Learning and memory with complex synaptic plasticity

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My research areas

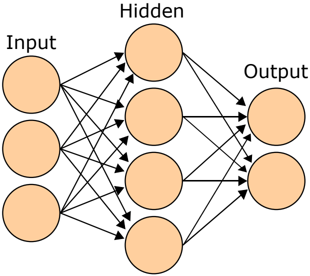
Learning and memory
Structure of synapses & function.
Learning v. remembering tradeoff.
Success & failure in trying to enhance learning.

Energy use in living systems
Energy cost of signalling/sensing.
Tradeoffs with accuracy & speed.
Thermodynamics $\leftrightarrow$ information geometry.

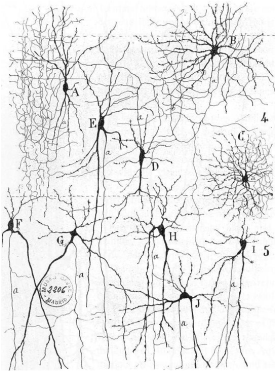
High dimensional statistics
Theory of random projections and the geometry of data.
Neural recordings as projections.

What is a synapse?

Comp-neuro/machine learning



Cellular biology



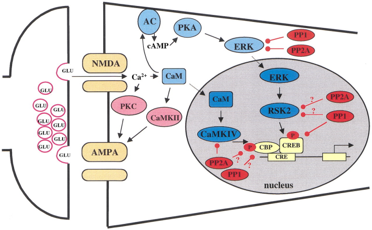
[Cajal (1899)]

What is a synapse?

Comp-neuro/machine learning

$$W_{ij}$$

Cellular biology



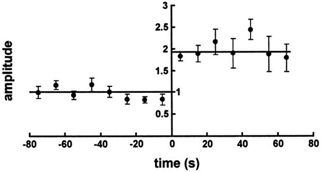
[Klann (2002)]

Storage capacity of synaptic memory

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

Assumes unbounded analogue synapses

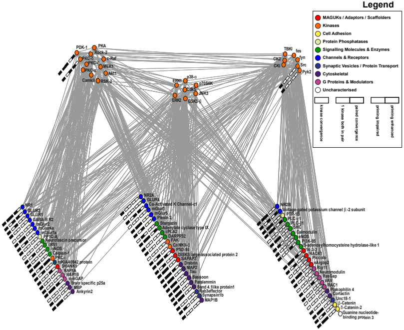
With discrete, finite synapses:
$\implies$ memory capacity $\sim \mathcal{O}(\log N)$.
[Amit and Fusi (1992), Amit and Fusi (1994)]



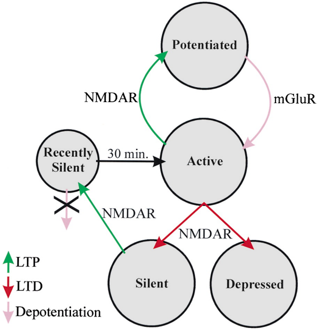
[Petersen et al. (1998), O'Connor et al. (2005)]

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

Synapses are complex

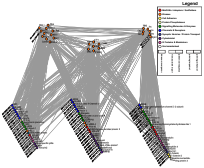


[Coba et al. (2009)]



[Montgomery and Madison (2002)]

Synapses are complex



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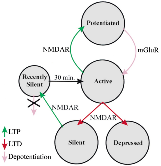
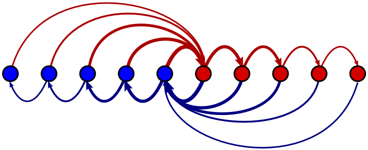


[Montgomery and Madison (2002)]

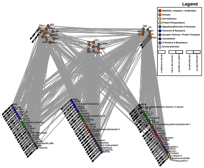
Cascade model



Capacity $\propto N^{2/3}$.

