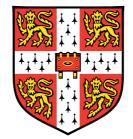
COMPUTATIONAL MODELLING OF SYNAPTIC FUNCTION

MÁTÉ LENGYEL

Computational and Biological Learning Lab Department of Engineering University of Cambridge



COMPUTATIONAL MODELLING OF SYNAPTIC PLASTICITY

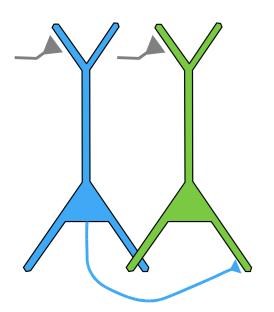
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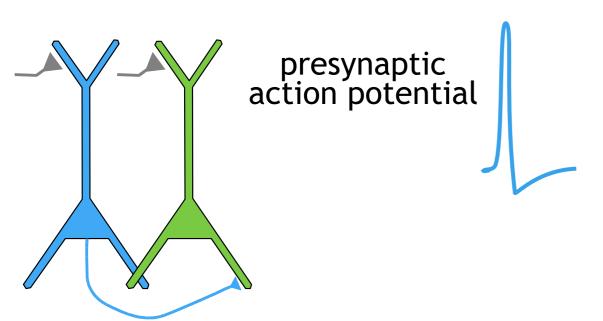


Synapses are computational devices that not only transmit action potential-encoded information, but also transform it. Neuronal information is often encoded by bursts or trains of action potentials. Synapses process such action potential bursts or trains in a synapsespecific manner that involves use-dependent changes in neurotransmitter release during the burst or train (referred to as short-term plasticity). In addition, synapses experience usedependent long-term changes in synaptic transmission that adjust the "gain" of a synapse, and operate either pre- and/or postsynaptically (referred to as long-term plasticity)

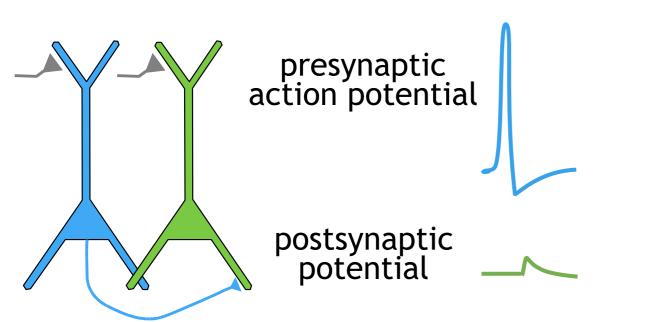
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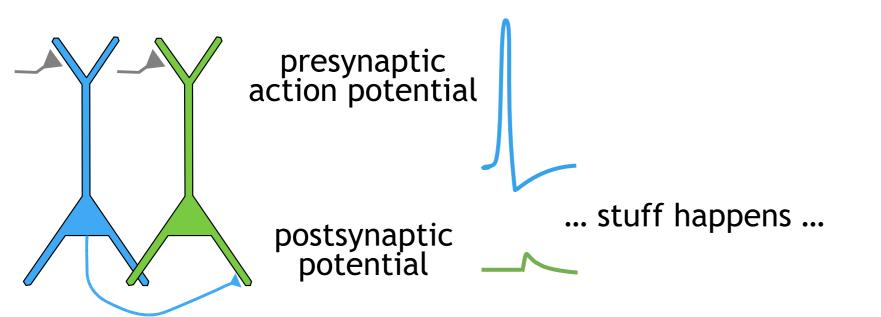
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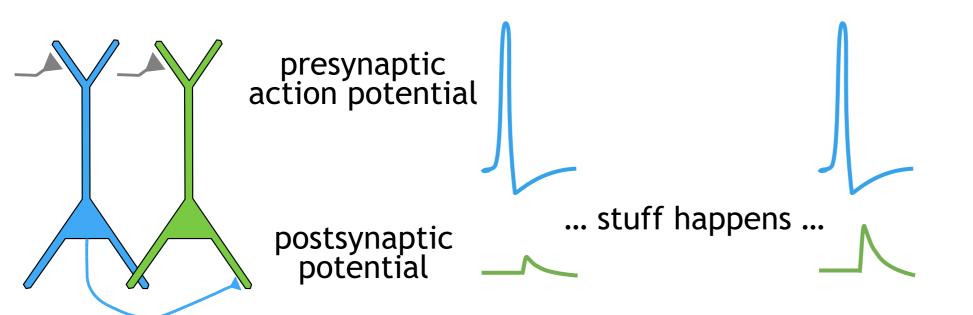
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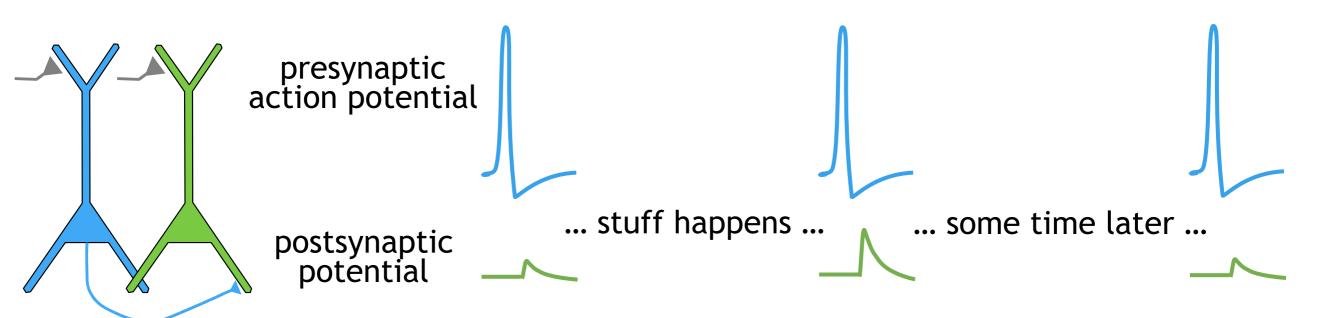
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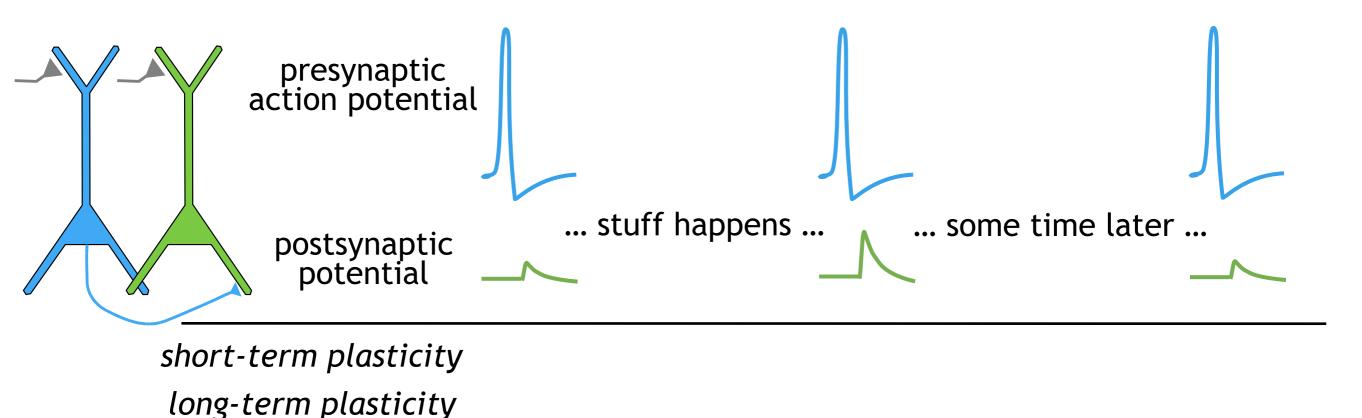
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Südhof, 2012

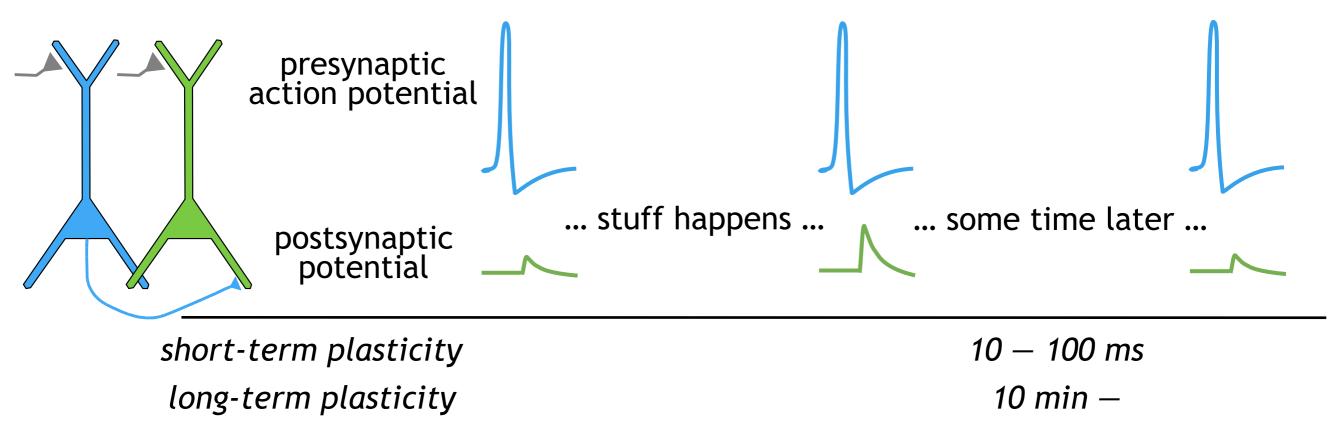
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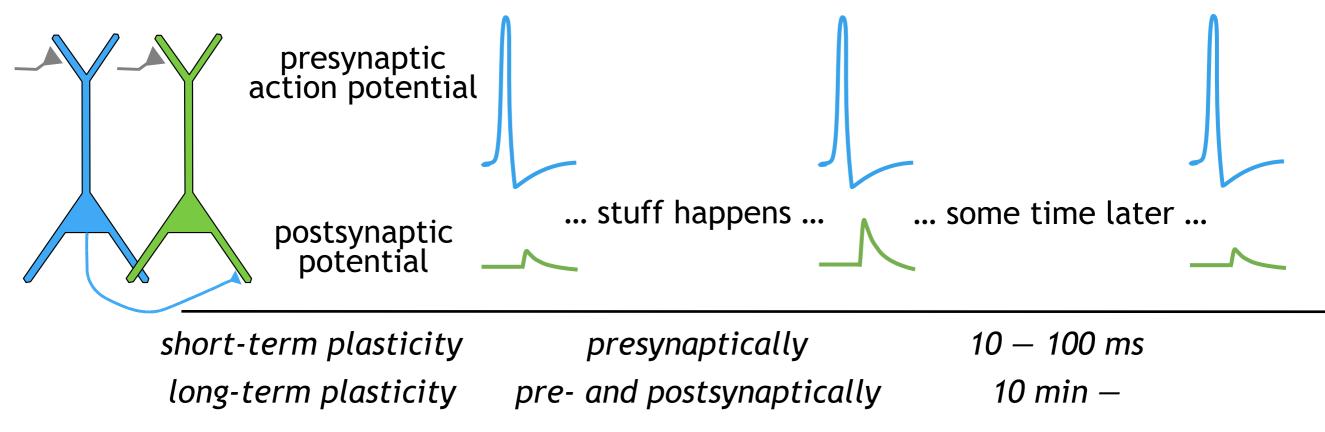
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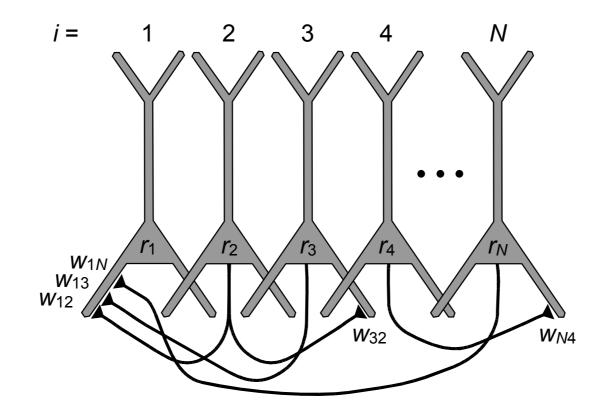
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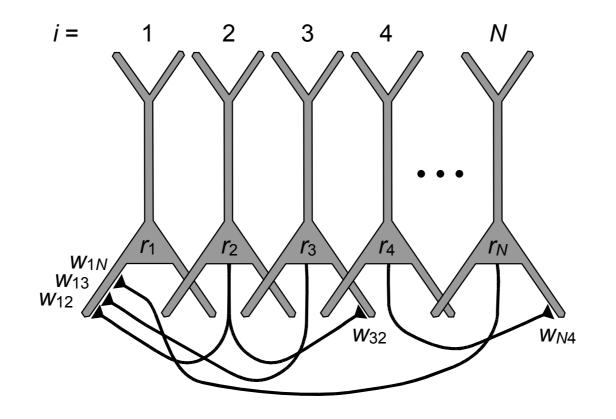
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COMPUTATION: BETWEEN CIRCUITS AND BEHAVIOUR



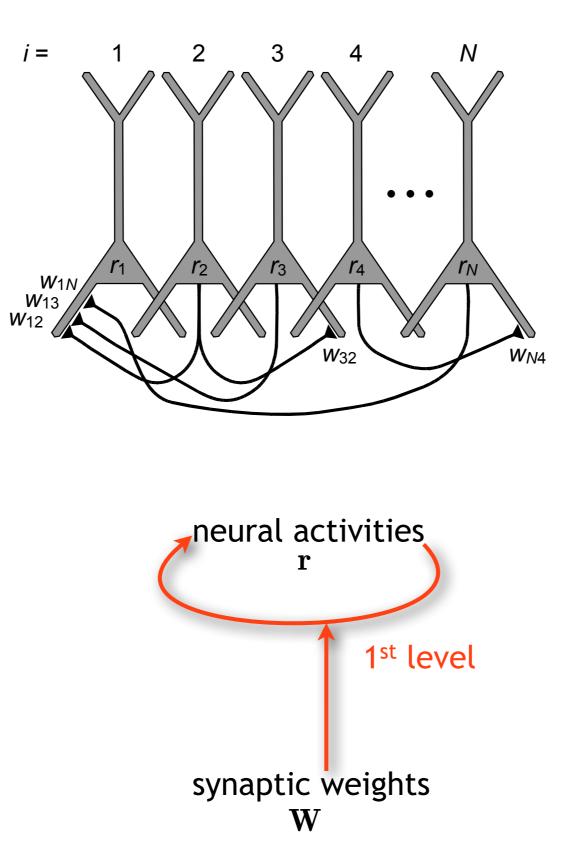
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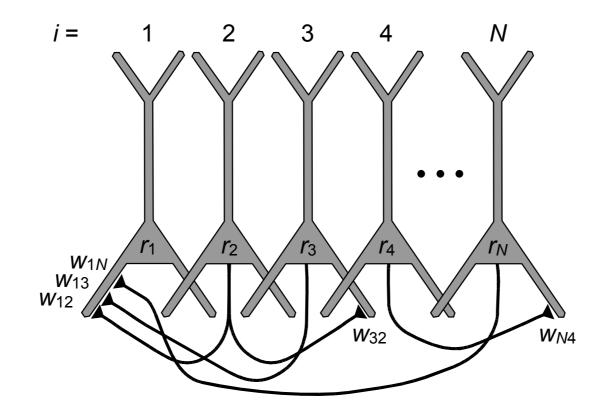


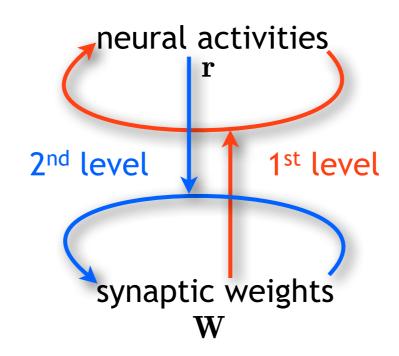


neural activities r

synaptic weights W







AUTOASSOCIATIVE MEMORY: AN EXAMPLE



I raised to my lips a spoonful of the tea in which I had soaked a morsel of the cake. ... And suddenly the memory returns. The taste was that of the little crumb of madeleine which on Sunday mornings at Combray, when I went to say good day to her in her bedroom, my aunt Léonie used to give me, dipping it first in her own cup of real or of lime-flower tea.

Marcel Proust: À la recherche du temps perdu

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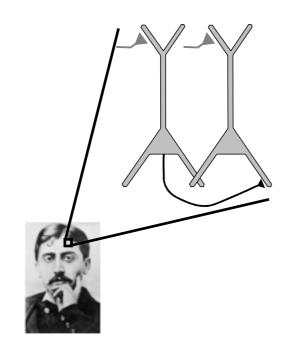
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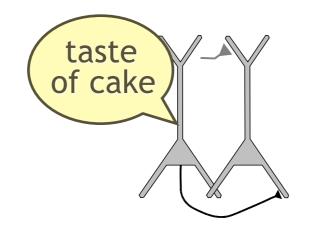
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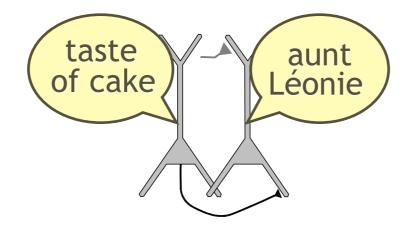
HOW DOES THIS HAPPEN?

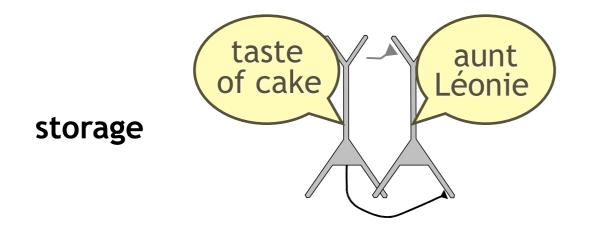


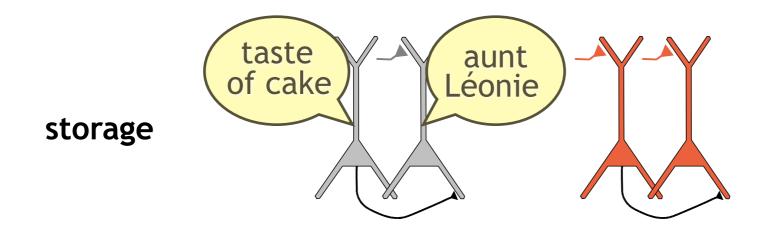


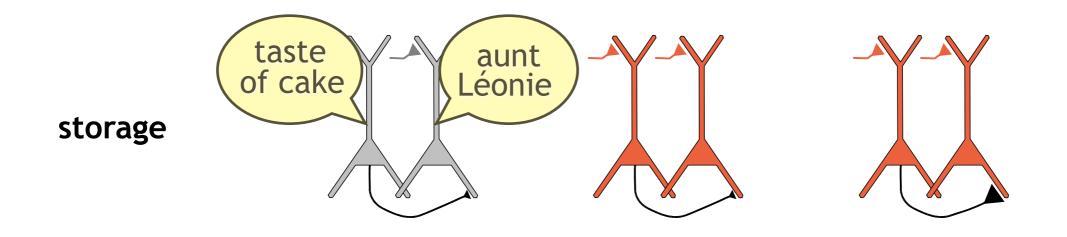




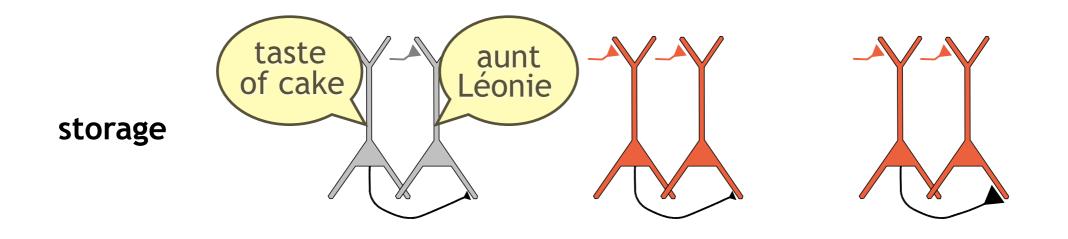




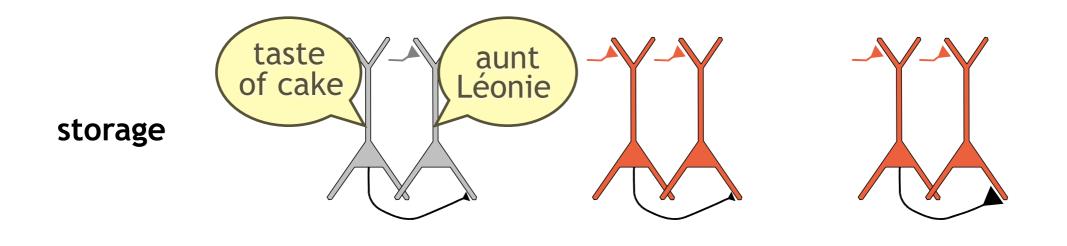




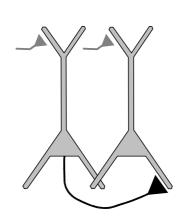
the Hebbian paradigm

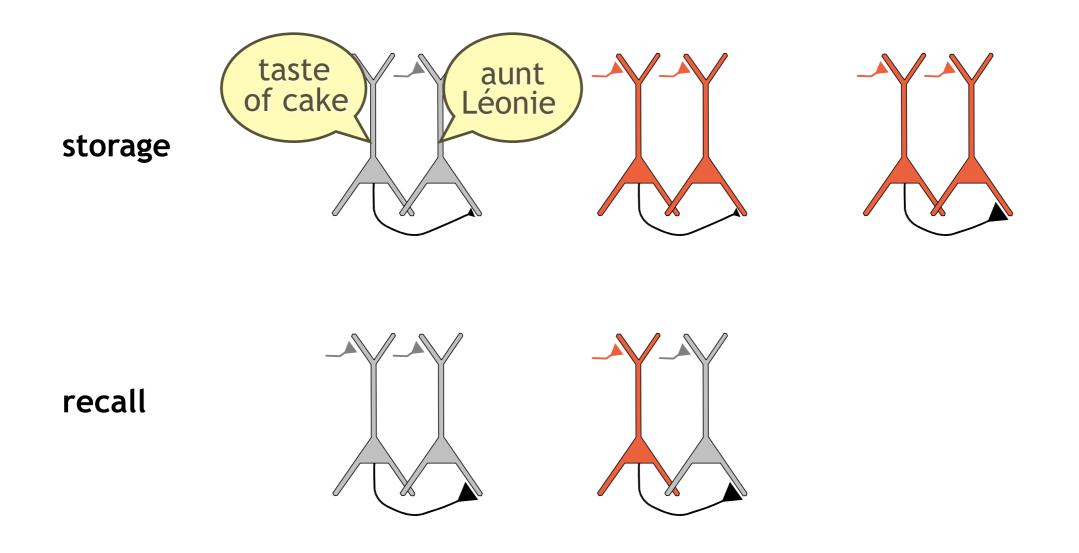


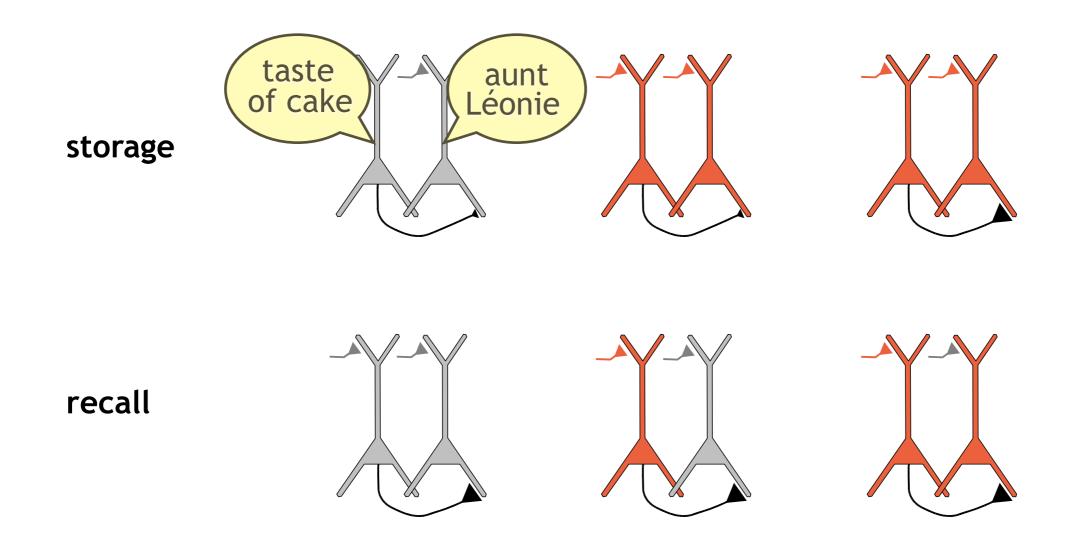
recall



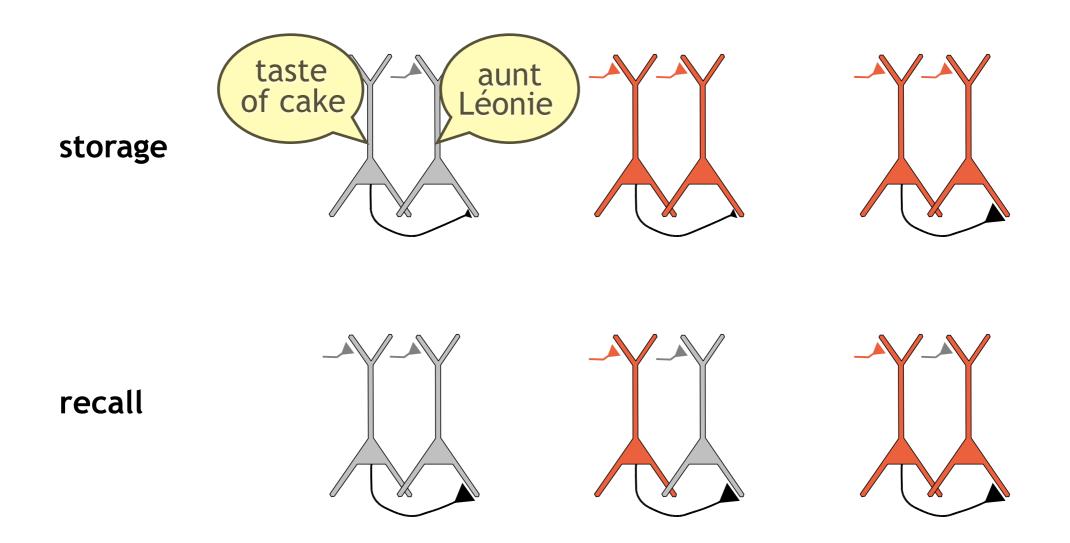




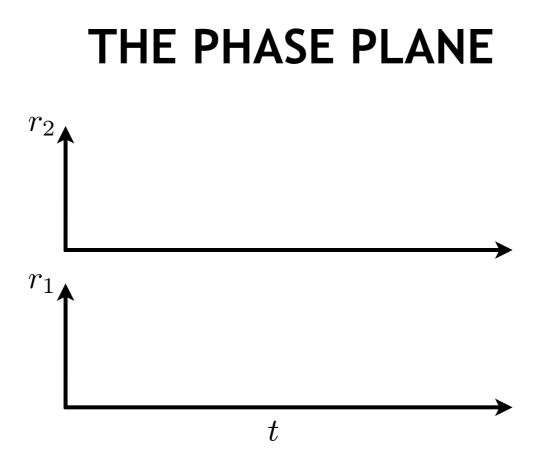


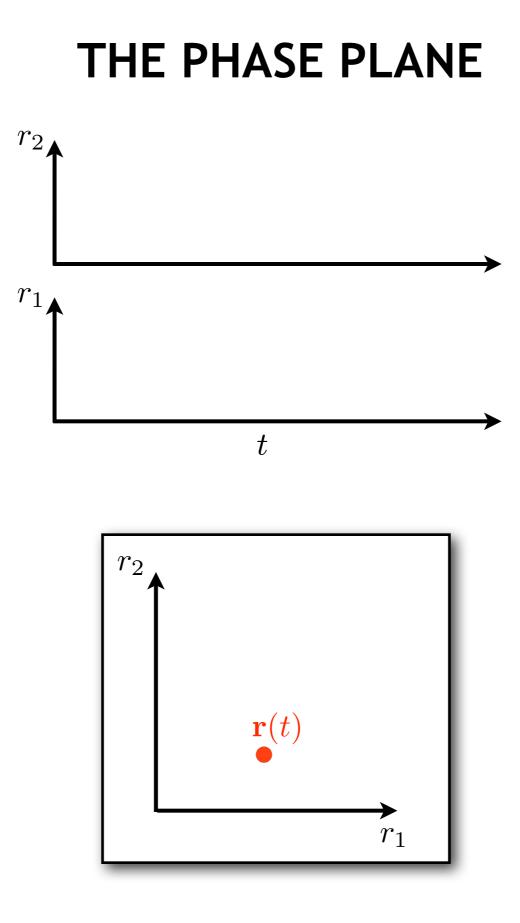


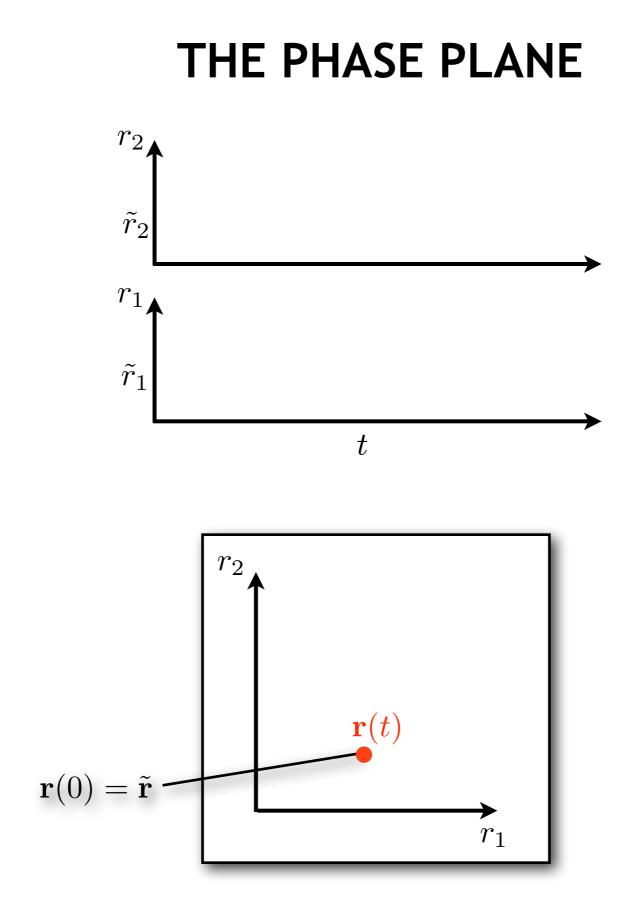
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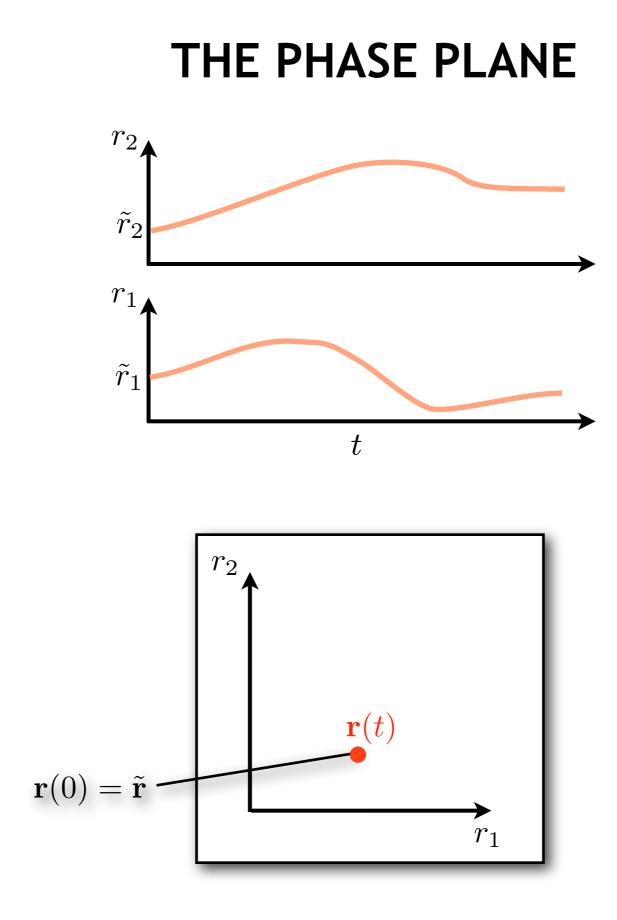
how does this work for **distributed representations**, without assuming aunt Léonie grandmother neurons ?

