

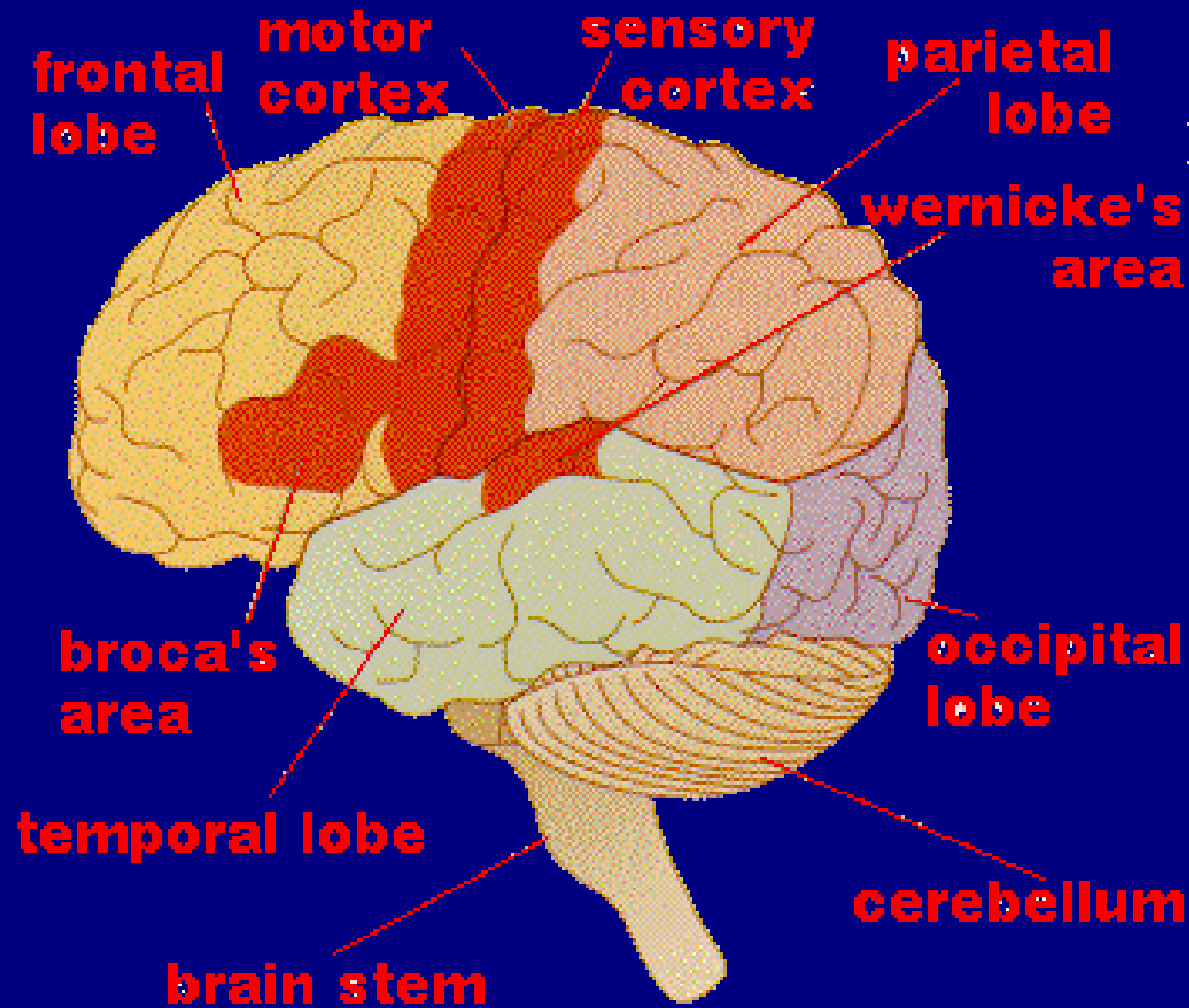
Atractores continuos y biestabilidad en la corteza cerebral

Albert Compte

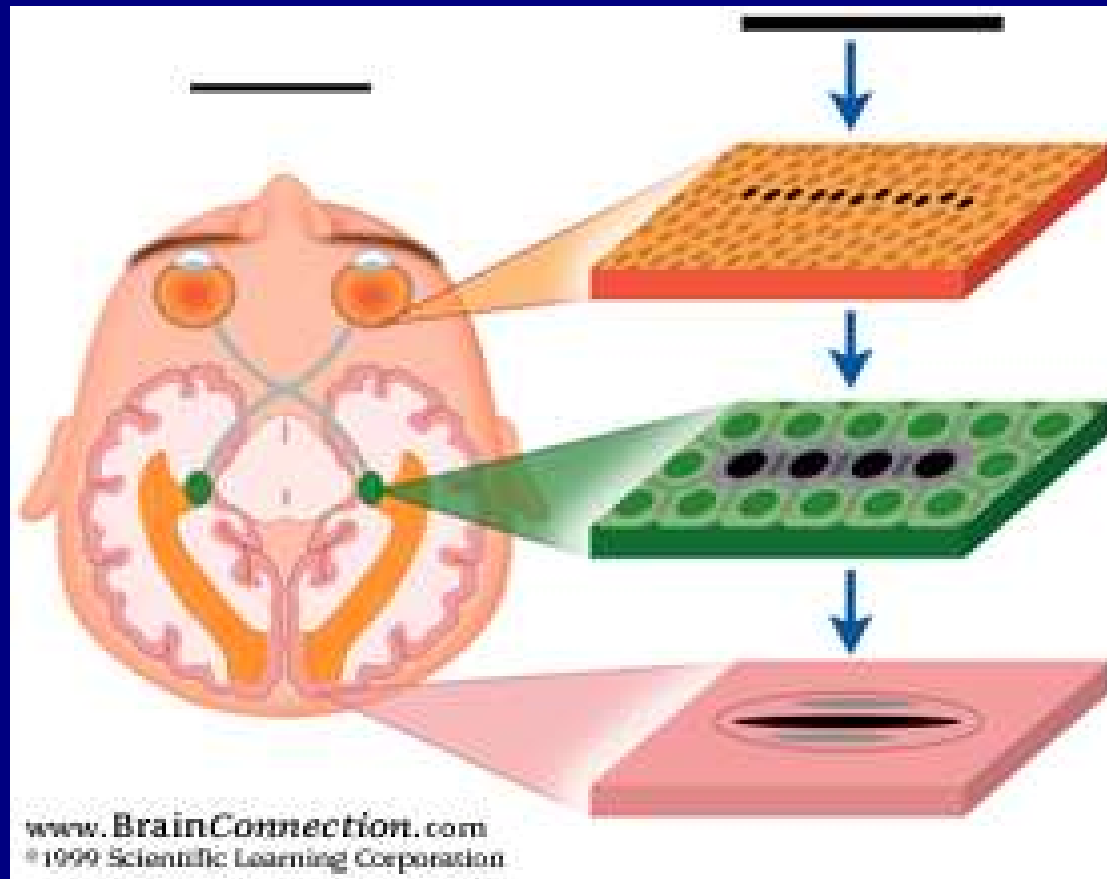
Instituto de Neurociencias de Alicante
UMH-CSIC

Murcia, septiembre 2004

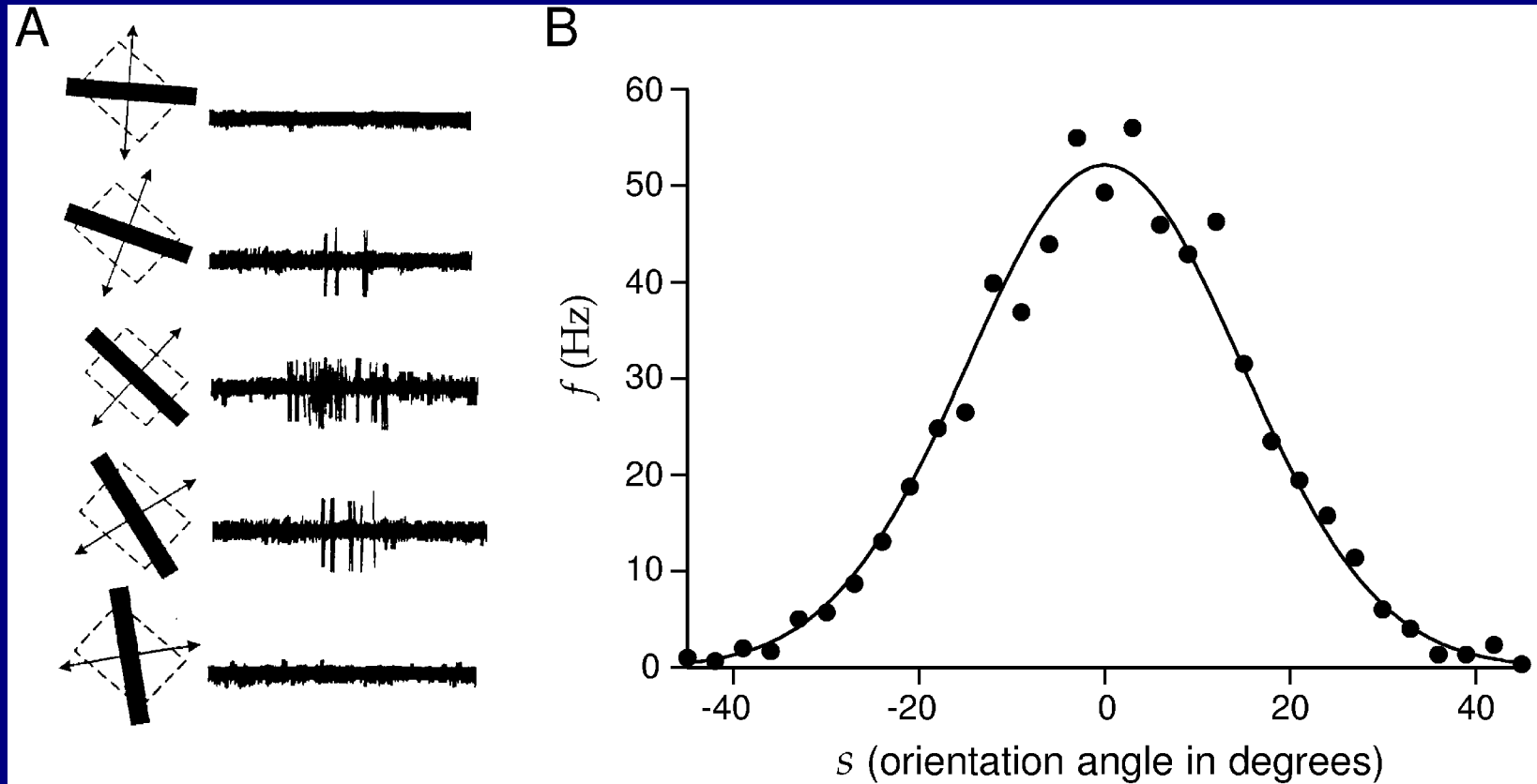
codificación de estímulos continuos en 3 áreas cerebrales



