Learning and memory with complex synaptic plasticity

based on work with Surya Ganguli

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Introduction

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

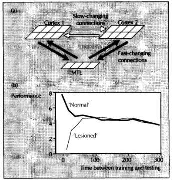
Semi-realistic models of synaptic plasticity have terrible memory without synaptic complexity.

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

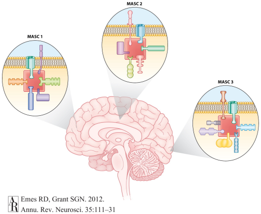


[Squire and Alvarez (1995)]

cf. Cerebellar cortex vs. cerebellar nuclei.

[Krakauer and Shadmehr (2006)]

Different synapses have different molecular structures.



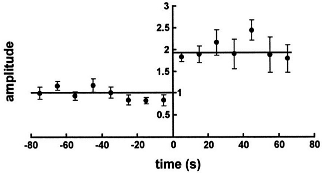
[Emes and Grant (2012)]

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:
$\implies$ new memories overwrite old.



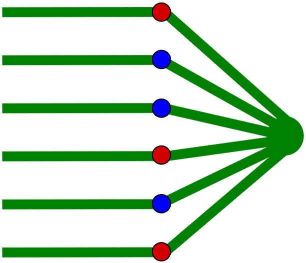
[Petersen et al. (1998), O'Connor et al. (2005)]

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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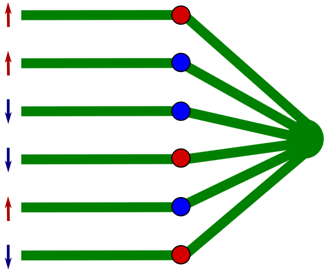

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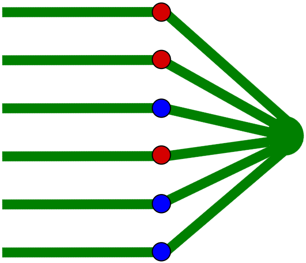

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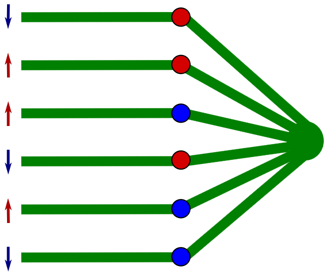

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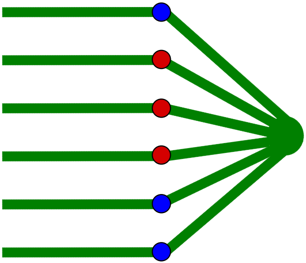

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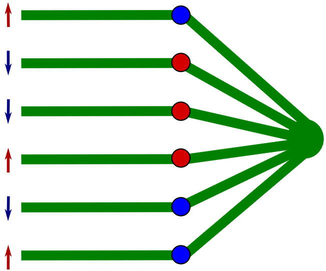

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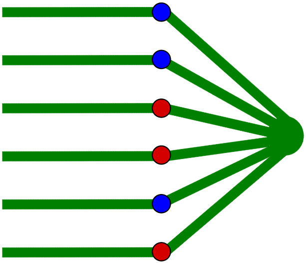

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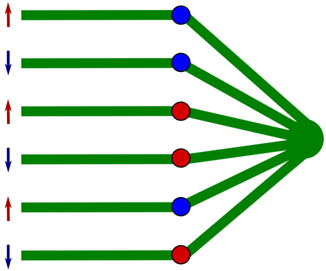
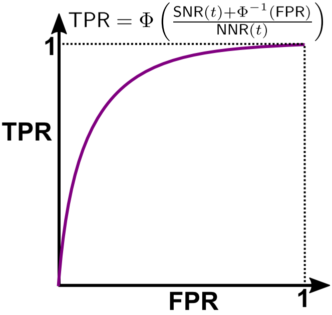


Later: presented with a pattern. Has it been seen before?

