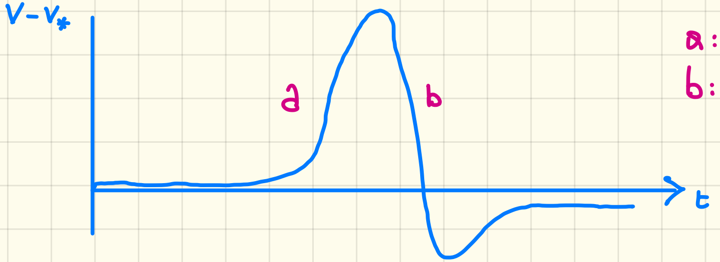
- Recall HH model and spike generation



a: Increase in g_{Na}, depolarisation
b: Increase in g_K, repolarisation

Currents: I_L, I_{Na}, I_K, State variables: (V, n, m, h)

n → K act. gate
h → K inact. gate
m → Na act. gate

- HH model is a nonlinear ODE in $\mathbb{R}^4$. (can be explored via time simulation and num. bif. analy.)
- We now study models that are analysable, at least in part.

  - Morris-Lecar
  - FitzHugh-Nagumo

  } ODEs in $\mathbb{R}^2$

  - Leaky Integrate-and-Fire
  - Quadratic Int. - and- Fire

  } non-smooth ODEs in $\mathbb{R}$

Morris-Lecar model. (barnacle giant muscle fiber)

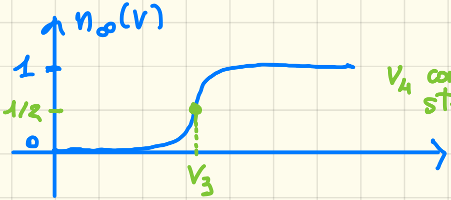
$$C\dot{V} = I - g_L(V-E_L) - g_K\, n\,(V-E_K) - g_{Ca}\, m_\infty(V)(V-E_{Ca})$$

$$\dot{n} = \frac{n_\infty(V) - n}{\tau(V)}$$

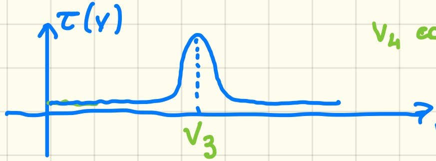
$$m_\infty(V) = \frac{1}{2}\left[1 + \tanh\left(\frac{V-V_1}{2}\right)\right]$$

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

$$\tau(V) = \frac{1}{\cosh\left(\frac{V-V_3}{2V_4}\right)}$$



V_4 controls steepness

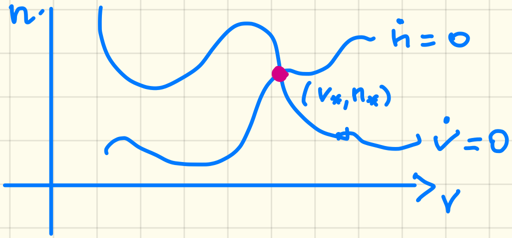


V_4 controls width.

ODE in $\mathbb{R}^2$ (V, n)

$$\dot{V} = f(V,n)$$
$$\dot{n} = g(V,n)$$

Recall facts for ODEs in $\mathbb{R}^2$



Steady state: (v_*, n_*) s.t. $f(v_*, n_*) = 0$
$g(v_*, n_*) = 0$

v-nullcline $= \{ (v,n) : f(v,n) = 0 \}$
n-nullcline $= \{ (v,n) : g(v,n) = 0 \}$

Nullclines partition $\mathbb{R}^2$ into ares with
$\dot{v} > 0, \dot{n} > 0$ $\nearrow$
$\dot{v} < 0, \dot{n} > 0$ $\nwarrow$
$\dot{v} < 0, \dot{n} < 0$ $\swarrow$
$\dot{v} > 0, \dot{n} < 0$ $\searrow$

How do perturbations $(\tilde{v}(t), \tilde{n}(t))$ to (v_*, n_*) behave? (later on, warn that excitability implies large perturb.).

