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Interdisciplinary work in neuroscience

Masters in Physics, PhD in Physics (interdisciplinary) @ Univ. of Buenos Aires

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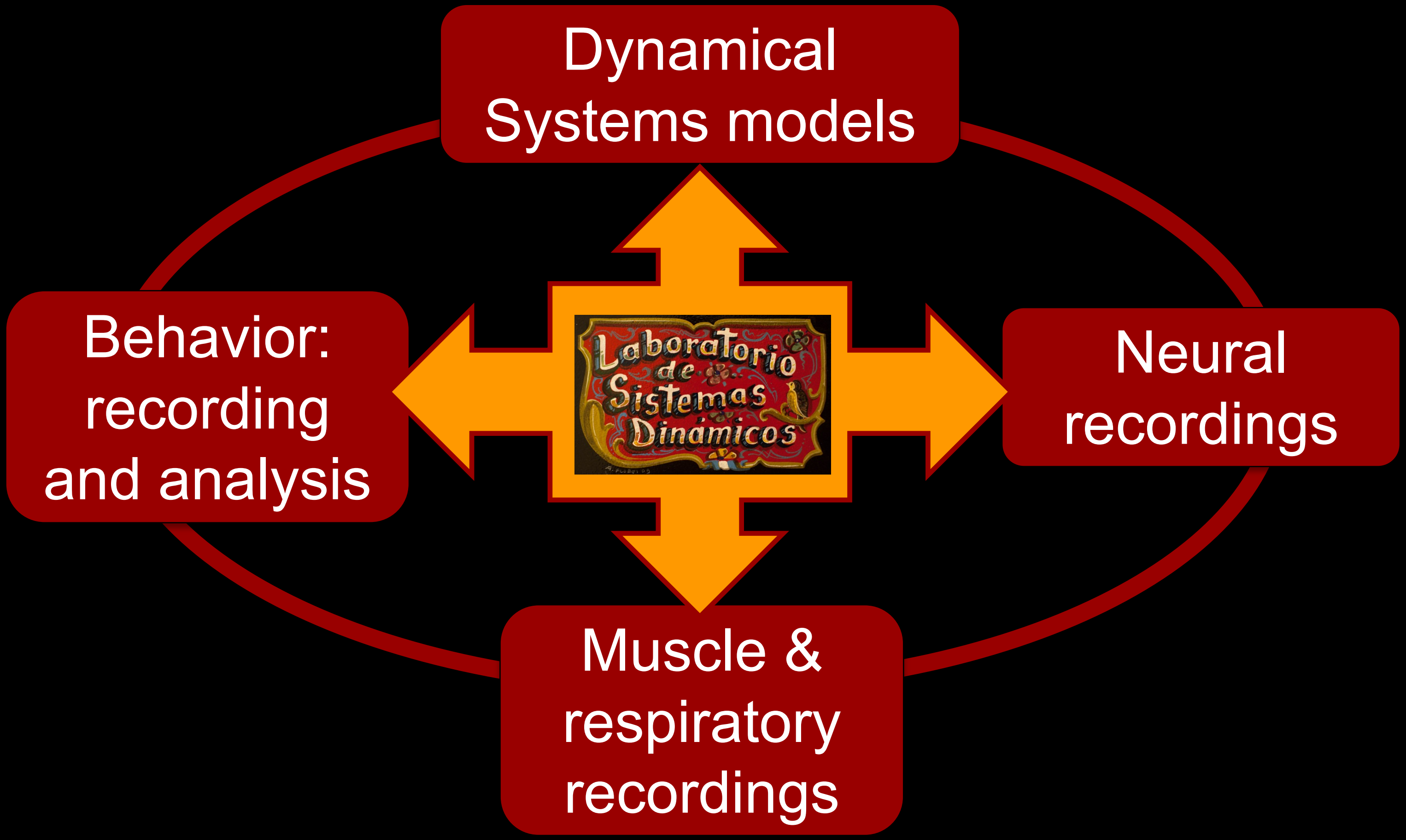
The goal of our research is to shed light on the **dynamical mechanisms involved in the perception and the generation of complex sounds** and to study the brain and the peripheral system in this process.



Lecture 1

Introduction to nonlinear dynamics and excitable systems

Lecture 2

Dynamical models for single neurons. Comparison with experimental data.

Lecture 3

The neuroethology perspective in neuroscience.
Case of study: models of vocal production in birds.

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Lecture 1
Introduction to nonlinear dynamics and excitable systems

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Dynamical Systems

Definition : set of **variables** that describe state of the system and a **law** that describes the evolution of the state variables with time

how the state of the system in the next moment of time depends on the input and its state in the previous moment of time

Example:
The Hodgkin-Huxley model
(4-dimensional dynamical system)
Its state is uniquely determined by the membrane potential, V , and the "gating variables" n, m, and h for persistent K+ and transient Na+ currents.
The evolution law is given by a **4-dimensional system of ordinary differential equations.**

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= \alpha_n(V)(1-n) - \beta_n(V)n \\
\dot{m} &= \alpha_m(V)(1-m) - \beta_m(V)m \\
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V)h\ ,
\end{aligned}
$$

Is this dynamical system nonlinear?

Nonlinear Dynamics

Nonlinear rules

Mechanisms responsible for governing the temporal evolution of a system

Let´s see…

$$
\begin{aligned}
C\,\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
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\end{aligned}
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\begin{aligned}
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\beta_m(V) &= 4 \exp\left(\frac{-V}{18}\right) \,, \\
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\beta_h(V) &= \frac{1}{\exp(\frac{30-V}{10}) + 1} \,.
\end{aligned}
$$

Dynamical Systems

Types of dynamical systems:

Differential equations

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
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\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V)h \,,
\end{aligned}
$$

Maps

Logistic map

$$x_{n+1} = r x_n (1 - x_n)$$

where x_n is a number between 0 and 1, which represents the ratio of existing population to the maximum possible population

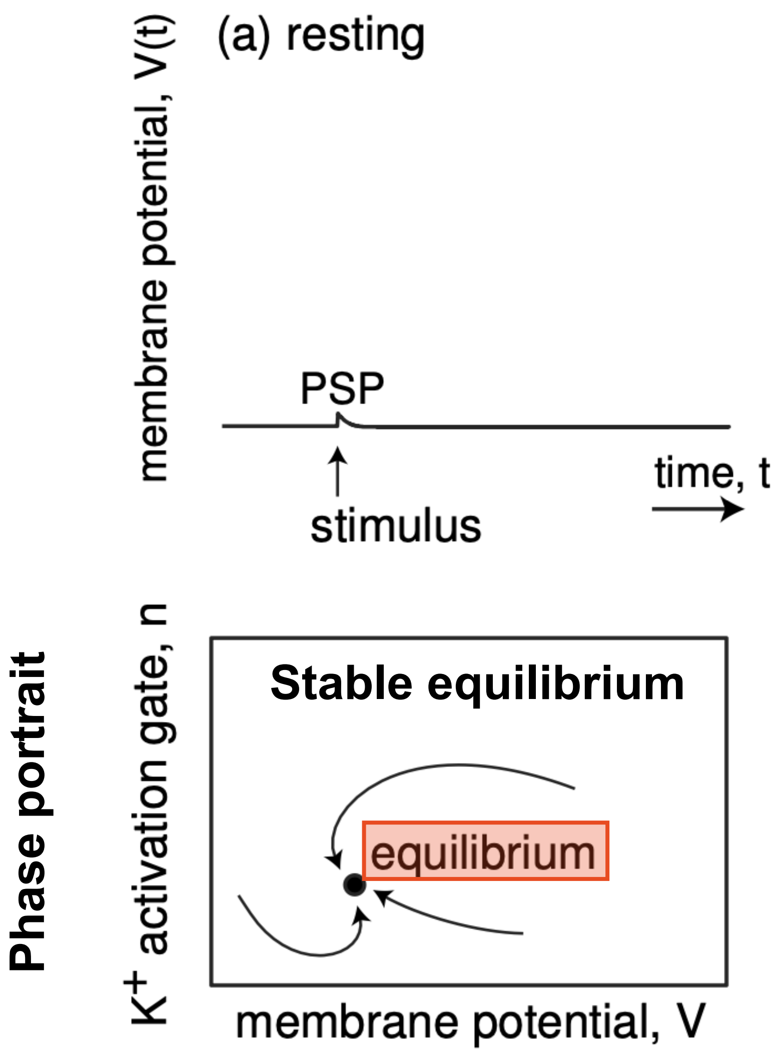
Chaos!

