Section 7 Dynamic System and Hodgkin-Huxley Model

Brief Conceptual Review and HW3

Binxu Wang

Nov. 1st , 2021

Review Contents

- Dynamic system analysis and stability

- Biophysics of Membrane and H-H model.

Dynamic System and Stability Analysis

Dynamic System is Everywhere…

- Mechanics, Astrophysics, Fluid dynamics, Solar dynamics …
- Robotics, Autonomous car…
- Gene interaction network; protein interaction (e.g. molecular clock?)…
- Single neurons; neural networks
- Epidemics, population dynamics…

Dynamic System Review

$$\dot{X} = f(X)$$

X is state variables

$f(X)$ defines the dynamics or motion.

Analysis View

$$f(X) = \dot{X} \approx \frac{\Delta X}{\Delta t}$$
$$\Delta X \approx f(X)\Delta \mathrm{t}$$
$$X(t + \Delta t) \approx X(t) + f(X)\Delta \mathrm{t}$$

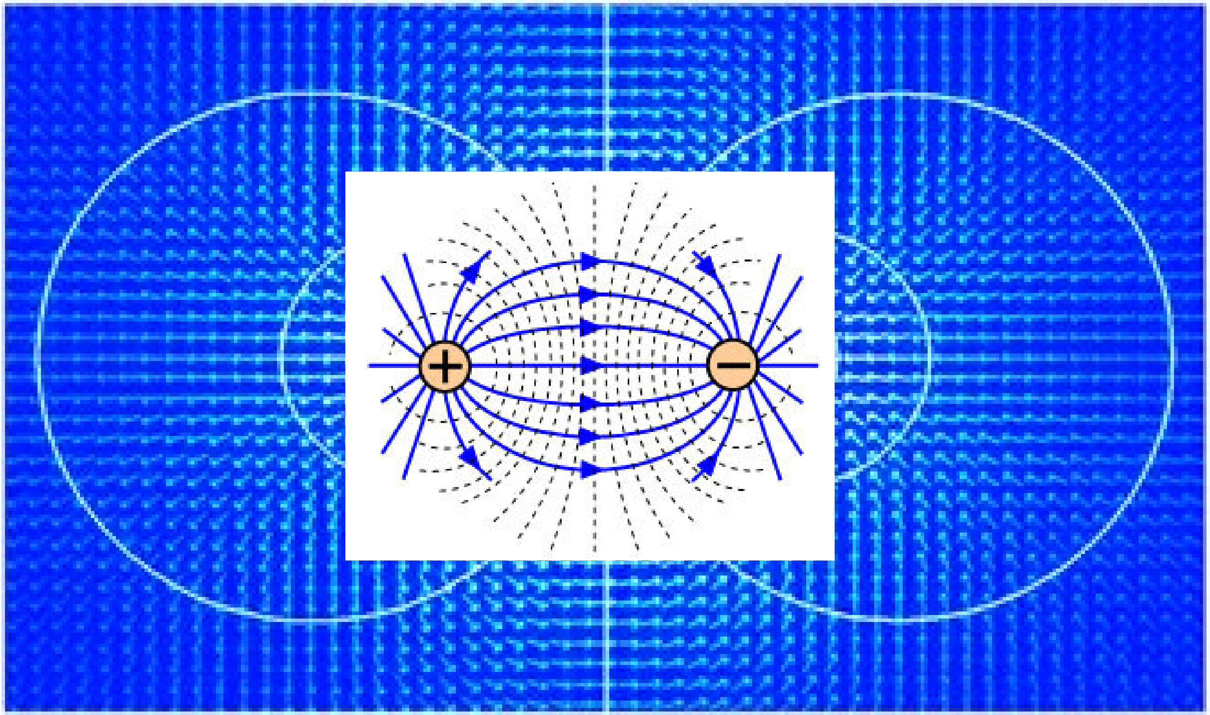
- ~ Euler method for integrating / solving ODE. (HW3, P2)
- A few ODE has analytical solutions $X(t)$
  - $X(t) = e^{kt}$, then $\dot{X} = ke^{kt} = kX$

Geometric View

- Differential equations define a vector field.
  - $f(X)$ is the vector at X
- Differential equations / Vector field can be integrated as a flow $X(t)$.
- Dynamics could be read out from the geometry of flow field.
  - Fixed points (attractor, repeller, saddle etc.)
  - Limit cycle

Physics example: Electric field and field "lines"

- Field lines are the *flow* defined by the vector field of $\vec{E}$

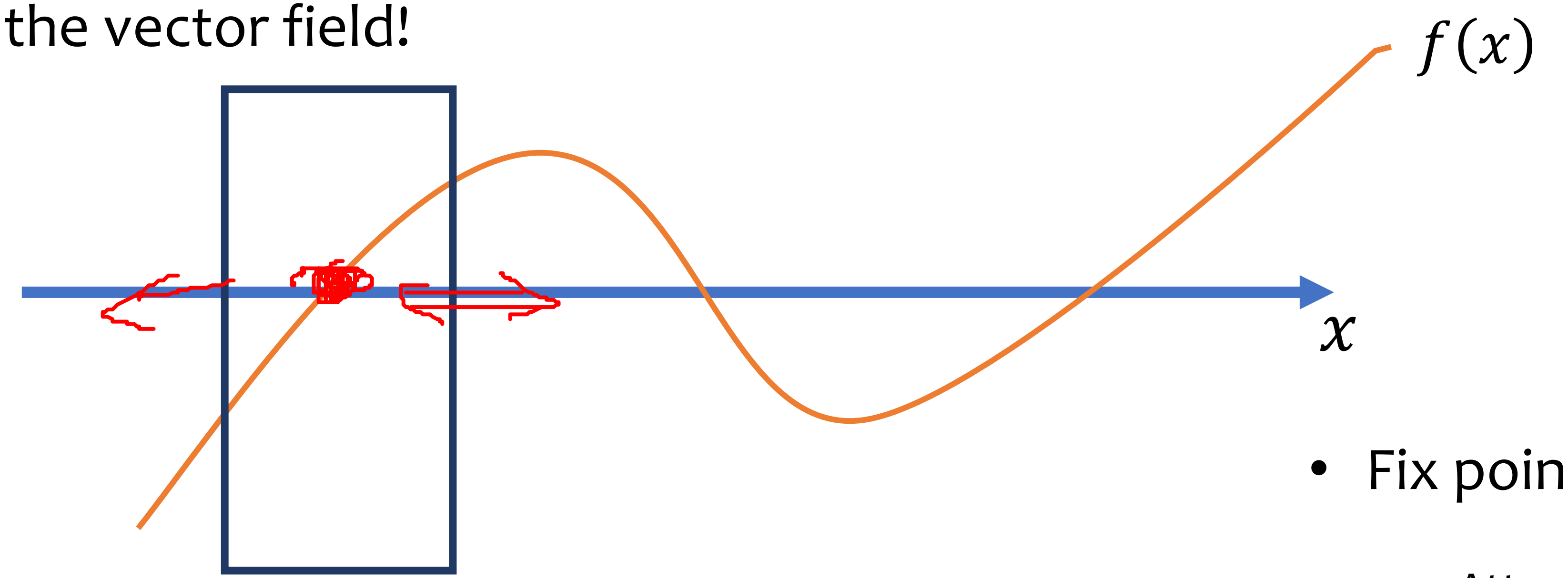


1-D Dynamic System

1-D function on a line

$$\dot{x} = f(x), x \in \mathbb{R}$$

Let's try reading the dynamics from the vector field!



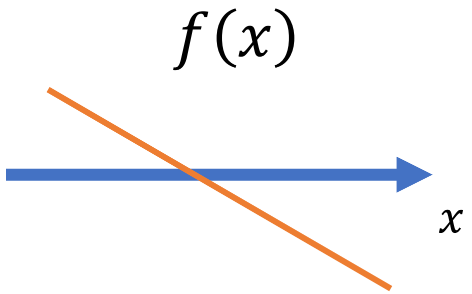
- Fix point
  - Attractor (stable fix point)
  - Repeller (unstable fix point)

Stability of Fix Point

- Fix point
  - $\dot{x} = f(x) = 0$
- Stable fix point, attractor

$$\begin{cases} f(x) < 0; x > x^* \\ f(x) > 0; x < x^* \end{cases}$$

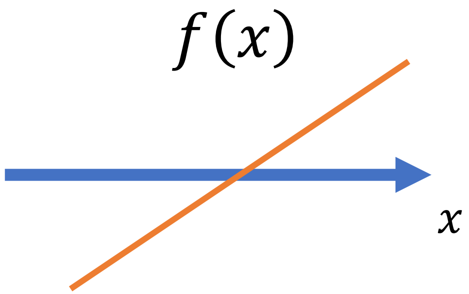
  - $\frac{df}{dx}|_{x^*} < 0$
  - Negative feedback



- Unstable fix point, repellor

$$\begin{cases} f(x) > 0; x > x^* \\ f(x) < 0; x < x^* \end{cases}$$

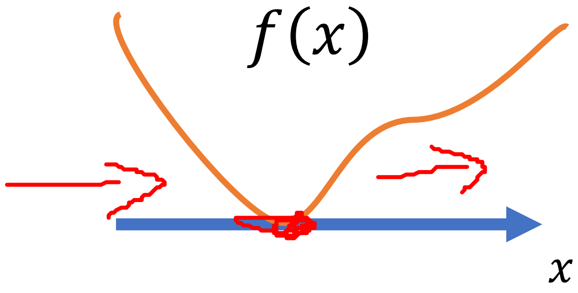
  - $\frac{df}{dx}|_{x^*} > 0$
  - Positive feedback

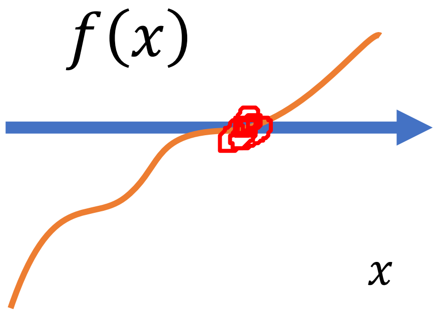


Analyze derivative / Jacobian of $f(x)$ is a theme for dynamic system.

What about the dynamics of these cases?

$$\left.\frac{df}{dx}\right|_{x^*} = 0$$





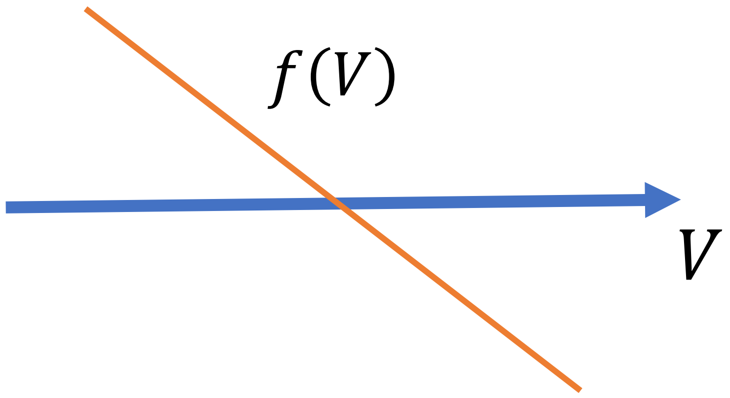
- Linearization / Jacobian method failed, need deeper analysis.
  - Look at the vector field.

