

Optimal synaptic strategies for different timescales of memory

Subhaneil Lahiri and Surya Ganguli

Stanford University, Applied Physics

February 26, 2016

What is a synapse?

What is a synapse?

Theorists

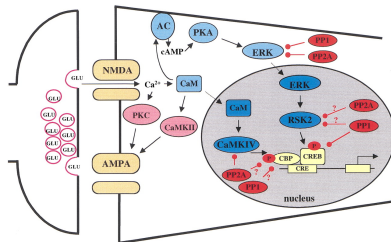
$$W_{ij}$$

What is a synapse?

Theorists

$$W_{ij}$$

Experimentalists



[Klann (2002)]

Storage capacity of synaptic memory

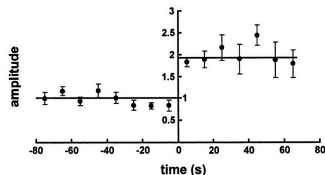
Hopfield, perceptron have capacity $\propto N$, ($\#$ synapses).

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)]

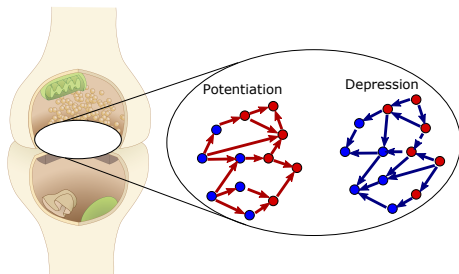
New memories overwrite old \implies stability-plasticity dilemma.

Models of complex synaptic dynamics



Models of complex synaptic dynamics

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

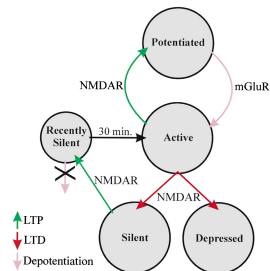
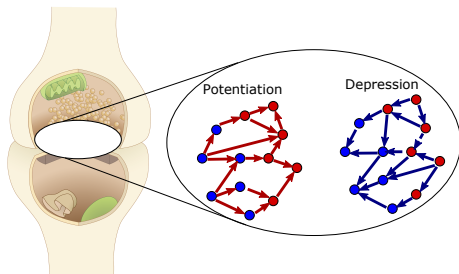


States: #AMPA, #NMDAR, NMDAR subunit composition,
CaMK II autophosphorylation, activating PKC, p38 MAPK,...

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

Models of complex synaptic dynamics

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



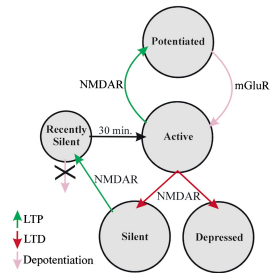
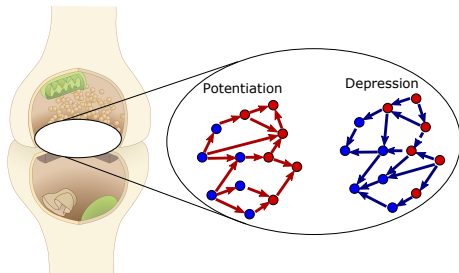
[Montgomery and Madison (2002)]

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

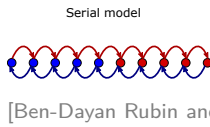
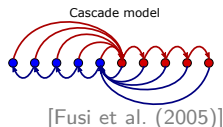
[Fusi et al. (2005), Fusi and Abbott (2007), Barrett and van Rossum (2008)]

Models of complex synaptic dynamics

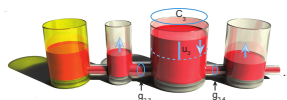
- Internal functional state of synapse \rightarrow synaptic weight. ● weak ● strong
- Candidate plasticity events \rightarrow transitions between states ● strong



