

# Modelling impaired and enhanced learning with enhanced plasticity

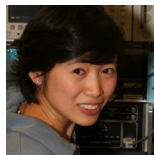
Subhaneil Lahiri, Barbara Nguyen-Vu, Grace Zhao, Aparna Suvrathan, Han-Mi Lee, Surya Ganguli, Carla Shatz and Jennifer Raymond

Stanford University, Applied Physics

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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But often: enhanced plasticity → impaired learning.

[Migaud et al. (1998), Uetani et al. (2000), Hayashi et al. (2004)]

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

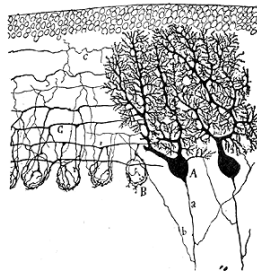
Simple synapses **cannot** explain behaviour. **Complex synapses** are required.  
→ predictions for synaptic physiology.

# Vestibulo-Ocular Reflex training

## VOR Increase Training

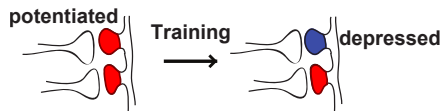


## VOR Decrease Training



[Cajal]

VOR increase: LTD in PF-Pk synapses.

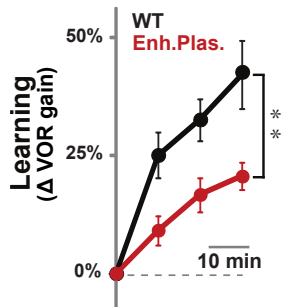


[du Lac et al. (1995), Boyden et al. (2004)]

# Enhanced plasticity impairs learning

**Expectation:** enhanced LTD → enhanced learning.

**VOR Increase  
Training**



**Experiment:** enhanced plasticity → impaired learning.

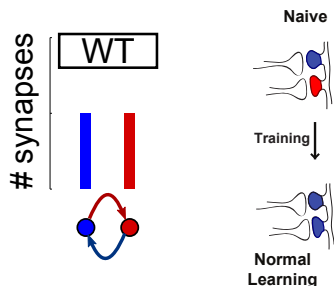
Knockout of MHC-I D<sup>b</sup>K<sup>b</sup> molecules in PF-Pk synapses

→ lower threshold for LTD

[McConnell et al. (2009)]

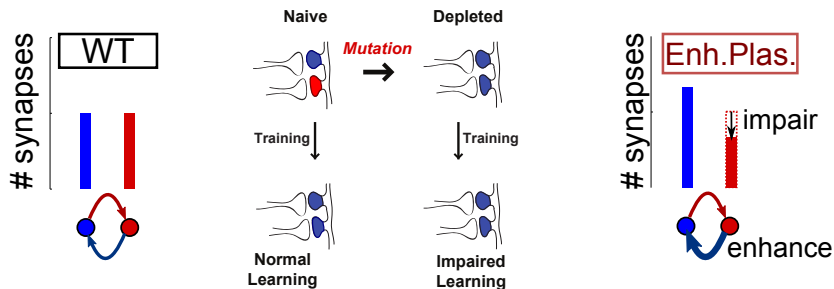
# Depletion hypothesis

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



# Depletion hypothesis

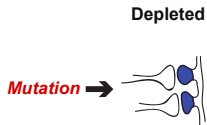
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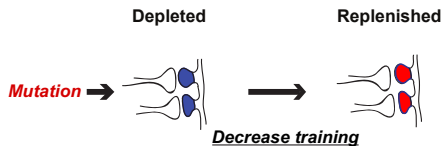
Question 1: depletion effect competes with enhanced intrinsic plasticity.  
Which effect is stronger?



