

Búsqueda de multiestabilidad en redes neuronales (caóticas)

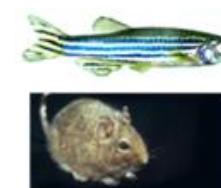
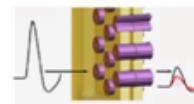
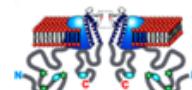
Patricio Orio Álvarez

Centro Interdisciplinario de Neurociencia de Valparaíso CINV
Universidad de Valparaíso



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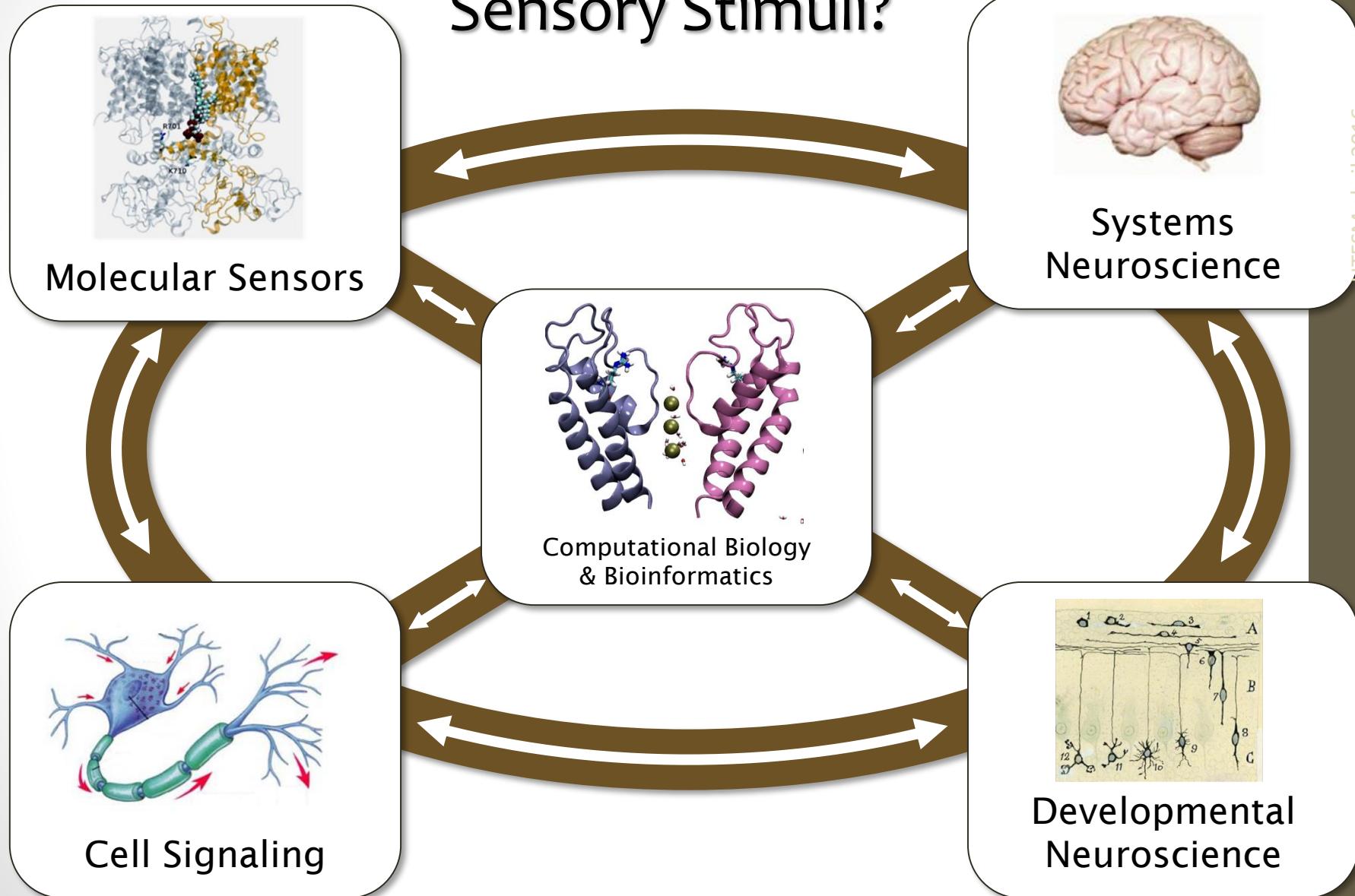
- Principal Investigator
 - Ramón Latorre
- Deputy Principal Investigator
 - Alan Neely
- Associated Investigators
 - Ana María Cárdenas
 - John Ewer
 - David Naranjo
 - Adrián Palacios
 - Kathleen Whitlock
 - Fernando González-Nilo
 - Tomás Pérez-Acle
 - Juan C. Sáez
- 9 Adjunct Researchers



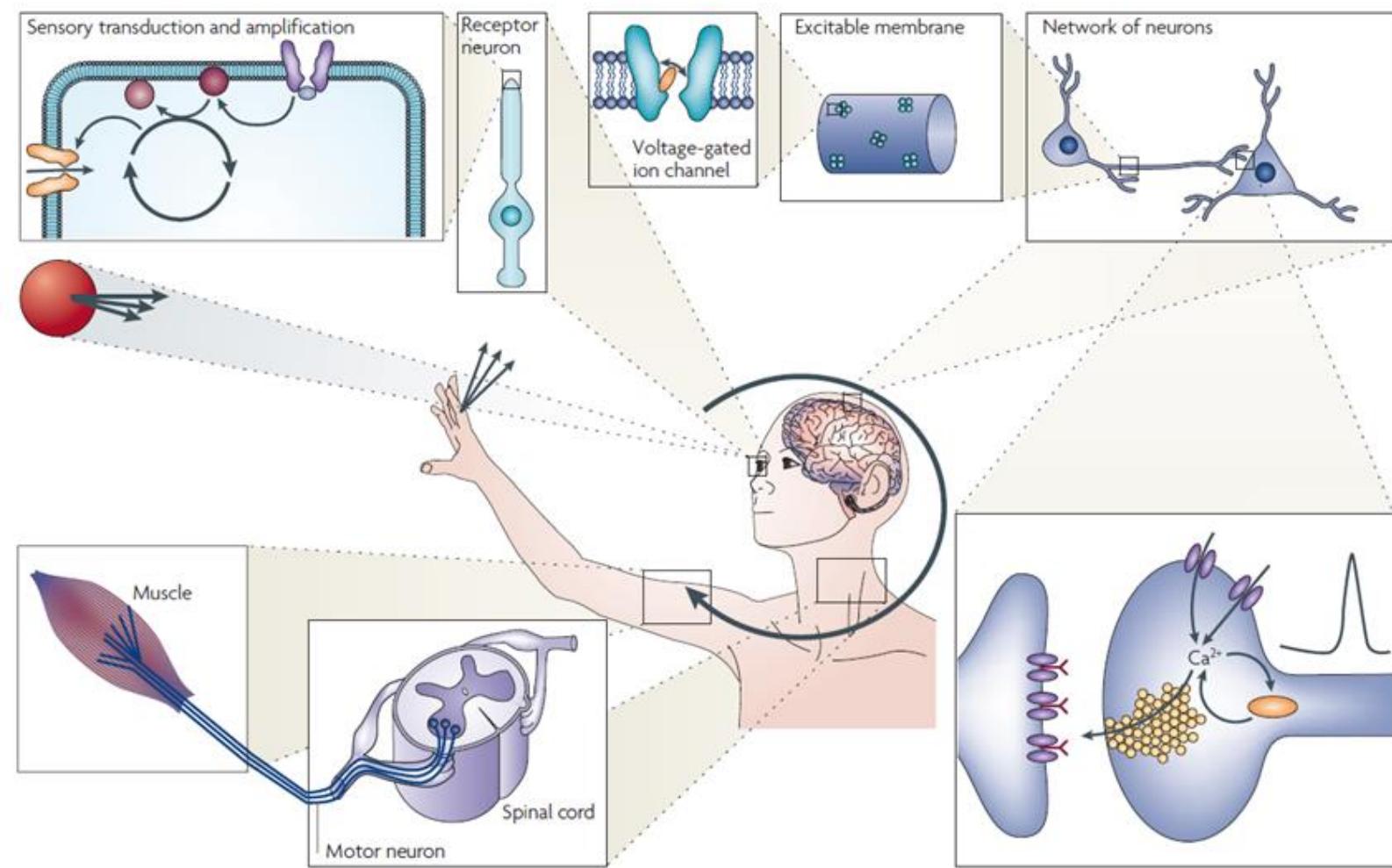
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Main Research Topic

How does the Nervous System respond to Sensory Stimuli?

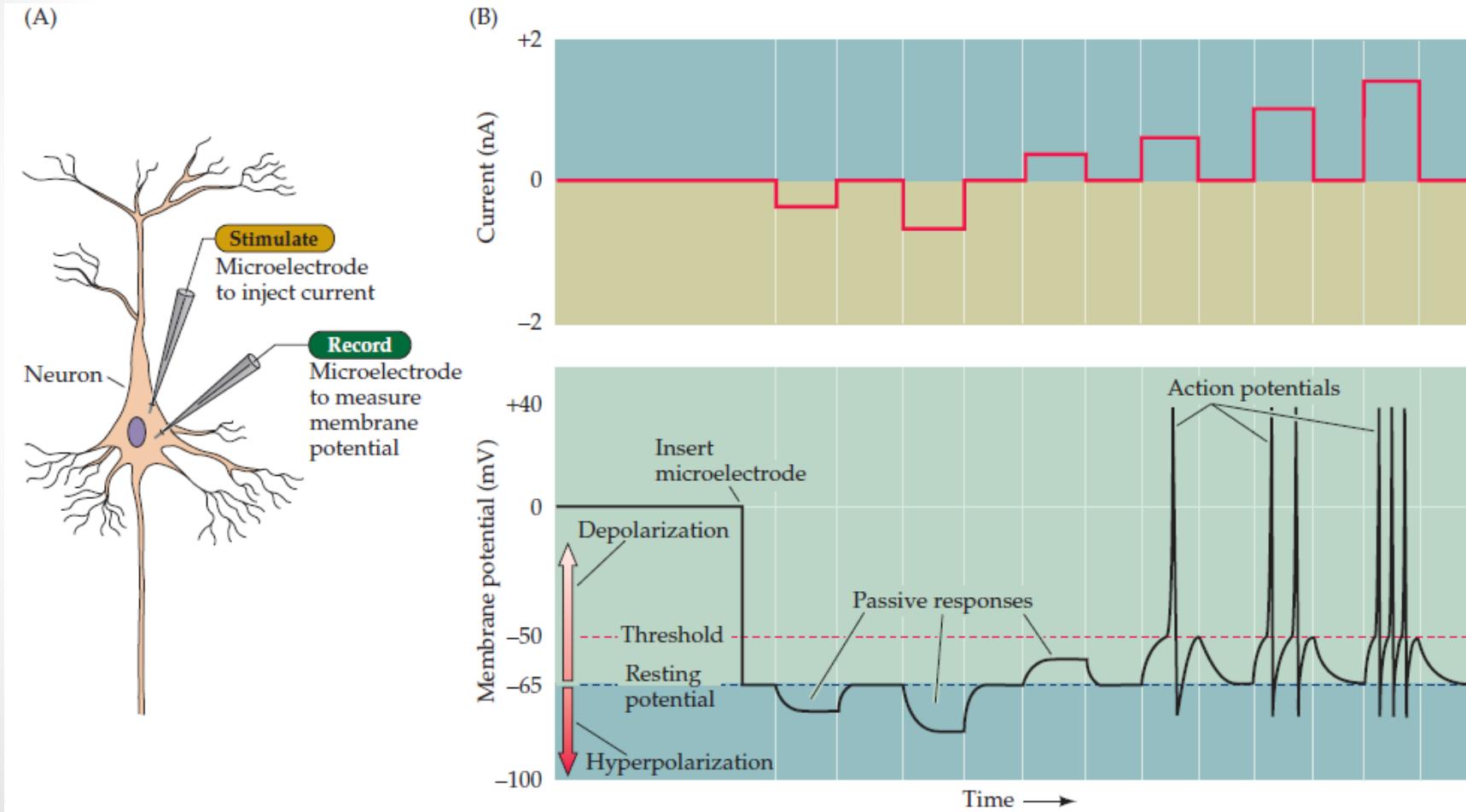


El sistema nervioso

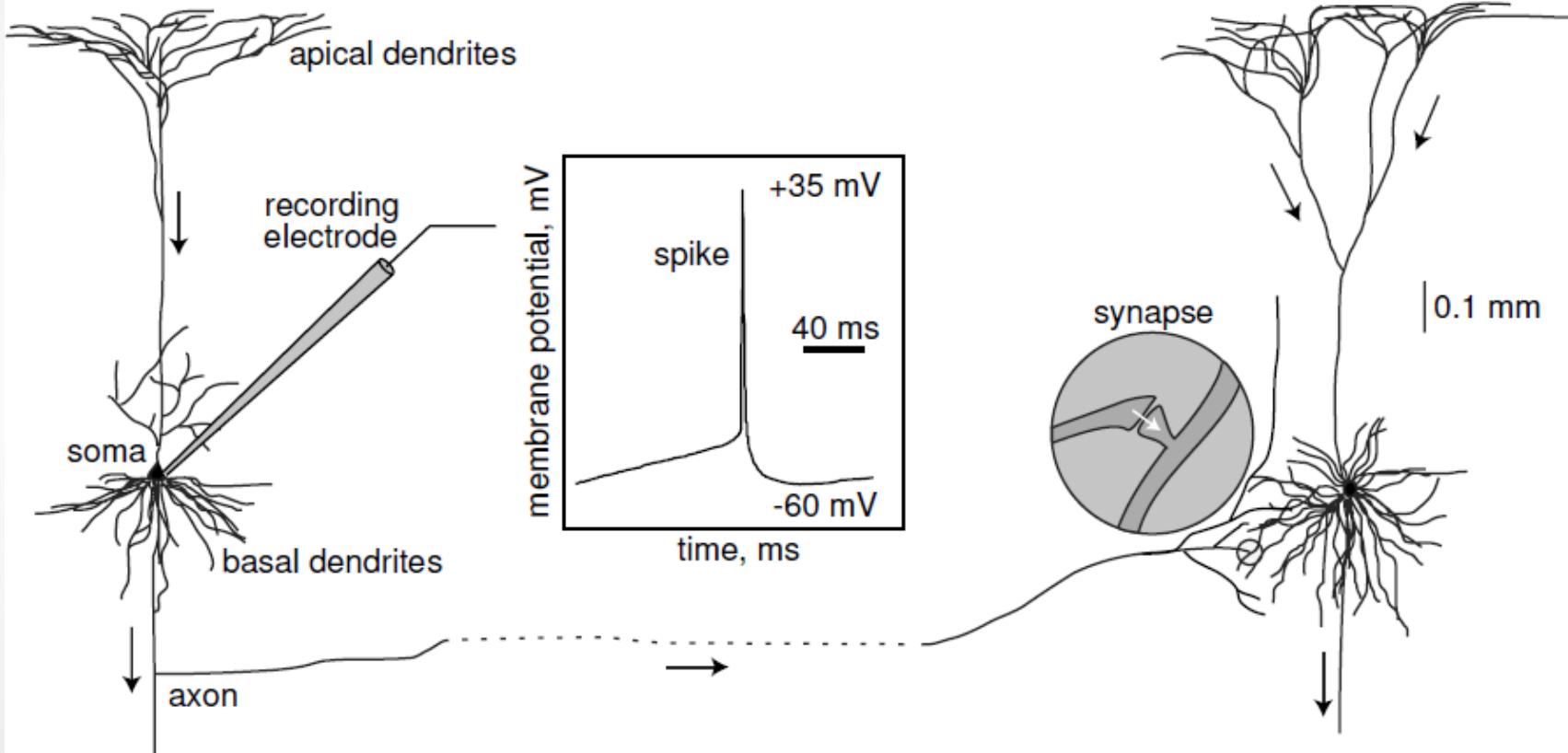


Adaptado de: Faisal A.A., Selen L. & Wolpert D.M.(2008). Noise in the nervous system. *Nat Rev Neurosci* 9:292-303

