Optimal synaptic strategies for different timescales of memory

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What is a synapse?

What is a synapse?

Theorists

$$W_{ij}$$

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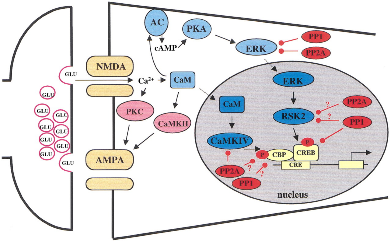
Theorists

$$W_{ij}$$

Experimenters



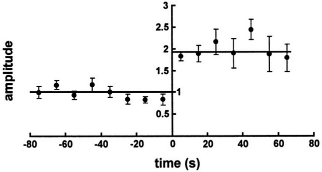
[Klann (2002)]

Storage capacity of synaptic memory

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

Assumes unbounded analog synapses

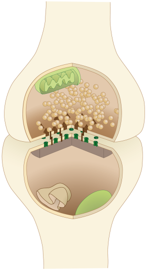
With discrete, finite synapses:
$\Longrightarrow$ memory capacity $\sim \mathcal{O}(\log N)$.
[Amit and Fusi (1992), Amit and Fusi (1994)]



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

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

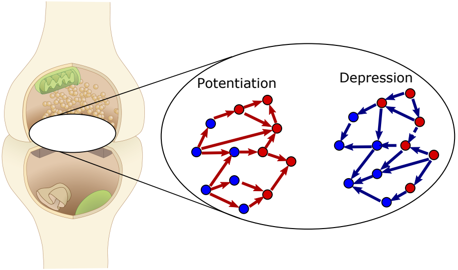
Models of complex synaptic dynamics



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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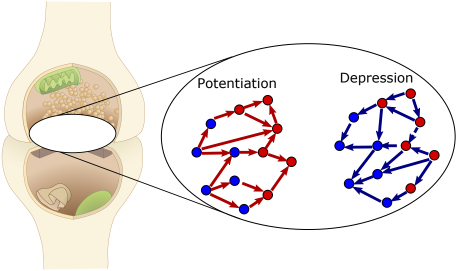

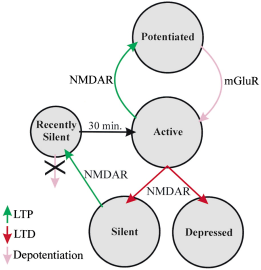

[Montgomery and Madison (2002)]

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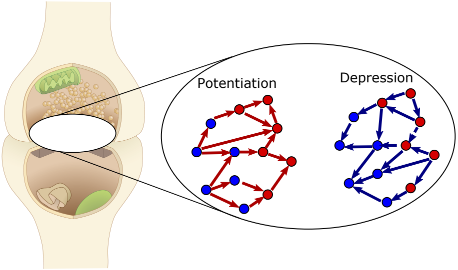

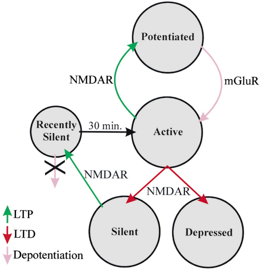

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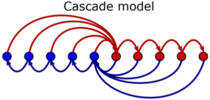
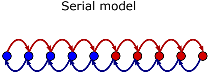
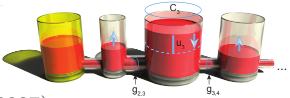


[Fusi et al. (2005)]

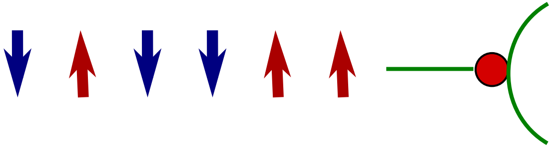


[Ben-Dayan Rubin and Fusi (2007), Leibold and Kempter (2008)]

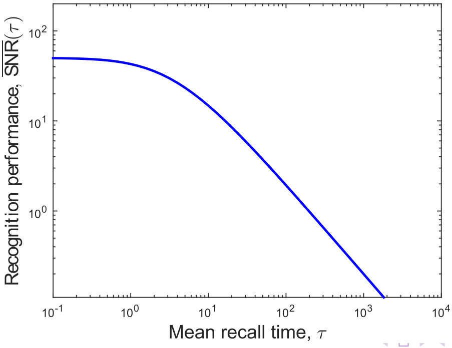


[Benna and Fusi (2015)]

Synaptic memory curves

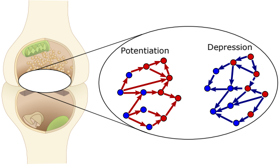


Synapses store a sequence of memories.

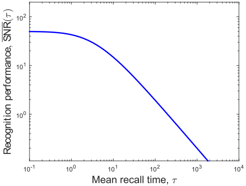


General principles relating structure and function?

