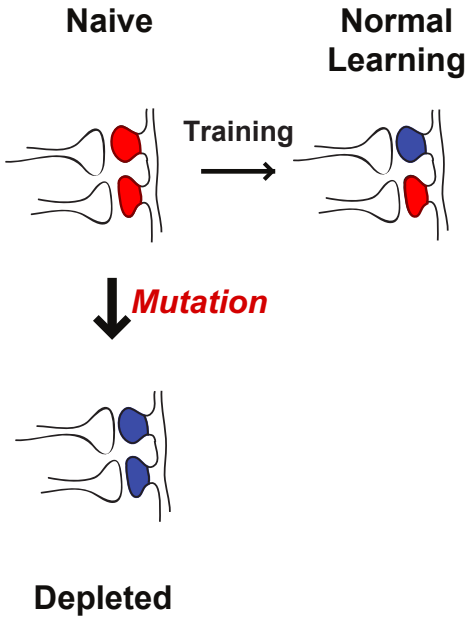

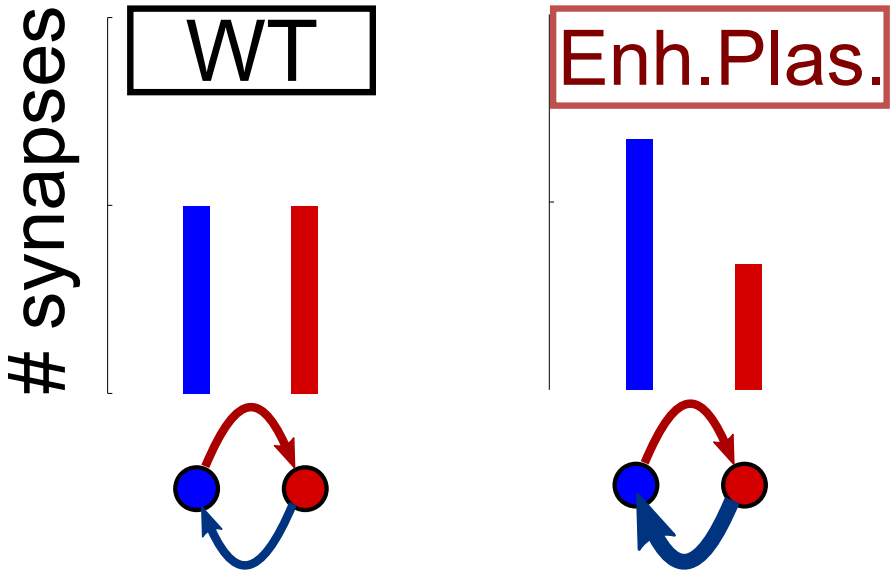

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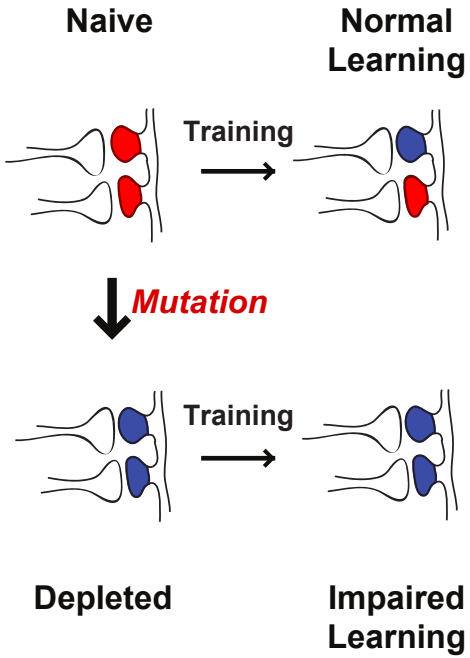
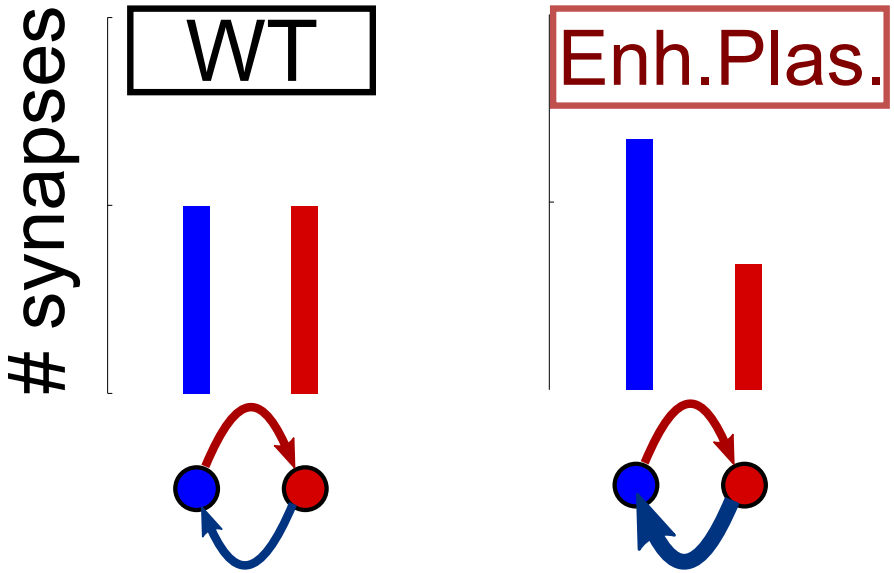
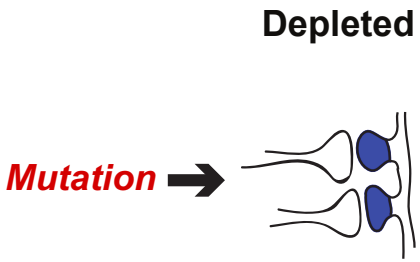




Question 1: depletion effect competes with enhanced intrinsic plasticity.
Which effect is stronger?

Replenishment by reverse-training



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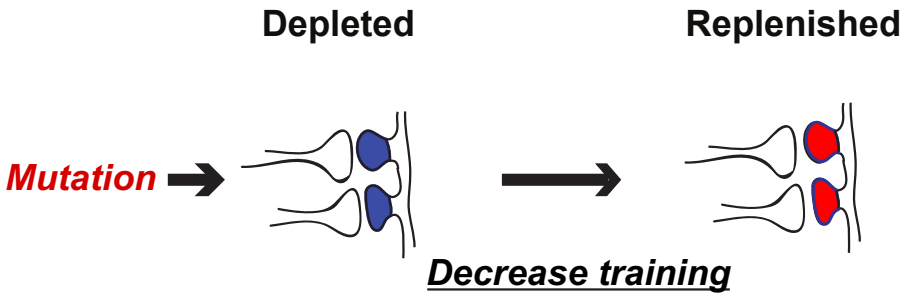

