

Neuronal Models - part III

Stefano Luccioli

Istituto Sistemi Complessi - CNR



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Single neuron models - 1

Single neuron models describe the **dynamics** of the membrane potential

● realistic models:

● **Hodgkin-Huxley model** - 4 variables → model for squid giant axon

$$C \frac{dV}{dt} = -G_{Na} m^3 h (V - V_{Na}) - G_K n^4 (V - V_K) - G_L (V - V_L) + I_{syn}$$

$$\frac{dX}{dt} = \alpha_X - X(\alpha_X + \beta_X) \quad X = n, m, h \quad \text{gating variables} \quad X = X(V, t)$$

$\alpha_X = \alpha_X(V)$ and $\beta_X = \beta_X(V)$ are **non linear** function of V

● models for other neurons

Single neuron models - 2

General form of a **bidimensional reduced** models

$$\frac{dV}{dt} = \frac{1}{\tau} (F(V, w) + RI(t))$$

$$\frac{dw}{dt} = \frac{1}{\tau_w} G(V, w)$$

- $V \rightarrow$ **membrane potential**, $w \rightarrow$ **recovery variable**
- $R = 1/g_L$, $\tau = RC$, τ_w is a constant

FitzHugh-Nagumo model

The equations for the **membrane potential** ("fast") and **recovery variable** ("slow") are

$$\dot{V} \equiv \frac{dV}{dt} = V - \frac{V^3}{3} - W + I \equiv f_1(V, W)$$

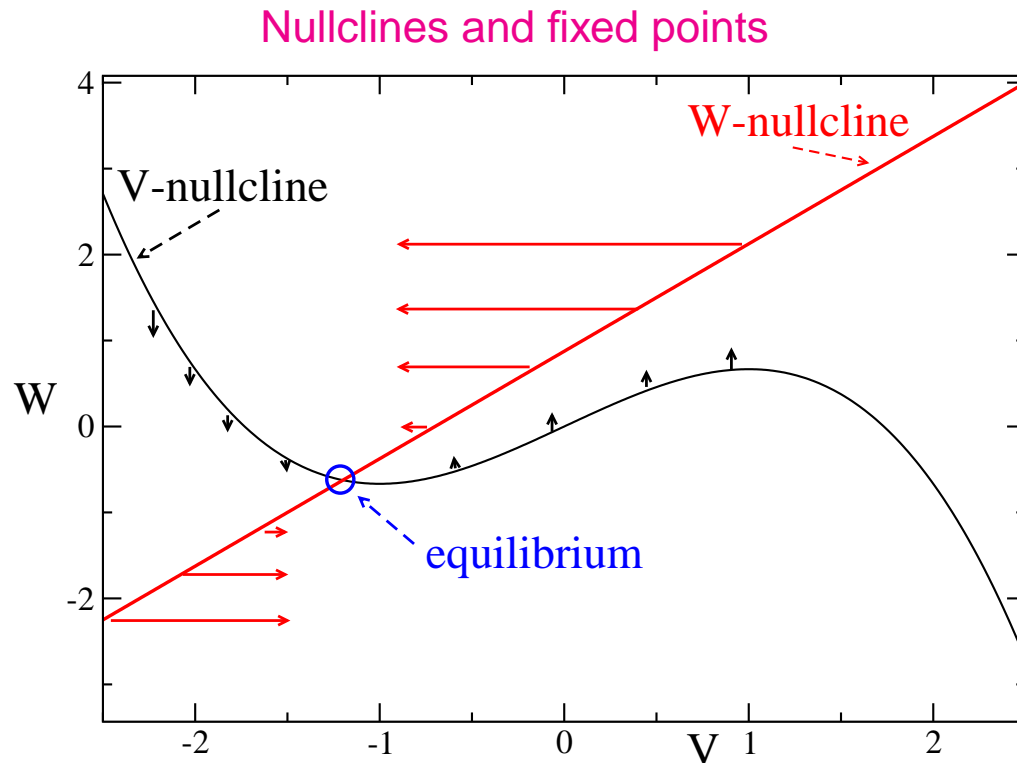
$$\dot{W} \equiv \frac{dW}{dt} = \phi(V + a - bW) \equiv f_2(V, W)$$

