Plasticity

- Spatial working memory: storing information in a continuum of attractors

- Memory in a noisy environment

- Short term plasticity: Tsodyks-Markram formalism and application to an ODR task

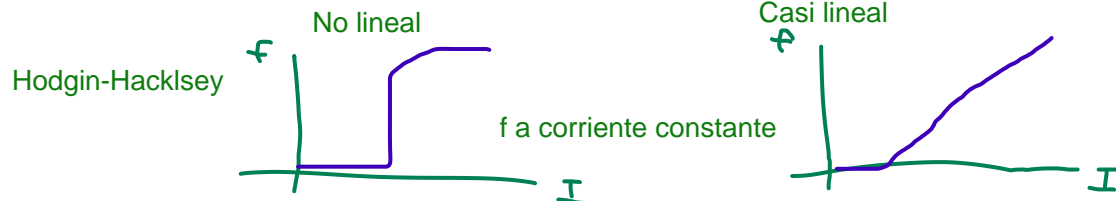# Spatial working memory and short term plasticity

Cuando vimos el modelo de Hopfield

- The models we have considered before are characterized by
- Discrete attractors
- Extremely non-linear neuron dynamics
- Both features favor the performance of the system as we have well defined attraction basins (cuencas de atracción bien definidas)

- What would be the most difficult case?
- Continuous attractors
- Quasi-linear dynamics

Ej: quiero recordar una posición. Pero alrededor de esa posición hay un continuo de posiciones que son igualmente posibles de recordar

La dinámica no es necesariamente no lineal (como la función signo)

No lineal

Hodgin-Hacklsey

f a corriente constante

Casi lineal

Spatial working memory and short term plasticity

- Continuous attractors
  - This will happen if we want to remember the value of a continuous variable (space, frequency, wavelength, etc)

- The non-linearity depends on
  - The intrinsic neuron dynamics
  - The level of noise: more noise will tend to linearize the effective f-I curve of the neurons   Las curvas tienden a suavizarse

Persistent Activity During an Oculomotor Delayed Response Task

Actividad de una neurona dada en la corteza pre-frontal (se mide con un electrodo)
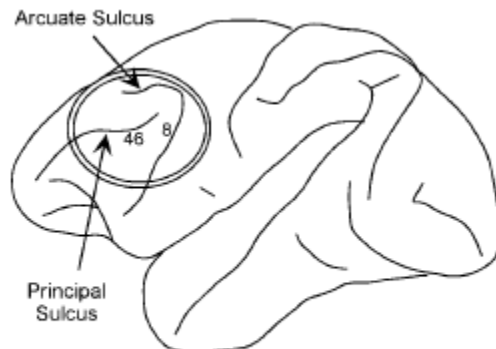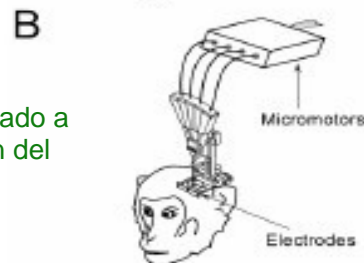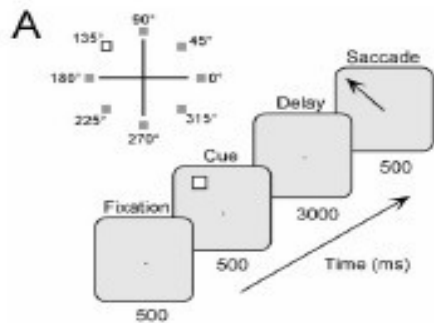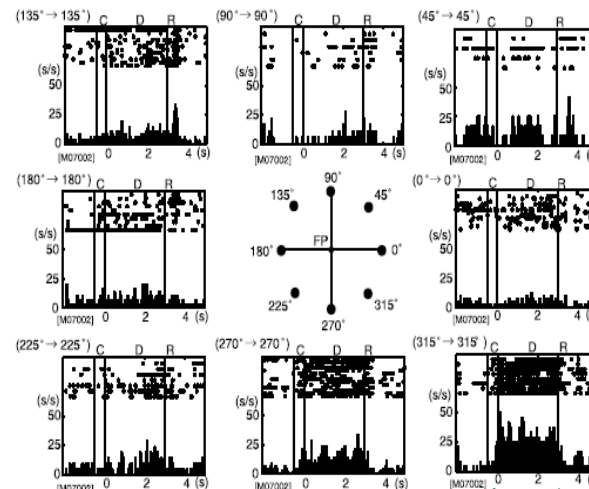
El mono está motivado a recordar la posición del estímulo

Intervalo de delay con gran actividad porque el mono está recordando

Funahashi, 2006

La tasa de disparo depende del ángulo!

preferido

no preferido

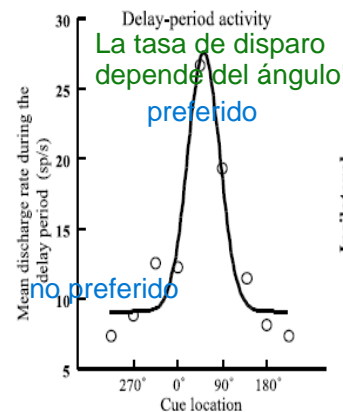A. Delay-period activity in the ODR task

B. Tuning curve

C. Best directions

Figure 1. Location of electrophysiological recording in dorsolateral pre-frontal cortex, centered on area *46* and the frontal eye fields (area *8*). This region included the caudal half of the principal sulcus and cortex lining the arcuate sulcus.
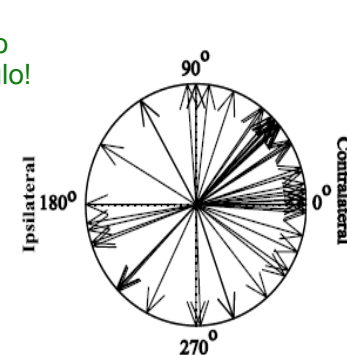
Fig. 2. Characteristics of delay-period activity observed in DLPFC neurons. (A) An example of directional delay-period activity. (B) An example of a tuning curve of directional delay-period activity. (C) Polar distribution of the best directions of delay-period activity. A majority of the best directions were directed toward the contralateral visual field.

Persistent Activity During the Delay Period is Highly Variable

proceso poissoniano

$$CV=[<ISI^2>-<ISI>^2]^{1/2}/<ISI>$$
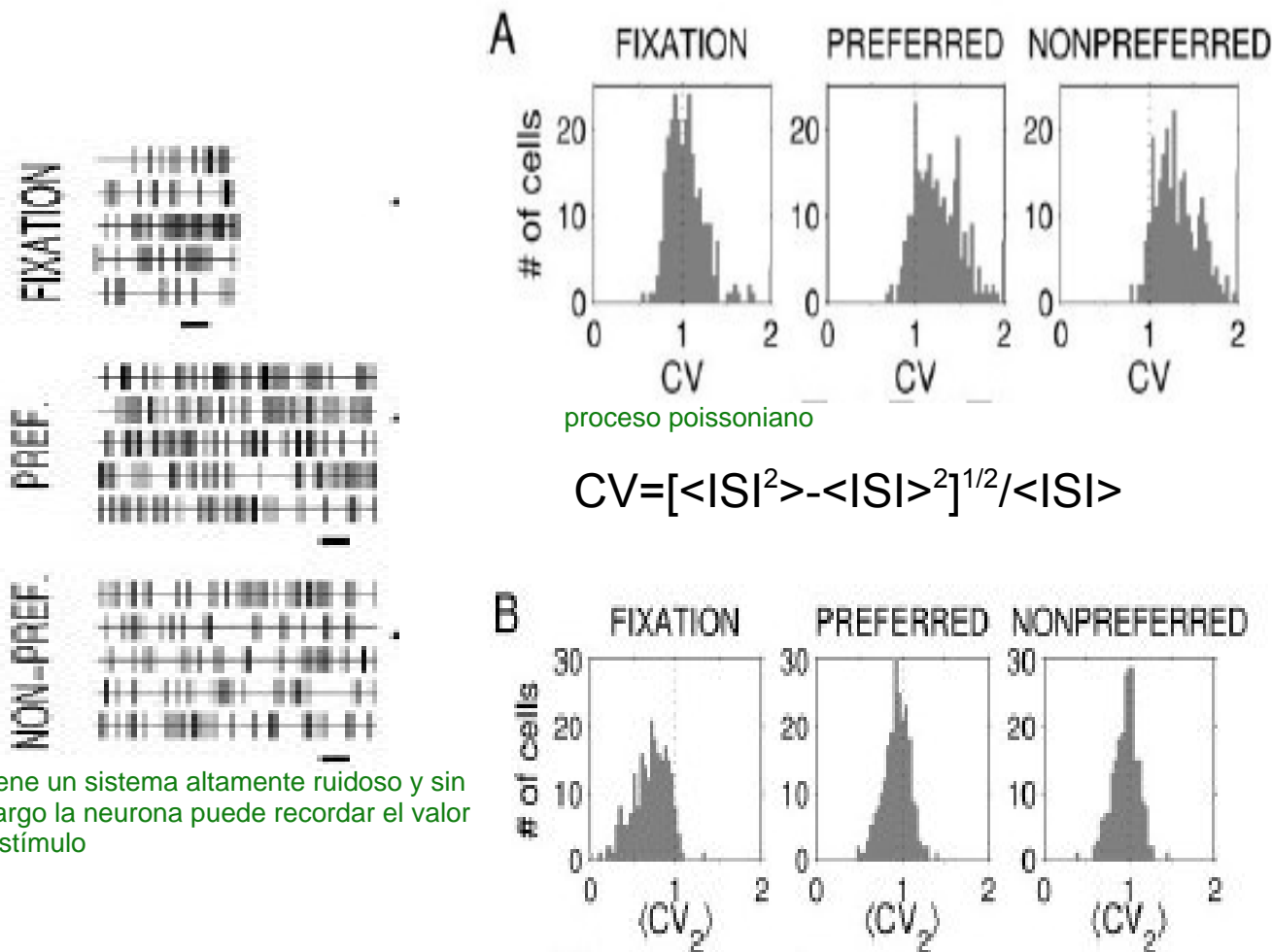
Se tiene un sistema altamente ruidoso y sin embargo la neurona puede recordar el valor del estímulo

Compte et al, 2003

$$<CV_2>=2<|ISI_{n+1}-ISI_n|/[ISI_{n+1}+ISI_n]>$$

Balance of excitation and inhibition explains irregular activity...

- N_E, N_I excitatory and inhibitory neurons
- K connections per neuron (average)
- 1 << K << N_E, N_I
- Synaptic efficacy O(1/sqrt(K))
- Average excitatory input O(sqrt(K))
- Average inhibitory input O(sqrt(K))
- Net input and fluctuations O(1)
  (van Vreeswijk and Sompolinsky, 1996)
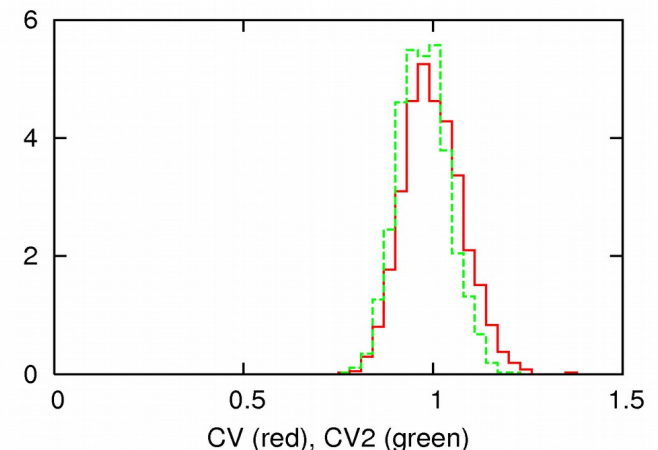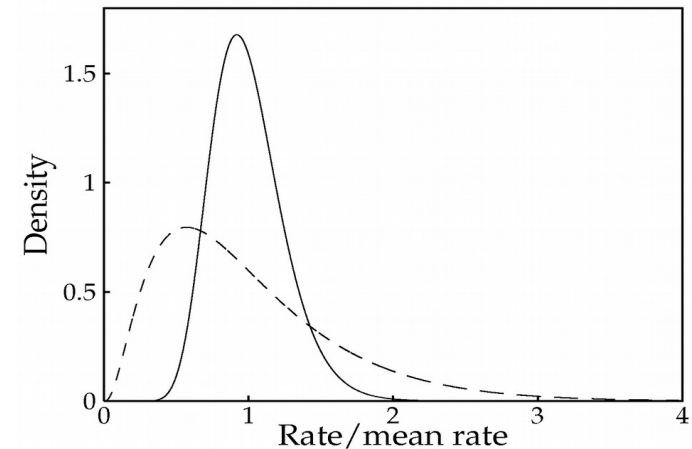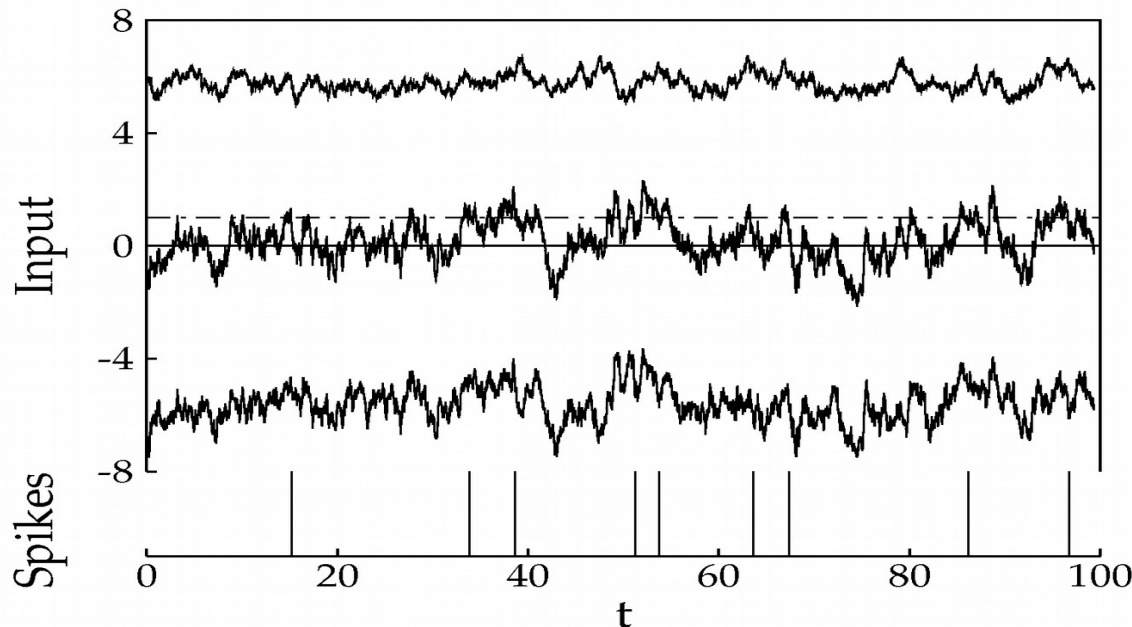
But this is problematic for having persistent states