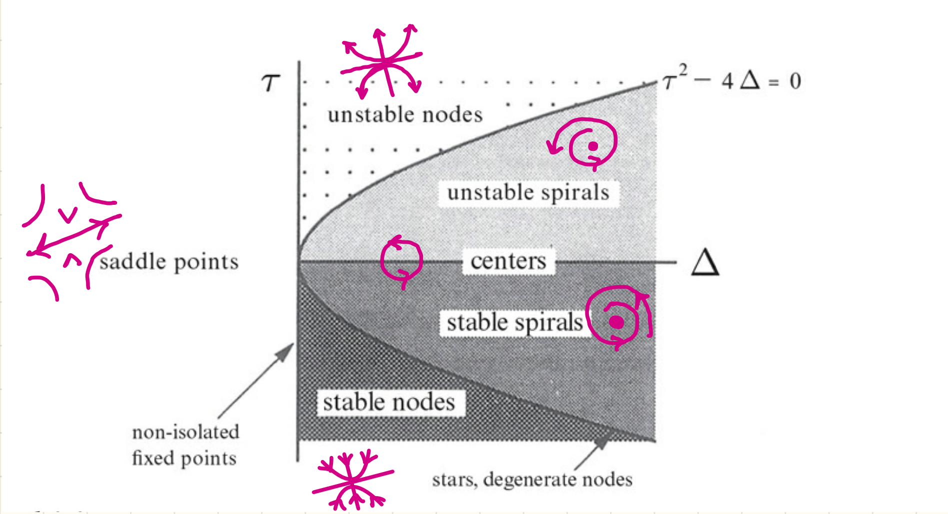
$$\frac{d}{dt}\begin{pmatrix} \tilde{v}(t) \\ \tilde{n}(t) \end{pmatrix} = J(v_*, n_*)\begin{pmatrix} \tilde{v}(t) \\ \tilde{n}(t) \end{pmatrix} + \mathcal{O}\left(\| (\tilde{v}(t), \tilde{n}(t)) \|^2 \right)$$

Eigenvalues λ_1, λ_2 of $J(v_*, n_*)$ determine the behaviour of soln. to

$$\frac{d}{dt}\begin{pmatrix} \tilde{v}(t) \\ \tilde{n}(t) \end{pmatrix} = J(v_*, n_*)\begin{pmatrix} \tilde{v}(t) \\ \tilde{n}(t) \end{pmatrix}$$

λ_1, λ_2 are soln. to

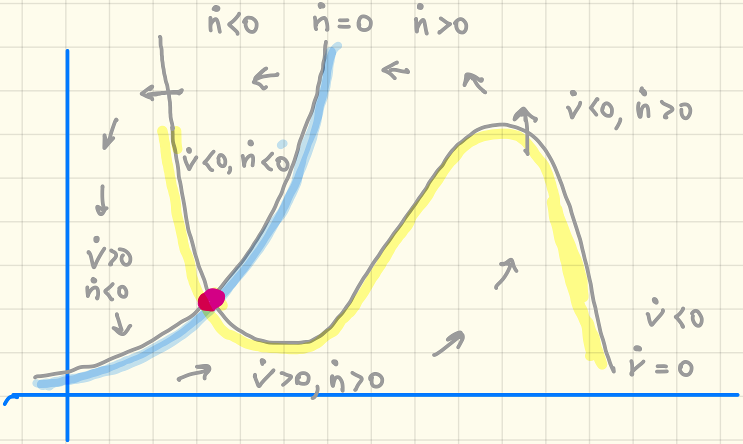
$$\lambda^2 - T\lambda + \Delta = 0, \qquad T = tr(J(v_*, n_*)), \quad \Delta = det(J(v_*, n_*))$$



Morris-Lecar model

$$f(v,n) = \frac{1}{c}\left[I_{app} - I(v,n) \right]$$

$$g(v,n) = \frac{n_\infty(v) - n}{\tau(v)}$$



n-nullcline

- $\tau(v) > 0$, hence

  $\{ n = n_\infty(v) \}$

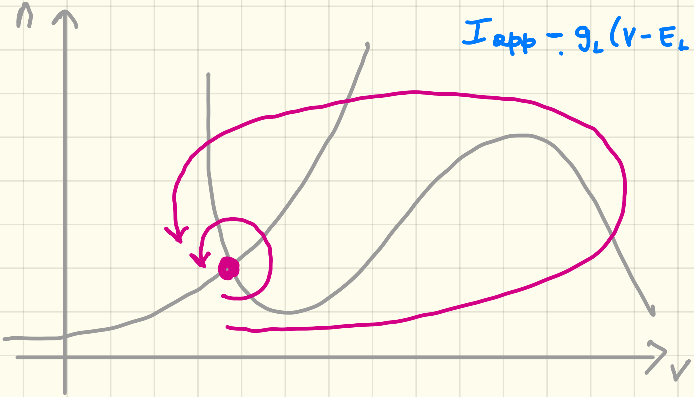
$n_\infty(v)$ is monotonic

v-nullcline

$$0 = I_{app} - g_L(v - E_L) - g_K n (V - E_K) - g_{Ca} m_\infty(v)(v - E_{Ca})$$