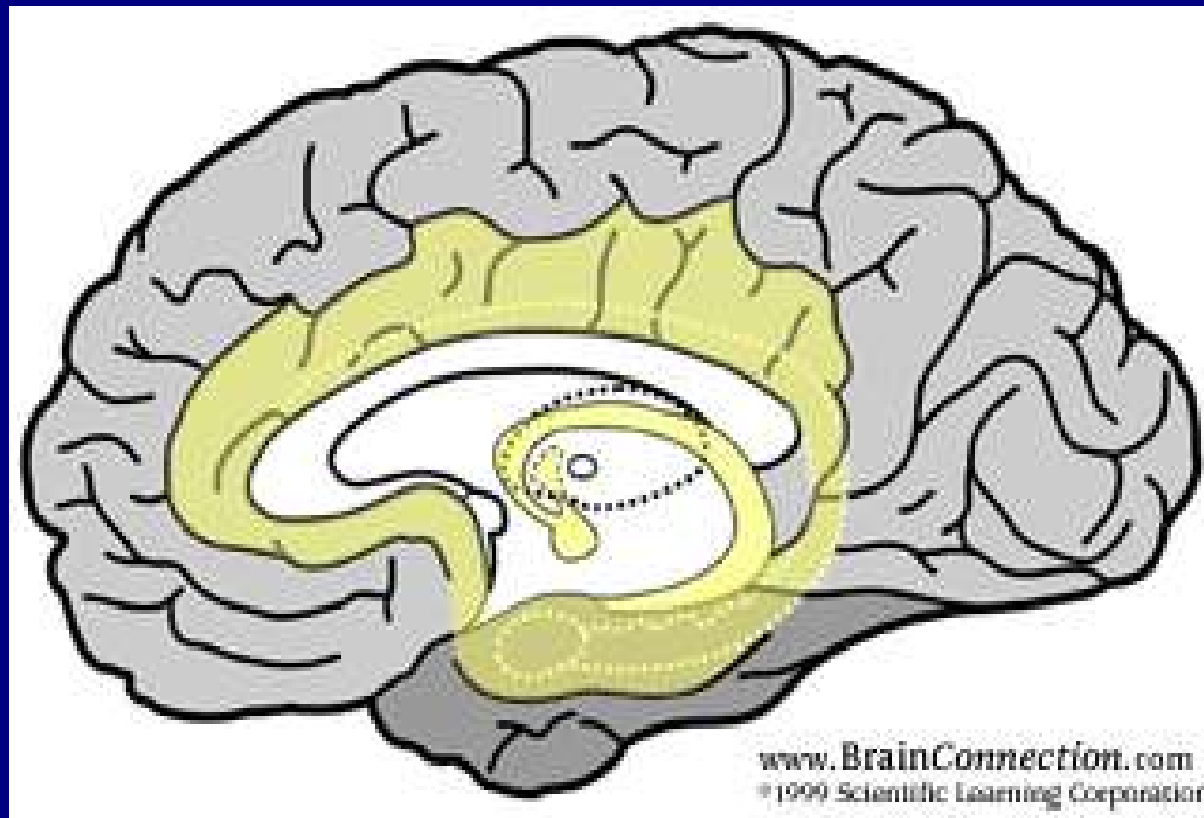
Visión – Respuestas en V1



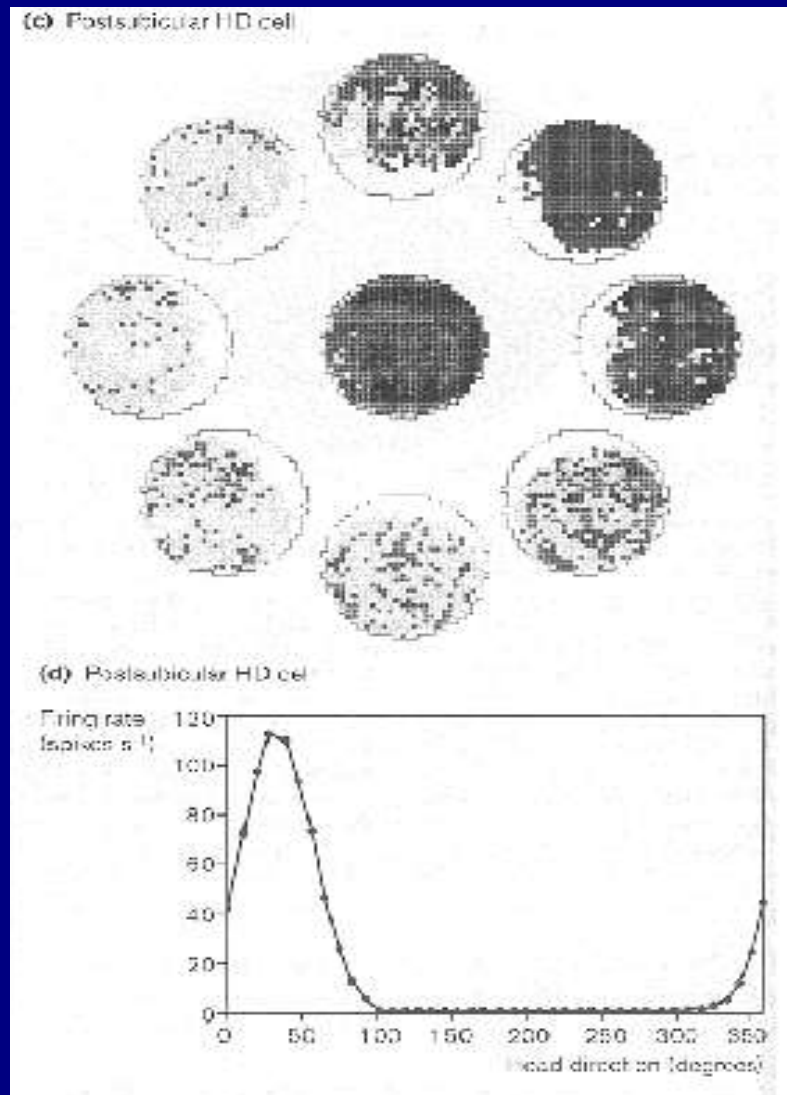
Visión – Respuestas en V1



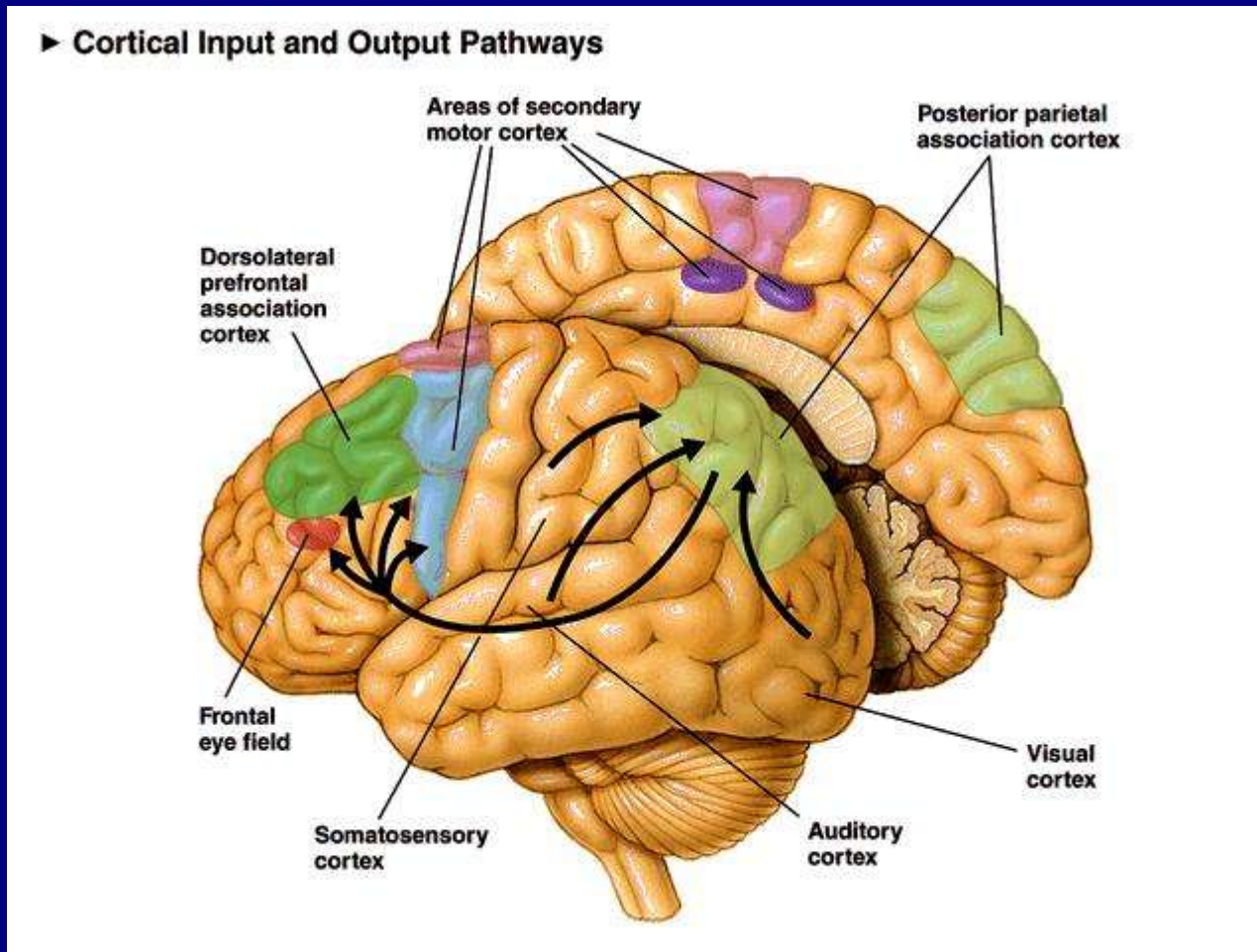
Head-direction cells en PoS



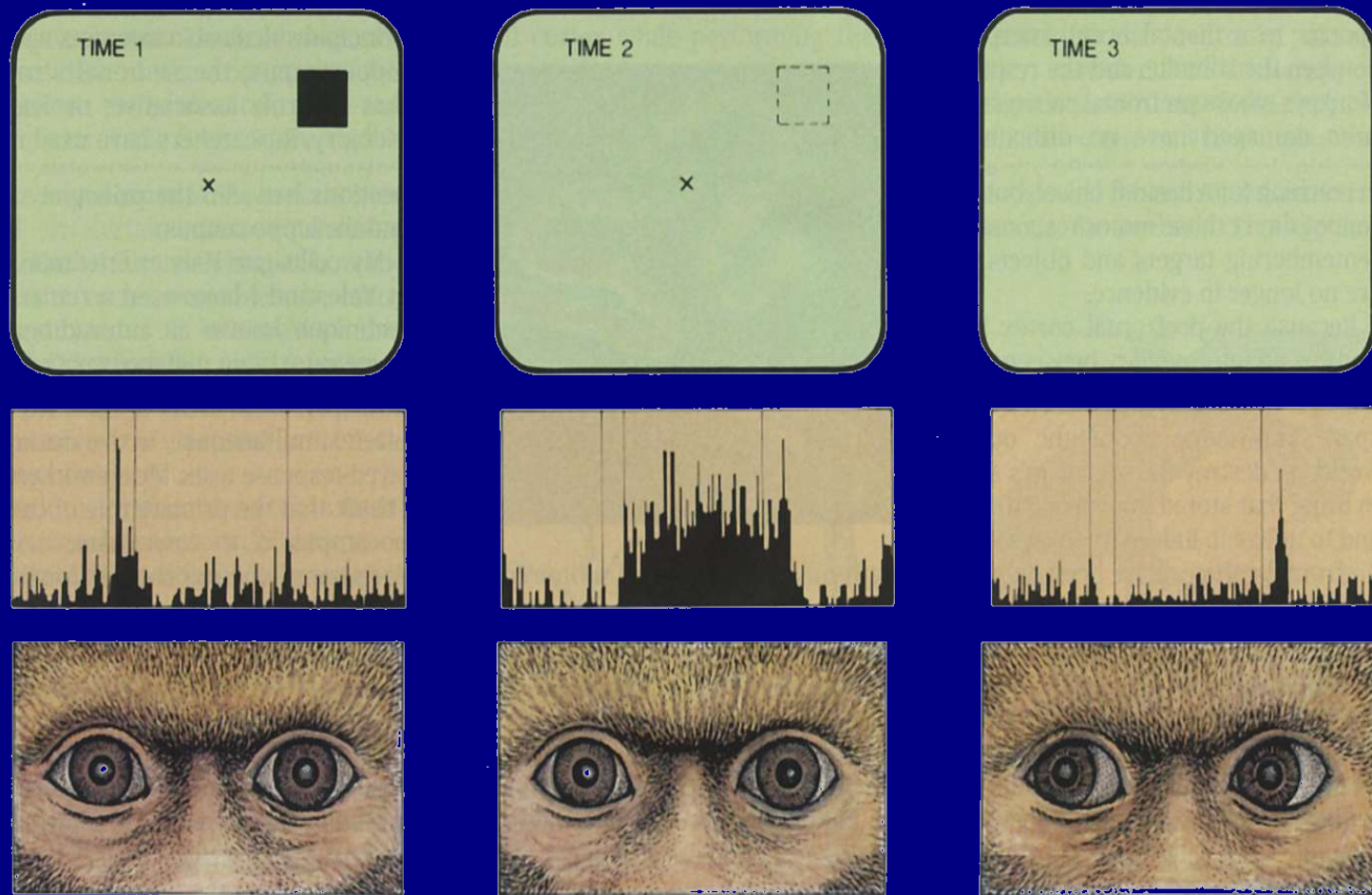
Head-direction cells en PoS



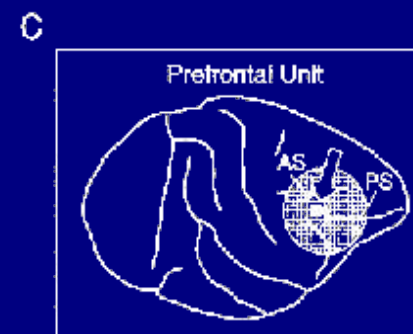
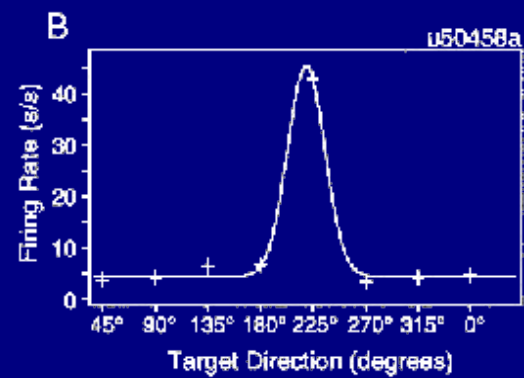
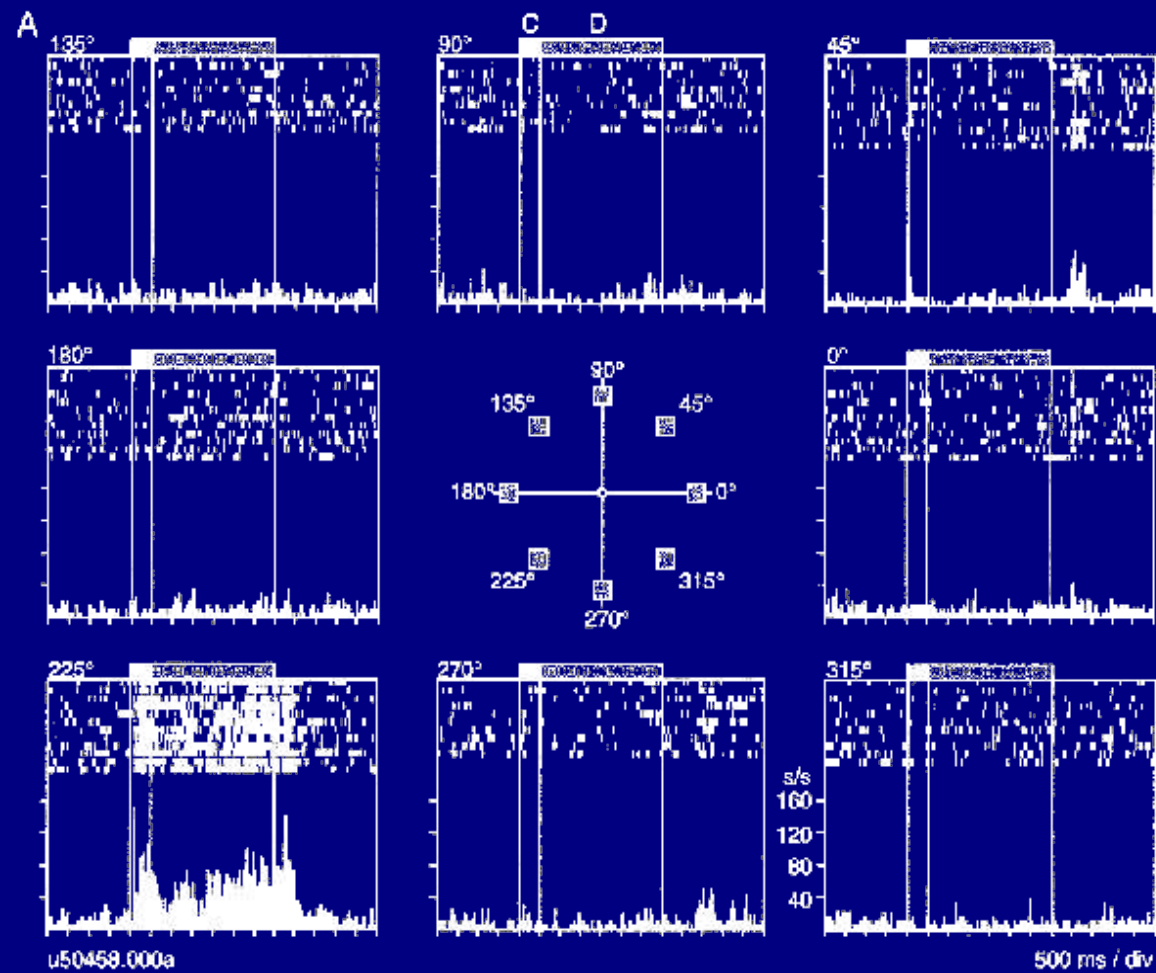
Actividad persistente en PFC



Actividad persistente en PFC



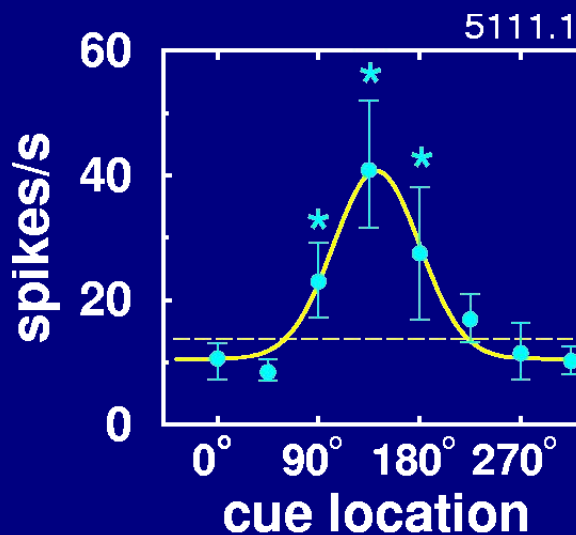
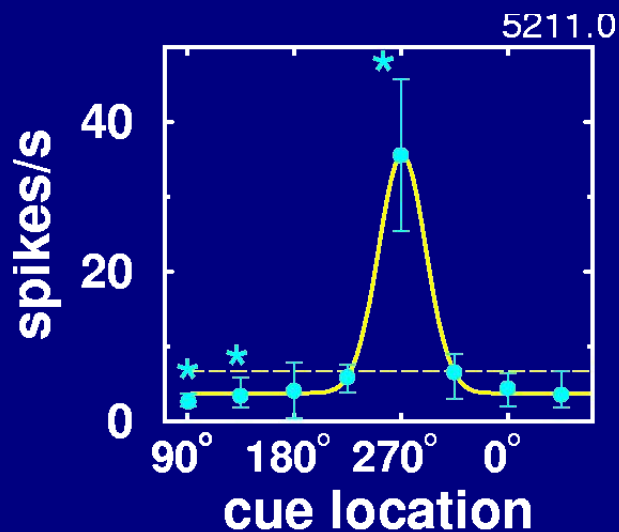
P. S. Goldman-Rakic, Scientific American, Sep 1992, p. 111



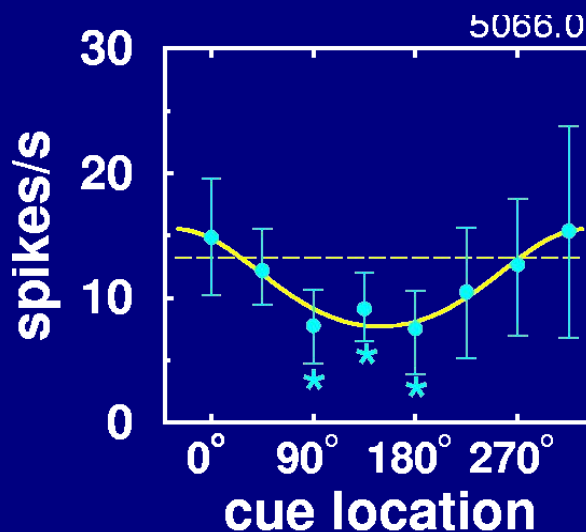
Chafee and Goldman-Rakic, J. Neurophysiol. **79**:2919 (1998)

Data from Funahashi *et al.*, J. Neurophysiol. **61**:331 (1989)

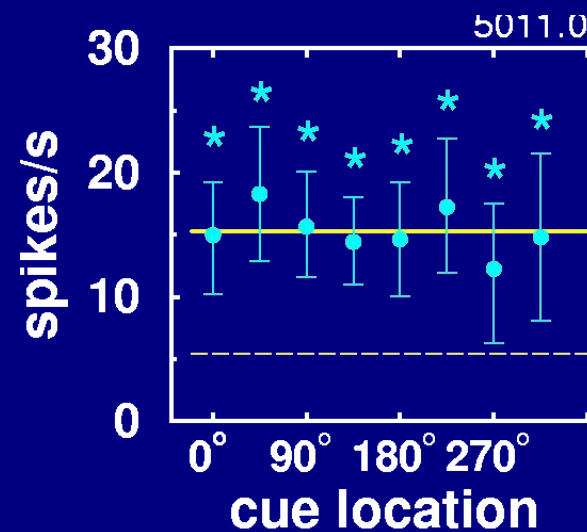
Upright tuning



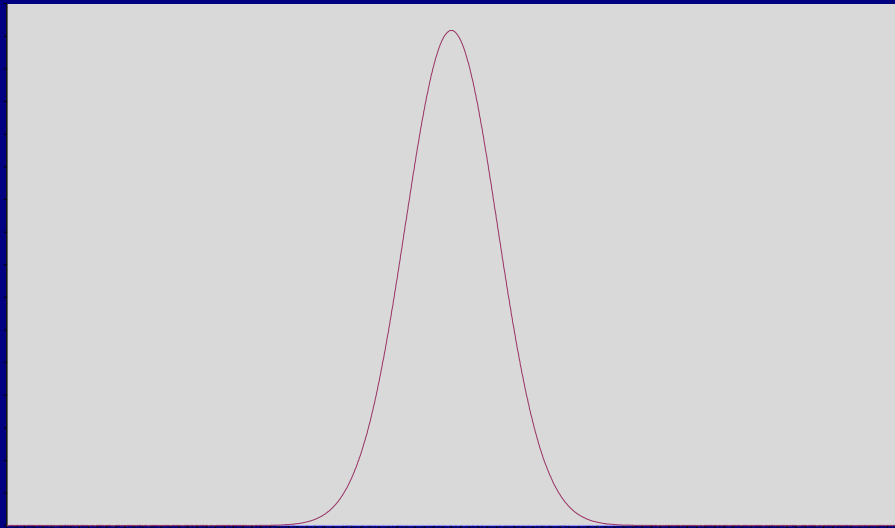
Inverted tuning



No tuning



Codificación continua por población en V1, PoS y PFC

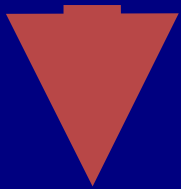


¿Atractor continuo como base de la
memoria espacial de corto alcance?

Los datos sugieren biestabilidad entre estados dinámicos en la red cortical de PFC

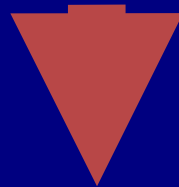
Ante el estímulo las tres áreas muestran actividad similar, pero en ausencia del estímulo...

V1



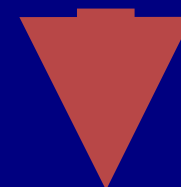
Actividad
espontánea
sin estructura

Head direction cells



Actividad
persistente y
estructurada

PFC

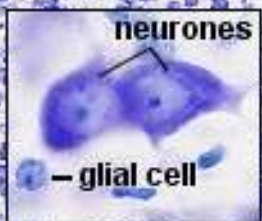
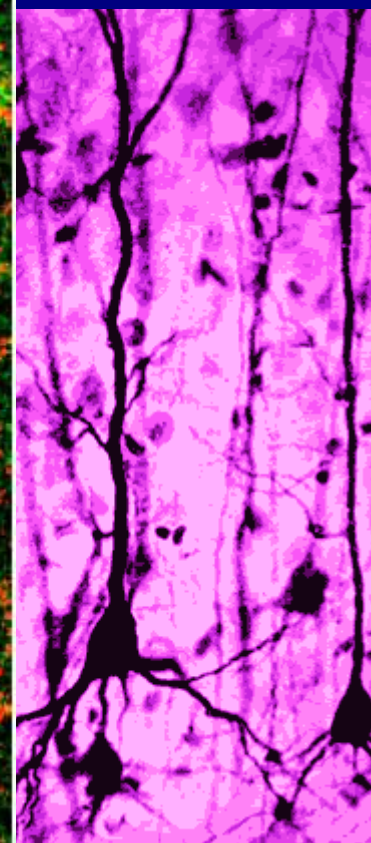
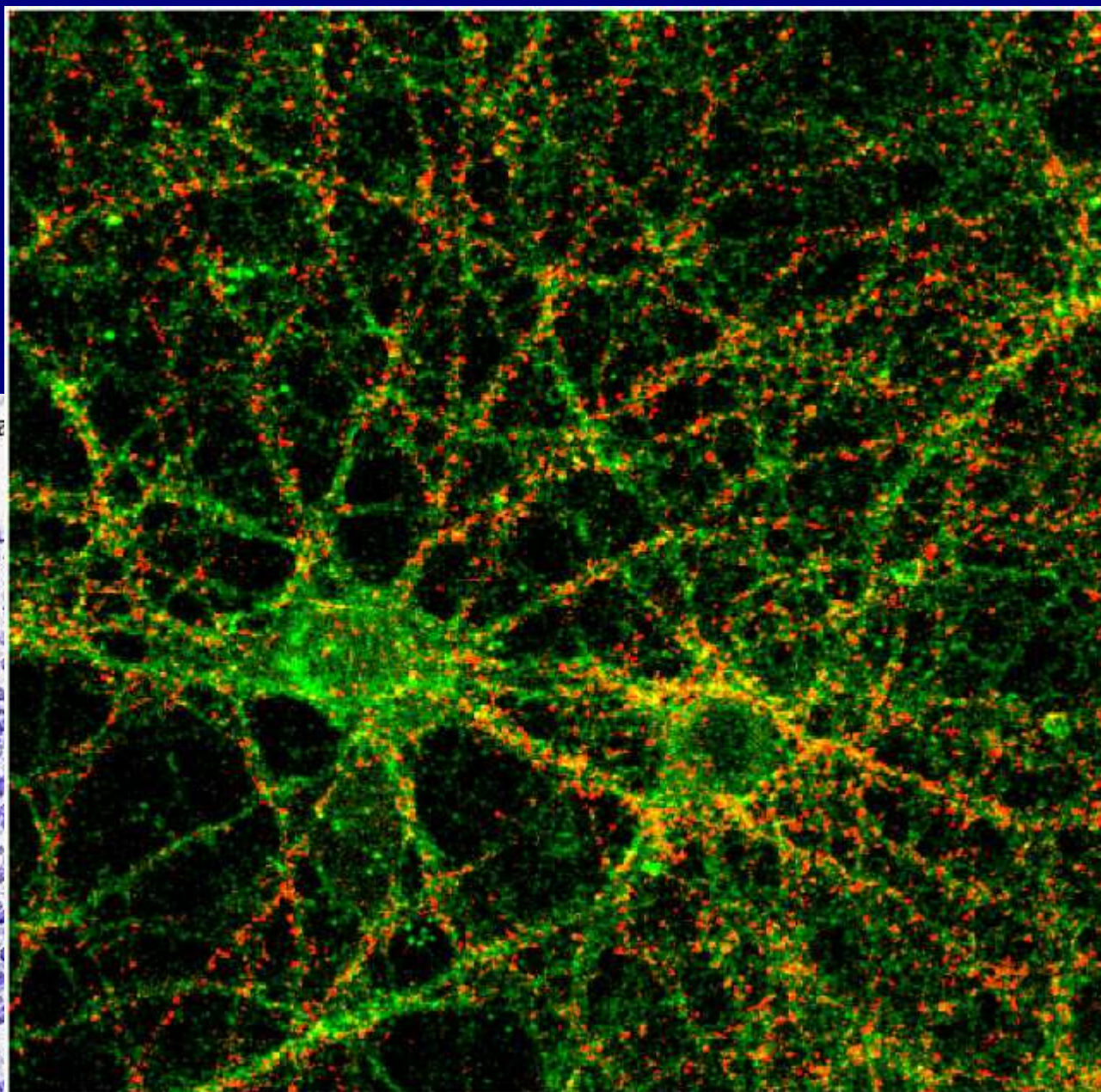
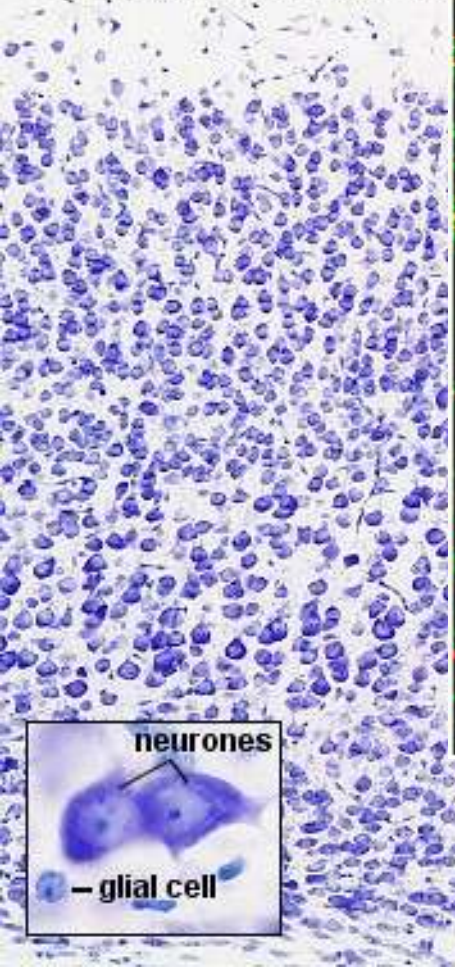


Actividad
espontánea o
persistente
estructurada
según historia
previa

Cuestiones

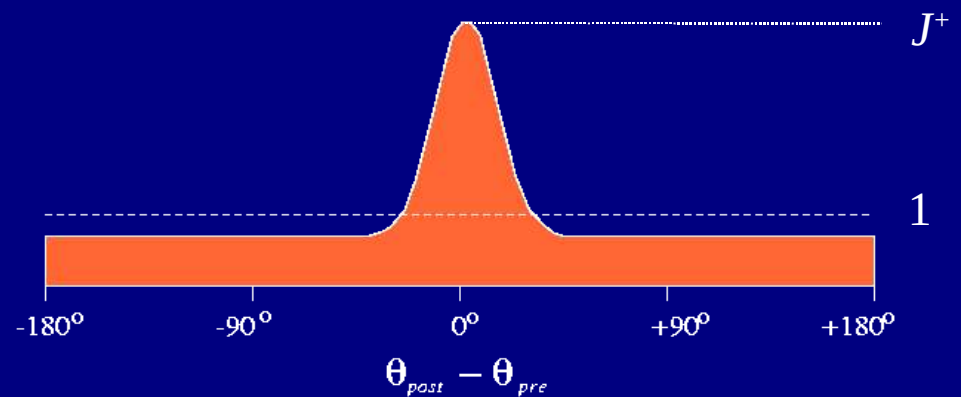
- ¿Tiene la corteza cerebral mecanismos capaces de generar esta biestabilidad?
- ¿Qué mecanismos son más críticos para los distintos aspectos: biestabilidad y persistencia?