- $f_E = F(h_E)$, $f_I = F(h_I)$
- f: firing rate; h: synaptic input; F: input-output transfer function

$$h_E = sqrt(K)\{G_{EE}\, f_E - G_{EI}\, f_I + I_E\}$$
$$h_I = sqrt(K)\{G_{IE}\, f_E - G_{II}\, f_I + I_I\}$$

- In the limit of very large K it must be

$$0 = G_{EE}\, f_E - G_{EI}\, f_I + I_E$$
$$0 = G_{IE}\, f_E - G_{II}\, f_I + I_I$$

Para que halla cancelación de valores medios es necesario cumplir esas ecuaciones que son lineales, no dando lugar a la multiestabilidad necesaria para tener ((varios atractores))

- There is a LINEAR relation between the firing rates and the external inputs. Single neuron input-output transfer function (**F**) is irrelevant

- **<u>Multistability is not possible between balanced states if synapses are linear</u>**

But this is problematic for having persistent states

- On the other hand, for finite values of connectivity some non-linearity is still present
- Some models work in this regime (e.g. Renart et al, 2007)
- They require an increasingly precise tuning of parameters as K increases
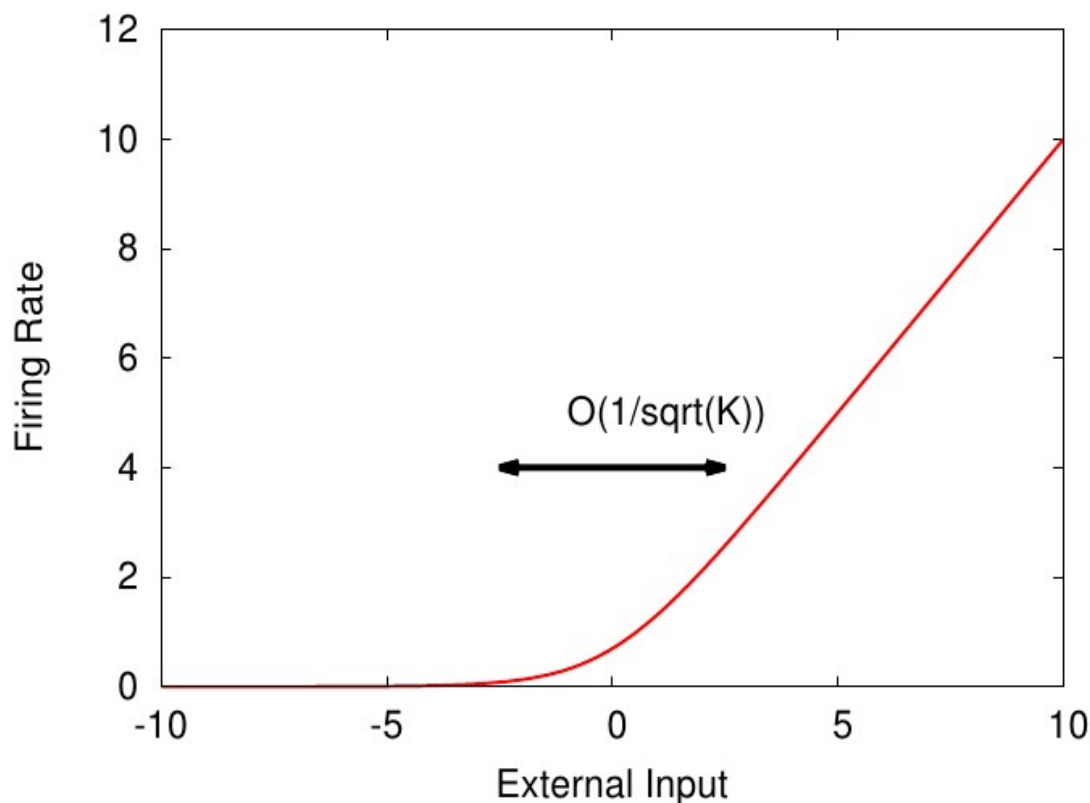
How can we reconcile balanced states and persistent states in a robust way?

- A possible solution:

  Non Linearities in Synapses e.g. Short Term Synaptic Plasticity

Modeling short term synaptic plasticity

- The synaptic connection is characterized by its absolute amount of 'resources,' which can be partitioned into three states: effective, inactive, and recovered
- If all the resources are activated by a presynaptic spike, this would generate the maximal possible response defined here as the absolute synaptic efficacy
- Each presynaptic spike activates a certain fraction of resources available in the recovered state, which then quickly inactivates with a time constant of a few milliseconds and recovers with a time constant of about 1 sec.
- This model could reflect various possible biophysical mechanisms of synaptic depression, such as receptor desensitization or depletion of synaptic vesicles

  (Tsodyks & Markram, 1997)
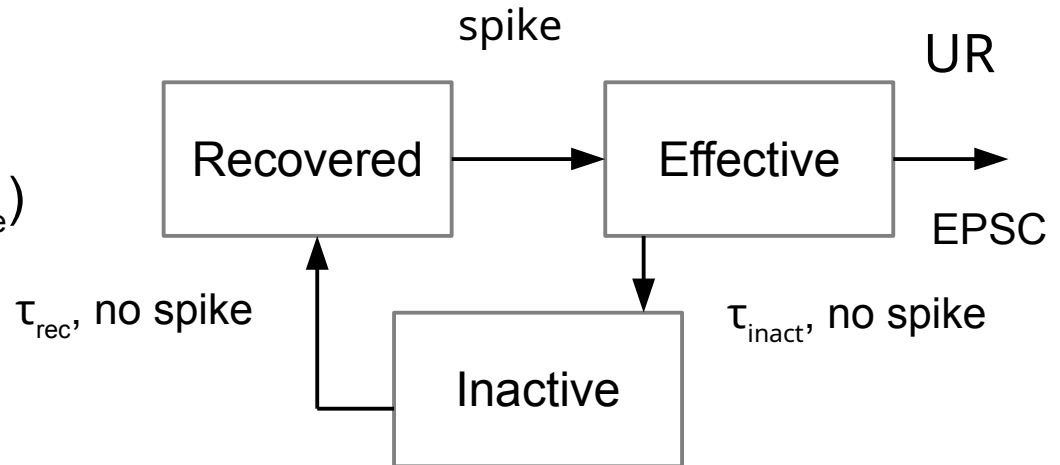
Modeling short term synaptic plasticity

Para resolver este problema se emplea la plasticidad

- Kinetic equations for each on of the three states are

$$dR/dt = I/\tau_{rec} - U\, R\, \delta(t-t_{spike})$$

$$dE/dt = -E/\tau_{inact} + U\, R\, \delta(t-t_{spike})$$

$$dI/dt = -I/\tau_{rec} + E/\tau_{inact}$$

where U is the utilization of synaptic efficacy parameter

- The size of the excitatory postsynaptic current (EPSC) for a periodic spike train of frequency f is (in the limit of small τ_{inact}):

$$EPSC \approx 1/(f\, \tau_{rec})$$

Modeling short term synaptic plasticity

- In Markram, Wang & Tsodyks, 1998, facilitation is included in the model
- The utilization of synaptic efficacy is increased at each spike

$$dR/dt = I/\tau_{rec} - u \, R \, \delta(t-t_{spike})$$

$$dE/dt = -E/\tau_{inact} + u \, R \, \delta(t-t_{spike})$$

$$dI/dt = -I/\tau_{rec} + E/\tau_{inact}$$

$$du/dt = (U-u)/\tau_{facil} + U(1-u) \, \delta(t-t_{spike})$$
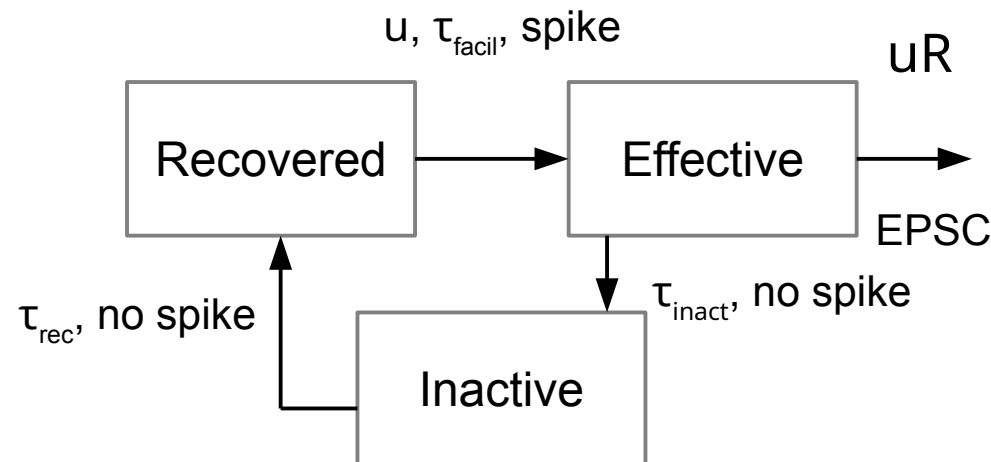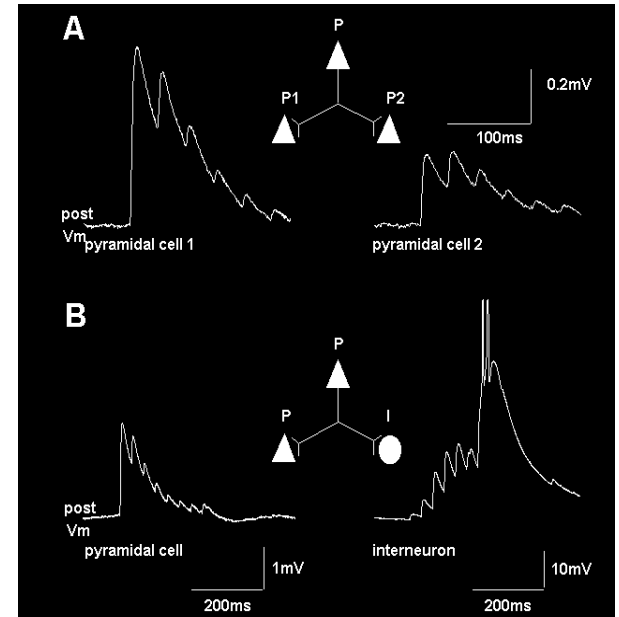
Modeling short term synaptic plasticity

- 4 Key Synaptic Parameters (in the limit of small τ_{inact}):

- Absolute strength : A
- Probability of release : U
- Depression time constant: τ_{rec}
- Facilitation time constant: τ_{facil}

(Markram, Wang & Tsodyks, 1998;
Tsodyks, Pawelzik & Markram, 1998)

- Effective synaptic efficacy at the time of n+1th spike: A u_{n+1} R_{n+1}

$$u_{n+1} = u_n \exp\left(\frac{-\Delta t}{\tau_{facil}}\right) + U\left(1 - u_n \exp\left(\frac{-\Delta t}{\tau_{facil}}\right)\right)$$

$$R_{n+1} = R_n(1 - u_{n+1})\exp\left(\frac{-\Delta t}{\tau_{rec}}\right) + 1 - \exp\left(\frac{-\Delta t}{\tau_{rec}}\right)$$

