

# Learning and memory with complex synaptic plasticity

Subhaneil Lahiri and Surya Ganguli

Stanford University, Applied Physics

February 17, 2016

# Introduction

Synaptic plasticity is often modelled as the change of a single number. But, there is a complex dynamical system inside a synapse.

We will study the entire space of a broad class of models of complex synapses to find upper bounds on their performance.

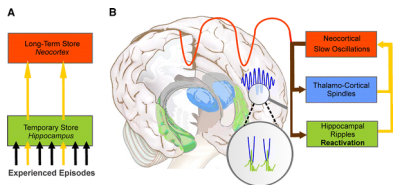
This leads to understanding of what structures are useful for storing memories for different timescales.

# Timescales of memory

Memories stored in different places  
for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]



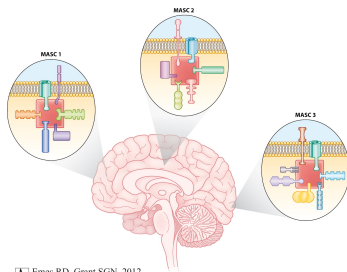
[Born and Wilhelm (2012)]

Also: Cerebellar cortex → nuclei.

[Attwell et al. (2002)]

[Cooke et al. (2004)]

Different synapses have different  
molecular structures.



[Emes RD, Grant SGN, 2012.  
Annu. Rev. Neurosci. 35:111–31]

[Emes and Grant (2012)]

# Storage capacity of synaptic memory

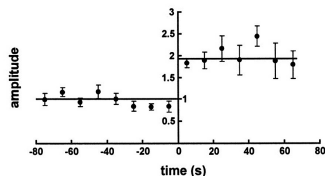
A classical perceptron has a capacity  $\propto N$ , ( $\#$  synapses).

Requires synapses' dynamic range also  $\propto N$ .

With discrete, finite synapses:

$\implies$  new memories overwrite old,

$\implies$  stability-plasticity dilemma.



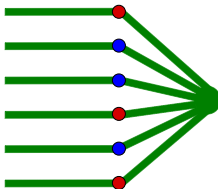
[Petersen et al. (1998), O'Connor et al. (2005)]

When we store new memories rapidly, memory capacity  $\sim \mathcal{O}(\log N)$ .

[Amit and Fusi (1992), Amit and Fusi (1994)]

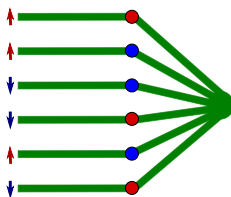
# Recognition memory

Synapses given a sequence of patterns (pot & dep) to store



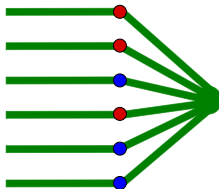
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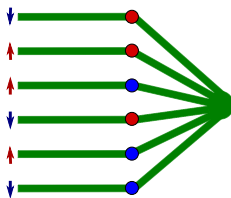
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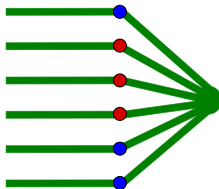
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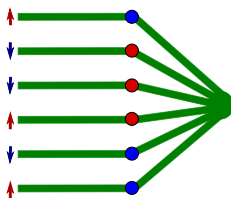
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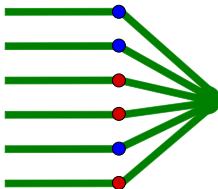
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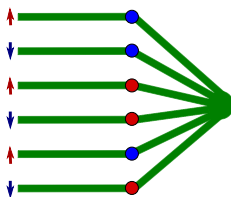
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Synapses given a sequence of patterns (pot & dep) to store



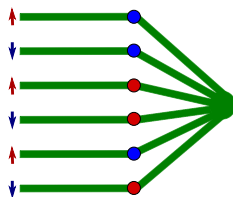
Later: presented with a pattern. Has it been seen before?

Compare  $\vec{s} \cdot \vec{w}(t)$  to threshold.

[Sommer and Dayan (1998)]

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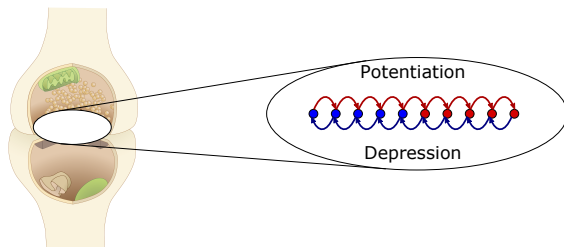
$$\text{SNR}(t) = \frac{\langle \vec{s} \cdot \vec{w}(t) \rangle - \langle \vec{s} \cdot \vec{w}(\infty) \rangle}{\sqrt{\text{Var}(\vec{s} \cdot \vec{w}(\infty))}}, \quad \overline{\text{SNR}}(\tau) = \int d\tau \frac{e^{-t/\tau}}{\tau} \text{SNR}(t).$$

