Learning and memory with complex synaptic plasticity

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Introduction

Synaptic plasticity is often modelled as the change of a single number (synaptic weight). In reality, there is a complex dynamical system inside a synapse.

Discrete models of synaptic plasticity have terrible memory without synaptic complexity.

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

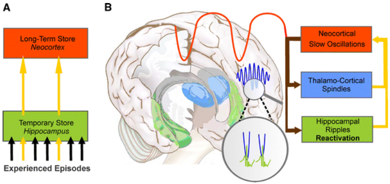
This leads to understanding of what structures are useful for storing memories for different timescales.

Timescales of memory

Memories stored in different places for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]



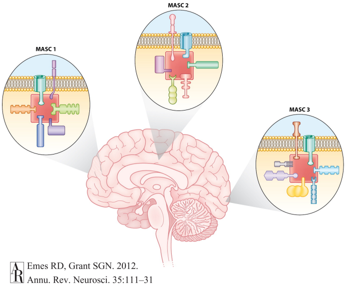
[Born and Wilhelm (2012)]

Also: Cerebellar cortex → nuclei.

[Attwell et al. (2002)]

[Cooke et al. (2004)]

Different synapses have different molecular structures.



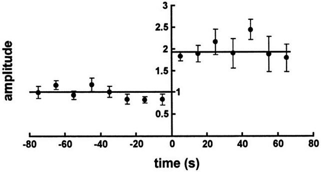
[Emes and Grant (2012)]

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:
$\Longrightarrow$ new memories overwrite old,
$\Longrightarrow$ stability-plasticity dilemma.



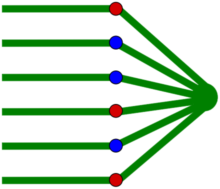
[Petersen et al. (1998), O'Connor et al. (2005)]

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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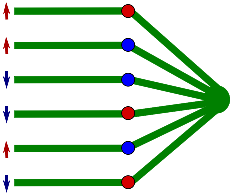

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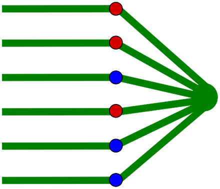

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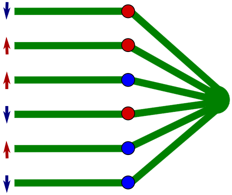

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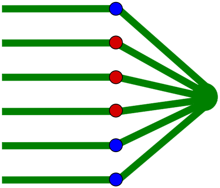

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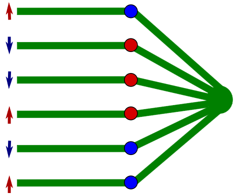

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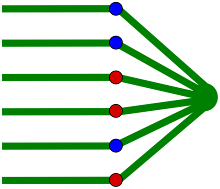

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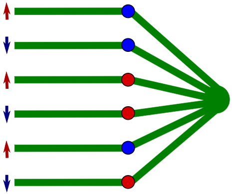

Later: presented with a pattern. Has it been seen before?

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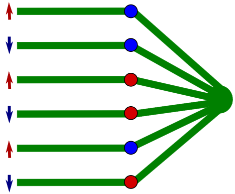

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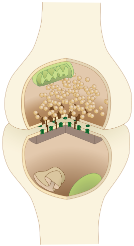
Compare $\vec{s}\cdot\vec{w}(t)$ to threshold. [Sommer and Dayan (1998)]