Forebrain, Cortex Giemsa



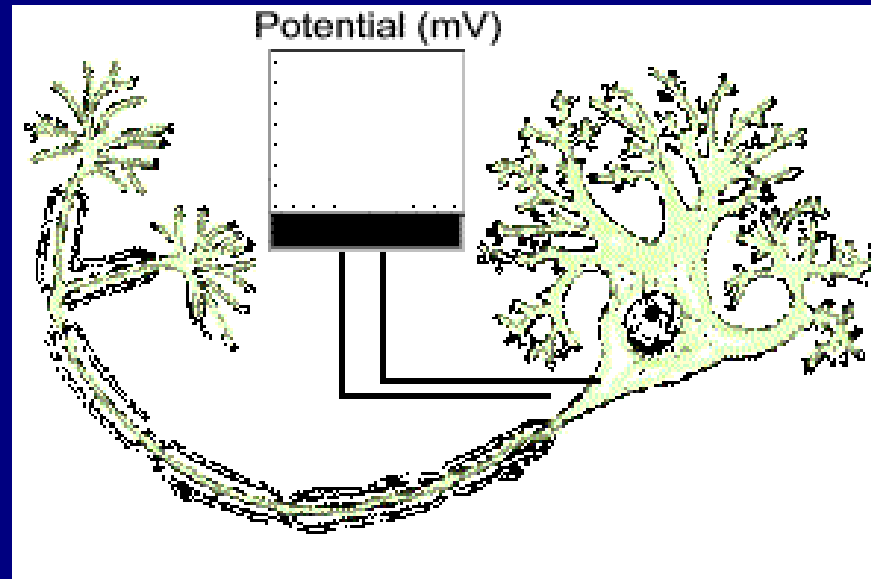
Un modelo de red

aproximamos la complejidad
de la conectividad cortical
(dendritas + axones) con
funciones de peso sináptico:



disponemos las neuronas en un anillo
unidimensional según su selectividad

Las neuronas de la red

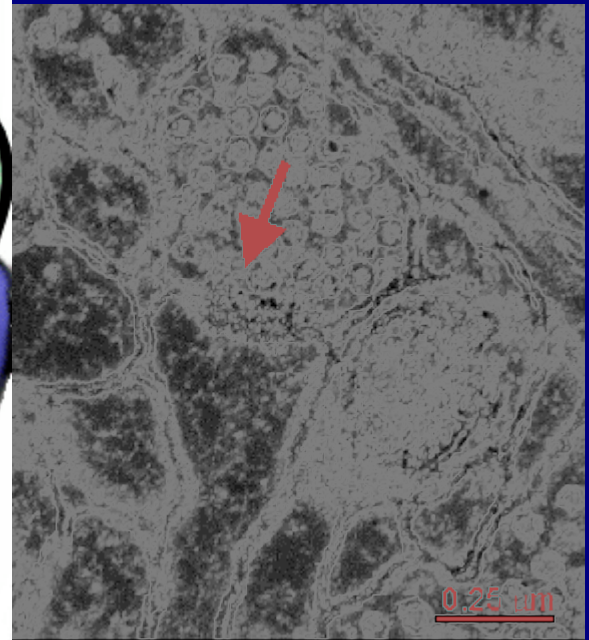
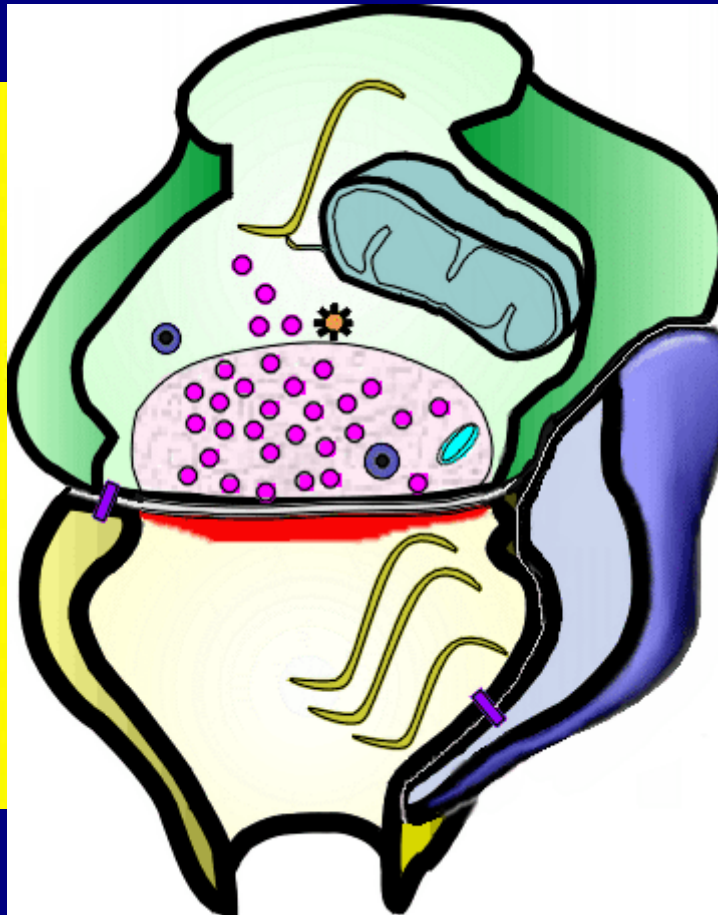
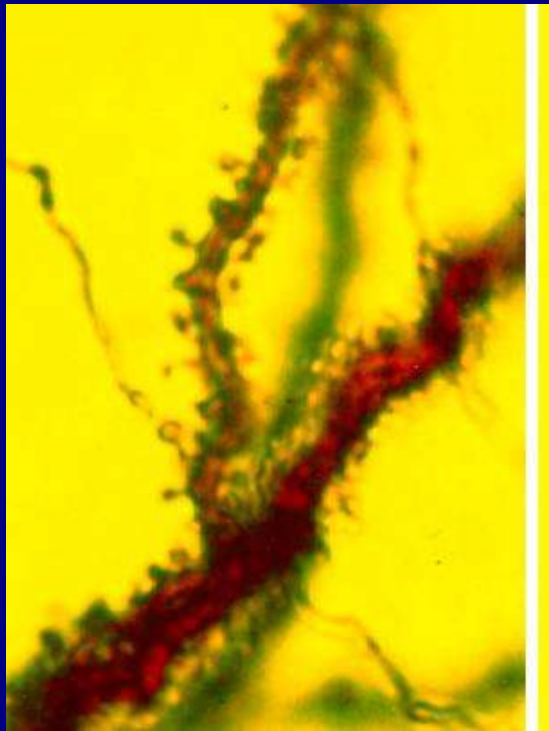


usamos el modelo de integración y disparo:

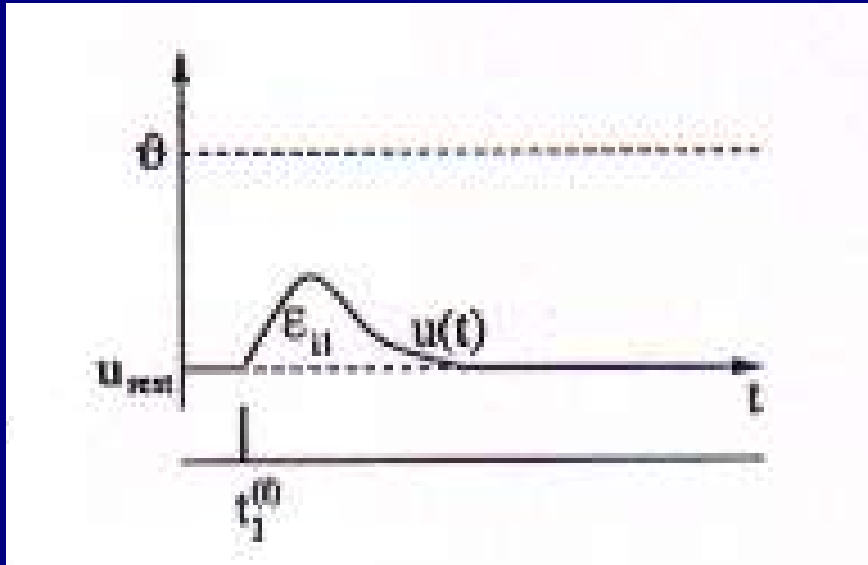
$$C_m \frac{dV}{dt} = -V + I(t)$$

$$\text{si } V(t) \geq V_{th} \Rightarrow V(t + \Delta t) = 0$$

Las conexiones: sinapsis



Las conexiones: sinapsis



$$\frac{ds}{dt} = (1-s)x - \frac{s}{\tau_s}$$

$$\frac{dx}{dt} = \sum_j \left(t - t_j \right) - \frac{x}{\tau_x}$$

$$I(t) = -g s(t) (V(t) - E_{syn})$$

inhibición $E_{syn} \simeq 0$

$\tau_s \simeq 10$ ms GABA_A

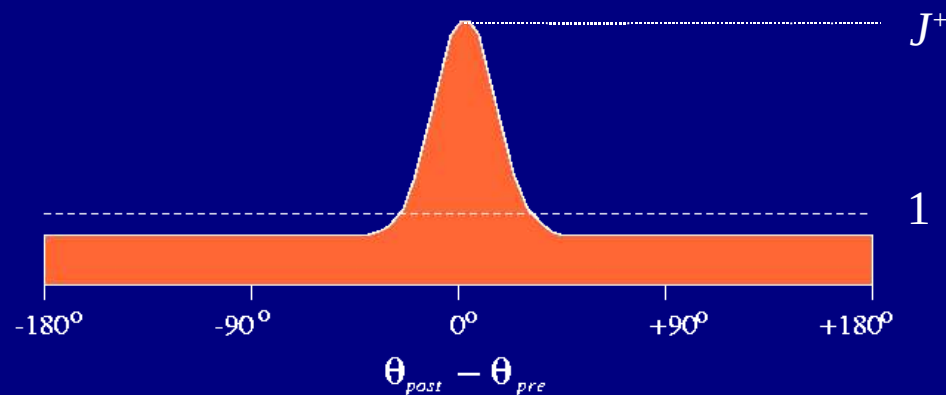
excitación $E_{syn} = 70$ mV ...

$\tau_s \simeq 100$ ms NMDA

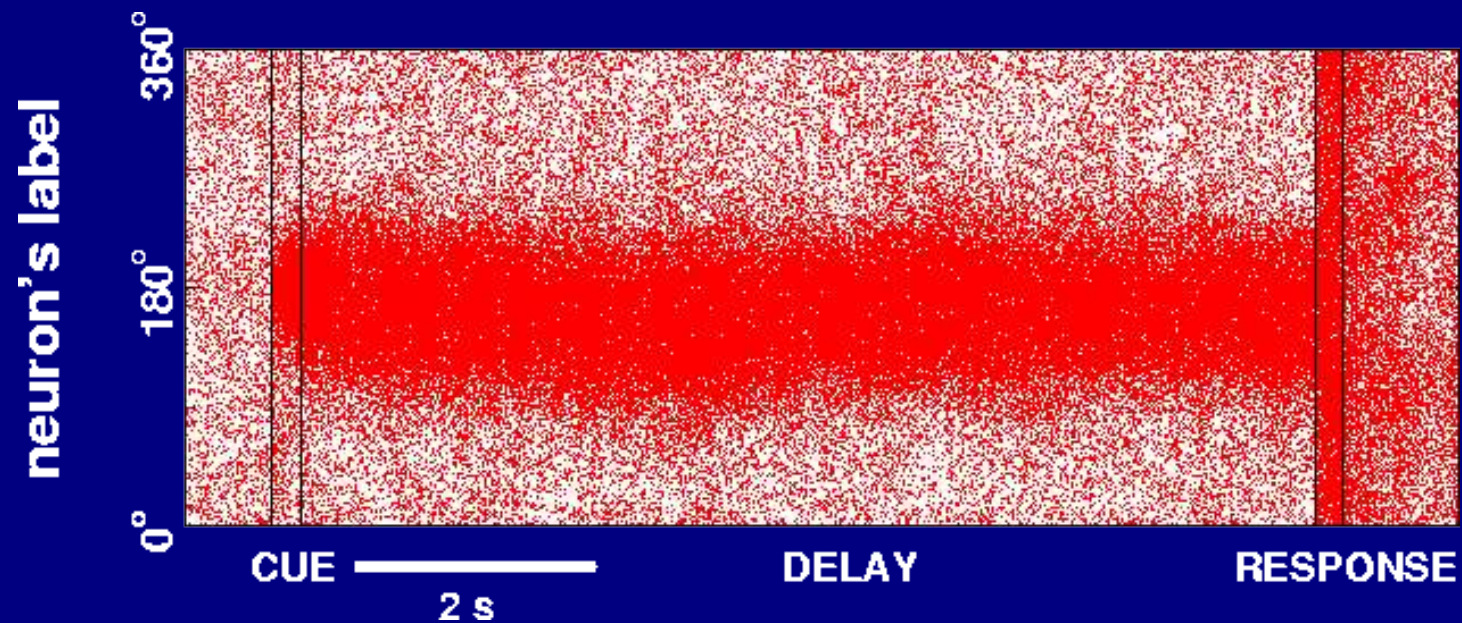
$\tau_s \simeq 2$ ms AMPA

Un modelo de red cortical para memoria de trabajo

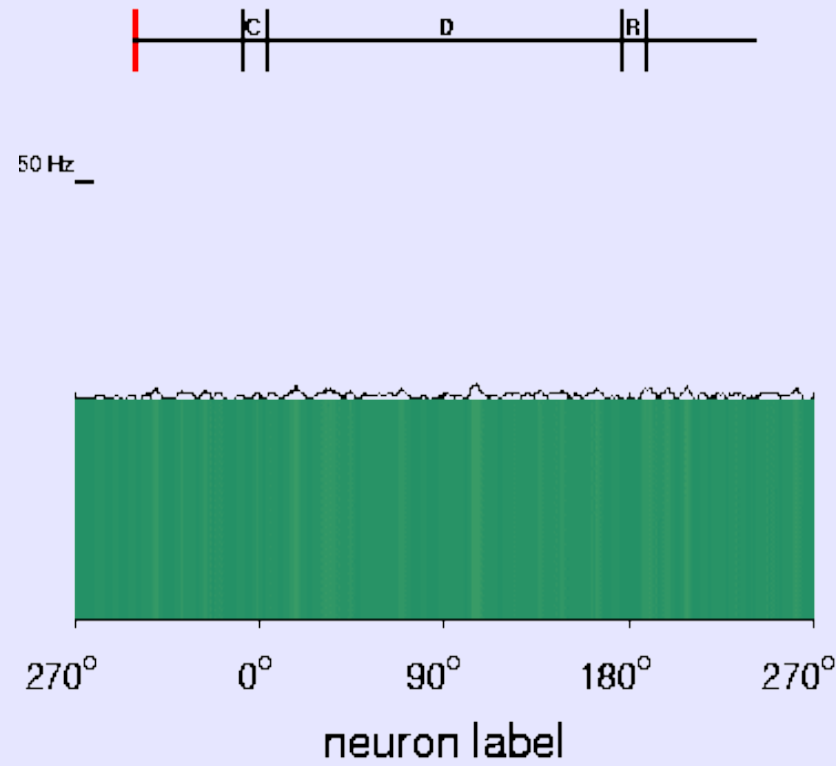
- 2 poblaciones de neuronas (excitatorias e inhibitorias) integrate-and-fire dispuestas en un anillo
- cinética sináptica realista a nivel biológico (AMPA, NMDA y $GABA_A$)
- excitación externa continua a través de canales AMPA con disparo de tipo Poisson
- conectividad E-a-E estructurada:



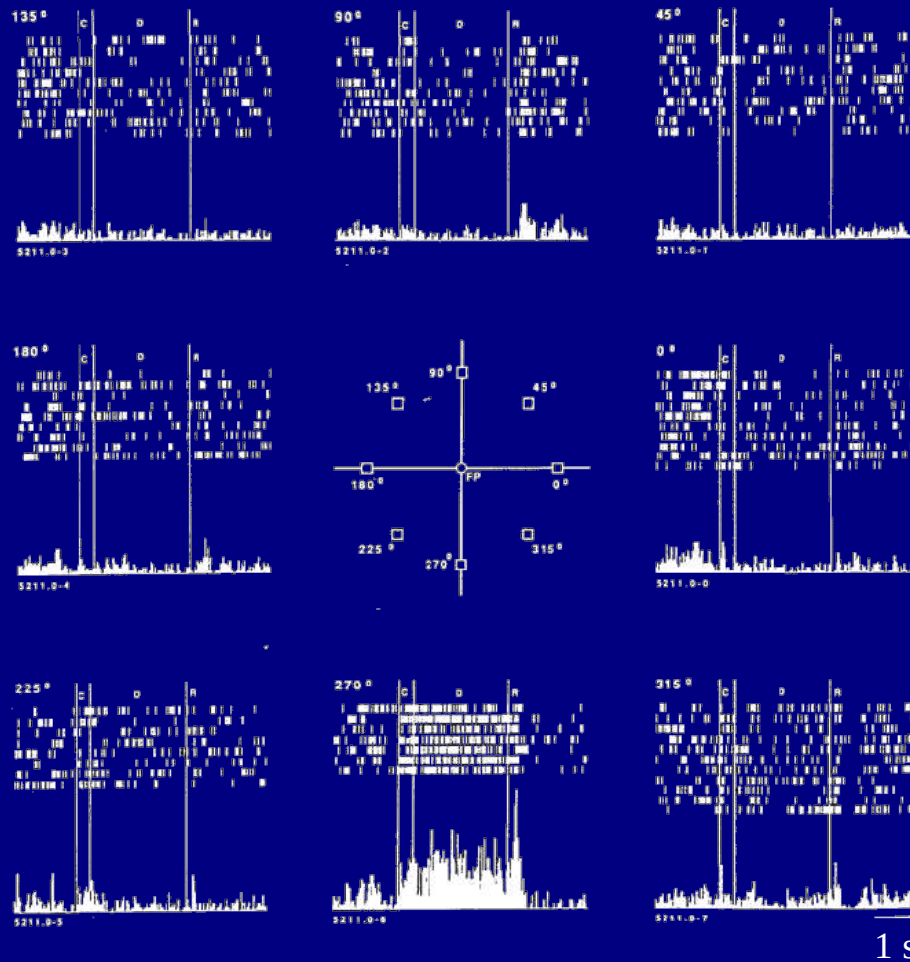
Funcionamiento del modelo de red



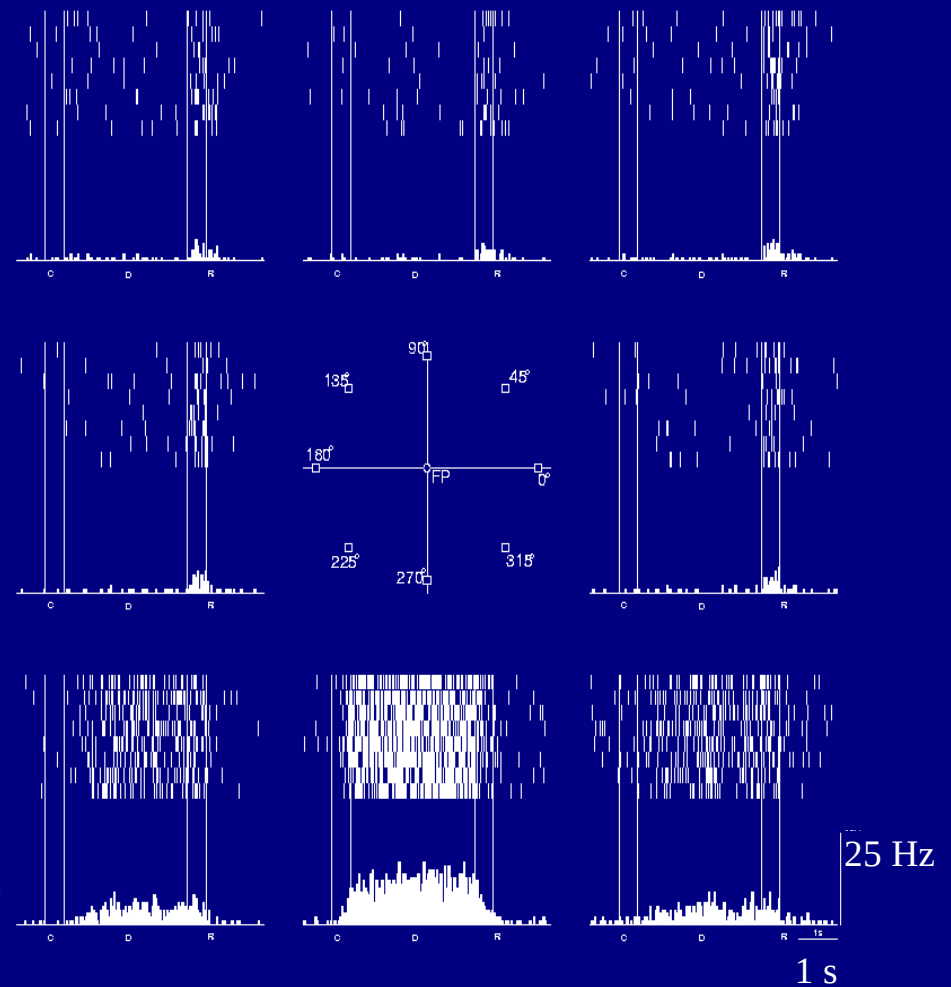
(Compte et al. Cerebral Cortex 10:910, 2000)



Experimento



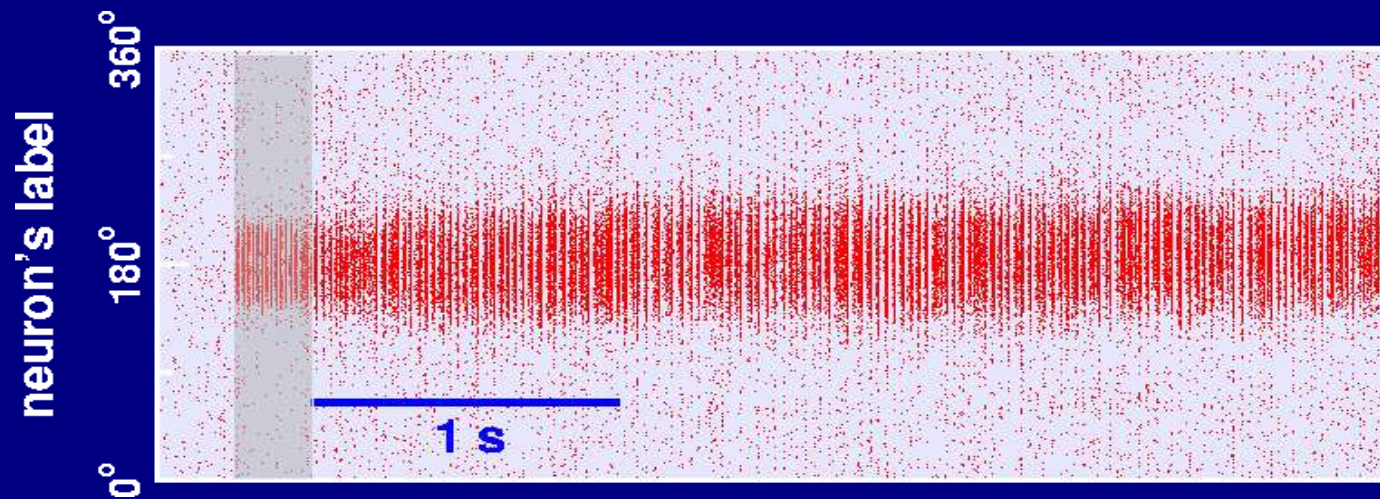
Simulación



Funahashi *et al.*, J. Neurophysiol. **61**:331 (1989)

