LECTURE 2

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Reminders from lecture 1

Principle of exchange stability

This is not a general result but it is good to have this “recipe” in mind to check the results.

Checkboard!!

Fold bifurcation

Assume F is **scalar** C^k, $k \geq 2$ in a neighborhood of $(0,0)$, and that it satisfies

$$F(0,0) = 0, \ \frac{\partial}{\partial u} F(0,0) = 0$$

and

$$\frac{\partial}{\partial \mu} F(0,0) := a \neq 0, \frac{\partial^2}{\partial^2 u} F(0,0) := 2b \neq 0.$$

Then, **a saddle-node bifurcation** occurs at $\mu = 0$. More precisely, in a neighbourhood of 0 in $\mathbb{R}$ for sufficiently small μ:

- if $ab < 0$ (resp. $ab > 0$) the ODE has 2 equilibria $u_\pm(\epsilon), \epsilon = \sqrt{\mu}$ for $\mu > 0$ (resp., for $\mu < 0$) , with opposite stabilities. Furthermore, the map $\epsilon \to u_\pm(\epsilon)$ is of class C^{k-2} in a neighbourhood of 0, and $u_\pm(\epsilon) = O(\epsilon)$.
- if $ab < 0$ (resp. $ab > 0$) the ODE has no equilibria for $\mu < 0$ (resp., for $\mu > 0$).

Hopf bifurcation

Assume F is $C^k, k \geq 5$ from $\mathcal{N}((0,0)) \in \mathbb{R}^n \times \mathbb{R}$ into $\mathbb{R}^n$, and that

$$F(0,0) = 0, \; L := \partial_u F(0,0) = 0.$$

Assume that two eigenvalues L are $\pm i\omega$ for some $\omega > 0$, all other being away from $i\mathbb{R}$. Then there is a *2d invariant manifold* onto which the ODE is conjugated to

$$\mathbb{C} \ni \dot{A} = (\mu \cdot a + i\omega)A + b|A|^2 A + O((|\mu| + |A|^2)^2)$$

with $\Re a, \Re b \neq 0$. Then, **a Hopf bifurcation** occurs at $\mu = 0$. More precisely, in a neighbourhood of 0 in $\mathbb{R}^n$ for sufficiently small μ:

- if $\Re a \Re b < 0$ (resp. $ab > 0$) the ODE has precisely one equilibrium $u(\mu)$ for $\mu < 0$ (resp., for $\mu > 0$), with $u(0) = 0$. This equilibrium is stable when $\Re b < 0$ and unstable when $\Re b > 0$.
- if $\Re a \Re b < 0$ (resp. $\Re a \Re b > 0$) the ODE possesses for $\mu > 0$ (resp., for $\mu < 0$) an equilibrium $u(\mu)$ and a unique periodic orbit $u^*(\mu) = O(\sqrt{|\mu|})$, which surrounds this equilibrium. The periodic orbit is stable when $\Re b < 0$ and unstable when $\Re b > 0$, whereas the

Center manifold

Center manifold: the case where $\Re\lambda = 0$

Consider u_{eq} equilibrium for $\dot{u} = \mathsf{F}(u;\alpha)$ at parameter value α_0, $\mathsf{F}(u_{eq};\alpha_0) = 0$. Write $u = u_{eq} + x$ and $\alpha = \alpha_0 + \mu$. It solves an equation like:

$$\dot{x} = \mathsf{L}x + \mathsf{R}(x;\mu),\ \mathsf{L} \in \mathcal{L}(\mathbb{R}^n),\ \mathsf{R} \in C^k(\mathcal{V}_x \times \mathcal{V}_\mu, \mathbb{R}^n), k \geq 2 \quad (1)$$

$$\mathsf{R}(0;0) = 0,\ d\mathsf{R}(0;0) = 0$$

Theorem 1/2

Write $\mathbb{R}^n = \mathcal{X}_c \oplus \mathcal{X}_h$ where $\mathcal{X}_h = \mathcal{X}_s \oplus \mathcal{X}_u$ and $\dim \mathcal{X}_c > 0$. Then, there is a neighborhood $\mathcal{O} = \mathcal{O}_x \times \mathcal{O}_\mu$ of $(0,0)$ in $\mathbb{R}^n \times \mathbb{R}^m$, a mapping $\Psi \in C^k(\mathcal{X}_c \times \mathbb{R}^m; \mathcal{X}_h)$ with

$$\Psi(0;0) = 0,\quad d_1\Psi(0;0) = 0$$

and a manifold $\mathcal{M}(\mu) = \{u_c + \Psi(u_c,\mu), u_c \in \mathcal{X}_c\}$ for $\mu \in \mathcal{V}_\mu$ such that:

1. $\mathcal{M}(\mu)$ is **locally invariant**, i.e., $x(0) \in \mathcal{M}(\mu) \cap \mathcal{O}_x$ and $x(t) \in \mathcal{O}_x$ for all $t \in [0,T]$ implies $x(t) \in \mathcal{M}(\mu)$ for all $t \in [0,T]$.

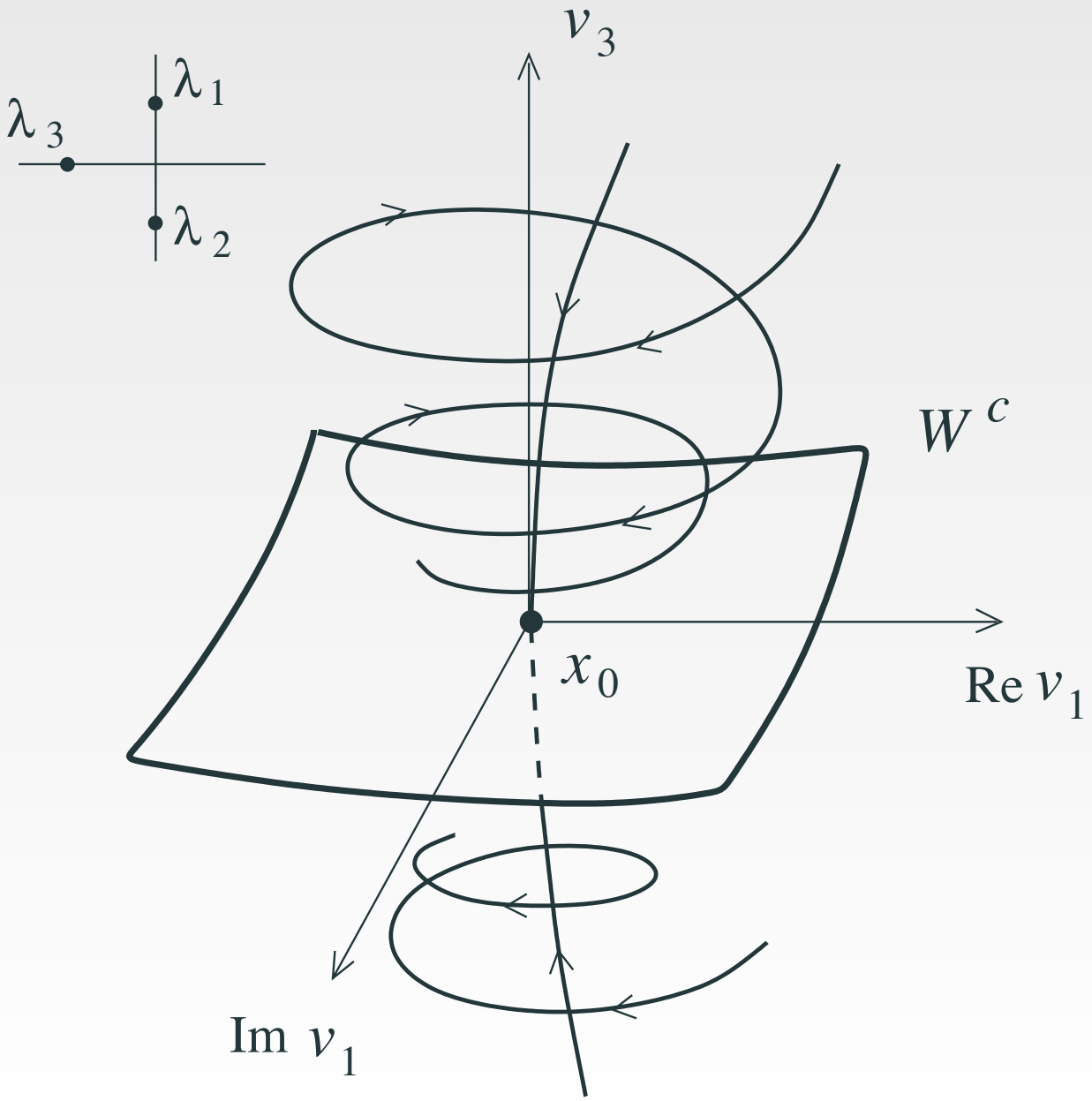
Theorem 2/2

2. $\mathcal{M}(\mu)$ contains the set of **bounded solutions** of (1) staying in $\mathcal{O}_x$ for all $t \in \mathbb{R}$, i.e. if x is a solution of (1) satisfying for all $t \in \mathbb{R}$, $x(t) \in \mathcal{O}_x$, then $x(0) \in \mathcal{M}(\mu)$.
3. (Parabolic case) if $n_+ = 0$, then $\mathcal{M}(\mu)$ is **locally attracting**, *i.e.* if x is a solution of (1) with $x(0) \in \mathcal{O}_x$ and $x(t) \in \mathcal{O}_x$ for all $t > 0$, then there exists $v(0) \in \mathcal{M}(\mu) \cap \mathcal{O}_c$ and $\tilde{\gamma} > 0$ such that

$$x(t) = v(t) + O(e^{-\tilde{\gamma}t}) \text{ as } t \to \infty$$

where v is a solution of (1) with initial condition $v(0)$.

Center manifold



Center manifold: Additional properties

1. The Center manifold is not unique. Uniqueness can be achieved if $\mathbf{R}$ is Lipschitzian with sufficiently small Lipschitz constant.
2. If $x_c(0) \in \mathcal{M}(\mu)$, then

$$\dot{x}_c = \mathbf{L}_c x_c + P_c \mathbf{R}(x_c + \Psi(x_c, \mu), \mu) \equiv f(x_c, \mu)$$

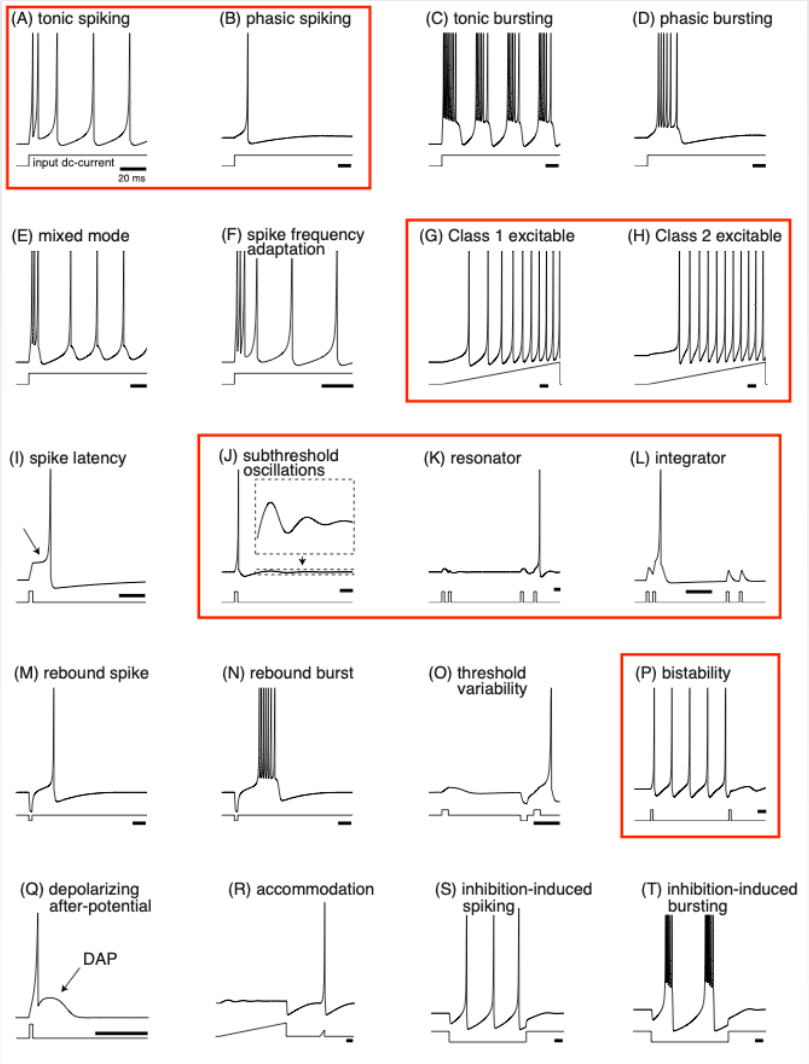
   where P_c is the projector on $\mathcal{X}_c$.
3. The local coordinates function satisfies

$$d\Psi(x_c, \mu) \cdot f(x_c) = P_h \mathbf{L} \cdot \Psi(x_c, \mu) + P_h \mathbf{R}(x_c + \Psi(x_c, \mu))$$

4. There are extensions for non-autonomous systems, with symmetries...
5. Extensions to Banach spaces possible in some cases
6. Taylor expansion of Ψ is uniquely determined.

Application to Neurosciences

Goal of this lecture: excitability



$\Rightarrow$ Have a geometric understanding of excitability

Reminder on the $I_{Na,p} + I_K$ model

This is a 2-dimensional simplification of the Hodgkin-Huxley model where we assume

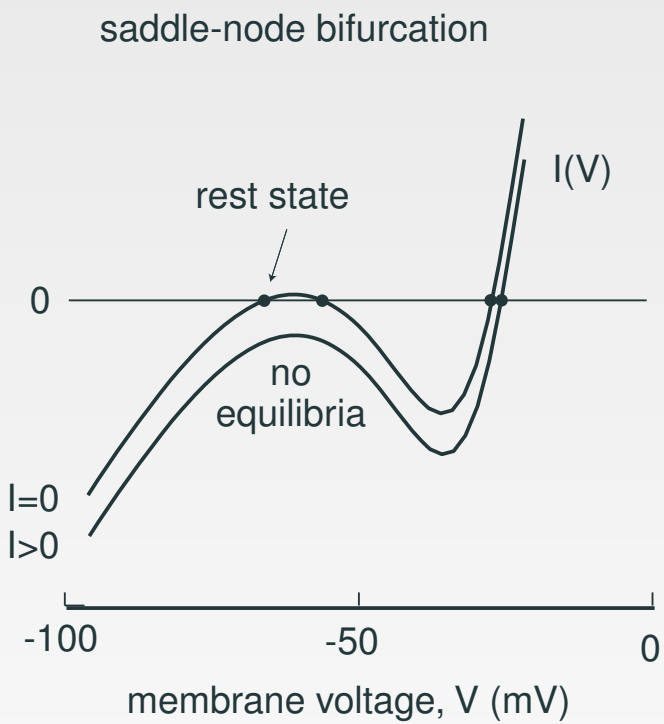
- a leak current
- a persistent Na-current with instantaneous kinetics
- a persistent K-current with slower kinetics

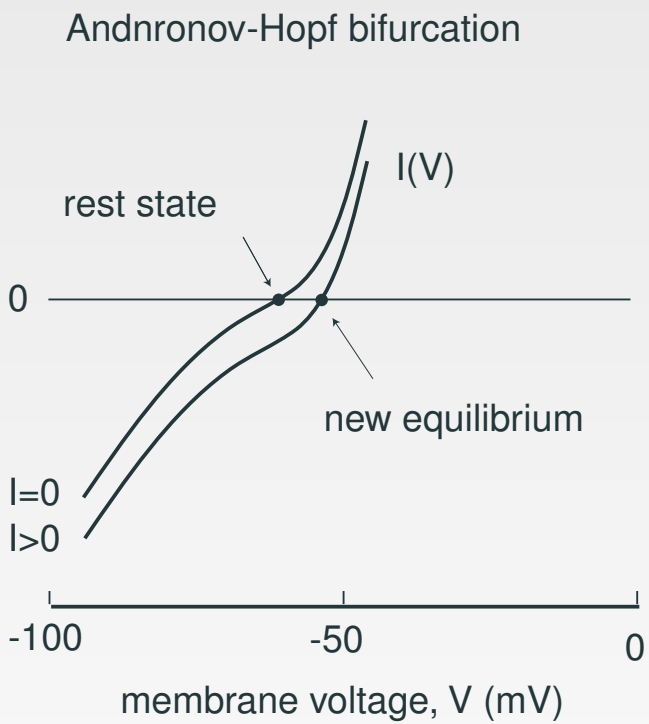
$$C\frac{dV}{dt} = I - \overbrace{\bar{g}_K n(V - E_K)}^{I_K} - \overbrace{\bar{g}_{Na} m_\infty(V)(V - E_{Na})}^{I_{Na}} - g_L(V - E_L) \equiv I(V)$$
$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau(V)}$$

where

$$(m, n)_\infty = \frac{1}{1 + exp[(V_{1/2} - V)/k]}$$

I-V CURVES IN THE $I_{Na,p} + I_K$ MODEL

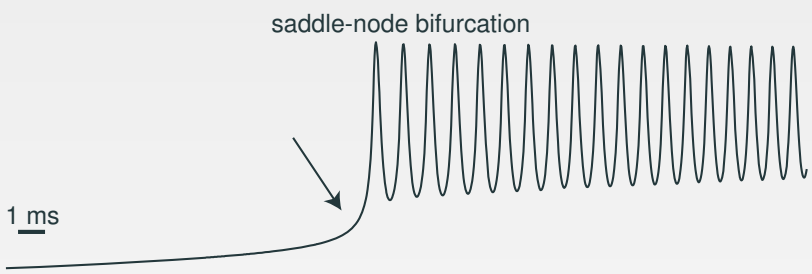


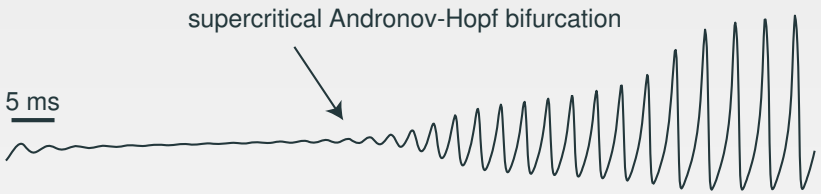


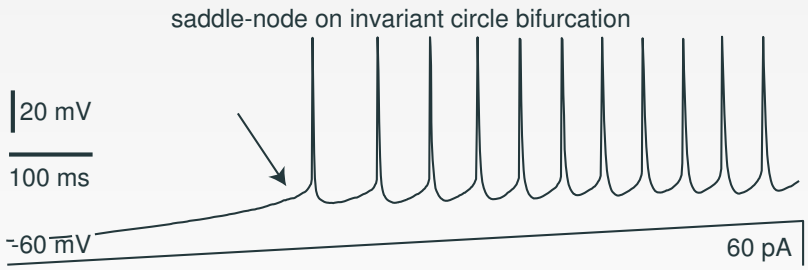
$$C\frac{dV}{dt} = I - \overbrace{\bar{g}_K n(V - E_K)}^{I_K} - \overbrace{\bar{g}_{Na} m_\infty(V)(V - E_{Na})}^{I_{Na}} - g_L(V - E_L) \equiv I(V)$$

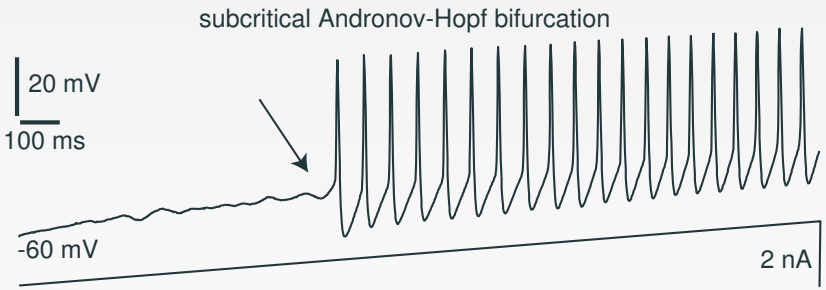
4 examples of codim 1 bifurcations (Figures from Izhikevich)

Transitions to tonic spiking: by which mechanism?









