Modeling synapses: Noise and dynamics

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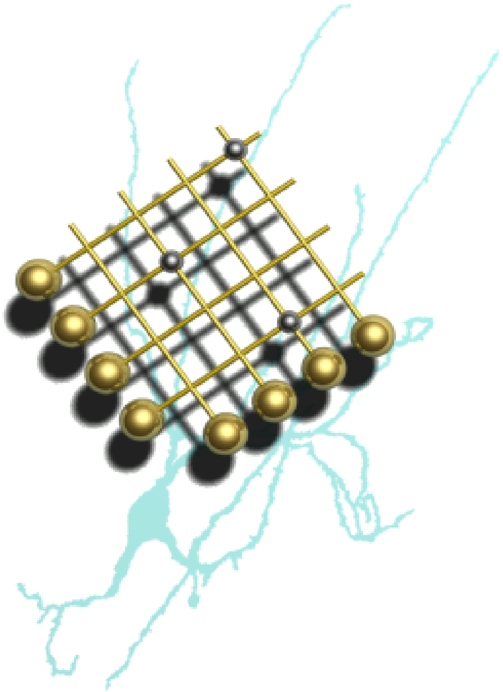
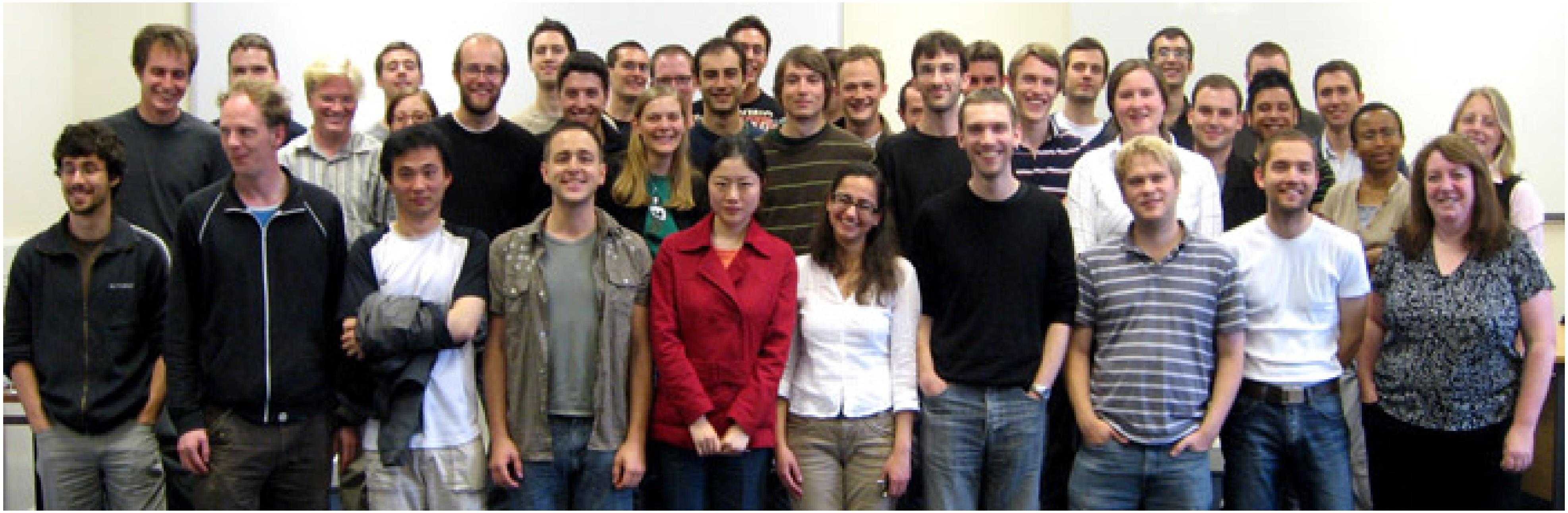


Lawrence York, Jesus Cortes, Cian O'Donnell,
Paul Clark,
Robert Smith (U Penn)

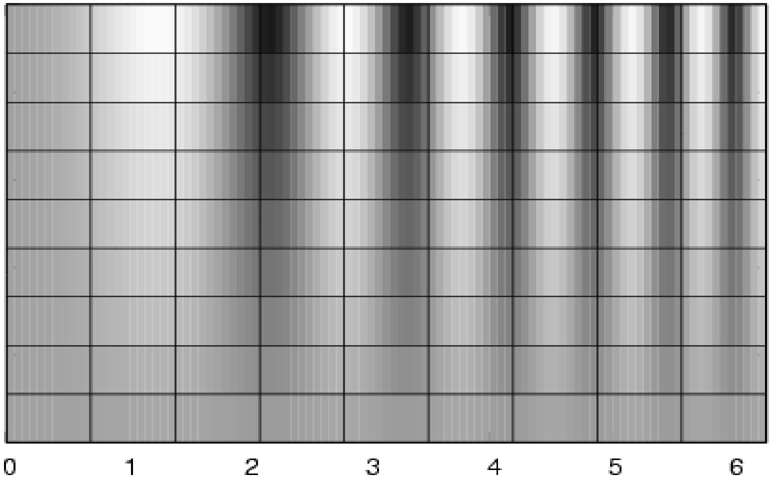
Adverts



Neuroinformatics
Doctoral Training Centre

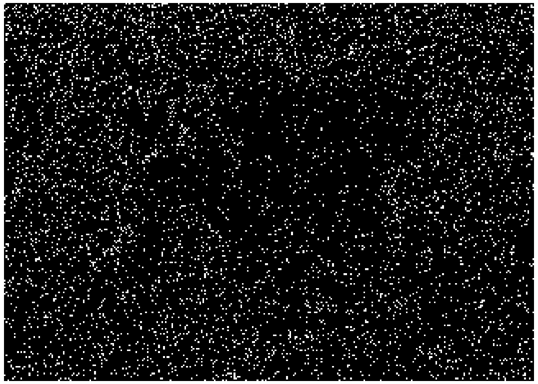
Links between synapses and perception in the visual system

Contrast perception (TUESDAY)



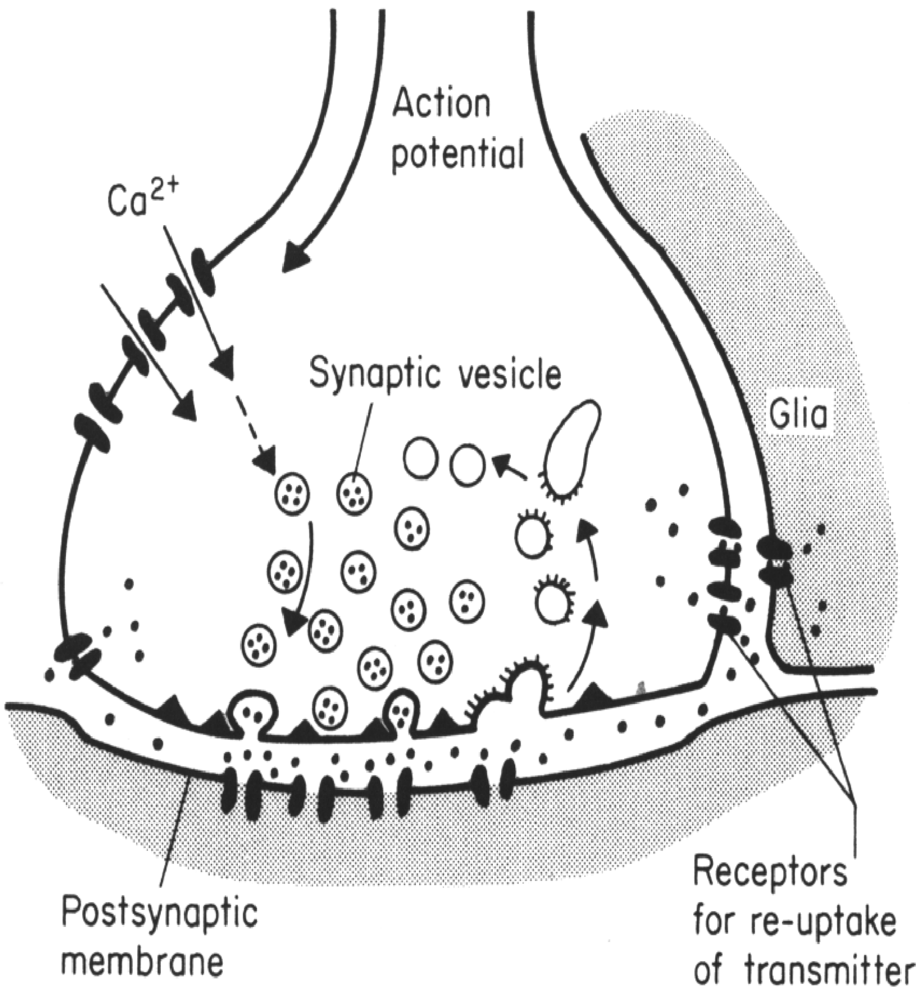
Synaptic requirements for night vision

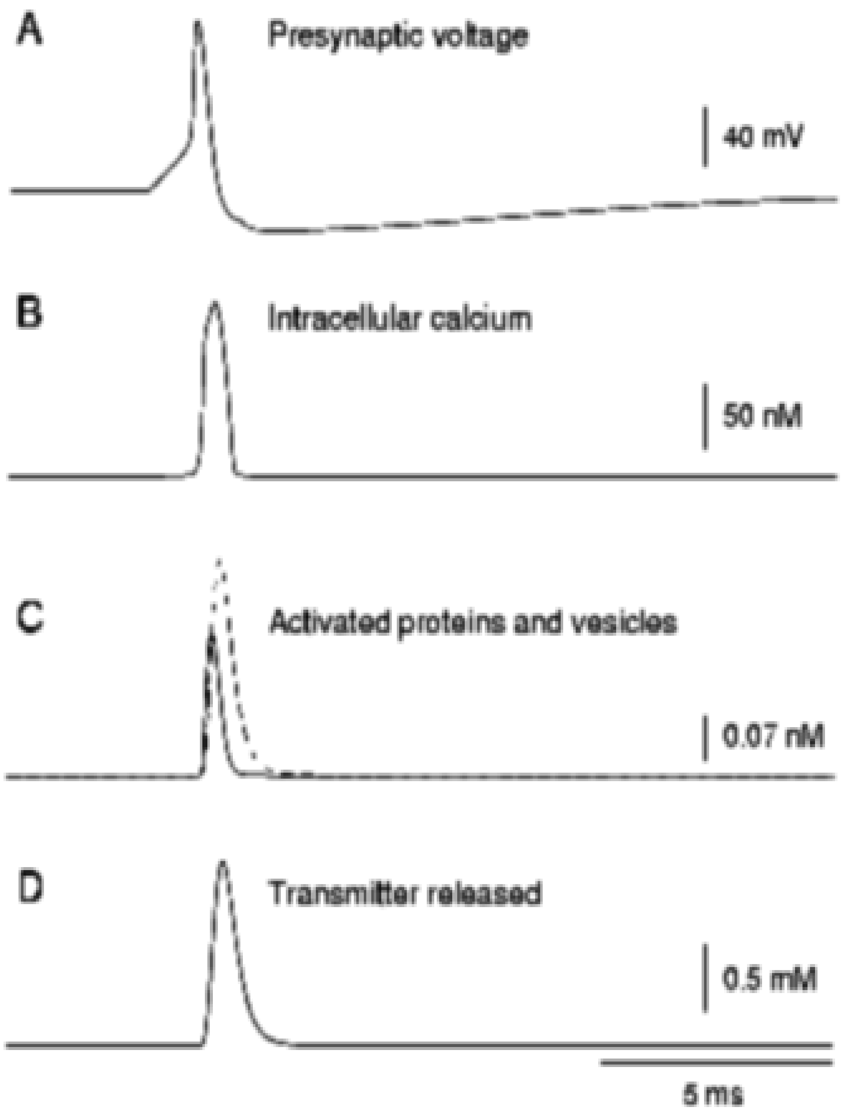
Day light



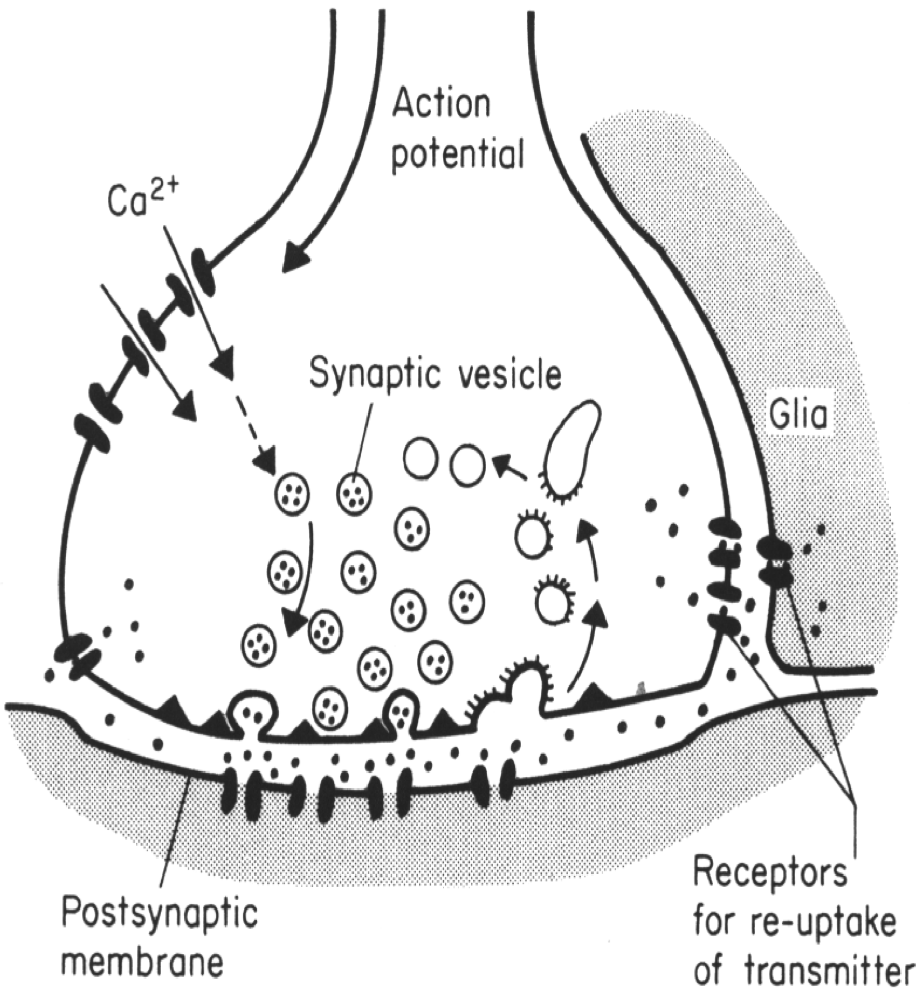
At night

The synapse


Action
potential
Ca2+
Synaptic vesicle
Glia
Postsynaptic
membrane
Receptors
for re-uptake
of transmitter