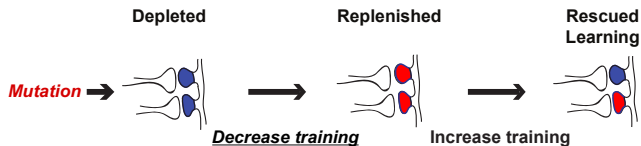
# Replenishment by reverse-training



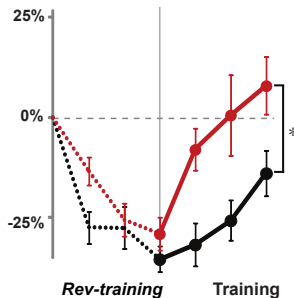
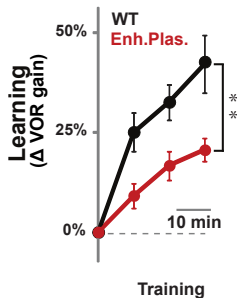
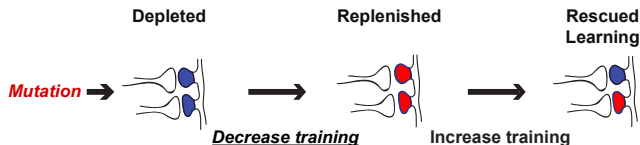
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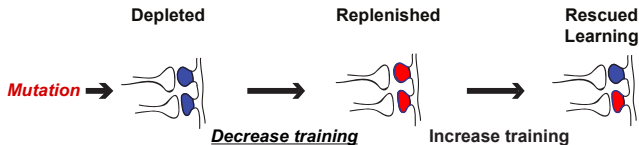
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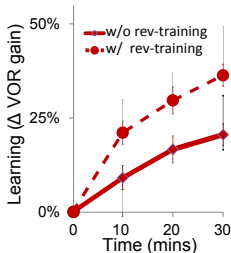
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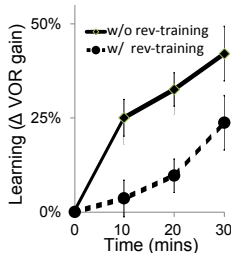
# Replenishment by reverse-training



Enh. Plast.

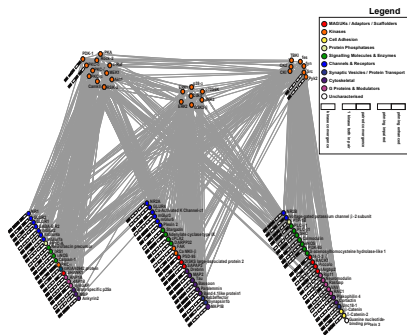


WT

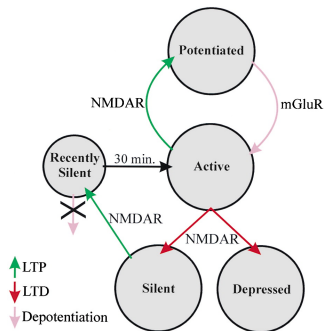


**Question 2:** How can *too much* replenishment impair learning?

# Synapses are complex



[Coba et al. (2009)]

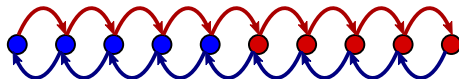


[Montgomery and Madison (2002)]