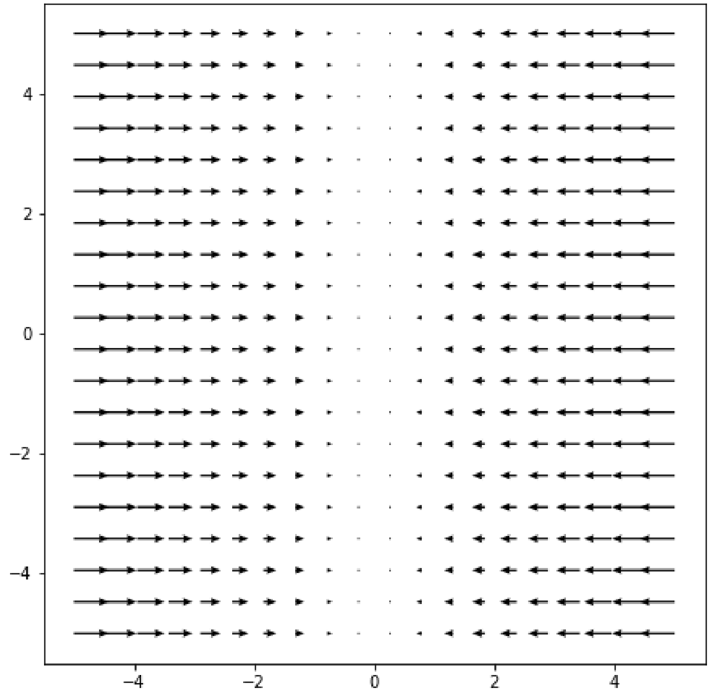
First-order dynamics

- *What is the flow of this system?*

$$\frac{dV}{dt} = -k(V - V_*)$$

  - $V(t) - V_* = (V(0) - V_*)e^{-kt}$





- Examples:
  - I&F Neurons without input
    - Decay to V_{rest}
  - Channel dynamics $h(t), m(t), n(t)$
    - chasing a moving target. $h_\infty(V), m_\infty(V), n_\infty(V)$

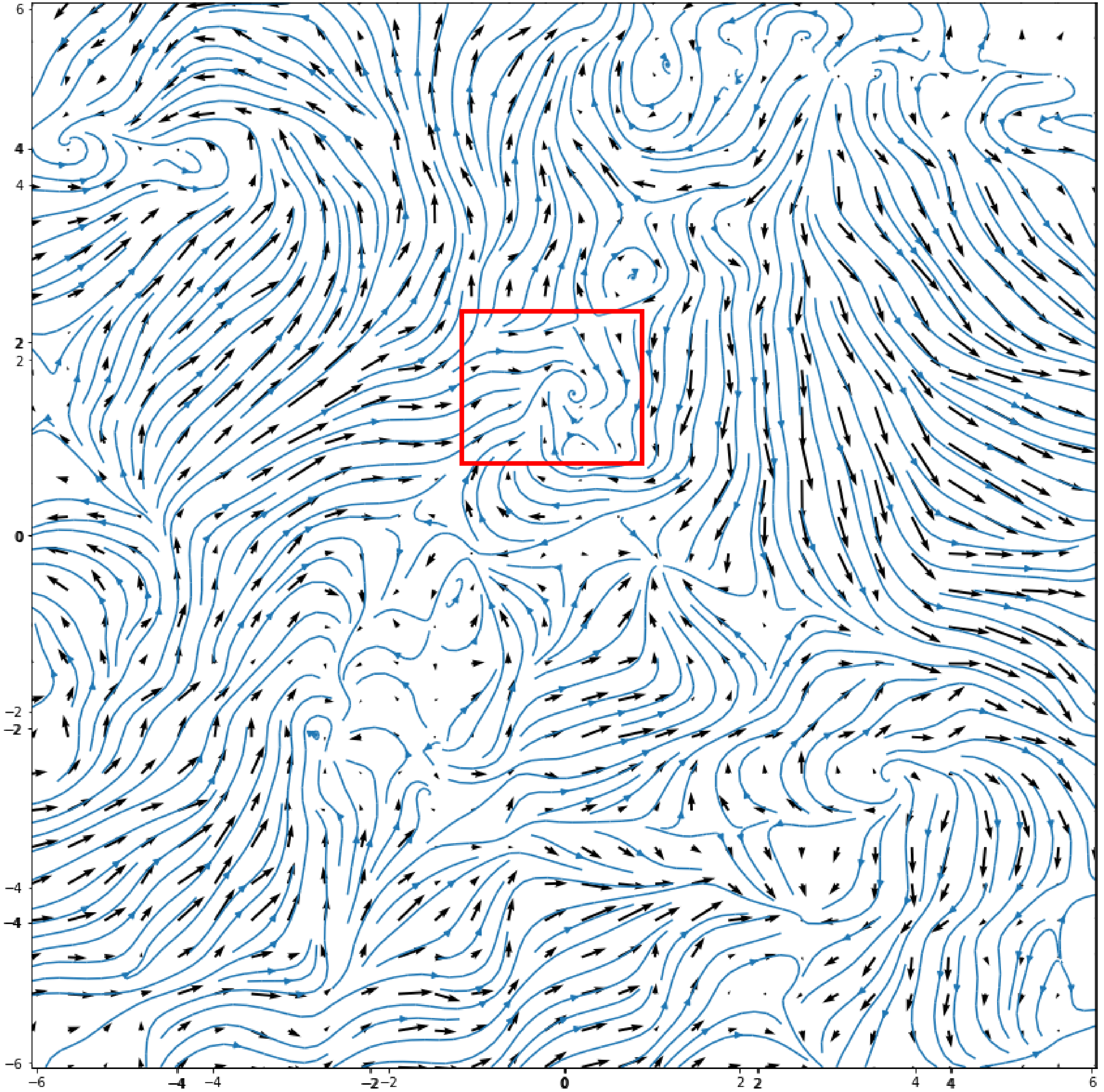
Reformulation of the equations for gating variables.

$$\dot{h} = \alpha(V)(1-h) - \beta(V)h$$
$$\dot{h} = \alpha(V) - (\alpha(V) + \beta(V))h$$

- $\dot{h} = -\frac{1}{\tau_h(V)}\left(h - h_\infty(V)\right)$
  - Time constant of recovery $\tau_h(V) = \frac{1}{\alpha(V)+\beta(V)}$
  - Equilibrium value $h_\infty(V) = \frac{\alpha(V)}{\alpha(V)+\beta(V)}$

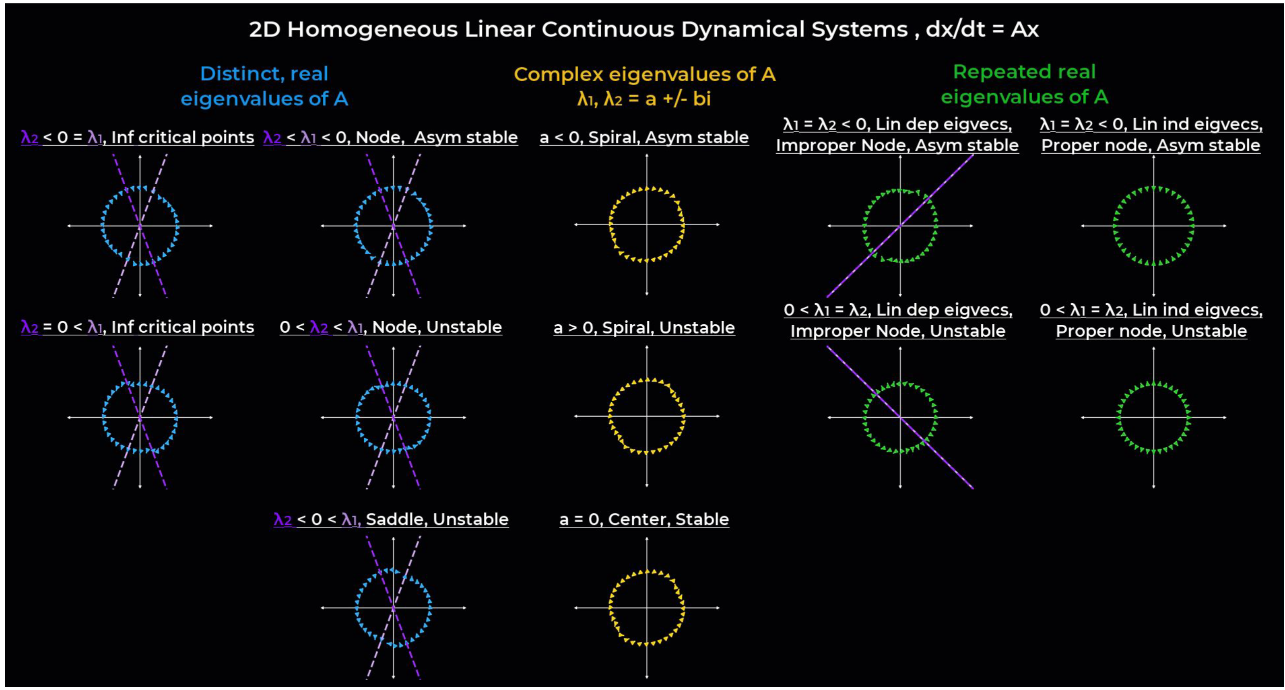
2-D Dynamic Systems

- $\dot{X} = f(X)$
  - $X \in \mathbb{R}^2, f: \mathbb{R}^2 \to \mathbb{R}^2$ usually nonlinear.
  - Vector field and flow on a plane!
  - Even complex dynamics have simple local motifs.



Motifs of complex dynamics: Linear system

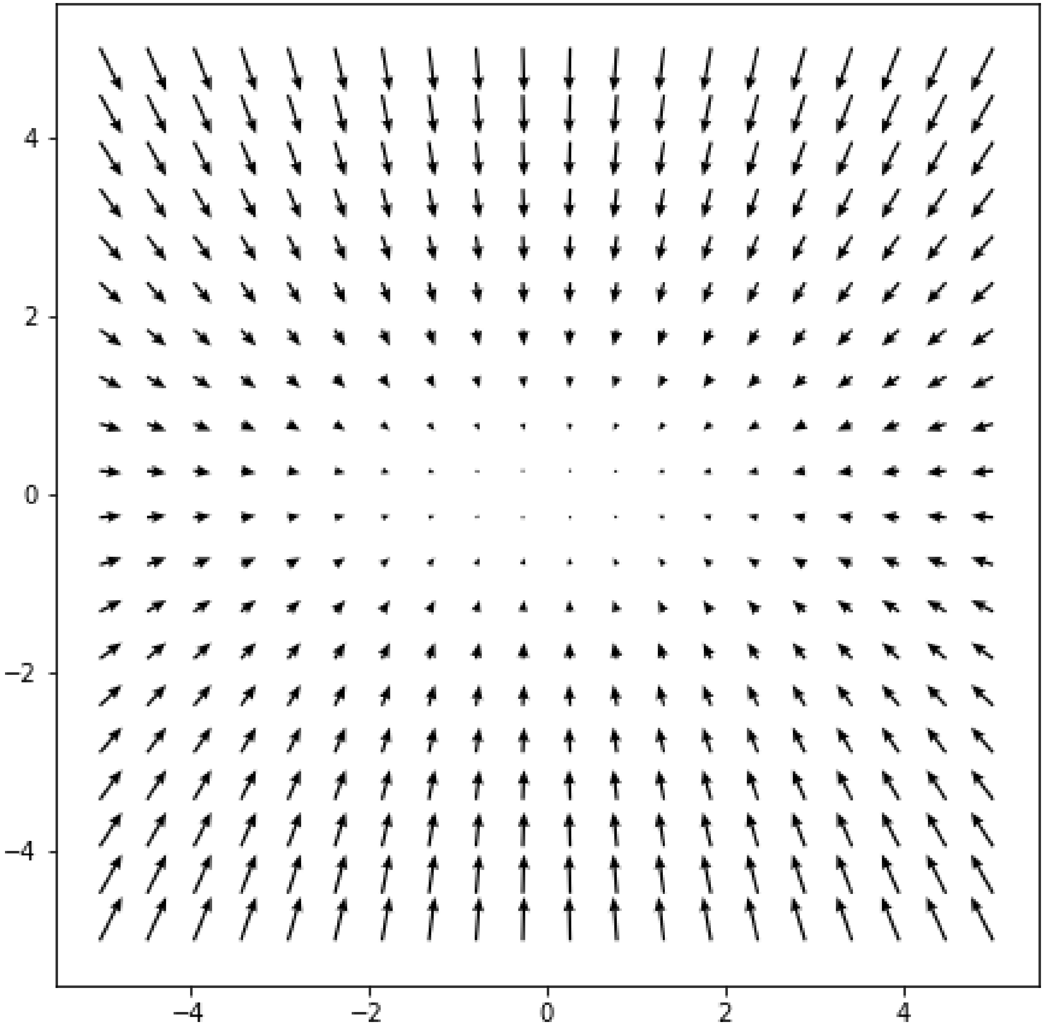
- 2-D Linear system
  - $\dot{X} = AX, X \in \mathbb{R}^2$
  - Analytically solved $X(t) = e^{At}X(0)$
  - Behavior fully classified.



