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

Stanford University, Applied Physics

July 24, 2013

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1. Acknowledge Barbara and Grace

Introduction

Learning requires synaptic plasticity.
Expect enhanced plasticity $\to$ 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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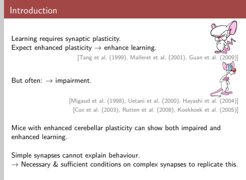
Mice with enhanced cerebellar plasticity can show both impaired and enhanced learning.

Simple synapses cannot explain behaviour.
→ Necessary & sufficient conditions on complex synapses to replicate this.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Outline

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

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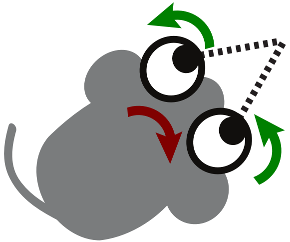
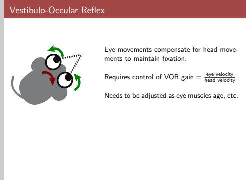
Vestibulo-Occular Reflex



Eye movements compensate for head movements to maintain fixation.

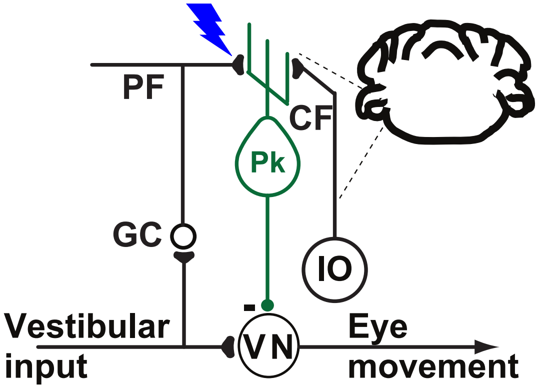
Requires control of VOR gain $= \frac{\text{eye velocity}}{\text{head velocity}}$.

Needs to be adjusted as eye muscles age, etc.



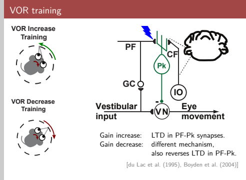
VOR Increase Training

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

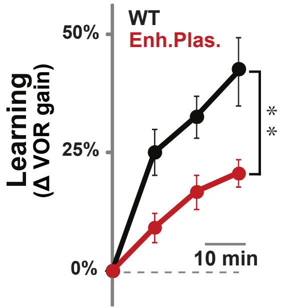
[McConnell et al. (2009)]

→ lower threshold for LTD → enhanced plasticity

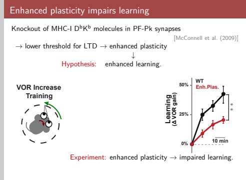
↓

Hypothesis: enhanced learning.

VOR Increase Training



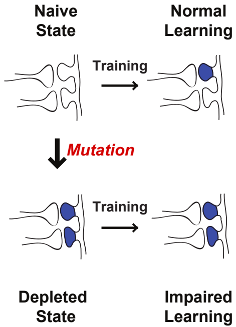
Experiment: enhanced plasticity → impaired learning.

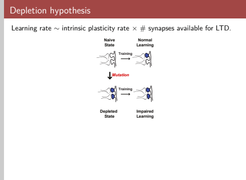


1. Major Histocompatibility Complex - involved in synaptic plasticity (Carla Shatz lab)
2. Easier LTD → expect better learning
3. Impairment of learning
4. Looking at change of VOR gain during gain-up training

Depletion hypothesis

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





1. Our model: baseline activity $\rightarrow$ saturation $\rightarrow$ less depression possible
2. Saturation has to compete with enhanced plsaticity. Which will win?