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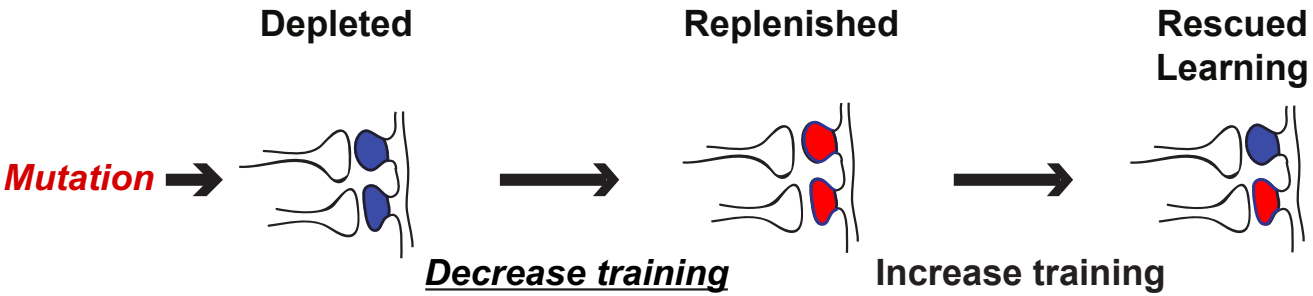

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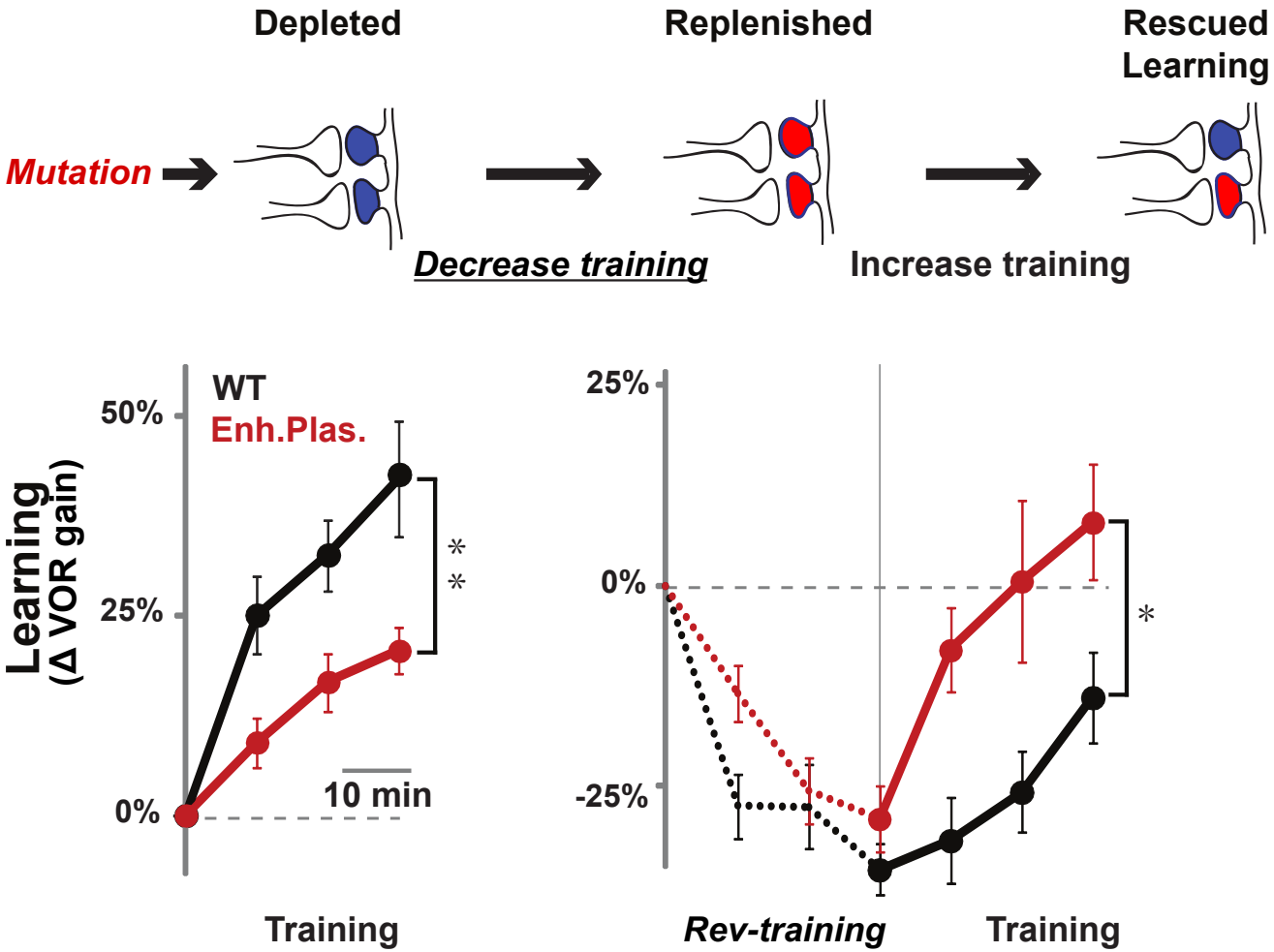

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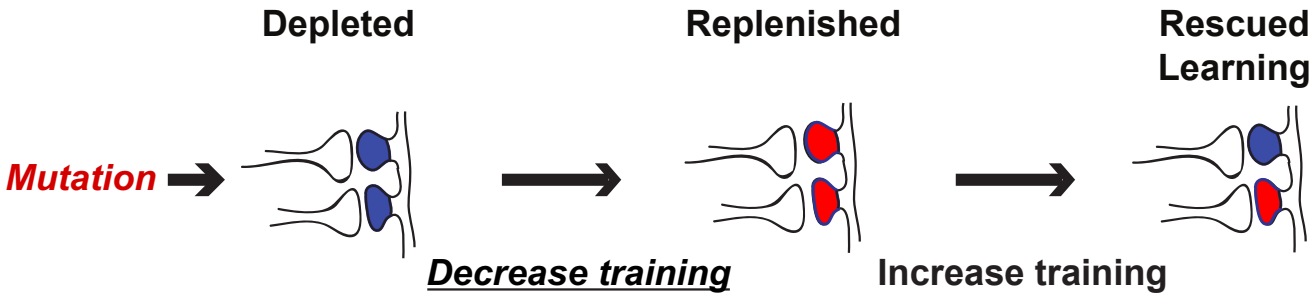

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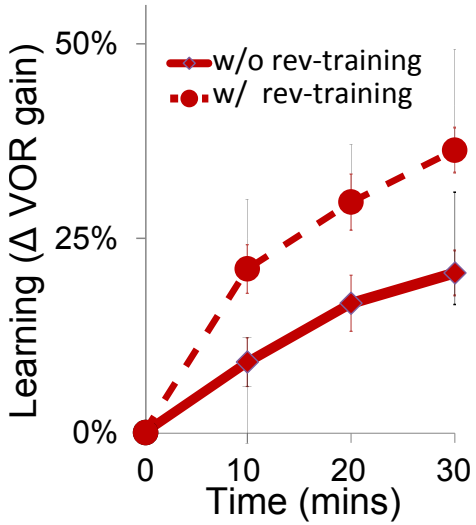