Quantifying memory quality

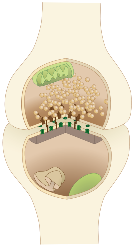
Have we seen pattern before? Test if $\vec{w}_{\text{ideal}} \cdot \vec{w}(t) \gtrless \theta$?
$\vec{w}_{\text{ideal}} \cdot \vec{w}(\infty) \sim$ null distribution $\implies$ ROC curve:



$$\mathrm{SNR}(t) = \frac{\langle \vec{w}_{\text{ideal}} \cdot \vec{w}(t) \rangle - \langle \vec{w}_{\text{ideal}} \cdot \vec{w}(\infty) \rangle}{\sqrt{\mathrm{Var}(\vec{w}_{\text{ideal}} \cdot \vec{w}(\infty))}},$$

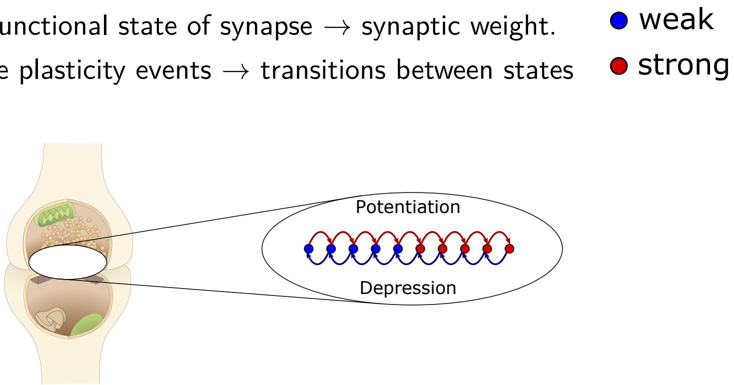
$$\mathrm{NNR}(t) = \sqrt{\frac{\mathrm{Var}(\vec{w}_{\text{ideal}} \cdot \vec{w}(t))}{\mathrm{Var}(\vec{w}_{\text{ideal}} \cdot \vec{w}(\infty))}}.$$

Models of complex synaptic dynamics



Models of complex synaptic dynamics

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



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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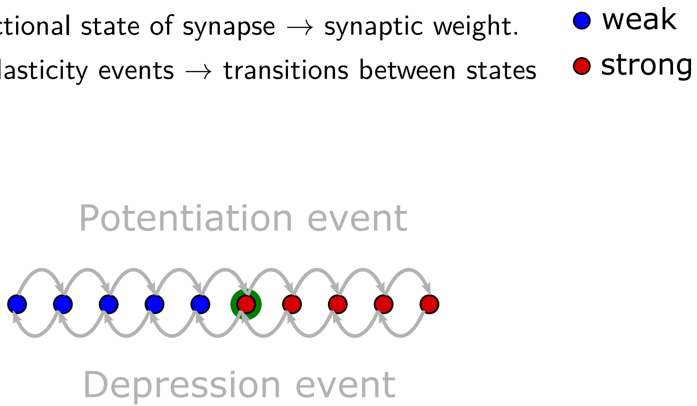

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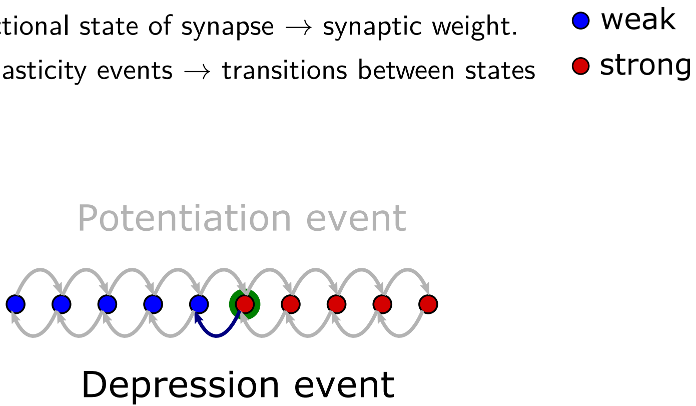

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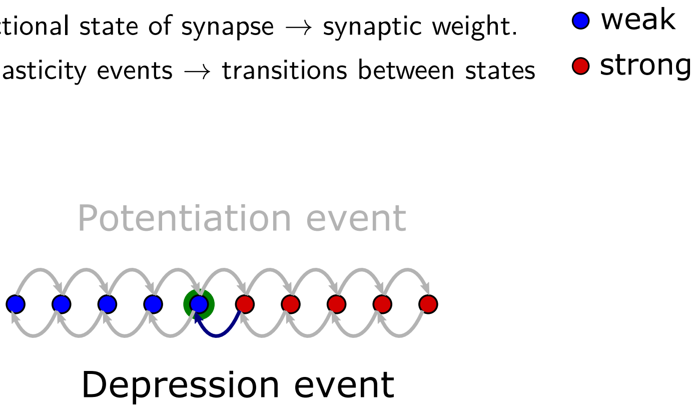

