# Optimal synaptic strategies for different timescales of memory

Subhaneil Lahiri and Surya Ganguli

Stanford University, Applied Physics

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# What is a synapse?

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Theorists

$$W_{ij}$$

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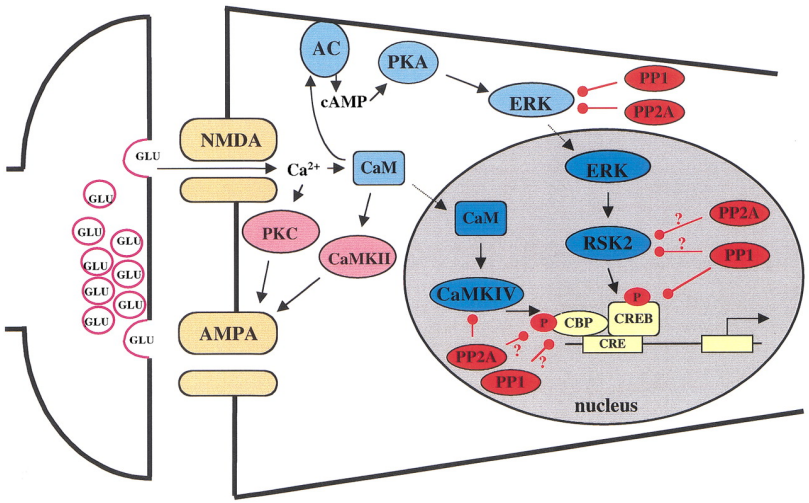
$W_{ij}$

Experimentalists




[Klann (2002)]

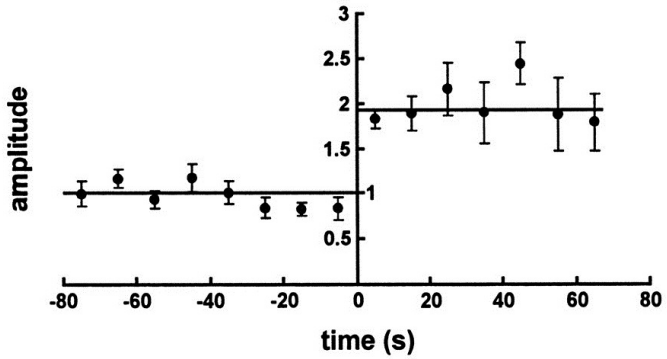
# Storage capacity of synaptic memory

Hopfield, perceptron have capacity $\propto N$, (# synapses).

Assumes unbounded analog synapses

With discrete, finite synapses:
$\implies$ memory capacity $\sim \mathcal{O}(\log N)$.

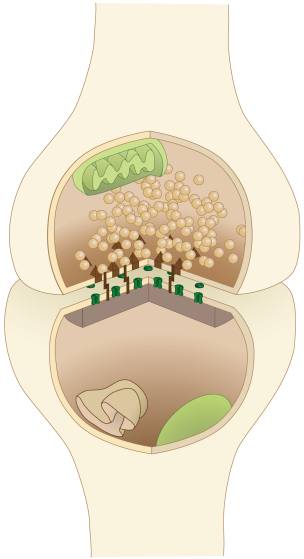
[Amit and Fusi (1992), Amit and Fusi (1994)]




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

New memories overwrite old $\implies$ stability-plasticity dilemma.