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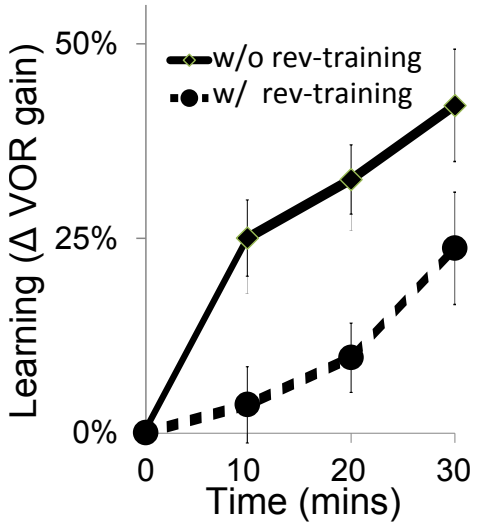
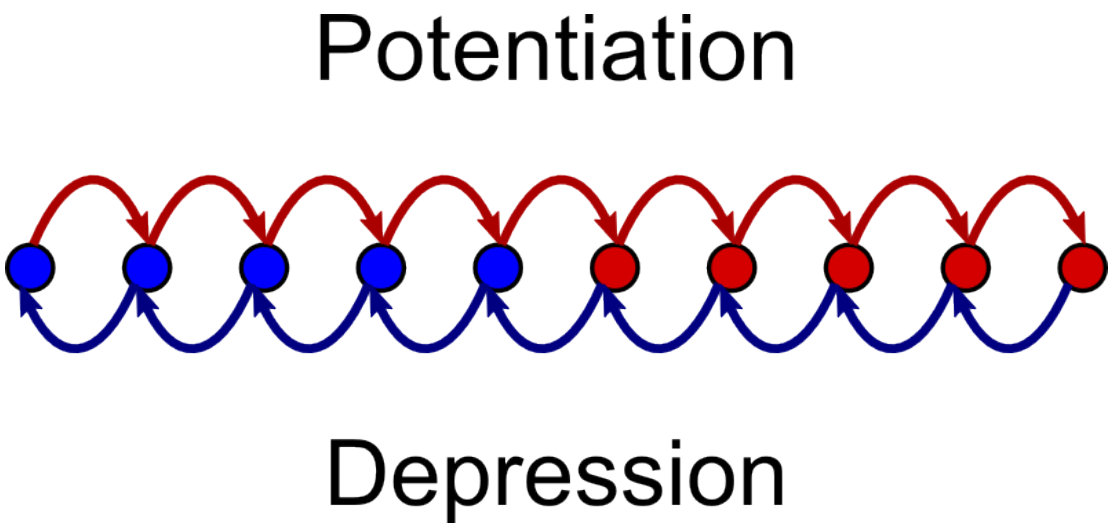


Question 2: How can *too much* replenishment impair learning?

Models of complex synaptic dynamics

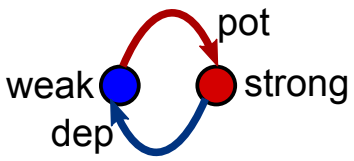
- Internal functional state of synapse $\rightarrow$ synaptic weight.
- Candidate plasticity events $\rightarrow$ transitions between states

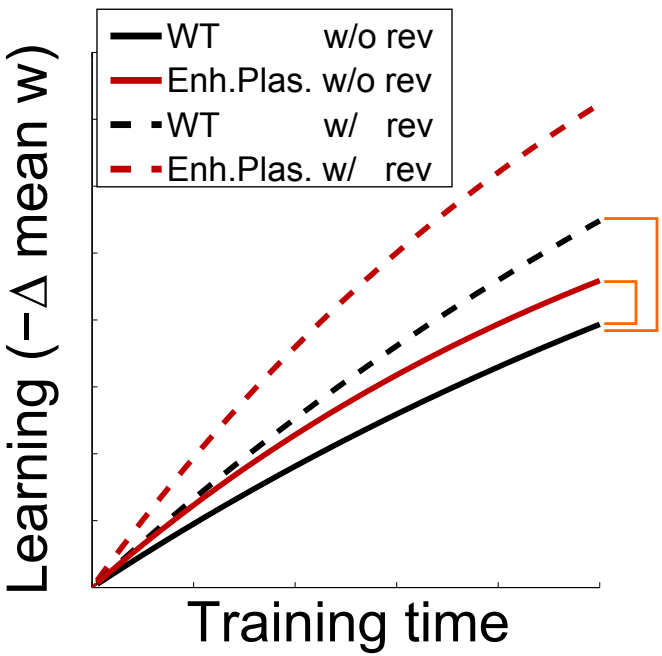


[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]
[Smith et al. (2006)]

