Modelling impaired and enhanced learning with enhanced plasticity

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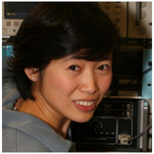
Stanford University

March 1, 2014

Barbara Nguyen-Vu



Grace Zhao

Introduction

Learning requires synaptic plasticity.
Expect: enhanced plasticity $\rightarrow$ enhanced learning.

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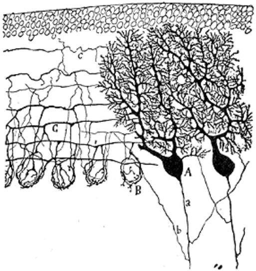
Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Simple synapses cannot explain behaviour. Complex synapses are required.
→ predictions for synaptic physiology.

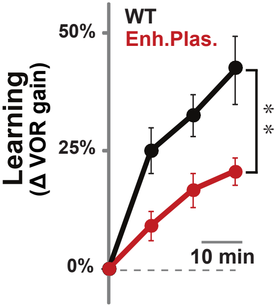


[Cajal]

VOR increase: LTD in PF-Pk synapses.

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

Expectation: enhanced LTD $\rightarrow$ enhanced learning.

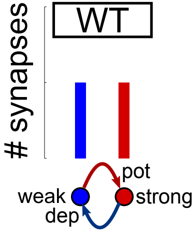


Experiment: enhanced plasticity $\rightarrow$ impaired learning.

Knockout of MHC-I K^bD^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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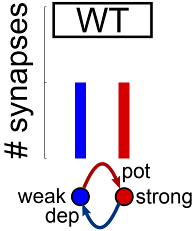
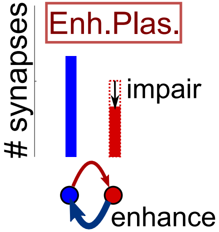
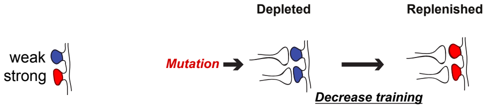




Question 1: depletion effect competes with enhanced intrinsic plasticity.
When is depletion effect stronger?

Replenishment by reverse-training

Replenishment by reverse-training



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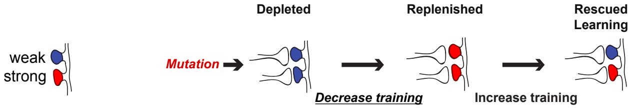

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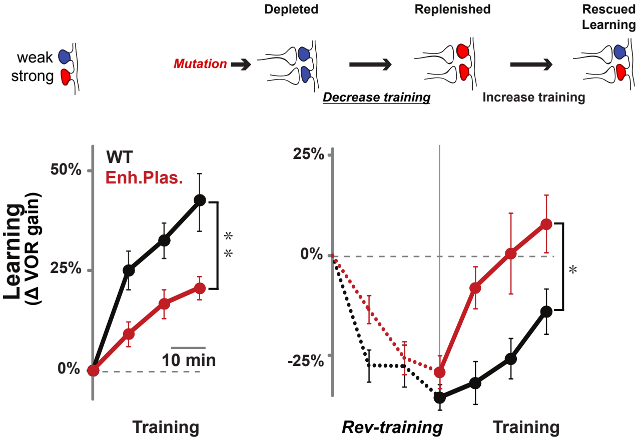

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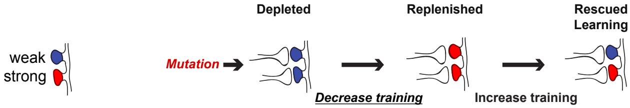
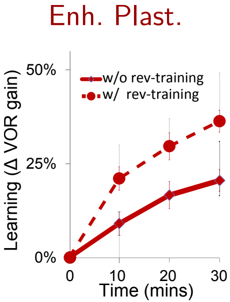
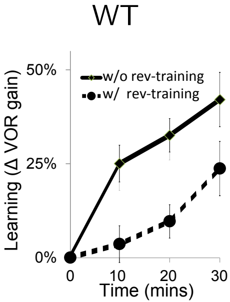
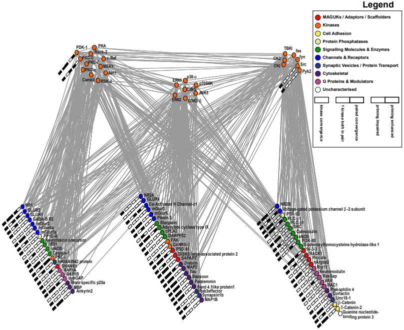