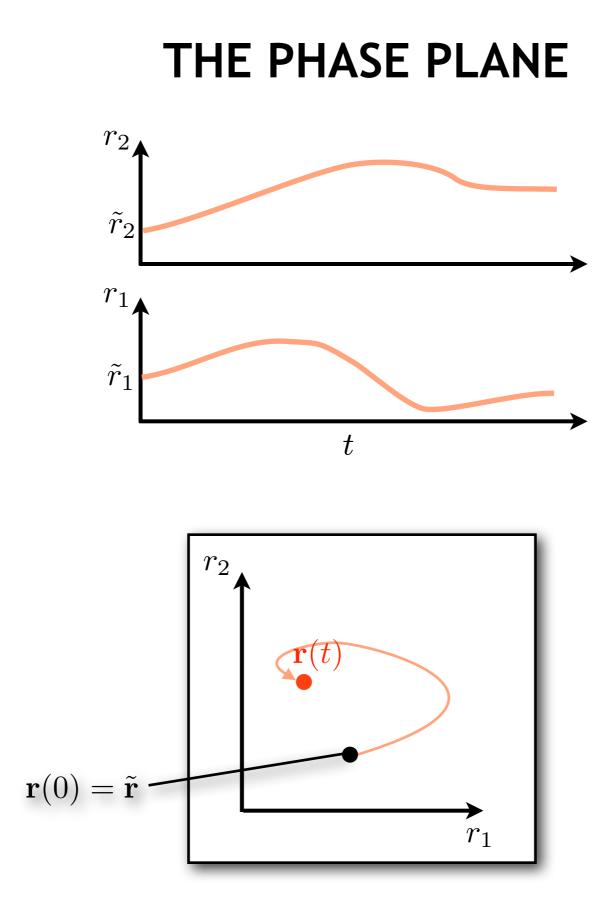




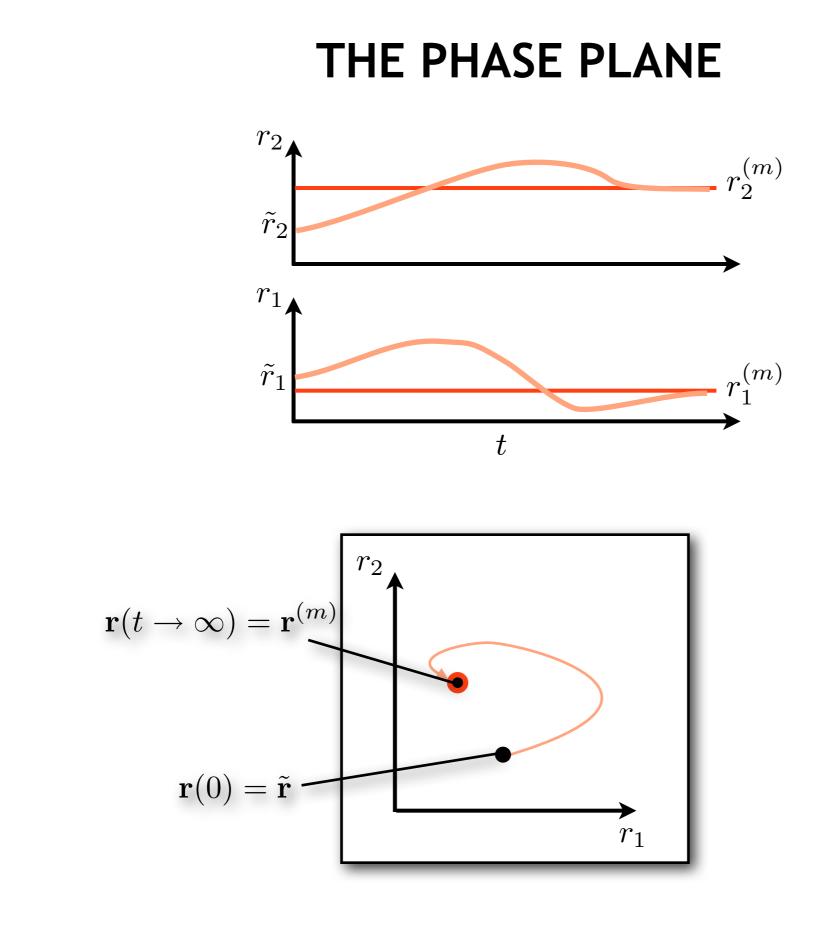


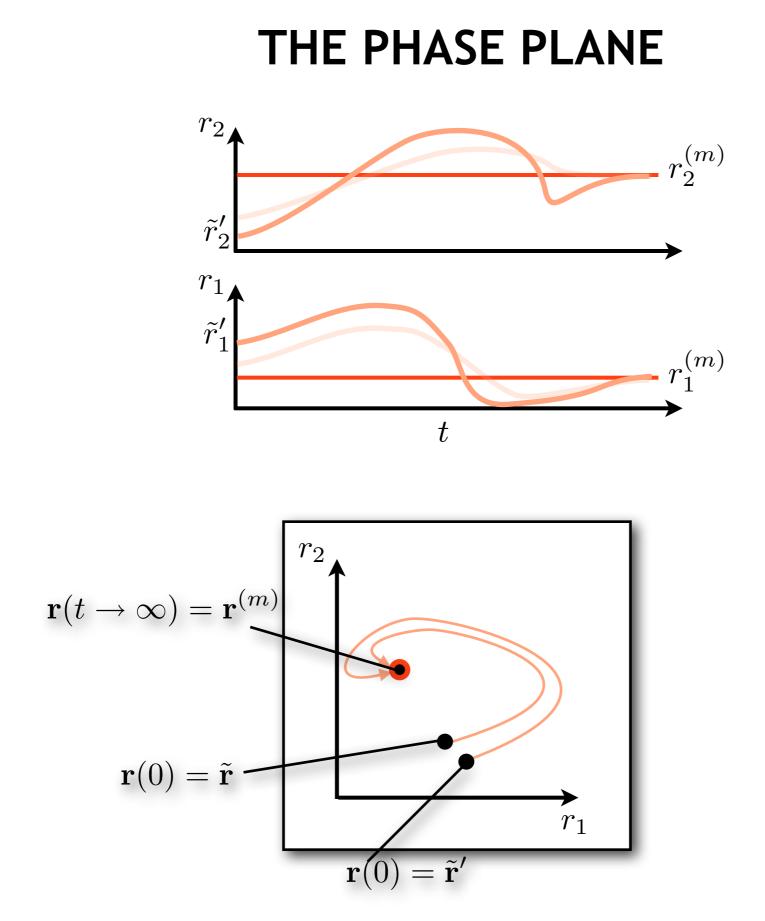
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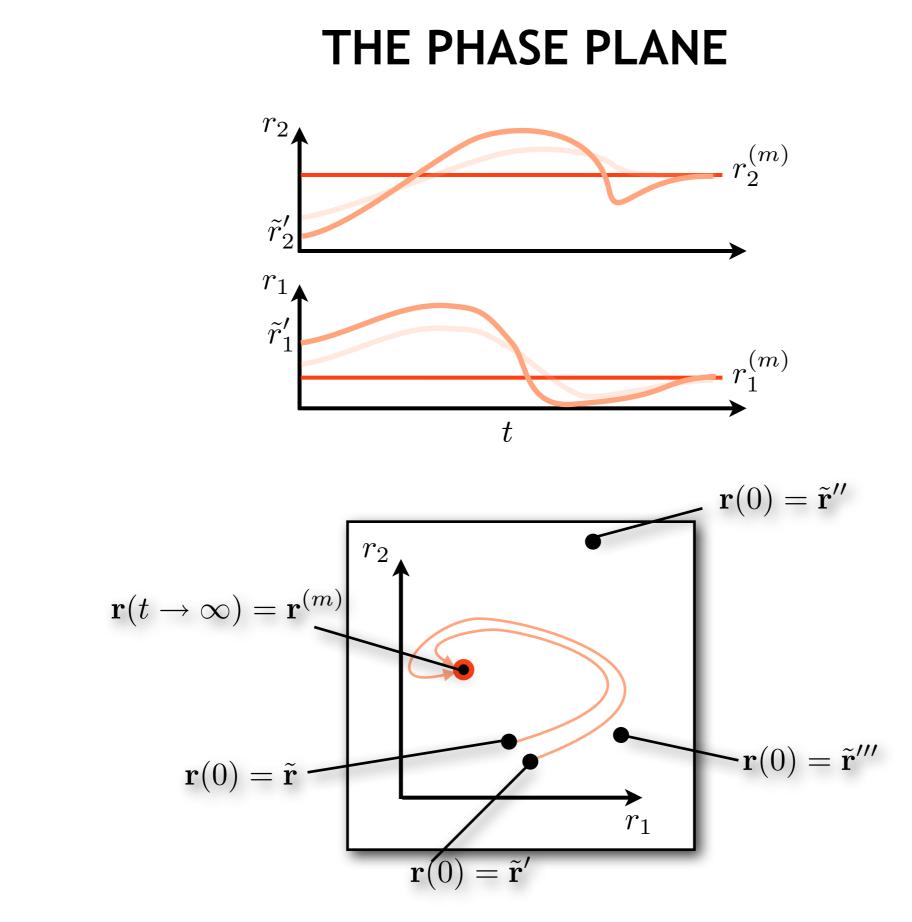


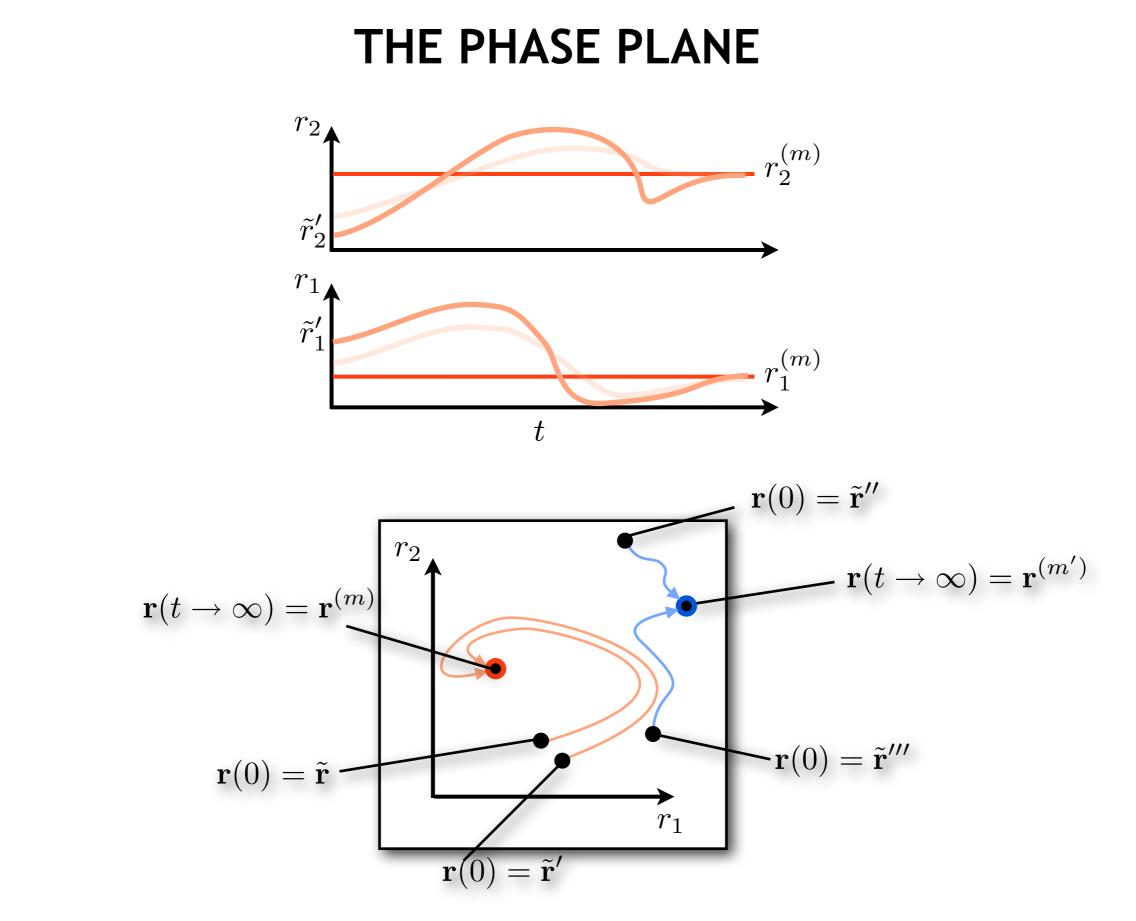


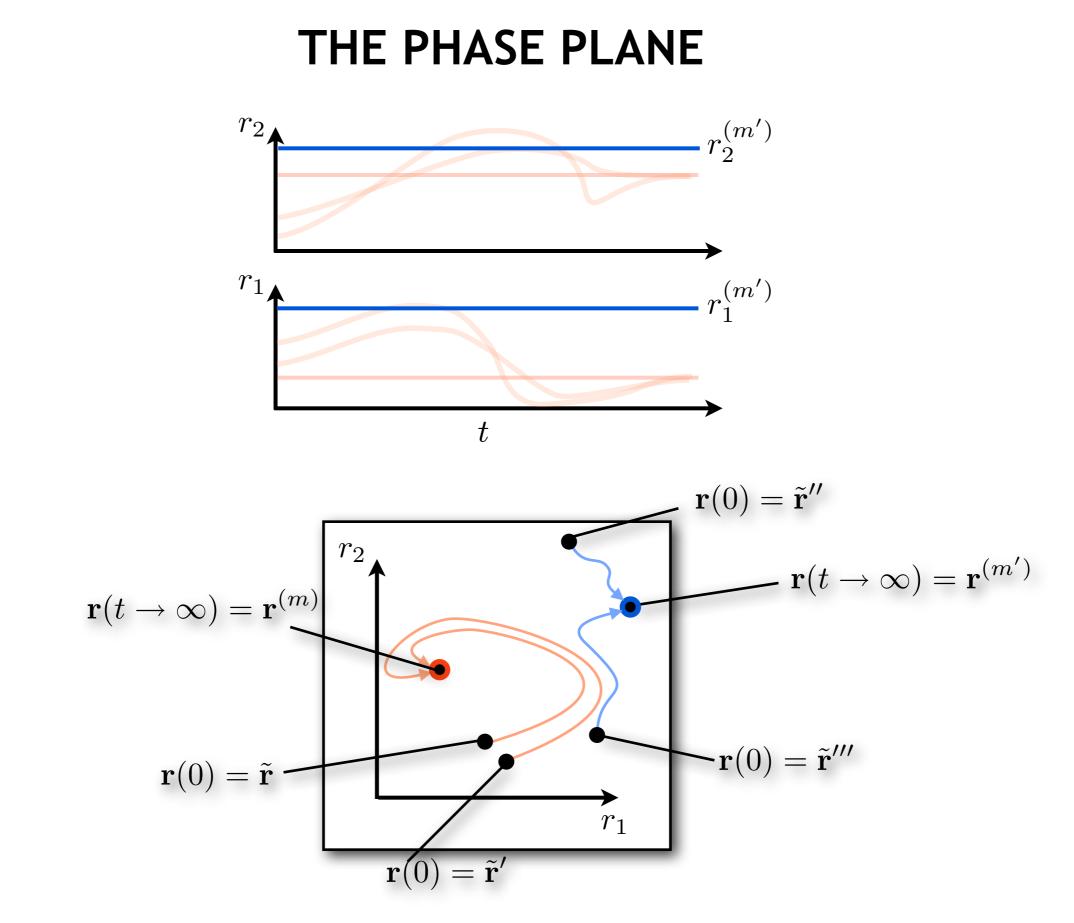
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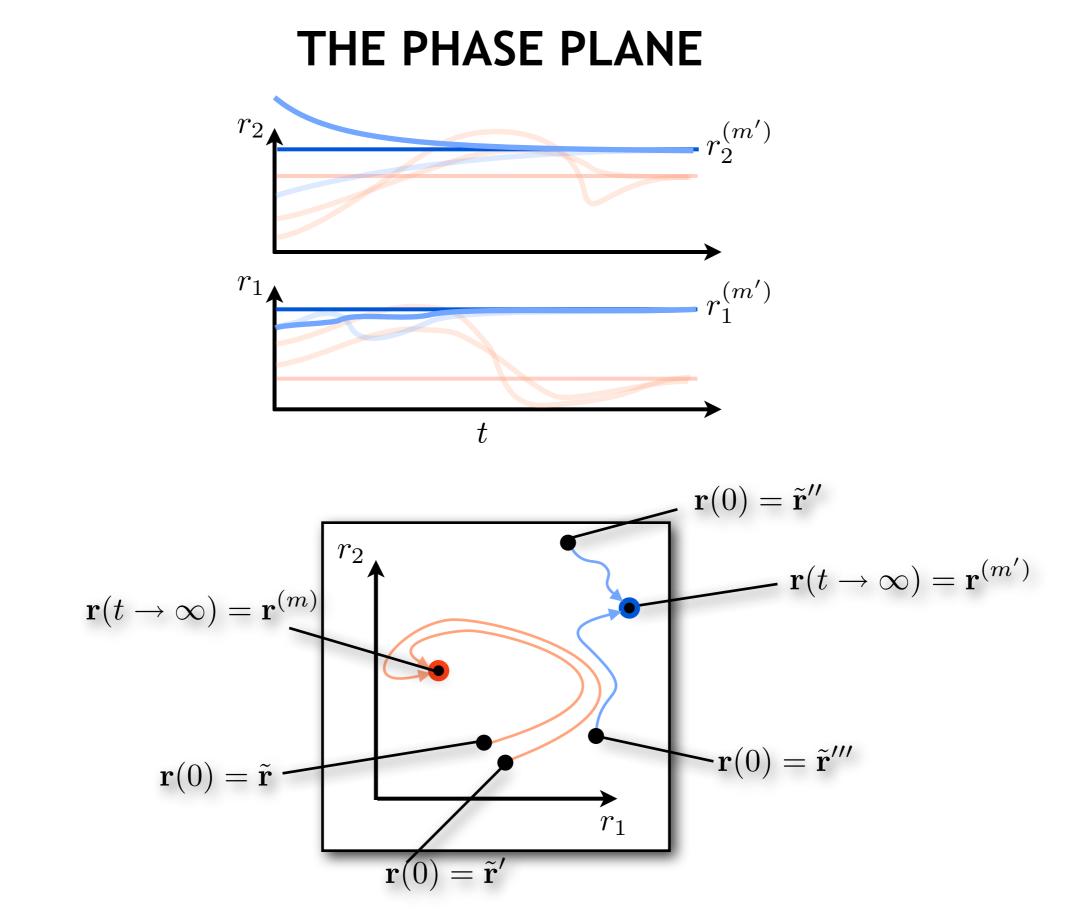














binary neurons

McCulloch & Pitts, 1943. A logical calculus of the ideas immanent in nervous activity.

recall: analogue neurons with a firing rate-based description

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$$\frac{dI_i}{dt} = -\frac{1}{\tau}I_i(t) + \sum_{j \neq i} W_{ij} r_j(t)$$

recall: analogue neurons with a firing rate-based description

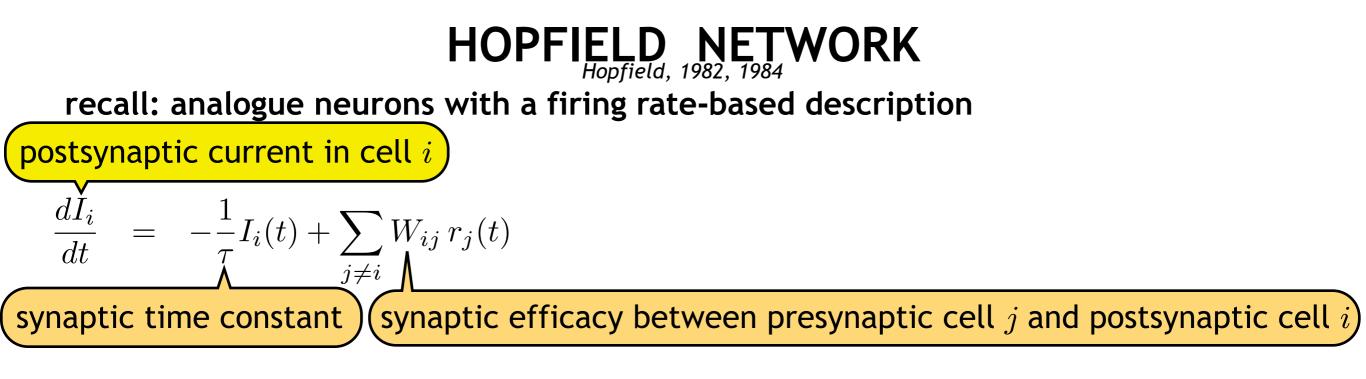
postsynaptic current in cell i

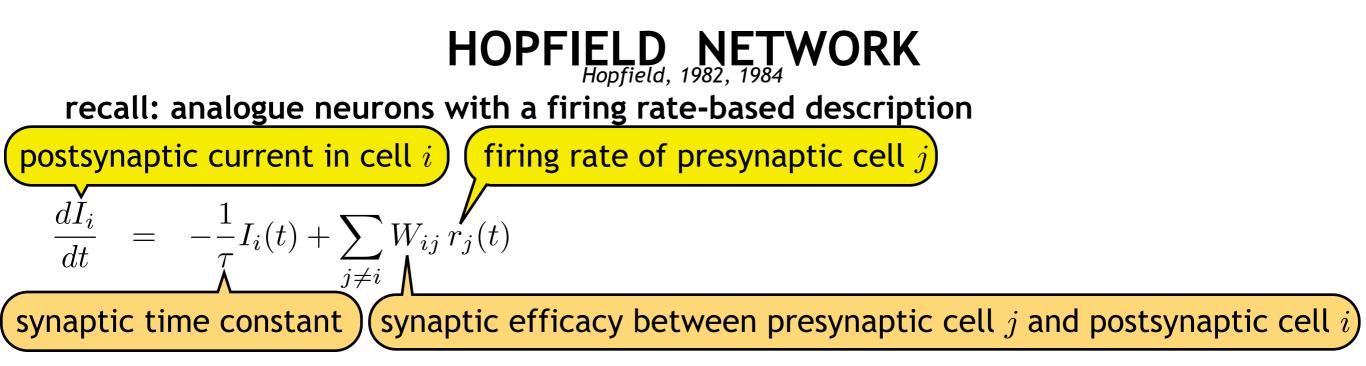
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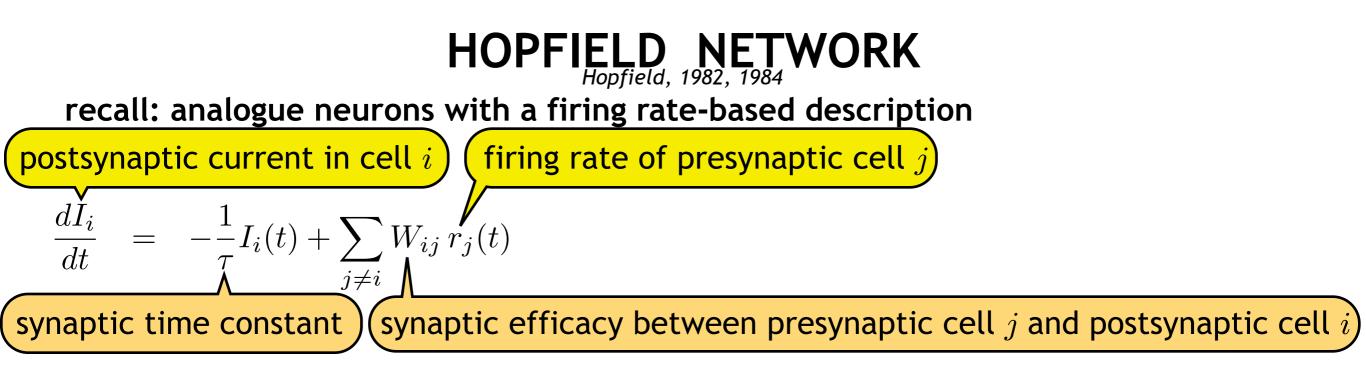
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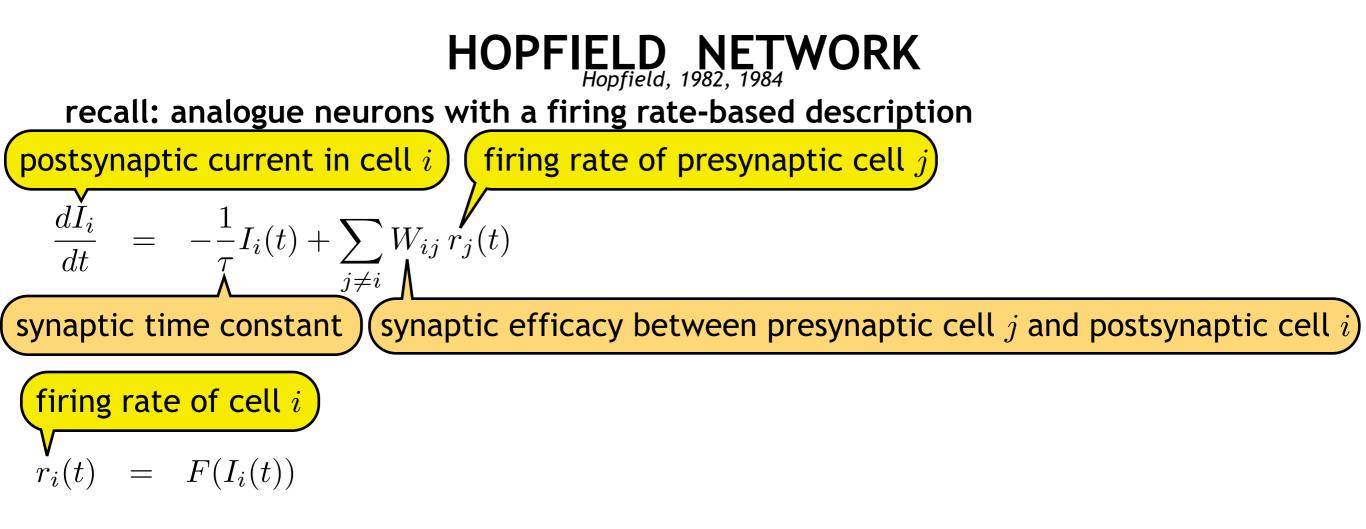
$$\frac{dI_{i}}{dt} = -\frac{1}{\tau}I_{i}(t) + \sum_{j \neq i} W_{ij} r_{j}(t)$$
synaptic time constant

