Medidas de fase y sincronía en osciladores neurales

Patricio Orio Álvarez

Centro Interdisciplinario de Neurociencia de Valparaíso CINV
Universidad de Valparaíso

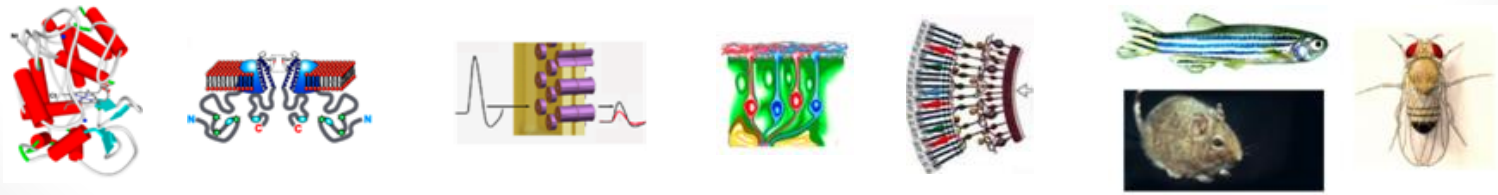
CENTRO INTERDISCIPLINARIO DE Neurociencia de Valparaíso

Facultad de Ciencias

Universidad de Valparaíso CHILE

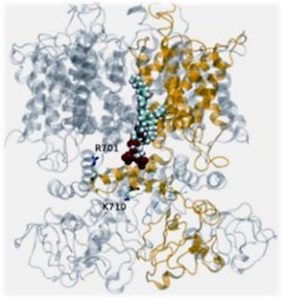
Centro Interdisciplinario de Neurociencia de Valparaíso – CINV

- 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



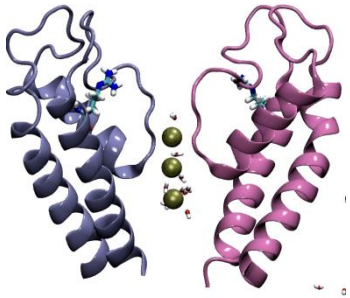
Main Research Topic

How does the Nervous System respond to Sensory Stimuli?