# Models of complex synaptic dynamics



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

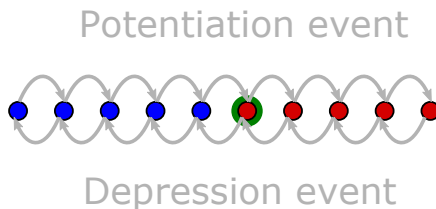


States: #AMPA, #NMDAR, NMDAR subunit composition,  
CaMK II autophosphorylation, activating PKC, p38 MAPK,...

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

# Models of complex synaptic dynamics

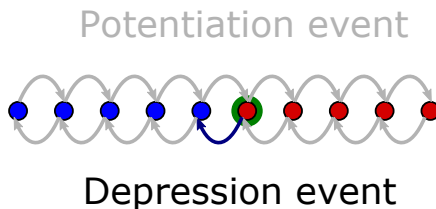
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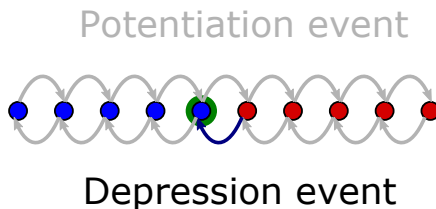
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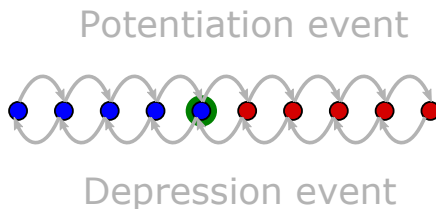
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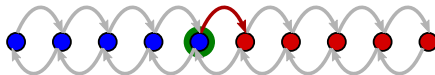
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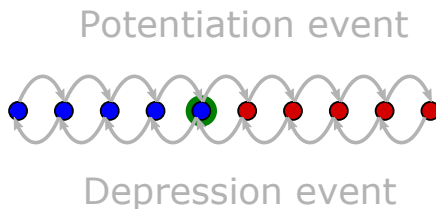
Potential event



Depression event

# Models of complex synaptic dynamics

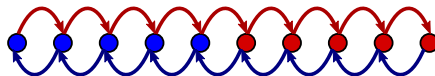
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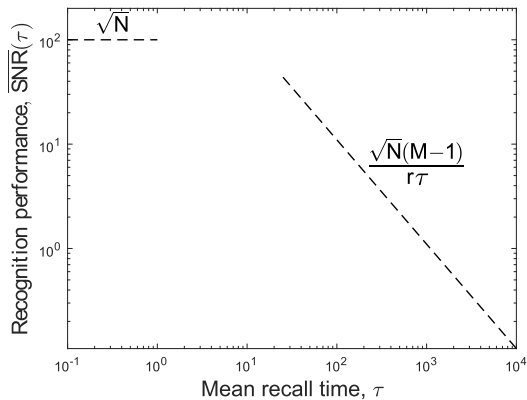
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Potentiation



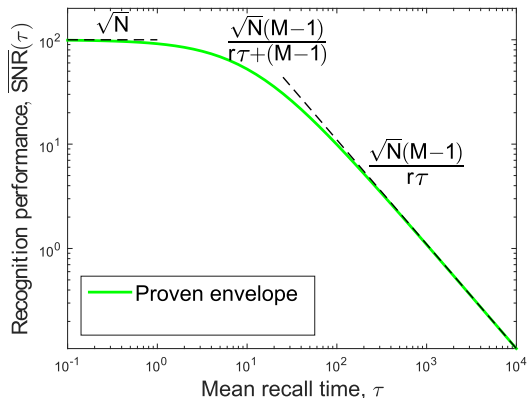
Depression

# Proven envelope: memory frontier



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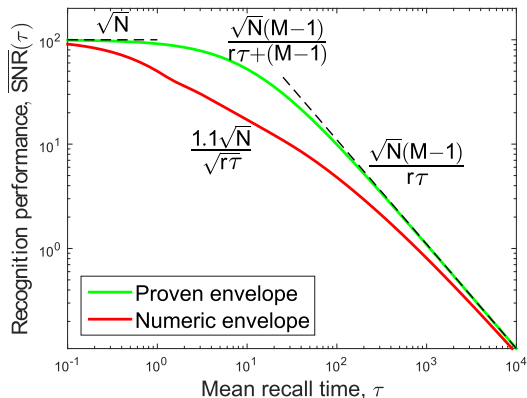
Upper bound on memory curve at *any* timescale.



