Mathematical Foundations of Neuroscience - Lecture 4. One dimensional systems.

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Winter 2009/2010

1d systems

To understand more complex multi-dimensional systems of ordinary differential equations it is valuable to first study one dimensional systems. Even though a single variable restricts the dynamic behavior of the system significantly, one dimensional systems exhibit a couple of interesting regimes like

- bistability (multistability)
- hysteresis
- slow transitions

They are also valuable as a simplest case to study bifurcations.

Simplifying neural model

How can one dimensional be relevant from neuroscientific point of view?

- One can strip Hodgkin-Huxley like neural models from conductances and assume only one ionic species is relevant
- One can assume that the activation kinetics of certain ions is instantaneous, that is the gating variable achieves its asymptotic value instantly
- Since activations and inactivations have different timescales, one dimensional systems are valuable to study fast currents in short timescales, where it can be assumed that all other parameters are constant

Let us depart from the Hodgkin-Huxley model:

$$C_m \frac{dV}{dt} = -g_L(V - E_L) - g_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) - g_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})$$
$$\frac{dm}{dt} = (m_\infty(V) - m)/\tau_m(V)$$
$$\frac{dn}{dt} = (n_\infty(V) - n)/\tau_n(V)$$
$$\frac{dh}{dt} = (h_\infty(V) - h)/\tau_h(V)$$

Lets assume that all parameters are normalized (e.g. $C_m = 1$ etc.). Furthermore lets assume there is only one ionic channel with only one gating variable.

We then arrive with:

$$\frac{dV}{dt} = -g_L(V - E_L) - gp(V - E)$$
$$\frac{dp}{dt} = (p_\infty(V) - m)/\tau(V)$$

We can assume that the gating variable is much faster than voltage. In this case $\tau(V)$ is very small in the entire relevant voltage range. In such case we can skip the second equation, and write $p = p_\infty(V)$. We end up with one dimensional system:

$$\frac{dV}{dt} = -g_L(V - E_L) - gp_\infty(V)(V - E)$$

By changing parameters E and the character of p (either activation or inactivation) we can obtain four models

	Inward current	outward current
activation gating	$I_{Na,p}$ (persistent sodium model)	I_K
inactivation gating	I_h	I_{Kir} (inverse rectifying)

We will use persistent sodium with leak as an example.

General 1d systems

The general 1d system can be expressed

$$\frac{dy(t)}{dt} = F(y(t), t)$$

- If the right hand side of the equation does not depend on time, the system is called autonomous. In other case the system is called nonautonomous (such systems are generally harder to deal with).
- Each solution to the equation $y(t)$ departing from some initial condition y_0 (that is $y(t_0) = y_0$) is called a trajectory.
- The mapping $\phi(y_0, t)$ which takes some initial condition and a time value and returns the value of solution departing from y_0 at time t is called a flow.

Linear systems

In the general case the solutions of 1d systems might not exist for every value of t (trajectories might diverge). It is also difficult to find solutions analytically. There are clever methods of solving differential equations, but they only work for certain special cases.

Nevertheless there are a couple of important special cases which can be solved analytically. These are linear equations of the form

$$\frac{dy(t)}{dt} = Ay(t) + B$$

It is easy to verify (via differentiation) that the solutions are:

$$y(t) = -\frac{B}{A} + \left(\frac{B}{A} + y_0\right) \cdot e^{A(t-t_0)}$$

When $t = t_0$ we have

$$y(t_0) = -\frac{B}{A} + \left(\frac{B}{A} + y_0\right) \cdot e^0 = -\frac{B}{A} + \frac{B}{A} + y_0 = y_0$$

for $t > t_0$

$$\frac{dy(t)}{dt} = \frac{d}{dt}\left(-\frac{B}{A} + \left(\frac{B}{A} + y_0\right) \cdot e^{A(t-t_0)}\right) =$$
$$= \left(\frac{B}{A} + y_0\right) A e^{A(t-t_0)} = A\left(-\frac{B}{A} + \left(\frac{B}{A} + y_0\right) e^{A(t-t_0)} + \frac{B}{A}\right) =$$
$$= A\left(-\frac{B}{A} + \left(\frac{B}{A} + y_0\right) e^{A(t-t_0)}\right) + B = Ay(t) + B$$

QED.