Neuronas y Potencial de Acción

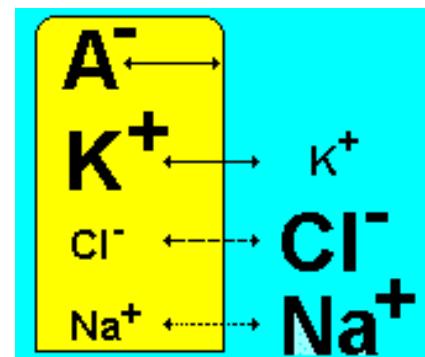
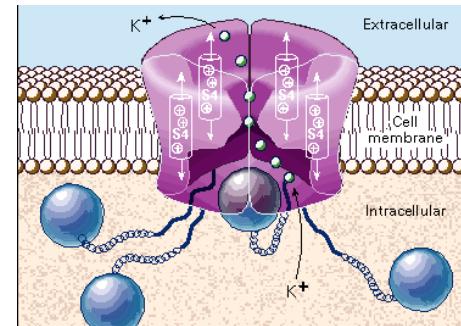
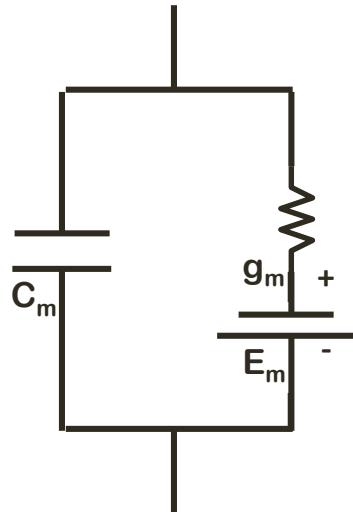
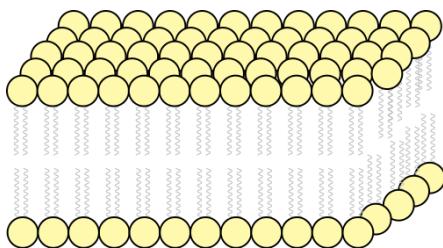


Propagación y transmisión sináptica



Origen de la excitabilidad

- Circuito Equivalente



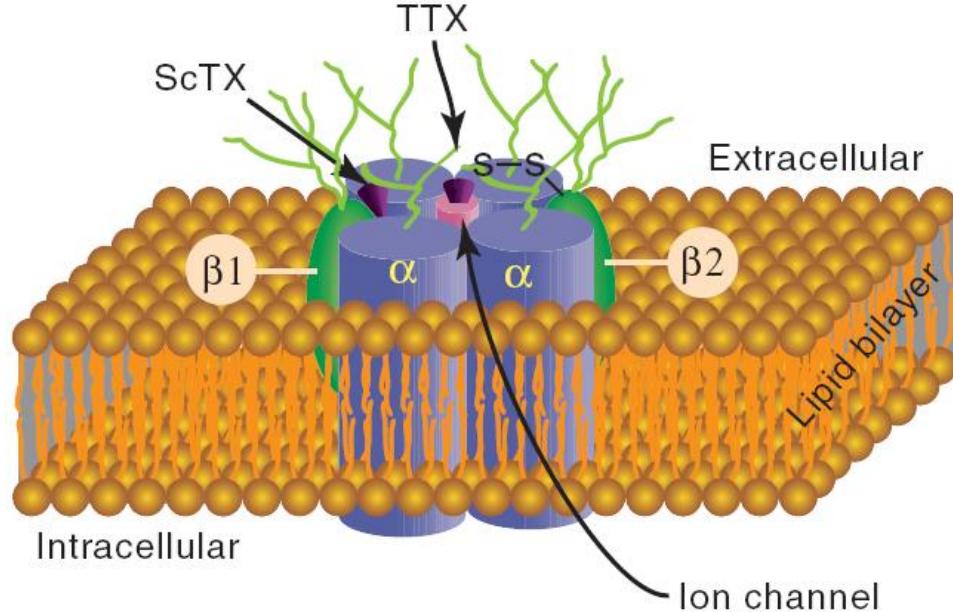
$$I_{memb} = I_C + I_{ion}$$

$$I_{memb} = C_m \frac{dV}{dt} + g_m(V - E_m)$$

$$C_m \frac{dV}{dt} = -g_m(V - E_m) + I_{ext}$$

Potenciales de acción ‘reales’

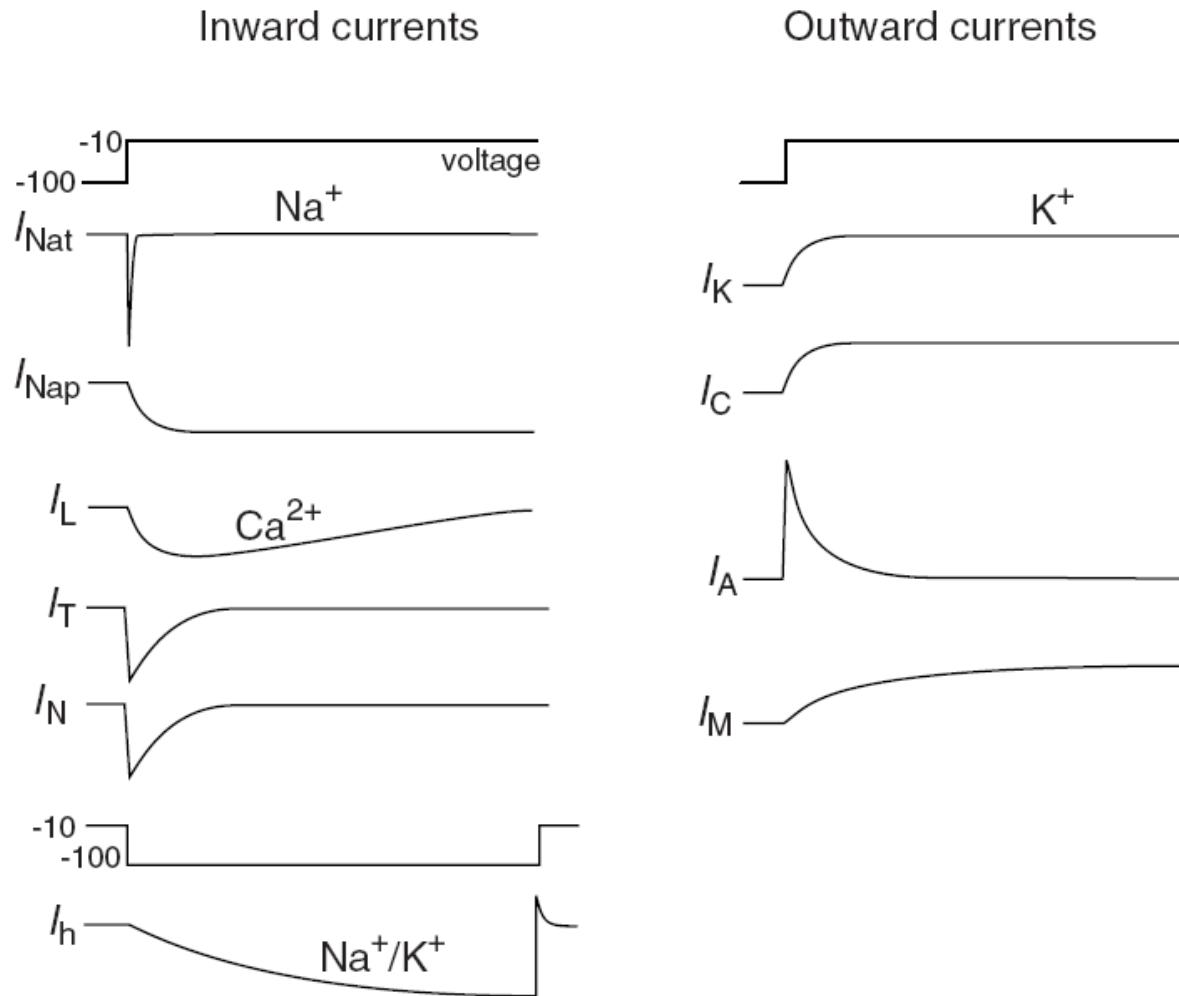
- Canales iónicos dependientes de voltaje



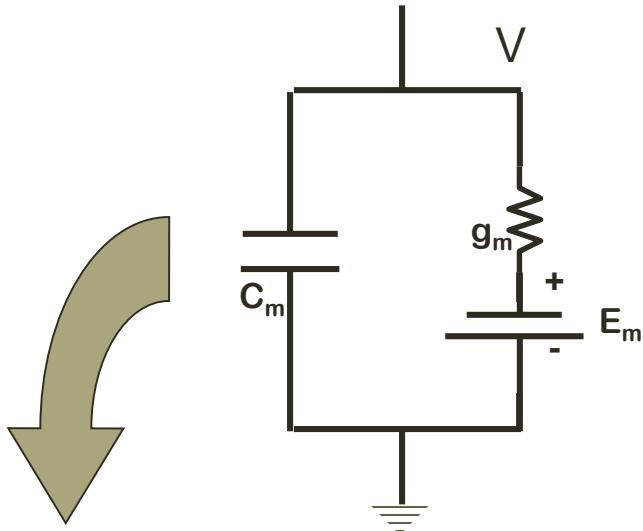
- Na^+
 - K^+
 - Ca^{2+}
 - Cl^-
 - Catiónicos
-
- Activados por despolarización
 - Activados por hiperpolarización
 - Inactivación

Canales dependientes de voltaje

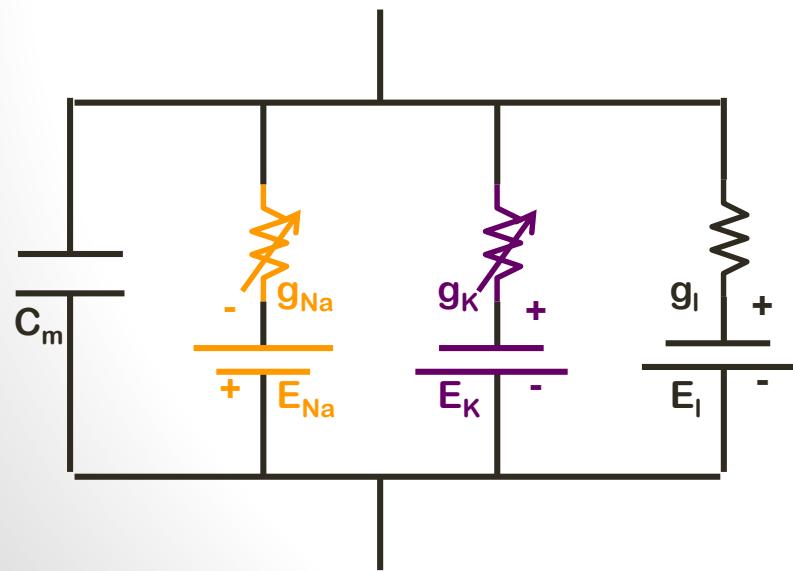
- La respuesta al voltaje no es instantánea



Incorporando canales ‘realistas’



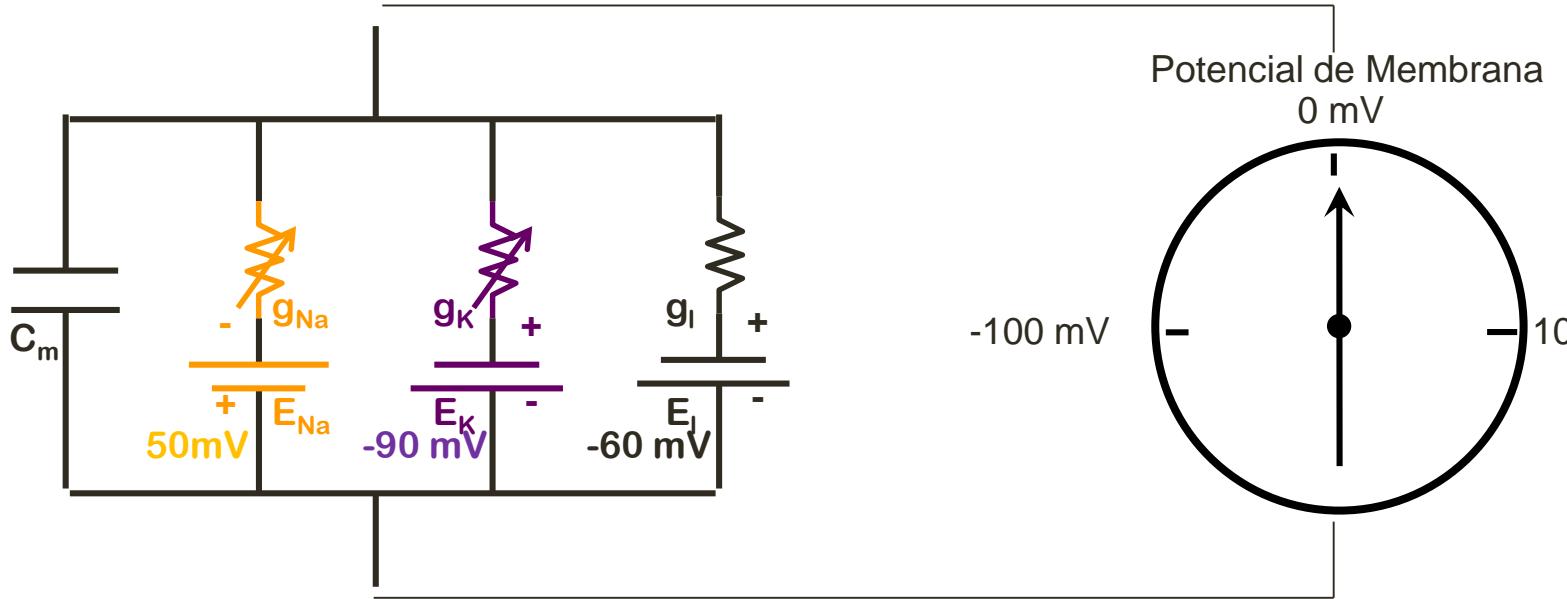
$$C_m \frac{dV}{dt} = -g_m(V - E_m) + I_{ext}$$



$$C_m \frac{dV}{dt} = - \sum_{i=K,Na,\dots} g_i(V - E_i) + I_{ext}$$

$$C_m \frac{dV(t)}{dt} = - \sum_i g_i(V, t)(V(t) - E_i) + I_{ext}(t)$$

Incorporando canales ‘realistas’



$$C_m \frac{dV}{dt} = - \sum_i g_i (V - E_i)$$

$$\frac{dV}{dt} = 0 \Rightarrow V_{eq} = \frac{\sum g_i E_i}{\sum g_i}$$

Ecuaciones de Hodgkin y Huxley

$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l),$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n,$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m,$$

$$C_M \frac{dV}{dt} = f(V, m, h, n)$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h,$$

