Lecture 6

2025-10-08

Electrophysiology of neural membrane; Circuit model of spiking neurons

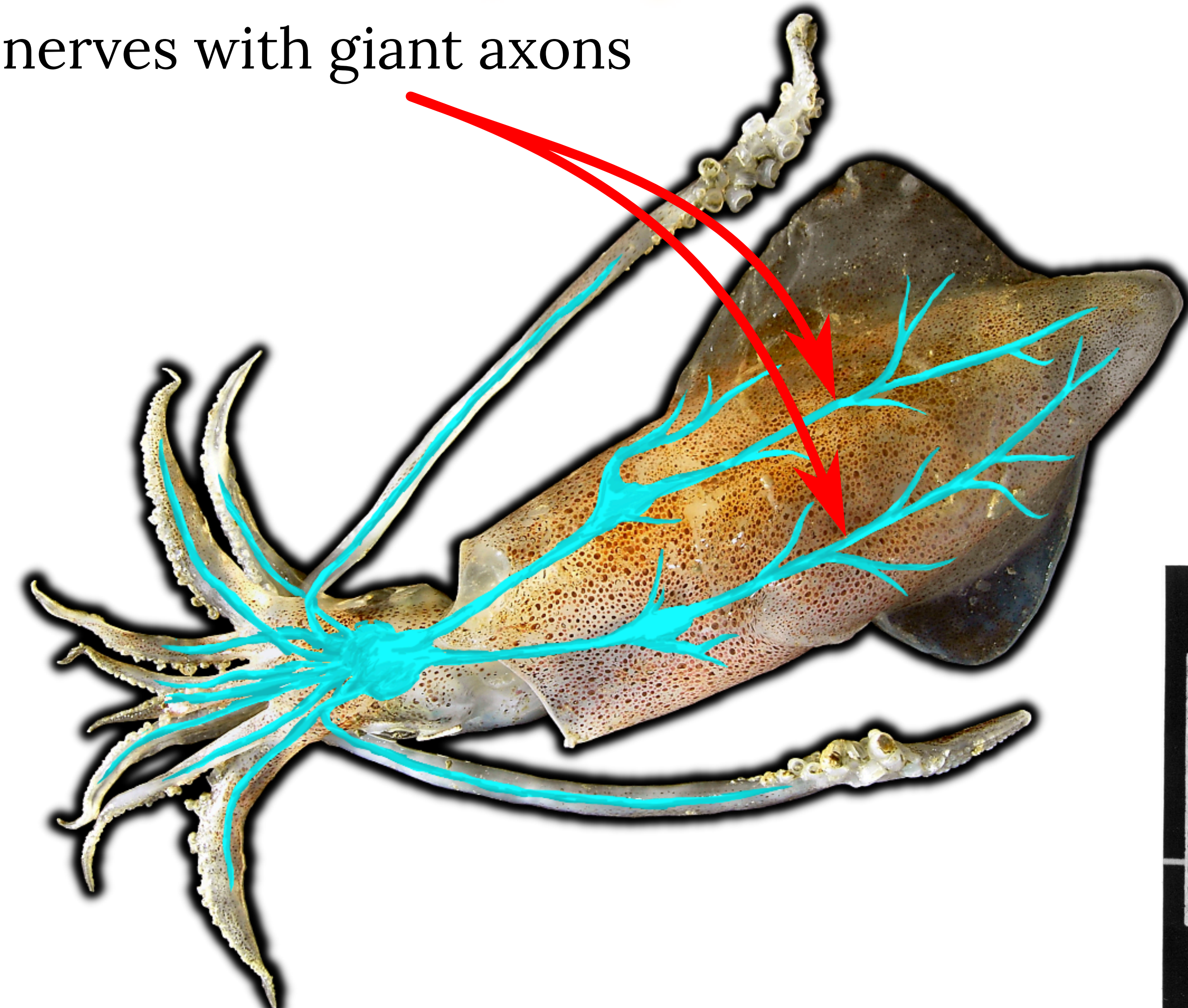
- Online slides: lec06-electrophy_circuit.html
- Code: code06.ipynb
- Homework: hw06.pdf