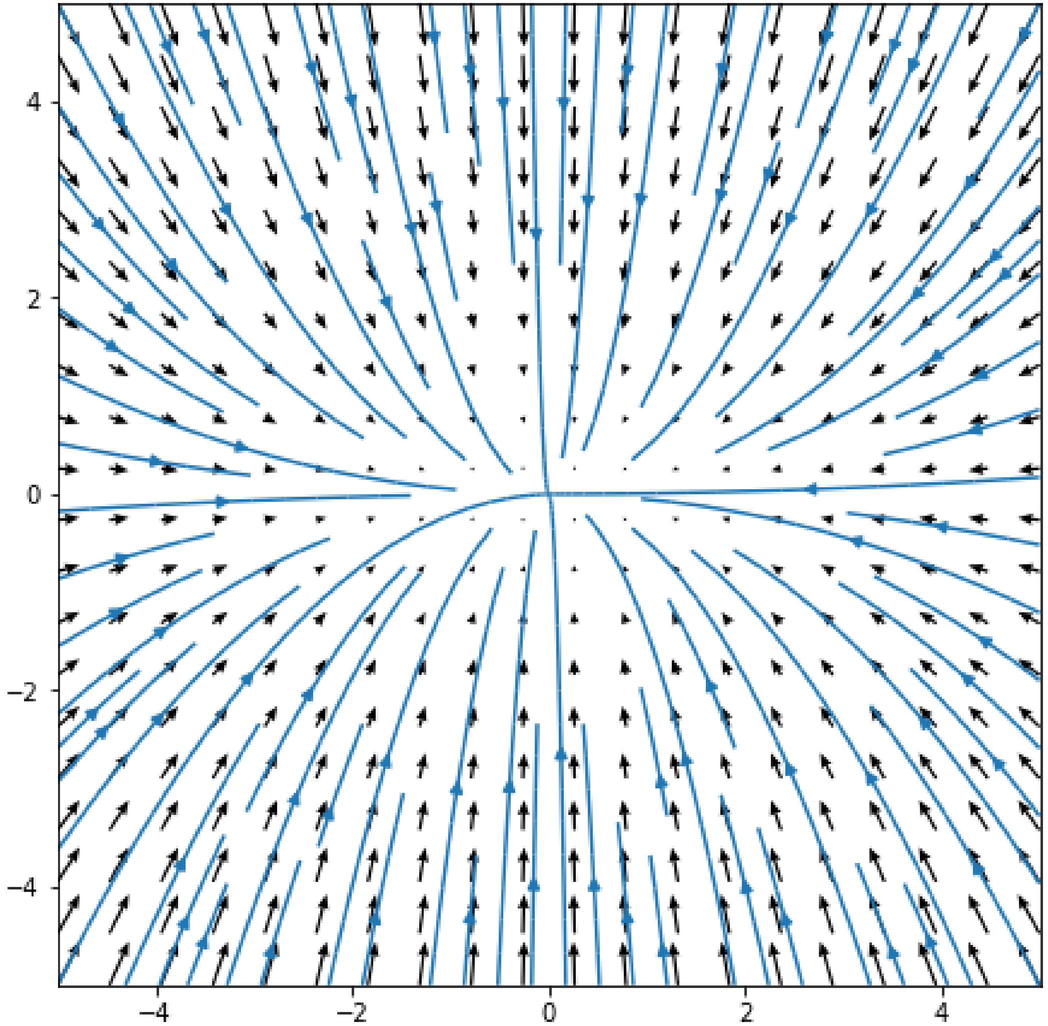
- Locally approximates nonlinear systems.
  - $f(X) \approx A(X - X^*)$ if $f(X^*) = 0$ is fixed point

2-D Linear System

$$\dot{X} = \begin{bmatrix} -1 & 0 \\ 0 & -2 \end{bmatrix} X \qquad \begin{cases} \dot{x} = -x \\ \dot{y} = -2y \end{cases}$$

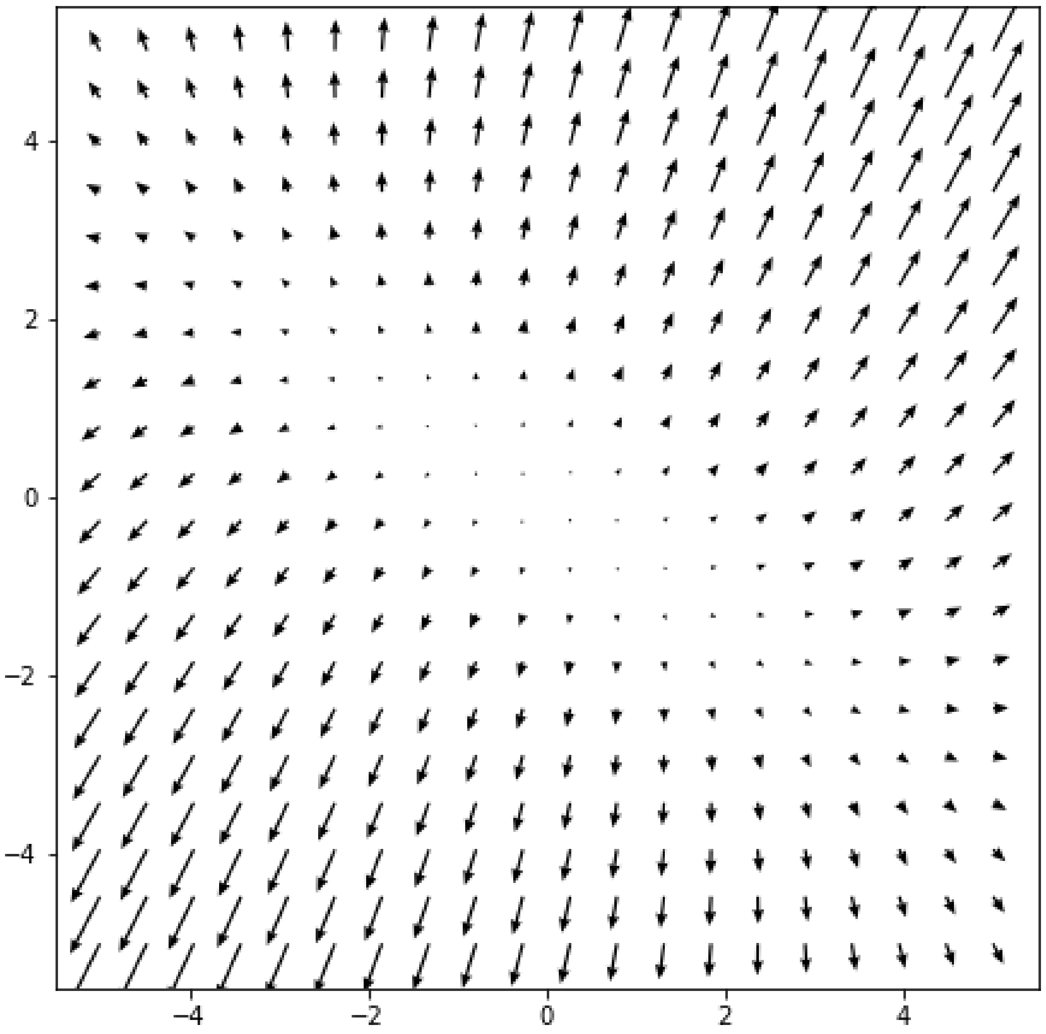


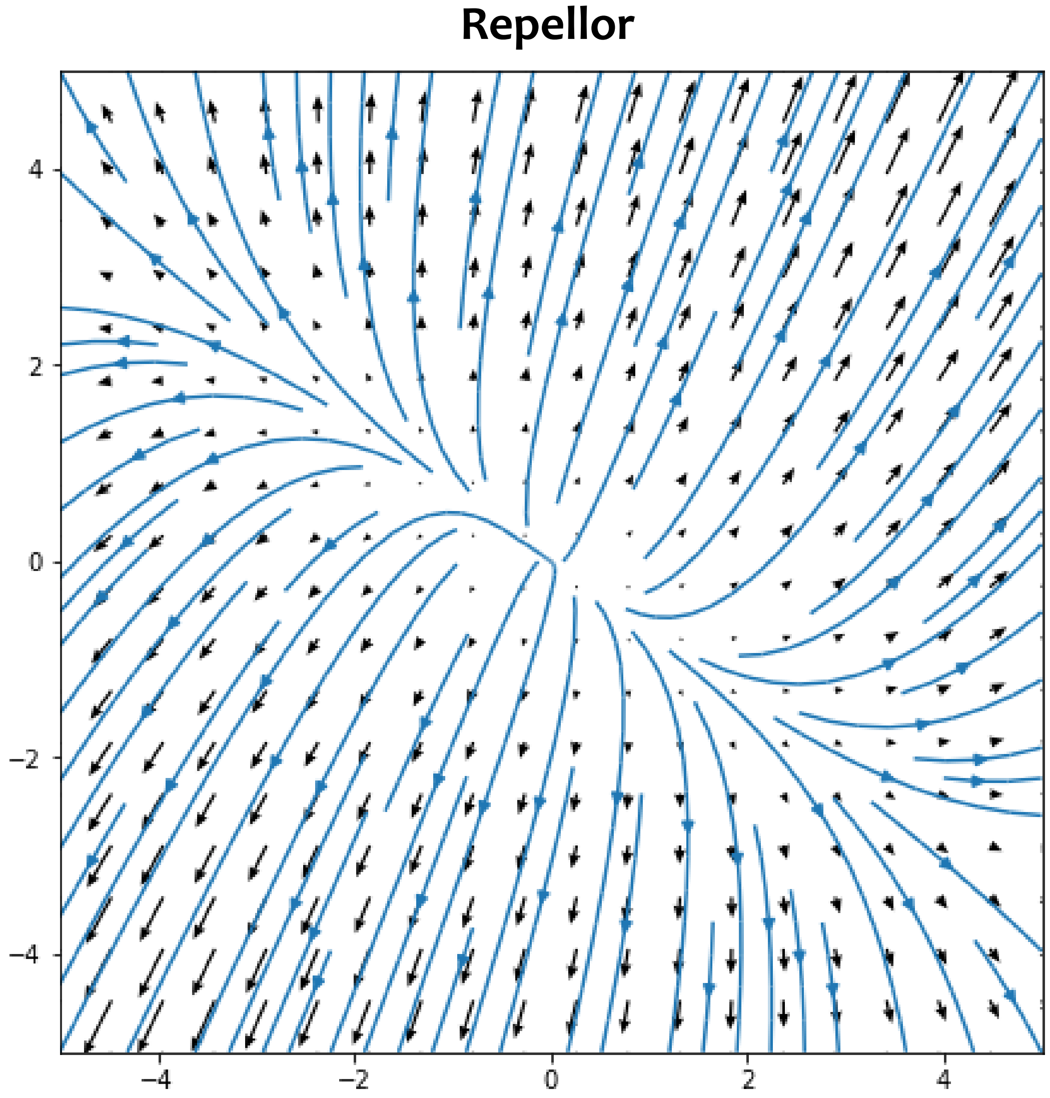
Attractor



2-D Linear System

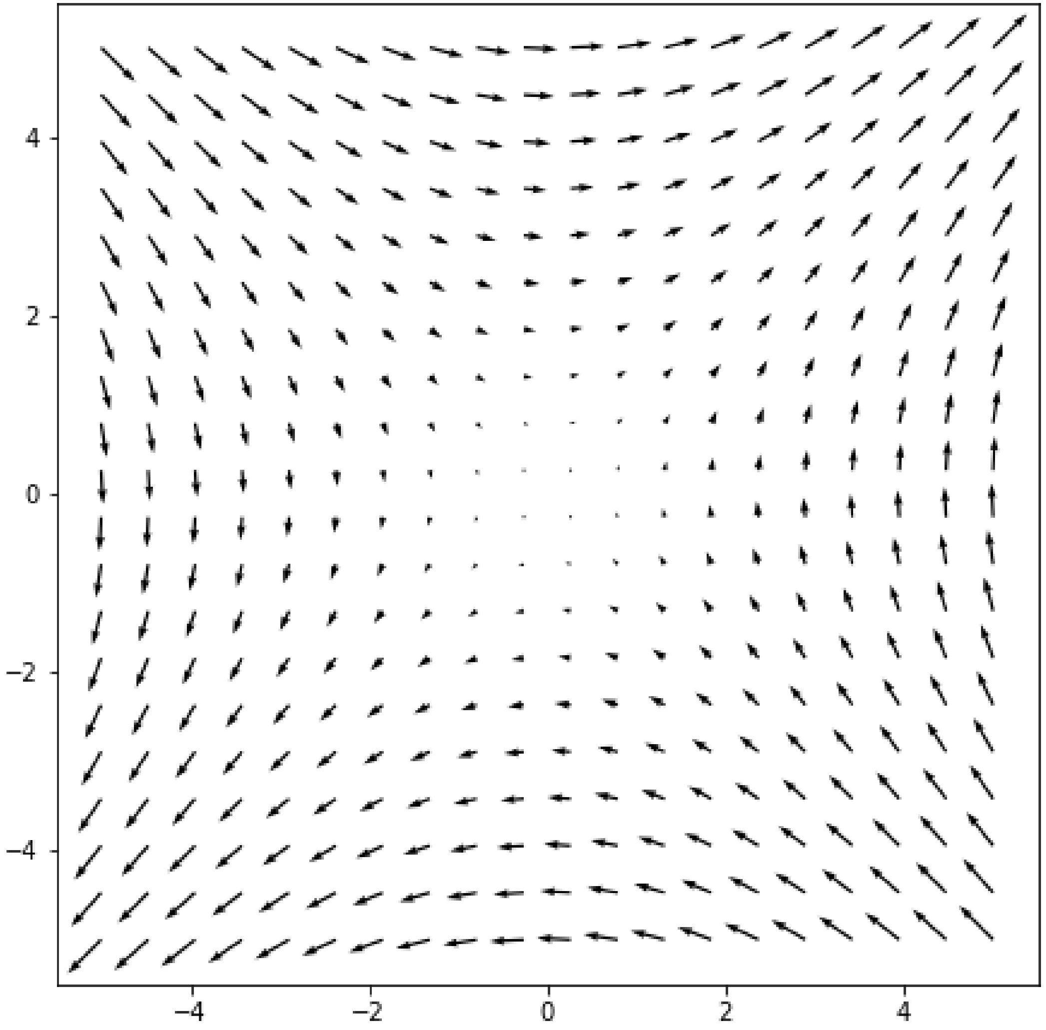
$$\dot{X} = \begin{bmatrix} 1 & 0.5 \\ 1 & 2 \end{bmatrix} X \qquad \begin{cases} \dot{x} = x + 0.5y \\ \dot{y} = 2y + x \end{cases}$$