$$\frac{dn}{dt} = g(V, n)$$

$$= 0.01 (V -$$

Canales de potasio dependientes de voltaje

$$\frac{dm}{dt} = j(V, m)$$

$$\beta_n = 0.$$

$$\frac{dh}{dt} = k(V, h)$$

$$\beta_m = 0.1 (V -$$

Canales de sodio dependientes de voltaje

$$\beta_m = 4$$

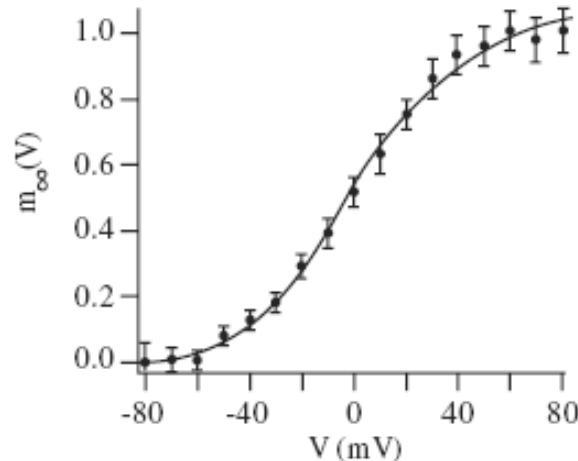
$$\alpha_h = 0.07 \exp(V/20),$$

$$\beta_h = 1 / \left(\exp \frac{V + 30}{10} + 1 \right).$$

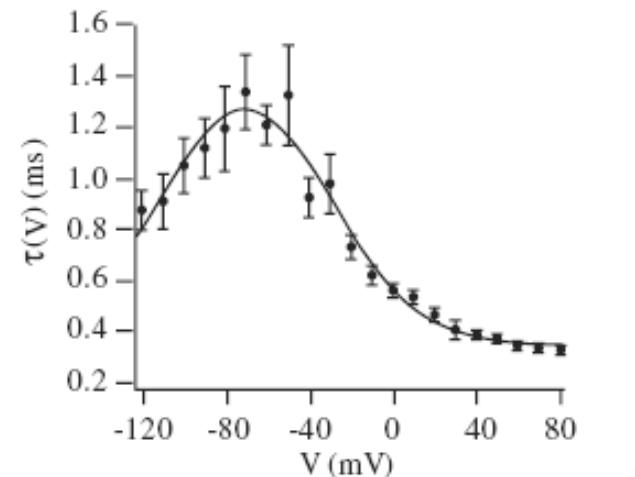
Modelando canales

$$I = C_m \frac{dV_m}{dt} + \sum_i g_i (V_m - E_i)$$

$$\frac{dO_i}{dt} = \frac{O_{i\infty}(V) - O_i}{\tau_i(V)}$$

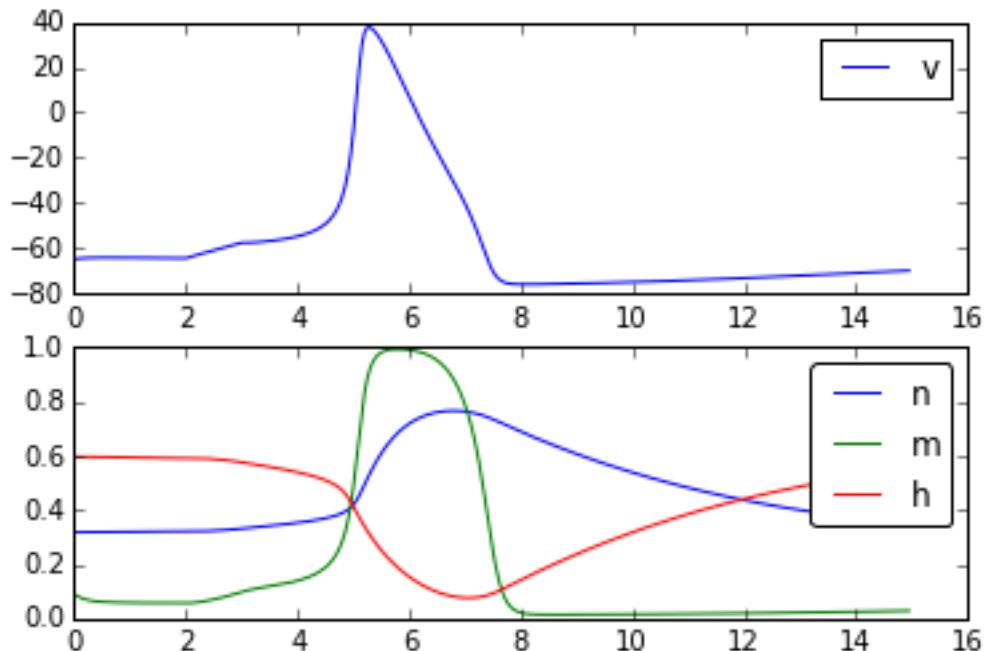


$$O_\infty(V) = P_{(O)}(V) = \frac{1}{1 + e^{\frac{-(V - V_{1/2})}{k}}}$$

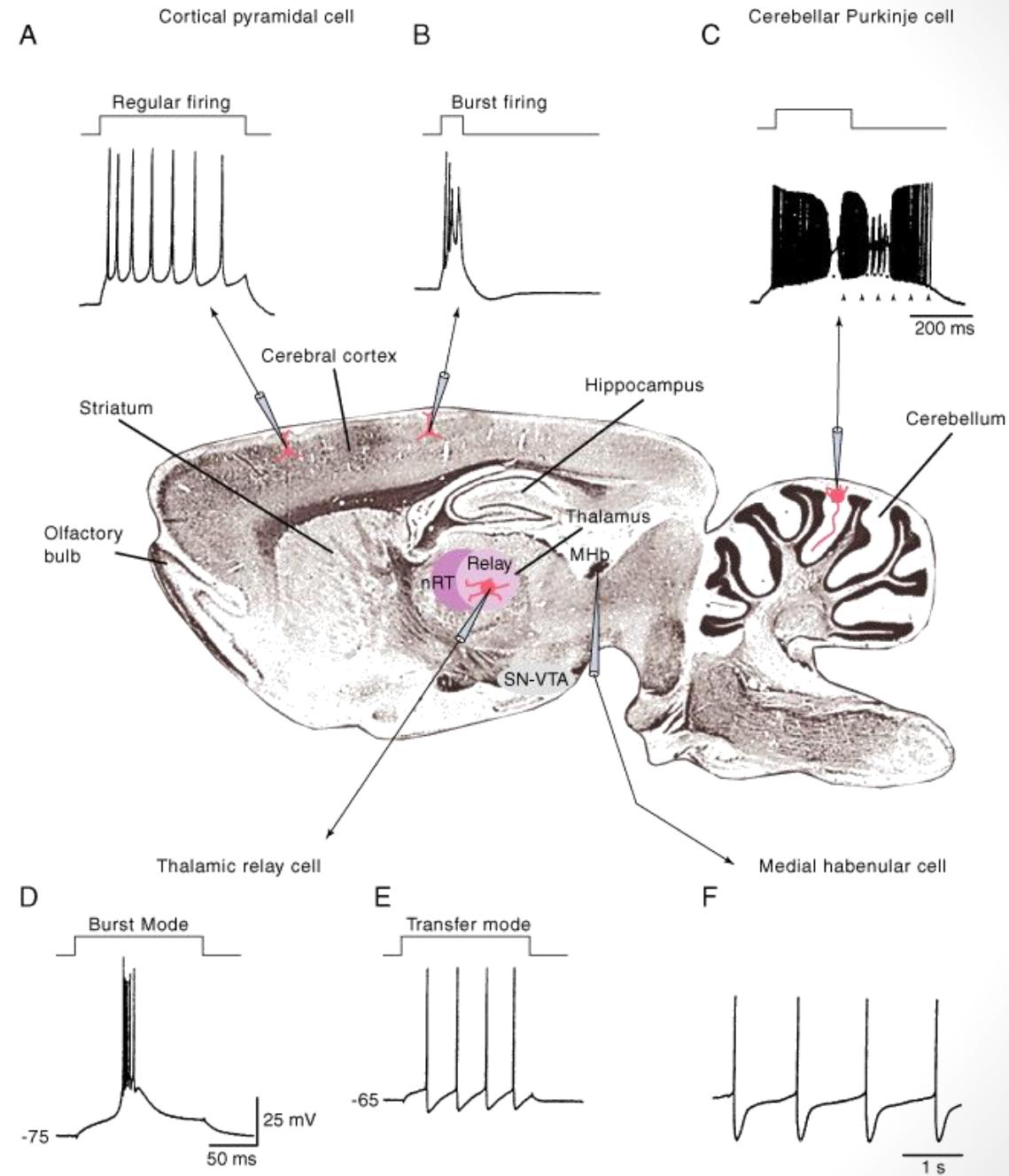


$$\tau(V) = C + Ae^{\frac{-(V_{\max} - V)^2}{\sigma^2}}$$

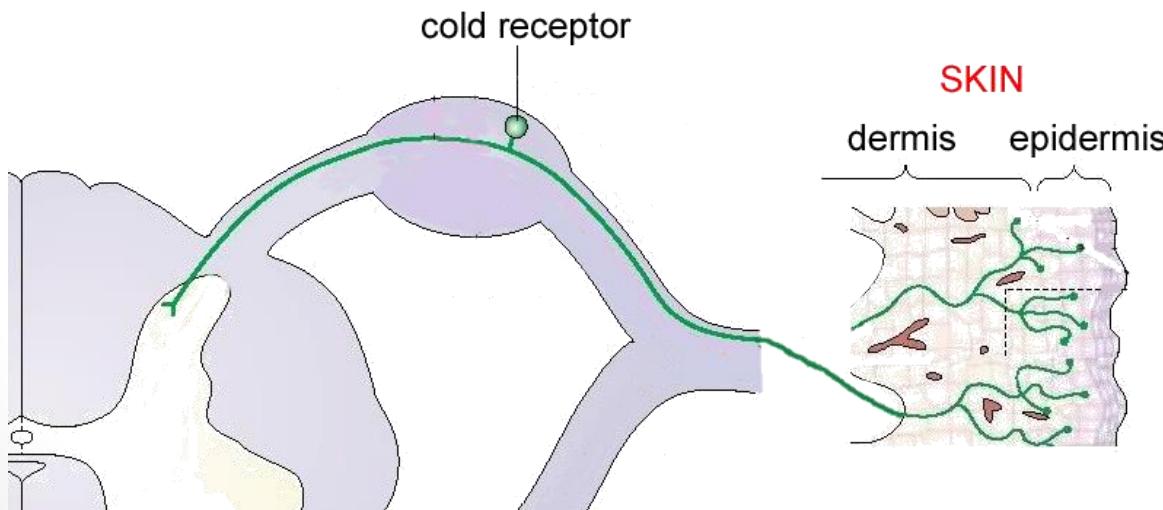
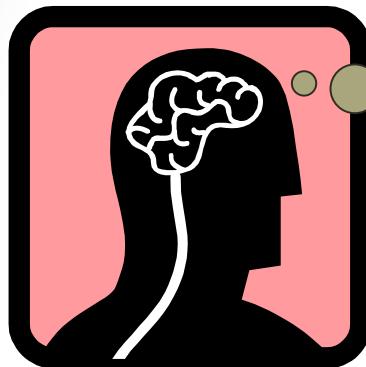
Modelo de H&H



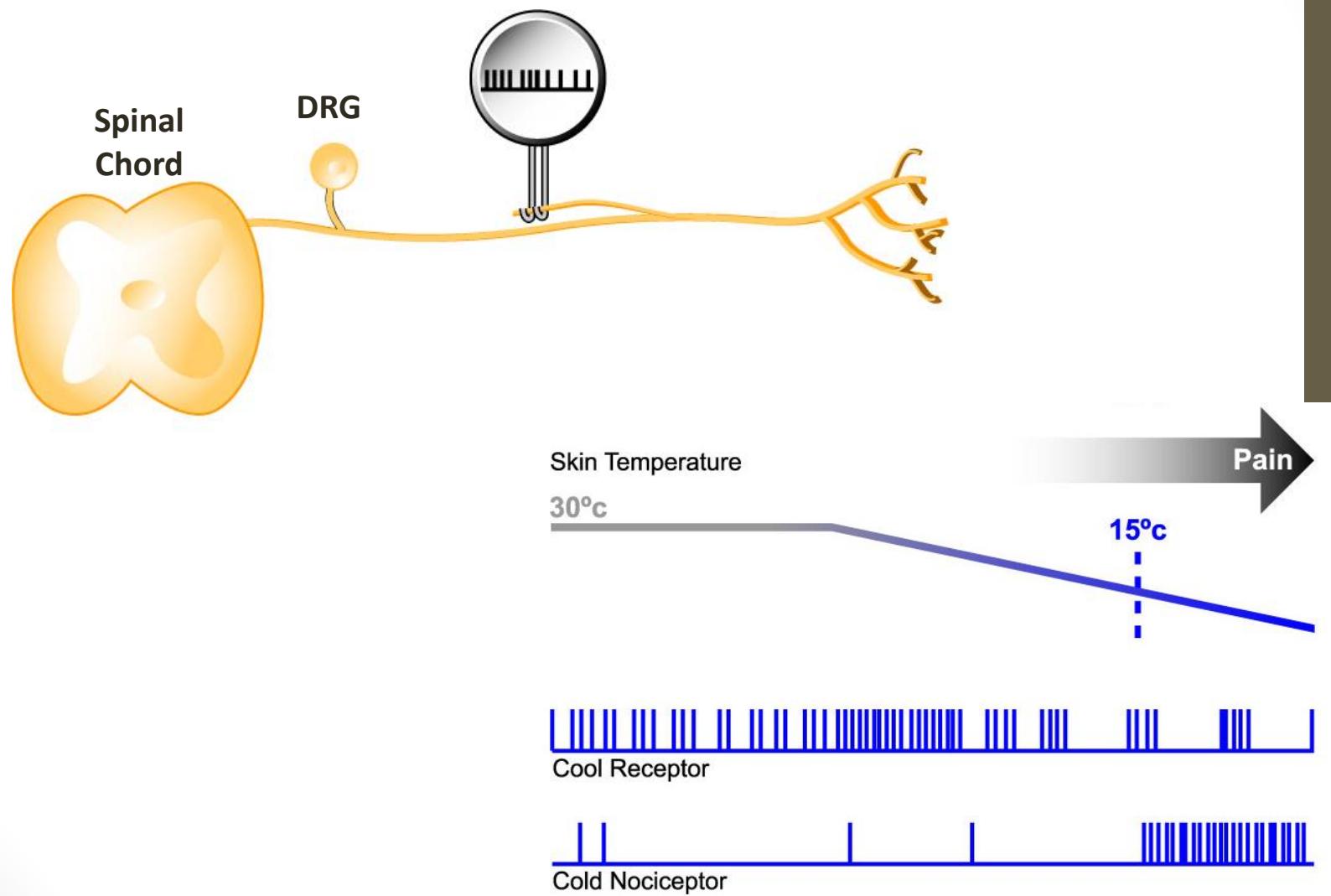
Diversidad de neuronas, diversidad de canales