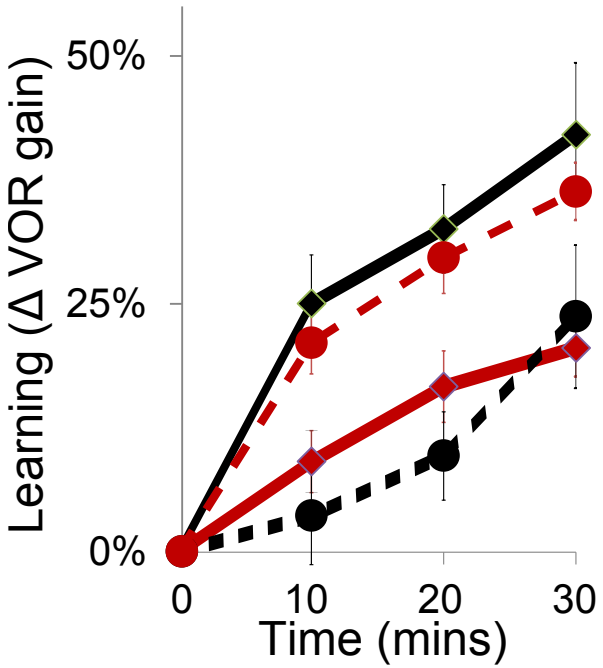
Simple synapses cannot explain the data

Binary synapse





VOR Increase Training



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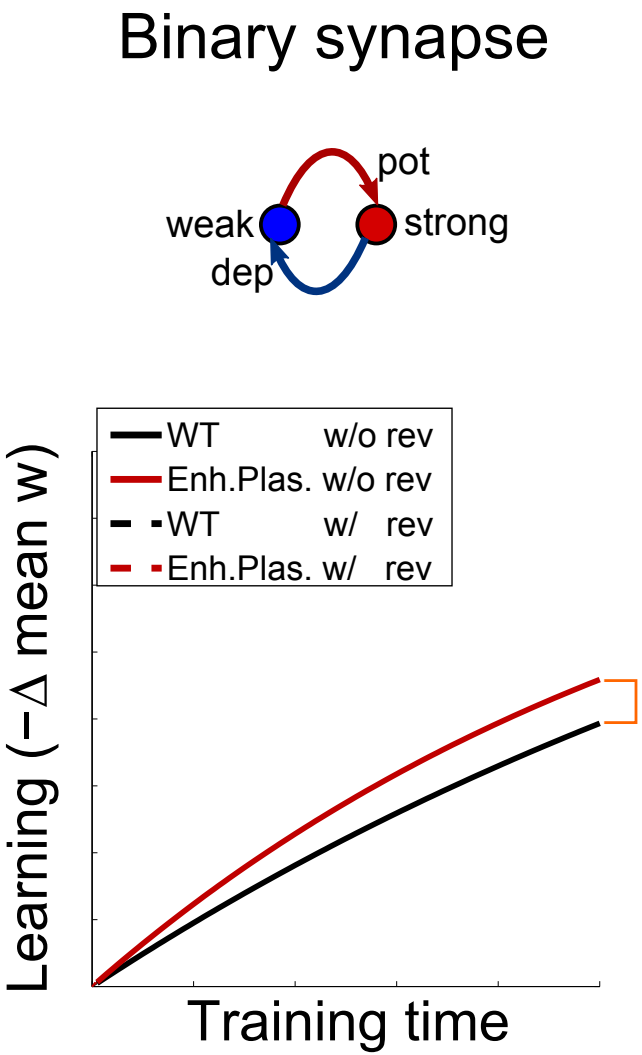

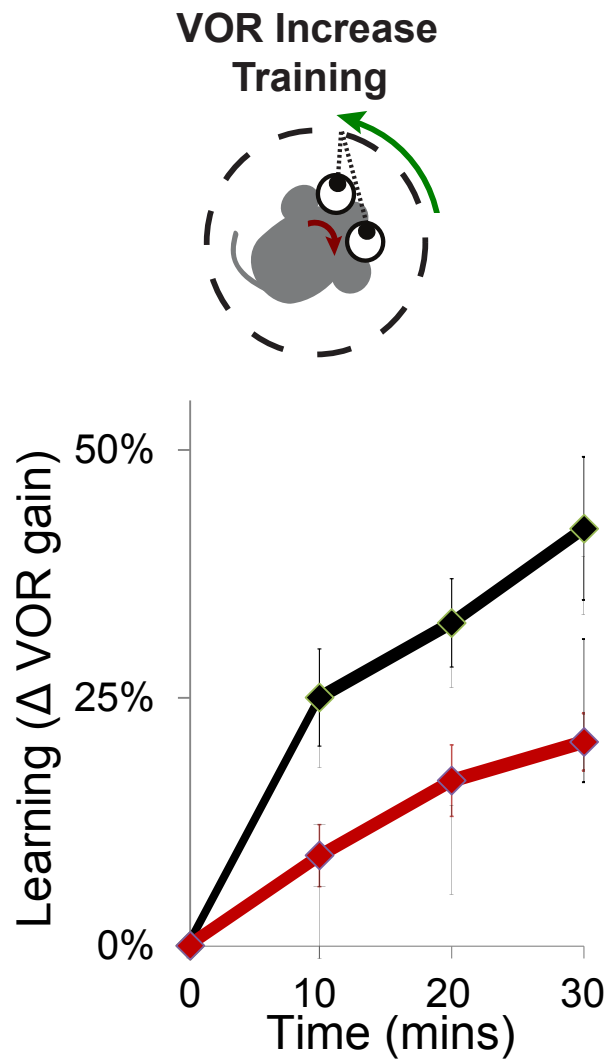

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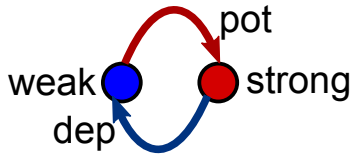
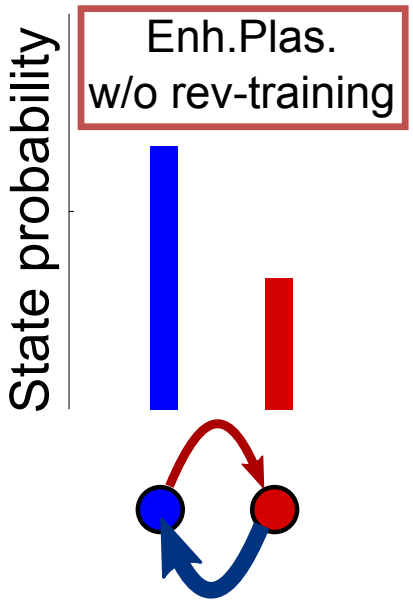


Initial distribution



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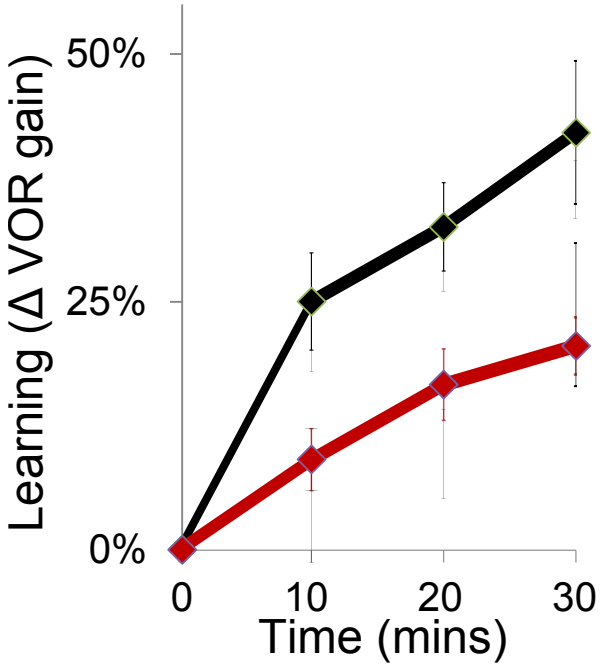