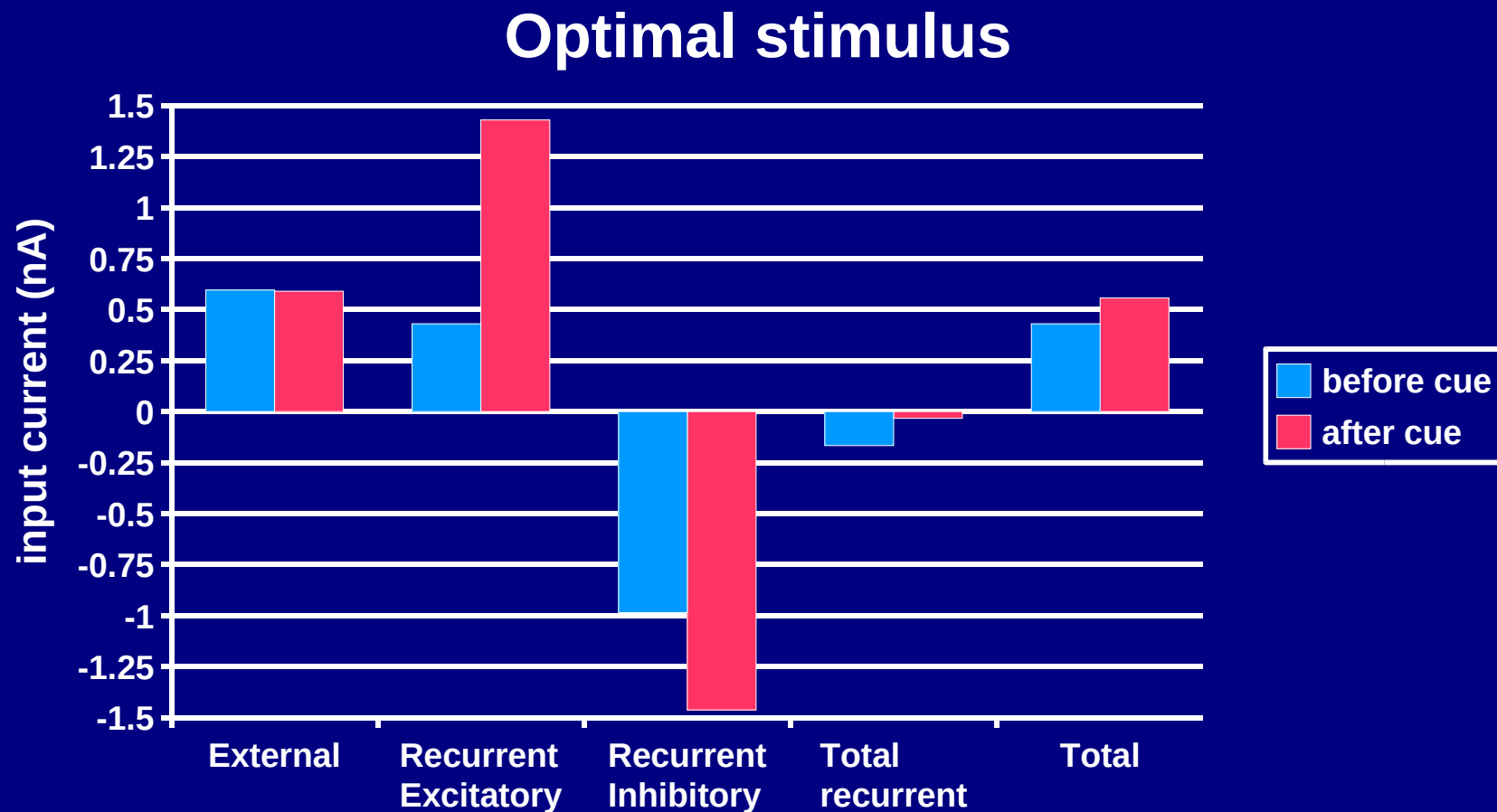
Mecanismos en el modelo

- Las sinapsis excitadoras de tipo NMDA con saturación y con cinética lenta estabilizan la actividad persistente a baja tasa de disparo



Mecanismos en el modelo

- La inhibición domina en las interacciones recurrentes para estabilizar la actividad espontánea



Estudiamos el modelo

- Plausibilidad biológica del mecanismo de reverberancia de red para la memoria de trabajo espacial con atractor continuo biestable con actividad espontánea
- La solución encontrada ¿es única? ¿es óptima? ¿es robusta?
- ¿Qué otros estados dinámicos puede generar la red?
- ¿Qué parámetros son especialmente críticos para la biestabilidad?

Reducción a un modelo simplificado

Simulación completa: $3 N_E + 3 N_I$ variables

Usamos la
aproximación
de difusión



Suponemos
disparo
asíncrono

Simulación de campo medio: $N_E + 1$ variables

Suponemos conectividad
 $W_{EE}(\Delta\theta) = 1 + J \cos \Delta\theta$



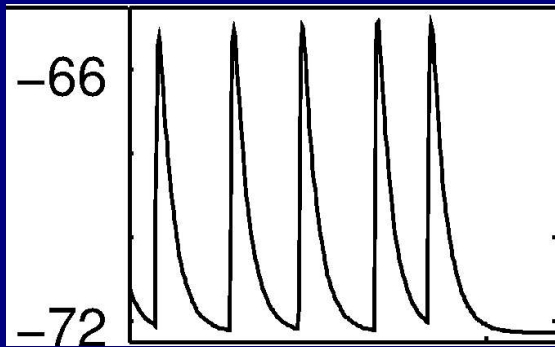
Sistema dinámico para componentes de Fourier: 3 variables

$$s_E(\theta) = \boxed{s_E^0} + \boxed{s_E^1} \cos \theta + \dots, \quad \boxed{s_I}$$

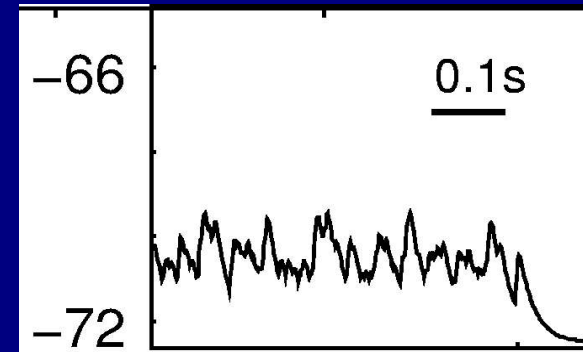
5 parámetros de conectividad libres: G_{EE} , J , G_{EI} , G_{IE} , G_{II}

Modelo de campo medio

disparo síncrono:



disparo asíncrono:



lo aproximamos por media +
desviación estándar x ruido
blanco Gaussiano

$$r = \frac{1}{\int_{\langle I \rangle}^{\langle I \rangle} du \sqrt{\exp(u^2) [1 + \operatorname{erf}(u)]}} + r_{ref}$$

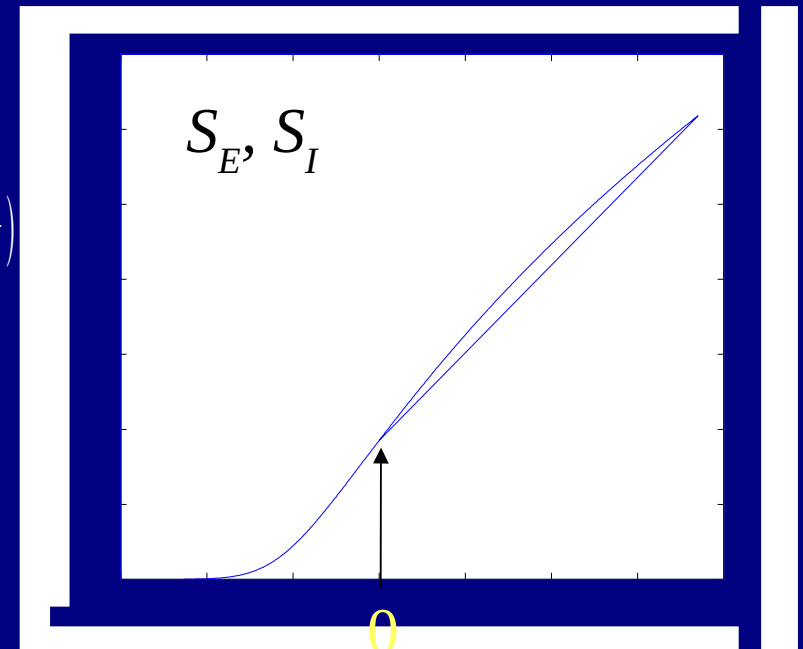
(Ricciardi 1977, Brunel and Sergi J. Theor Biol 1998)

$$\frac{dV}{dt} = -V + \langle I \rangle + \sqrt{\dots} \quad (t)$$

$$r = 1 / \left(\text{tiempode } 1 \text{ rpasopor } V_{th} \right)$$

Modelo de campo medio

$$\begin{aligned} \frac{\partial s_E(\cdot, t)}{\partial t} &= -s_E(\cdot, t) + S_E(I_E(\cdot, t)) \\ \frac{ds_I(t)}{dt} &= -s_I(t) + S_I(I_I(t)) \end{aligned}$$



corriente recurrente

$$I_E(\cdot, t) = \frac{G_{EE}}{2} \int_{-}^{\cdot} W_{EE}(\cdot - \cdot') s_E(\cdot', t) d\cdot' - G_{IE} s_I(t)$$

$$I_I(t) = \frac{G_{EI}}{2} \int_{-}^{\cdot} s_E(\cdot', t) d\cdot' - G_{II} s_I(t)$$

tomamos:

$$W_{EE} \left(\begin{matrix} s_E(t) \\ s_I(t) \end{matrix} \right) = 1 + J \cos \left(\begin{matrix} s_E(t) \\ s_I(t) \end{matrix} \right)$$

$$s_E(t) = s_E^0(t) + s_E^1(t) \cos + s_E^2(t) \cos 2 + \dots$$

y lo reducimos a un sistema dinámico de 3 ecs.

$$\left\{ \begin{aligned} \frac{ds_E^0}{dt} &= -s_E^0 + \frac{1}{2} \int S_E(I_E(t)) dt \\ \frac{ds_E^1}{dt} &= -s_E^1 + \frac{1}{2} \int S_E(I_E(t)) \cos dt \\ \frac{ds_I^0}{dt} &= -s_I^0 + S_I(I_I(t)) \end{aligned} \right.$$

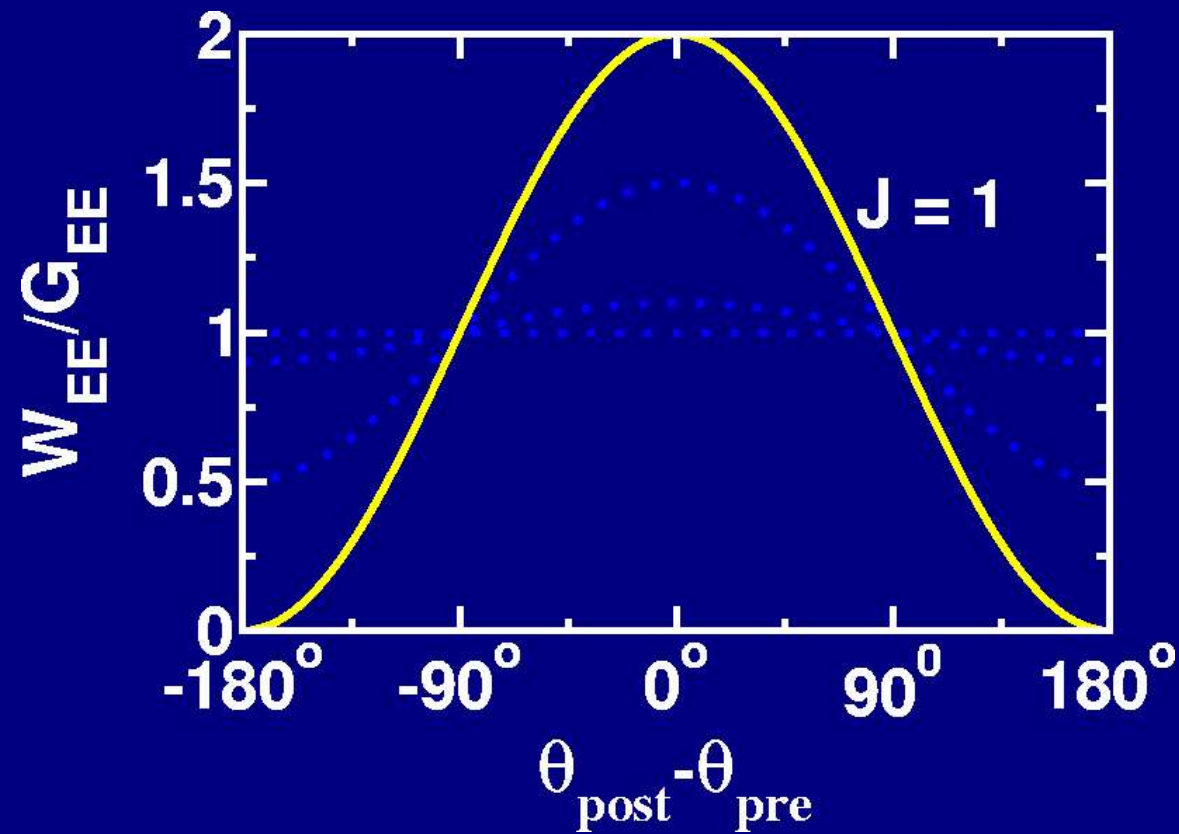
con $I_E(t) = G_{EE}s_E^0(t) + \frac{1}{2}JG_{EE}s_E^1(t) \cos - G_{IE}s_I^0(t)$

$$I_I(t) = G_{EI}s_E^0(t) - G_{II}s_I^0(t)$$

parámetros del sistema: $J, G_{EE}, G_{EI}, G_{IE}, G_{II}$

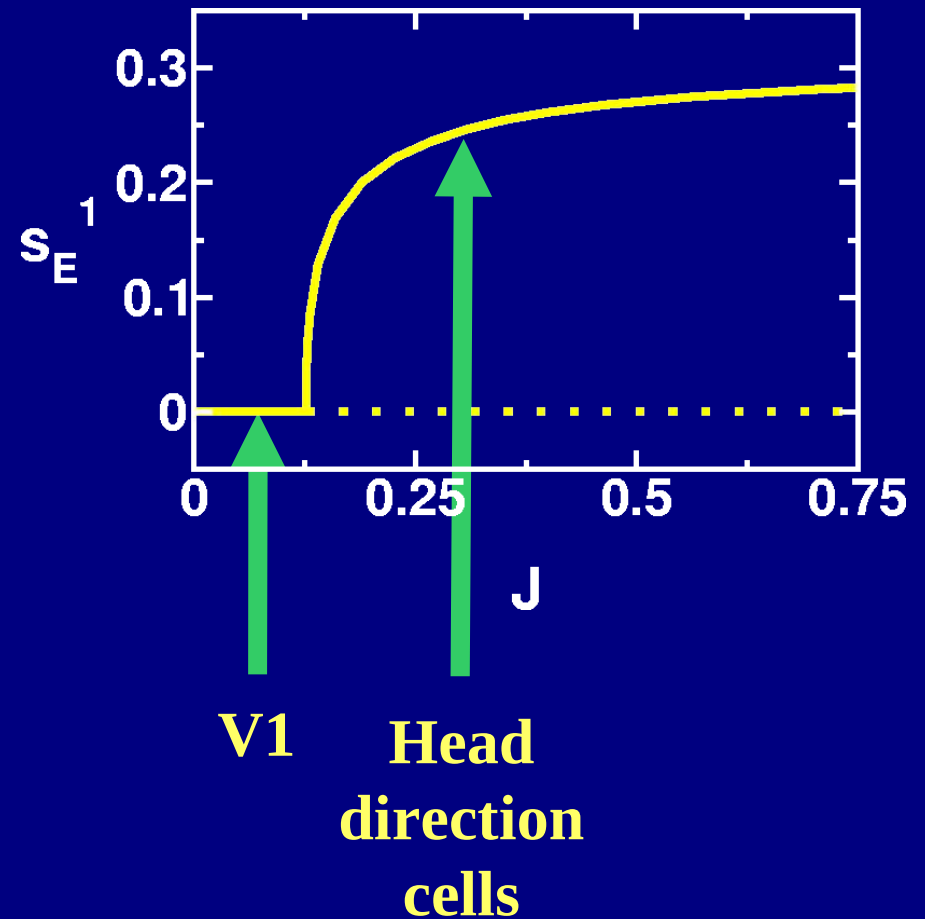
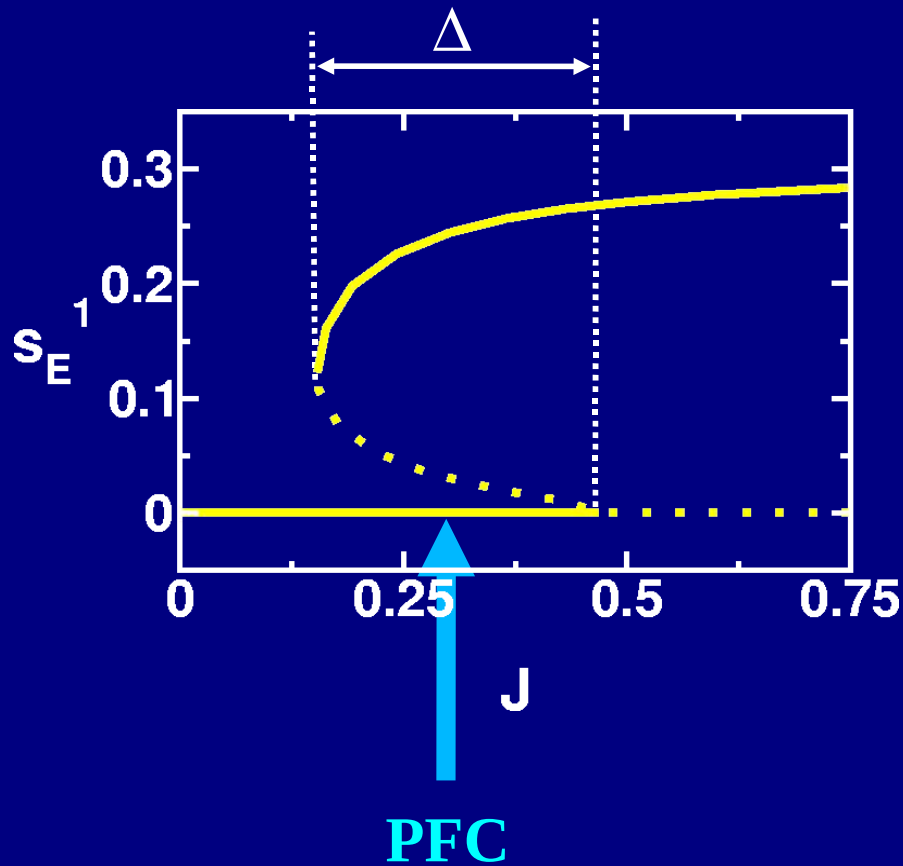
Bistability

$$W_{EE}(\theta_{\text{post}} - \theta_{\text{pre}}) = 1 + \mathbf{J} \cos(\theta_{\text{post}} - \theta_{\text{pre}})$$



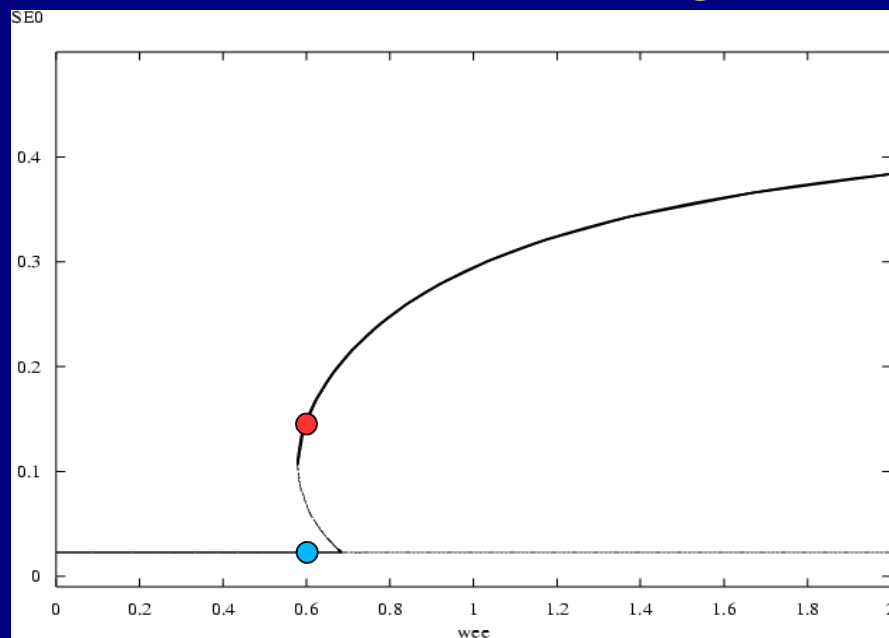
Bistability

$$W_{EE}(\theta_{post} - \theta_{pre}) = 1 + \mathbf{J} \cos(\theta_{post} - \theta_{pre})$$