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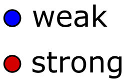

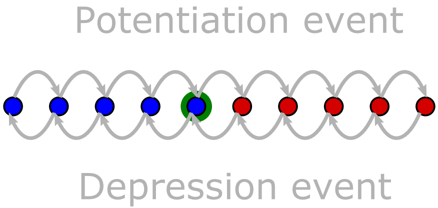

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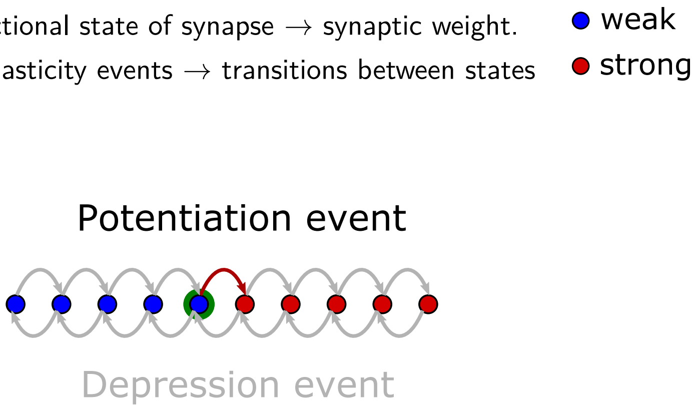

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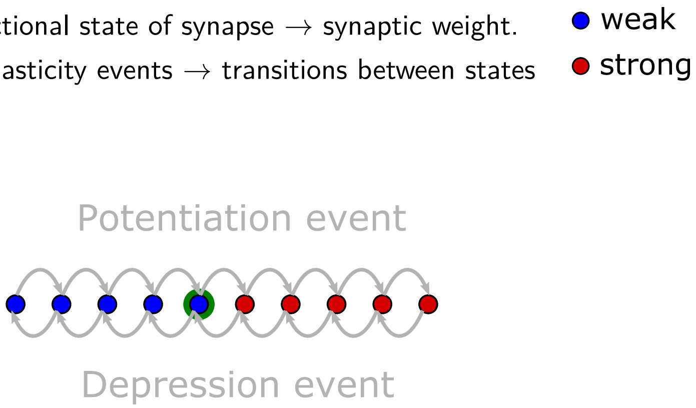

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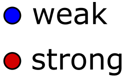
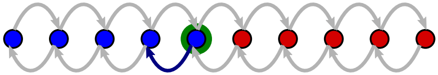


Potentiation event



Depression event

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

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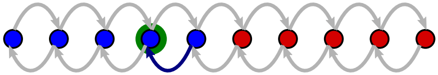
● weak
● strong

Potentiation event



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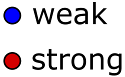

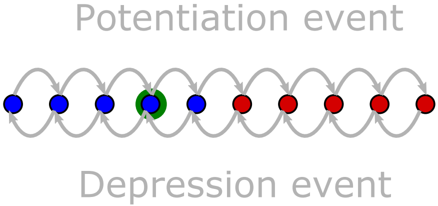

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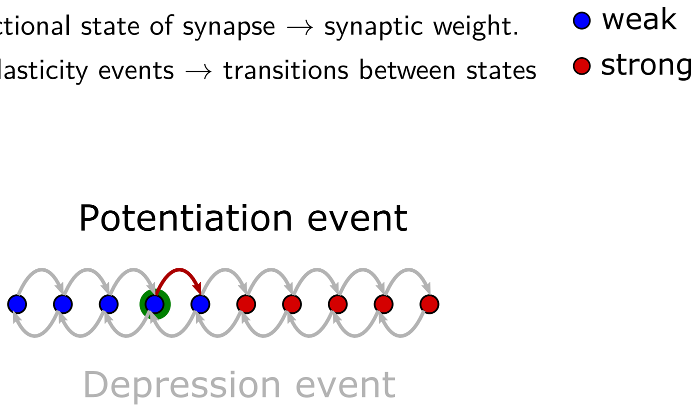