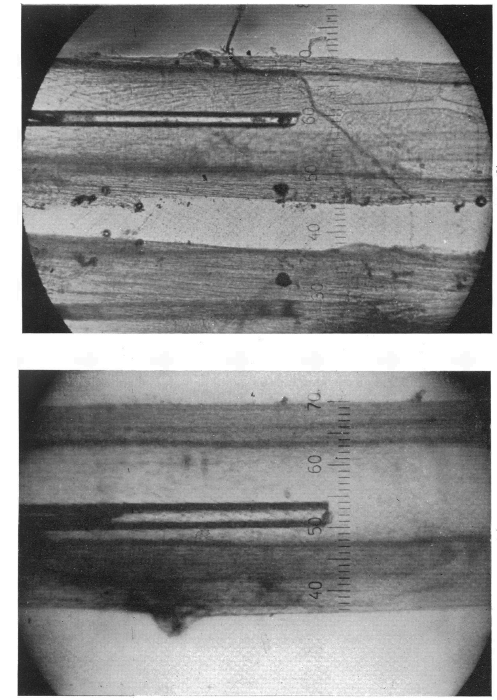
Username: `cns`, Password: `nycu2025`

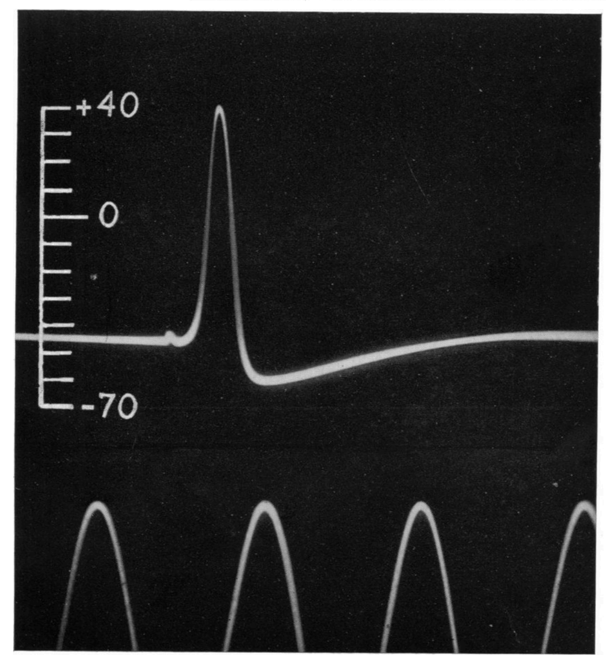
Laboratory of Computing Biological Networks

Giant axons of a squid

nerves with giant axons

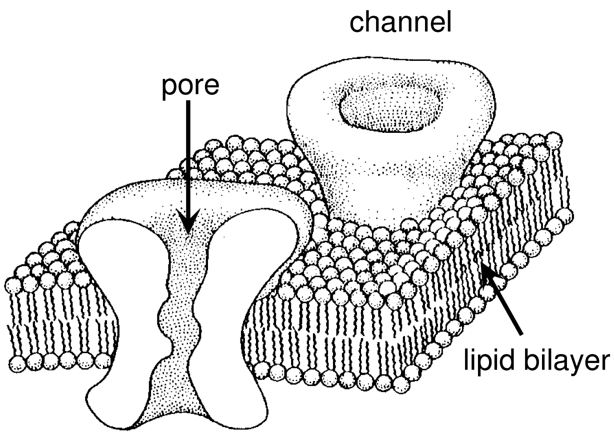






Hodgkin and Huxley (1952)

Some quantitative descriptions



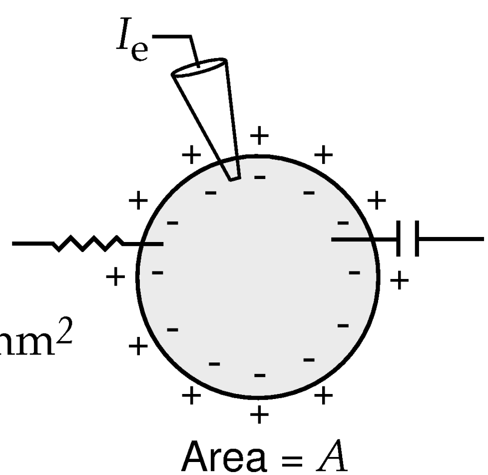
- Lipid bilayer thickness: 4~8 nm
- Channels can be selective to types of ions
- Potential comparable to thermal noise
- Intracellular resistivity 1~3 kΩ mm
- Specific membrane capacitance 10 nF/mm^2
- Cell surface area: 0.01~0.1 mm^2
- Total membrane capacitance: 0.1~1 nF