In particular equation

$$\frac{dy(t)}{dt} = -Ay(t)$$

has a simple analytic solution

$$y(t) = y_0 e^{-A(t-t_0)}$$

which can be simulated efficiently

$$y(t+1) = \alpha \cdot y(t)$$

where $\alpha = e^{-A\tau}$ is precomputed (τ is the time step)

Another important special case is the so called homogeneous linear equation of the form

$$\frac{d^n y(t)}{dt^n} + A_1 \frac{d^{n-1} y(t)}{dt^{n-1}} + \ldots + A_{n-1} \frac{dy(t)}{dt} + A_n y(t) = 0$$

Euler noticed that substituting $y(t) = e^{zt}$ leads to a following expression:

$$z^n e^{zt} + A_1 z^{n-1} e^{zt} + \ldots + A_{n-1} z^1 e^{zt} + A_n e^{zt} = 0$$

Dividing by e^{zt} yields

$$z^n + A_1 z^{n-1} + \ldots + A_{n-1} z + A_n = 0$$

the so called characteristic polynomial. Now assume z_i is a root of the characteristic polynomial.

- In such case $e^{z_i x}$ is a solution of the differential equation. Since the equation (and the differential operator) are linear, then functions $e^{z_i x}$ for all roots z_i of characteristic equation form a linear basis and any solution is a linear combination.
- In the general case if the root z_i has multiplicity m then for any $k \in \{1, 2, ..., m-1\}$ $x^k e^{z_i x}$ is a solution (this is much harder to see!!!), and any linear combination of such solutions is also a solution.
- If the coefficients of the equation are real, then roots of the characteristic equation are complex conjugates. In such case one can obtain the real basis of solutions by taking $u_i = \frac{e^{z_i x} + e^{\overline{z_i} x}}{2} =$ and $v_i = \frac{e^{z_i x} - e^{\overline{z_i} x}}{2i}$

Phase line analysis

- The basic factor determining the behavior of trajectories is the right hand side function $F(y(t))$. Lets assume for a moment that it does not depend on time.
- Since $y(t) \in \mathbb{R}$ the domain of F is $\mathbb{R}$. We will call the real line a this context a *phase line* (which should not be confused with the *time line* that is the domain of t).
- The phase line contains all the possible states of the system (which in this case are real numbers), but in general a *phase space* can be multidimensional. On the contrary the domain of t is always $\mathbb{R}$, at least for ODE.
- Plotting $F(y)$ for $y \in \mathbb{R}$ gives a whole lot of information, which we will learn to read.

Equilibria

- First of all, note that if for some y_c $F(y_c) = 0$, we have

$$\frac{dy}{dt} = F(y_c) = 0$$

  and consequently a trajectory that originates in y_c remains constant forever (since its derivative is zero)!
- We call such a y_c an equilibrium. As we will soon see, there are different types of equilibria.
- If F is positive (negative) for some point, the trajectory at that point will be increasing (decreasing respectively)
- We will assume that F is a continuous and differentiable function. How can F look like near y_c ?

Equilibria

- There are five qualitatively different cases in which $F(y_c) = 0$
  1. $F'(y_c) > 0$
  2. $F'(y_c) < 0$
  3. $F'(y_c) = 0$ and $F''(y_c) = 0$
  4. $F'(y_c) = 0$ and $F''(y_c) > 0$
  5. $F'(y_c) = 0$ and $F''(y_c) < 0$
- The first two we will call hyperbolic while the latter three non-hyperbolic. The last two we will also call degenerate.
- There is also possibility that the second derivative is not defined at all. We will skip these pathological cases for now.