Modeling short term synaptic plasticity

- $U, \tau_{rec}, \tau_{facil}$ control the relation between depression and facilitation.
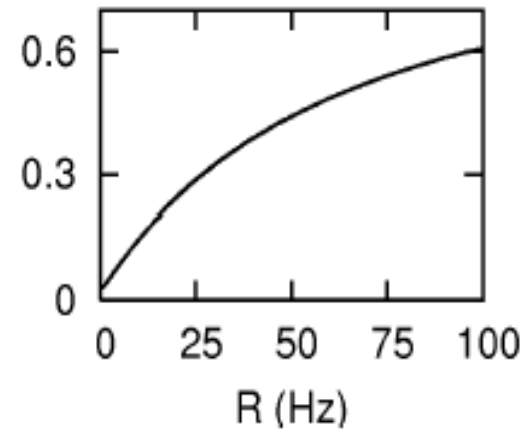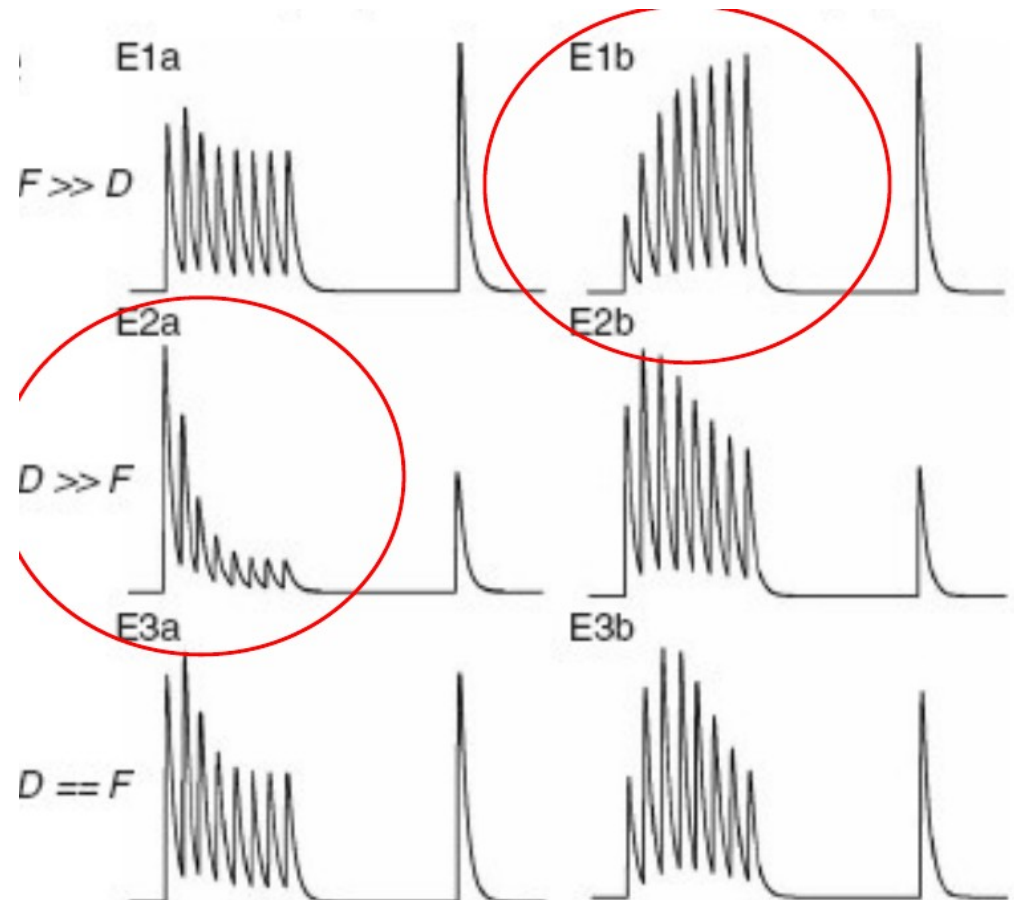
- For periodic spike trains:
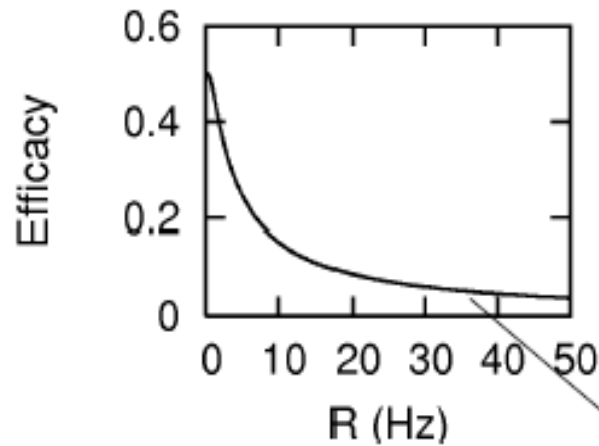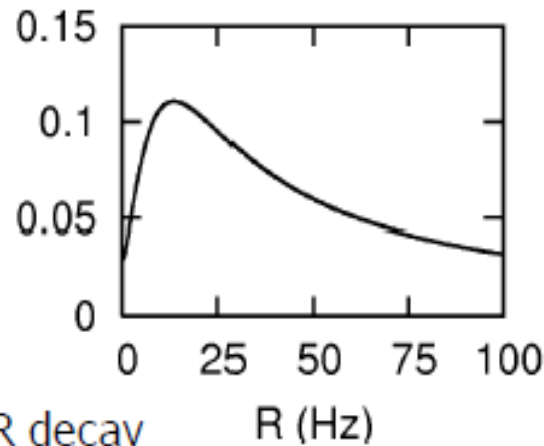
Modeling short term synaptic plasticity

- Diversity in the pre-frontal cortex

- $F=\tau_{facil}$
  $D=\tau_{rec}$

  Wang et al. (2006)

Modeling short term synaptic plasticity

- How will this system behave in a network

- Some kind of self-consistent calculation is necessary

- Mean field theory: Mongillo et al. PRL (2012)

- Two populations of LIF neurons with sparse connectivity (K connections per neuron K<<N)

- Coupling strengths proportional to $1/K^{1/2}$

- If we have plasticity only in the E→E connections the final result is that the firing rates can be evaluated by multiplying J_{EE} by p_R

- P_R can be evaluated self-consistently

Modeling short term synaptic plasticity

- Two population network with sparse connectivity and plasticity in the E->E connections
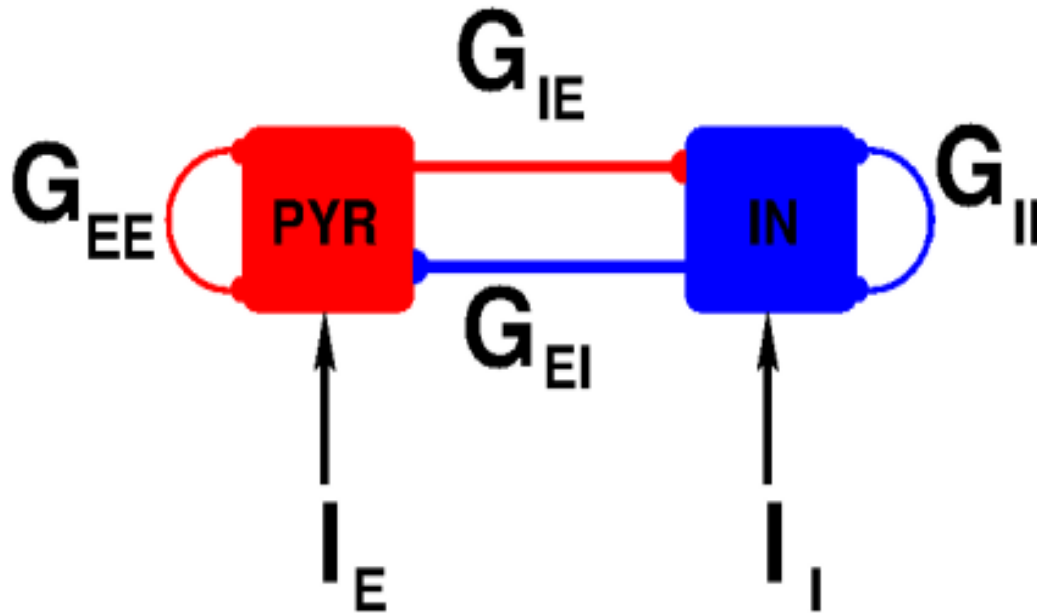
Modeling short term synaptic plasticity
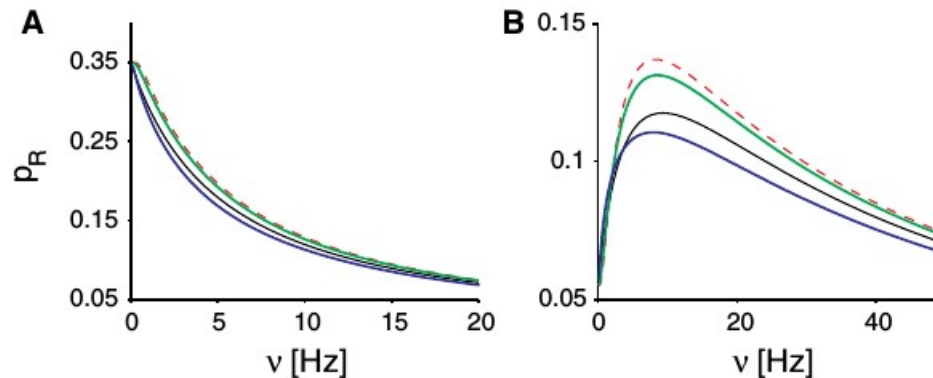
- For instance

FIG. 1 (color online). The probability of release p_R vs the spiking rate ν for different ISI pdfs. From top to bottom: δ function (red dashed), inverse Gaussian with CV = 0.5 (green), exponential (black), inverse Gaussian with CV = 1.5 (blue). (a) Depressing transmission: p_R decreases with increasing ν. Parameters: $U = 0.35$, $\tau_F = 150$ ms, $\tau_D = 700$ ms. (b) Facilitating transmission: p_R first increases, then decreases with increasing ν. Parameters: $U = 0.055$, $\tau_F = 650$ ms, $\tau_D = 200$ ms.

- This generates additional NON-LINEARITY

Modeling short term synaptic plasticity

- Introducing a firing rate dependence in the E->E connections, the balance equations become:

$$0 = G_{EE} \, p_R(f_E) \, f_E - G_{EI} \, f_I + I_E$$
$$0 = G_{IE} \, f_E - G_{II} \, f_I + I_I$$

- Mean field equations for leaky integrate-and fire neurons (Mongillo et al, 2012)

- $p_R(f_E)$ depends very weakly on the statistics of the spike trains
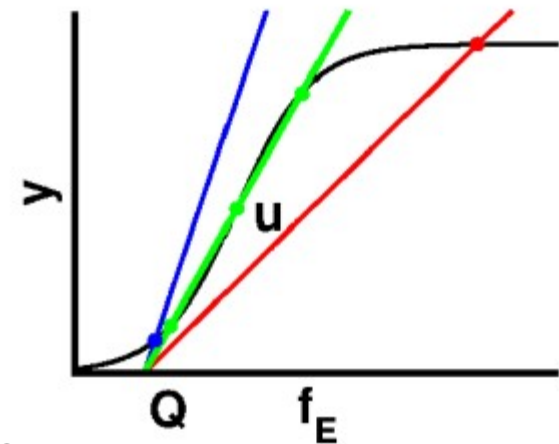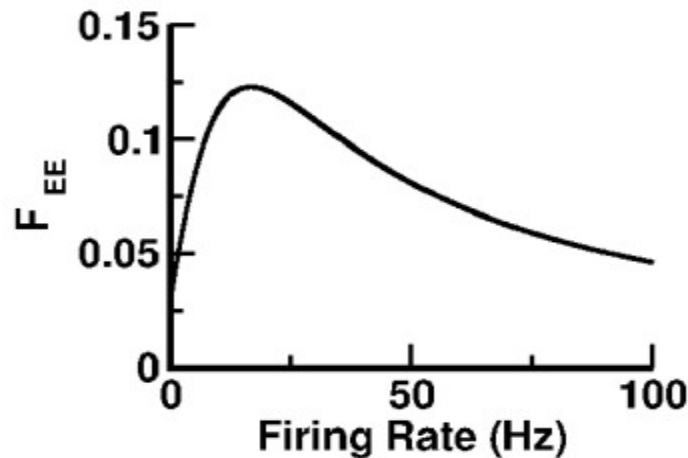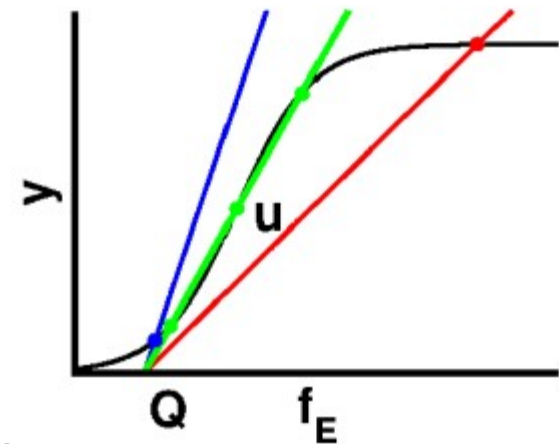
Short term synaptic plasticity allows bistability in unstructured network