A
Presynaptic voltage
40 mV
B
Intracellular calcium
50 nM
C
Activated proteins and vesicles
0.07 nM
D
Transmitter released
0.5 mM
5 ms

The synapse



<u>Table of contents:</u>

- synapse models and synaptic noise
- synaptic non-linearities
- release probability

<u>Not discussed:</u>

- pre-synaptic receptors
- LTP
- receptor insertion/diffusion
- release biophysics
- synaptic integration on dendrites
- spines

PART 1: Synaptic channel models

Synaptic currents

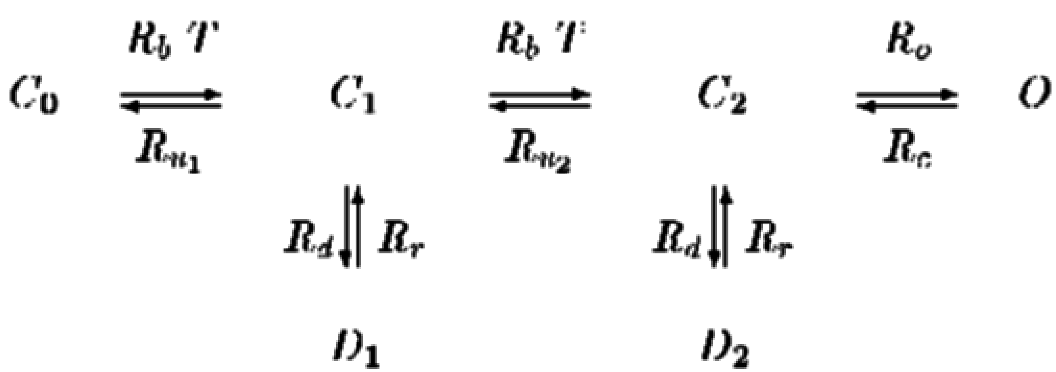
- Current based, e.g.

$$I_{syn} = I_0 \exp(-t/\tau_{syn})$$

- Conductance based, e.g.

$$I_{syn} = g_{syn}[V(t) - V_{syn}^{rev}] \exp(-t/\tau_{syn})$$

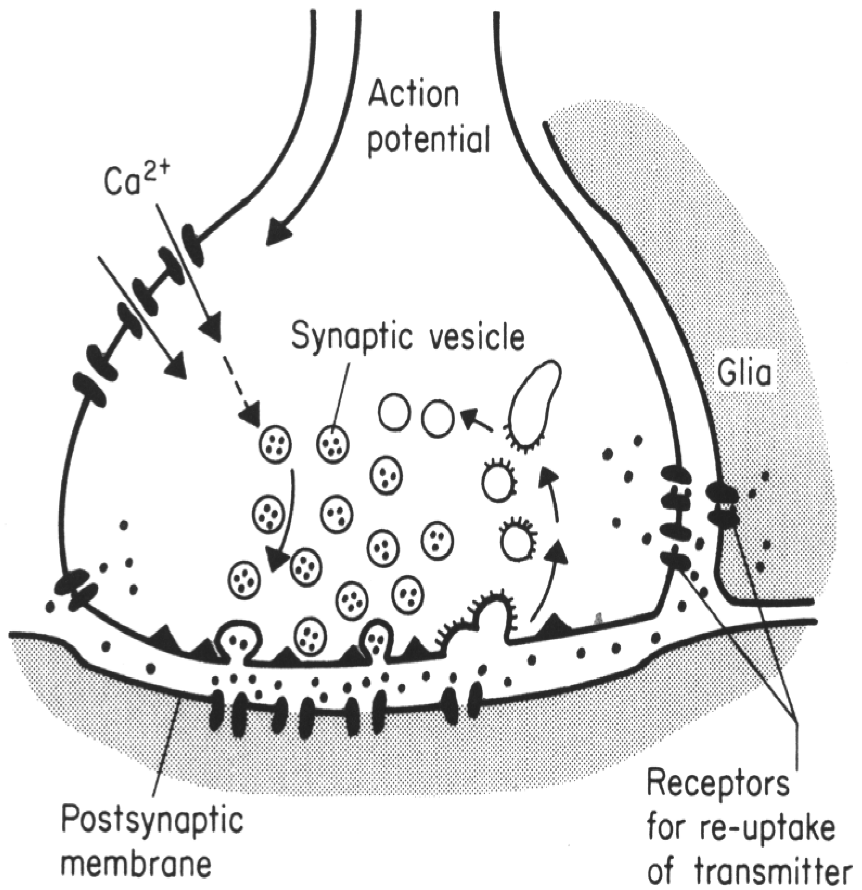
- Full state diagram: e.g. AMPA channel



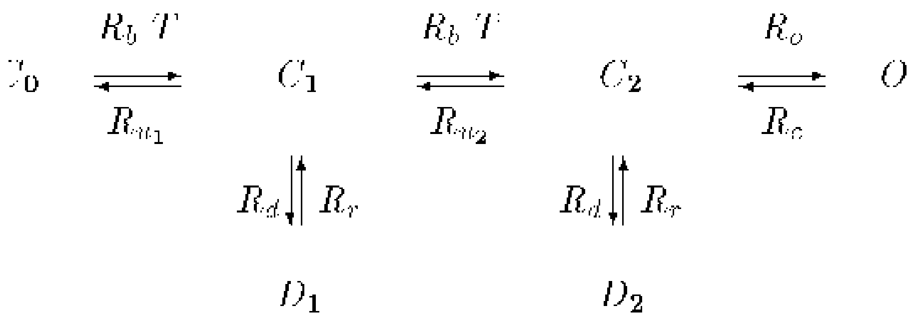
Noise in synaptic input

Synaptic current is noisy because

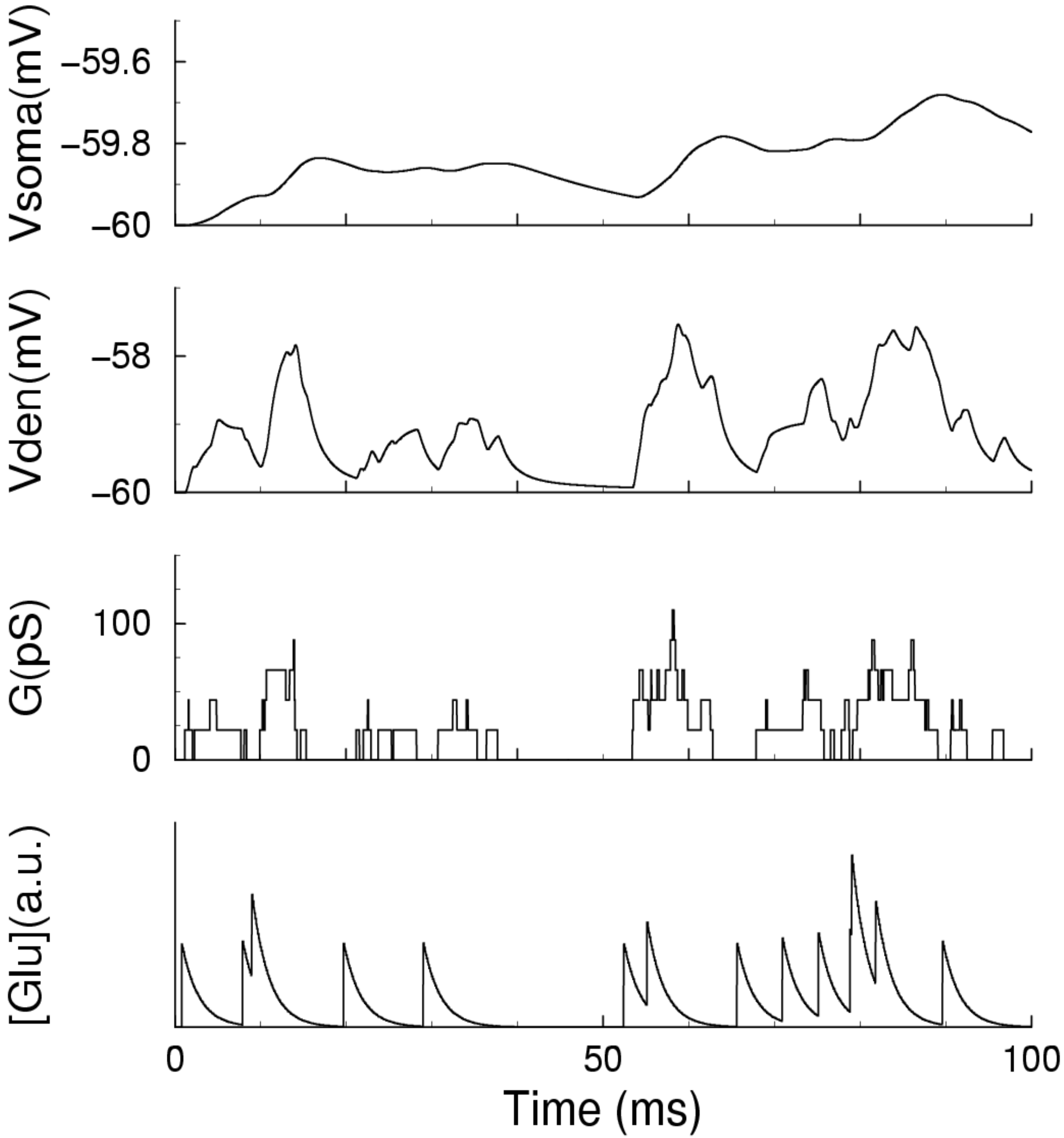
- vesicles vary in size
- vesicle release is stochastic
- variation in release location
- synaptic channel opening is stochastic



Synaptic currents simulation



Markov diagrams can be simulated
Stochastically
or
deterministically



Markov formulation

$$C \Leftrightarrow C' \Leftrightarrow O$$

State vector *s*, given occupation of each state $\frac{d\vec{s}}{dt} = W.\vec{s}$

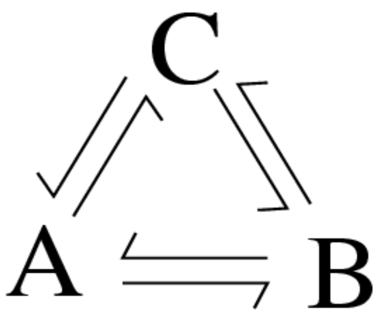
$$W = \begin{pmatrix} -kT & \alpha & 0 \\ kT & -k'T-\alpha & \alpha' \\ 0 & k'T & -\alpha' \end{pmatrix} \qquad \lambda = \{0, \lambda_{1,} \lambda_2\}$$

$$\vec{s}(t) = \vec{s}_\infty + \vec{c}_1 \exp(-t/\lambda_1) + \vec{c}_2 \exp(-t/\lambda_2)$$

Preserve probability $\frac{d \sum \vec{s}}{dt} = 0$

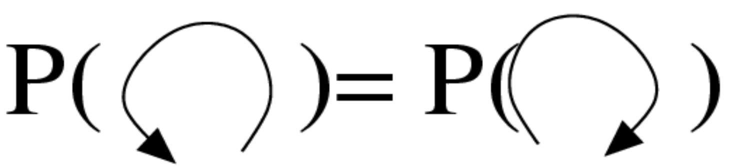
Markov formulation

Detailed balance (statistical physics)



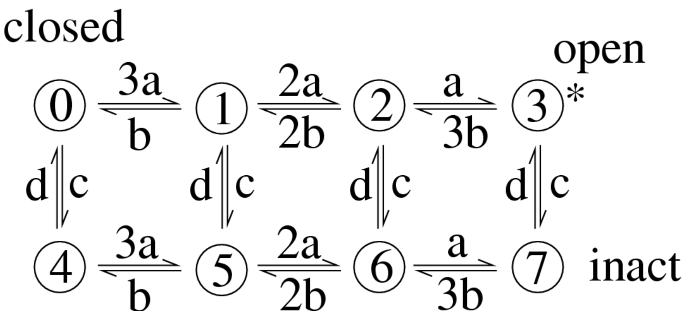
In equilibrium detailed balance should hold.

Without detailed balance, looping would be possible.