Dayan & Abbott 2002

$\Delta V = I_e R_m$

$R_m = r_m / A$

$r_m \approx 1\ \mathrm{M\Omega\ mm^2}$

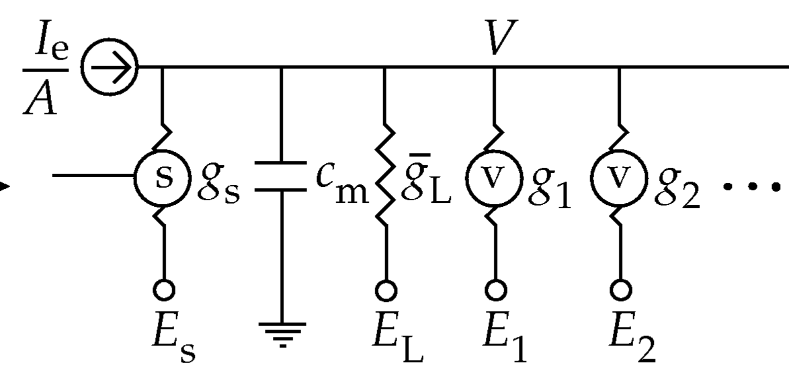


$Q = C_m V$

$C_m = c_m A$

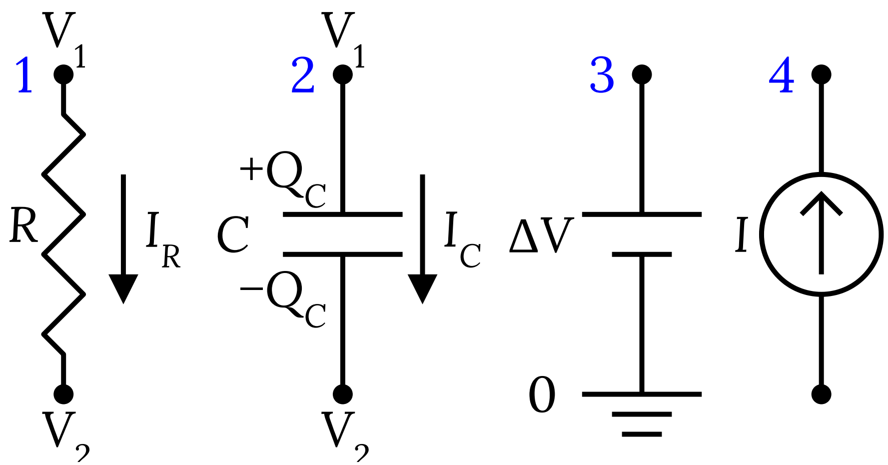
$c_m \approx 10\ \mathrm{nF/mm^2}$

Circuit model of cell membrane



E: reversal potentials

Electrical circuits



1. Resistor (Ohm's law)

$$V_R = V_1 - V_2 = I_R R$$

2. Capacitor

$$CV_C = C(V_1 - V_2) = Q_C$$

3. Voltage source
4. Current source

Conductance $G = 1/R$.
Additive connection:

- Serial: $R = R_1 + R_2$
- Parallel: $G = G_1 + G_2$

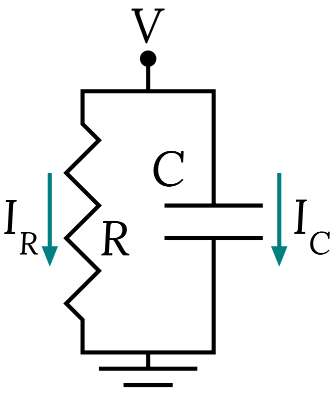
Charge is the accumulation of current: $I_C = dQ_C/dt$,

$$C\frac{dV_C}{dt} = I_C$$

Kirchhoff's laws

- Voltage differences around closed loops sum to 0.
- Sum of all currents into a point must be 0.

