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

Subhaneil Lahiri

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1. Acknowledge Barbara and Grace

Introduction

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

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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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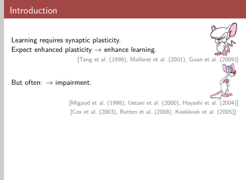

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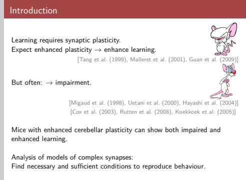
Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Analysis of models of complex synapses:
Find necessary and sufficient conditions to reproduce behaviour.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Outline

- Cerebellar learning of mice with enhanced plasticity
- Complex synaptic models

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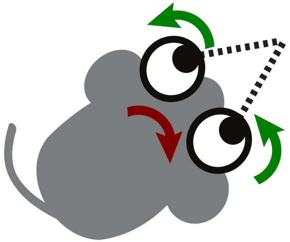
Vestibulo-Occular Reflex



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.

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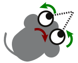

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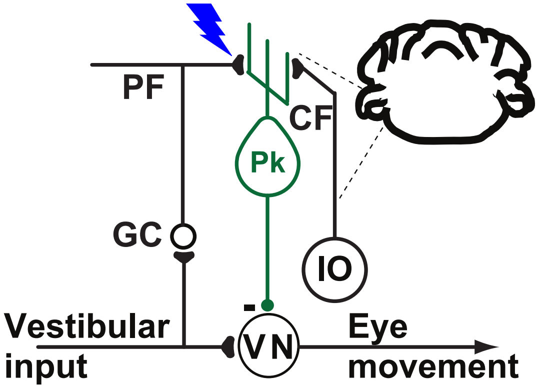
VOR training

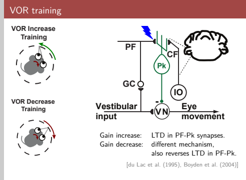
VOR Increase Training

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)]

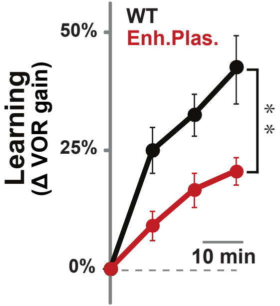


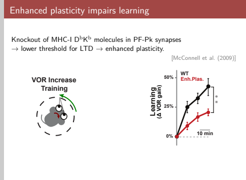
1. trick brain into thinking VOR gain needs adjusting my moving visual stimulu
2. anti-phase → increase gain
3. in phase → decrease gain
4. Gain change involves cerebellum
5. If we enhanced plasticity here: expect enhanced learning

Enhanced plasticity impairs learning

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

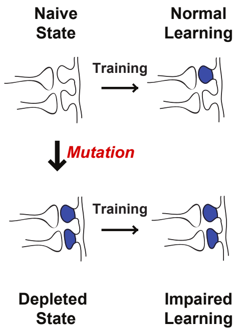
[McConnell et al. (2009)]

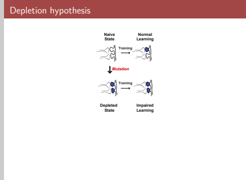




1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD $\rightarrow$ expect better learning
3. Impairment of learning
4. Looking at change of VOR gain during gain-up training

Depletion hypothesis





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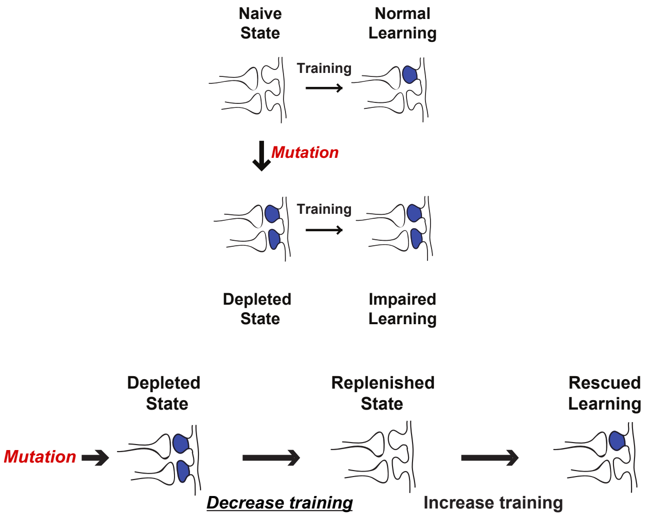
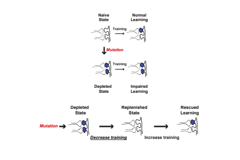
2. Saturation has to compete with enhanced plsaticity. Which will win?