[Fusi et al. (2005)]

Synapses are complex



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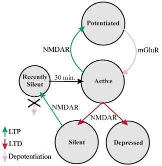

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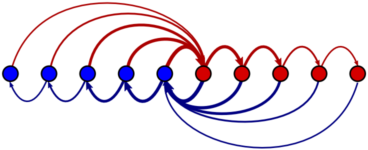


Capacity $\propto N^{2/3}$. [Fusi et al. (2005)]

Capacity $\propto N$. [Benna and Fusi (2016)]

My approach

We want to study the structure-function relationship of biological processes.

Not trying to build a *single* model.

Instead, we build a broad framework of models to find:

- $\rightarrow$ underlying mechanisms and principles.
- $\rightarrow$ trade-offs between aspects of performance (e.g. learning vs. memory).
- $\rightarrow$ properties of models that best manage these trade-offs.

Outline

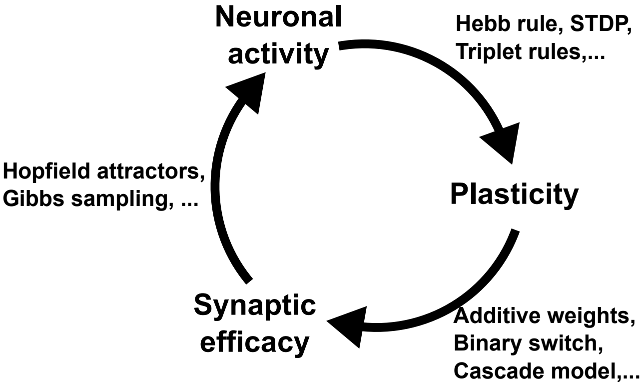
1. Memory over different timescales
   - Quantifying memory quality
   - Frontiers of memory
   - Implications of memory limits

Section 1

Memory over different timescales

"A memory frontier for complex synapses", S Lahiri and S Ganguli.
Adv. Neural Inf. Process. Syst. 26, pp. 1034–1042, (2013).
NeurIPS 2013 Outstanding Paper Award.

Synaptic learning and memory



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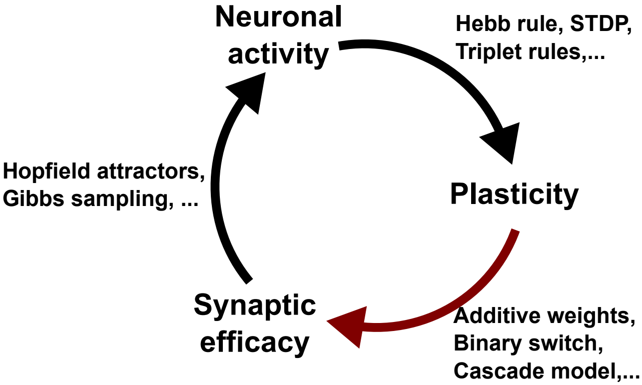
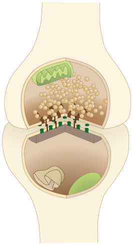


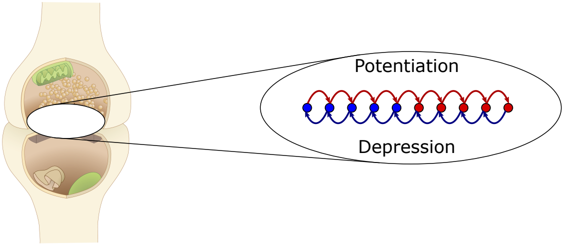
Models of complex synaptic dynamics



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)]
[Smith et al. (2006), Lahiri and Ganguli (2013)]

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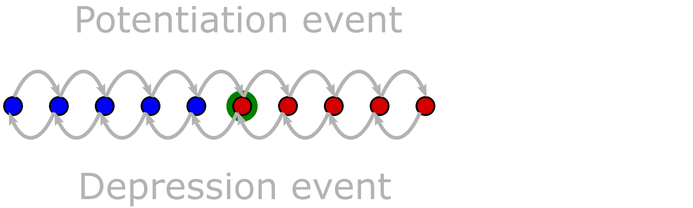