RC circuit



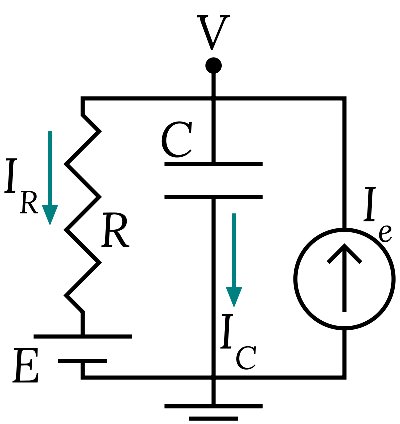
From Kirchhoff's laws, $I_C + I_R = 0$ thus

$$C\frac{dV}{dt} = I_C = -I_R = -\frac{V}{R}$$

Solution:

$$V(t) = V(0)\exp\left(-\frac{t}{RC}\right)$$

Simple passive membrane model



$$C\frac{dV}{dt} = \frac{E-V}{R} + I_e$$

Solution: $V(t) = V_\infty + [V(0) - V_\infty]\exp(-t/\tau)$

$V_\infty = E + RI_e$ and $\tau = RC$.

Exponential relaxation with time constant τ...

About the membrane and ion channels

- specific membrane resistence r_m ($= 1/g_\mathrm{m}$)
- membrane time constant τ_m
- equilibrium potential, reversal potential E
- depolarization/hyperpolarization
- shunting conductances
- inhibitory and excitatory synapses
- specific membrane current

$$i_\mathrm{m} = \sum_i g_i (V - E_i)$$

- leakage current, resting potential (lumping up the time-independent parts):

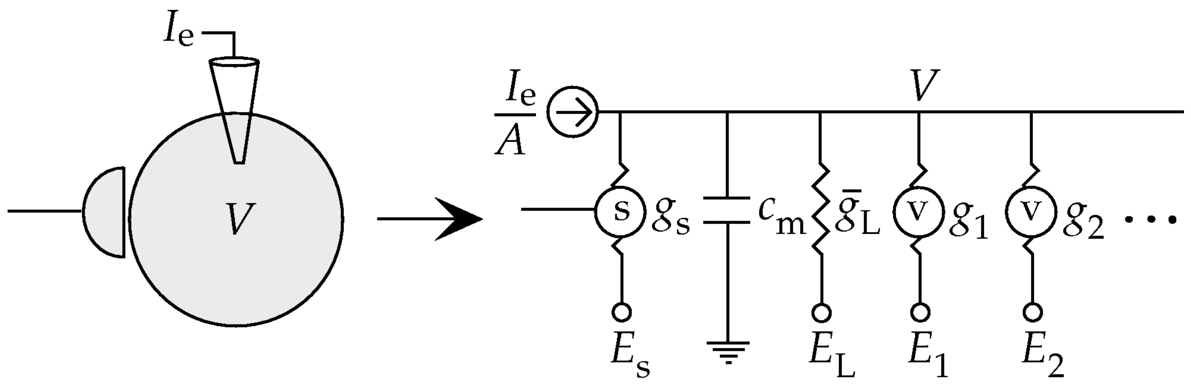
$$\bar{g}_\mathrm{L}(V - E_\mathrm{L})$$

Single-compartment models

Models describing the membrane potential of a neuron by a single variable V (i_{m} is positive outward)

$$c_{\mathrm{m}} \frac{dV}{dt} = -i_{\mathrm{m}} + \frac{I_e}{A}$$

Equivalent circuit



In general, membrane potential can vary with the location on the membrane: Multiple-compartment models; Potential field;...

Integrate-and-fire model

Consider single leakage term $i_{\mathrm{m}} = \bar{g}_{\mathrm{L}}(V - E_{\mathrm{L}})$,

$$c_{\mathrm{m}} \frac{dV}{dt} = -\bar{g}_{\mathrm{L}}(V - E_{\mathrm{L}}) + \frac{I_e}{A}$$

Multiply with $r_{\mathrm{m}} = 1/\bar{g}_{\mathrm{L}}$, using $c_{\mathrm{m}} r_{\mathrm{m}} = \tau_{\mathrm{m}}$ and total membrane resistance $R_{\mathrm{m}} = r_{\mathrm{m}}/A$:

$$\tau_{\mathrm{m}} \frac{dV}{dt} = E_{\mathrm{L}} - V + R_{\mathrm{m}} I_e \tag{5.9}$$

augmented by threshold V_{th} and reset V_{reset} potentials. Resting potential is E_{L}.