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

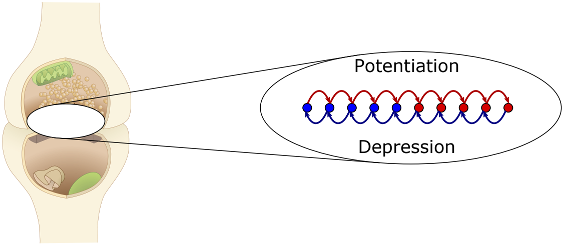
Models of complex synaptic dynamics



Models of complex synaptic dynamics

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

● weak
● strong



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

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

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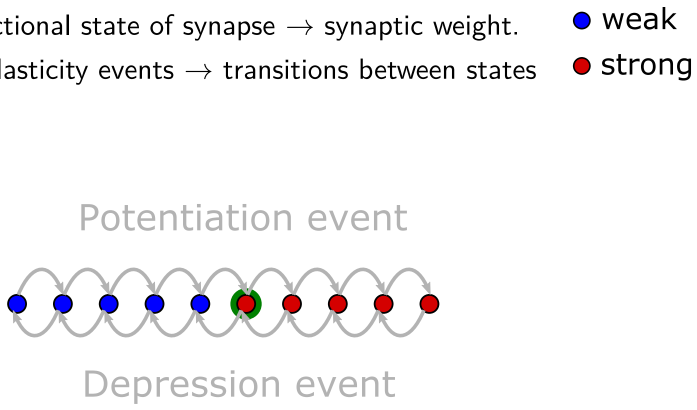

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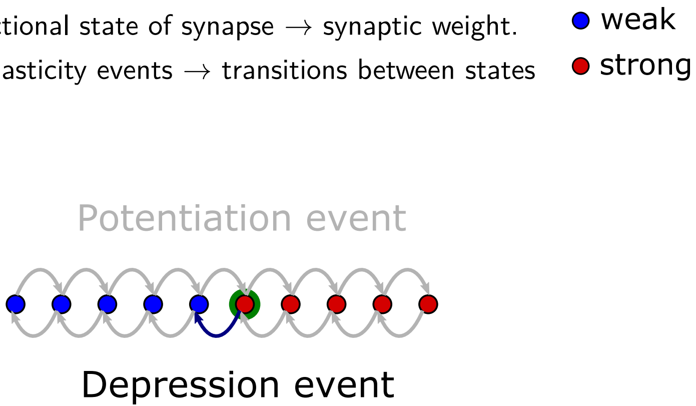

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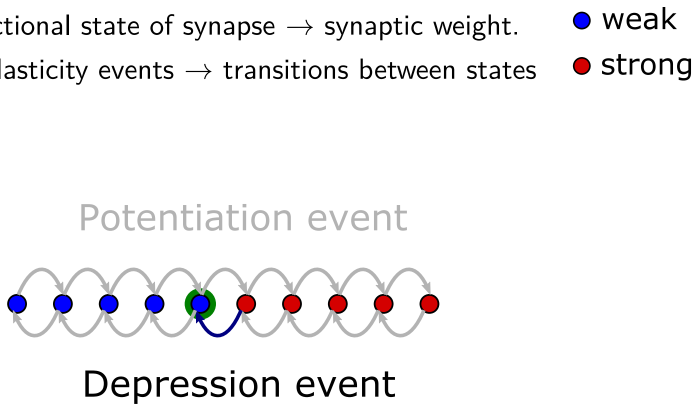

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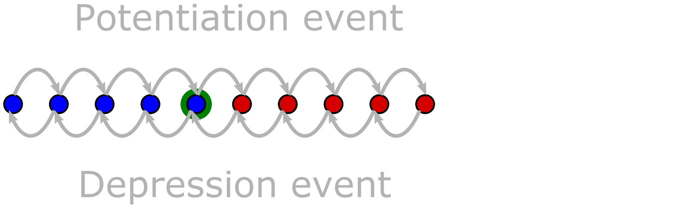