Phase portraits

The power of the dynamical systems approach to neuroscience (and to many other sciences) is that we can tell many things about a system without knowing all the details that govern the system evolution.

Phase portraits

Quiescent neuron whose membrane potential is resting



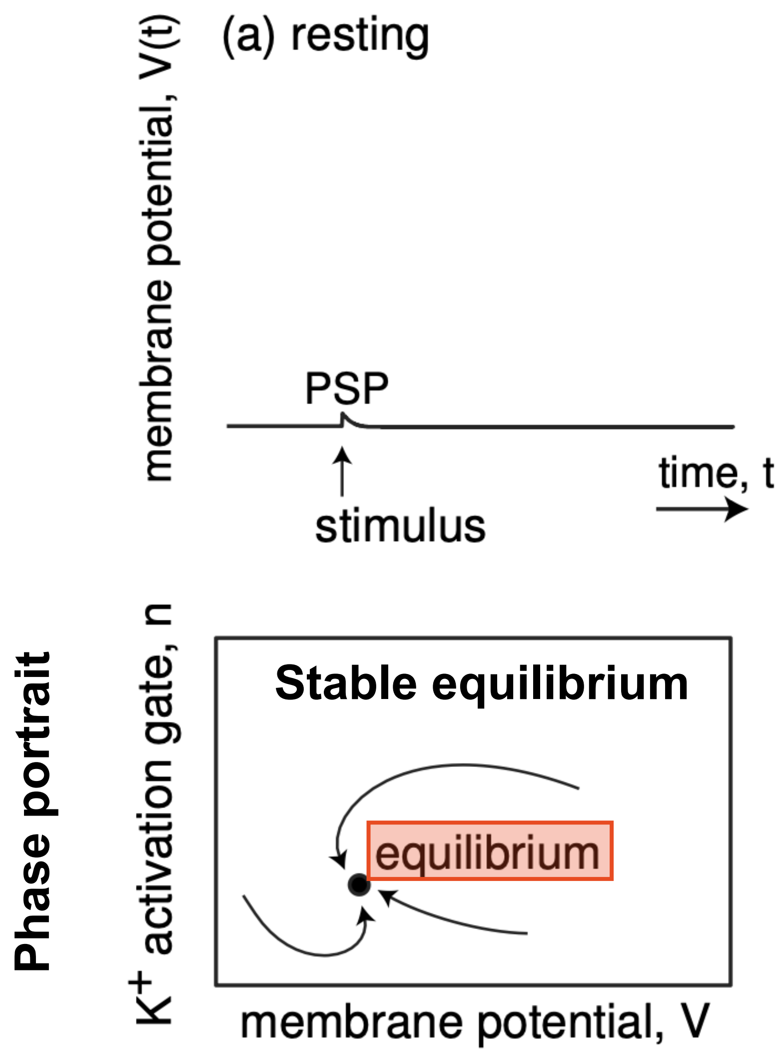
Isn´t it amazing that we can reach such a conclusion without knowing the equations that describe the neuron’s dynamics?

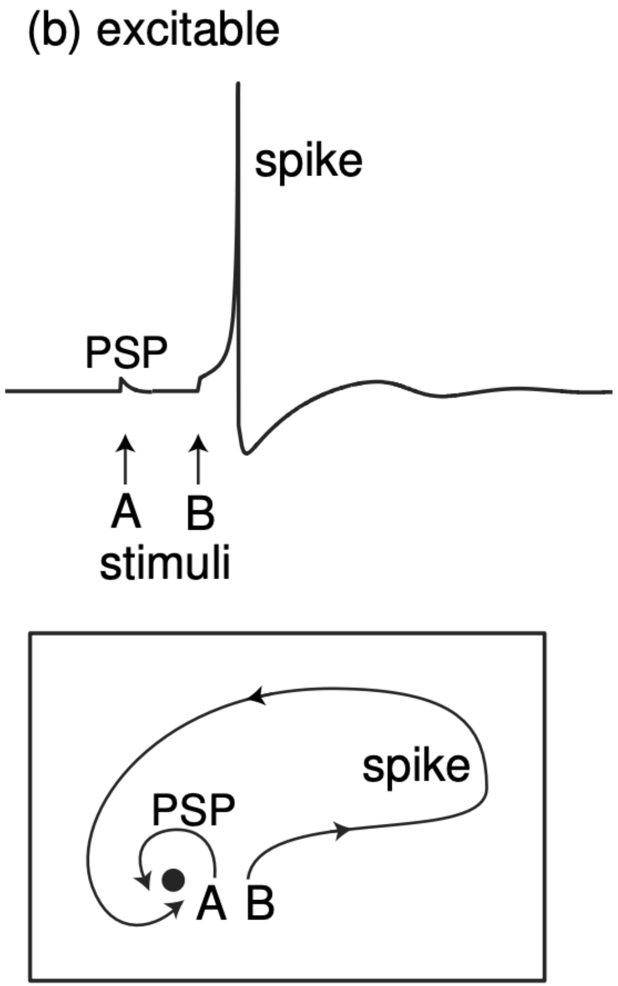
We do not even know the number of variables needed to describe the neuron

Phase portraits

Quiescent neuron whose membrane potential is resting

Neuron in an excitable mode





Small perturbations **(A)** result in small excursions from the equilibrium (**PSP**, postsynaptic potential).

Larger perturbations **(B)**, are amplified by the neuron's intrinsic dynamics and result in the **spike response.**