- $a > 0, b > 0, \phi = \tau/\tau_w > 0$
- here $a = 0.7, b = 0.8, \phi = 0.08$

For $\Delta t \ll 1$ the movement is in the direction of the **flux field** $\dot{\vec{r}} = (\dot{V}, \dot{W})$, i.e.

$$(\Delta V, \Delta W) \simeq (\dot{V}, \dot{W})\Delta t$$

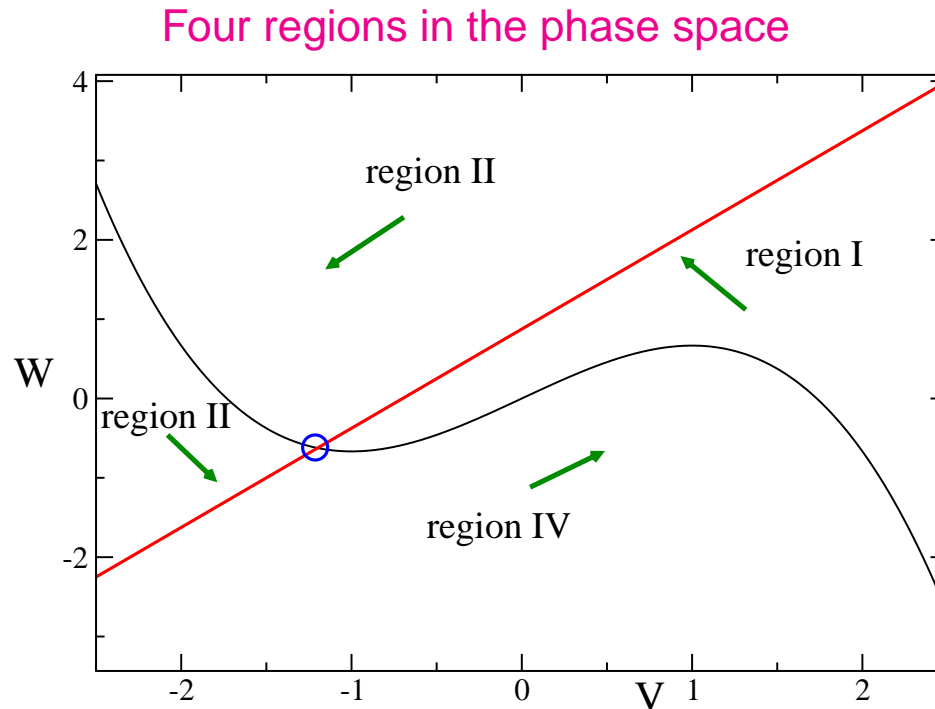
FitzHugh-Nagumo model



- **V-nullcline** \Leftrightarrow curve $\dot{V} = 0 \rightarrow W = V - V^3/3 + I \rightarrow$ on *V-nullcline* $\dot{\vec{r}} = (0, \dot{W})$
- **W-nullcline** \Leftrightarrow curve $\dot{W} = 0 \rightarrow W = (V + a)/b \rightarrow$ on *W-nullcline* $\dot{\vec{r}} = (\dot{V}, 0)$
- **fixed point** (or **equilibrium**) (intersection between nullclines) $\Leftrightarrow (\dot{V}, \dot{W}) = (0, 0)$

For $b < 1 \rightarrow$ one fixed point $\forall I \rightarrow \vec{r}^* = (\bar{V}, \bar{W})$

FitzHugh-Nagumo model



Phase space (V,W) divided in **four regions** according to the sign of the components of the flux field (\dot{V}, \dot{W}) :

