Neuronal Models - part III

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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 $\rightarrow$ model for squid giant axon

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

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

  $\alpha_X = \alpha_X(V)$ 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

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

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

.

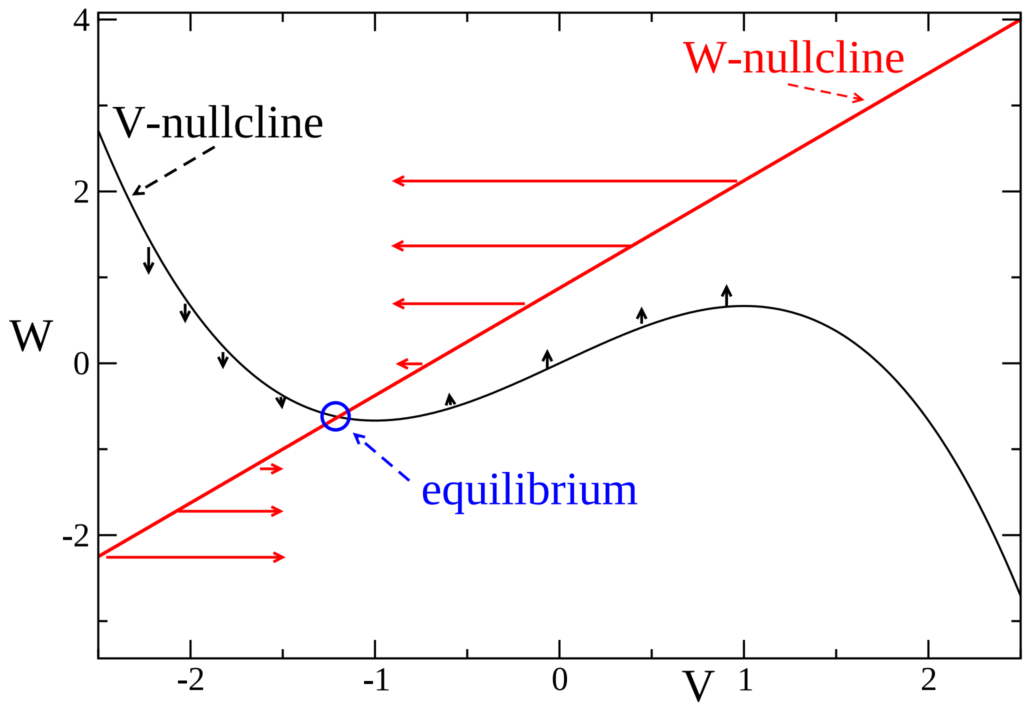
- $a > 0$, $b > 0$, $\phi = \tau/\tau_w > 0$
- here $a = 0.7$, $b = 0.8$, $\phi = 0.08$

