

# Optimal synaptic strategies for different timescales of memory

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# What is a synapse?

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Theorists

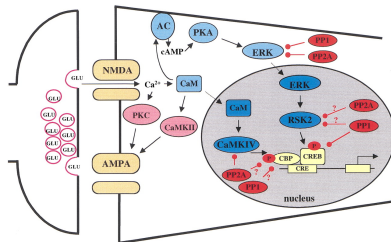
$$W_{ij}$$

# What is a synapse?

Theorists

$$W_{ij}$$

Experimentalists



[Klann (2002)]

# Storage capacity of synaptic memory

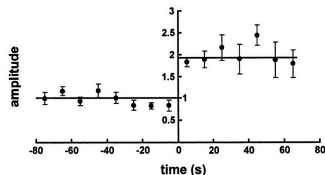
Hopfield, perceptron have capacity  $\propto N$ , ( $\#$  synapses).

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)]

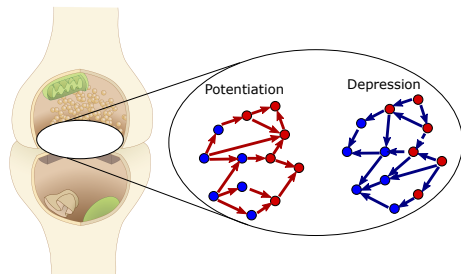
New memories overwrite old  $\implies$  stability-plasticity dilemma.

# Models of complex synaptic dynamics



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

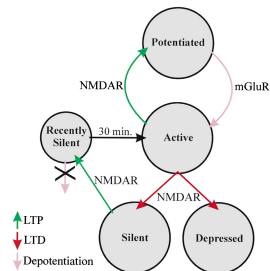
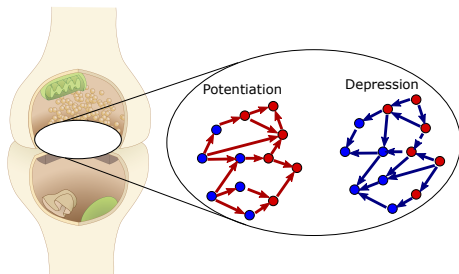


States: #AMPA, #NMDAR, NMDAR subunit composition,  
CaMK II autophosphorylation, activating PKC, p38 MAPK,...

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

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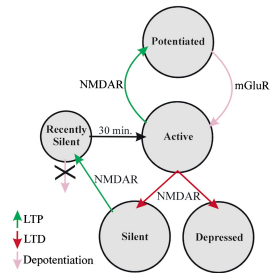
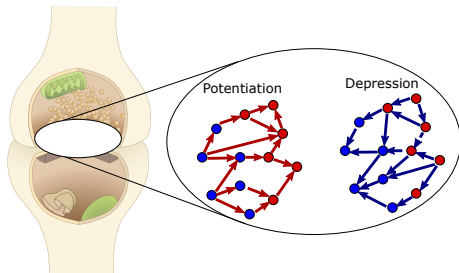
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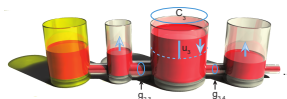
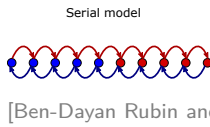
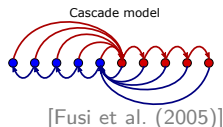


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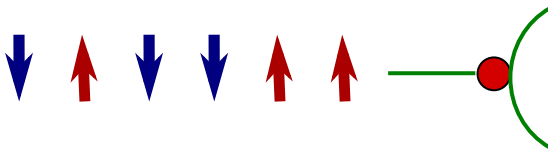
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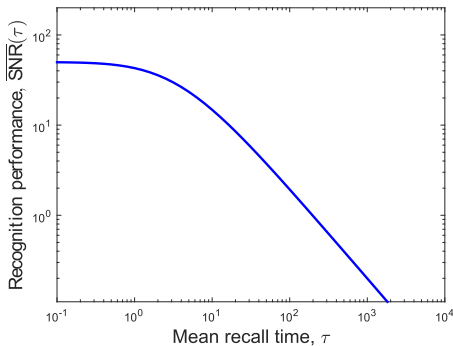
[Montgomery and Madison (2002)]



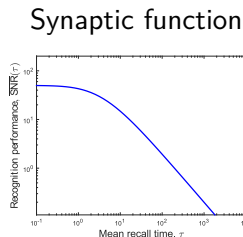
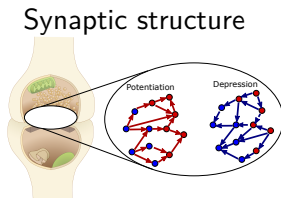
# Synaptic memory curves



Synapses store a sequence of memories.



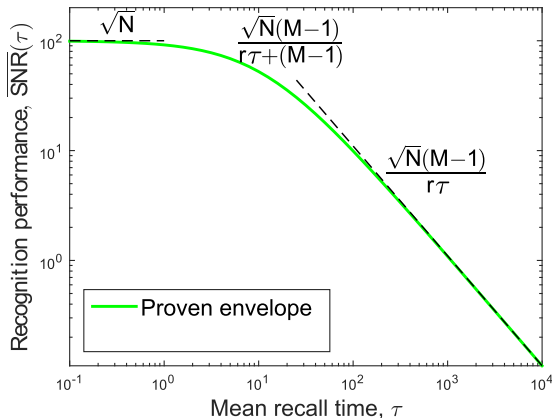
# General principles relating structure and function?