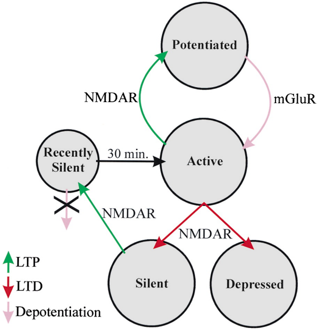


Question 2: How can replenishment *ever* impair learning?

Synapses are complex



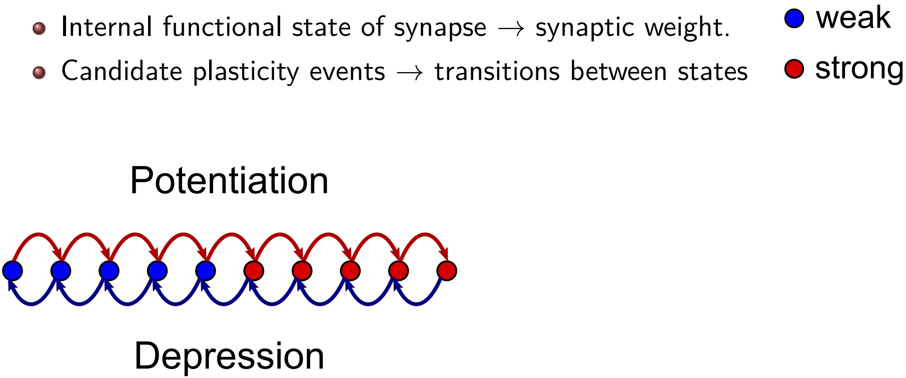
[Coba et al. (2009)]



[Montgomery and Madison (2002)]

Models of complex synaptic dynamics

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



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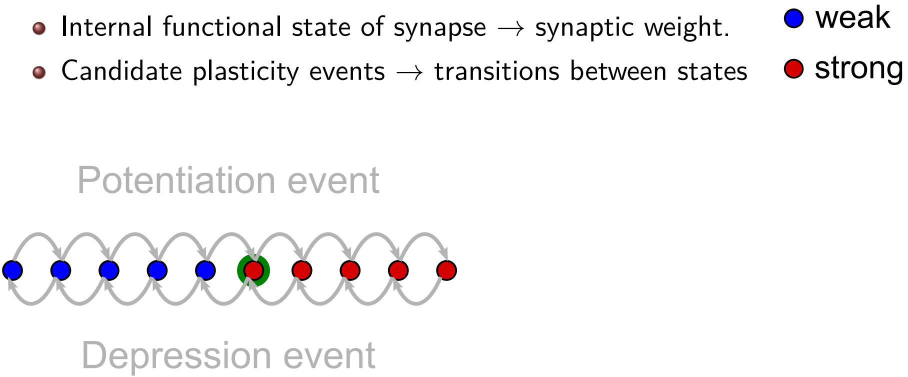

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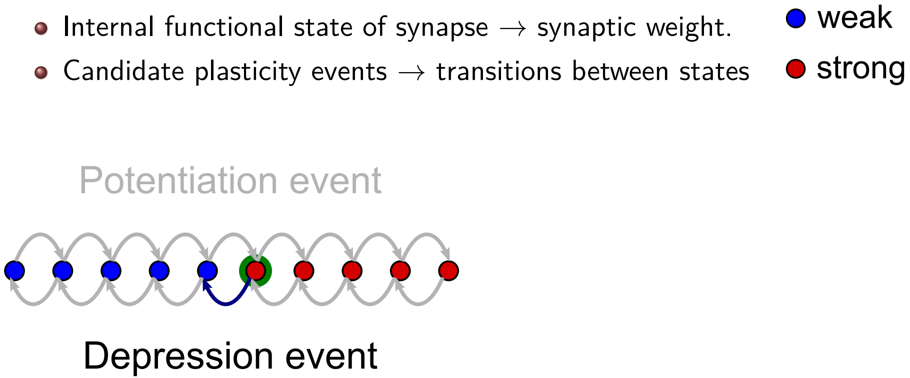