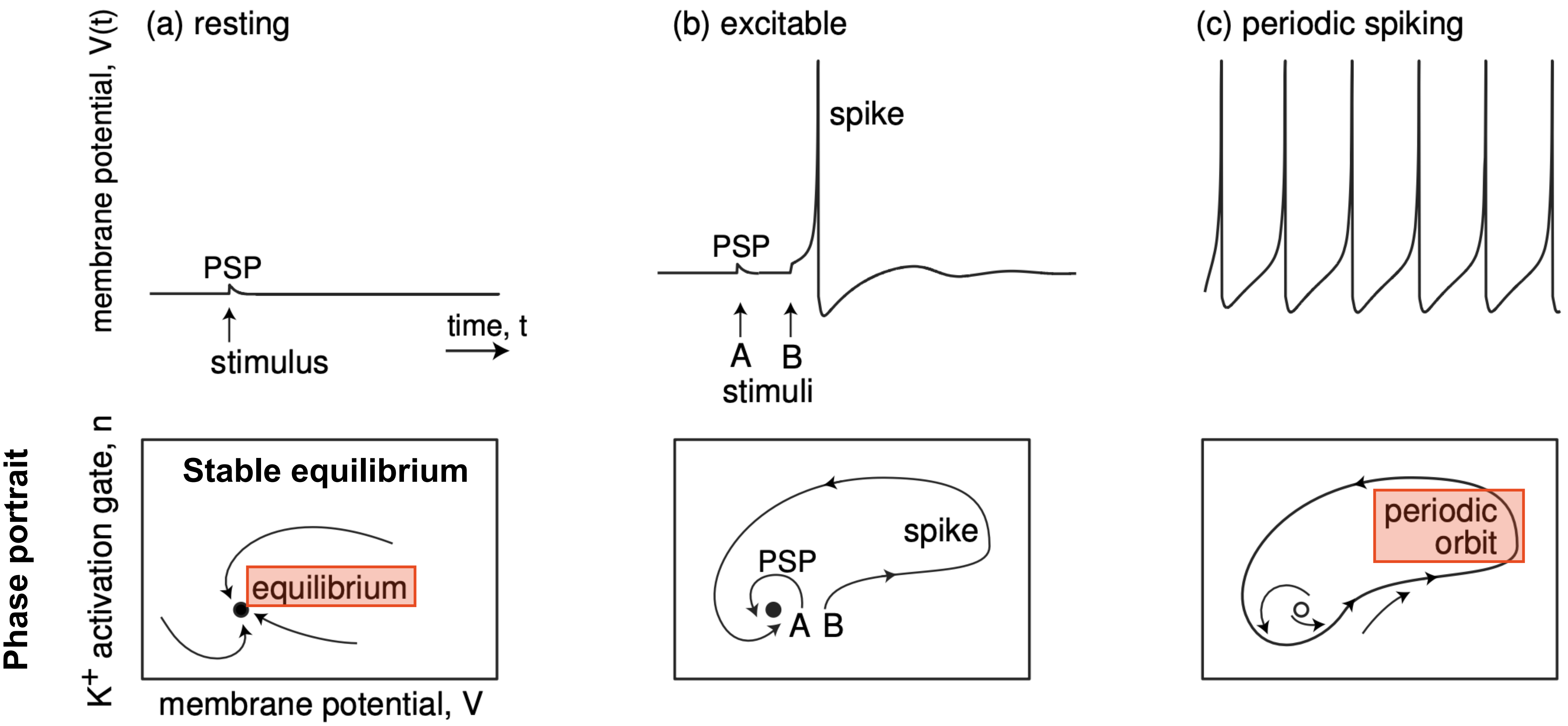
Excitable system

Phase portraits

Quiescent neuron whose membrane potential is resting

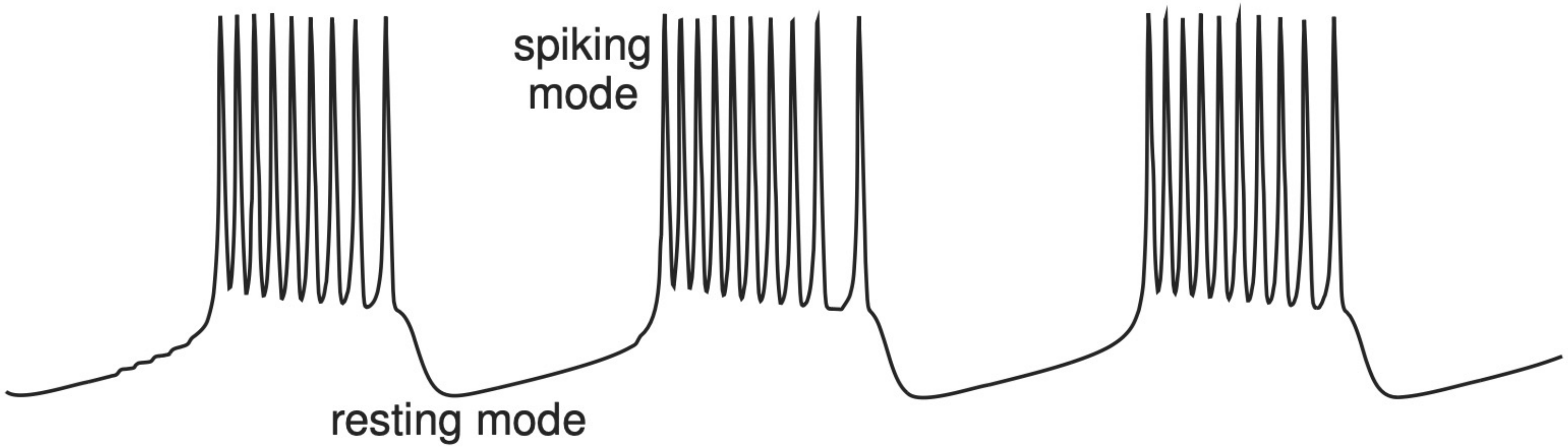
Neuron in an excitable mode

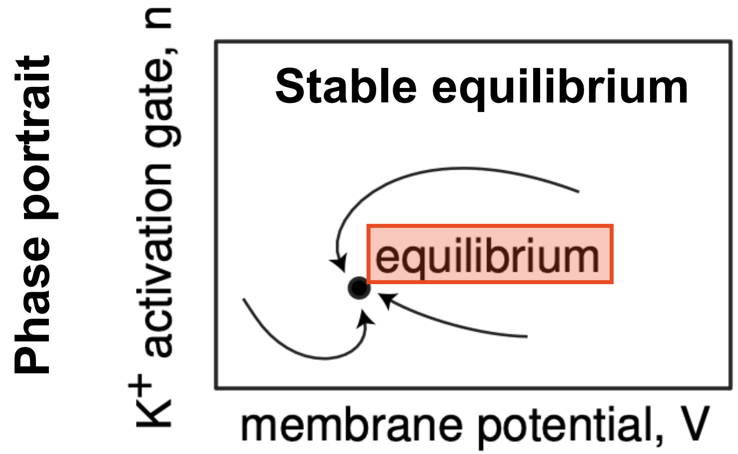
Pacemaker neuron

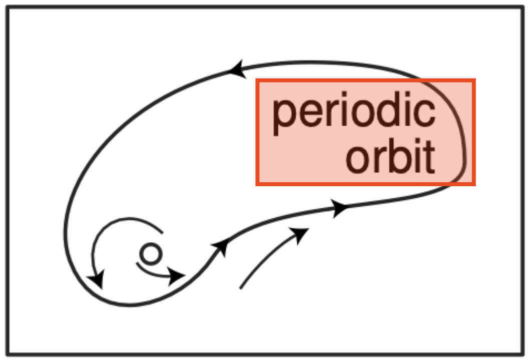


Phase portraits

Equilibria and **limit cycles** can coexist, so a neuron can be switched from one mode to another by a transient input







Bifurcations

Qualitative changes

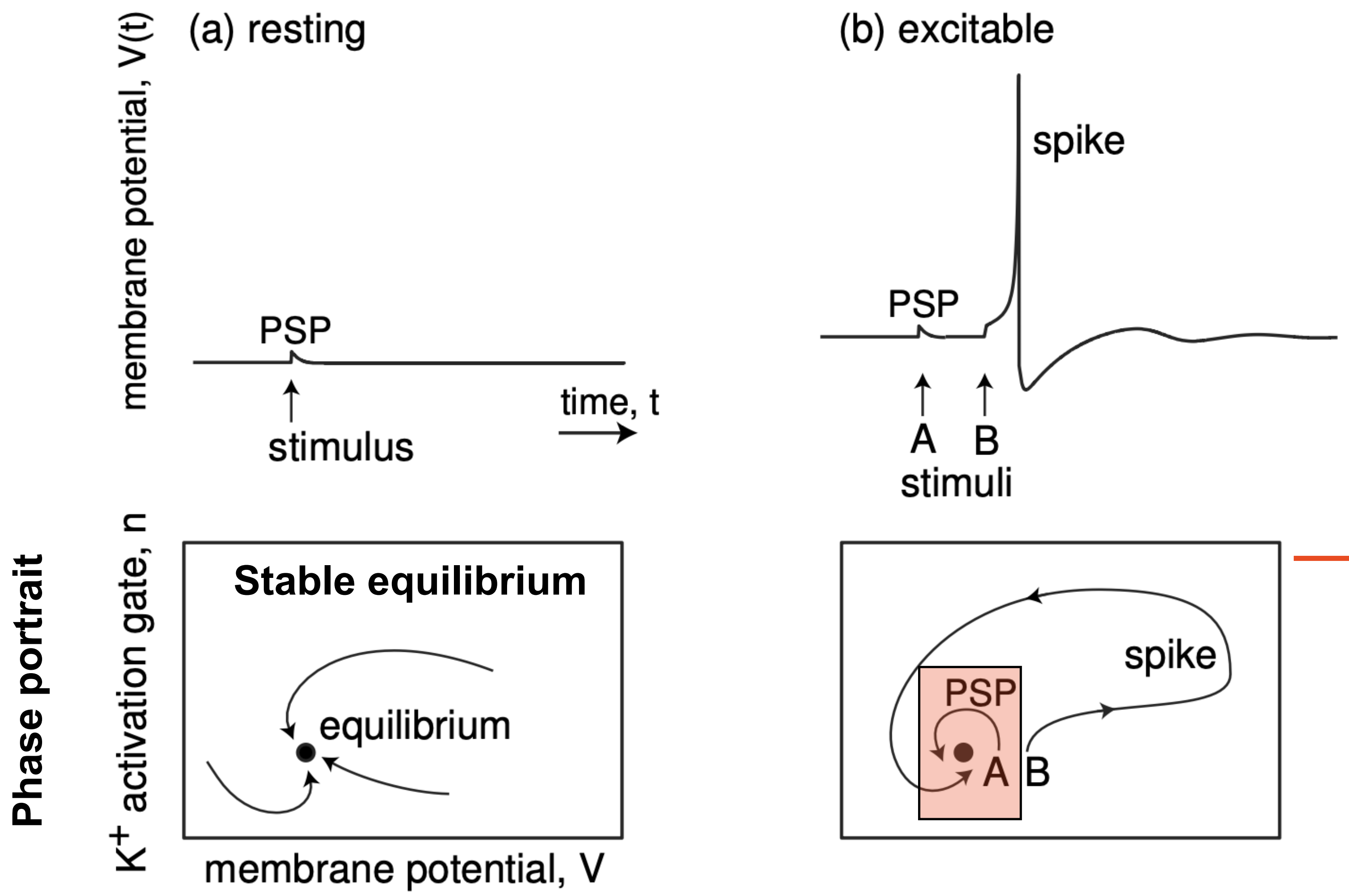
What is a bifurcation?