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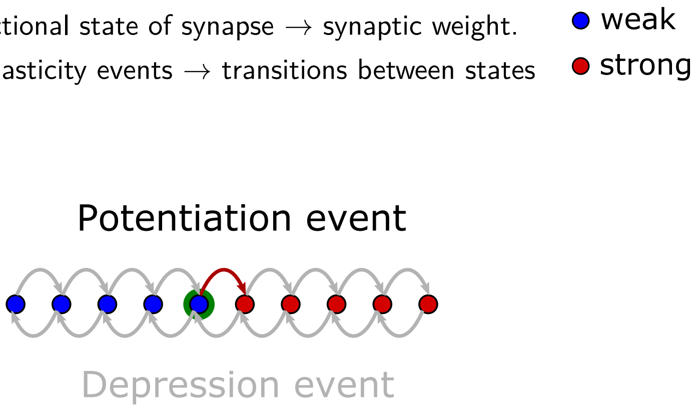

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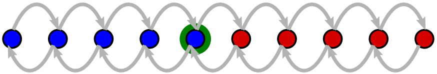

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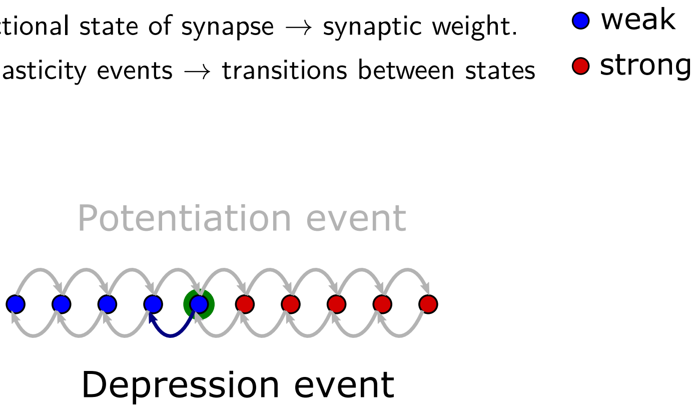

Metaplasticity: change propensity for plasticity
(independent of change in synaptic weight).

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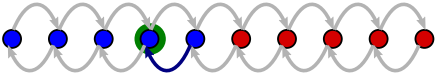
Potentiation event



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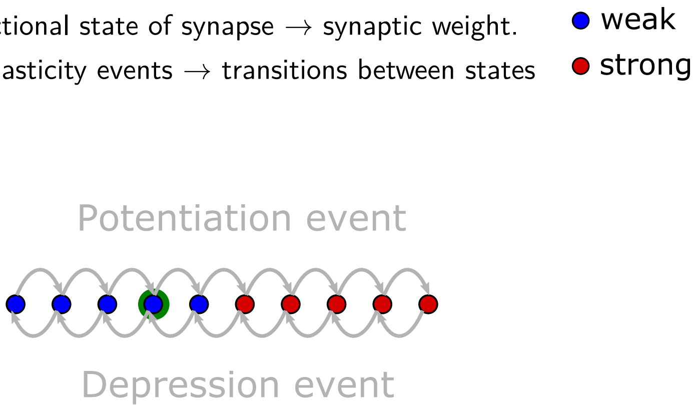

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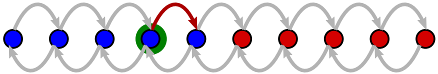

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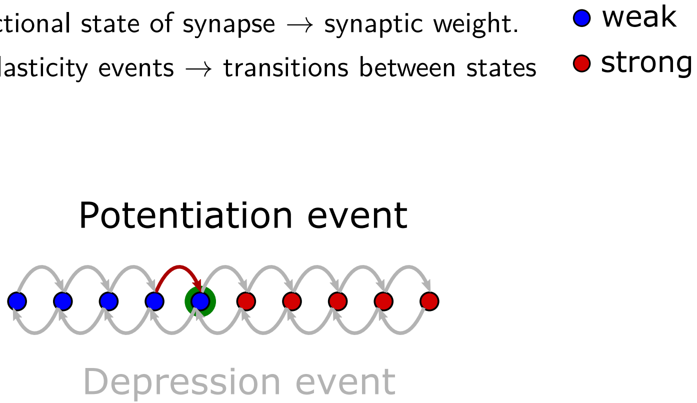