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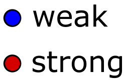

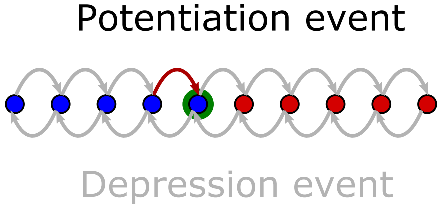

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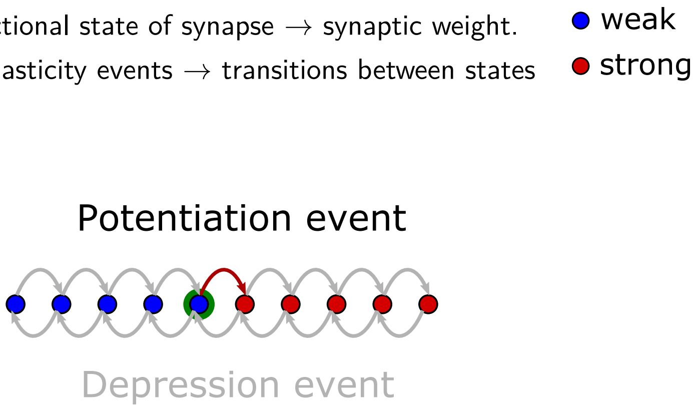

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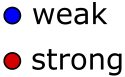

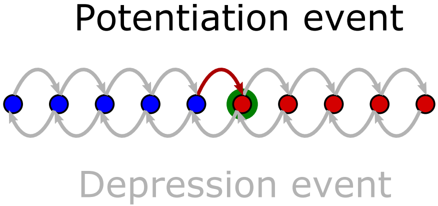

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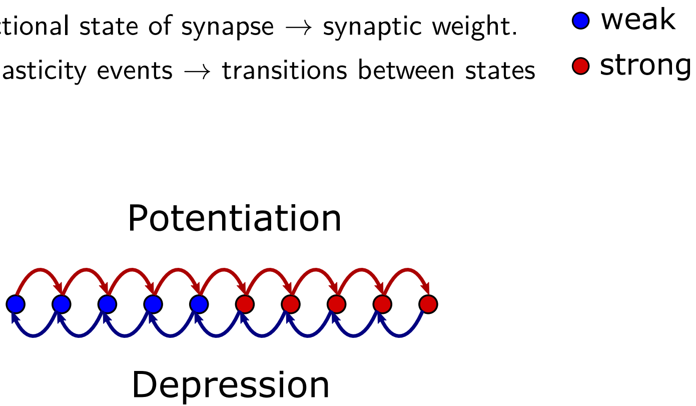

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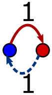
Upper bounds on measures of memory

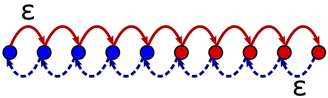
Initial SNR:

$$\mathsf{SNR}(0) = \overline{\mathsf{SNR}}(0) \leq \sqrt{N}.$$



Area under curve:

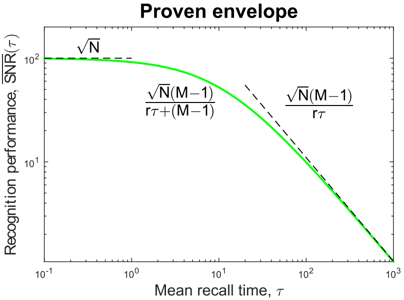
$$\mathcal{A} = \int_0^\infty \mathrm{d}t\ \mathsf{SNR}(t) = \lim_{\tau\to\infty} \tau\,\overline{\mathsf{SNR}}(\tau) \leq \sqrt{N}(M-1)/r.$$



[Lahiri and Ganguli (2013)]

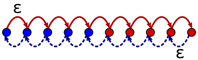
Proven envelope: memory frontier

Upper bound on memory curve at *any* time.



