Physiological Modeling

Parametric

- *Structural*
- *System Components*
- *Differential Equations*

Nonparametric

- *Functional*
- *System Kernels*
- *Integral Equations*

Functional and Structural Identification of Systems

I. Input-output relationships in a 'Black-Box' approach

In the absence of detailed information about the system's inner structure, stimulus-response experiments are performed. This leads to functional identification when prediction of response to an arbitrary stimulus is achieved.

II. Interactions between the component of the system which indicate how does the system work

This is achieved by breaking open the 'black box' and looking inside at the various components. This leads to structural identification of the system.

Parametric Models

Rate Processes

- Laws governing the rate of change of quantities such as
  distance (limb movements, diffusion of ions, ...),
  concentration (ions, drugs, ...),
  current (ionic, cellular, ...),
  voltage (cellular, surface, ...).

- Dynamical systems characterized by differential equations.

- Perspectives:
  Conceptual, geometrical
  mathematical, physiological

DYNAMICAL SYSTEMS

LINEAR

Superposition principle holds

FIXED

TIME VARYING

NONLINEAR

Superposition principle does not hold

Second Order Systems

Consider two first order systems

$$\frac{dx}{dt} = k_1 x$$

$$\frac{dy}{dt} = k_2 y$$

Cross couple the two systems

$$\dot{x} = k_1 x + c_1 y$$

$$\dot{y} = k_2 y + c_2 x$$

$$\therefore \quad \ddot{x} = k_1 \dot{x} + c_1 \dot{y}$$

$$= (k_1 + k_2)\dot{x} - (k_1 k_2 - c_1 c_2) x$$

$$\ddot{x} - (k_1 + k_2)\dot{x} + (k_1 k_2 - c_1 c_2) x = 0$$

$$\boxed{\ddot{x} + P\dot{x} + Q x = 0}$$

where

$$P = -(k_1 + k_2) \triangleq \text{Damping Coefficient}$$

$$Q = (k_1 k_2 - c_1 c_2) \triangleq \text{Stiffness Coefficient}$$

1. Time Invariant Linear Systems

$$\ddot{x} + P\dot{x} + Qx = F$$

2. Time Varying Linear Systems

$$\ddot{x} + P(t)\dot{x} + Q(t)x = F$$

♫

P and Q are functions of the $\boxed{\text{independent}}$ variable "t".

3. Nonlinear Systems

$$\ddot{x} + P(x)\dot{x} + Q(x)x = F$$

♫

P and Q are functions of the $\boxed{\text{dependent}}$ variable "x".

If $P(x) = \alpha\,[x^2 - 1]$

$Q(x) = \omega^2$

$\Rightarrow$ The Van der Pol equation.

A Geometrical View of Second Order Systems

Consider a linear system

$$\ddot{x} + P\dot{x} + Qx = 0$$

Free Running

Case 1 : Undamped Harmonic Oscillator
$P = 0$

$$\ddot{x} + Qx = 0$$

The second order differential equation can be written as two first order simultaneous differential equations

Let $\dot{x} = y$

then $\dot{y} = -Qx$

The xy plane is called the phase plane or state plane as it represents the totality of all possible states of the system.