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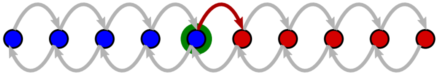

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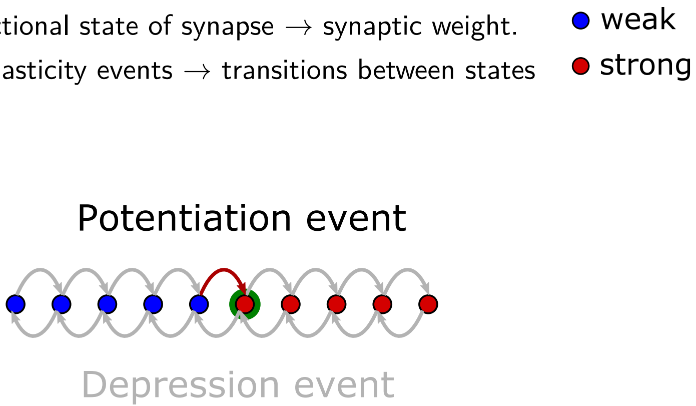

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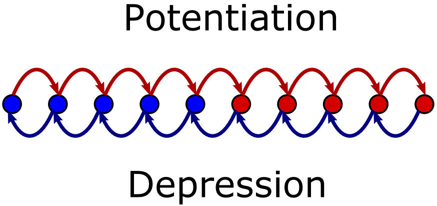

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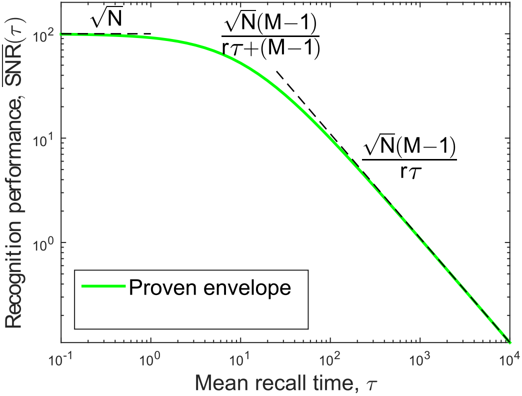
Proven envelope: memory frontier

Upper bound on memory curve at *any* time.



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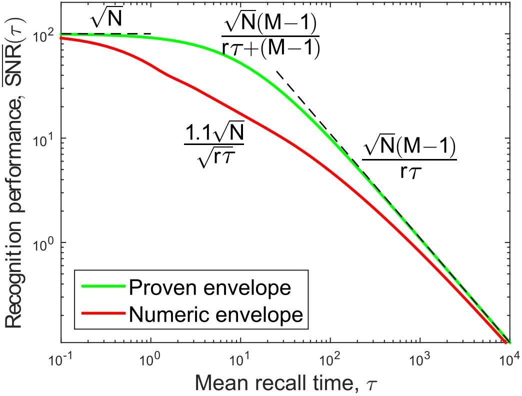
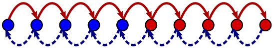
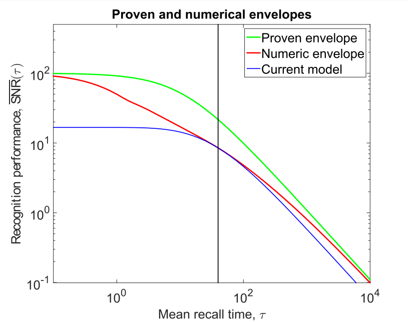
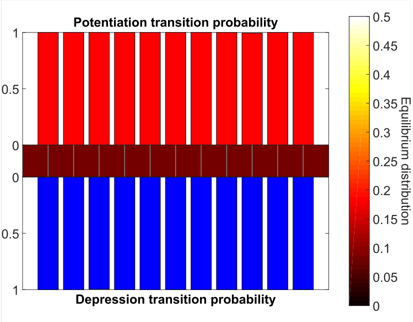


Serial topology:



Models that maximise memory for one timescale





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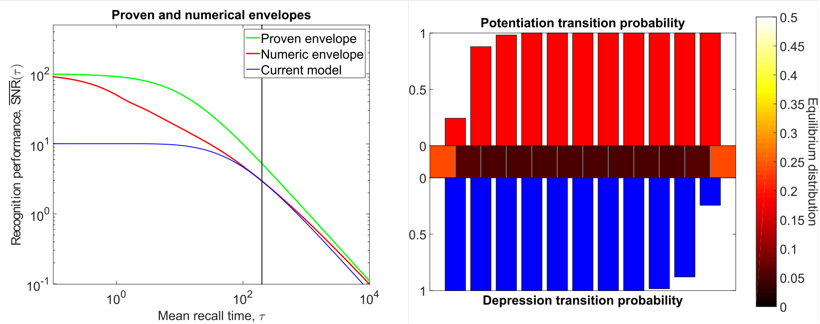

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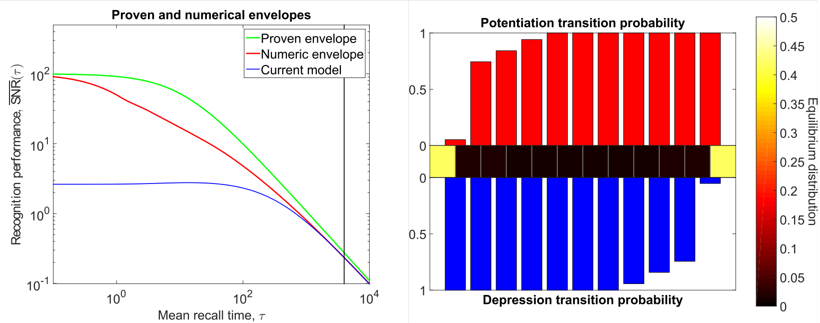

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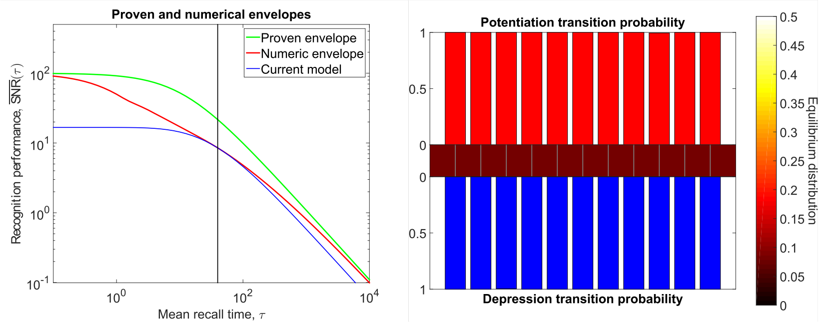

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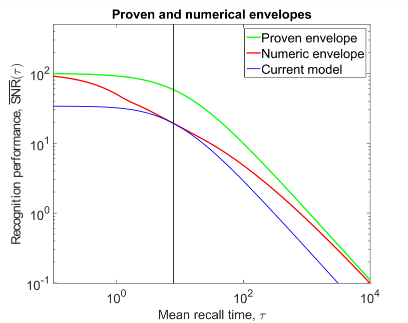