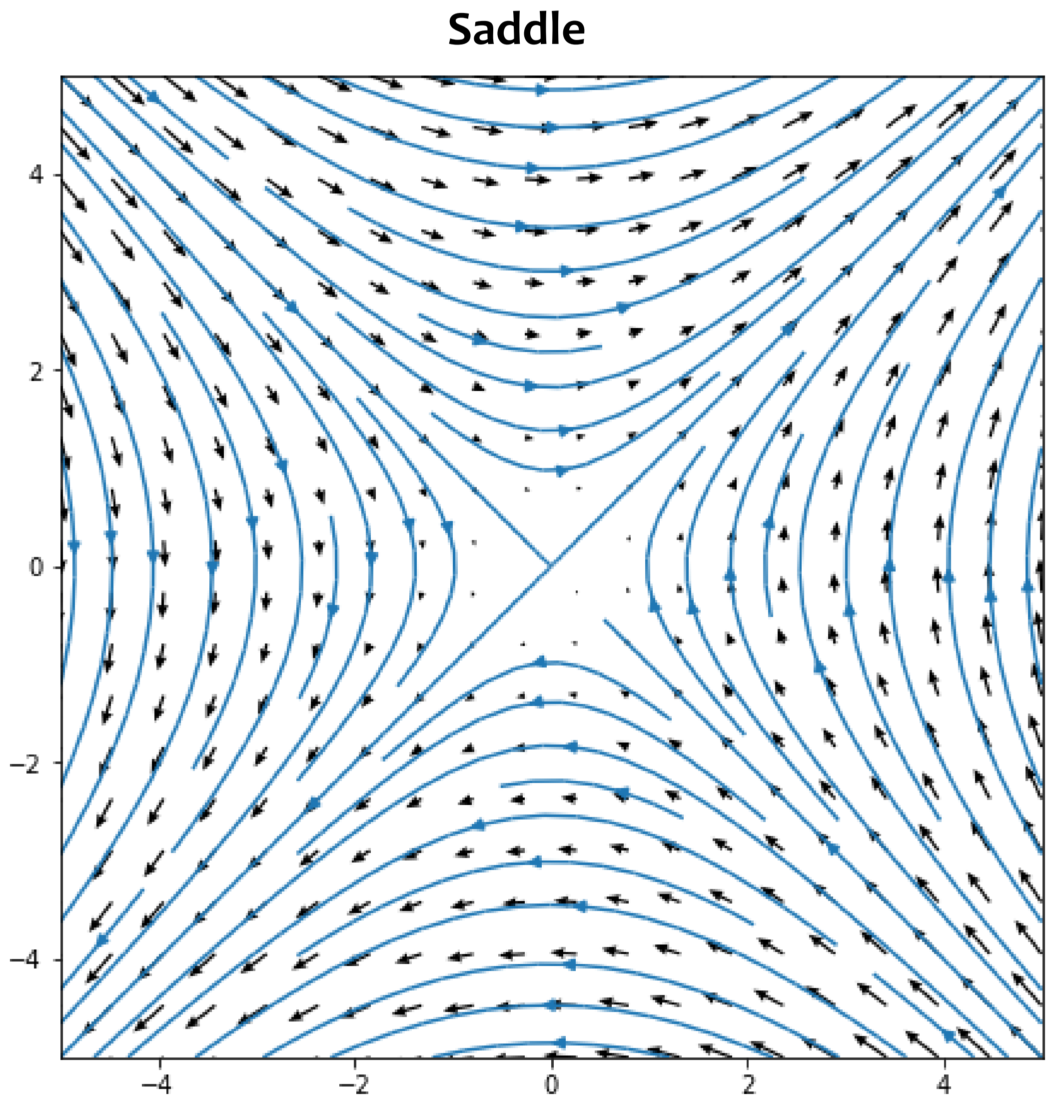




2-D Linear System

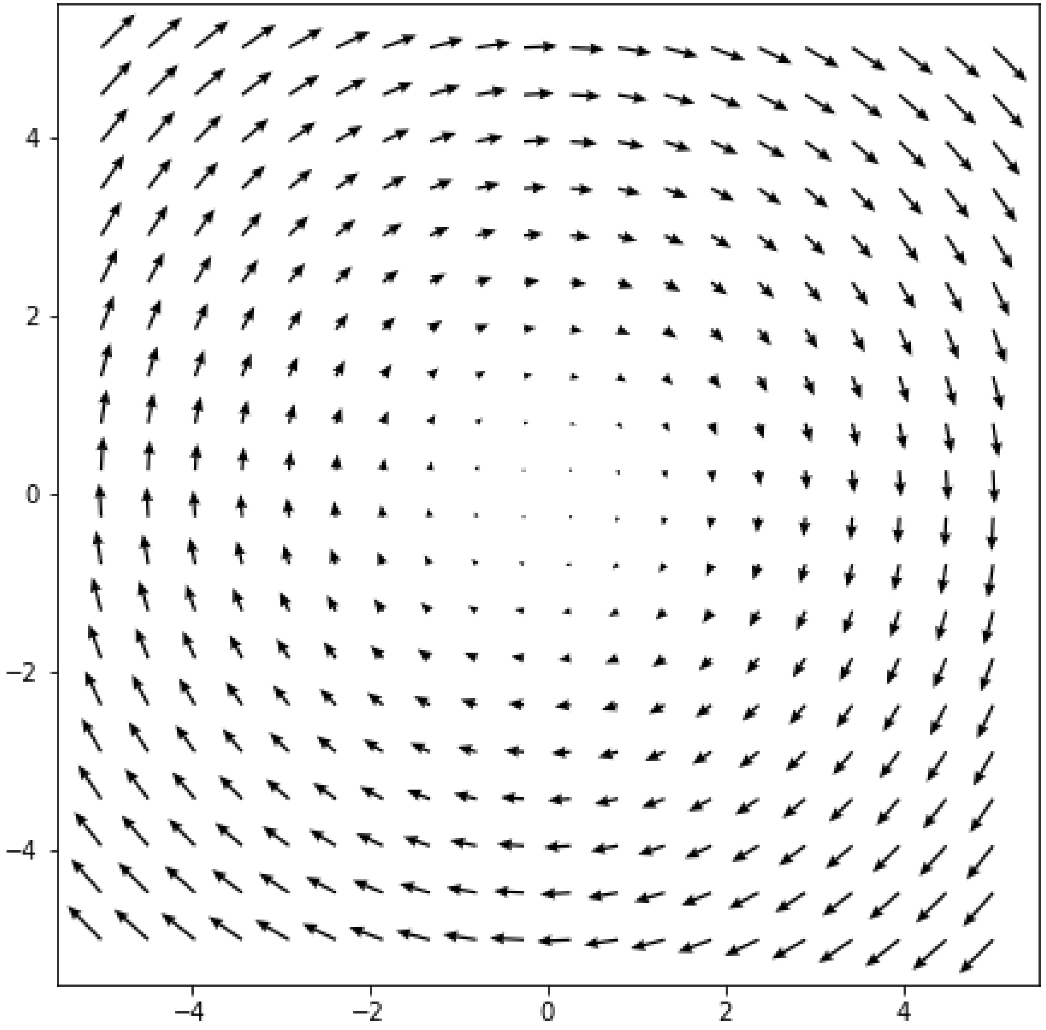
$$\dot{X} = \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix} X \qquad \begin{cases} \dot{x} = y \\ \dot{y} = x \end{cases}$$

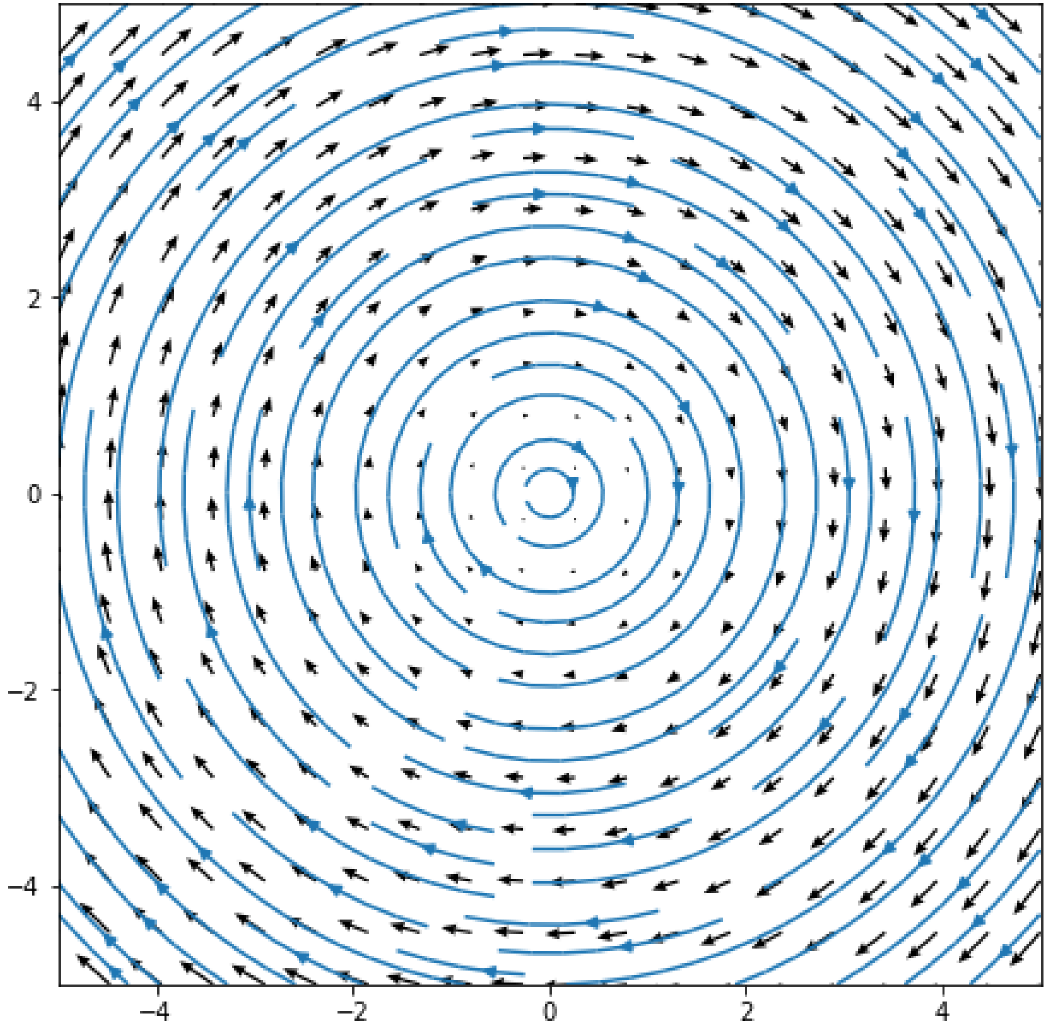




2-D Linear System

$$\dot{X} = \begin{bmatrix} 0 & 1 \\ -1 & 0 \end{bmatrix} X \qquad \begin{cases} \dot{x} = y \\ \dot{y} = -x \end{cases}$$