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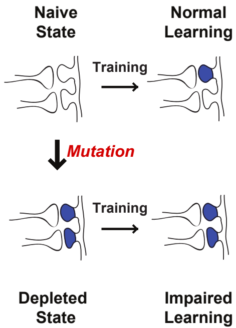
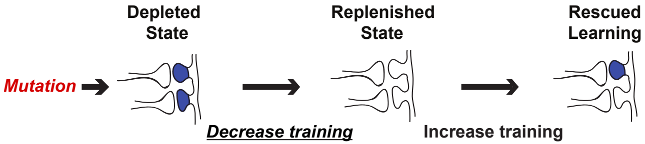
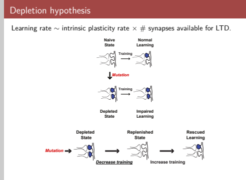
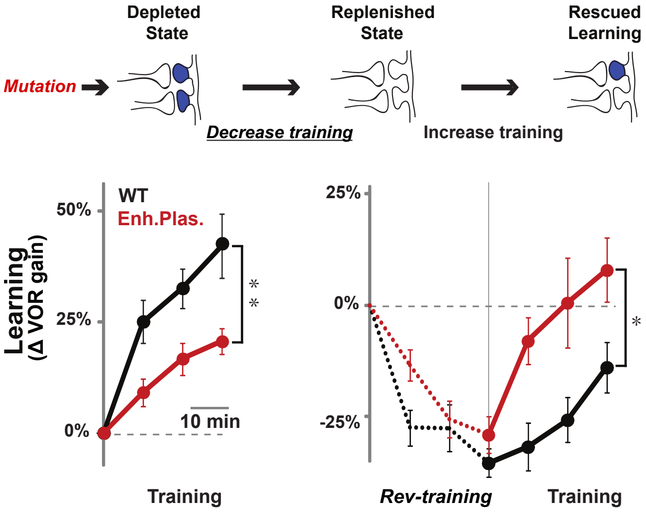






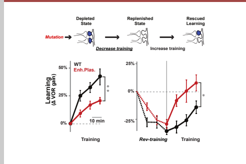
1. Our model: baseline activity $\to$ saturation $\to$ less depression possible
2. Saturation has to compete with enhanced plsaticity. Which will win?
3. Prediction: replenish with rev-training $\to$ rescue



2013-07-24

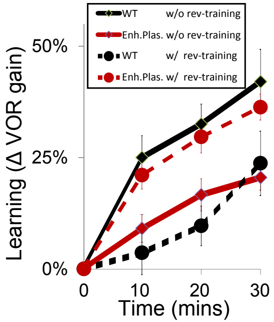
Impaired learning with enhanced plasticity

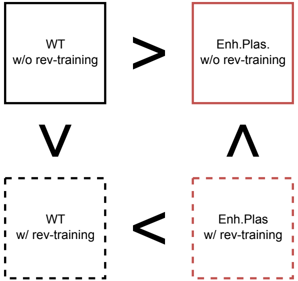
└─Replenishment by reverse-training

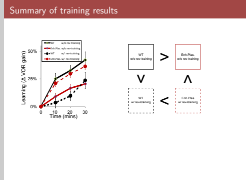


1. precede gain inc training w/ gain dec rev-training: reverses LTD
2. but behaviour from elsewhere → not modelled
3. Focus on gain inc part

Summary of training results







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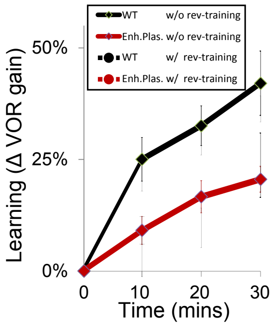
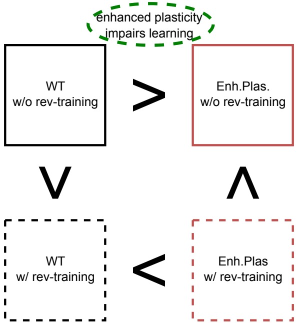
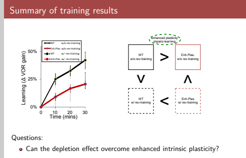




Questions:

- Can the depletion effect overcome enhanced intrinsic plasticity?