To eliminate time and obtain the integral curves

$$\boxed{\frac{dy}{dx} = \frac{\dot{y}}{\dot{x}}} = -Q\,\frac{x}{y}$$

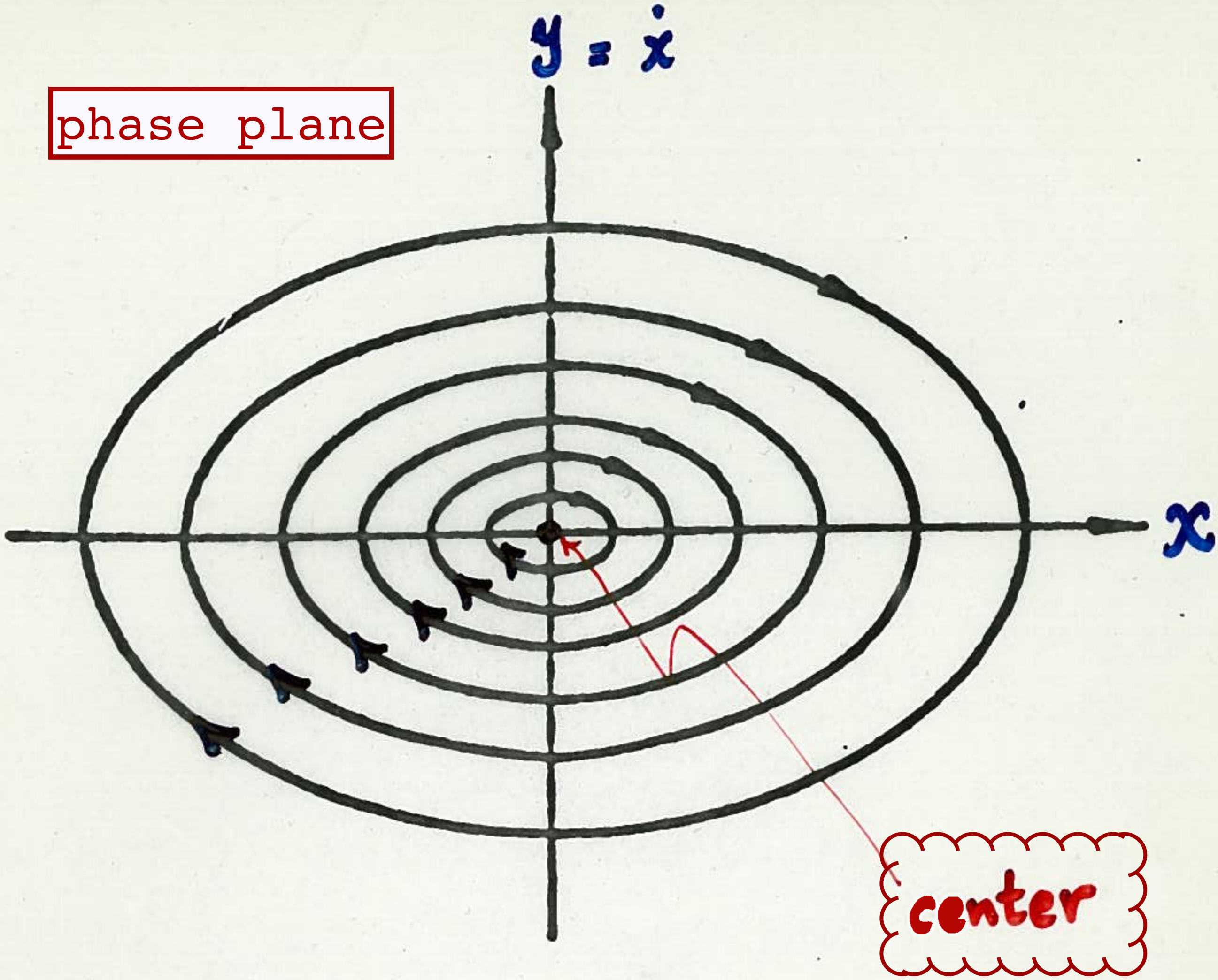
$$x\,dx + \frac{1}{Q}\,y\,dy = 0$$

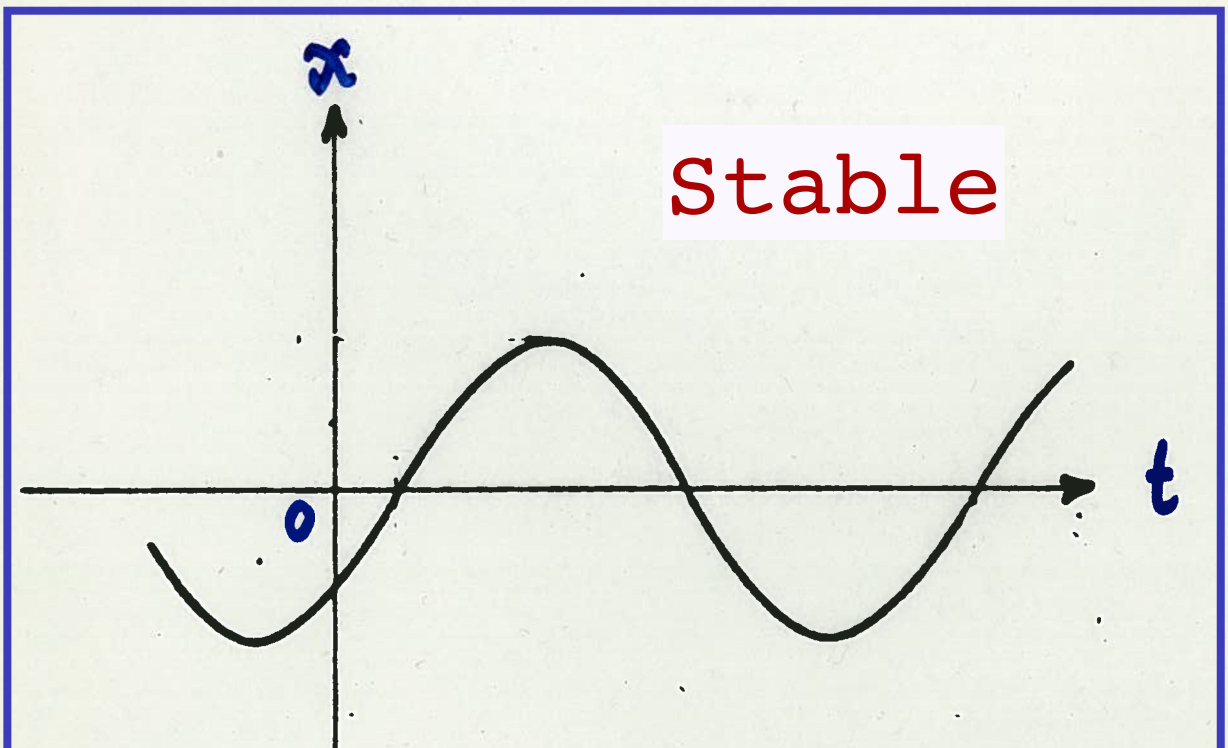
$$\boxed{\frac{x^2}{A} + \frac{y^2}{AQ} = 1}$$

A is a constant of integration

These are the trajectories of motion of the state point on the state plane.

They are also called trajectories of state or paths of phase.


phase plane
$y = \dot{x}$
x
center


x
Stable
0
t

* A Singular Point is a state point at which $\boxed{\dot{x} = \dot{y} = 0}$.