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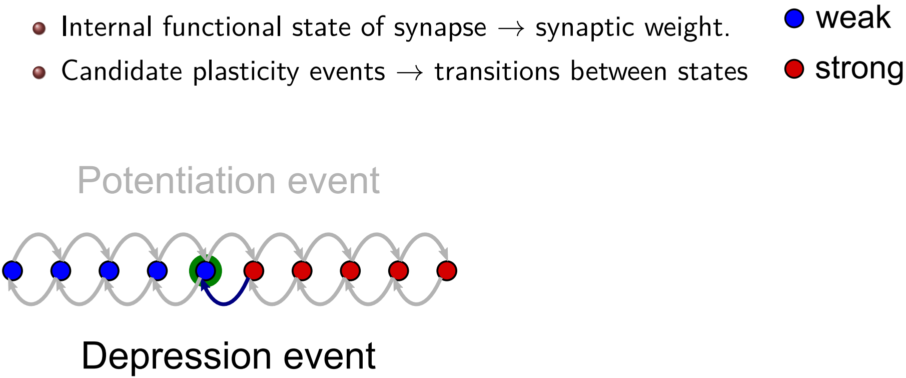

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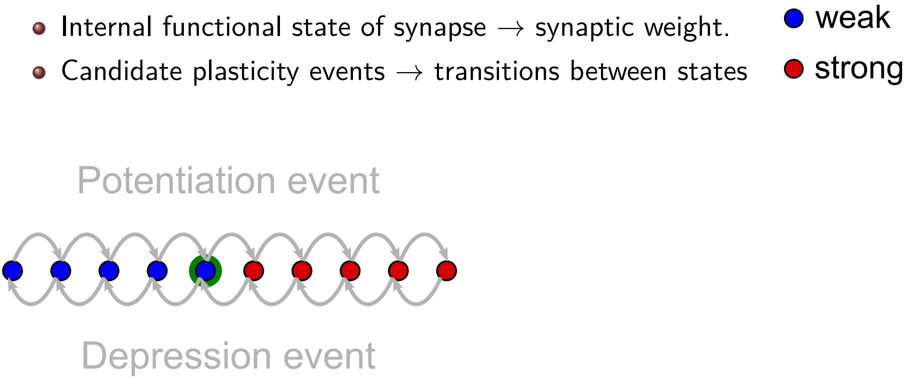

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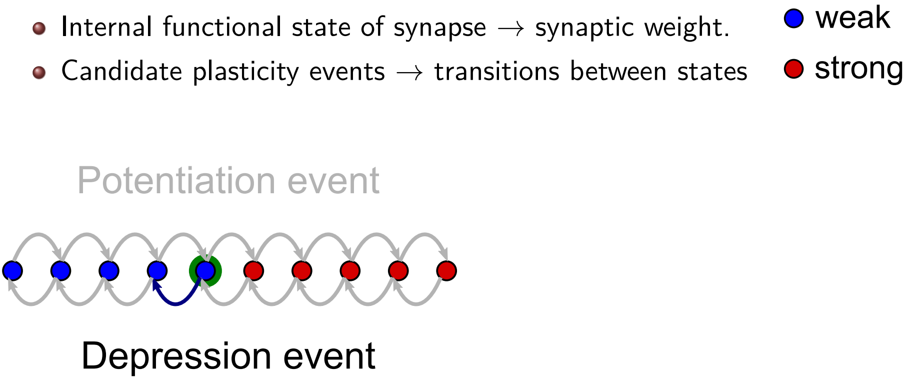