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

Nullclines and fixed points

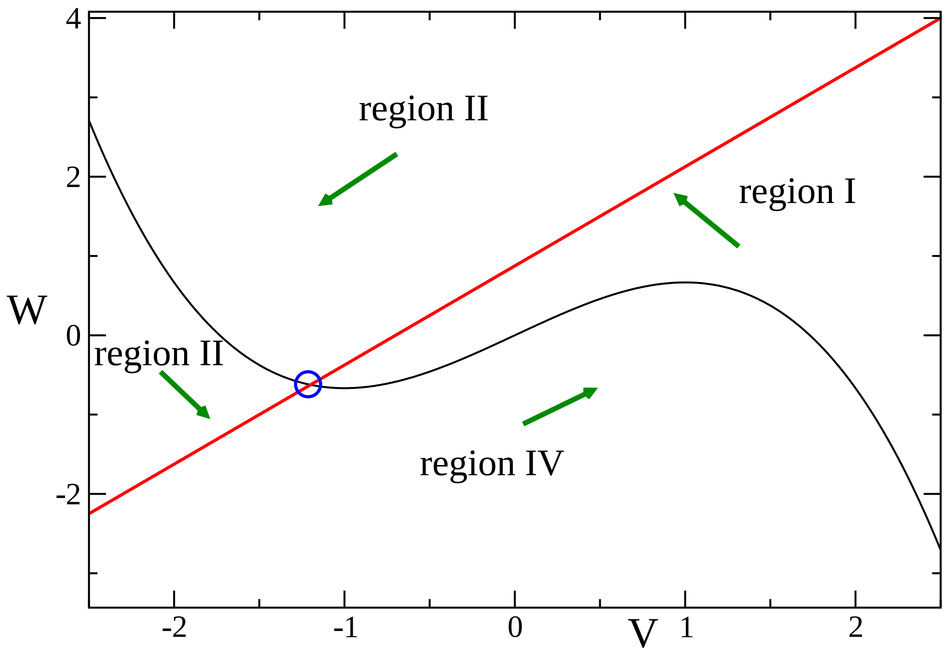


- V-nullcline $\Leftrightarrow$ curve $\dot{V} = 0 \rightarrow W = V - V^3/3 + I \rightarrow$ on *V-nullcline* $\dot{\vec{r}} = (0, \dot{W})$
- W-nullcline $\Leftrightarrow$ curve $\dot{W} = 0 \rightarrow W = (V + a)/b \rightarrow$ on *W-nullcline* $\dot{\vec{r}} = (\dot{V}, 0)$
- fixed point (or equilibrium)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

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

FitzHugh-Nagumo model

Four regions in the phase space



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 $(\overline{V}, \overline{W})$:

$$\delta\dot{\vec{r}} = \left[\begin{array}{cc} \frac{\partial f_1}{\partial v} & \frac{\partial f_1}{\partial w} \\ \frac{\partial f_2}{\partial v} & \frac{\partial f_2}{\partial w} \end{array} \right]_{(\overline{V},\overline{W})} \delta\vec{r} = \left[\begin{array}{cc} (1-\overline{V}^2) & -1 \\ \phi & -b\phi \end{array} \right] \delta\vec{r} \equiv J(\overline{V}, \overline{W})\delta\vec{r}$$

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

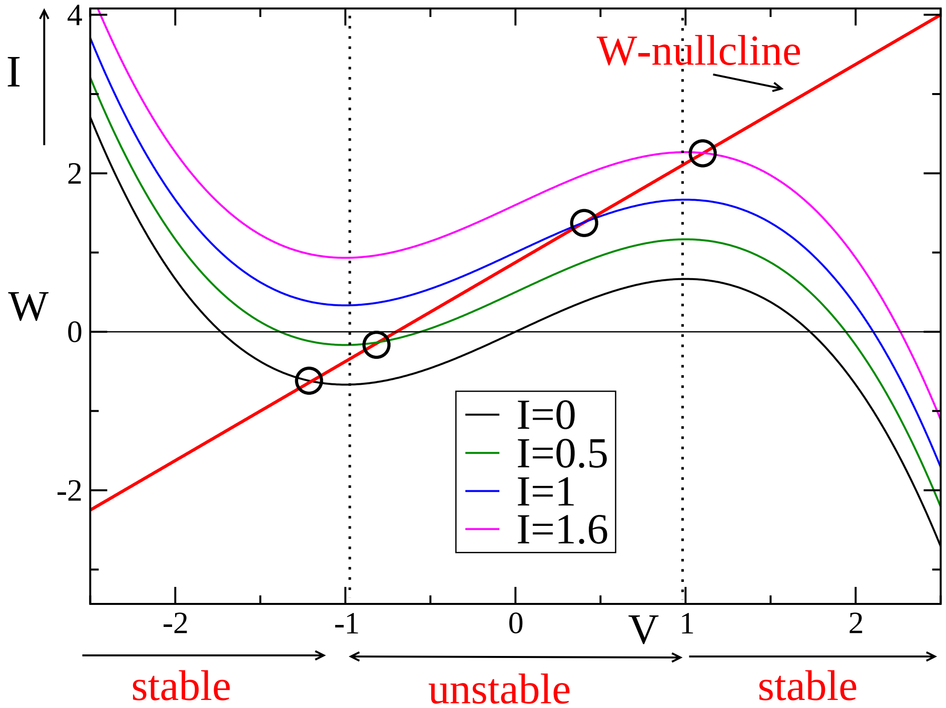
$$\delta\vec{r}(t) = c_1\vec{r}_1 e^{\lambda_1 t} + c_2\vec{r}_2 e^{\lambda_2 t}$$