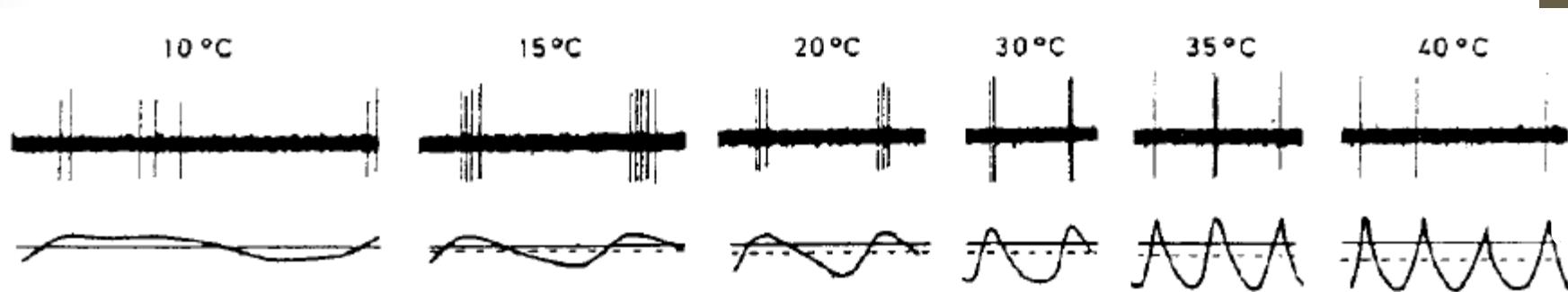
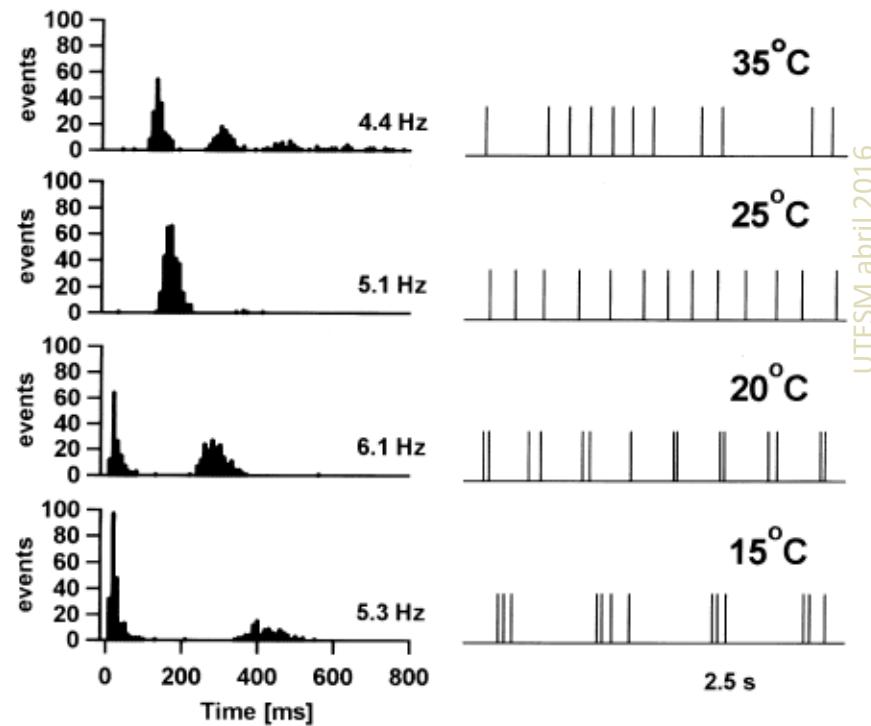
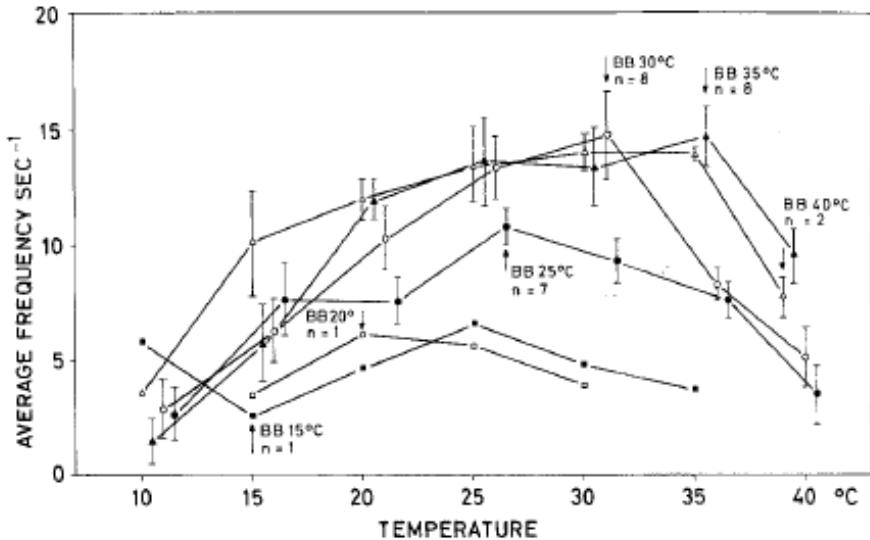
Terminaciones nerviosas sensibles a frío



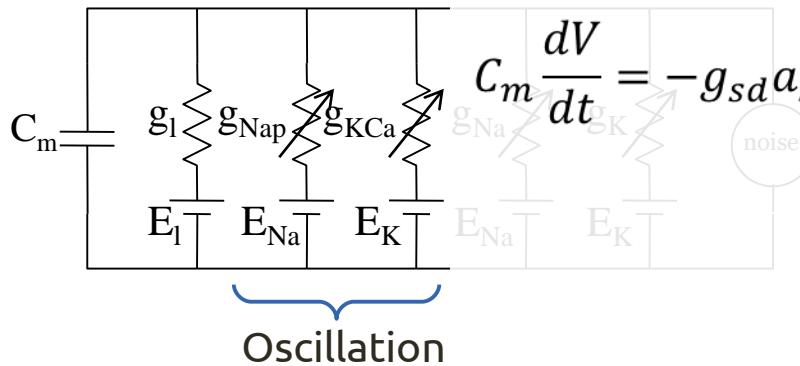
Cold Sensitive Nerve endings and fibers



Static Temperature Coding



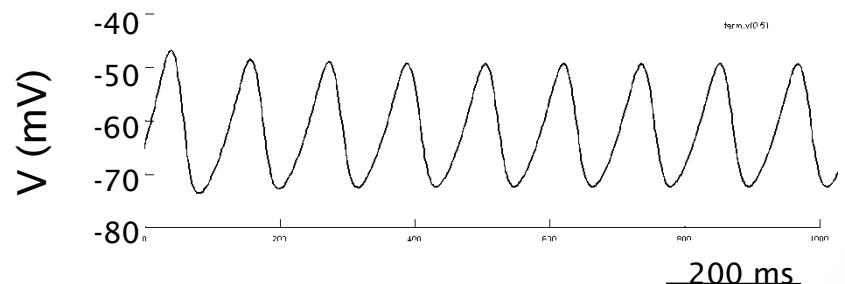
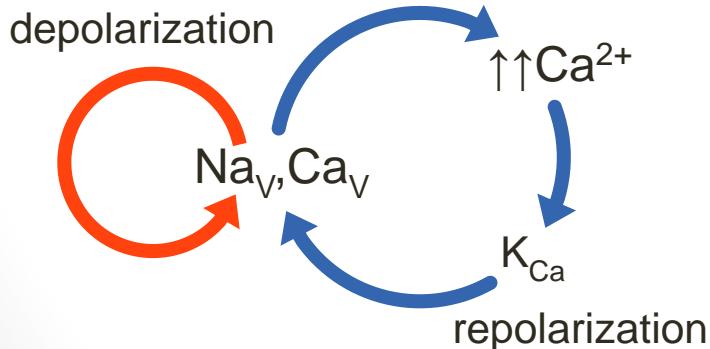
Huber & Braun's model of cold-modulated oscillation



$$C_m \frac{dV}{dt} = -g_{sd}a_{sd}(V - E_{Na}) - g_{sr}a_{sr}(V - E_K) - g_l(V - E_l)$$

$$\frac{da_{sd}}{dt} = \varphi_T \frac{a_{sd}^\infty - a_{sd}}{\tau_{sd}}$$

$$\frac{da_{sr}}{dt} = \varphi_T \frac{\eta I_{sd} - \kappa a_{sr}}{\tau_{sr}}$$

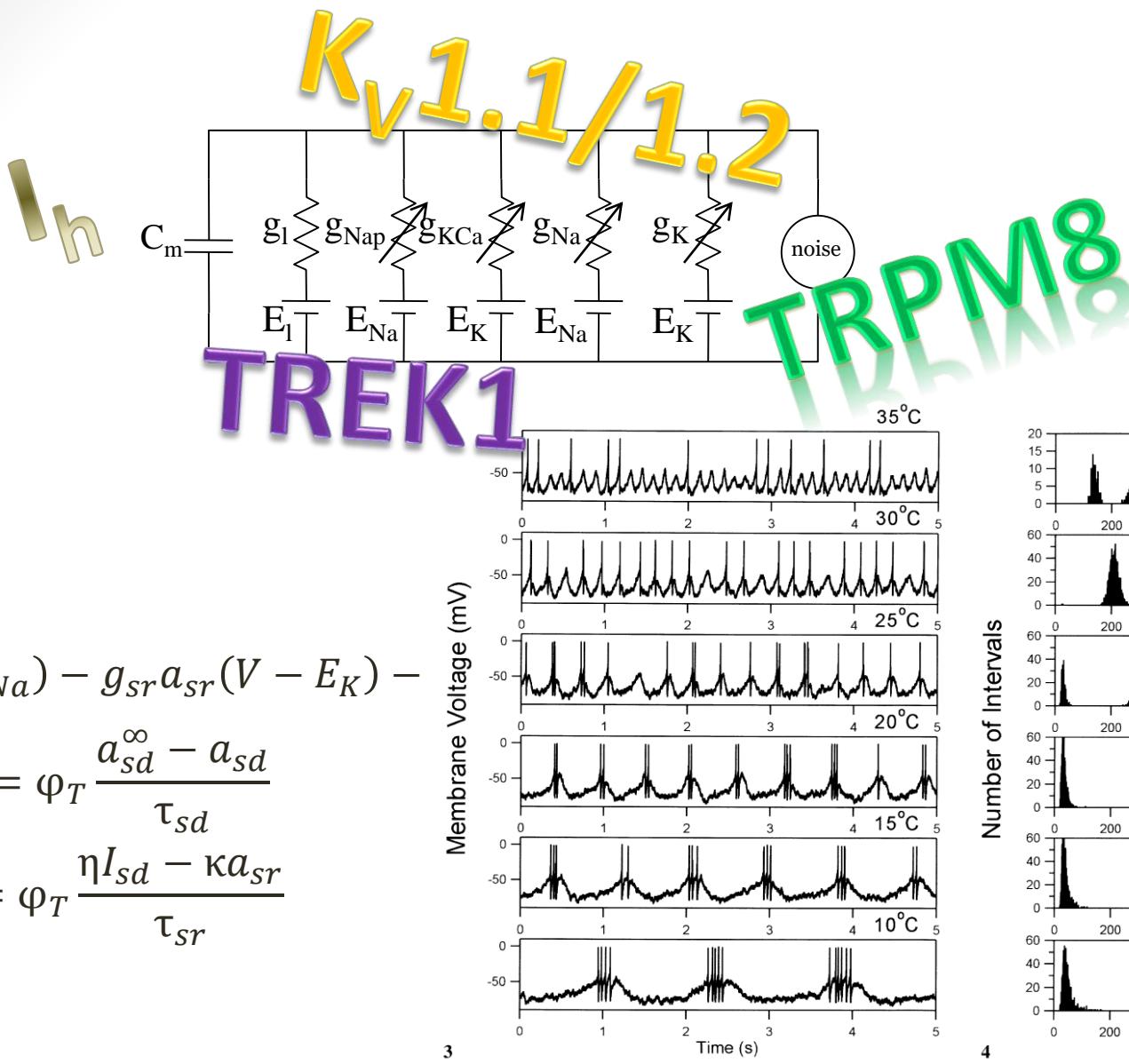


Braun, H.A. *et al* (1998) Int. J. Bif. Chaos
 Huber, M.T. *et al* (2000) Chaos Sol. Fract.

$$da_{sd}(V - E_{Na}) - g_{sr}a_{sr}(V - E_K) -$$

$$\frac{da_{sd}}{dt} = \varphi_T \frac{a_{sd}^\infty - a_{sd}}{\tau_{sd}}$$

$$\frac{da_{sr}}{dt} = \varphi_T \frac{\eta I_{sd} - \kappa a_{sr}}{\tau_{sr}}$$



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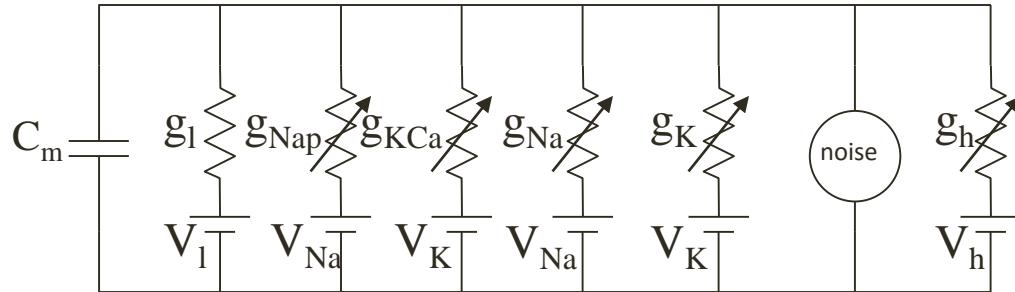
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Braun, H.A. et al (1998) Int. J. Bif. Chaos
 Huber, M.T. et al (2000) Chaos Sol. Fract.

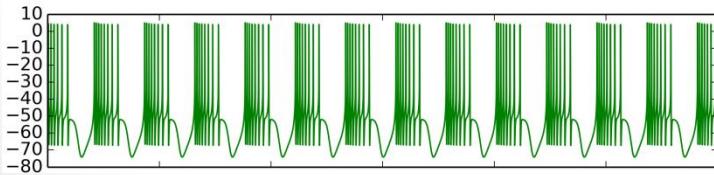
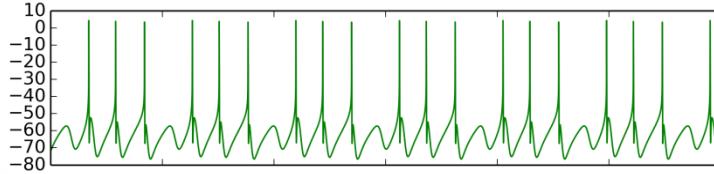
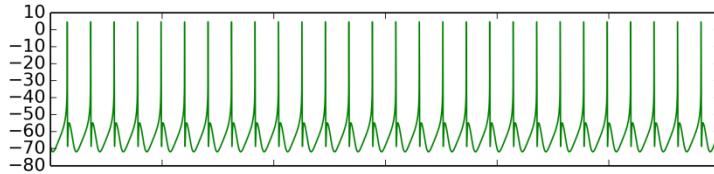
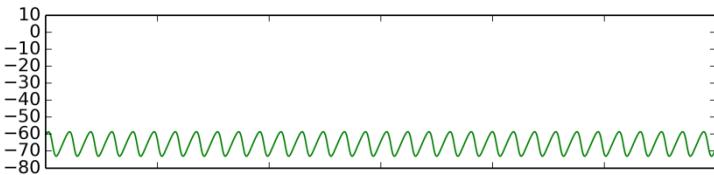
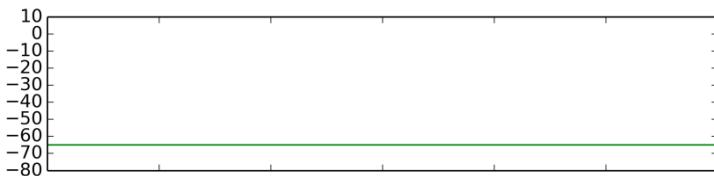
Huber-Braun + Ih model



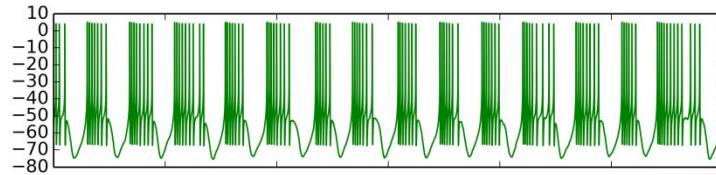
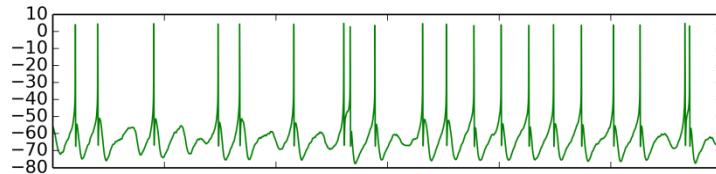
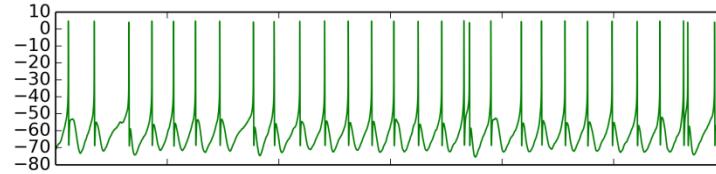
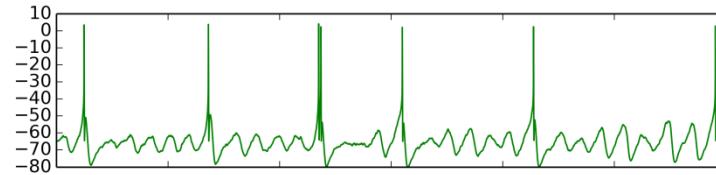
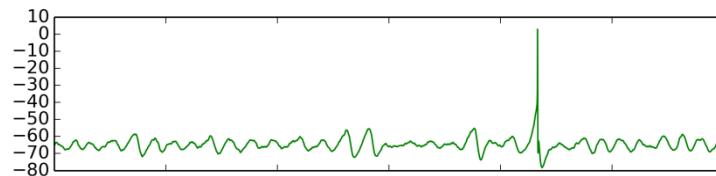
- Experimental results obtained with HCN1^(-/-) mice are better explained by a compensation with the related channel HCN2.
- Kinetics of HCN1 give the oscillations the right period.