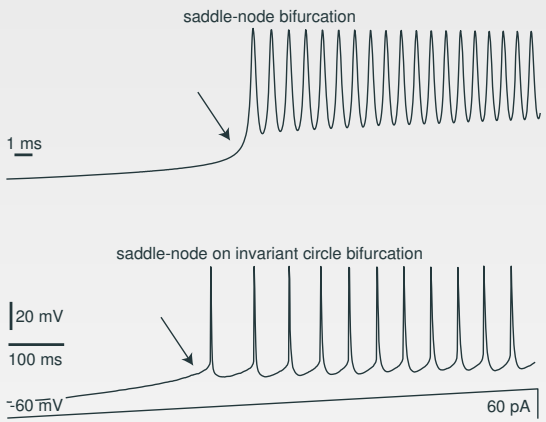
Last 2 are in-vitro recordings

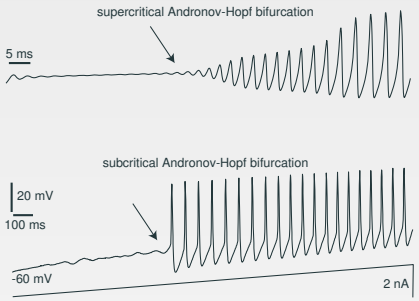
Codim 1 bifurcations of equilibria

Outline

Transitions from resting to spiking.

Quasi-static change in I, bifurcations?

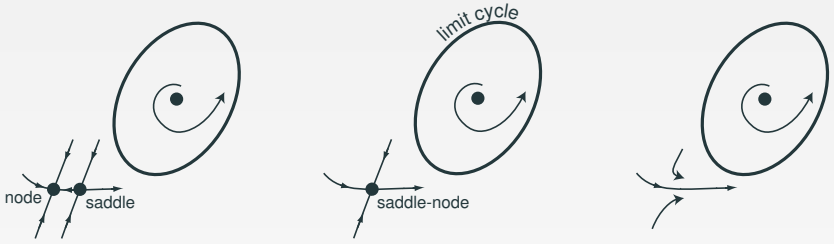


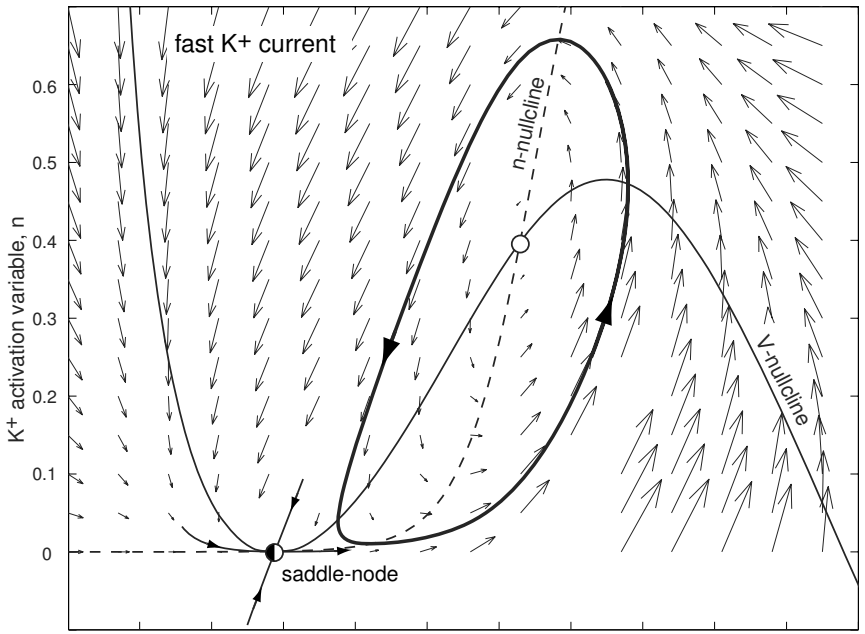


Bifurcation of an equilibrium	**Fast subthreshold oscillations**	**Amplitude of spikes**	**Frequency of spikes**
saddle-node	no	nonzero	nonzero
saddle-node on invariant circle	no	nonzero	$A\sqrt{I-I_{\mathrm{b}}} \to 0$
supercritical Andronov-Hopf	yes	$A\sqrt{I-I_{\mathrm{b}}} \to 0$	nonzero
subcritical Andronov-Hopf	yes	nonzero	nonzero

Saddle-node bifurcation 1/2

Figures from Izhikevitch, $I_{Na,p} + I_K$ model





Saddle-node bifurcation 2/2

- the bifurcation occurs at $I_p = 4.51, (V_p, n_p) = (-61, 0.0007)$
- We can compute the center manifold

$\Rightarrow$ Useful to understand when SN occurs and codim 2 bifuractions

Saddle-node bifurcation 2/2

- the bifurcation occurs at $I_p = 4.51, (V_p, n_p) = (-61, 0.0007)$
- We can compute the center manifold
- we check that

$$a = \frac{1}{2}\partial_V^2 f(V_p, I_p) \neq 0 \quad c = \partial_I f(V_p, I_p) \neq 0$$

$\Rightarrow$ Useful to understand when SN occurs and codim 2 bifuractions

Saddle-node bifurcation 2/2

- the bifurcation occurs at $I_p = 4.51, (V_p, n_p) = (-61, 0.0007)$
- We can compute the center manifold
- we check that

$$a = \frac{1}{2}\partial_V^2 f(V_p, I_p) \neq 0 \quad c = \partial_I f(V_p, I_p) \neq 0$$

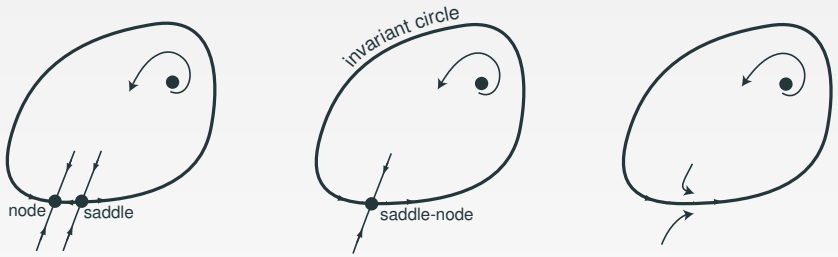
- We have the "normal form"

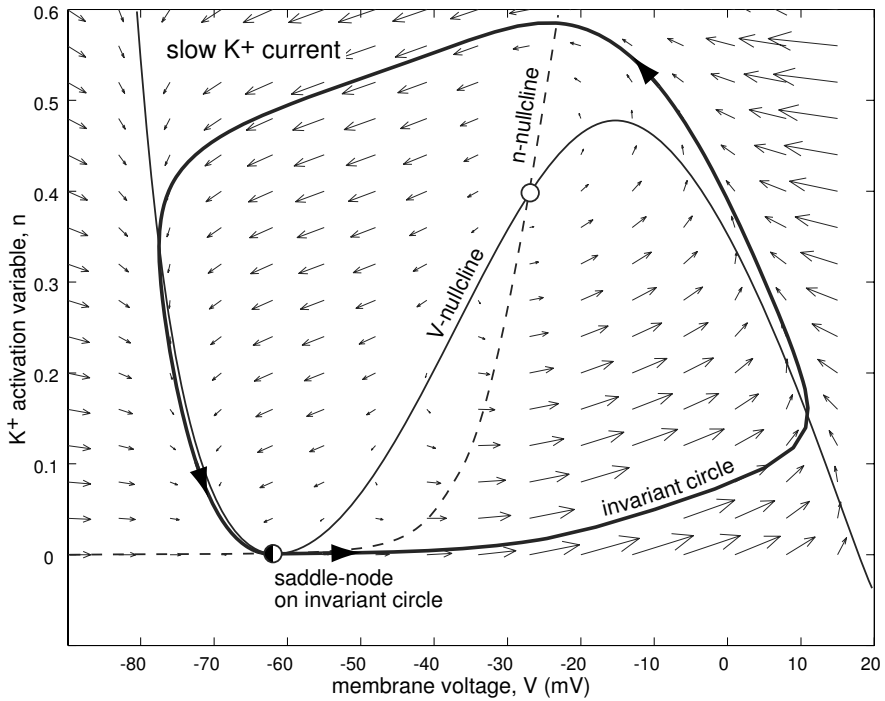
$$\dot{V} = c(I - I_p) + a(V - V_p)^2 + \cdots \quad a = 0.1887, c = 1$$

$\Rightarrow$ Useful to understand when SN occurs and codim 2 bifuractions

Saddle-node bifurcation on invariant cycle (SNIC) 1/2

(Figures from Izhikevitch, $I_{Na,p} + I_K$ model with high threshold, $\tau(V) = 1$) Also called **Saddle-node homoclinic bifurcation**

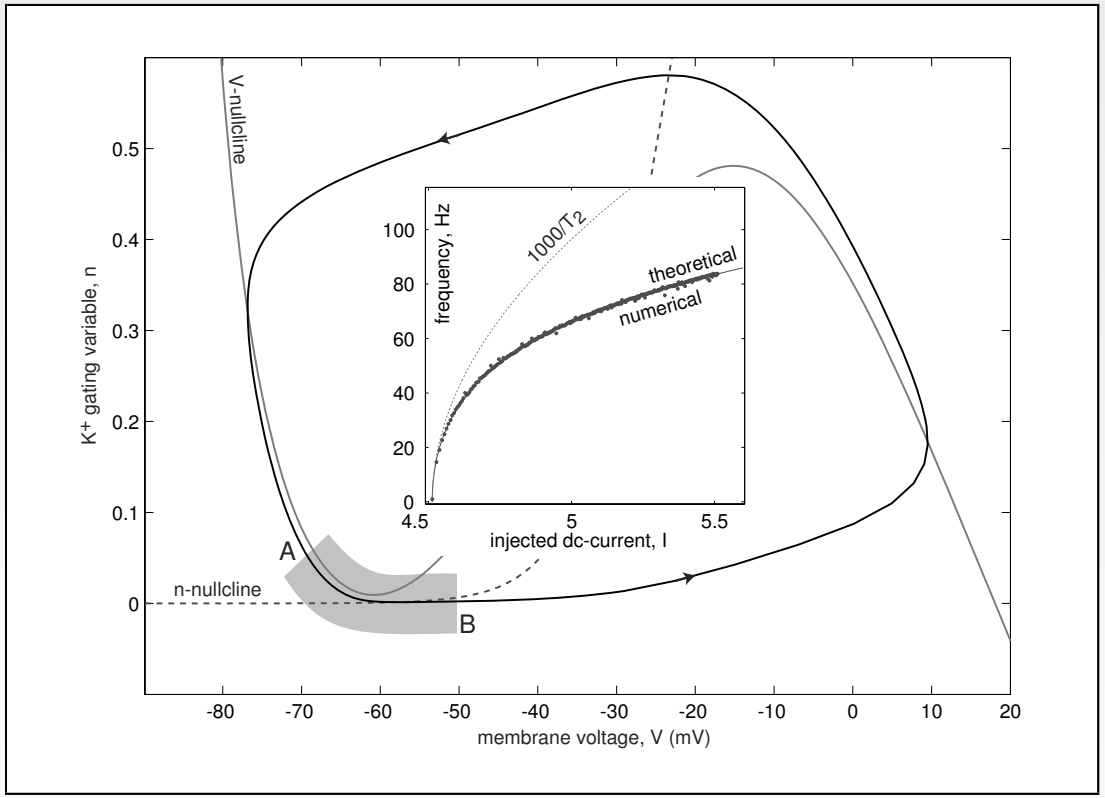




Saddle-node bifurcation on invariant cycle (SNIC) 2/2

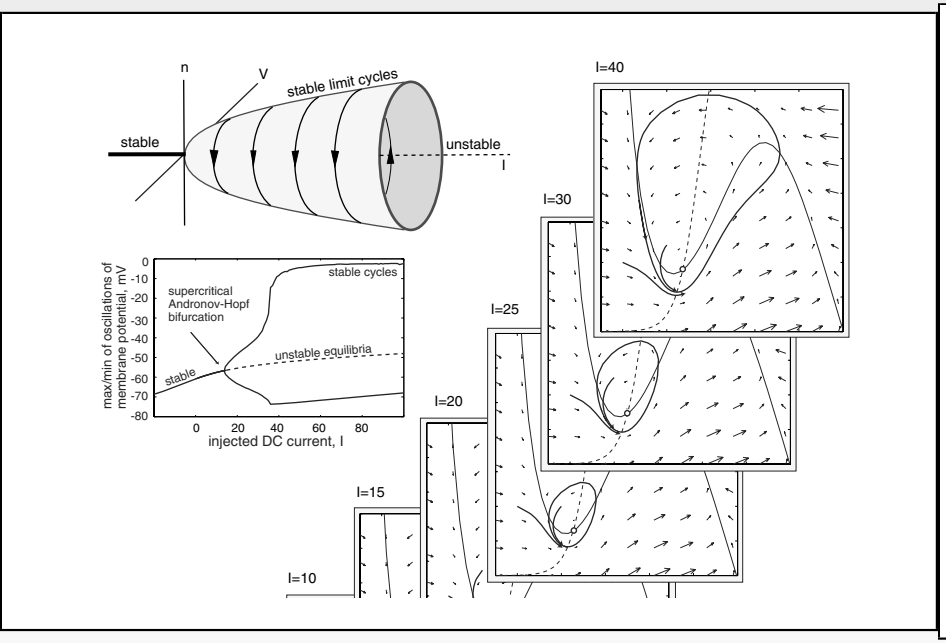
(Saddle-node homoclinic bifurcation)

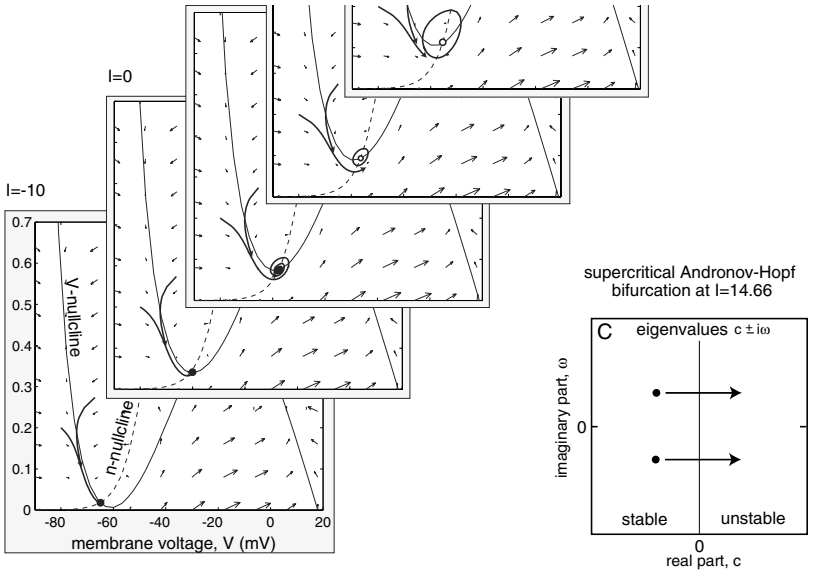
- Time from A to B
  $T_2 \approx \frac{\pi}{\sqrt{ac(I-I_p)}}$
- Action potential duration $T_1 \approx 4.7ms$
- Firing frequency
  $\omega = \frac{1000}{T_1+T_2}$