Depletion hypothesis





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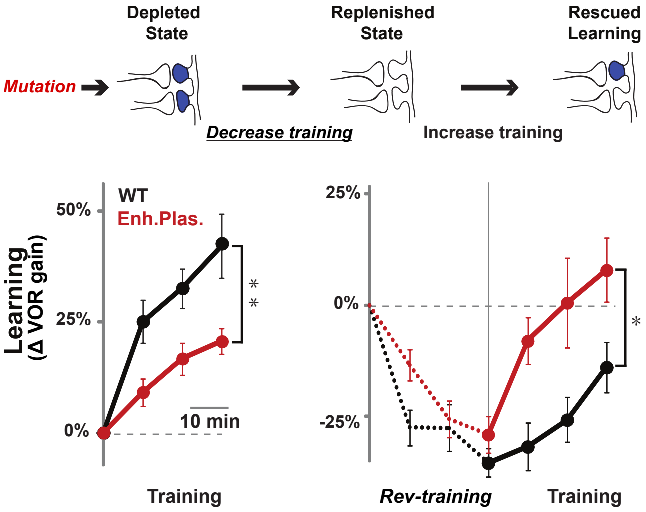
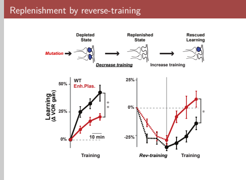
3. Prediction: replenish with rev-training → rescue

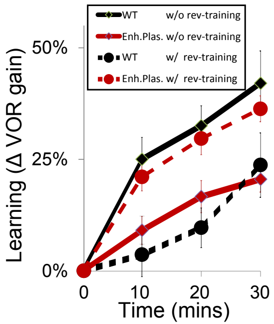
Replenishment by reverse-training

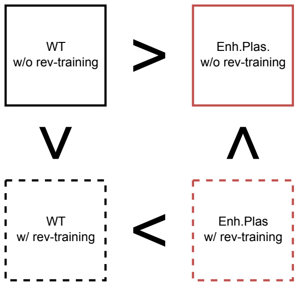




1. precede gain inc training w/ gain dec rev-training: reverses LTD
2. but behaviour from elsewhere → not modelled
3. Focus on gain inc part

Summary of training results





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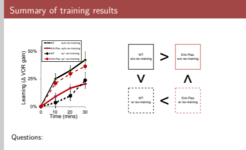

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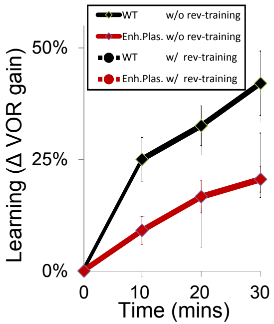

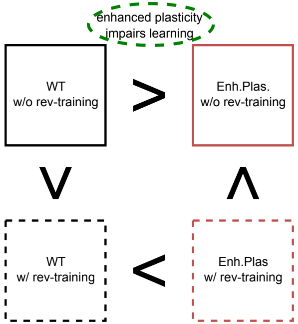

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- Can the depletion effect overcome intrinsic plasticity?

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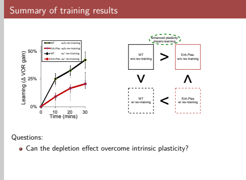

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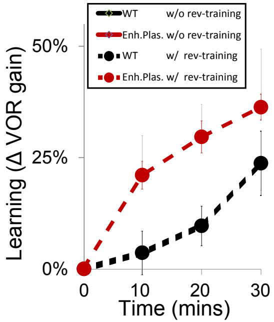

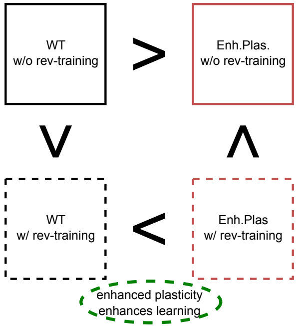

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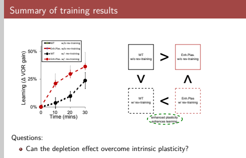

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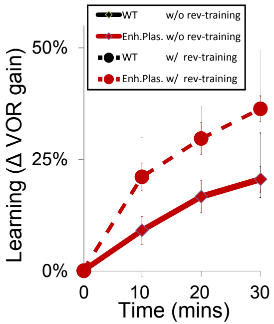