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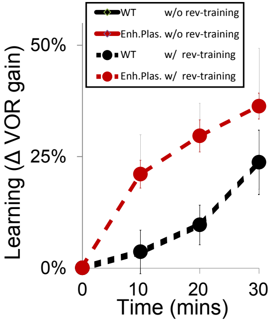

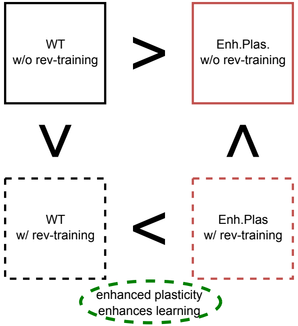

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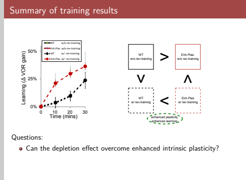

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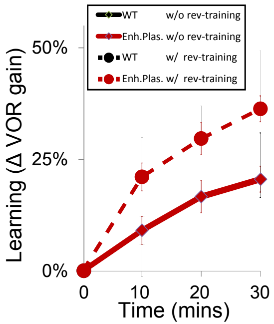

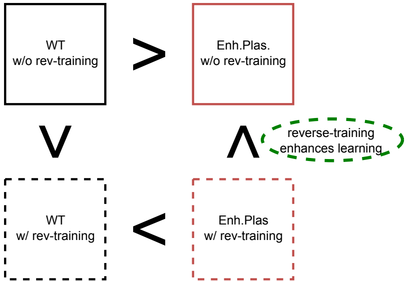

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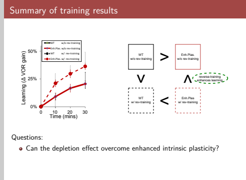

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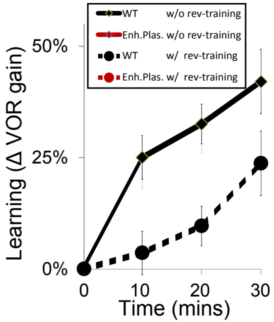

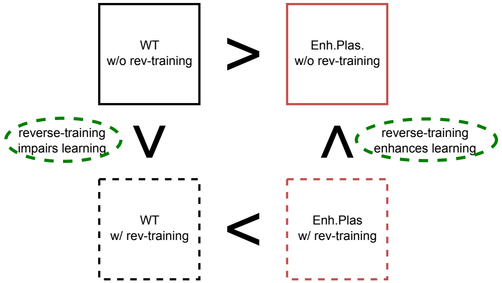

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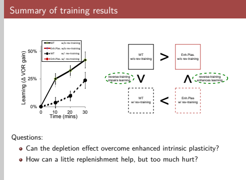

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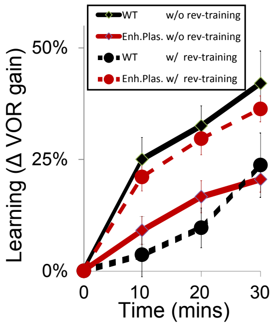

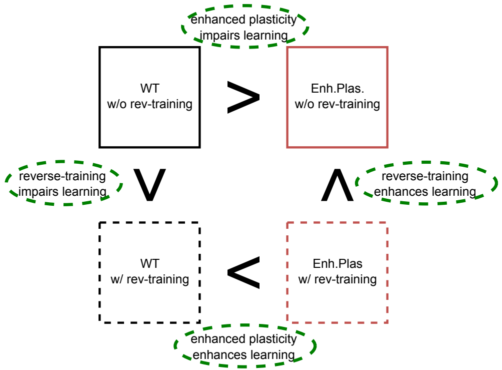

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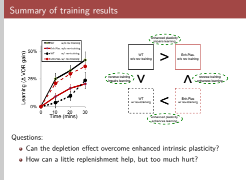

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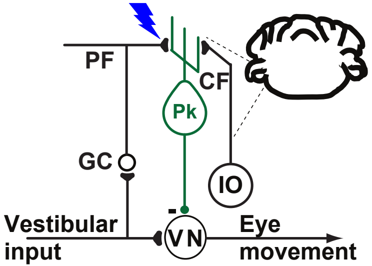
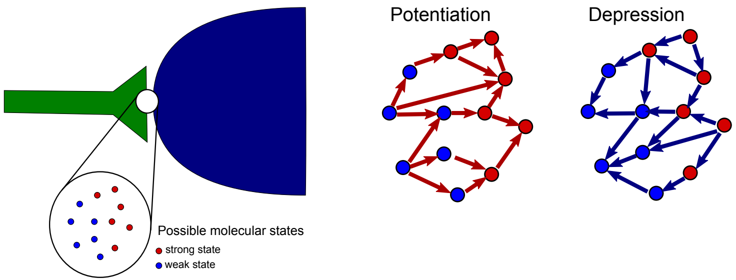
9. Summarize: Enh.Plas. can impair/enhance. Rev can impair/enhance
10. Diagonal comparisons: parameter fitting. Depend on size of mut vs. rev