$\Rightarrow$ Exercise with θ-model or SN normal form

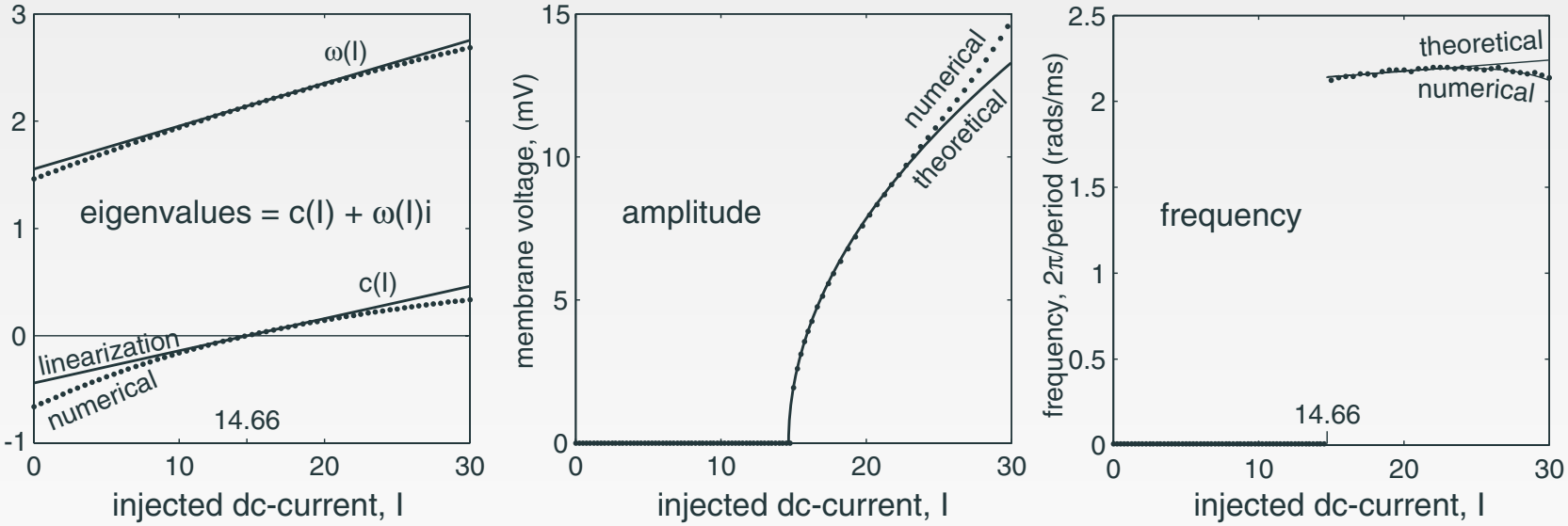
Supercritical Andronov-Hopf bifurcation 1/2



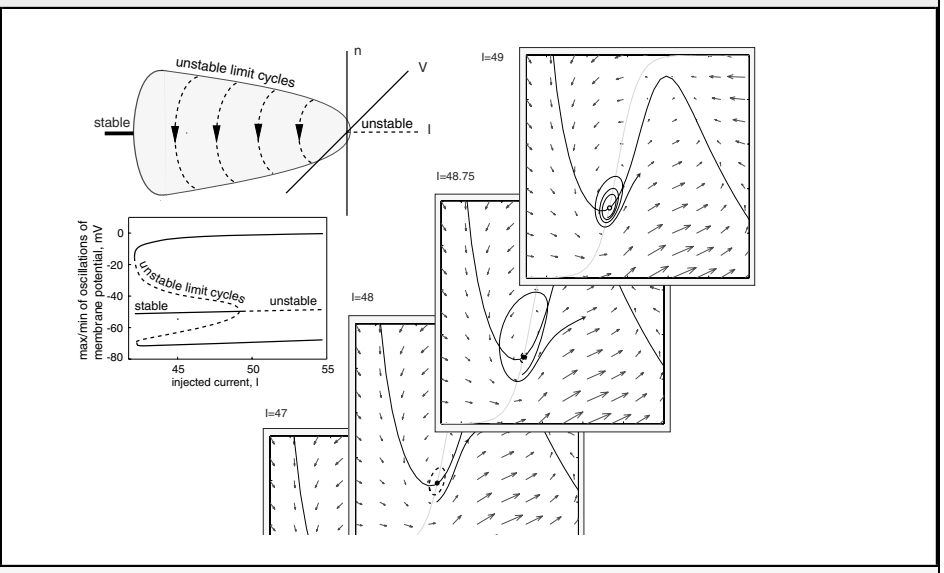


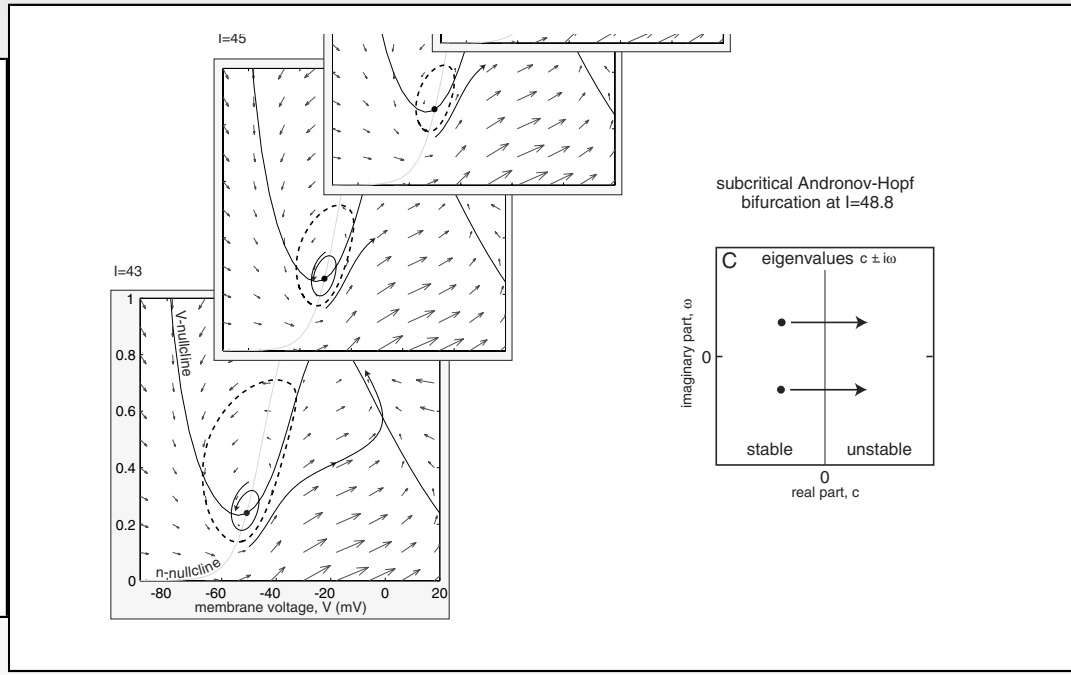
Supercritical Andronov-Hopf bifurcation 2/2

$I_{Na,p} + I_K$ model with low threshold

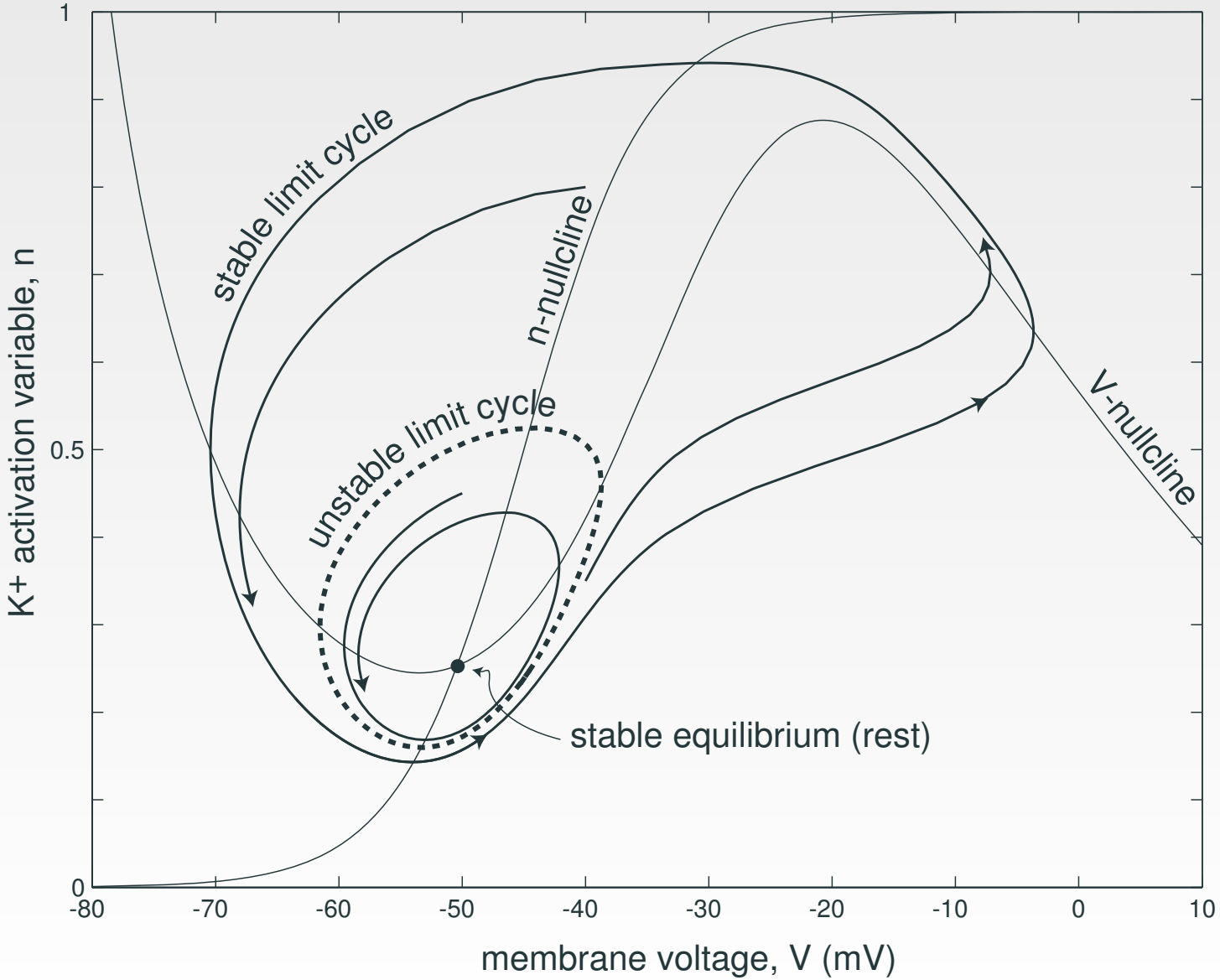


Subcritical Andronov-Hopf bifurcation

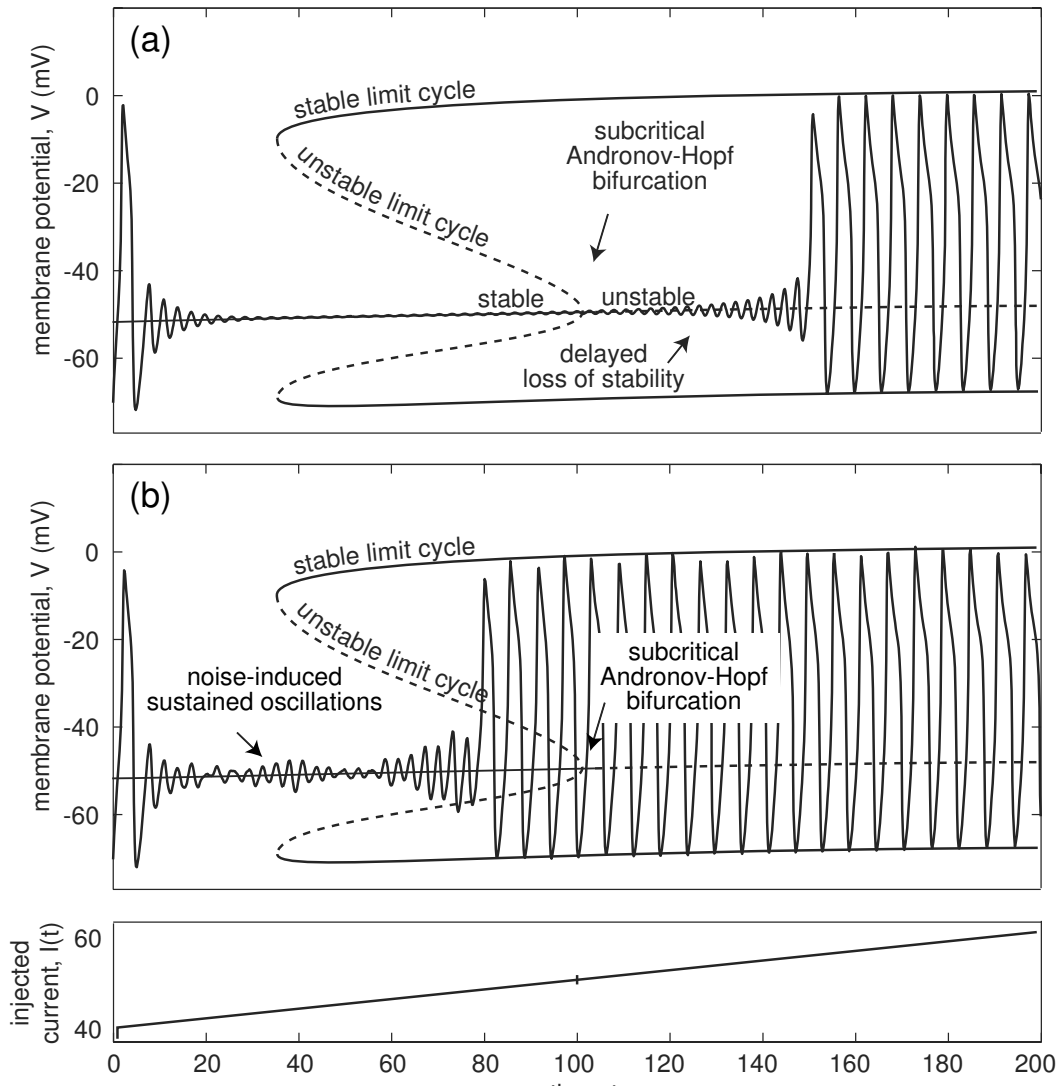




Bistability in the $I_{Na,p} + I_K$ model (To be explained later)

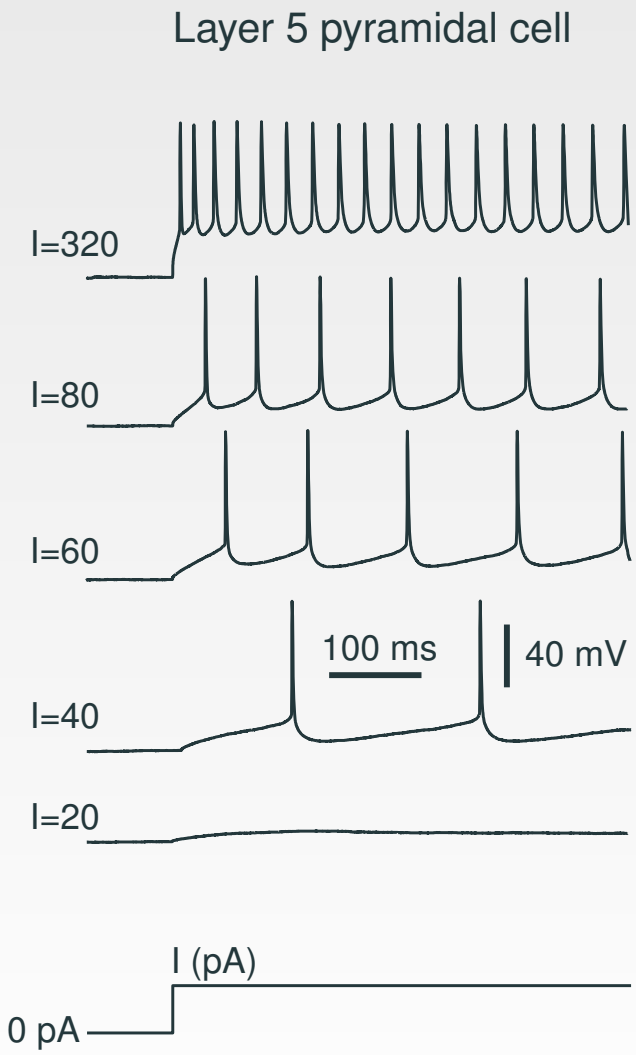


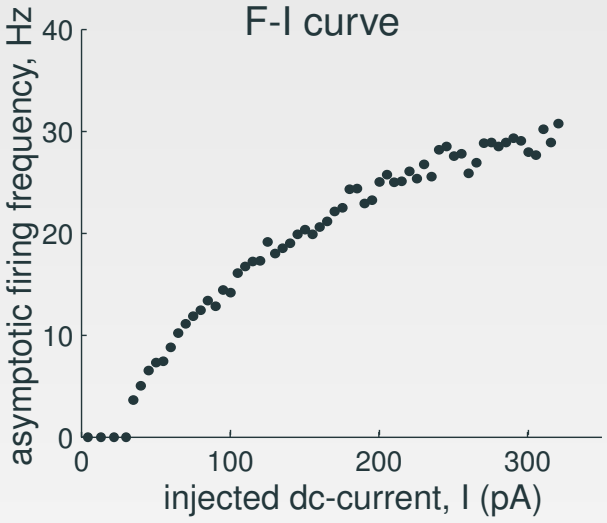
Delayed loss of stability (To be analyzed later (also)...)