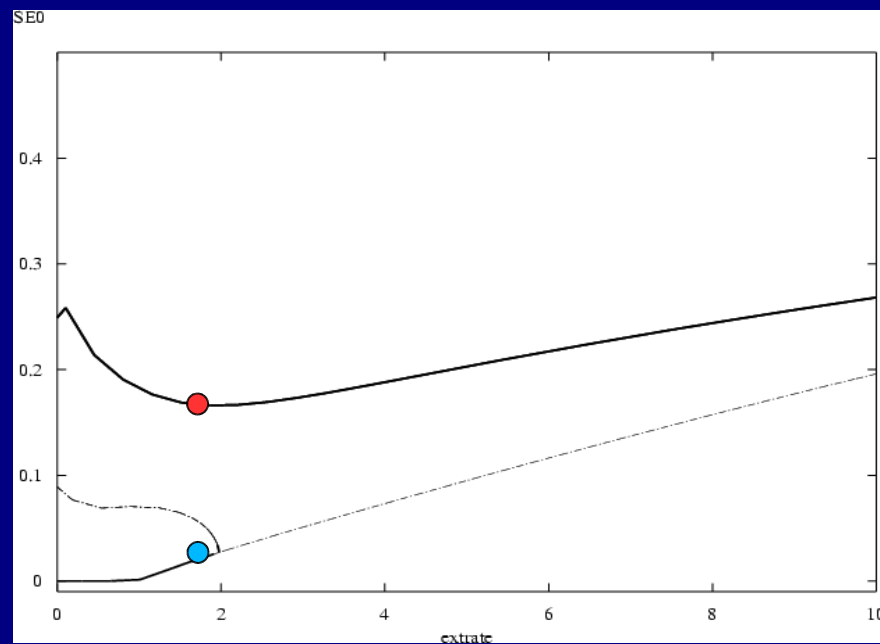
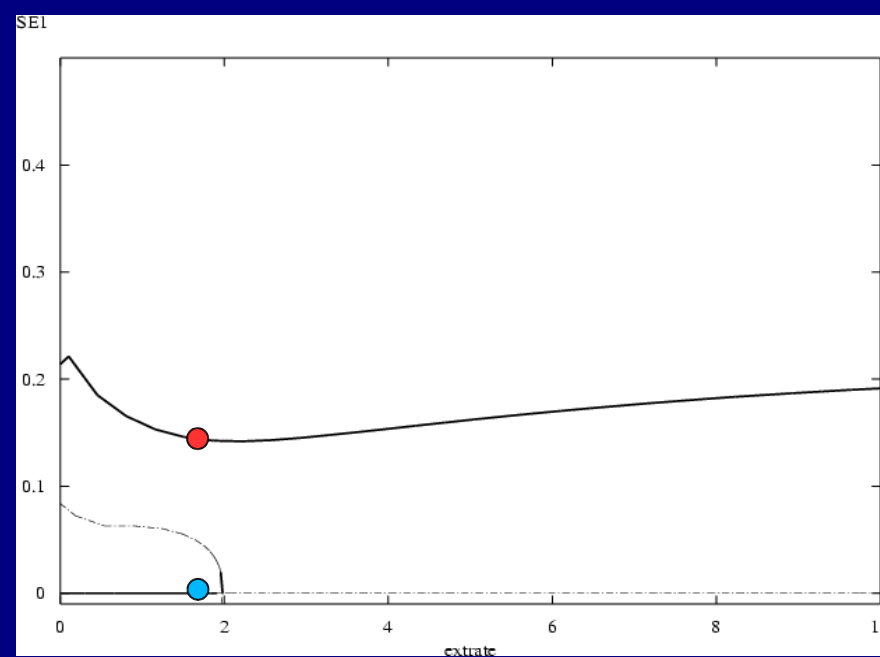
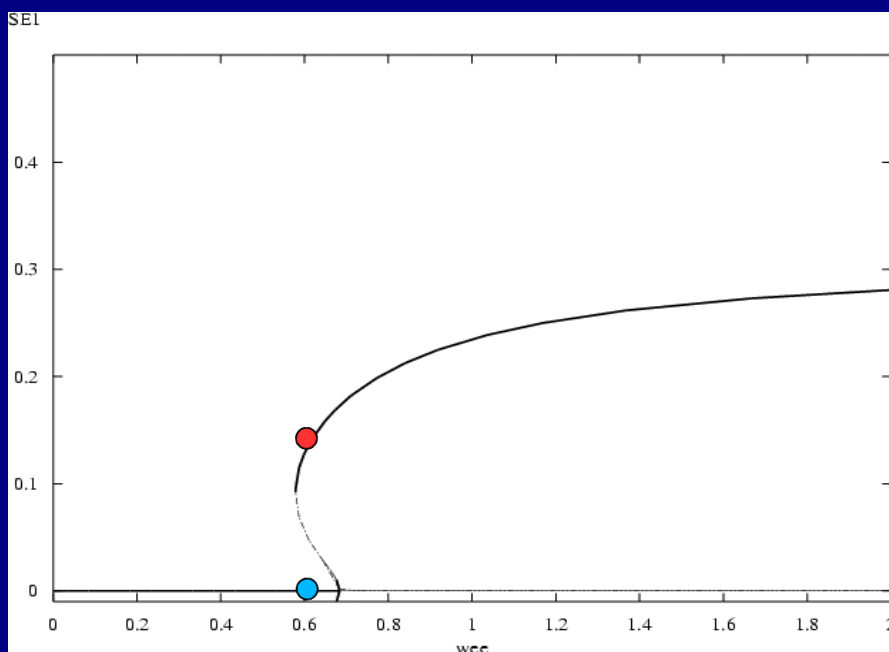
J

rango 14%

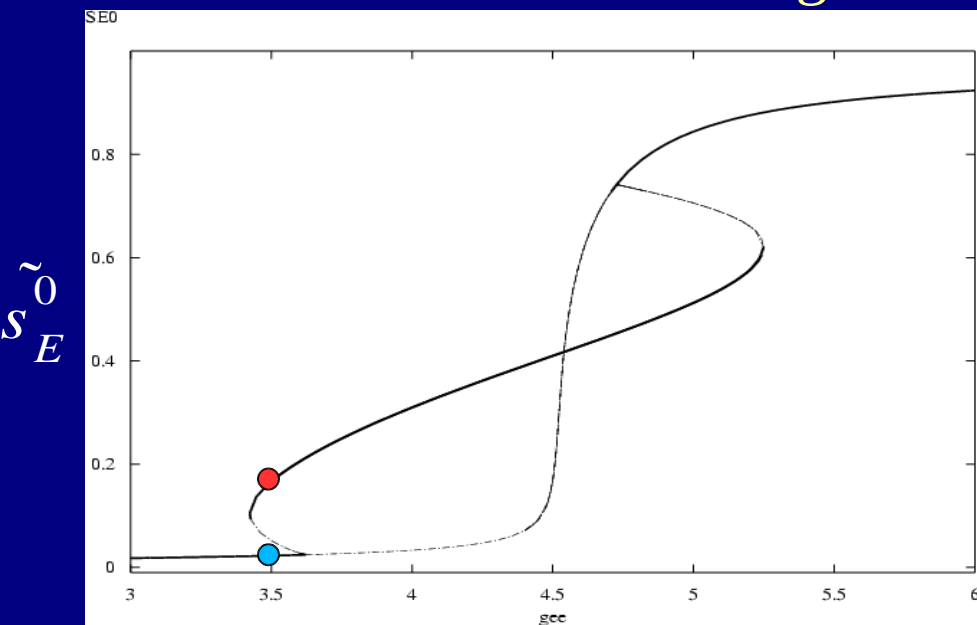
 $s_E^{\sim 0}$ 

rate externo

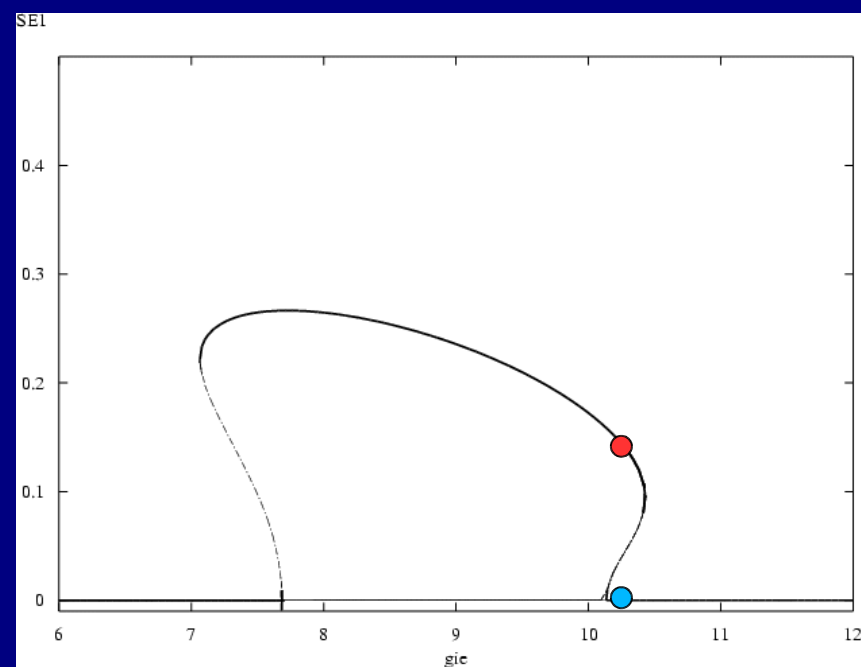
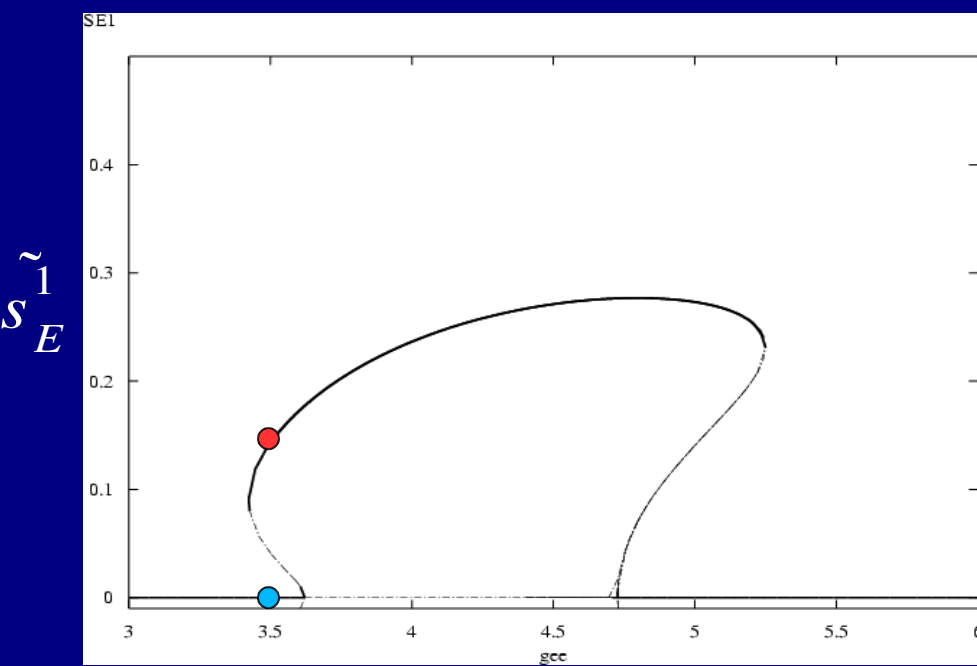
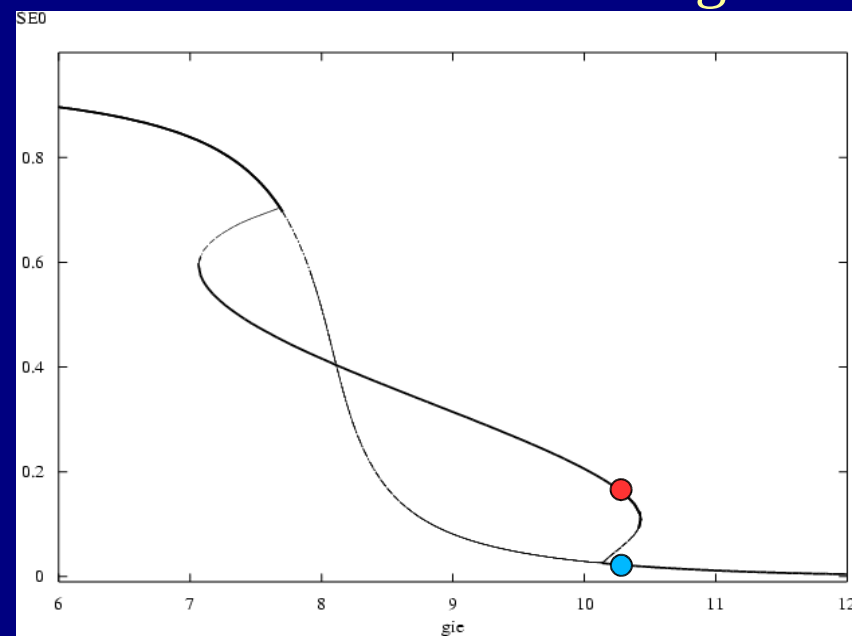
rango 200%

 $s_E^{\sim 1}$ 

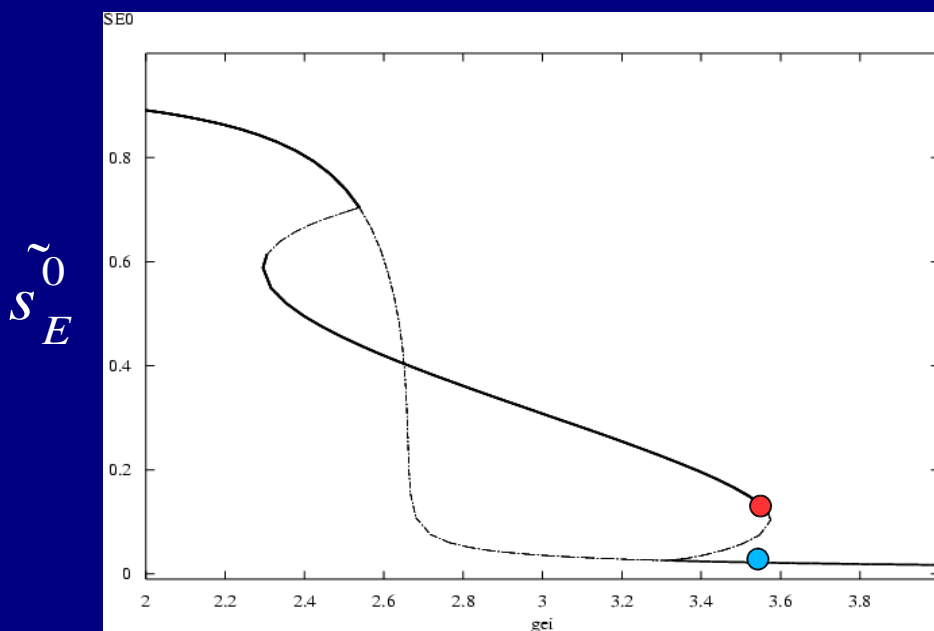
G_{EE} rango 7%



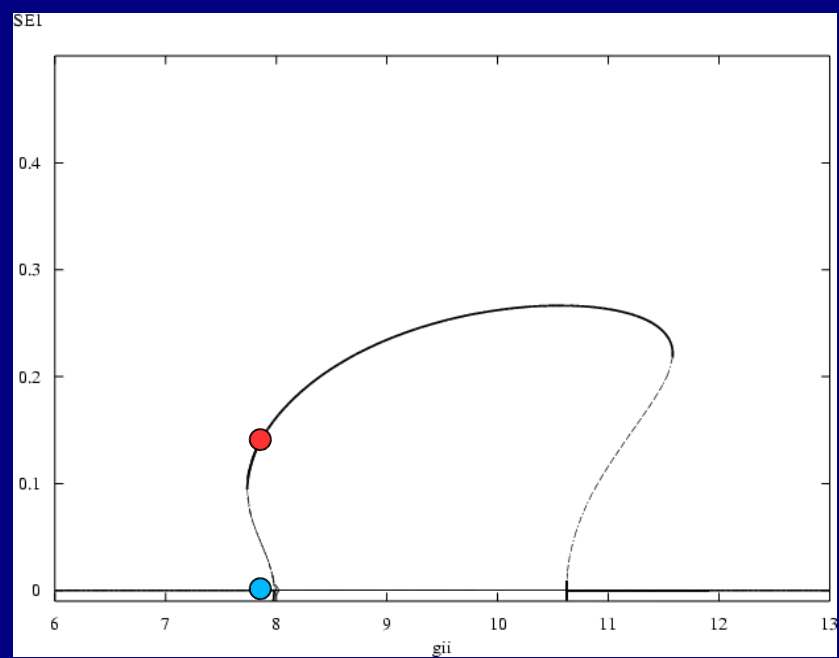
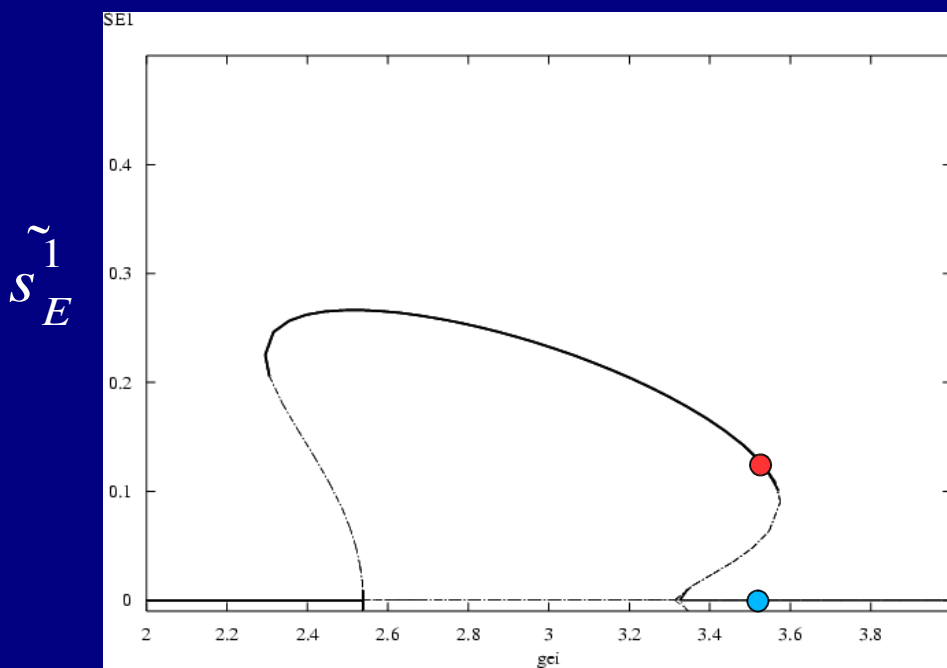
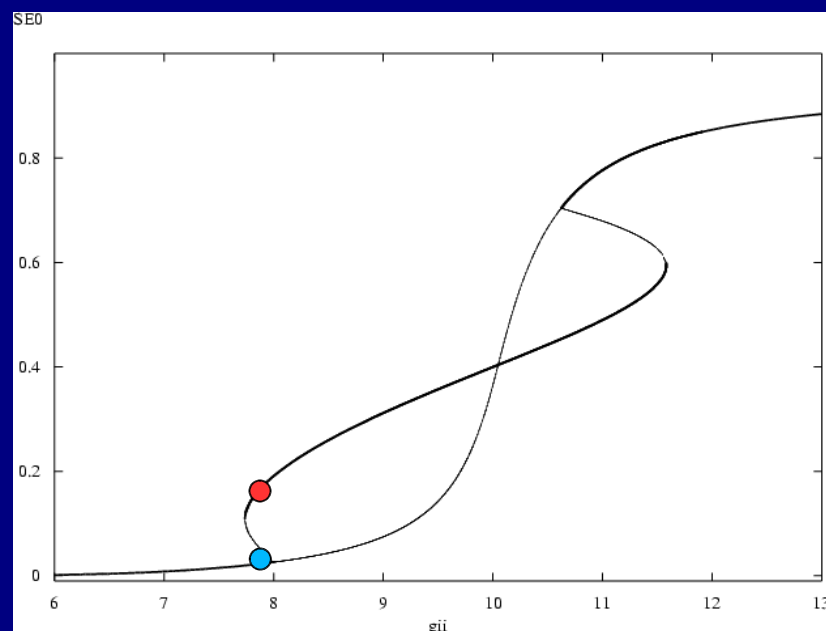
G_{IE} rango 2%