The equation for the integral curve becomes indeterminate at a singular point.

$$\boxed{\text{There is an equilibrium state at a singular point which may be either stable or unstable.}}$$

Periodic motion on the trajectories of the state point, since an ellipse has finite length and since phase velocity is not zero any where on the trajectory.

$$\boxed{\text{Phase velocity} = \bar{v}_\phi = \dot{x}\,\bar{i} + \dot{y}\,\bar{j}}$$

$$|\bar{v}_\phi| = \sqrt{y^2 + Q^2 x^2} > 0 \quad \text{for } x, y \neq 0$$

A closed trajectory represents a periodic phenomenon.

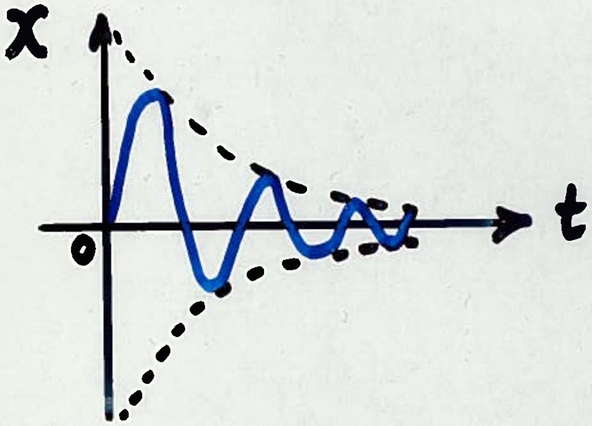
Case 2 : Damped Free Running Oscillator $P \neq 0$