Initial SNR:

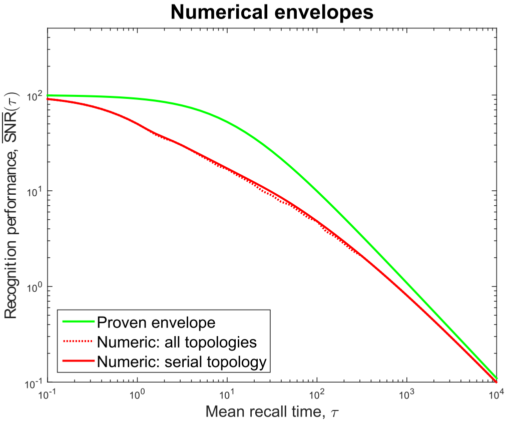
Late times:



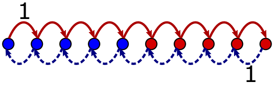
[Lahiri and Ganguli (2013)]

No model can ever go above this envelope. Is it achievable?

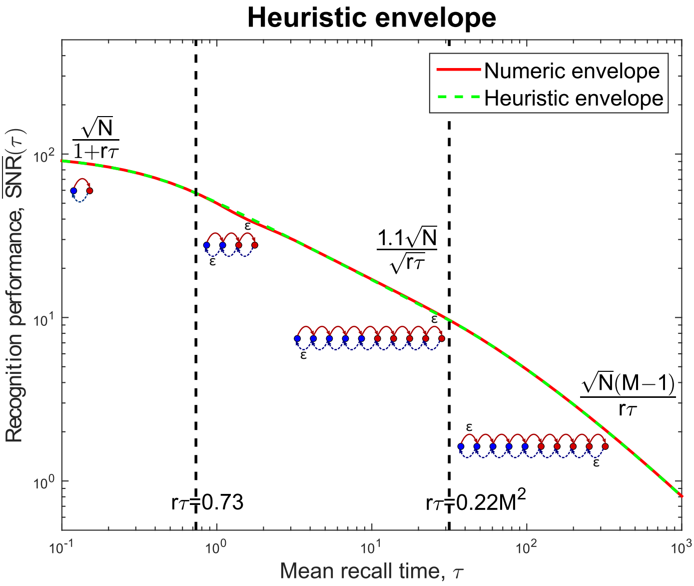
Achievable envelope



Serial topology:



Heuristic envelope



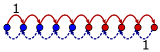
Synaptic structures for different timescales of memory

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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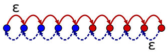

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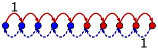

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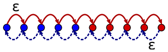

short & wide $\longrightarrow$ long & thin

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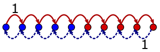

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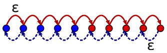


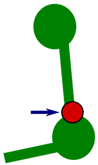
short & wide $\longrightarrow$ long & thin

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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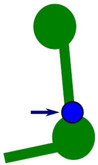

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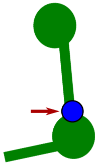

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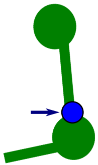

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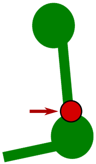

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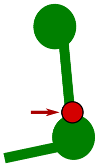

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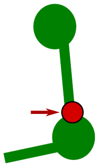


EM algorithms:

Sequence of hidden states $\rightarrow$ estimate transition probabilities
Transition probabilities $\rightarrow$ estimate sequence of hidden states

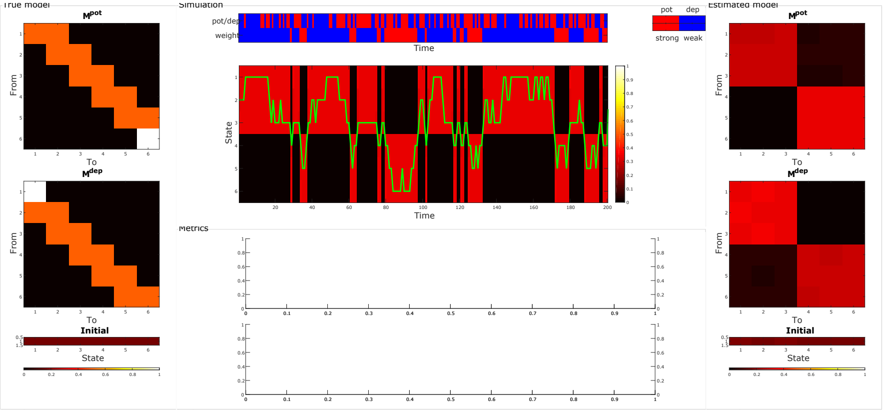
[Baum et al. (1970), Rabiner and Juang (1993), Dempster et al. (2007)]

Spectral algorithms:

Compute $P(w_1), P(w_1, w_2), P(w_1, w_2, w_3), \ldots$ from data,
from model.