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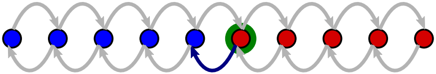
Potentiation event



Depression event

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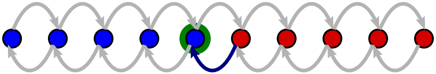

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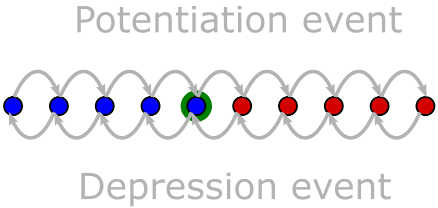

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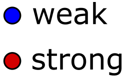

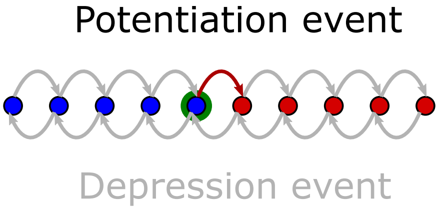

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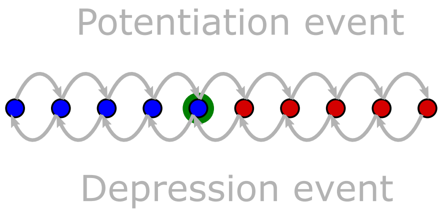

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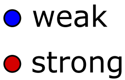

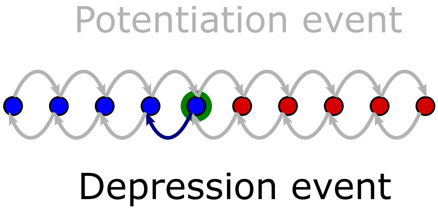

Metaplasticity: change propensity for plasticity
(independent of change in synaptic weight).

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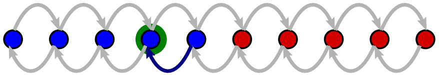

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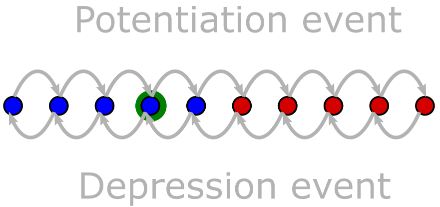

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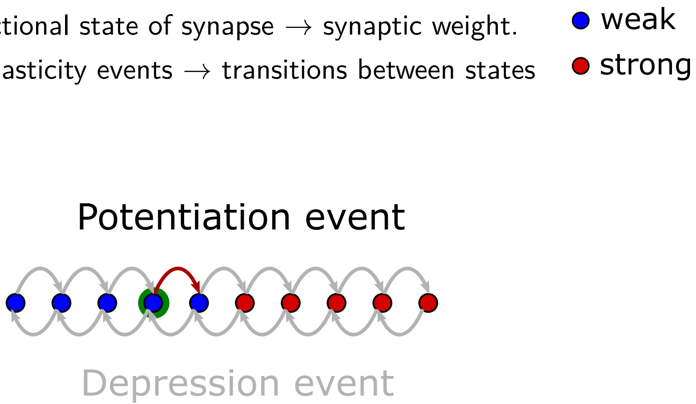

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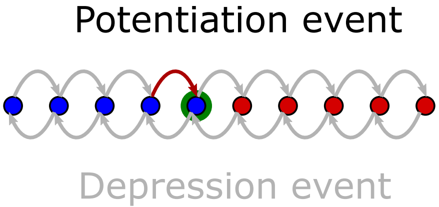

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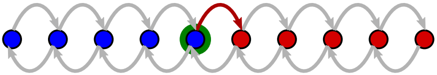

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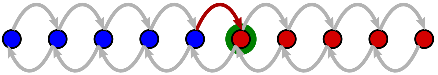

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Models of complex synaptic dynamics