$$n = \frac{I_{app} - g_L(v - E_L) - g_{Ca} m_\infty(v)(v - E_{Ca})}{g_K (v - E_K)} \longrightarrow \text{cubic like}$$

$$I_{app} - g_L(V-E_L) - g_K n (V-E_K) - g_{Ca} m_\infty(V)(V-E_{Ca})$$



(V_*, n_*) is determined by $\quad n_* = m_\infty(V_*), \quad I_{app} = I(n_*, V_*)$

$$J(n_*, V_*) = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

$a = 1/c\left[-g_L - g_K n_* - g_{Ca} m_\infty(V_*) - g_{Ca} m'_\infty(V_*)(V_* - E_{Ca})\right]$

$b = 1/c\left[-g_K (V_* - E_K)\right]$

$c = \varphi\, n'_\infty(V_*)/\tau(V_*) - \cancel{\varphi(n_\infty(V_*) - n_*)/\tau(V_*)}$ $= 0$ as $n_* = m_\infty(V_*)$.

$d = -\varphi/\tau(V_*)$

Assume: $E_K < V_* < E_{Ca}$

a may be $\gtrless 0$ depending on $m'_\infty(V_*)$

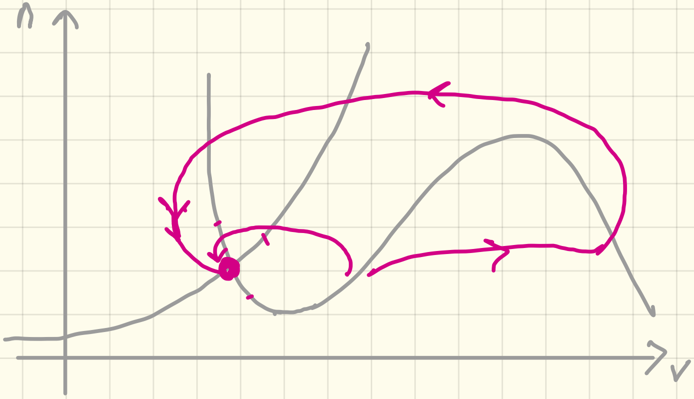
$b < 0$

$c > 0$

$d < 0$

V-nullcline: $f(v(s), n(s)) = 0, \quad s \in I_s \Rightarrow \partial_v f(v(s), n(s)) \frac{dv}{ds}(s) + \partial_n f(v(s), n(s)) \frac{dn}{ds}(s) = 0$

$$\frac{dn}{dv}(s) = -\frac{\partial_v f(v(s), n(s))}{\partial_n f(v(s), n(s))}$$ at $s = s_* \rightsquigarrow$ rest $\boxed{\frac{dn}{dv} = -a/b}$ $\quad \boxed{\frac{dn}{dv} = -\frac{c}{d}}$ n-nullcline

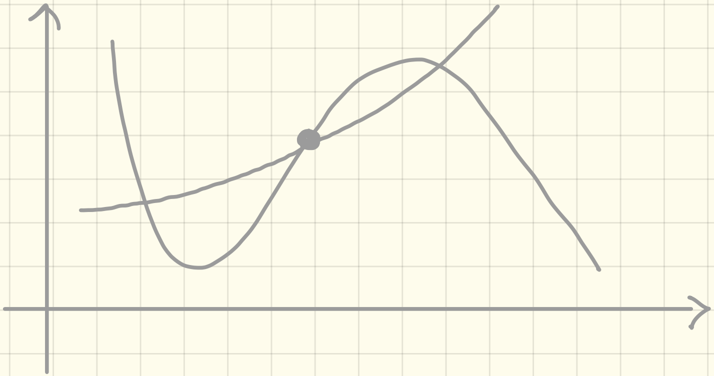


$$J = \begin{bmatrix} a & b \\ c & d \end{bmatrix}, \quad a<0 \quad b<0 \quad c>0 \quad d<0$$