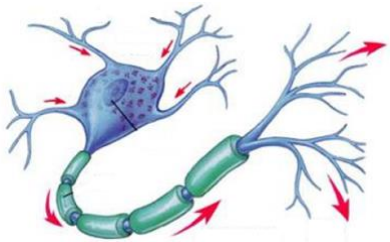


Molecular Sensors

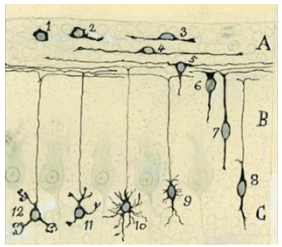
Systems Neuroscience



Computational Biology & Bioinformatics

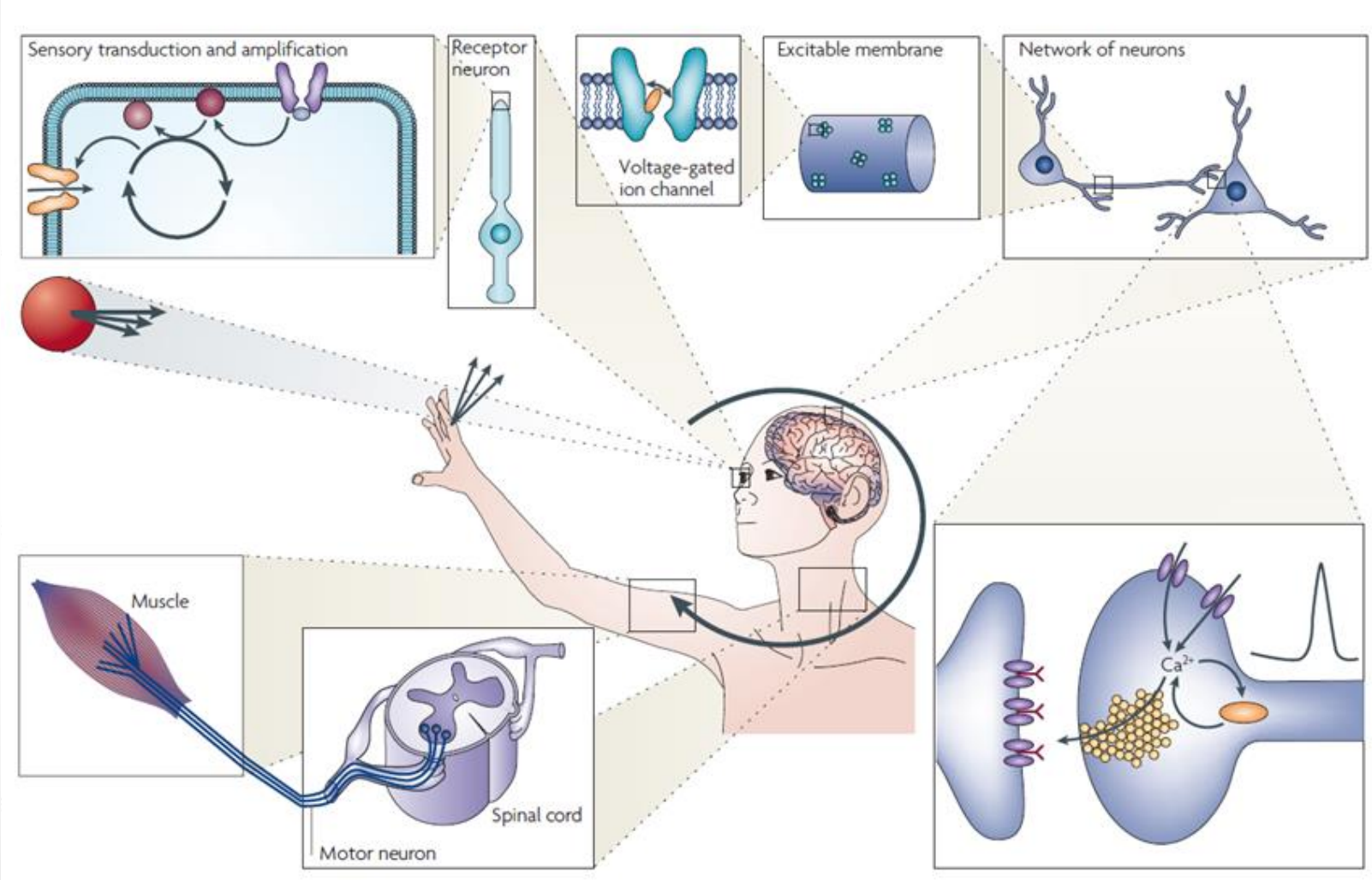


Cell Signaling



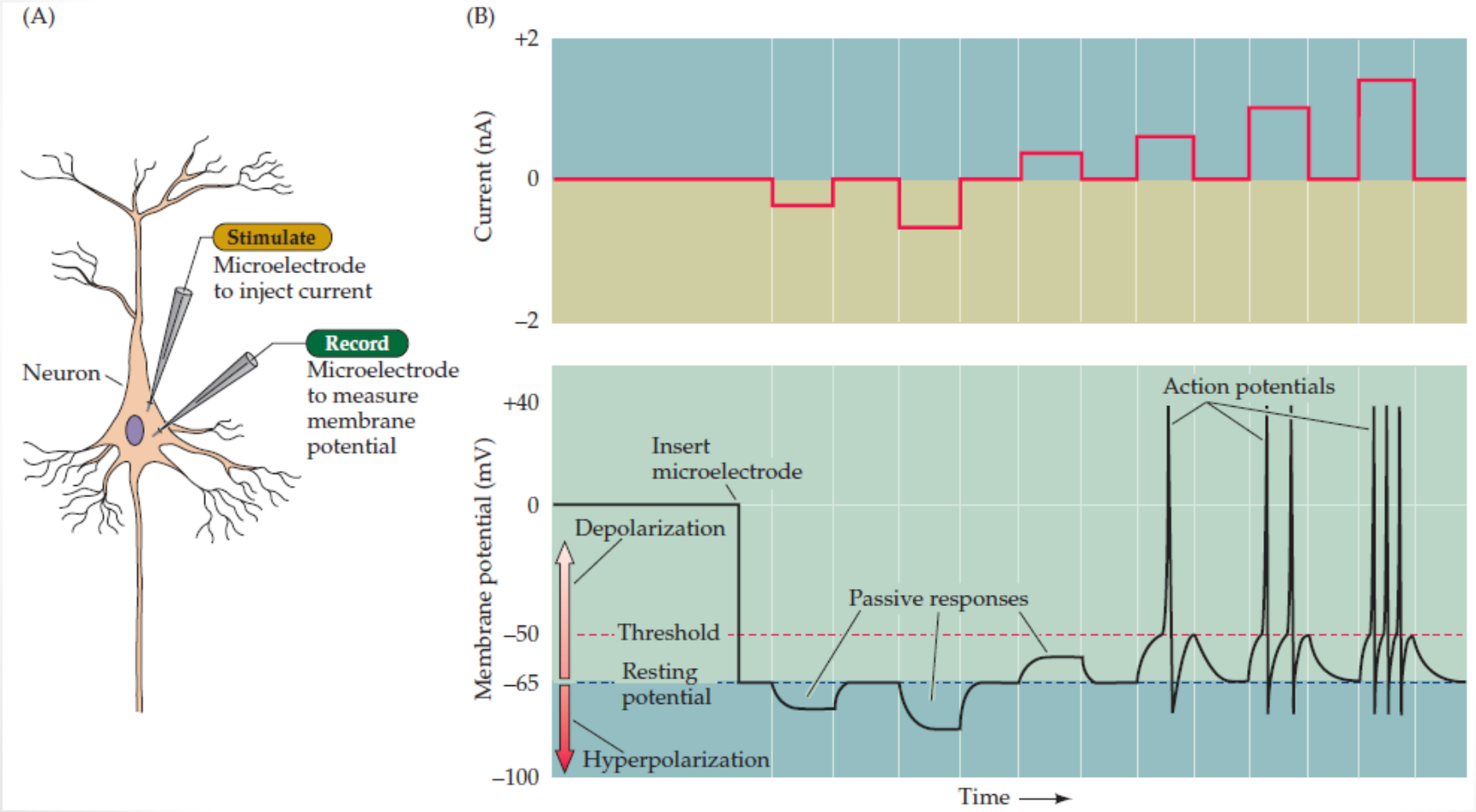
Developmental Neuroscience

El sistema nervioso

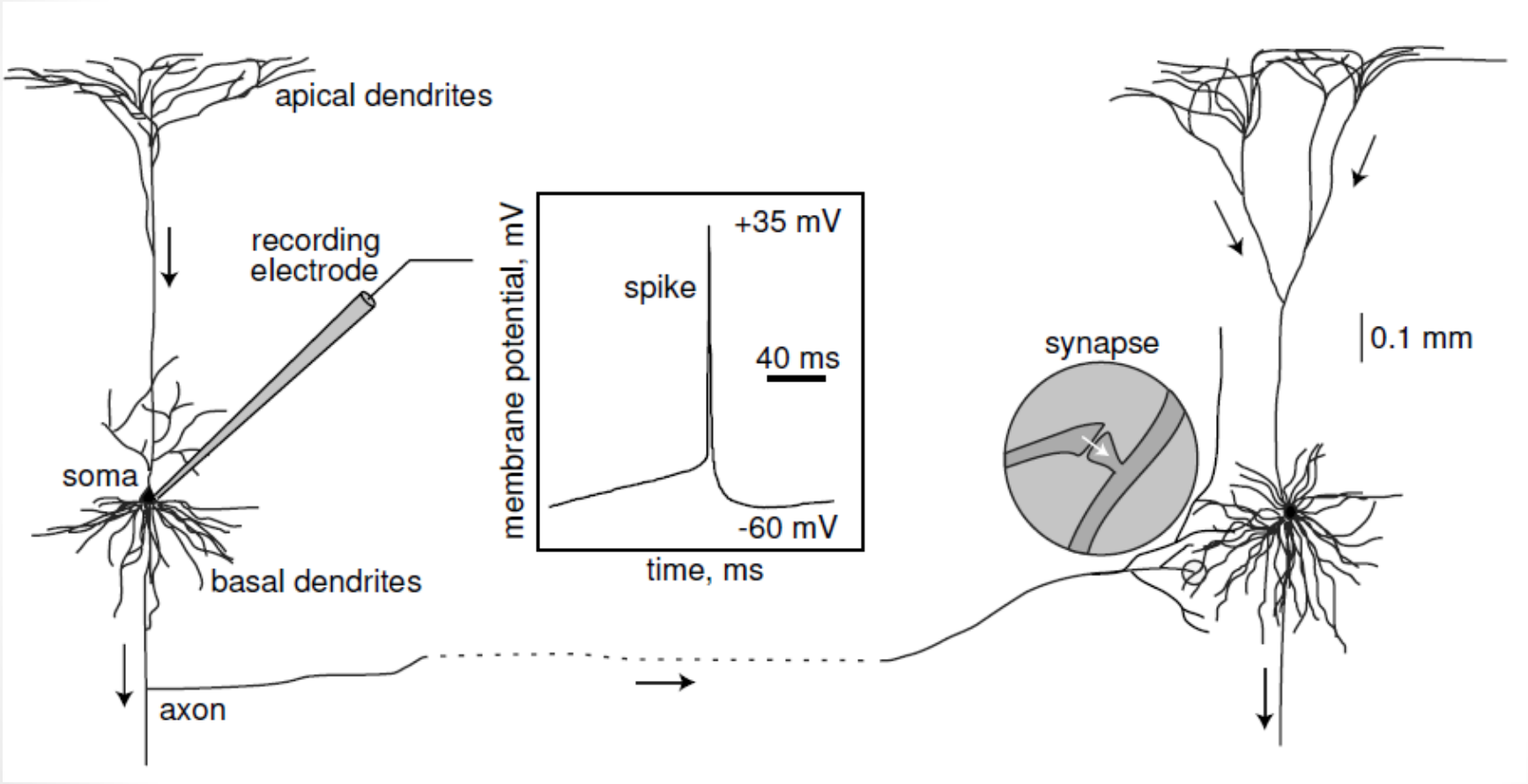


Adaptado de: Faisal A.A., Selen L. & Wolpert D.M.(2008). Noise in the nervous system. *Nat Rev Neurosci* **9**:292-303