Excitability

Hodgkin's Classification, Class I (Figures from Izhikevich)



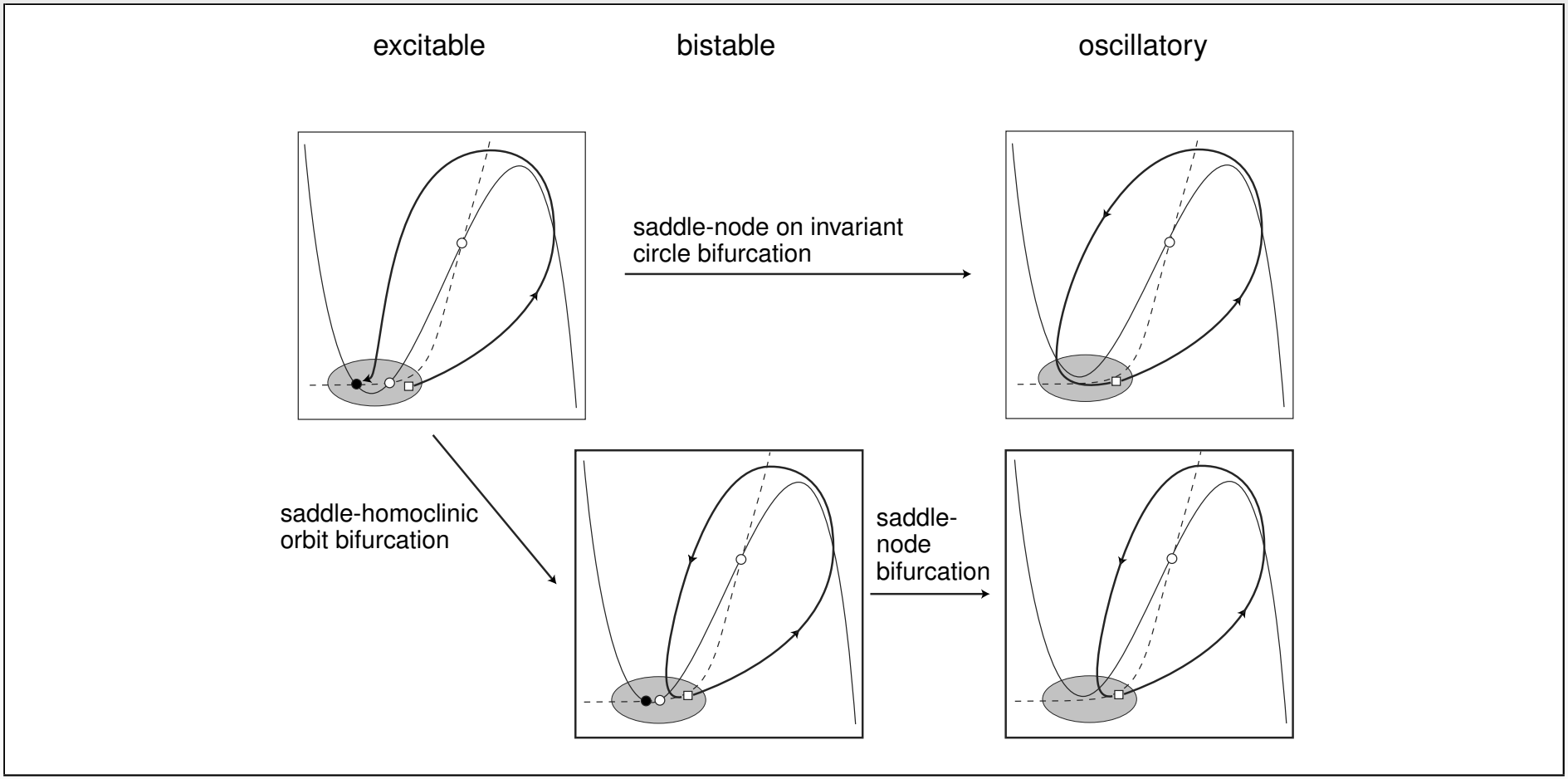


- Action potentials can be generated with arbitrarily low frequency, depending on the strength of the applied current.

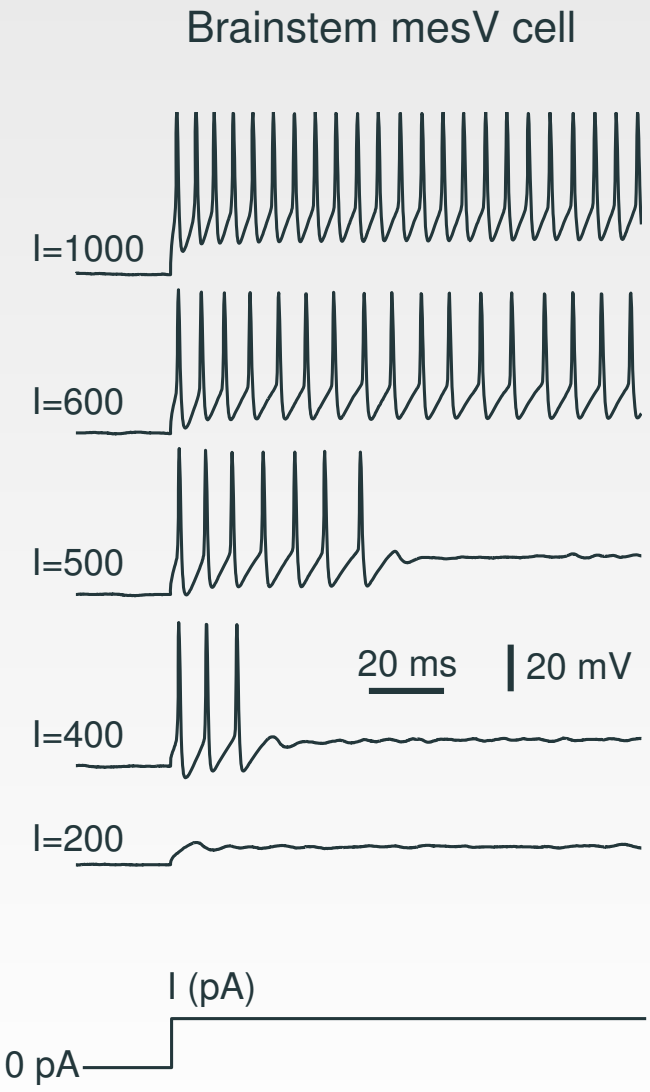
  $\Rightarrow$ encodes stim. strength

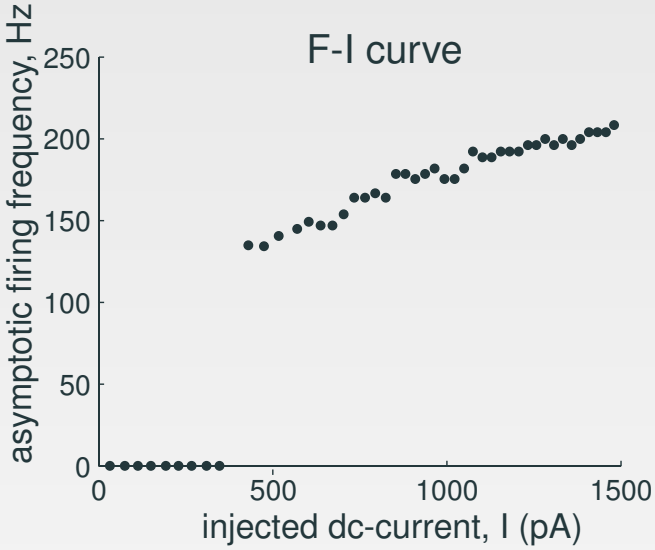
Hodgkin's Classification: Class I

Transition of excitable systems to oscillatory ones. **Period varies.**



Hodgkin's Classification, Class II (Figures from Izhikevich)



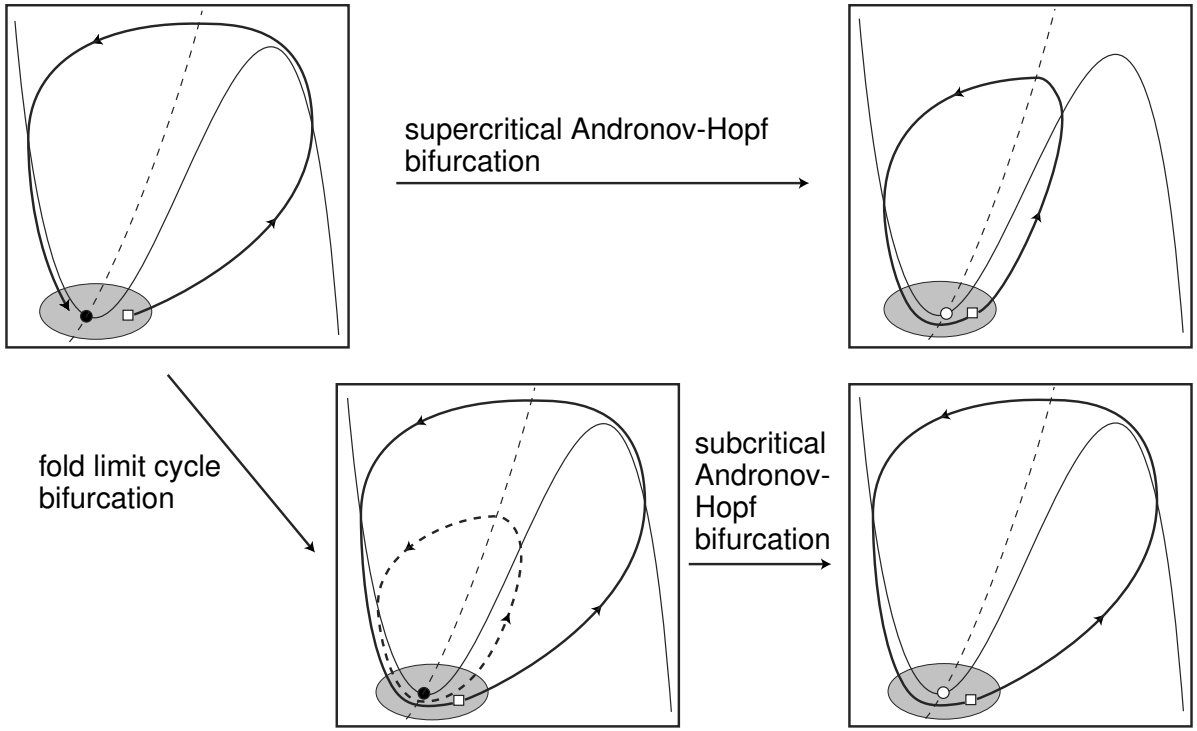


- Action potentials are generated in a certain frequency band that is relatively insensitive to changes in the strength of the applied current.

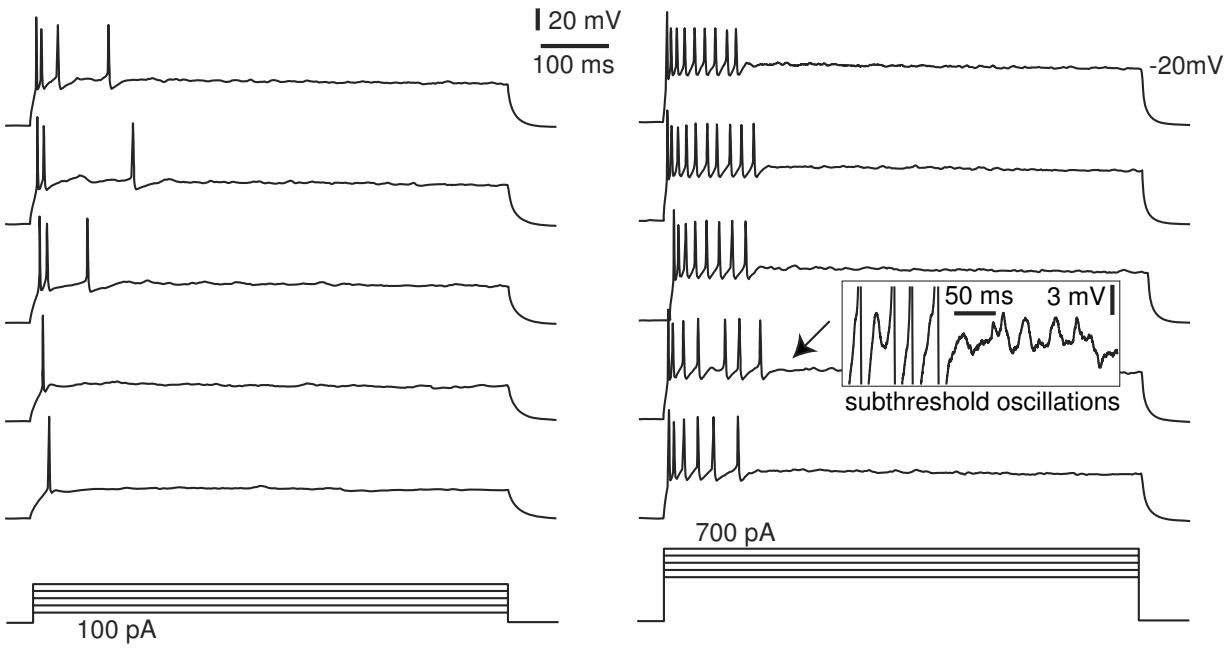
  $\Rightarrow$ encodes threshold.

Hodgkin's Classification: Class II

Period varies weakly.



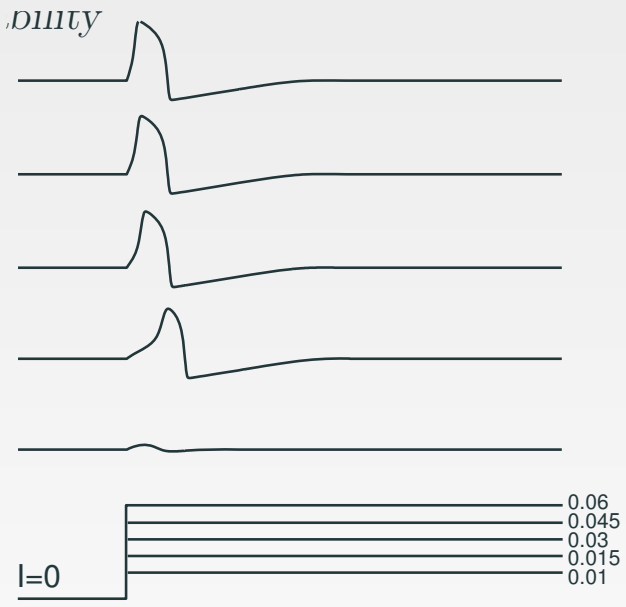
Hodgkin's Classification, Class III (Figures from Izhikevich)

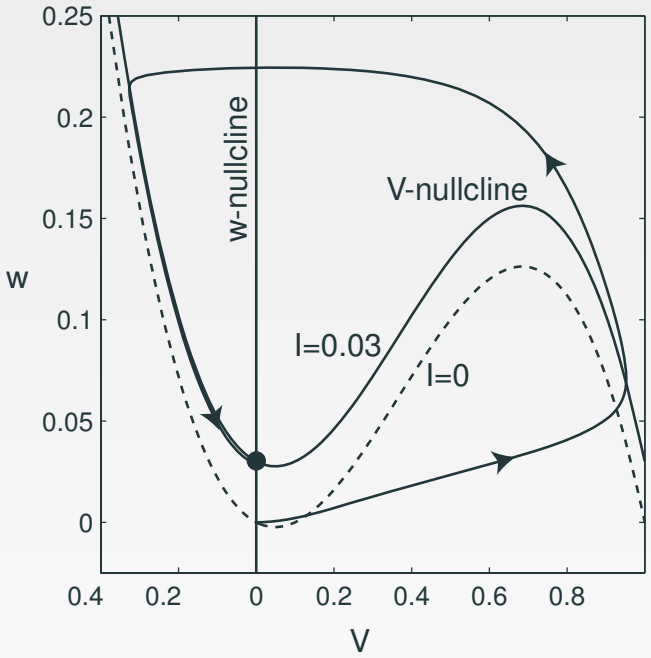


- L5 Pyramidal neuron in rat visual cortex. One spike is generated in response to a current step. Repetitive (tonic) spiking can be generated only for extremely strong injected currents or not at all.

Hodgkin's Classification, Class III (Figures from Izhikevich)

Class 3 neural excitability occurs when the resting state remains stable for any fixed I in a biophysically relevant range