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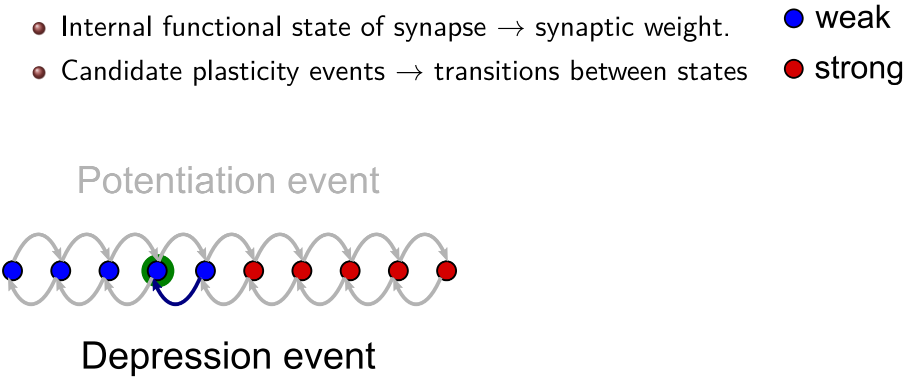

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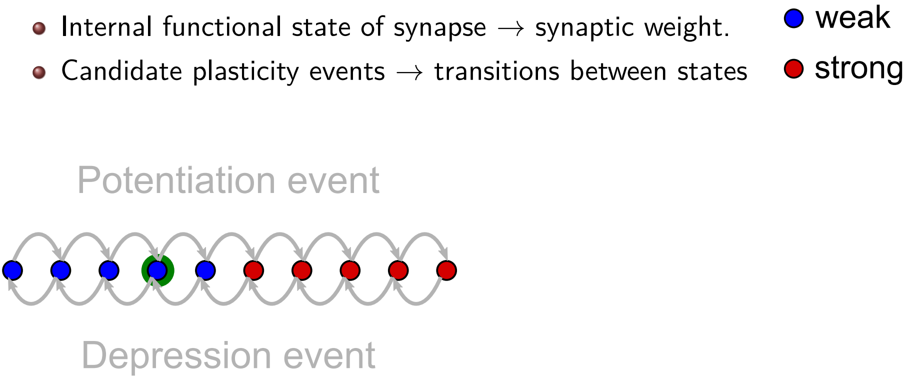

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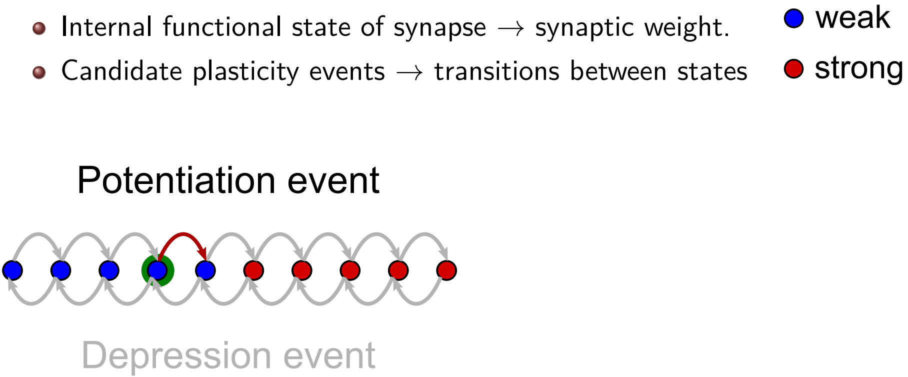

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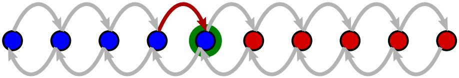
weak