Neuronas y Potencial de Acción

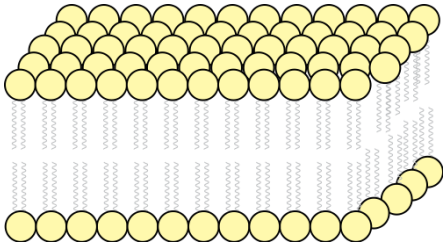


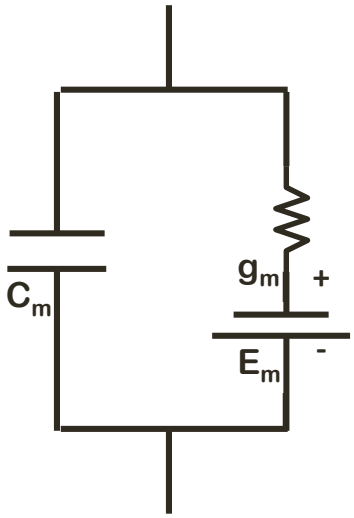
Propagación y transmisión sináptica

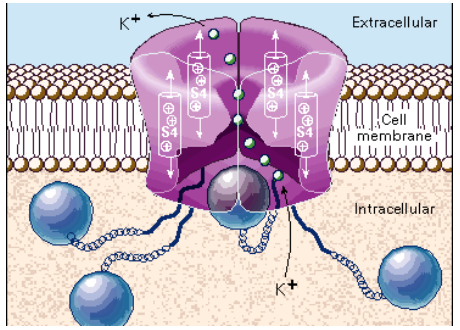


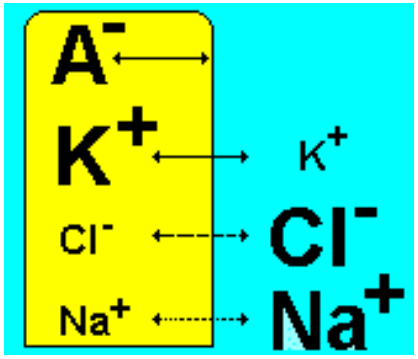
Origen de la excitabilidad

- Circuito Equivalente









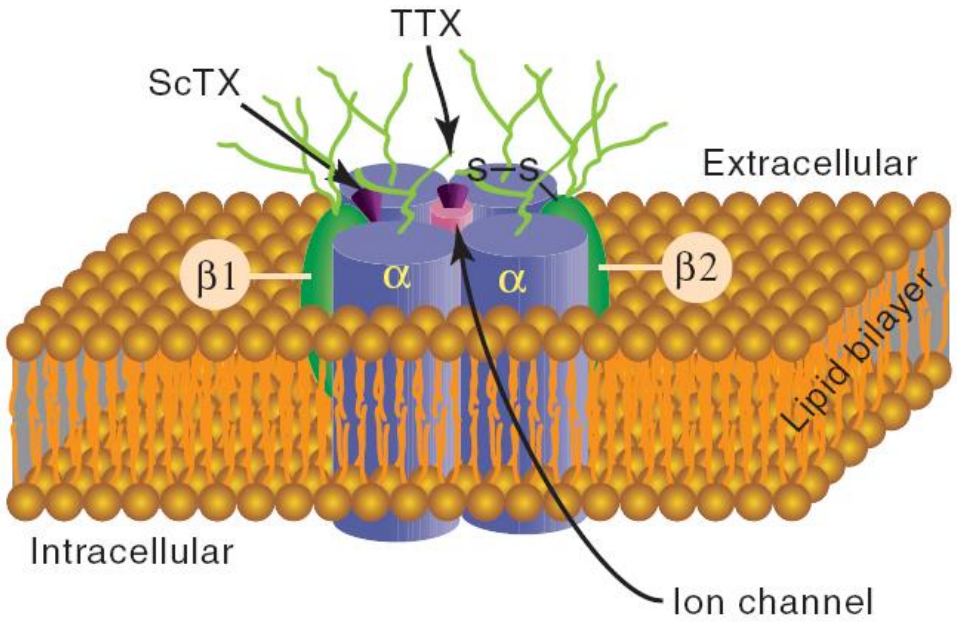
$$I_{memb} = I_C + I_{ion}$$

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

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

Potenciales de acción 'reales'