In diagrams without loops, detailed balance is trivial.

$$W_{ij} s_j^{equil} = W_{ji} s_i^{equil}$$



Markov formulation

$$C \Leftrightarrow C' \Leftrightarrow O$$

Suppose equilibrium has been reached (e.g. transmitter in the bath). Autocorrelation function

$$c(t) = \int dt' s(t') s(t' + t)$$

Autocorrelation has two time-constants in this case: $1/\lambda_1, 1/\lambda_2$

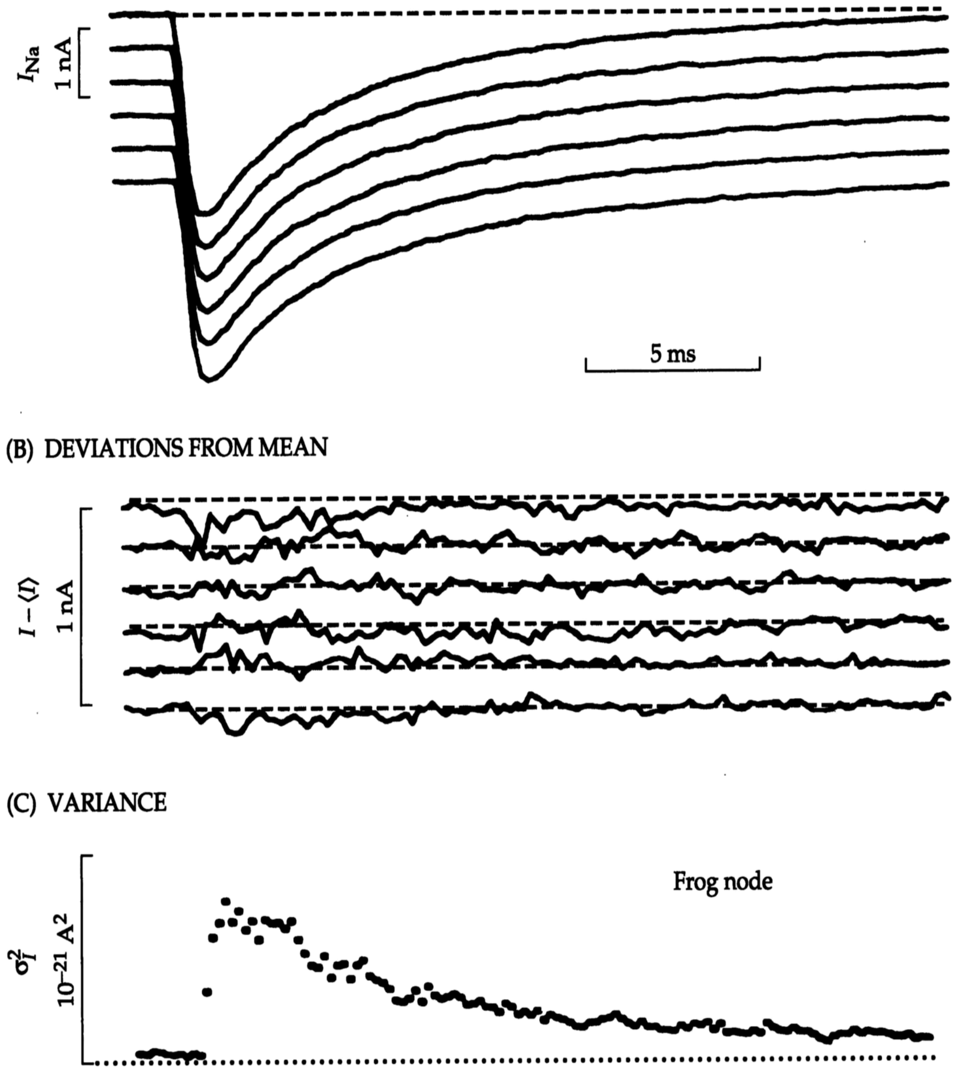
Wiener-Khichin theorem:

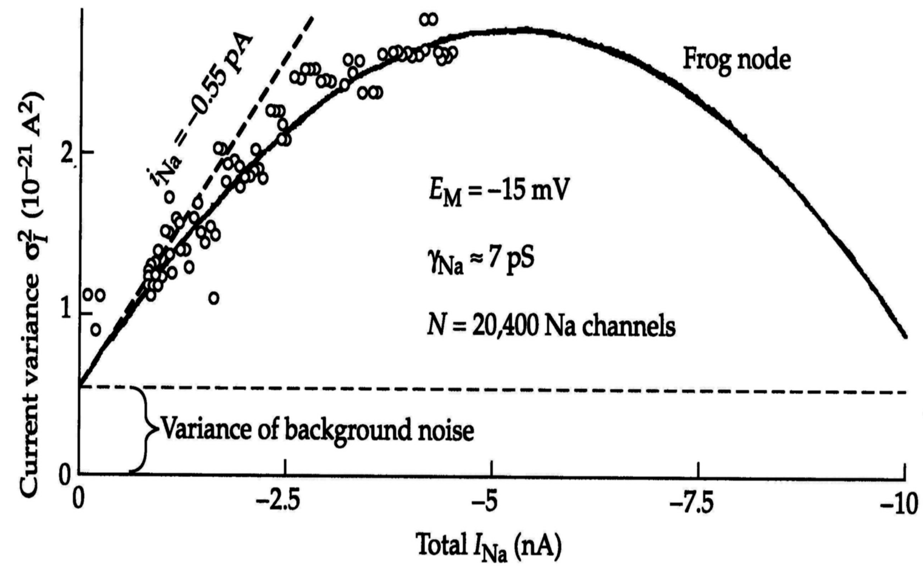
$$PSD(f) = 4 \int_0^\infty c(t) \cos(2\pi f t) dt$$

$$PSD(f) = \frac{w(0)}{\prod_i [1 + (2\pi f / \lambda_i)^2]}$$

The channel dynamics determine the noise spectrum

Using the noise: Noise analysis





Binomial distribution: *n* out *N* are open

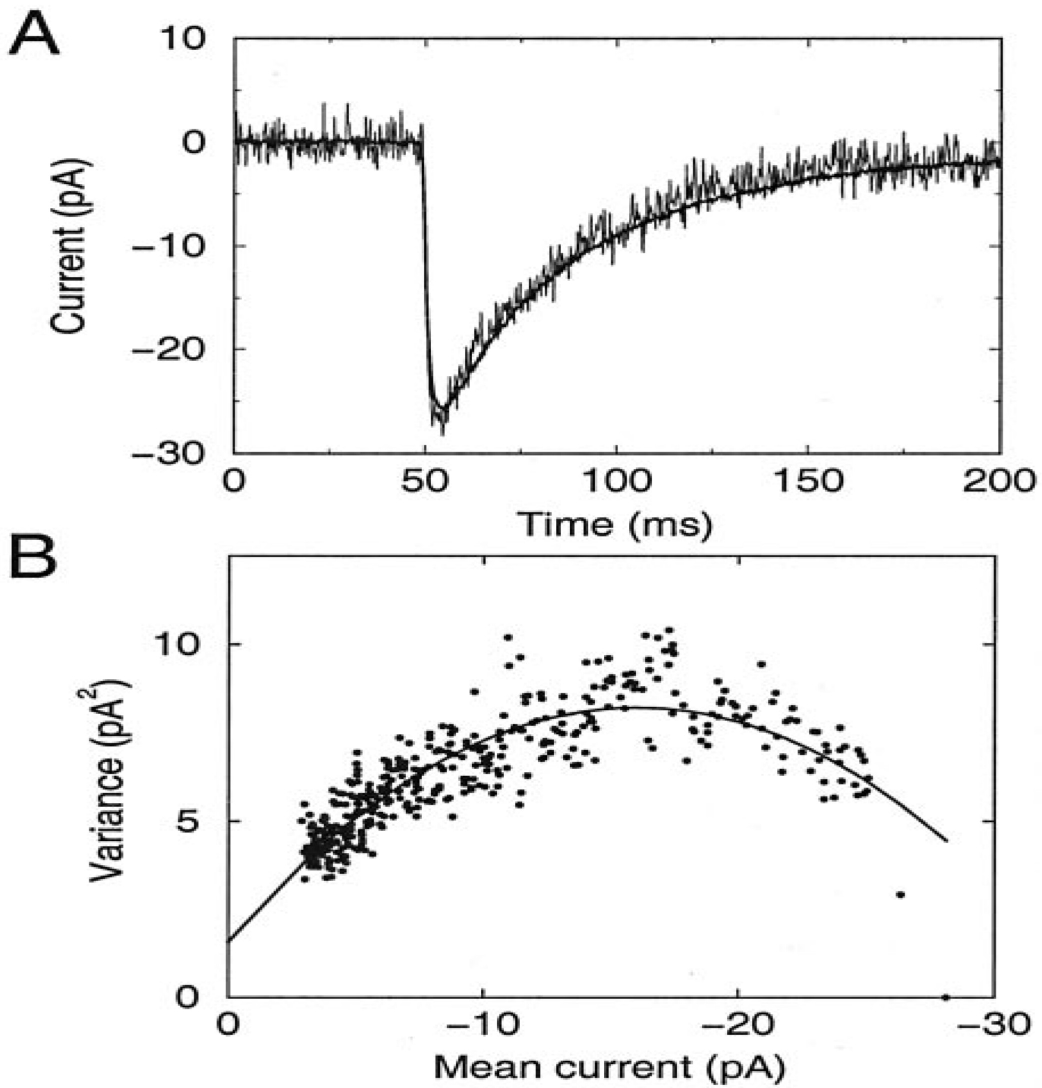
$$\langle I(t)\rangle = i_0 N p(t)$$

$$\langle \delta I^2(t)\rangle = i_0^2 N p(t)[1-p(t)]$$

$$\langle \delta I^2(t)\rangle = i_0 \langle I(t)\rangle - \langle I(t)\rangle^2 / N$$

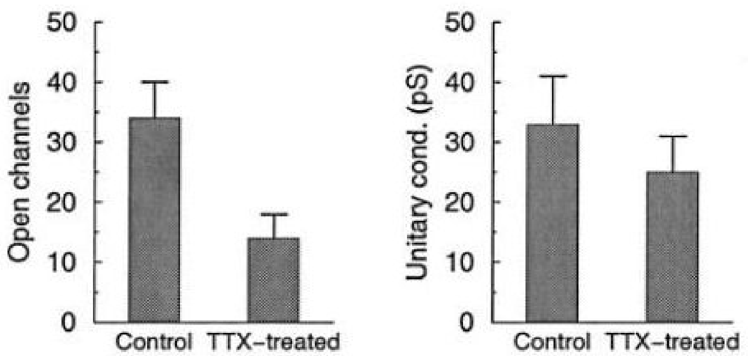
[Hille's book, Sigworth '80]

Using the noise: Noise analysis



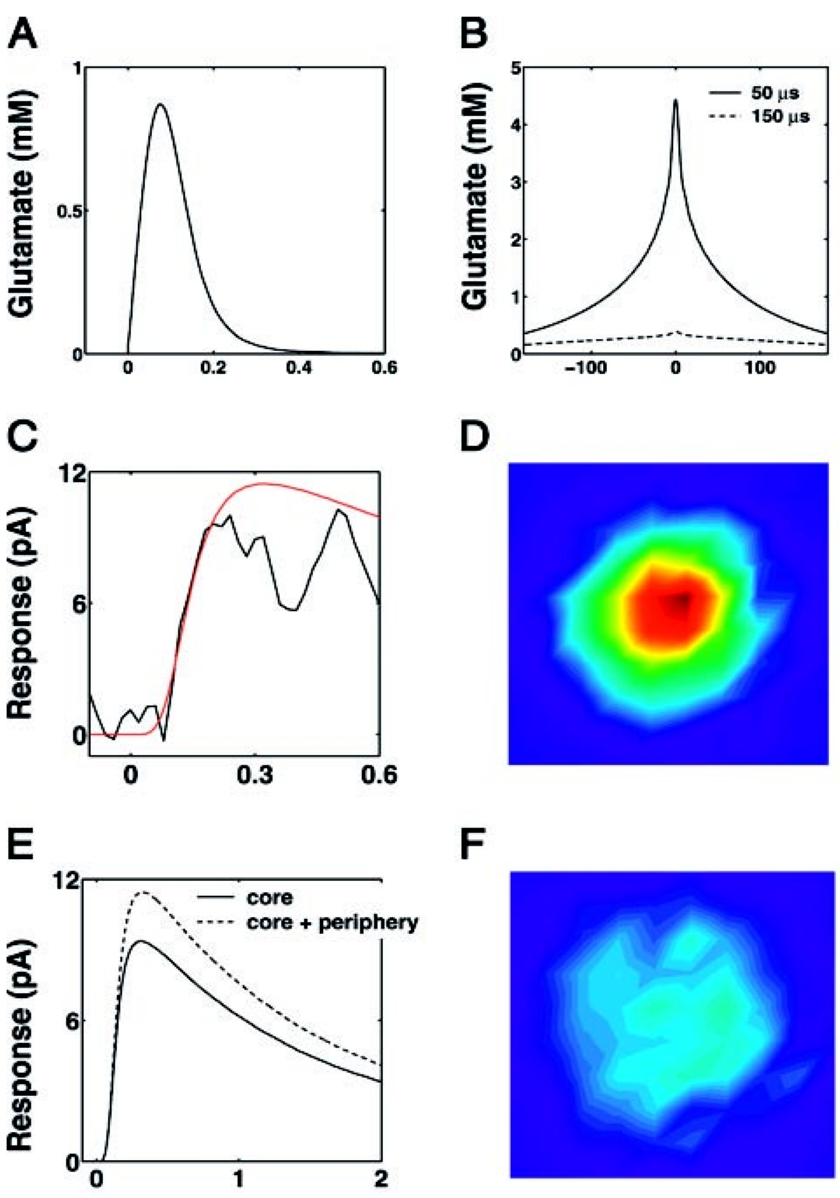
[Killman, van Rossum, Turrigiano '02]

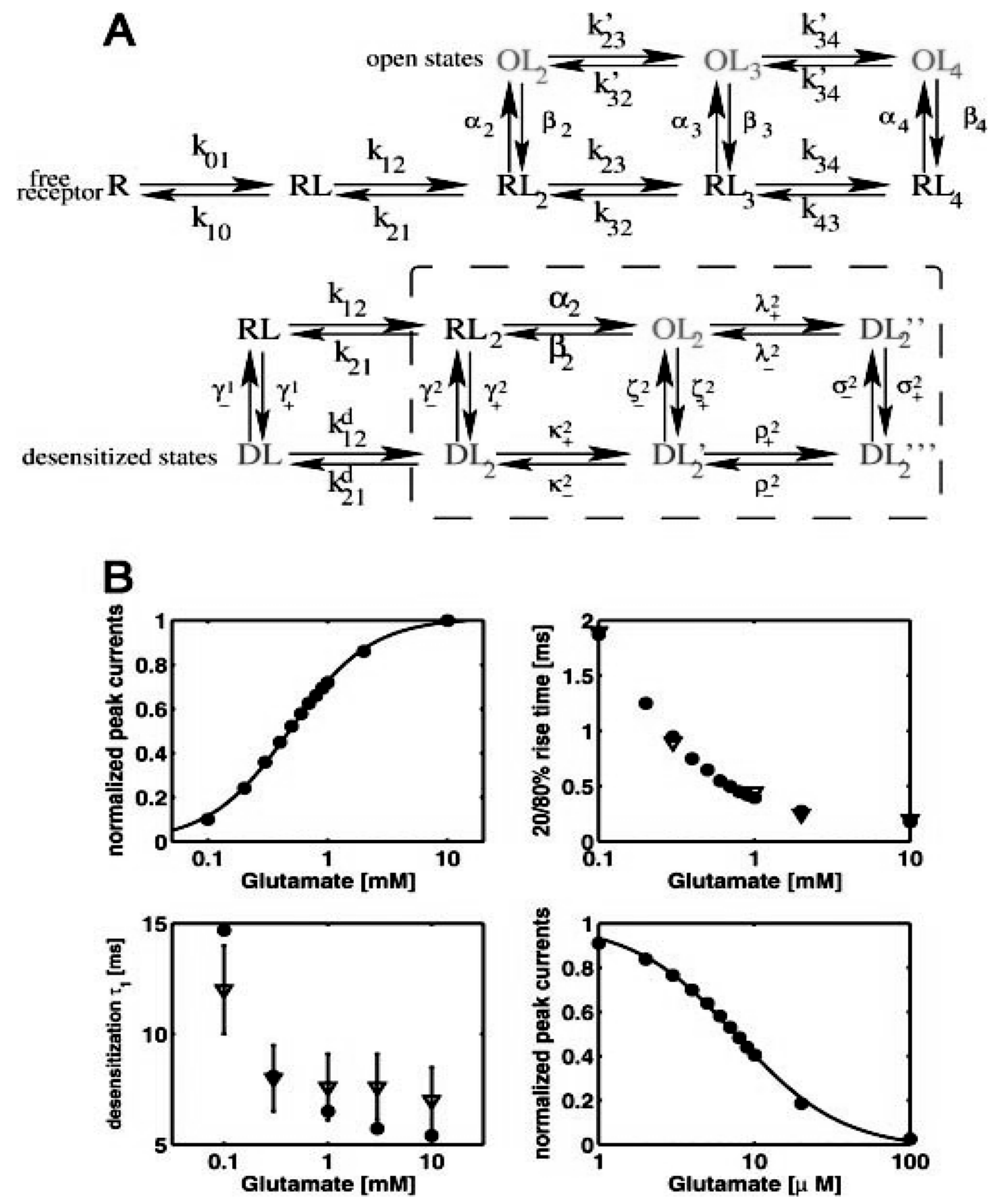
Noise analysis in practice:
  baseline subtraction,
  onset alignment,
  background noise, ...