- The input-output transfer at population level are non-linear
- This allows to have bistability:

Synapse with facilitation and depression
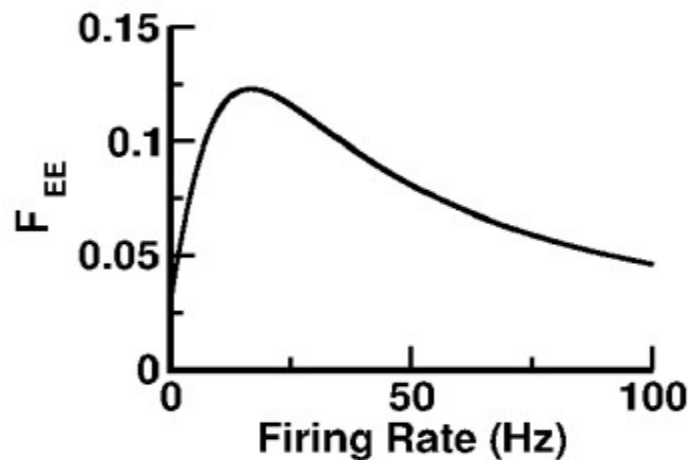
For a given value of the coupling two stable solutions

$$f_E F_{EE}(f_E)=(f_E-Q)/J \equiv y$$
$$Q=(G_{II} I_E/G_{EI} - I_I)/G_{IE}$$
$$J=G_{II} G_{EE}/(G_{EI} G_{IE})$$

Short term synaptic plasticity allows bistability in unstructured network

- Bistability in a wide region of the parameter space:

Phase diagram
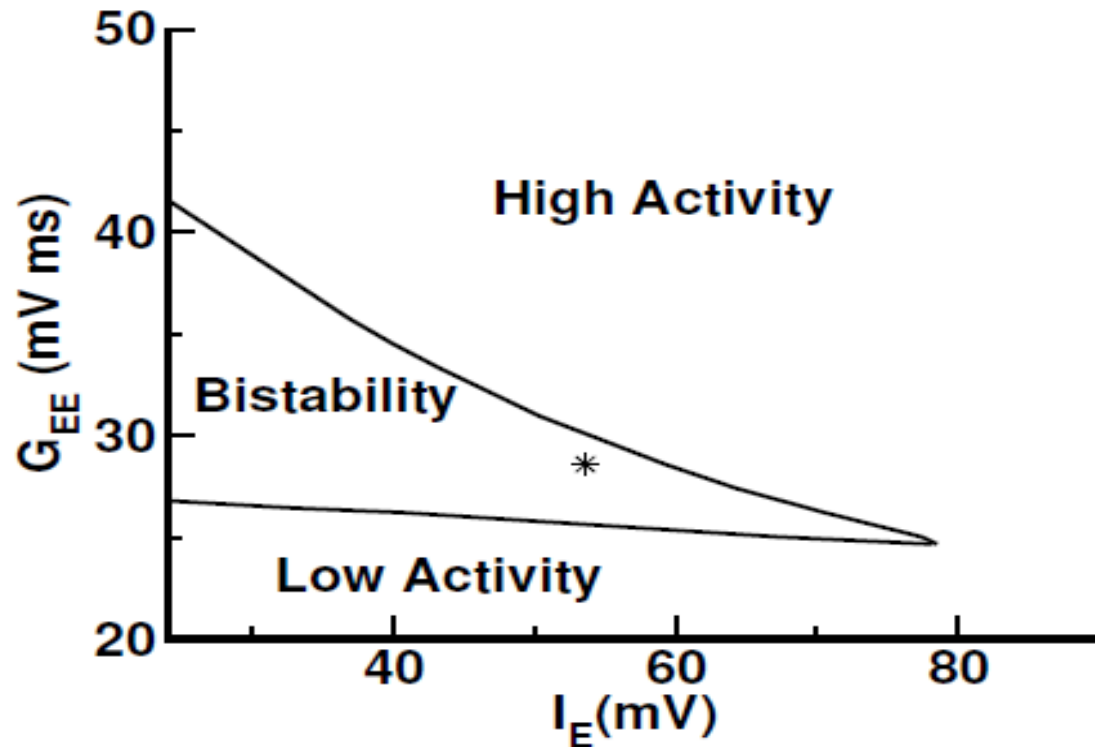
Short term synaptic plasticity allows bistability in unstructured networks

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For a given value of the coupling two stable solutions

$$f_E\ F_{EE}(f_E) = (f_E - Q)/J \equiv y$$
$$Q = (G_{II}\ I_E/G_{EI} - I_I)/G_{IE}$$
$$J = G_{II}\ G_{EE}/(G_{EI}\ G_{IE})$$

Short term synaptic plasticity allows bistability in unstructured networks

- Switch between DOWN and UP states
- These two states are balanced and display high temporal variability (CV approx. 1)
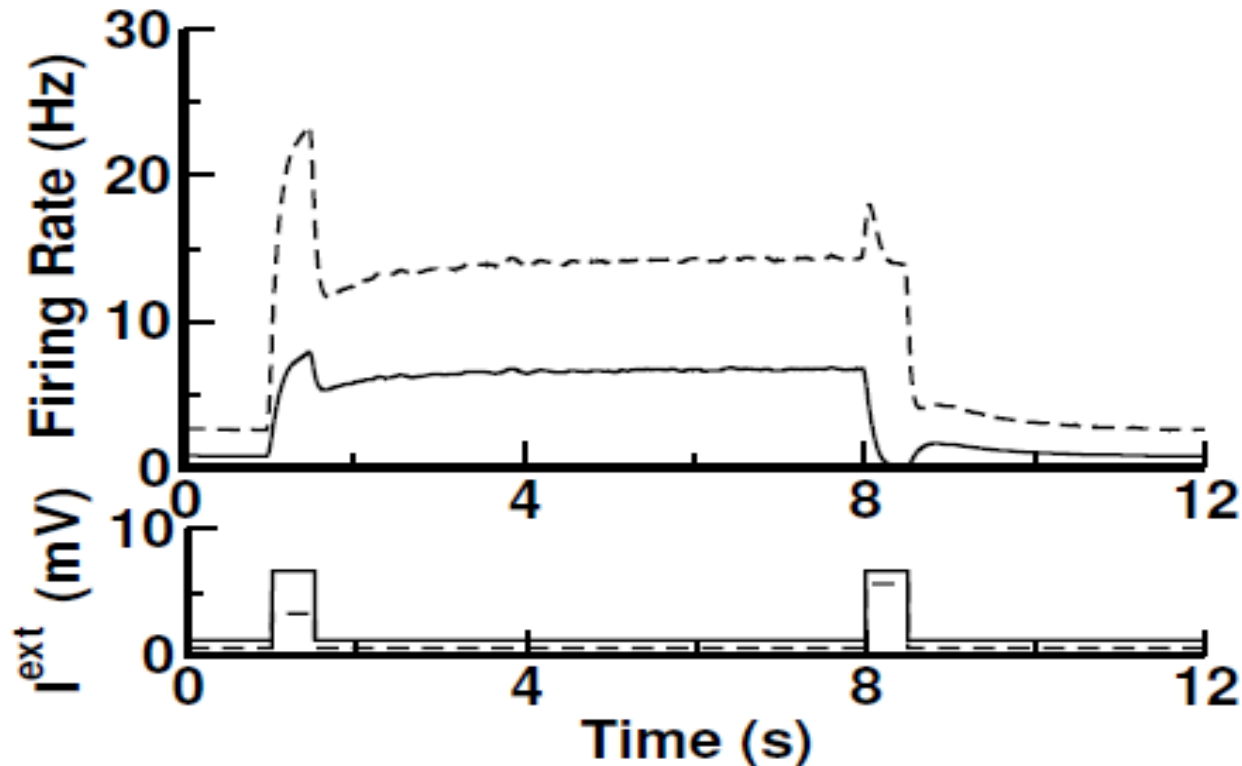
Short term synaptic plasticity allows multistability

- But is it possible to have a continuum of states?

  - Coexistence of a low-rate homogeneous state and an infinite number of high-rate spatially modulated states

  - That can be achieved with spatially modulated interactions: more probability of connections if the neurons are located at similar spatial locations

  - The specific state should be chosen by a cue-dependent transient stimulus (Hansel & Mato ,2012)

The Model for the ODR task

- N_E excitatory (PYR) and N_I inhibitory neurons (IN)
- Ring: architecture: probability of connections depends on the distance along the ring.
- Average number of connections per neuron: K
- Interactions: exponential time dependence.
  Excitation:
  mixture of AMPA and NMDA
  Inhibition: $GABA_A$
- E->E interactions are facilitating
- External input is time dependent to simulate the task
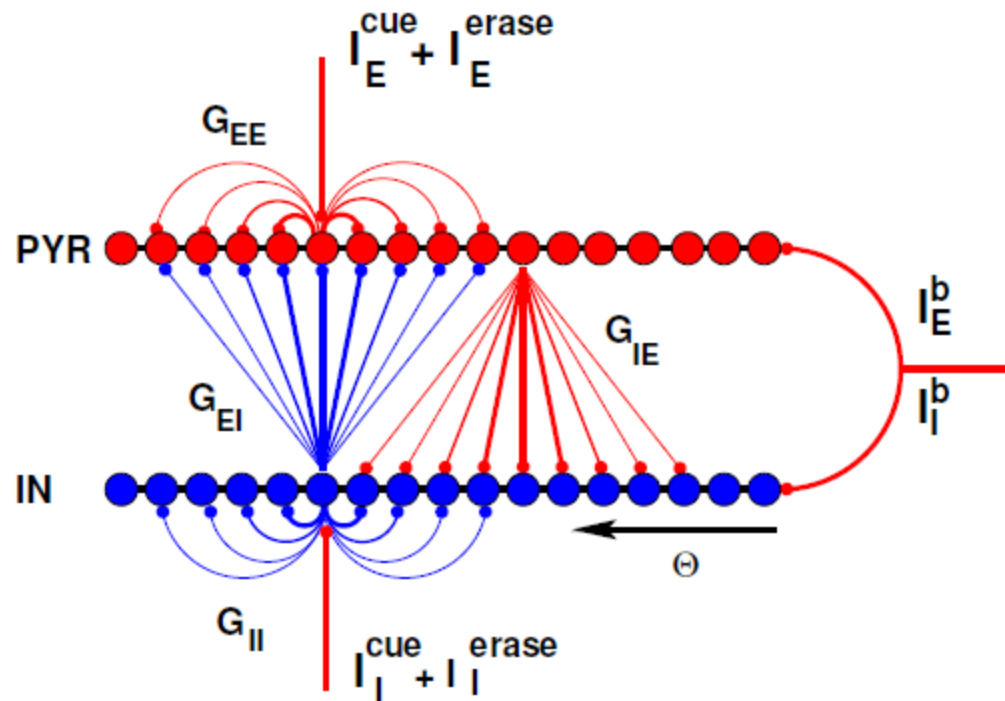
The Model for the ODR task

- Leaky Integrate-and-Fire neurons

- N_E =64000, N_I =16000 (some simulations up to 256000)

- K=1600 (EE, IE) or 400 (EI,II) (some simulations up to 8000)

- t_{AMPA}= 3 ms, t_{NMDA}= 50 ms, t_{GABA}= 4 ms

- U=0.03, τ_r=250 ms, τ_f=450 ms (plasticity only in E->E connections)

- Probability of connections: Gaussian function σ=60 degrees (EE, II, EI) or 70 degrees (IE)