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

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

FitzHugh-Nagumo model

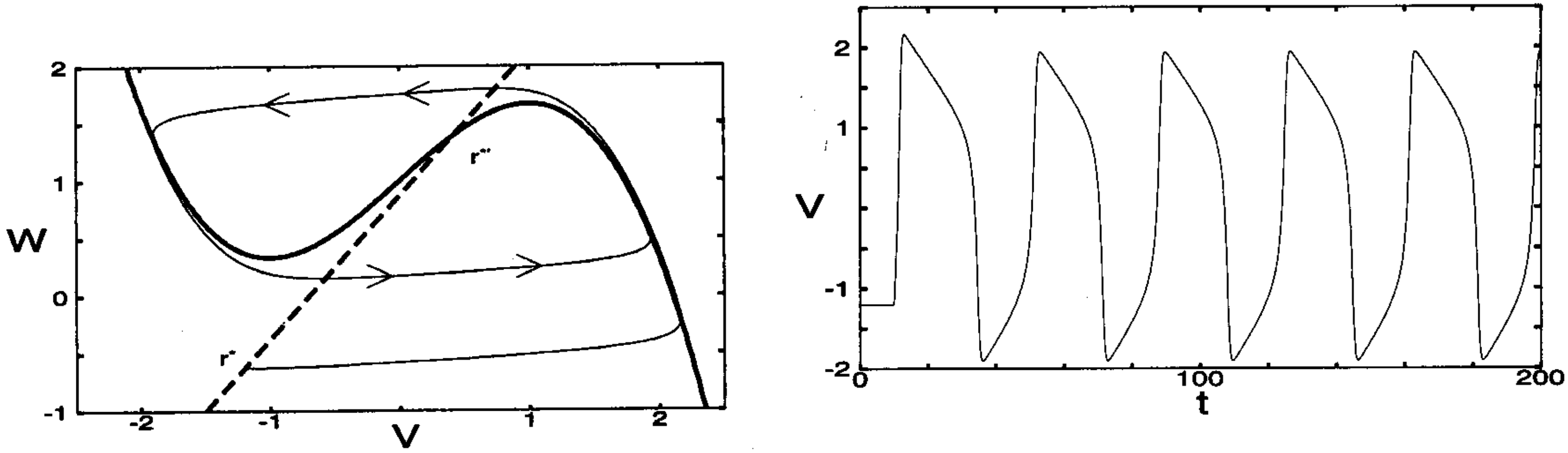
Stability of the fixed point for $I \neq 0$