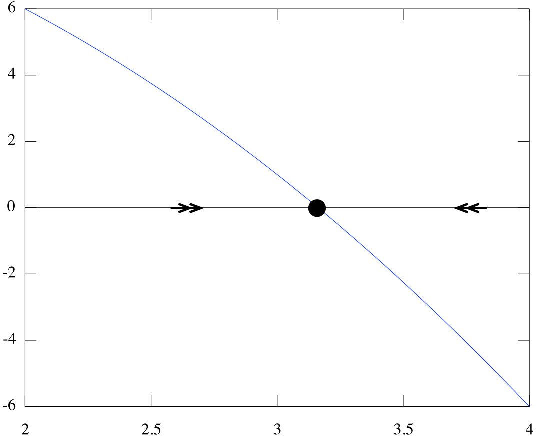


Figure: $F' < 0$ - stable attracting hyperbolic equilibrium

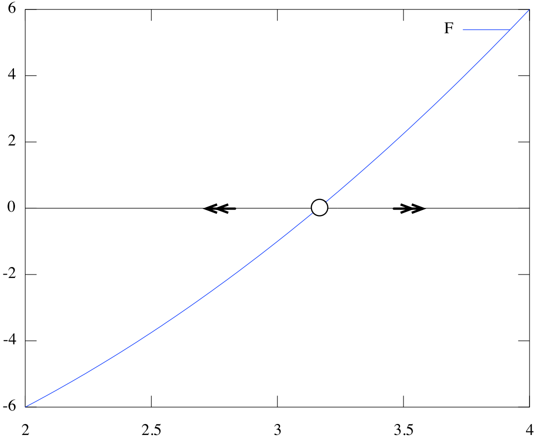


Figure: $F' > 0$ - unstable repelling hyperbolic equilibrium

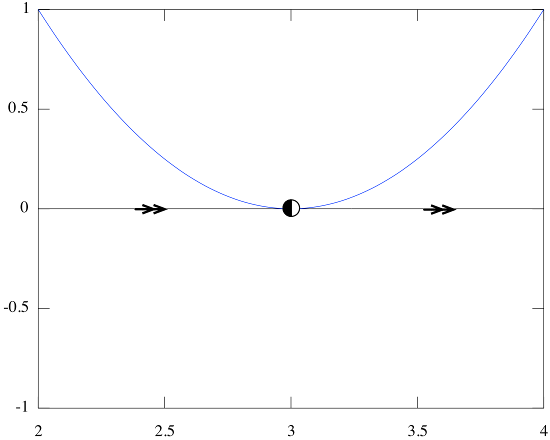


Figure: $F' = 0$, $F'' = 0$ - semi stable non-hyperbolic equilibrium

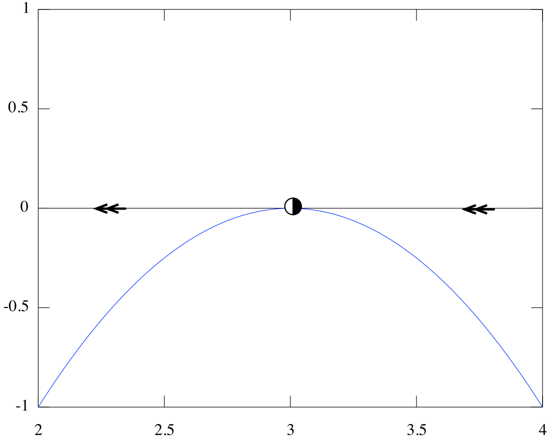


Figure: $F' = 0,\ F'' = 0$ - semi stable non-hyperbolic equilibrium

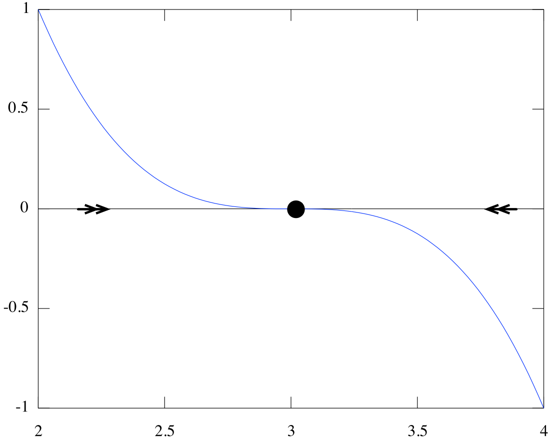


Figure: $F' = 0$, $F'' < 0$ - stable degenerate non-hyperbolic equilibrium

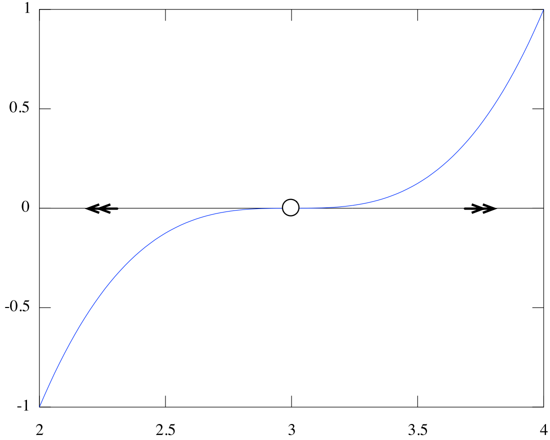


Figure: $F' = 0$, $F'' > 0$ - unstable degenerate non-hyperbolic equilibrium

- Simple 1d systems can exhibit interesting phenomena
- A system can have a multiple stable equilibria (multi - stability). In particular two stable equilibria lead to bistability
- When a system is (multi) bistable, it can be pushed by some input stimulus and rest at one of the equilibria. Then it could be pushed again into different stable equilibrium. In a sense, the system exhibits memory. This phenomenon is called hysteresis.

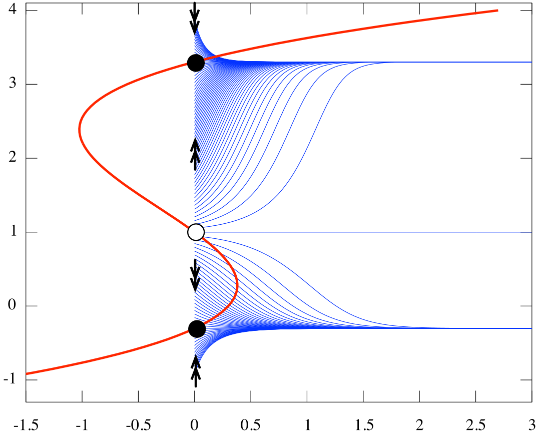


Figure: Bistability. Function F denoted in red is plotted such that abscissa is vertical. In blue are plotted sample trajectories with time on the horizontal axis.

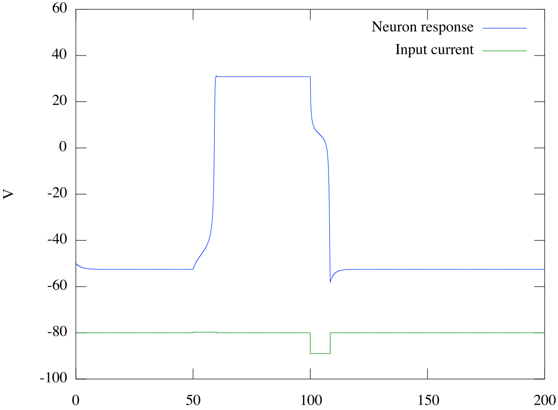