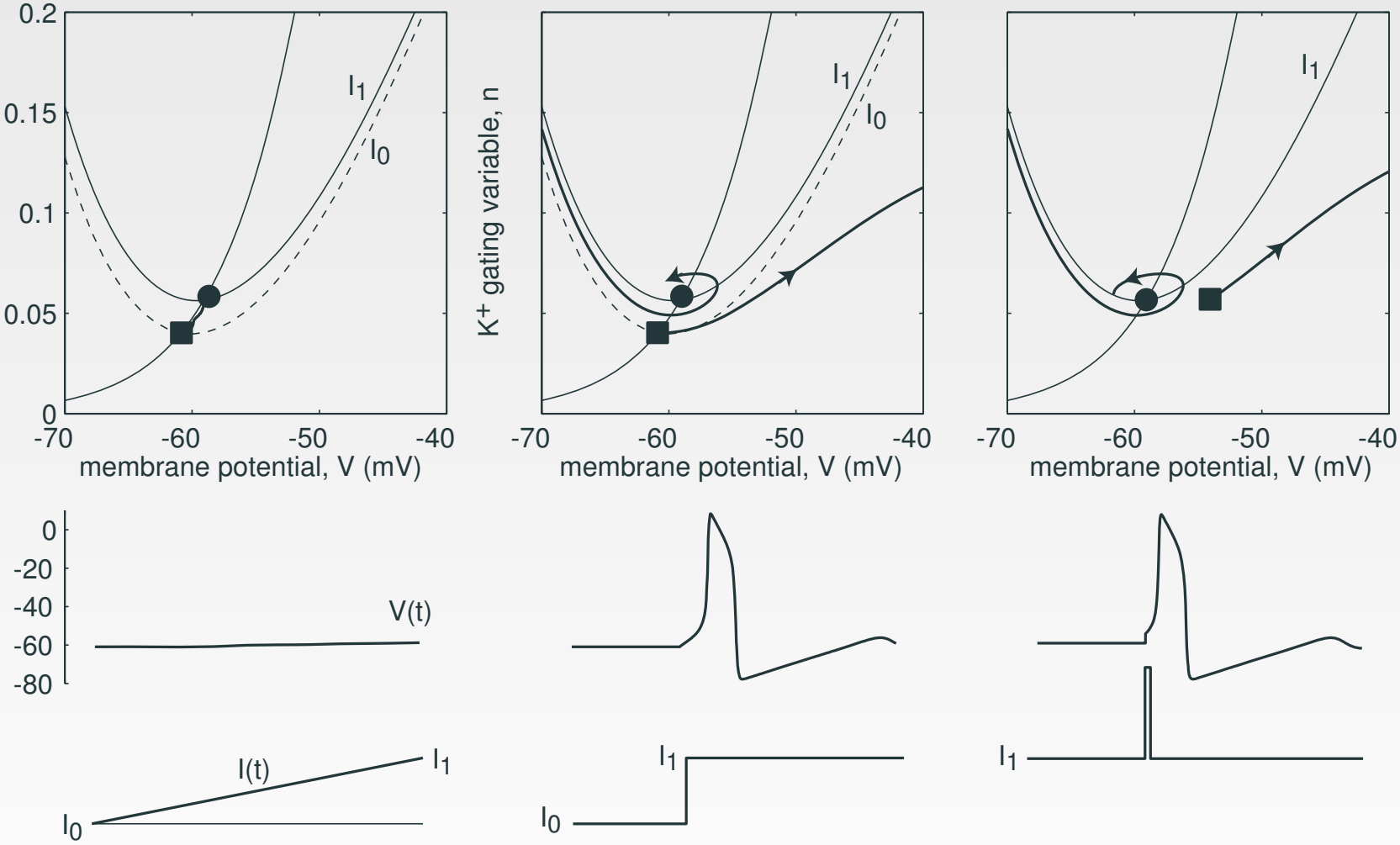




Example of the Fitzhugh-Nagumo model

$\dot{V} = V(a - V)(V - 1) - w + I,\ \dot{w} = bV - cw,\ a = 0.1,\ b = 0.01$

Ramps, Steps, and Shocks



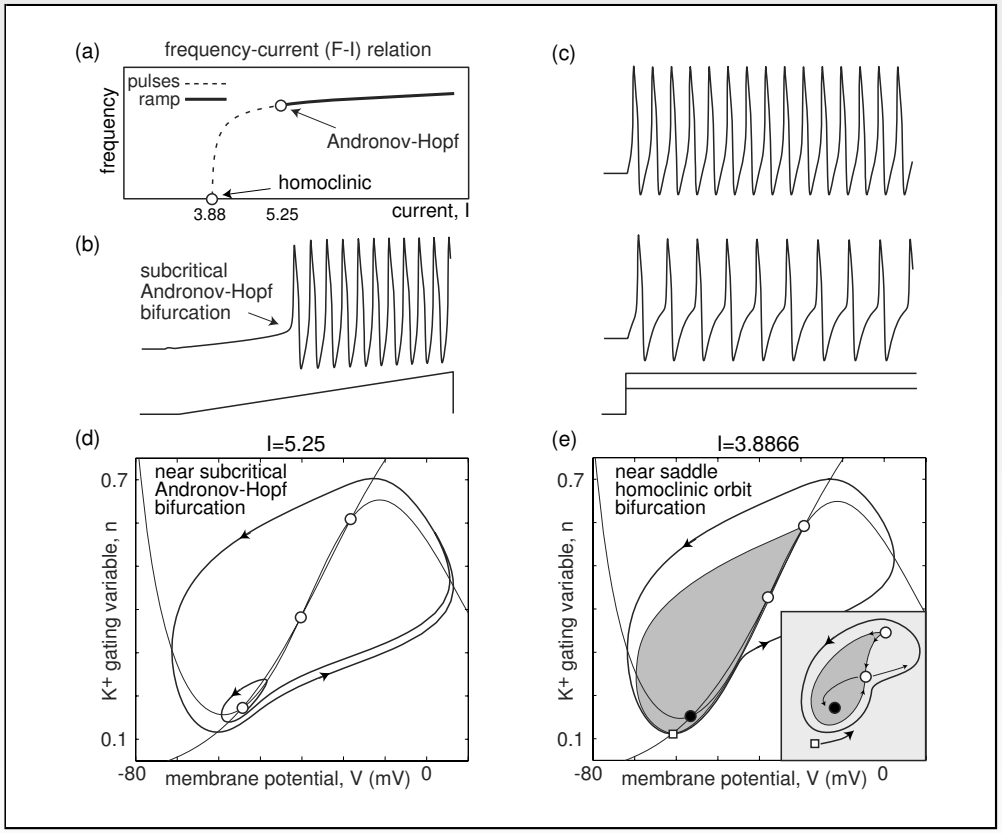
slow ramp from I_0 to I_1

step from I_0 to I_1

shock pulse at I_1

The $I_{Na,p} + I_K$ model, Class I or II?

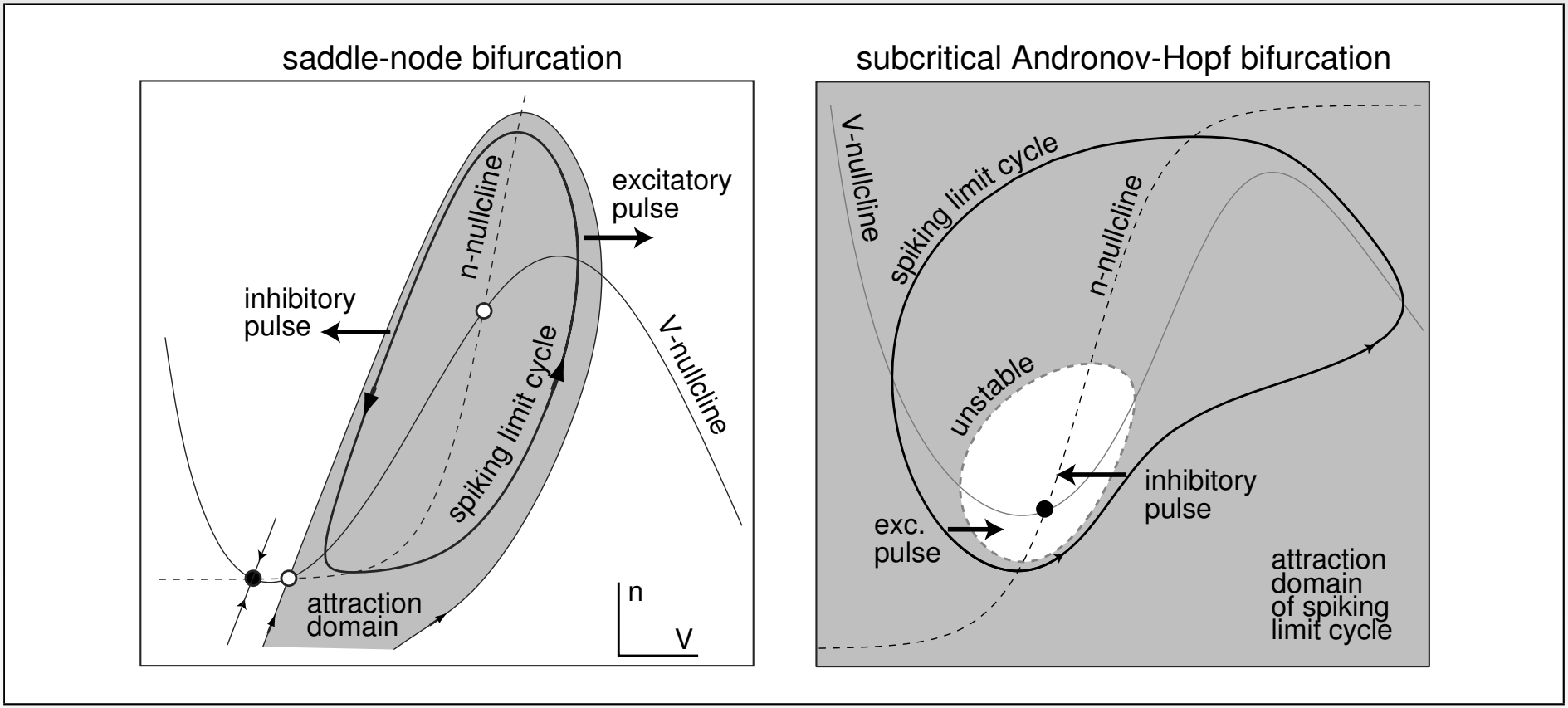
Bistability equilibrium - periodic orbit.



- Class II for ramps, I for Steps
- subcr. AH at $I = 5.25$ for ramps
- Saddle homoclinic for $I \approx 3.89$ for steps
- near BT

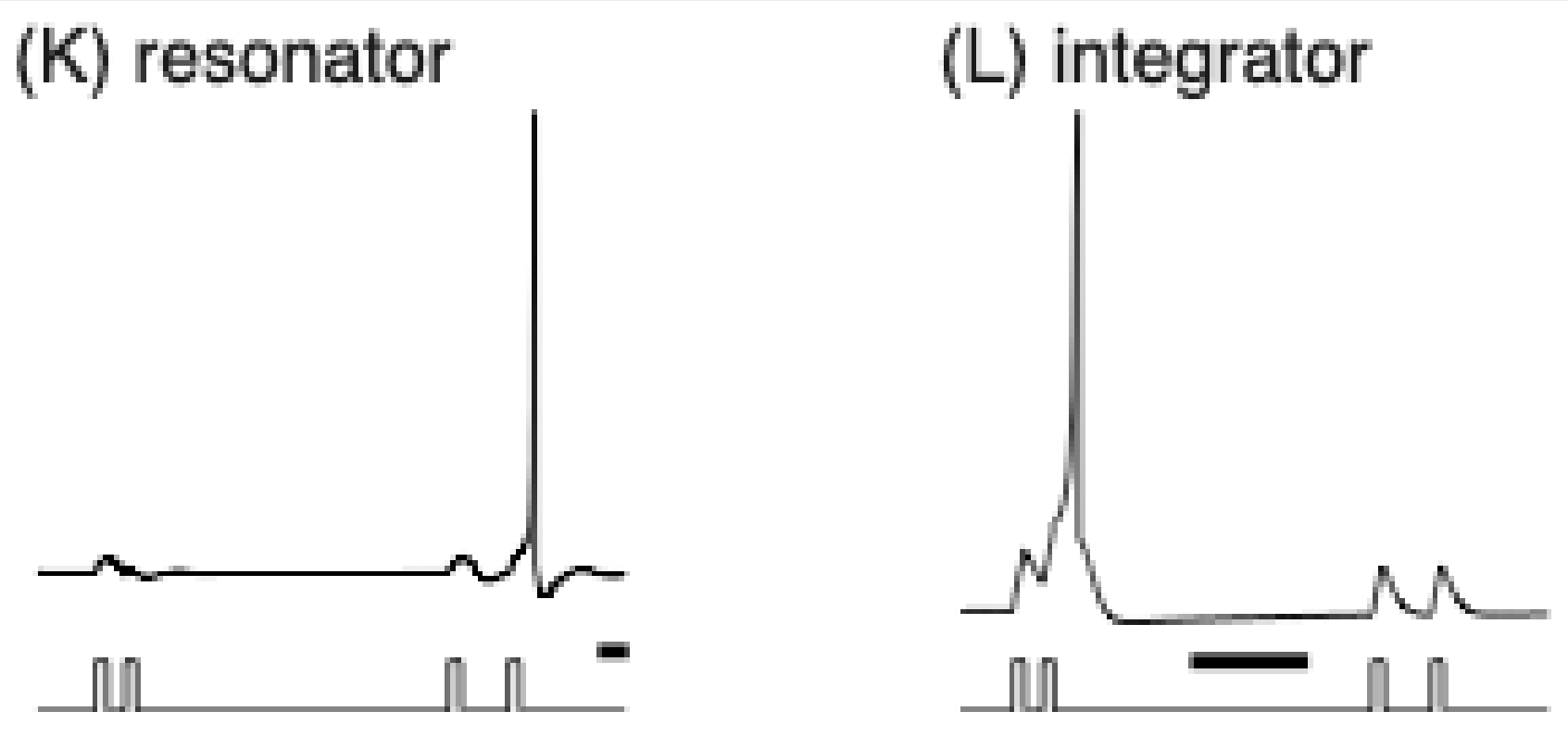
Gray: attraction domain for resting state.

Bistability

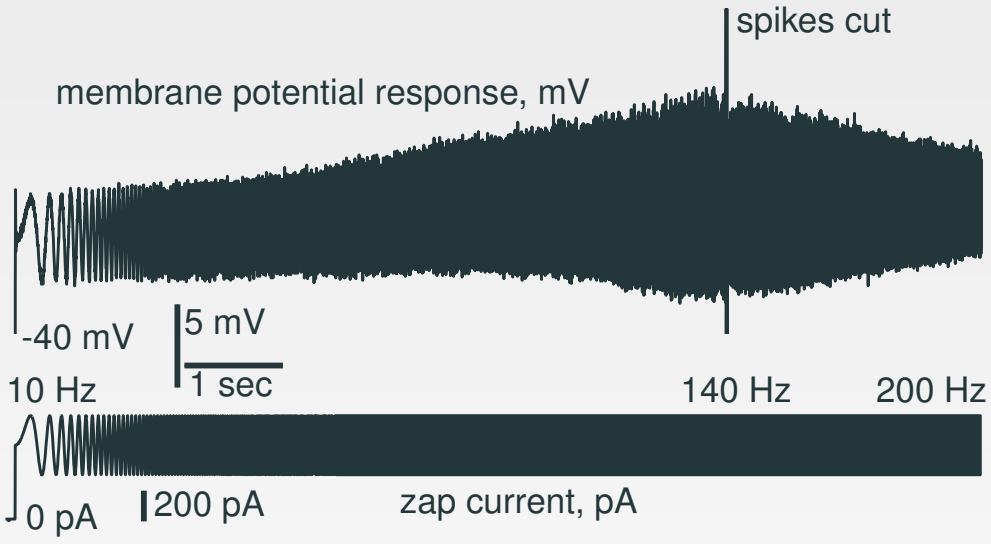


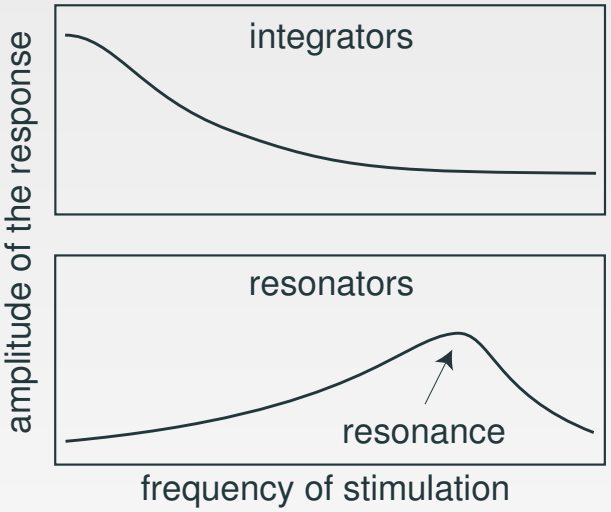
Excitatory / inhibitory pulses can shift the neuron from its resting state to repetitive firing.

Integrators vs. Resonators 1/2



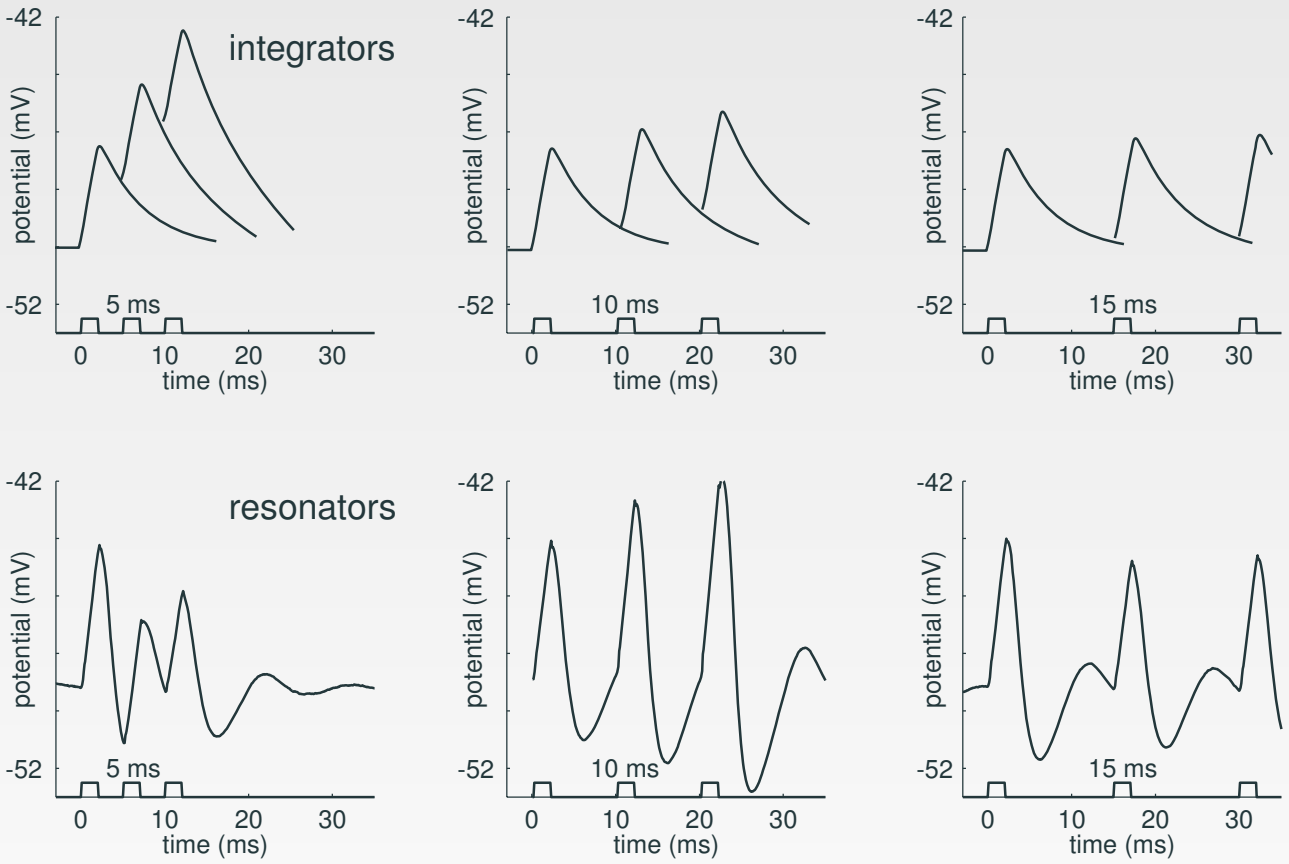
Integrators vs. Resonators 1/2





1. Presence of sub-threshold oscillations
2. Exp. mechanism to test their presence

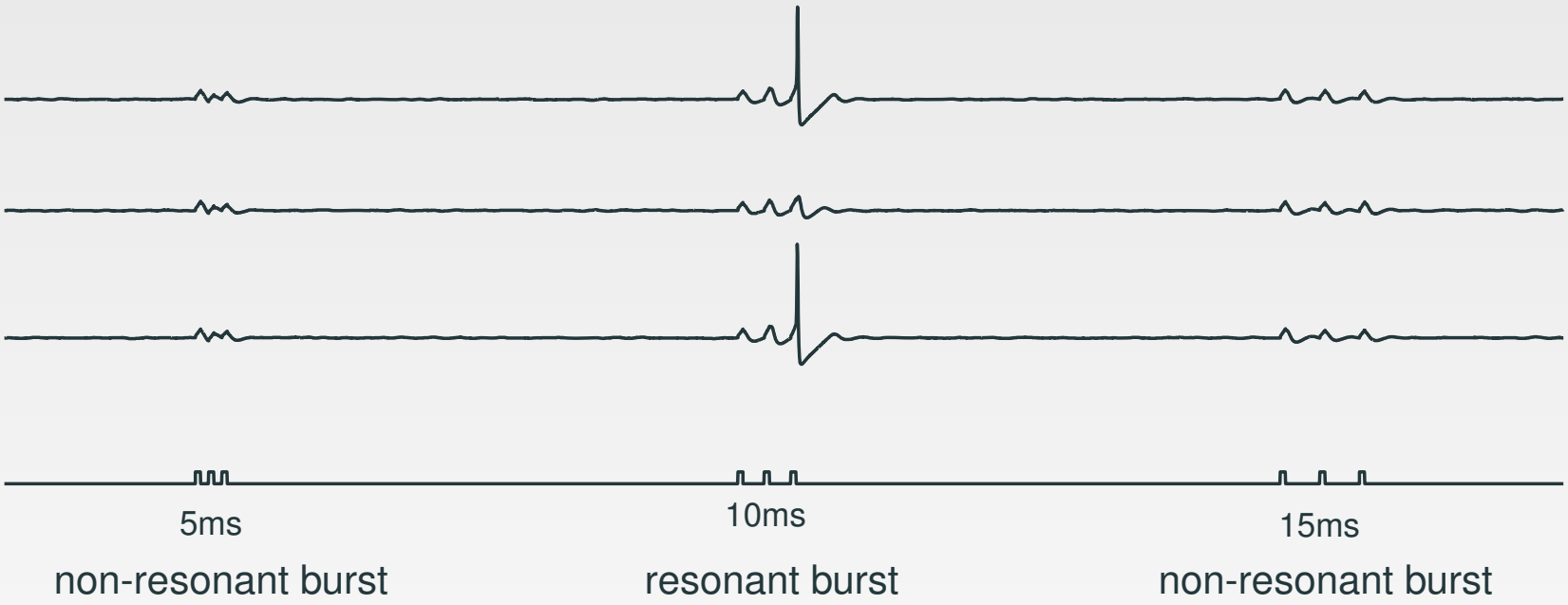
Integrators vs. Resonators 2/2



Integrators prefer high frequencies: detect coincidences.