# Models of complex synaptic dynamics

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

Potential



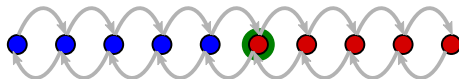
Depression

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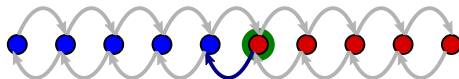
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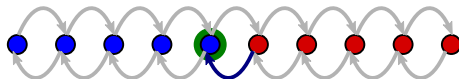
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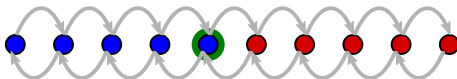
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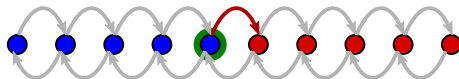
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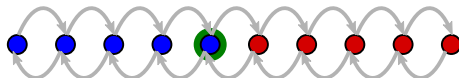
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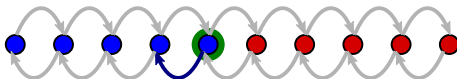
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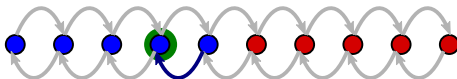
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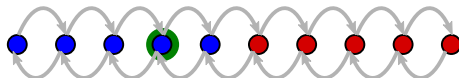
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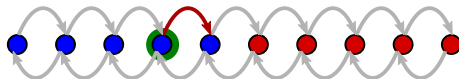
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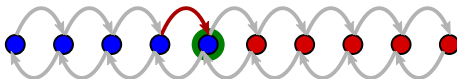
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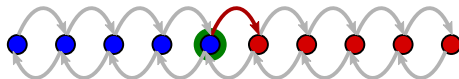
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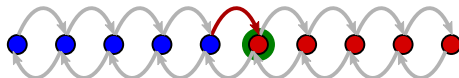
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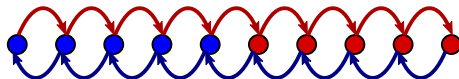
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Potential



Depression

Mutation: trans. probs.

Training: plast. event rates

Learning: synaptic weight

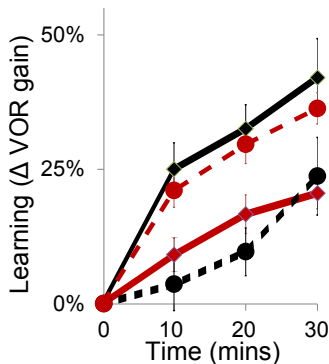
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# Simple synapses cannot explain the data

Multistate synapse

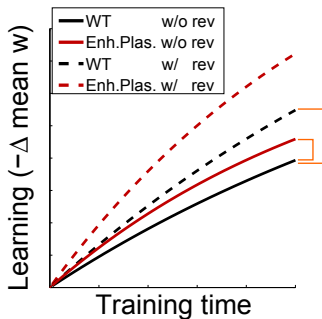
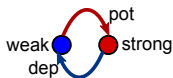


VOR Increase Training

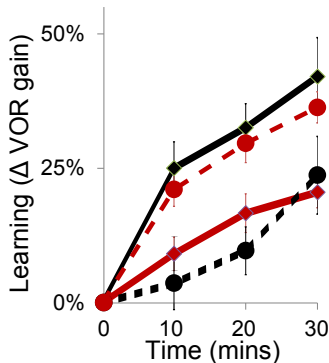


# Simple synapses cannot explain the data

## Binary synapse

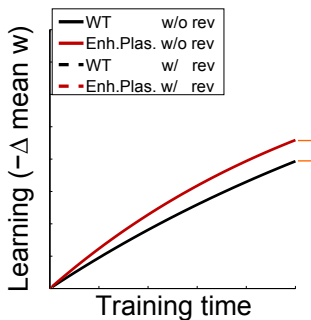


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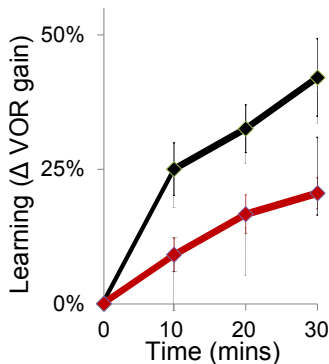


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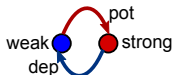
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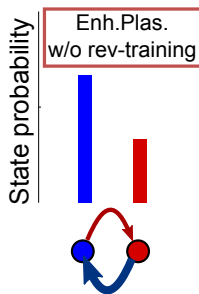


# Simple synapses cannot explain the data

## Binary synapse



## Initial distribution



depletion effect

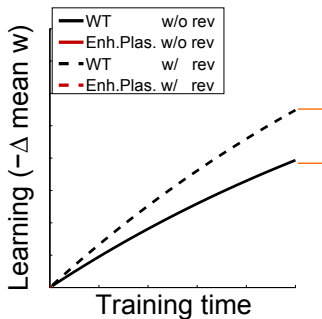
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enhanced plasticity