Synaptic structure



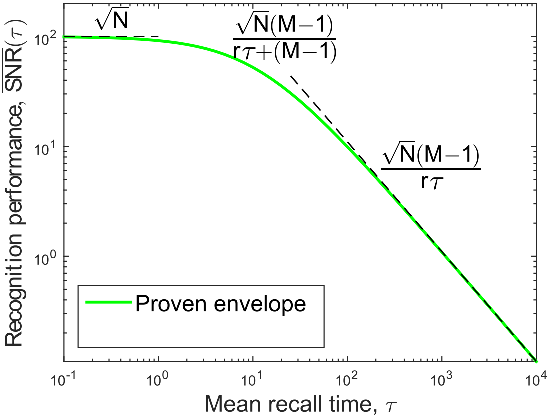
Synaptic function



- 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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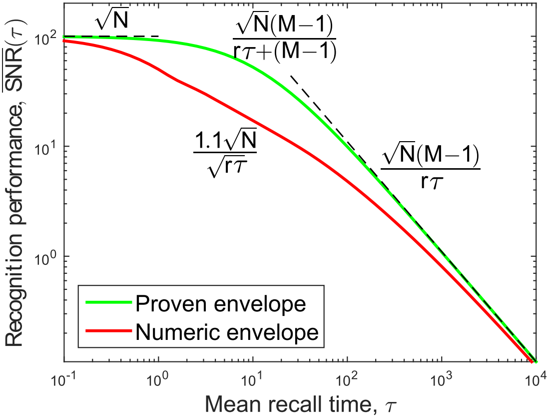
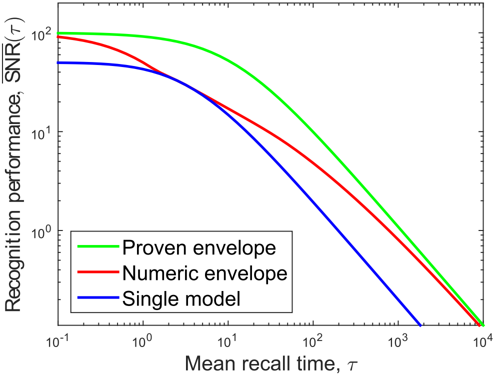
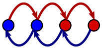


Models that maximize memory for one timescale





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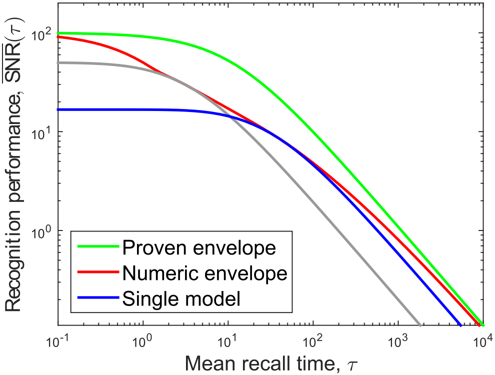

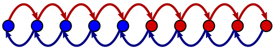

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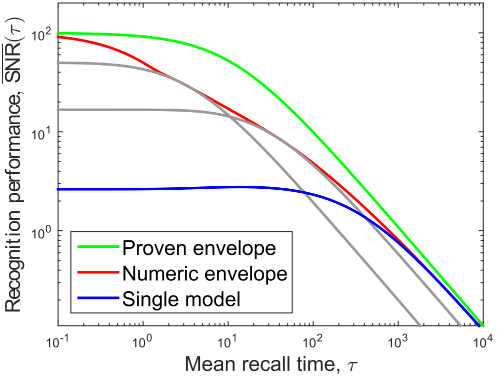
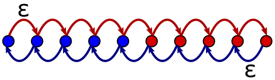
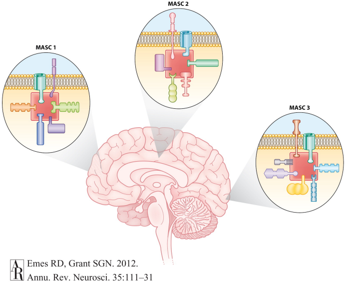




Synaptic diversity and timescales of memory

Different synapses have different molecular structures.



[Emes and Grant (2012)]

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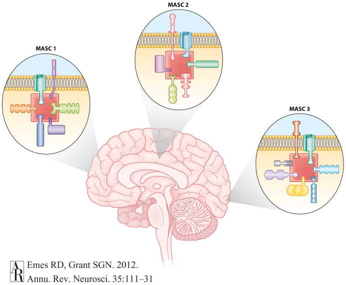
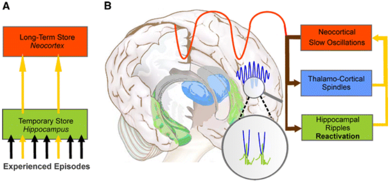


[Emes and Grant (2012)]

Memories stored in different places for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]



[Born and Wilhelm (2012)]

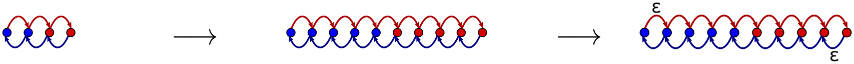
Also: Cerebellar cortex → nuclei.

[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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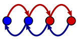
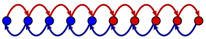
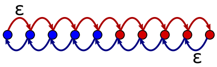


$\longrightarrow$

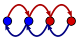
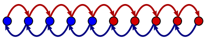
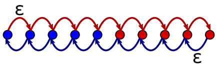


$\longrightarrow$



short topology $\longrightarrow$ long topology

Synaptic structure and function: general principles

Short timescale	$\longrightarrow$	Intermediate timescale	$\longrightarrow$	Long timescale
	$\longrightarrow$		$\longrightarrow$	
short topology	$\longrightarrow$	long topology		
		deterministic synapse	$\longrightarrow$	stochastic synapse

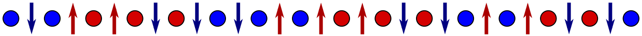
Experimental tests?

Traditional experiments:

Experimental tests?

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

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33

Technical detail: ordering states

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

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

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

[Kemeny and Snell (1960)]

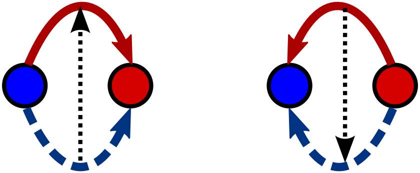
We define:

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

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