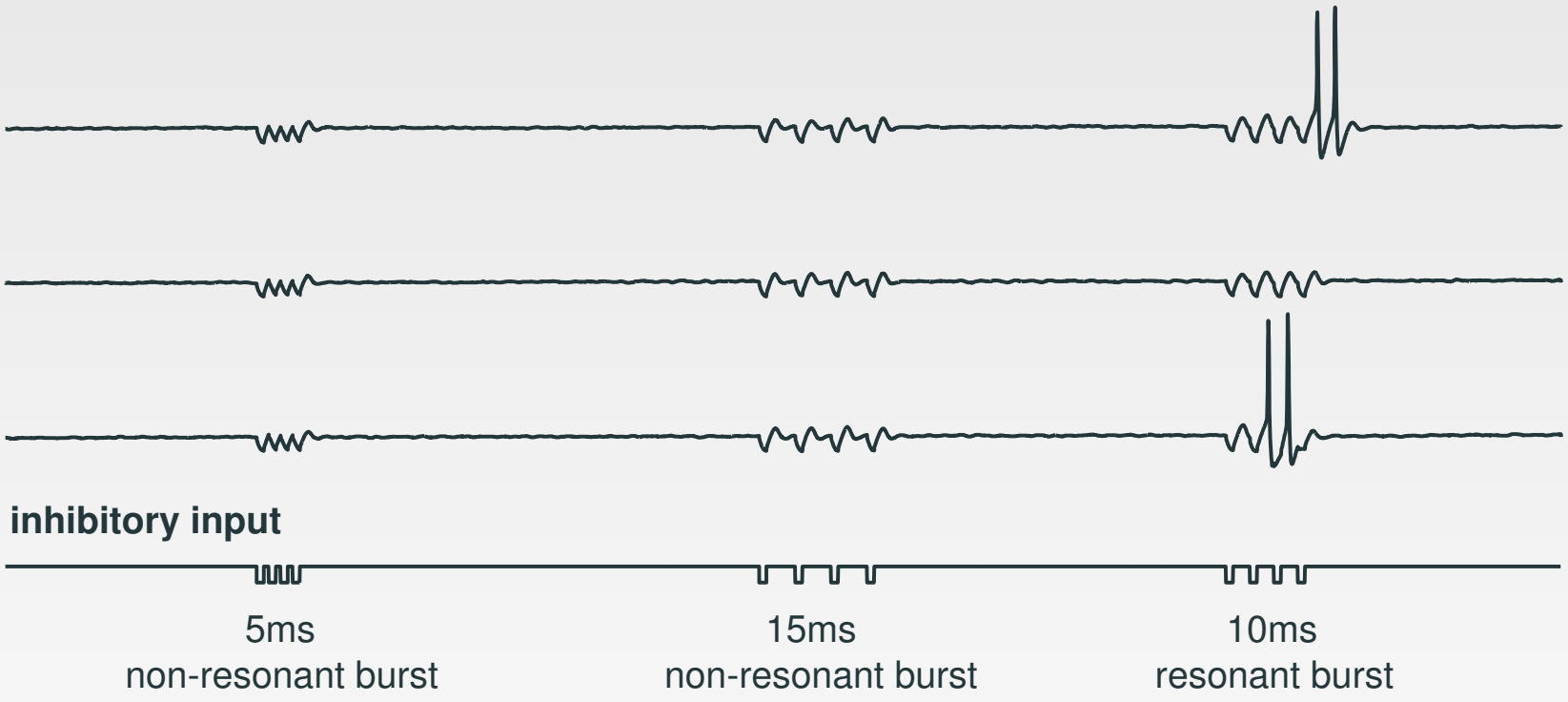
Resonators are selective in a frequency band.

Selective response: excitation or inhibition



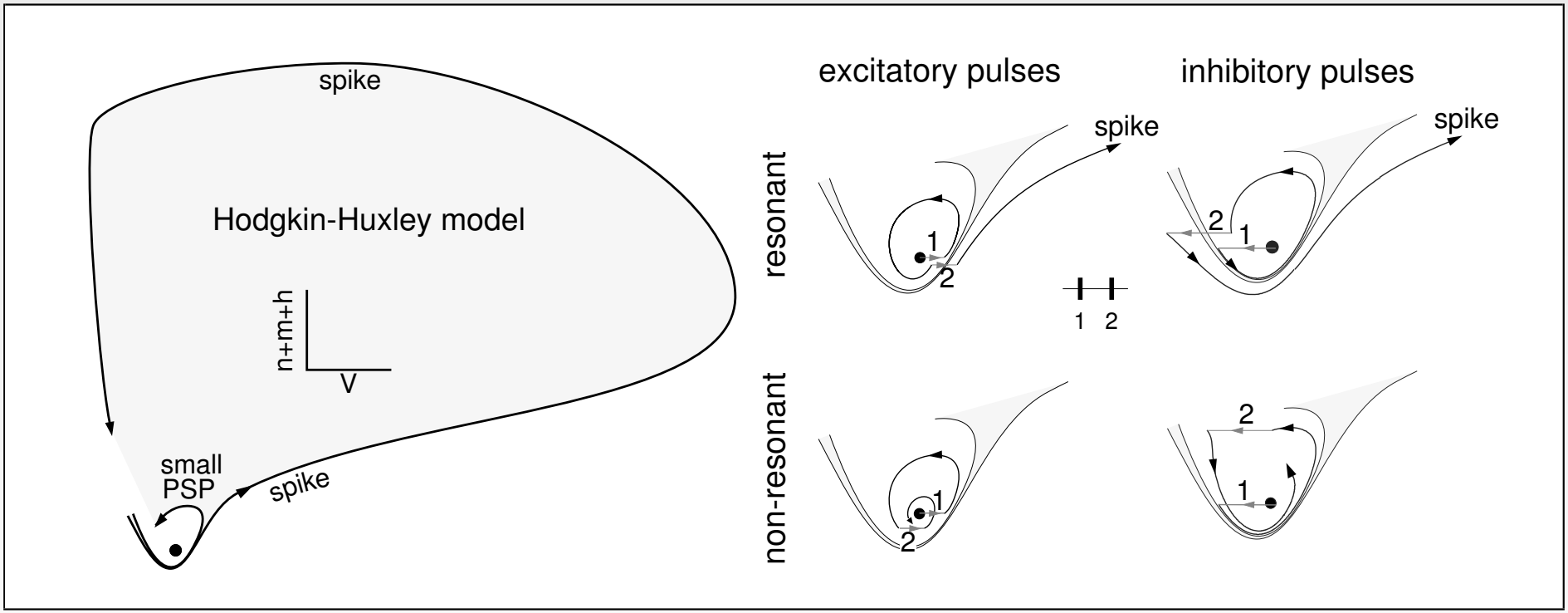
Mesencephalic V neurons in brainstem having subthreshold membrane oscillations with a natural period around 9 ms. Three consecutive voltage traces are shown to demonstrate some variability of the result

Selective response: excitation or inhibition



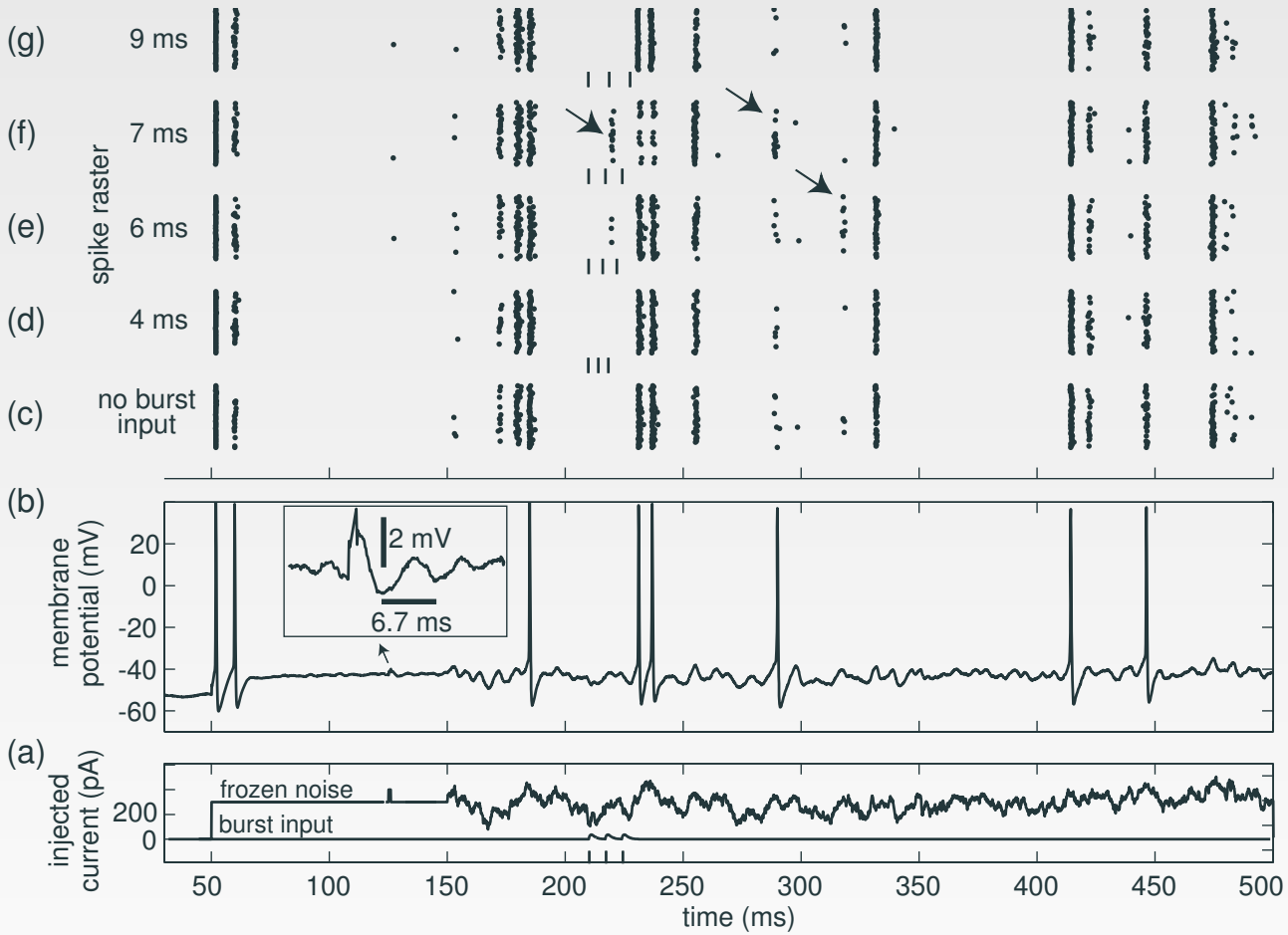
Experimental observations of selective response to inhibitory resonant burst in mesencephalic V neurons in brainstem having oscillatory potentials with the natural period around 9 ms. (Modified from Izhikevich et al. 2003).

Selective response: excitation or inhibition, Geometrical explanation



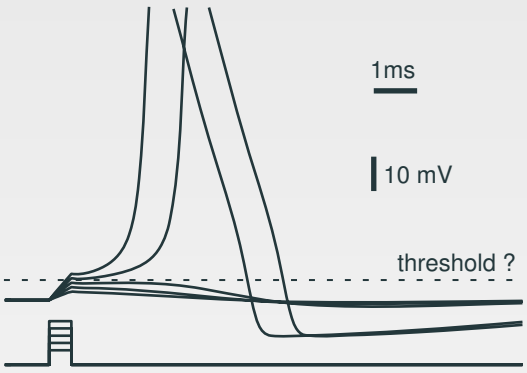
Important temporal coherence of pulses.

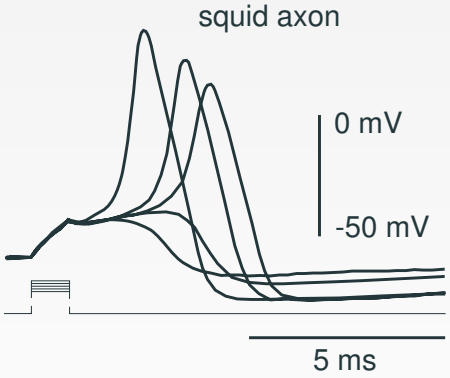
Influence of synaptic bombardment, Frozen noise experiment

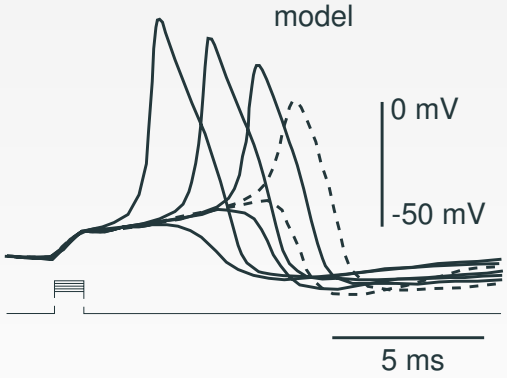


In vitro exp., sub-th. oscillations.