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

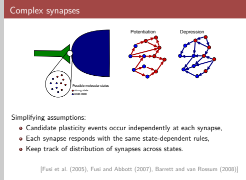
Complex synapses



Simplifying assumptions:

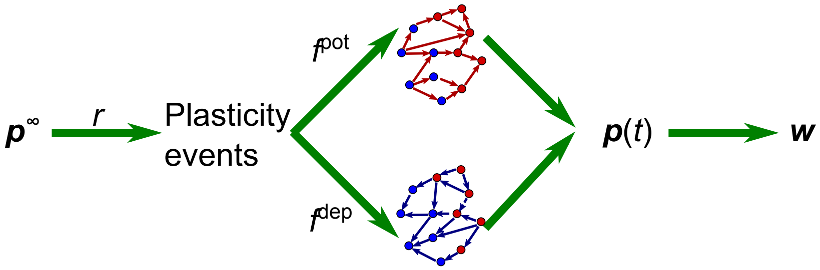
- Candidate plasticity events occur independently at each synapse,
- Each synapse responds with the same state-dependent rules,
- Keep track of distribution of synapses across states.

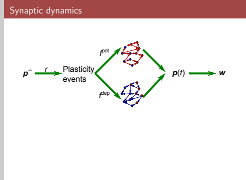
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]



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. allows us to concentrate on synapse, not neuron/network
6. 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.
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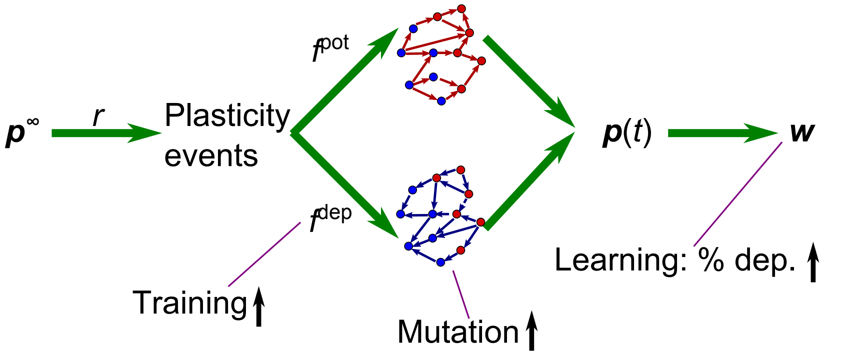
4. fraction pot/dep
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.

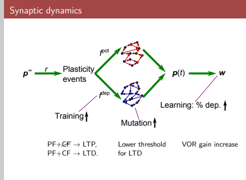
Synaptic dynamics



PF+$\cancel{\text{CF}}$ → LTP,
PF+CF → LTD.

Lower threshold for LTD

VOR gain increase



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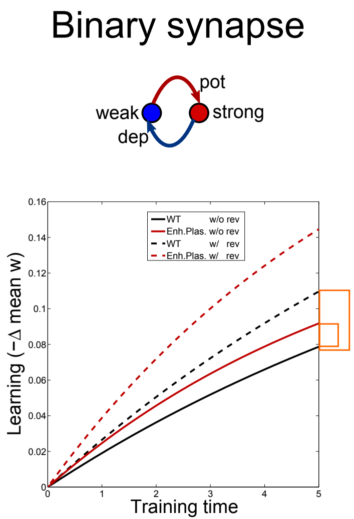
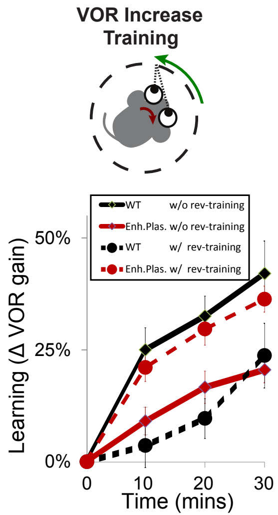
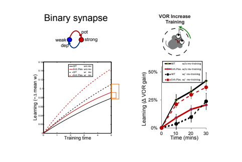
5. probs changed by Markov matrices, prob $i \to j$
6. Readout: synaptic weight vec when in each state.
7. Mutation: lower threshold → increase transition probs
8. Training: Changes statistics of LTP/LTD. Only parameters we have. Don't care about r.
9. Learning: Only output we have. Don't keep track of synaptic identity.