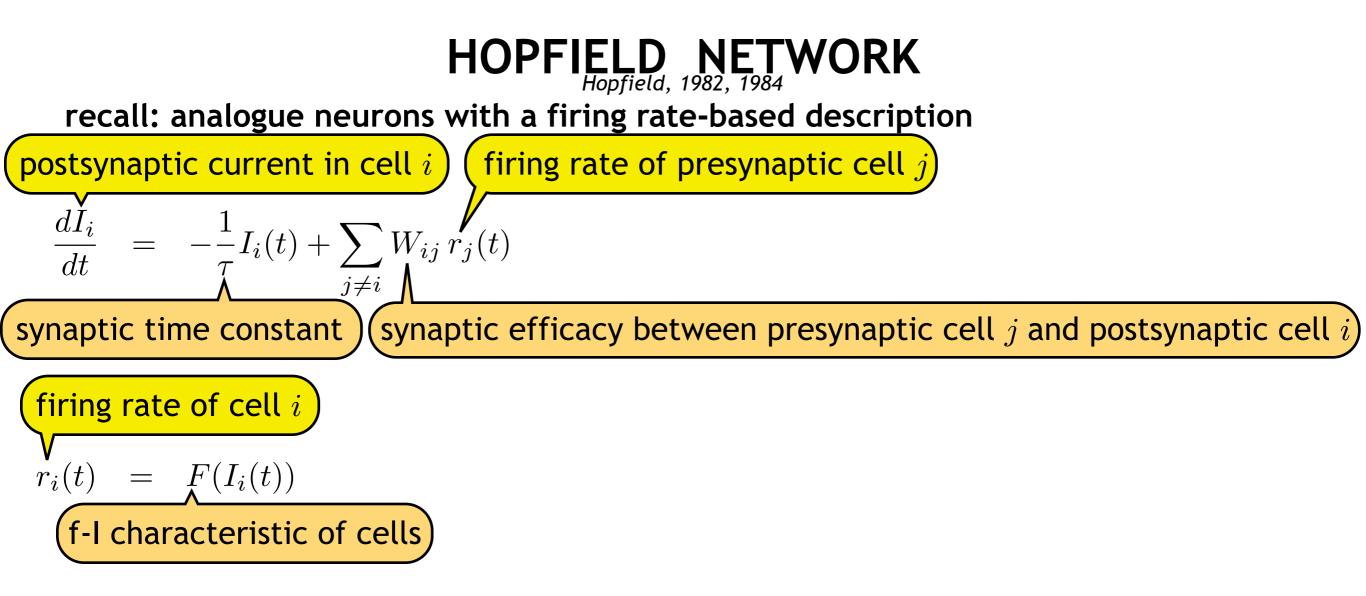


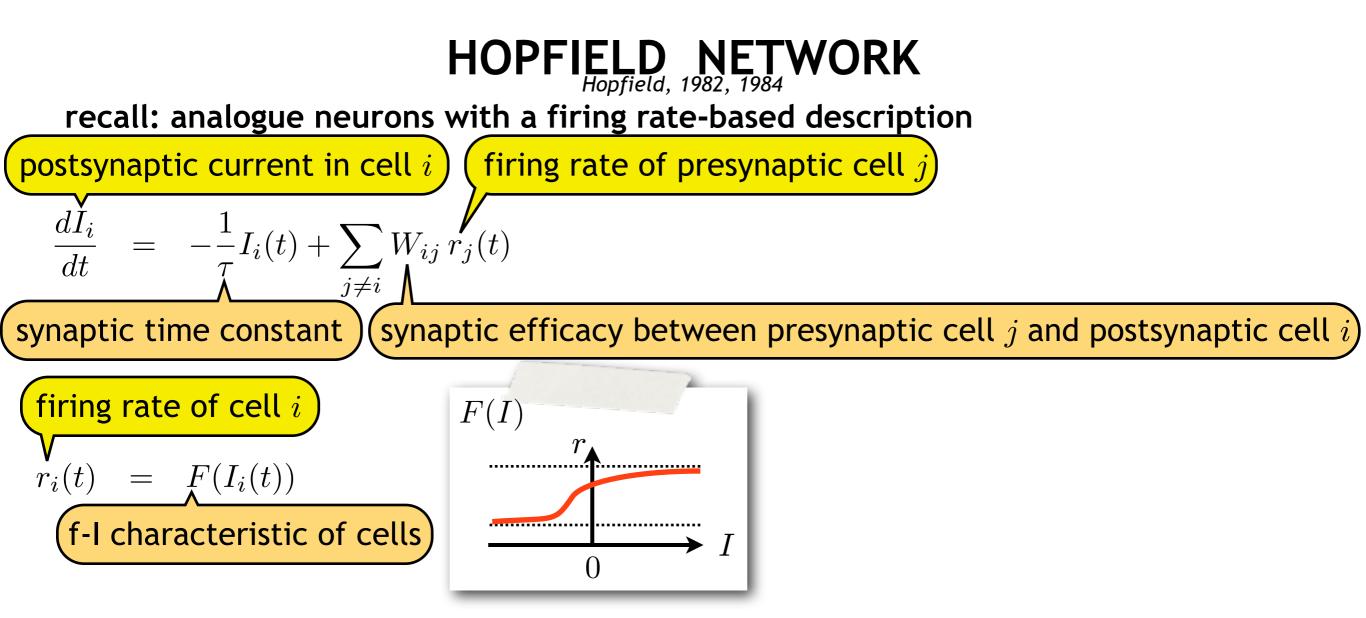


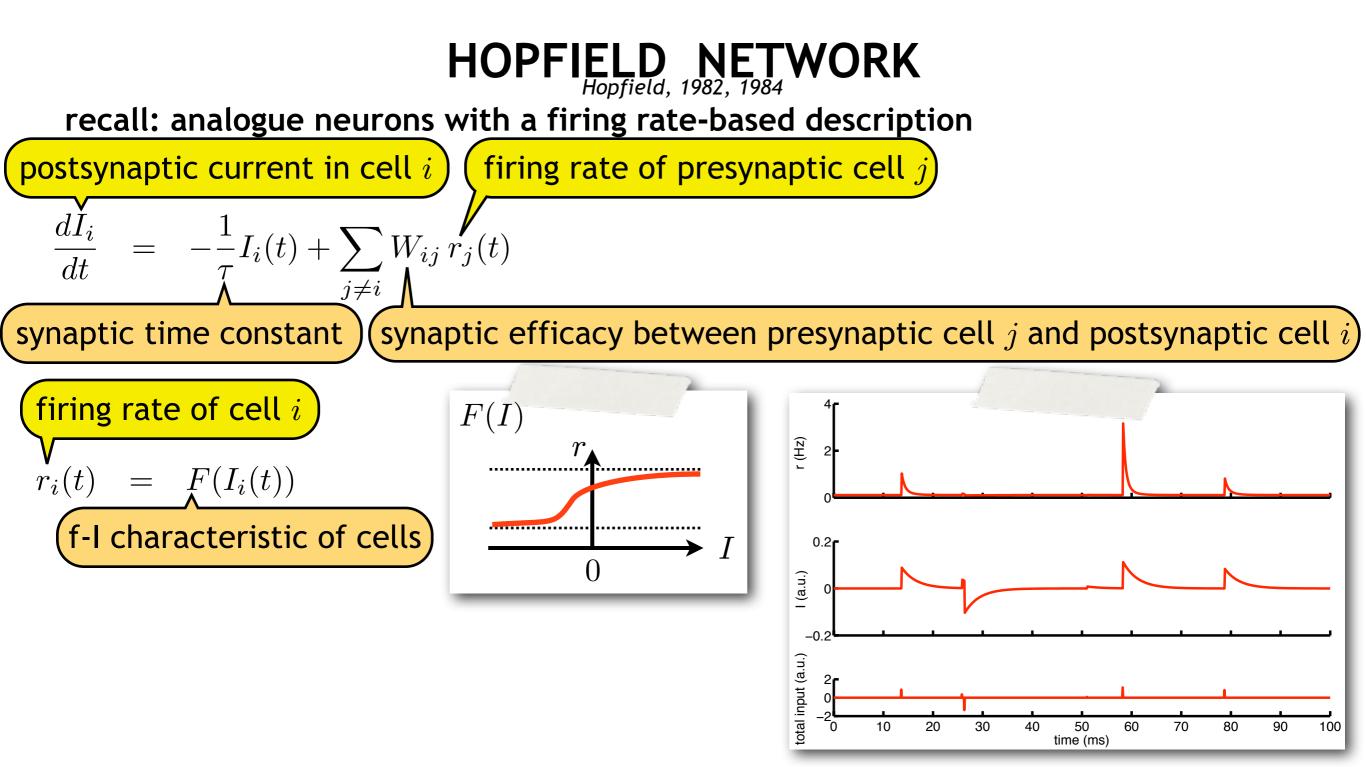


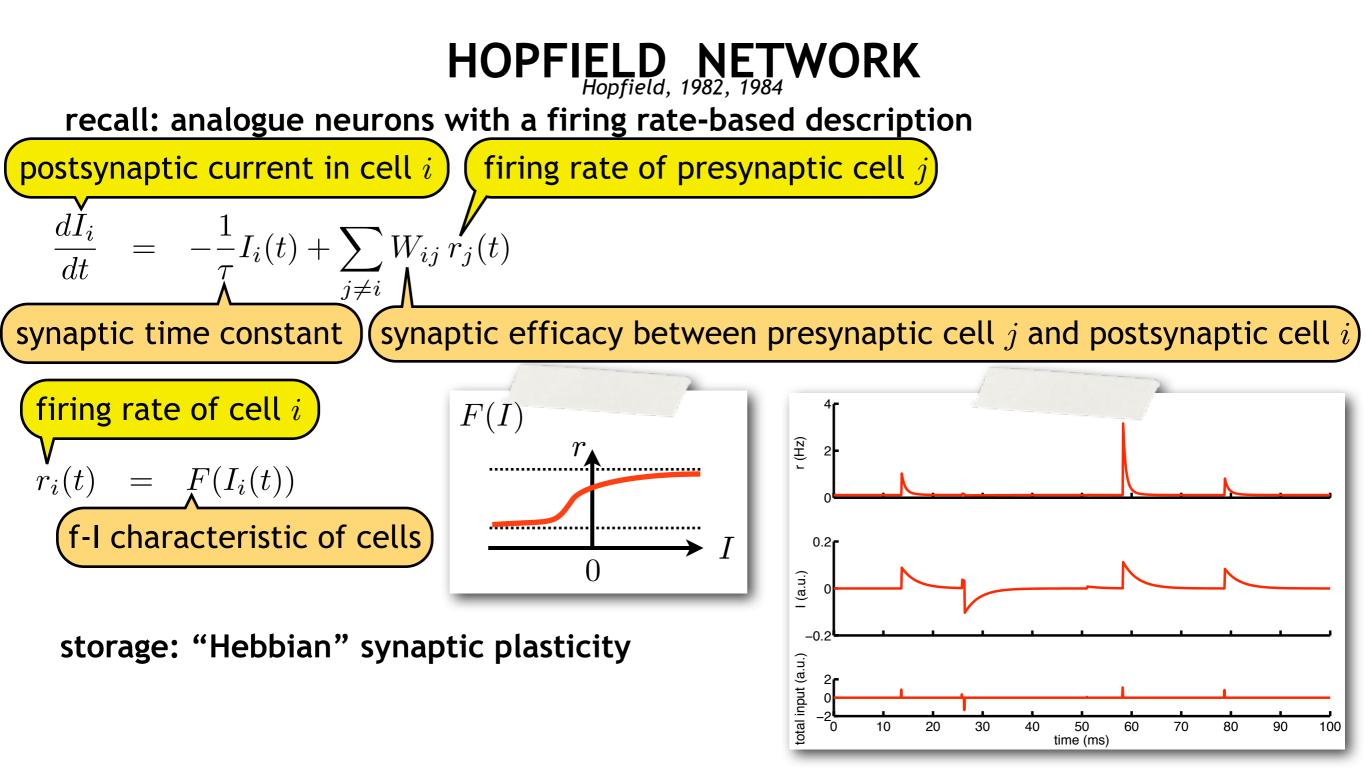
$$r_i(t) = F(I_i(t))$$

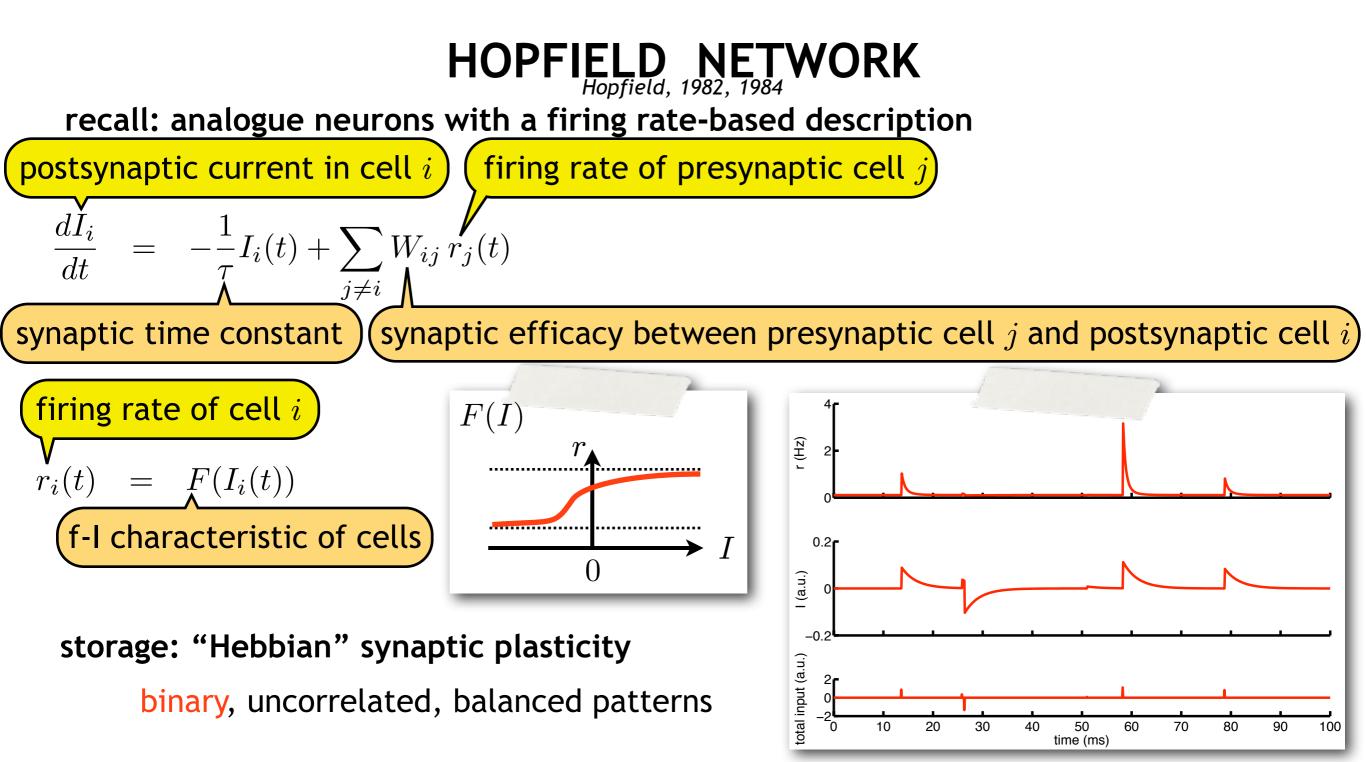


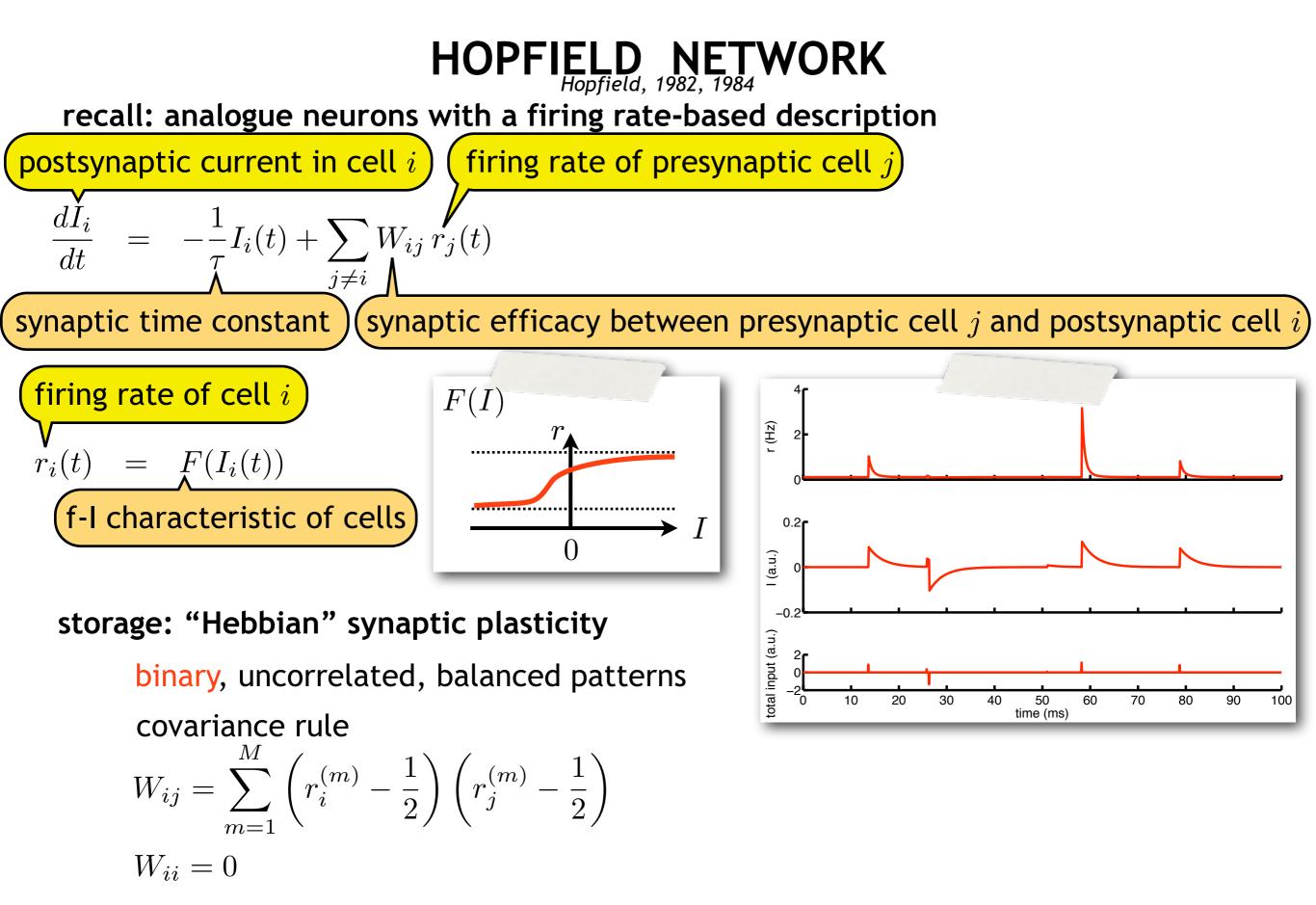


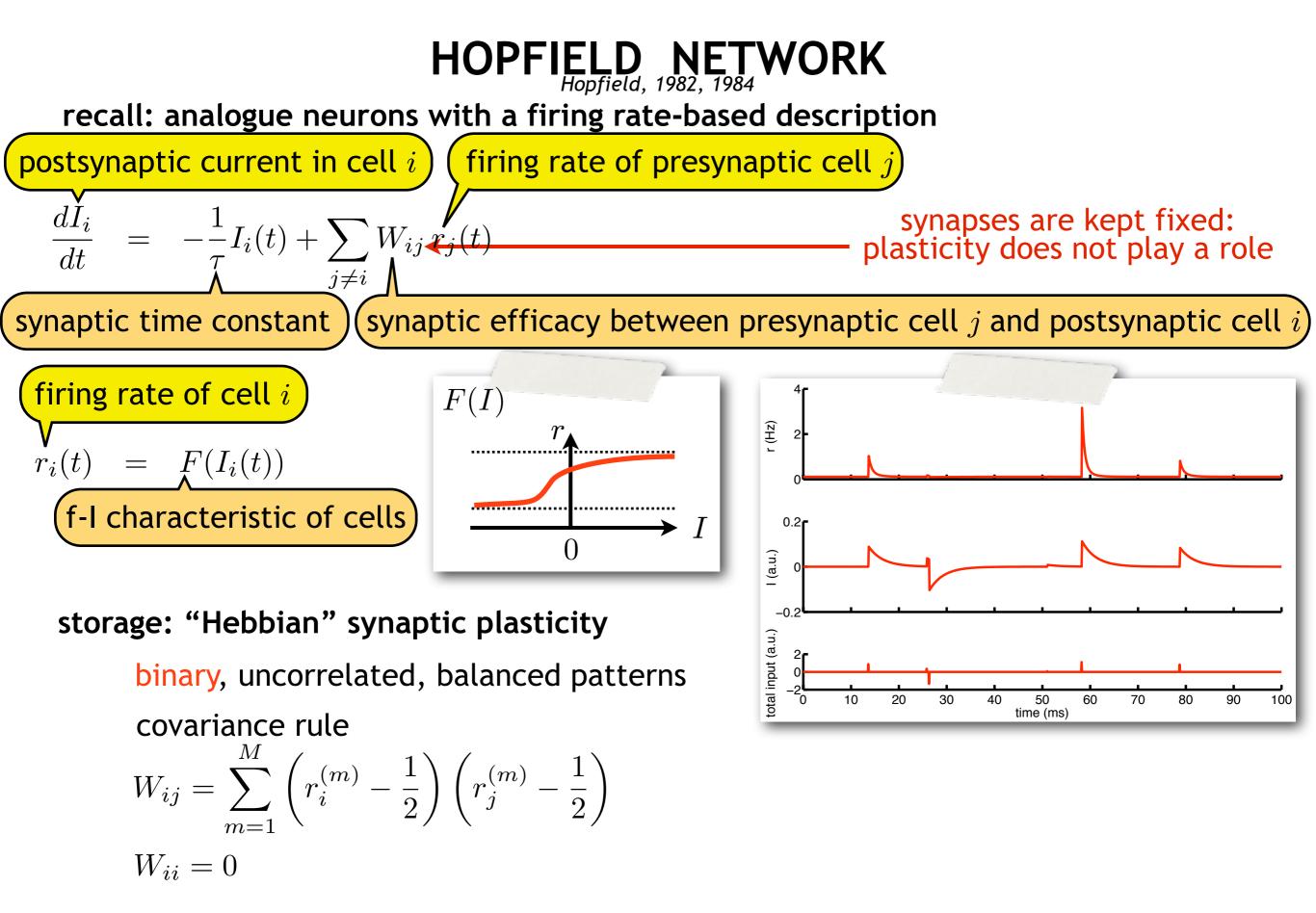


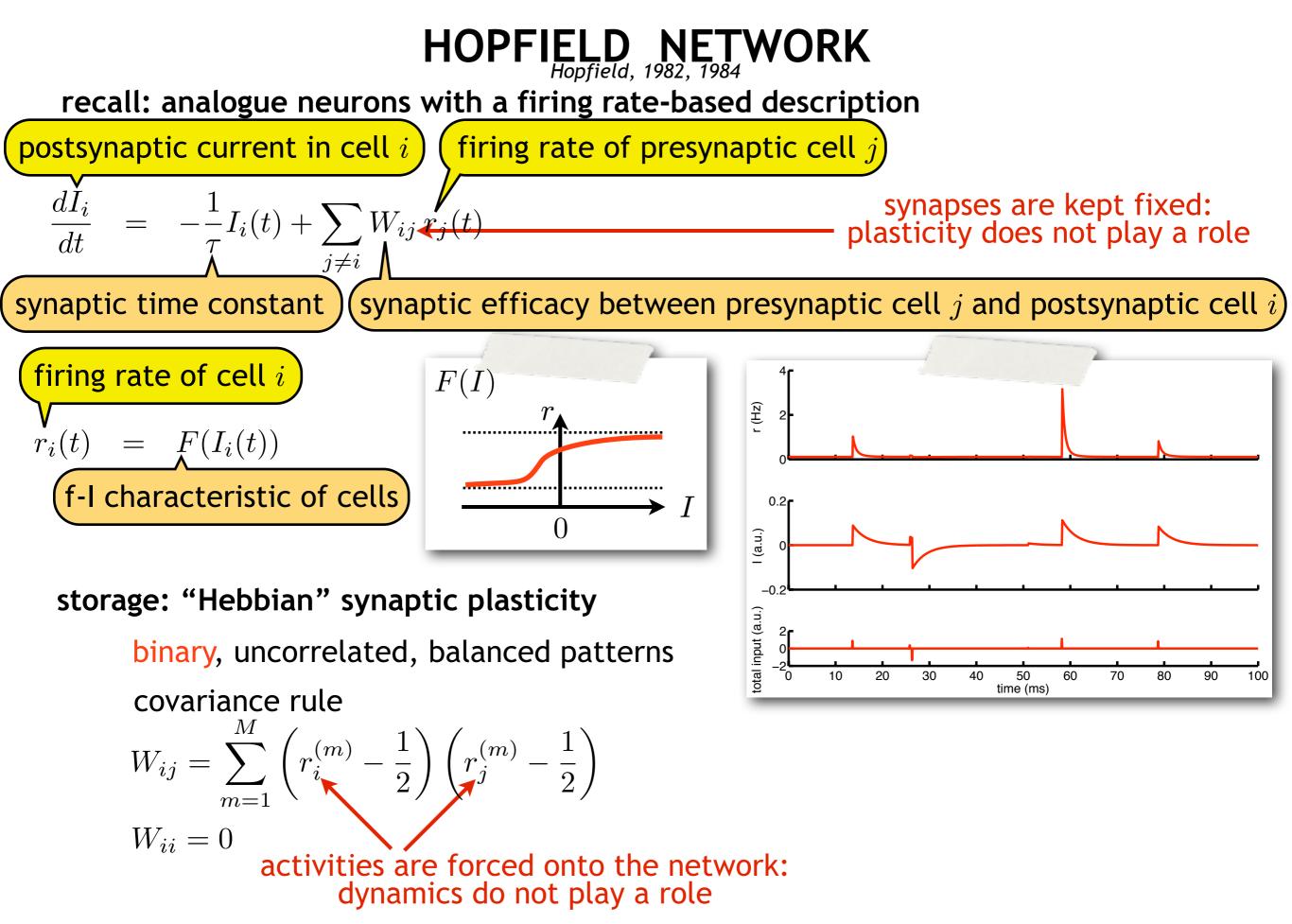












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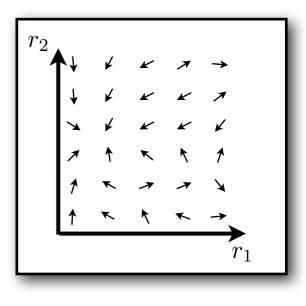
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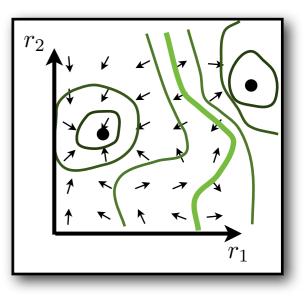
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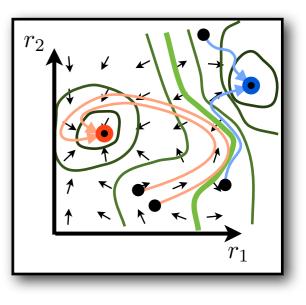
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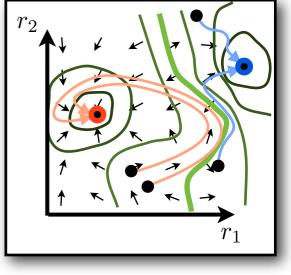


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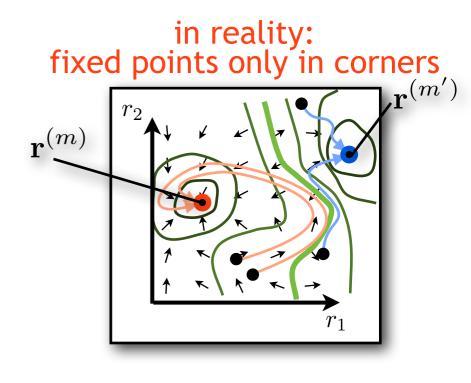


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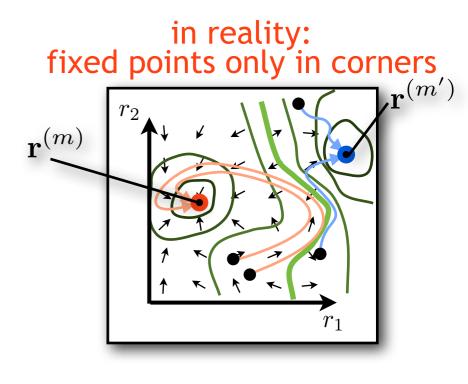




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- 2. stored patterns are fixed points



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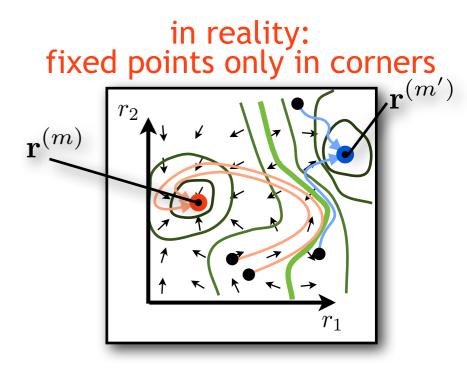


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stable?2. stored patterns are fixed points

sources of recall errors:

• stored patterns are unstable fixed points



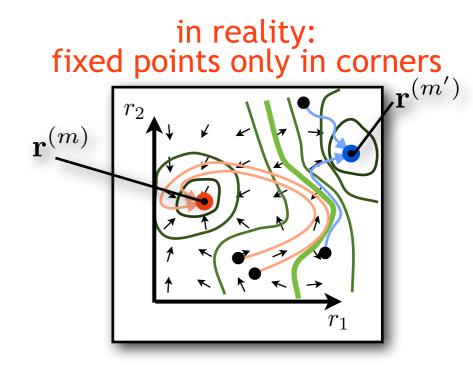
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stable?

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sources of recall errors:

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- stored patterns are not fixed points



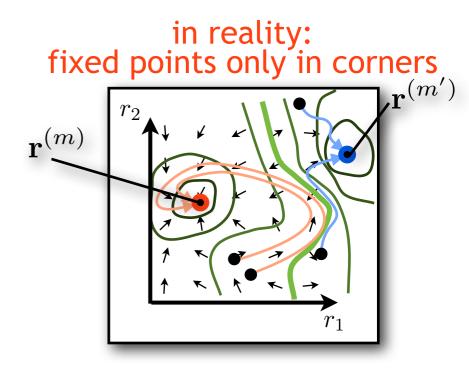
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stable?

2. stored patterns are fixed points on average

sources of recall errors:

- stored patterns are unstable fixed points
- stored patterns are not fixed points



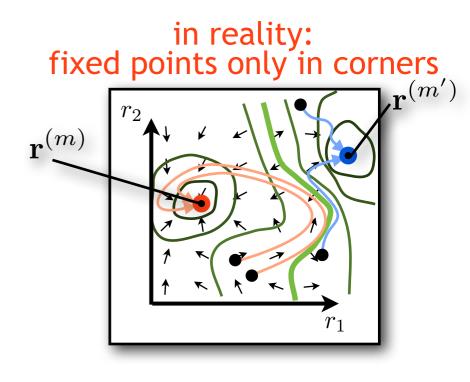
- \rightarrow equations for Hopfield network are like the equations describing 'spin glasses'
- \rightarrow same maths apply!
- 1. network dynamics have stable fixed points if we can show that there exists an 'landscape' (energy or Lyapunov) function $E(\mathbf{r})$
 - the dynamics of r are such that the it never moves upwards on the landscape $E(\mathbf{r}(t + \Delta t)) \leq E(\mathbf{r}(t))$
 - the landscape has finite depth (lower bounded) $E(\mathbf{r}) \geq 0$

stable?

2. stored patterns are fixed points on average

sources of recall errors:

- stored patterns are unstable fixed points
- stored patterns are not fixed points
- spurious attractors



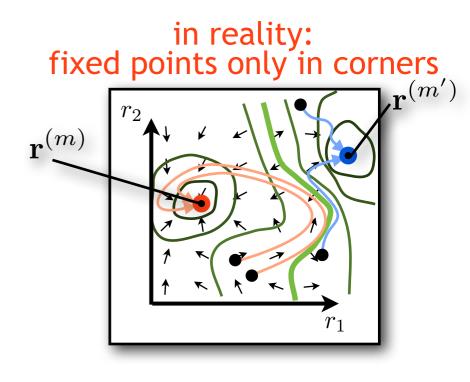
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stable?

2. stored patterns are fixed points on average (other stable fixed points?)

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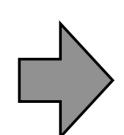
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 $\mathbf{r}^{(m)}$

in reality:

fixed points only in corners

possible to analyse mathematically: capacity, phase transitions, etc.



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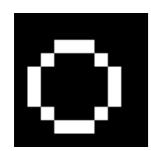
e.g. capacity is determined by

capacity, phase transitions, etc.

 $\frac{\rm number \ of \ stored \ patterns}{\rm number \ of \ synapses/cell}$

stored patterns



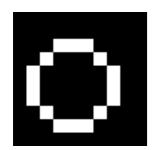


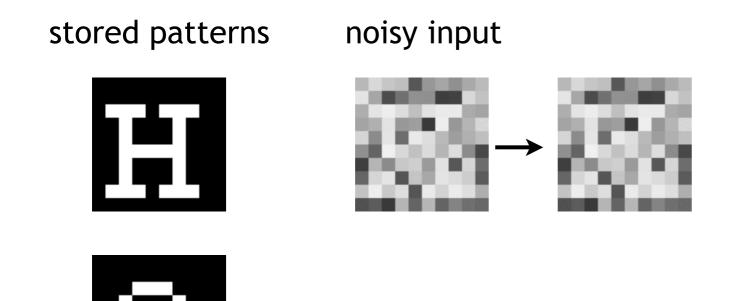
stored patterns

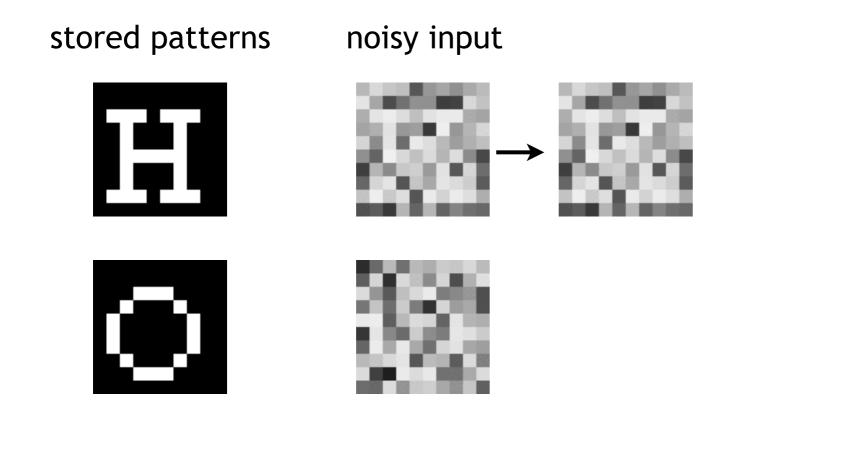


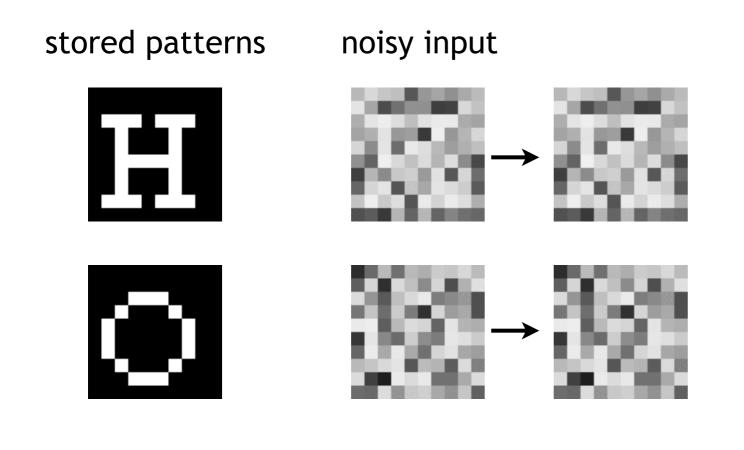
noisy input

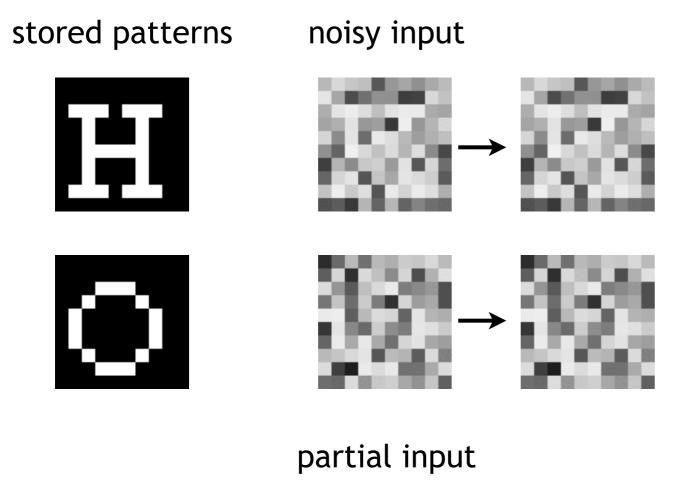




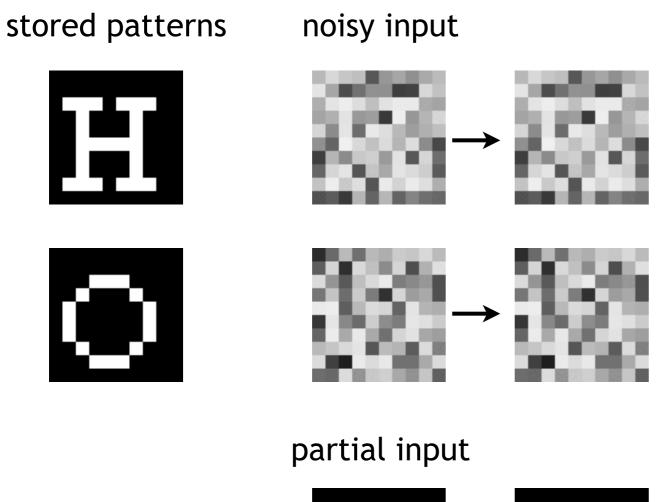


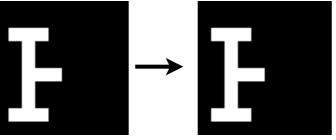


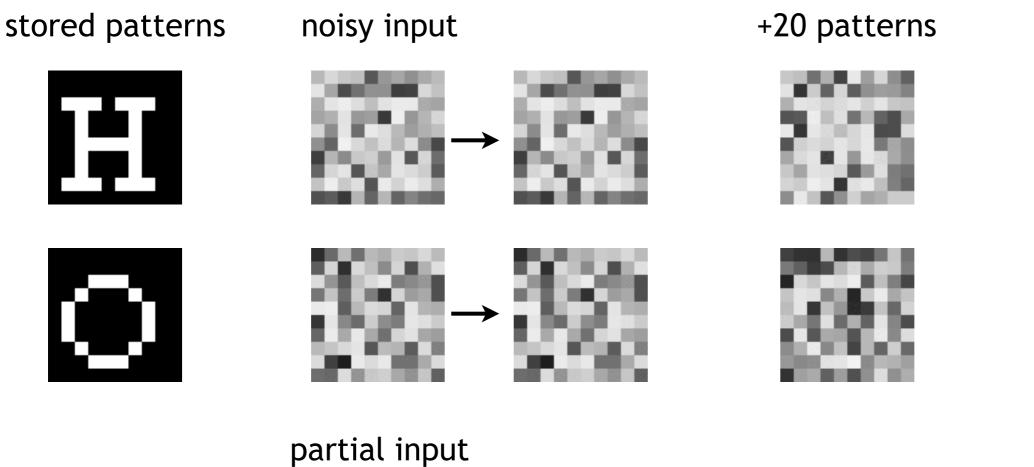




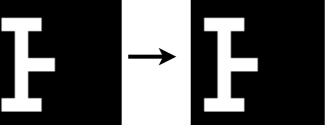


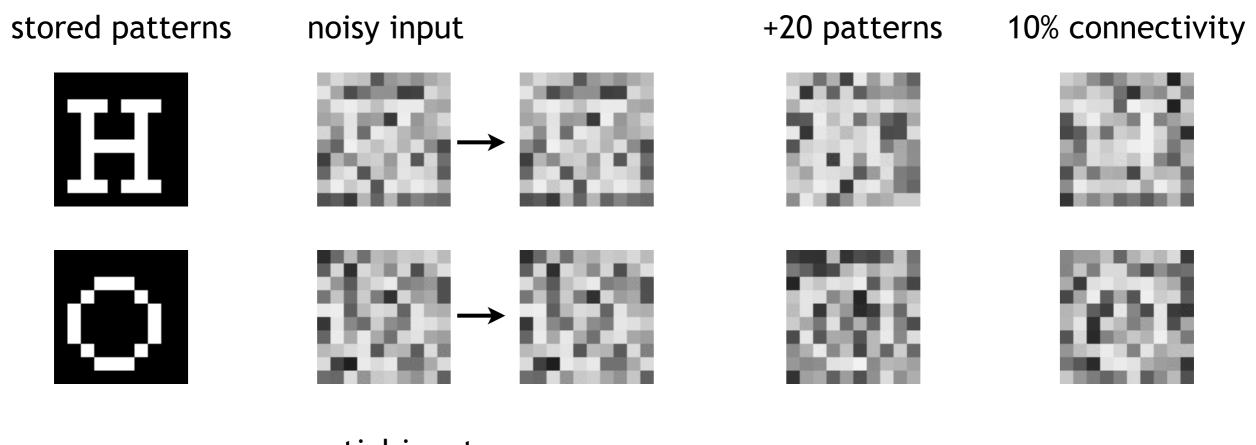




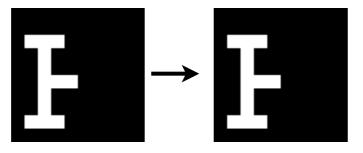


partial input





partial input



the Hopfieldian paradigm

• memories are represented as *distributed* patterns of activity

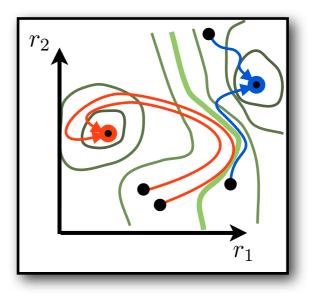
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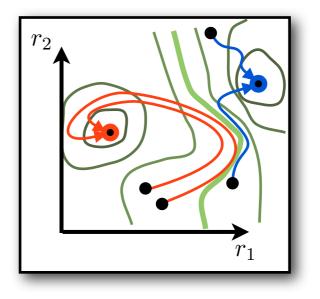
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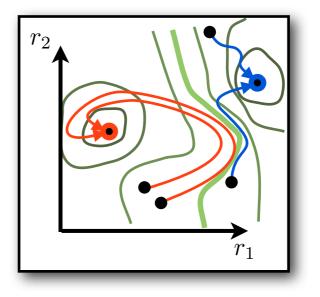
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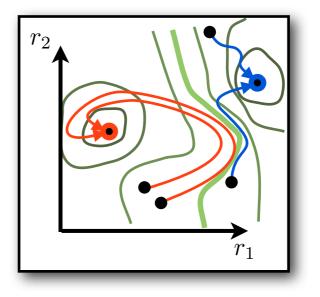


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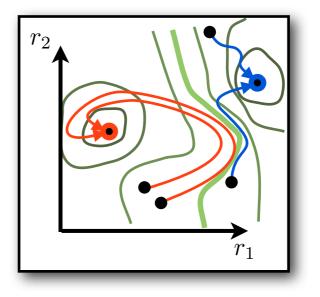


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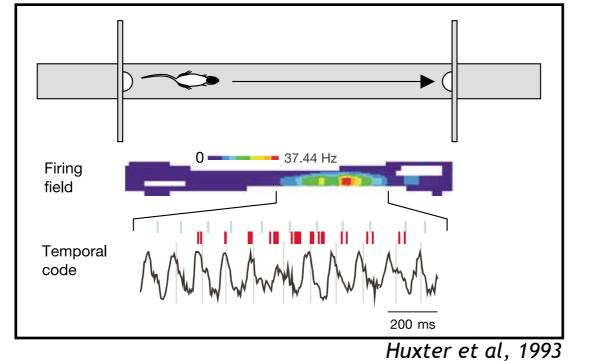
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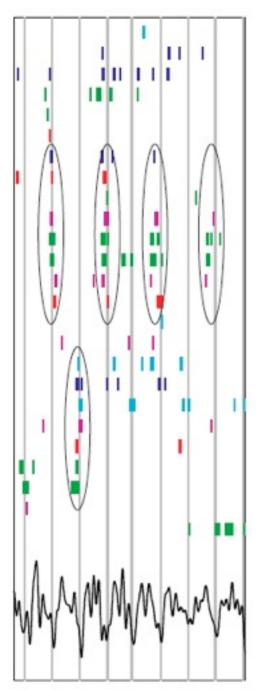


challenges:

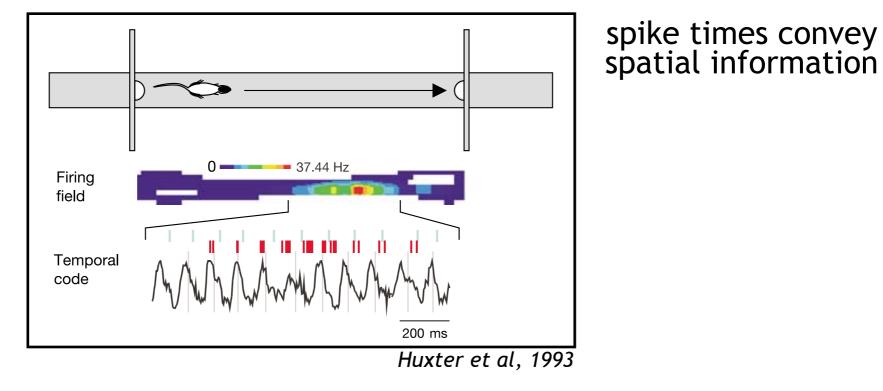
- general theory (different learning rules, network dynamics) : hard to find the corresponding energy function
- analogue-valued memories
- spike timings, oscillations



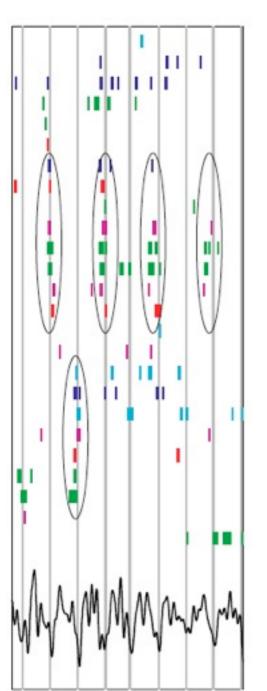
spike times convey spatial information



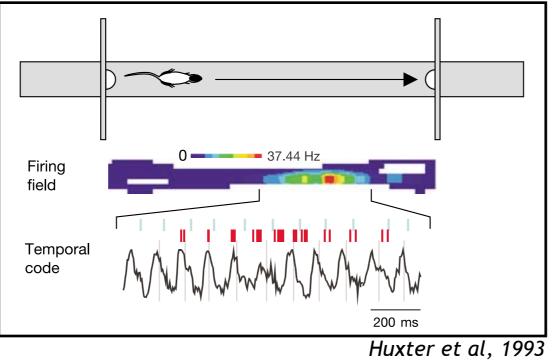
Harris & al, 2003



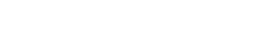
spatio-temporal firing patterns consistently reappear during awake behavior



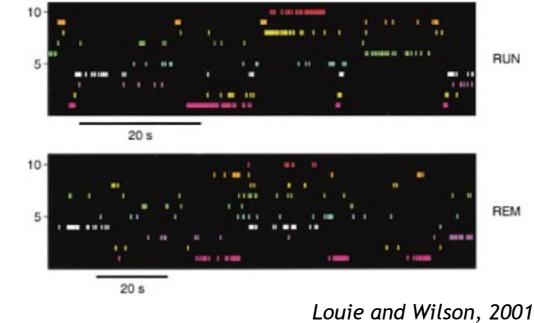
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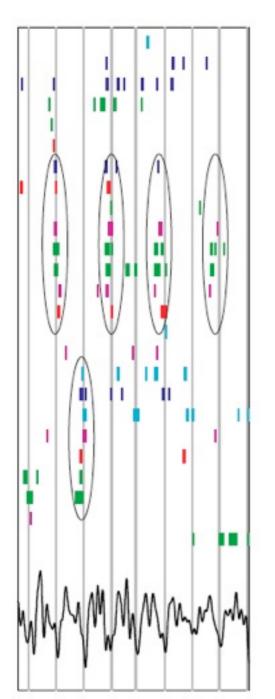
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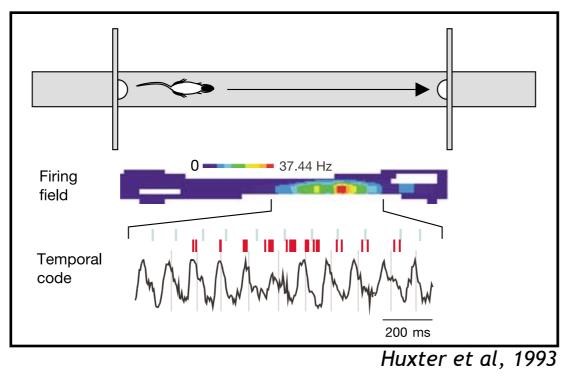
spatio-temporal firing patterns consistently reappear during awake behavior ... and sleep



Máté Lengyel | Computational modelling of synaptic function MPS-UCL Symposium on Computational Psychiatry, 18 Sept 2012 http://www.eng.cam.ac.uk/~m.lengyel 12



Harris & al, 2003



spatio-temporal firing patterns consistently reappear during awake behavior ... and s

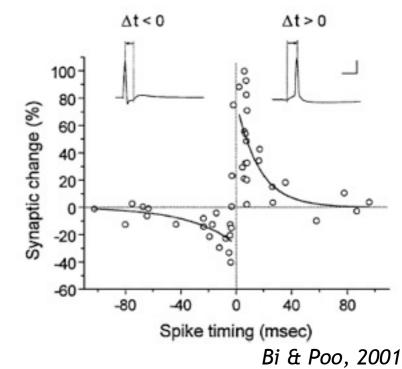
20 s

20 s

10

spike times convey spatial information





Máté Lengyel | Computational modelling of synaptic function

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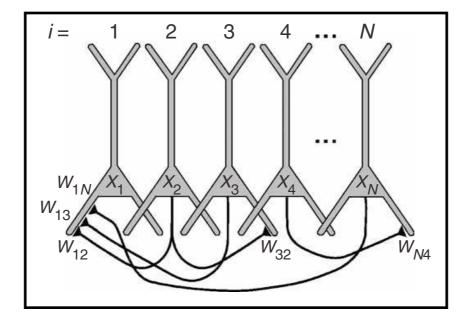
Louie and Wilson, 2001

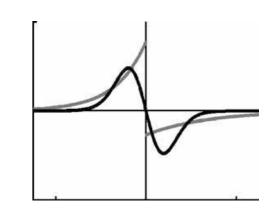
... and sleep

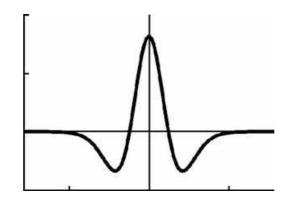
RUN

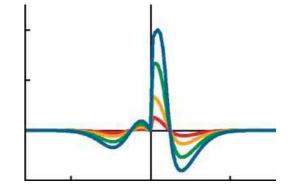
REM

MEMORY RETRIEVAL AS PROBABILISTIC INFERENCE

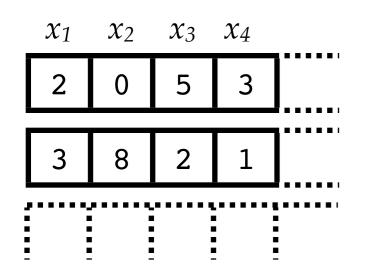


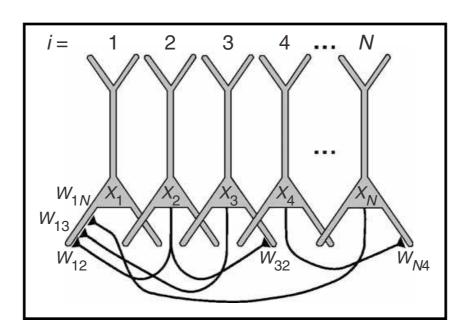


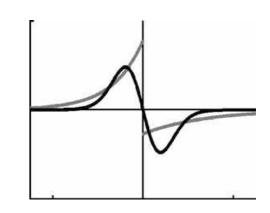


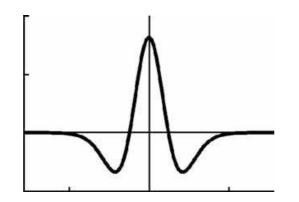


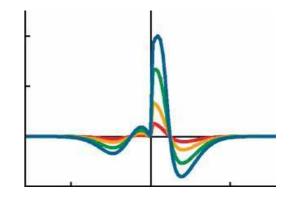
stored activities



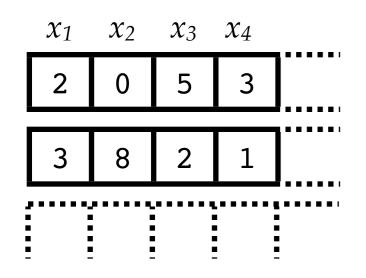


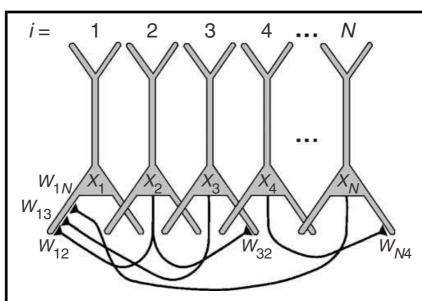




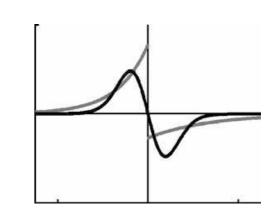


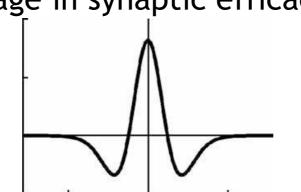
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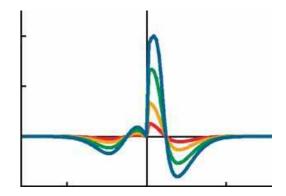




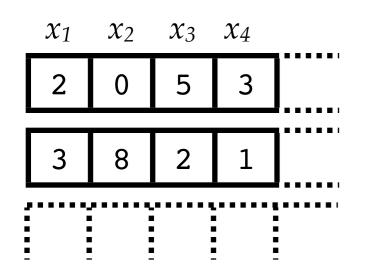
storage in synaptic efficacies

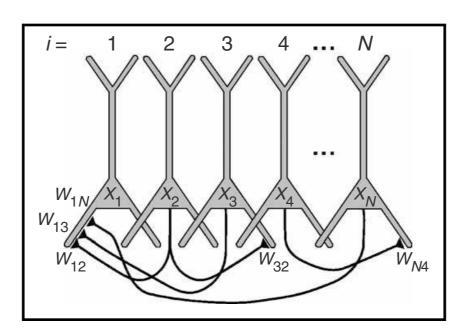






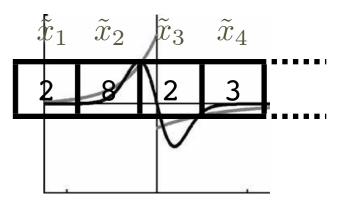
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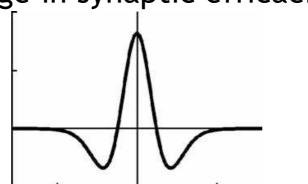