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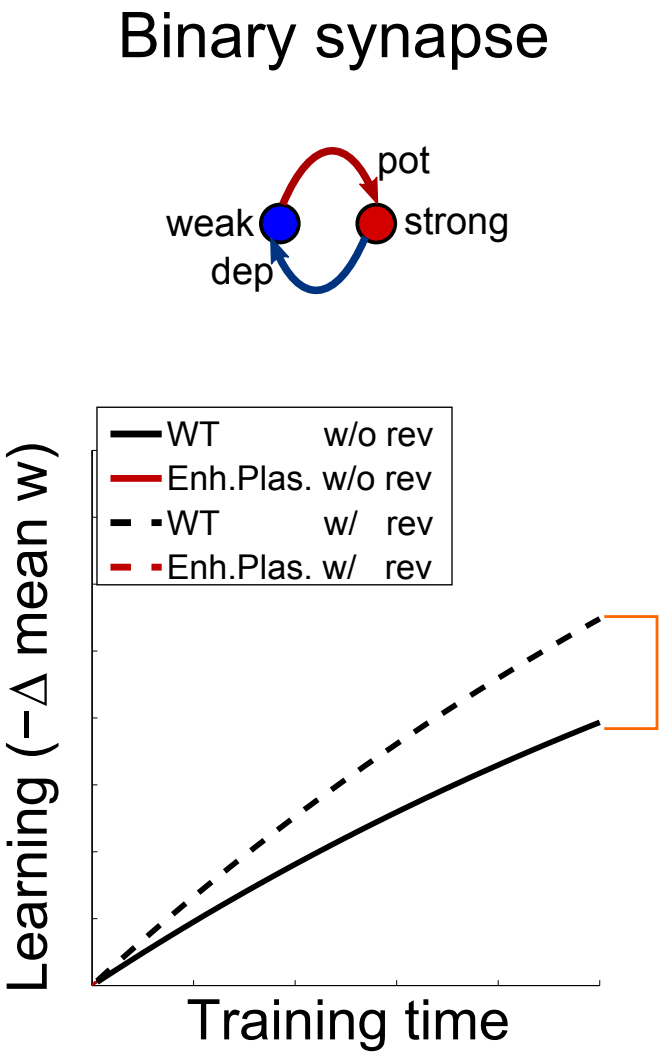

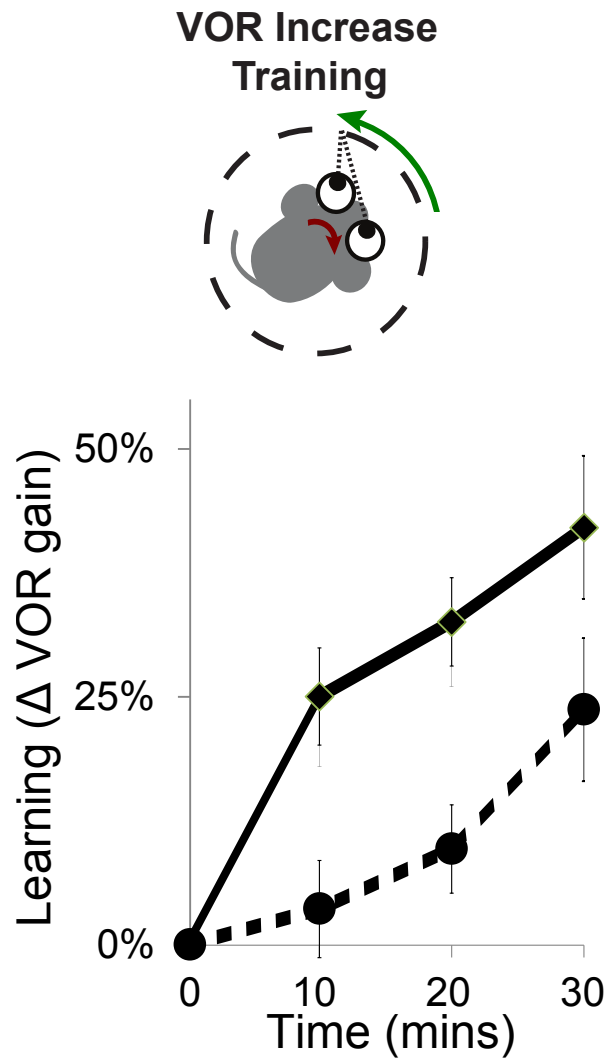

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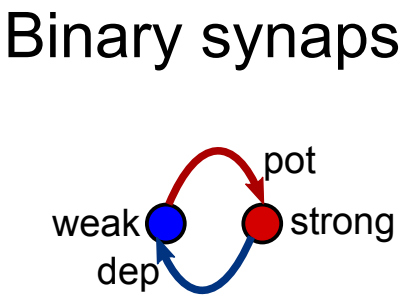
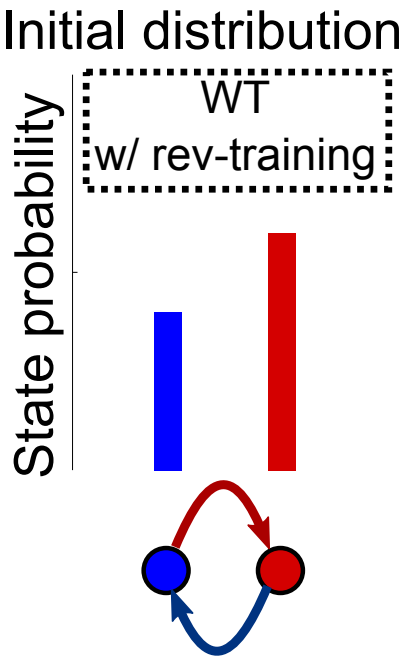
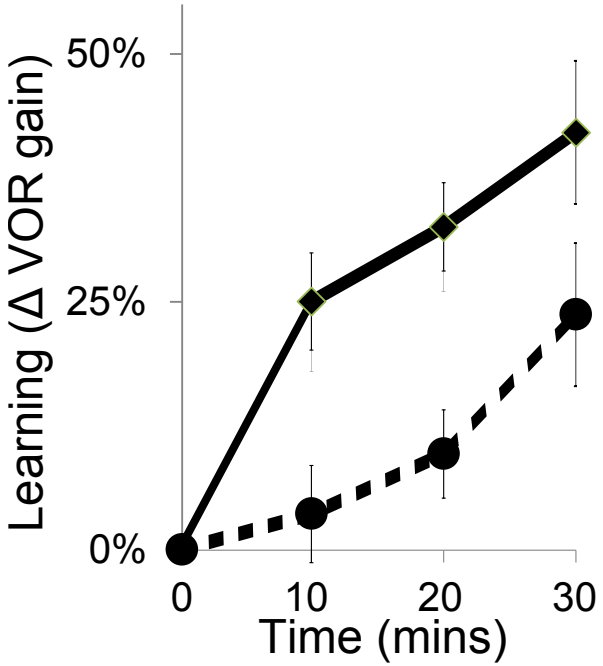
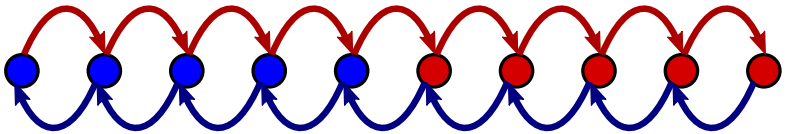