Figure: Hysteresis in $I_{Na,p}$ (persistent sodium model). Small input current causes the model to jump into excited state (higher stable equilibrium). Since the model lacks inactivation or potassium, the activation is persistent. Larger negative current can force the system back into the rest equilibrium.

Phase portraits

- Phase portraits are a convenient way to qualitatively describe properties of the dynamical system
- One begins the construction of a phase portrait with the plot of right hand side function F
- Then one finds its roots, that is the equilibrium points. By looking at the plot one can easily verify the type of equilibrium point
- Lastly one can determine attraction domains and convergence rates

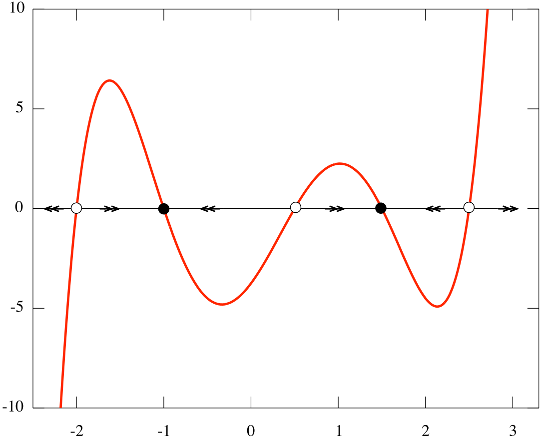


Figure: Phase portrait

Topological equivalence

- Two dynamical systems with essentially identical phase portraits behave in similar ways. The rate of convergence of certain trajectories may differer, nevertheless there is the same structure of equilibria and attraction domains.
- The keyword here is *essentially identical*. What does this mean?
- We will assume two phase portrait essentially identical when there exist continuous, invertible mapping from one to the other phase line that preserves all equilibria and attraction domains
- Two systems with topologically equivalent phase portraits we will call equivalent