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

FitzHugh-Nagumo model

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



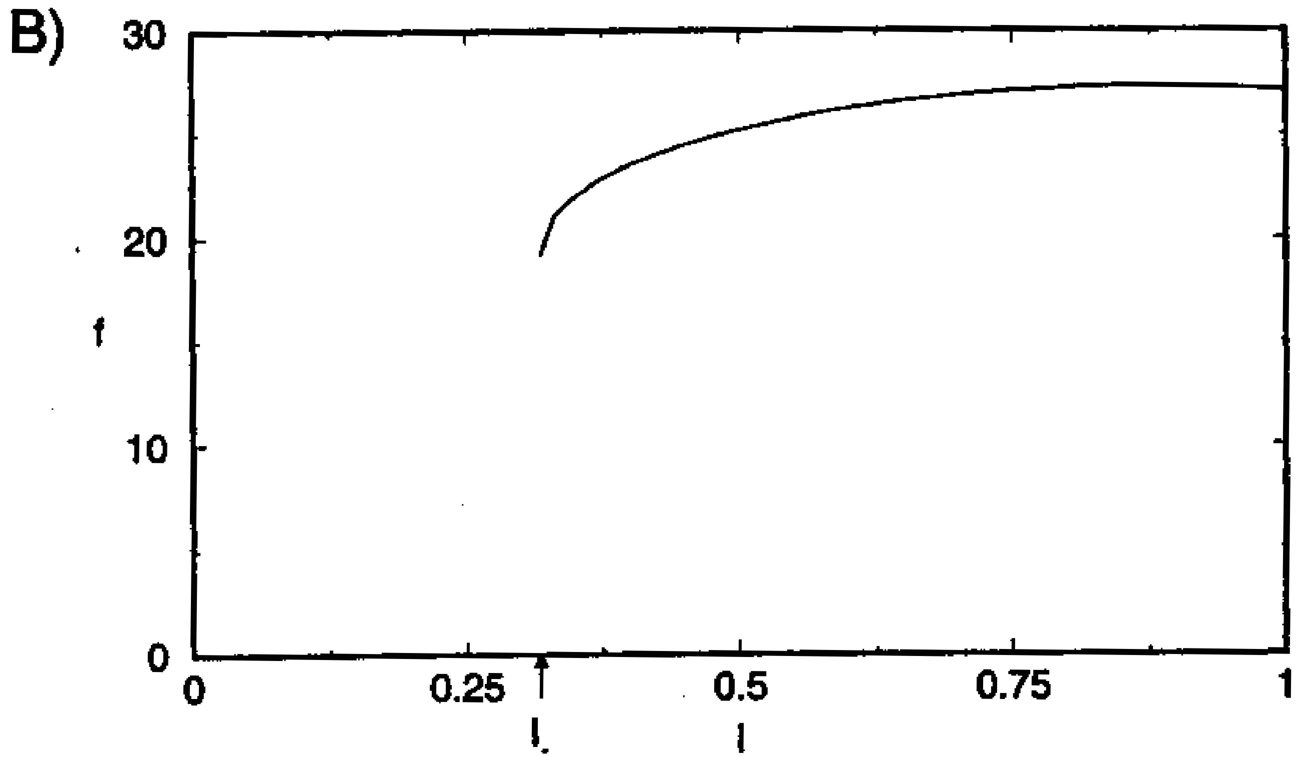
Existence of a stable limit cycle (periodic sequence of action potentials):

- 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 V-nullcline)