- Canales iónicos **dependientes de voltaje**

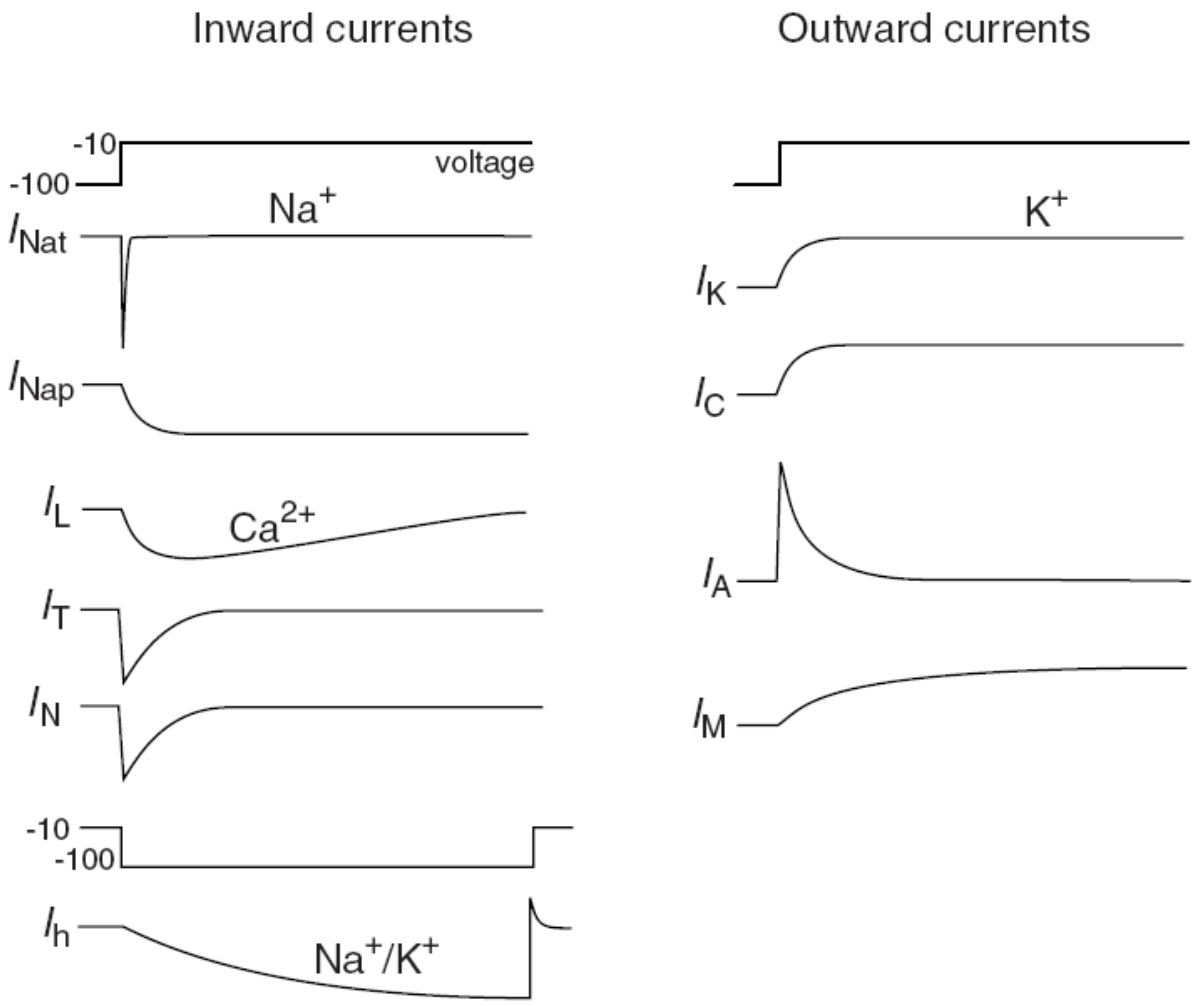


- Na^+
- K^+
- Ca^{2+}
- Cl^-
- Catiónicos

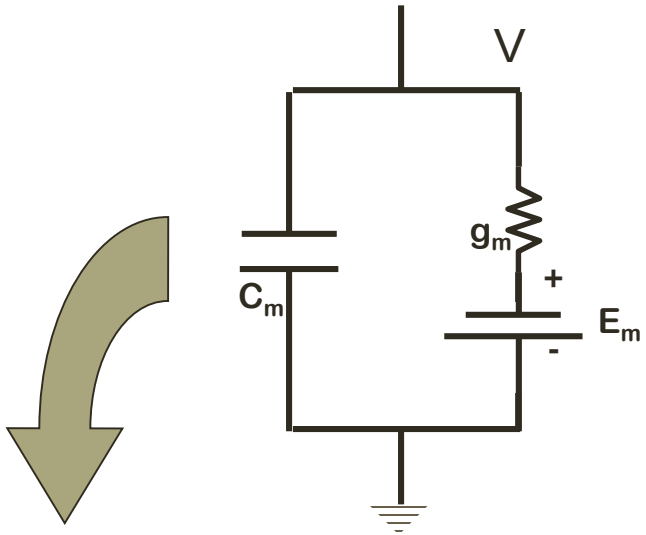
- Activados por **despolarización**
- Activados por **hiperpolarización**
- Inactivación

Canales dependientes de voltaje

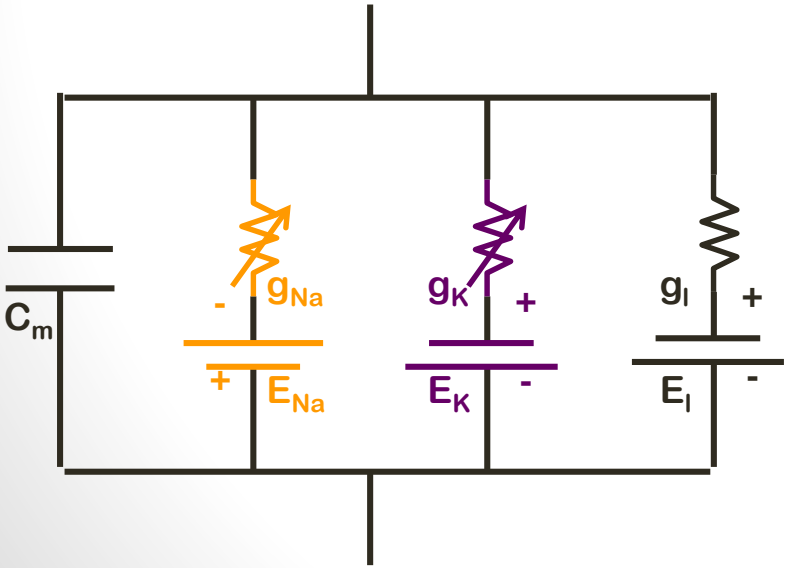
- **La respuesta al voltaje no es instantánea**



Incorporando canales 'realistas'