The network displays cue related multistability
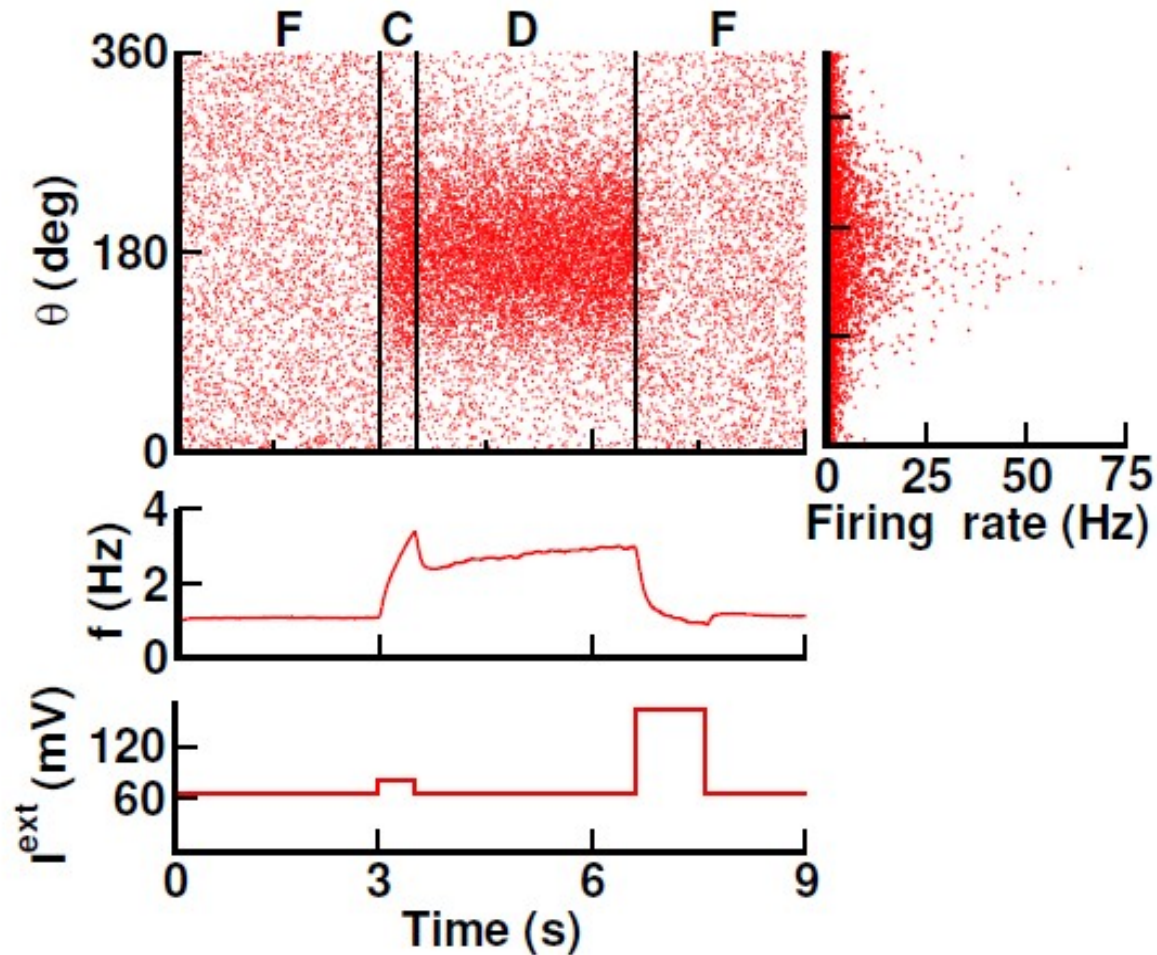
The network displays cue related multistability
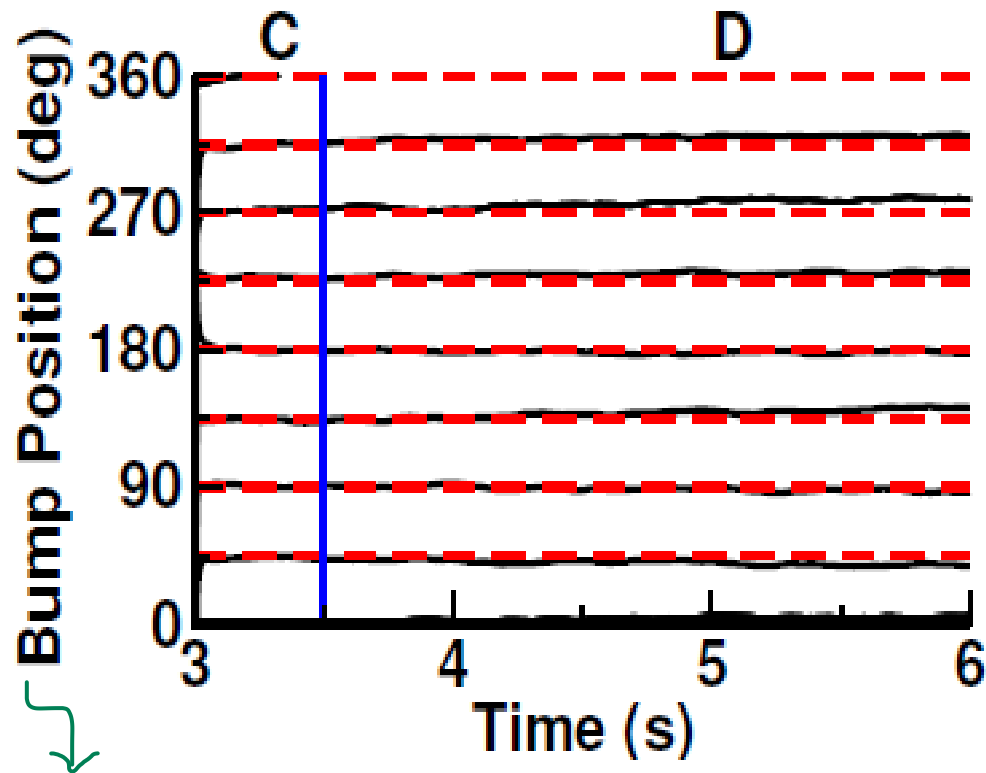
Cada línea negra es un experimento distinto y representa el centro de masa

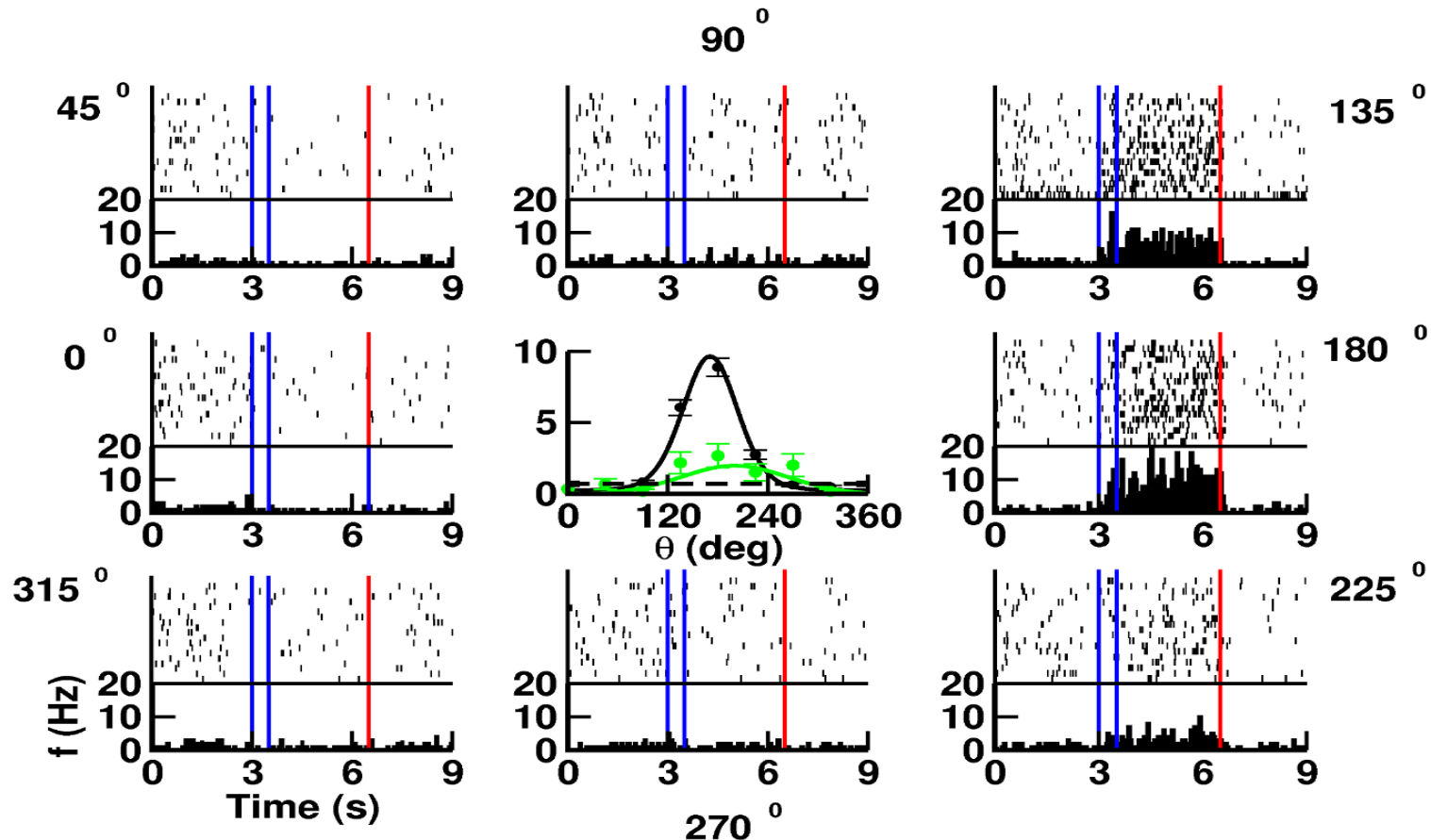En qué posición (angular) está centrada la actividad

Both baseline and delay states are balanced

- Red: excitatory input
- Blue: inhibitory input
- Black: total input
- Green: total input + 1.5 SD
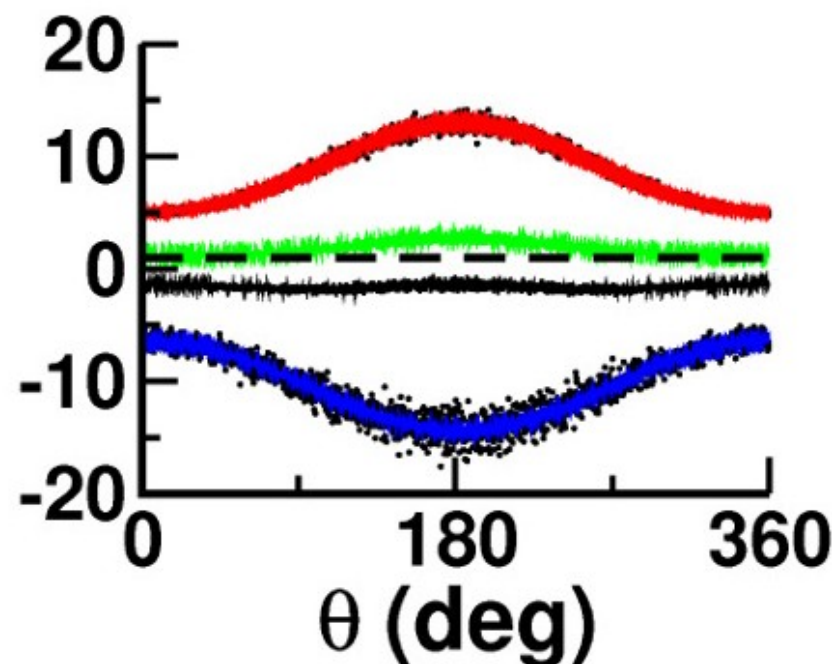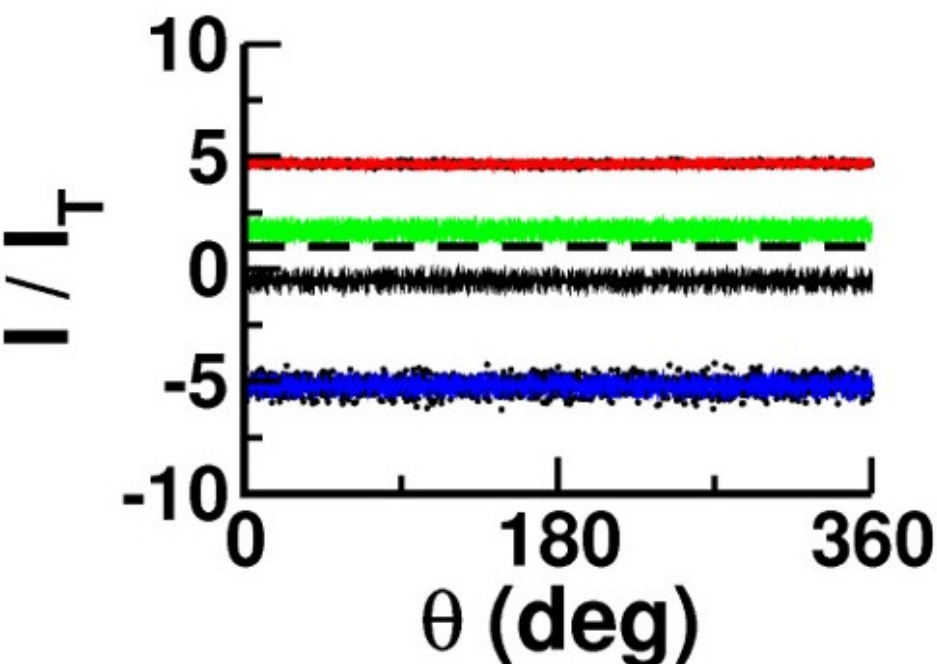
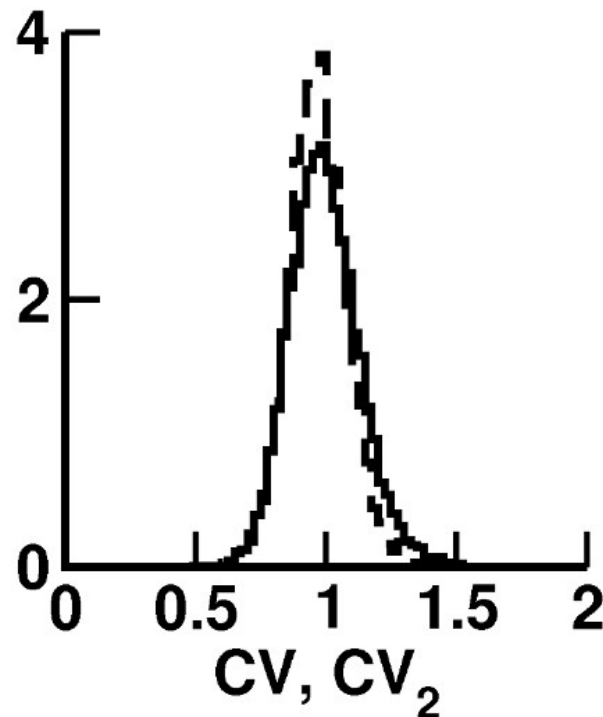# Both baseline and delay activities are highly irregular
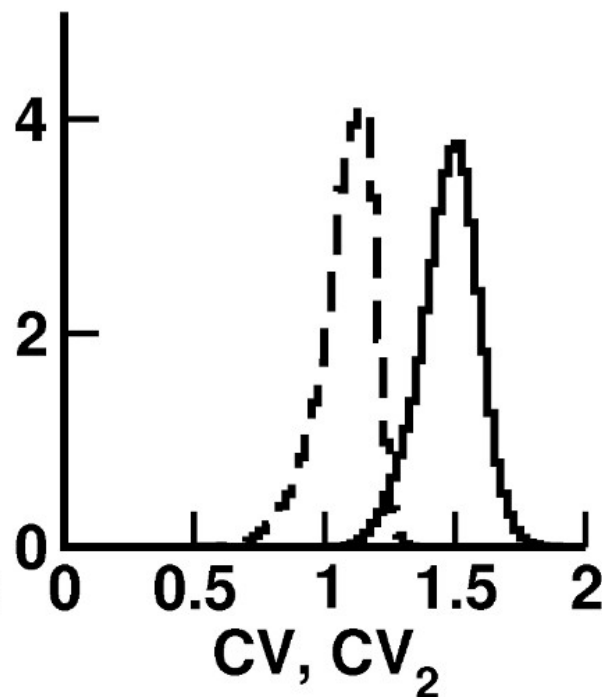
- Black: tuning curve during delay
- Green: tuning curve during cue