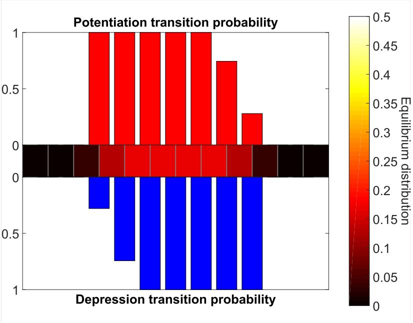

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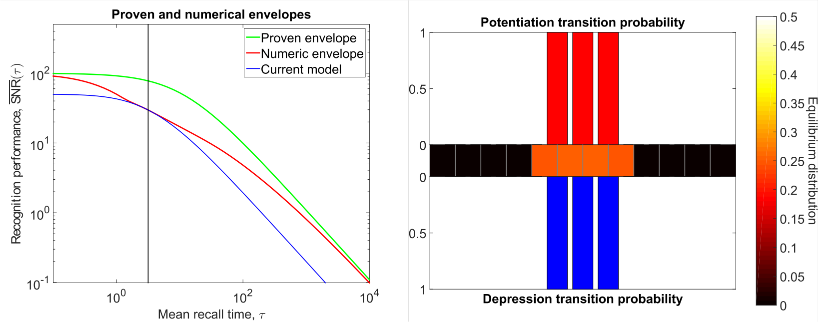

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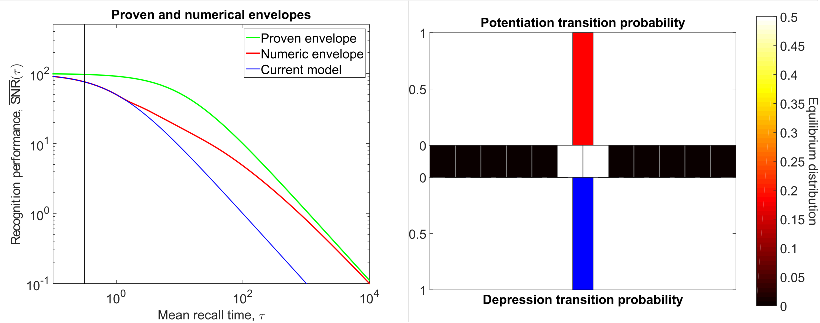


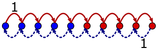
Synaptic structures for different timescales of memory

Real synapses limited by molecular building blocks.
Evolution had larger set of priorities.

What can we conclude?

Short timescales $\longrightarrow$ Intermediate timescales $\longrightarrow$ Long timescales

$\longrightarrow$



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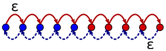

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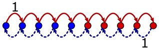

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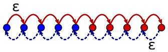

short & wide $\longrightarrow$ long & thin

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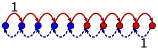
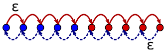
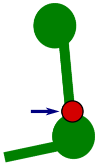
	$\longrightarrow$		$\longrightarrow$	
short & wide	$\longrightarrow$	long & thin		
		strong transitions	$\longrightarrow$	weak transitions

Proposed Experimental design

Subject a synapse to a sequence of candidate plasticity events.

Observe the changes in synaptic efficacy.



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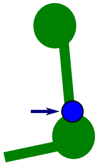

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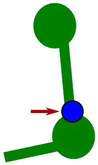

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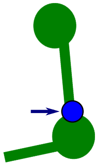

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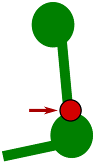

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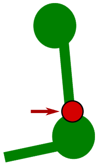

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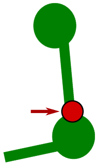
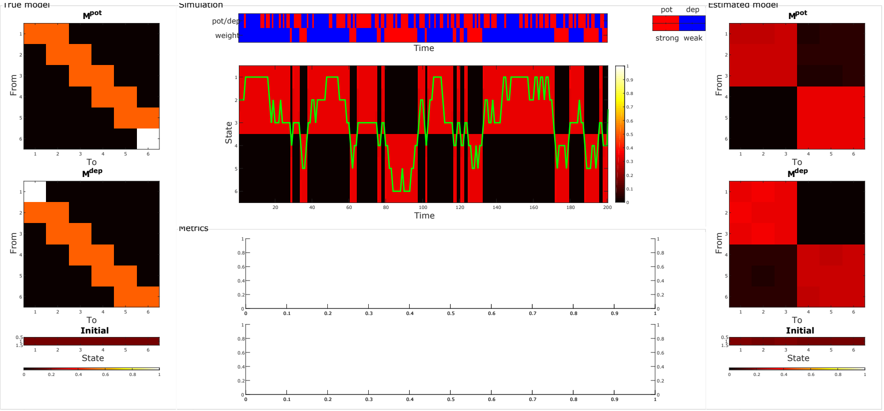