$$\ddot{x} + P\dot{x} + Qx = 0$$

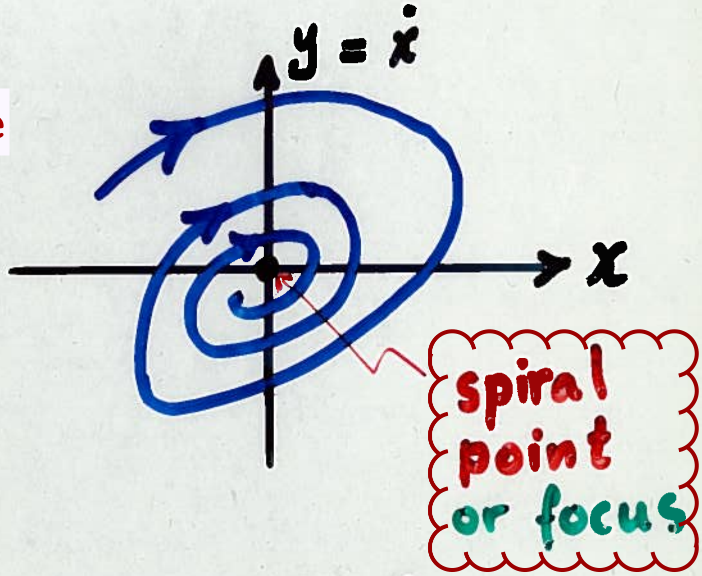
For $4Q > P^2$, solution is

$$x = C\,e^{-\frac{P}{2}t} \sin\left(\sqrt{Q - \frac{P^2}{4}}\,t + \phi\right)$$

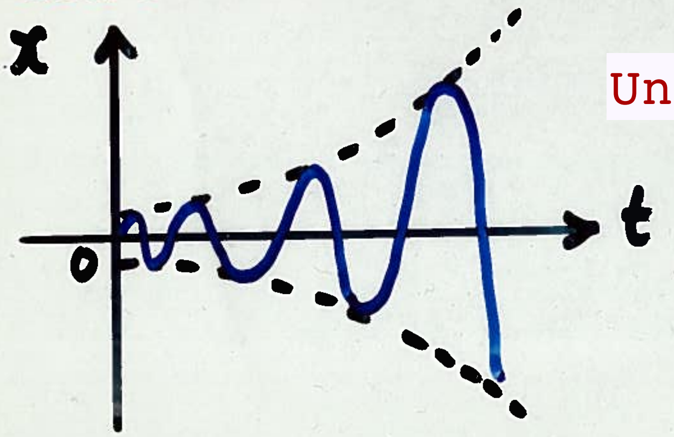
For $P > 0$



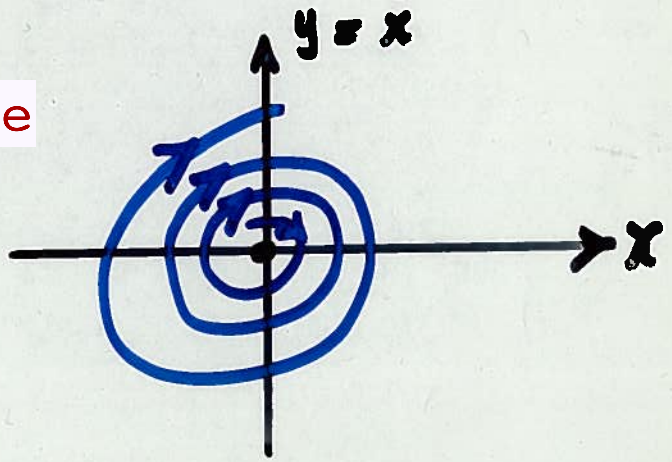
Stable



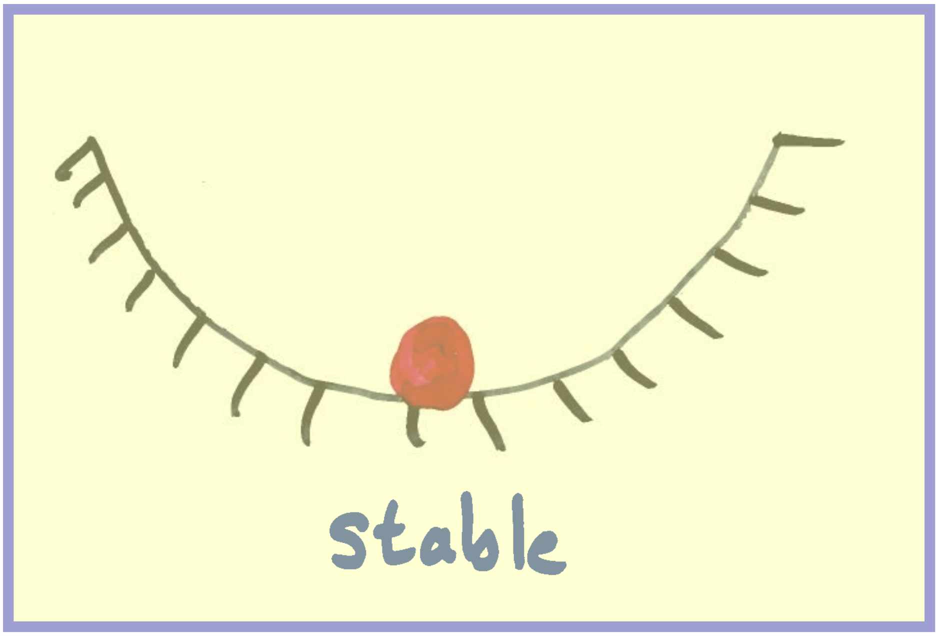
For $P < 0$



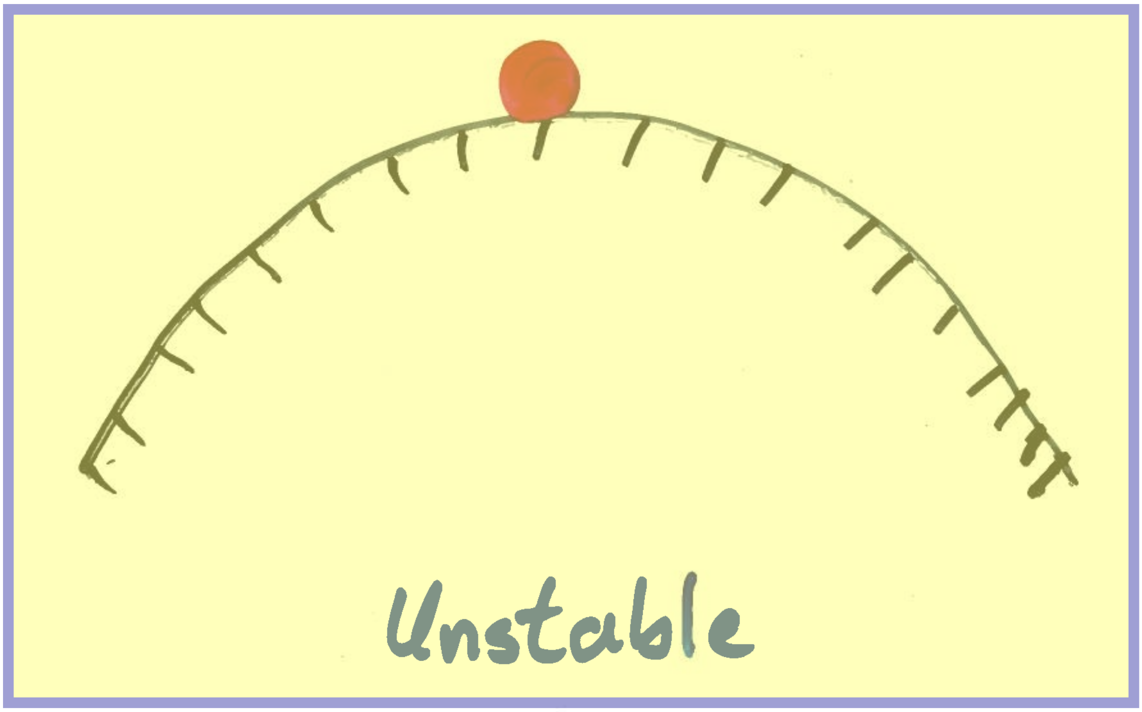
Unstable



Absolute Stability



- Check through perturbations

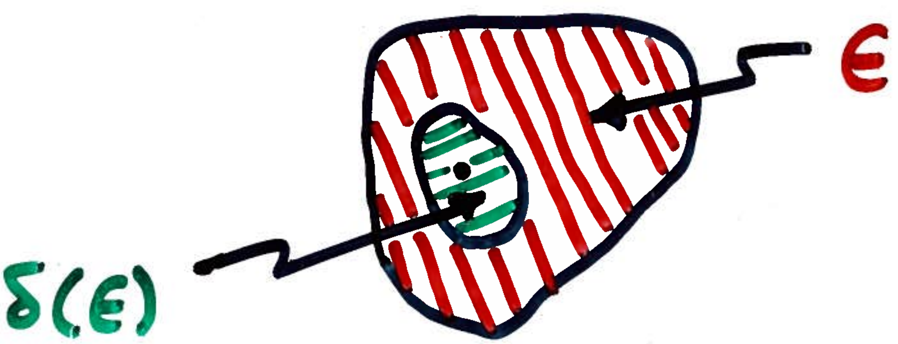


Stability of a State of Equilibrium

1. **Absolute Stability** (Asymptotic Stability)

For any perturbation the system returns (after a sufficiently long interval) arbitrarily close to the position of equilibrium.