Both baseline and delay activities are highly irregular
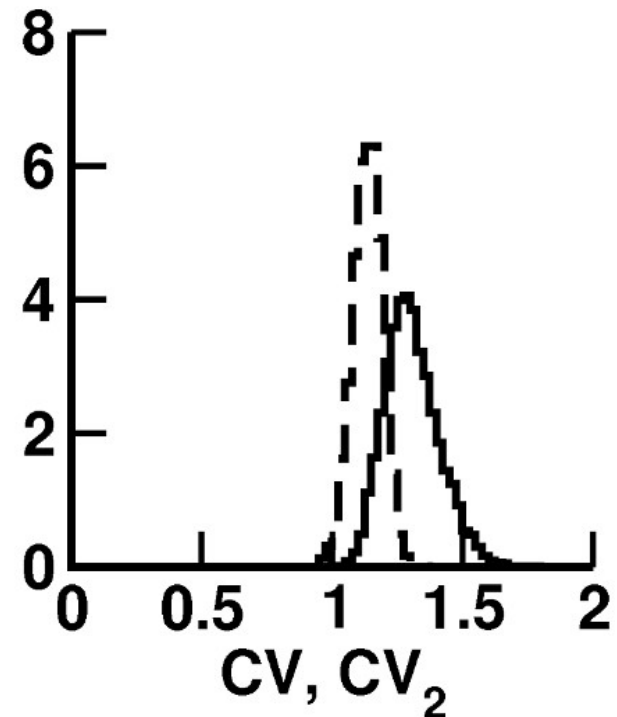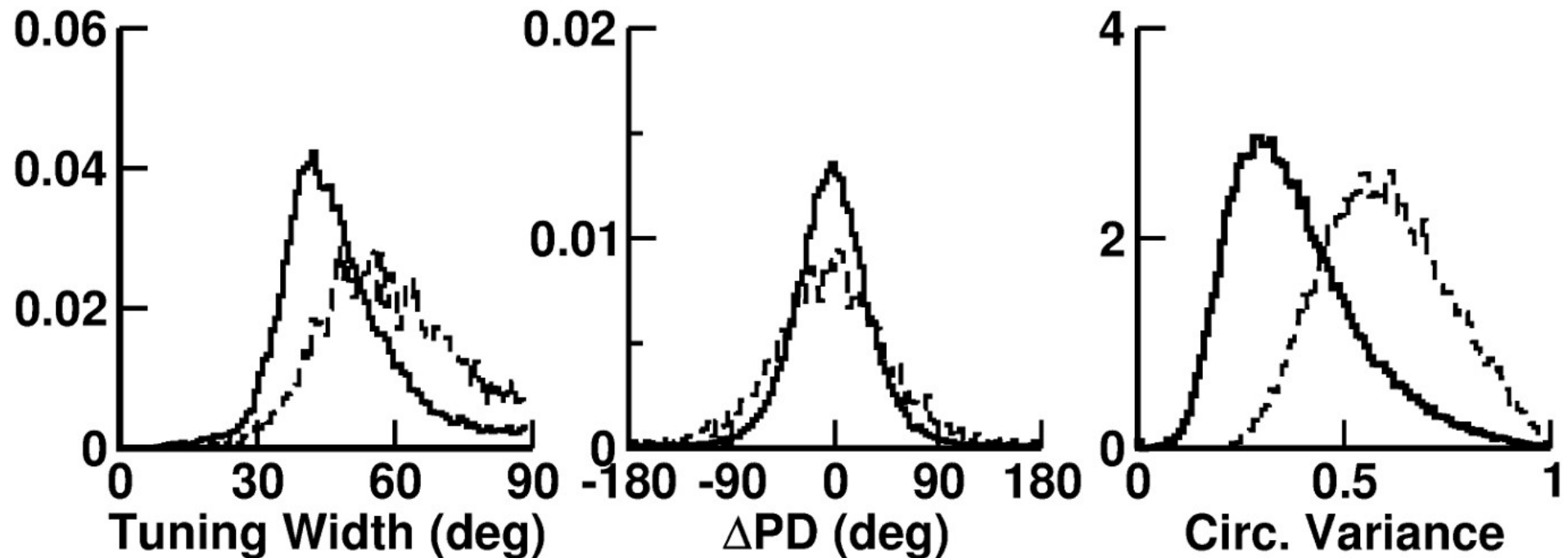
- Solid line E pop
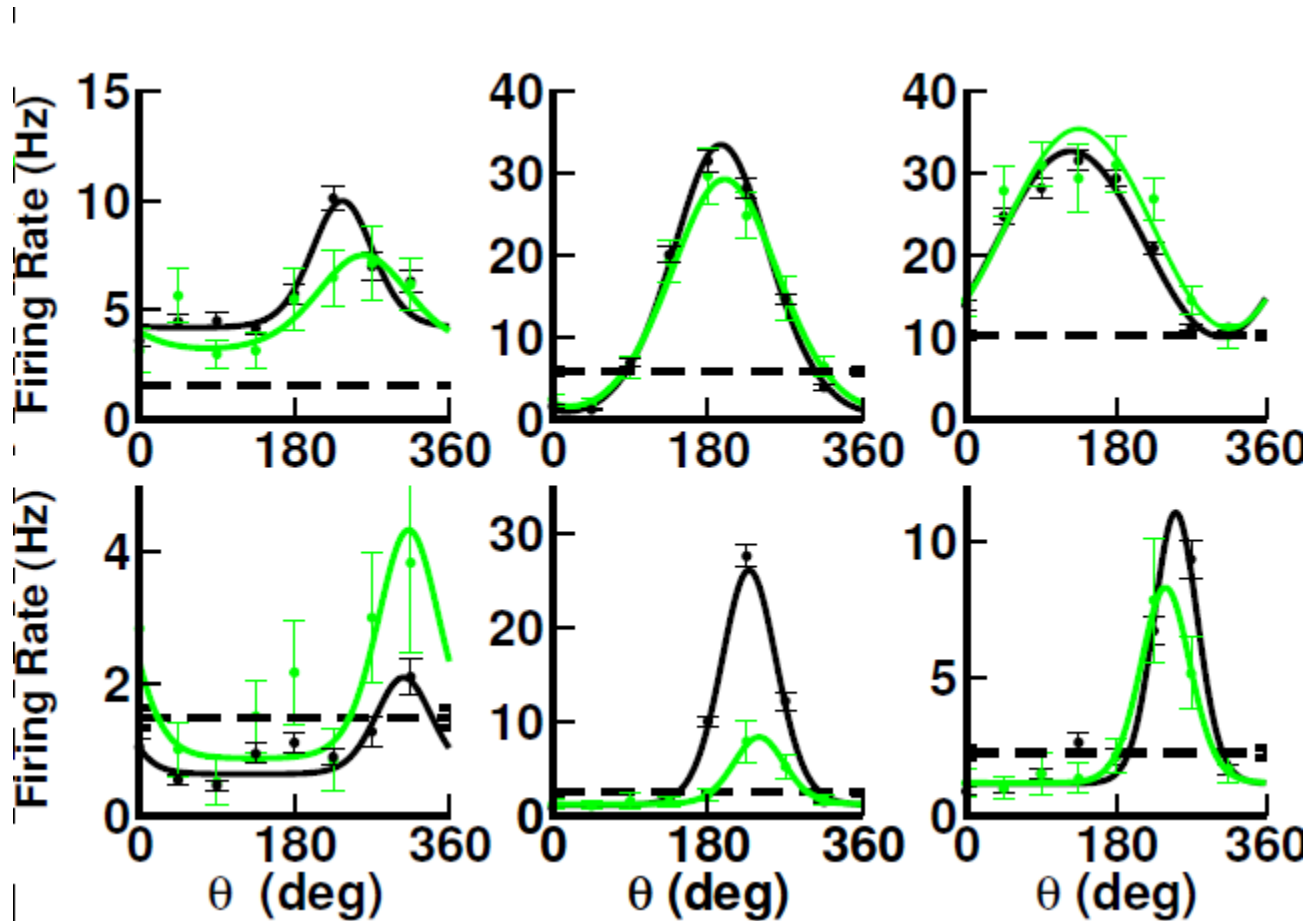- Dashed line: I pop

Tuning properties are heterogeneous

- Solid line E pop
- Dashed line: I pop
- ΔPD: Preferred direction – position on the ring
- Circular Variance=$1-c_1/c_0$, where c_n is the nth Fourier component of the tuning curve
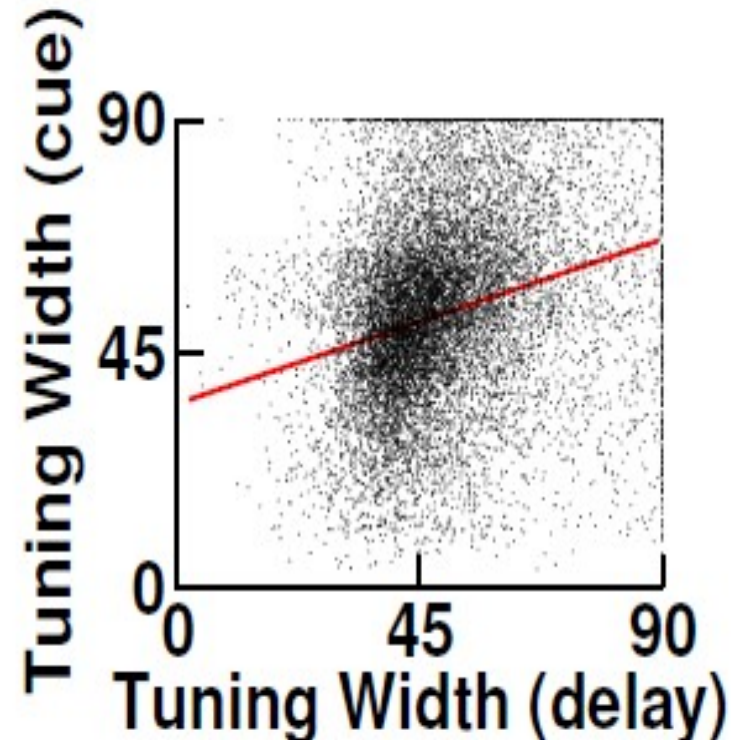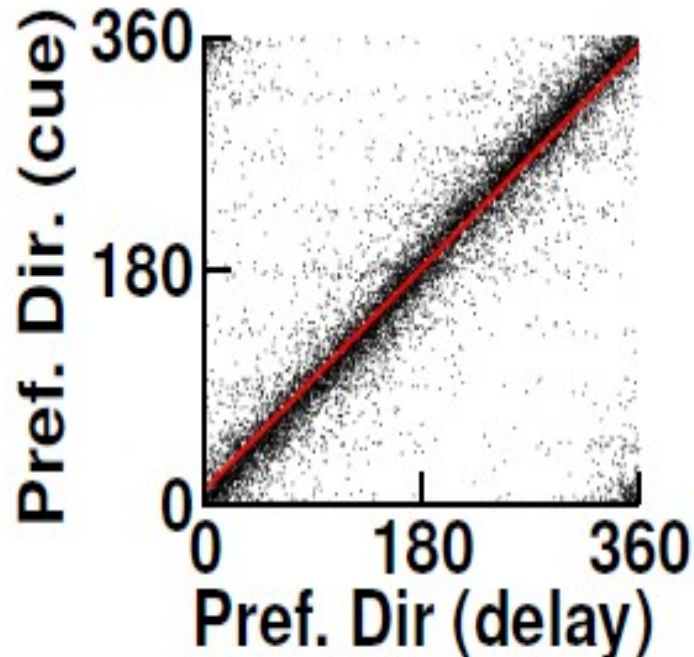
Tuning properties are heterogeneous