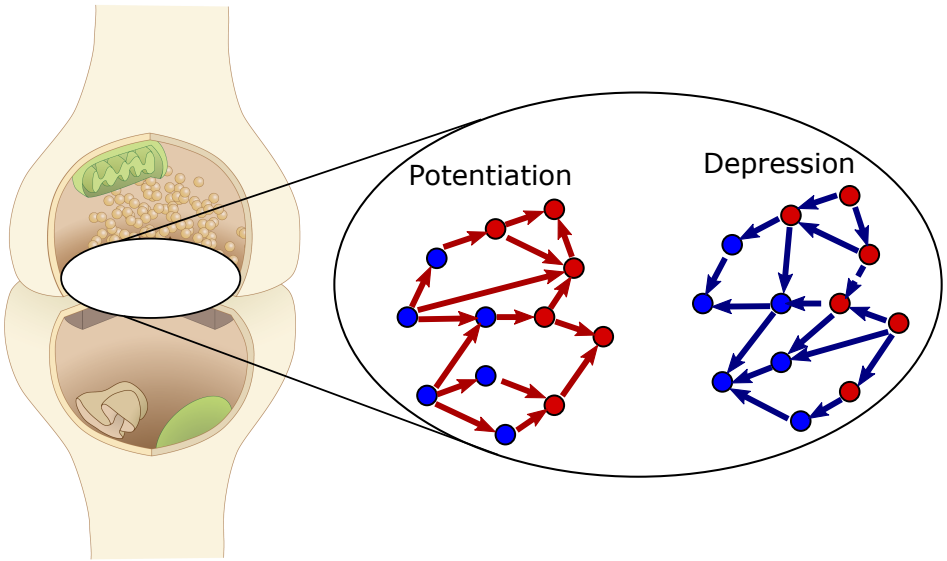
# Models of complex synaptic dynamics



# Models of complex synaptic dynamics

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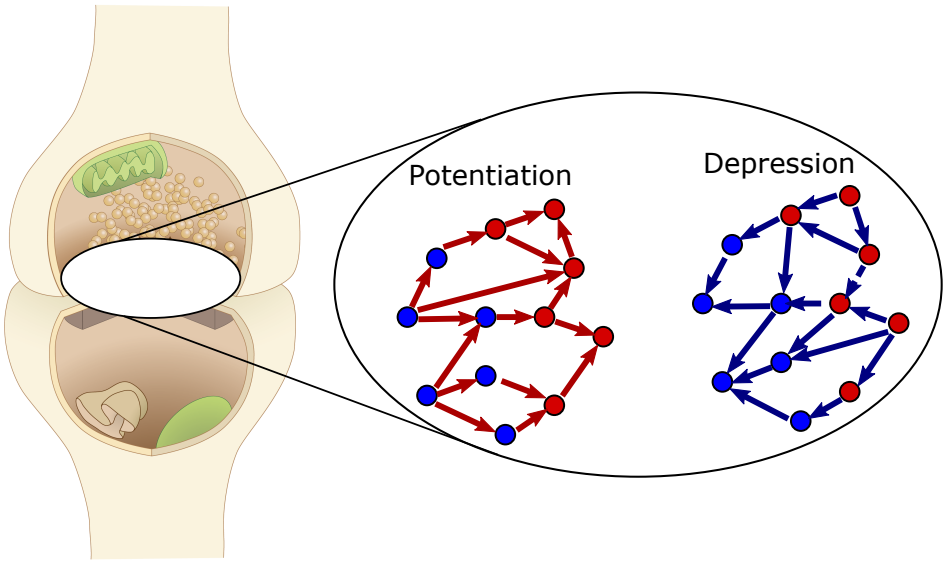


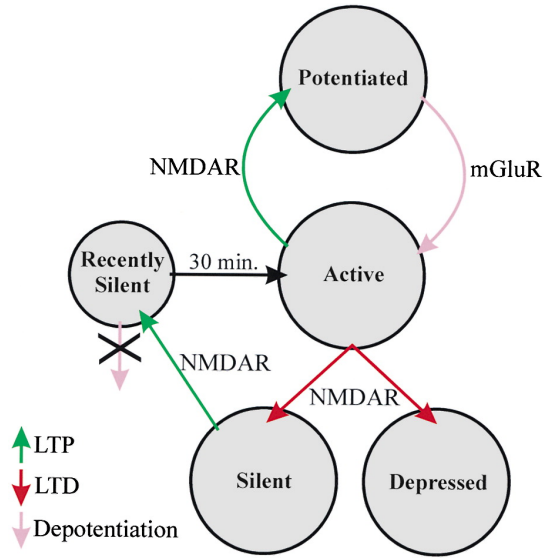


[Montgomery and Madison (2002)]

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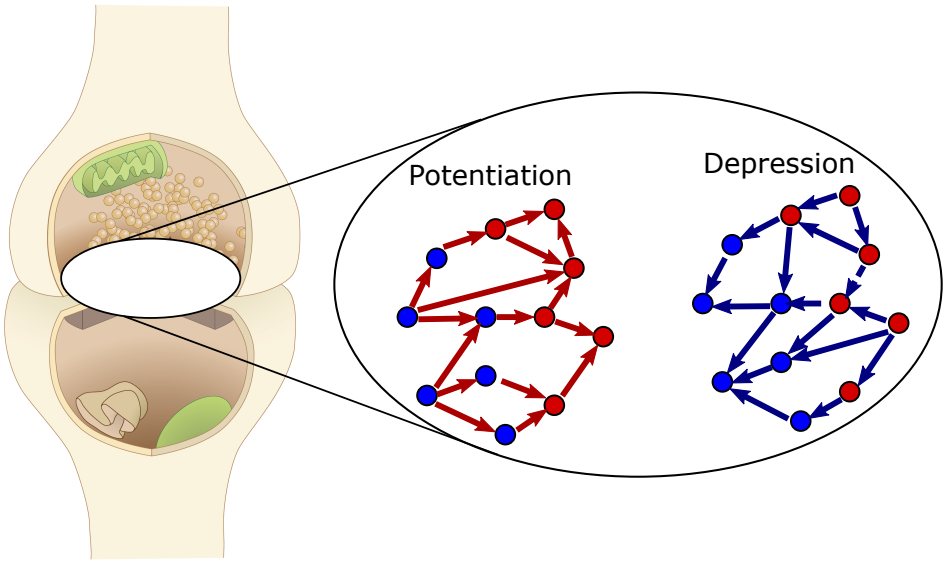