Firing rate of integrate-and-fire model

For constant I_e, from reset following a spike to the next spike we have t_{isi}, $V(t_{\text{isi}}) =$

$$V_{\text{th}} = E_{\text{L}} + R_{\text{m}} I_e + (V_{\text{reset}} - E_{\text{L}} - R_{\text{m}} I_e) \exp(-t_{\text{isi}}/\tau_{\text{m}}).$$

Interspike-interval firing rate (for $R_{\text{m}} I_e > V_{\text{th}} - E_{\text{L}}$)

$$r_{\text{isi}} = \frac{1}{t_{\text{isi}}} = \left(\tau_{\text{m}} \ln\left(\frac{R_{\text{m}} I_e + E_{\text{L}} - V_{\text{reset}}}{R_{\text{m}} I_e + E_{\text{L}} - V_{\text{th}}}\right)\right)^{-1}$$

$$\approx \left[\frac{E_{\text{L}} - V_{\text{th}} + R_{\text{m}} I_e}{\tau_{\text{m}}(V_{\text{th}} - V_{\text{reset}})}\right]_+ \qquad (5.12)$$

Spike-rate adaptation and refractoriness

IF assumptions: • Instant action potential • Linear current

$$\tau_{\mathrm{m}} \frac{dV}{dt} = E_{\mathrm{L}} - V + R_{\mathrm{m}} I_e$$

Solving ordinary differential equation

Continuous dynamics

$$\frac{dy(t)}{dt} = f[t, y(t)]$$

Discrete time steps

$$t_n = t_0 + n\Delta t \quad \Rightarrow \quad t_{n+1} = t_n + \Delta t$$

Euler method

$$y_{n+1} = y_n + \Delta t f(t_n, y_n)$$

Local truncation error: $O(\Delta t^2)$

Higher order methods

Runge–Kutta method (RK4)

$$y_{n+1} = y_n + \frac{\Delta t}{6}(k_1 + 2k_2 + 2k_3 + k_4)$$

$$\begin{aligned}
k_1 &= f(t_n, y_n) \\
k_2 &= f(t_n + \frac{\Delta t}{2}, y_n + \frac{\Delta t}{2}k_1) \\
k_3 &= f(t_n + \frac{\Delta t}{2}, y_n + \frac{\Delta t}{2}k_2) \\
k_4 &= f(t_n + \Delta t, y_n + \Delta t k_3)
\end{aligned}$$