- Black: tuning curve during delay
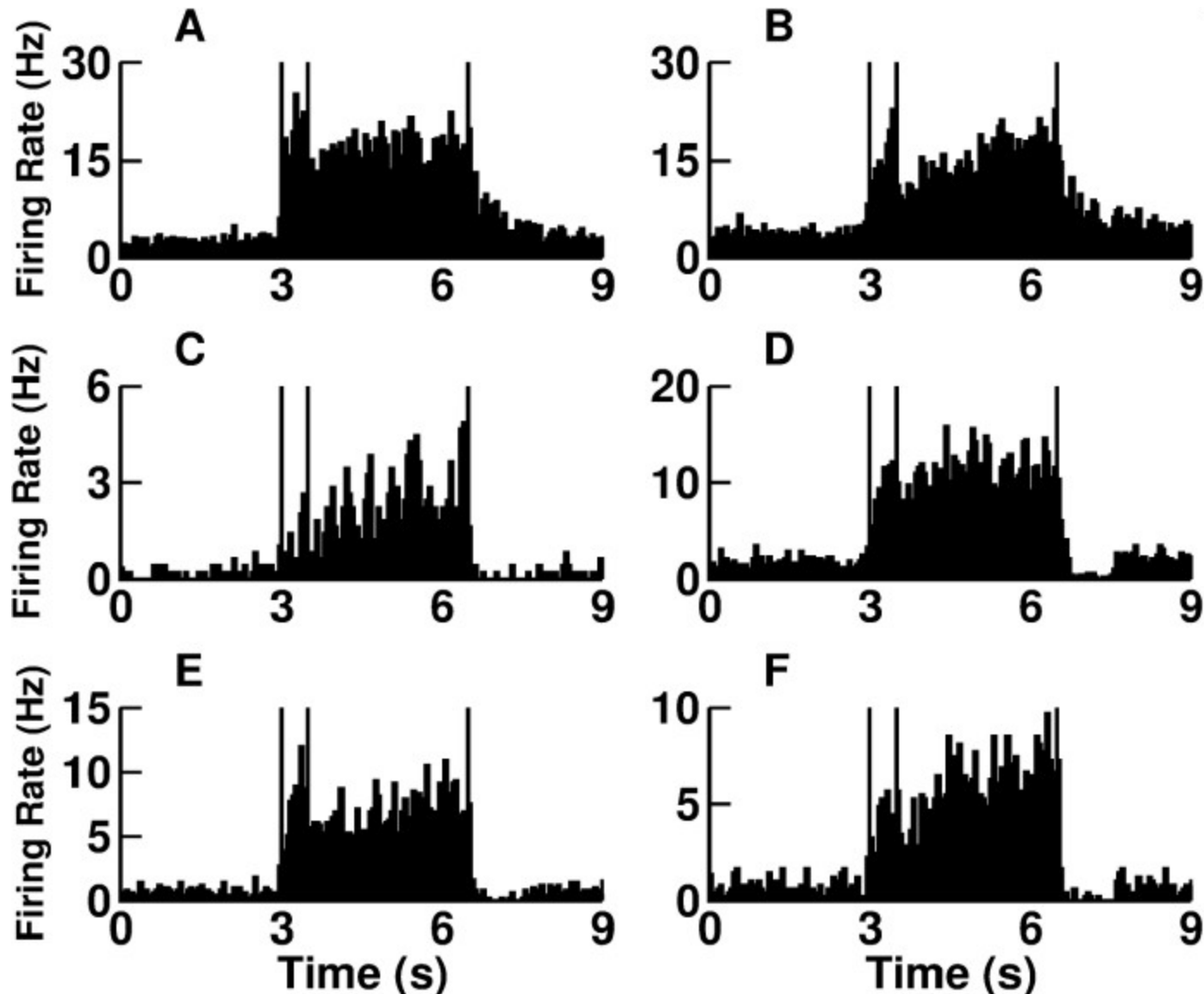- Green: tuning curve during cue

Tuning properties are heterogeneous

- Preferred directions are strongly correlated between cue and delay but tuning widths are not
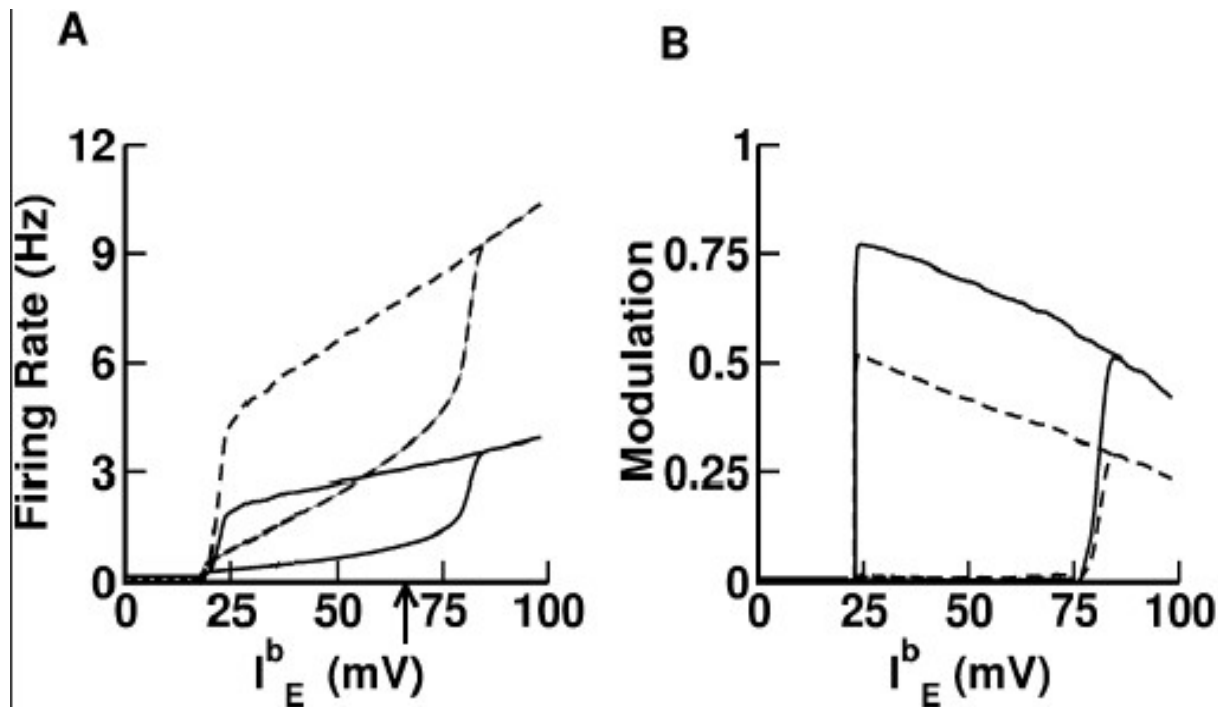
Dynamics during cue period is also heterogeneous

Multistability exists in a broad range of external inputs

- Solid line E pop
- Dashed line: I pop
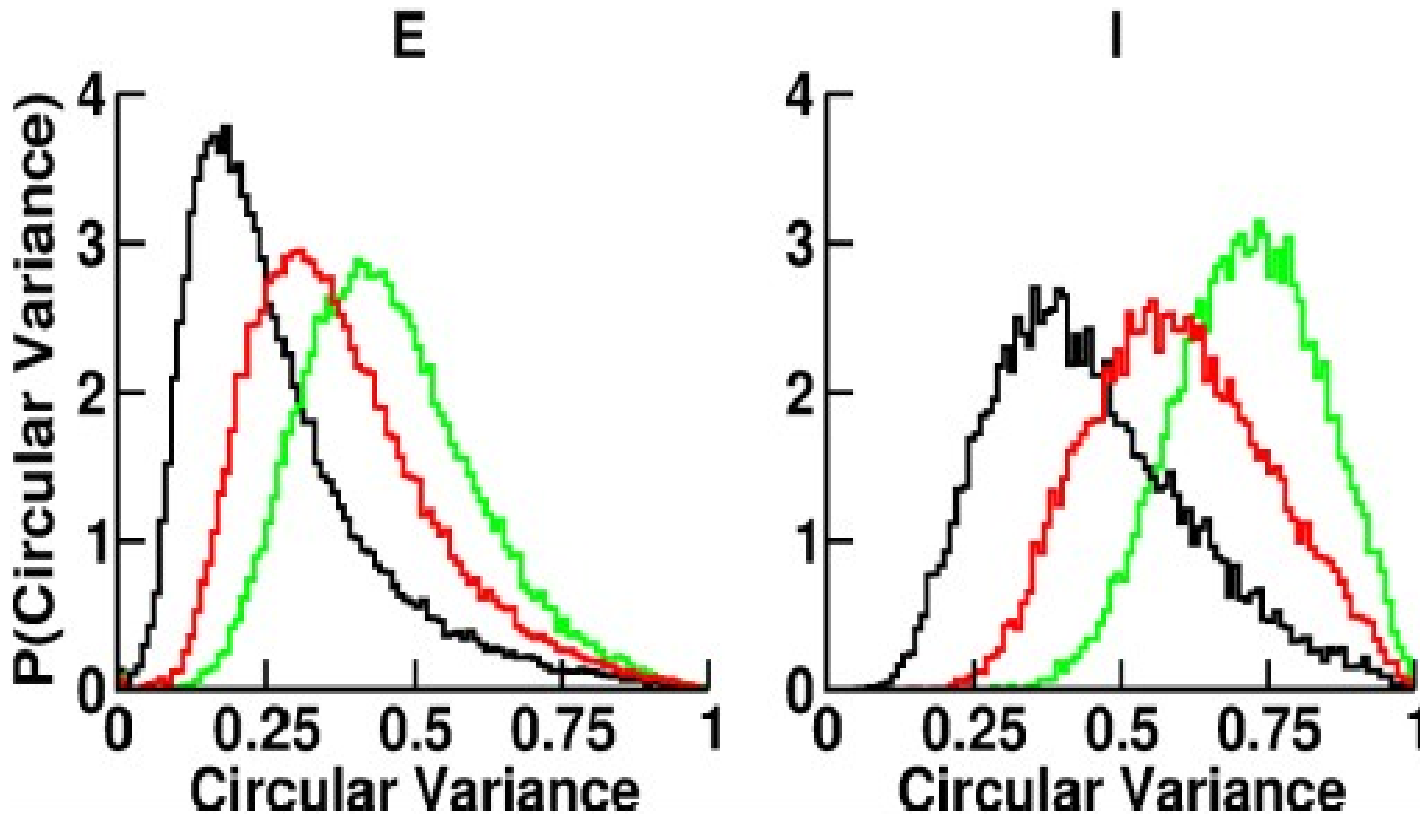
$m_E(\Theta, t) = m_0 + m_1 \cos(\Theta - \Theta_0) + ...$

Population averaged = m_0

Normalized spatial modulation = m_1 / m_0

But the modulation depends on σ

- $\sigma_{II} = \sigma_{EI} = 40$ deg (green)
- $\sigma_{II} = \sigma_{EI} = 60$ deg (red)
- $\sigma_{II} = \sigma_{EI} = 70$ deg (black)