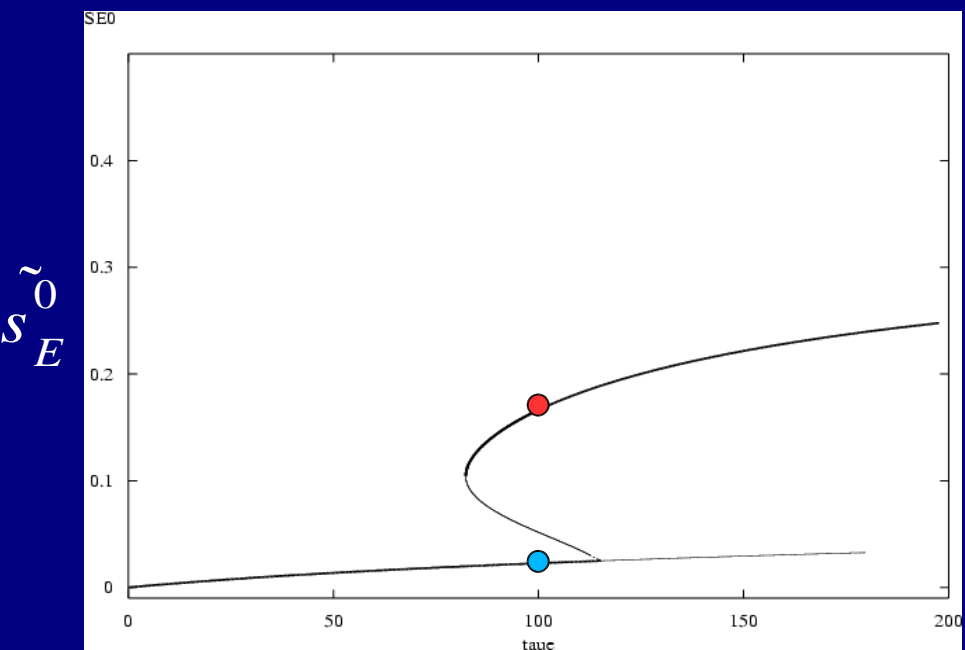
G_{EI} rango 7%



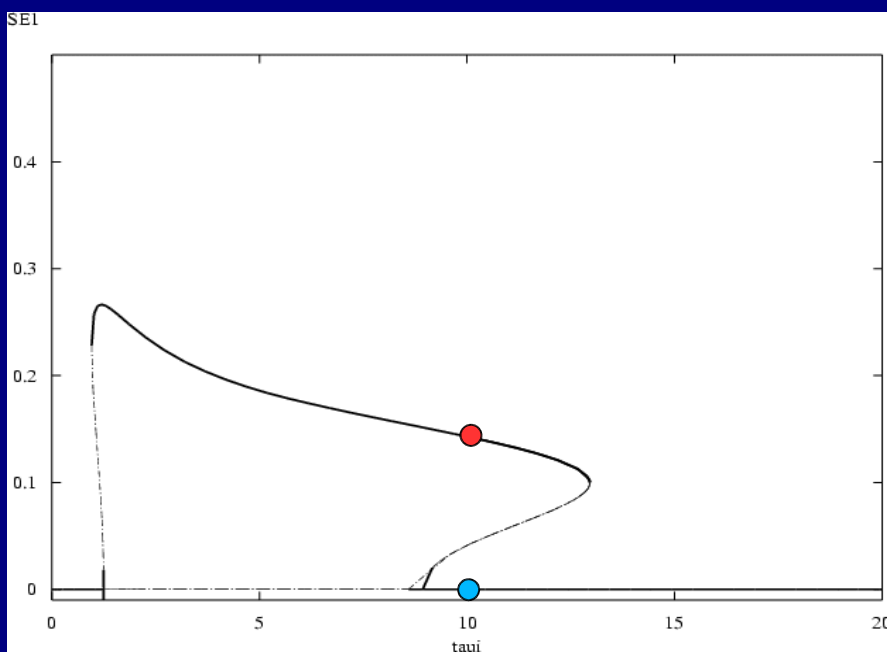
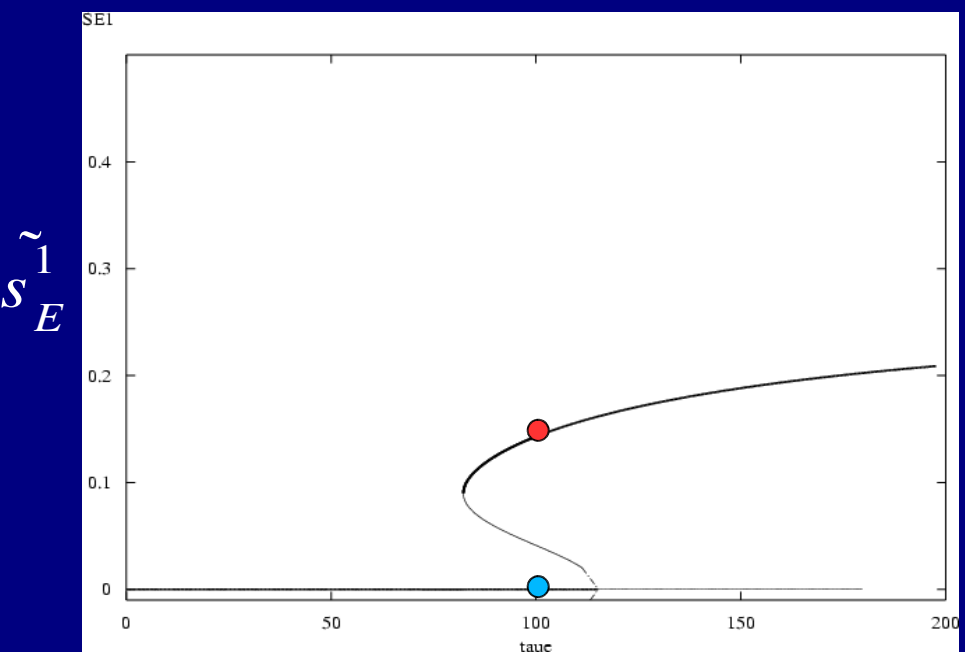
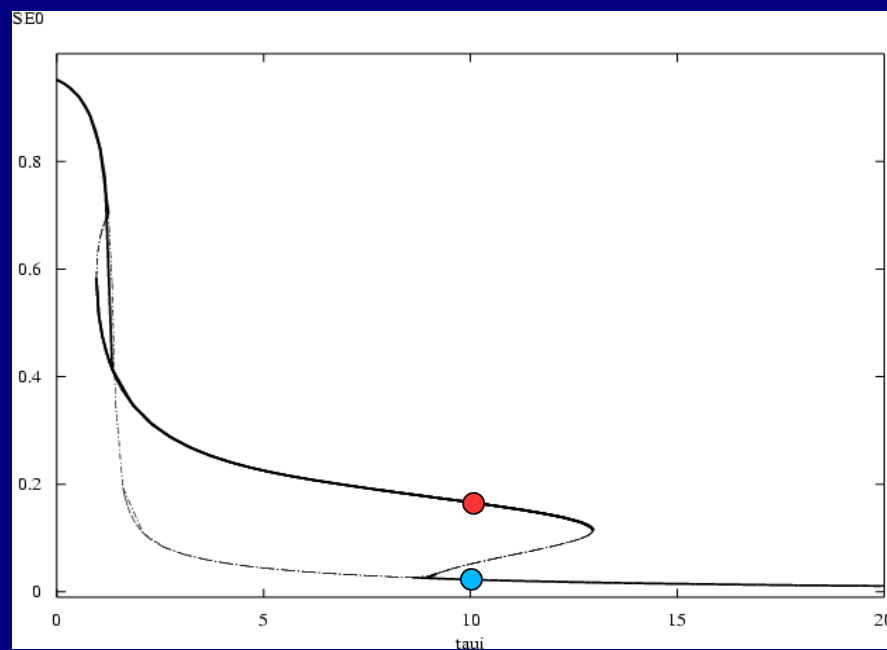
G_{II} rango 4%

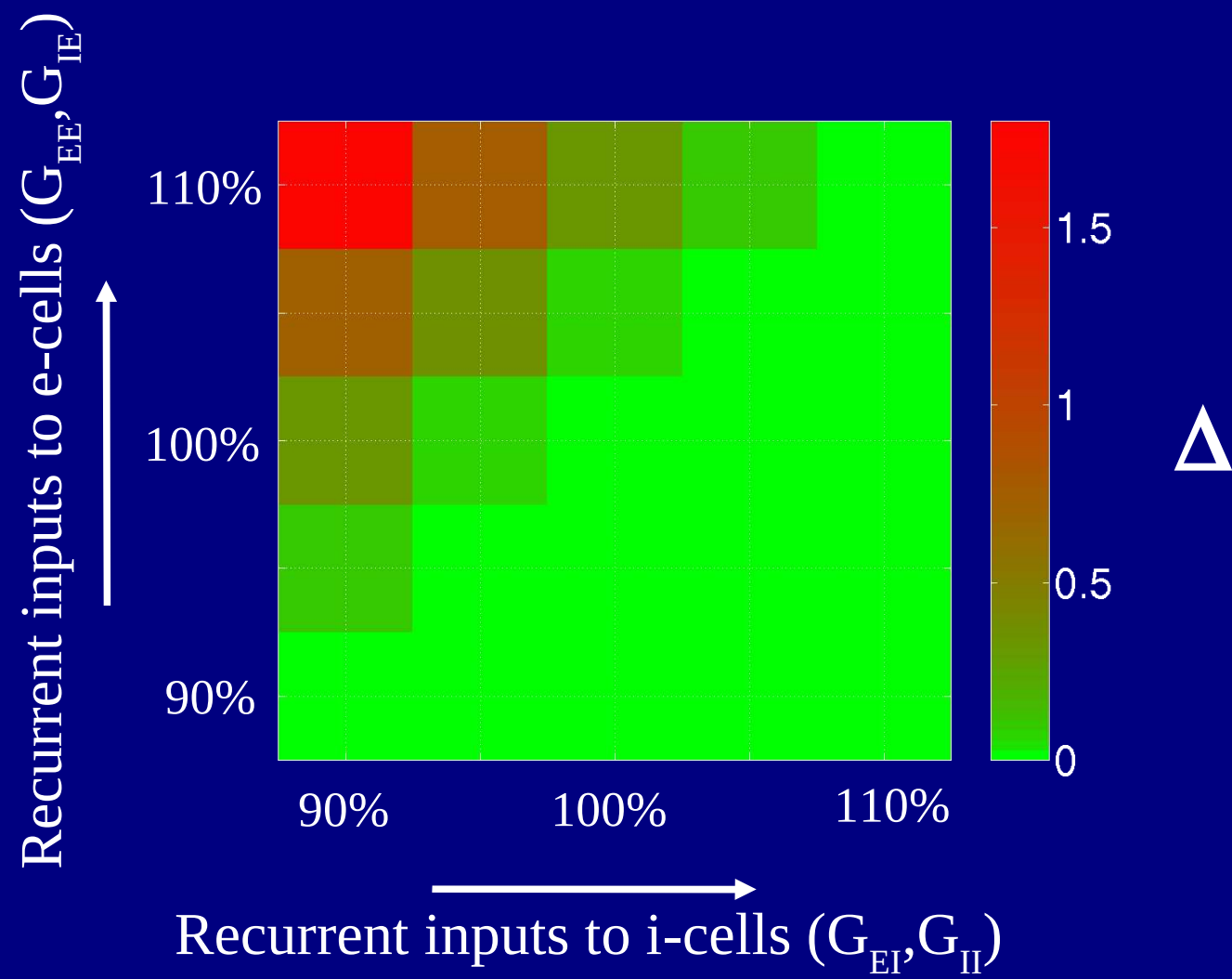


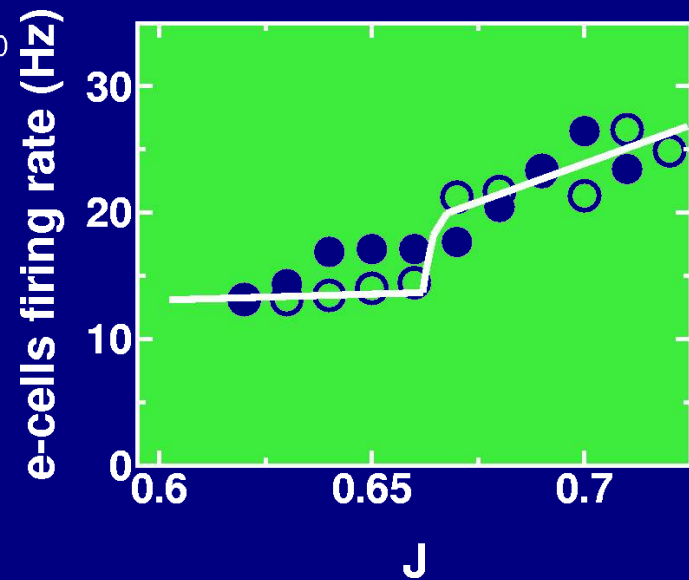
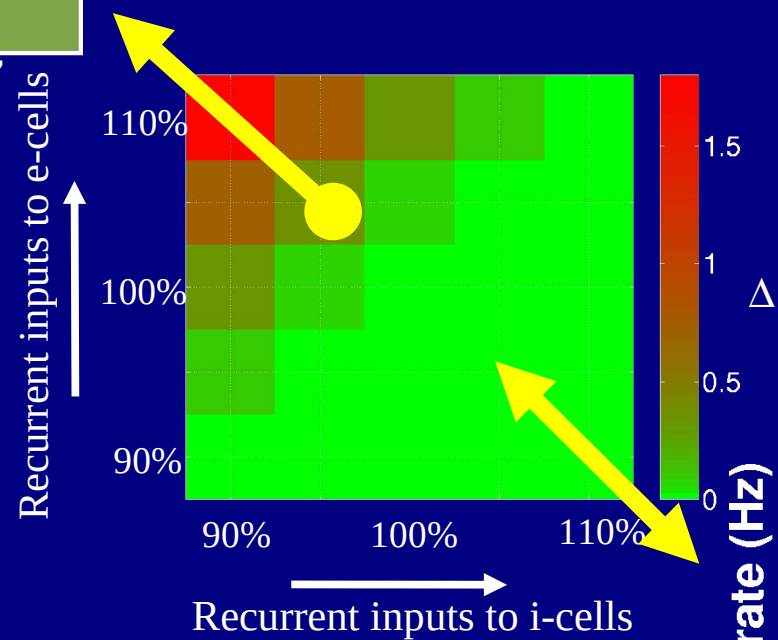
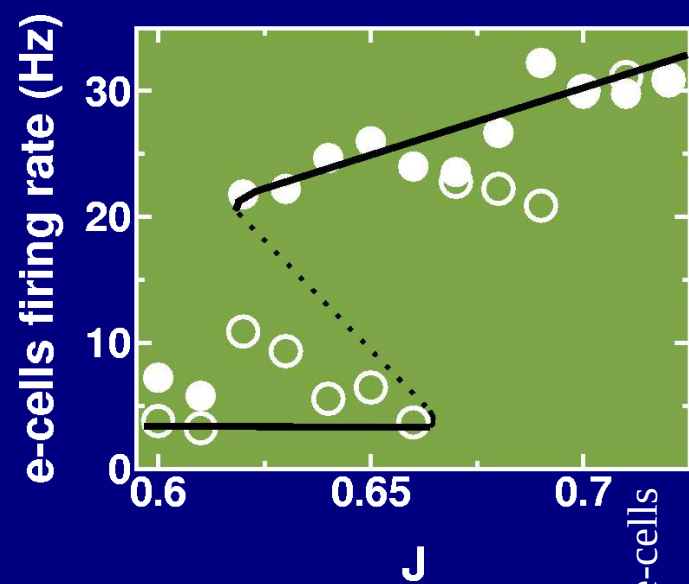
τ_E rango 36%



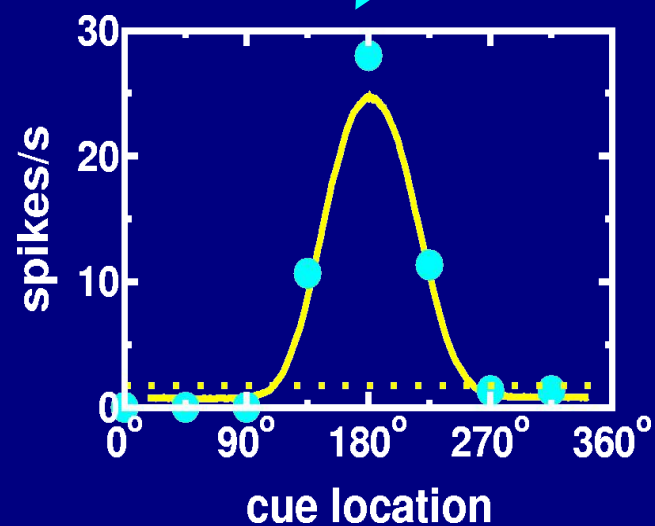
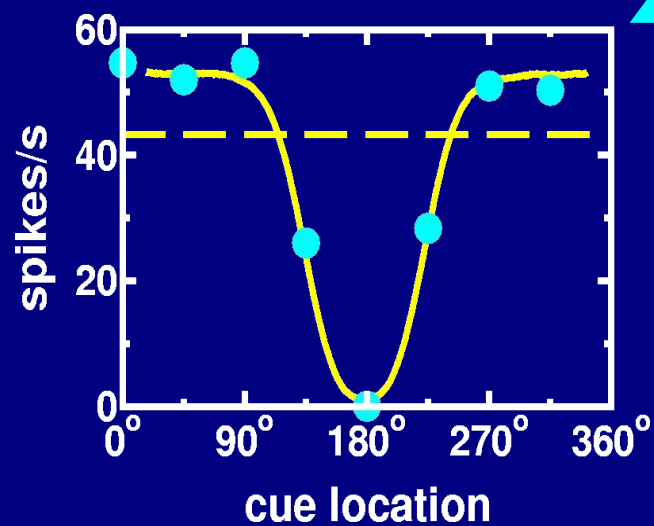
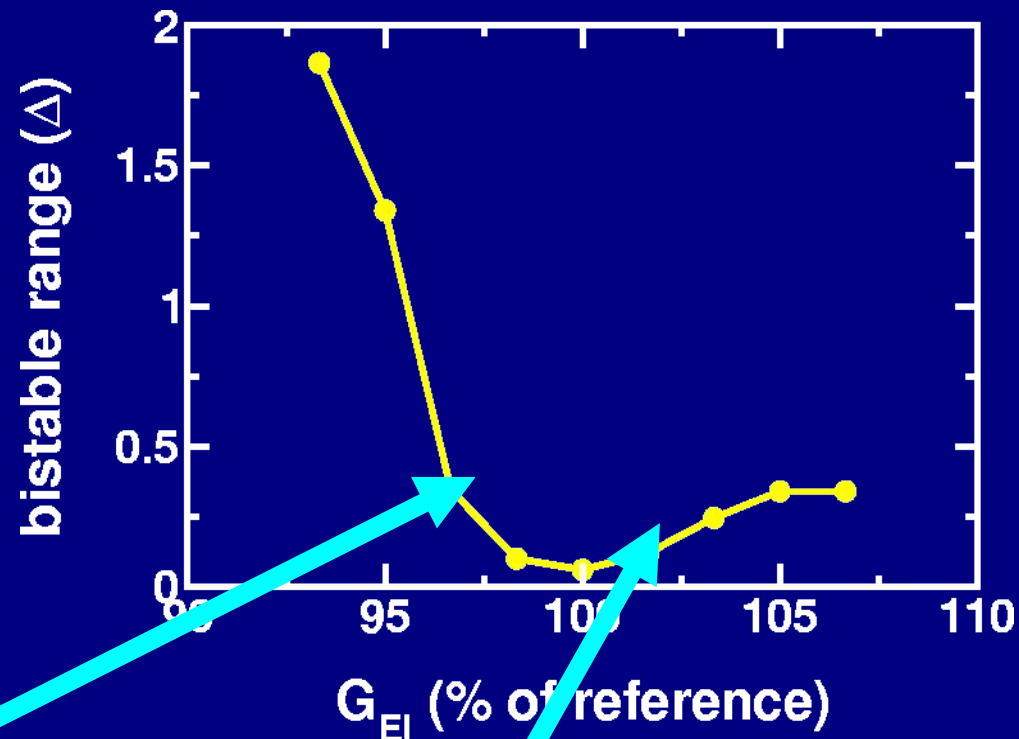
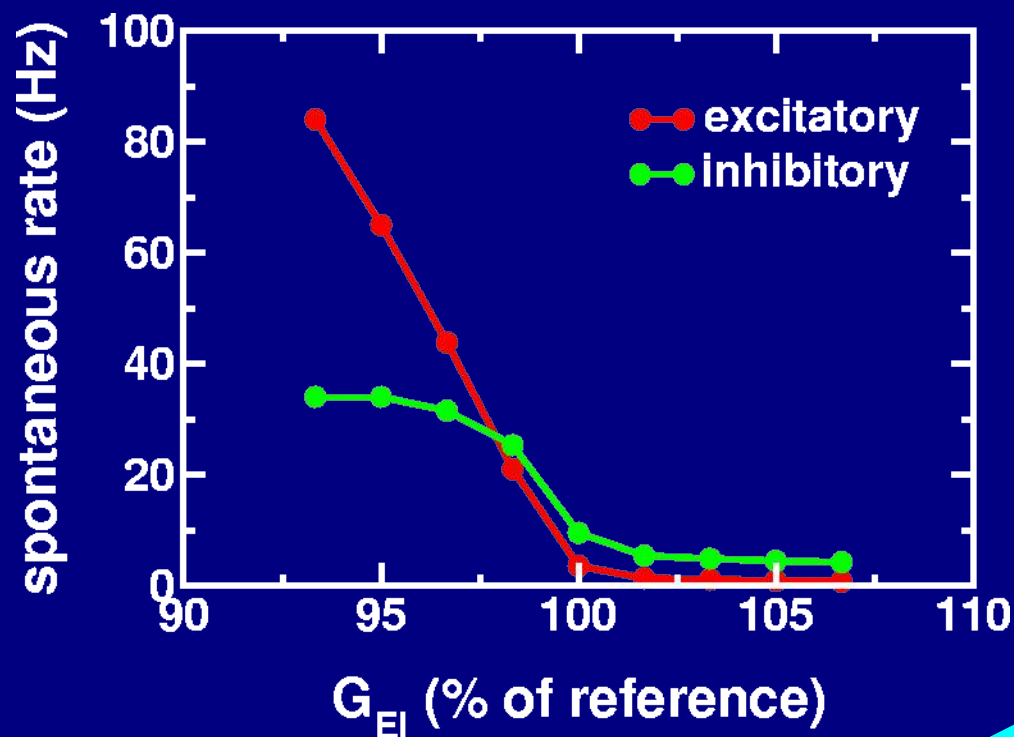
τ_I rango 42%





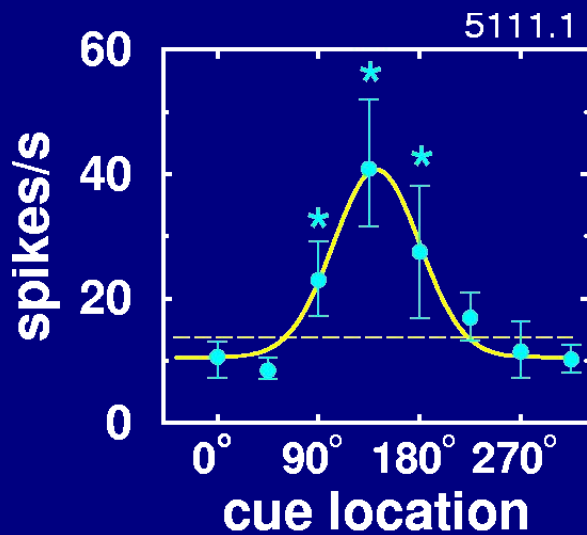
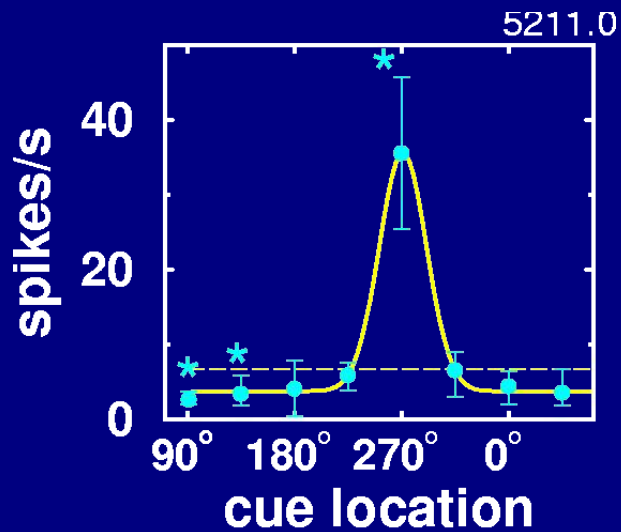


Inhibition

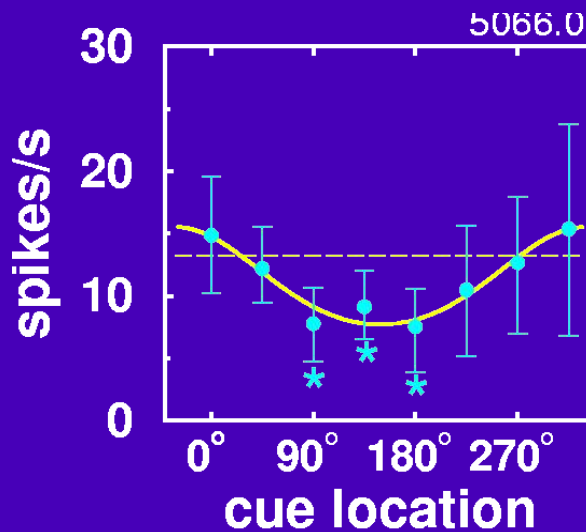


Data from Funahashi et al. J. Neurophysiol. **61**:331 (1989)