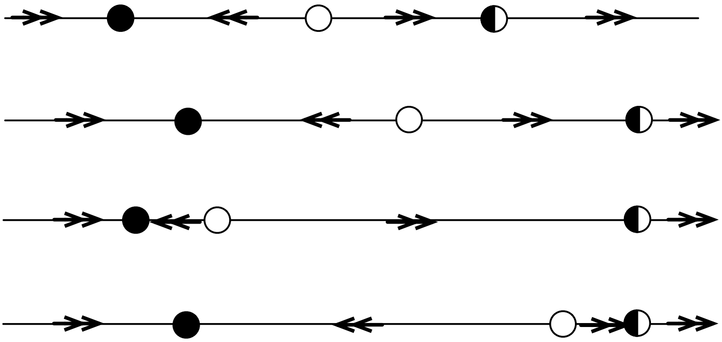


Figure: Equivalent phase portraits. Note the number, order and type of equilibria remains intact. The respective attraction domains may get stretched but they never vanish completely.

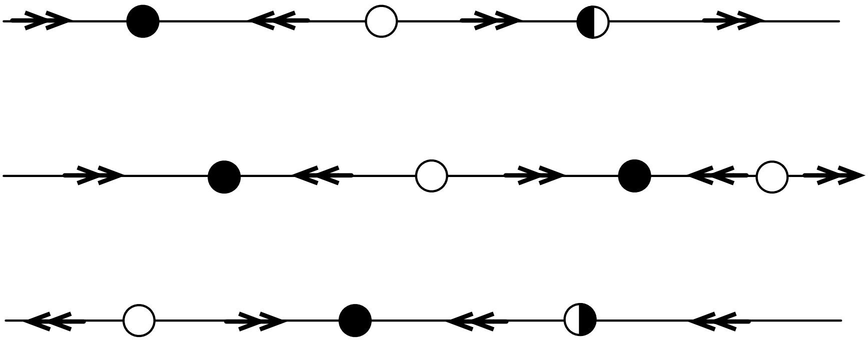


Figure: Non-equivalent phase portraits. Either the number or type of equilibria doesn't match. Some attraction domains may vanish.

Local equivalence

- The total equivalence of the whole phase portrait is a rather strong notion
- Many real world systems are not totally equivalent, but locally their phase portraits look alike. In particular biological systems like neurons can be equivalent in biologically plausible voltage range, but may differ at extreme voltages
- In such case it is useful to introduce local equivalence in which case the continuous mapping mentioned a few slides earlier is restricted to only some subsets of the phase line
- It is particularly useful to associate a dynamical system in the vicinity of hyperbolic equilibrium with its linear approximation. Under certain assumptions such association can be complete, that is linear systems completely determines the systems behavior sufficiently close to the equilibrium

Hartman-Grobman Theorem

- Hartman-Grobman Theorem states that near a hyperbolic equilibrium the system is equivalent to its linearization
- The equivalence here is somewhat stronger: not only trajectories follow the same directions, but sufficiently near the equilibrium trajectories of original and linear systems are indistinguishable.
- Formally the theorem states that there is a homeomorphism working from some open subset E to some open subset L (both containing the equilibrium) which for some time segment $[0, T]$ continuously transforms each trajectory $f(x_e, t), x_e \in E, t \in [0, T]$ into $f_l(x_l, t), x_l \in L, t \in [0, T]$.
- Therefore unless the equilibrium is non-hyperbolic, it is sufficient to study linear system. We will get back to Hartman-Grobman Theorem with two dimensional systems.

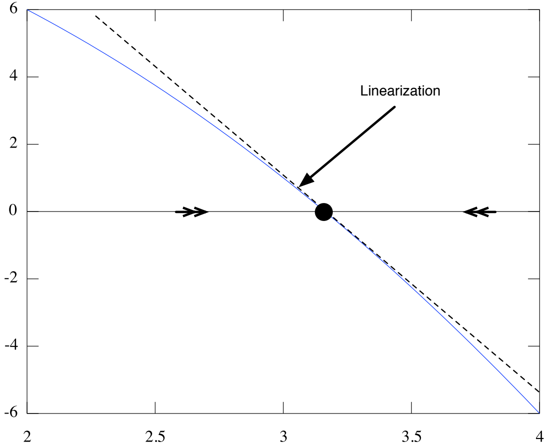


Figure: Linear approximation of the system at the equilibrium.