- region I $\rightarrow \dot{V} < 0, \dot{W} > 0$
- region II $\rightarrow \dot{V} < 0, \dot{W} < 0$
- region III $\rightarrow \dot{V} > 0, \dot{W} < 0$
- region IV $\rightarrow \dot{V} > 0, \dot{W} > 0$

FitzHugh-Nagumo model

Linear stability analysis of the fixed point for $I = 0$

- Evolution of a "small" perturbation $\delta\vec{r} = (\delta V, \delta W)$ around (\bar{V}, \bar{W}) :

$$\delta\dot{\vec{r}} = \begin{bmatrix} \frac{\partial f_1}{\partial v} & \frac{\partial f_1}{\partial w} \\ \frac{\partial f_2}{\partial v} & \frac{\partial f_2}{\partial w} \end{bmatrix}_{(\bar{V}, \bar{W})} \delta\vec{r} = \begin{bmatrix} (1 - \bar{V}^2) & -1 \\ \phi & -b\phi \end{bmatrix} \delta\vec{r} \equiv J(\bar{V}, \bar{W}) \delta\vec{r}$$

- solving the spectral problem for $J(\bar{V}, \bar{W}) \rightarrow \lambda_{1,2}$ eigenvalues, $\vec{r}_{1,2}$ eigenvectors, $c_{1,2}$ constants:

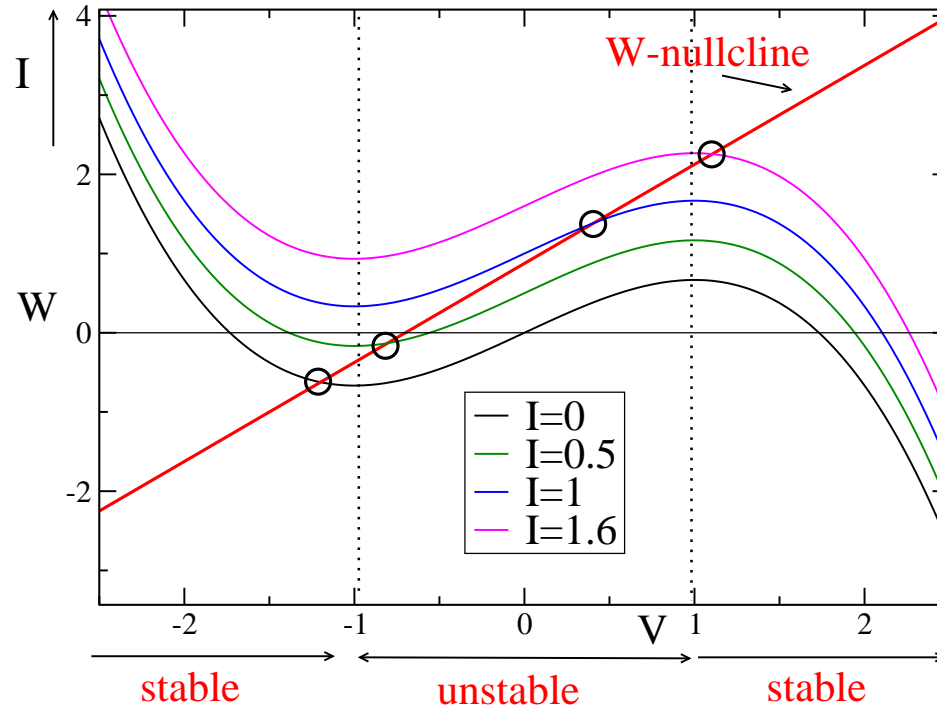
$$\delta\vec{r}(t) = c_1 \vec{r}_1 e^{\lambda_1 t} + c_2 \vec{r}_2 e^{\lambda_2 t}$$

$$\lambda_{1,2} = \frac{-(\bar{V}^2 - 1 + b\phi) \pm \sqrt{(\bar{V}^2 - 1 + b\phi)^2 - 4\phi}}{2} \equiv \alpha \pm i\omega$$