[Hsu et al. (2008)]

Fitting algorithm



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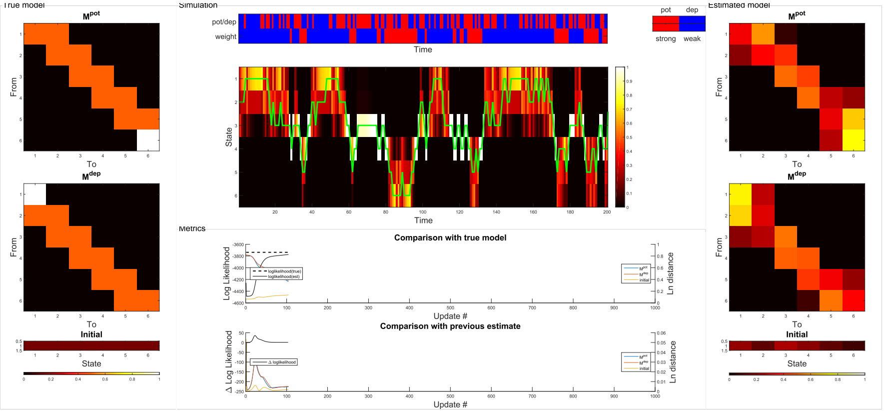

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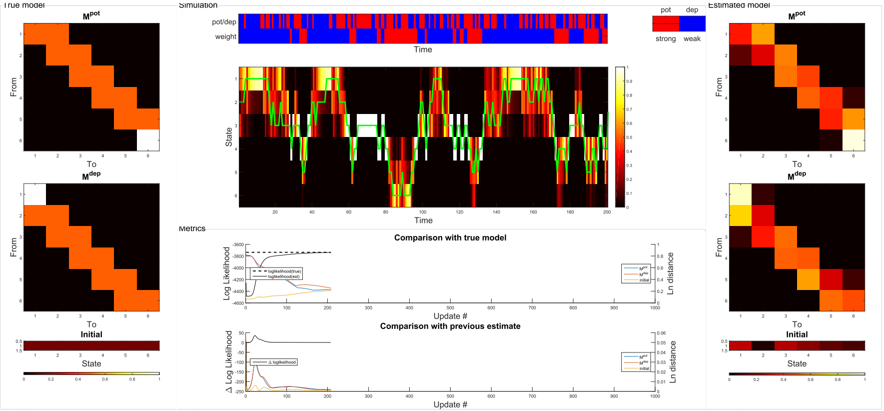