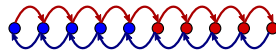


# Proven envelope: memory frontier

Upper bound on memory curve at *any* timescale.



Serial topology:



# Synaptic structures for different timescales of memory

Short timescales



→

Intermediate timescales



→

Long timescales



# Synaptic structures for different timescales of memory

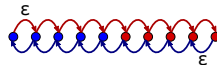
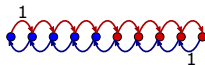
Short timescales



Intermediate timescales



Long timescales



short & wide



long & thin

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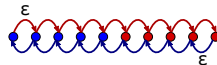
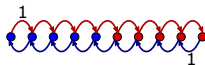
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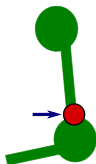
strong transitions



weak transitions

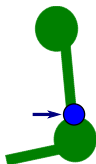
# Proposed Experimental design

Subject a synapse to a sequence of candidate plasticity events.  
Observe the changes in synaptic efficacy.



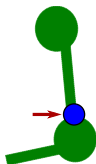
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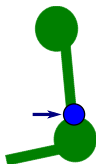
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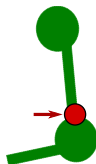
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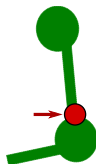
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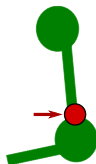
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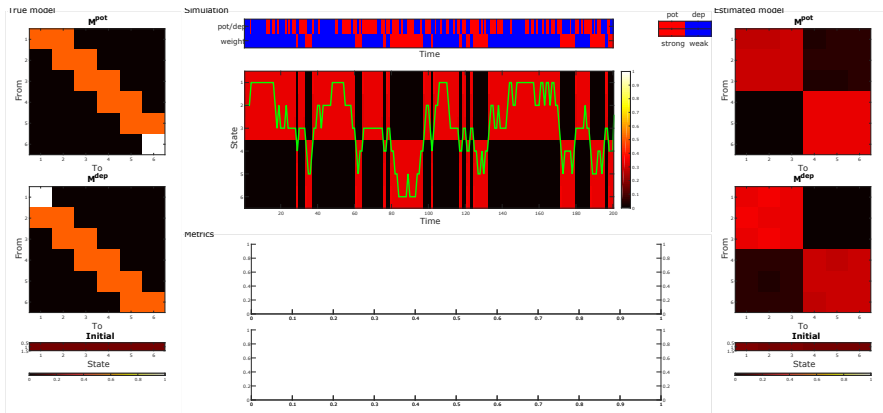
## EM algorithms:

Sequence of hidden states  $\rightarrow$  estimate transition probabilities

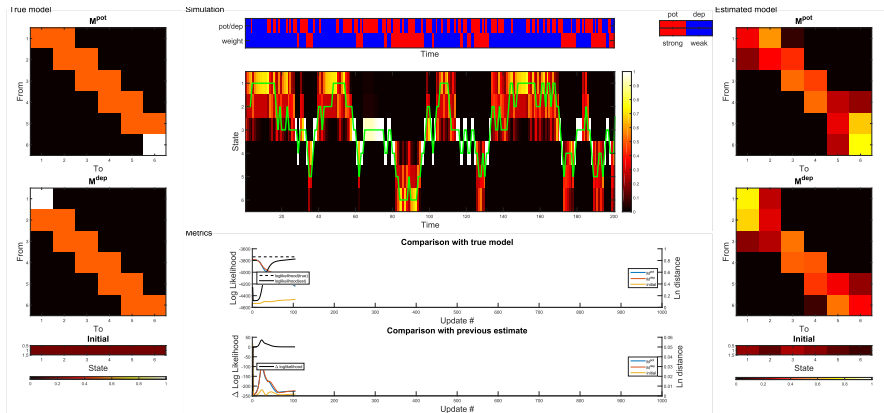
Transition probabilities  $\rightarrow$  estimate sequence of hidden states

[Baum et al. (1970), Rabiner and Juang (1993), Dempster et al. (2007)]