These synapses are close to the soma (inhibitory).

Model with geometry [Raghavachari & Lisman '04]





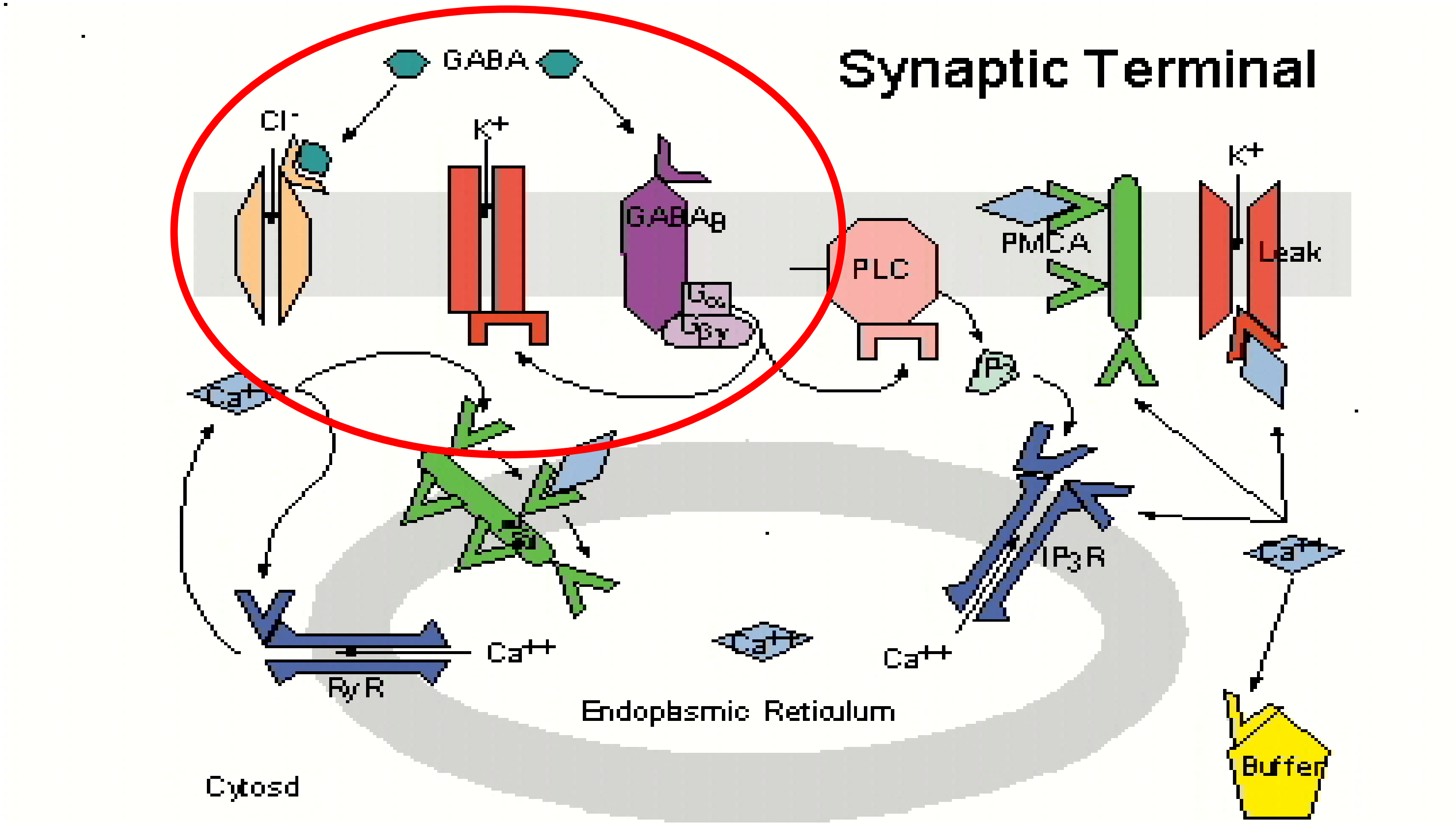
PART 2: Post synaptic non-linearities

Post-synaptic complications

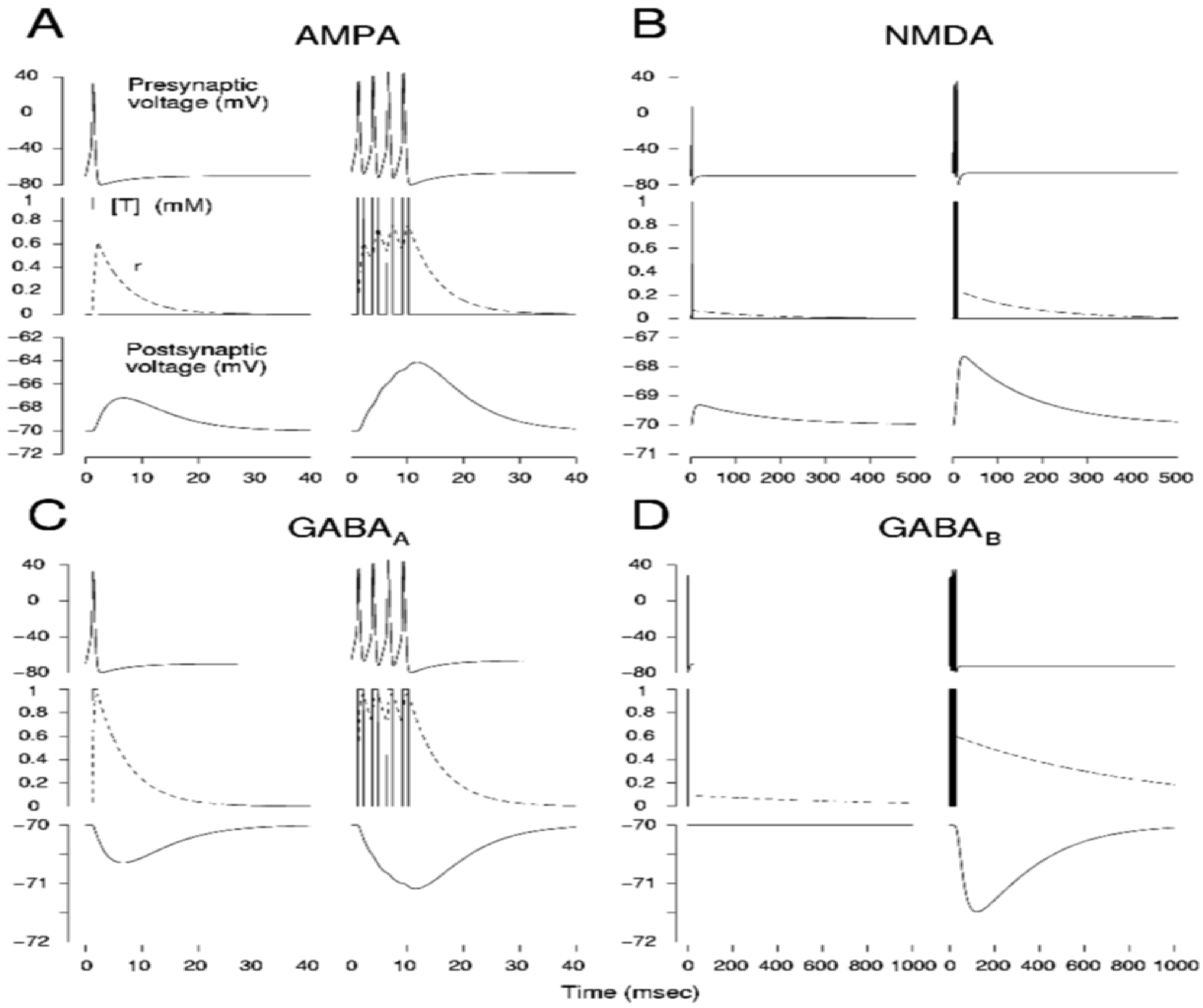
Second messenger synapses, channel opening is caused by activated membrane bound messenger.

Example in cortex: GABAb, mGluR

Retina: mGluR



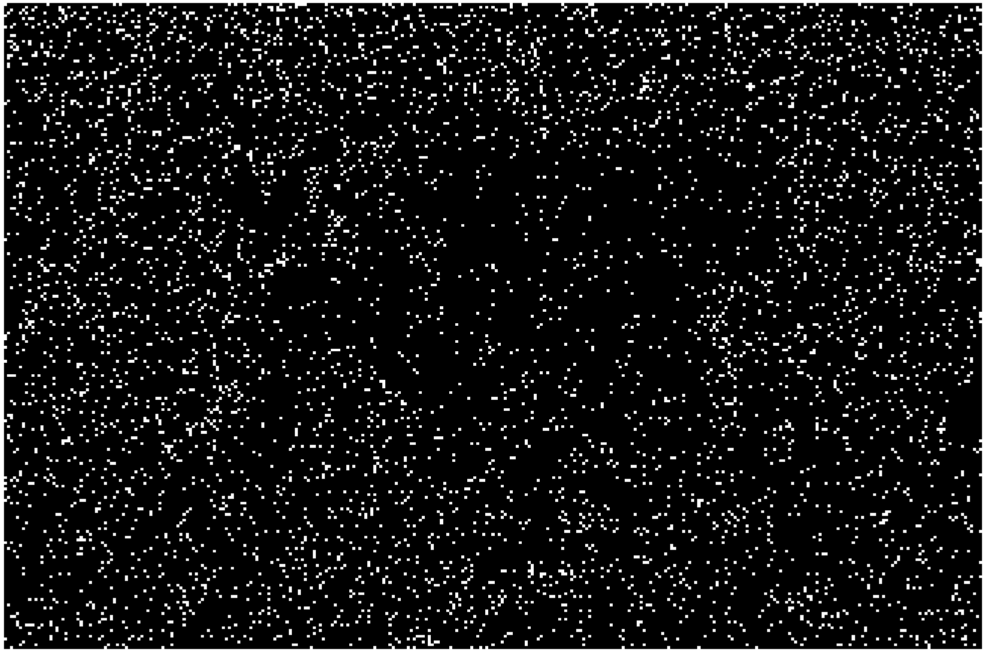
GABAb


A
AMPA
Presynaptic voltage (mV)
[T] (mM)
r
Postsynaptic voltage (mV)
B
NMDA
C
GABA_A
D
GABA_B
Time (msec)

Second messenger: noise removal at rod to rod-bipolar synapse

Day light

Scotopic : 1 photon / rod / 10 min

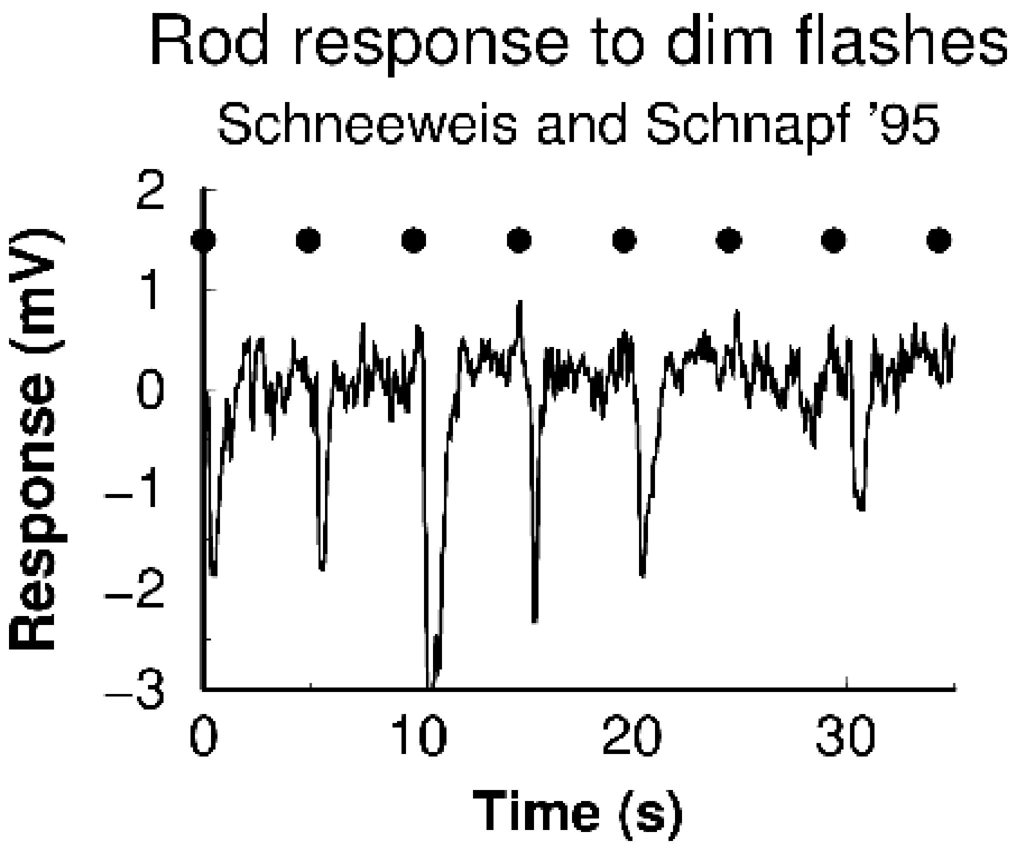


Retinal performance:

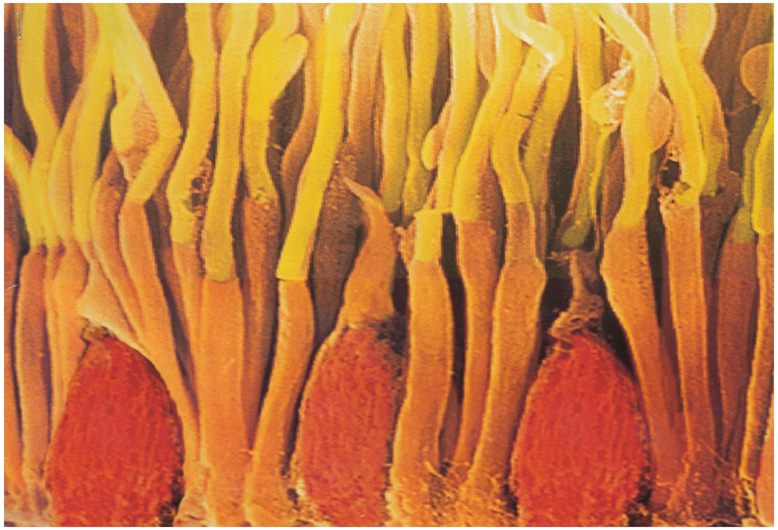
- Miss at most 75% of photons: *false negative* rate < 75 %
- *False positives*: less than dark light (0.01 /rod /sec)

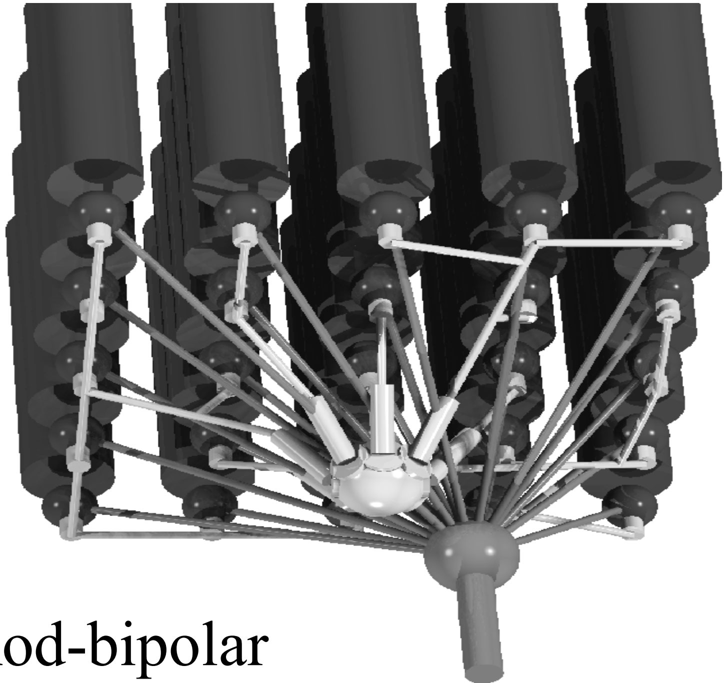
[van Rossum & Smith 1998, Clark & van Rossum 2006]

Rod pathway circuitry

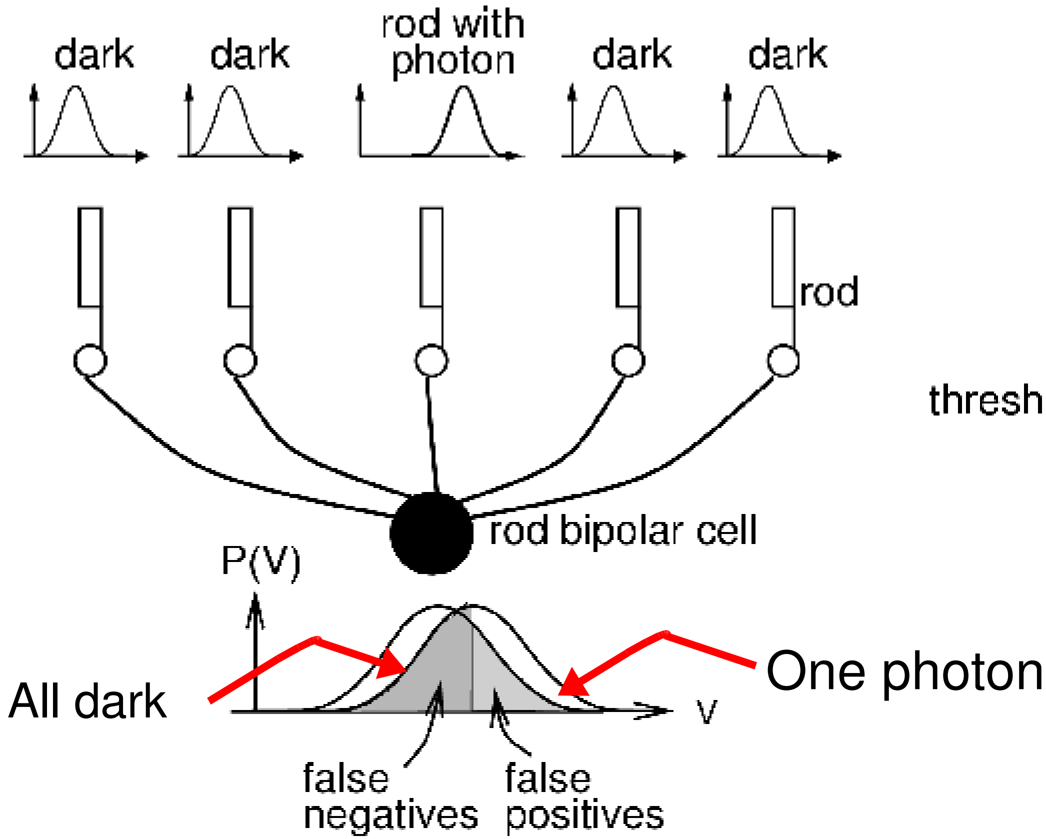


Note: 20% intrinsic noise

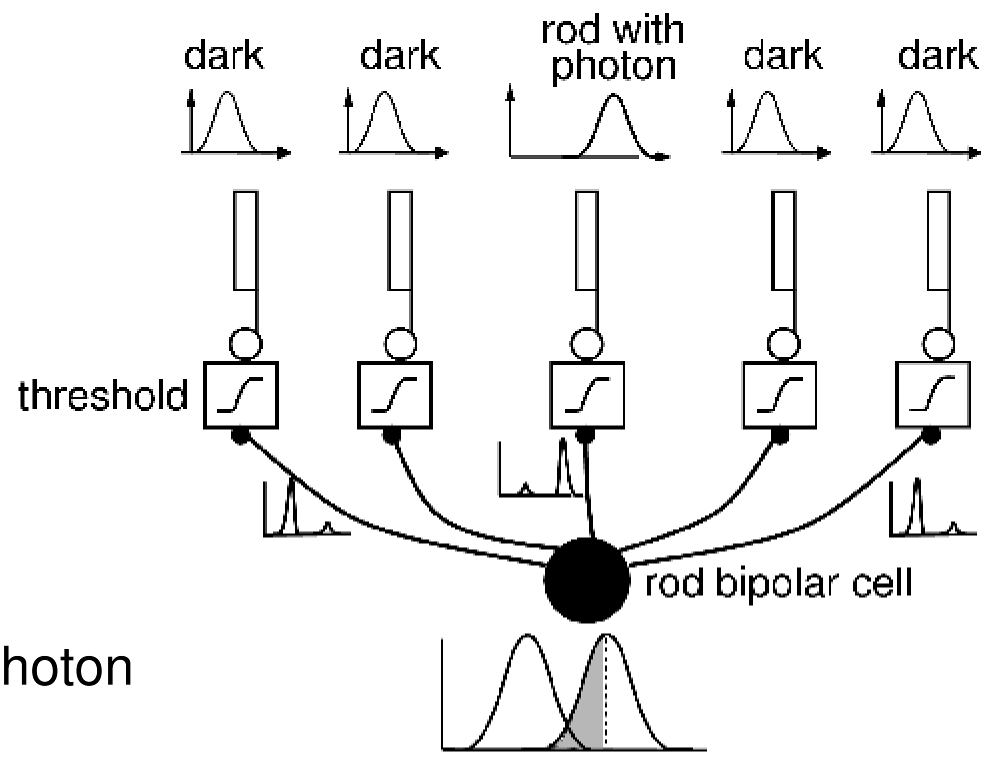




The need for a thresholding synapse



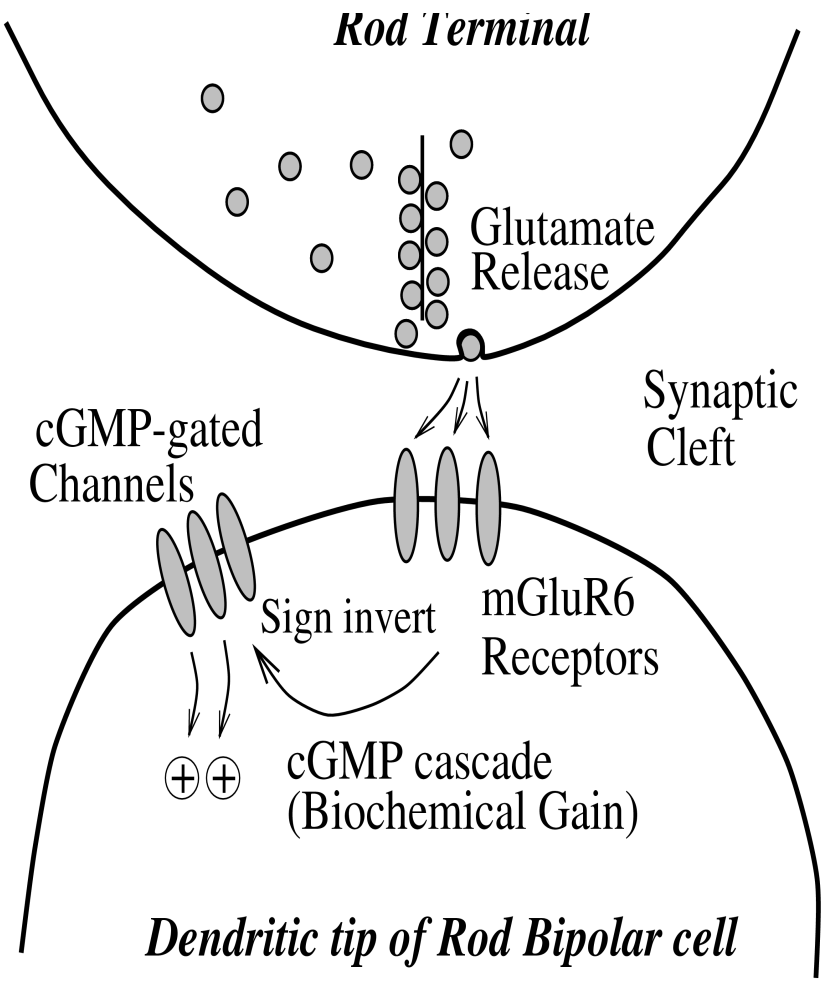
No threshold: many errors

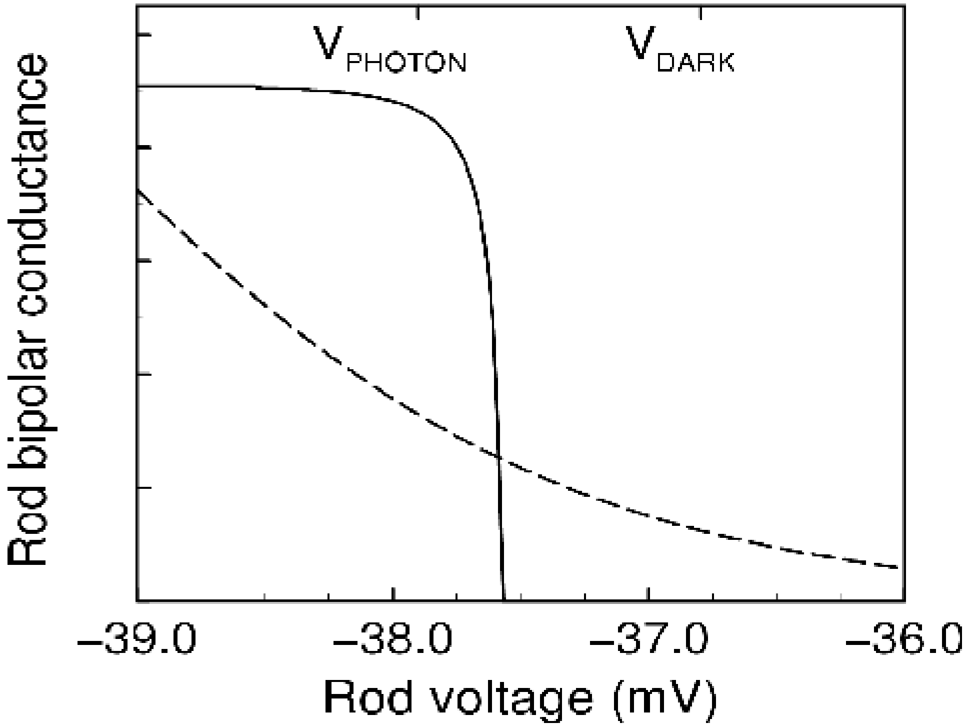


Thresholding: keep errors small

- Simple pooling is bad [Baylor et al 1984].
- Threshold before summing
- Set threshold high (reject many events).