Simple synapses cannot explain the data



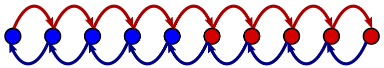


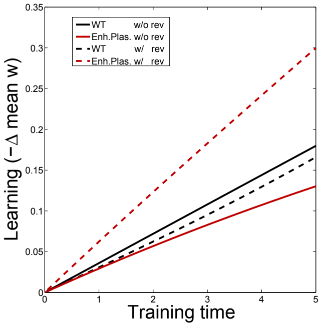


1. Binary fails – mathematical proof for any params
2. Enh.Plas: faster depression wins over bias
3. pre: reduces/reverses bias. always helps.

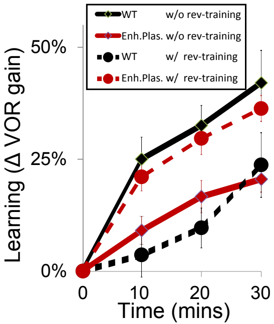
Complex synapses can explain the data

Serial synapse

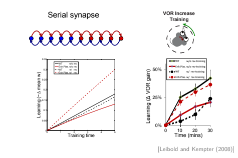




VOR Increase Training

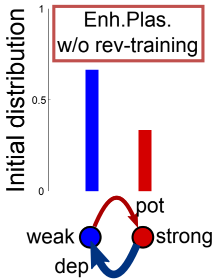


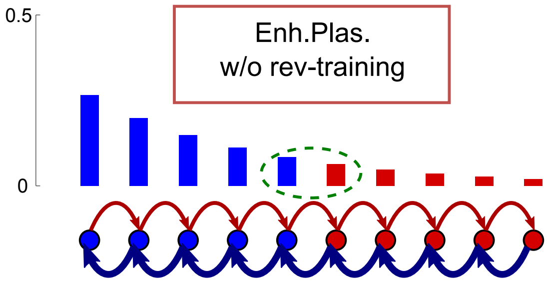
[Leibold and Kempter (2008)]



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

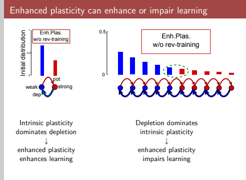
Enhanced plasticity can enhance or impair learning





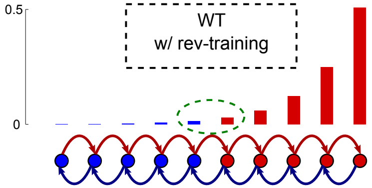
Intrinsic plasticity dominates depletion
↓
enhanced plasticity enhances learning

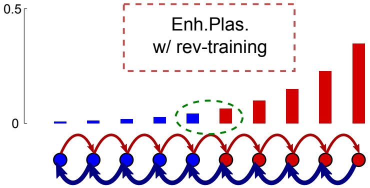
Depletion dominates intrinsic plasticity
↓
enhanced plasticity impairs learning



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

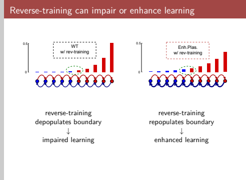
Reverse-training can impair or enhance learning





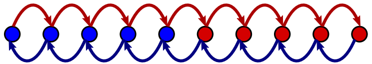
reverse-training
depopulates boundary
↓
impaired learning

reverse-training
repopulates boundary
↓
enhanced learning



1. rev-training: little repopulates boundary
2. Too much pushes to other side, depopulates boundary
3. this effect is absent in any simple synapse

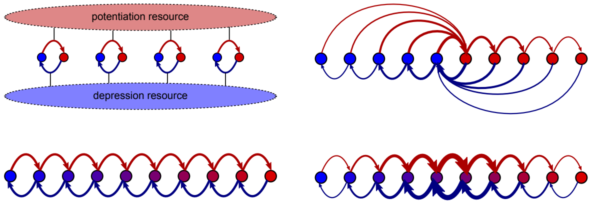
Essential features



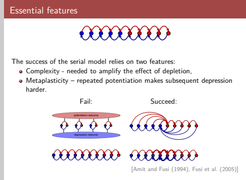
The success of the serial model relies on two features:

- 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)]



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

Conclusions

- 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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Tradeoff: learning vs. remembering

What about memory?