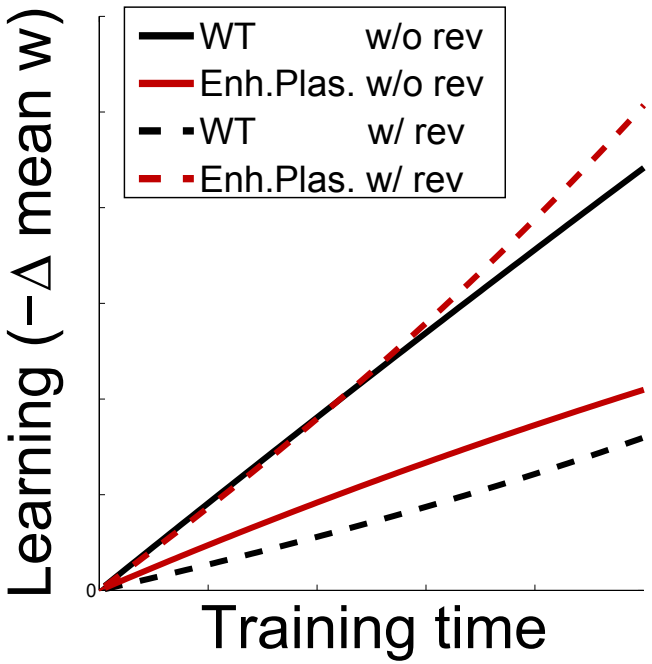




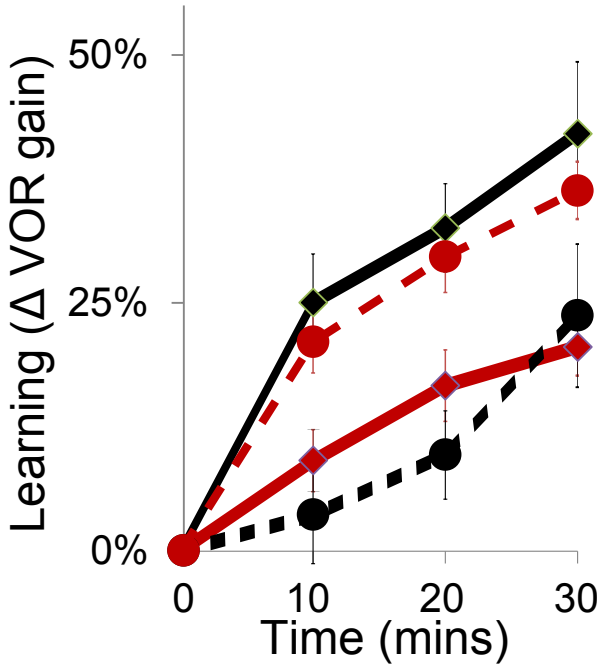
Complex metaplastic synapses can explain the data

Serial synapse





VOR Increase Training



[Leibold and Kempter (2008)]

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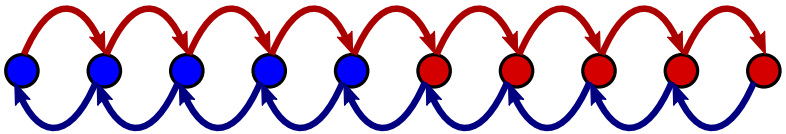

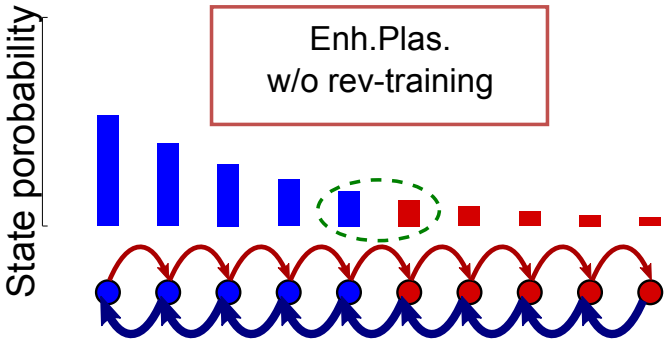

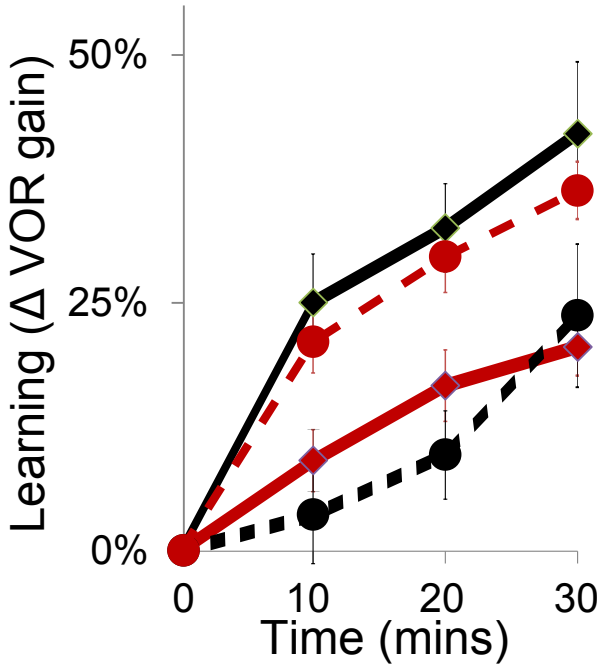

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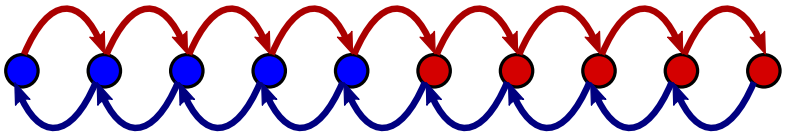

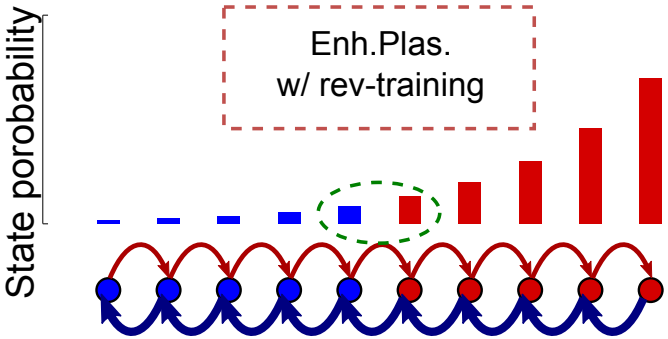

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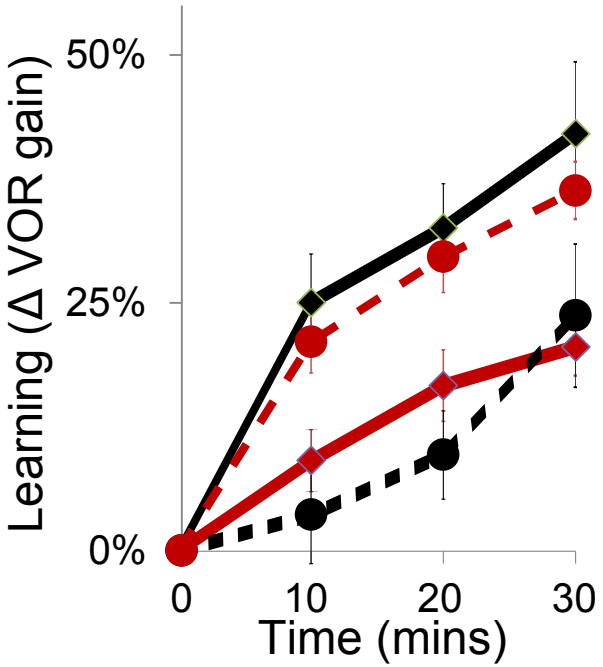