Second messenger synapse



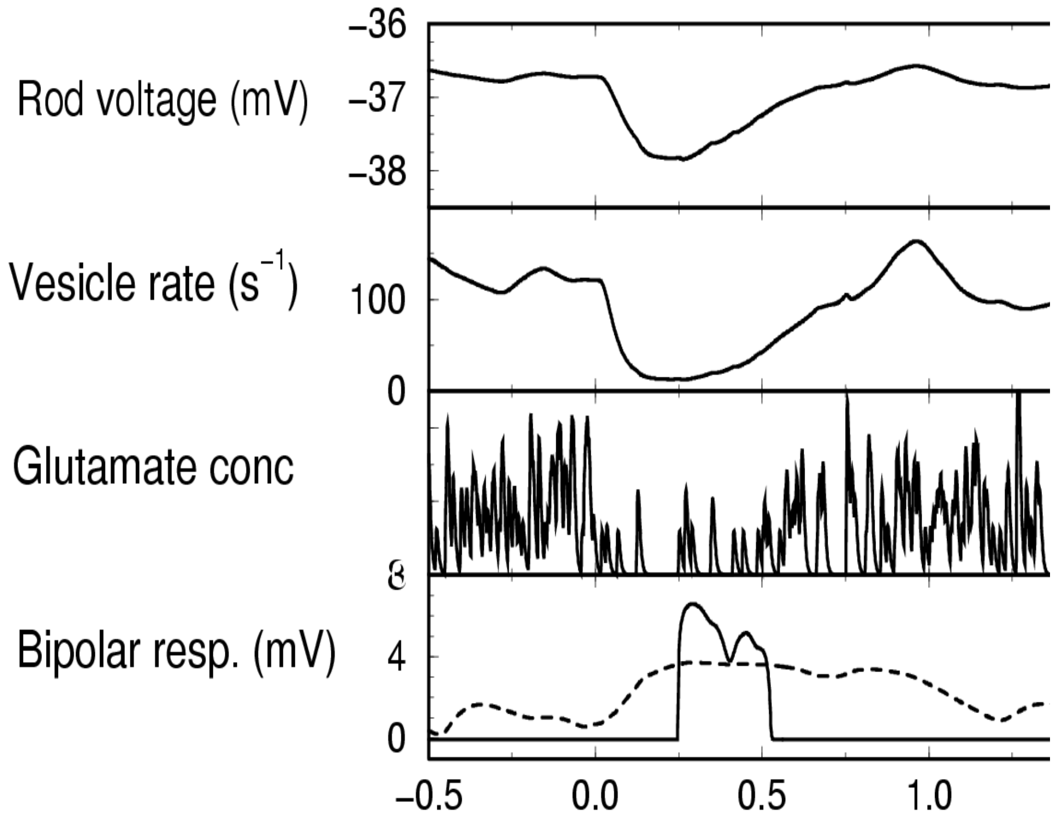


$$[cGMP] = 1 - c_{gain}[Glu]_{bound}$$

$$but \quad [cGMP] > 0$$

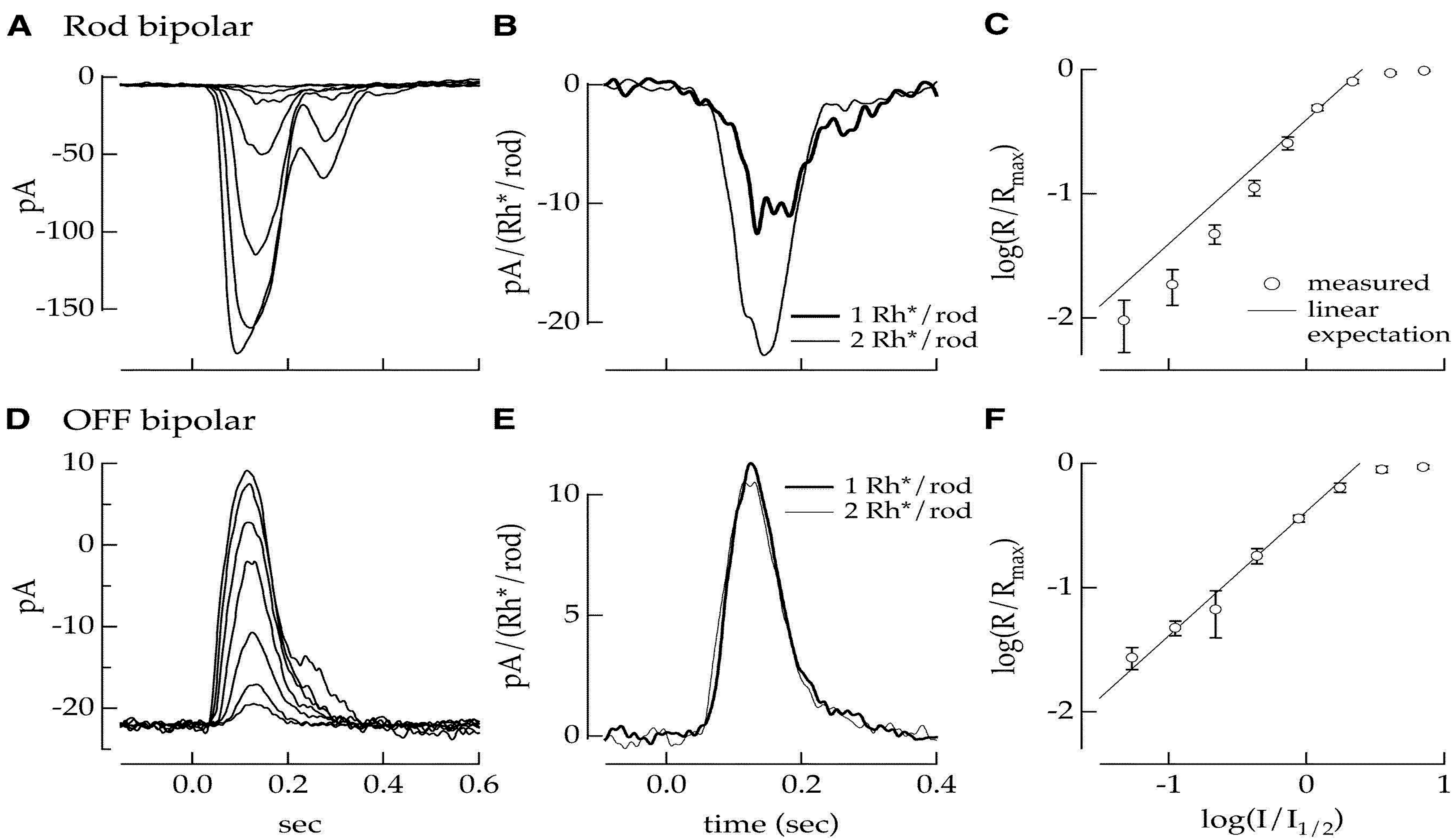
$$g = \frac{[cGMP]}{k_2 + [cGMP]}$$

Second messenger synapse



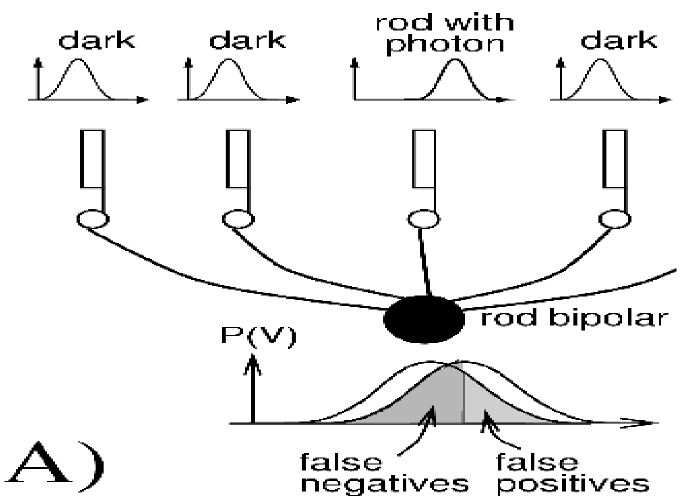
- Requires high vesicle release rate. About 80 ves/sec for Poisson release.
- Experiments confirm model [Sampath & Rieke, '04]
- Only 0-2 channels open in the dark, 30 open for single photon response.

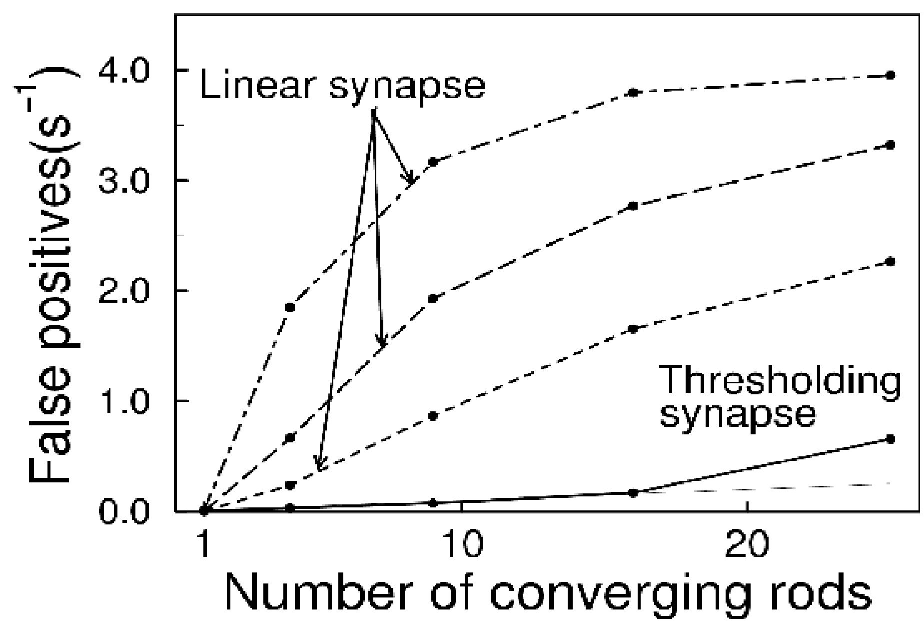
Experimental evidence

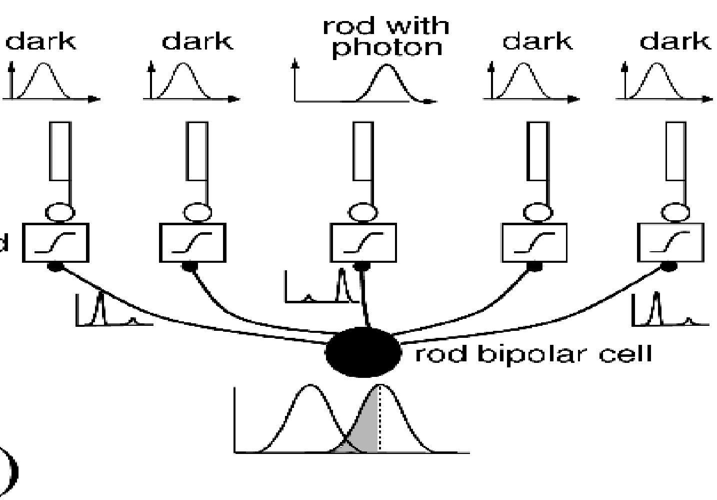


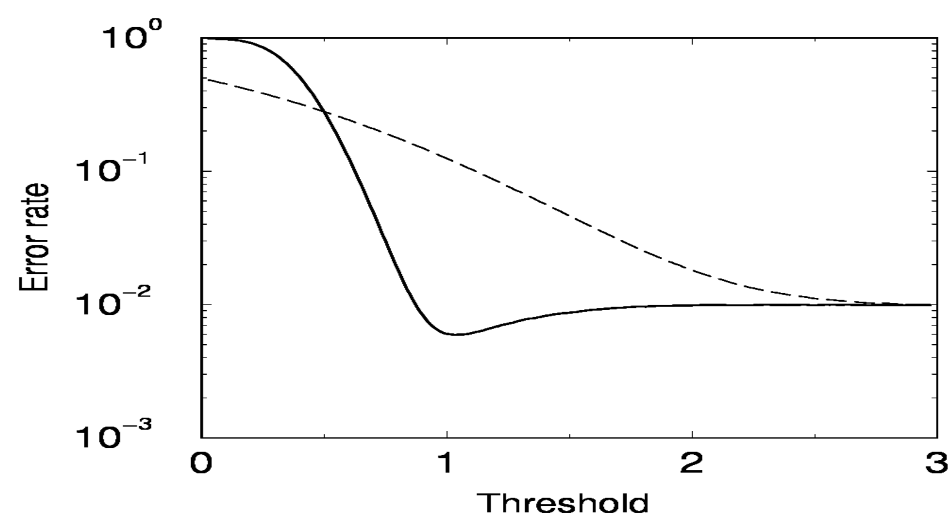
Data from Field & Rieke 2002.