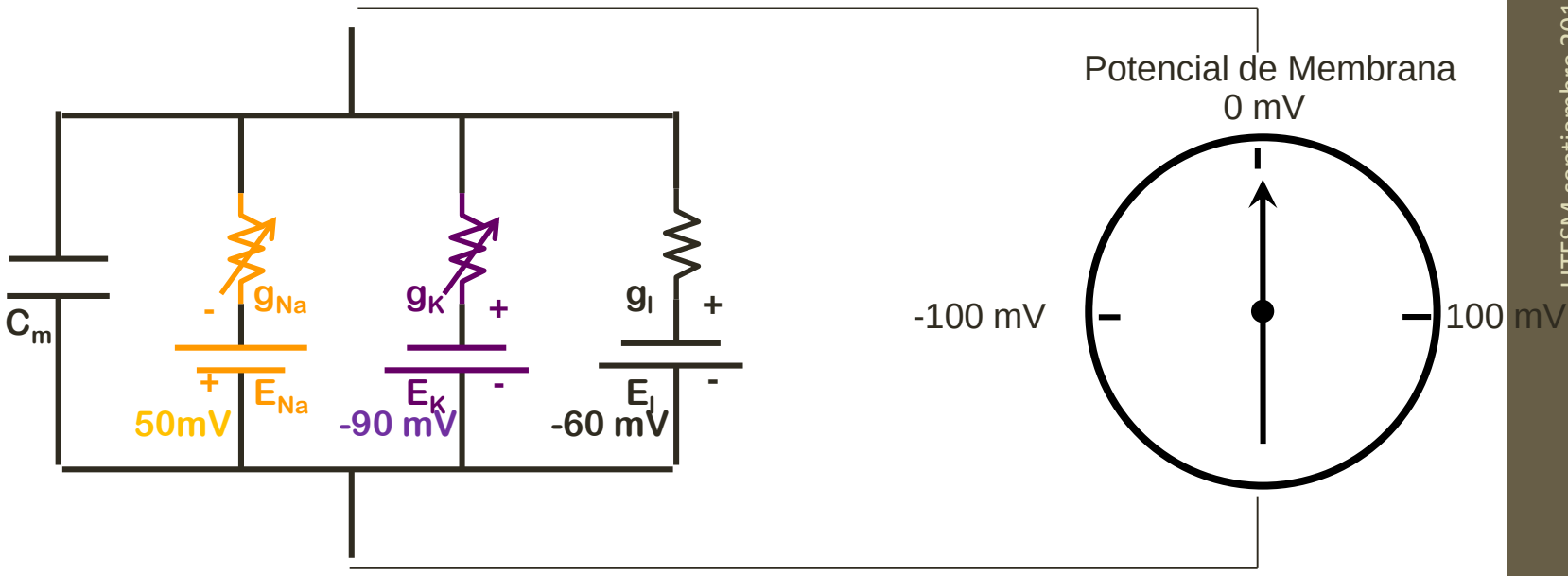
$$C_m \frac{dV}{dt} = -g_m(V - E_m) + I_{ext}$$



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

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

Incorporando canales 'realistas'



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

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

Ecuaciones de Hodgkin y Huxley

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

$$dn/dt = \alpha_n (1 - n) - \beta_n n,$$

$$dm/dt = \alpha_m (1 - m) - \beta_m m,$$

$$dh/dt = \alpha_h (1 - h) - \beta_h h,$$

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

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

Canales de potasio dependientes de voltaje

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

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

Canales de sodio dependientes de voltaje

$$= 0{\cdot}01\,(V$$

$$\beta_n = 0{\cdot}$$

$$V +$$

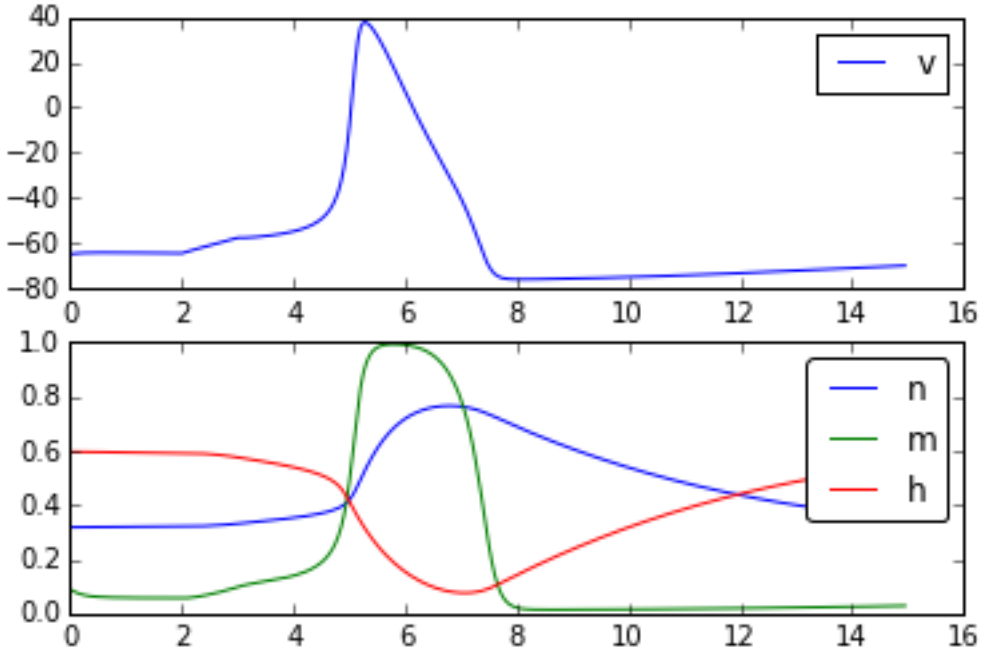
$$\beta_m = 4$$

$$\alpha_h = 0{\cdot}07 \exp(V/20),$$

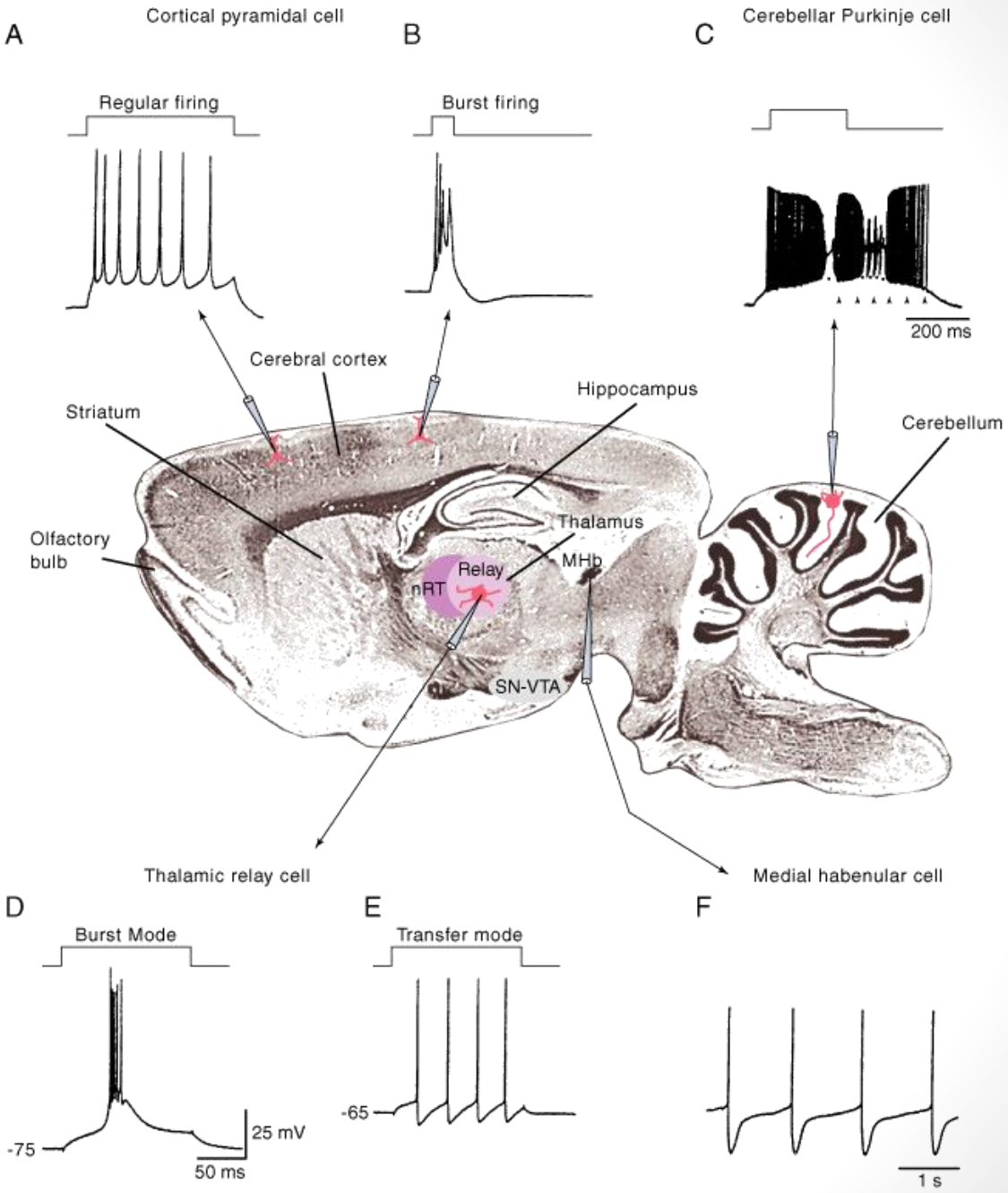
$$\beta_h = 1 \Big/ \left(\exp \frac{V + 30}{10} + 1 \right).$$

Hodgkin A.L., and Huxley A.F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* **117**: 500-544