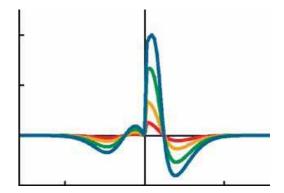


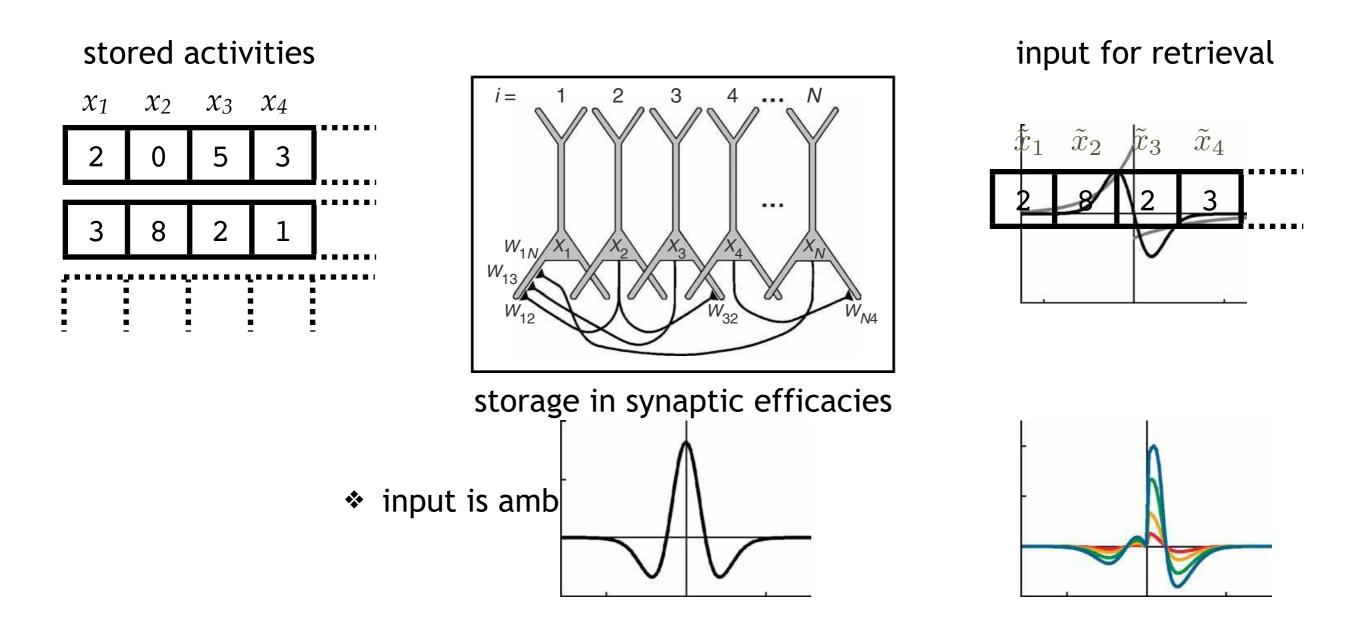
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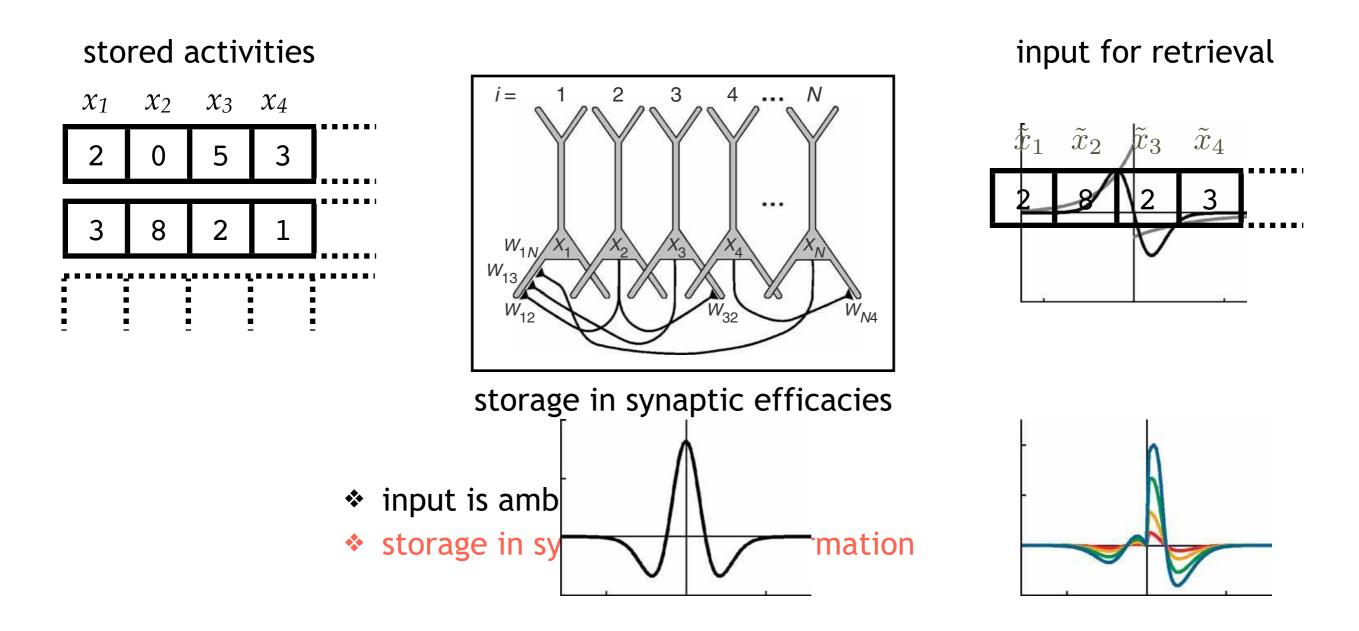


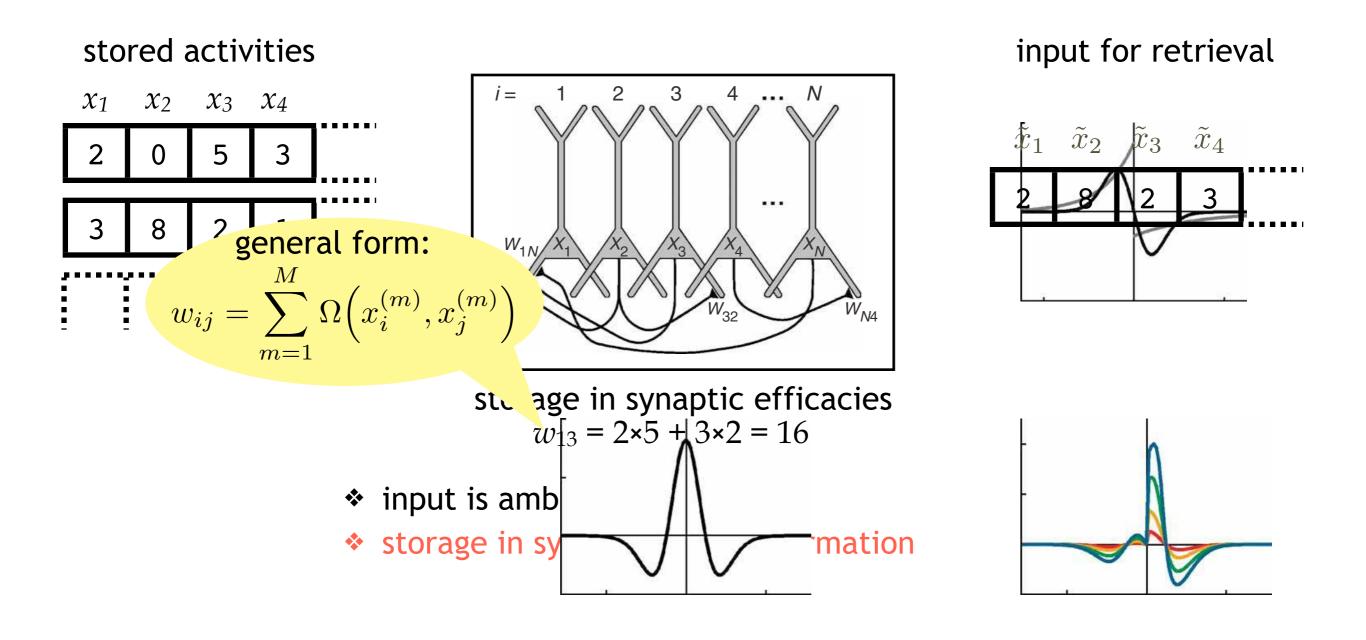


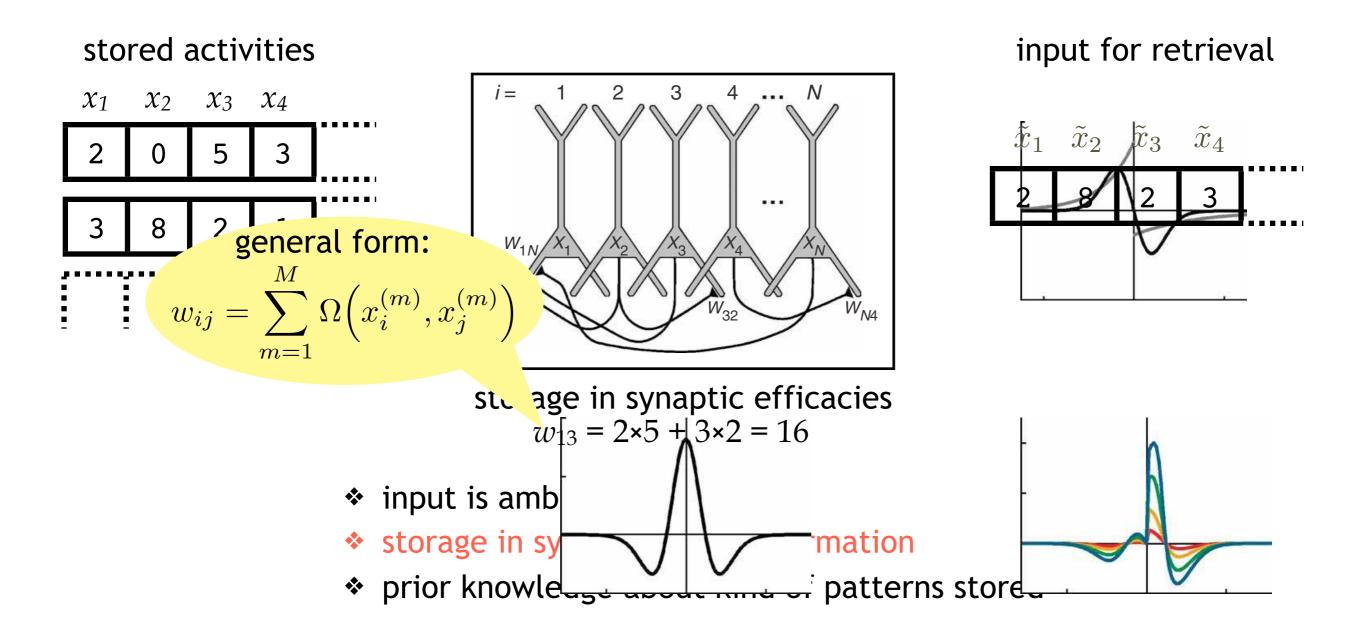


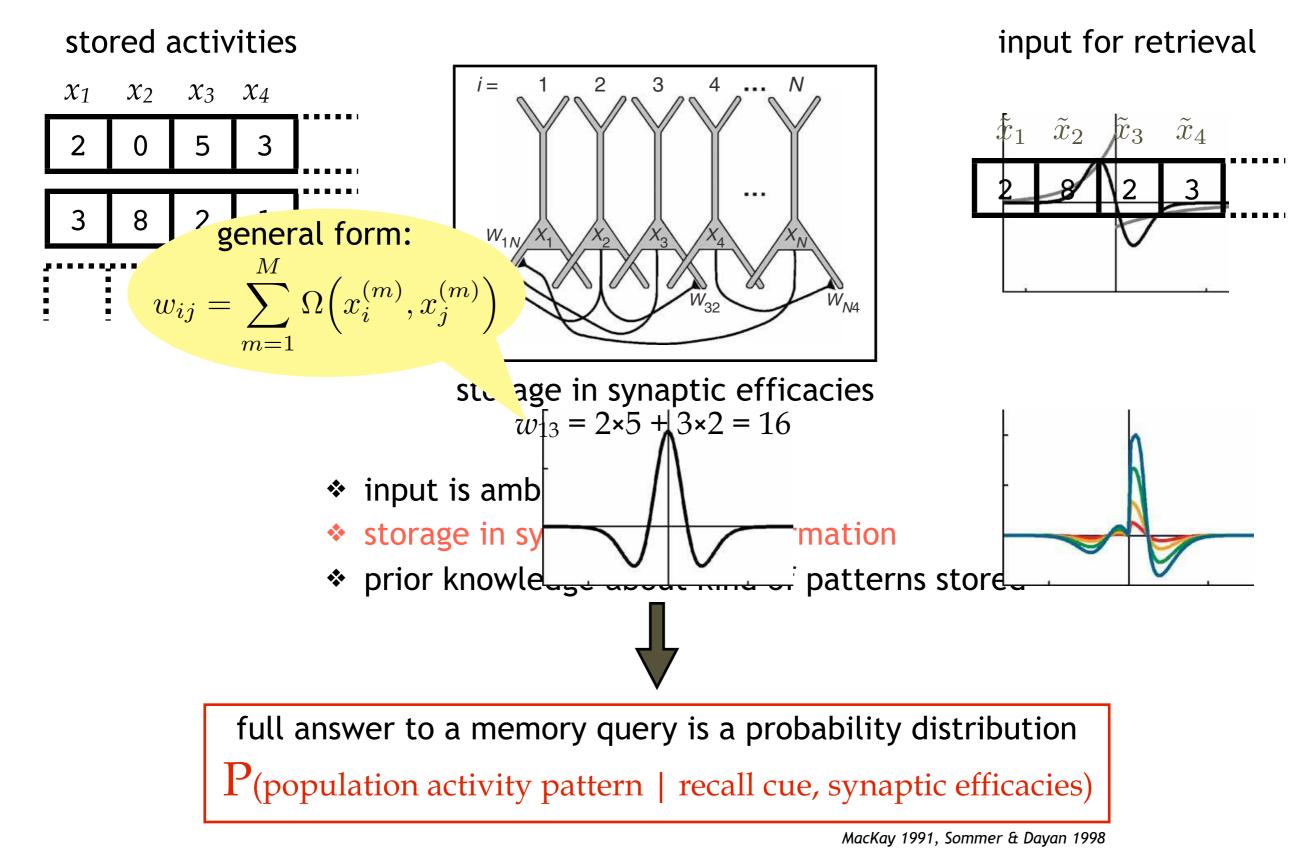












UNDERSTANDING THE POSTERIOR

P(population activity pattern | recall cue, synaptic efficacies)

UNDERSTANDING THE POSTERIOR $P(\mathbf{x}|\tilde{\mathbf{x}}, \mathbf{W})$

$\begin{array}{l} \textbf{UNDERSTANDING THE POSTERIOR} \\ P(\mathbf{x}|\tilde{\mathbf{x}},\mathbf{W}) \, \propto \, P(\mathbf{x}) \, \ P(\tilde{\mathbf{x}}|\mathbf{x}) \, \ P(\mathbf{W}|\mathbf{x}) \end{array}$

UNDERSTANDING THE POSTERIOR $P(\mathbf{x}|\tilde{\mathbf{x}}, \mathbf{W}) \propto P(\mathbf{x}) P(\tilde{\mathbf{x}}|\mathbf{x}) P(\mathbf{W}|\mathbf{x})$

the probability that pattern \mathbf{x} is chosen to be stored

 $P(\mathbf{x})$



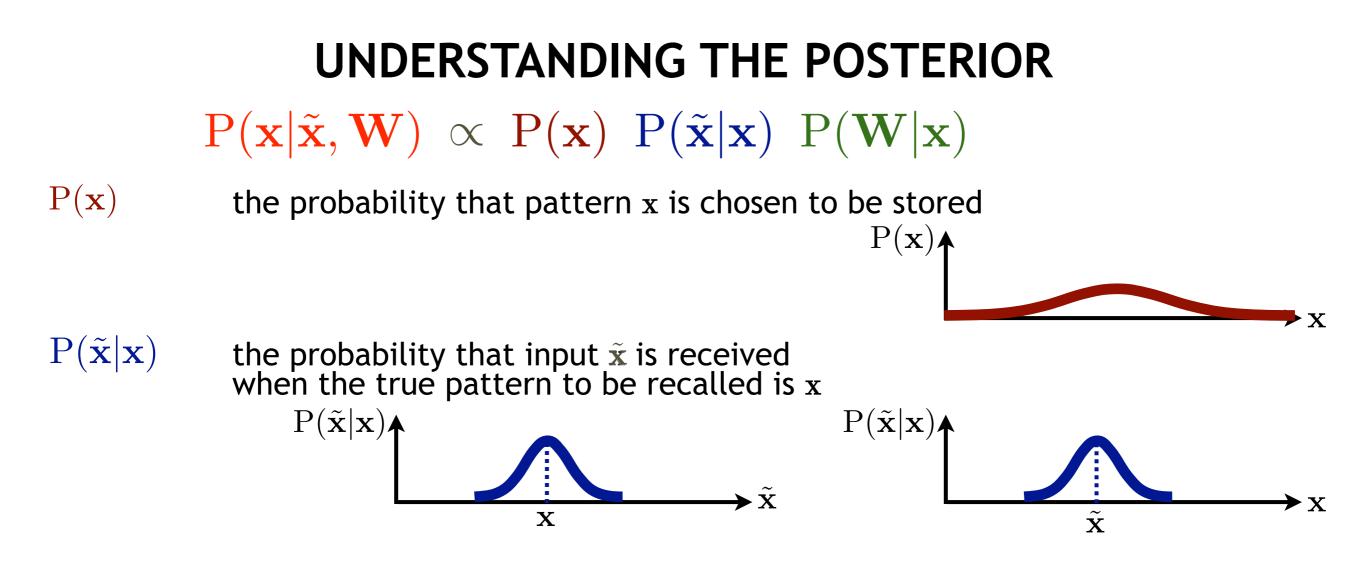
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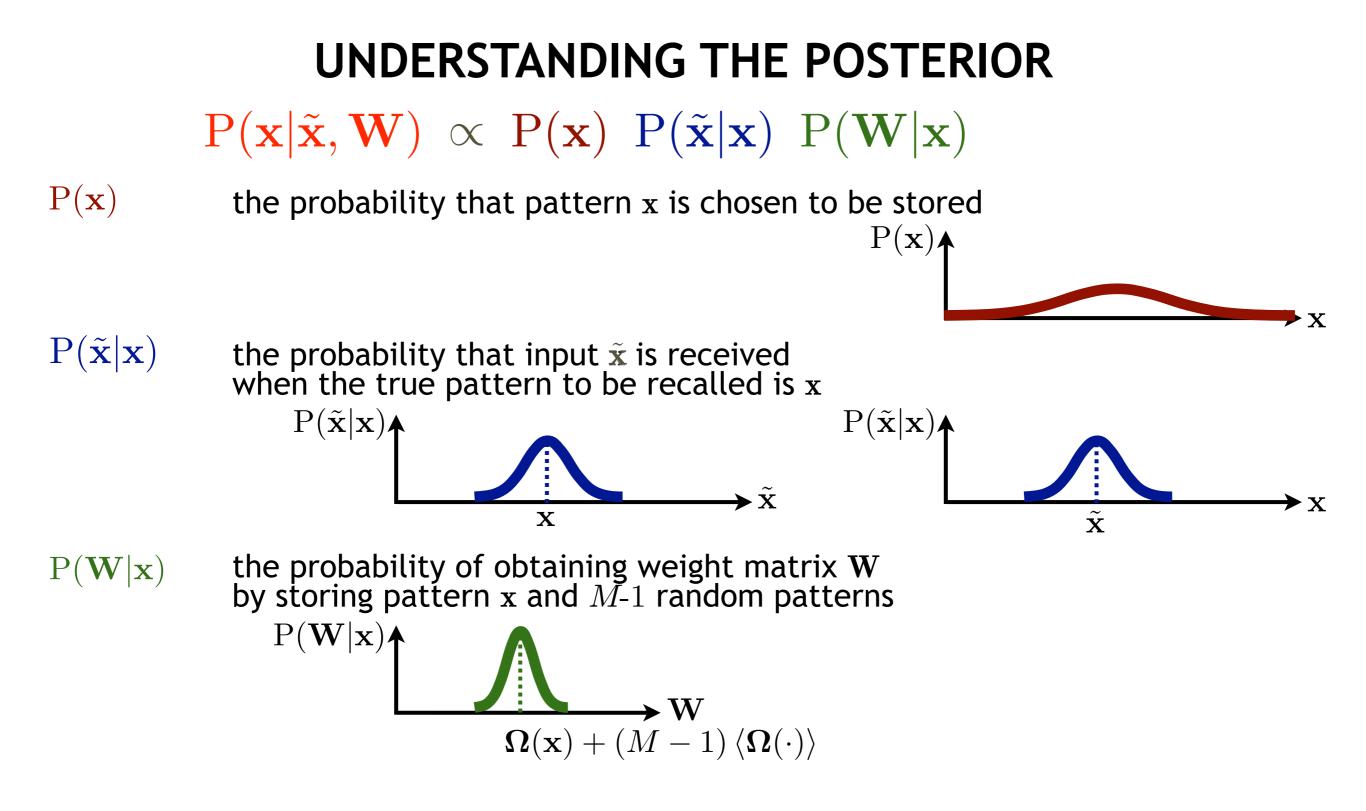
Х

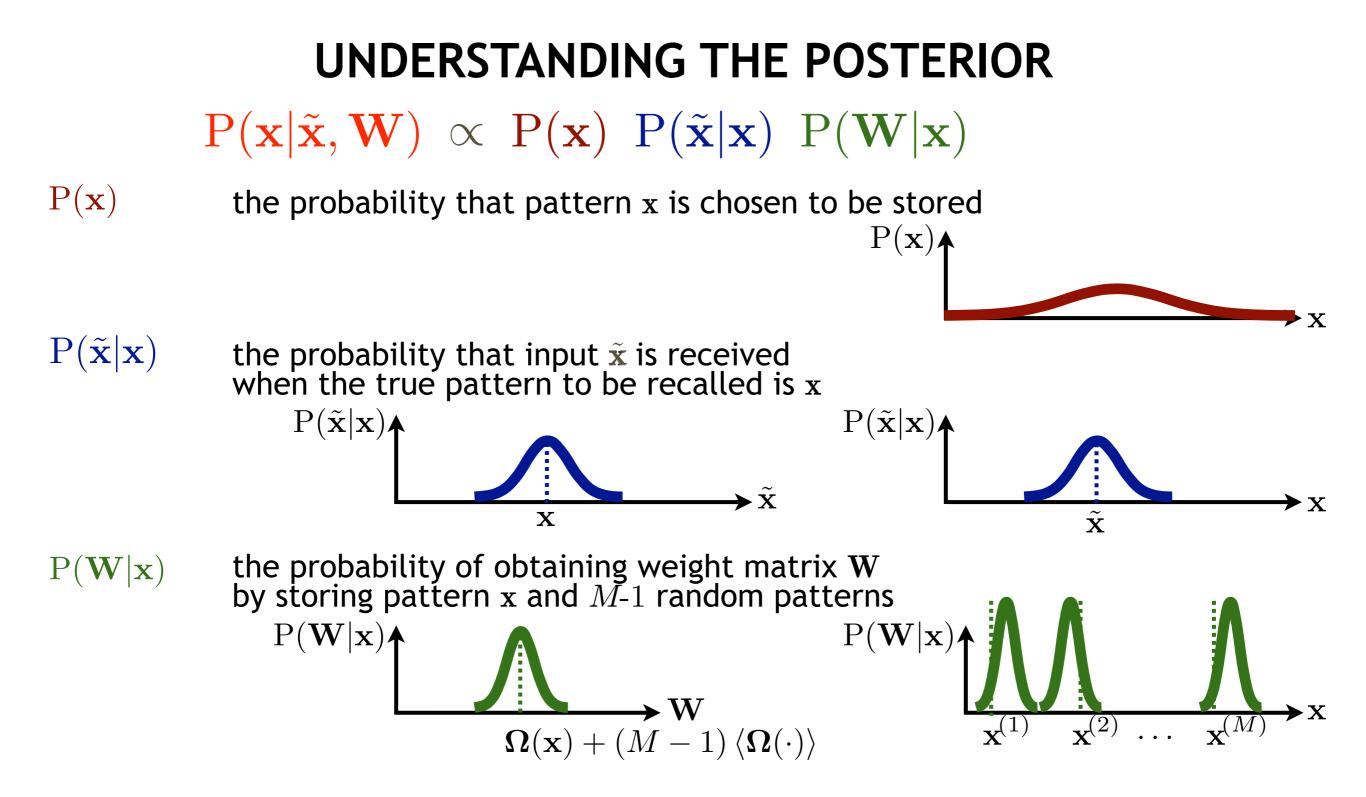
 $\tilde{\mathbf{x}}$

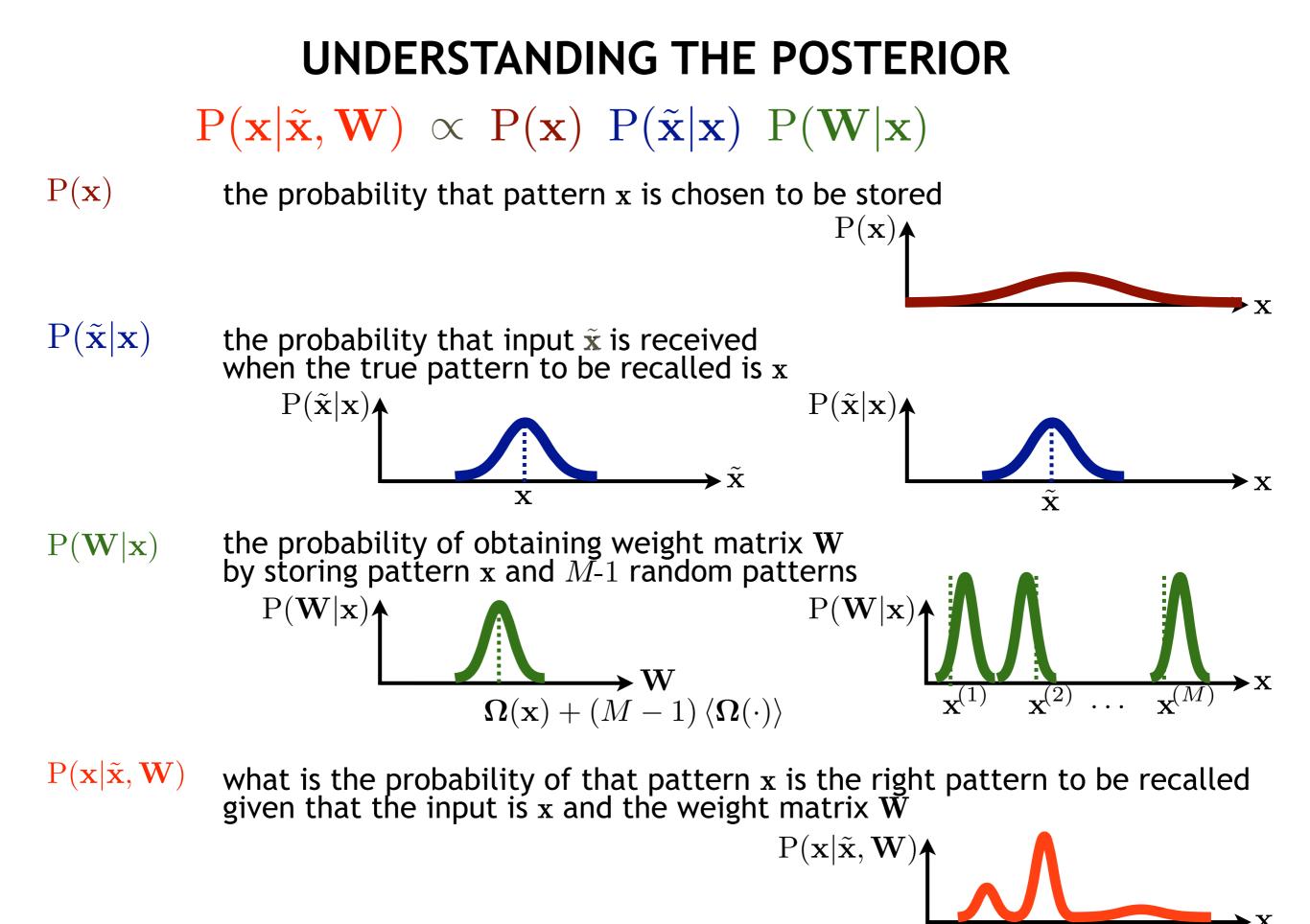
 $P(\tilde{\mathbf{x}}|\mathbf{x})$

14







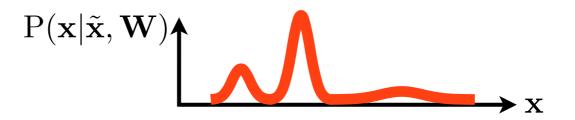


MAXIMUM A POSTERIORI INFERENCE

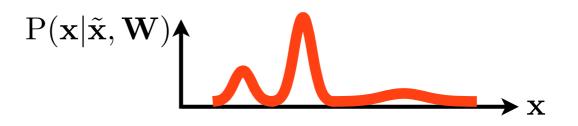
- memories are represented as distributed patterns of activity
- assume particular learning rule
- **assume** particular network dynamics
- → **find** energy function

MAXIMUM A POSTERIORI INFERENCE

- memories are represented as distributed patterns of activity
- **assume** particular learning rule
- **define** energy function
- → derive network dynamics

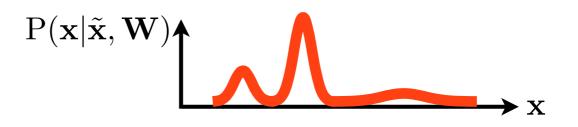


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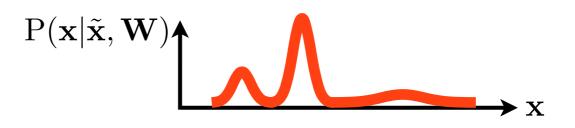
$$\frac{d}{dt}x_i \propto \frac{\partial}{\partial x_i} \log P(\mathbf{x}|\tilde{\mathbf{x}}, \mathbf{W})$$

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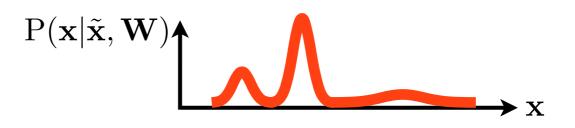
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$$P(\mathbf{x}|\tilde{\mathbf{x}}, \mathbf{W}) \longrightarrow \mathbf{x}$$

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$$rac{d}{dt}x_i\propto\ldots+\sum_j w_{ij}~rac{\partial}{\partial x_i}\Omega(x_i,x_j)$$
Lengyel et al, Nat Neurosci 2005

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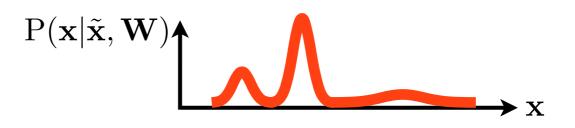


network dynamics implements gradient ascent on the (log) posterior

$$\frac{d}{dt}x_i \propto \frac{\partial}{\partial x_i} \log P(\mathbf{x}) + \frac{\partial}{\partial x_i} \log P(\tilde{\mathbf{x}}|\mathbf{x}) + \frac{\partial}{\partial x_i} \log P(\mathbf{W}|\mathbf{x})$$
$$\approx \frac{\partial}{\partial x_i} \log P(x_i) + \frac{\partial}{\partial x_i} \log P(\tilde{x}_i|x_i) + \frac{1}{2} \sum_j \frac{\partial}{\partial x_i} \log P(w_{ij}|x_i, x_j)$$

 $\frac{d}{dt}x_i \propto \ldots + \sum_j w_{ij} \frac{\partial}{\partial x_i} \Omega(x_i, x_j)$ interactions should be scaled by synaptic weights

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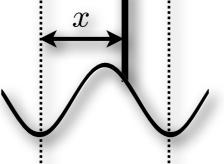
network dynamics implements gradient ascent on the (log) posterior

$$\frac{\partial}{\partial x_i} \cos P(\mathbf{x}) + \frac{\partial}{\partial x_i} \log P(\mathbf{x}) + \frac{\partial}{\partial x_i} \log P(\tilde{\mathbf{x}}|\mathbf{x}) + \frac{\partial}{\partial x_i} \log P(\mathbf{W}|\mathbf{x})$$
$$\approx \frac{\partial}{\partial x_i} \log P(x_i) + \frac{\partial}{\partial x_i} \log P(\tilde{x}_i|x_i) + \frac{1}{2} \sum_j \frac{\partial}{\partial x_i} \log P(w_{ij}|x_i, x_j)$$