Bifurcations

Quiescent neuron whose membrane potential is resting

Neuron in an excitable mode

Qualitative changes



If the dynamical system goes from **(a)** to **(b)**, is it going through a bifurcation?

No bifurcation!

This dynamical system contains (a)

The differences between **(A)** and **(B)** are the initial conditions.

There is not a **qualitative change**

Bifurcations

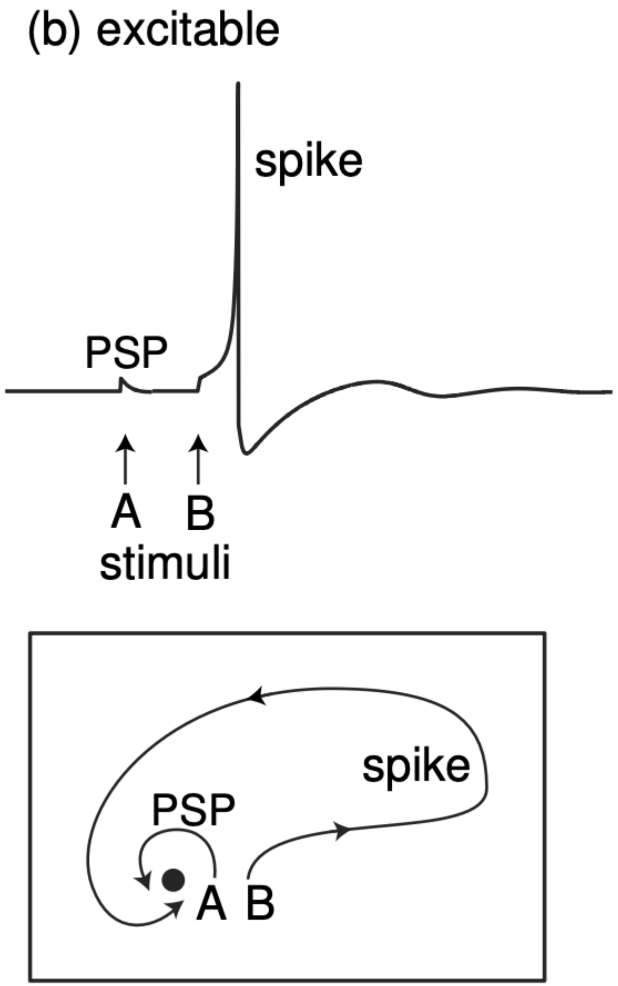
If the dynamical system goes from **(b)** to **(c)**, is it going through a bifurcation?

Let´s see…
(b) : stable fix point
(c) : unstable fix point and a limit cycle.

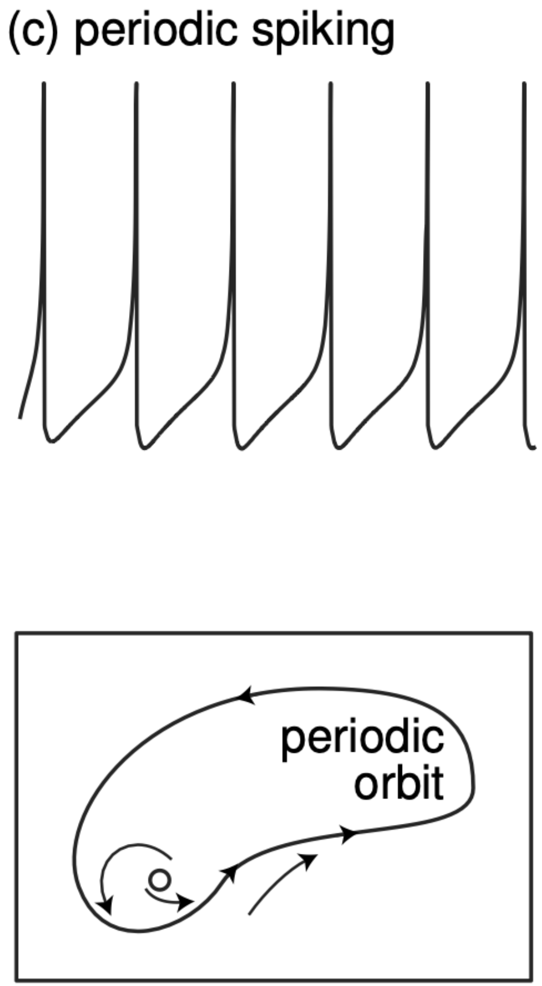
There is a **qualitative change**

Bifurcation!