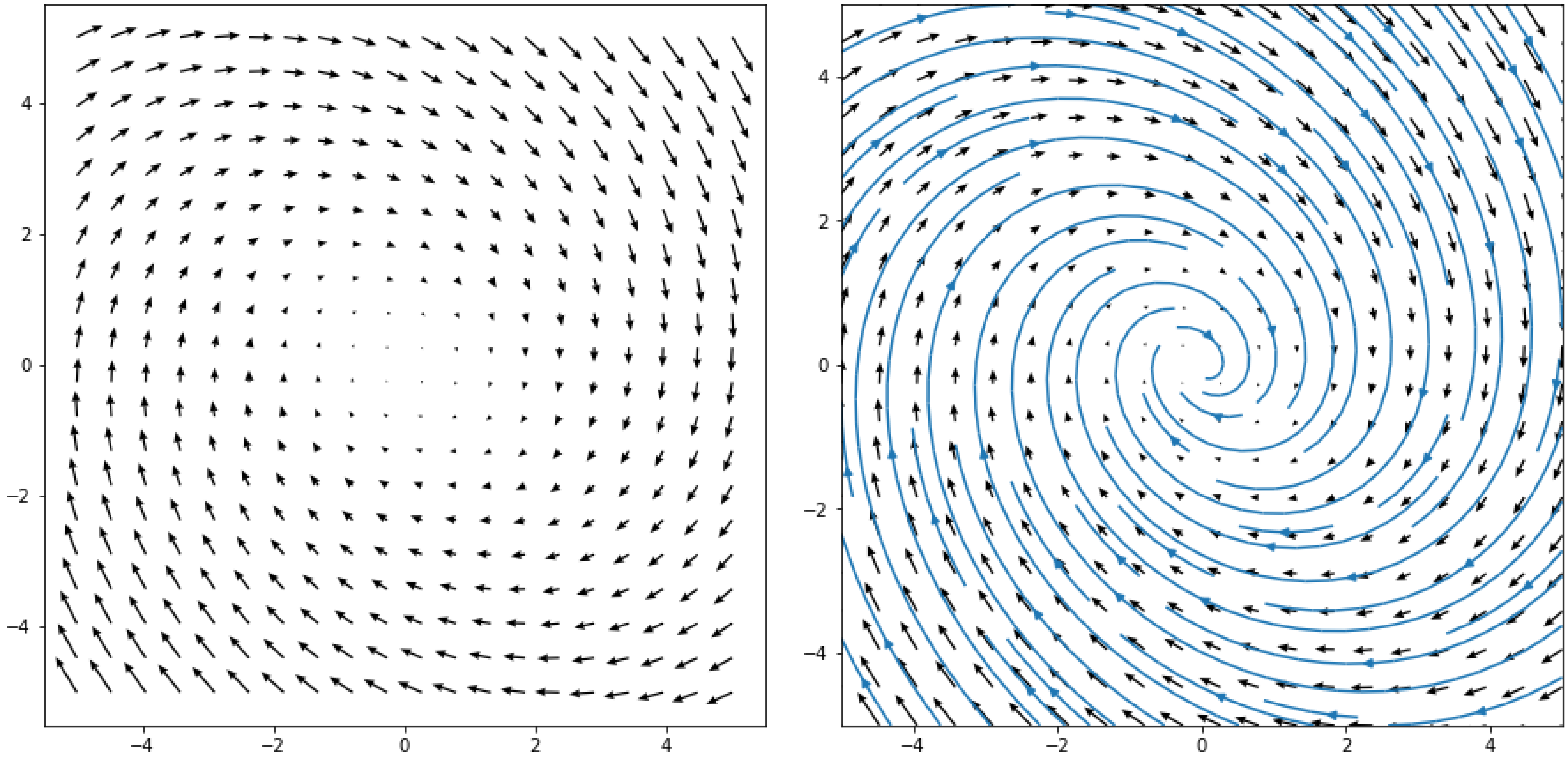




2-D Linear System

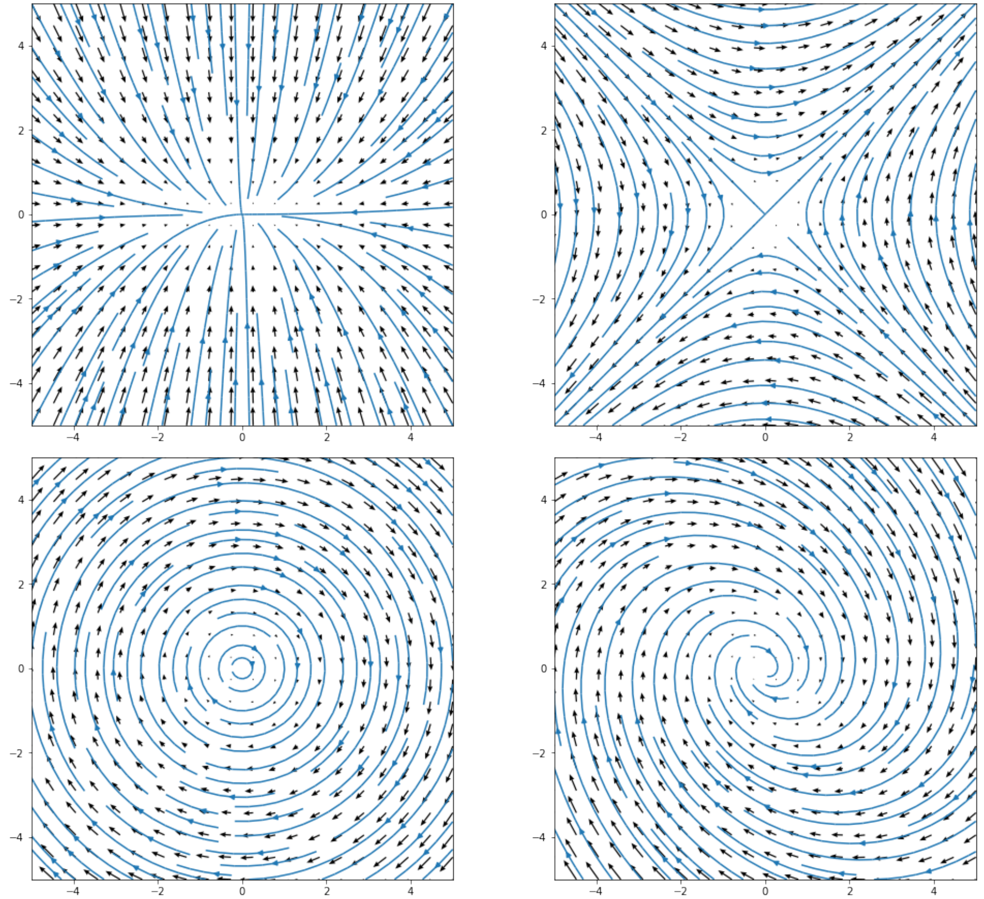
$$\dot{X} = \begin{bmatrix} -0.1 & 1 \\ -1 & -0.5 \end{bmatrix} X \qquad \begin{cases} \dot{x} = y - 0.1x \\ \dot{y} = -x - 0.5y \end{cases}$$

Stable Spiral



Eigenvalue is the Key

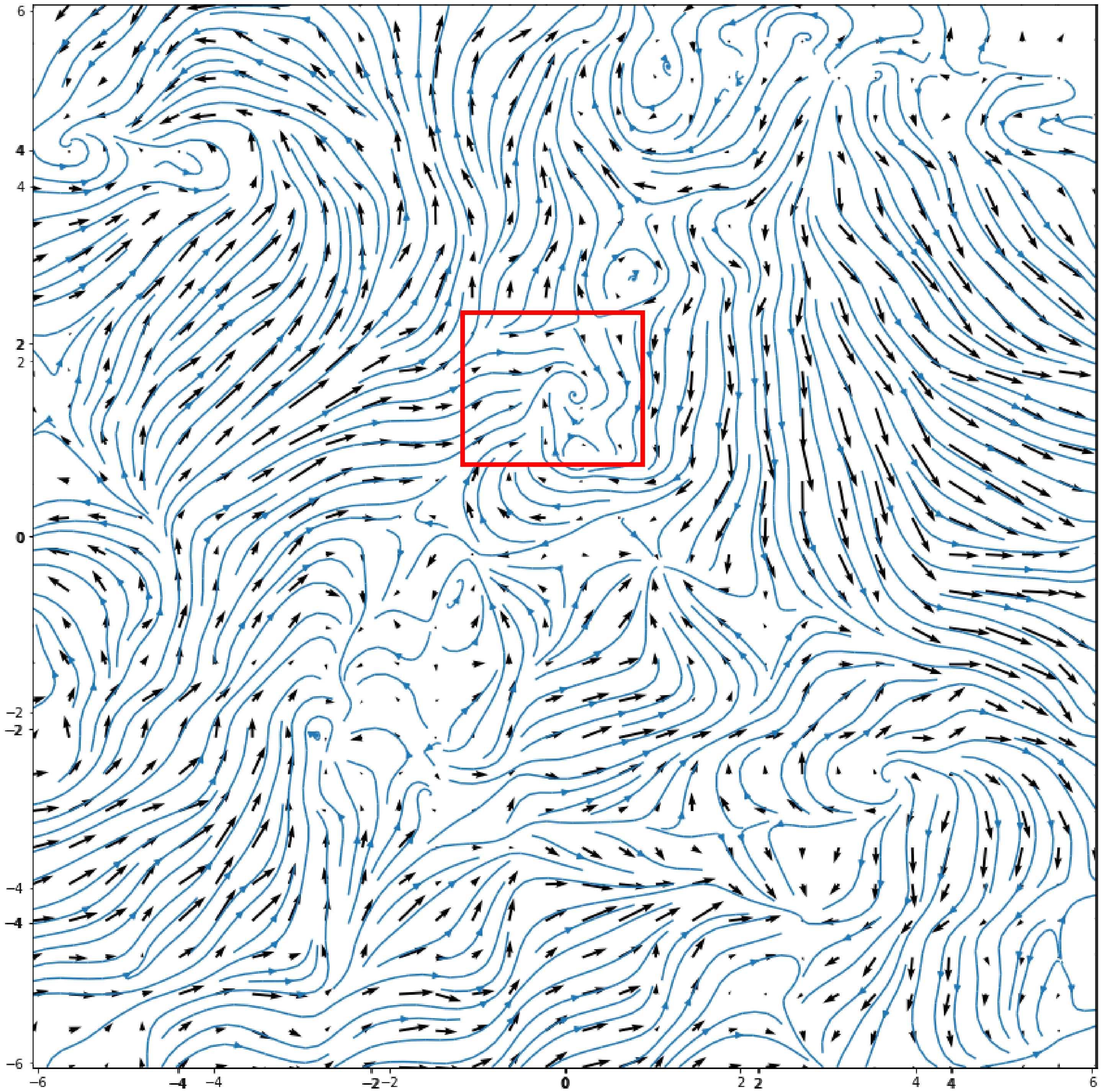
- Real eigenvalues
  - Attractor: $\lambda_1 < 0, \lambda_2 < 0$
  - Repeller: $\lambda_1 > 0, \lambda_2 > 0$
  - Saddle: $\lambda_1 < 0, \lambda_2 > 0$
- Complex eigenvalues
  - Center: $\lambda_1 = bi, \lambda_2 = -bi$
  - Stable Spiral: $\lambda_1 = a + bi, \lambda_2 = a - bi;\ a < 0$
  - Unstable Spiral: $\lambda_1 = a + bi, \lambda_2 = a - bi;\ a > 0$



- Sufficient and necessary condition for asymptotic stability of $\dot{X} = AX$
  - $Real(\lambda) < 0$ for all eigenvalue.

Locally Analysis of 2-D Nonlinear Systems

- $\dot{X} = f(X)$
  - $X \in \mathbb{R}^2, f: \mathbb{R}^2 \to \mathbb{R}^2$ usually nonlinear.
  - Vector field and flow on a plane!
  - Even complex dynamics have simple local motifs.