Modos de disparo del modelo

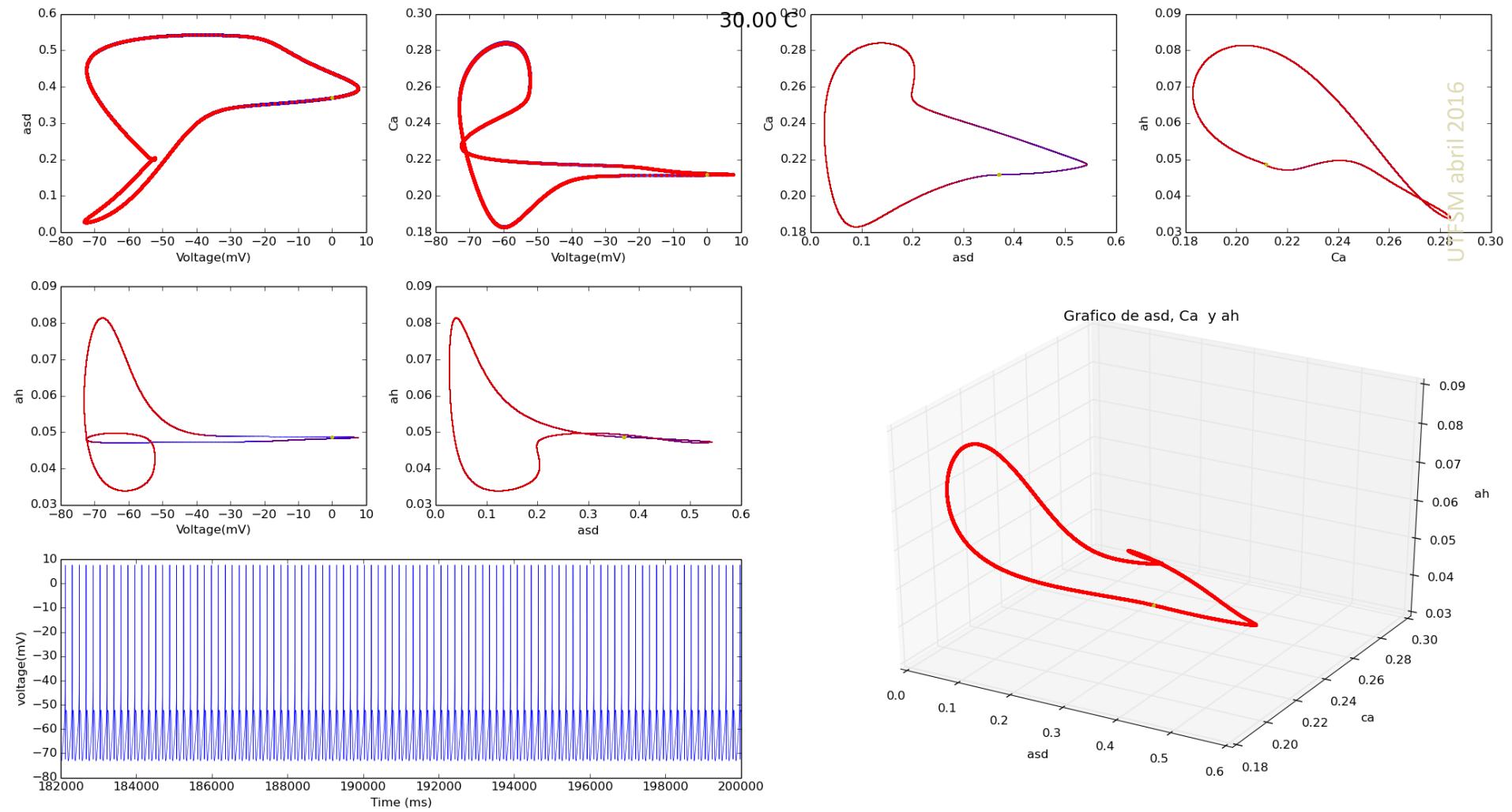
Simulación determinista



Simulación estocástica



Ongoing work: characterizing chaotic dynamics



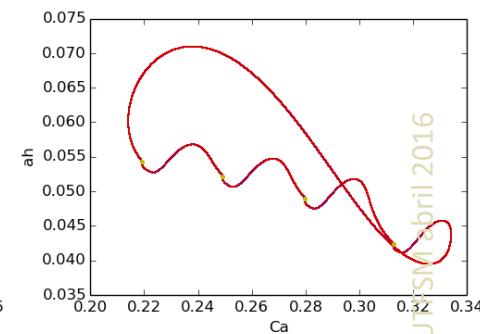
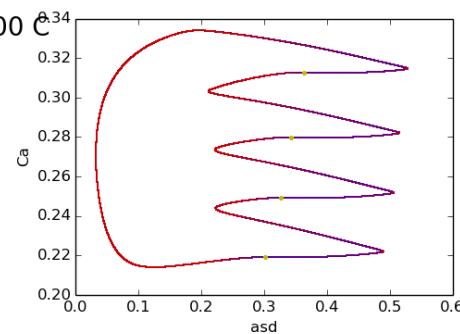
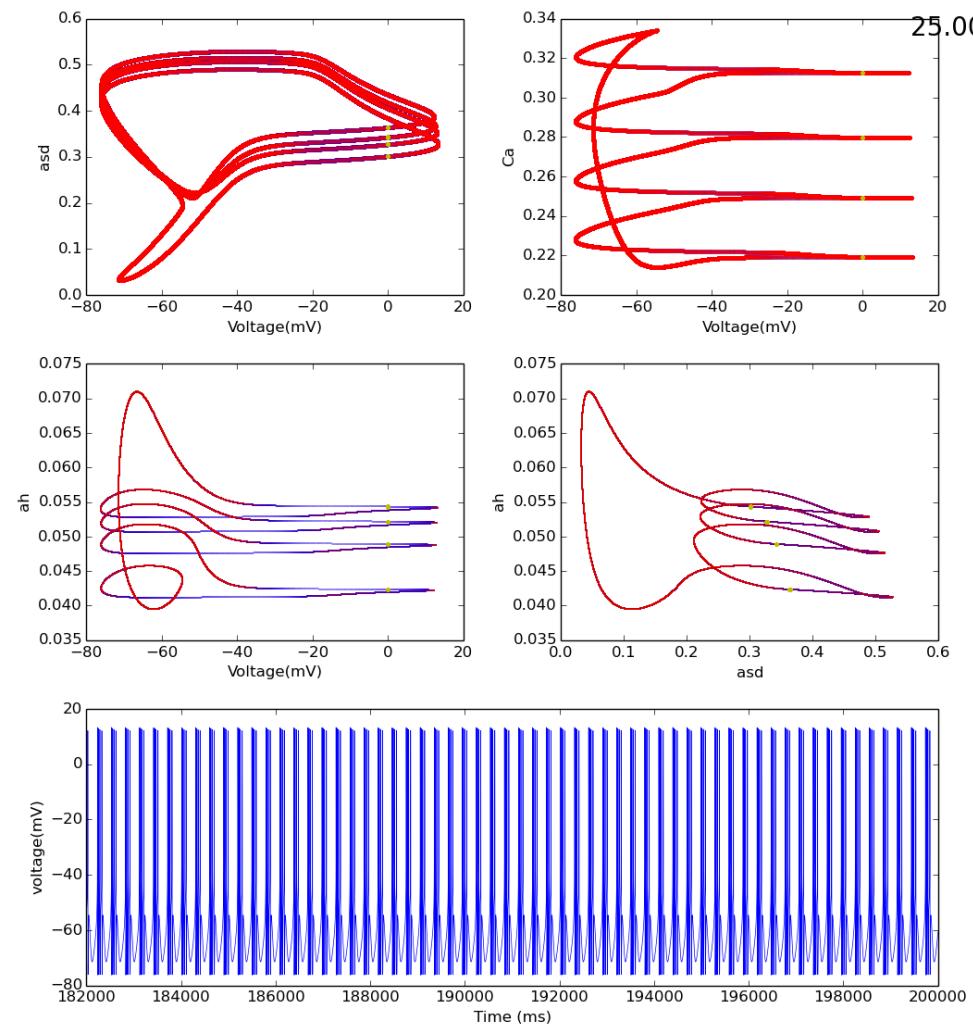
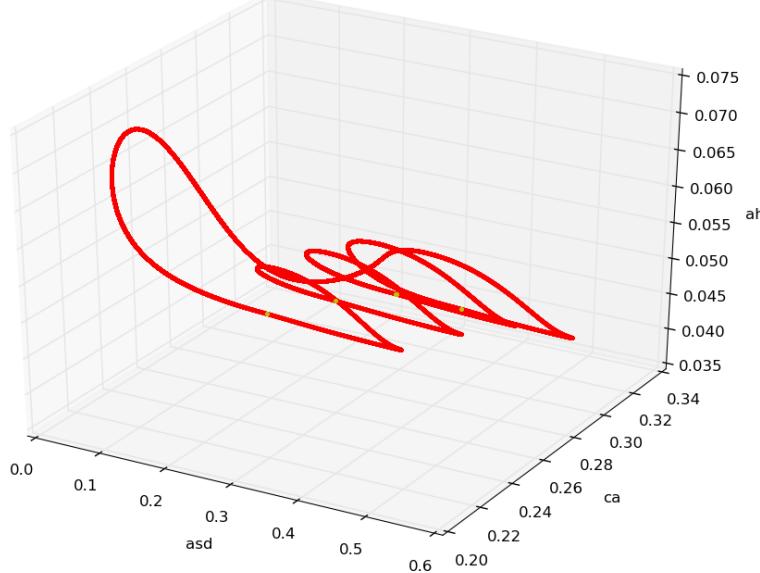
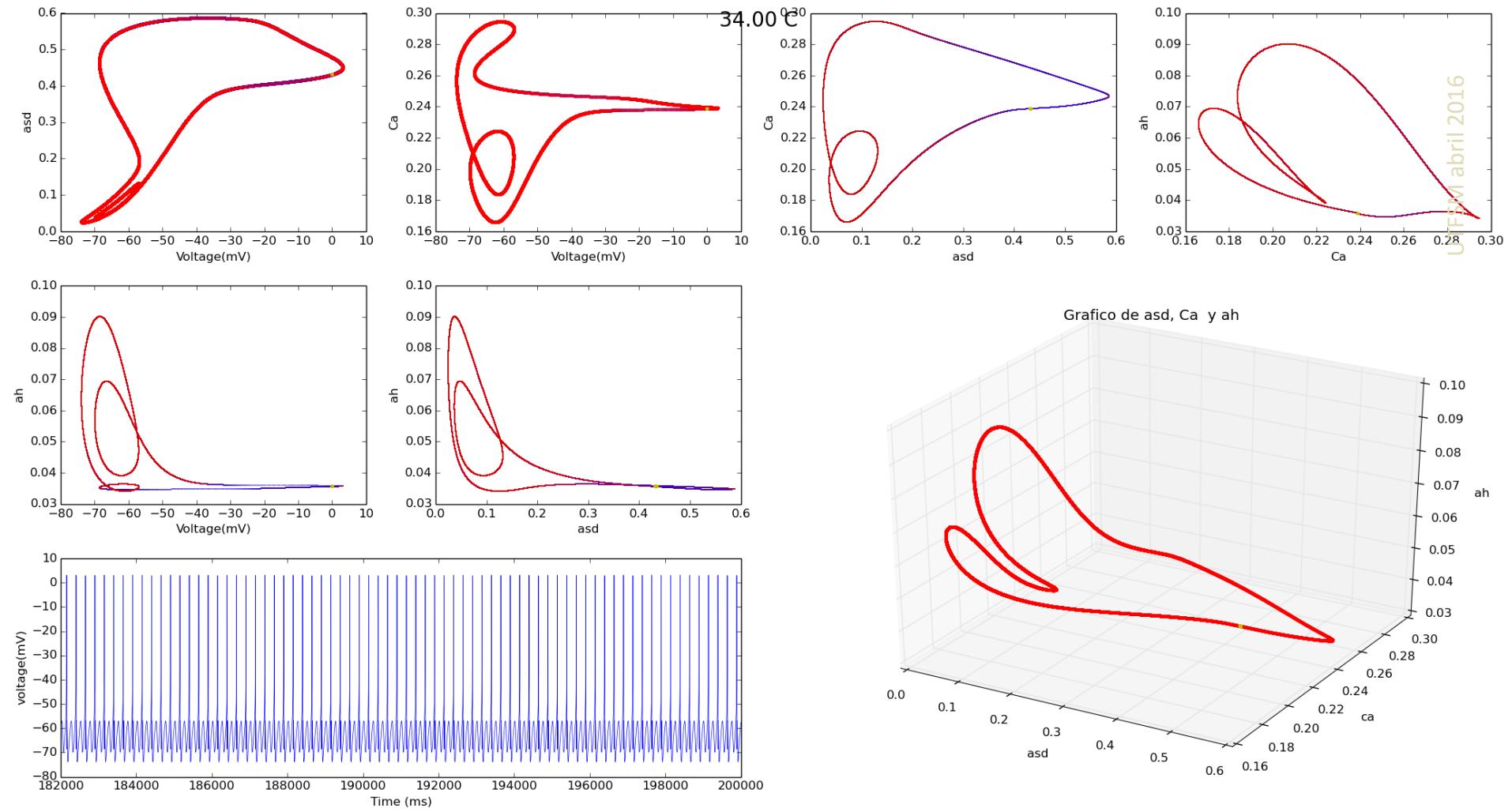
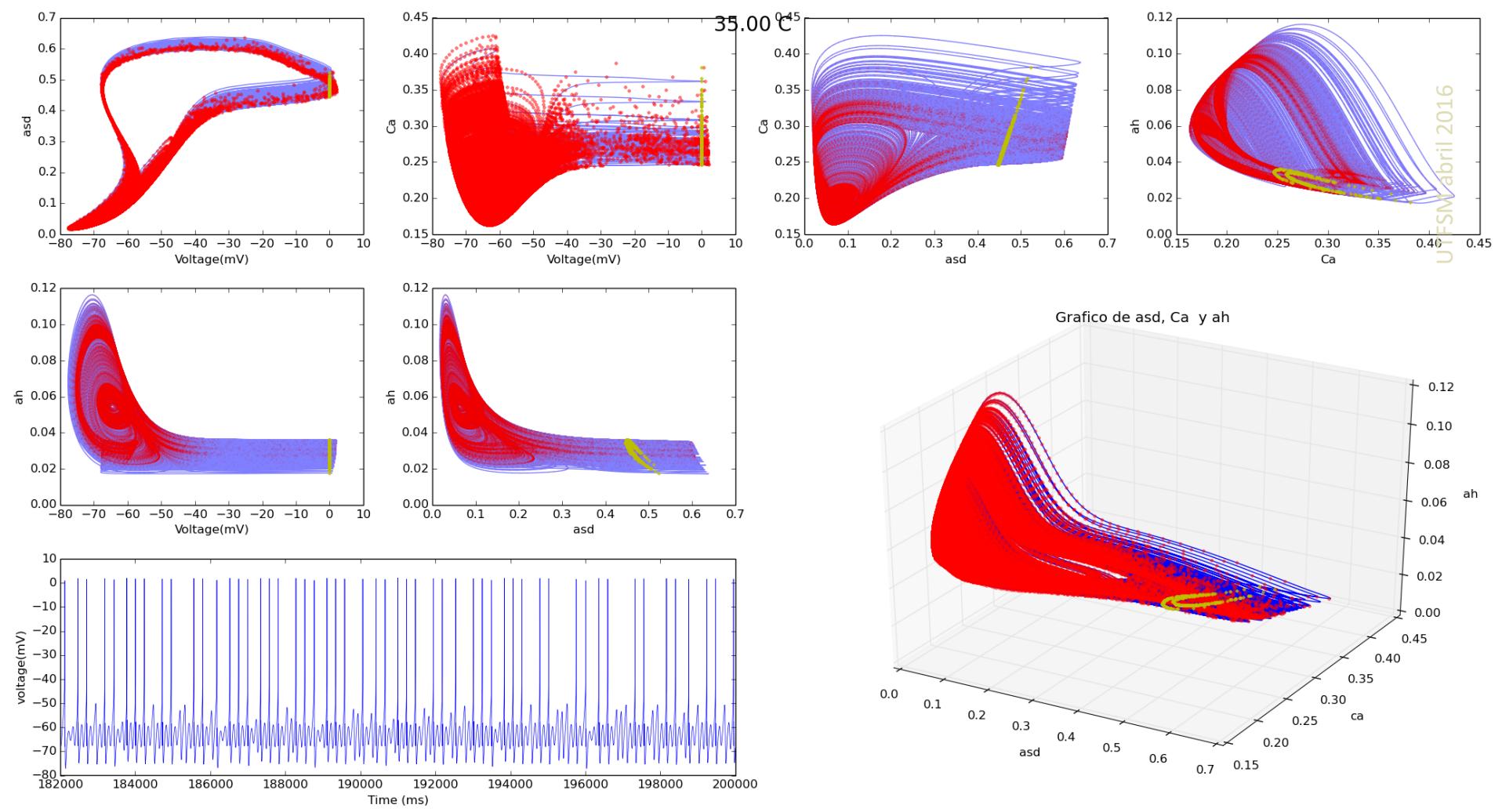