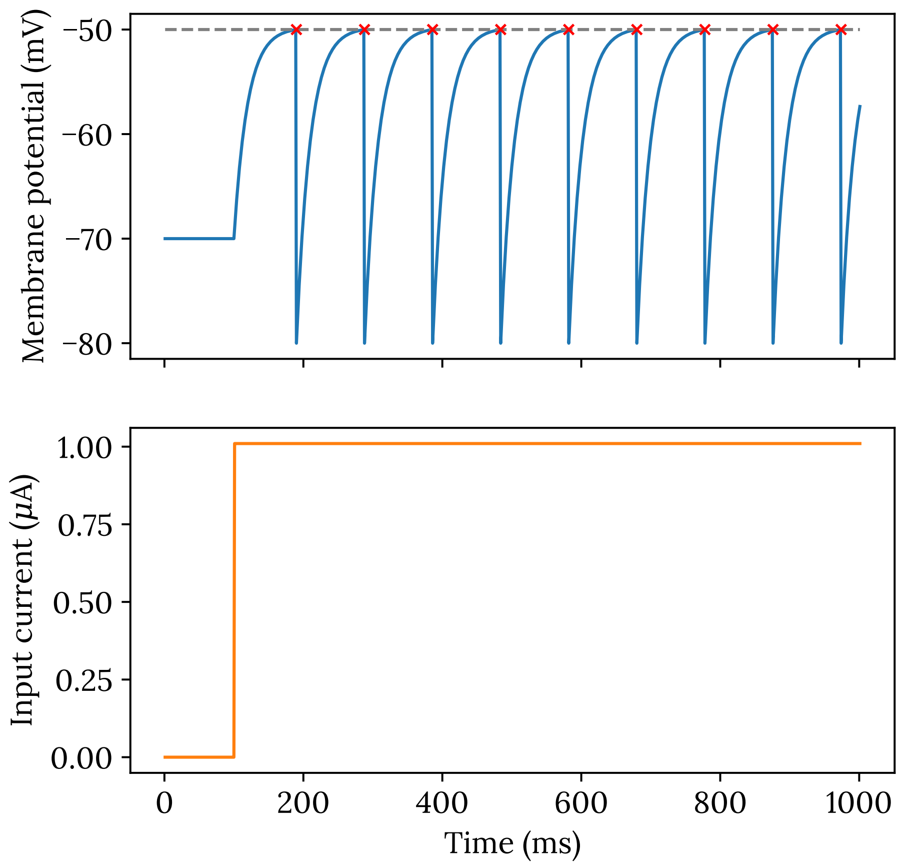
Local truncation error: $O(\Delta t^5)$

Integrate-and-fire again

$$\tau \frac{dV}{dt} = E_{\mathrm{L}} - V + R_{\mathrm{m}} I_e$$

Symbol	Variable	Description
E_{L}	`el`	Resting potential
R_{m}	`mr`	Membrane resistance
τ_{m}	`tm`	Membrane time constant
V_{th}	`th`	Firing threshold
V_{reset}	`vr`	Reset potential
I_e	`ie`	External input current
$V(0)$	`vi`	Initial membrane potential
V	`vm`	Membrane potential
Δt	`dt`	time between frames

Euler method for LIF




```
tt = 1000  # Simulate for 1s
ti = 0     # Time
# Traces
tis = []  # Time frames (ms)
vms = []  # Membrane potential (mV)
spt = []  # Spike train
ies = []  # Input current (μA)
ti = 0
vm = el
while ti<=tt:
  ie = 0 if ti<100 else 1.01
  dvt = (el-vm+mr*ie)/tm
  vm += dt*dvt
  ti += dt
  if sp:=vm>th: vm = vr
  tis.append(ti)
  vms.append(vm)
  spt.append(sp)
  ies.append(ie)
```

Tech notes:

- Trinary operator
- Walrus operator

Functionalized Integrate-and-fire code

—Reusable function with integrator function as argument

*We package the code into a function as discussed earlier so it can be reused for different parameter values. Even algorithmic parts can also be parameterized by passing **functions** as parameters.*

```python
def integrate_fire_traces(tt,dt,vi=el,ies=None,itg=euler_step):
   '''Solve integrate-and-fire model for traces

   Parameters
   ----------
   tt :  Simulated time duration
   dt :  Time step size
   vi :  Initial membrane potential
   ies : Input current trace
   itg : Integrator function

   Return
   ------
   tis :  Time frames
   vms :  Membrane potential trace
   spt :  Spike train
   '''
   nf = int(tt/dt)
   if ies is None: ies = np.zeros(nf)
   ti = 0
   vm = vi
   # Traces
   tis = []   # Time frames
   vms = []   # Membrane potential
   spt = []   # Spike train
   for i in range(nf):
      ie = ies[i%len(ies)]
      vm = itg(vm,lambda x:(el-x+mr*ie)/tm,dt)
      if sp:=vm>th: vm = vr
      ti += dt
      tis.append(ti)
      vms.append(vm)
      spt.append(sp)
   return np.array(tis),np.array(vms),np.array(spt)
```

Functionalized integrators

```
def euler_step(y,f,dt):
    dyt = f(y)
    y += dt*dyt
    return y
```

```
def runge_kutta(y,f,dt):
    k1 = f(y)
    k2 = f(y+k1*dt/2)
    k3 = f(y+k2*dt/2)
    k4 = f(y+k3*dt)
    y += dt*(k1+2*(k2+k3)+k4)/6
    return y
```

☆ Here we consider only dynamics without explicity time dependence. The integrators are defined as functions taking the time-derivative function `f` as a parameter. These integrator functions can themselves be passed as argument values to the `integrate_fire_traces` function. This code pattern can be repeated allowing generation of different combinations of models and algorithms with minimal additional coding efforts.