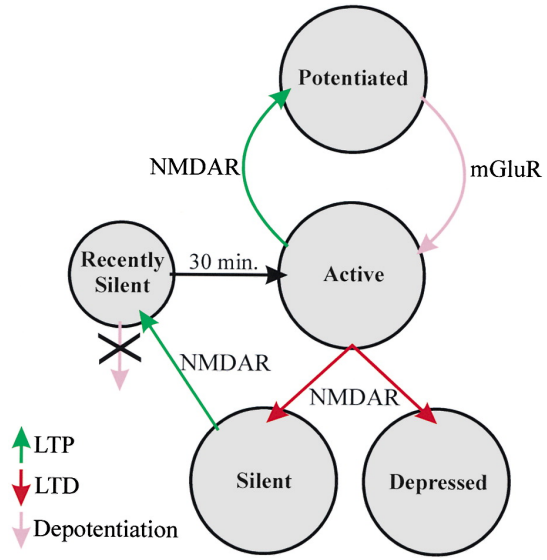


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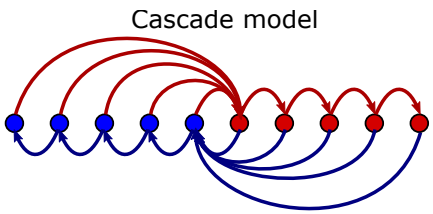
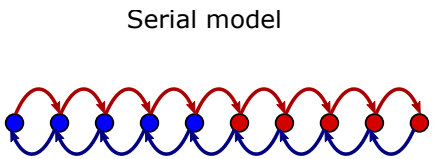
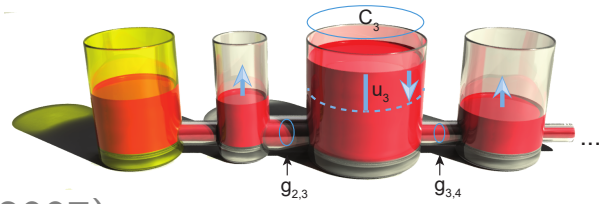



[Fusi et al. (2005)]

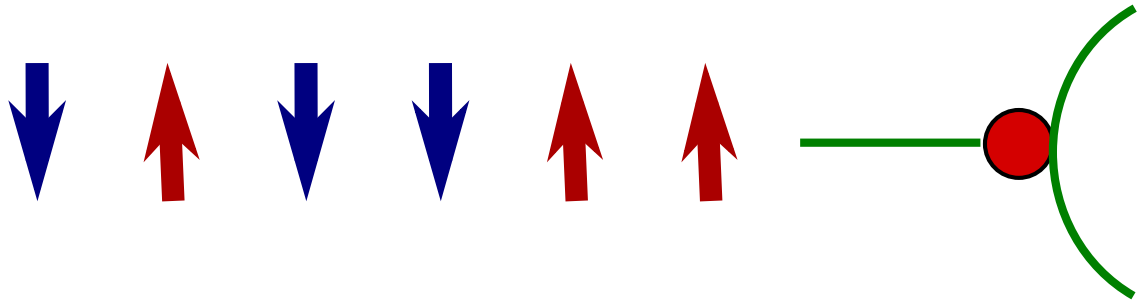



[Ben-Dayan Rubin and Fusi (2007), Leibold and Kempter (2008)]