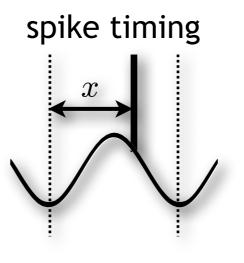
 $\frac{d}{dt}x_i \propto \ldots + \sum_j w_{ij} \frac{\partial}{\partial x_i} \Omega(x_i, x_j)$ interactions should be scaled by synaptic weights matching between storage and recall Lengyel et al, Nat Neurosci 2005

representation

spike timing

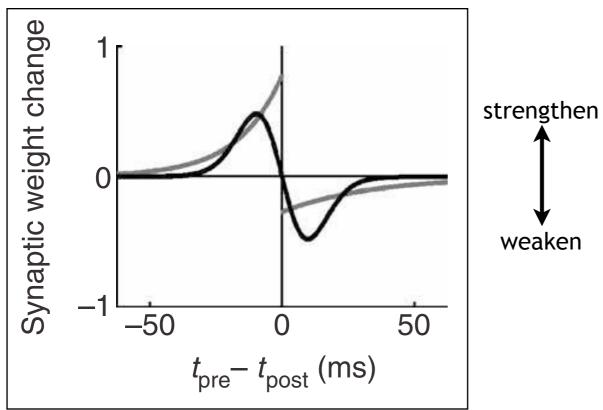


representation



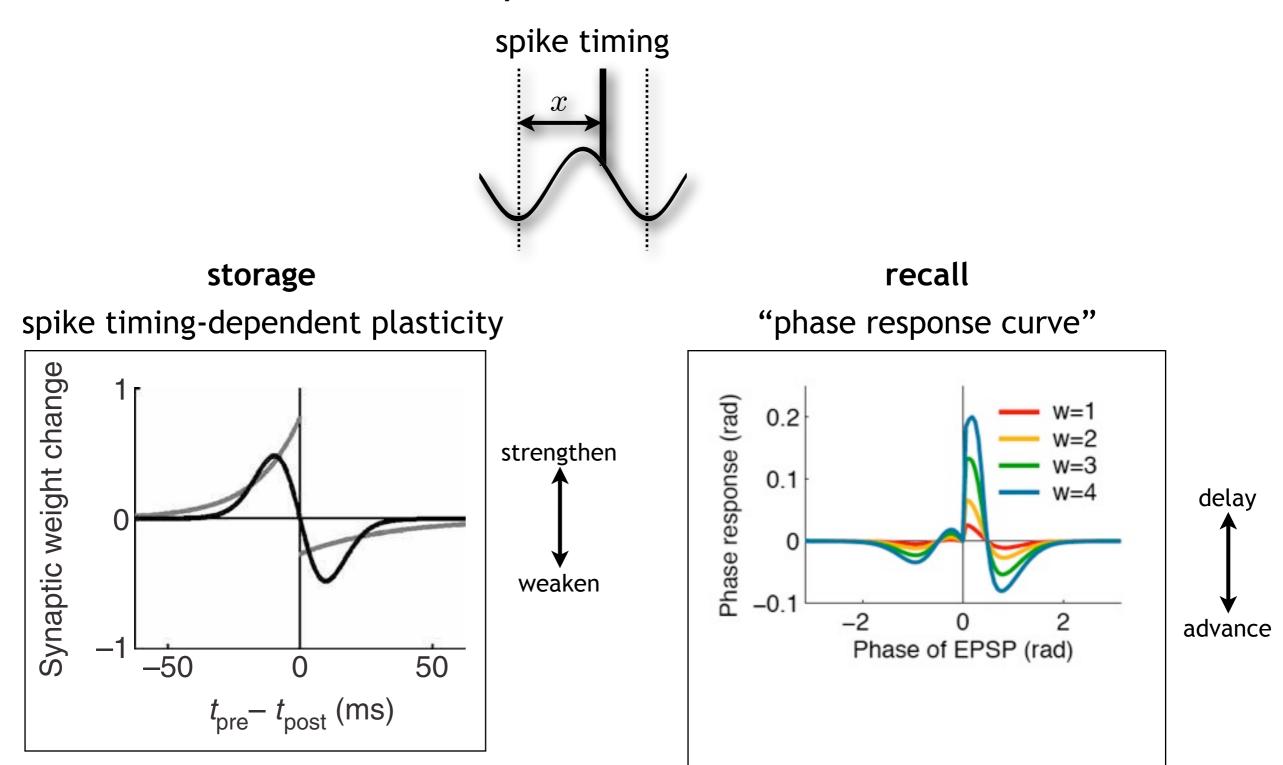
storage

spike timing-dependent plasticity



16

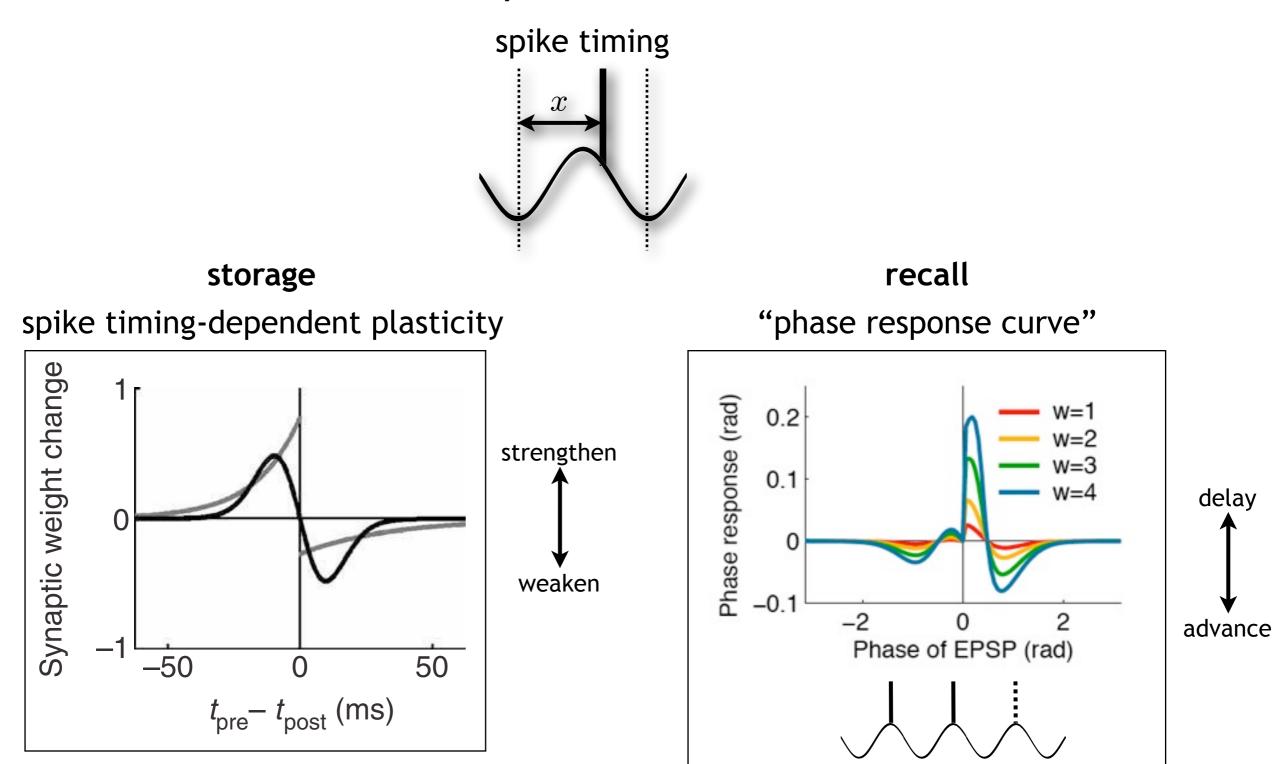
representation



Lengyel et al, Nat Neurosci 2005

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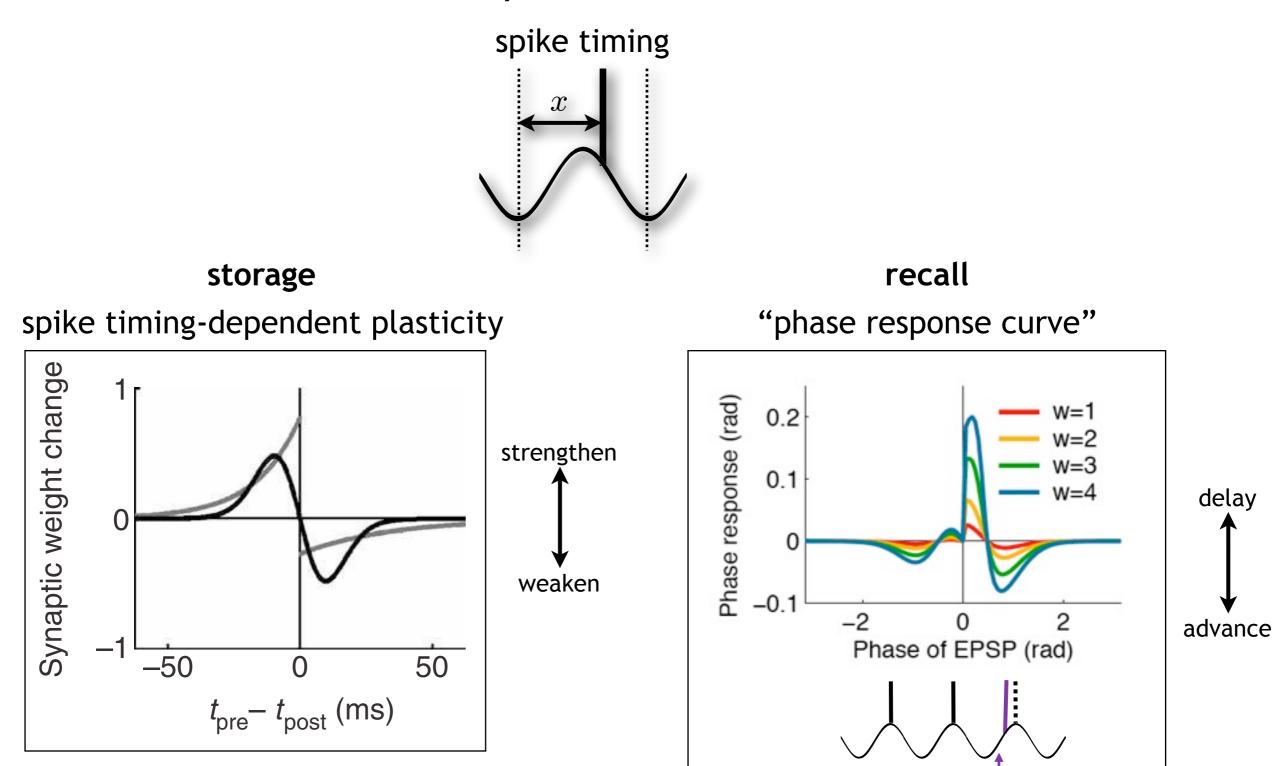
representation



Lengyel et al, Nat Neurosci 2005

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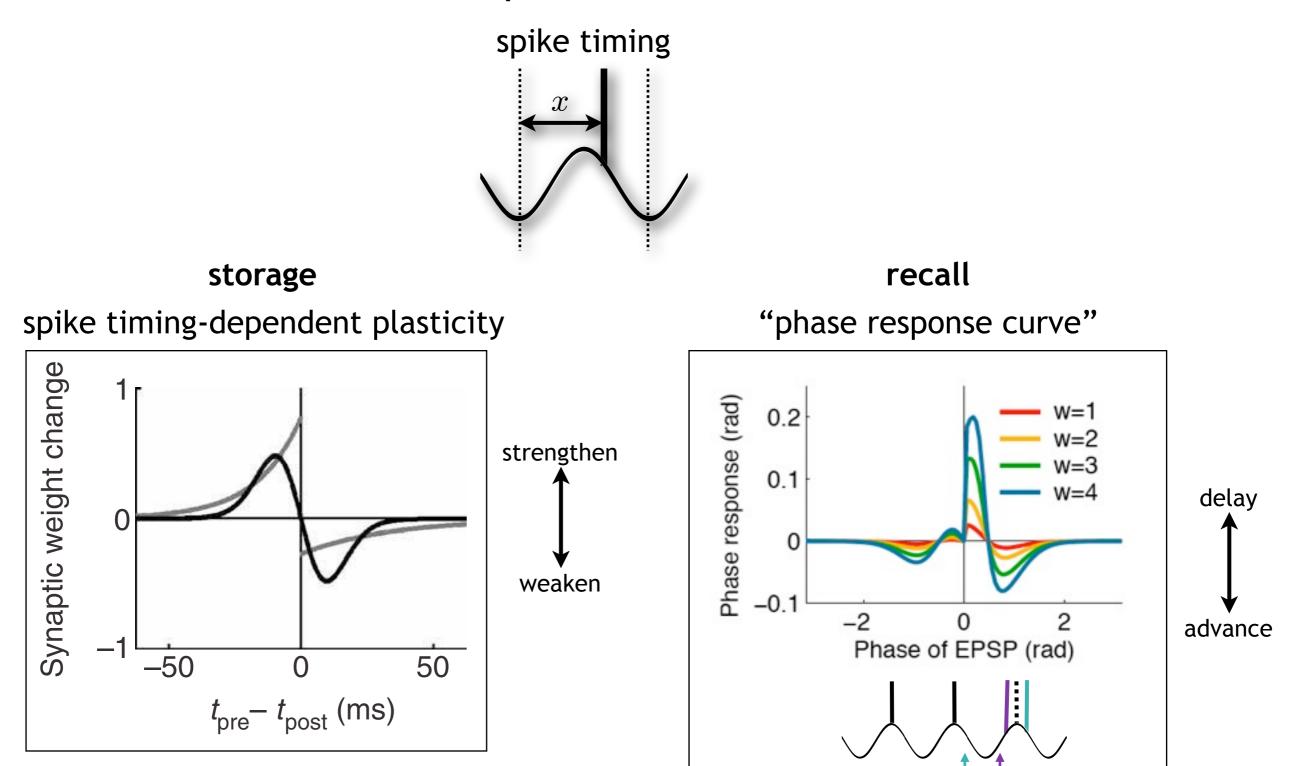
representation



Lengyel et al, Nat Neurosci 2005

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representation

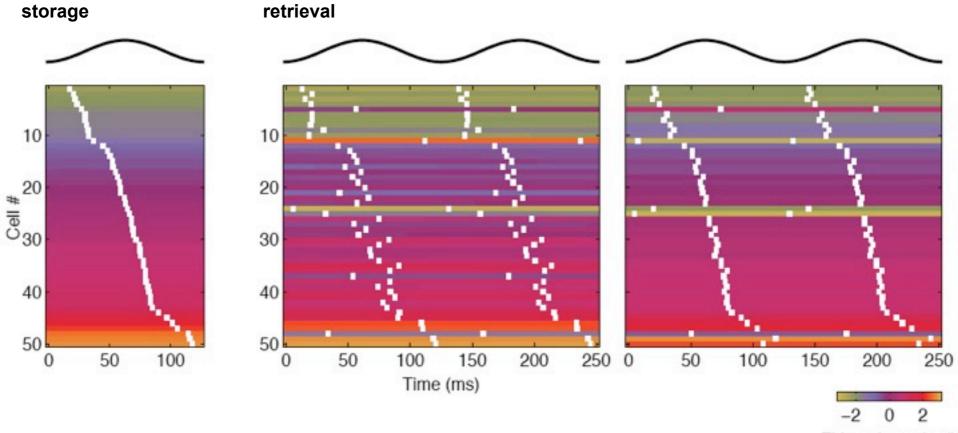


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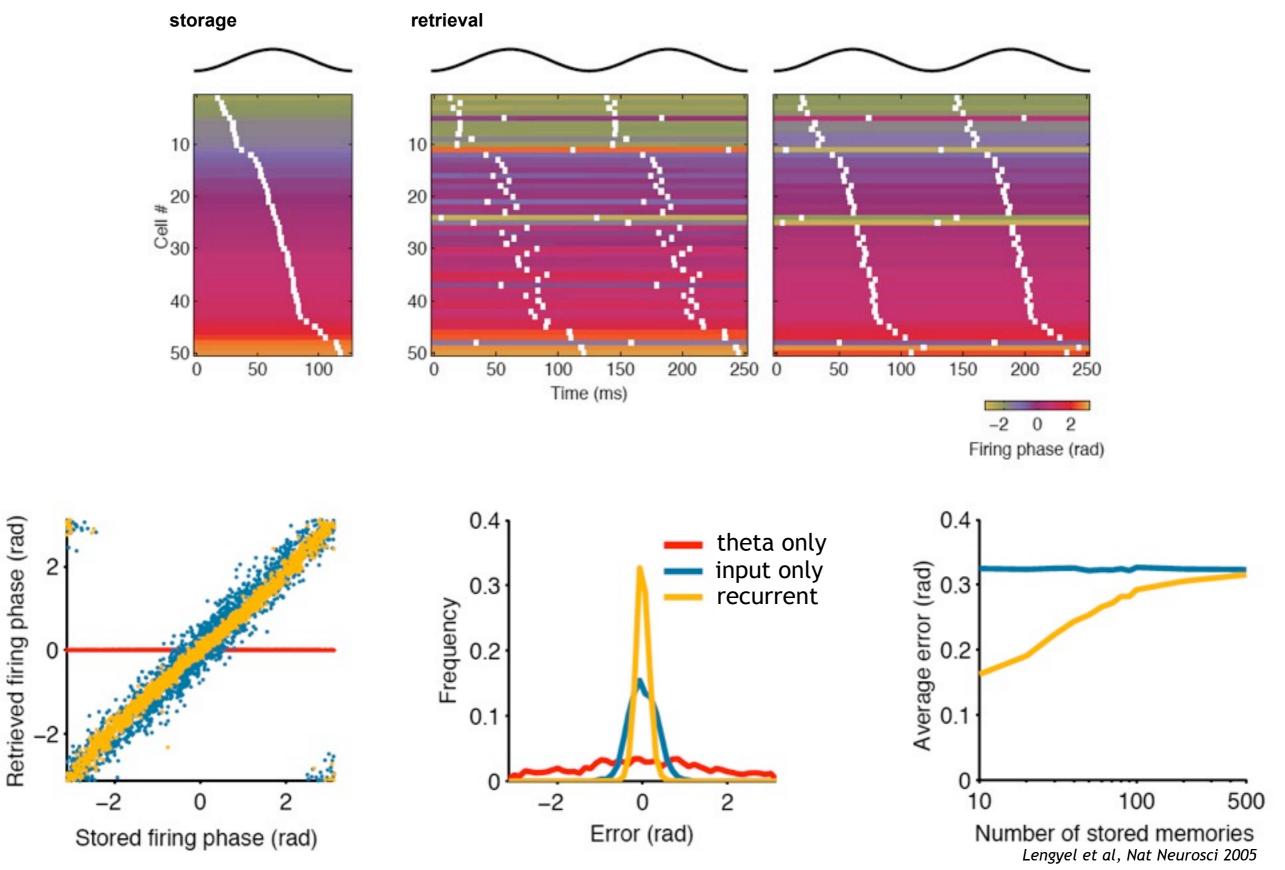
Lengyel et al, Nat Neurosci 2005

PERFORMANCE OF NETWORK



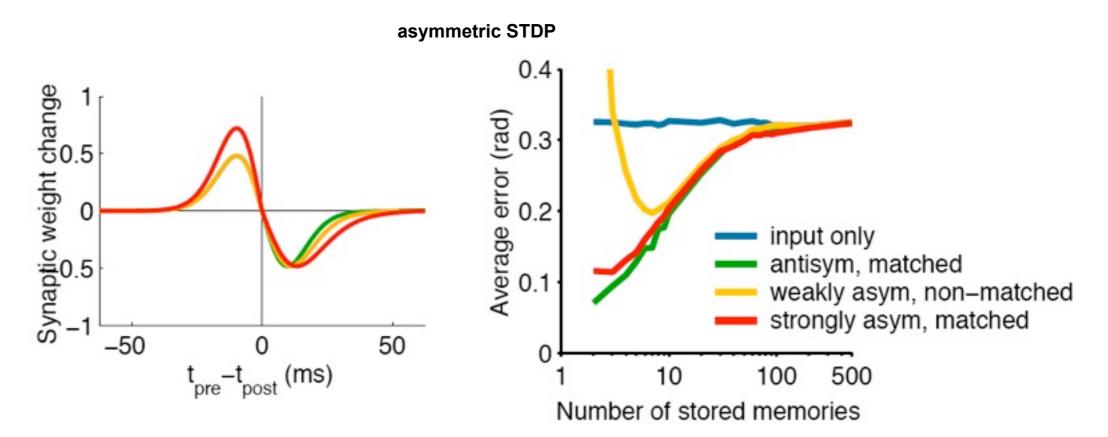
Firing phase (rad)

PERFORMANCE OF NETWORK

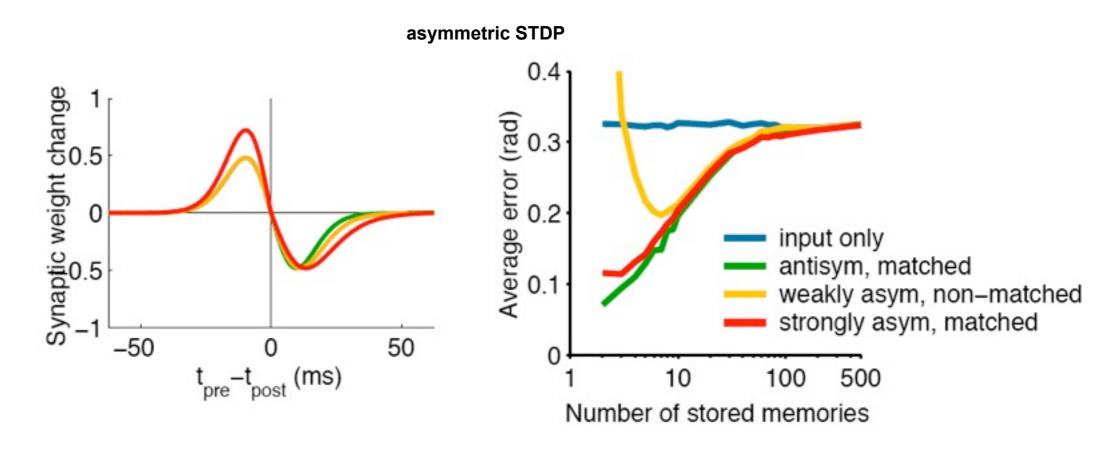


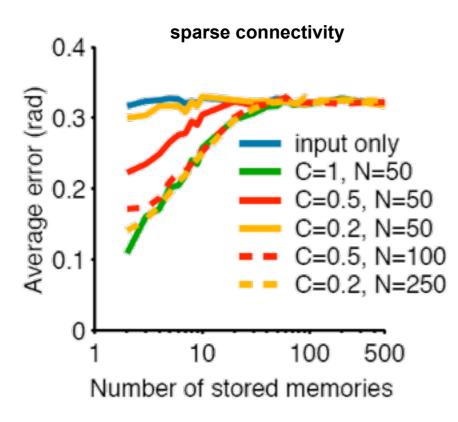
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ROBUSTNESS OF RECALL PERFORMANCE

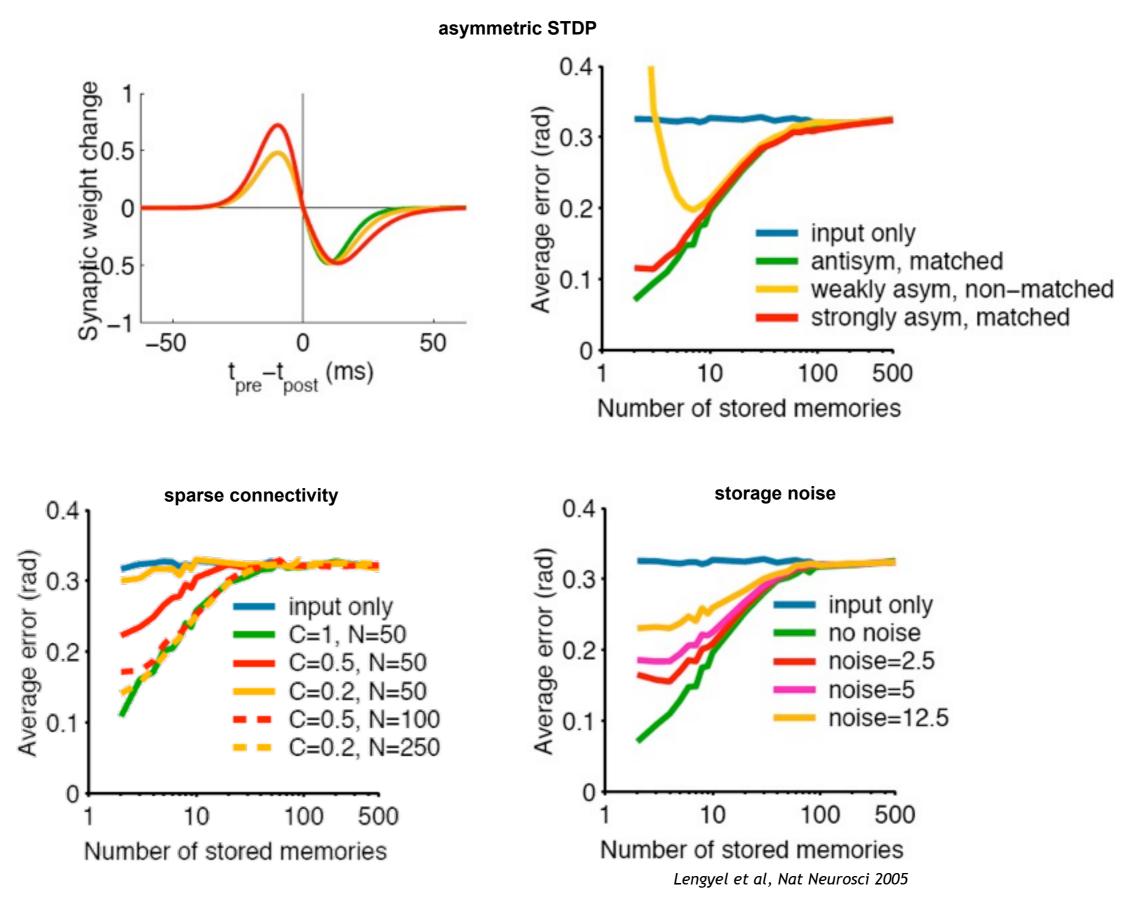


ROBUSTNESS OF RECALL PERFORMANCE



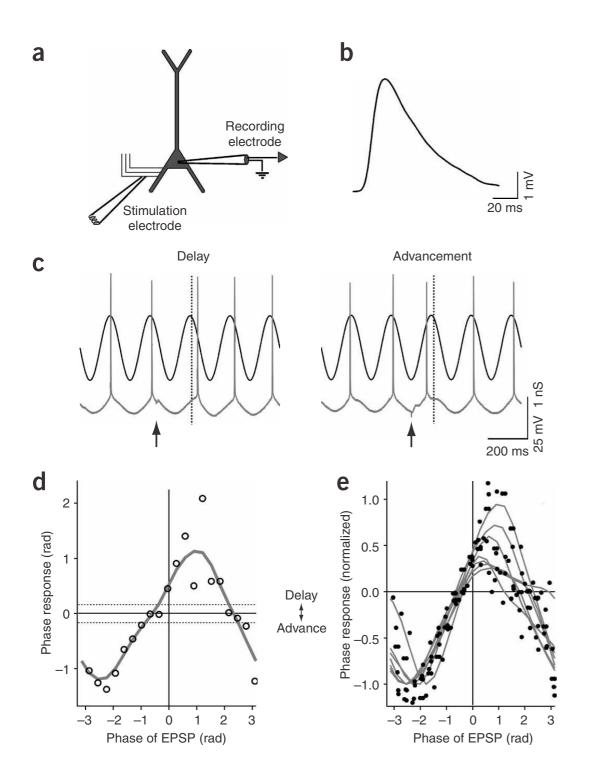


ROBUSTNESS OF RECALL PERFORMANCE

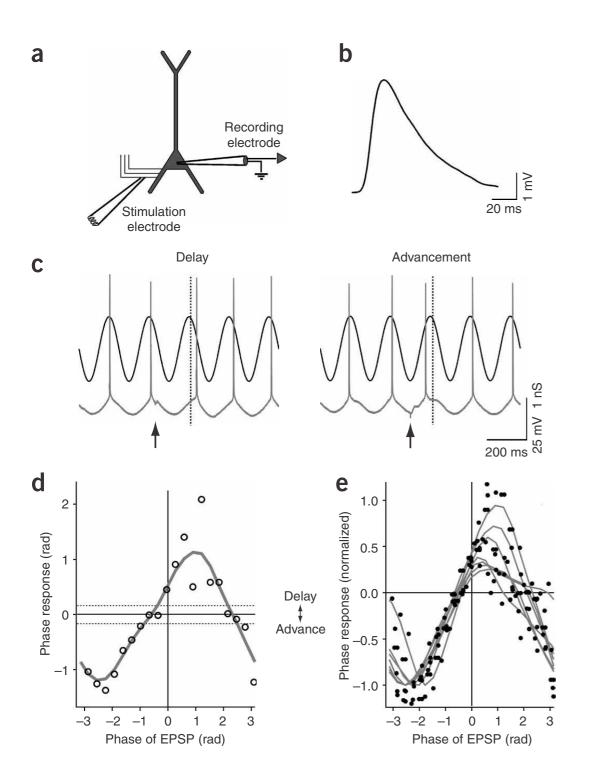


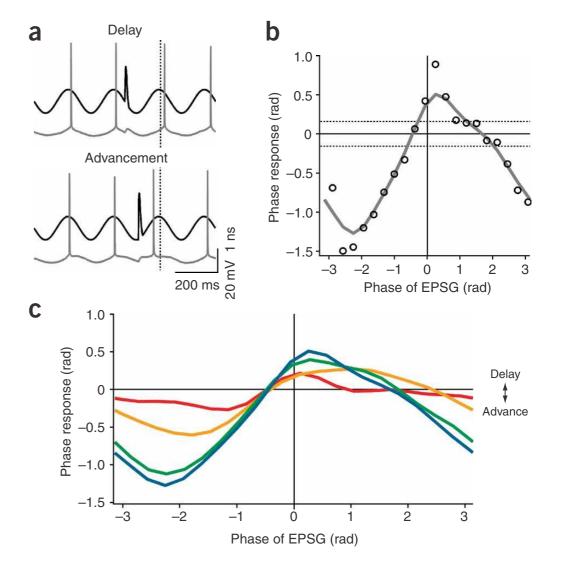
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TESTING THE PREDICTION IN VITRO



TESTING THE PREDICTION IN VITRO

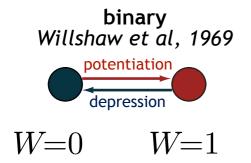


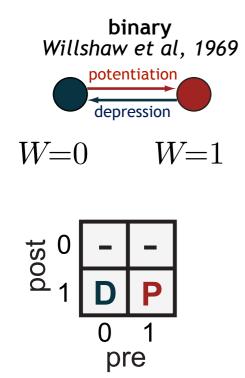


Lengyel et al, Nat Neurosci 2005

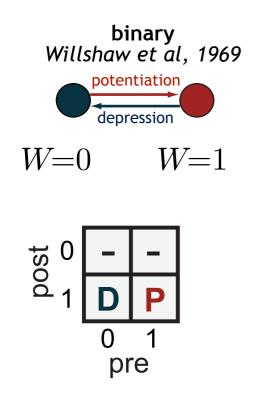
$$W_{ij} = \sum_{m=1}^{M} \Omega\left(x_i^{(m)}, x_j^{(m)}\right)$$

$$W_{ij} = \sum_{m=1}^{M} \Omega\left(x_i^{(m)}, x_j^{(m)}\right) \rightarrow \text{unlimited dynamic range ...}$$

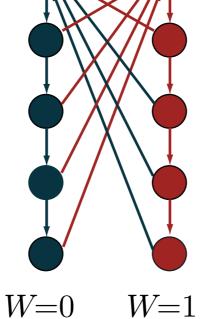


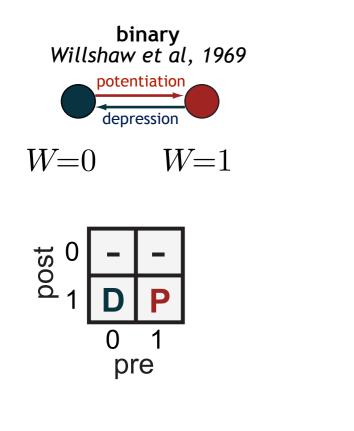


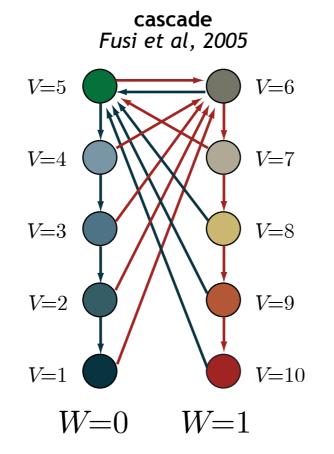
synapses with limited dynamic range



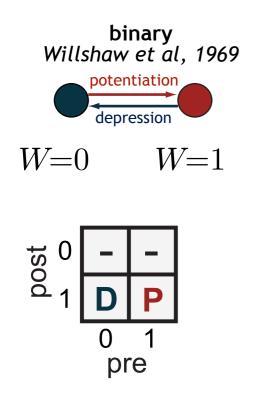
cascade Fusi et al, 2005

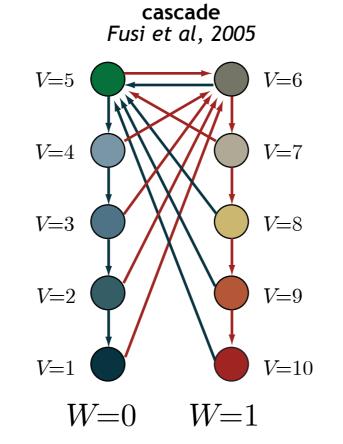




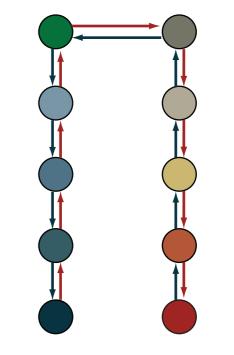


synapses with limited dynamic range

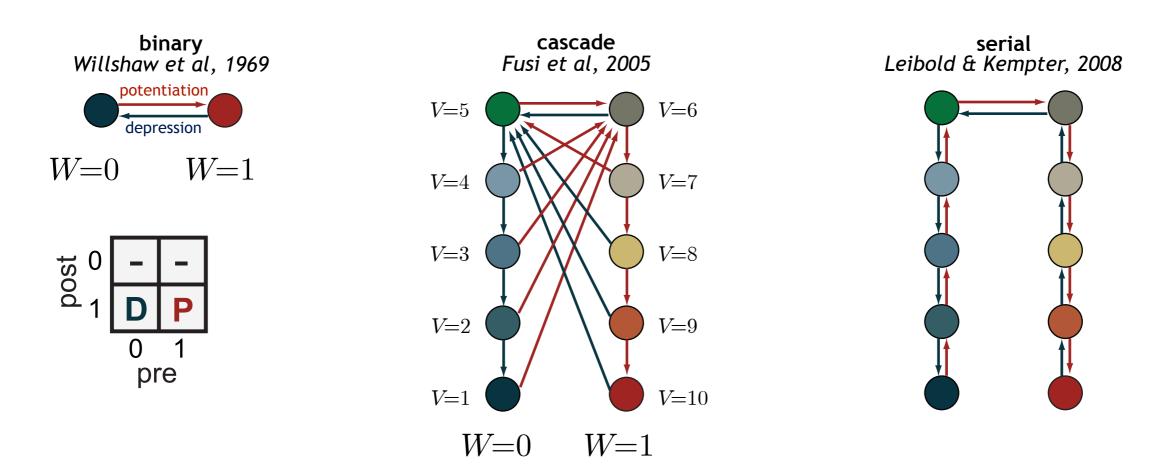




serial Leibold & Kempter, 2008



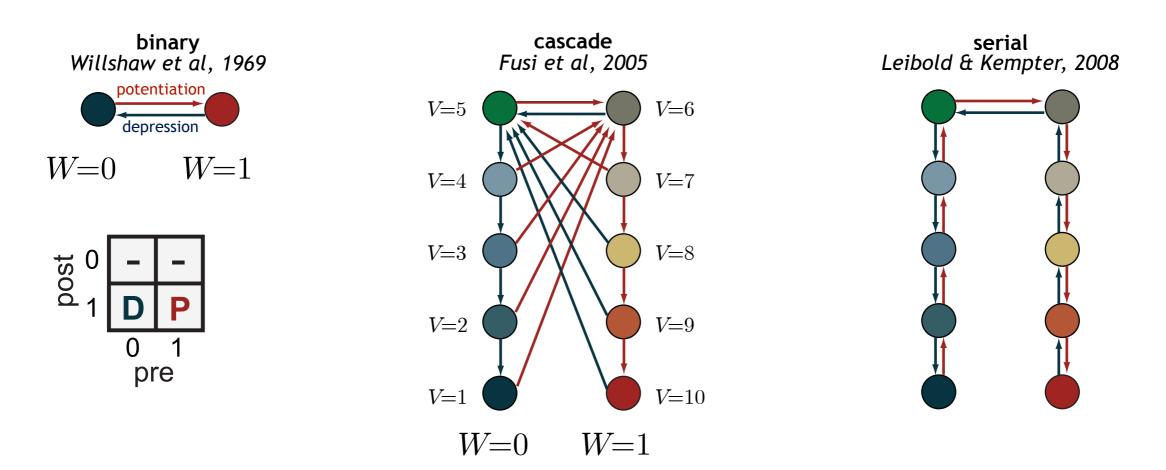
synapses with limited dynamic range



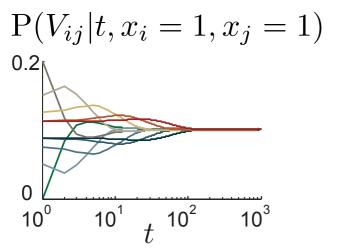
... lead to palimpsest memories

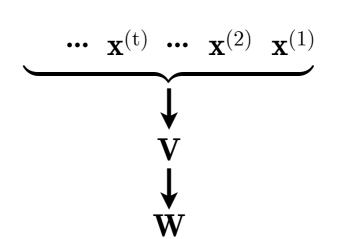
$$P(V_{ij}|t, x_i = 1, x_j = 1)$$

synapses with limited dynamic range



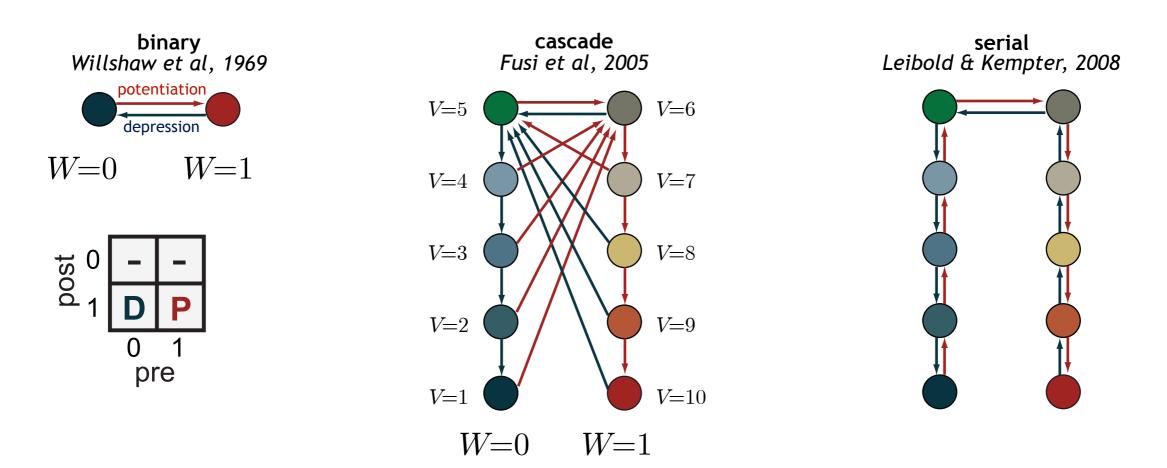
... lead to palimpsest memories



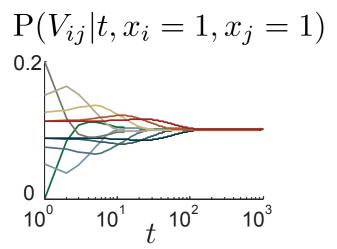


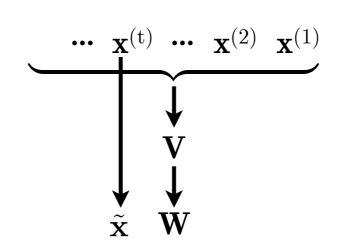
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synapses with limited dynamic range



... lead to palimpsest memories

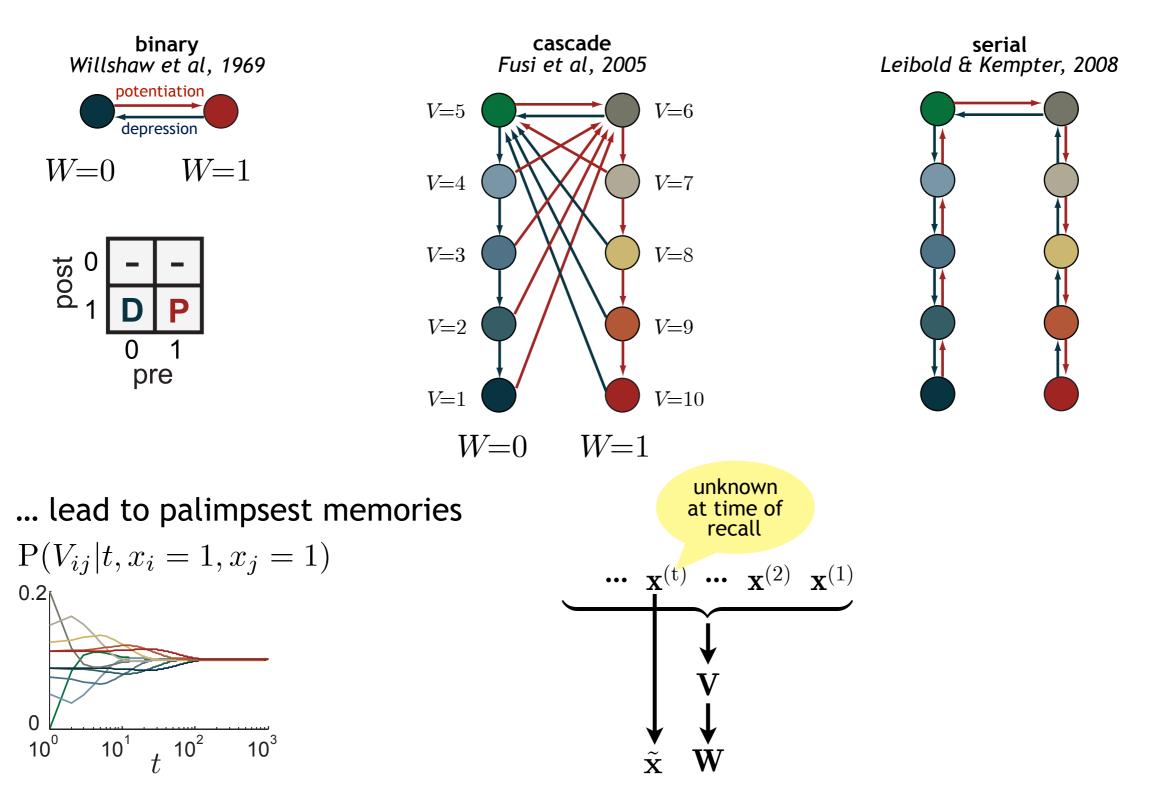




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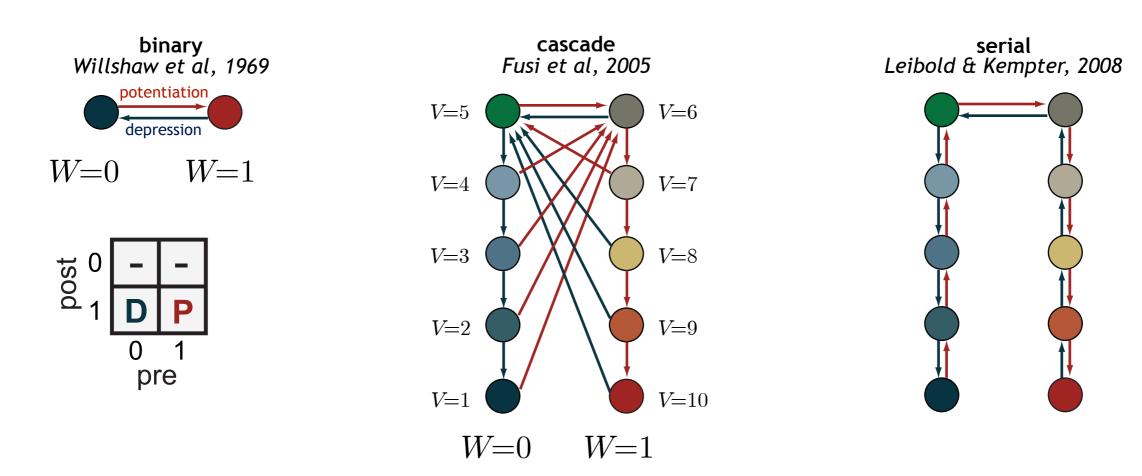
synapses with limited dynamic range