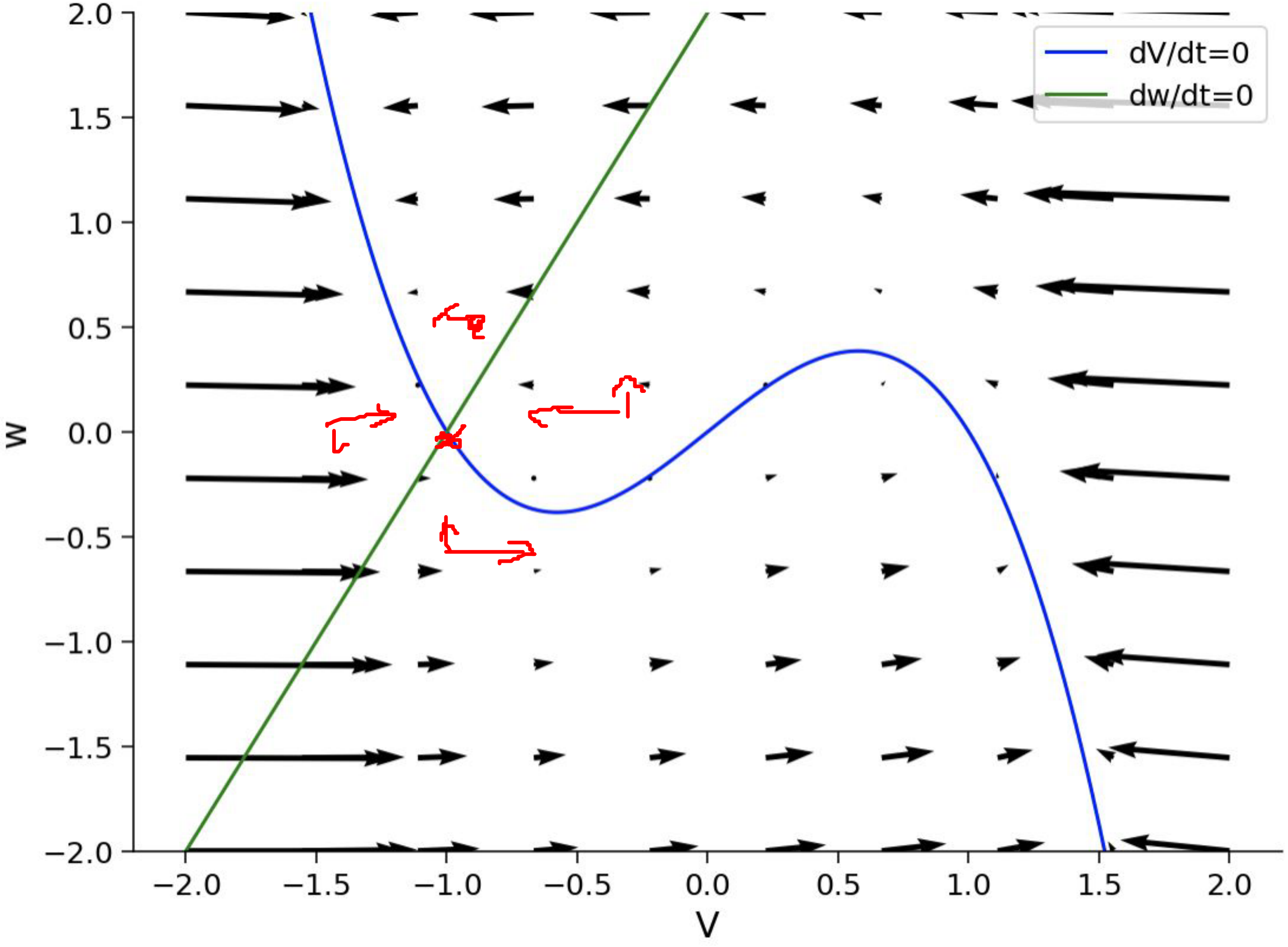
Example: FitzHugh-Nagumo Model

$$\frac{dV}{dt} = V - V^3 - W + I$$

$$\frac{dW}{dt} = 0.08(V + 0.7 - 0.8W)$$

- Note the 0.08
  - What that mean for the vector field? Dynamics?
  - Great speed / time scale difference in V and W

Nullcline for Qualitative Analysis

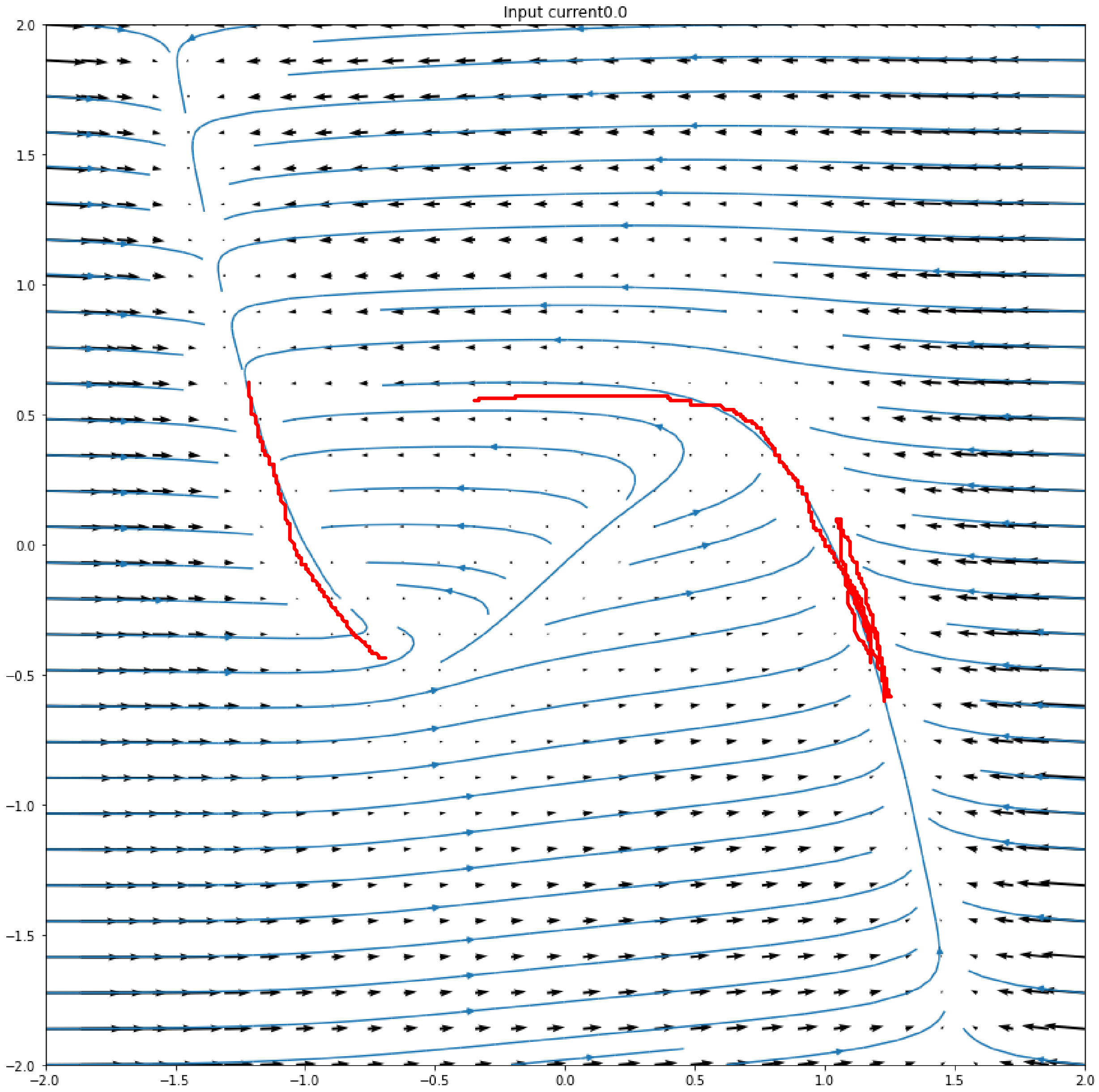


Mystery of Spiking: How can a constant input generate oscillatory response?!

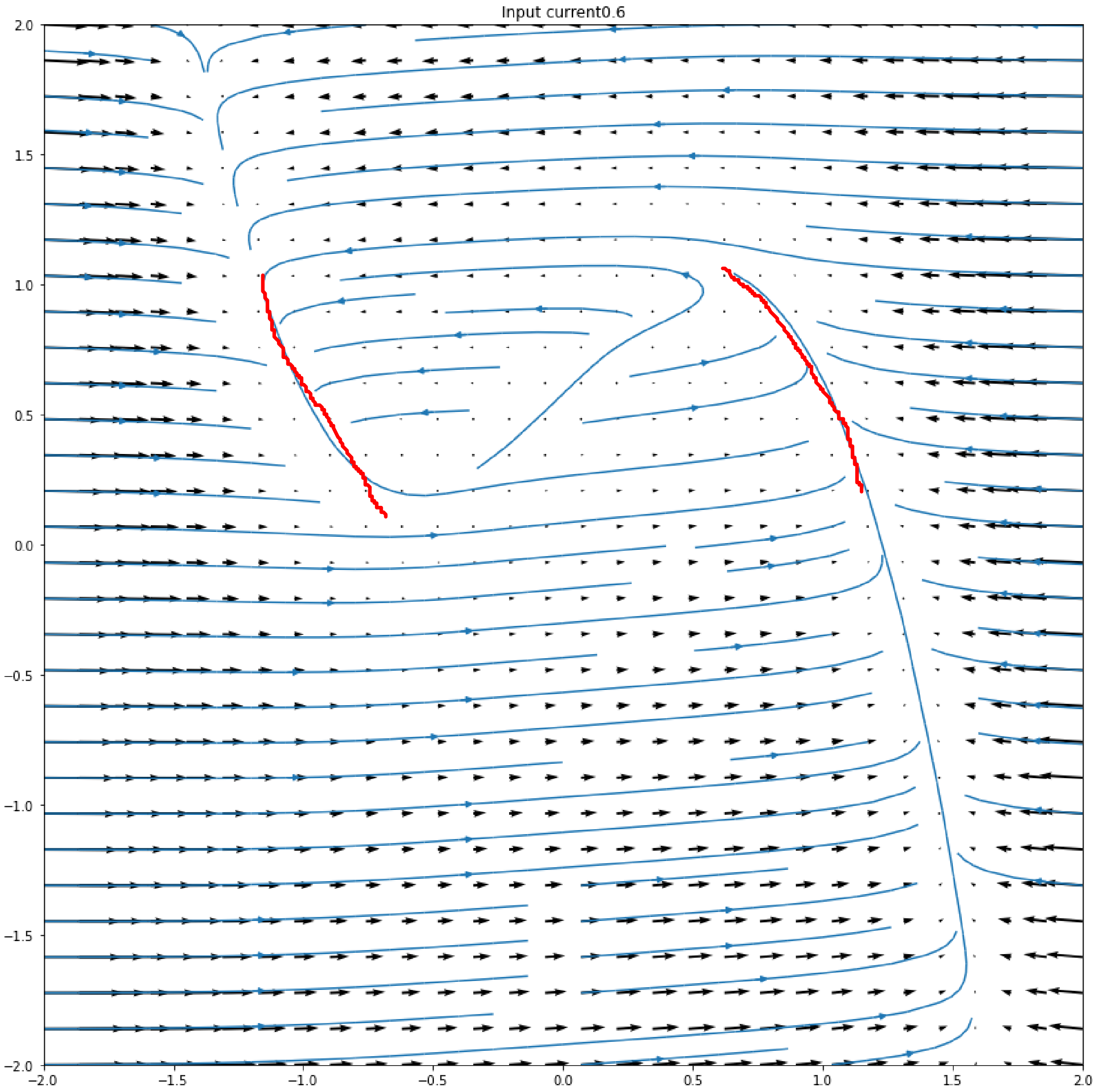
Limit cycle is the answer! Only exist in nonlinear system > 2D.

No limit cycle in 1-D system, need to manual reset.