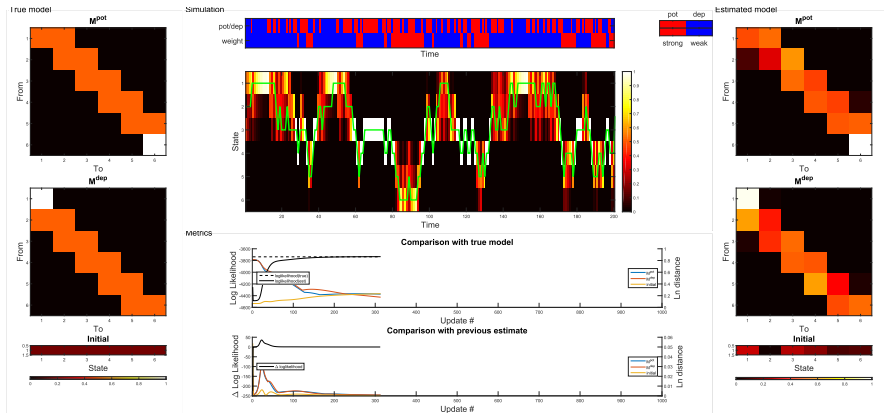
# Simulated experiment



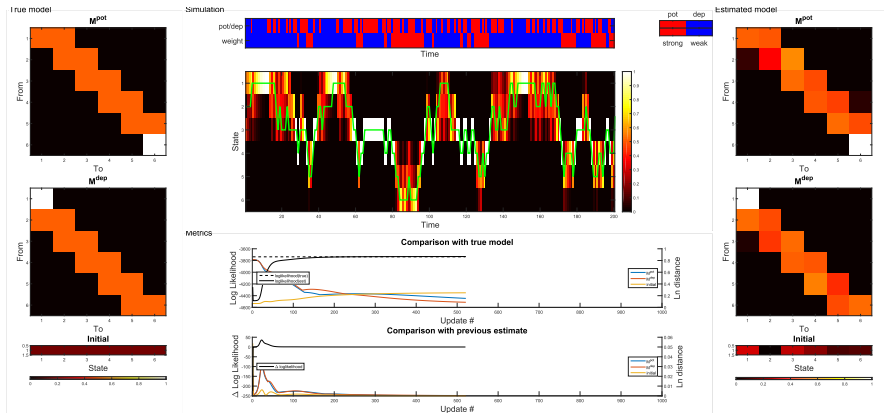
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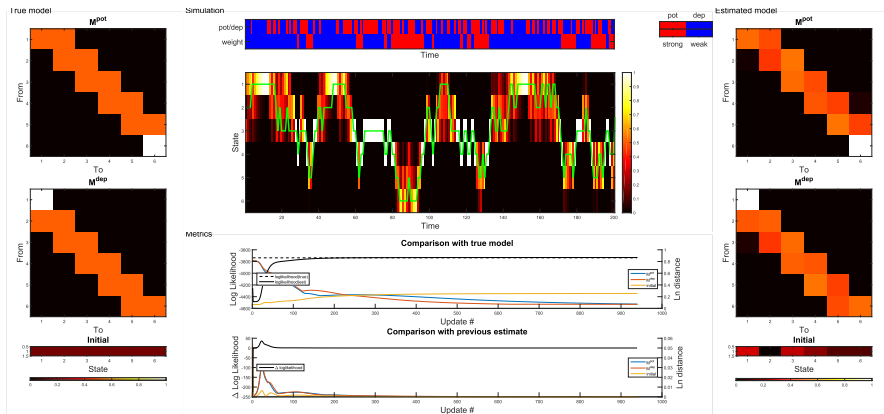
# Simulated experiment



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# Simulated experiment





- We have formulated a general theory of learning and memory with complex synapses.
- We find a memory envelope: a single curve that cannot be exceeded by the memory curve of *any* synaptic model.
- We understood which types of synaptic structure are useful for storing memories for different timescales.

# Acknowledgements

## Thanks to:

- Surya Ganguli
- Stefano Fusi
- Marcus Benna
- David Sussillo
- Jascha Sohl-Dickstein

## Funding:

- Swartz foundation
- Stanford Bio-X
- Genentech

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*Finite markov chains.*

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## Technical detail: ordering states

Let  $\mathbf{T}_{ij}$  = mean first passage time from state  $i$  to state  $j$ . Then:

$$\eta = \sum_j \mathbf{T}_{ij} \mathbf{p}_j^\infty,$$

is independent of the initial state  $i$  (Kemeney's constant).

[Kemeny and Snell (1960)]

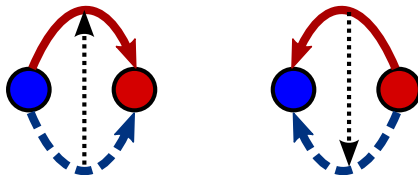
We define:

$$\eta_i^+ = \sum_{j \in \text{strong}} \mathbf{T}_{ij} \mathbf{p}_j^\infty, \quad \eta_i^- = \sum_{j \in \text{weak}} \mathbf{T}_{ij} \mathbf{p}_j^\infty.$$

They can be used to arrange the states in an order (increasing  $\eta^-$  or decreasing  $\eta^+$ ). [back](#)

# Technical detail: upper/lower triangular

With states in order:



Endpoint: potentiation goes right, depression goes left.

[back](#)