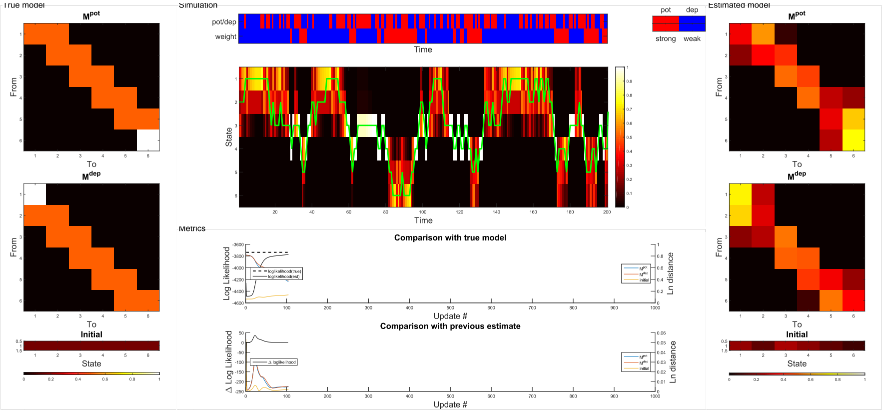
EM algorithms:

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)]

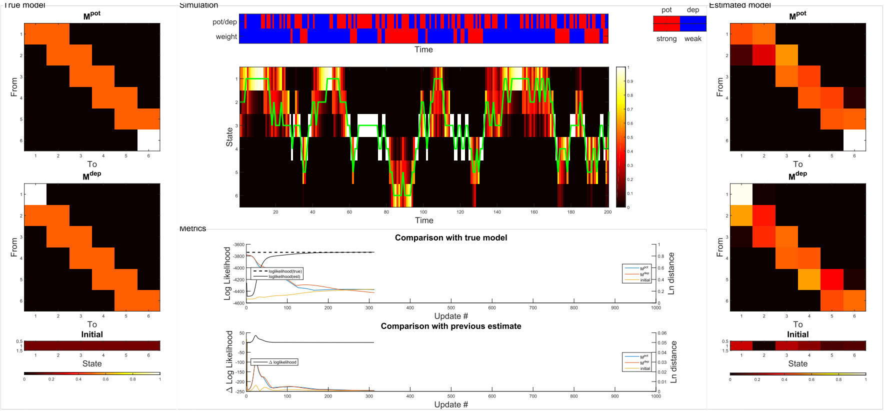
Fitting algorithm





True model
Simulation
Estimated model
Metrics
pot/dep
weight
Time
pot
dep
strong
weak
State
From
To
Initial
Comparison with true model
Comparison with previous estimate
Log Likelihood
Δ Log Likelihood
Ln distance
Update #
loglikelihood(true)
loglikelihood(est)
Δ loglikelihood
initial