strong

Potentiation event



Depression event

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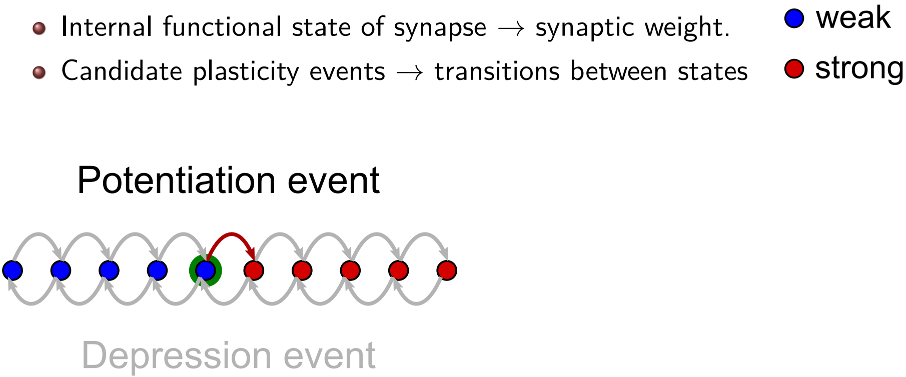

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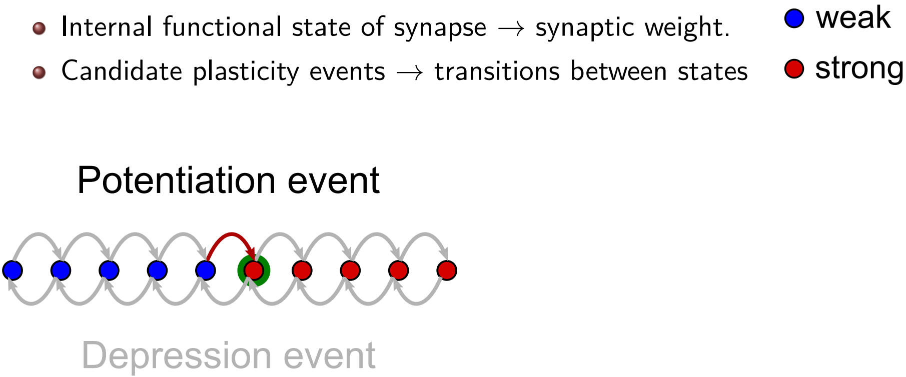

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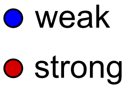

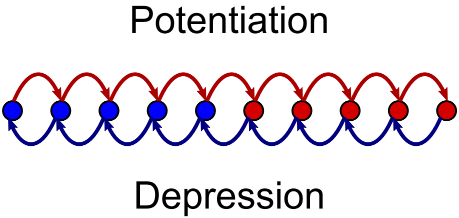

Mutation: trans. probs.

Training: rates of pot/dep events

Learning: synaptic weight

[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]
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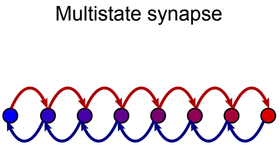
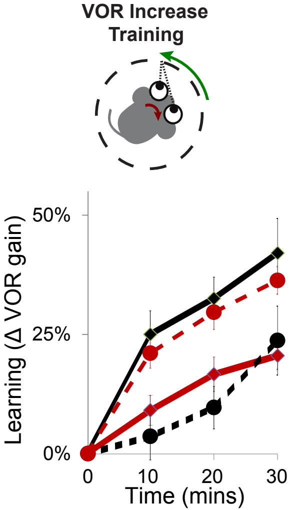
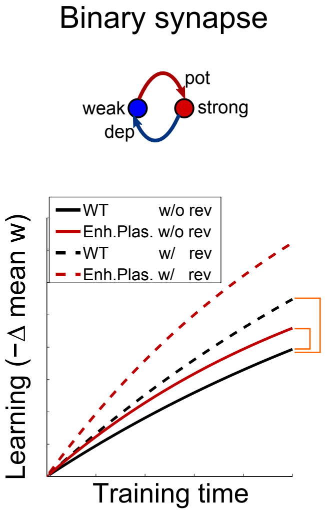
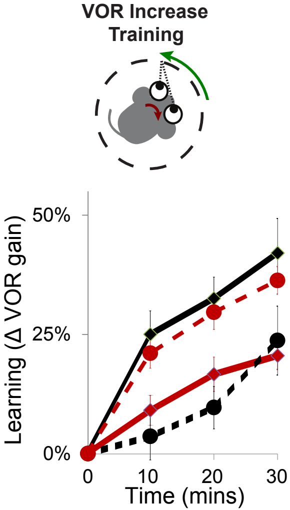
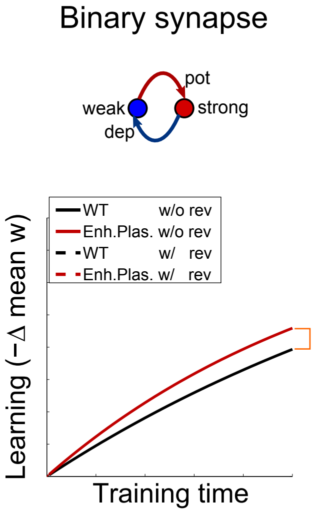
Simple synapses cannot explain the data