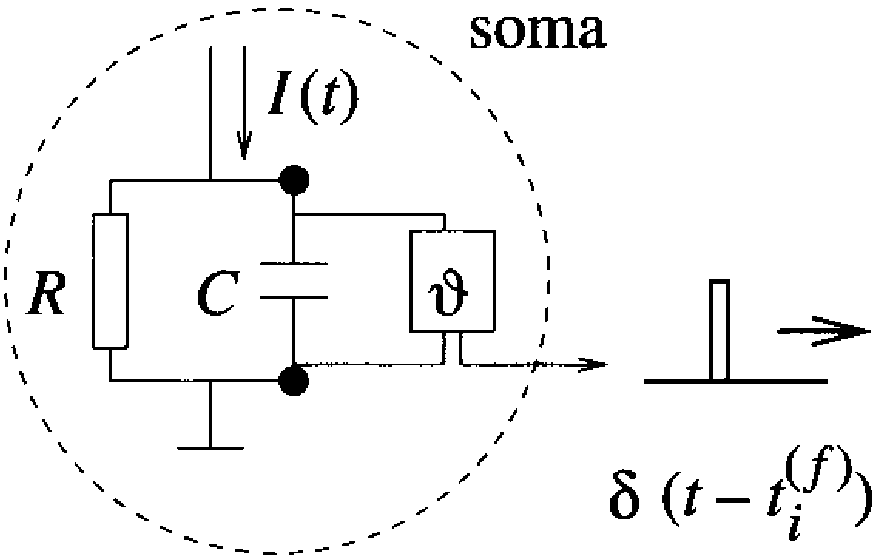
FitzHugh-Nagumo model

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



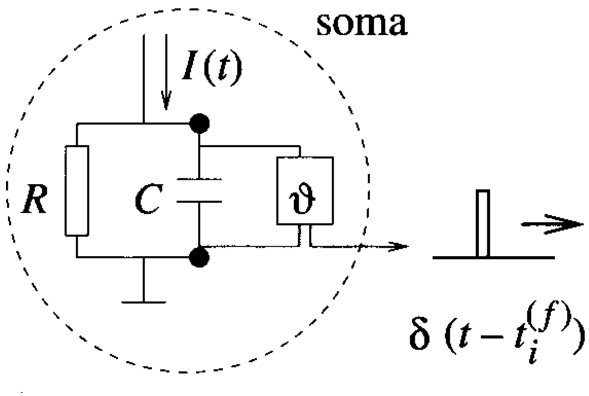
- 1-dimension model $\rightarrow$ dynamics of membrane potential V
- formal model $\rightarrow$ only dynamics below the firing threshold θ

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



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

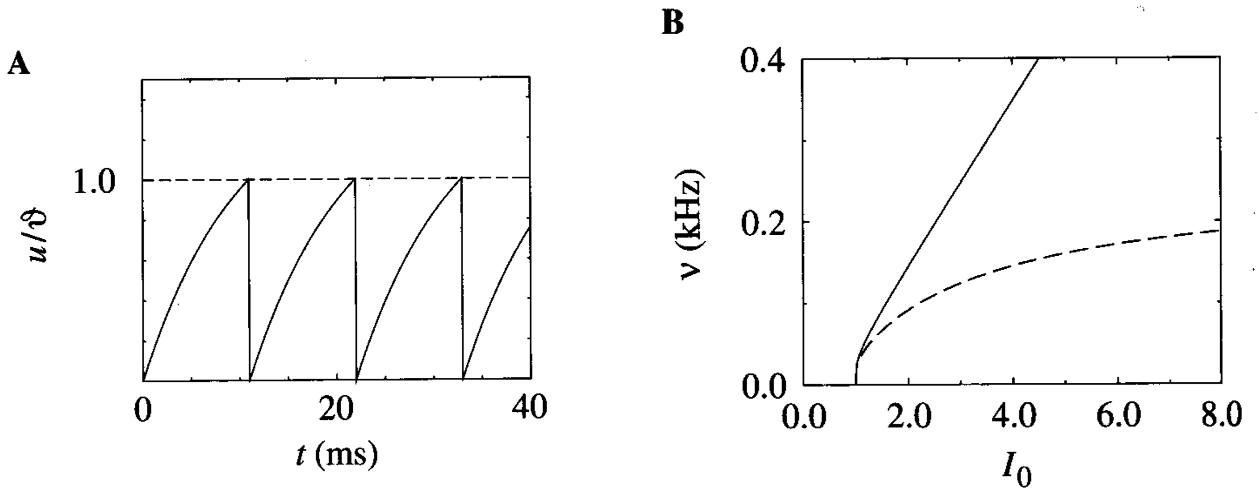
$$V(t_f^-) = \theta \qquad \rightarrow \qquad \text{spike emission} \quad \delta(t - t_f)$$

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

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

Leaky-integrate-and-fire

Response to a constant current I_0



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

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

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

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

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):