$T = \mathrm{tr}\, J < 0$

$\Delta = \det J > 0$

(v_*, n_*) is stable.



$$J = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \quad a>0,\ b<0,\ c>0,\ d<0$$

$T = \mathrm{tr}\, J = a + d \quad \gtrless 0$

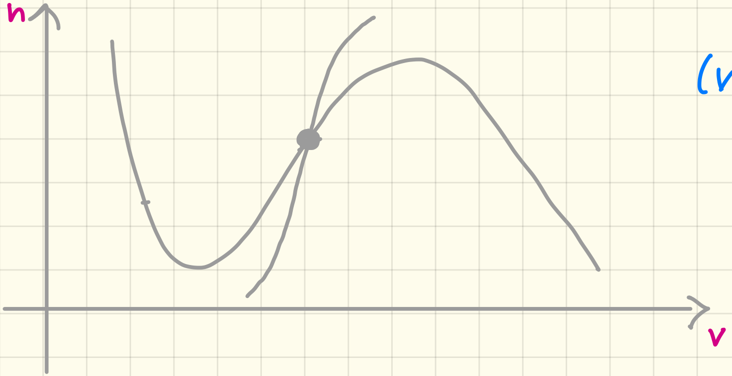
$\Delta = \det J = ad - bc \quad < 0$ because