- $\alpha < 0 \rightarrow$ **stable fixed point** (stable spiral) and the whole plane is the basin of attraction
 \rightarrow the neuron is **silent (no spikes!)**

FitzHugh-Nagumo model

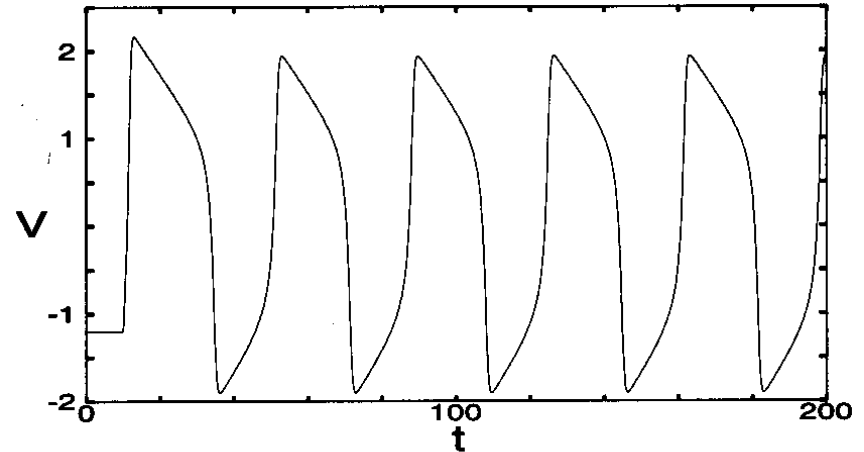
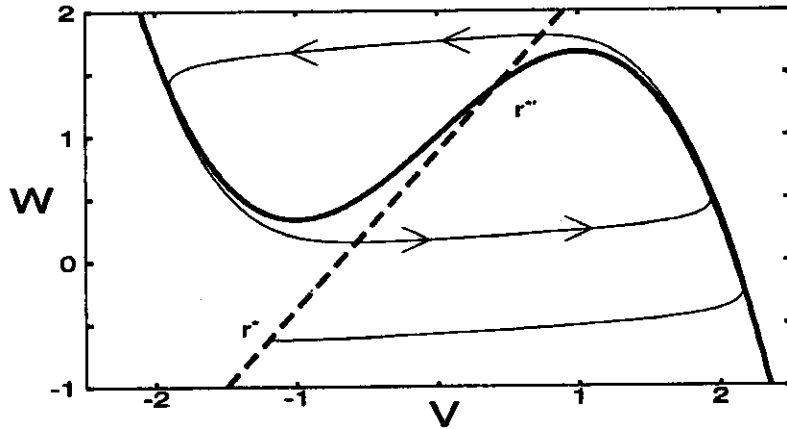
Stability of the fixed point for $I \neq 0$



- same formula for $\lambda_{1,2}$ but now $(\bar{V} = \bar{V}(I), \bar{W} = \bar{W}(I))$
- $\alpha(I) = -(\bar{V}(I)^2 - 1 + b\phi)/2$
 - $\bar{V} < -\sqrt{1 - b\phi} \Leftrightarrow I < I_- \rightarrow \alpha < 0$ (stable fixed point)
 - $|\bar{V}| < \sqrt{1 - b\phi} \Leftrightarrow I_- < I < I_+ \rightarrow \alpha > 0$ unstable fixed point
 - $\bar{V} > +\sqrt{1 - b\phi} \Leftrightarrow I > I_+ \rightarrow \alpha < 0$ (stable fixed point)