FitzHugh–Nagumo model

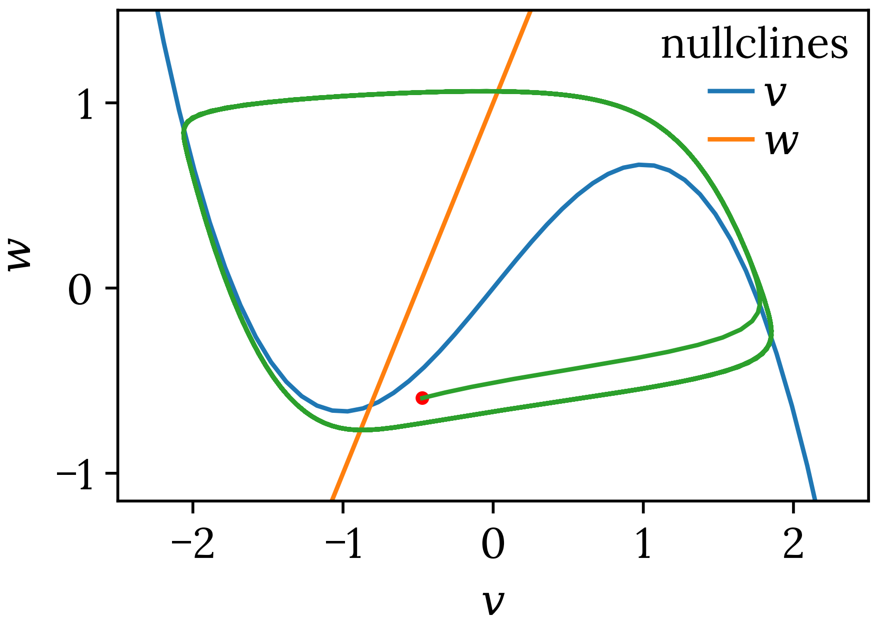
A simply model that can generate action potentials

$$\frac{dv}{dt} = v - \frac{v^3}{3} - w + RI_{\text{ext}}$$
$$\tau \frac{dw}{dt} = v + a - bw$$

- Two-variable model (Minimally required for continuous AP)
- With fast variable v and slow variable w
- Can be in one of multiple regimes: excitable or oscillatory