- Simple synapses have poor memory storage capacity.
  Synaptic complexity is needed for rescue.
  [Amit and Fusi (1992), Amit and Fusi (1994)]

- 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)]

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

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

The frontiers of complex synaptic memory

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References I

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"Genetic enhancement of learning and memory in mice".
Nature, 401(6748):63–69, (Sep, 1999) .
3 4 5

Gaël Malleret, Ursula Haditsch, David Genoux, Matthew W. Jones, Tim V.P. Bliss, Amanda M. Vanhoose, Carl Weitlauf, Eric R. Kandel, Danny G. Winder, and Isabelle M. Mansuy.
"Inducible and Reversible Enhancement of Learning, Memory, and Long-Term Potentiation by Genetic Inhibition of Calcineurin".
Cell, 104(5):675 – 686, (2001) .
3 4 5

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└References

References I

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References II

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"HDAC2 negatively regulates memory formation and synaptic plasticity".
Nature, 459(7243):55–60, (May, 2009) .
3 4 5

M. Migaud, P. Charlesworth, M. Dempster, L. C. Webster, A. M. Watabe, M. Makhinson, Y. He, M. F. Ramsay, R. G. Morris, J. H. Morrison, T. J. O'Dell, and S. G. Grant.
"Enhanced long-term potentiation and impaired learning in mice with mutant postsynaptic density-95 protein".
Nature, 396(6710):433–439, (Dec, 1998) .
3 4 5

References II
J. S. Guan, S. J. Haggarty, E. Giacometti, J. H. Dannenberg, N. Joseph, J. Gao, T. J. Nieland, Y. Zhou, X. Wang, R. Mazitschek, J. E. Bradner, R. A. DePinho, R. Jaenisch, and L. H. Tsai.
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N. Uetani, K. Kato, H. Ogura, K. Mizuno, K. Kawano, K. Mikoshiba, H. Yakura, M. Asano, and Y. Iwakura.
"Impaired learning with enhanced hippocampal long-term potentiation in PTPdelta-deficient mice".
EMBO J., 19(12):2775–2785, (Jun, 2000) .
3 4 5

Mansuo L Hayashi, Se-Young Choi, B.S.Shankaranarayana Rao, Hae-Yoon Jung, Hey-Kyoung Lee, Dawei Zhang, Sumantra Chattarji, Alfredo Kirkwood, and Susumu Tonegawa.
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Neuron, 42(5):773 – 787, (2004) .
3 4 5

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└References

References III

N. Uetani, K. Kato, H. Ogura, K. Mizuno, K. Kawano, K. Mikoshiba, H. Yakura, M. Asano, and Y. Iwakura.
"Impaired learning with enhanced hippocampal long-term potentiation in PTPdelta-deficient mice".
EMBO J., 19(12):2775–2785, (Jun, 2000) .

Mansuo L Hayashi, Se-Young Choi, B.S.Shankaranarayana Rao, Hae-Yoon Jung, Hey-Kyoung Lee, Dawei Zhang, Sumantra Chattarji, Alfredo Kirkwood, and Susumu Tonegawa.
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References IV

Patrick R Cox, Velia Fowler, Bisong Xu, J.David Sweatt, Richard Paylor, and Huda Y Zoghbi.
"Mice lacking tropomodulin-2 show enhanced long-term potentiation, hyperactivity, and deficits in learning and memory".
Molecular and Cellular Neuroscience, 23(1):1 – 12, (2003) .
3 4 5

Kris Rutten, Dinah L. Misner, Melissa Works, Arjan Blokland, Thomas J. Novak, Luca Santarelli, and Tanya L. Wallace.
"Enhanced long-term potentiation and impaired learning in phosphodiesterase 4D-knockout (PDE4D-/-) mice".
European Journal of Neuroscience, 28(3):625–632, (2008) .
3 4 5

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"Mice lacking tropomodulin-2 show enhanced long-term potentiation, hyperactivity, and deficits in learning and memory".
Molecular and Cellular Neuroscience, 23(1):1 – 12, (2003) .