Binary synapse
pot
weak
strong
dep
WT w/o rev
Enh.Plas. w/o rev
WT w/ rev
Enh.Plas. w/ rev
Learning (−Δ mean w)
Training time


VOR Increase
Training
50%
25%
0%
Learning (Δ VOR gain)
0
10
20
30
Time (mins)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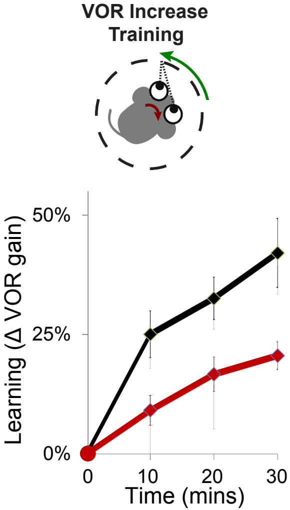
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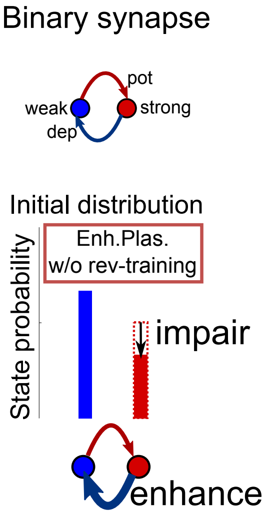
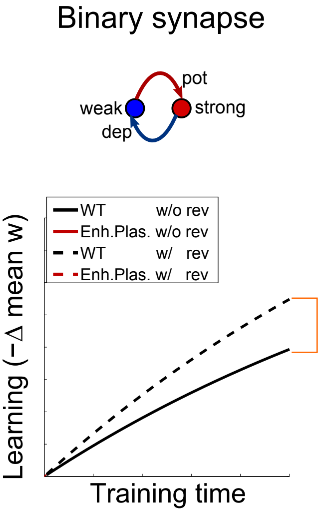


depletion effect

$<$

enhanced plasticity

$\Longrightarrow$ enhanced learning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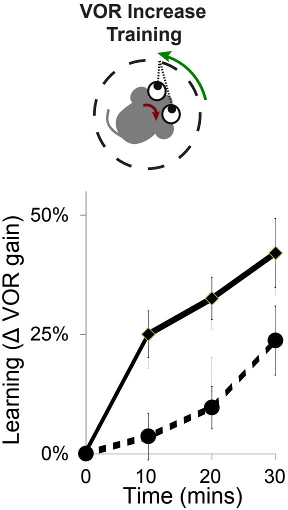
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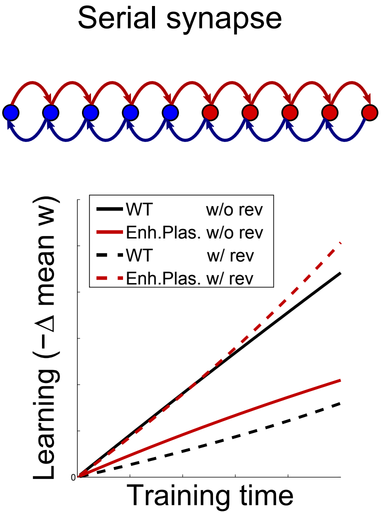
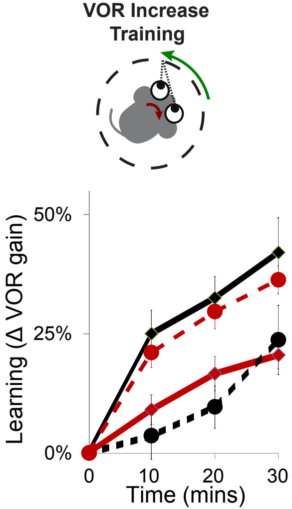
Complex metaplastic synapses can explain the data