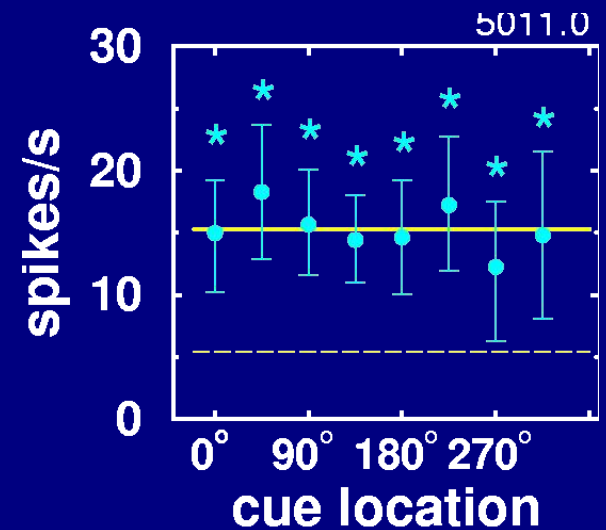
Upright tuning



Inverted tuning

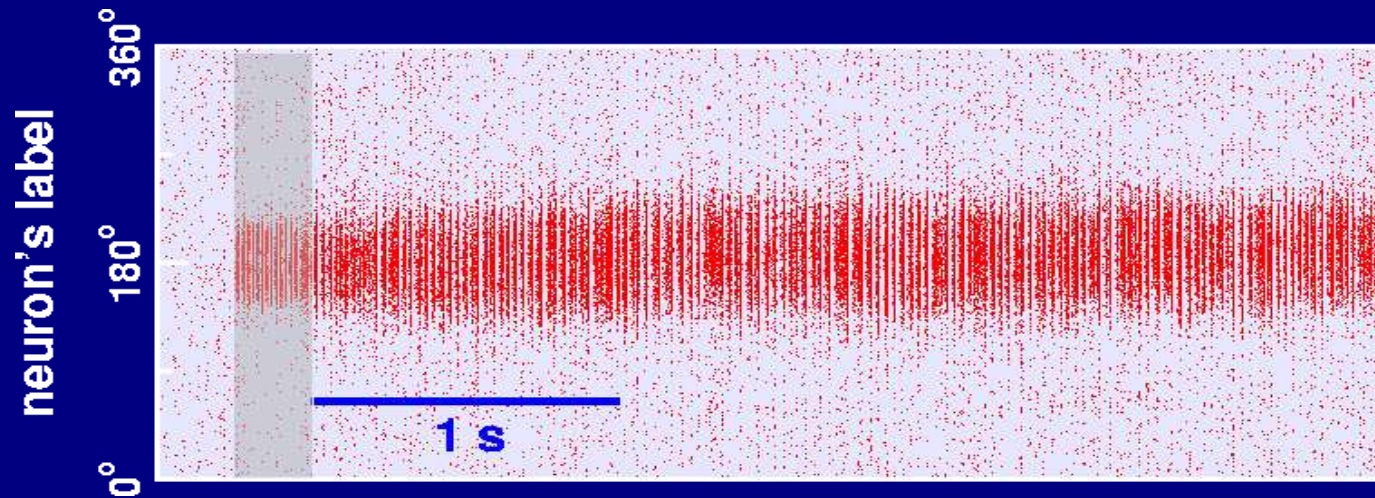


No tuning



Mechanisms for model function

- Slow-decaying, saturating excitatory synapses (NMDA) stabilize low-rate persistent state



Las neuronas:

$N_E + N_I$ ecs.

$$C_m \frac{dV_i^{E,I}}{dt} = -V_i^{E,I} + I_i^{E,I}(t)$$

$$\text{si } V_i^{E,I}(t) \geq V_{th} \Rightarrow V_i^{E,I}(t + \tau) = 0$$

Las conexiones:

$$I_i^{E,I}(t) = g_E^{E,I} (70 - V_i^{E,I}(t)) \sum_j W_E^{E,I}(i-j) s_j^E(t) - \dots \\ g_I^{E,I} V_i^{E,I}(t) \sum_j W_I^{E,I}(i-j) s_j^I(t) + I_{ext,i}^{E,I}(t)$$

Excitación externa:

$$I_{ext,i}^{E,I}(t) = g_{ext}^{E,I} (70 - V_i^{E,I}(t)) s_{ext,i}^{E,I}(t)$$

Las sinapsis:

$2N_E + 2N_I$ ecs.

$$\frac{ds_i^E}{dt} = (1 - s_i^E) \sum_j \left(t - \left\lceil T_i^E \right\rceil_j \right) - \frac{s_i^E}{\tau_s^E}$$

$$\frac{ds_i^I}{dt} = \sum_j \left(t - \left\lceil T_i^I \right\rceil_j \right) - \frac{s_i^I}{\tau_s^I}$$

$$\frac{ds_{ext,i}^{E,I}}{dt} = \sum_j \left(t - \left\lceil T_{ext,i}^{E,I} \right\rceil_j \right) - \frac{s_{ext,i}^{E,I}}{\tau_{ext}^{E,I}}$$

Las neuronas:

$$C_m \frac{dV_i^{E,I}}{dt} = -V_i^{E,I} + \langle I_i^{E,I} \rangle + I_{ext}^{E,I} \quad (t)$$

$$r_i^{E,I} = 1 / \text{tiempo de primer paso por } V_{th}$$

Las conexiones:

$$\langle I_i^E \rangle = g_{EE} (70 - V_i^E) \sum_j W(i-j) \langle s_j^E \rangle - \dots \\ g_{IE} V_i^E \langle s^I \rangle + \langle I_{ext}^E \rangle$$

$$\langle I^I \rangle = g_{EI} (70 - V^I) \frac{1}{N_E} \sum_j \langle s_j^E \rangle - \dots \\ g_{II} V^I \langle s^I \rangle + \langle I_{ext}^I \rangle$$

Excitación externa:

$$\langle I_{ext}^{E,I} \rangle = g_{ext}^{E,I} (70 - V_i^{E,I}) \langle s_{ext}^{E,I} \rangle$$

Las sinapsis:

$$\frac{d\langle s_i^E \rangle}{dt} = \left(1 - \langle s_i^E \rangle \right) \left\langle \sum_j \left(t - \left\lfloor T_i^E \right\rfloor_j \right) \right\rangle - \frac{\langle s_i^E \rangle}{\tau_s^E}$$

$$\frac{d\langle s^I \rangle}{dt} = \left\langle \sum_j \left(t - \left\lfloor T_i^I \right\rfloor_j \right) \right\rangle - \frac{\langle s^I \rangle}{\tau_I}$$

$$\frac{d\langle s_{ext}^{E,I} \rangle}{dt} = \left\langle \sum_j \left(t - \left\lfloor T_{ext,i}^{E,I} \right\rfloor_j \right) \right\rangle - \frac{\langle s_{ext}^{E,I} \rangle}{\tau_{ext}^{E,I}}$$

Las neuronas:

$$C_m \frac{dV_i^{E,I}}{dt} = -V_i^{E,I} + I_i^{E,I}$$

$$r_i^{E,I} = 1 / \text{tiempo de primer paso por } V_{th}$$

Las conexiones:

$$I_i^E = g_{EE} (70 - \langle V_i^E \rangle) \sum_j w(i,j) \langle s_j^E \rangle - \dots$$

$$g_{IE} \langle V_i^E \rangle \langle s^I \rangle + I_{ext}^E$$

$$I^I = g_{EI} (70 - \langle V^I \rangle) \frac{1}{N_E} \sum_j \langle s_j^E \rangle - \dots$$

$$g_{II} \langle V^I \rangle \langle s_j^I \rangle + I_{ext}^I$$

Excitación externa:

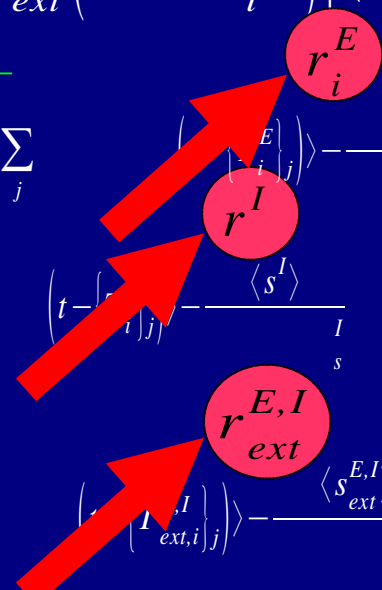
$$I_{ext}^{E,I}(t) = g_{ext}^{E,I} (70 - V_i^{E,I}) \left[\langle s_{ext}^{E,I} \rangle + \frac{E,I}{ext} (t) \right]$$

Las sinapsis:

$$\frac{d\langle s_i^E \rangle}{dt} = (1 - \langle s_i^E \rangle) \left\langle \sum_j \left(\frac{1}{\tau_{ij}^E} - \frac{\langle s_j^E \rangle}{\tau_{ij}^E} \right) \right\rangle - \frac{\langle s_i^E \rangle}{\tau_s^E}$$

$$\frac{d\langle s^I \rangle}{dt} = \left\langle \sum_j \left(\frac{1}{\tau_{ij}^I} - \frac{\langle s_j^I \rangle}{\tau_{ij}^I} \right) \right\rangle - \frac{\langle s^I \rangle}{\tau_s^I}$$

$$\frac{d\langle s_{ext}^{E,I} \rangle}{dt} = \left\langle \sum_j \left(\frac{1}{\tau_{ext,i}^{E,I}} - \frac{\langle s_{ext,i}^{E,I} \rangle}{\tau_{ext,i}^{E,I}} \right) \right\rangle - \frac{\langle s_{ext}^{E,I} \rangle}{\tau_{ext}^{E,I}}$$



Estado estacionario:

$$\langle s_i^E \rangle_\infty = \frac{E}{s} r_i^E / \left(1 + \frac{E}{s} r_i^E \right)$$

$$\langle s^I \rangle_\infty = \frac{I}{s} r^I$$

$$\langle s_{ext}^{E,I} \rangle_\infty = \frac{ext}{ext} r_{ext}^{E,I}$$

$$\frac{E,I}{ext} = \sqrt{\frac{r_{ext}^{E,I}}{ext}}$$

Las neuronas:

$$r_i^{E,I} = \frac{1}{\int_{\left(I_i^{E,I}, E, I\right)}^{\left(I_{ref}^{E,I} + \frac{E, I}{m}, E, I\right)} du \sqrt{\quad} \exp\left(u^2\right) \left[1 + \operatorname{erf}\left(u\right)\right]}$$

(Ricciardi 1977, Brunel and Sergi J. Theor Biol 1998)

Las conexiones:

$$I_i^E = G_{EE} \sum_j W(i-j) \langle s_j^E \rangle - G_{IE} \langle s^I \rangle + G_{ext}^E \langle s_{ext}^E \rangle$$

$$I_i^I = G_{EI} \frac{1}{N_E} \sum_j \langle s_j^E \rangle - G_{II} \langle s^I \rangle + G_{ext}^I \langle s_{ext}^I \rangle$$

$$r_{ext}^{E,I} = G_{ext}^{E,I} \sqrt{r_{ext}^{E,I}}$$

Las sinapsis:

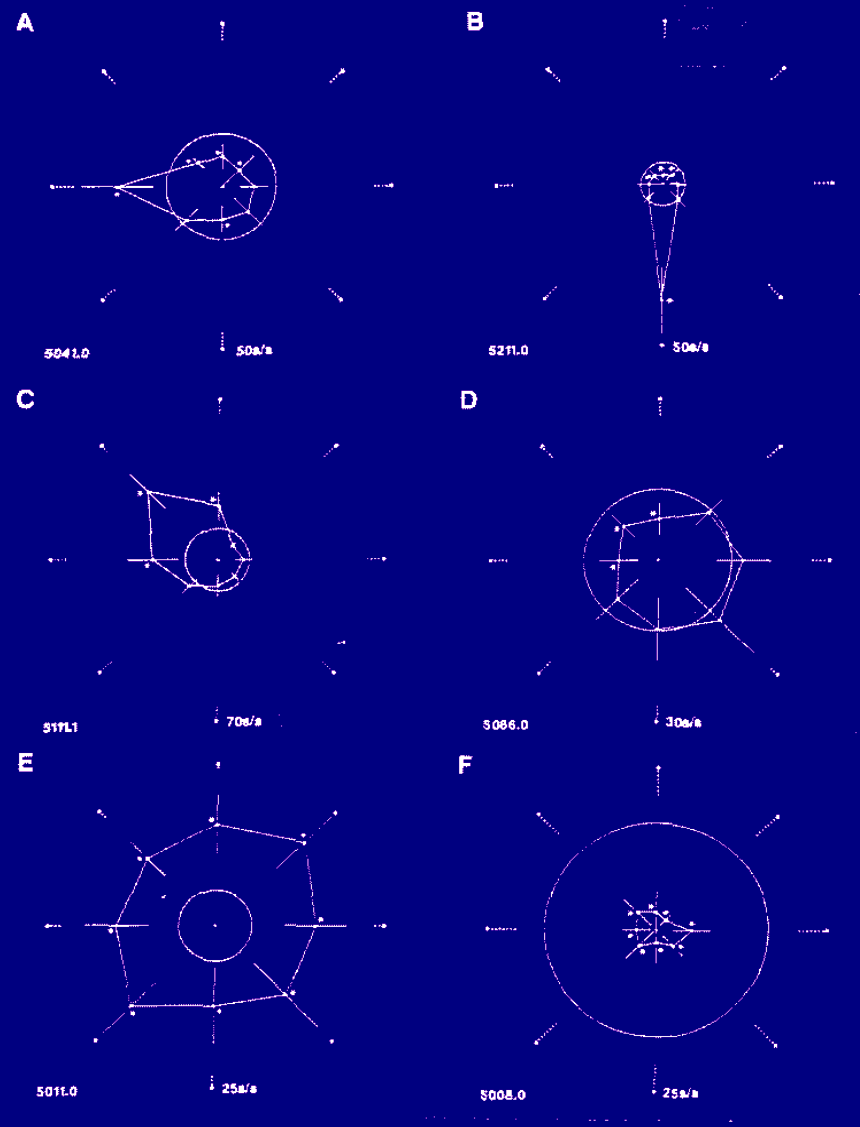
$N_E + 1$ ecs.

$$\frac{d\langle s_i^E \rangle}{dt} = \frac{\langle s_i^E \rangle_\infty - \langle s_i^E \rangle}{\tau_{Es}}$$

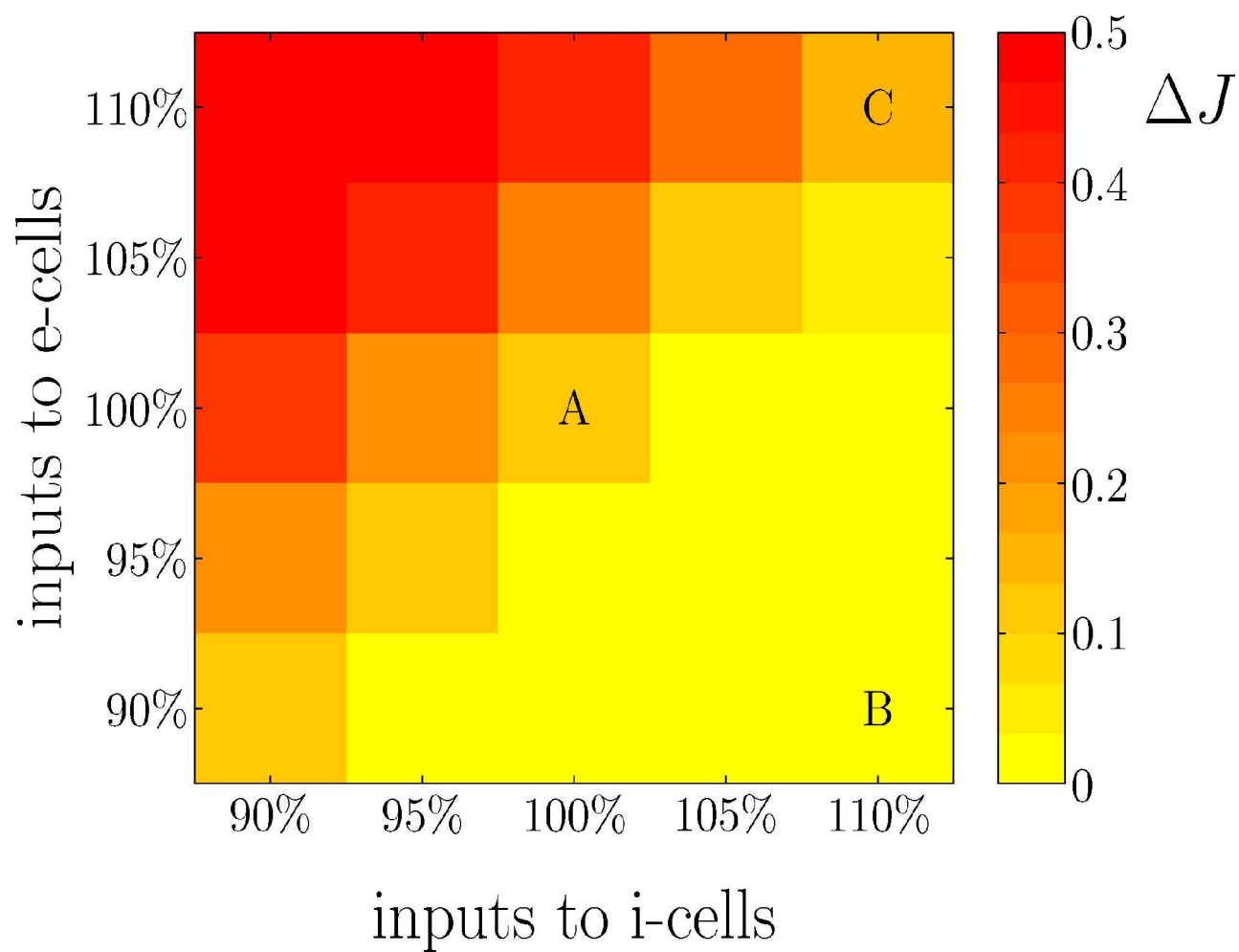
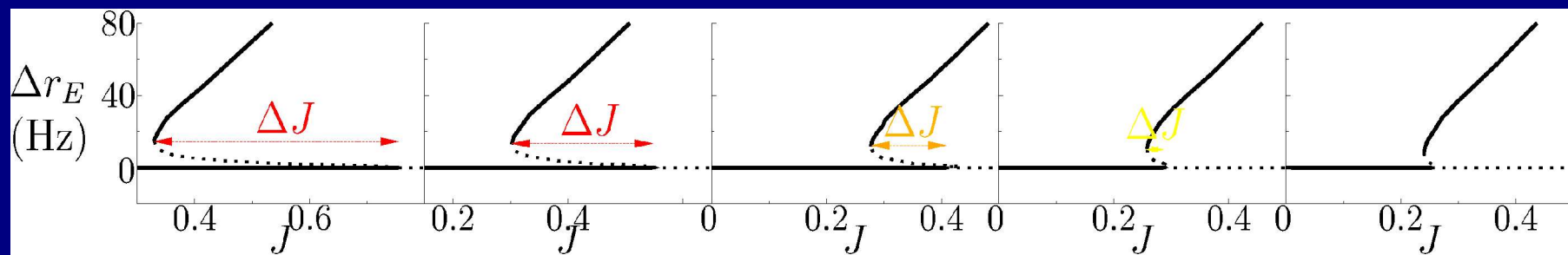
$$\langle s_i^E \rangle_\infty = \frac{\tau_s^E r_i^E}{\left(1 + \tau_s^E r_i^E\right)}$$