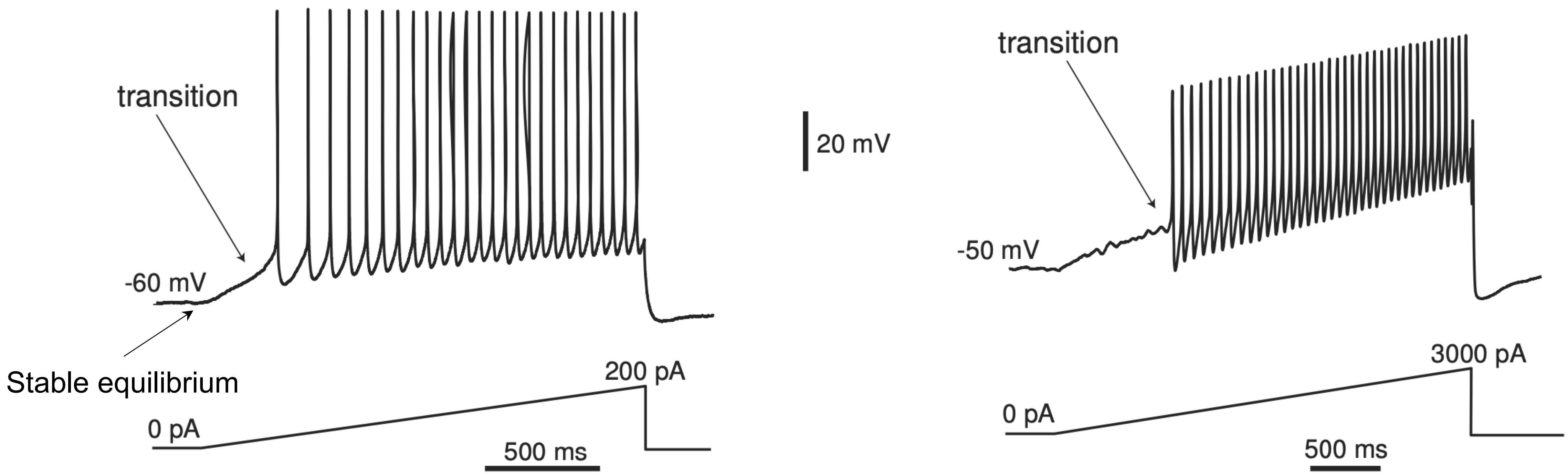
Neuron in an excitable mode



Pacemaker neuron



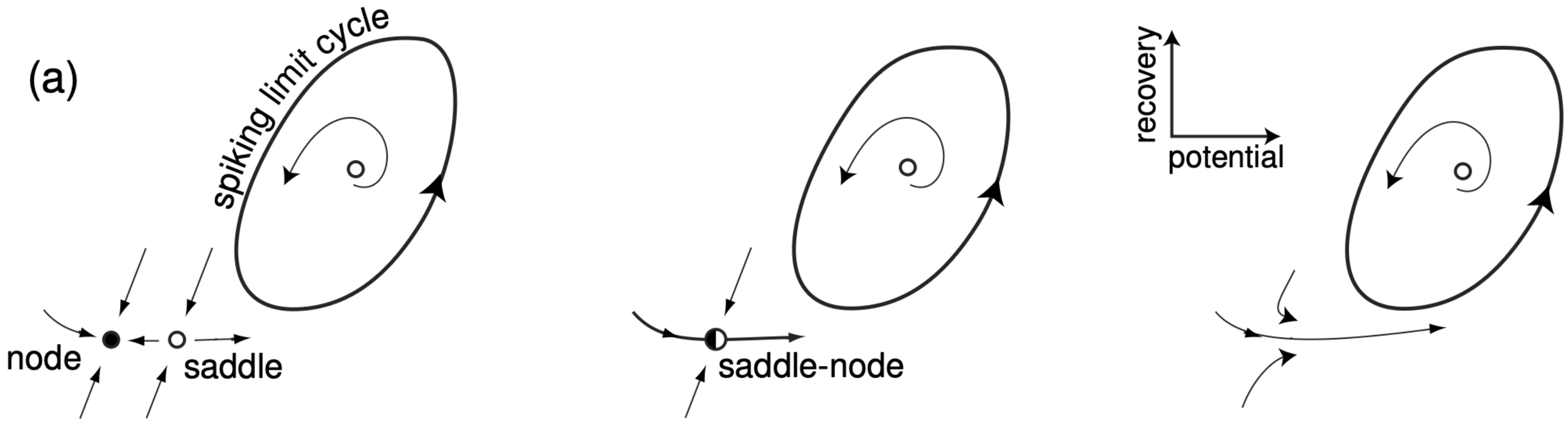
Bifurcations



As the magnitude of the injected current slowly increases, the neurons bifurcate from resting (equilibrium) mode to tonic spiking (limit cycle) mode.

Bifurcations

Equilibrium state leading to the transition from **resting** to **periodic spiking** behavior in neurons.
(codimension-1, i.e., 1 control parameter)



Saddle-node bifurcation

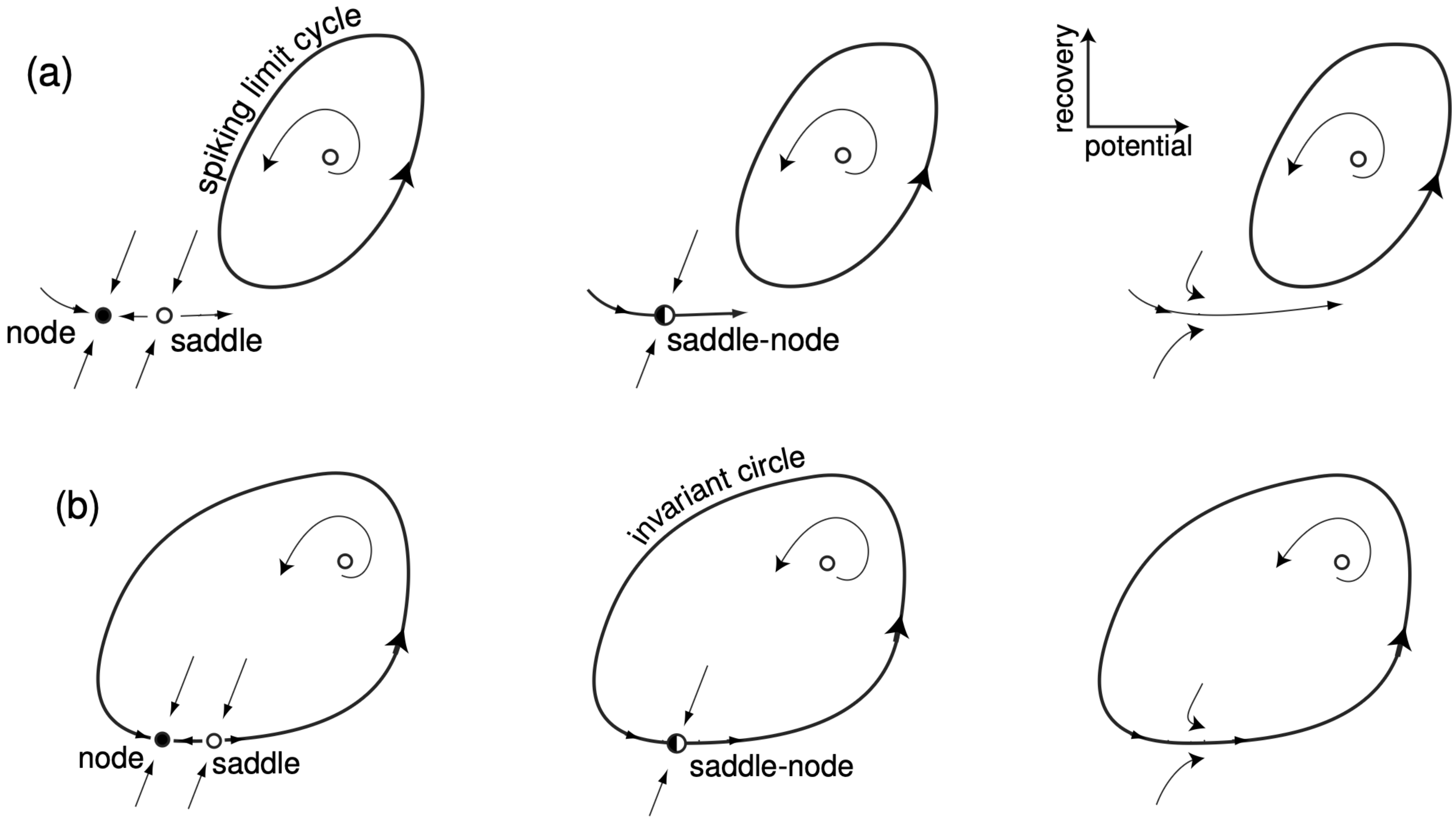
Depending on the initial conditions, the neuron may spike (or decay to the stable resting position) or burst

Bifurcation point

The saddle and node colapse and annihilate each other.
Only the limit cycle survives

Bifurcations

Equilibrium state leading to the transition from **resting** to **periodic spiking** behavior in neurons.
(codimension-1, i.e., 1 control parameter)

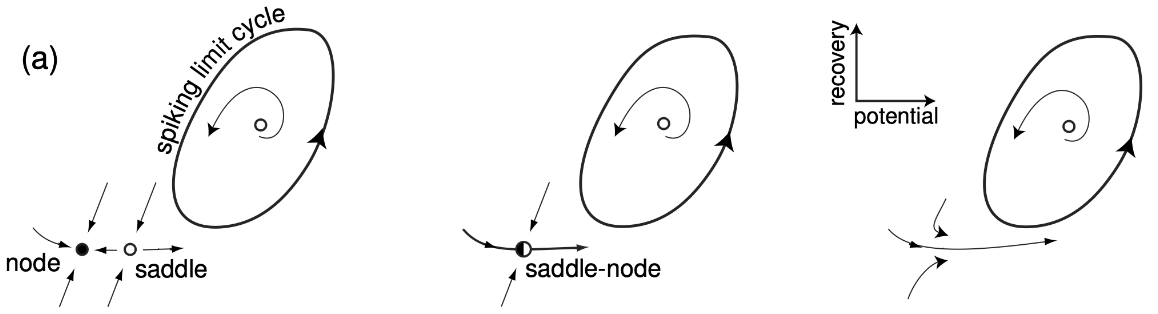


Saddle-node bifurcation

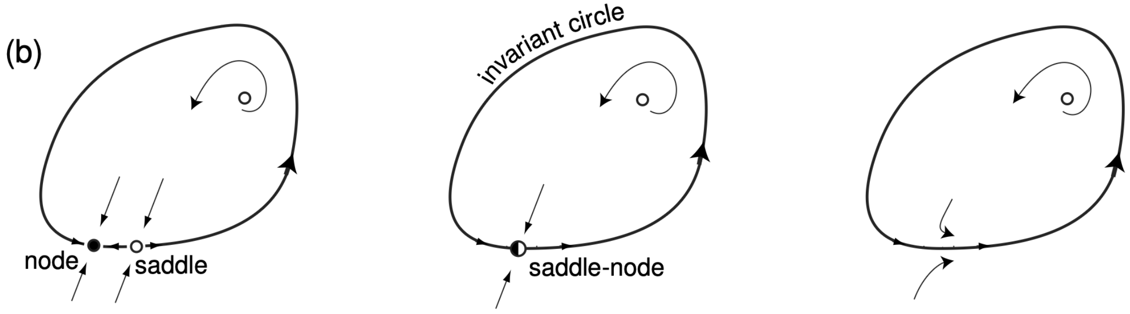
Saddle-node on invariant circle bifurcation