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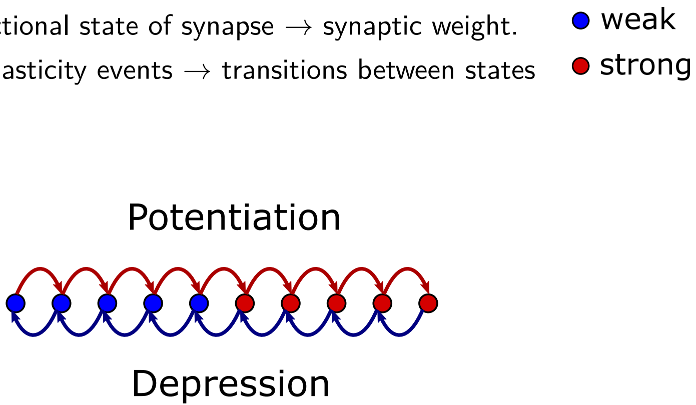

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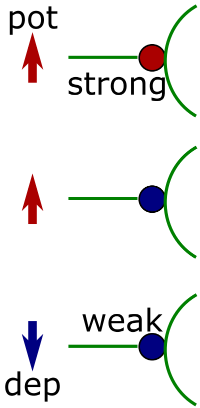
Synaptic memory curves



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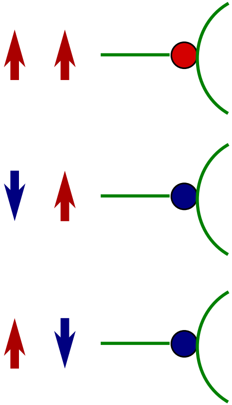

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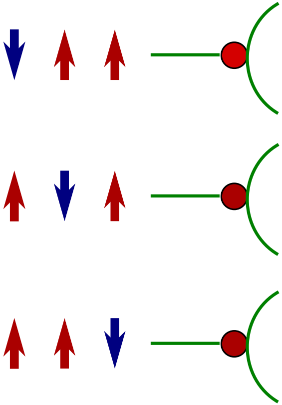

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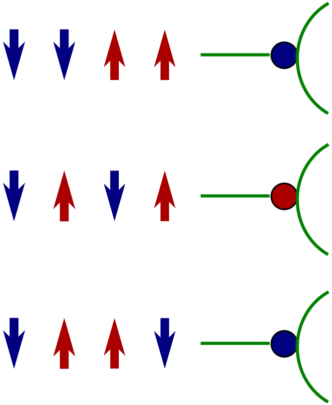

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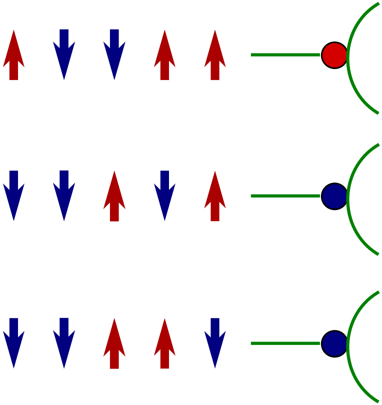

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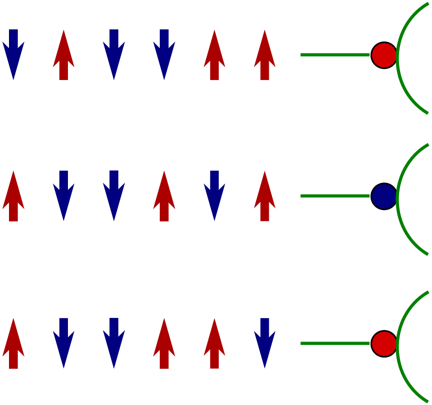

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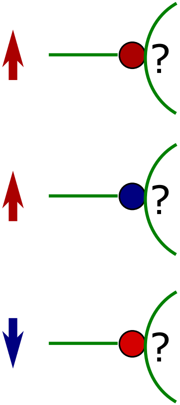

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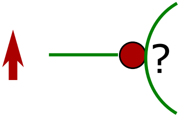
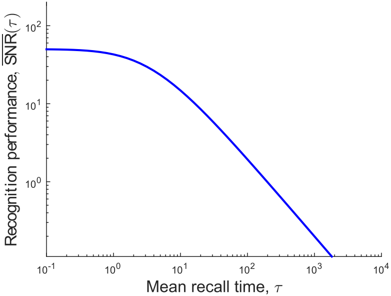


Recognition memory: has this pattern been seen before?
Performance described by SNR of $\vec{w}(t) \cdot \vec{w}_{\text{test}}$.