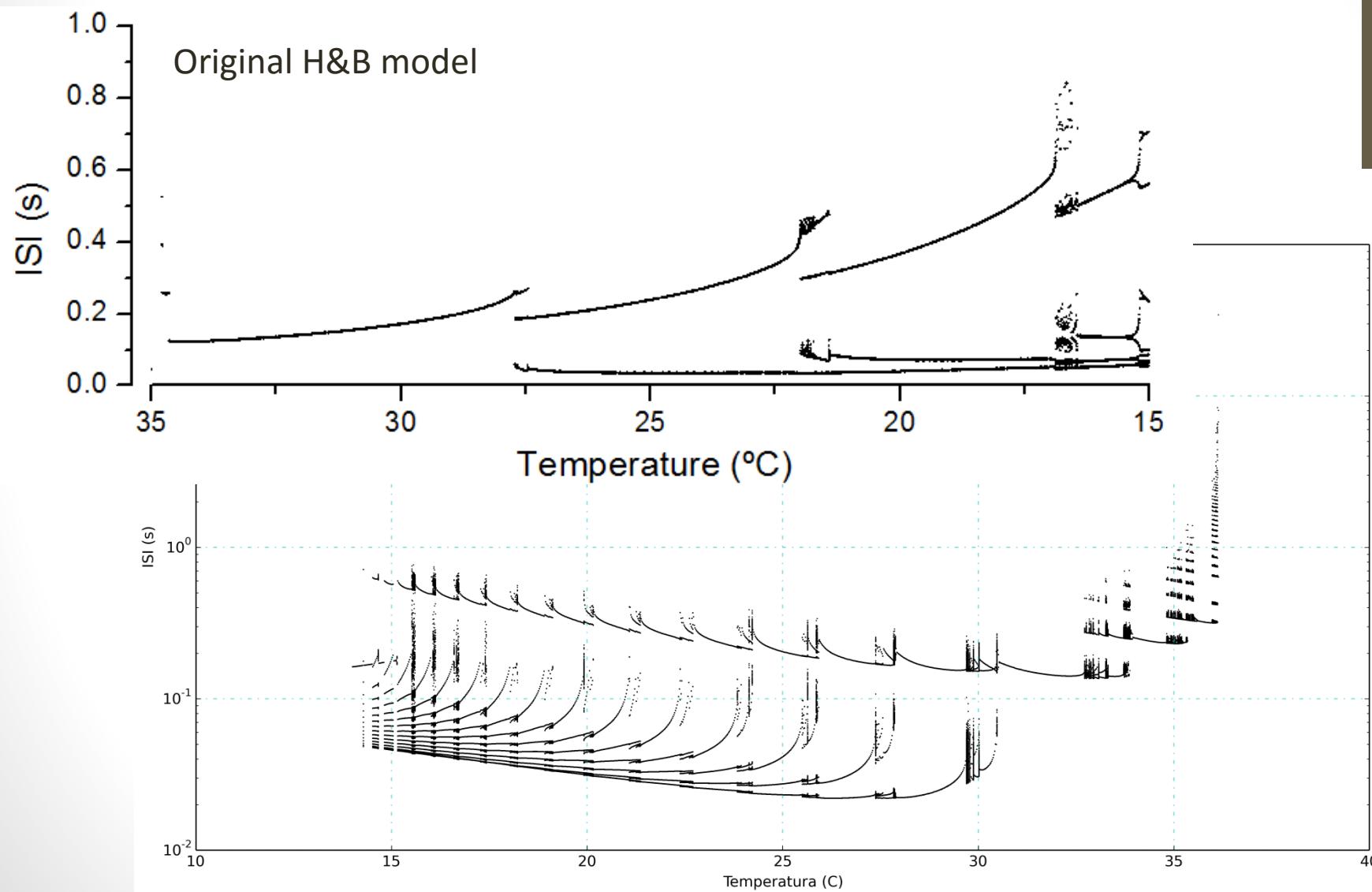
Grafico de asd , Ca y ah





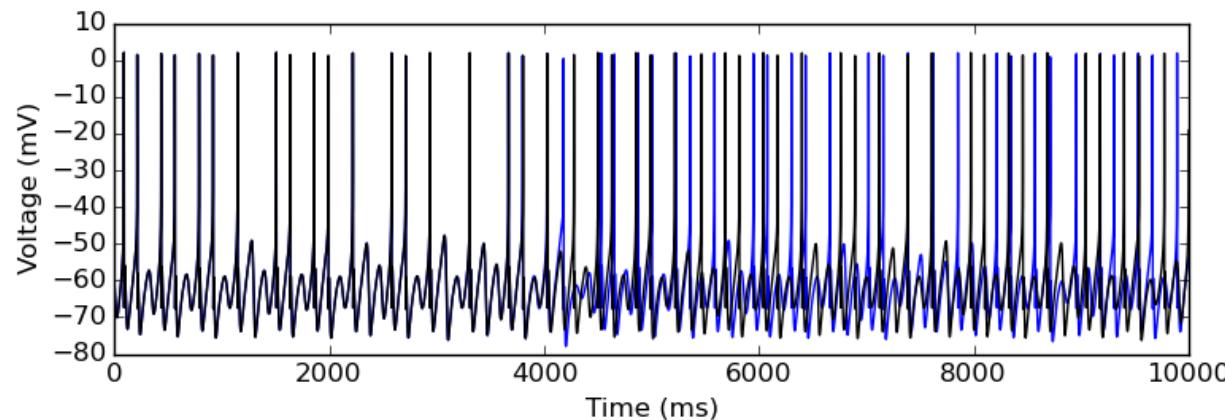
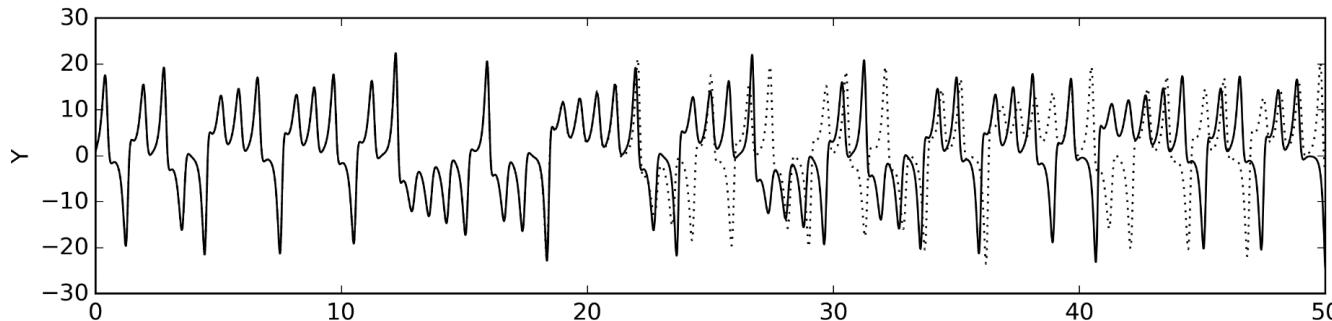


(apparent) Chaotic dynamics in H&B + Ih model



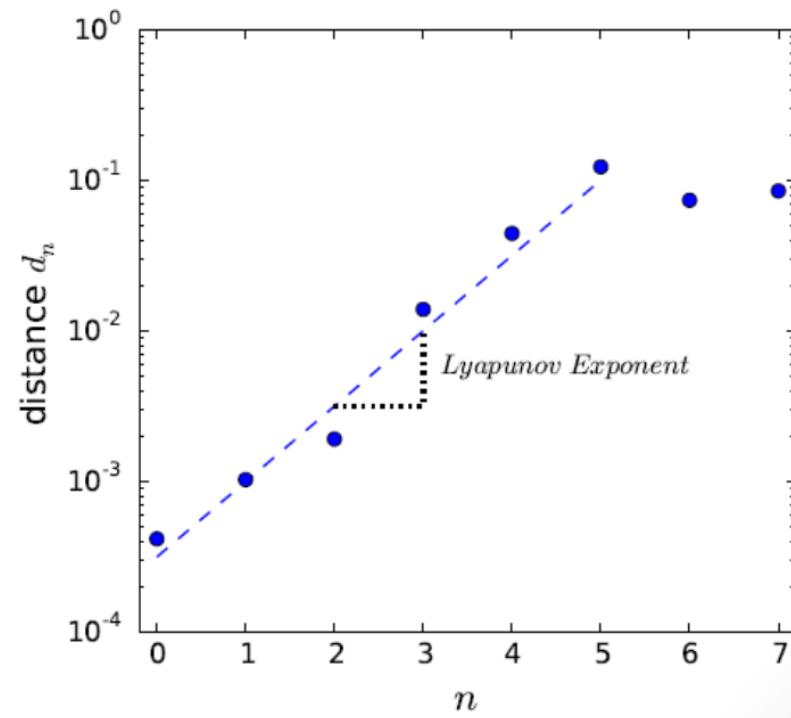
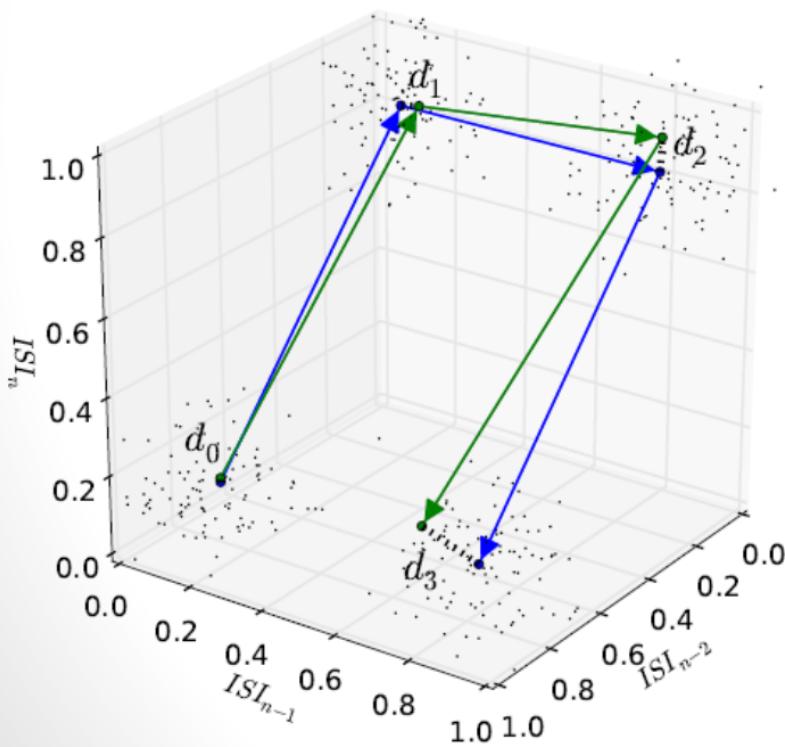
Caos

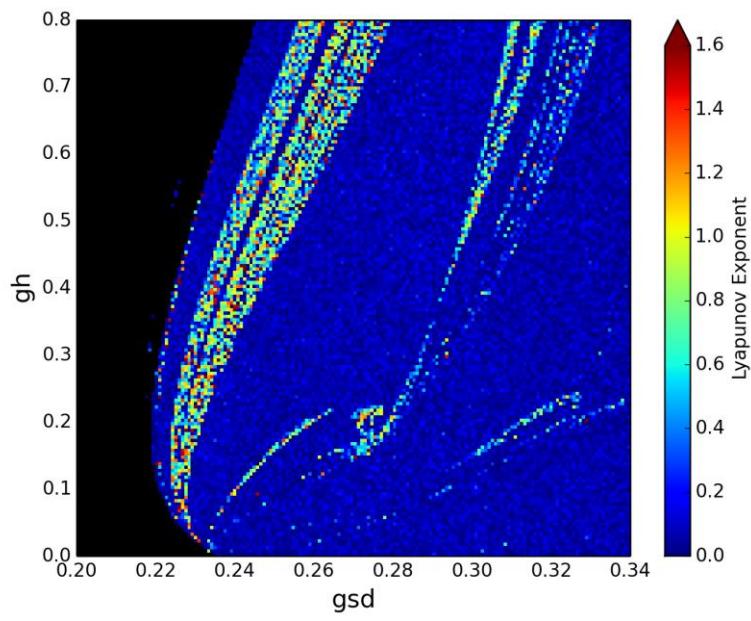
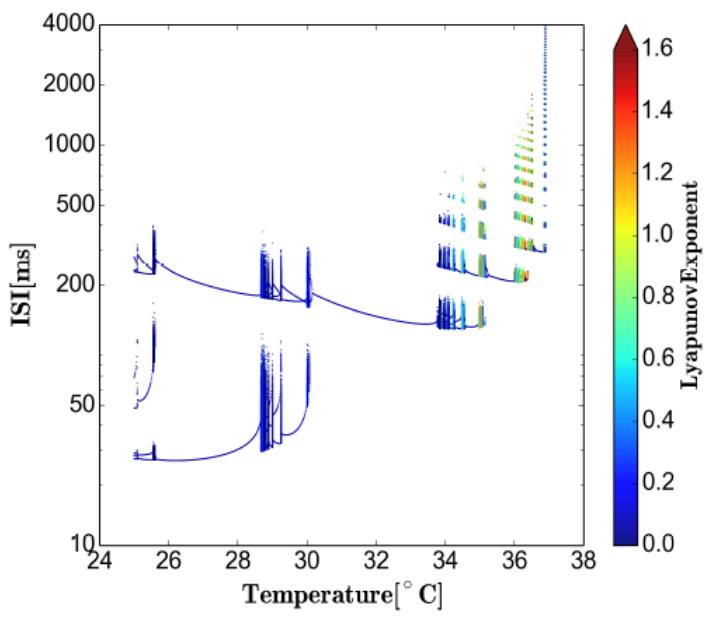
- Comportamiento *aperiódico* a largo plazo de un sistema *determinístico*, exhibiendo alta *dependencia de las condiciones iniciales*.