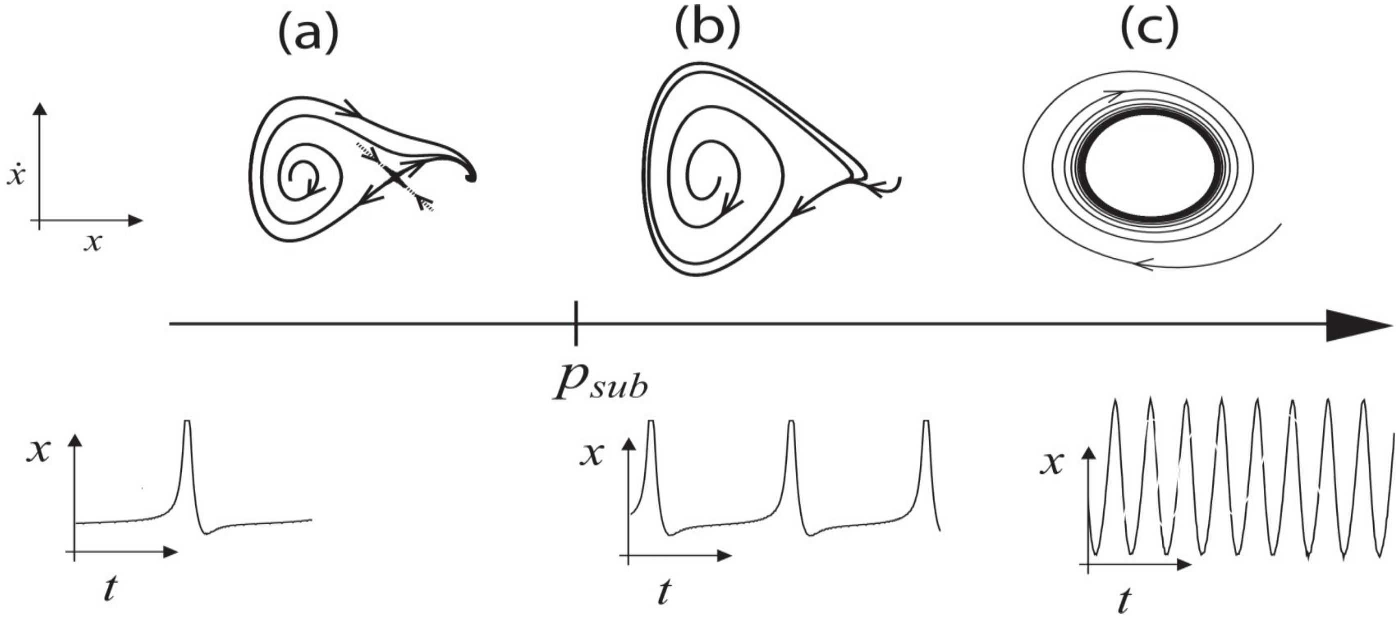
Bifurcations

Saddle-node bifurcation



Saddle-node on invariant circle bifurcation





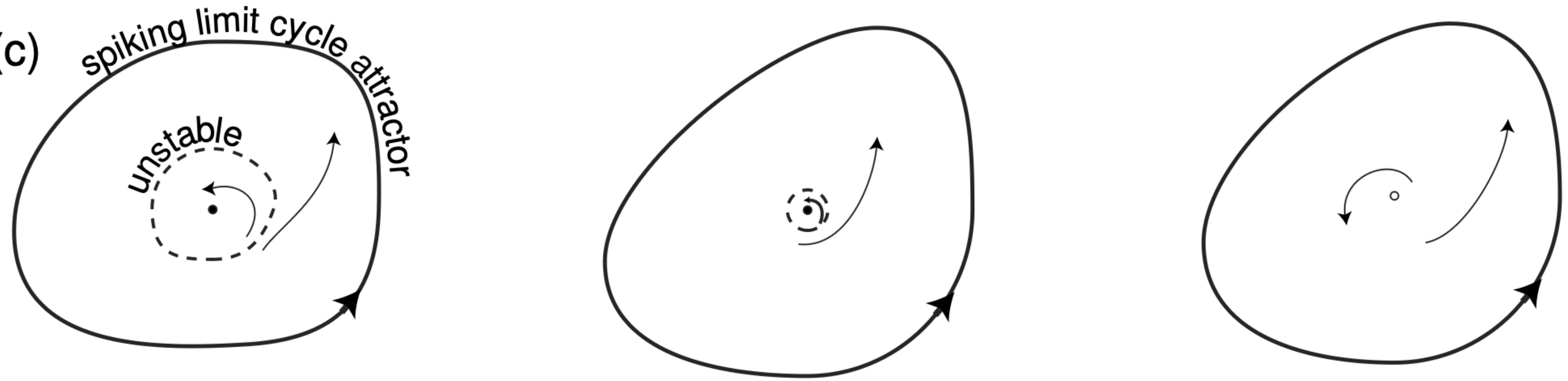
Saddle-node ghost

Saddle-node on invariant circle bifurcation

Bifurcations

Equilibrium state leading to the transition from **resting** to **periodic spiking** behavior in neurons.
(codimension-1, i.e., 1 control parameter)

(c)

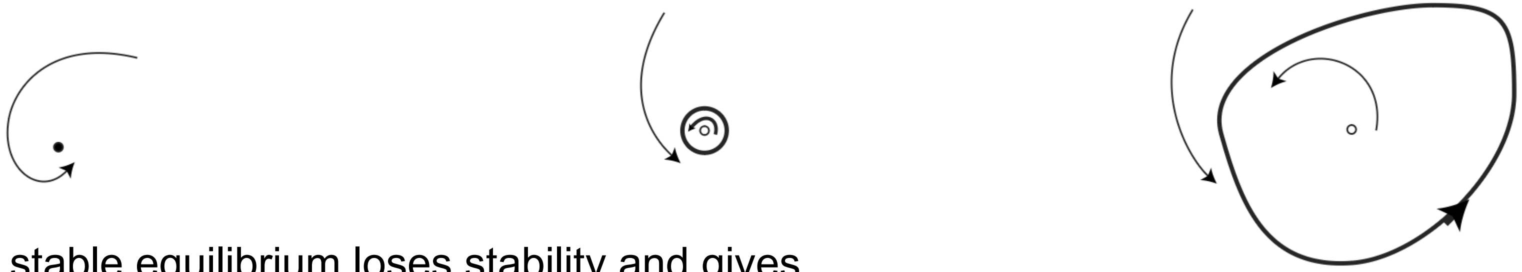


A small unstable limit cycle shrinks to a stable equilibrium and makes it lose stability

The only stable state is the limit cycle

Subcritical Andronov-Hopf bifurcation

(d)



The stable equilibrium loses stability and gives birth to a small-amplitude limit cycle attractor

As the magnitude of the injected current increases, the amplitude of the limit cycle increases, and it becomes a full-size spiking limit cycle