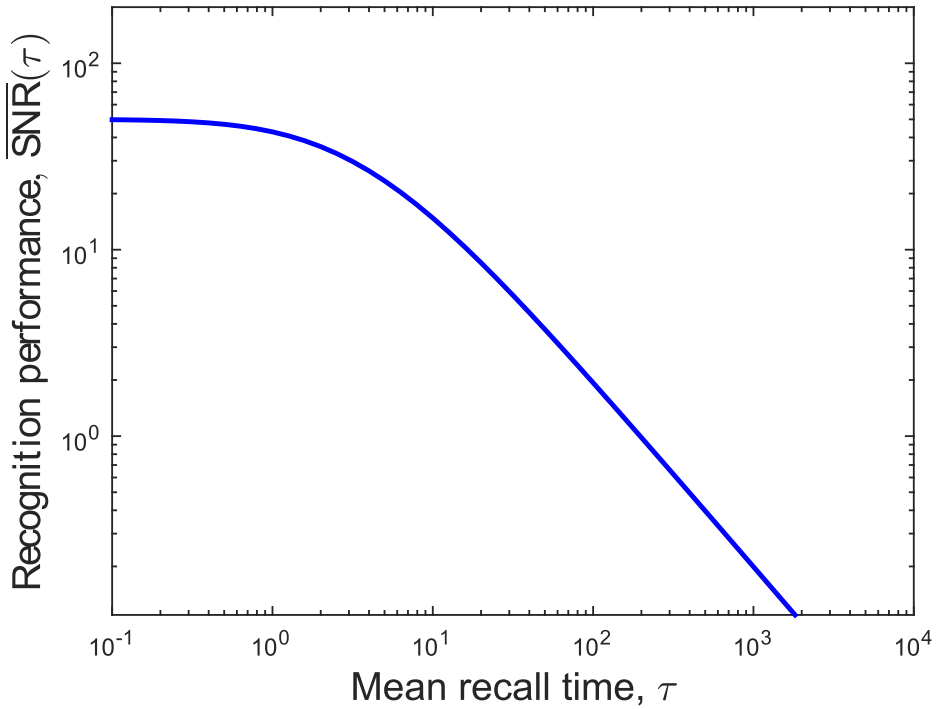



[Benna and Fusi (2015)]

# Synaptic memory curves

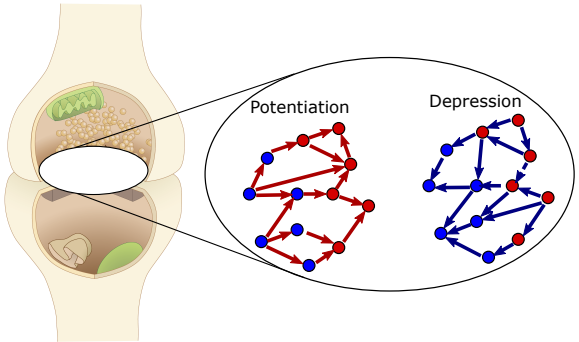


Synapses store a sequence of memories.