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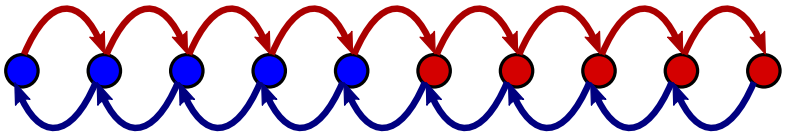

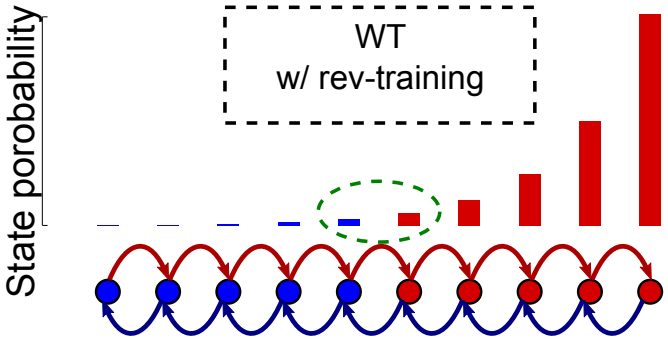

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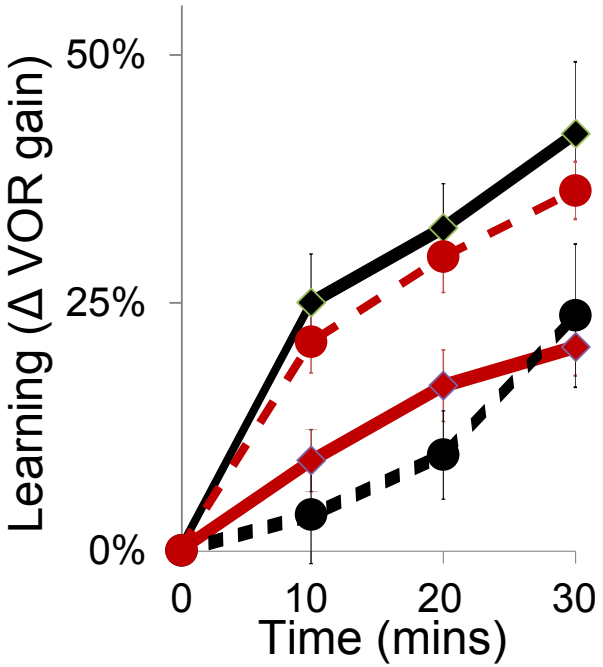

[Leibold and Kempter (2008)]

Conclusions

- Diverse behavioural patterns:
  Enhanced plasticity $\rightarrow$ enhance/impair learning (prior experience).
  Reverse-training $\rightarrow$ enhance/impair learning (plasticity rates).

- Predictions for synaptic physiology:
  Synaptic complexity: necessary to amplify depletion.
  Synaptic stubbornness: repeated potentiation makes subsequent depression harder.

- We used behaviour to constrain the dynamics of synaptic plasticity

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Aparna Suvrathan

Carla Shatz
Han-Mi Lee

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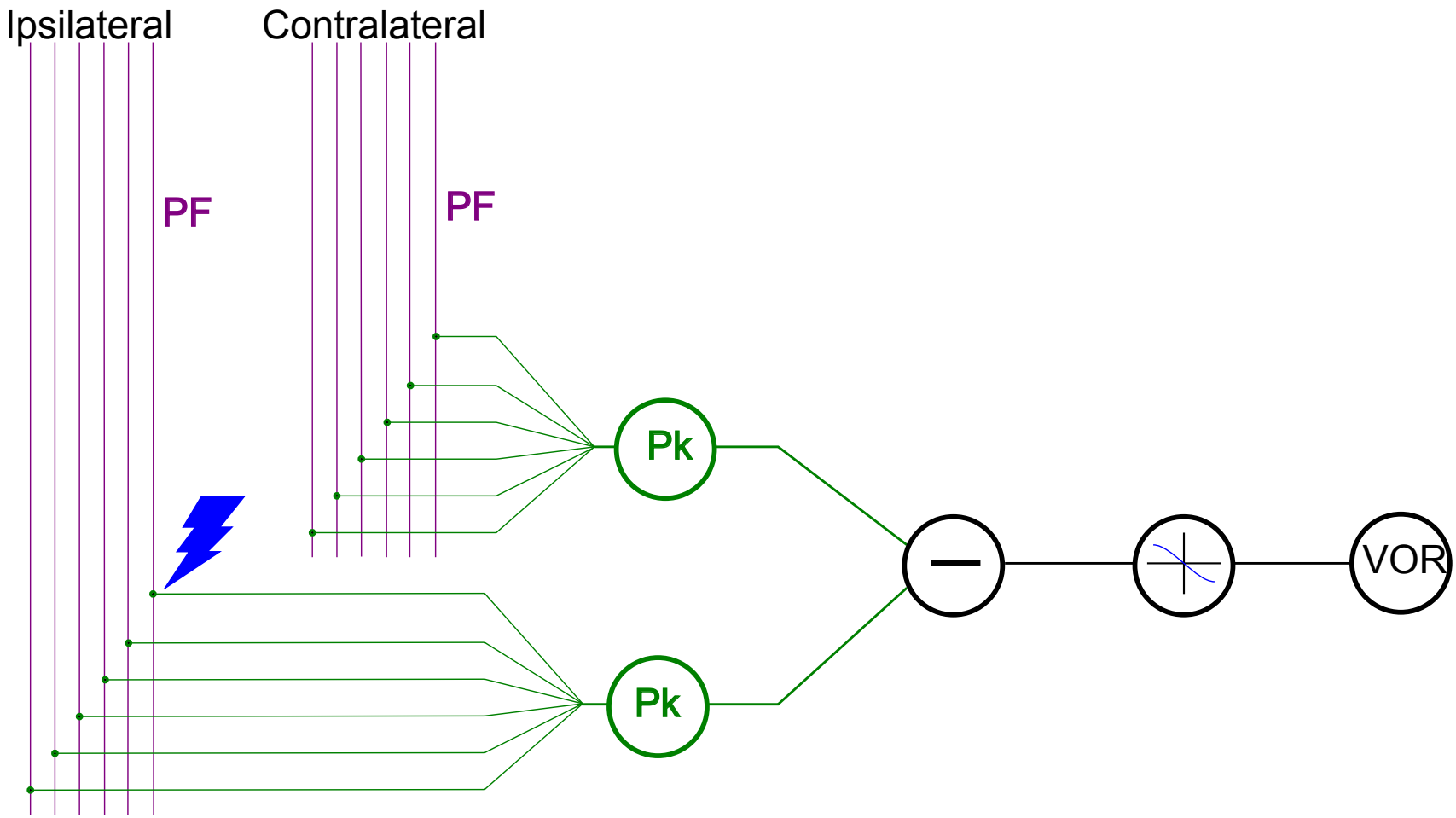
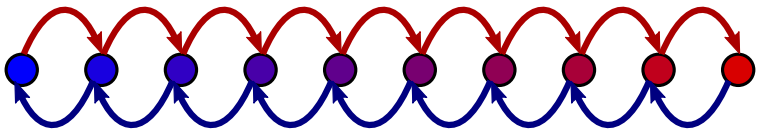
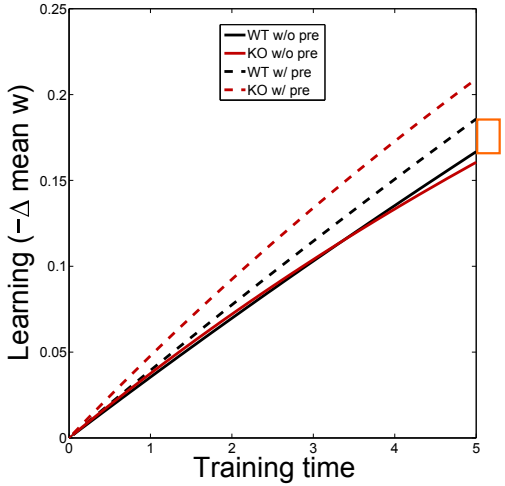
Model of circuit