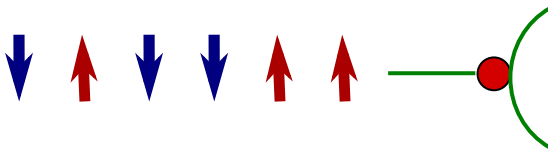
[Montgomery and Madison (2002)]



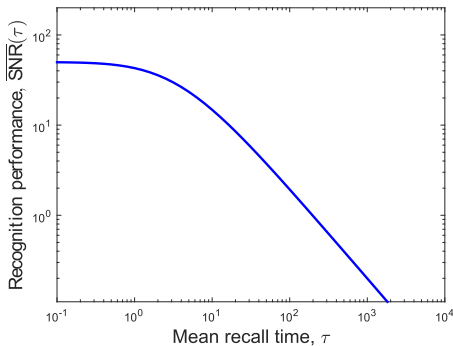
Leibold and Kempter (2008)]



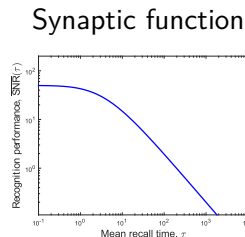
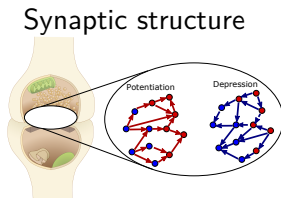
Synaptic memory curves



Synapses store a sequence of memories.



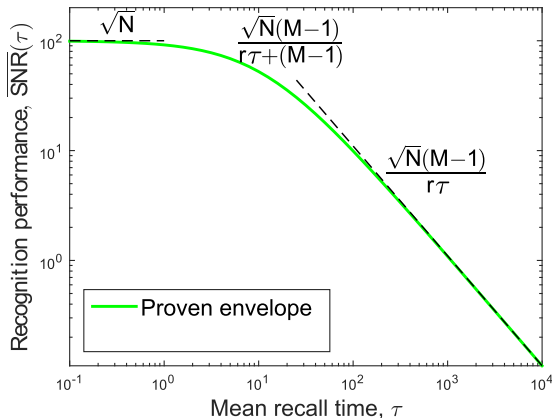
General principles relating structure and function?



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

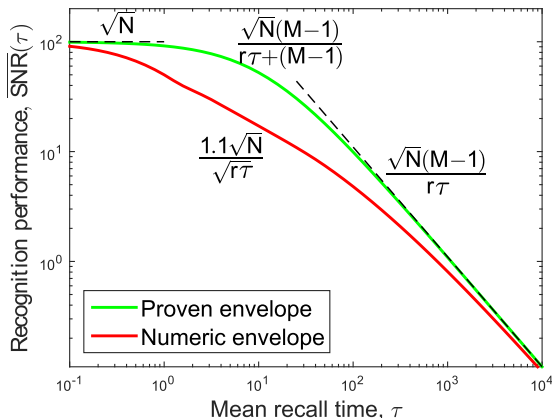
Proven envelope: memory frontier

Upper bound on memory curve at *any* timescale.

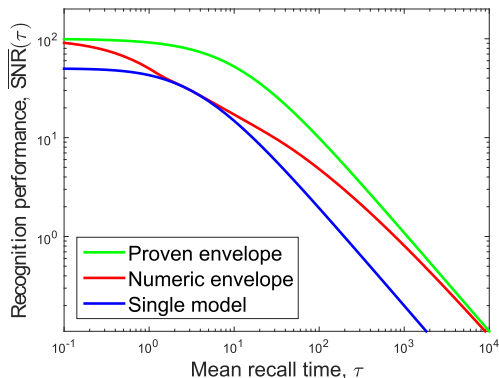


Proven envelope: memory frontier

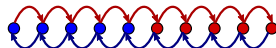
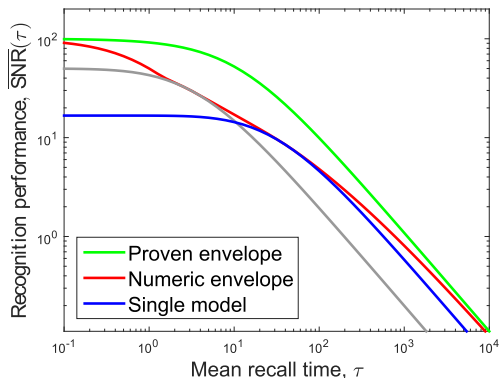
Upper bound on memory curve at *any* timescale.