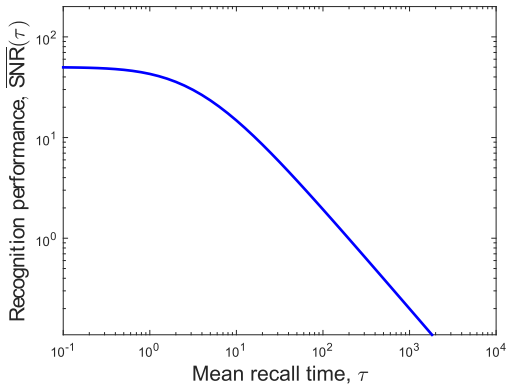


# General principles relating structure and function?

Synaptic structure



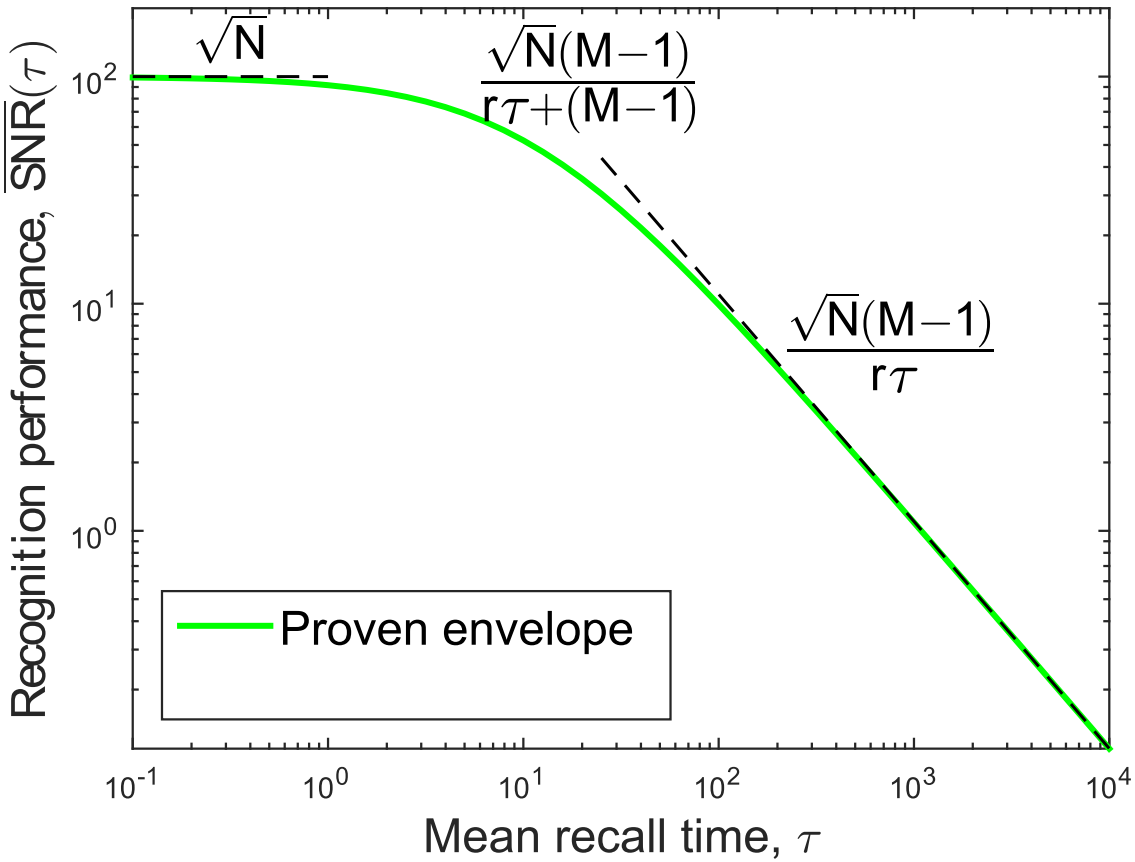

Synaptic function




- What are the fundamental limits of memory?
- Which models achieve these limits?
- What are the theoretical principles behind the optimal models?

# Proven envelope: memory frontier

Upper bound on memory curve at *any* timescale.



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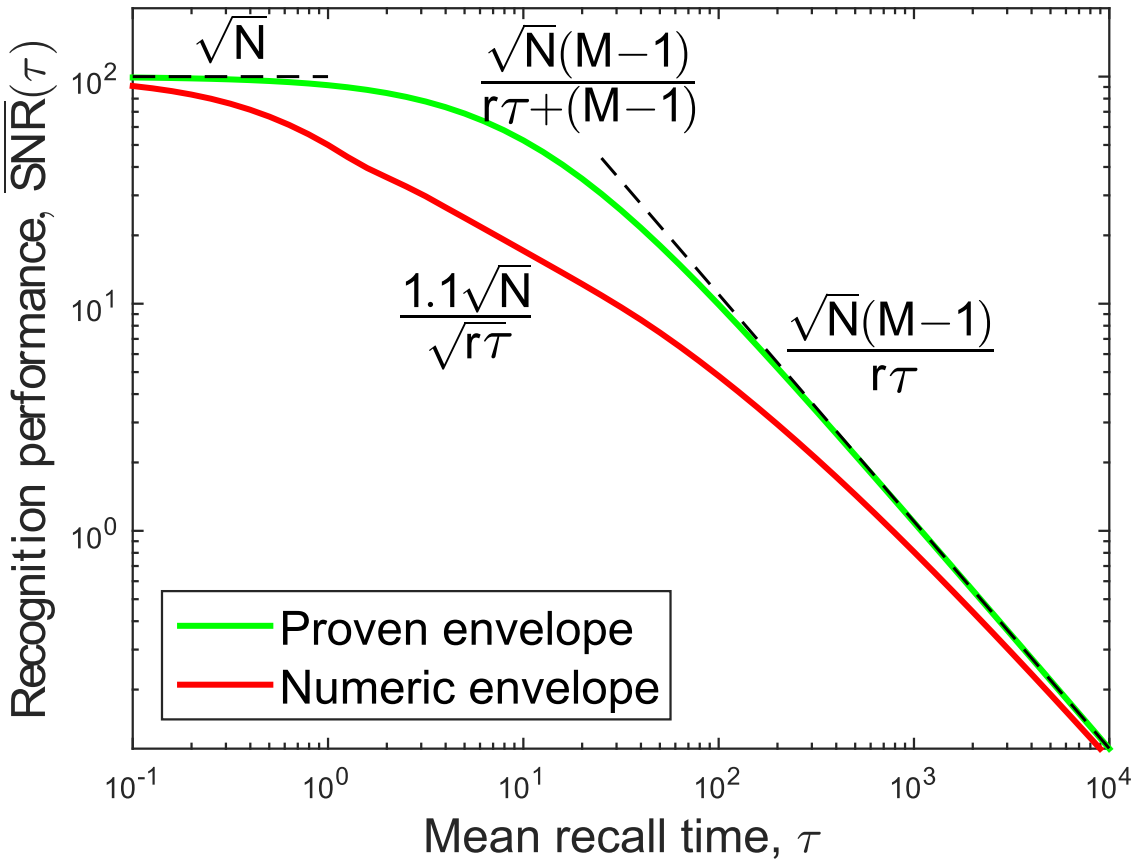
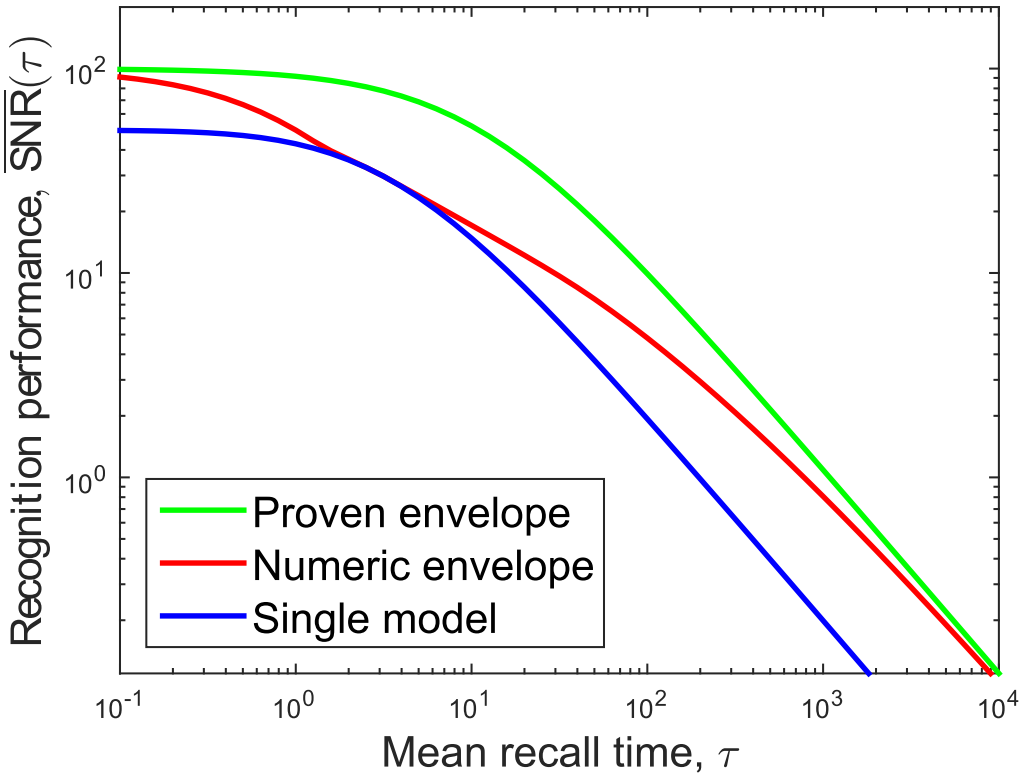
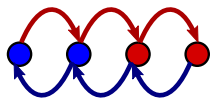