Fitting algorithm



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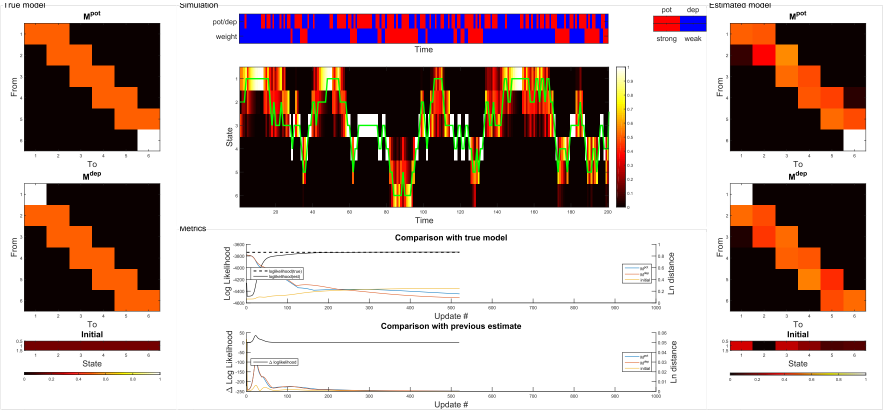
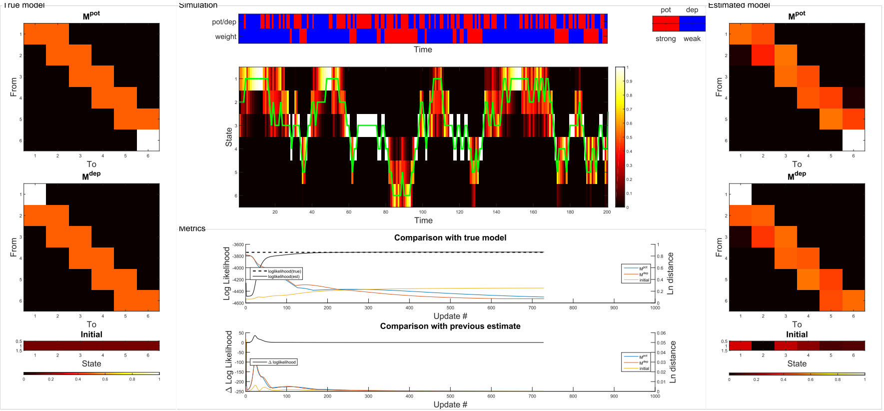
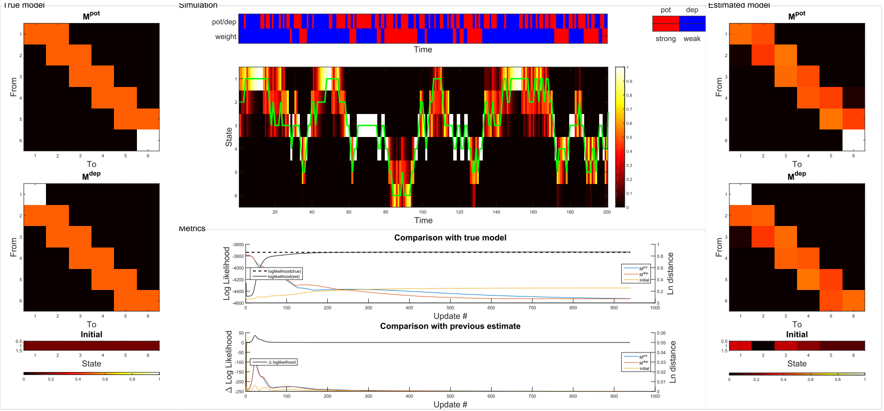


Fitting algorithm



Fitting algorithm



Summary

- 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.
- Synaptic complexity (M internal states) raises the memory envelope linearly in M for times $> \mathcal{O}(M^2)$.
- We understood which types of synaptic structure are useful for storing memories for different timescales.

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Technical detail: ordering states

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

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

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

[Kemeny and Snell (1960)]

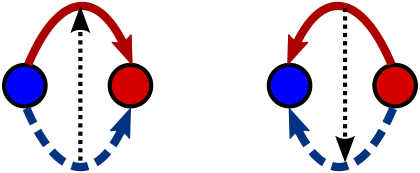
We define:

$$\eta^+_i = \sum_{j \in \text{strong}} \mathbf{T}_{ij} \mathbf{p}^\infty_j , \qquad \eta^-_i = \sum_{j \in \text{weak}} \mathbf{T}_{ij} \mathbf{p}^\infty_j .$$

They can be used to arrange the states in an order (increasing η^- or decreasing η^+). back

Technical detail: upper/lower triangular

With states in order:



Endpoint: potentiation goes right, depression goes left.

back