Performance with thresholding synapse

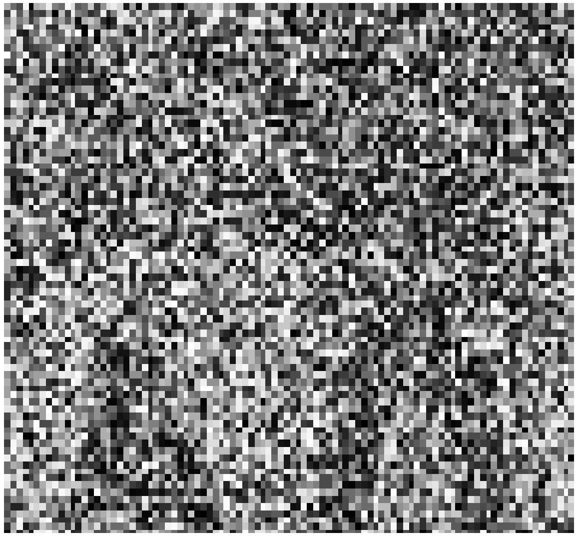








Simulation of visual perception

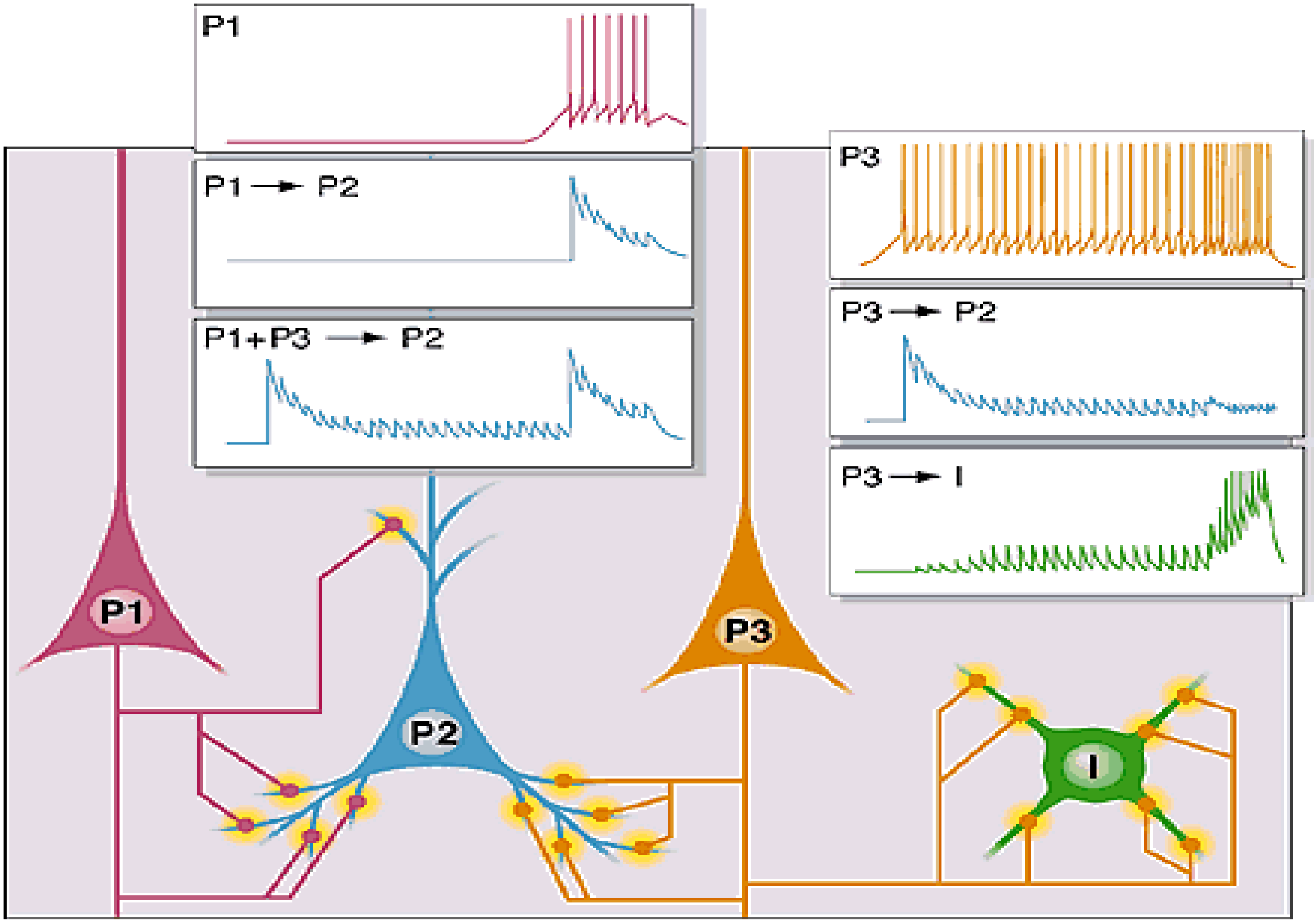


Different synapses, different perception
Low level modeling with high level consequences

Other applications ?
Detection of single, binary signal amidst many, noisy inputs

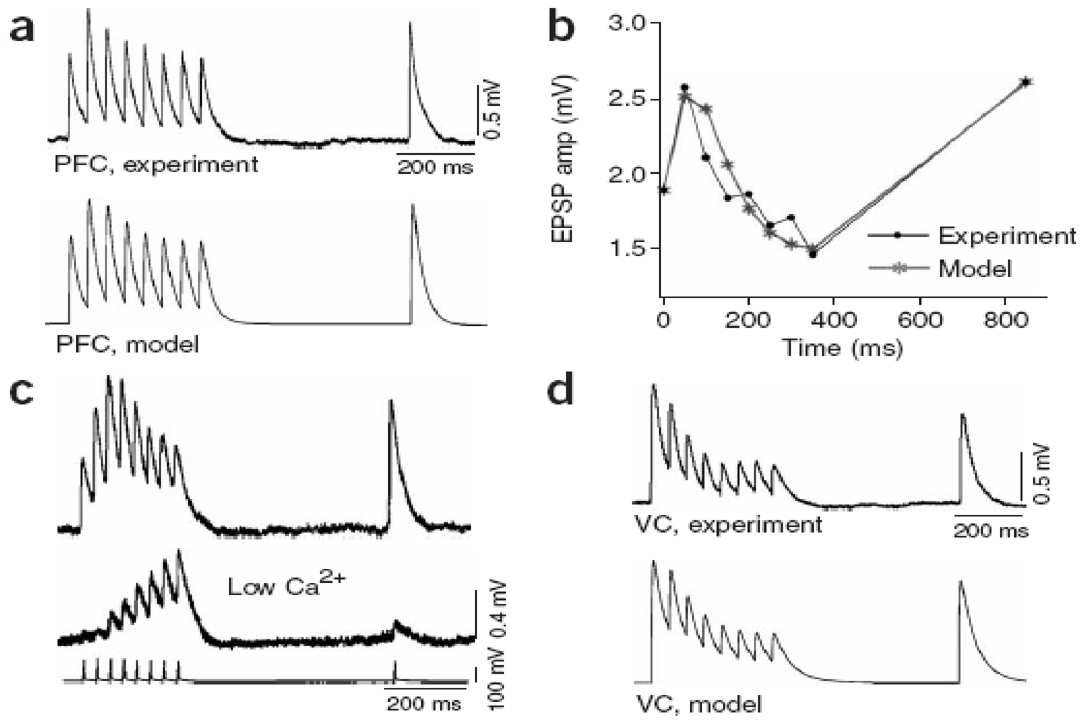
PART 3: Synaptic depression and network dynamics

Short term synaptic depression



Short term synaptic depression

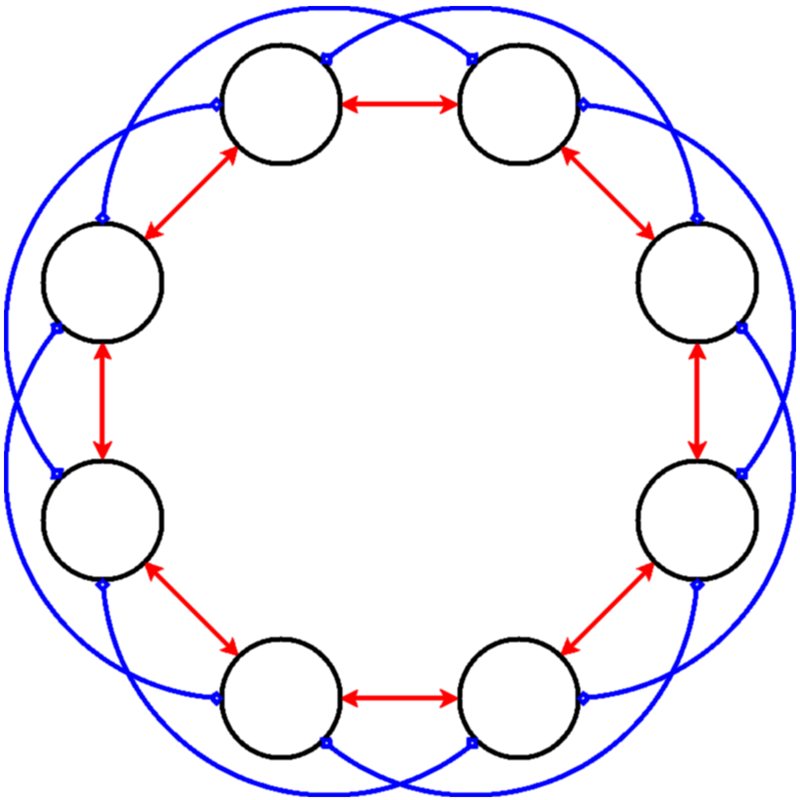
[Markram et al '98]

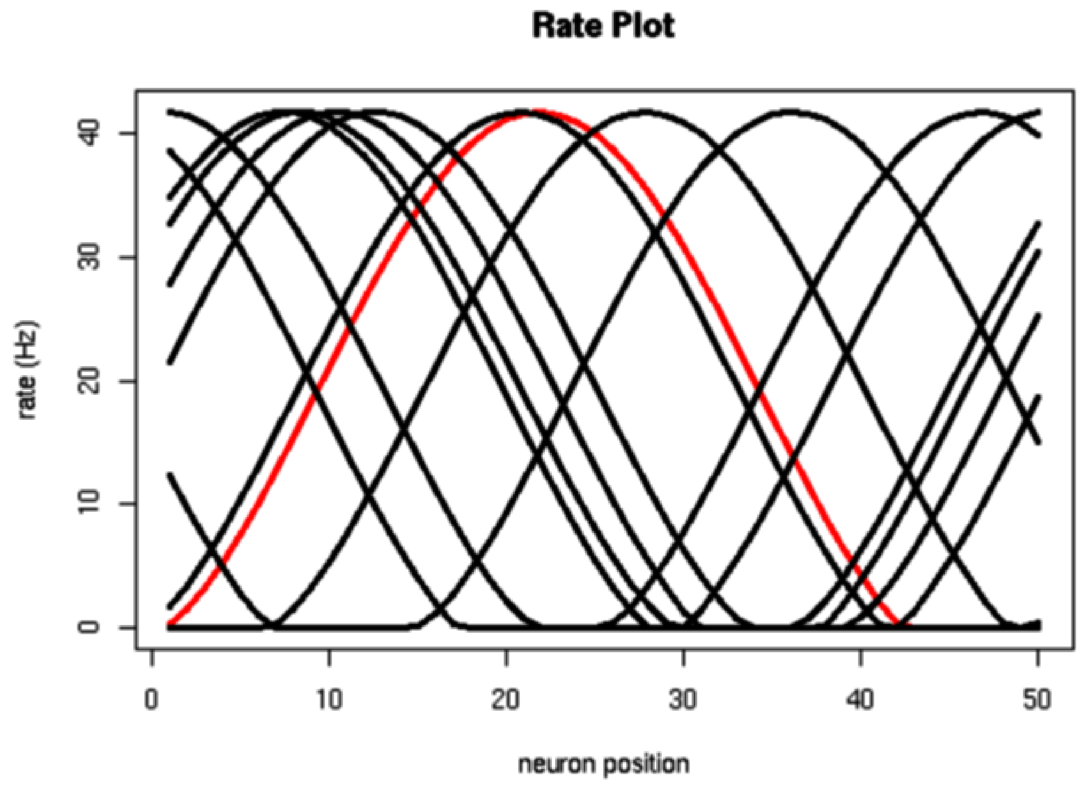


[Wang et al 2007]

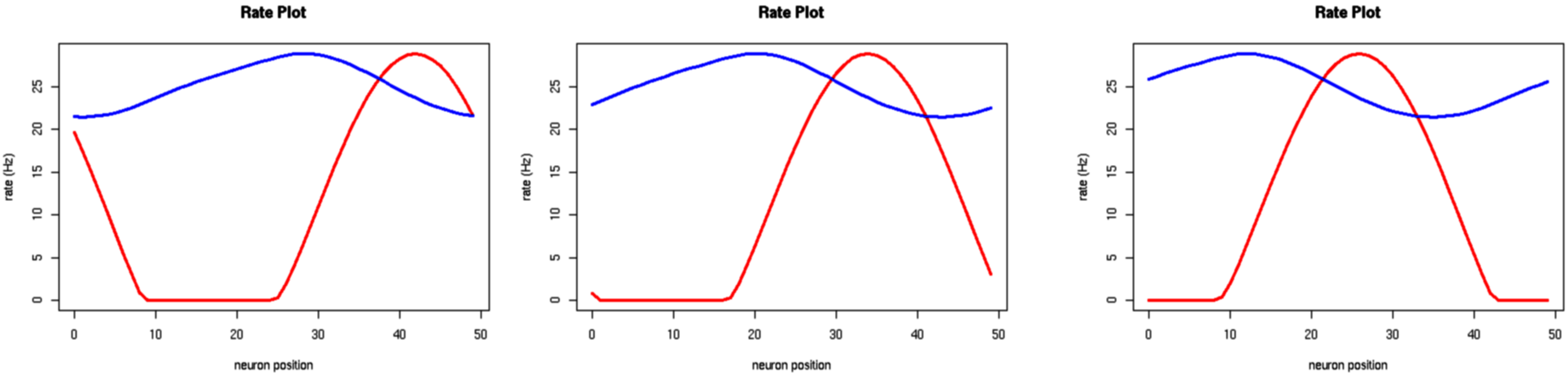
Ring attractor network

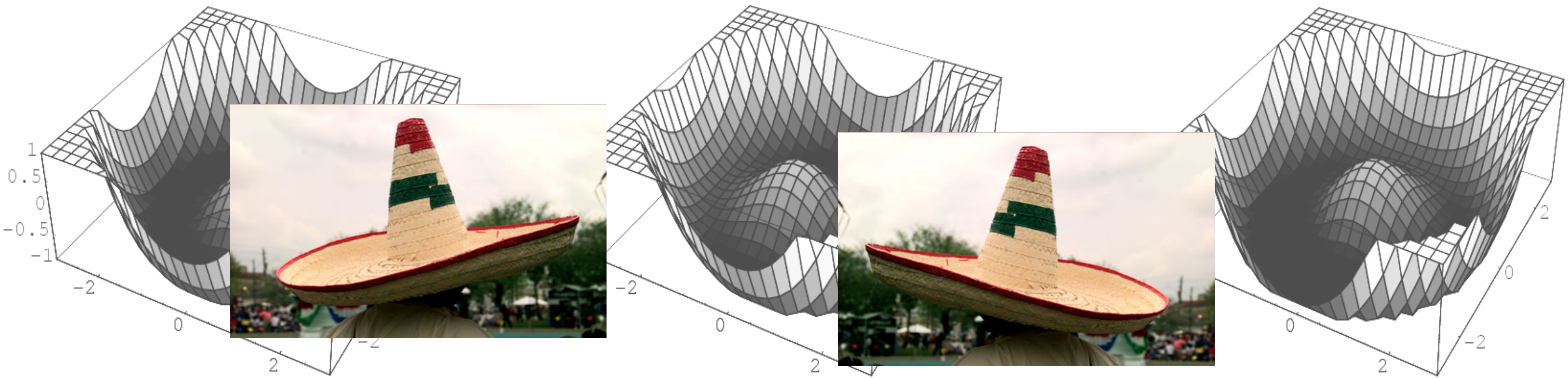
- Ring network with centre-surround profile
- With strong enough recurrence: line-attractors