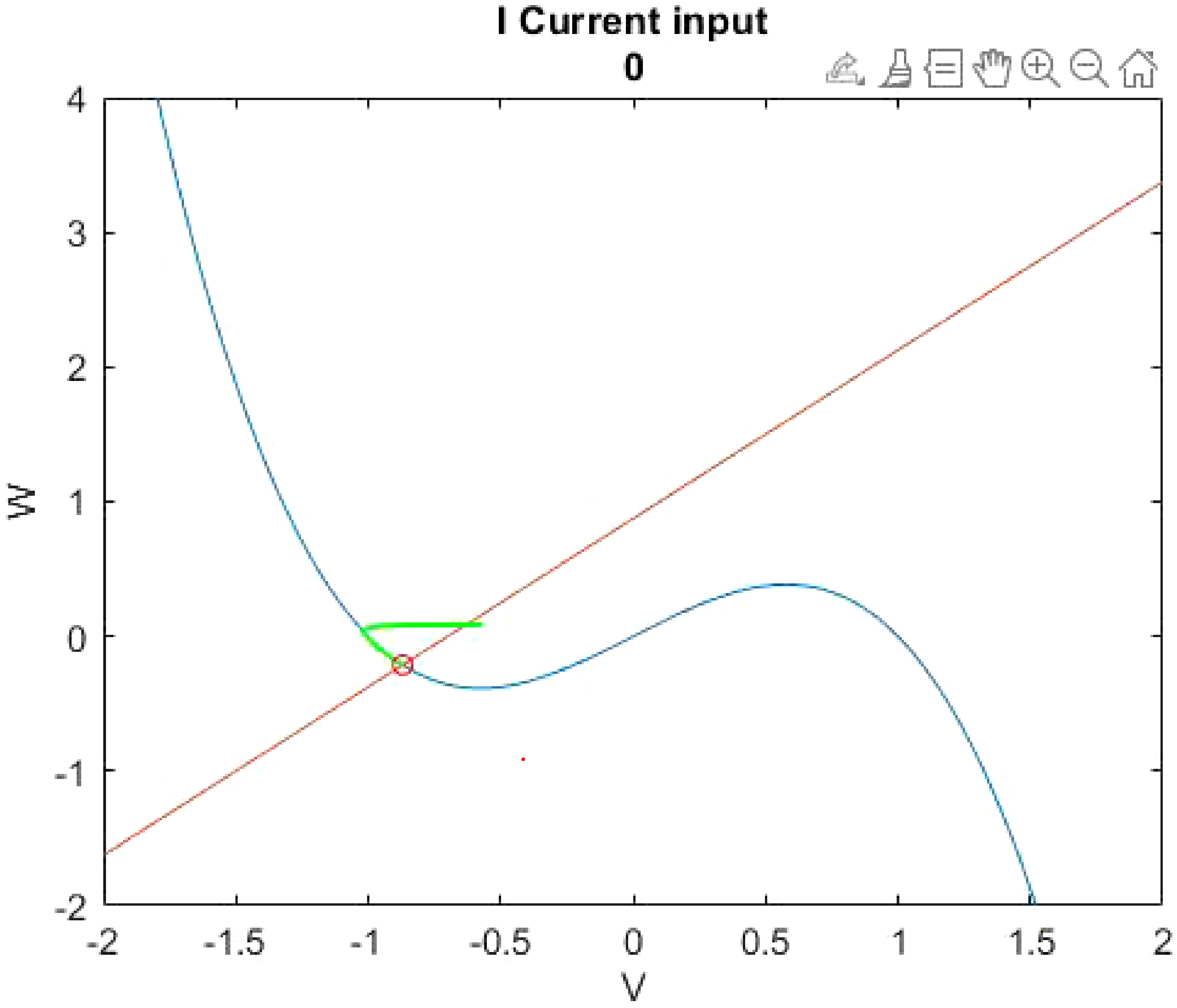
Vector field without Spike / Limit Cycle



Vector field with Spike / Limit Cycle



Proof Our Intuition by Simulation



Hodgkin-Huxley Model and Biophysics Review

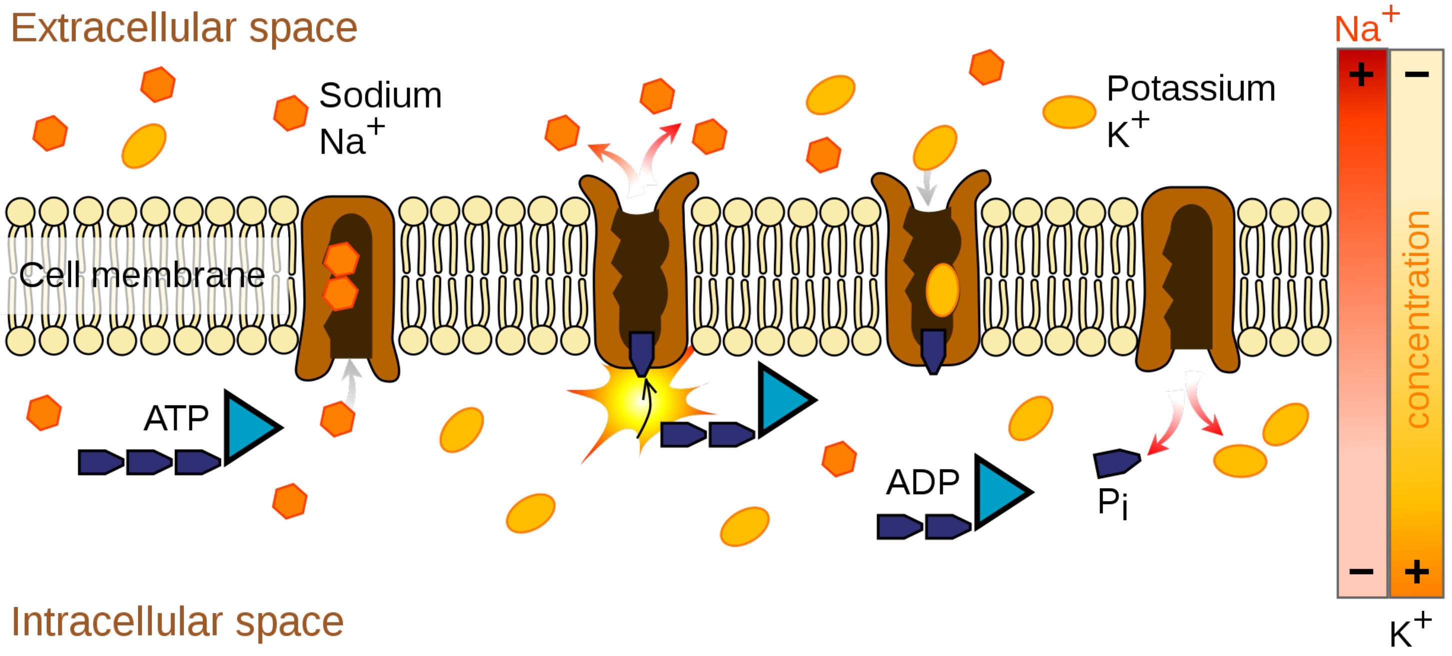
All models are wrong, some are useful.

--George Box

H-H is one of those hyper useful models…

Why there is a difference of electric potential across cellular membrane?

- What are some key players?
  - Semi-permeability of membrane
  - Ion(s)
  - Ion pumps
  - Concentration gradient



Reversal Potential / Nernst Potential

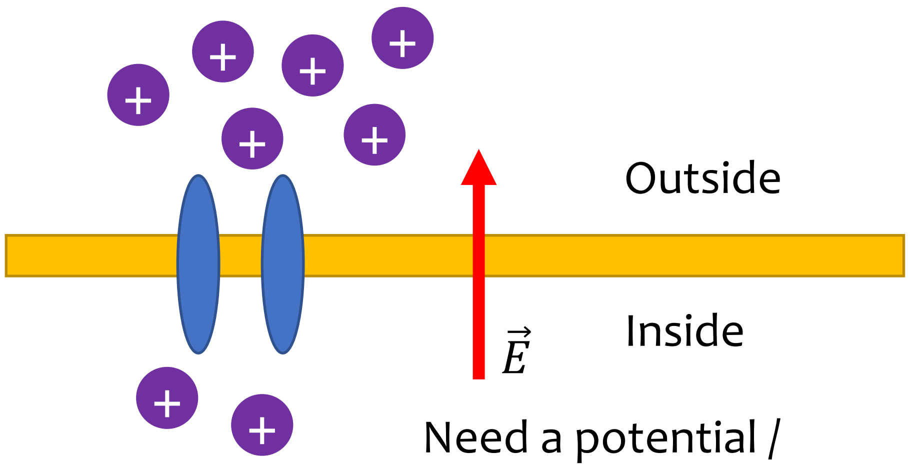
- The electric field / potential to balance the diffusion due to concentration gradient
- Quick derivation from Boltzmann distribution

$$\frac{\exp(-qV_{out}\beta)}{\exp(-qV_{in}\beta)} = \frac{n_{out}}{n_{in}}$$

$$\Delta V_{in-out} = \frac{1}{q\beta} \ln \frac{n_{out}}{n_{in}}$$

$$q = e, \beta = 1/k_B T$$

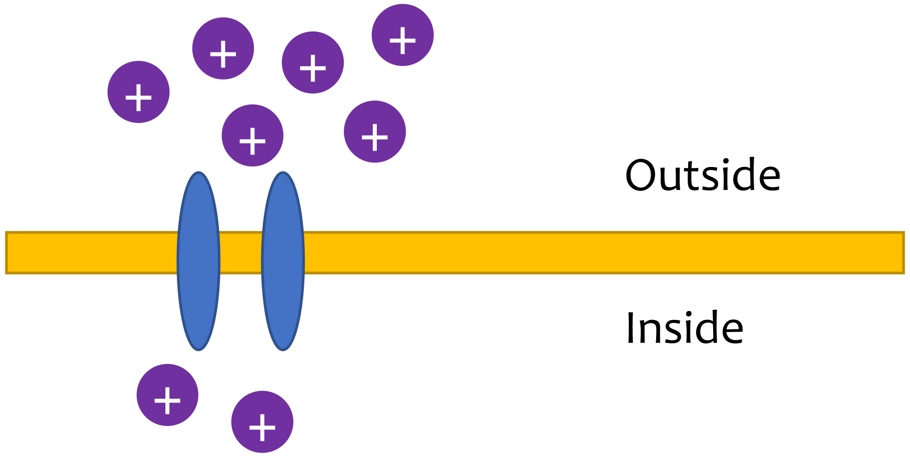
$$R = N_A k_B; F = eN_A$$



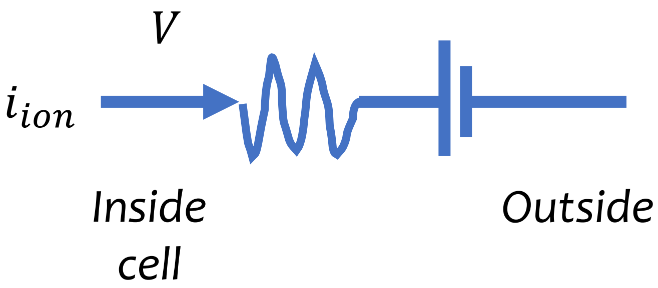
Need a potential / electric field to counterbalance the diffusion.

Model for One Channel / Ion

- $i_{ion} = g_{ion}(V - E_{ion})$
  - Driving force
  - $\times$
  - Conductance



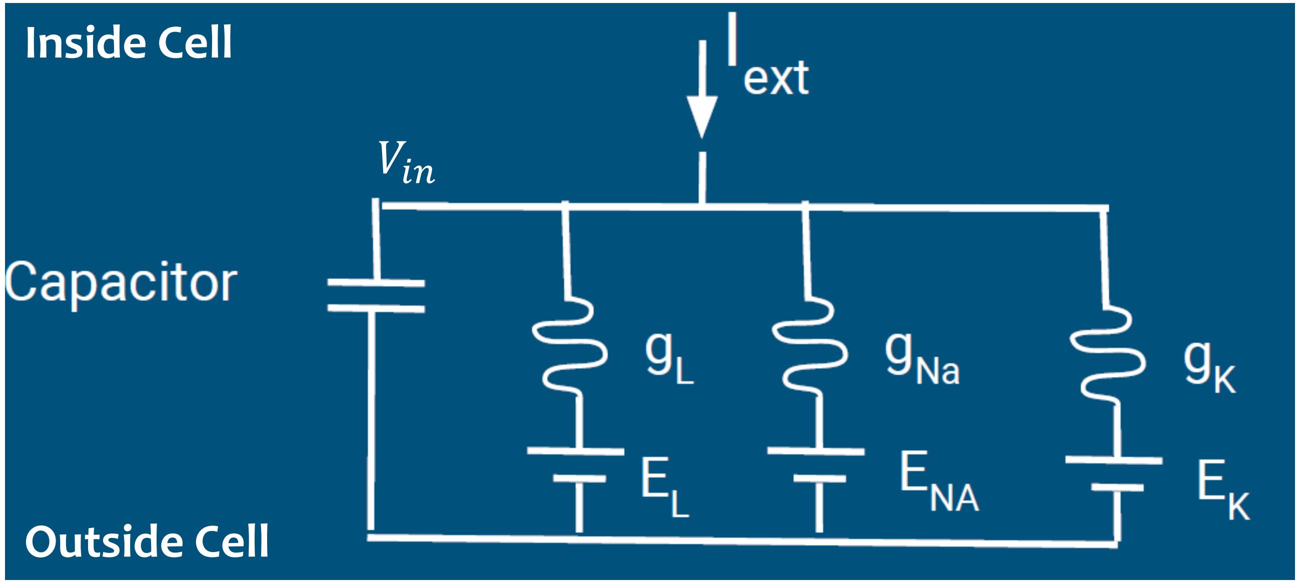
- When $V < E_{ion}$ what's the direction of ion flow?