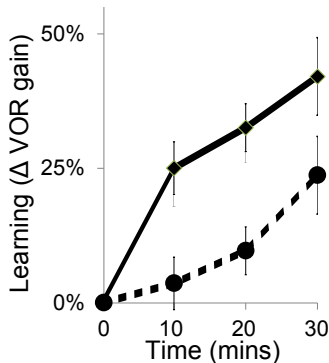
⇒ enhanced learning

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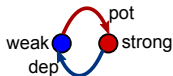


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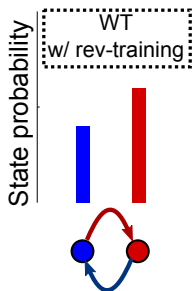


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## Initial distribution



reverse training



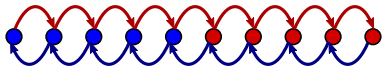
replenishment



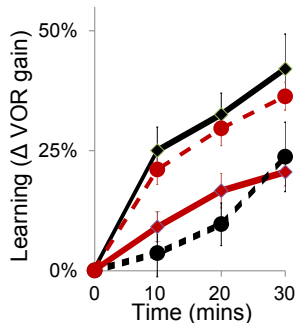
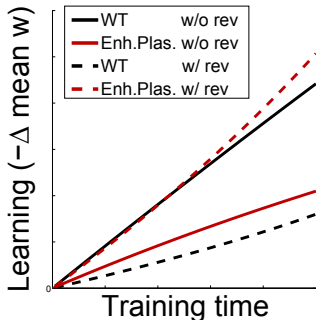
enhanced learning

# Complex metaplastic synapses can explain the data

## Serial synapse



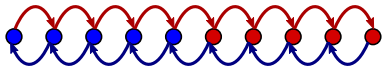
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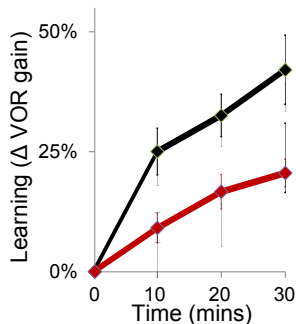
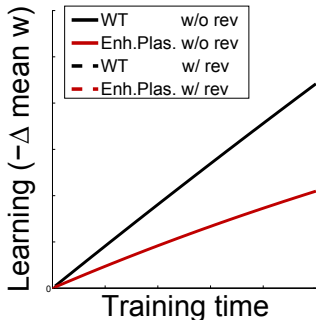
[Leibold and Kempter (2008), Ben-Dayan Rubin and Fusi (2007)]

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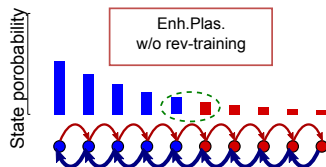
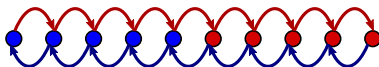
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# Complex metaplastic synapses can explain the data

## Serial synapse



amplified depletion

>

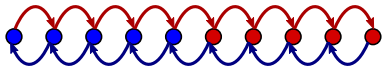
enhanced plasticity

⇒ impaired learning

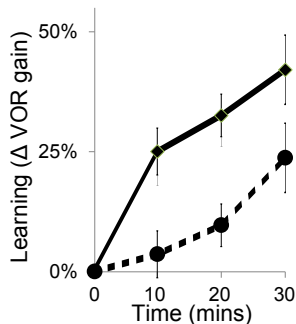
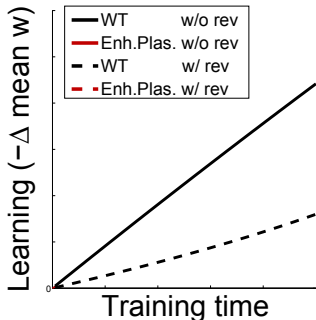
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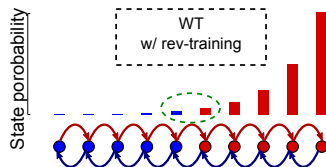
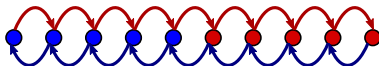
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# Complex metaplastic synapses can explain the data