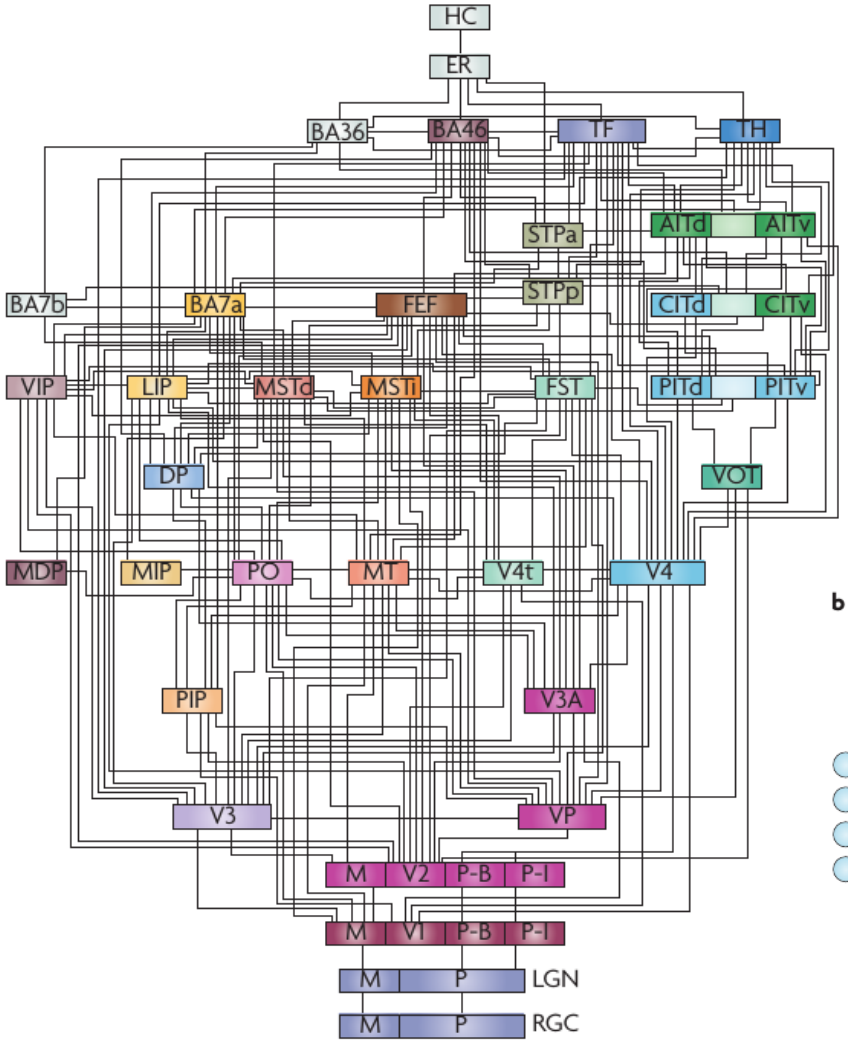
Modelo de H&H

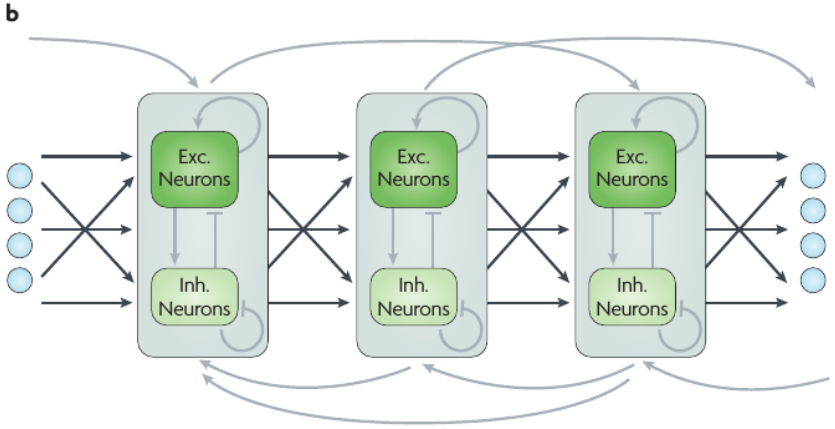


Diversidad de neuronas, diversidad de canales



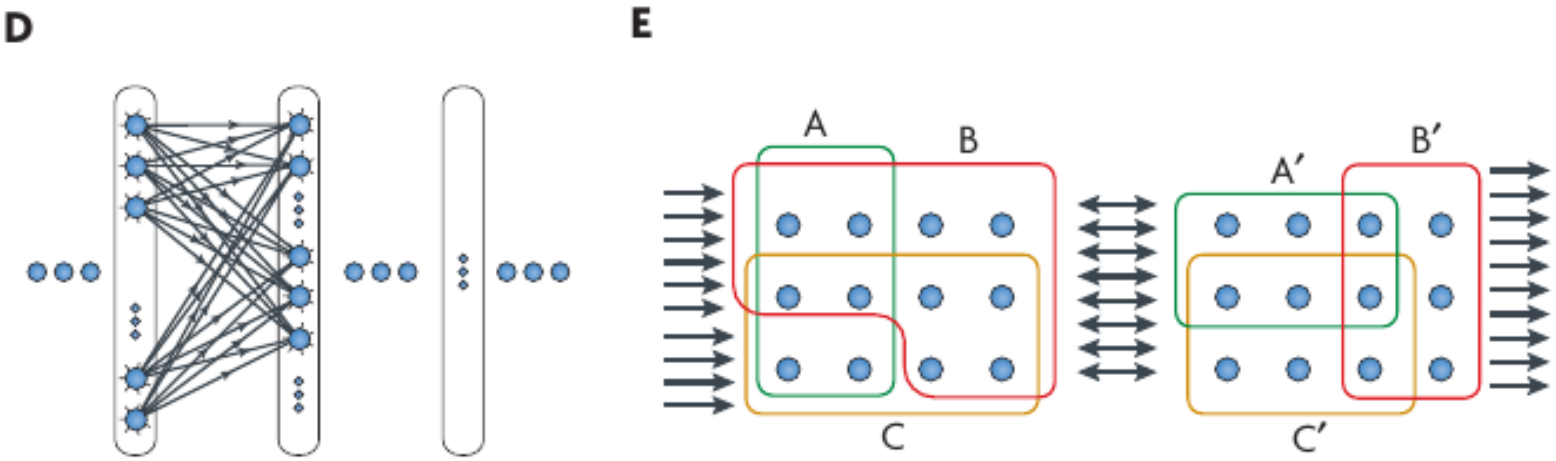
Las neuronas forman redes

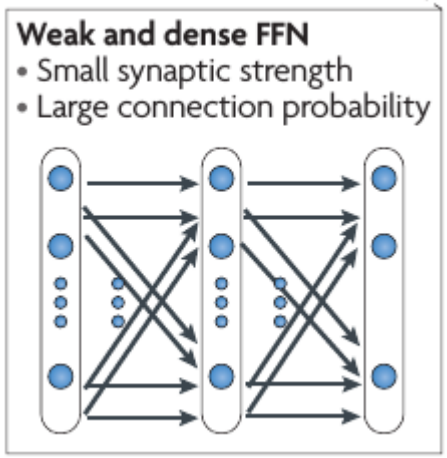


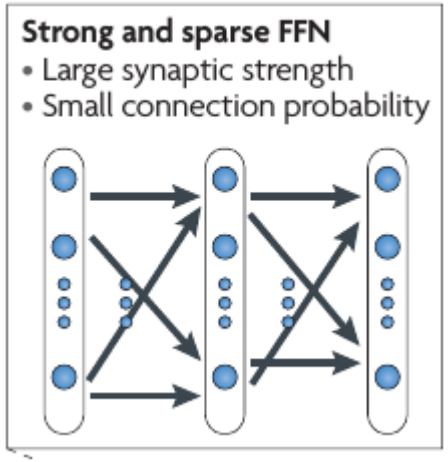


Kumar *et al.* (2010) *Nat Rev Neurosci*

FFNs y Neural Assemblies

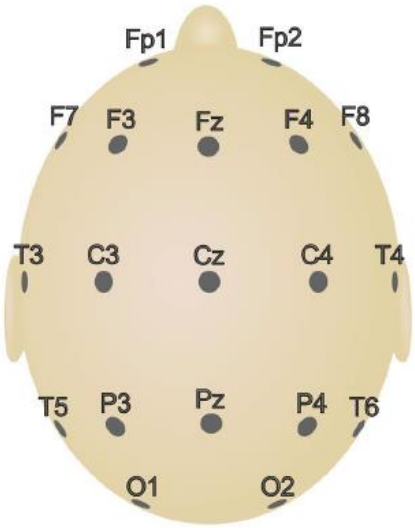


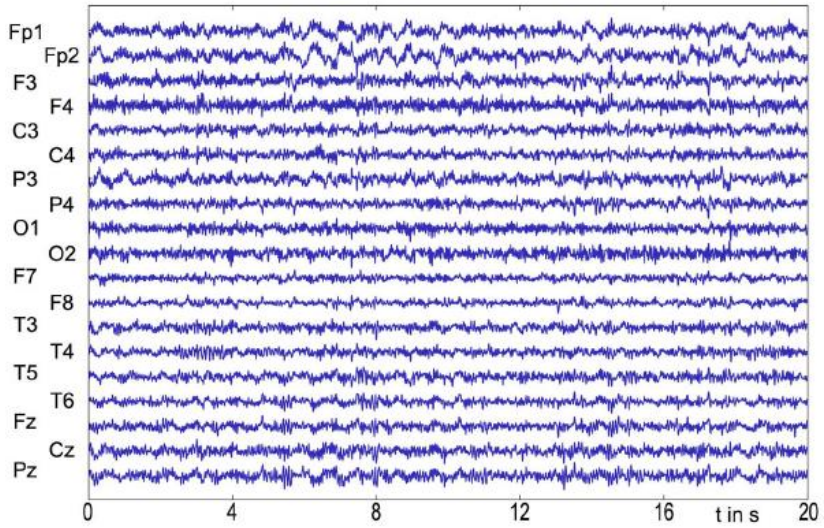




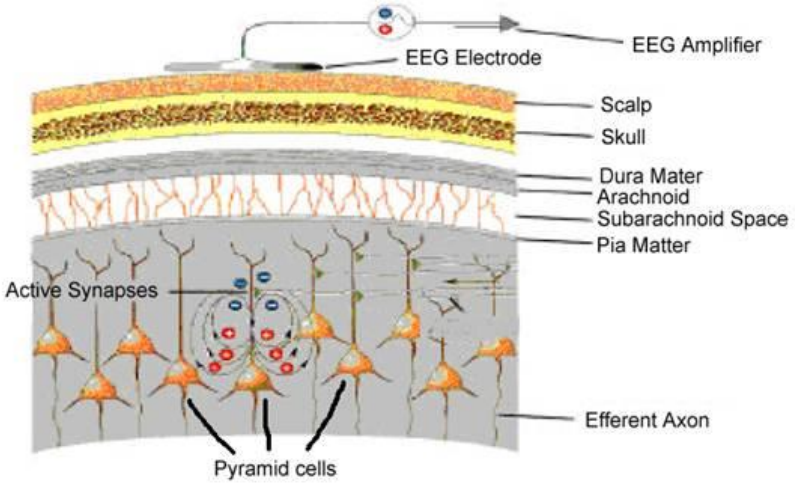
Kumar *et al.* (2010) *Nat Rev Neurosci*