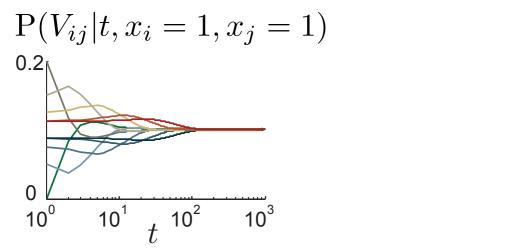
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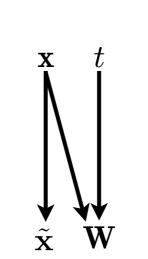
synapses with limited dynamic range



... lead to palimpsest memories

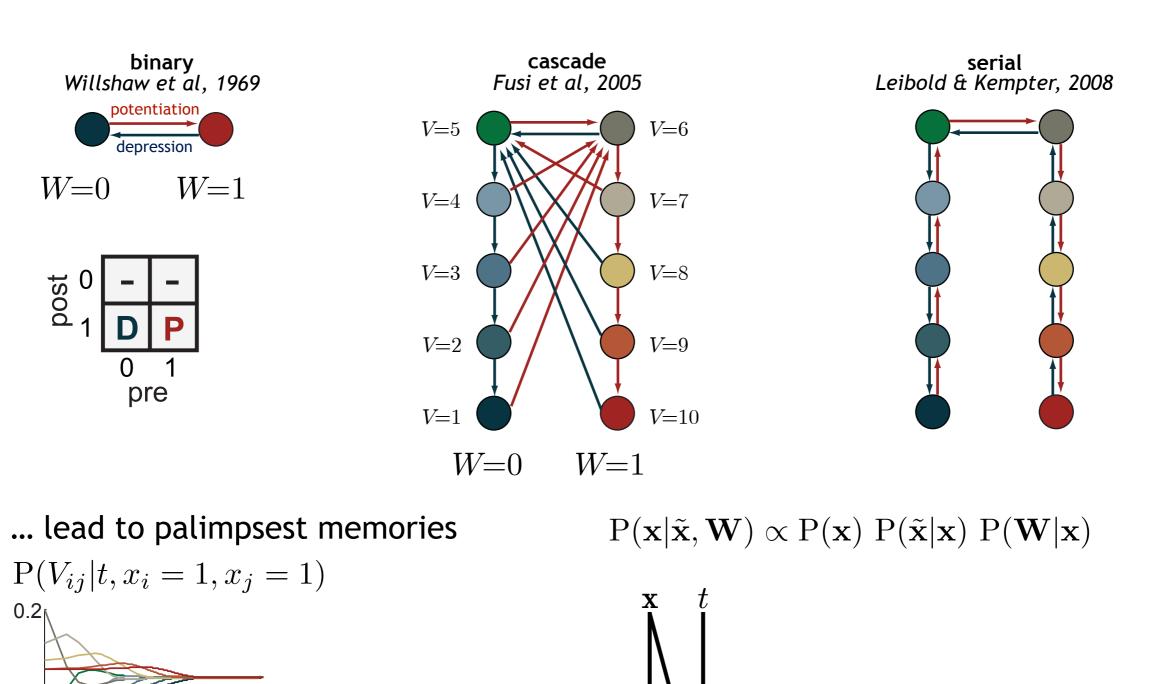


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synapses with limited dynamic range



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10¹

 t^{10^2}

10³

0

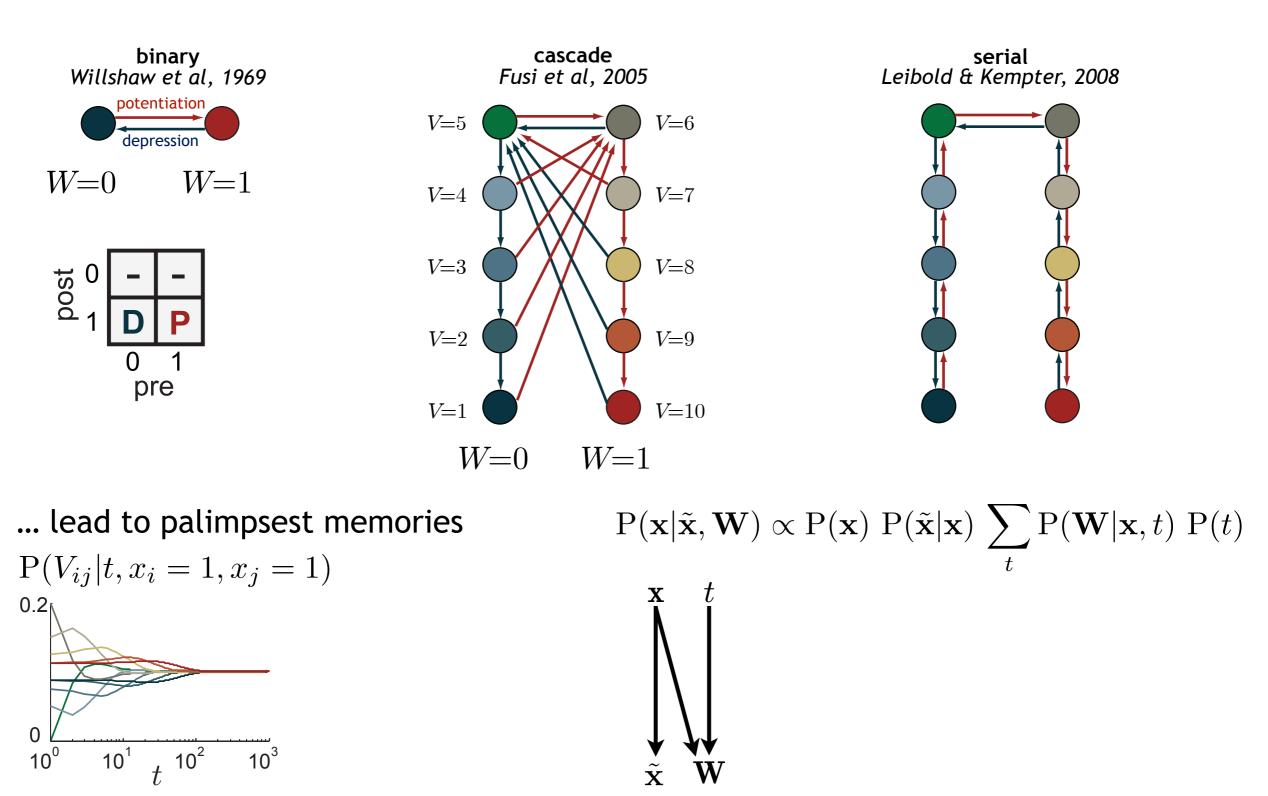
10⁰

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X

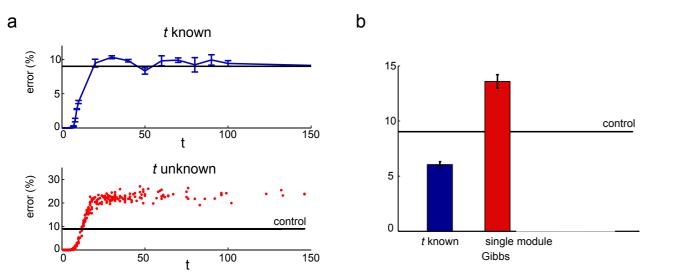
W

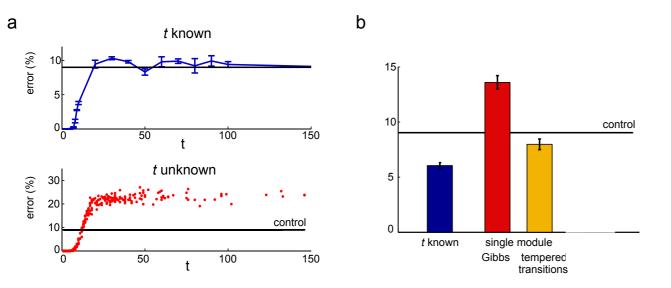
synapses with limited dynamic range

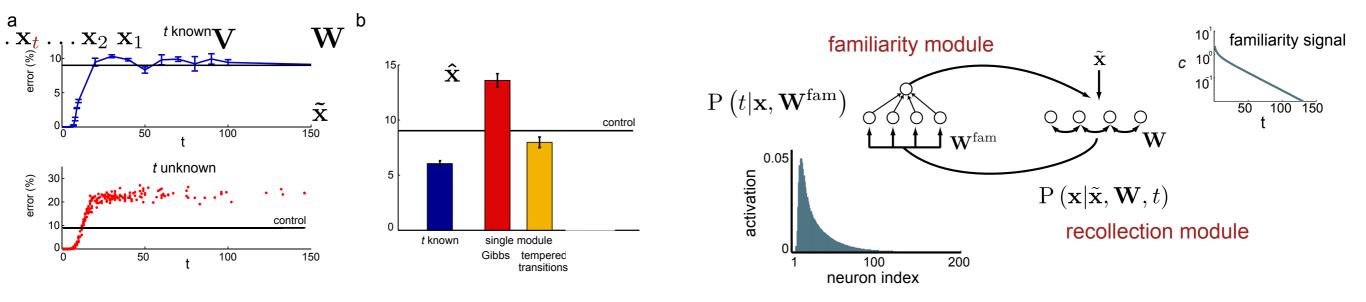


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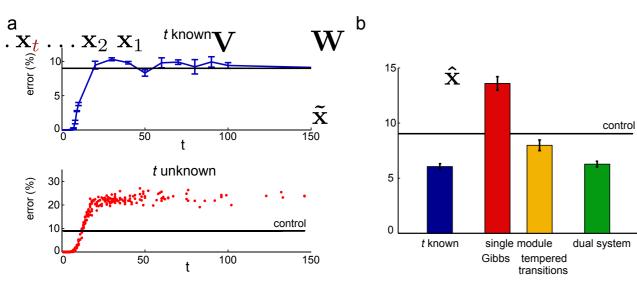
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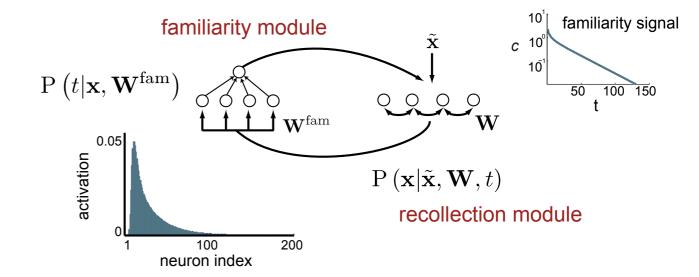






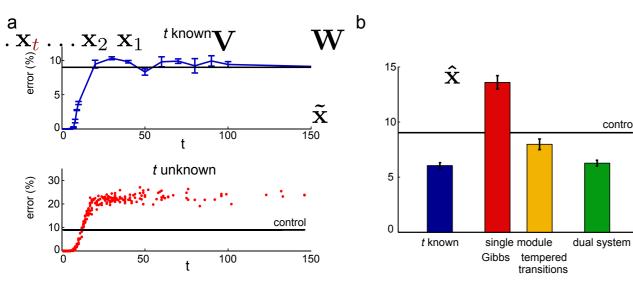
 $P(\mathbf{x}|\mathbf{W}, \mathbf{\tilde{x}}) \propto P(\mathbf{W}|\mathbf{x}) \cdot P(\mathbf{\tilde{x}}|\mathbf{x}) \cdot P(\mathbf{x})$

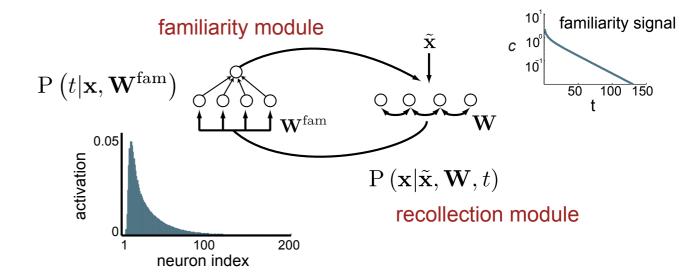




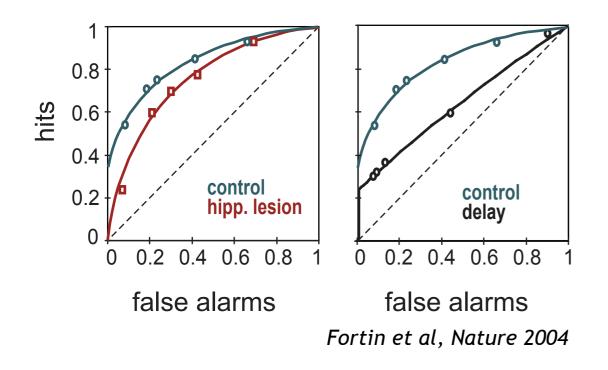
 $P(\mathbf{x}|\mathbf{W}, \mathbf{\tilde{x}}) \propto P(\mathbf{W}|\mathbf{x}) \cdot P(\mathbf{\tilde{x}}|\mathbf{x}) \cdot P(\mathbf{x})$

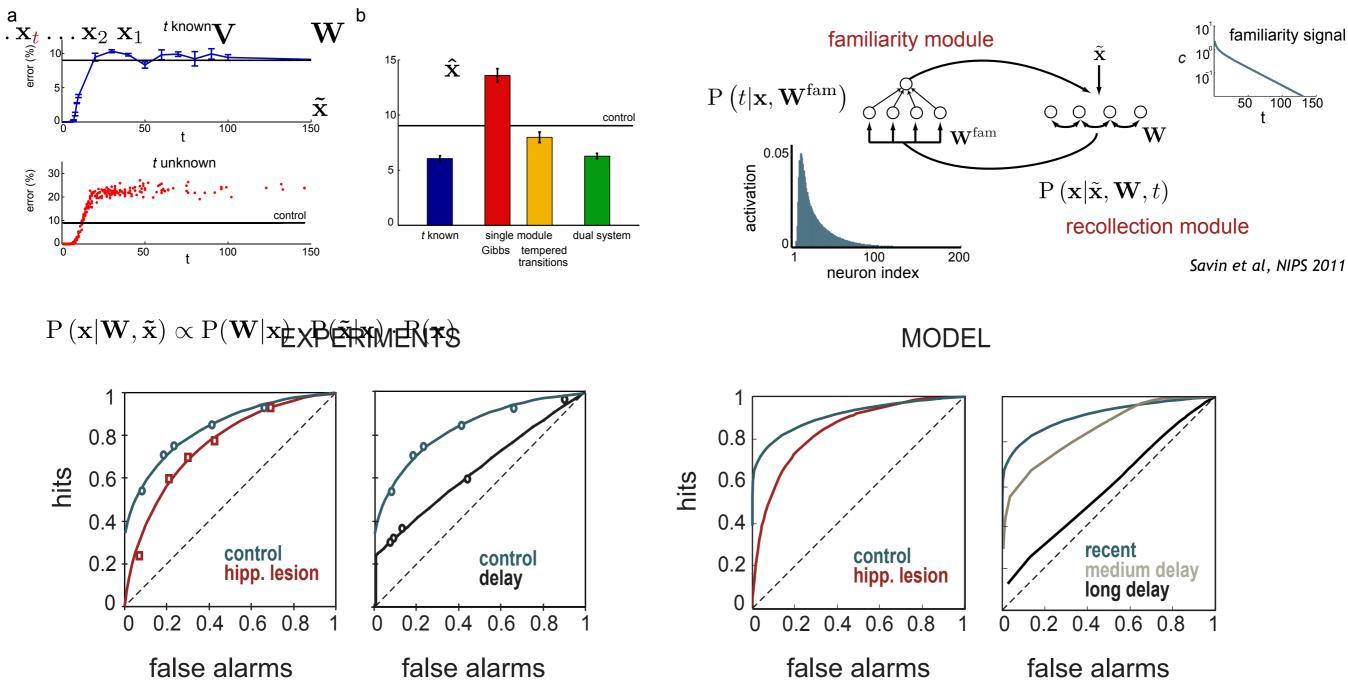
control





$P(\mathbf{x}|\mathbf{W}, \mathbf{\tilde{x}}) \propto P(\mathbf{W}|\mathbf{x}, \mathbf{\tilde{x}}) \in \mathbb{R}$



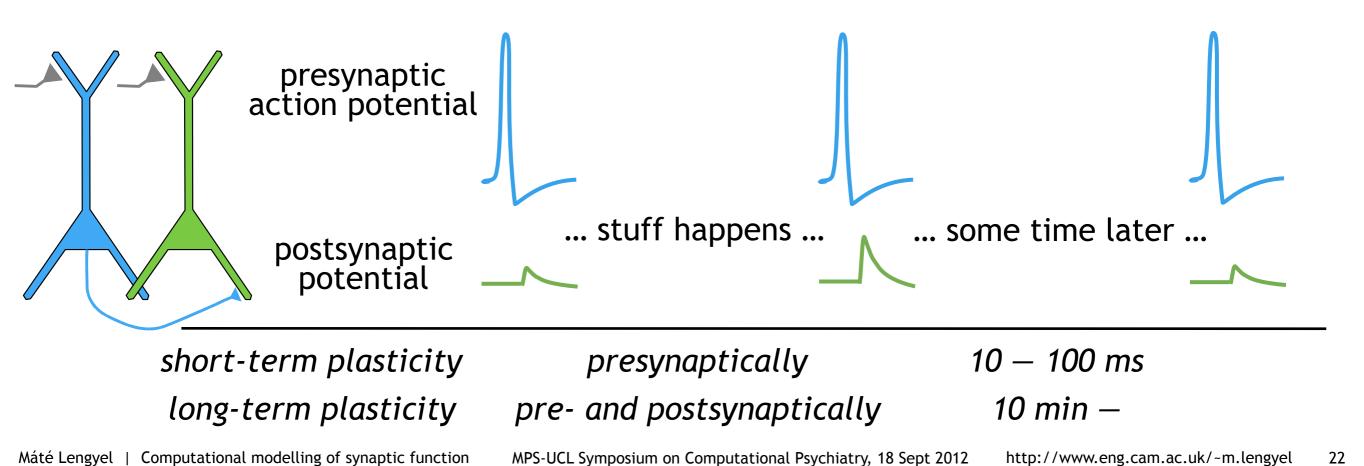


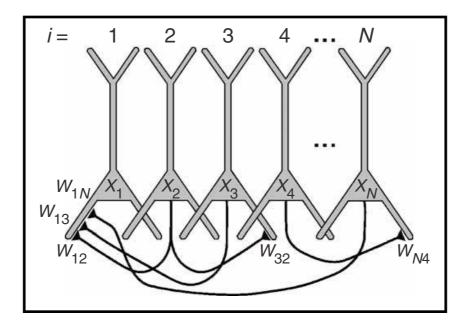
Fortin et al, Nature 2004

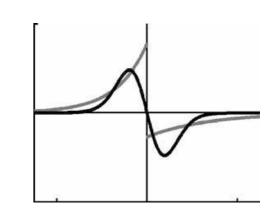
SYNAPTIC PLASTICITY

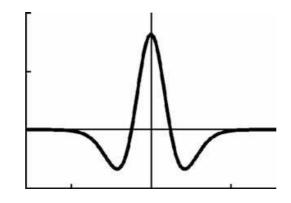
Synapses are computational devices that not only transmit action potential-encoded information, but also transform it. Neuronal information is often encoded by bursts or trains of action potentials. Synapses process such action potential bursts or trains in a synapsespecific manner that involves use-dependent changes in neurotransmitter release during the burst or train (referred to as short-term plasticity). In addition, synapses experience usedependent long-term changes in synaptic transmission that adjust the "gain" of a synapse, and operate either pre- and/or postsynaptically (referred to as long-term plasticity)

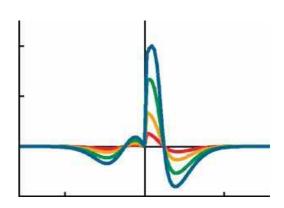
Südhof, 2012

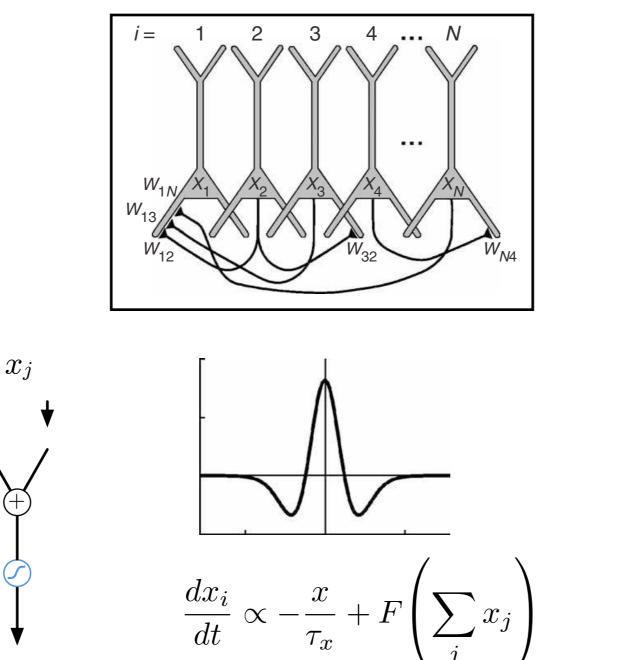


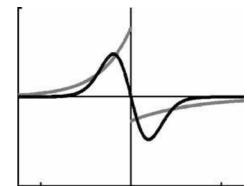


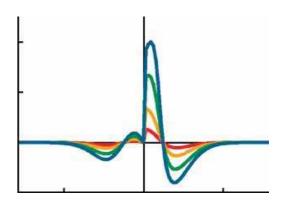




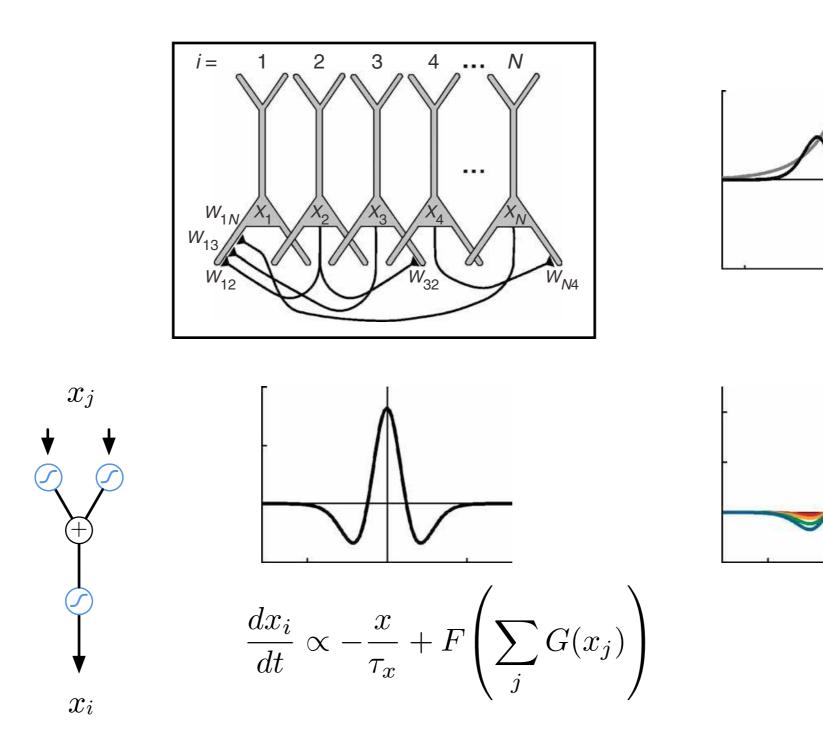


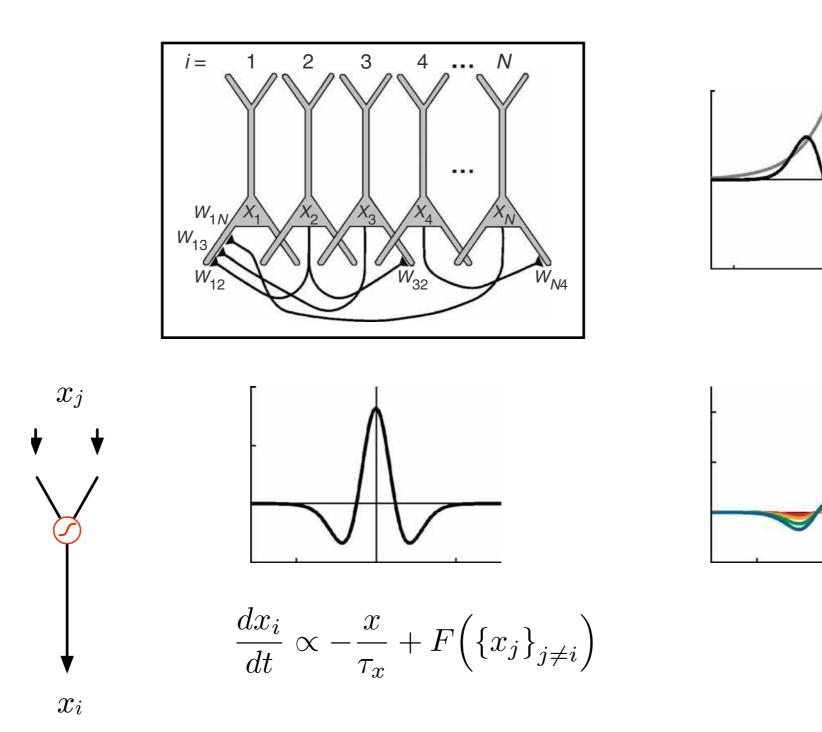


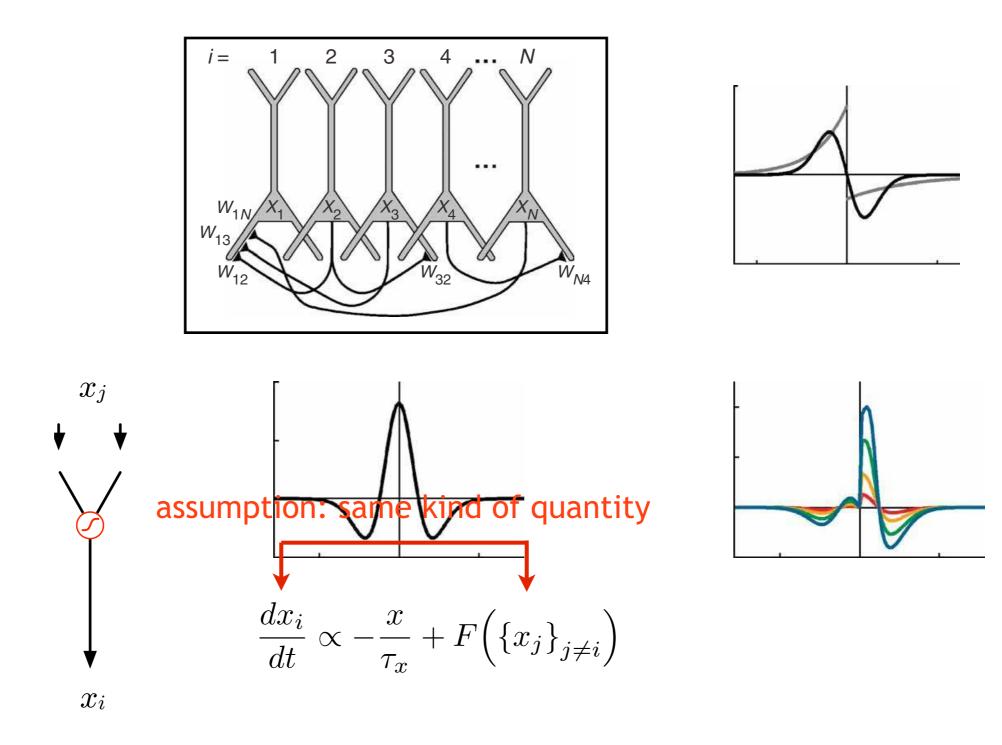




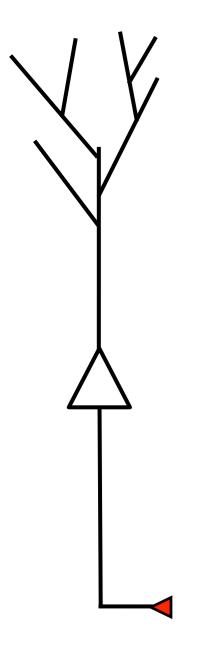
 x_i





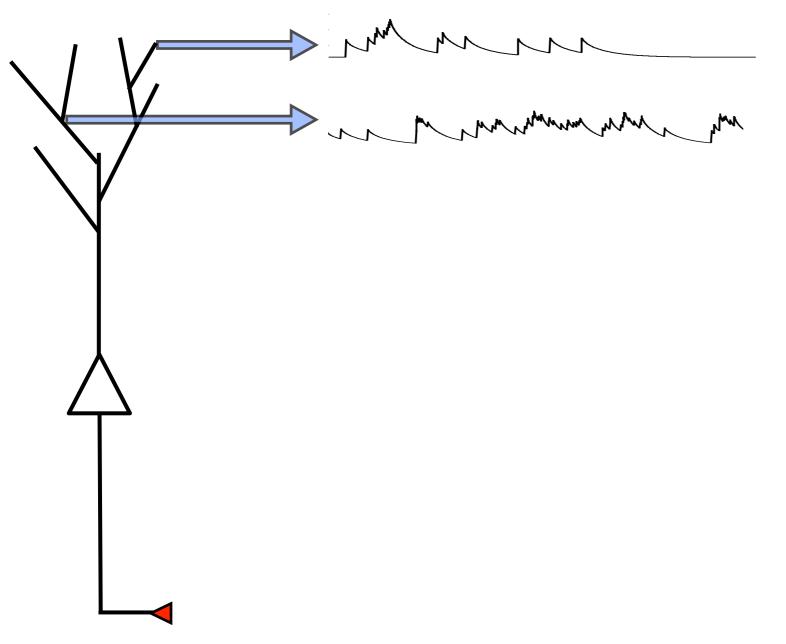


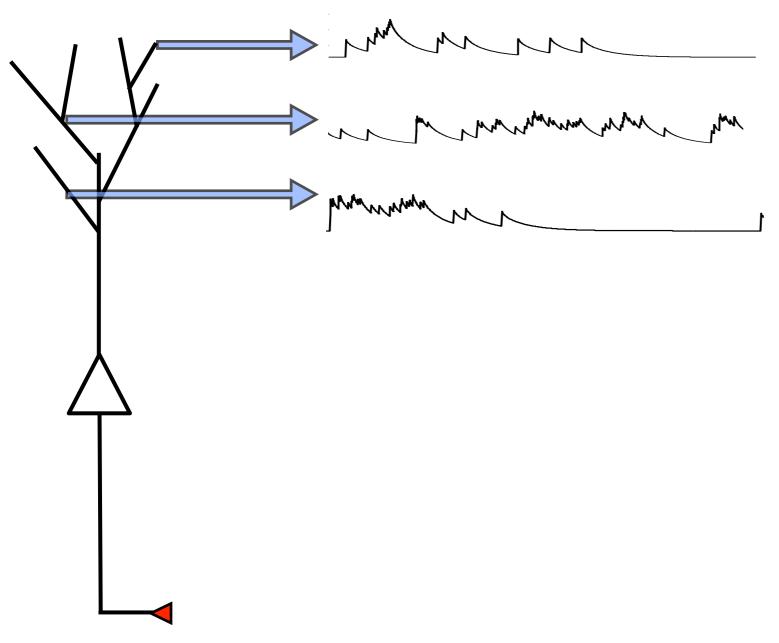
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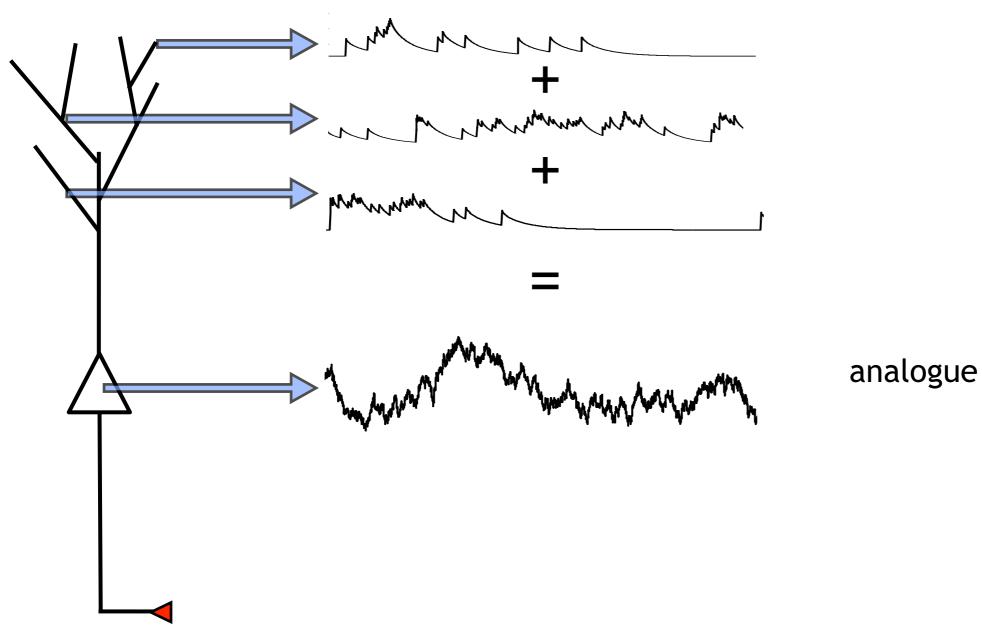


NW

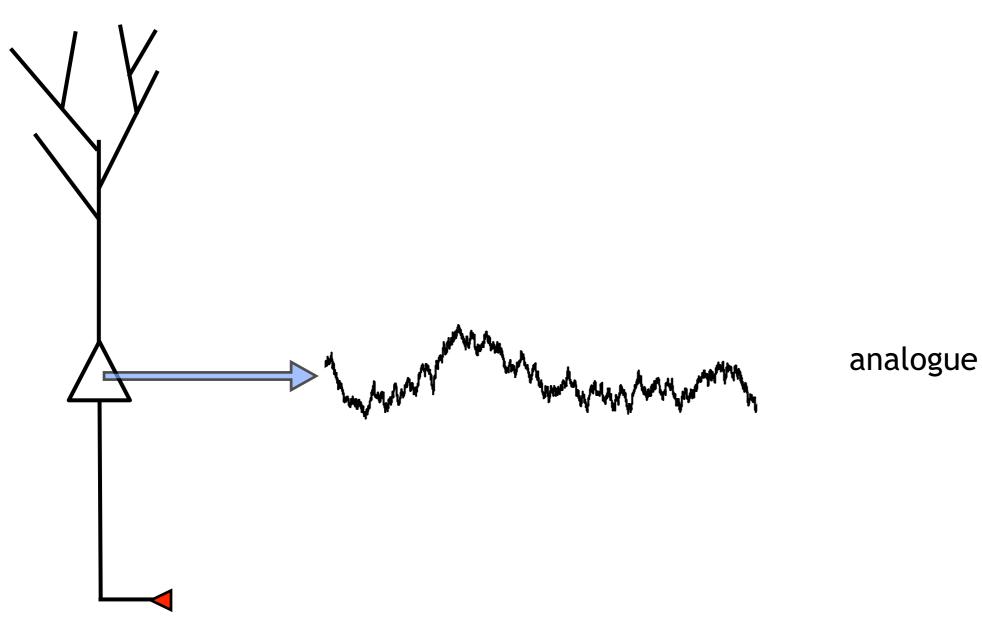
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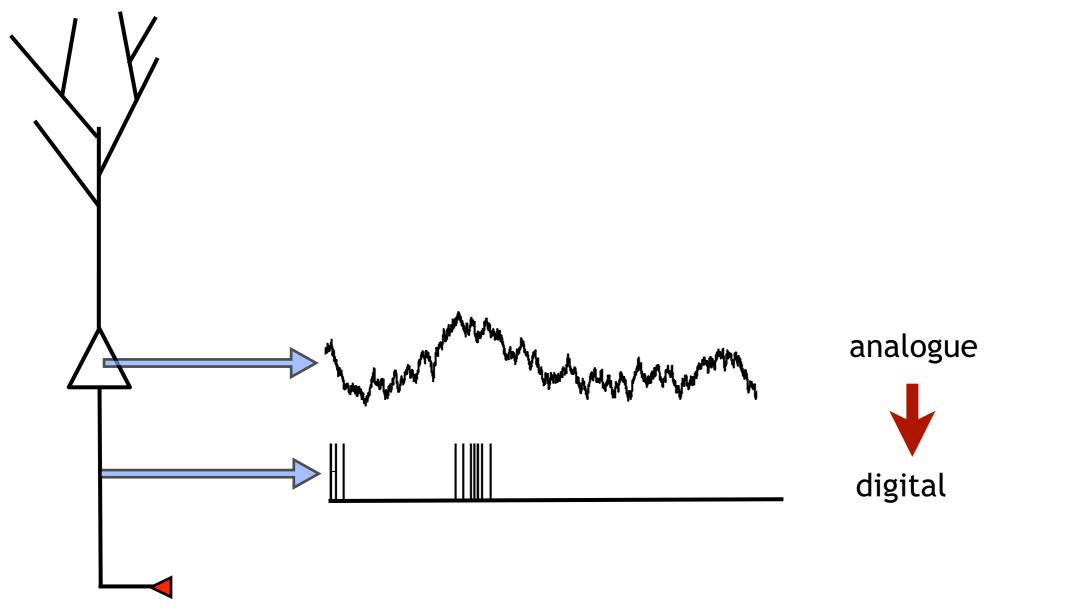