FitzHugh-Nagumo model

Stable attractor for $I_- < I < I_+$: limit cycle



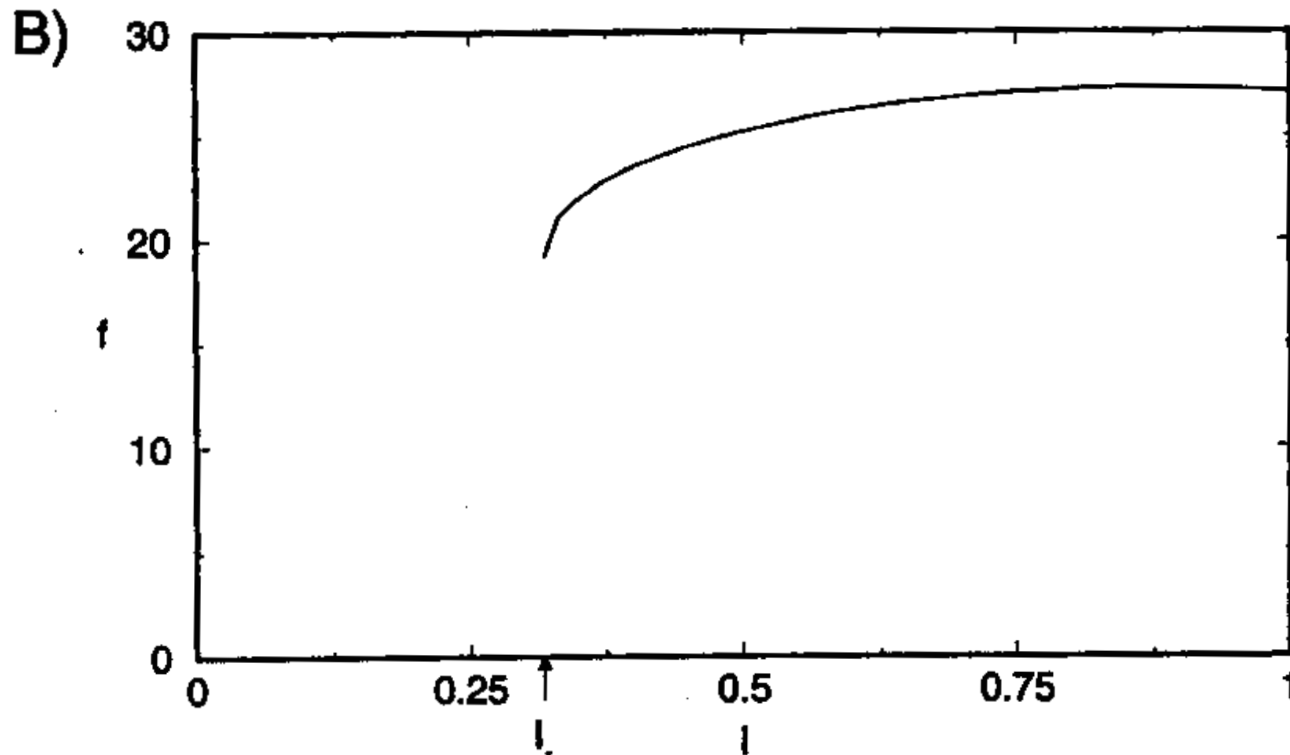
Existence of a **stable** limit cycle (periodic sequence of **action potentials**):

- qualitative reasoning:
 - for $V, W \gg 1 \Rightarrow \frac{d}{dt}(V^2 + W^2) \simeq -V^4 < 0$ (the flux is attracting)
 - unstable fixed point (outgoing flux from fixed point)
- rigorously \rightarrow Poincaré-Bendixson Theorem (only in 2-dimensions)

Shape of action potentials (remind $\phi \ll 1$) \Rightarrow **fast** raising/depolarization - **slow** relaxing (along V -nullcline) - **fast** decreasing - **slow** recovery (along W -nullcline)