Threshold definition: not obvious





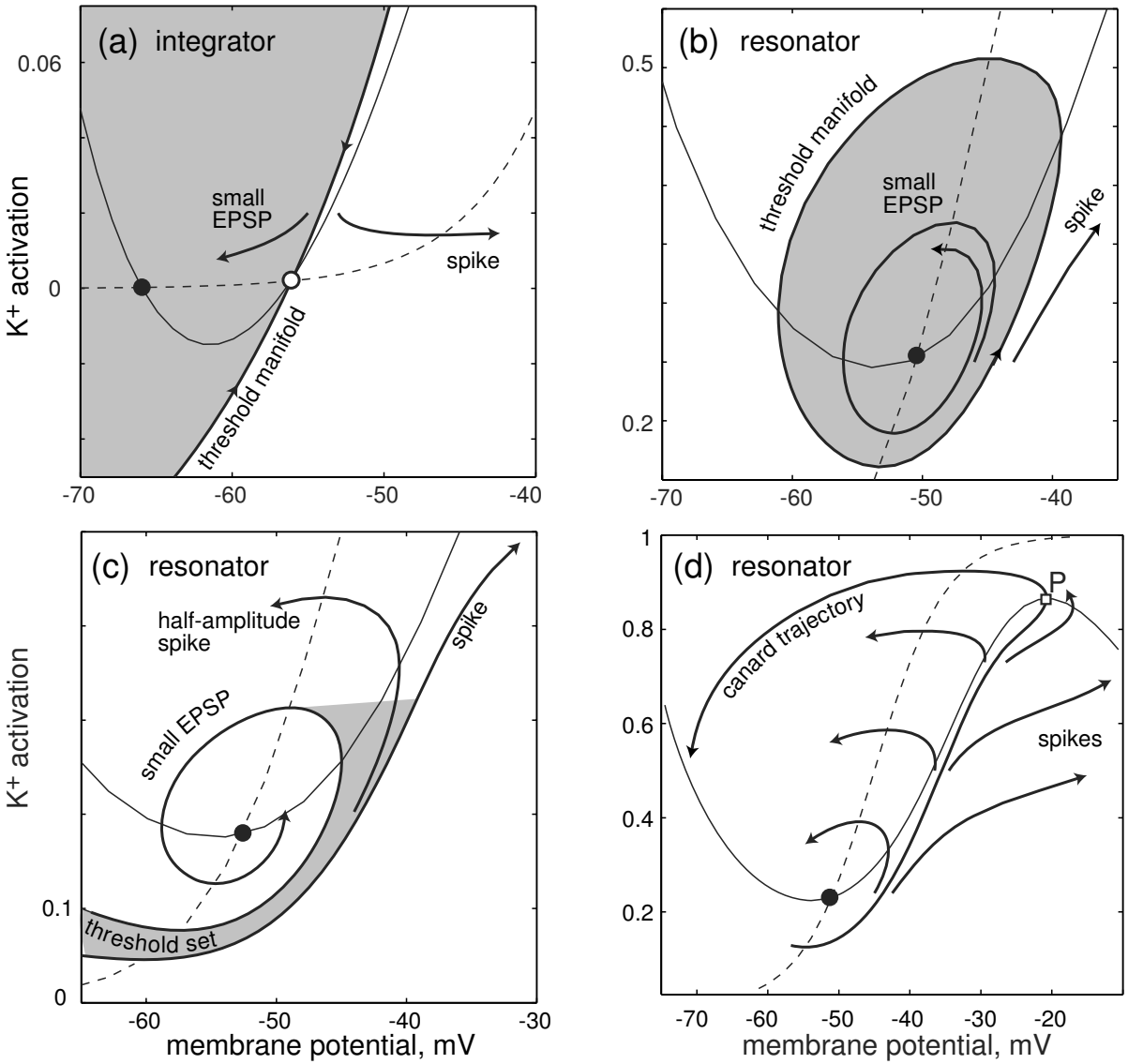


Threshold manifolds for the $I_{Na,p} + I_K$ model

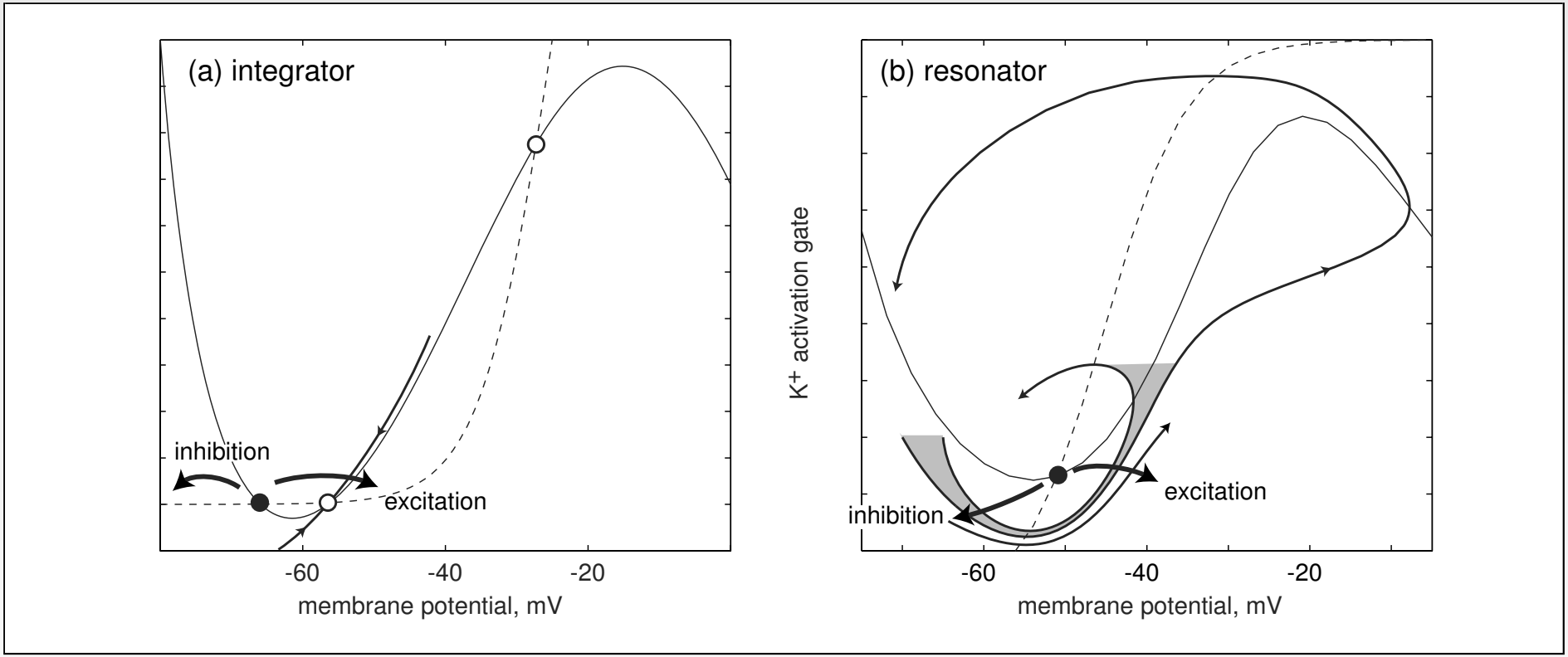
FitzHugh (1955) noticed that **thresholds, if they exist, are never numbers but manifolds**, e.g., curves in two-dimensional systems.

- Integrators (close to saddle-node bifurcation) have a threshold manifolds, given by stable manifold of fold point.
- For resonators, it depends on bifurcation type
  - Bistable regime: (close to sub. AH): the unstable LC is a th. manifold.
  - In all other cases, there is no well defined th. manifold.

Threshold manifolds for the $I_{Na,p} + I_K$ model

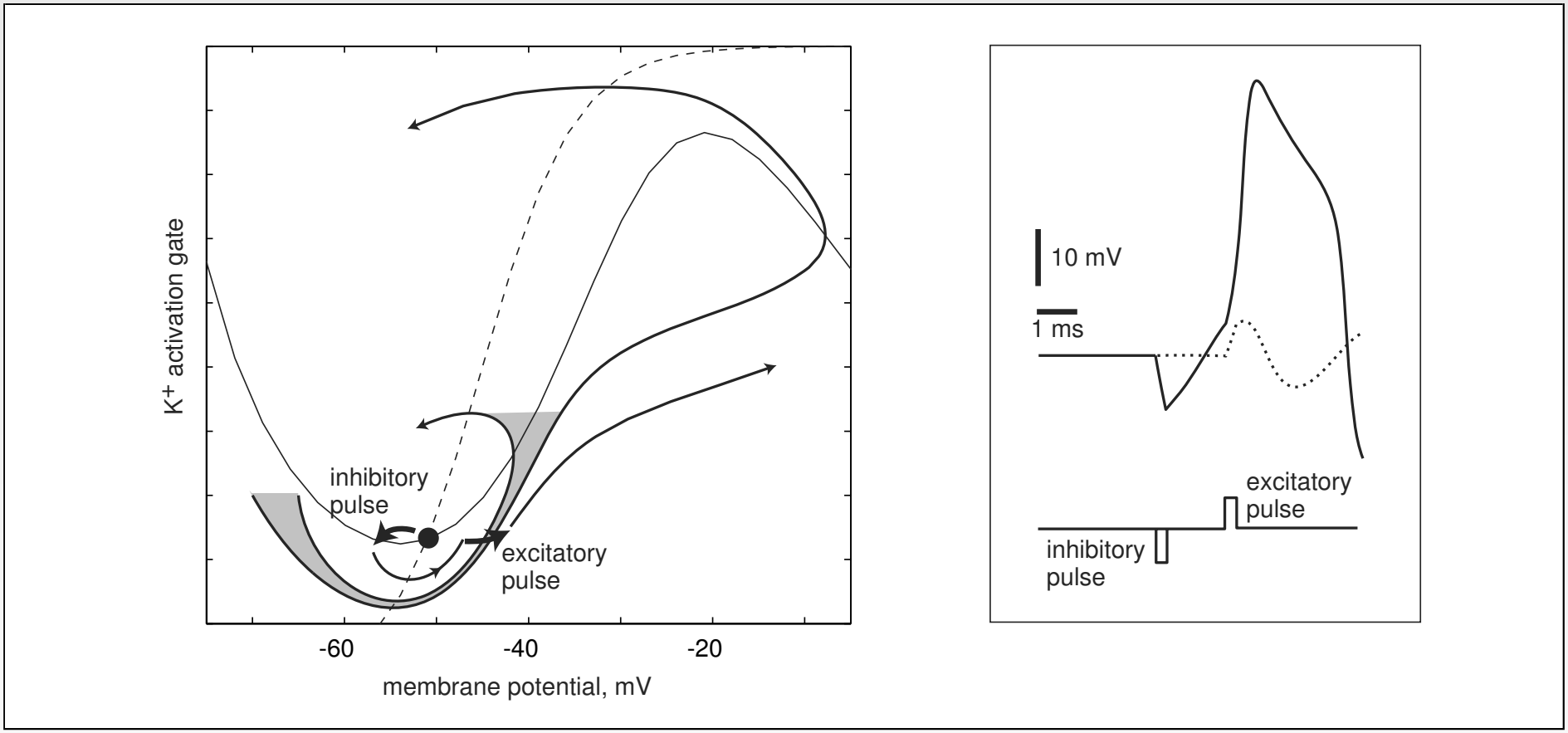


Spike emission: excitation or inhibition?



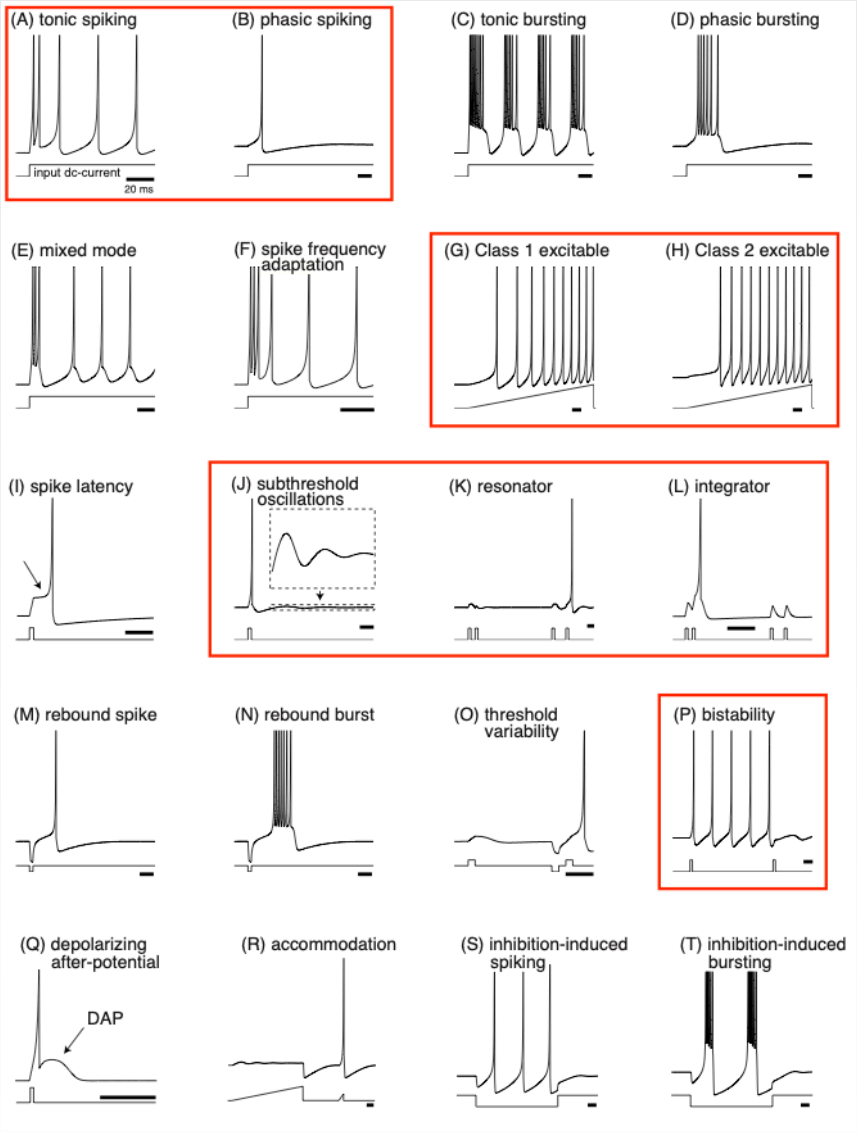
An integrator cannot spike in response to a hyper-polarizing current, a resonator can.

Spike emission: excitation or inhibition?

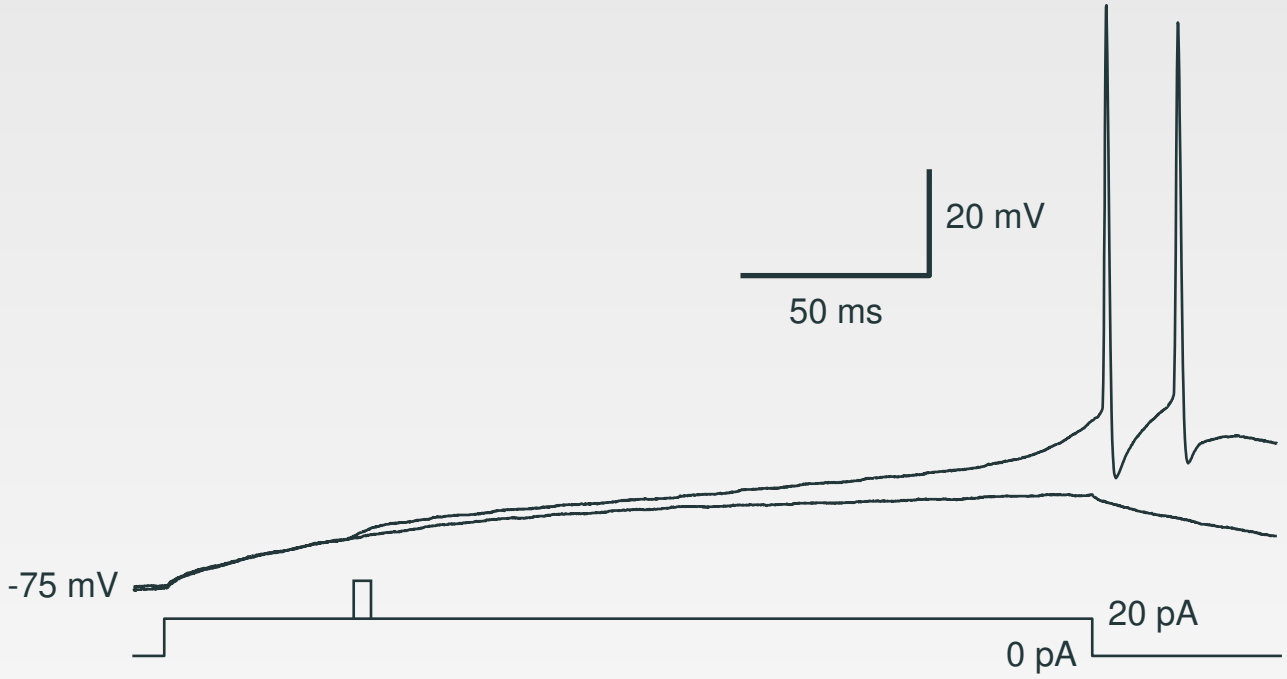


An hyper-polarizing current (inhib.) can enhance the effect of subsequent excitatory pulses.

Spiking behaviours



Latency to first spike (In Vitro)