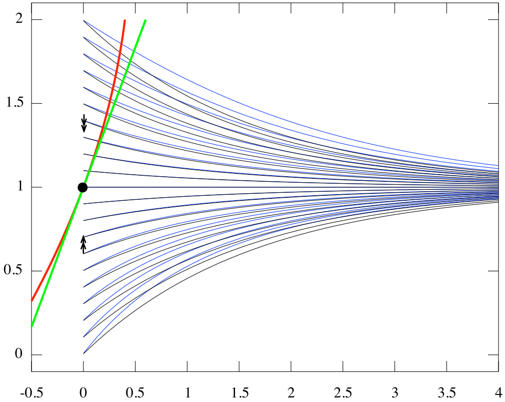


Figure: Linear approximation of the system at the equilibrium. The trajectories corresponding to the linear system are marked in black, whereas those of the original system are blue. Sufficiently close to the equilibrium both black and blue trajectories look the same.

Bifurcations

- Now lets assume, that the right hand side function $F(y(t), I)$ depends on some parameter, say I
- By changing the parameter, the shape of the function can change, and consequently the phase portrait might undergo a qualitative change
- Such an event, which transforms one phase portrait into topologically non-equivalent other is called a bifurcation.
- Bifurcations are in the focus of our interest, since as we will se, they are responsible for various dynamical behaviors
- A prominent example of a bifurcation in 1d systems is the *saddle node bifurcation* in which stable and unstable equilibrium annihilate in a continuous manner

Saddle node bifurcation

How to check is the system $\frac{dy}{dt} = F(y, I)$ is at a bifurcation with values y_{sn}, I_{sn}? It has to satisfy three conditions:

- Non hyberbolicity (at y_{sn}):

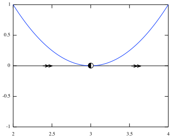
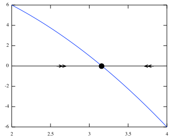
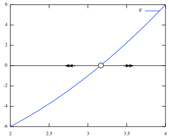
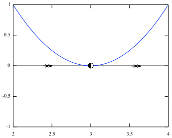
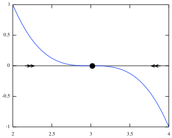
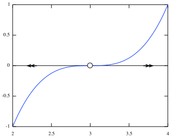
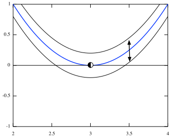
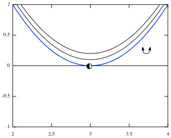
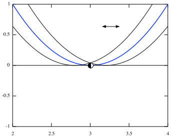
$$\frac{\partial F(y, I_{sn})}{\partial y} = 0$$

- Non degeneracy (at y_{sn}):

$$\frac{\partial^2 F(y, I_{sn})}{\partial y^2} \neq 0$$

- Traversality (at I_{sn}):

$$\frac{\partial F(y_{sn}, I)}{\partial I} \neq 0$$

Saddle node		
 non-hyperbolic	 hyperbolic	 hyperbolic
 non-degenerate	 degenerate	 degenerate
 traversal	 not traversal	 not traversal