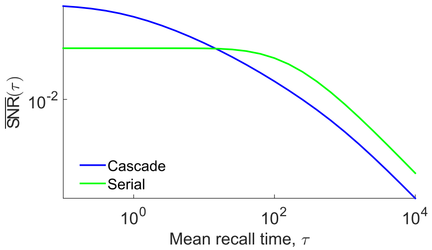


Specific models of complex synaptic dynamics

Two example models of complex synapses.

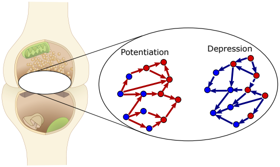
[Fusi et al. (2005), Leibold and Kempter (2008), Ben-Dayan Rubin and Fusi (2007)]

These have different memory storage properties

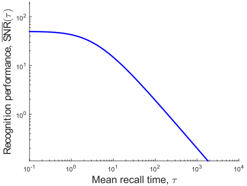


General principles relating structure and function?

Synaptic structure



Synaptic function

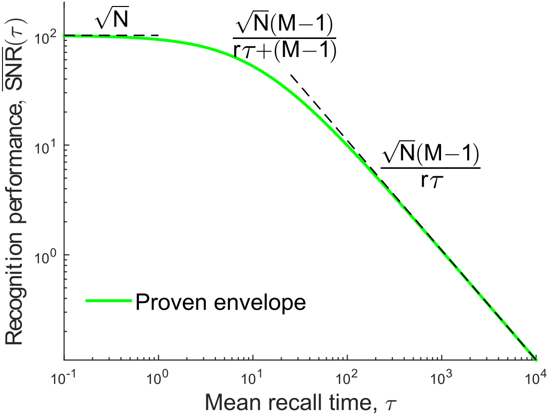


- What are the fundamental limits of memory?
- Which models achieve these limits?
- What are the theoretical principles behind the optimal models?

Proven envelope: memory frontier

Upper bound on memory curve at *any* timescale.

N: # synapses,
M: # states.



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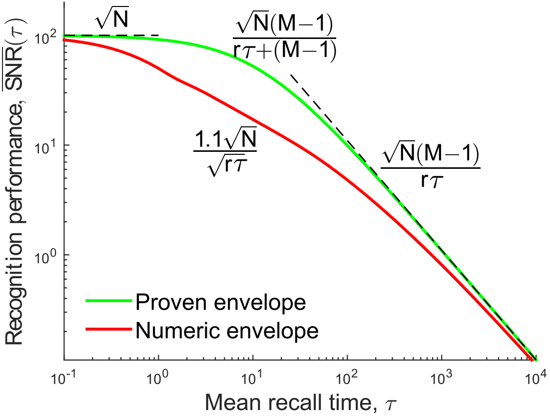
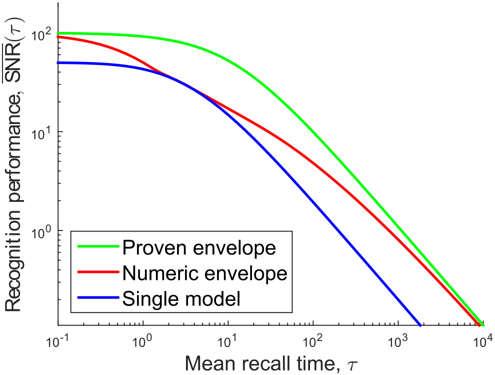
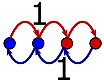