Oscilaciones de masas neurales

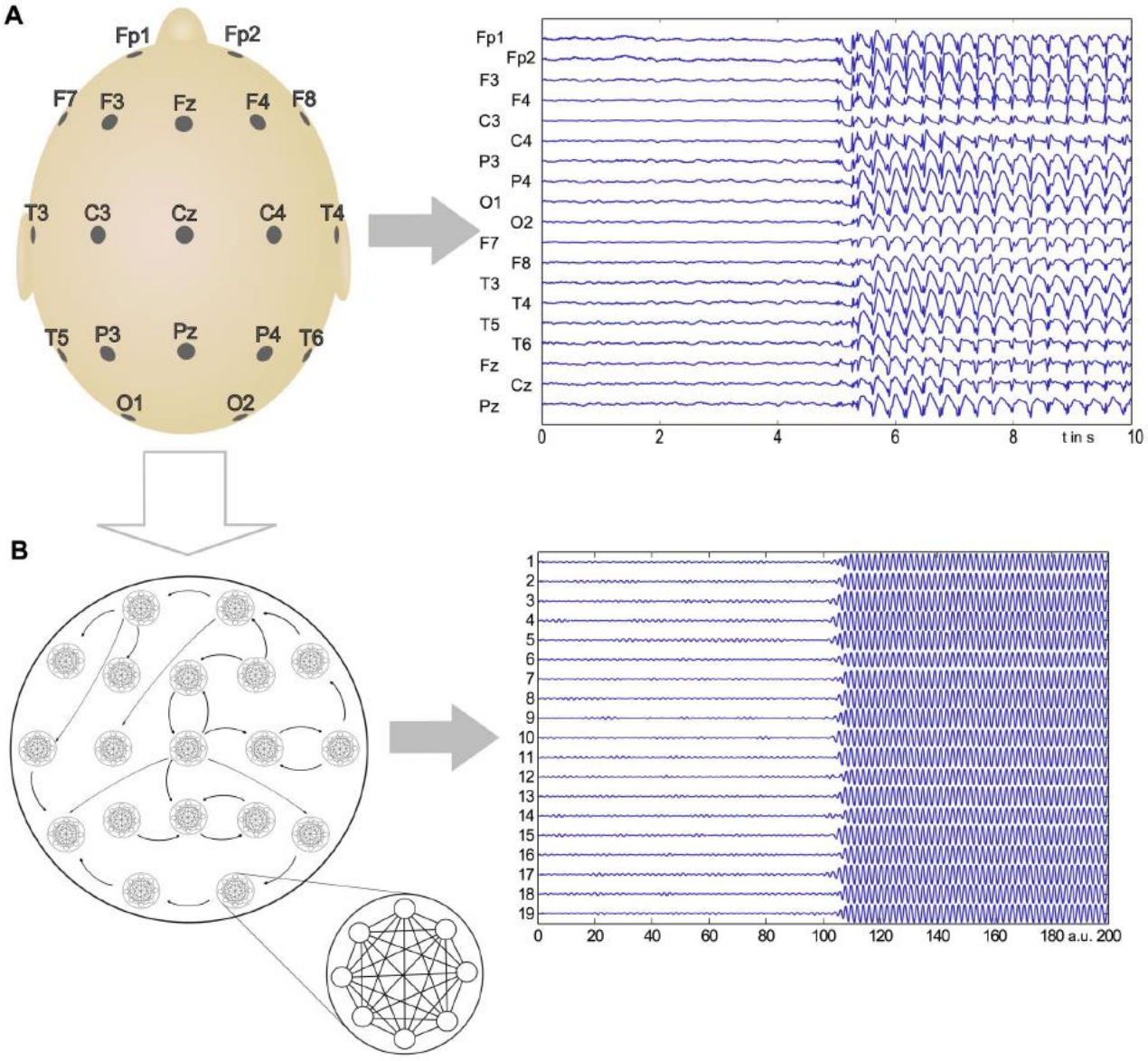




EEG



Oscilaciones de masas neurales

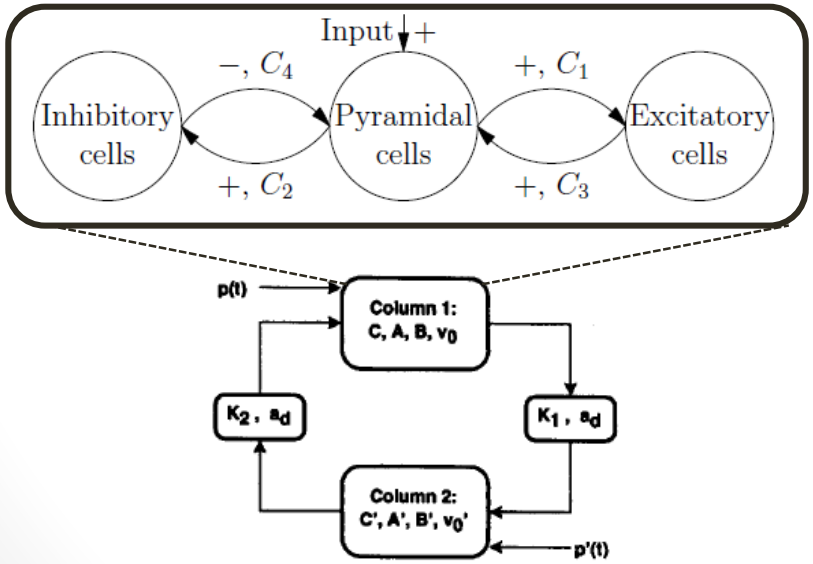


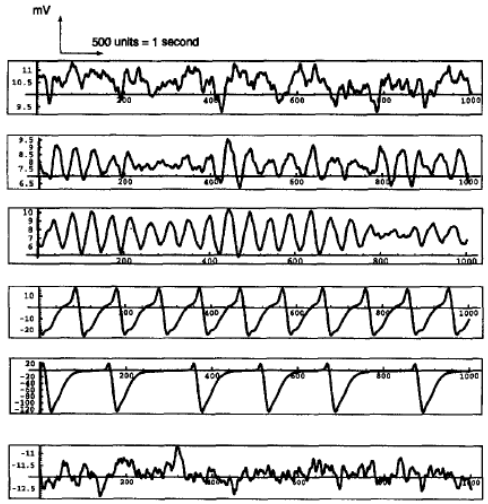
Modelos de masas neuronales

- CTRNN – Continuous Time Recurrent Neural Networks

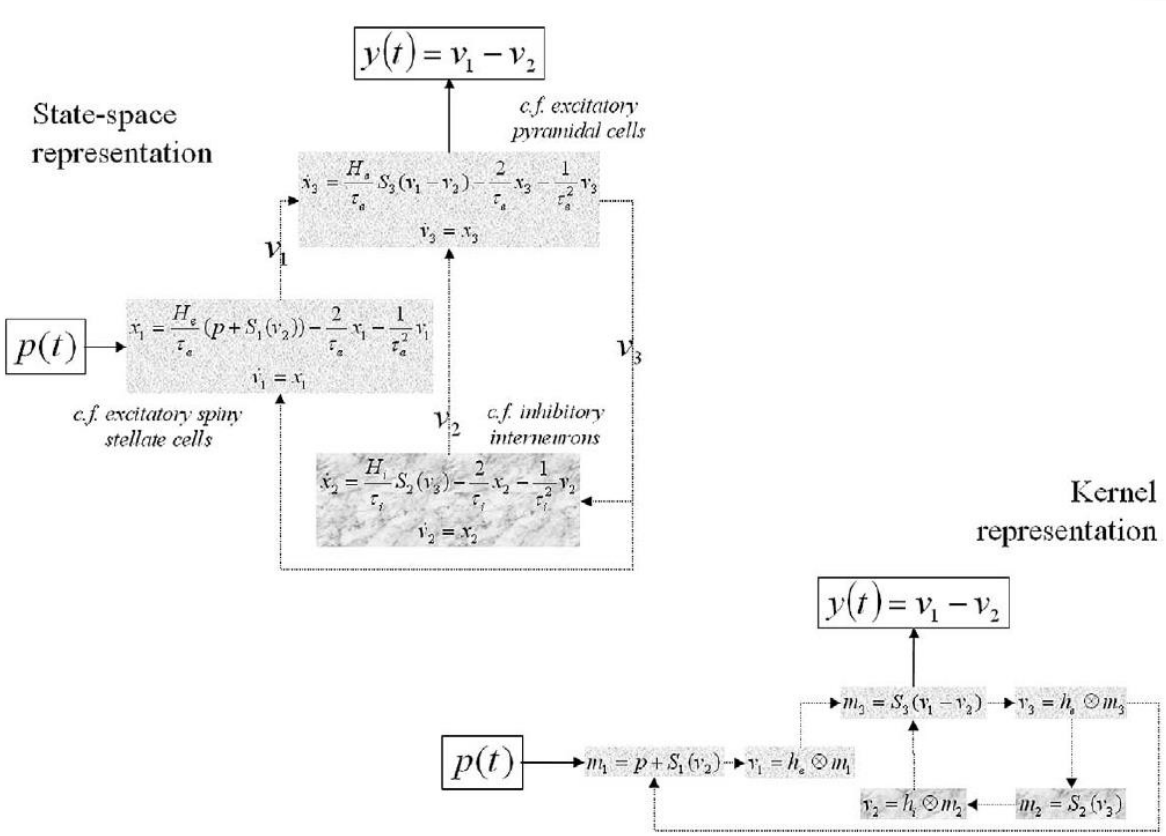
$$\frac{dy_i}{dt} = \frac{1}{\tau_i}\left(-y_i + \sum_{j=1}^{N} w_{ji}\sigma(y_j + \theta_j) + I_i\right) \qquad \sigma(x) = \frac{1}{1+e^{-x}}$$

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





NMMs



$$\dot{y}_0(t) = y_3(t)$$

$$\dot{y}_3(t) = Aa\ \mathrm{Sigm}[y_1(t) - y_2(t)] - 2a y_3(t) - a^2 y_0(t)$$

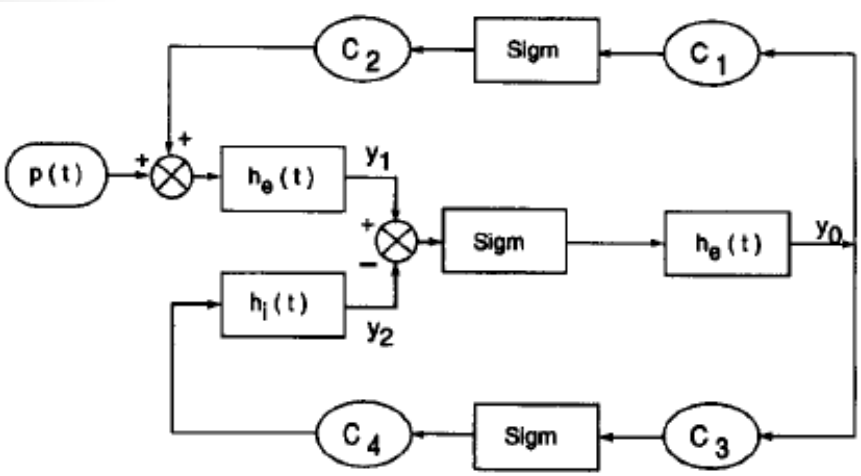
$$\dot{y}_1(t) = y_4(t)$$

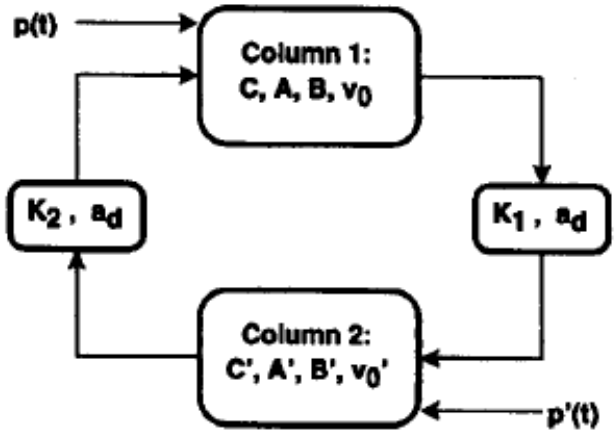
$$\dot{y}_4(t) = Aa\{p(t) + C_2\ \mathrm{Sigm}[C_1 y_0(t)]\} - 2a y_4(t) - a^2 y_1(t)$$

$$\dot{y}_2(t) = y_5(t)$$

$$\dot{y}_5(t) = Bb\{C_4\ \mathrm{Sigm}[C_3 y_0(t)]\} - 2b y_5(t) - b^2 y_2(t)$$

2 NMM nodes


C 2
Sigm
C 1
p(t)
+
+
h e (t)
y1
+
Sigm
h e (t)
y0
−
h i (t)
y2
C 4
Sigm
C 3


p(t)
Column 1:
C, A, B, v0
K2 , ad
K1 , ad
Column 2:
C', A', B', v0'
p'(t)

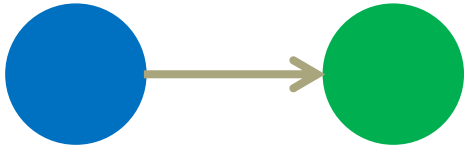
Osciladores de Kuramoto

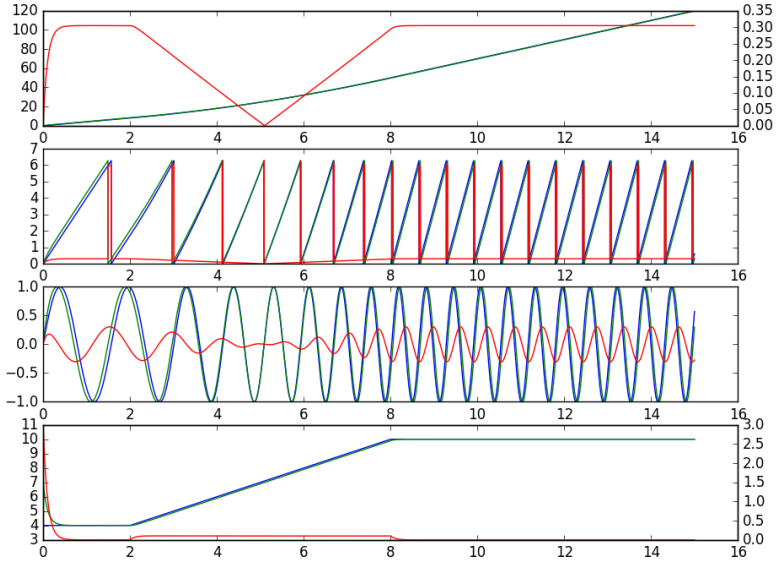
$$\frac{d\theta_i}{dt} = \omega_i + \sum_j w_{ij} \sin(\omega_j - \omega_i)$$

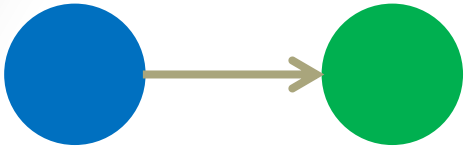
ω_i frecuencia natural (preferida) de i

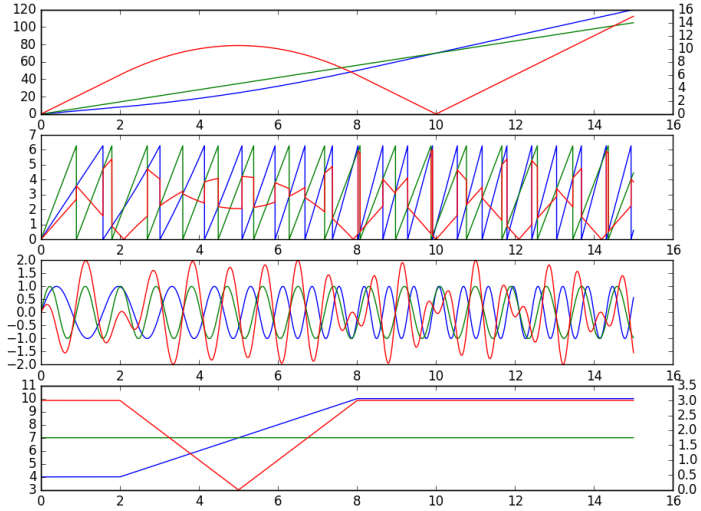
w_{ij} 'peso' de la conexión $j \rightarrow i$