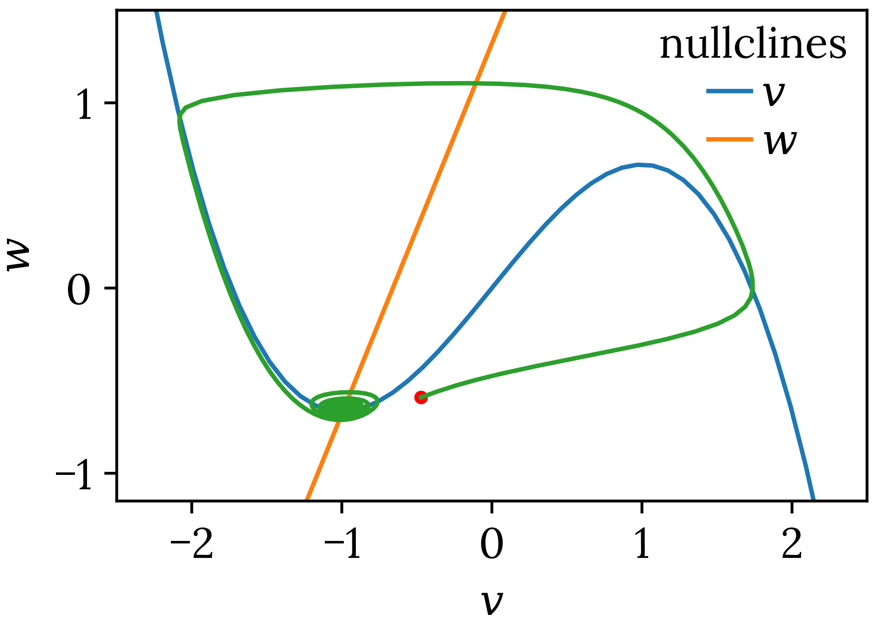
State space of FhN model

Oscillatory



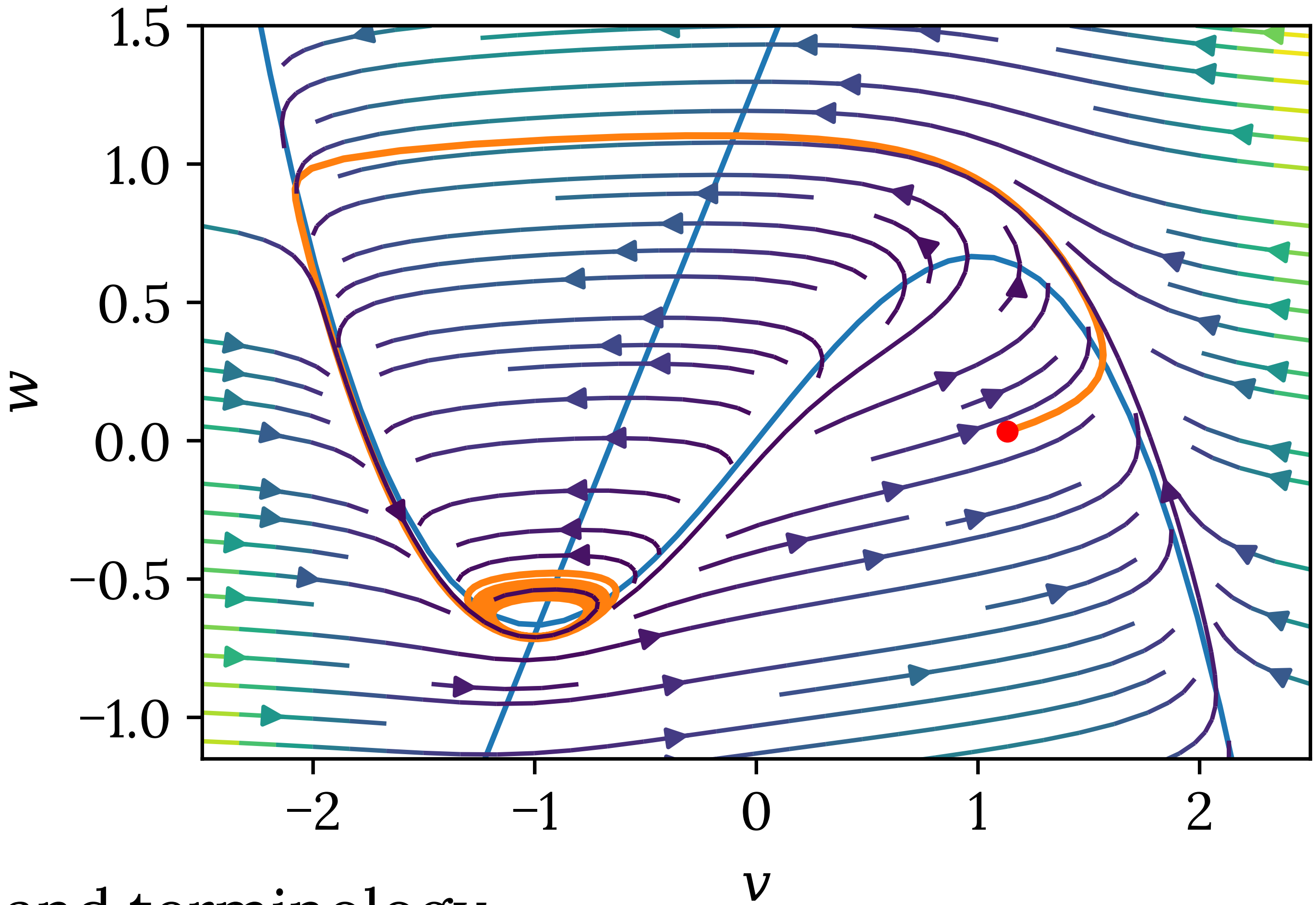
$$a, b, \tau = 0.5, 0.5, 10$$

Excitable



$$a, b, \tau = 0.66, 0.5, 10$$

Flow of FhN state



Concepts and terminology

- nullclines
- fixed points
- limit cycles