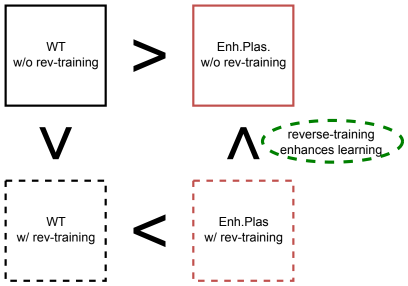

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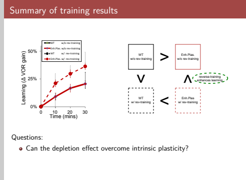

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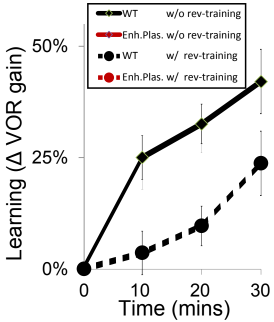

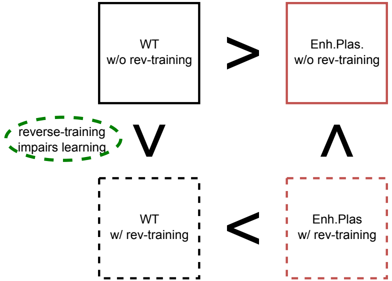

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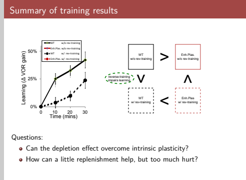

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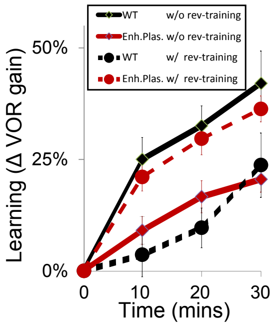

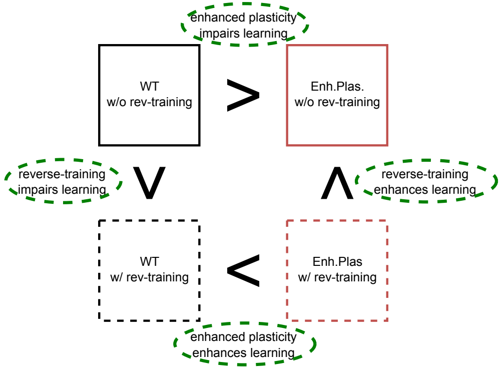

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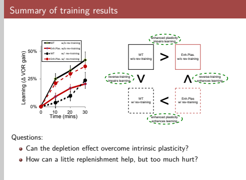

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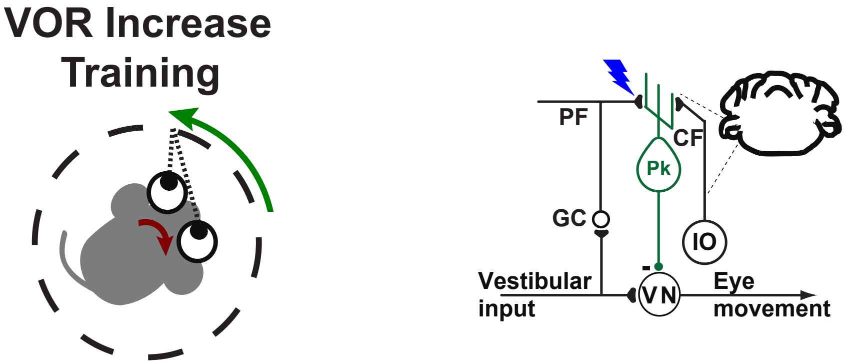
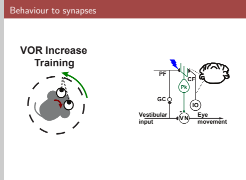
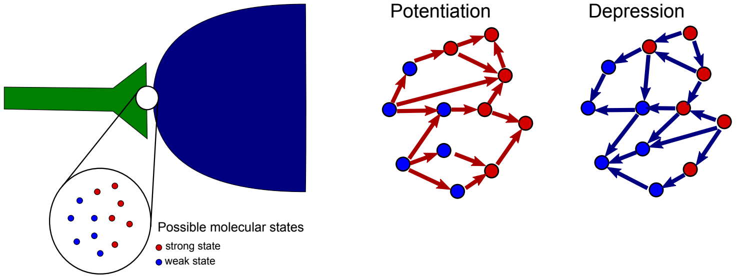