# Models that maximize memory for one timescale



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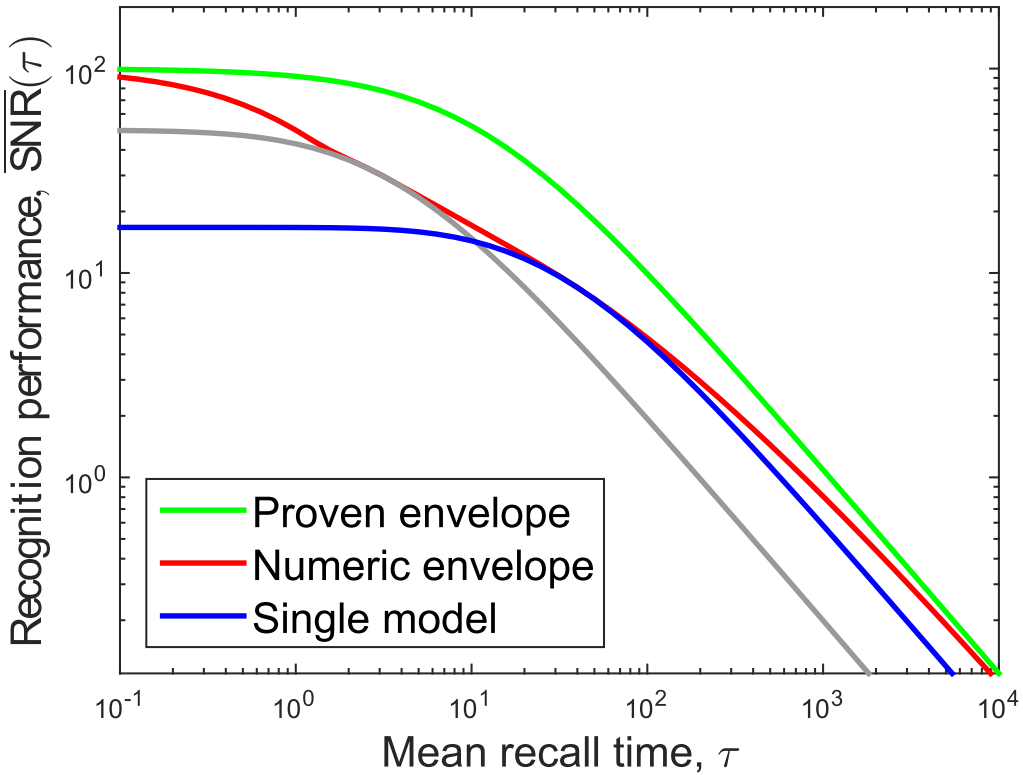