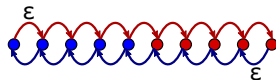
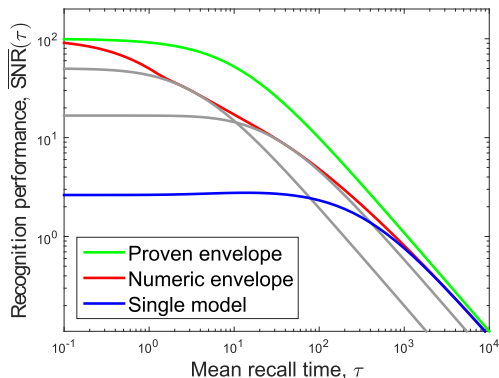
Models that maximize memory for one timescale



Models that maximize memory for one timescale

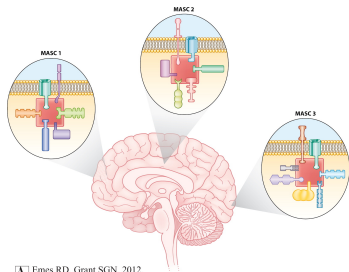


Models that maximize memory for one timescale



Synaptic diversity and timescales of memory

Different synapses have different molecular structures.

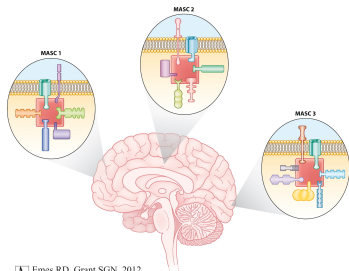


Emes RD, Grant SGN, 2012.
Annu. Rev. Neurosci. 35:111–31

[Emes and Grant (2012)]

Synaptic diversity and timescales of memory

Different synapses have different molecular structures.



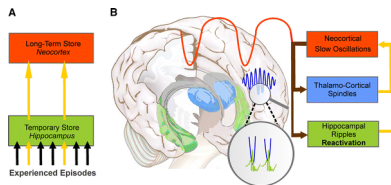
Emes RD, Grant SGN. 2012.
Annu. Rev. Neurosci. 35:111–31

[Emes and Grant (2012)]

Memories stored in different places for different timescales

[Squire and Alvarez (1995)]

[McClelland et al. (1995)]



[Born and Wilhelm (2012)]

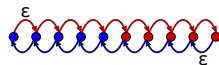
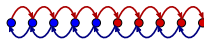
Also: Cerebellar cortex → nuclei.

[Attwell et al. (2002)]

[Cooke et al. (2004)]

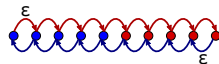
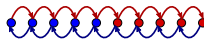
Synaptic structure and function: general principles

Short timescale \longrightarrow Intermediate timescale \longrightarrow Long timescale



Synaptic structure and function: general principles

Short timescale \longrightarrow Intermediate timescale \longrightarrow Long timescale



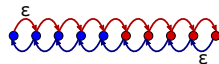
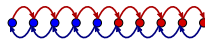
short topology



long topology

Synaptic structure and function: general principles

Short timescale \longrightarrow Intermediate timescale \longrightarrow Long timescale



short topology



long topology

deterministic synapse



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

Acknowledgements

Thanks to:

- **Surya Ganguli**
- Stefano Fusi
- Marcus Benna
- David Sussillo
- Jascha Sohl-Dickstein

Funding:

- Swartz foundation
- Stanford Bio-X
- Genentech

References I



Eric Klann.