1. Focus on synapses. See if we can understand this behaviour.

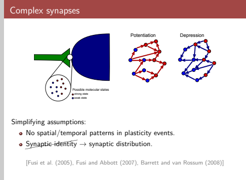
Complex synapses



Simplifying assumptions:

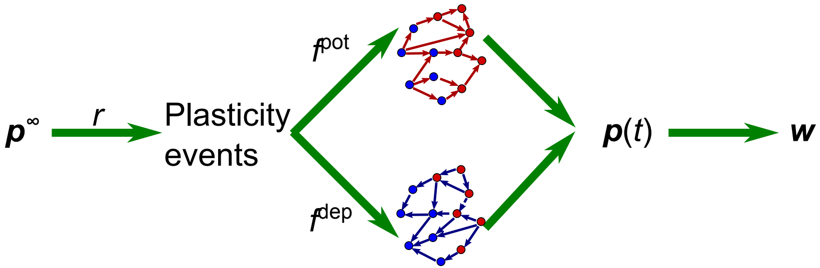
- No spatial/temporal patterns in plasticity events.
- ~~Synaptic identity~~ → synaptic distribution.

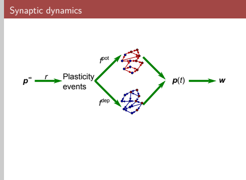
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]



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. pot/dep occur randomly
6. allows us to concentrate on synapse, not neuron/network
7. This is a question about synaptic populations after all.

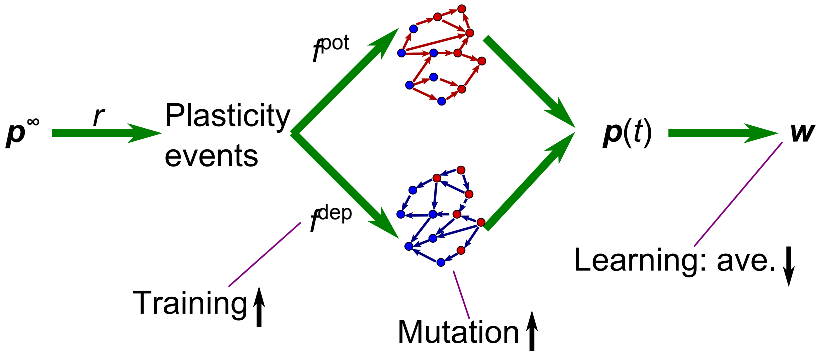
Synaptic dynamics

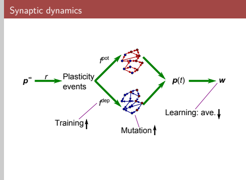




1. stoch process has steady state distribution.
2. Prior activity puts it in this state. row vec.
3. plasticity events at rate r
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

Synaptic dynamics





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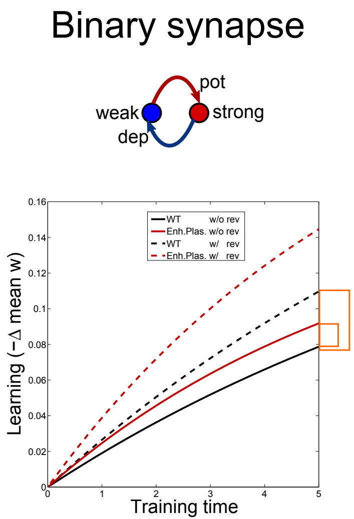
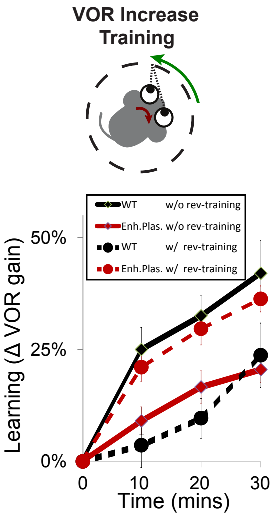
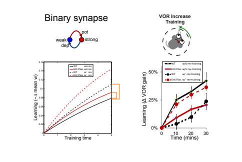
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold → increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r.
9. Learning: Only output we have. Don't keep track of synaptic identity.
10. Same PF+CF input → same $r, f^{\text{pot}}, f^{\text{dep}}$ in each case.
11. Input to Pk, some linear combination of $\mathbf{w}$'s.