2. **Lyapunov Stability**



A state of equilibrium is stable if, for any assigned region ϵ of possible deviations there is a region $\delta(\epsilon)$ such that no motion beginning within $\delta(\epsilon)$, ever reaches the boundary of ϵ.

♬ An equilibrium point is stable (in the Lyapunov sense) if all trajectories starting at nearby points stay nearby; otherwise it is unstable. It is asymptotically stable (or have absolute stability) if all trajectories starting at nearby points not only stay nearby but also tend to the equilibrium point as time approaches infinity.

♬ Absolute stability is a stronger stability condition than Lyapunov stability.

Lyapunov Stability of Singular Points

Let $\dot{x} = \mathcal{F}_1(x, y)$

$\dot{y} = \mathcal{F}_2(x, y)$

Let $\underset{\sim}{v} = \begin{bmatrix} x \\ y \end{bmatrix}$ and $\underset{\sim}{\mathcal{F}} = \begin{bmatrix} \mathcal{F}_1 \\ \mathcal{F}_2 \end{bmatrix}$

$$\therefore \quad \dot{\underset{\sim}{v}} = \underset{\sim}{\mathcal{F}}(\underset{\sim}{v})$$

Linearization around a singular point $\hat{\underset{\sim}{v}}$

$$\Rightarrow \Delta \underset{\sim}{\mathcal{F}}(\underset{\sim}{v}) = \underset{\sim}{A} \, \Delta \underset{\sim}{v}$$

Taylor series

$$\underset{\sim}{A} = \left. \frac{\partial \underset{\sim}{\mathcal{F}}}{\partial \underset{\sim}{v}} \right|_{\underset{\sim}{v} = \hat{\underset{\sim}{v}}}$$