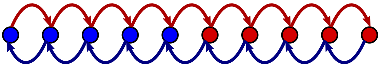


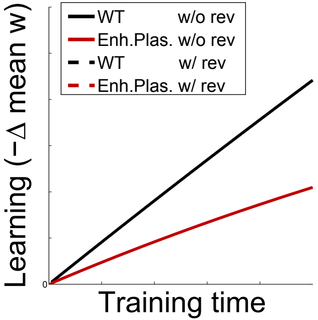


[Leibold and Kempter (2008), Ben-Dayan Rubin and Fusi (2007)]

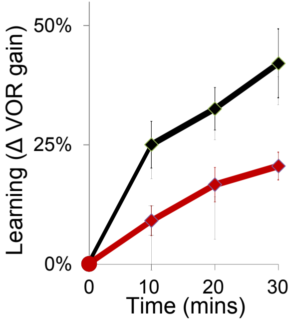
Complex metaplastic synapses can explain the data

Serial synapse





VOR Increase Training



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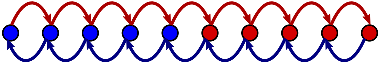

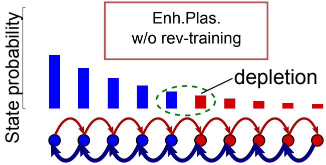

amplified depletion

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enhanced plasticity

$\Longrightarrow$ impaired learning

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

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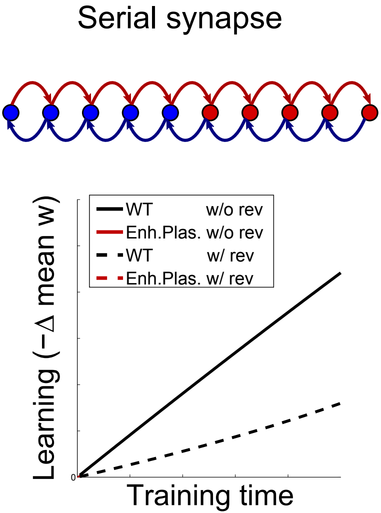

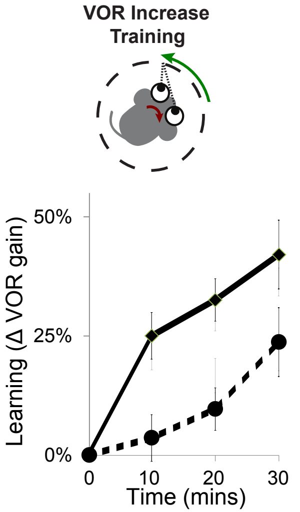

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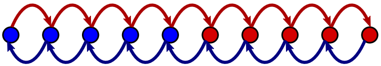
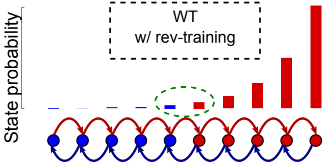




reverse training

+

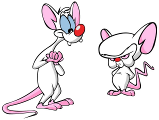
"stubborn" metaplasticity

$\Longrightarrow$ impaired learning

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

Conclusions

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



- enhanced LTD vs. depletion $\rightarrow$ learning outcome.

- 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

Acknowledgements

Surya Ganguli
Madhu Advani
Peiran Gao
Niru Maheswaranathan
Ben Poole
Jascha Sohl-Dickstein
Kiah Hardcastle
Jay Sarkar

Jennifer Raymond
Barbara Nguyen-Vu
Grace Zhao
Aparna Suvrathan

Carla Shatz
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Funding: Swartz Foundation, Stanford Bio-X Genentech fellowship.