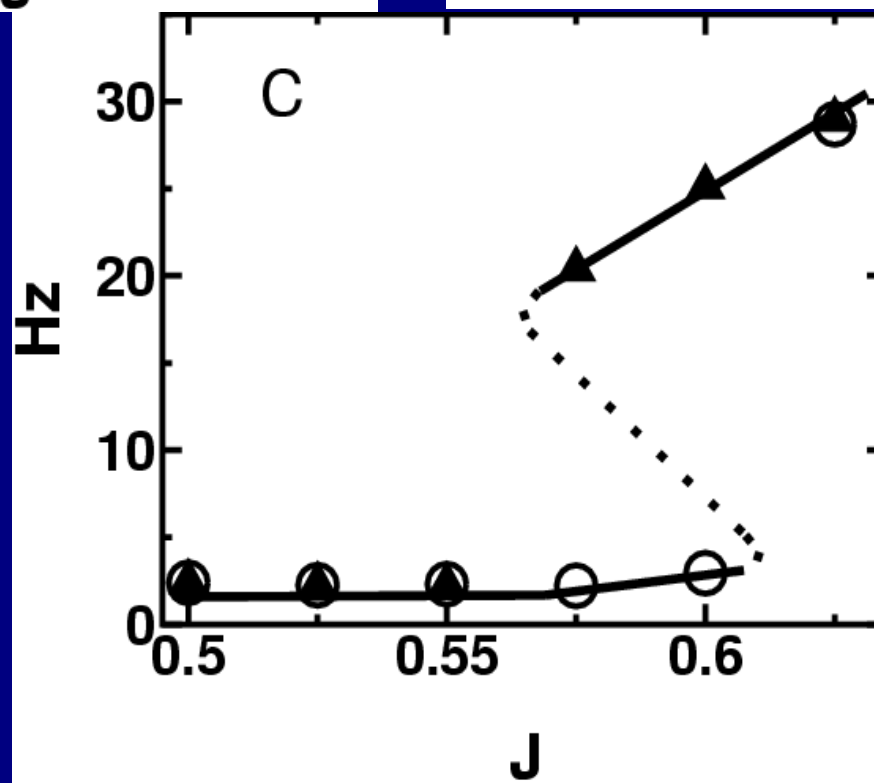
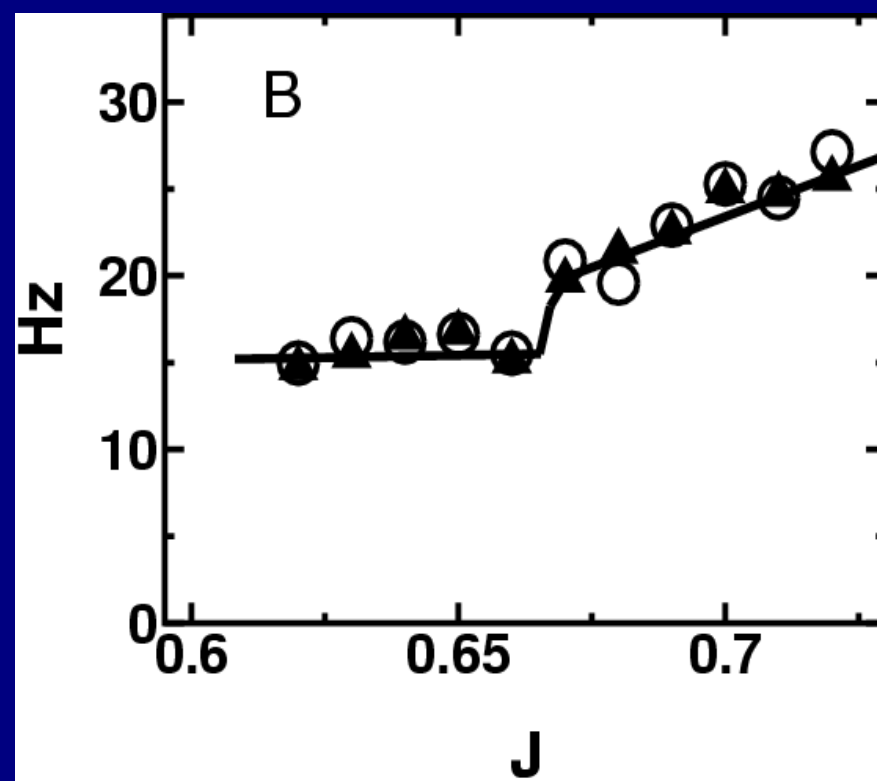
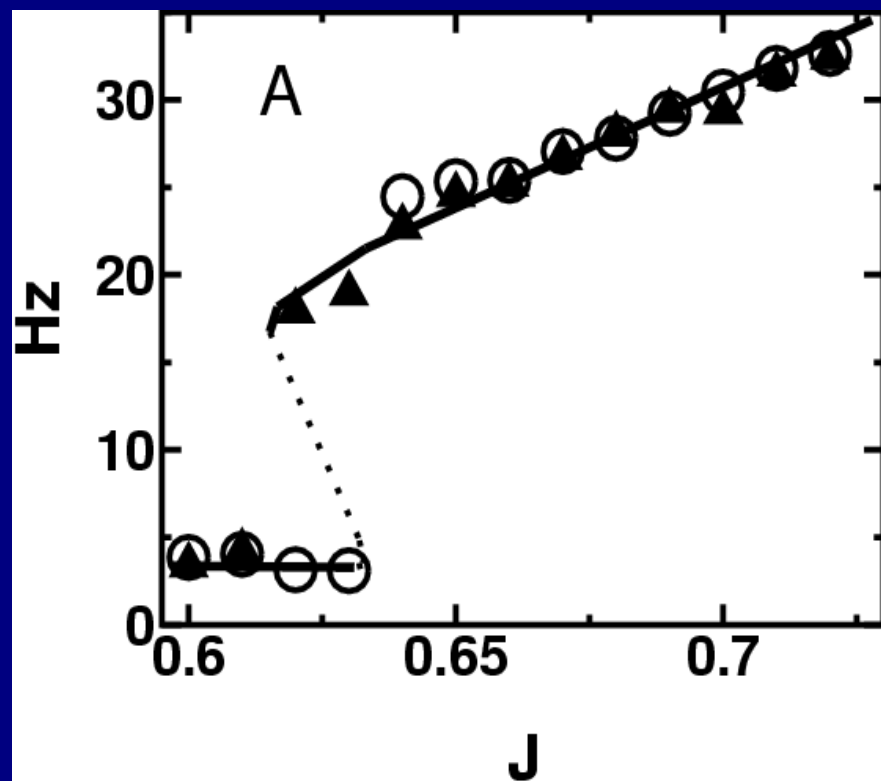
$$\frac{d\langle s^I \rangle}{dt} = \frac{\langle s^I \rangle_\infty - \langle s^I \rangle}{\tau_{Is}}$$

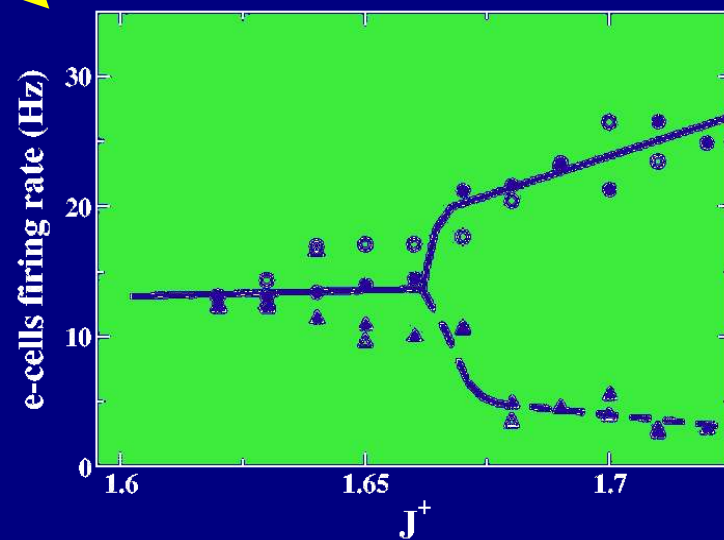
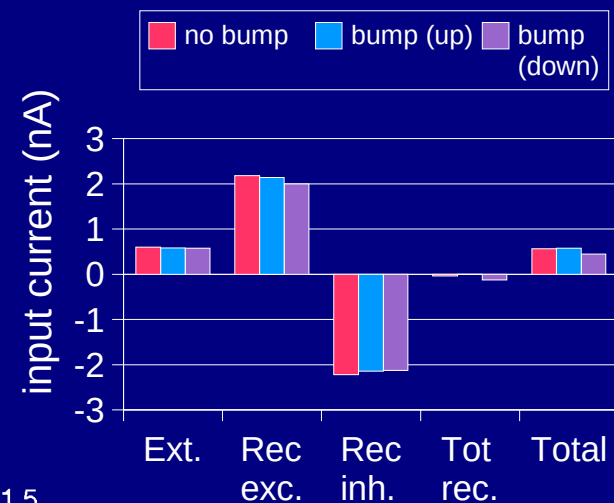
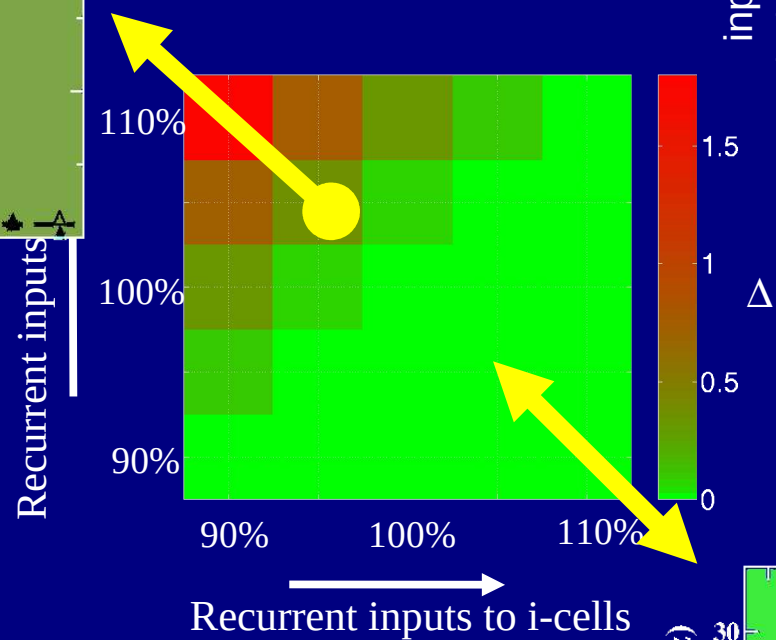
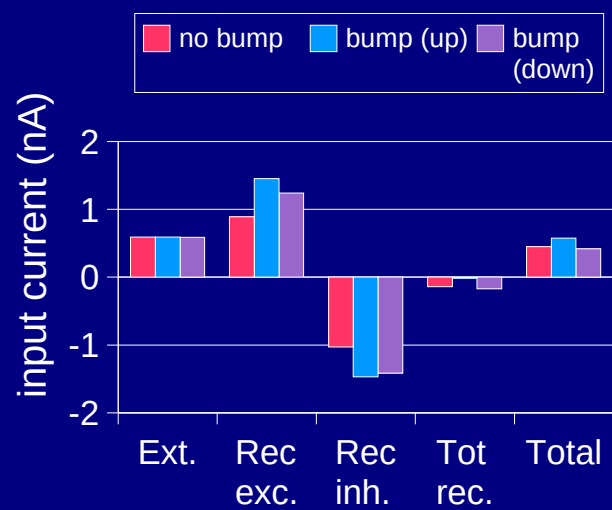
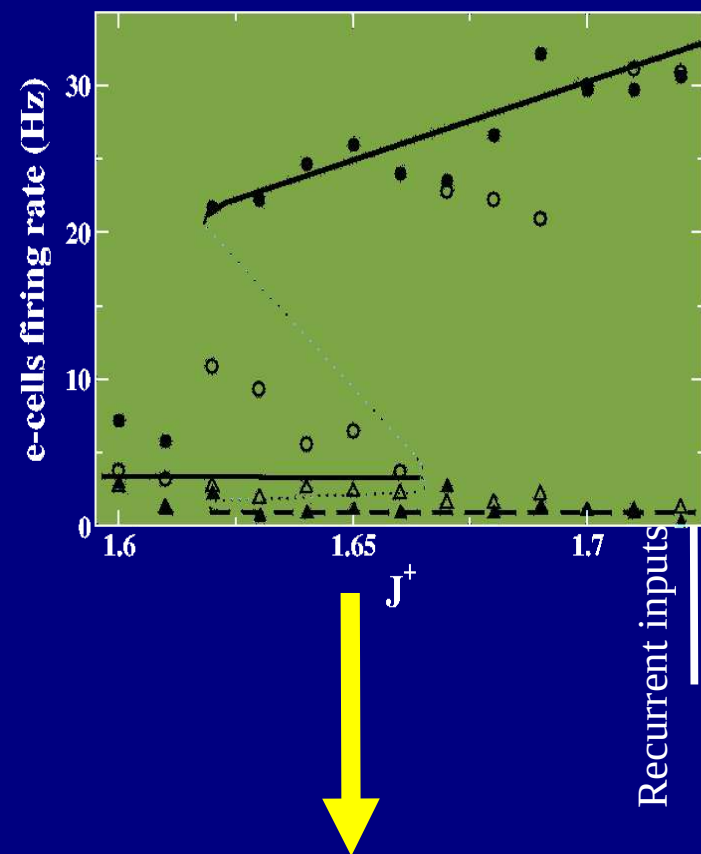
$$\langle s^I \rangle_\infty = \tau_s^I r^I$$



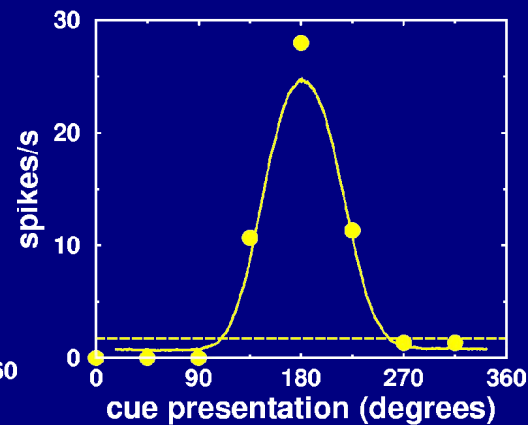
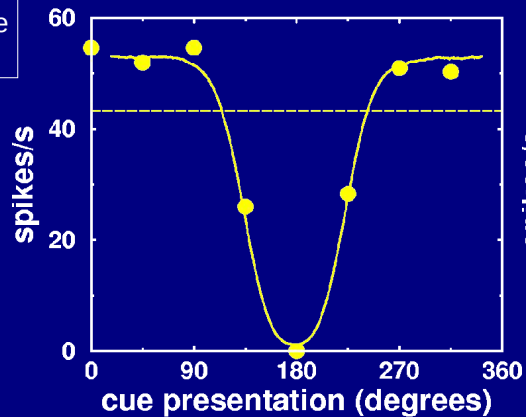
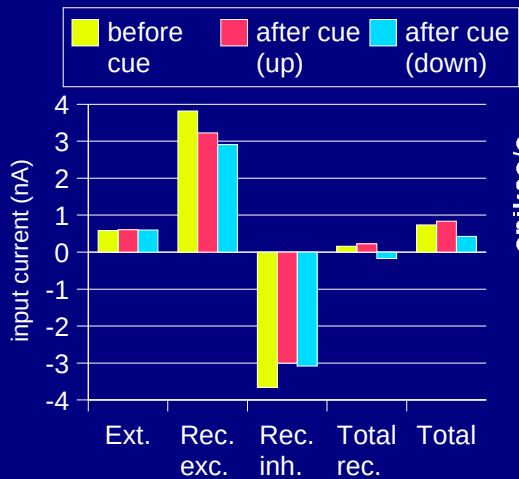
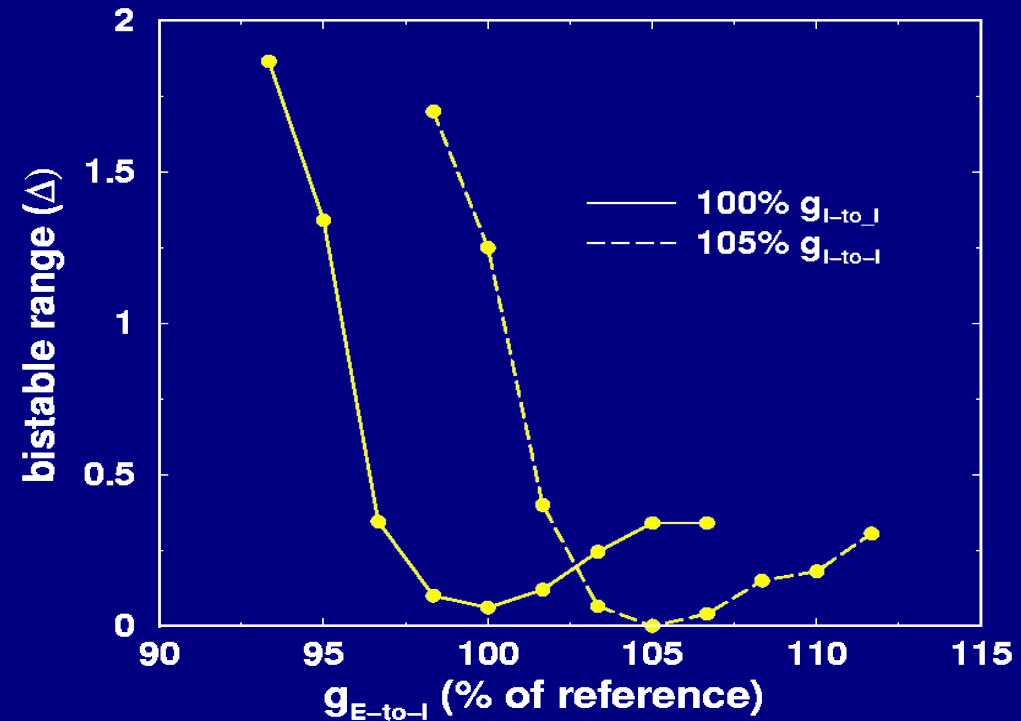
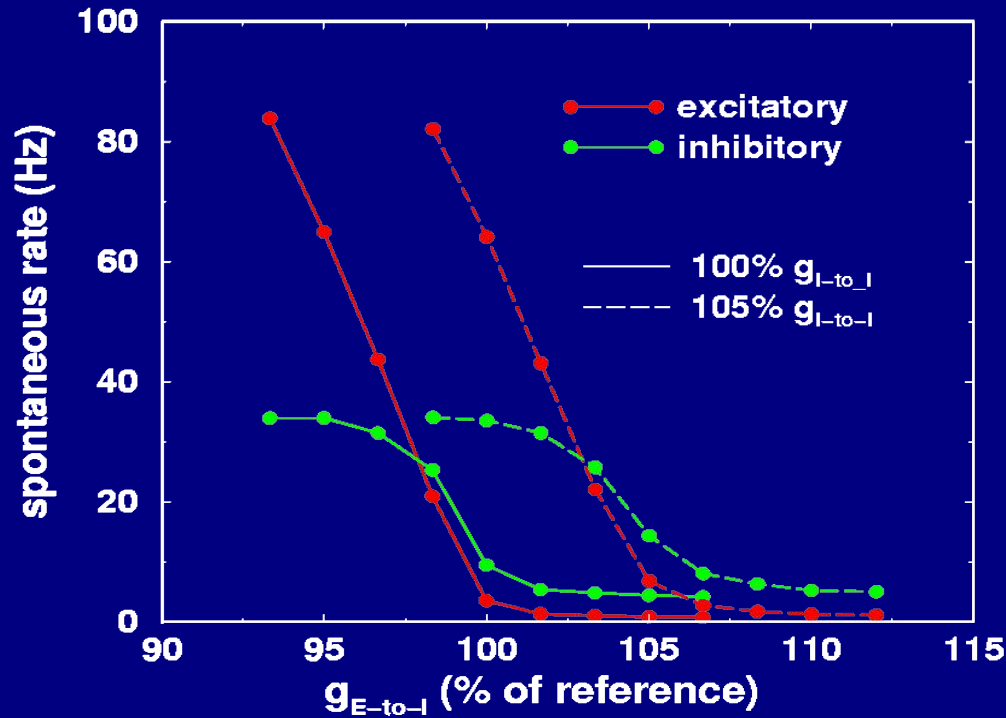
Funahashi *et al.*, J. Neurophysiol. 61, 331 (1989)

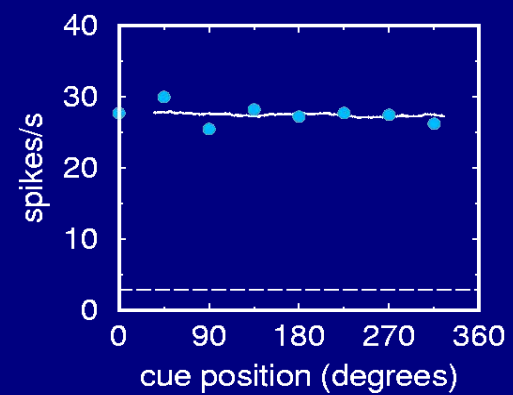
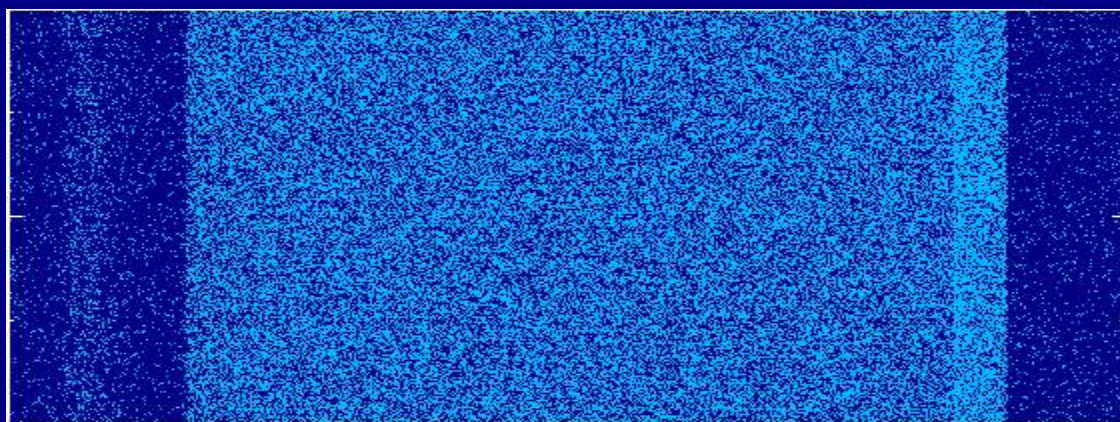
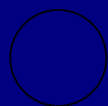
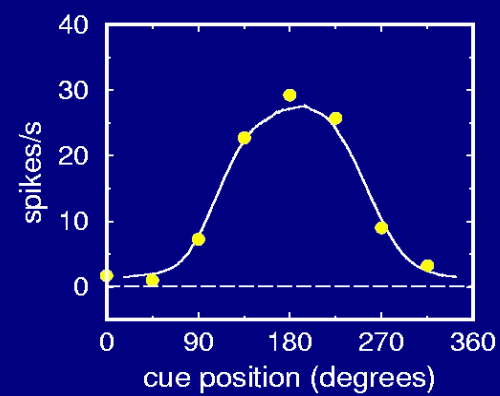
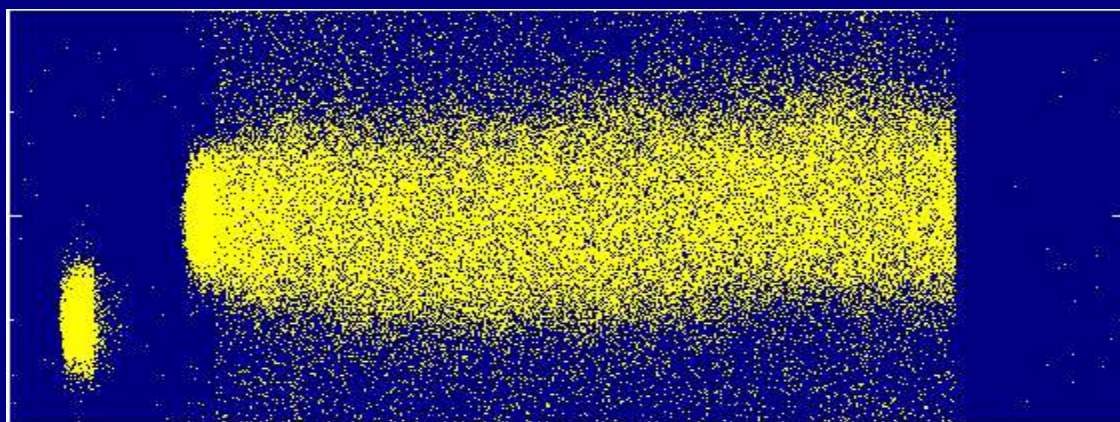
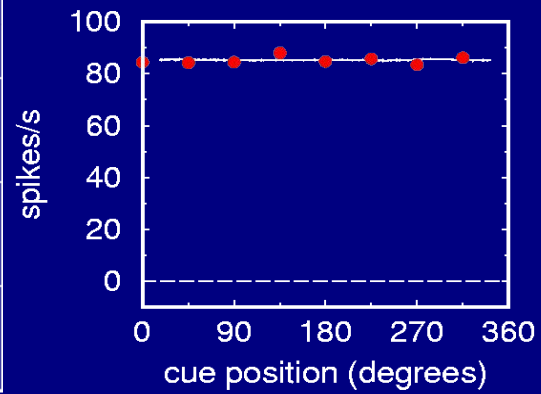
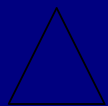






Inhibition





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