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

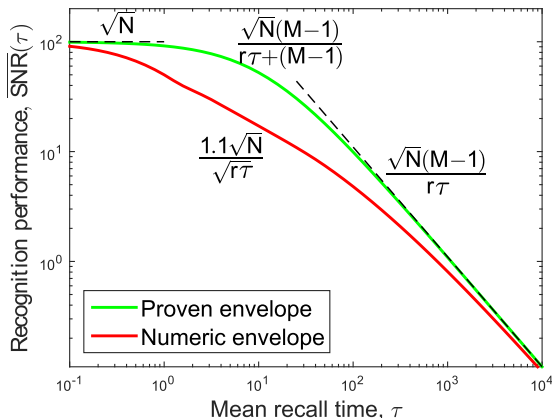
# Proven envelope: memory frontier

Upper bound on memory curve at *any* timescale.

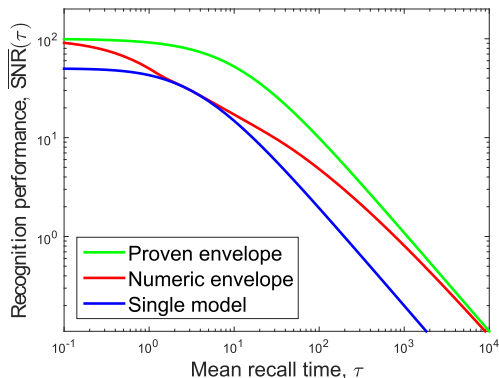


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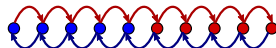
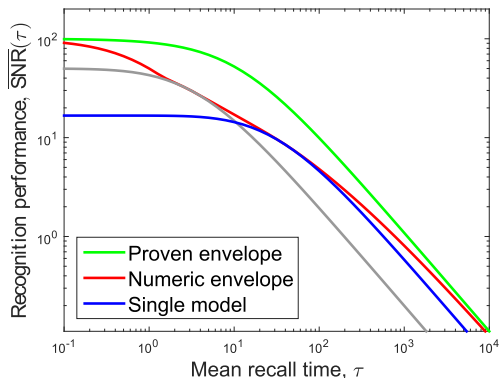
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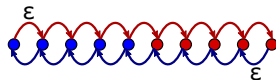
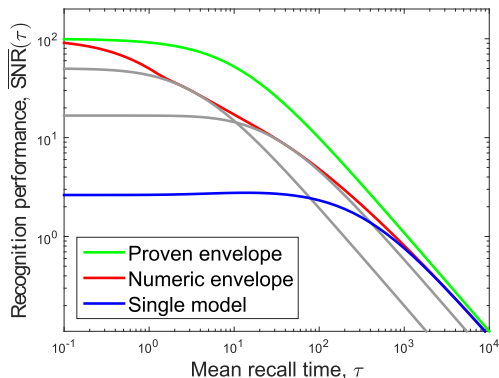
# Models that maximize memory for one timescale



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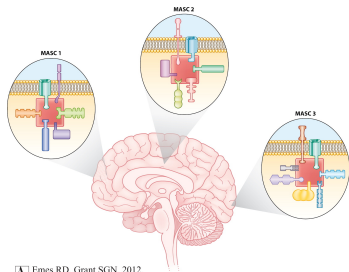
# Models that maximize memory for one timescale





# Synaptic diversity and timescales of memory

Different synapses have different molecular structures.

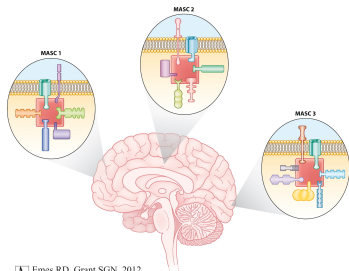


Emes RD, Grant SGN, 2012.  
Annu. Rev. Neurosci. 35:111–31

[Emes and Grant (2012)]

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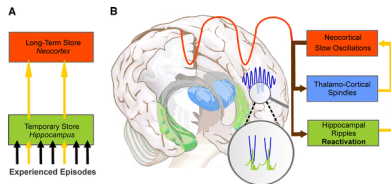
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[Emes and Grant (2012)]

Memories stored in different places for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]



[Born and Wilhelm (2012)]

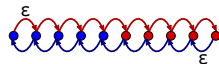
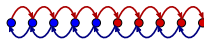
Also: Cerebellar cortex → nuclei.

[Attwell et al. (2002)]

[Cooke et al. (2004)]

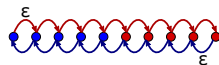
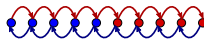
# Synaptic structure and function: general principles

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



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short topology



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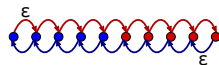
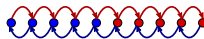
Short timescale



Intermediate timescale



Long timescale



short topology



long topology

deterministic synapse



stochastic synapse

# Experimental tests?

Traditional experiments:



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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



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