Travel grant: Gatsby Charitable Foundation, Qualcomm Incorporated, Brain Corporation, Evolved Machines.

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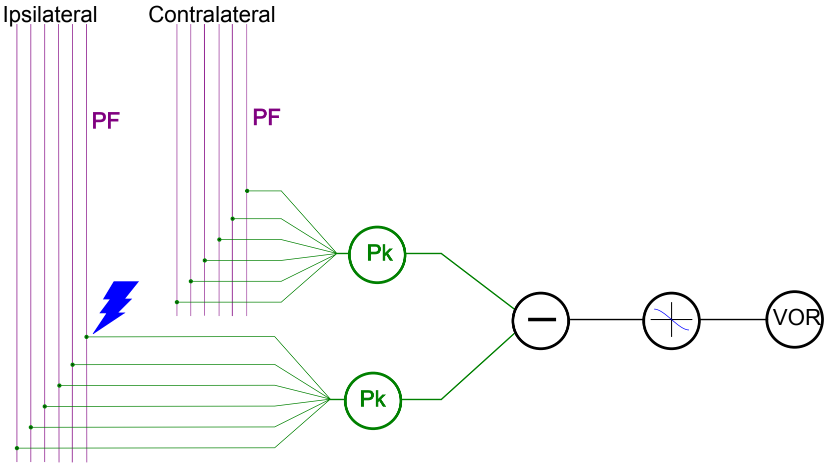
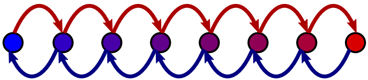
Model of circuit

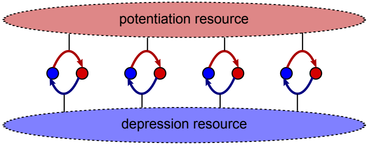


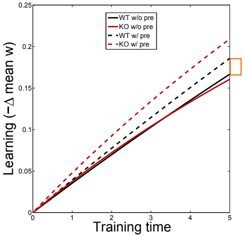
Other models that fail

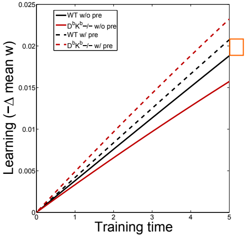
Multistate synapse



Pooled resource model



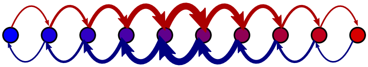


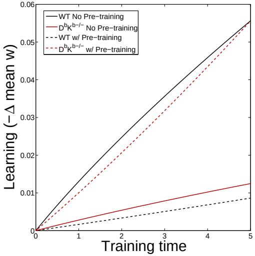


[Amit and Fusi (1994)]

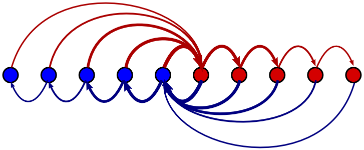
Other models that work

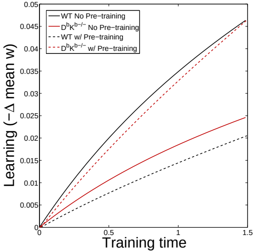
Non-uniform multistate model





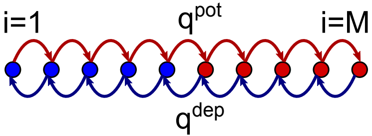
Cascade model





[Fusi et al. (2005)]

Mathematical explanation



Serial synapse: $\mathbf{p}_i^{\infty} \sim \mathcal{N}\left(\frac{q^{\text{pot}}}{q^{\text{dep}}}\right)^{i}$.

Learning rate $\sim \mathbf{p}_{M/2}^{\infty}\left(\frac{q^{\text{dep}}}{q^{\text{pot}}}\right) = \mathcal{N}\left(\frac{q^{\text{pot}}}{q^{\text{dep}}}\right)^{\frac{M}{2}-1}$.

For $M > 2$: larger $q^{\text{dep}} \implies$ slower learning.

For $M = 2$: larger $q^{\text{dep}} \implies$ larger $\mathcal{N} \implies$ faster learning.