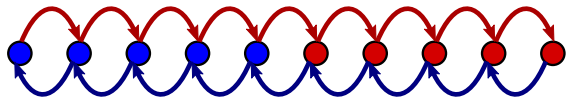

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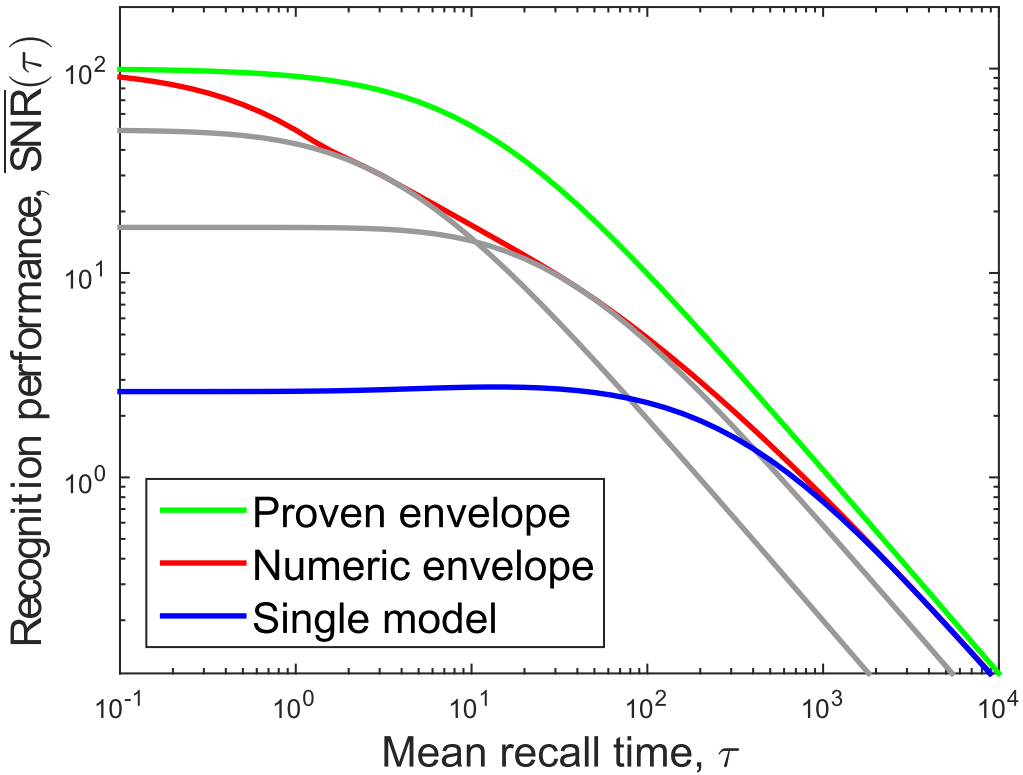
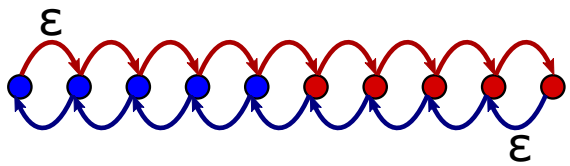
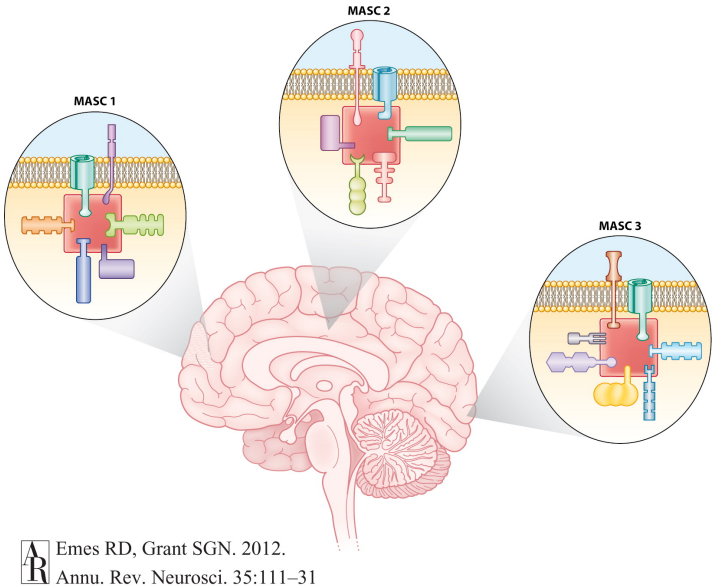


# Synaptic diversity and timescales of memory

Different synapses have different molecular structures.