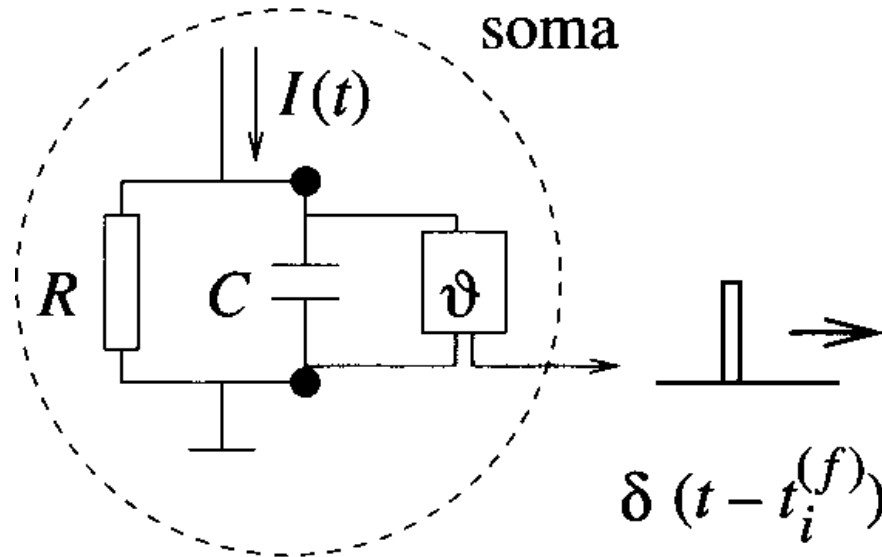
FitzHugh-Nagumo model

Gain function: frequency (f) versus stimulation current (I)



- type-I neuronal model \rightarrow arbitrarily small frequency (*leaky-integrate-and-fire*)
- type-II neuronal model \rightarrow periodic firing starts with finite frequency (Hodgkin-Huxley, FitzHugh-Nagumo)

Leaky-integrate-and-fire



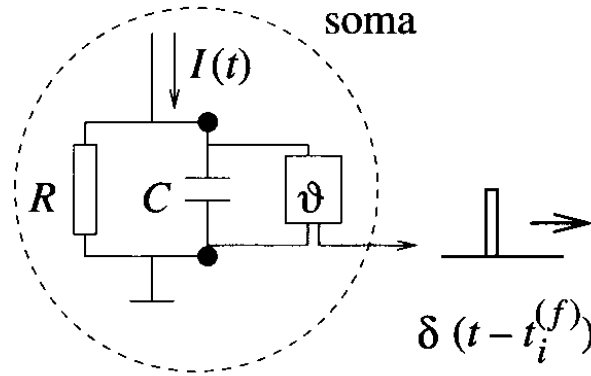
- 1-dimension model \rightarrow dynamics of membrane potential V
- **formal** model \rightarrow **only** dynamics **below** the **firing threshold** θ

Recalling **passive electric properties** of the membrane (R and C):

$$\text{Nodes Law} \rightarrow I(t) = I_R(t) + I_C(t) = \frac{V(t)}{R} + C \frac{dV(t)}{dt}$$