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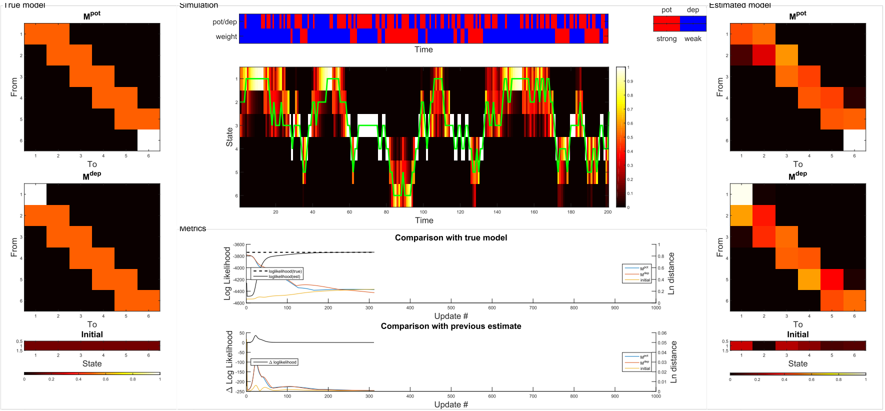
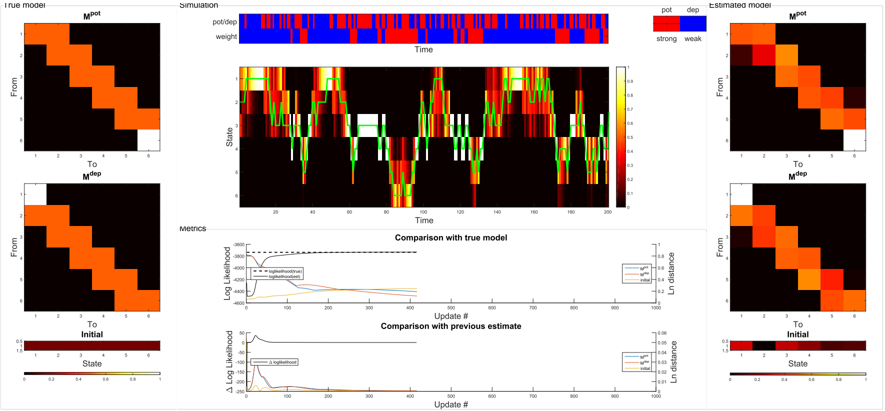
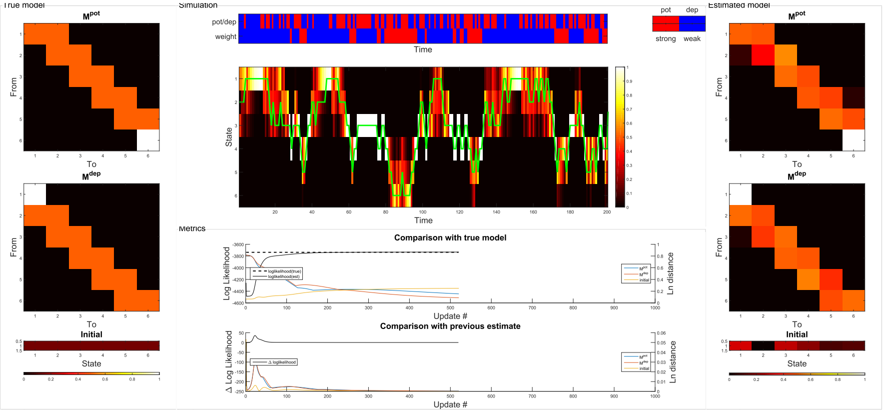
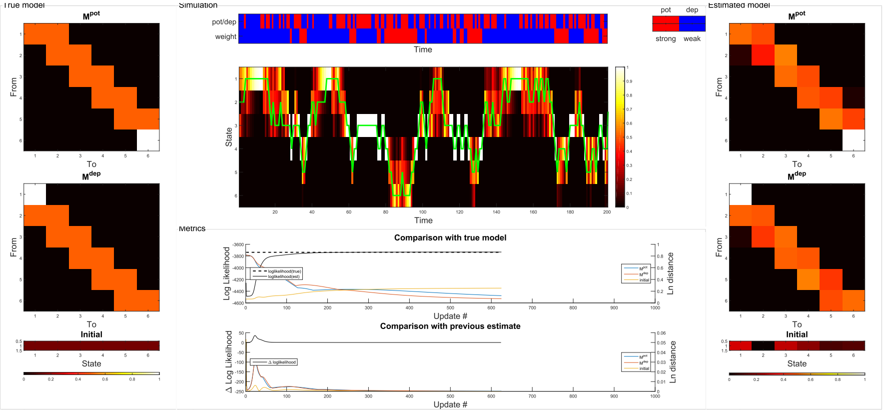