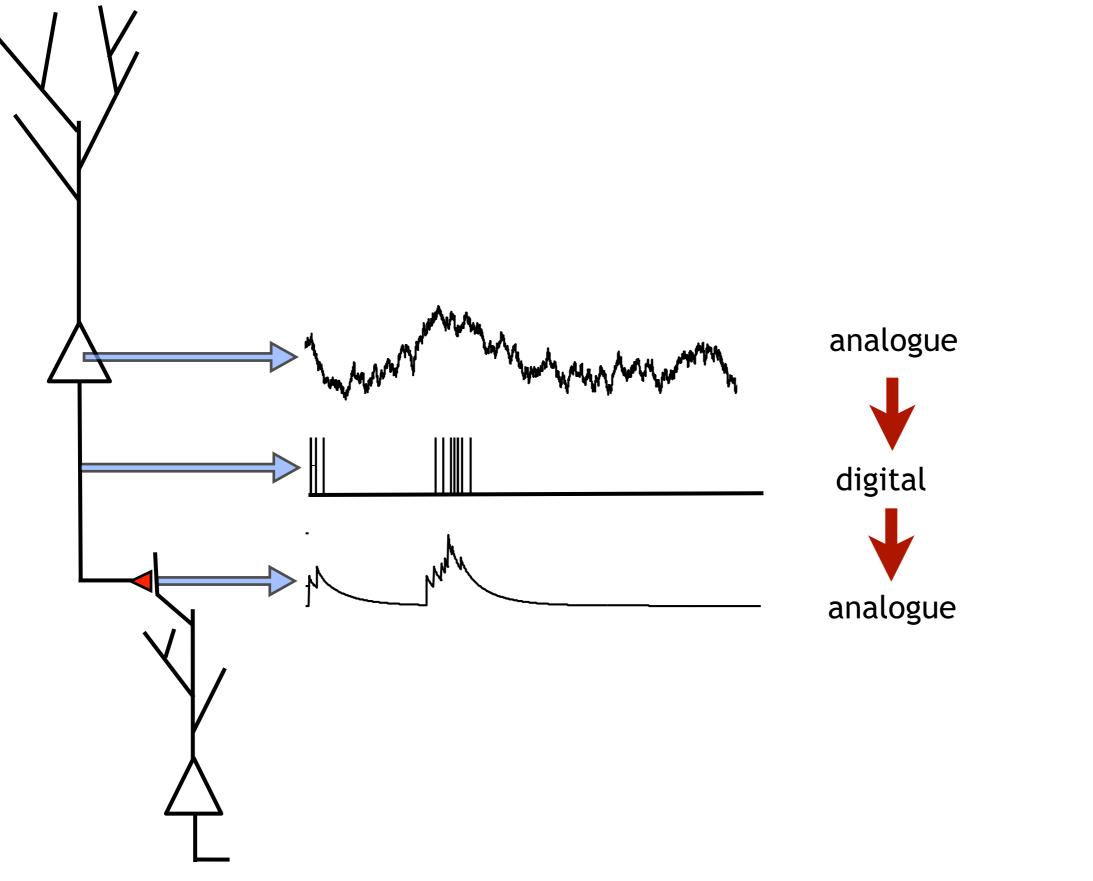


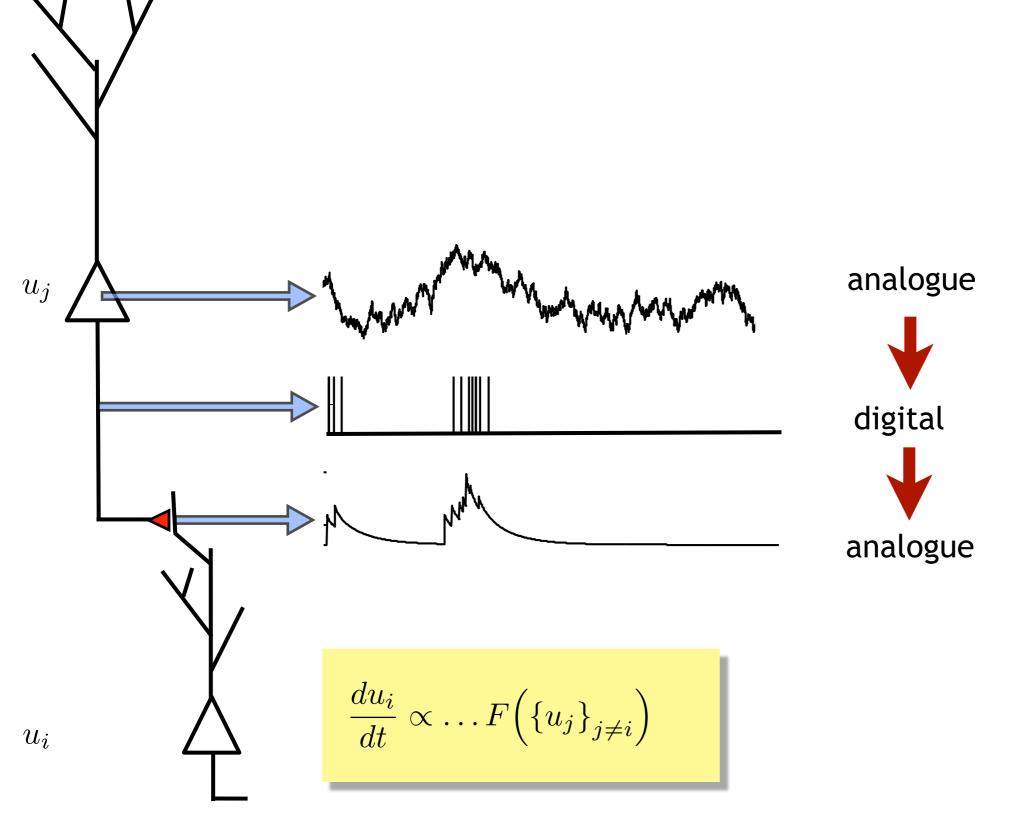
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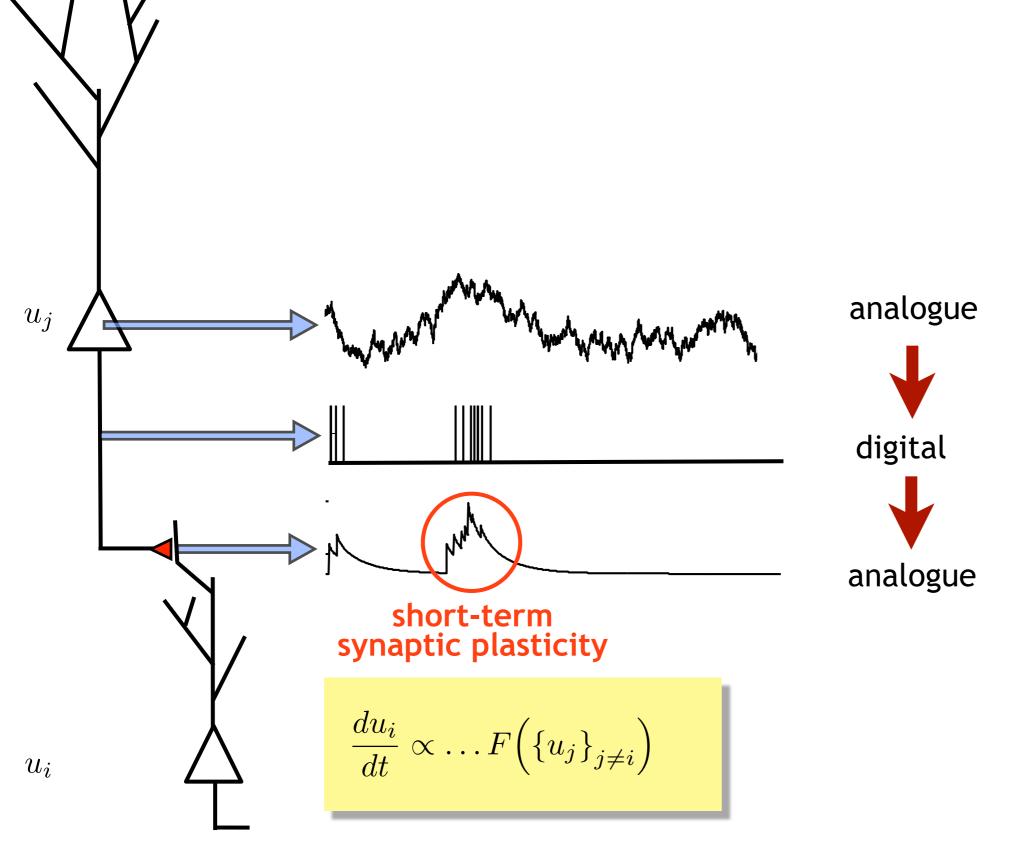
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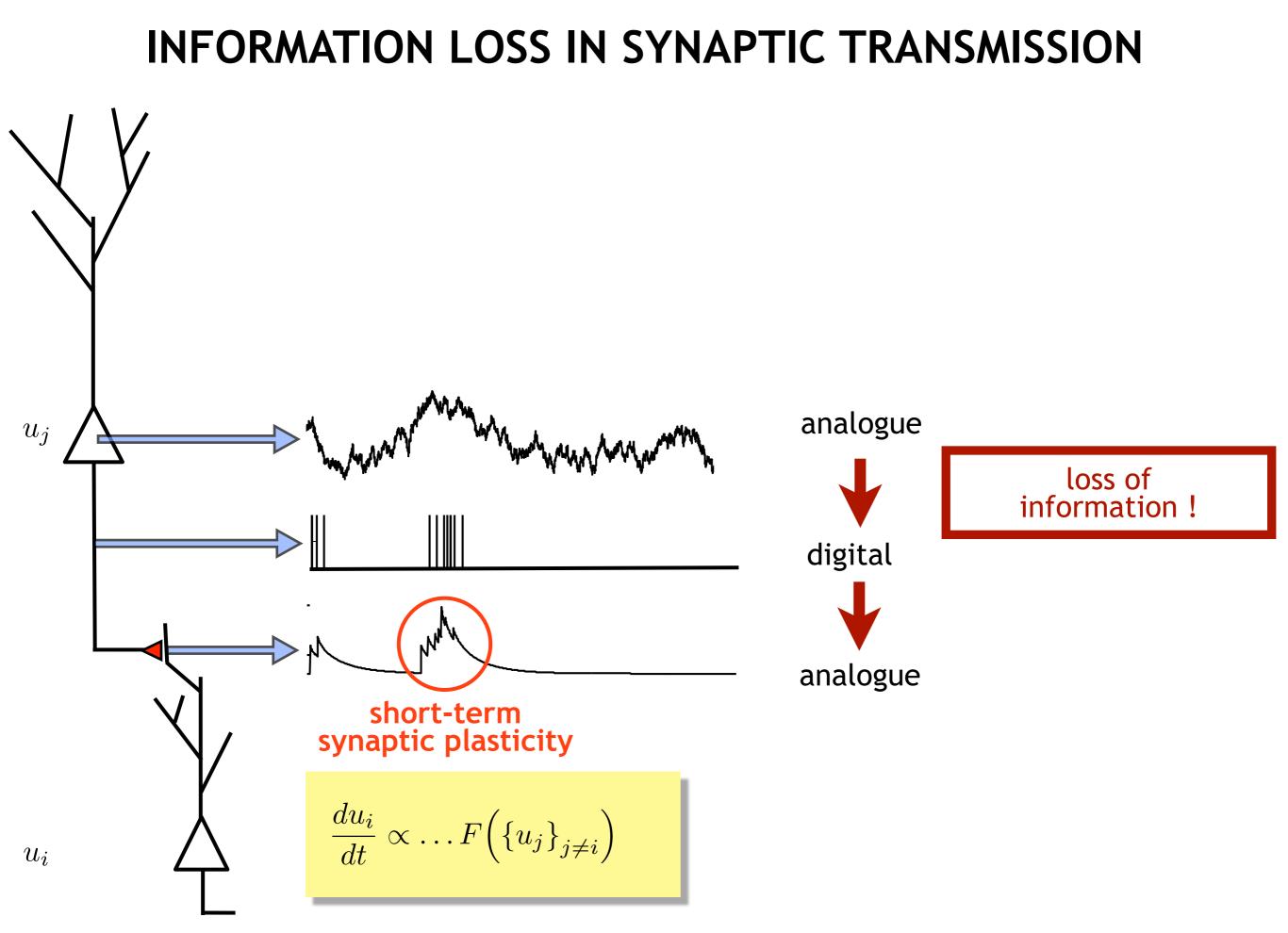




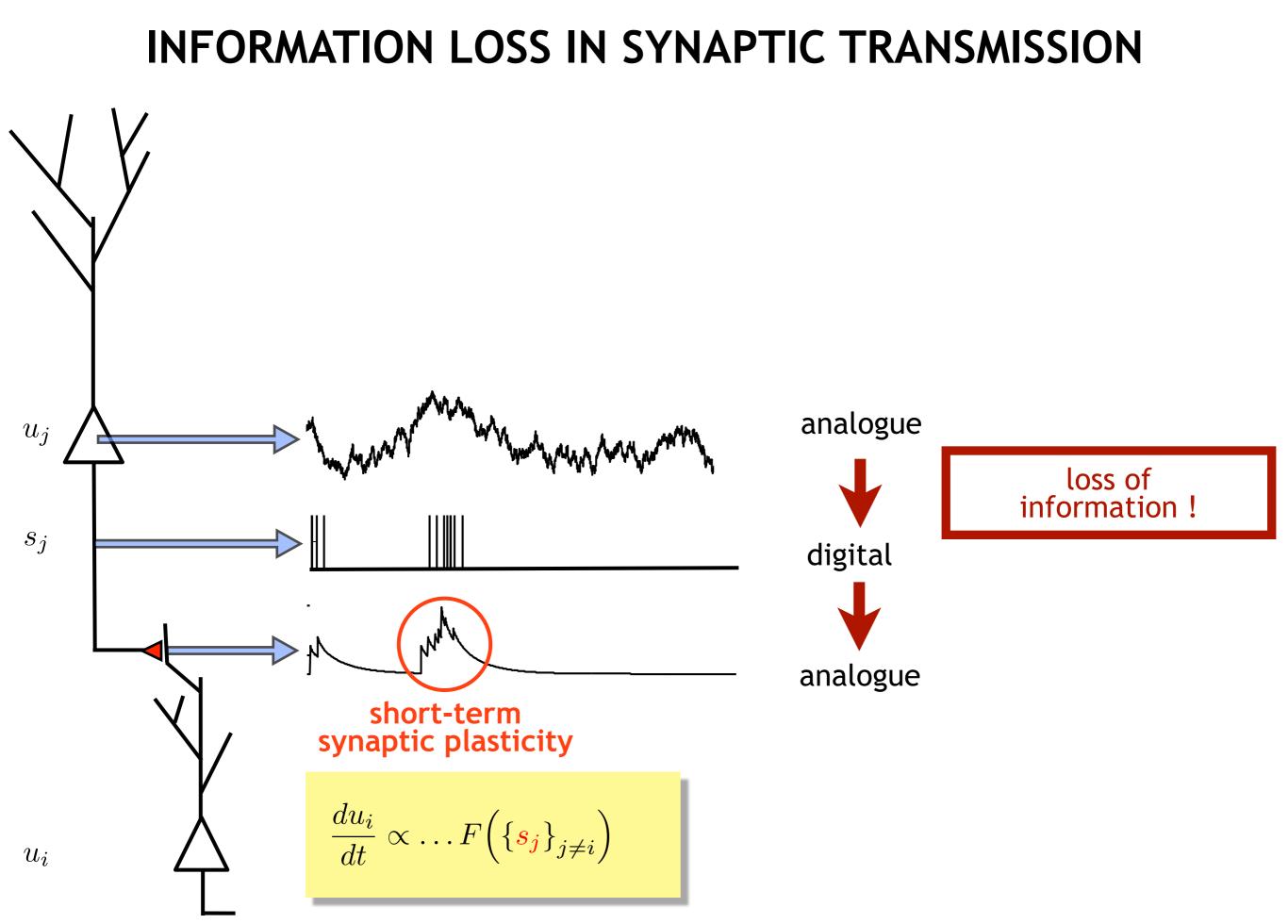


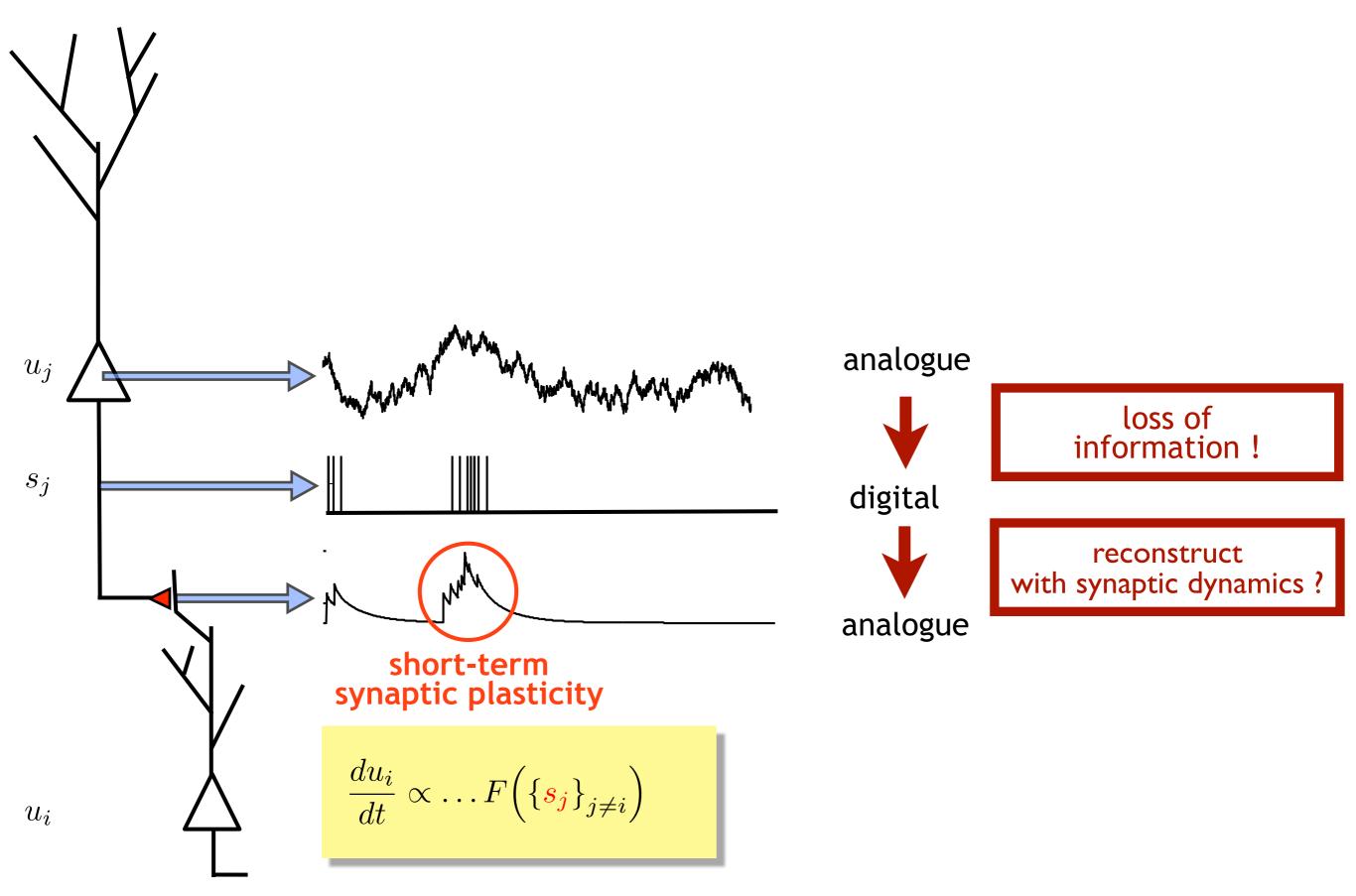
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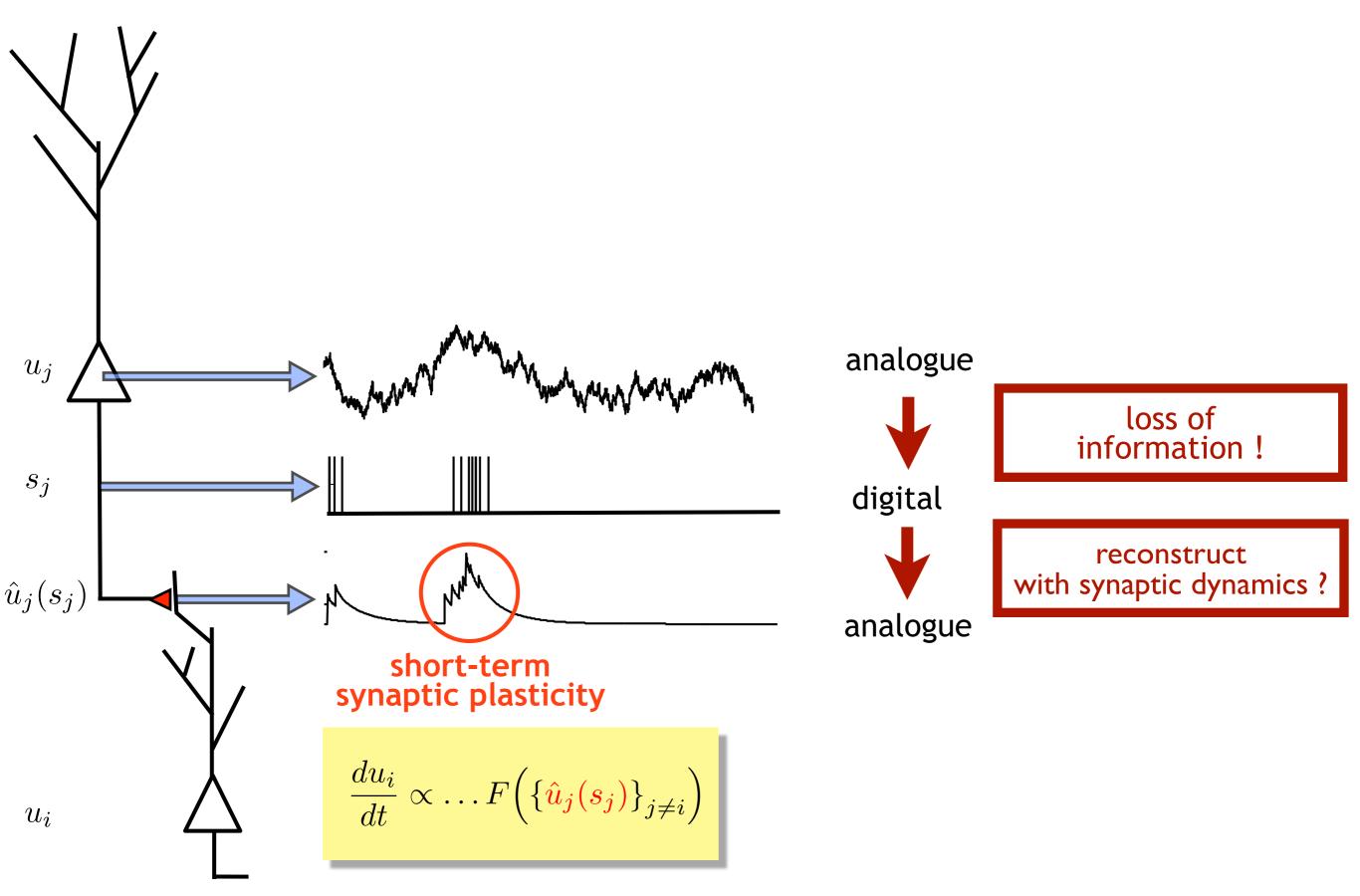


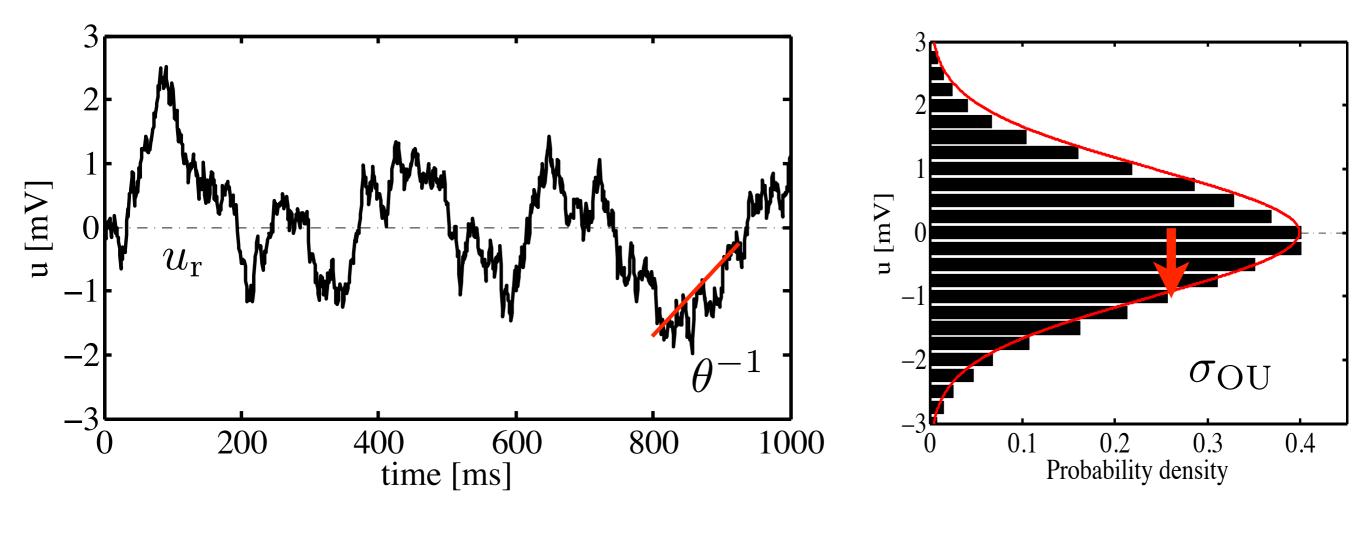


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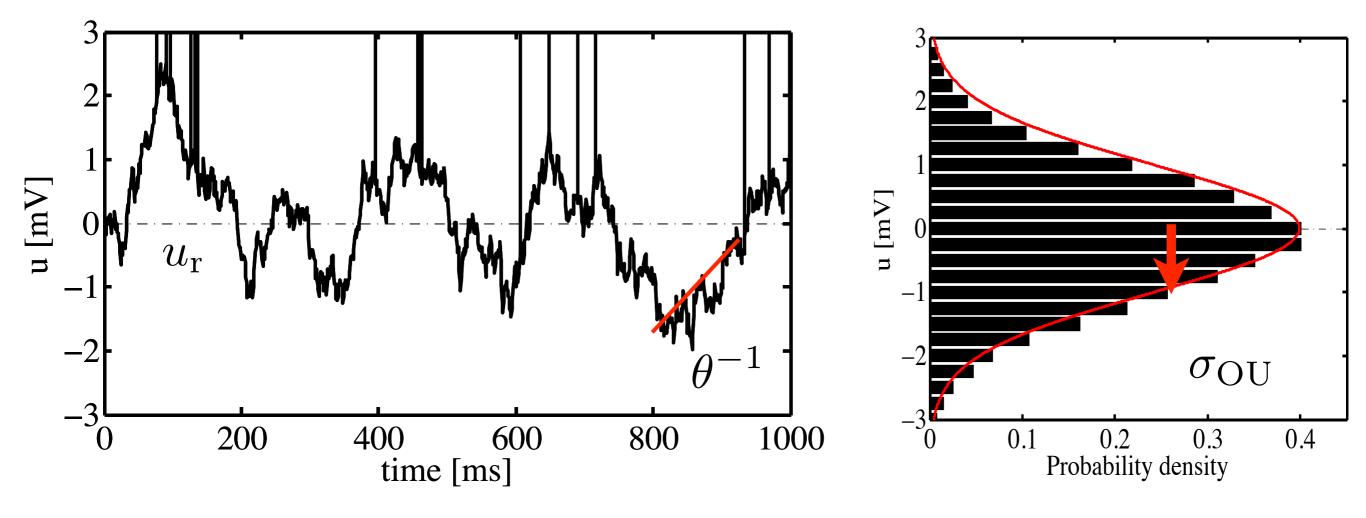






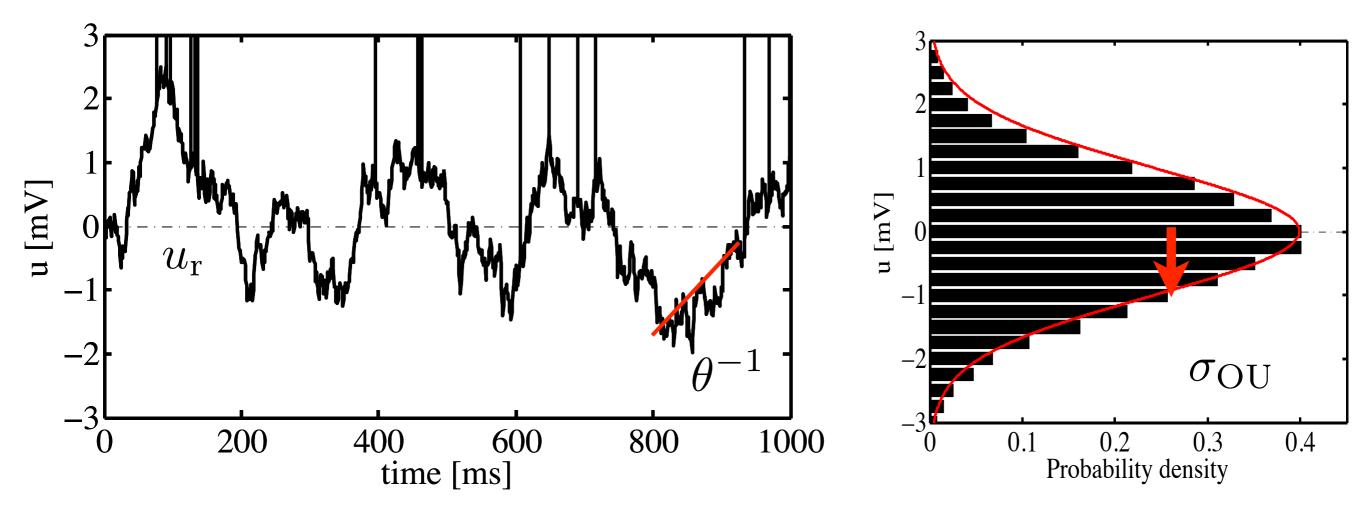


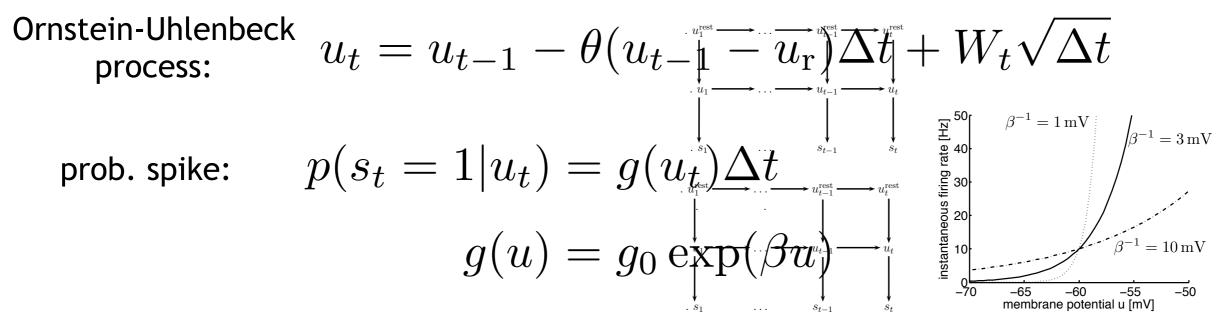
Ornstein-Uhlenbeck process: $u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t\sqrt{\Delta t}$



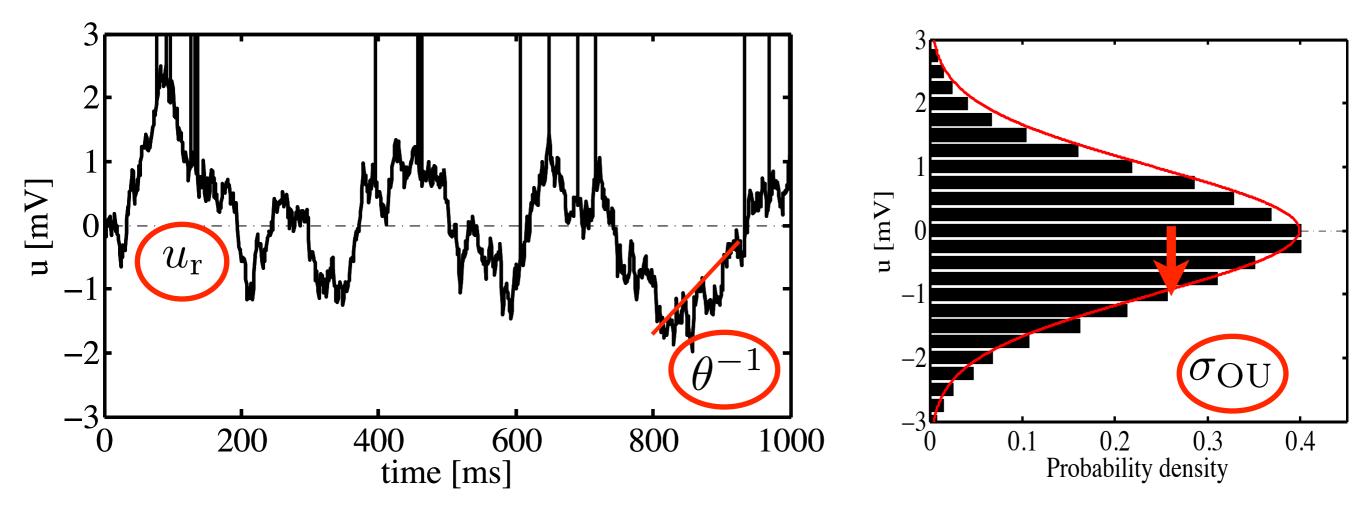
Ornstein-Uhlenbeck process: $u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t\sqrt{\Delta t}$

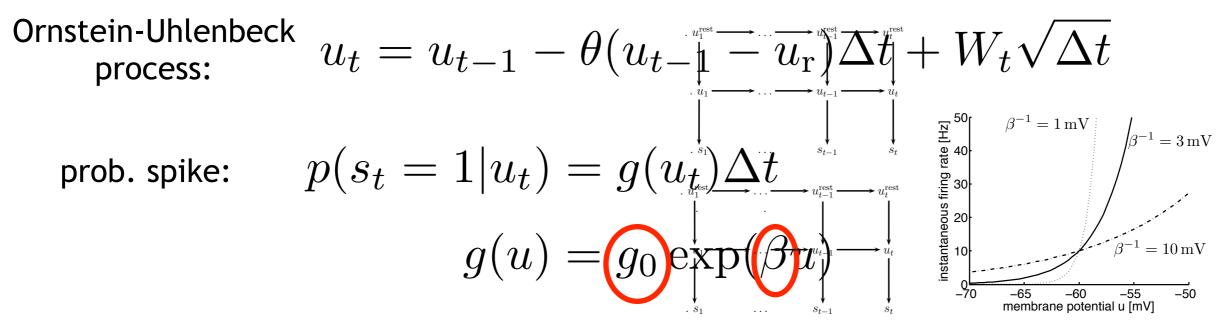
prob. spike: $p(s_t = 1 | u_t) = g(u_t) \Delta t$





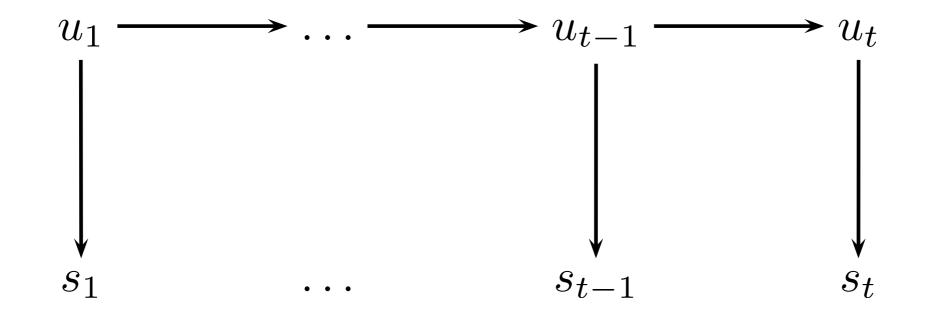
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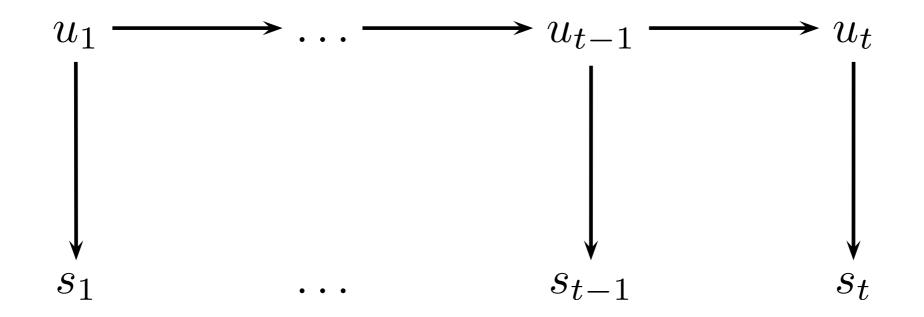
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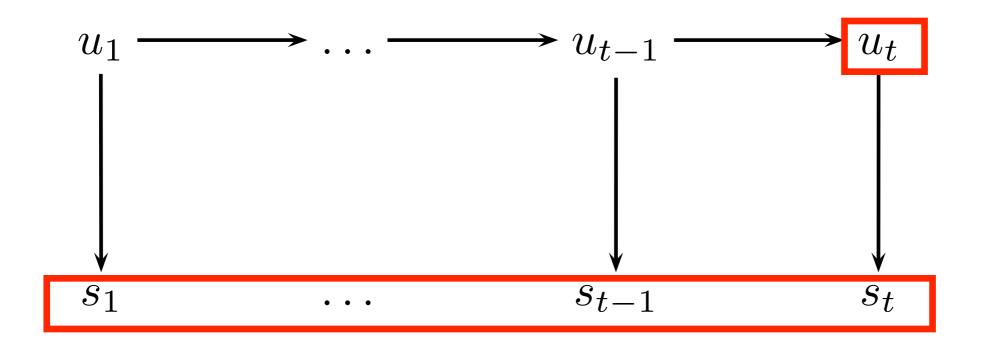