## Serial synapse



reverse training  
+  
“stubborn” metaplasticity  
⇒ impaired learning

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



# Conclusions

- Diverse behavioural patterns:  
Enhanced plasticity → enhance/impair learning (prior experience).  
Reverse-training → 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

# Acknowledgements

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Aparna Suvrathan

**Carla Shatz**

Han-Mi Lee

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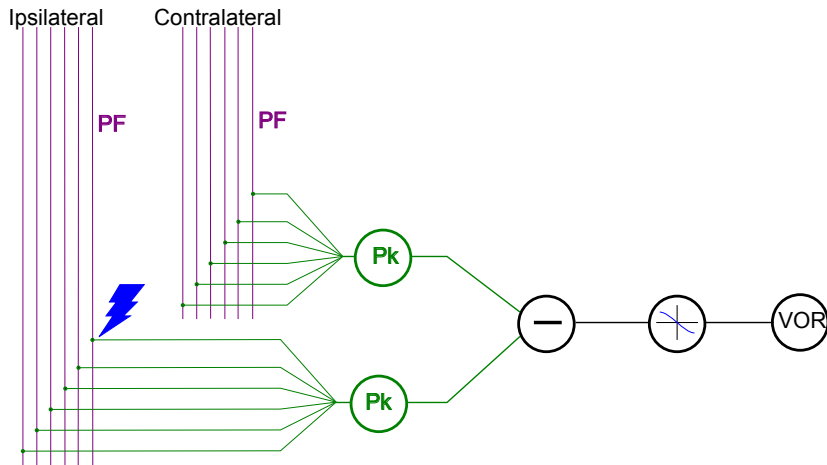
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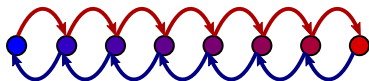
# Model of circuit



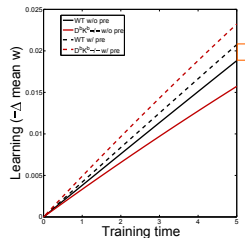
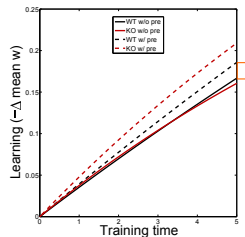
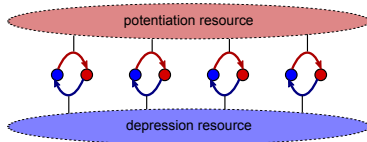


# Other models that fail

## Multistate synapse



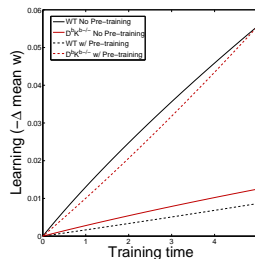
## Pooled resource model



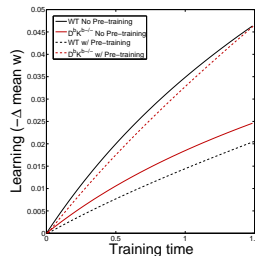
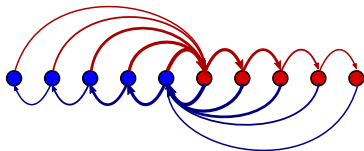
[Amit and Fusi (1994)]

# Other models that work

Non-uniform multistate model

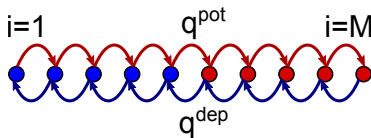


Cascade model



[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.