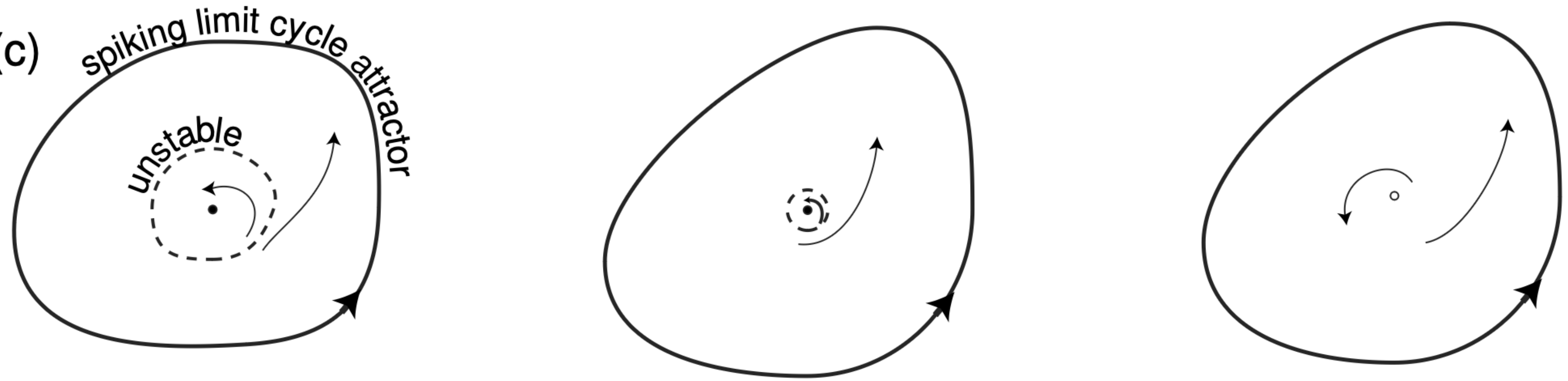
Supercritical Andronov-Hopf bifurcation

Bifurcations

Equilibrium state leading to the transition from **resting** to **periodic spiking** behavior in neurons.
(codimension-1, i.e., 1 control parameter)

Bi-stable

(c)



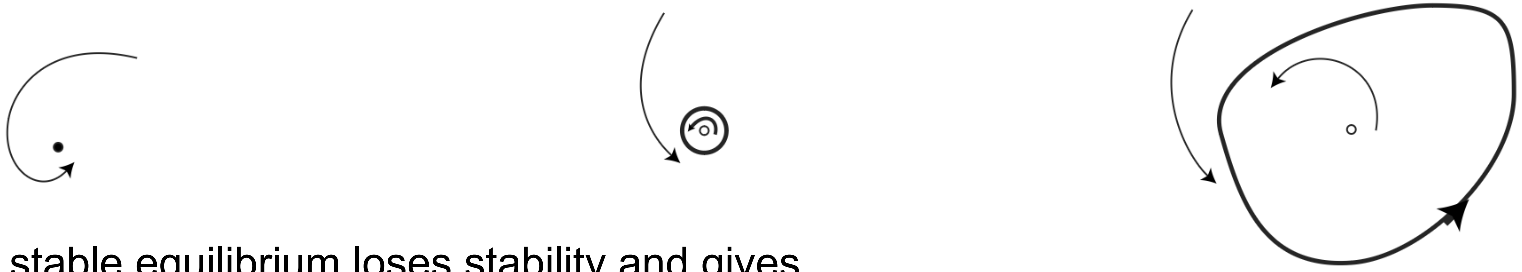
A small unstable limit cycle shrinks to a stable equilibrium and makes it lose stability

Subcritical Andronov-Hopf bifurcation

The only stable state is the limit cycle

(d)

Mono-stable



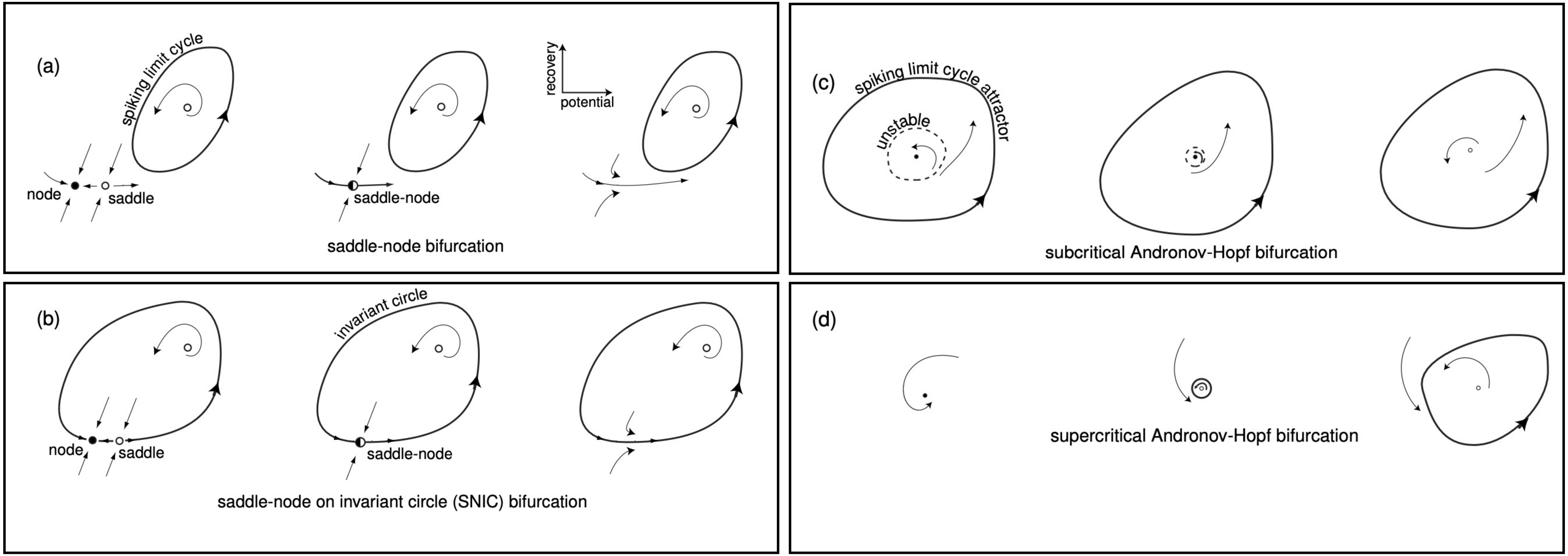
The stable equilibrium loses stability and gives birth to a small-amplitude limit cycle attractor

Supercritical Andronov-Hopf bifurcation

Bifurcations

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

Bifurcations



Building models

First of all: you need neural recordings!
(from your own experiments or from a collaborator)

To make a model of a neuron: put the right kind of currents together and tune the parameters so that the model can fire spikes like the ones recorded.

Another way is to determine what kind of bifurcations the neuron undergoes and how the bifurcations depend on neuromodulators and pharmacological blockers.

These approaches can be complementary.

Interdisciplinary work

Respect the different “ideologies”

The Hodgkin – Huxley model

Using **pioneering experimental techniques** of that time, Hodgkin and Huxley (1952) determined that the squid axon carries three major currents:

- Voltage-gated persistent K^+ current with four activation gates (resulting in the term n^4 in the equation below, where n is the activation variable for K^+);
- Voltage-gated transient Na^+ current with three activation gates and one inactivation gate (the term m^3h below)
- Ohmic leak current, I_L, which is carried mostly by Cl^- ions.