$-a/b > -c/d \Rightarrow -ad + bc > 0$

slope of n-nullcline $= -c/d$

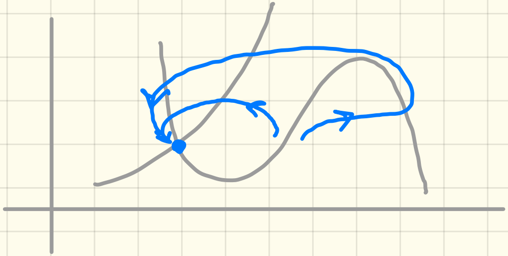
slope of v-nullcline $= -a/b$

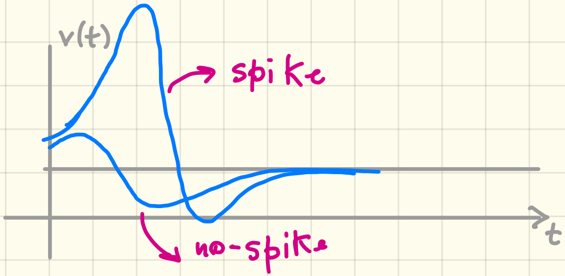
(v_*, n_*) is unstable



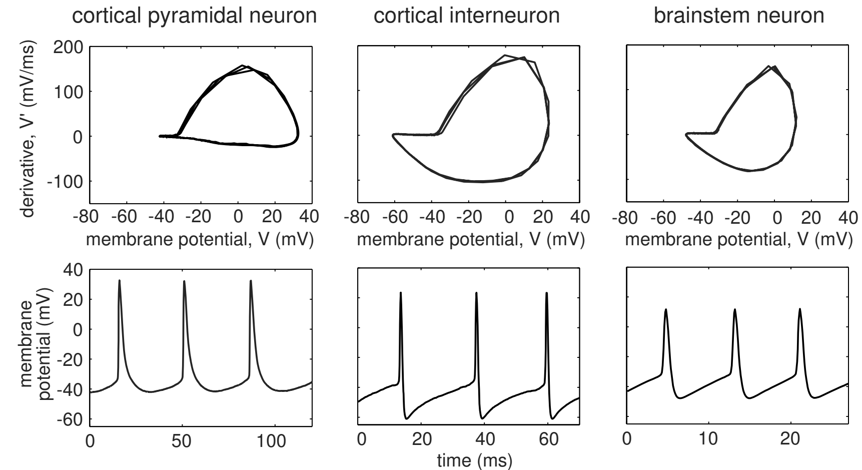
(v_*, n_*) is stable if $a+d<0$

unstable if $a+d>0$





This all-or-none response is often indicated by saying the cell is **Excitable**



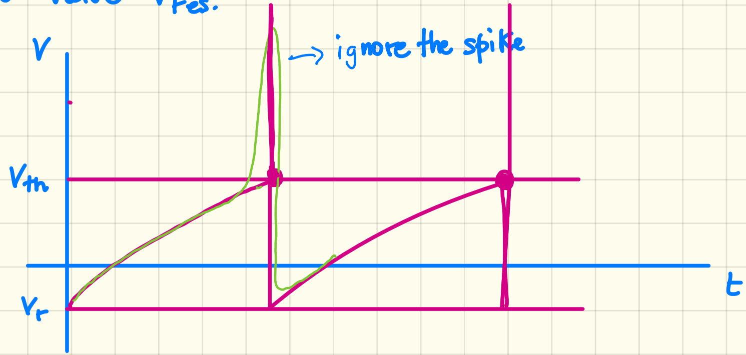
cortical pyramidal neuron
cortical interneuron
brainstem neuron
derivative, V' (mV/ms)
200
100
0
-100
-80 -60 -40 -20 0 20 40
membrane potential, V (mV)
membrane potential (mV)
40
20
0
-20
-40
-60
0 50 100
0 20 40 60
0 10 20
time (ms)

Integrate-and-fire model:

- Prescribe a simple dynamic for $v(t)$ → integrate

$$\dot{v}(t) = I - g_L(v - E_L) \qquad (1)$$

- Assume (1) is valid until v hits a threshold value V_{th} → fire.
  when this occurs, say that the cell has fired. Reset v to a value V_{res}.



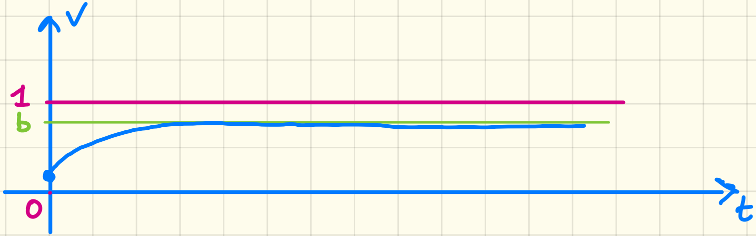
What type of dynamical system is this?
Which property does it have?

One can show that, by rescaling V, t, the system can be written as

$$\begin{cases} \dot{V}(t) = b - V(t) & \text{if } V(t) \in [0,1) \\ \text{if } V=1, \text{ then set } V=0. \end{cases}$$

⟶ sloppy definition

Case I: $b < 1$



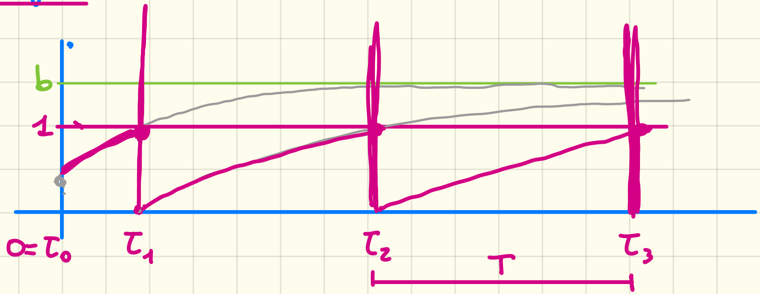
Let $v_0 \in [0,1)$

$v(t) = b + (v_0 - b)e^{-t}$ for all t.

There are no spikes if b is constant (subthreshold behaviour). If $b = f(t)$ then spiking may occur. This is an excitable regime

Case II: $b \geq 1$

$$\boxed{\begin{aligned} & v(t) = b + (A_i - b)e^{-(t-\tau_{i-1})} \quad t \in [\tau_{i-1}, \tau_i] \\ & A_1 = v_0 \\ & A_i = 0 \quad i > 1. \end{aligned}}$$



T satisfies the equation $1 = v(T)$, hence

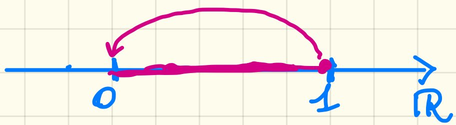
$$1 = b - be^{-T} \Rightarrow e^{-T} = 1 - 1/b \Rightarrow \boxed{T = -\ln(1 - 1/b)}$$