Kris Rutten, Dinah L. Misner, Melissa Works, Arjan Blokland, Thomas J. Novak, Luca Santarelli, and Tanya L. Wallace.
"Enhanced long-term potentiation and impaired learning in phosphodiesterase 4D-knockout (PDE4D-/-) mice".
European Journal of Neuroscience, 28(3):625–632, (2008) .

References V

S.K.E. Koekkoek, K. Yamaguchi, B.A. Milojkovic, B.R. Dortland, T.J.H. Ruigrok, R. Maex, W. De Graaf, A.E. Smit, F. VanderWerf, C.E. Bakker, R. Willemsen, T. Ikeda, S. Kakizawa, K. Onodera, D.L. Nelson, E. Mientjes, M. Joosten, E. De Schutter, B.A. Oostra, M. Ito, and C.I. De Zeeuw.

"Deletion of *FMR1* in Purkinje Cells Enhances Parallel Fiber LTD, Enlarges Spines, and Attenuates Cerebellar Eyelid Conditioning in Fragile X Syndrome".

Neuron, 47(3):339 – 352, (2005) .

3 4 5

S du Lac, J L Raymond, T J Sejnowski, and S G Lisberger.

"Learning and Memory in the Vestibulo-Ocular Reflex".

Annual Review of Neuroscience, 18(1):409–441, (1995) .

8

References V

S.K.E. Koekkoek, K. Yamaguchi, B.A. Milojkovic, B.R. Dortland, T.J.H. Ruigrok, R. Maex, W. De Graaf, A.E. Smit, F. VanderWerf, C.E. Bakker, R. Willemsen, T. Ikeda, S. Kakizawa, K. Onodera, D.L. Nelson, E. Mientjes, M. Joosten, E. De Schutter, B.A. Oostra, M. Ito, and C.I. De Zeeuw.

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"CEREBELLUM-DEPENDENT LEARNING: The Role of Multiple Plasticity Mechanisms".
Annual Review of Neuroscience, 27(1):581–609, (2004) .
8

Michael J. McConnell, Yanhua H. Huang, Akash Datwani, and Carla J. Shatz.
"H2-Kb and H2-Db regulate cerebellar long-term depression and limit motor learning".
Proc. Natl. Acad. Sci. U.S.A., 106(16):6784–6789, (2009) .
9

References VI
Edward S. Boyden, Akira Katoh, and Jennifer L. Raymond.
"CEREBELLUM-DEPENDENT LEARNING: The Role of Multiple Plasticity Mechanisms".
Annual Review of Neuroscience, 27(1):581–609, (2004) .
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Proc. Natl. Acad. Sci. U.S.A., 106(16):6784–6789, (2009) .

References VII

S. Fusi, P. J. Drew, and L. F. Abbott.
"Cascade models of synaptically stored memories".
Neuron, 45(4):599–611, (Feb, 2005) .
20 27

S. Fusi and L. F. Abbott.
"Limits on the memory storage capacity of bounded synapses".
Nat. Neurosci., 10(4):485–493, (Apr, 2007) .
20

A. B. Barrett and M. C. van Rossum.
"Optimal learning rules for discrete synapses".
PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .
20

References VII

S. Fusi, P. J. Drew, and L. F. Abbott.
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Neuron, 45(4):599–611, (Feb, 2005) .

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A. B. Barrett and M. C. van Rossum.
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PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .

References VIII

Christian Leibold and Richard Kempter.
"Sparseness Constrains the Prolongation of Memory Lifetime via Synaptic Metaplasticity".
Cerebral Cortex, 18(1):67–77, (2008) .
24

D. J. Amit and S. Fusi.
"Learning in neural networks with material synapses".
Neural Computation, 6(5):957–982, (1994) .
27 29

D. J. Amit and S. Fusi.
"Constraints on learning in dynamic synapses".
Network: Computation in Neural Systems, 3(4):443–464, (1992) .
29

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Christian Leibold and Richard Kempter.
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