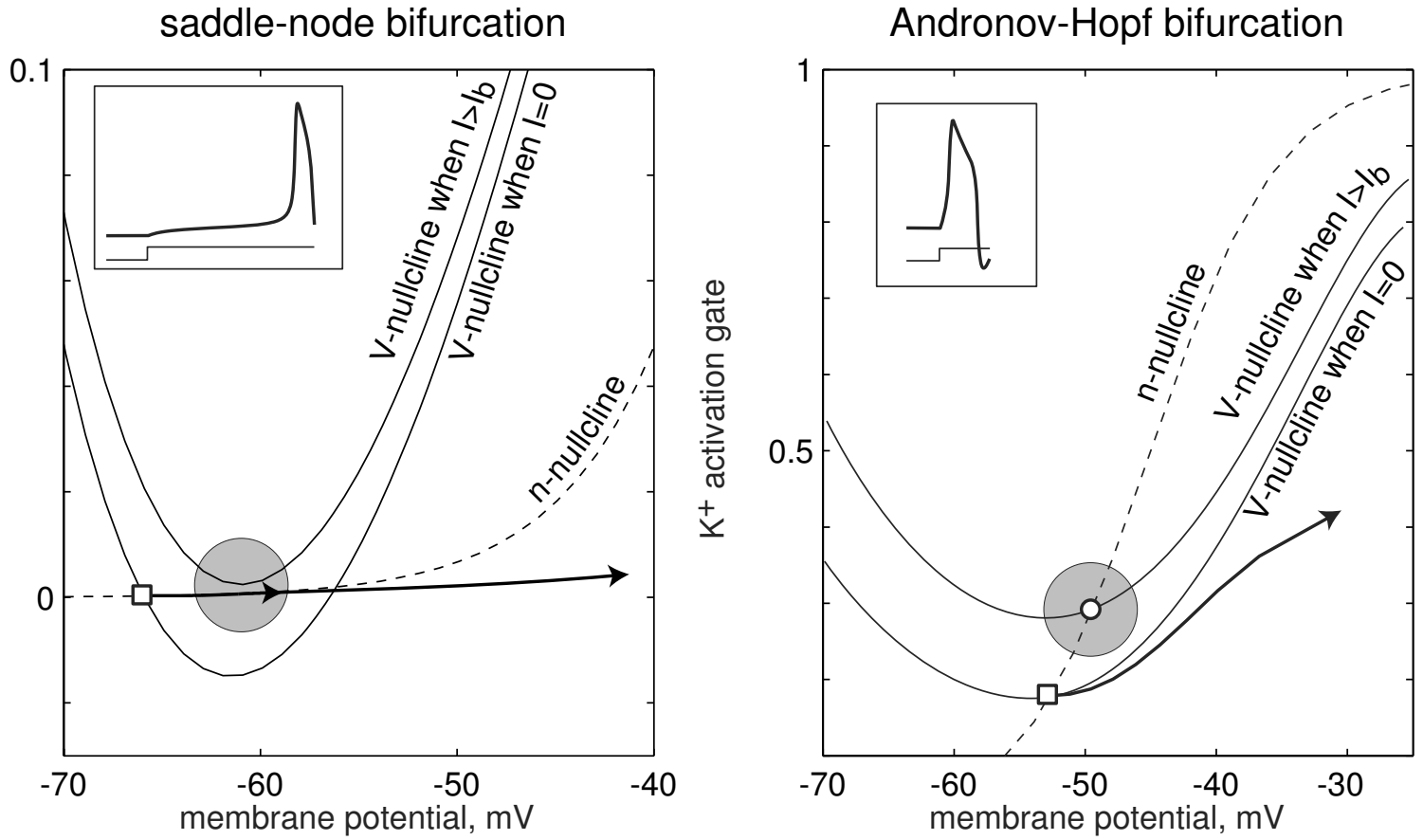


Property of integrators

Allow coding of input strengh in latency to first spike

Less sensitive to noise, since only prolonged inputs can cause spikes

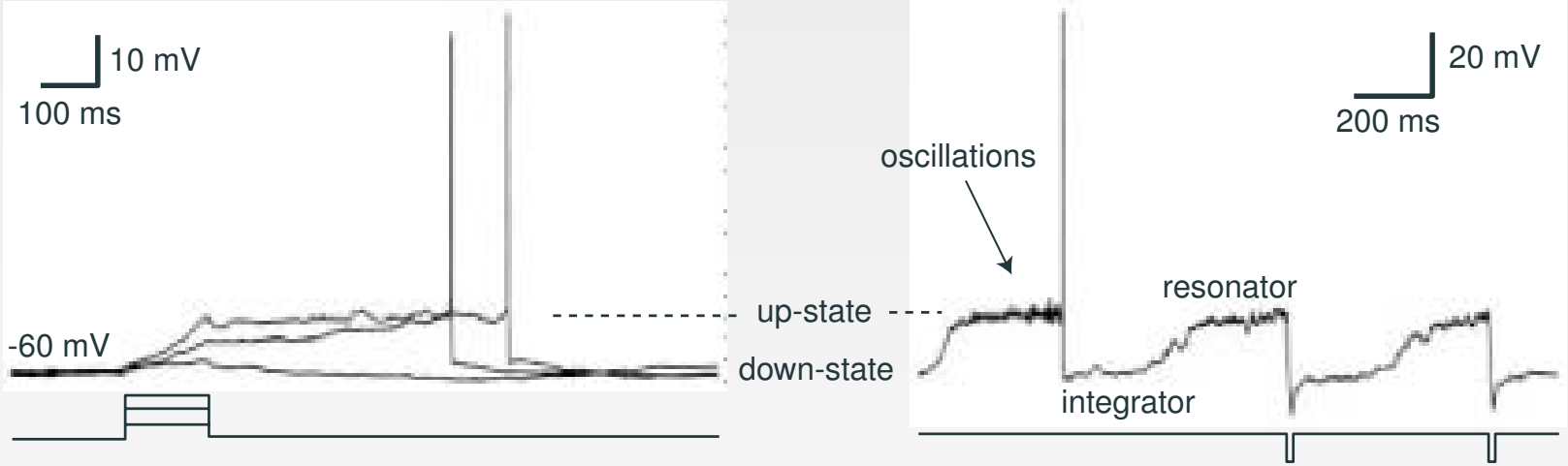
Latency to first spike



Flipping from an Integrator to a Resonator

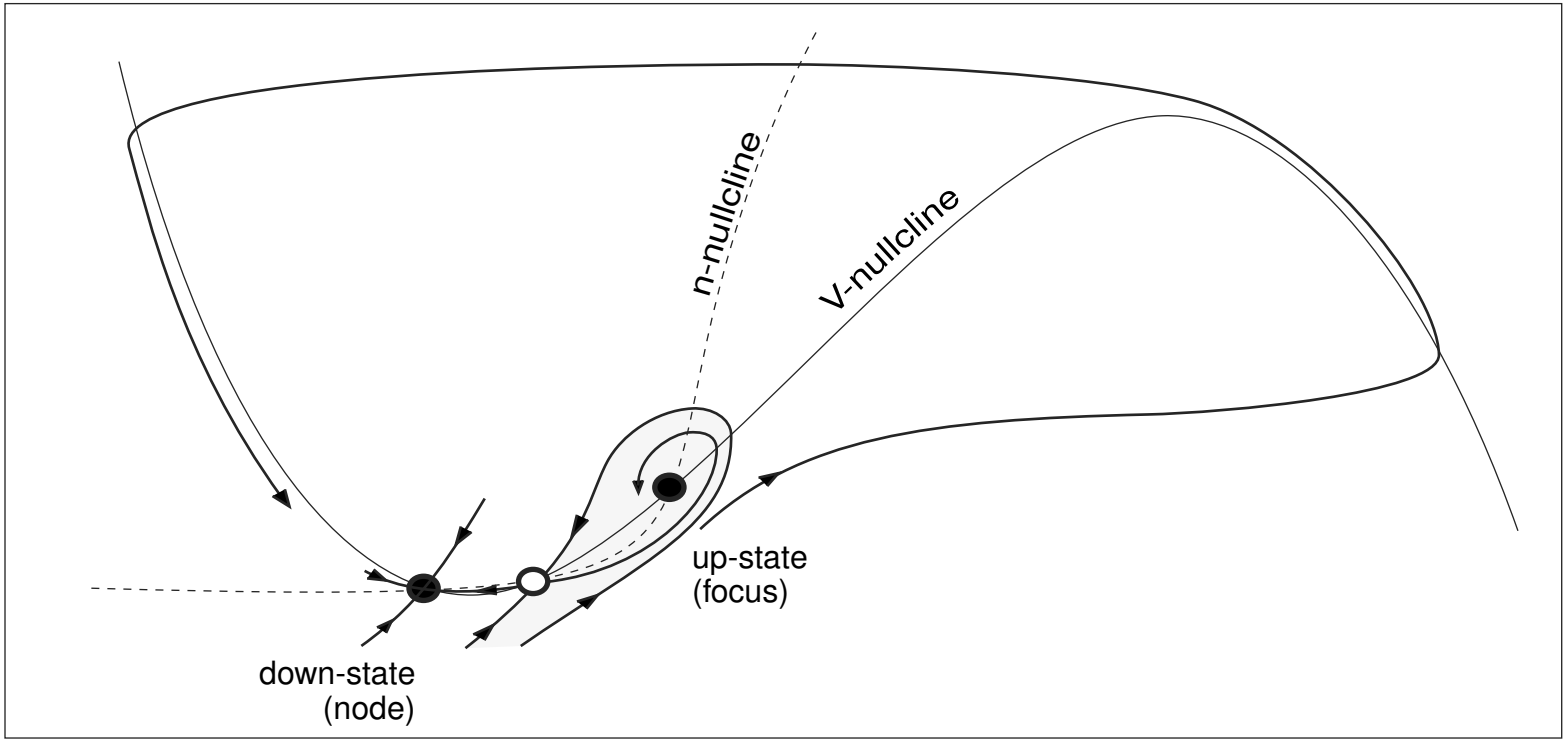
- Mitral cells can be switched from being integrators to being resonators by synaptic input.
- For resonators, it depends on bifurcation type

Integrator → Resonator 1/2



Multistability of equilibria.

Integrator → Resonator 2/2

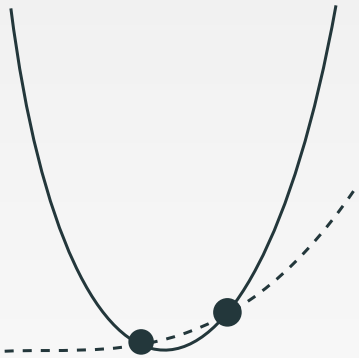


Gray: attraction domain for UP state.

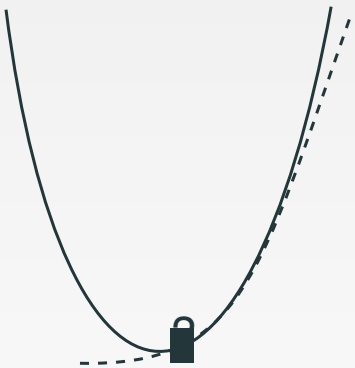
BT coming into play?

Need to combine in 2d a SN with a AH:

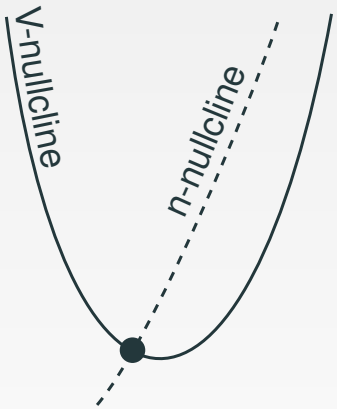
integrator
(saddle-node bifurcation)



?

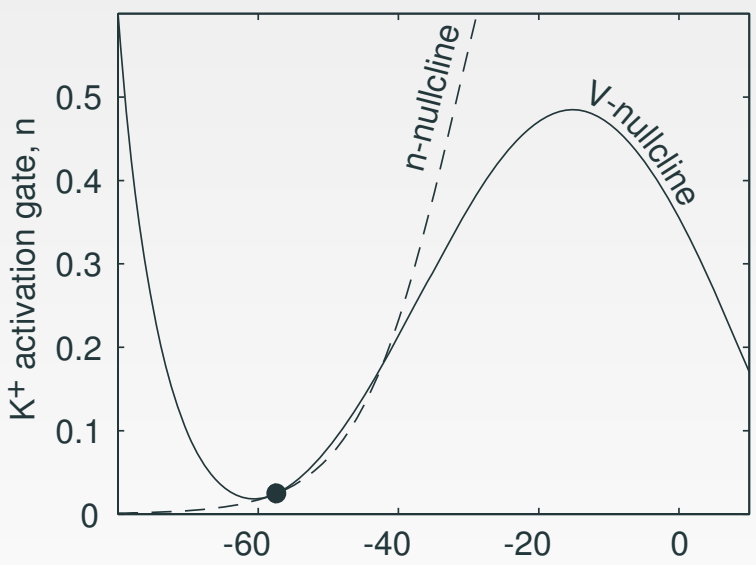


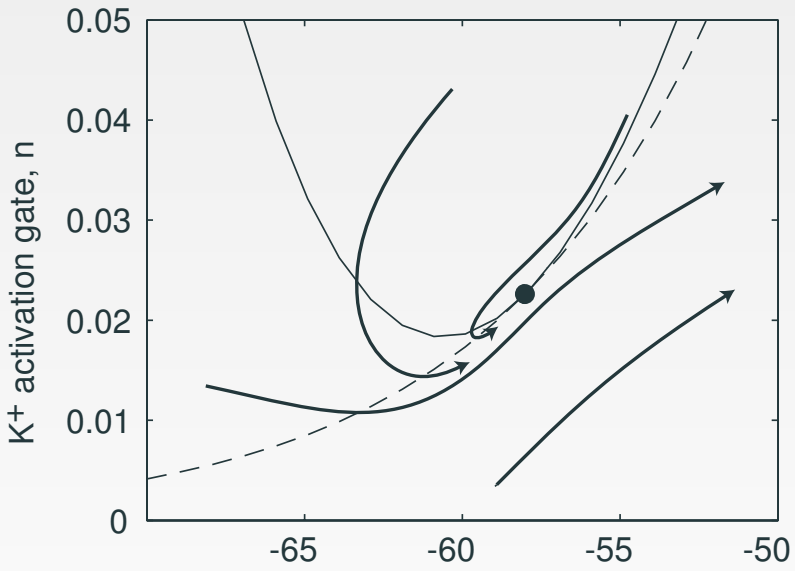
resonator
(Andronov-Hopf bifurcation)



Bogdanov-Takens 1/3

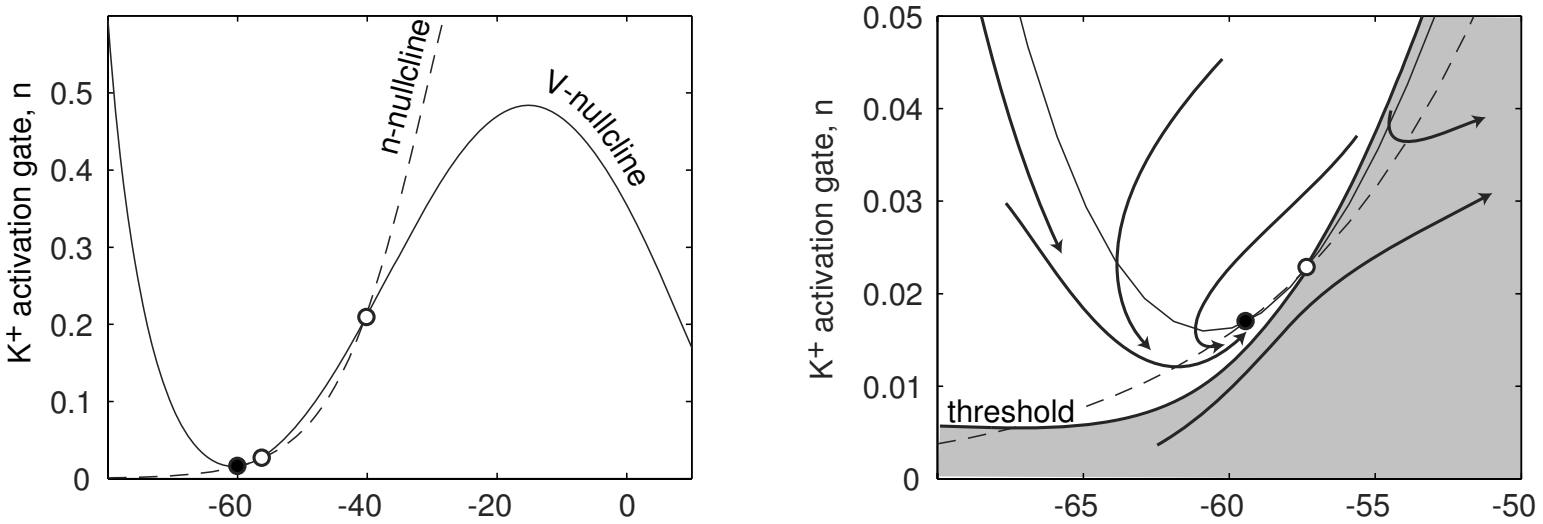
In the $I_{Na,p} + I_K$ model (parameters $E_L, V_{1/2}$), the nullclines are parallel close to the left knee of the fast nullcline





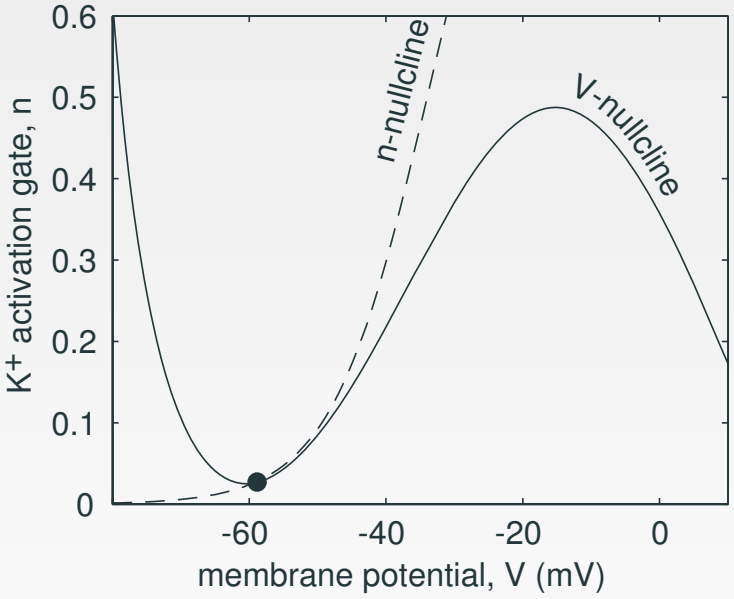
Bogdanov-Takens 2/3

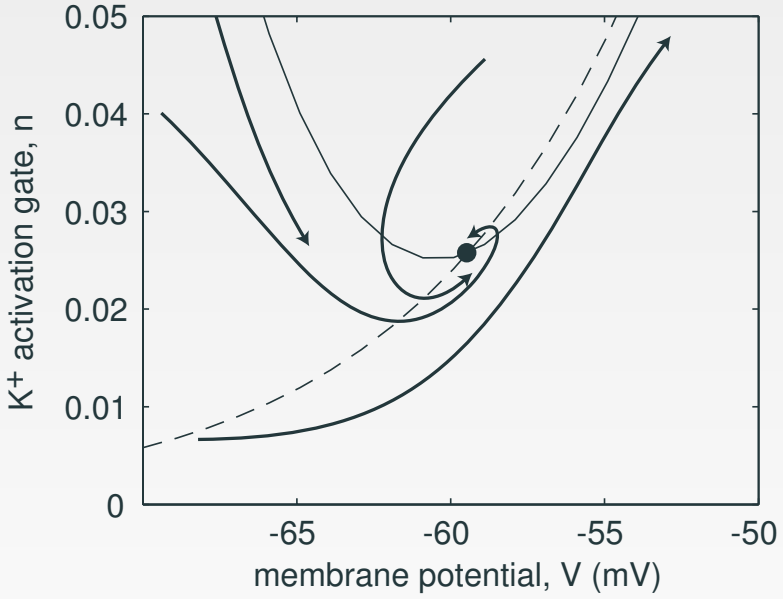
A small change in the parameter $V_{1/2}$ can give a Saddle-Node: i.e. an integrator



Bogdanov-Takens 3/3

or a resonator via a stable focus.





Summary

Summary 1/2

subthreshold oscillations \ coexistence of resting and spiking states	YES (bistable)	NO (monostable)
NO (integrator)	saddle-node	saddle-node on invariant circle
YES (resonator)	subcritical Andronov-Hopf	supercritical Andronov-Hopf

⇒ How does this impact network dynamics, ongoing research

Summary 2/2

properties	integrators		resonators	
bifurcation	saddle-node on invariant circle	saddle-node	subcritical Andronov-Hopf	supercritical Andronov-Hopf
excitability	class 1	class 2	class 2	class 2
oscillatory potentials	no		yes	
frequency preference	no		yes	
I-V relation at rest	non-monotone		monotone	
spike latency	large		small	
threshold and rheobase	well-defined		may not be defined	
all-or-none action potentials	yes		no	
co-existence of resting and spiking	no	yes	yes	no
post-inhibitory spike or facilitation (brief stimuli)	no		yes	
inhibition-induced spiking	no		possible	