Models that maximise memory for one timescale





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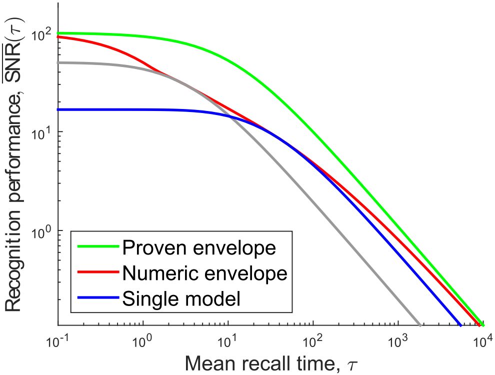

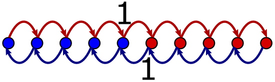

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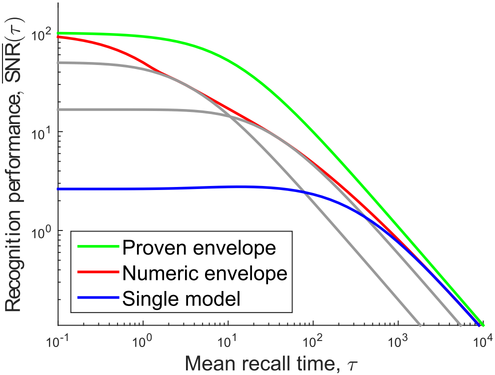
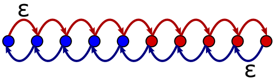
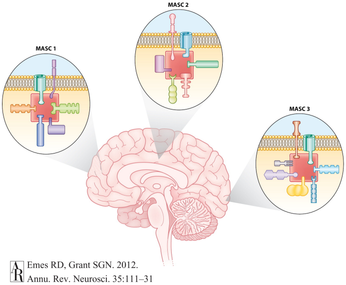




Synaptic diversity and timescales of memory

Different synapses have different molecular structures.



[Emes and Grant (2012)]

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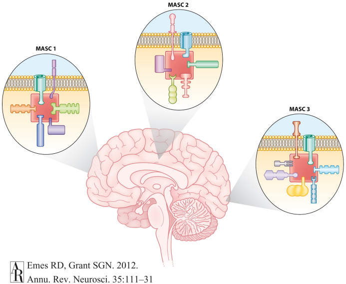
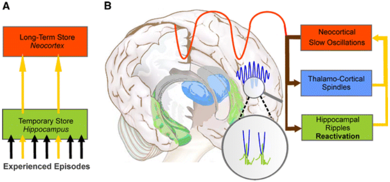


[Emes and Grant (2012)]

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)]

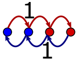
[Cooke et al. (2004)]

Synaptic structure and function: general principles

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

What can we conclude?

Short timescale $\longrightarrow$ Moderate timescale $\longrightarrow$ Long timescale



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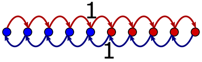

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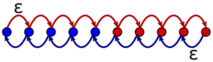

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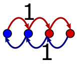
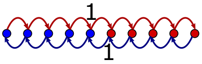
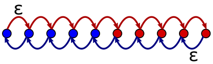
What can we conclude?

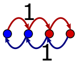
Short timescale	$\longrightarrow$	Moderate timescale	$\longrightarrow$	Long timescale
	$\longrightarrow$		$\longrightarrow$	
short topology	$\longrightarrow$	long topology		

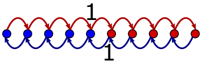
Synaptic structure and function: general principles

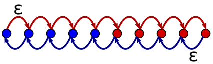
Real synapses limited by molecular building blocks.
Evolution had larger set of priorities.

What can we conclude?

Short timescale $\longrightarrow$ Moderate timescale $\longrightarrow$ Long timescale



$\longrightarrow$


$\longrightarrow$


short topology $\longrightarrow$ long topology

deterministic synapse $\longrightarrow$ stochastic synapse

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

Future directions

Learning and memory

- Experimental tests.
- Multiple presentations.
- Correlations.
- More realistic tasks.
- Relation to molecular structure?

Energy use in living systems

- Include space as well as time.
- Coarse graining: molecules $\to$ cells $\to$ systems.