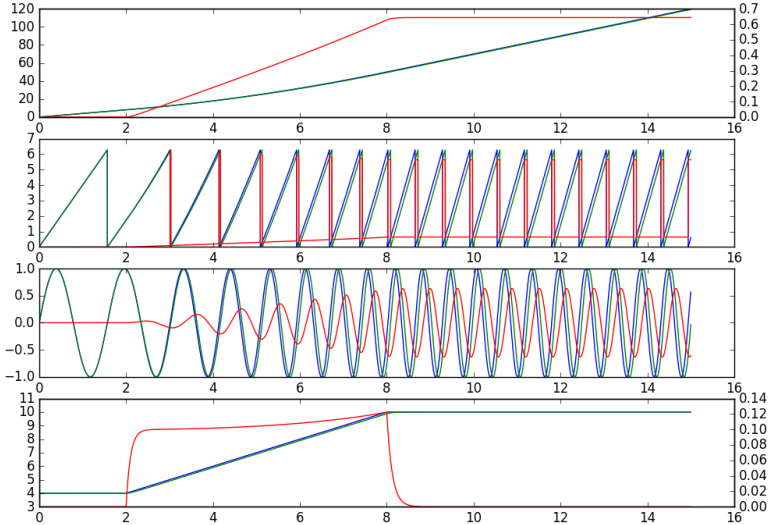
Si $w_{ij} > 0, w_{ji} = 0 \Rightarrow$ Maestro-esclavo

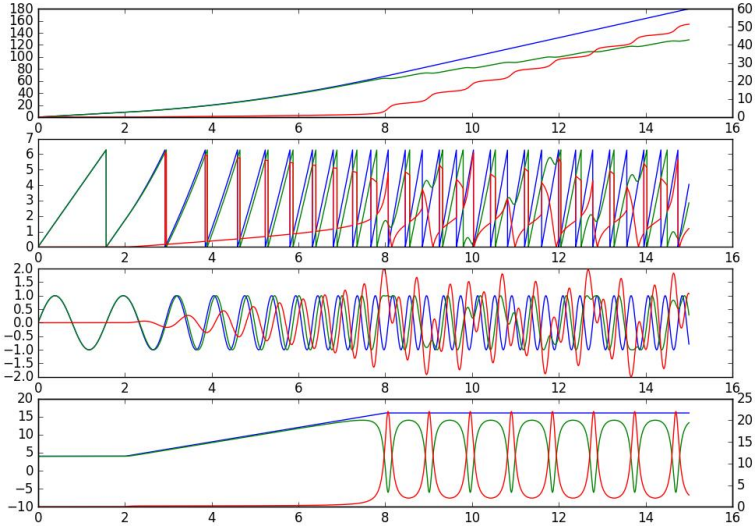




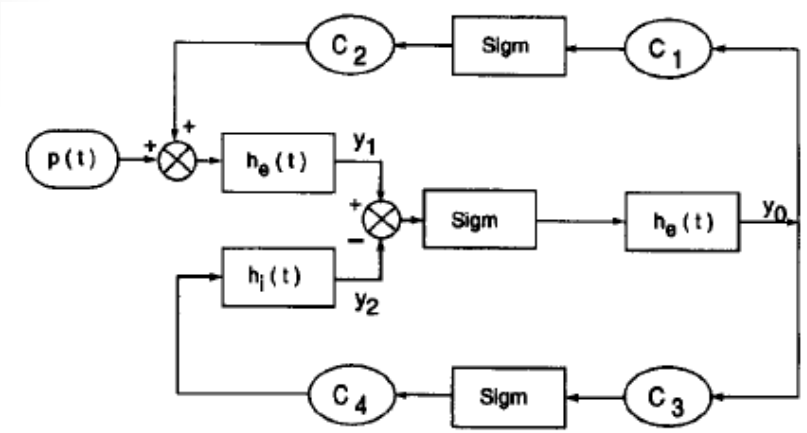


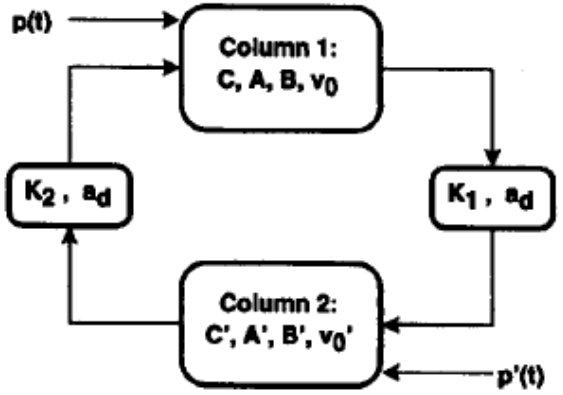


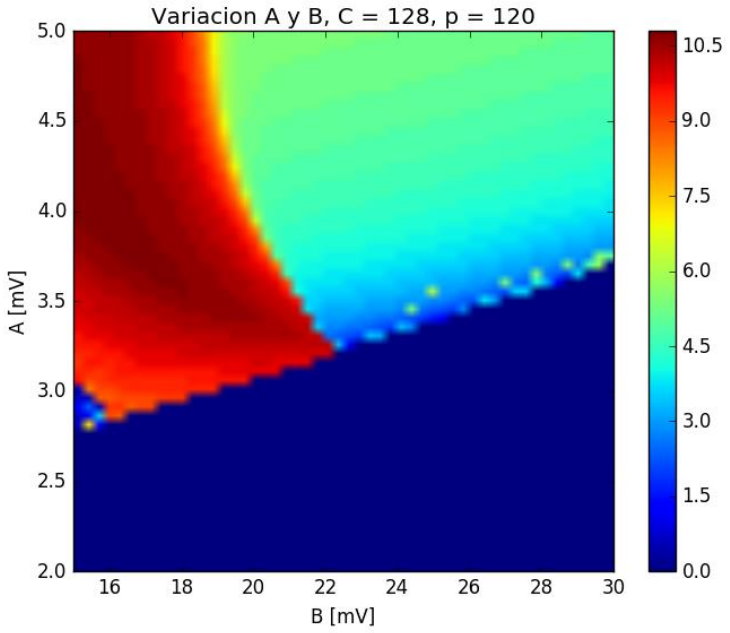


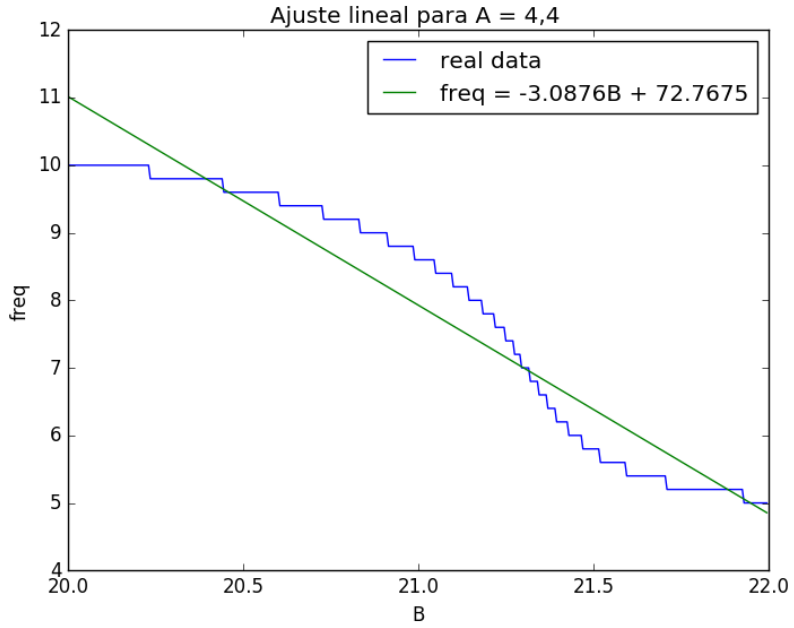


¿Pasa lo mismo con NMMs?









Problemas:

- Osciladores no sinusoidales: ¿ocurre lo mismo que en Kuramoto?
  - Paso 1: medir fase y frecuencia instantánea
  - Observar relaciones fase/frecuencia cuando el ‘maestro’ cambia su frecuencia
  - Extender a un maestro dado por pulsos, en vez de otro oscilador.