[Emes and Grant (2012)]

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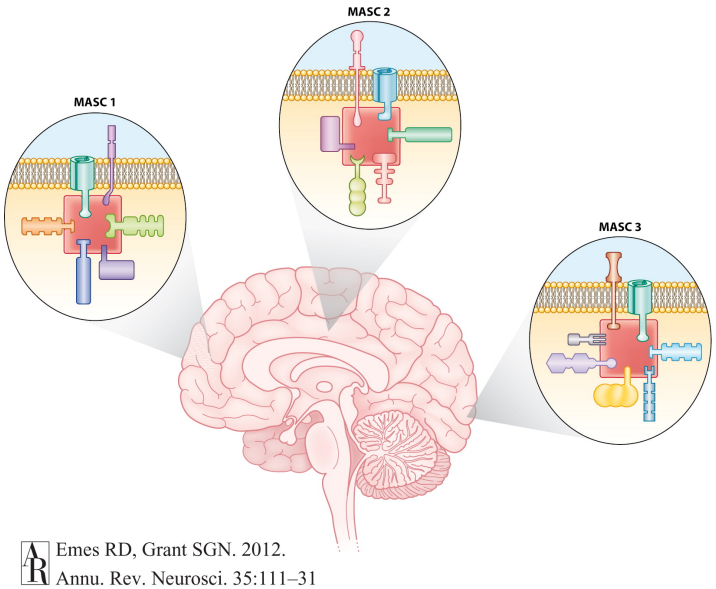
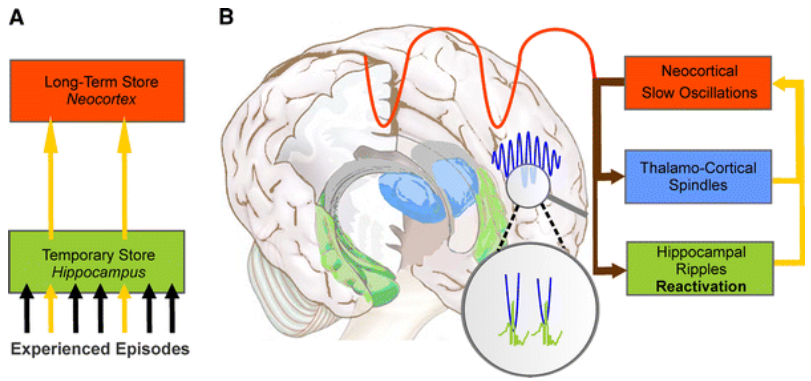



[Emes and Grant (2012)]

Memories stored in different places for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]




[Born and Wilhelm (2012)]

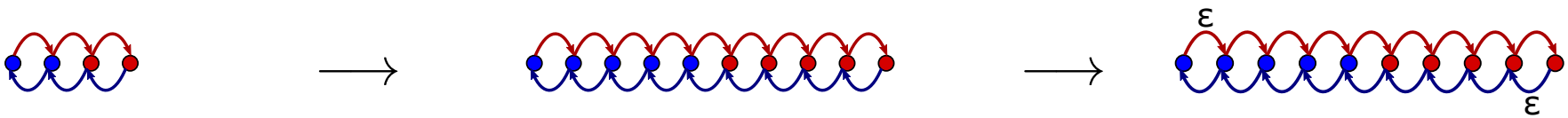
Also: Cerebellar cortex $\rightarrow$ nuclei.

[Attwell et al. (2002)]

[Cooke et al. (2004)]

# Synaptic structure and function: general principles

Short timescale $\longrightarrow$ Intermediate timescale $\longrightarrow$ Long timescale



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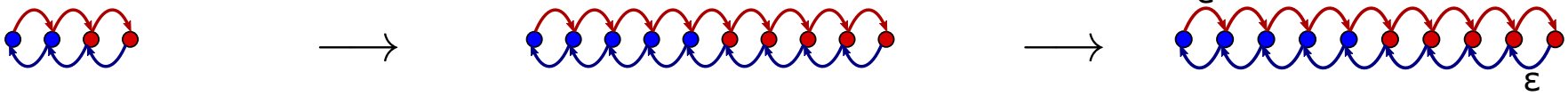


short topology $\longrightarrow$ long topology

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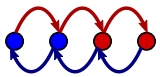
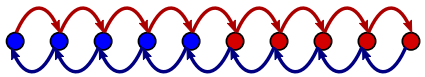

$\longrightarrow$

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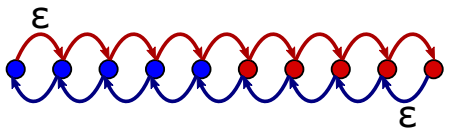


short topology $\longrightarrow$ long topology

deterministic synapse $\longrightarrow$ stochastic synapse

# Experimental tests?

Traditional experiments:

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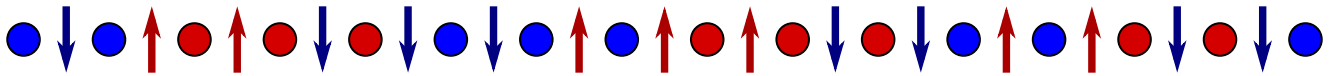
Traditional experiments:

To fit a model: long sequence of small plasticity events.
Observe the changes in synaptic efficacy.



# 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.
- We understood which types of synaptic structure are useful for storing memories for different timescales.
- We studied more than a single model. We studied *all possible models*, to extract general principles relating synaptic structure to function

# Acknowledgements

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- Marcus Benna
- David Sussillo
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33

# 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:

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

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