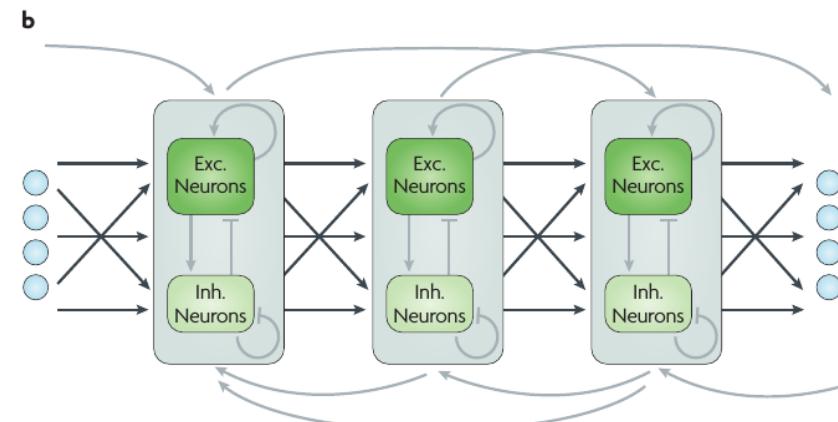
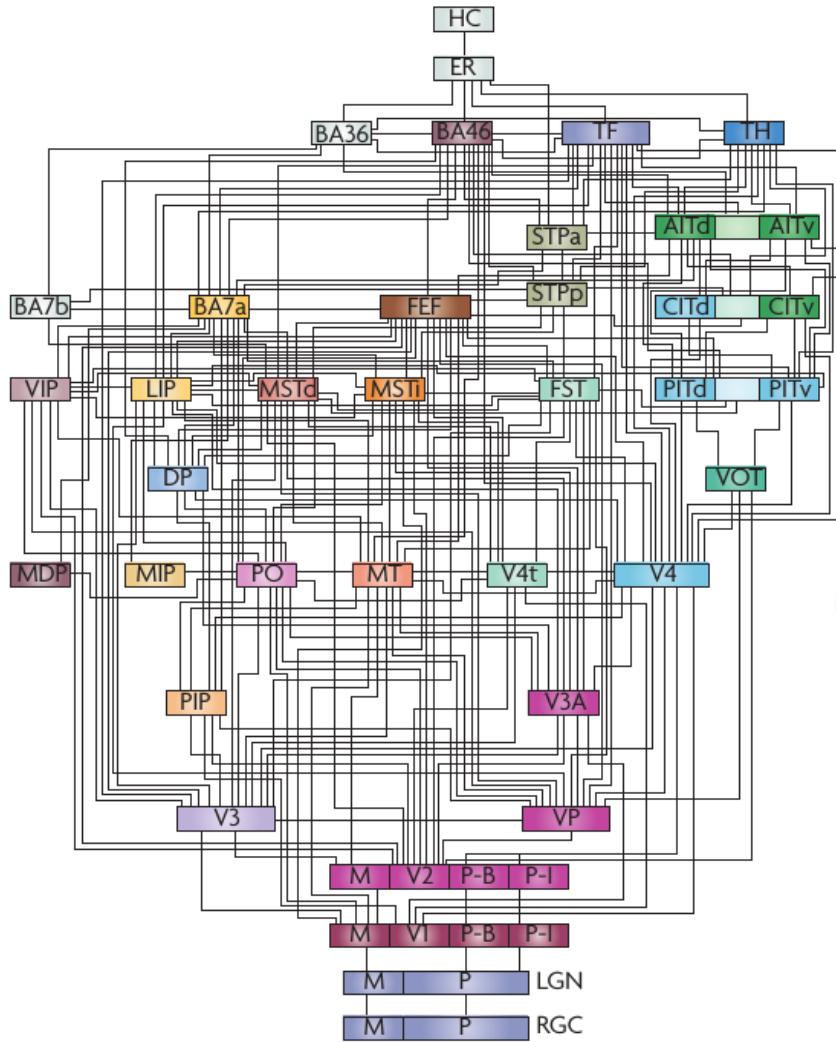
Medir (o demostrar?) caos

- Exponente de Lyapunov → divergencia exponencial de trayectorias inicialmente cercanas





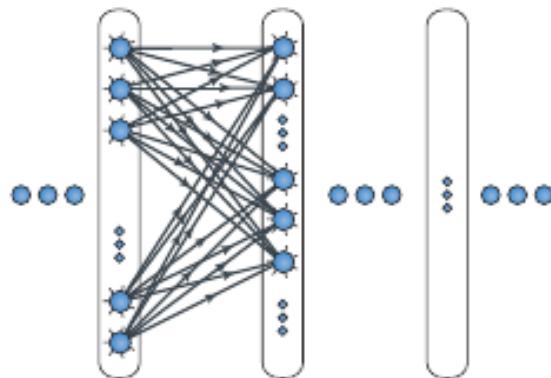
Las neuronas forman redes



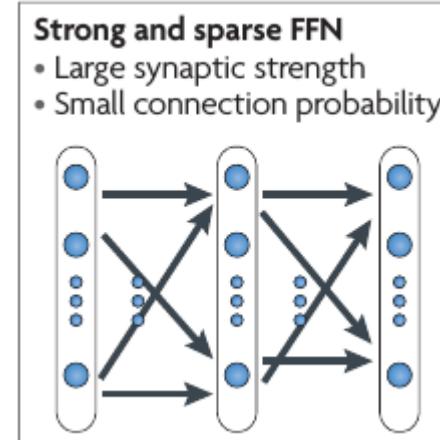
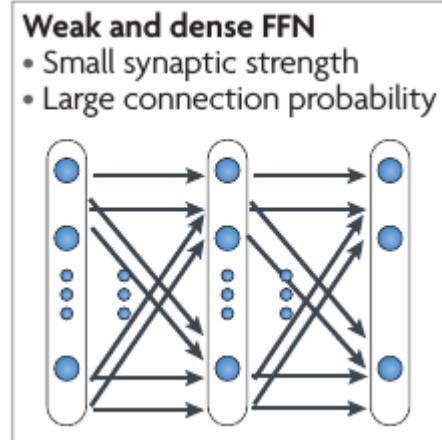
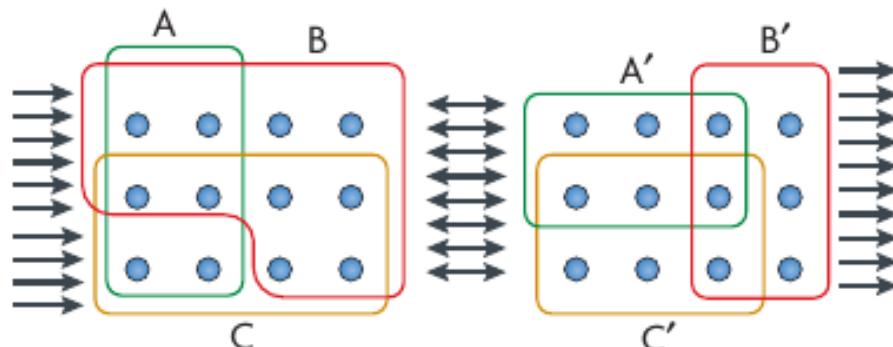
Kumar et al. (2010) *Nat Rev Neurosci*

FFNs y Neural Assemblies

D

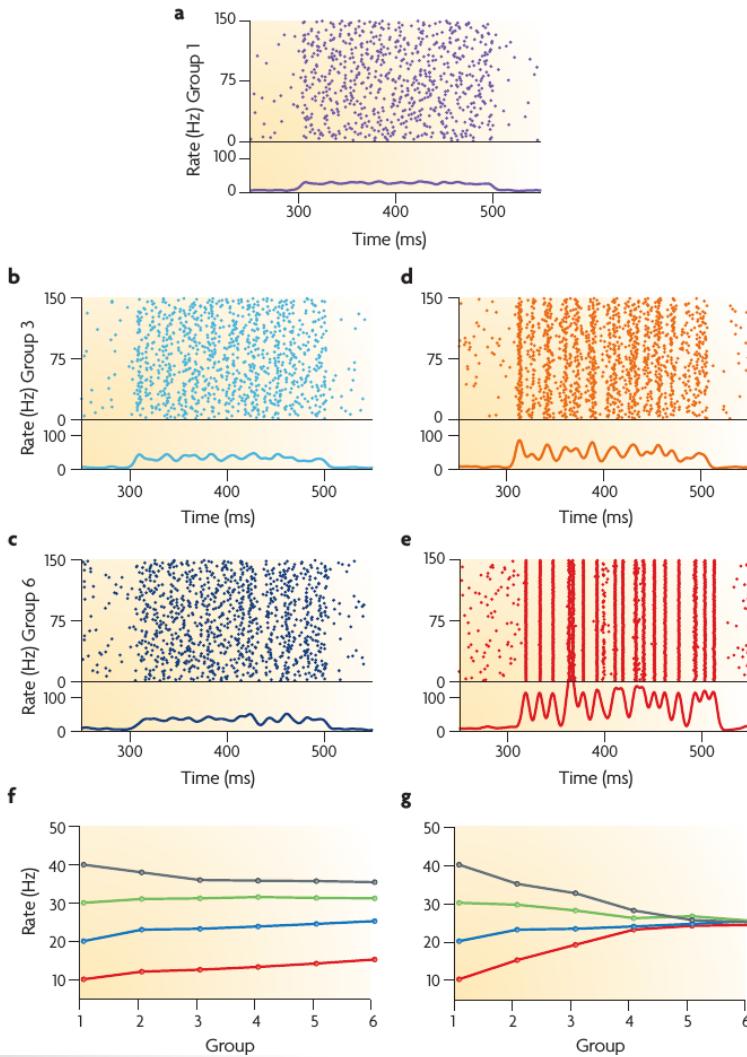


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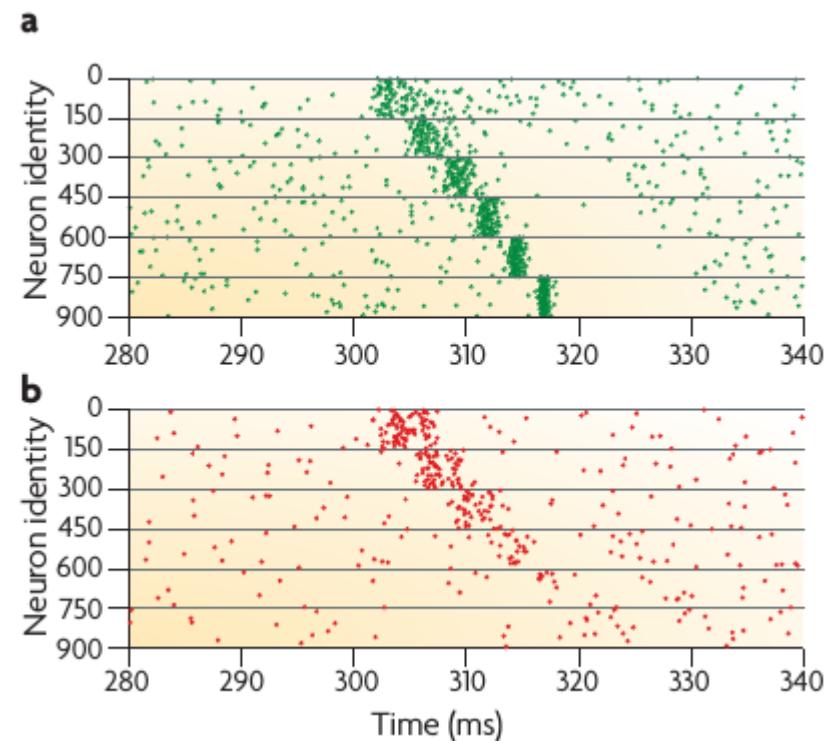


Efecto de la naturaleza de la red

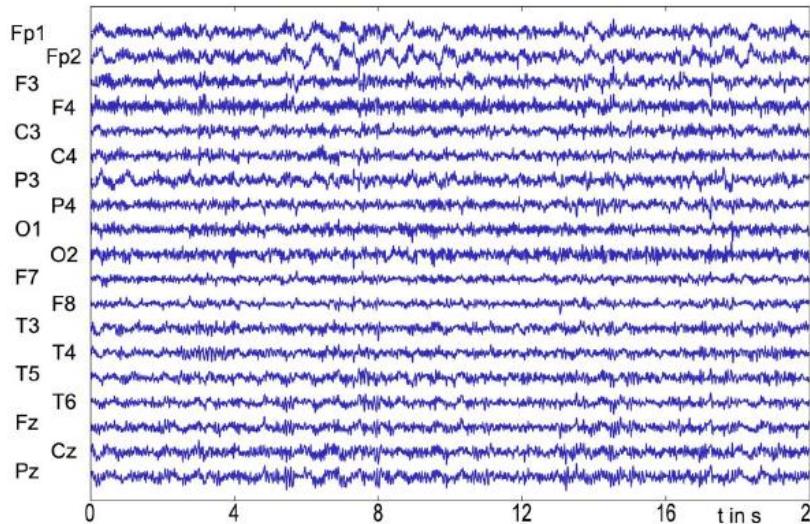
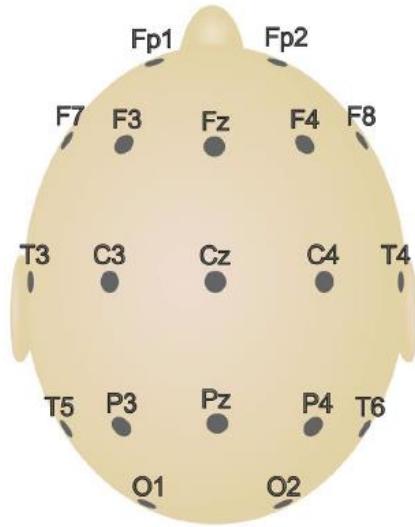
Rate coding