“Metaplastic Protein Phosphatases”.

Learning and Memory, 9(4):153–155, (2002) ,
<http://learnmem.cshlp.org/content/9/4/153.full.pdf+html>.

2

3

4



D. J. Amit and S. Fusi.

“Constraints on learning in dynamic synapses”.

Network: Computation in Neural Systems, 3(4):443–464, (1992) .

5



D. J. Amit and S. Fusi.

“Learning in neural networks with material synapses”.

Neural Computation, 6(5):957–982, (1994) .

5

References II



Carl C. H. Petersen, Robert C. Malenka, Roger A. Nicoll, and John J. Hopfield.

“All-or-none potentiation at CA3-CA1 synapses”.

Proc. Natl. Acad. Sci. U.S.A., 95(8):4732–4737, (1998) .

5



Daniel H. O'Connor, Gayle M. Wittenberg, and Samuel S.-H. Wang.

“Graded bidirectional synaptic plasticity is composed of switch-like unitary events”.

Proc. Natl. Acad. Sci. U.S.A., 102(27):9679–9684, (2005) .

5

References III



Johanna M. Montgomery and Daniel V. Madison.

“State-Dependent Heterogeneity in Synaptic Depression between Pyramidal Cell Pairs”.

Neuron, 33(5):765 – 777, (2002) .

6 7 8 9



S. Fusi, P. J. Drew, and L. F. Abbott.

“Cascade models of synaptically stored memories”.

Neuron, 45(4):599–611, (Feb, 2005) .

7 8 9



S. Fusi and L. F. Abbott.

“Limits on the memory storage capacity of bounded synapses”.

Nat. Neurosci., 10(4):485–493, (Apr, 2007) .

7 8

References IV



A. B. Barrett and M. C. van Rossum.

“Optimal learning rules for discrete synapses”.

PLoS Comput. Biol., 4(11):e1000230, (Nov, 2008) .

7

8



Daniel D Ben-Dayan Rubin and Stefano Fusi.

“Long memory lifetimes require complex synapses and limited sparseness”.

Frontiers in computational neuroscience, 1(November):1–14, (2007) .

9



Christian Leibold and Richard Kempter.

“Sparseness Constrains the Prolongation of Memory Lifetime via Synaptic Metaplasticity”.

Cerebral Cortex, 18(1):67–77, (2008) .

9

References V



Marcus K. Benna and Stefano Fusi.

“Computational principles of biological memory”.

(2015) , [arXiv:1507.07580 \[q-bio.NC\]](#).

9



Richard D. Emes and Seth G.N. Grant.

“Evolution of Synapse Complexity and Diversity”.

Annual Review of Neuroscience, 35(1):111–131, (2012) .

17

18



Larry R Squire and Pablo Alvarez.

“Retrograde amnesia and memory consolidation: a neurobiological perspective”.

Current Opinion in Neurobiology, 5(2):169–177, (April, 1995) .

17

18

References VI



James L McClelland, Bruce L McNaughton, and Randall C O'Reilly.

“Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory.”, 1995.

17

18



Jan Born and Ines Wilhelm.

“System consolidation of memory during sleep.”.

Psychological research, 76(2):192–203, (mar, 2012) .

17

18



Phillip J.E. Attwell, Samuel F. Cooke, and Christopher H. Yeo.

“Cerebellar Function in Consolidation of a Motor Memory”.

Neuron, 34(6):1011–1020, (jun, 2002) .

17

18



Samuel F Cooke, Phillip J E Attwell, and Christopher H Yeo.

“Temporal properties of cerebellar-dependent memory consolidation.”.

The Journal of neuroscience : the official journal of the Society for Neuroscience, 24(12):2934–41, (mar, 2004) .

17

18



J.G. Kemeny and J.L. Snell.

Finite markov chains.

Springer, 1960.