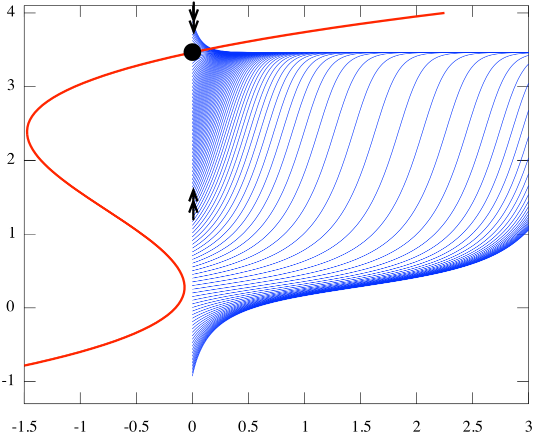


Figure: Saddle node bifurcation

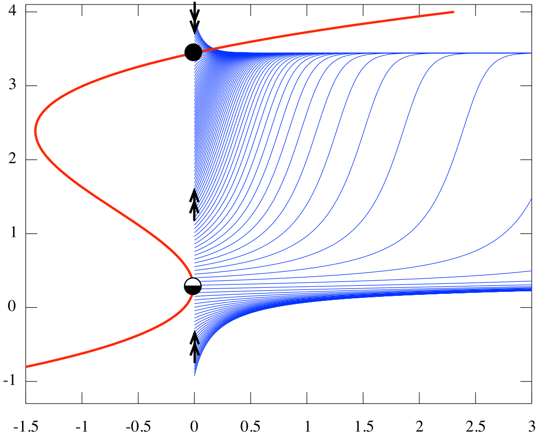
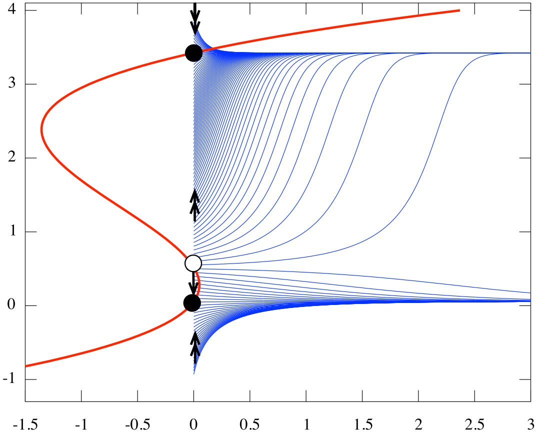


Figure: Saddle node bifurcation



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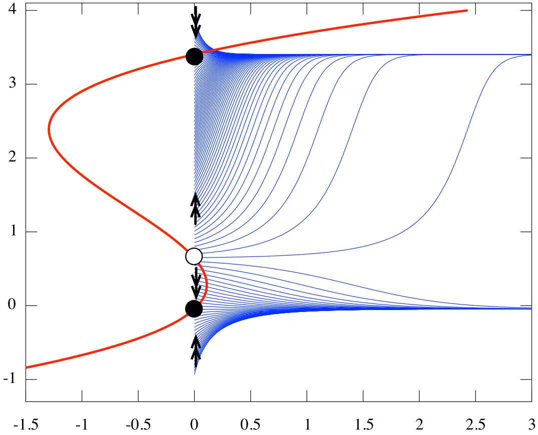


Figure: Saddle node bifurcation

Slow transition

- The behavior of trajectories may signal that the system is near a bifurcation
- One of such symptoms is the slow transition
- When the system is near the saddle node bifurcation, trajectories passing the so called attractor ruins are being slowed down
- Even though the attracting equilibrium does not exist, its ghost manages to keep the trajectories near for a while, before they follow to another attractor

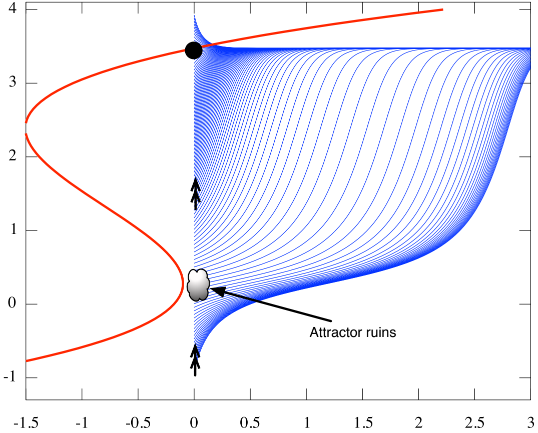


Figure: Slow transition. The attractor ruins, though formally not an equilibrium point significantly slows down trajectories.

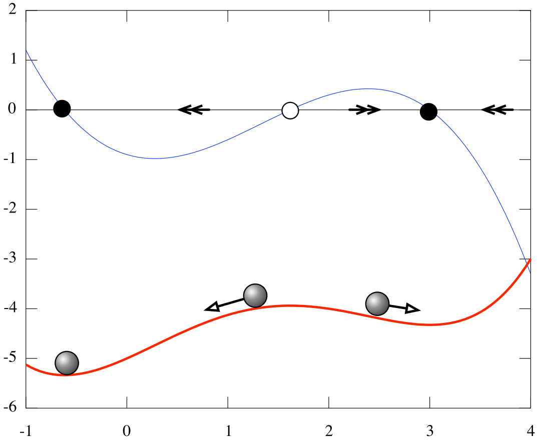
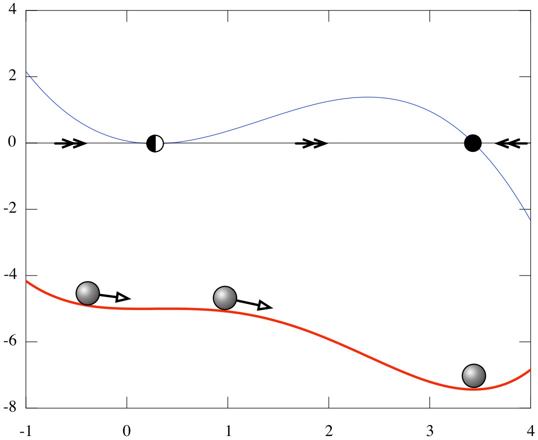