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
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\alpha_n(V) &= 0.01 \frac{10 - V}{\exp(\frac{10-V}{10}) - 1} \, , \\
\beta_n(V) &= 0.125 \exp\left(\frac{-V}{80}\right) \, , \\
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\end{aligned}
$$

The Hodgkin – Huxley model

Using **pioneering experimental techniques** of that time, Hodgkin and Huxley (1952) determined not only the equations but **measured all the parameters values** :

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
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\alpha_h(V) &= 0.07 \exp\left(\frac{-V}{20}\right) \,, \\
\beta_h(V) &= \frac{1}{\exp(\frac{30-V}{10}) + 1} \,.
\end{aligned}
$$

Values of shifted Nernst equilibrium potentials (so that $V_{rest} = 0$) :

$$E_{\mathrm{K}} = -12 \text{ mV} \,, \qquad E_{\mathrm{Na}} = 120 \text{ mV} \,, \qquad E_{\mathrm{L}} = 10.6 \text{ mV};$$

Values of maximal conductances:

$$\bar{g}_{\mathrm{K}} = 36 \text{ mS/cm}^2 \,, \qquad \bar{g}_{\mathrm{Na}} = 120 \text{ mS/cm}^2 \,, \qquad g_{\mathrm{L}} = 0.3 \text{ mS/cm}^2.$$

Value of membrane capacitance:

$$C = 1\,\mu\text{F/cm}^2$$

The Hodgkin – Huxley model

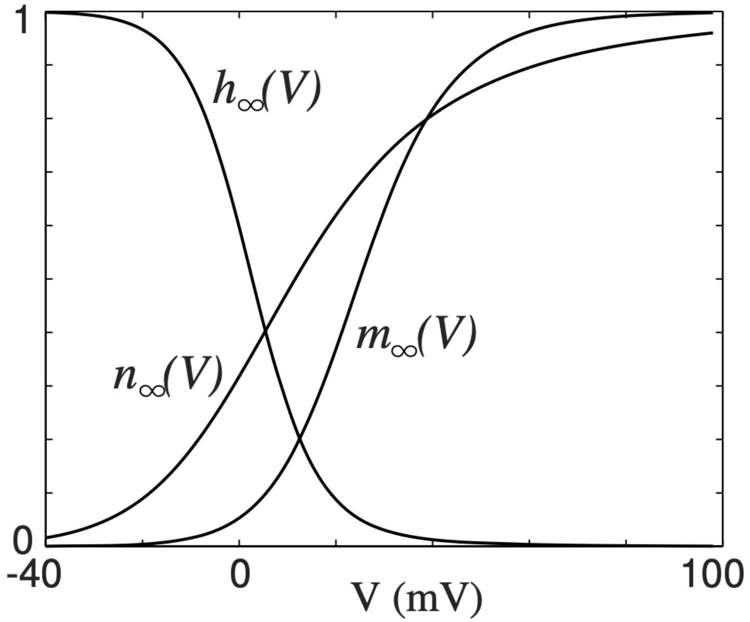
The functions α(V) and β(V) describe the transition rates between open and closed states of the channels

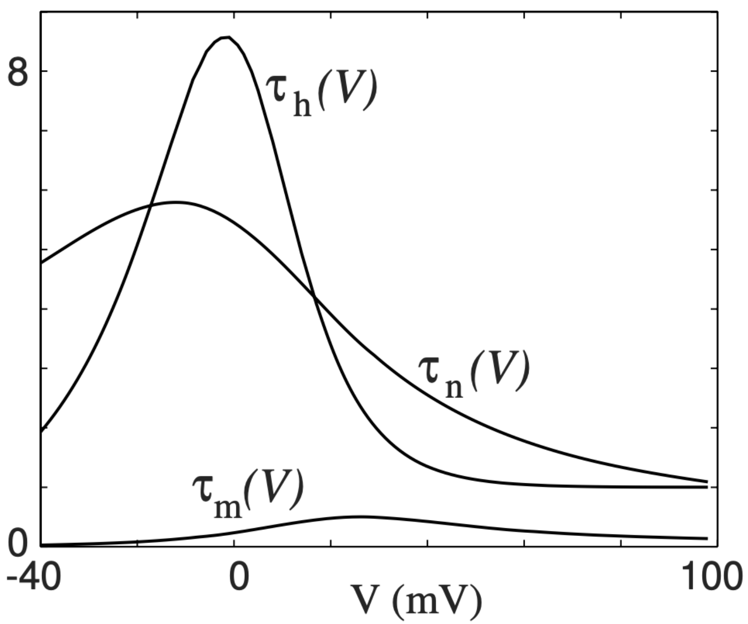
The notation presented before was used only for historical reasons.
It is more convenient to use:

$$\begin{aligned} \dot{n} &= (n_\infty(V) - n)/\tau_n(V) \ , \\ \dot{m} &= (m_\infty(V) - m)/\tau_m(V) \ , \\ \dot{h} &= (h_\infty(V) - h)/\tau_h(V) \ , \end{aligned}$$

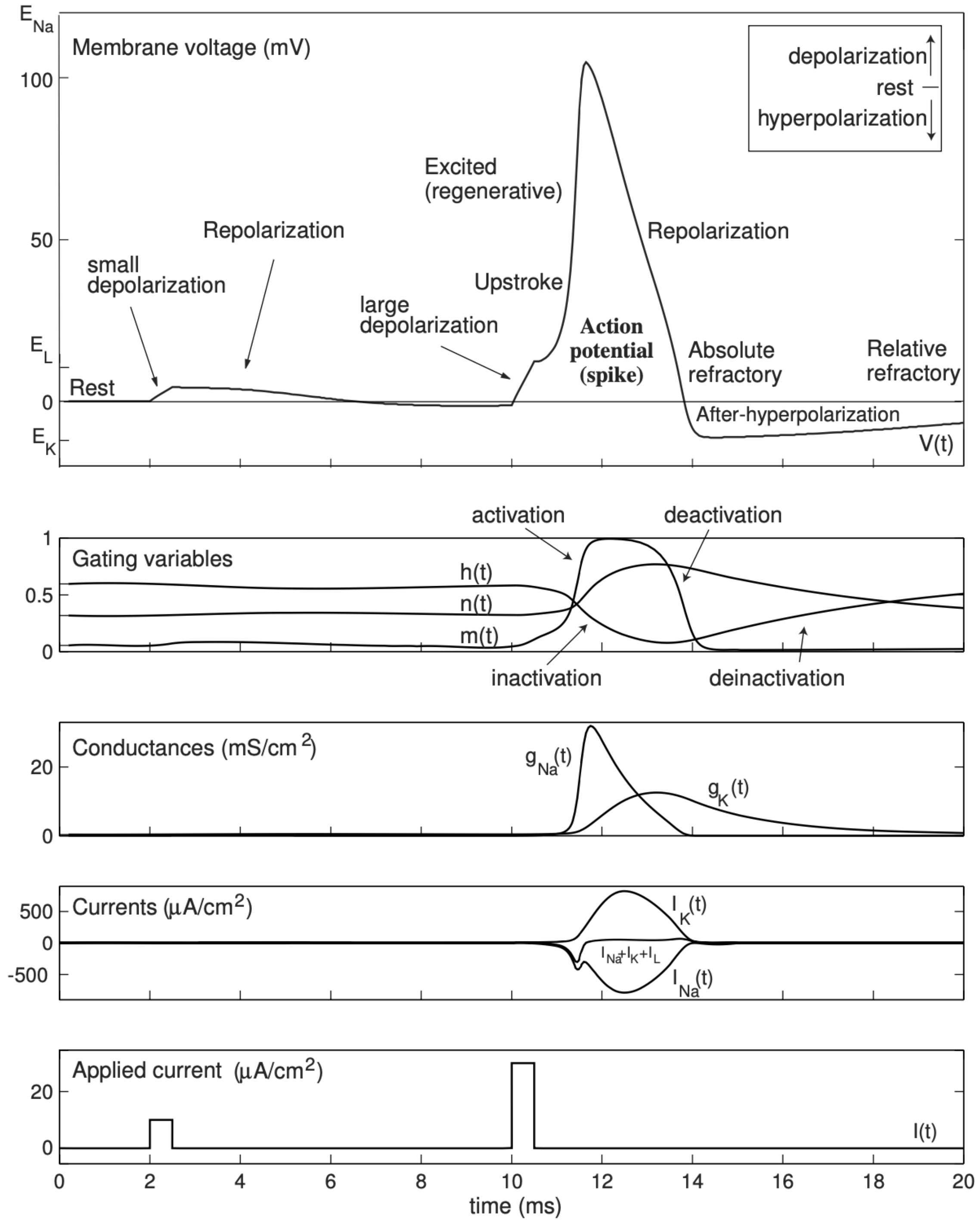
where

$$n_\infty = \alpha_n/(\alpha_n + \beta_n) \ , \qquad \tau_n = 1/(\alpha_n + \beta_n) \ ,$$
$$m_\infty = \alpha_m/(\alpha_m + \beta_m) \ , \qquad \tau_m = 1/(\alpha_m + \beta_m) \ ,$$
$$h_\infty = \alpha_h/(\alpha_h + \beta_h) \ , \qquad \tau_h = 1/(\alpha_h + \beta_h)$$





The Hodgkin – Huxley model



To be continued…