Leaky-integrate-and-fire

Full model



$$\tau_m \frac{dV(t)}{dt} = -V(t) + RI(t) \quad t < t_f \quad (\tau_m = RC)$$

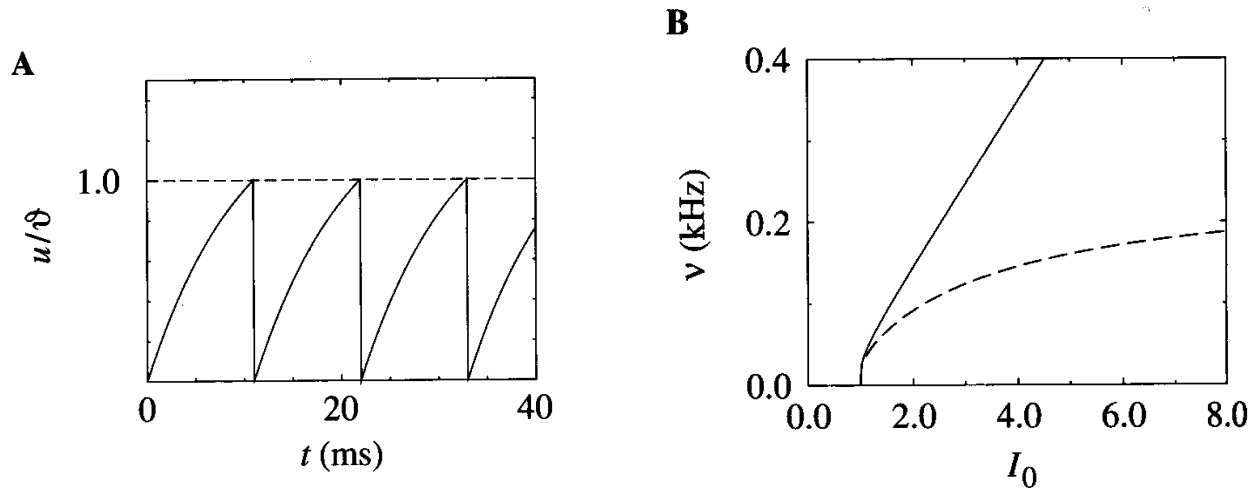
$$V(t_f^-) = \theta \quad \rightarrow \quad \text{spike emission } \delta(t - t_f)$$

$$V(t) = V_r \quad t_f^+ < t < t_f^+ + \Delta_{abs}$$

$V_r \Rightarrow$ rest potential $\Delta_{abs} \Rightarrow$ absolute refractoriness

Leaky-integrate-and-fire

Response to a constant current I_0



$$V(t) = RI_0(1 - e^{-t/\tau_m}) \quad \text{if } V(t=0) = V_r \equiv 0$$

- $RI_0 < \theta \rightarrow V(\infty) = RI_0$ (silent neuron, no spikes!)
- $RI_0 > \theta \rightarrow$ periodic sequence of spikes with period T^{tot}

$$T^{tot} = T + \Delta_{abs}$$

$$T = \tau_m \ln \frac{RI_0}{RI_0 - \theta} \quad (\text{given by } V(T) = \theta)$$

Morris-Lecar Model - 1

Conductance-based bidimensional model for membrane potential V and recovery variable w :

$$C \frac{dV}{dt} = I - g_{Ca} m_0(V)(V - E_{Ca}) - g_K w(V - E_K) - g_L(V - E_L)$$

$$\frac{dw}{dt} = -\frac{1}{\tau(V)}(w - w_0(V))$$

m_0, w_0, τ nonlinear function of V (reproducing the "shape" of Hodgkin-Huxley variables):