Simple synapses cannot explain the data

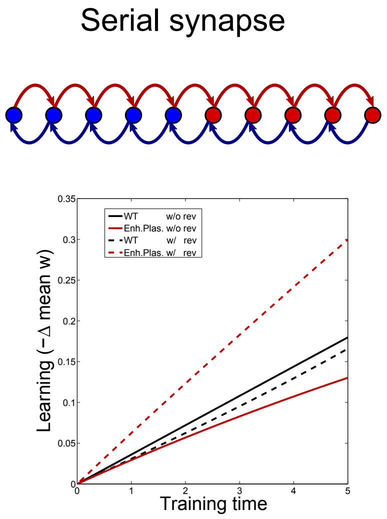


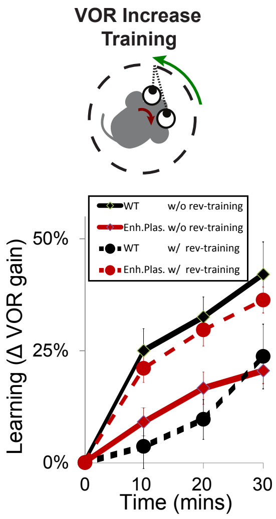




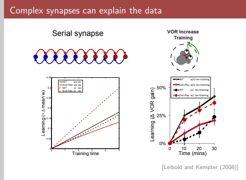
1. Binary fails – mathematical proof for any params
2. Enh.Plas: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.

Complex synapses can explain the data



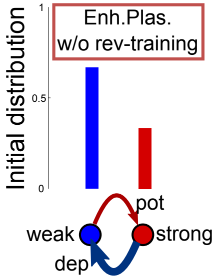


[Leibold and Kempter (2008)]

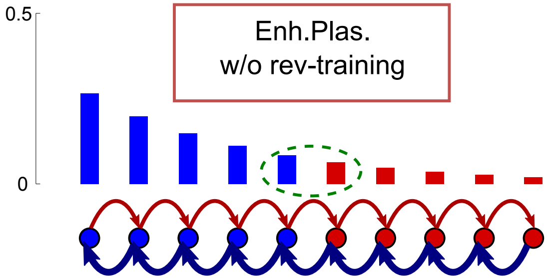


1. Serial: still only two weights. Works.
2. Understand by looking at distributions before training

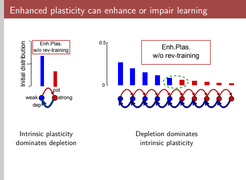
Enhanced plasticity can enhance or impair learning



Intrinsic plasticity dominates depletion

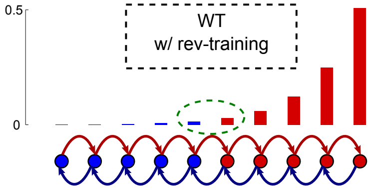


Depletion dominates intrinsic plasticity



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
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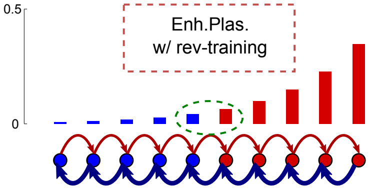

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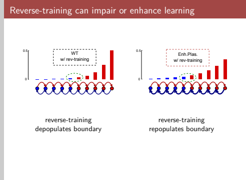
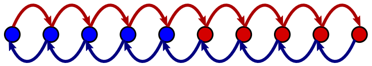
repopulates boundary



1. rev-training: little repopulates boundary
2. Too much pushes to other side, depopulates boundary

Essential features

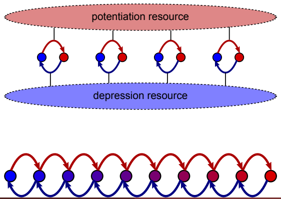
Serial synapse



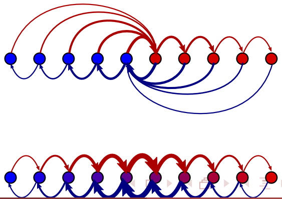
The success of the serial model relies on two features:

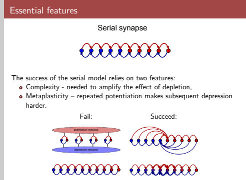
- Complexity - needed to amplify the effect of depletion,
- Metaplasticity – repeated potentiation makes subsequent depression harder.

Fail:



Succeed:





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

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

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