The bump drifts at very long times

Si se deja pasar mucho tiempo todo termina en 2 ángulos. ¿Por qué? Idealmente yo quiero que todos los ángulos sean igual de probables, sin embargo, no todos son equivalentes sino que hay algunos más probables que otros. Esto es consecuencia de que sistemas de atractores continuos no son robustos, es decir, no son estructuralmente estables como los atractores discretos.
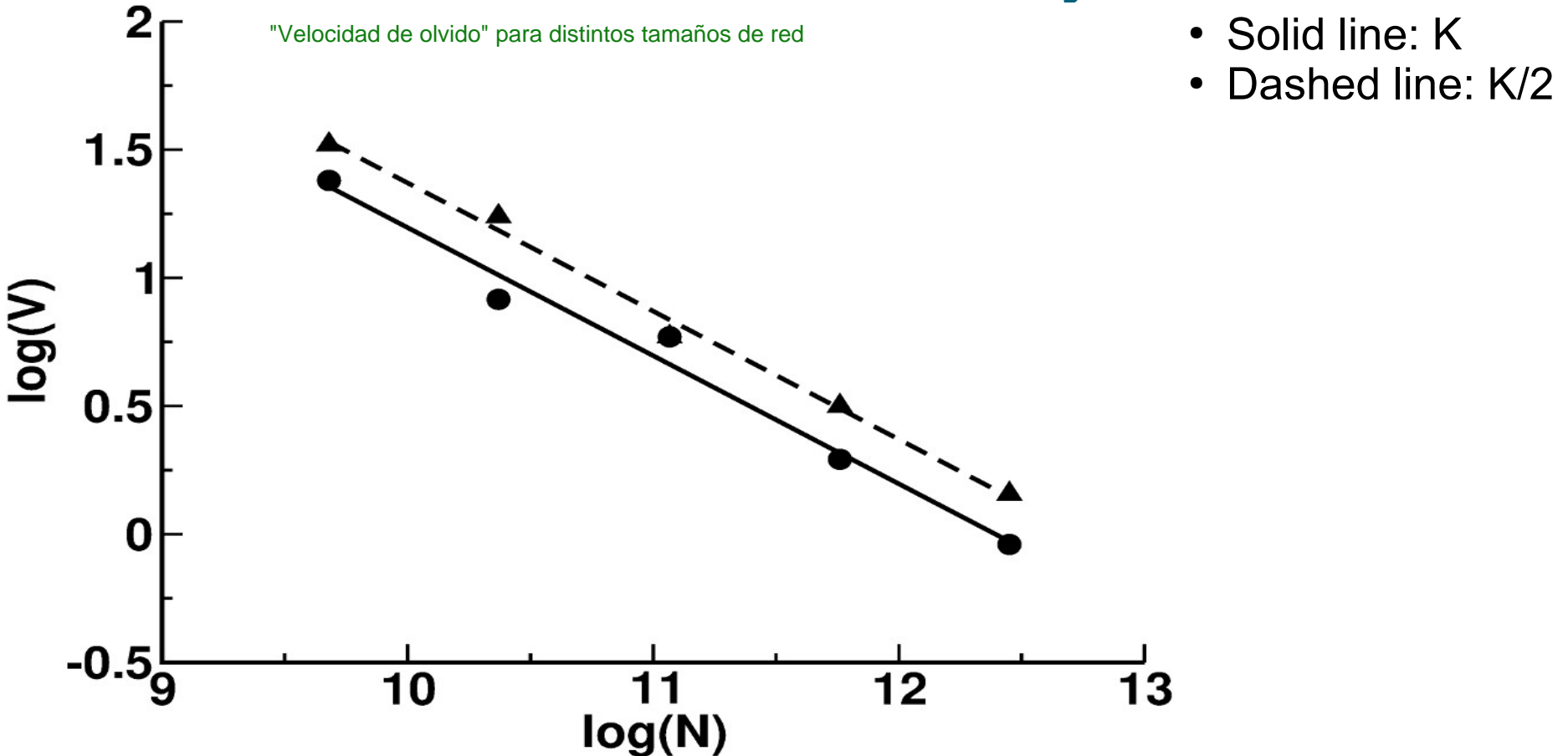
Tiempo en el que me olvido de la condición inicial.
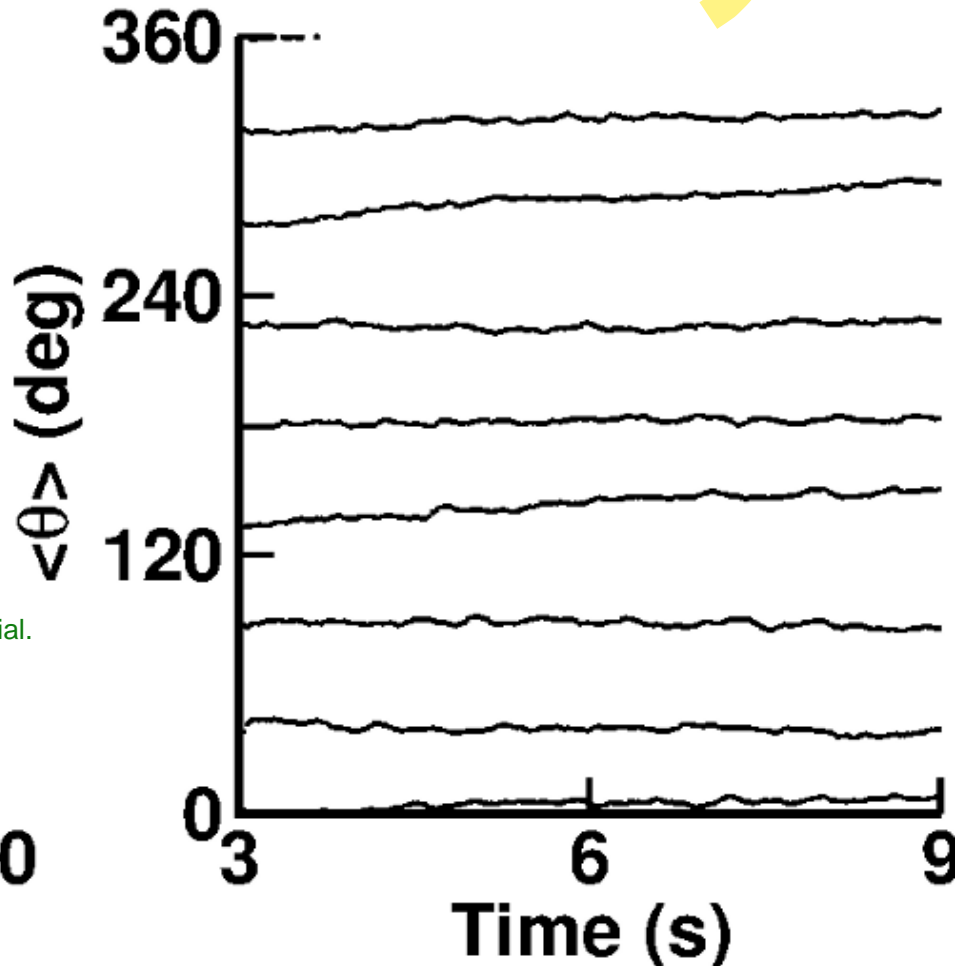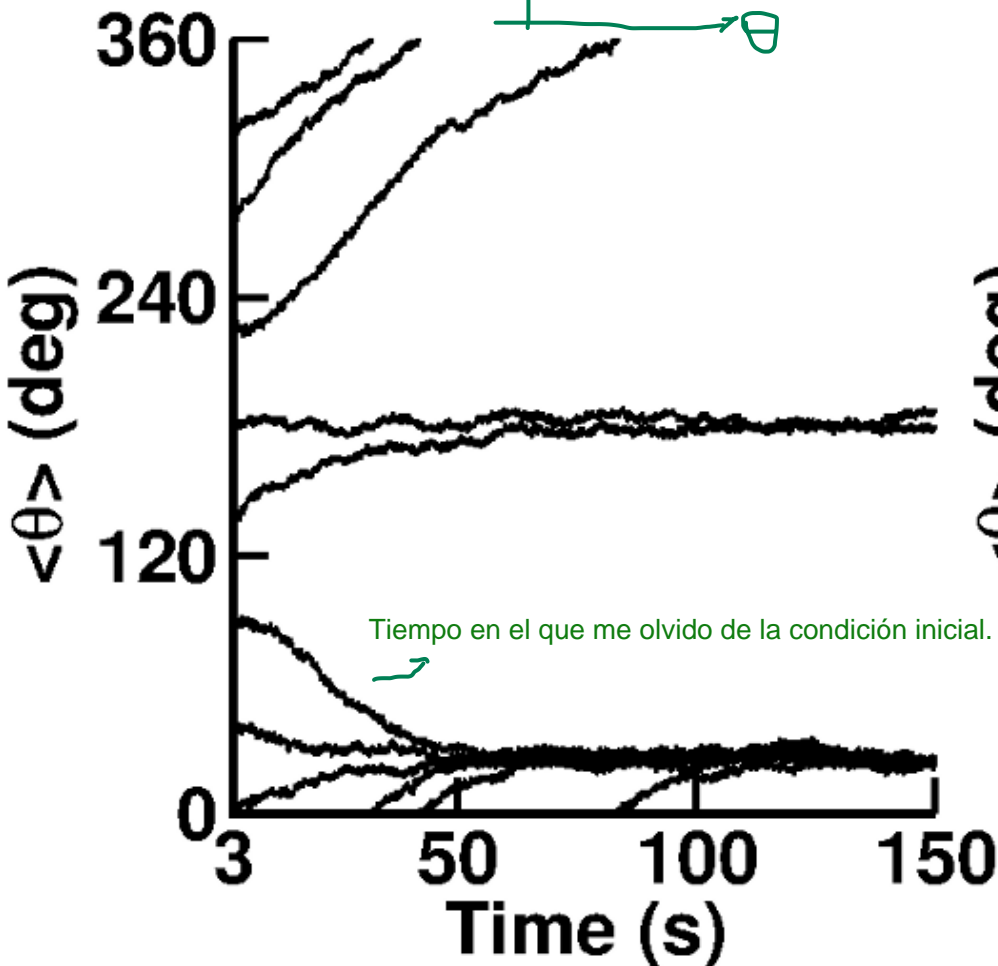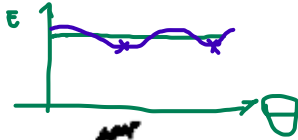
The velocity is constant at long times

- Σ: average quadratic displacement of the bump
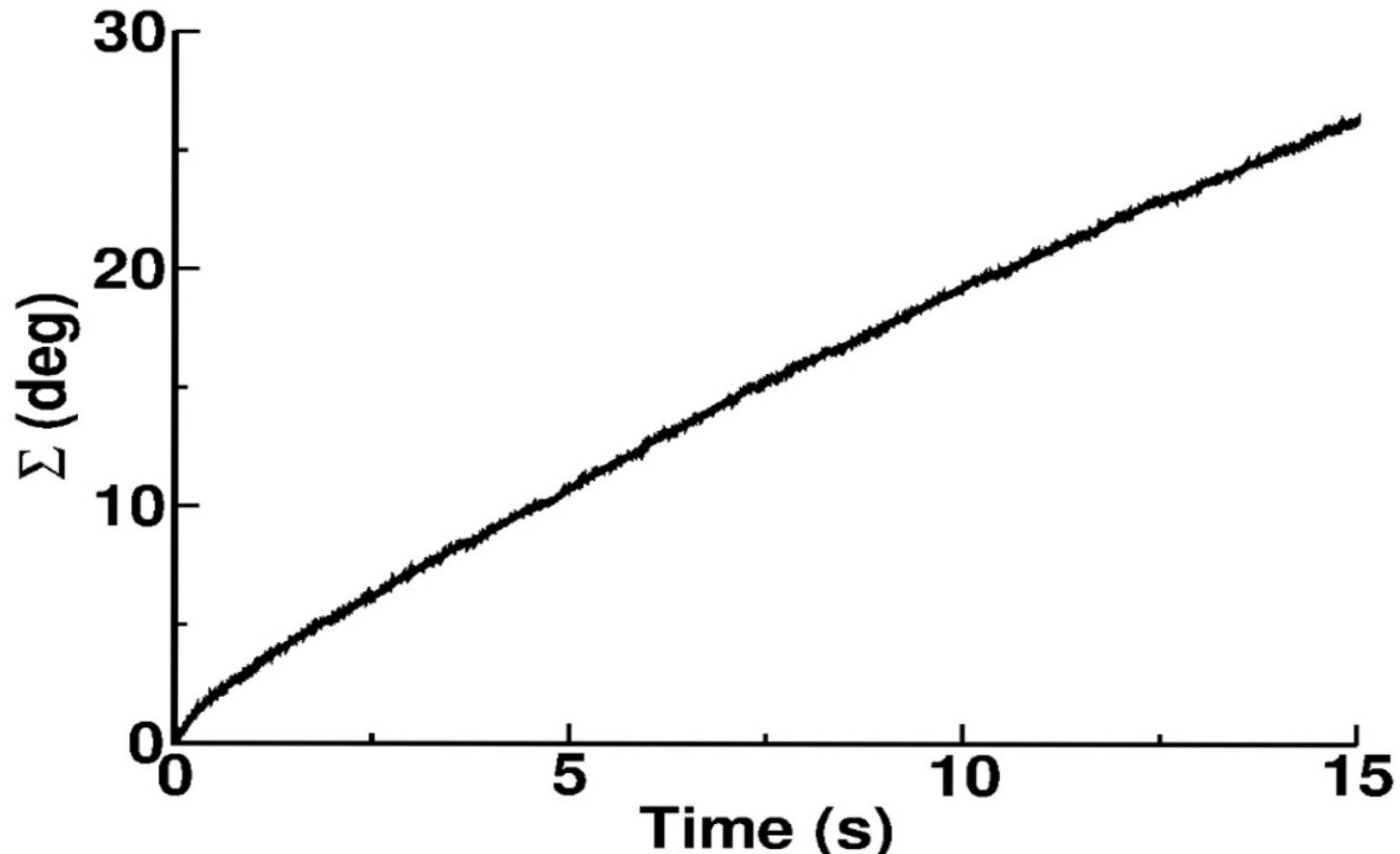
Velocity decreases with the size of the network and the connectivity

"Velocidad de olvido" para distintos tamaños de red

- Solid line: K
- Dashed line: K/2

For plausible size and connectivity one can easily obtain a drift of 0.5− 1 degrees/sec, in line with experimental data (White et al. 1994, Ploner et al. 1998).

Summary of the properties of the model

- Balanced state in cue and delay periods

- Highly variable activity (CV approx. 1)

- Highly heterogeneous neuronal properties (tuning widths, preferred directions)

- Heterogeneous dynamics during the delay period

- Slowly drifting bump

- Robust with respect to changes in external input, values of couplings, spatial width of the probability of connections, number of connections, parameters of the synaptic plasticity

Next lecture

- Metaplasticity

- Reinforcement Learning