We can now give a more rigorous definition:

$$\dot{v}(t) = b - v(t) \qquad t \in \bigcup_{i \in \mathbb{N}} [\tau_i, \tau_{i+1})$$

$$v(0) = v_0$$

$$\lim_{t \to \tau_i^+} v(t) = \lim_{t \to \tau_i^-} v(t) - 1 \quad , \quad i \geq 1$$



where $\{\tau_i\}_{i \in \mathbb{N}}$ are defined by:

$$\tau_0 = 0$$

$$\tau_i = \inf \left\{ t > \tau_{i-1} : \lim_{t \nearrow \tau^i} v(t) = 1, \ \lim_{t \nearrow \tau^i} \dot{v}(t) > 0 \right\}$$

Tutorial:

$$\dot{v} = v(v-a)(1-v) - w + I \quad a \in (0,1),\ \varepsilon > 0,\ \gamma \geq 0,\ I \in \mathbb{R}$$
$$\dot{w} = \varepsilon(v - \gamma w)$$

Set $I=0$. Then $(v,w) = (0,0)$ is a steady state and $J(0,0)$ is given by

$$J = \begin{bmatrix} -a & -1 \\ \varepsilon & -\varepsilon\gamma \end{bmatrix}, \qquad \operatorname{tr} J = -a - \varepsilon\gamma, \qquad \det J = a\varepsilon\gamma + \varepsilon$$

If $a > 0$, then $\operatorname{tr} J < 0$, $\det J > 0$ $\Rightarrow$ $(0,0)$ is stable.

If $\det J < 0$ or if $\det > J$ and $\operatorname{tr} J > 0$, then $(0,0)$ is unstable

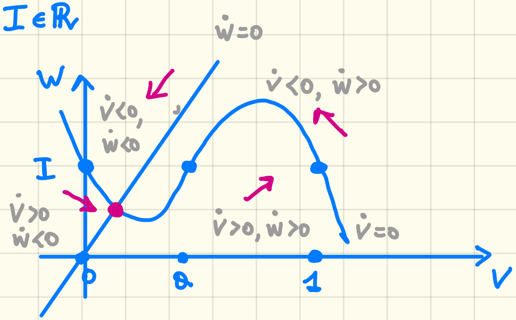
$\det J < 0 \iff a\varepsilon\gamma + \varepsilon < 0 \iff a < -\gamma$

$\det J > 0$ and $\operatorname{tr} J < 0 \iff a > -\gamma$ and $-a - \varepsilon\gamma > 0 \iff a \in (-\gamma, -\varepsilon\gamma)$

Therefore $a \in (-\infty, -\gamma) \cup (-\gamma, \varepsilon\gamma)$ implies $(0,0)$ is linearly unstable

$\dot{v} = v(v-a)(1-v) - w + I \quad a \in (0,1),\ \varepsilon > 0,\ \gamma \geq 0,\ I \in \mathbb{R}$

$\dot{w} = \varepsilon(v - \gamma w)$



Nullclines:

w-nullcline $\quad w = v/\gamma$

v-nullcline $\quad v(v-a)(1-v) + I = w$

Fixed points satisfy

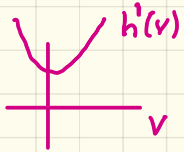
$$w_* = v_*/\gamma, \quad v_*(v_*-a)(1-v_*) - v_*/\gamma + I = 0 \Rightarrow I = h(v_*) = v_*/\gamma - v_*(v_*-a)(1-v_*)$$

Let $p(v) = h(v) - I$, which is cubic.

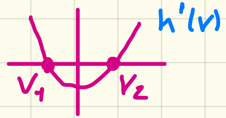
$$p'(v) = h'(v) = \frac{1}{\gamma} - \frac{d}{dv}\left[(v^2 - av)(1-v)\right] = \frac{1}{\gamma} - \frac{d}{dv}\left[v^2 - v^3 - av + av^2\right] = \frac{1}{\gamma} + \frac{d}{dv}\left[v^3 - (a+1)v^2 + av\right]$$

$$= 3v^2 - 2(a+1)v + a + \frac{1}{\gamma}$$

$h'(v)$ is a convex parabola so there are 2 possibilities:



- the equation $3v^2 - 2(a+1)v + a + \frac{1}{\gamma} = 0$ has no real roots, in which case $h'(v) > 0$ for all $v \in \mathbb{R}$