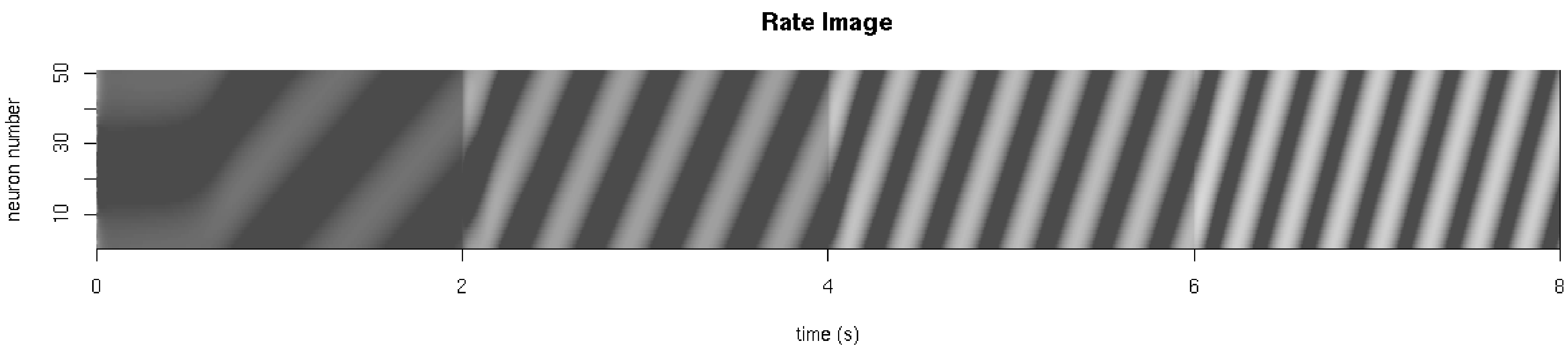
Ring attractor network

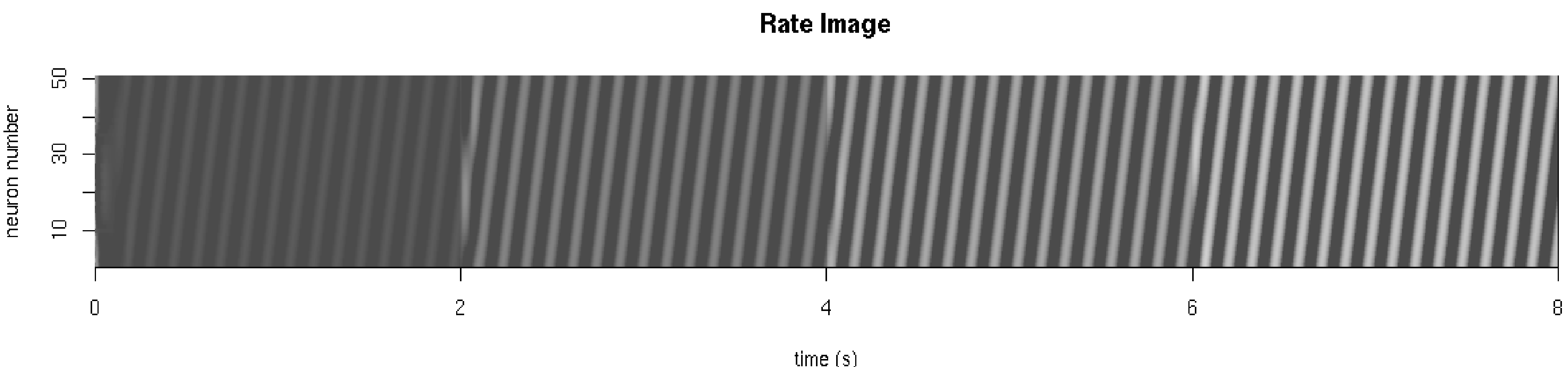




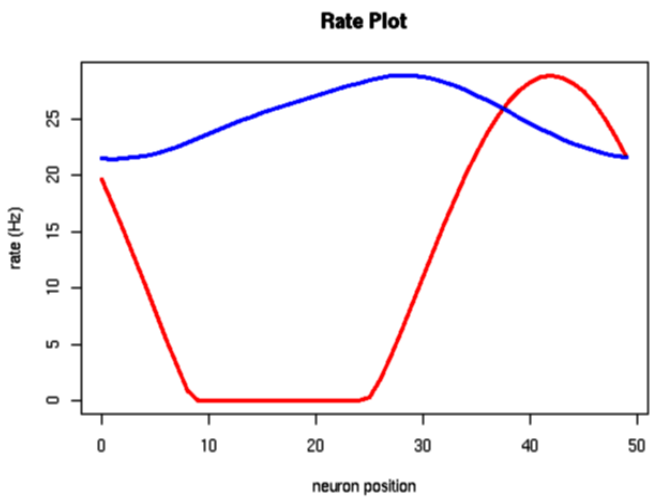
Destabilization, rotating attractors

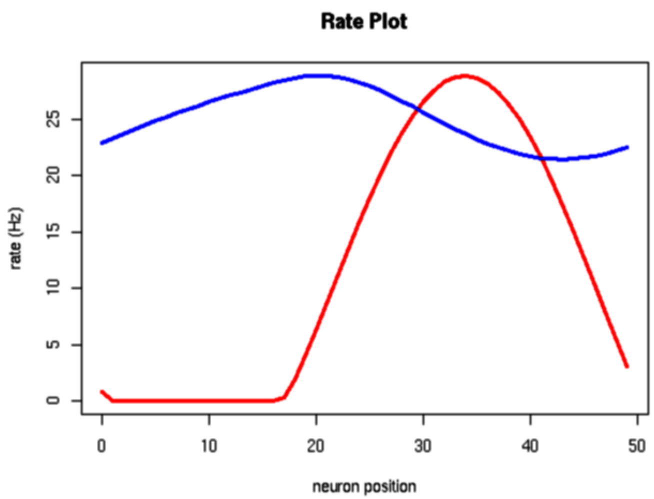
- With depressing synapses, rotating solution
- The rotation speed depends on uniform background current
- With spike rate adaptation, speed is fixed[Hansel and Sompolinsky]

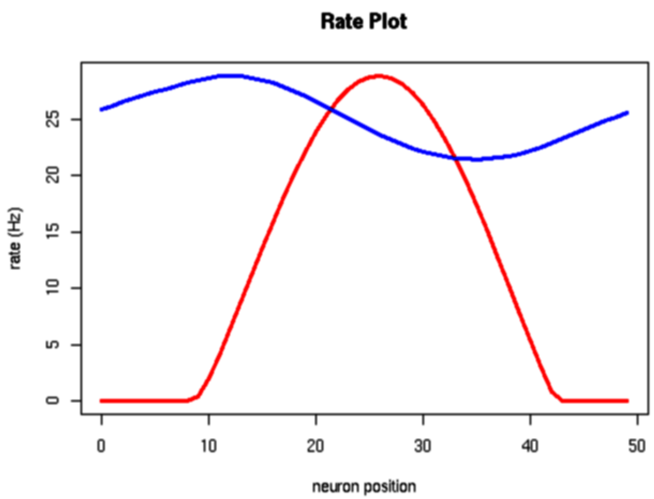




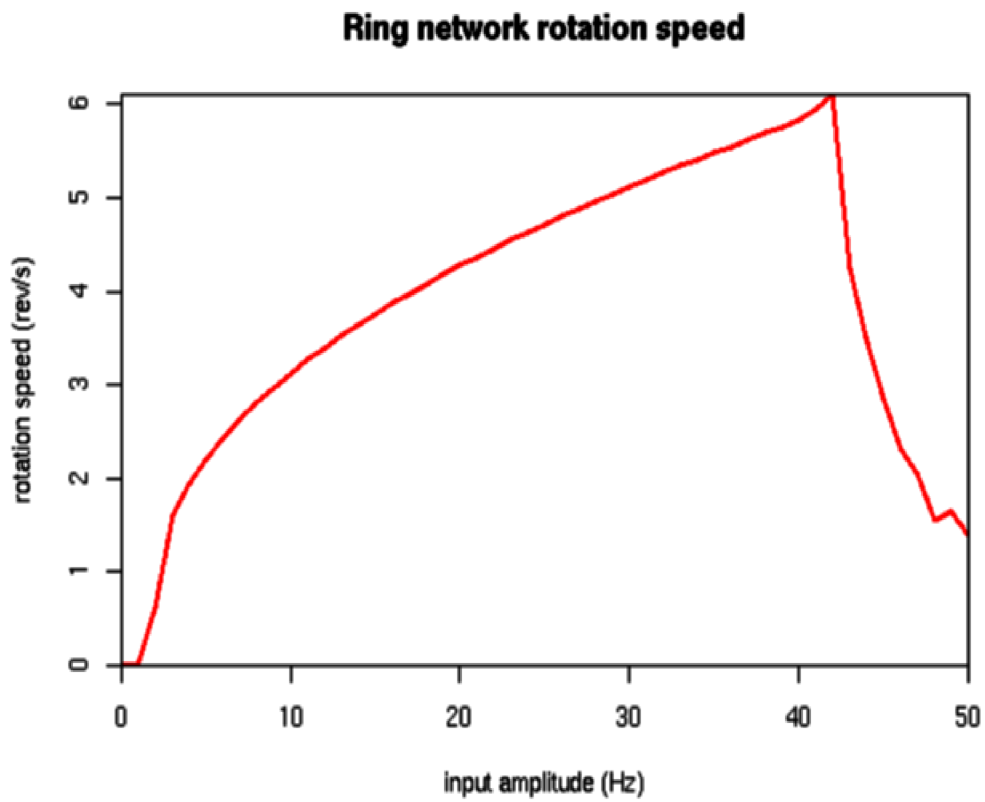
Ring attractor network





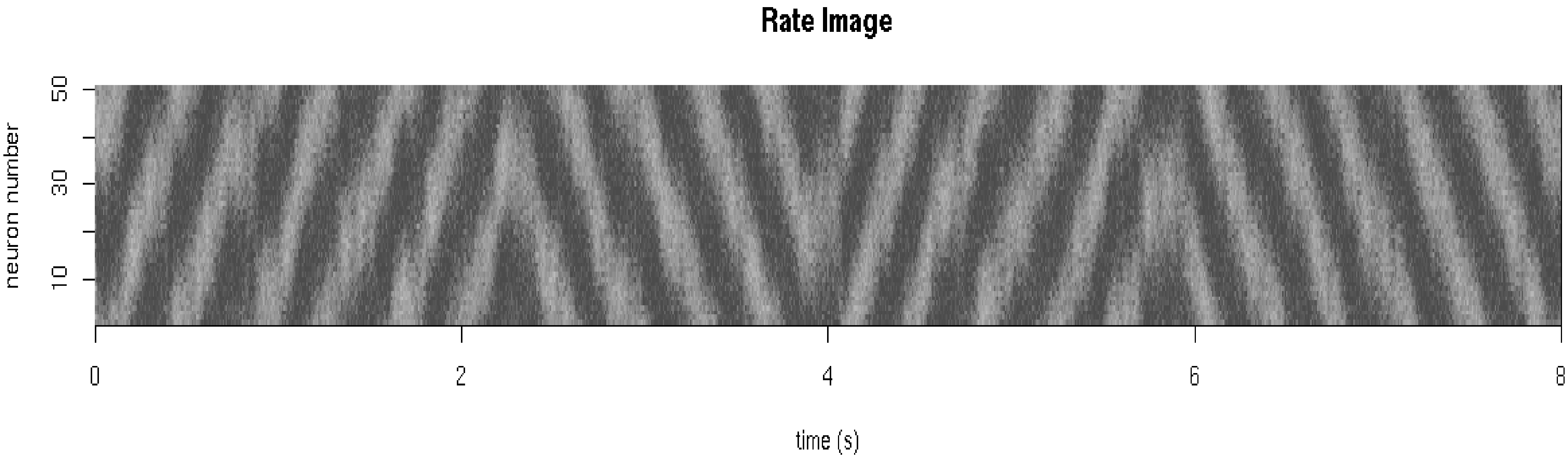


Rotation speed

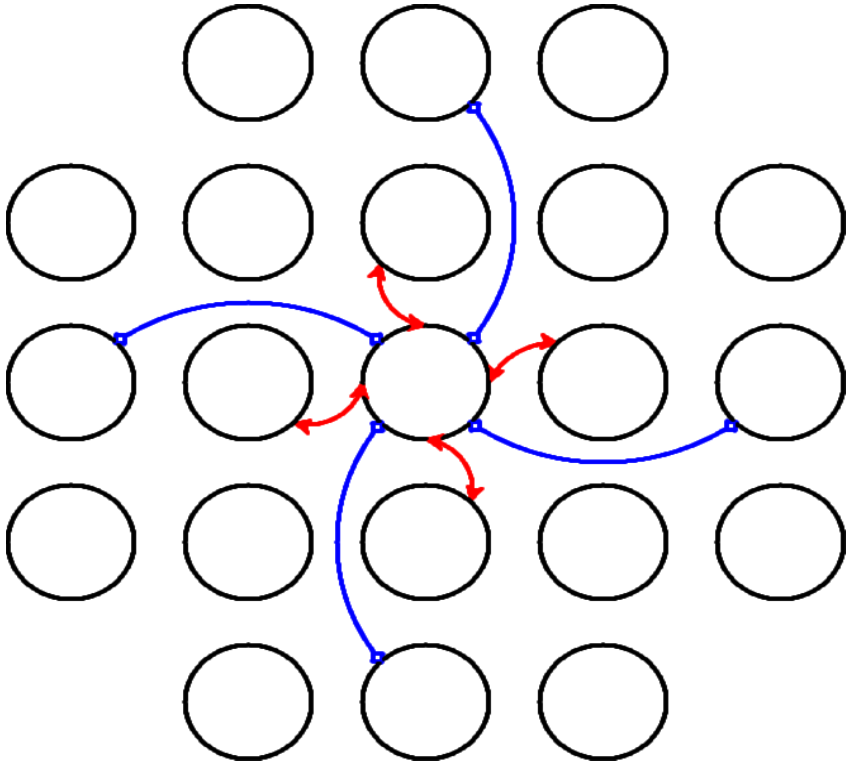


Possible application: pattern generation with variable frequency.

Alternative solutions in the presence of noise



2 dimensional field



Movies...

Conclusions

- Synapses are not only a way to do connect neurons
- They can have rich behavior: Non-linear, noisy, dynamical
- And this is reflected on a systems level