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

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

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

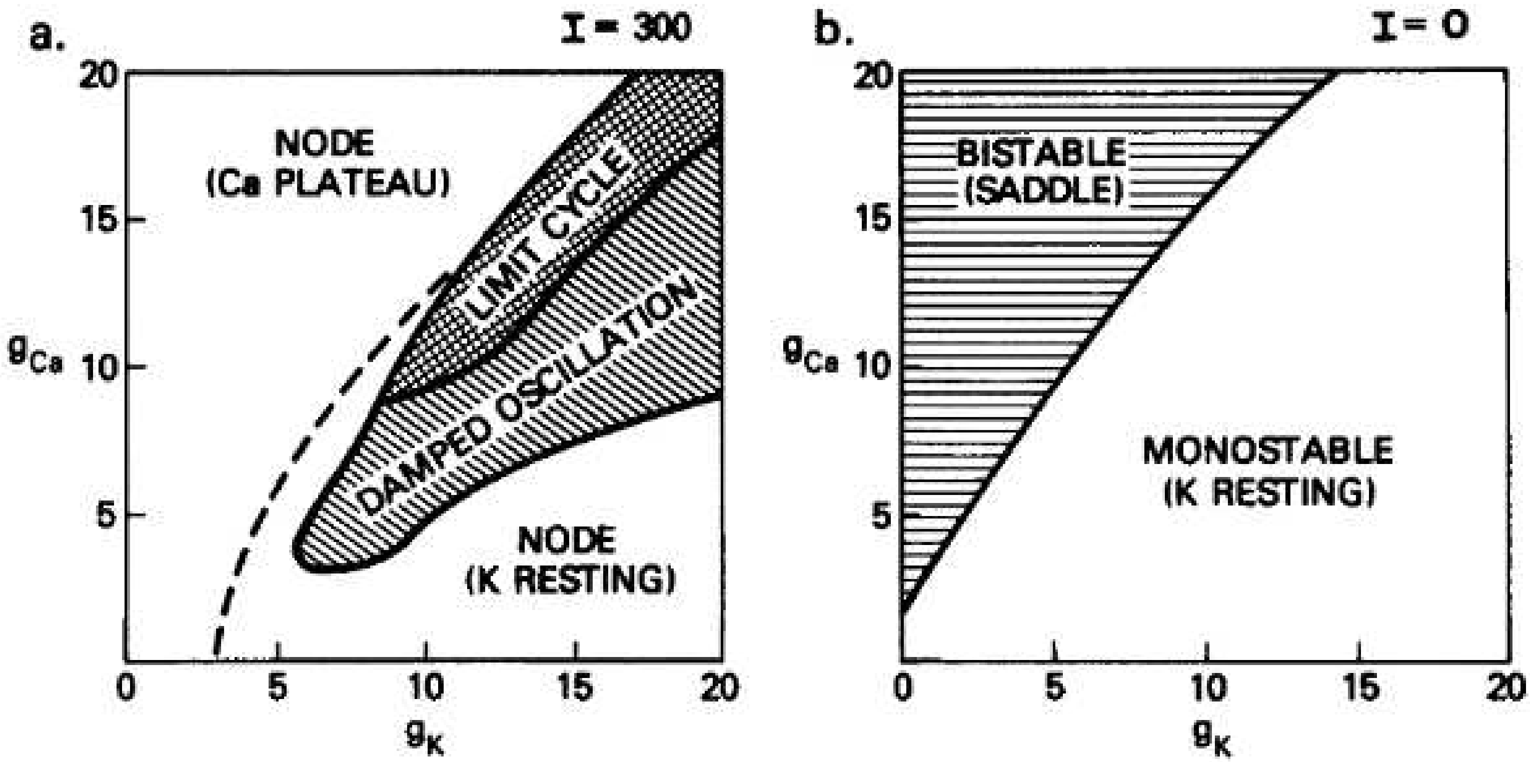
$V_1, V_2, V_3, V_4, \tau_w$ are parameters

Morris-Lecar Model - 2

- Ca^{++}-channels, K^{+}-channels $\rightarrow$ voltage-activated $\rightarrow$ nonlinear conductances
- g_L $\rightarrow$ 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)

[a] C. Morris and H. Lecar, H. Voltage oscillations in the barnacle giant muscle fiber. Biophys. J. 35, 193 (1981)