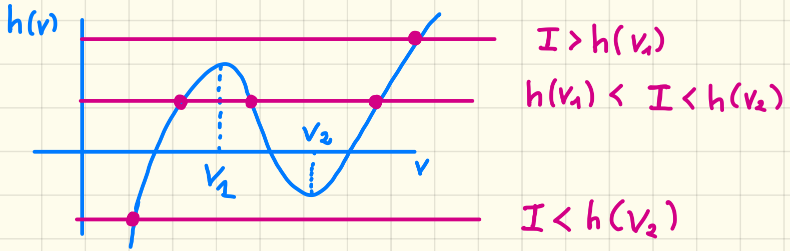


- the equation $3v^2 - 2(a+1)v + a + \frac{1}{\gamma} = 0$ has two real roots $v_1 \leq v_2$, hence $h'(v) \geq 0$ for $v \leq v_1 \cup v \geq v_2$, and negative otherwise

We find $V_{1,2} = (a+1) \pm \sqrt{(a+1)^2 - 3a - 3/\gamma}$, hence :

- if $\gamma < \dfrac{3}{1-a+a^2}$, then there are no real roots. We conclude $p(v)$ is strictly monotonic increasing and on $\mathbb{R}$ to $\mathbb{R}$, so it must have a unique root. There is only 1 equilibrium (v_*, w_*)

- if $\gamma \geq \dfrac{3}{1-a+a^2}$, then $h(v) \leq 0$ for $v \in [V_1, V_2]$, and negative otherwise. Depending on the value of I, $p(v) = h(v) - I$ has 1 or 3 roots .



If $I = h(V_1)$, or $I = h(v_2)$ then there are 3 roots, 2 of which are identical.

From $\dot{V} = f(V) - w + I$, $\dot{w} = \varepsilon V - \varepsilon \gamma w$ we get $J(V,w) = \begin{bmatrix} f'(V) & -1 \\ \varepsilon & -\varepsilon\gamma \end{bmatrix}$

Hence $\operatorname{tr} J(V_*, w_*) = f'(V_*) - \varepsilon\gamma = -3V_*^2 + 2(a+1)V_* - a - \varepsilon\gamma$.

$$\operatorname{tr} J(V_*, w_*) = 0 \iff -3V_*^2 + 2(a+1)V_* - a - \varepsilon\gamma = 0$$

$$V_{*1,2} = \frac{(a+1) \pm \sqrt{a^2 - a + 1 - 3\gamma\varepsilon}}{3} \qquad (*) \qquad \varepsilon < \frac{1 - a + a^2}{3\gamma}$$

$$3\varepsilon\gamma < a^2 - a + 1$$

If $\varepsilon < \frac{1}{3\gamma}(a^2 - a + 1)$, then V_{*1}, V_{*2} are distinct.

Let $I_{*1} = h(V_{*1})$, $I_{*2} = h(V_{*2})$, For each $I = I_{*j}$, $j = 1,2$ we have

- One equilibrium $E_i = (V_{*i}, V_{*i}/\gamma)$
- $\operatorname{Tr} J(E_i) = 0$
- $\det J(E_i) = -\varepsilon\gamma f'(V_{*i}) + \varepsilon$. Since $f(V) = V/\gamma - h(V)$ we have

$$\det J(E_i) = -\varepsilon\gamma \left(\frac{1}{\gamma} - h'(V_{*i}) \right) + \varepsilon = \varepsilon\gamma h'(V_{*i}) > 0 \rightsquigarrow \text{see sketch above.}$$

- The eigenvalues of $J(E_i)$ are of the form $\lambda_{1,2} = \pm i\omega$, $\omega = |\varepsilon\gamma h'(V_{*i})|$.

For the numerical experiment we have:

$a = 0.1$, $\varepsilon = 0.02$, $\gamma = 1$ hence $\gamma < \frac{3}{1-a+a^2}$, and we have 1 equilibrium for each value of I.

We also have $\varepsilon < \frac{1}{3\gamma}(a^2 - a + 1)$, therefore we expect two values of currents

$I_{*1} = h(V_{*1})$ and $I_{*2} = h(V_{*2})$, at which the Jacobian has purely complex eigenvals.

These currents are computed as follows:

$V_{*1,2}$ are computed using (*) and give:

$$V_{*1} \cong 0.593, \quad V_{*2} \cong 0.674,$$

$$I_{*1} \cong 0.062, \quad I_{*2} \cong 0.55$$

Going back to the numerical experiment, we see that these are the values of the current at which oscillations are born, or are destroyed, respectively.