$$m_0(V) = \frac{1}{2} \left[1 + \tanh\left(\frac{V - V_1}{V_2}\right) \right]$$

$$w_0(V) = \frac{1}{2} \left[1 + \tanh\left(\frac{V - V_3}{V_4}\right) \right]$$

$$\tau(V) = \frac{\tau_w}{\cosh\left(\frac{V - V_3}{V_4}\right)}$$

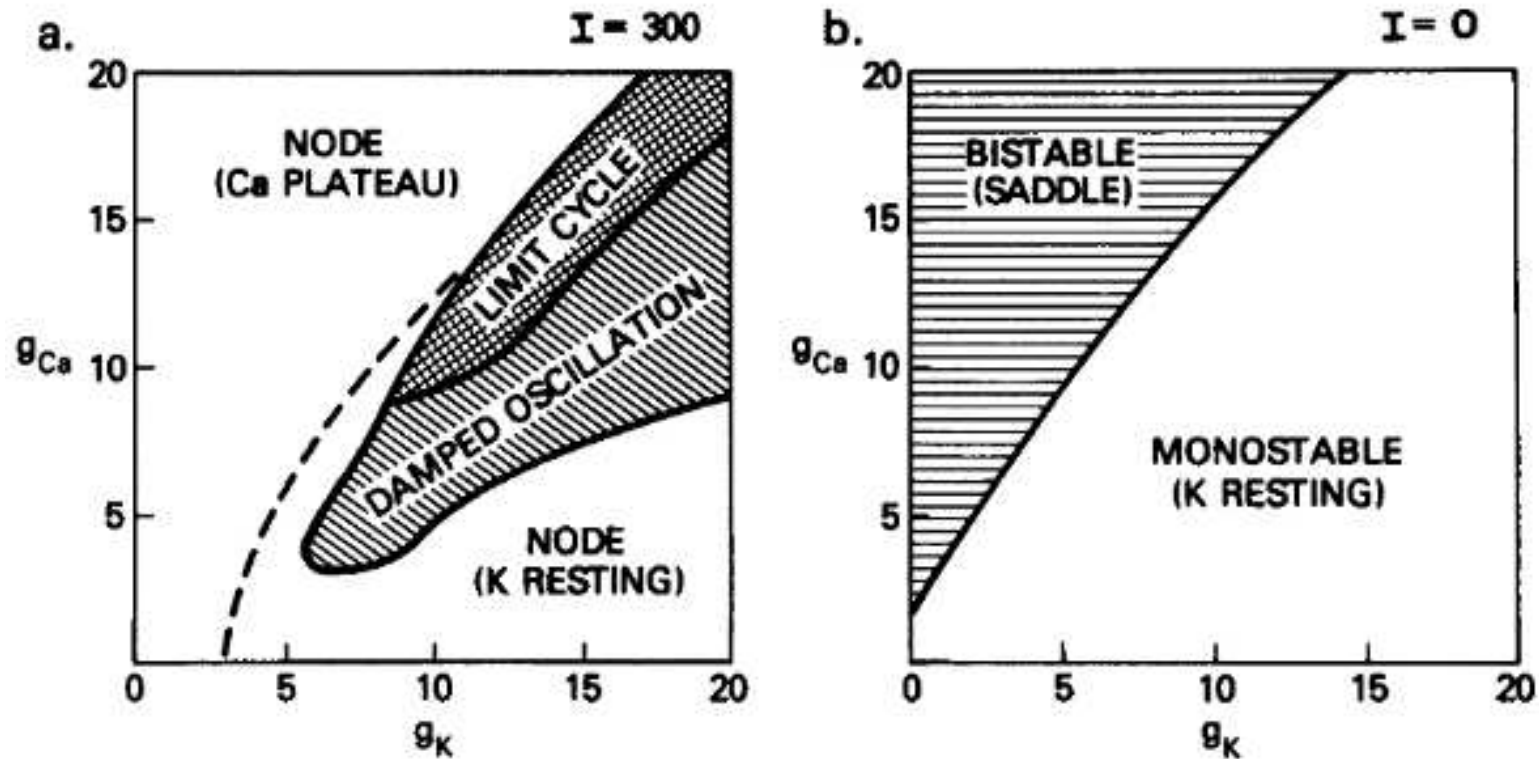
$V_1, V_2, V_3, V_4, \tau_w$ are parameters

Morris-Lecar Model - 2

- Ca^{++} -channels, K^+ -channels → voltage-activated → nonlinear conductances
- g_L → linear conductance
- comparison "2d-reduced" Hodgkin-Huxley/Morris-Lecar:

current terms	"2d-reduced" Hodgkin-Huxley	Morris-Lecar
Ca^{++} (Na^+) current	$m_0(V)^3(b - w)$	$m_0(V)$
K^+ current	w^4	w

Morris-Lecar Model - 3



- $I = 0 \rightarrow$ no damped oscillations/no limit cycle (shaded region: two stable nodes and a saddle, unshaded region: one stable node)
- **limit cycle** for certain values of I, g_{Ca}, g_K ^a (crosshatched region: stable limit cycle and unstable fixed point, unshaded region: one stable node)

^aC. Morris and H. Lecar, H. Voltage oscillations in the barnacle giant muscle fiber. Biophys. J. 35, 193 (1981)