Fitting algorithm

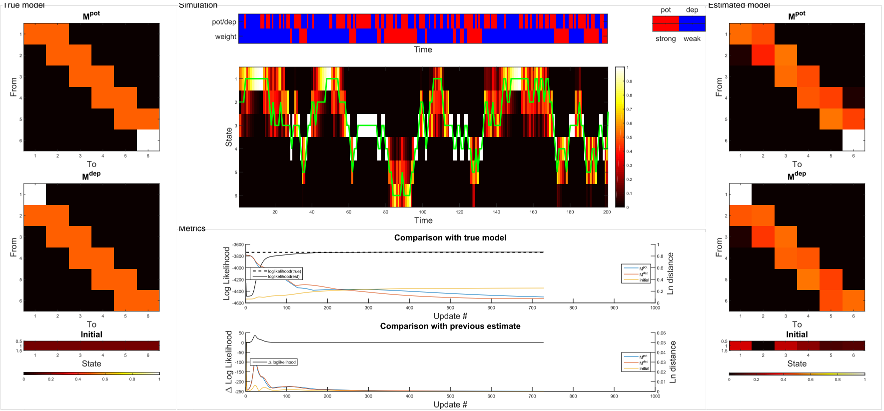


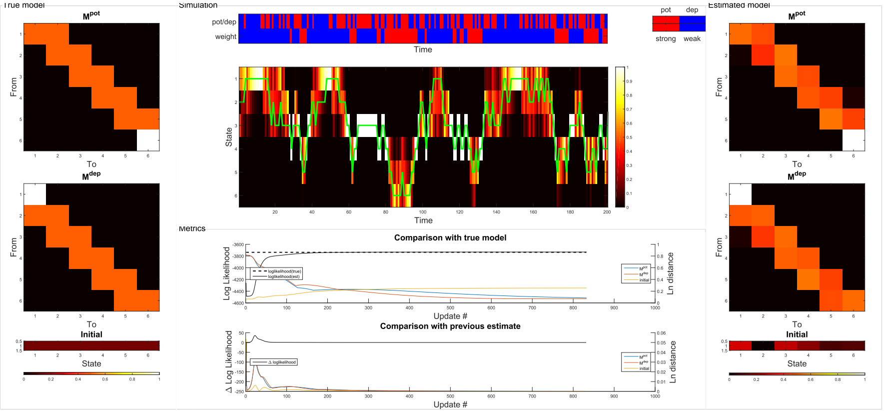
Fitting algorithm



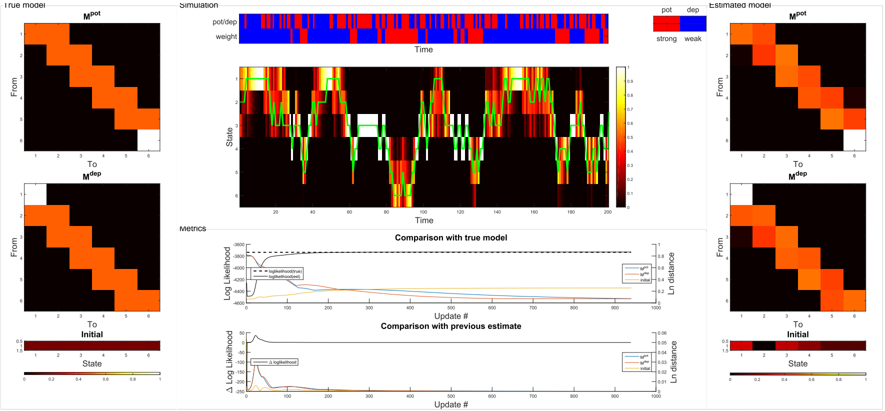

True model
Simulation
Estimated model
M^pot
M^dep
From
To
Initial
State
pot/dep
weight
Time
pot
dep
strong
weak
Metrics
Comparison with true model
Log Likelihood
Ln distance
Update #
loglikelihood(true)
loglikelihood(est)
initial
Comparison with previous estimate
Δ Log Likelihood
Δ loglikelihood

Fitting algorithm




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

Fitting algorithm



Experimental problems

- Need single synapses.
- Need long sequences of plasticity events.
- Need to control types of candidate plasticity events.
- Need to measure synaptic efficacies.

When we patch the postsynaptic neuron $\rightarrow$ Ca washout.

Summary

- We have formulated a general theory of learning and memory with complex synapses.
- The area under the memory curve of any model $<$ linear chain with same equilibrium distribution.
- 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 $> \mathcal{O}(M)$.
- We understood which types of synaptic structure are useful for storing memories for different timescales.
- Gap between envelope and what we can achieve at early times?
- Trade-off between SNR at different times?

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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)]

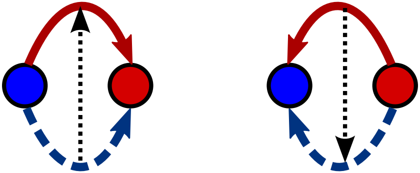
We define:

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

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