Figure: Mechanistic interpretation of the bifurcation. The red plot is minus integral of the blue function (shifted a bit down for better readability). The ball rolling on the integral follows the trajectories of the dynamical system.



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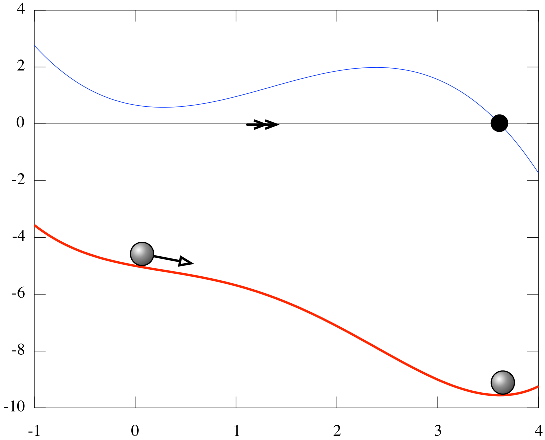

Figure: Mechanistic interpretation of the bifurcation. The red plot is minus integral of the blue function (shifted a bit down for better readability). The ball rolling on the integral follows the trajectories of the dynamical system.

Quadratic Integrate and fire neuron

- Note that the simplest possible system that may undergo saddle-node bifurcation is

$$\frac{dy(t)}{dt} = y(t)^2 + a$$

  so that the right hand side function F is a square parabola, and parameter a controls the shift of the curve over the axis.
- Such a simplest equation that is able to reproduce a certain bifurcation is sometimes called a topological normal form for that bifurcation. Surprisingly the normal form for saddle node bifurcation is one of the simplest spiking models!

Quadratic Integrate and fire neuron

- The model defined

$$\frac{dV(t)}{dt} = V(t)^2 + I$$

  where I is a parameter (input current).
- The equation has an analytic solution

$$V(t) = \frac{1}{c(I) - t}$$

  for some constant $c(I)$, so the trajectories diverge at $c(I)$ to infinity. Infinite membrane potential does not make any sense, therefore we will asume that after reaching certain value V_{peak} the voltage variable is reset $V = 0$.

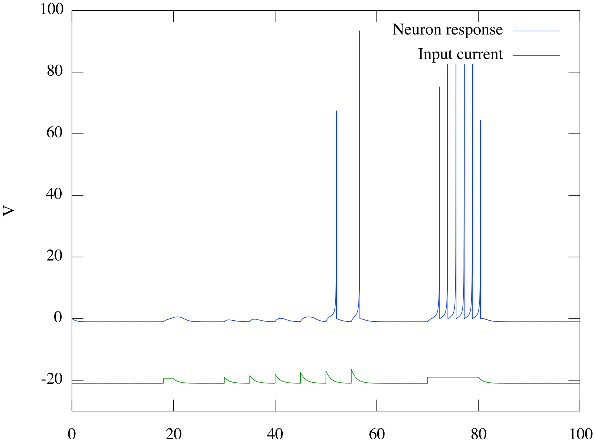

Figure: It turns out that quadratic integrate and fire model, even though very simple, can fairly well reproduce neuronal excitability.

- 1d systems are the simplest possible equations, nevertheless they exhibit many important dynamical features
- Some neural models can be simplified into a 1d system. The description in such case is not complete, but sufficient to study short timescale dynamics where slow variables can be assumed constant
- 1d systems undergo bifurcations, qualitative changes to the phase portrait which result in different dynamics
- Bifurcation is a very universal concept. Many different systems behave in similar manner because they undergo the same bifurcation. Many similar systems behave differently because they rest in different phase portrait regimes