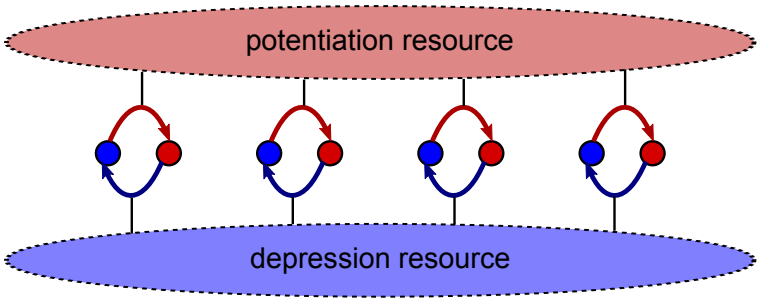
Other models that fail

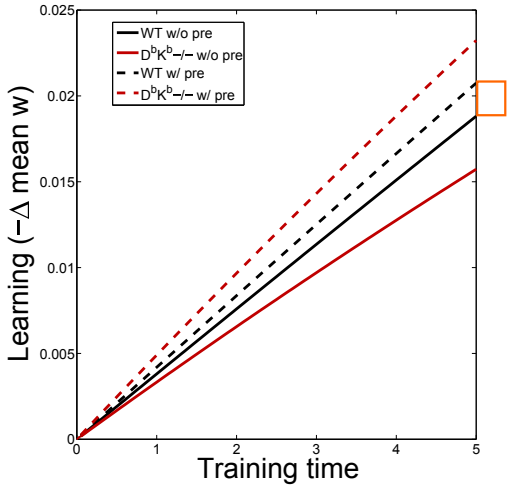
Multistate model





Pooled resource model

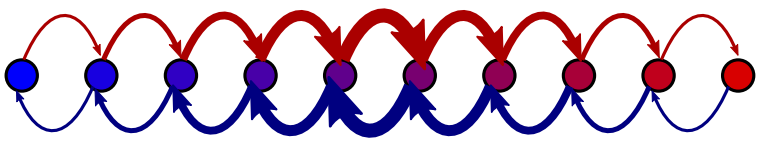


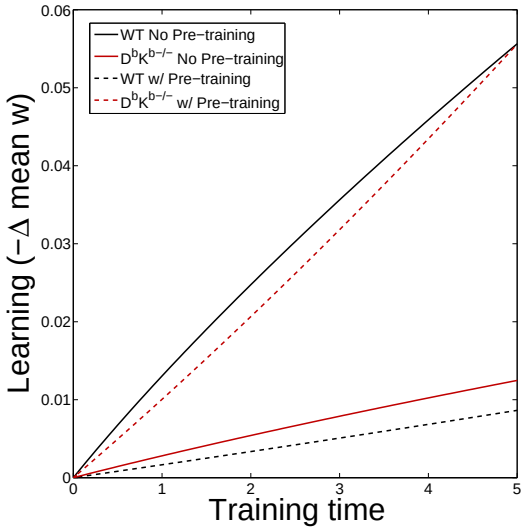


[Amit and Fusi (1994)]

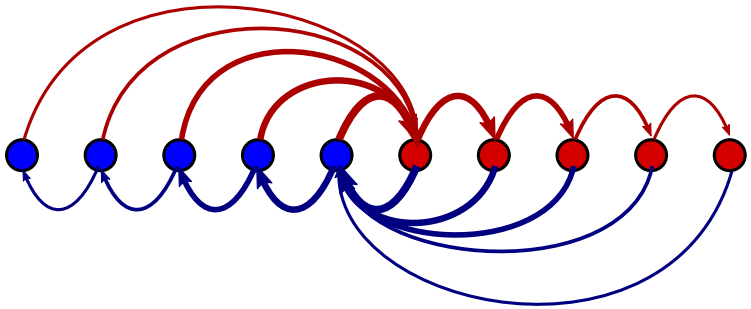
Other models that work

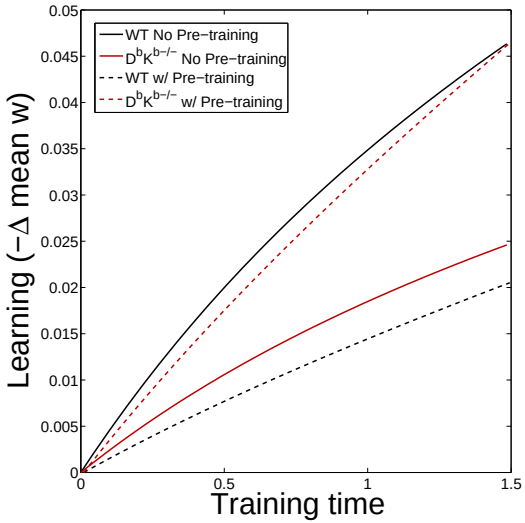
Non-uniform multistate model





Cascade model





[Fusi et al. (2005)]