High dimensional statistics

- Theory of noisy random projections.

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Summary

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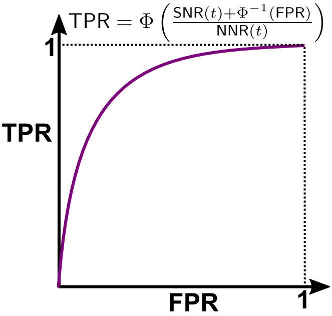
Quantifying memory quality

Test if $\vec{w}_{\text{ideal}} \cdot \vec{w}(t) \gtrless \theta$?

[Sommer and Dayan (1998)]



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

$$\overline{\text{SNR}}(\tau) = \int \mathrm{d}\tau \, \frac{\mathrm{e}^{-t/\tau}}{\tau} \, \text{SNR}(t).$$

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

Also: KL divergence, Chernoff distance, . . .

Parameters for synaptic dynamics

$$f^{\text{pot/dep}} = \text{fraction of events that are pot/dep},$$

pot. event: $M_{ij}^{\text{pot}} = \text{transition prob. } i \to j,$ $\qquad \mathbf{W}^{\text{pot}} = f^{\text{pot}}(\mathbf{M}^{\text{pot}} - I),$

dep. event: $M_{ij}^{\text{dep}} = \text{transition prob. } i \to j,$ $\qquad \mathbf{W}^{\text{dep}} = f^{\text{dep}}\big(\mathbf{M}^{\text{dep}} - I\big).$

Constraints:

$$f^{\text{pot/dep}}, \mathbf{M}_{ij}^{\text{pot/dep}} \in [0,1], \qquad f^{\text{pot}} + f^{\text{dep}} = \sum_j \mathbf{M}_{ij}^{\text{pot/dep}} = 1.$$

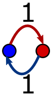
Memory curve given by

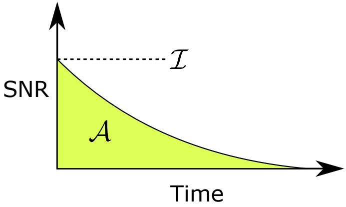
$$\begin{aligned} \overline{\text{SNR}}(\tau) &= \sqrt{N}\, \boldsymbol{\pi} \left(\mathbf{W}^{\text{pot}} - \mathbf{W}^{\text{dep}}\right) \left[\mathbf{I} - r\tau \left(\mathbf{W}^{\text{pot}} + \mathbf{W}^{\text{dep}}\right)\right]^{-1} \mathbf{w}. \\ &= \sqrt{N} \sum_a \frac{\mathcal{I}_a}{1 + r\tau/\tau_a}. \end{aligned}$$

Upper bounds on measures of memory

Initial SNR:

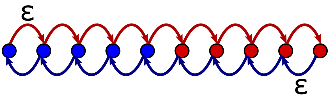
$$\mathcal{I} = \mathrm{SNR}(0) = \sum_a \mathcal{I}_a \leq \sqrt{N}.$$





Area under curve:

$$\mathcal{A} = \int_0^\infty \mathrm{SNR}(t)\,\mathrm{d}t = \sum_a \mathcal{I}_a \tau_a \leq \sqrt{N}(M-1)/r.$$



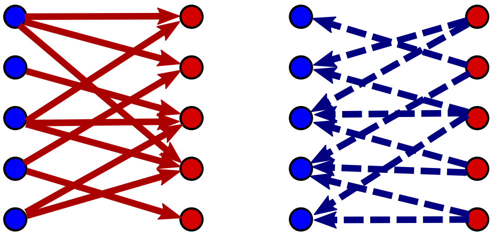
[Lahiri and Ganguli (2013)]

Initial SNR as flux

Initial SNR is closely related to flux between strong & weak states

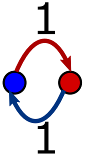
$$\mathrm{SNR}(0) \leq \frac{4\sqrt{N}}{r}\,\boldsymbol{\Phi}_{-+}.$$

Max when potentiation guarantees $\mathbf{w} \to +1$,
depression guarantees $\mathbf{w} \to -1$.