- Why called reversal potential?

Membrane as Circuit

- What are the cellular correspondence of these?
  - Battery ⇔
    - Gradient of Ion Concentration
  - Capacitor ⇔
    - Membrane Lipid bilayer
  - Conductor / Resistor ⇔
    - Ion Channels



- General equation of membrane potential
  - $C\frac{dV}{dt} + \sum_{ion} g_{ion}(V - E_{ion}) = I_{ext}$

Voltage equation

$$C_m \frac{dV}{dt} = -g_{Na}(V - E_{Na}) - g_K(V - E_K) - g_L(V - E_L) + I_{ext}$$

- Na+ channel open
  - -> pull up the Voltage
- K+ channel open
  - -> pull down the Voltage
- Leaky channel
  - -> return to resting
- C_m
  - Capacity ~ time constant

Squid Axon

Ion	Conc in	Conc out	Equilibrium Potential
Na+	50	440	55
K+	400	20	-76
Cl-	40	560	-66
Ca++	0.4	10	145

Mammalian Neuron

Ion	Conc in	Conc out	Equilibrium Potential
Na+	18	145	56
K+	135	3	-102
Cl-	7	20	-76
Ca++	0.0001	1.2	125

Dynamics of Channel

- Voltage dependency.

$$\dot{m} = \alpha(V)(1-m) - \beta(V)m$$

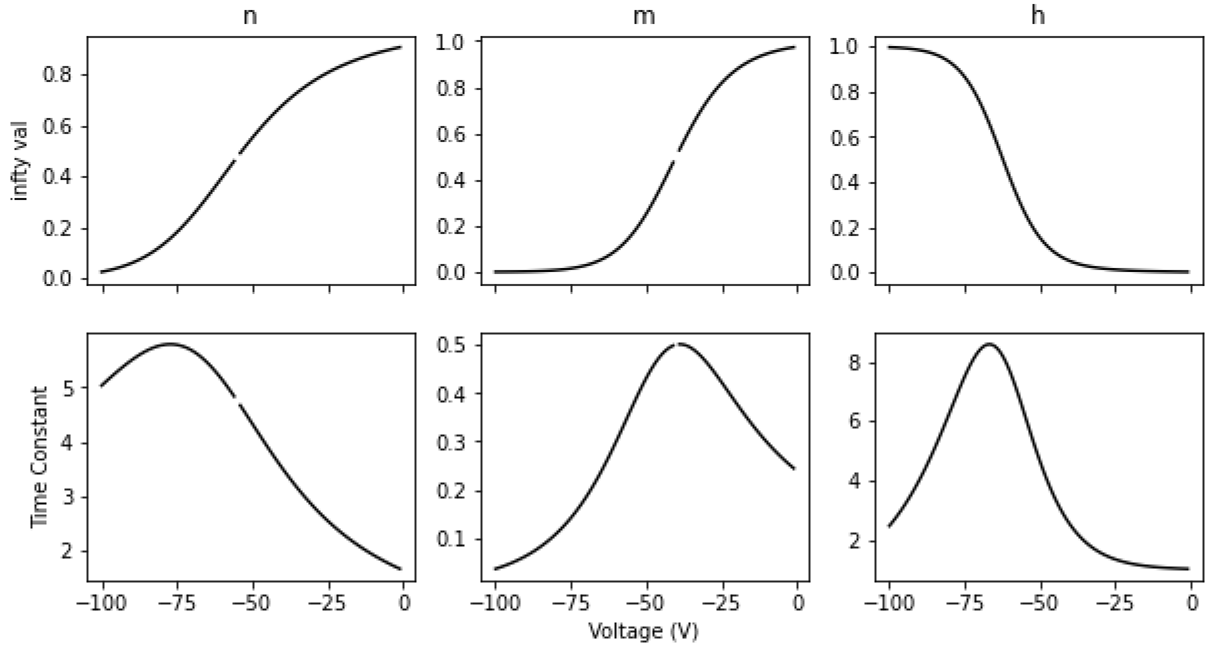
$$\dot{m} = -\frac{1}{\tau_m(V)}\left(m - m_\infty(V)\right)$$

$$m_\infty(V) = \frac{\alpha(V)}{\alpha(V)+\beta(V)}$$

$$\tau_m = \frac{1}{\alpha(V)+\beta(V)}$$

- Chasing a moving equilibrium
- Extreme case, fast convergence

$$m(t) = m_\infty(V(t))$$



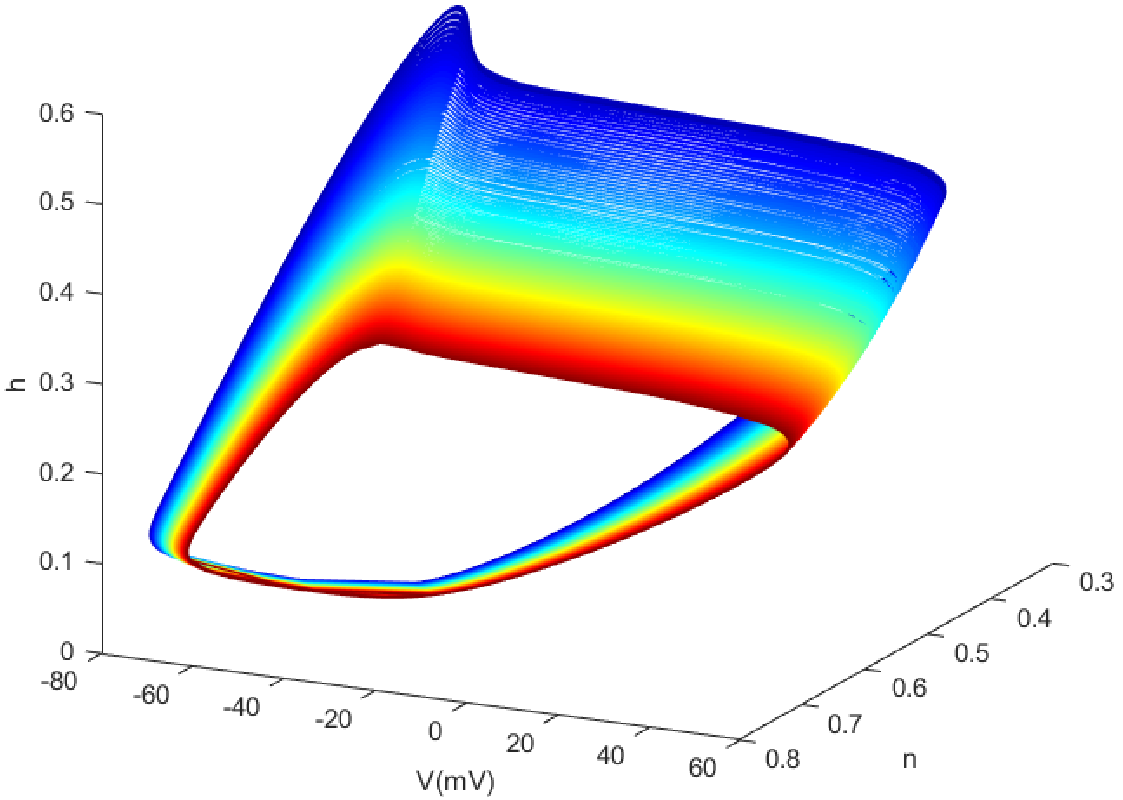
Modified from HW3

- Gating dynamics

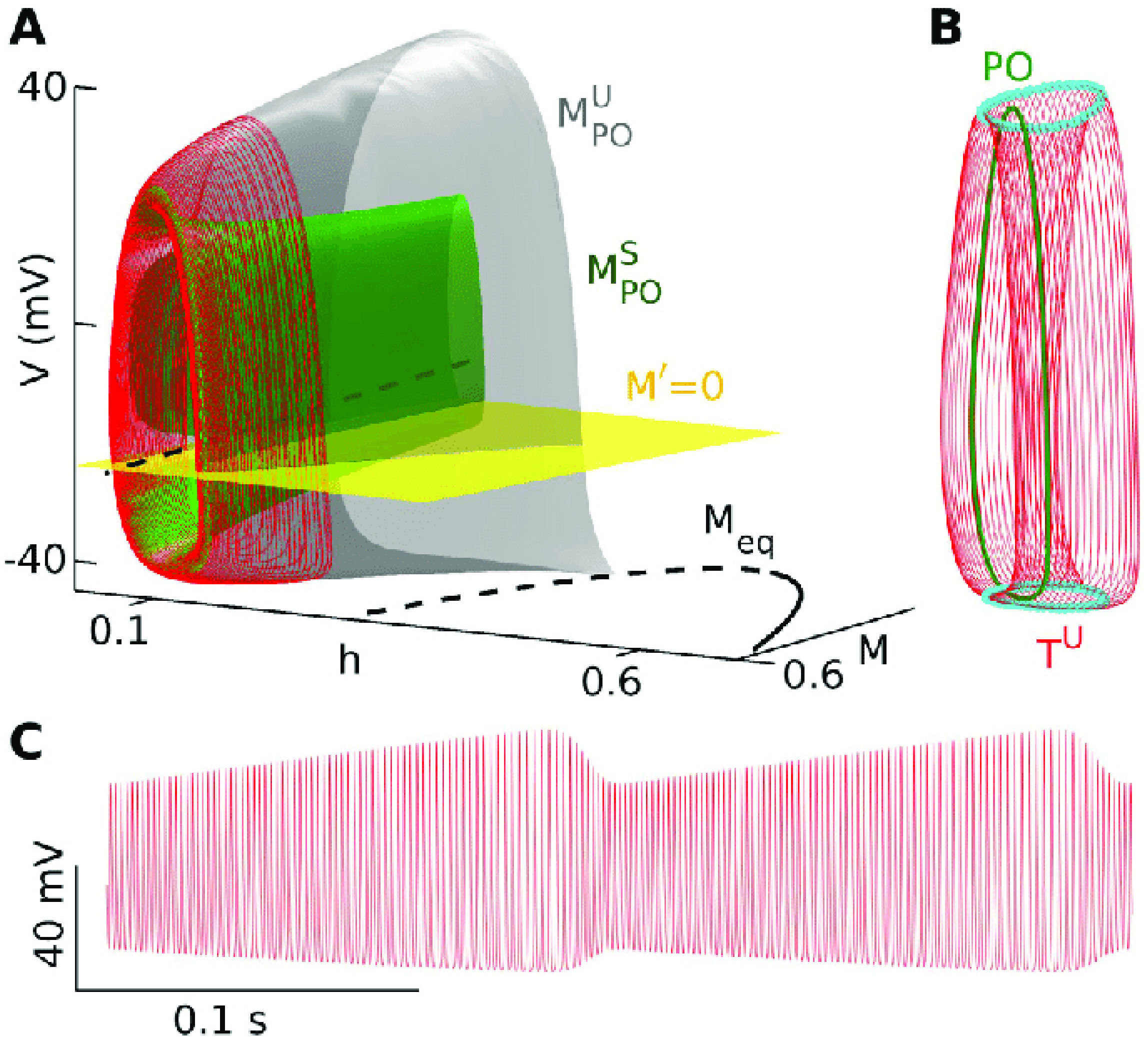
$$g_{Na} = \overline{g_{Na}} m^3 h$$

$$g_K = \overline{g_K} n^4$$

H-H model in phase space



Blue to Red color correspond to low to high current level (my matlab)



https://www.researchgate.net/figure/a-3D-h-M-V-phase-space-projection-of-the-Purkinje-cell-model-at-I-app-29487_fig6_328254161

Other Views of the H-H Manifold