Ornstein-Uhlenbeck
$$u_t = u_{t-1} - \theta(u_{t-1} - u_r)\Delta t + W_t\sqrt{\Delta t}$$

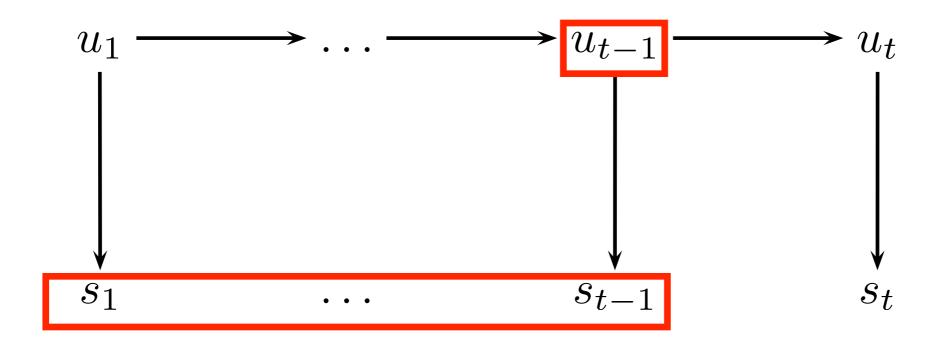
process: $p(s_t = 1|u_t) = g(u_t)\Delta t$
 $g(u) = g_0 \exp(\beta u)$



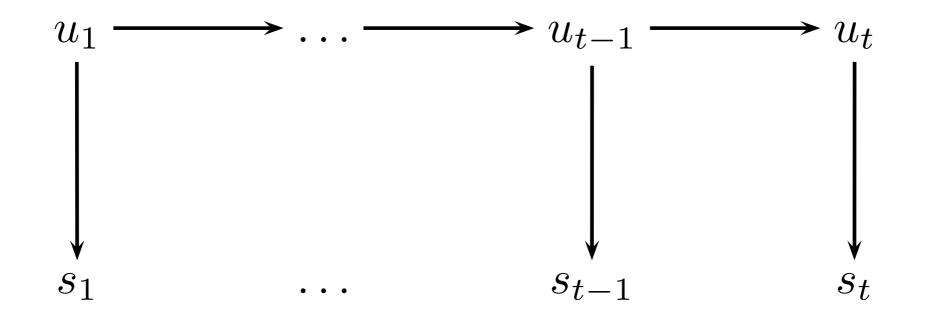
$$p(u_t|s_{1...t}) \propto p(s_t|u_t) \int p(u_t|u_{t-1}) p(u_{t-1}|s_{1...t-1}) du_{t-1}$$



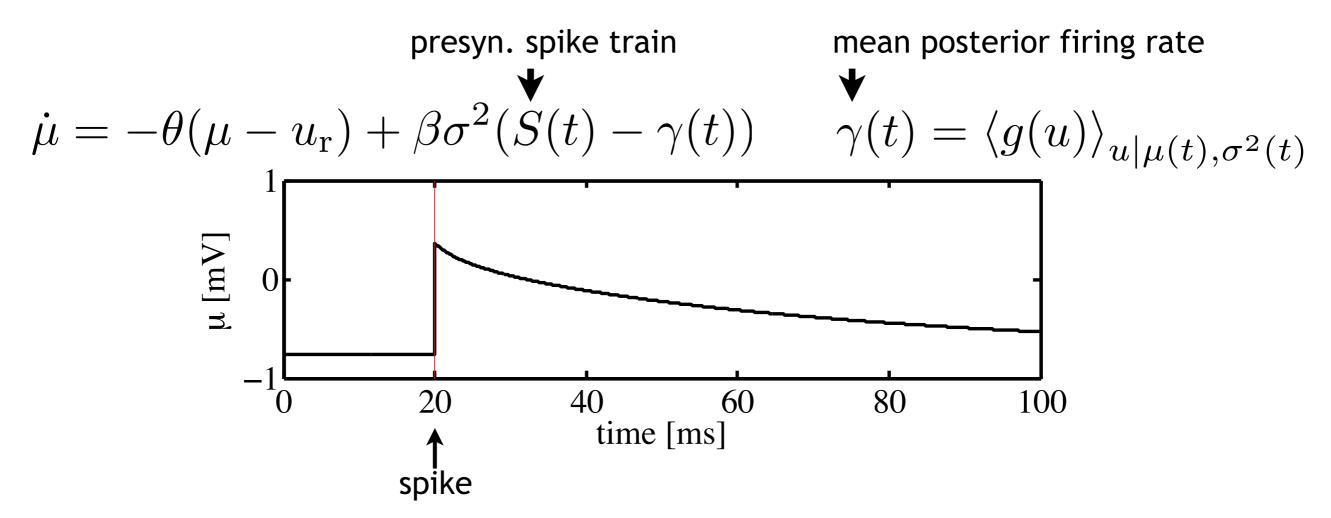
$$p(u_t|s_{1...t}) \propto p(s_t|u_t) \int p(u_t|u_{t-1}) p(u_{t-1}|s_{1...t-1}) du_{t-1}$$



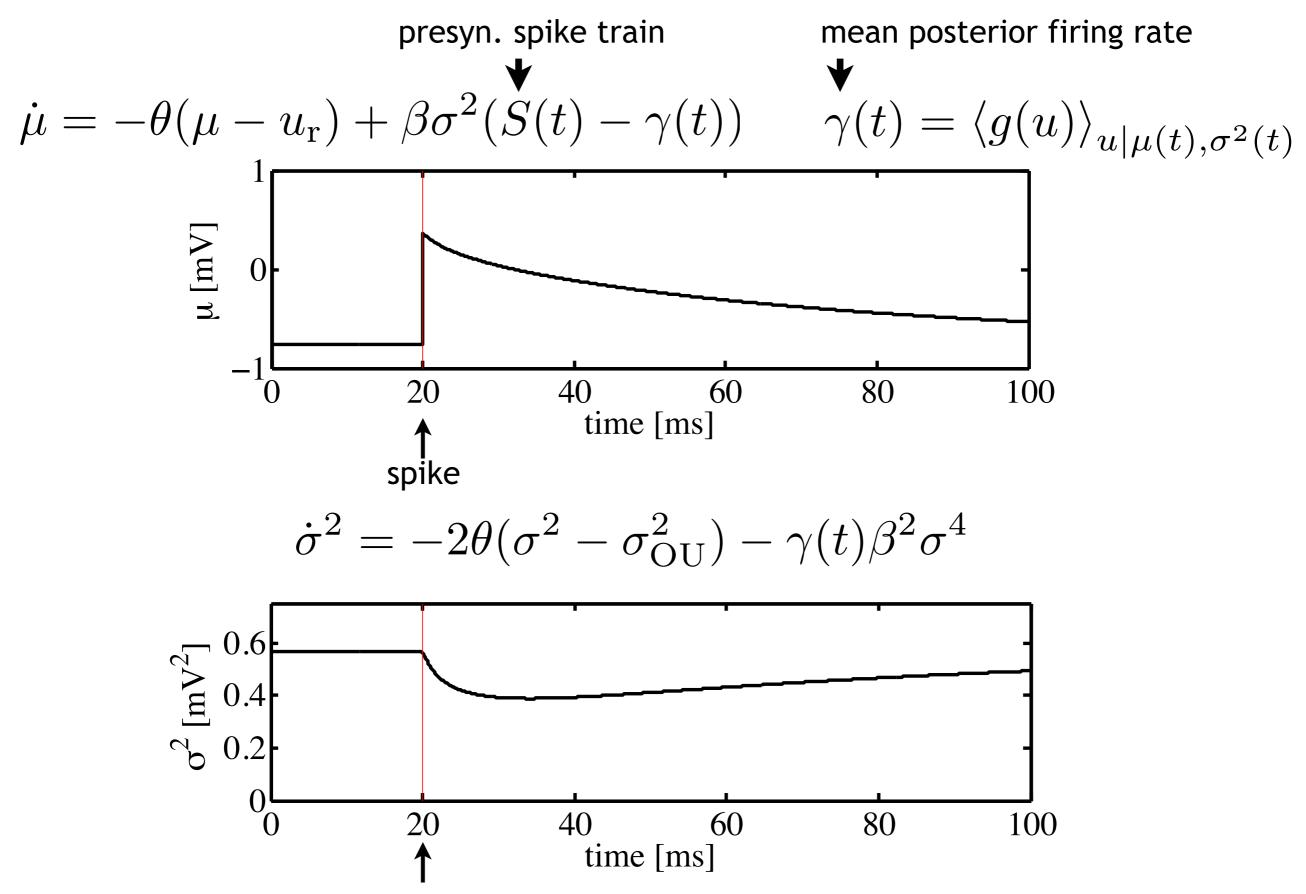
$$p(u_t|s_{1...t}) \propto p(s_t|u_t) \int p(u_t|u_{t-1}) p(u_{t-1}|s_{1...t-1}) du_{t-1}$$



DYNAMICS OF THE OPTIMAL ESTIMATOR



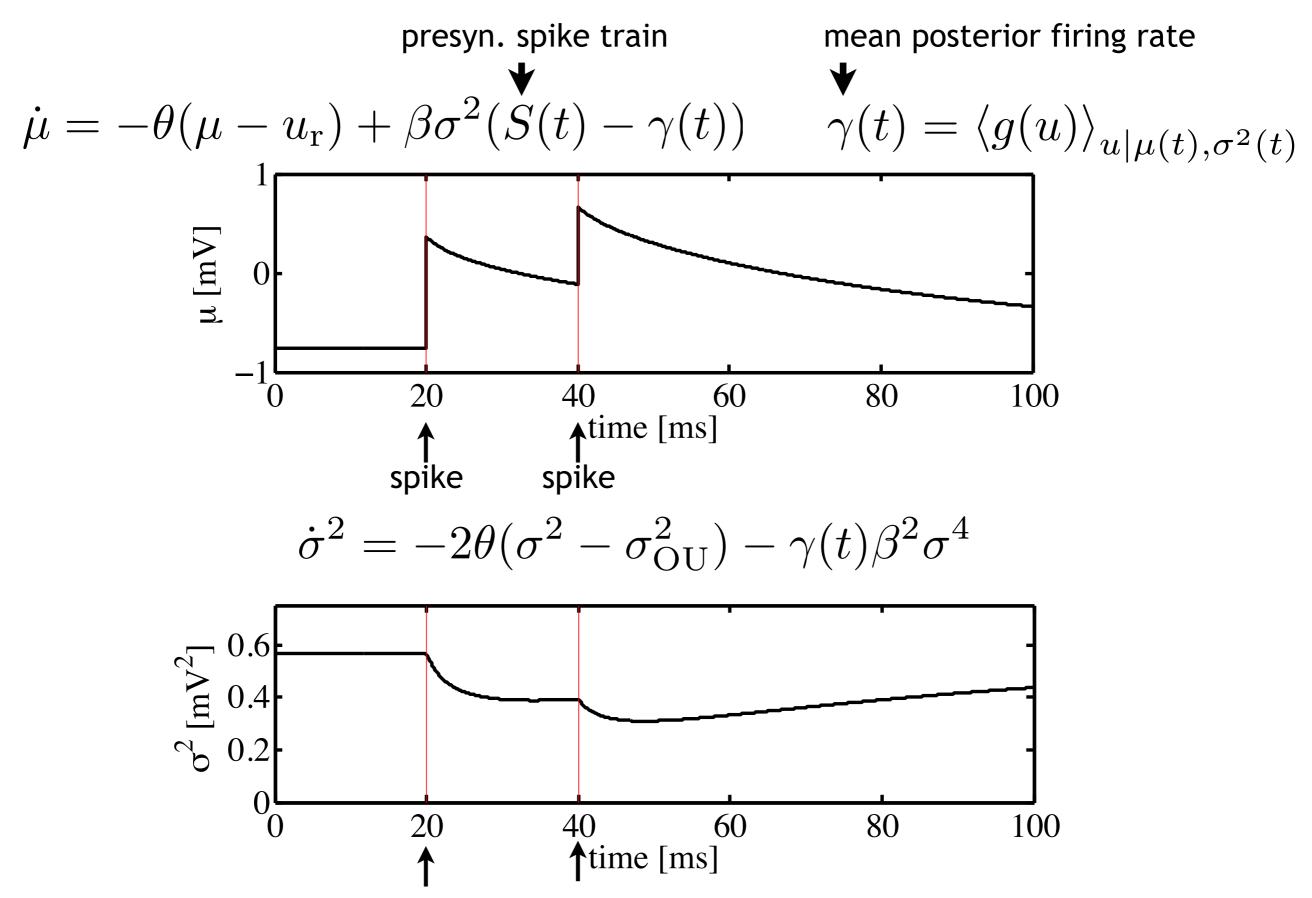
DYNAMICS OF THE OPTIMAL ESTIMATOR



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DYNAMICS OF THE OPTIMAL ESTIMATOR



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RELATION TO SHORT-TERM PLASTICITY

"biophysical" model of dynamic synapse

postsynaptic membrane potential

$$\frac{dv}{dt} = \frac{v_0 - v}{\tau_{\rm m}} + J x S(t)$$

synaptic resource

$$\frac{dx}{dt} = \frac{1-x}{\tau_{\rm D}} - Y \, x \, S(t)$$

Tsodyks et al., 1998

RELATION TO SHORT-TERM PLASTICITY

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synaptic resource

$$\frac{dx}{dt} = \frac{1-x}{\tau_{\rm D}} - Y \, x \, S(t)$$

Tsodyks et al., 1998

optimal estimator (in the limit)

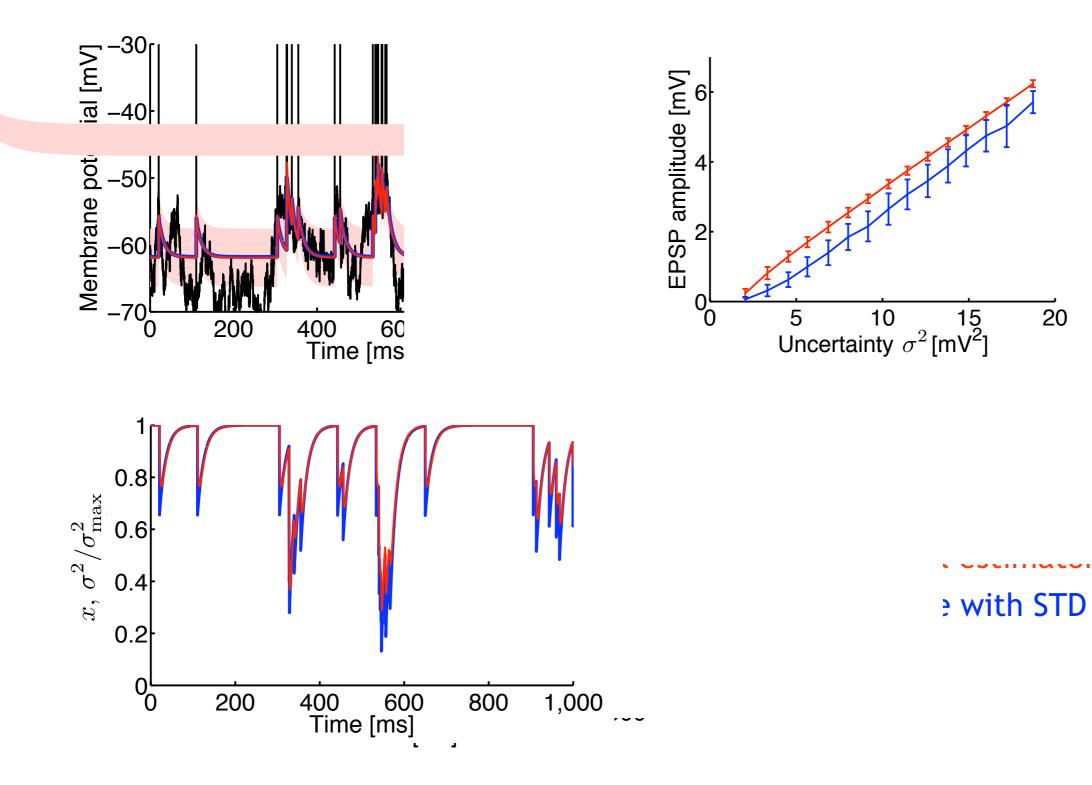
mean estimate

$$\frac{d\hat{u}}{dt} = \frac{\hat{u}_0 - \hat{u}}{\tau_{\rm m}} + J \,\sigma_{\rm u}^2 \,S(t)$$

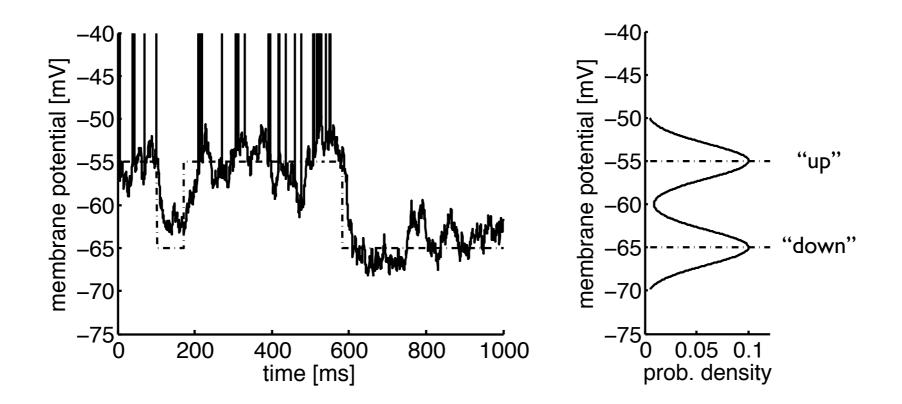
estimator uncertainty

$$\frac{d\sigma_{\rm u}^2}{dt} = \frac{1 - \sigma_{\rm u}^2}{\tau_{\rm D}} - Y \,\sigma_{\rm u}^2 \,S(t)$$

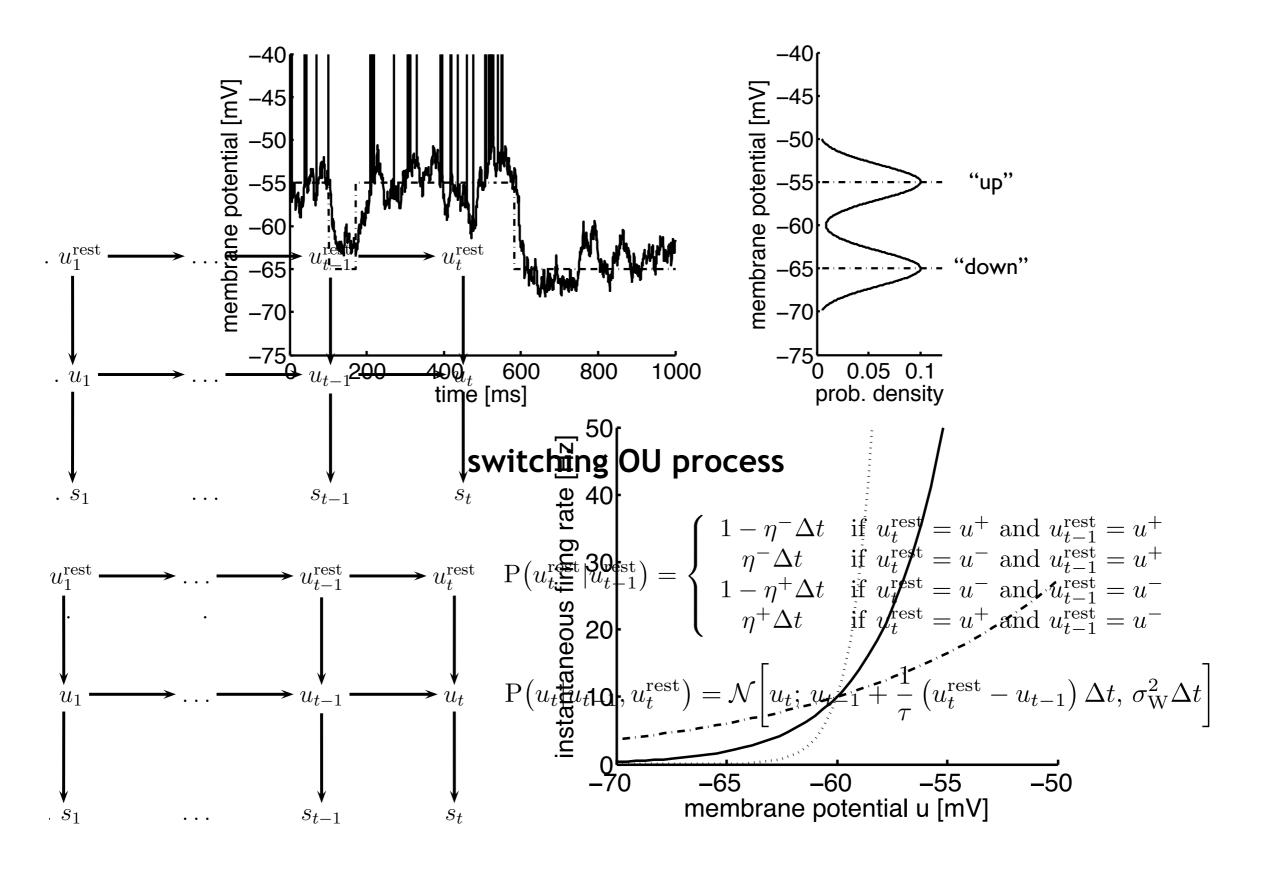
Pfister et al., NIPS 2009 Pfister et al., Nat Neurosci 2010



AN EXTENSION: "UP" AND "DOWN"



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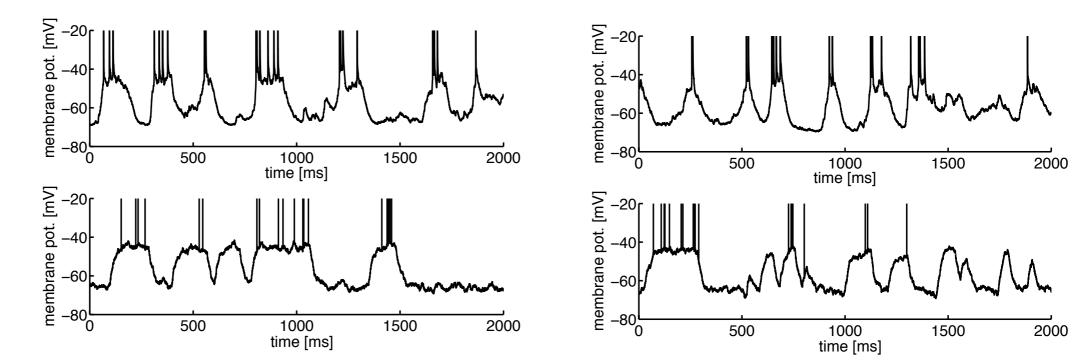


THE SWITCHING OU PROCESS

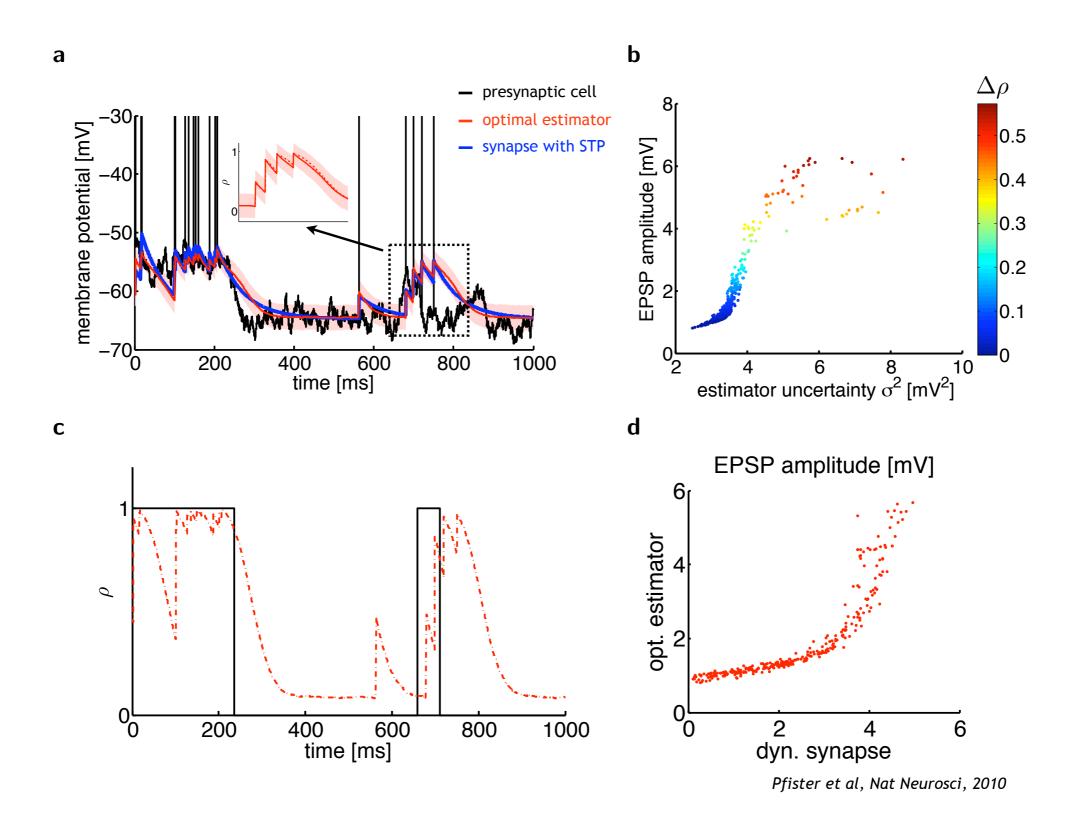


Gentet et al, 2010

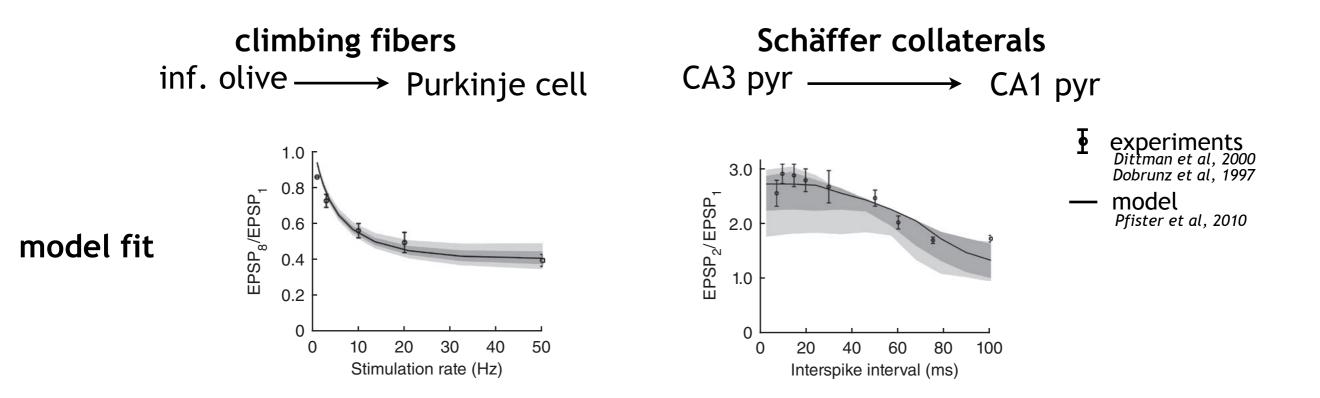




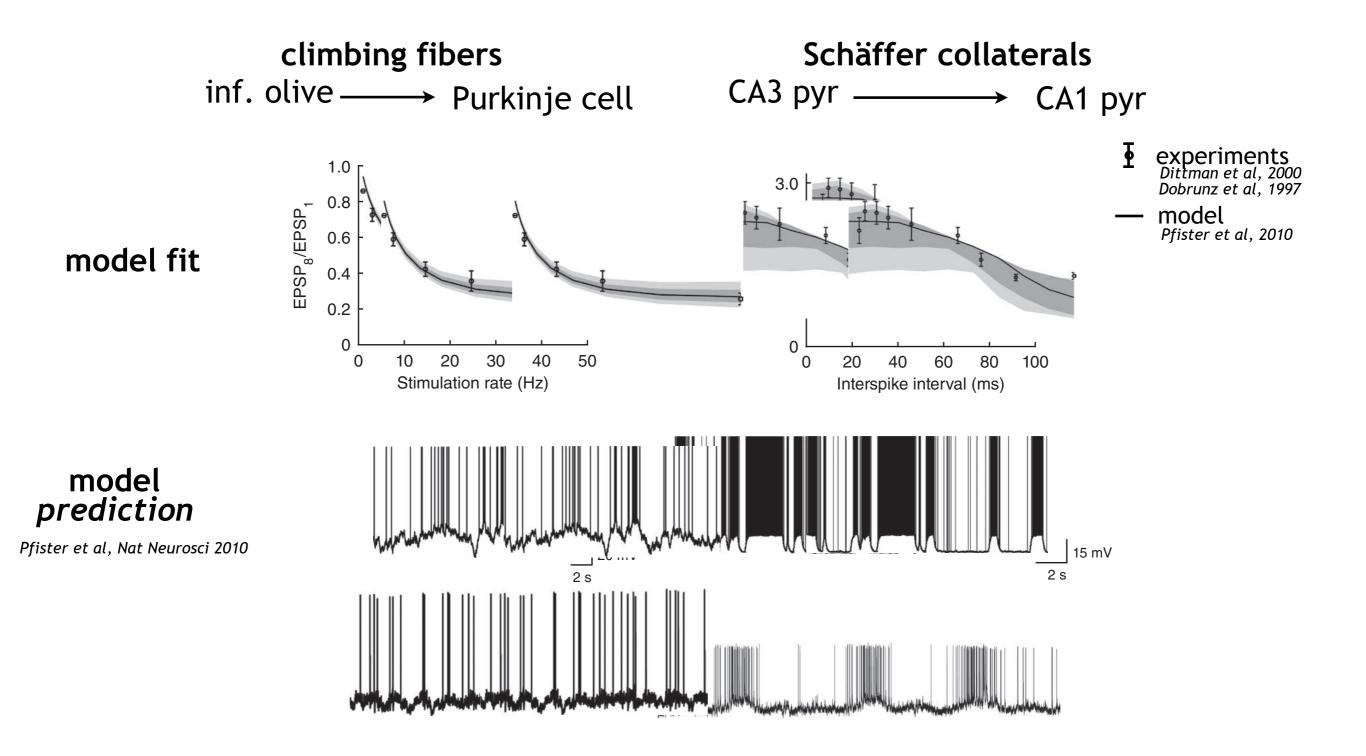
SYNAPSES WITH STP AS OPTIMAL ESTIMATORS



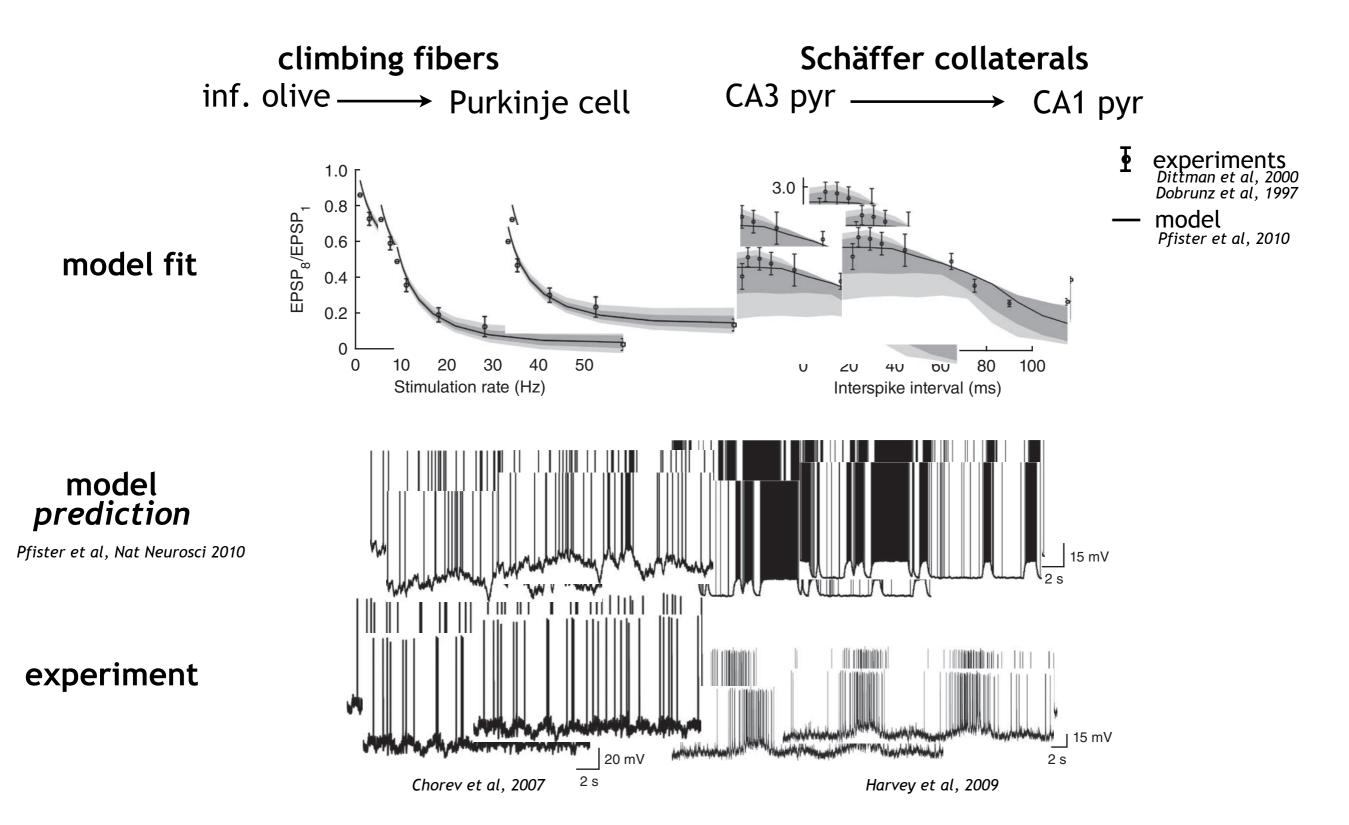
MATCHING STP PARAMETERS TO NATURAL MEMBRANE POTENTIAL STATISTICS



MATCHING STP PARAMETERS TO NATURAL MEMBRANE POTENTIAL STATISTICS

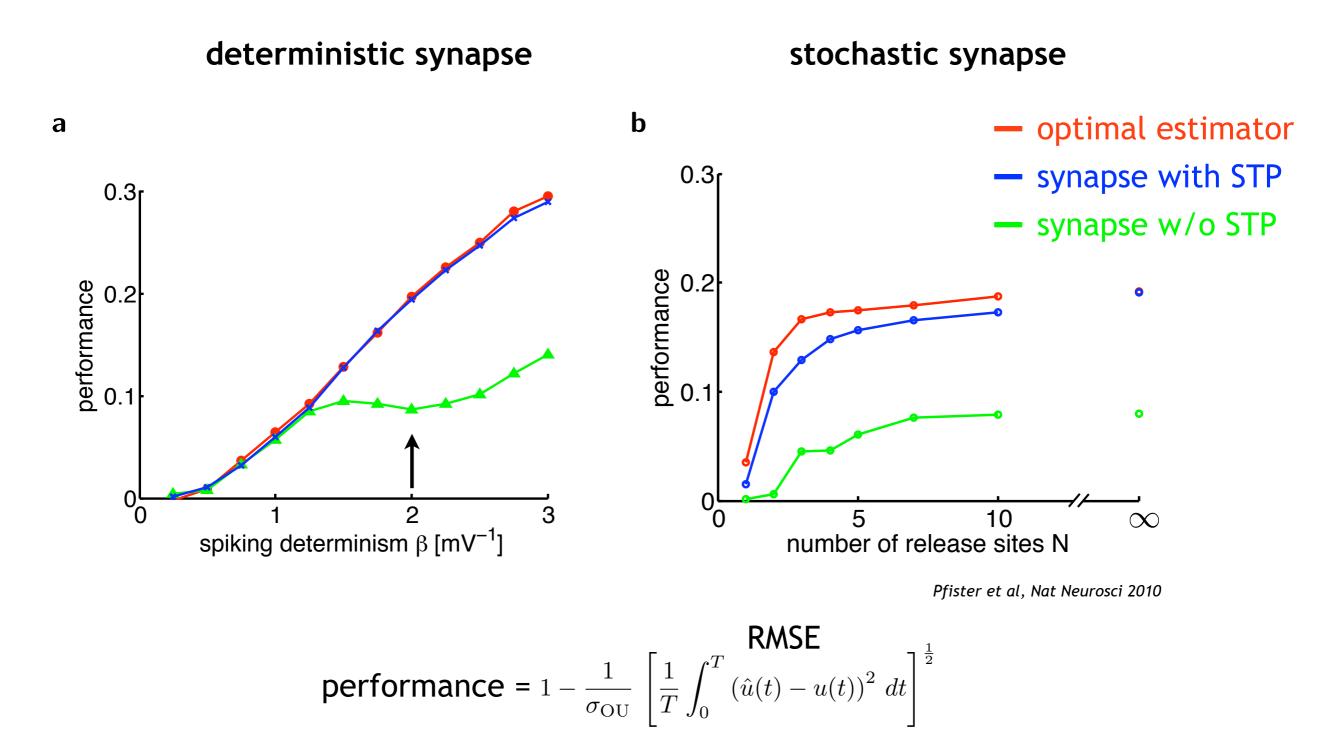


MATCHING STP PARAMETERS TO NATURAL MEMBRANE POTENTIAL STATISTICS



Máté Lengyel | Computational modelling of synaptic function MPS-UCL Symposium on Computational Psychiatry, 18 Sept 2012 http://www.eng.cam.ac.uk/~m.lengyel 34

THE ADVANTAGE OF STP



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