Two-state model

Two-state model equivalent to previous slide:

Transitions: 

$$\implies \mathrm{SNR}(t) = \sqrt{N}\,(4f^{\mathrm{pot}}f^{\mathrm{dep}})\,\mathrm{e}^{-rt}.$$

Maximal initial SNR:

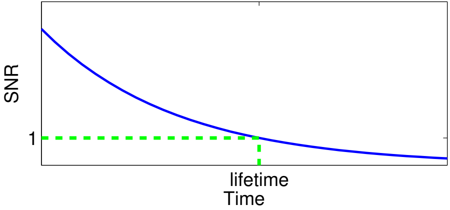
$$\mathrm{SNR}(0) \le \sqrt{N}.$$

Area under memory curve

$$\mathcal{A} = \int_0^\infty \mathrm{d}t\ \mathrm{SNR}(t), \qquad \overline{\mathrm{SNR}}(\tau) \to \frac{\mathcal{A}}{\tau} \quad \text{as} \quad \tau \to \infty.$$

Area bounds memory lifetime:

$$\mathrm{SNR}(\text{lifetime}) = 1$$
$$\implies \quad \text{lifetime} < \mathcal{A}.$$



This area has an upper bound:

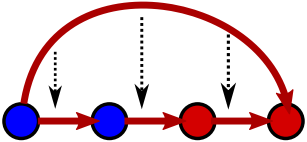
$$\mathcal{A} \leq \sqrt{N}(M-1)/r.$$

Saturated by a model with linear chain topology.

Proof of area bound

For any model, we can construct perturbations that

- preserve equilibrium distribution,
- increase area.



details

e.g. decrease "shortcut" transitions, increase bypassed "direct" ones.
Endpoint: linear chain

The area of this model is

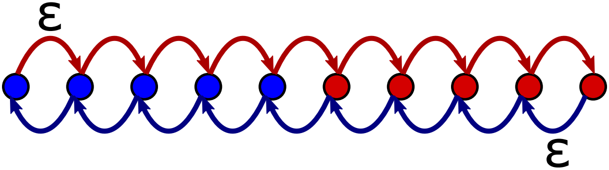
$$A = \frac{2\sqrt{N}}{r} \sum_k \pi_k \left| k - \langle k \rangle \right| .$$

Max: equilibrium probability distribution concentrated at both ends.

[Barrett and van Rossum (2008)]

Saturating model

Make end states "sticky"



Has long decay time, but terrible initial SNR.

$$\lim_{\varepsilon \to 0} A = \sqrt{N}(M-1)/r.$$

Technical detail: ordering states

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

$$\eta = \sum_j \mathbf{T}_{ij} \boldsymbol{\pi}_j,$$

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

[Kemeny and Snell (1960)]

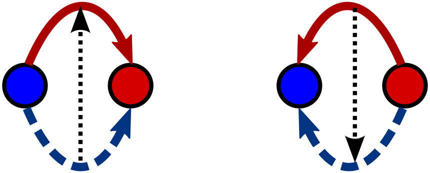
We define:

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

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

Technical detail: upper/lower triangular

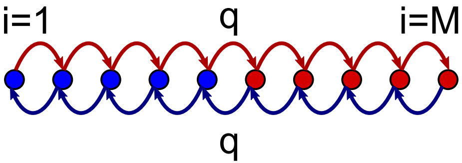
With states in order:



Endpoint: potentiation goes right, depression goes left.

back

Intuition for using topology



$$\mathcal{I} \propto q, \qquad \max_a \tau_a \propto \frac{1}{q},$$

$$\mathcal{I} \propto \frac{1}{M}, \qquad \max_a \tau_a \propto M^2,$$

$$\Longrightarrow$$

Stochasticity: $\mathcal{I} \propto \dfrac{1}{\tau_{\text{max}}}$,

Topology: $\mathcal{I} \propto \dfrac{1}{\sqrt{\tau_{\text{max}}}}$.

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