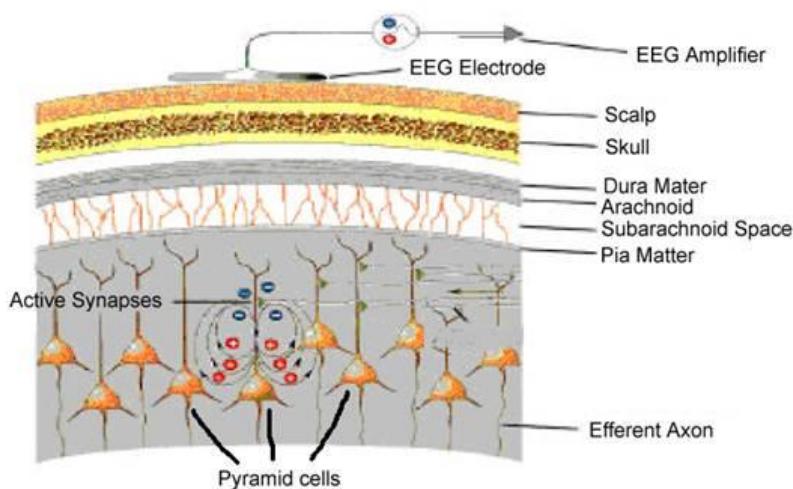
Temporal coding



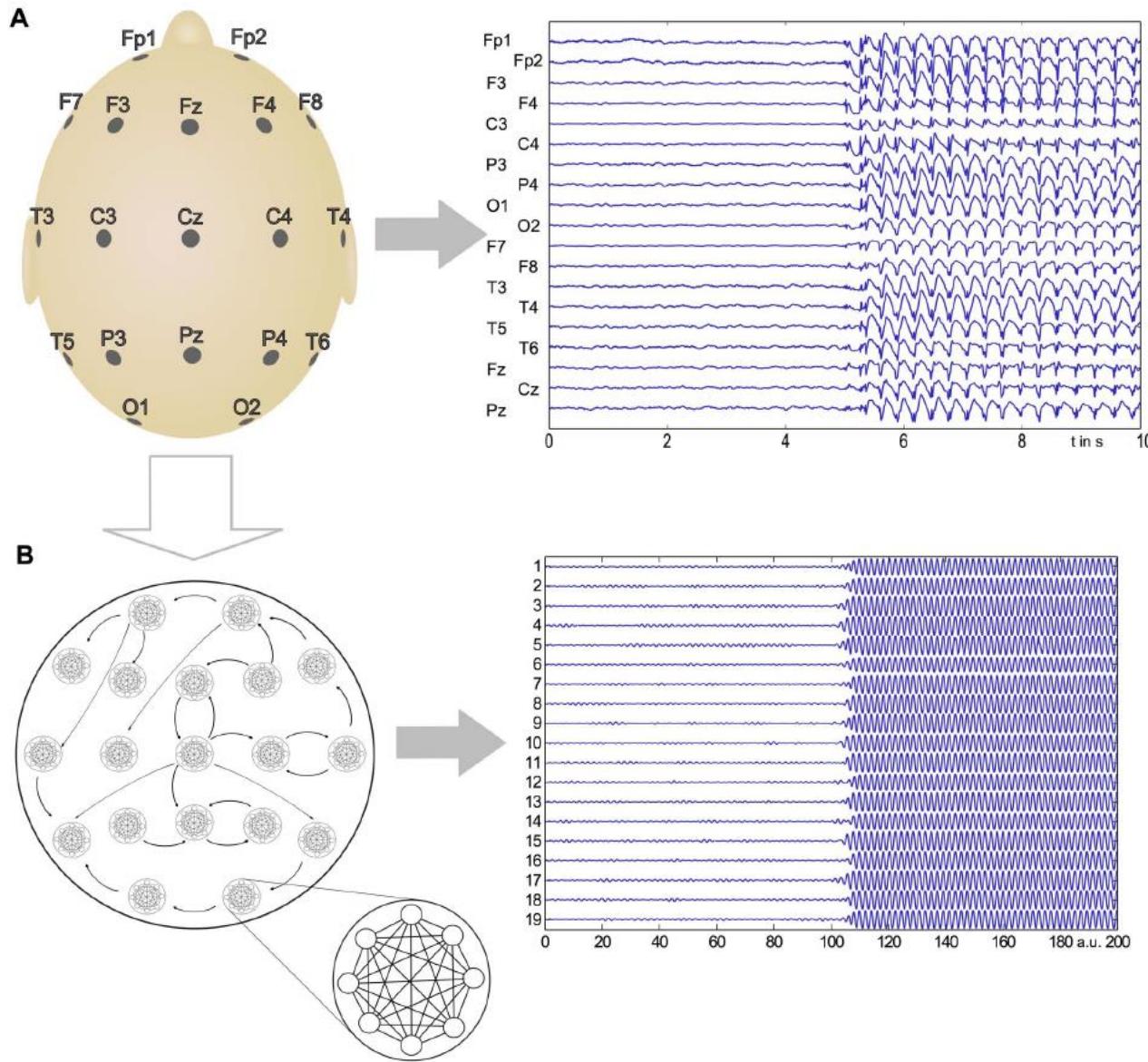
Oscilaciones de masas neurales



EEG



Oscilaciones de masas neurales

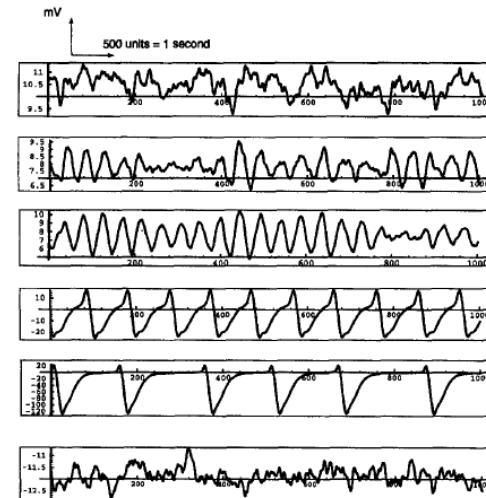
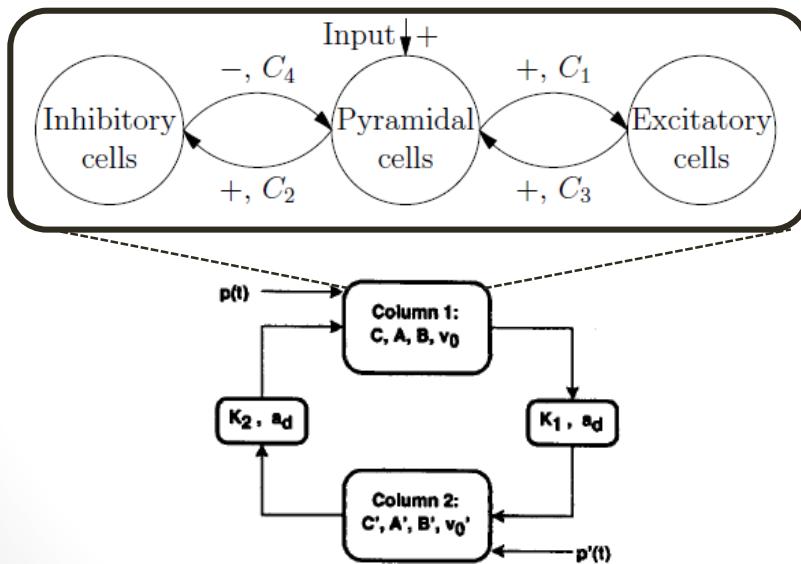


Modelos de masas neuronales

- CTRNN – Continuous Time Recurrent Neural Networks

$$\frac{dy_i}{dt} = \frac{1}{\tau_i} \left(-y_i + \sum_{j=1}^N w_{ji} \sigma(y_j + \theta_j) + I_i \right) \quad \sigma(x) = \frac{1}{1+e^{-x}}$$

- Neural Mass Models (NMMs): simulación de columnas corticales



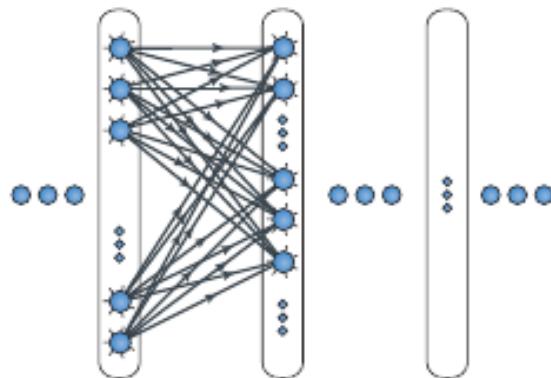
¿Qué efecto(s) tiene
el caos?

Problema a tratar

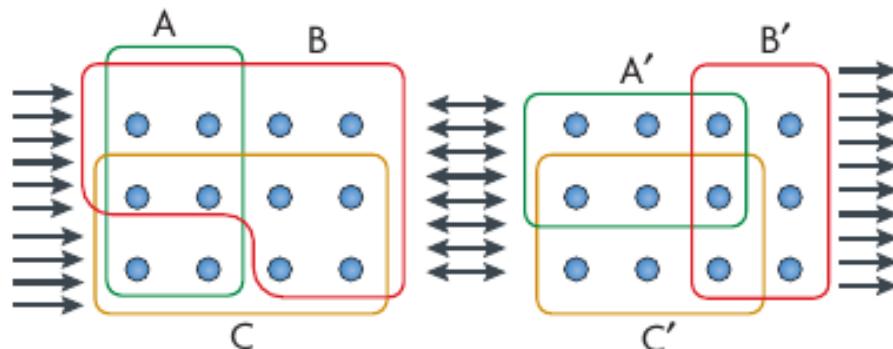
- En una red de neuronas oscilatorias, ¿qué diferencia hace que ellas tengan dinámica caótica?
 - Se asume que el caos permite una mayor exploración del espacio de estados del sistema
- Muchos estudios, numéricos y analíticos que caracterizan el caos en modelos.
 - **Pocos estudios que comparan sistemáticamente el efecto del caos.**

FFNs y Neural Assemblies

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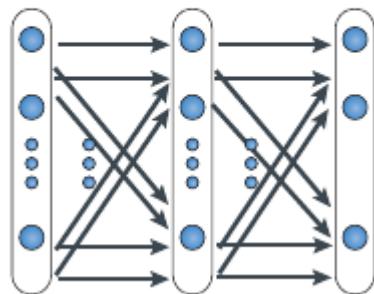


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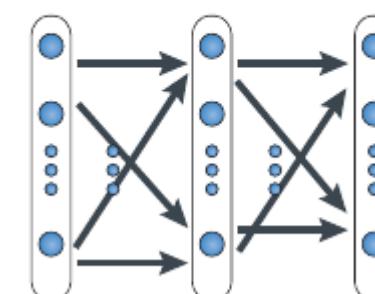
Weak and dense FFN

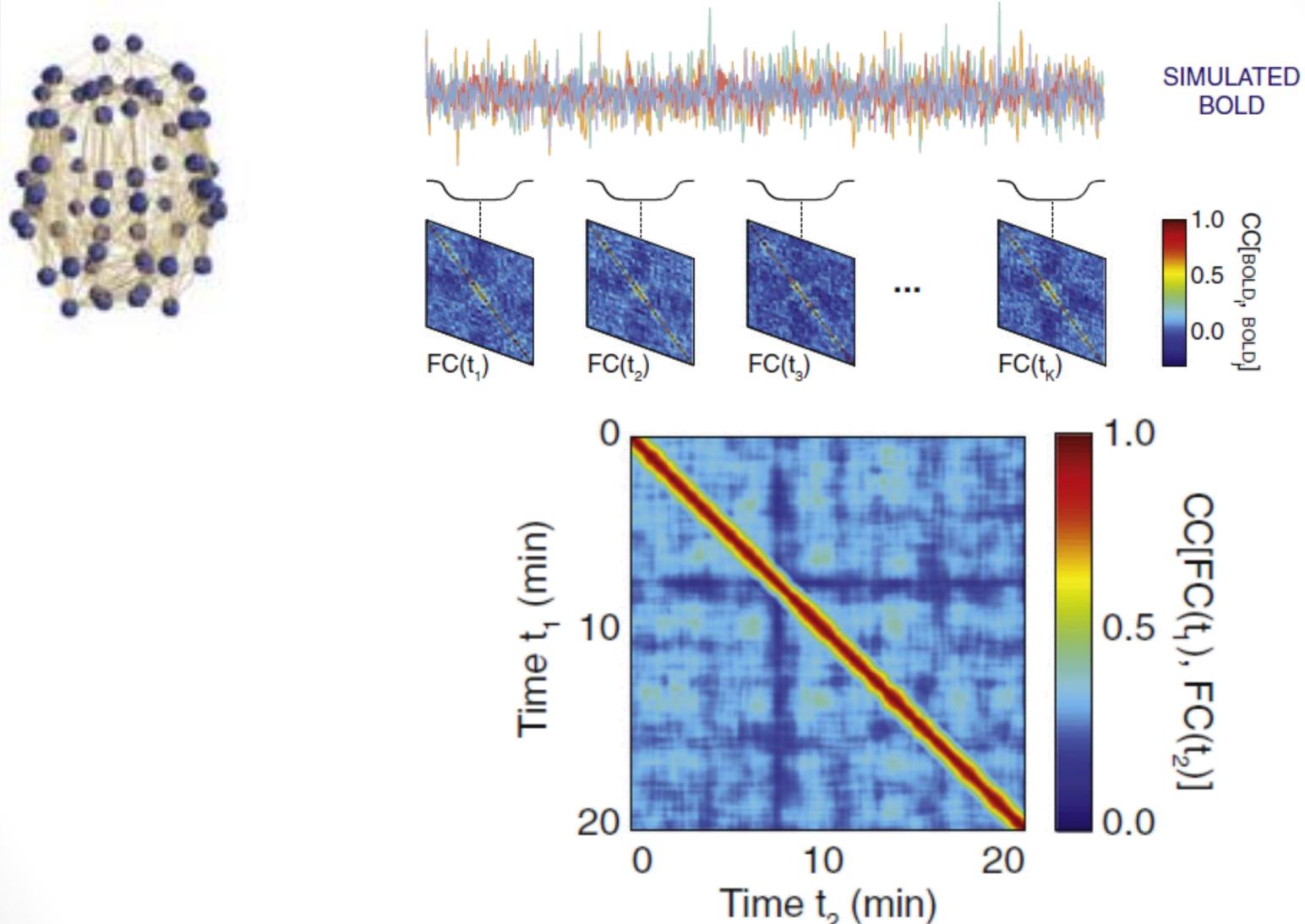
- Small synaptic strength
- Large connection probability



Strong and sparse FFN

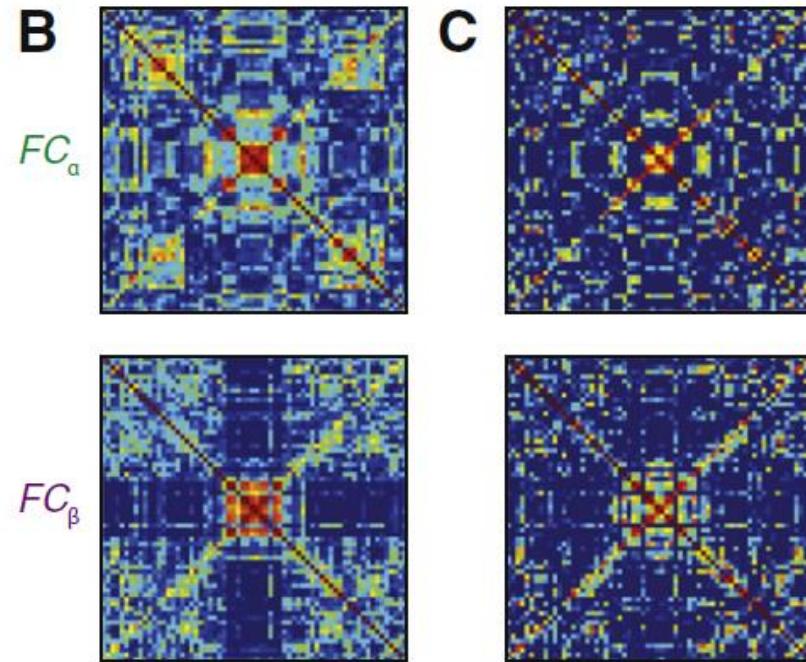
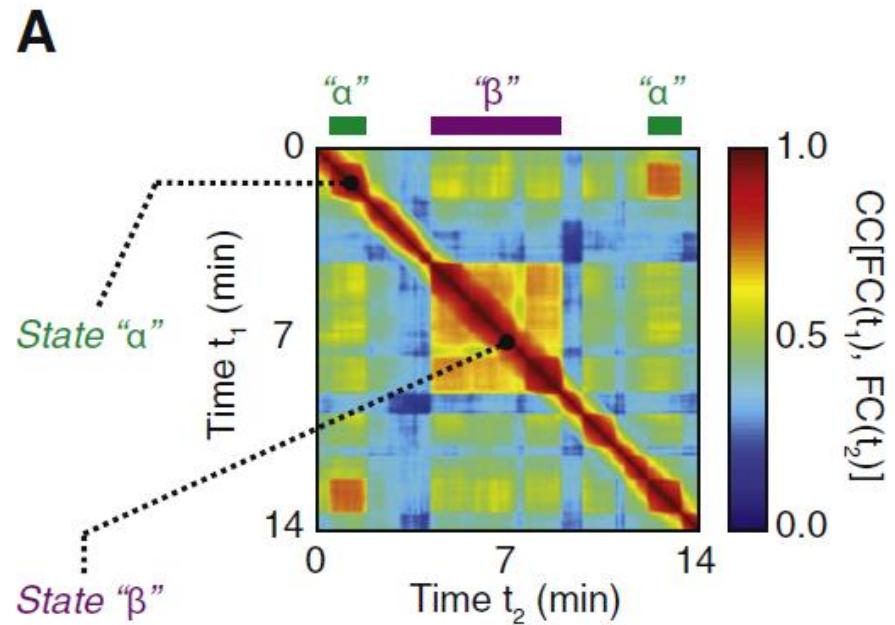
- Large synaptic strength
- Small connection probability





Functional connectivity dynamics: Modeling the switching behavior of the resting state





Pasos a trabajar

- Definir e implementar una métrica para medir el grado de sincronía de las neuronas (trazos de voltaje), diferente a correlación de Pearson
 - Sugerencias: coherencia de fase / ISI distance
- Definir e implementar métrica para medir similitud entre las diferentes matrices de correlación(coherencia, sincronía)
 - Buscar en paper de Hansen (2015)