$\Rightarrow$ Jacobian Matrix $= \dfrac{\partial \underset{\sim}{\mathcal{F}}}{\partial \underset{\sim}{v}} = \begin{bmatrix} \dfrac{\partial \mathcal{F}_1}{\partial x} & \dfrac{\partial \mathcal{F}_1}{\partial y} \\ \dfrac{\partial \mathcal{F}_2}{\partial x} & \dfrac{\partial \mathcal{F}_2}{\partial y} \end{bmatrix}$

$$\det(\underset{\sim}{A} - \hat{\lambda} \underset{\sim}{I}) = 0$$

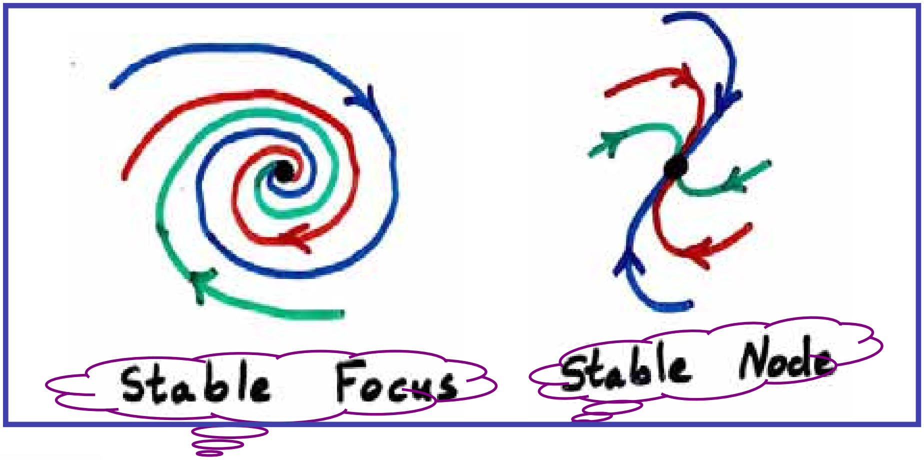
$\Rightarrow$ eigen values of $\underset{\sim}{A}$

$\hat{\lambda}_1 = \alpha_1 + i\beta_1$ and $\hat{\lambda}_2 = \alpha_2 + i\beta_2$

	$\beta_1 = -\beta_2$	$\beta_1 = \beta_2 = 0$
$\alpha_1 = \alpha_2 = 0$	stable centre	–
$\alpha_1 < 0$, $\alpha_2 < 0$	stable focus	stable node
$\alpha_1 > 0$, $\alpha_2 > 0$	unstable focus	unstable node
$\alpha_1 > 0$, $\alpha_2 < 0$	–	unstable saddle point

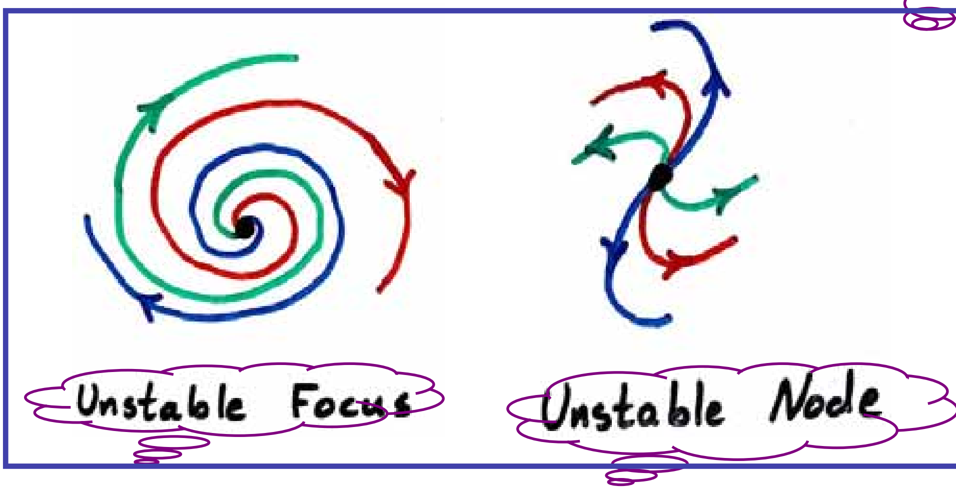
♫ In general, for an nth order system, an equilibrium state is stable if the eigen values of the Jacobian matrix have no positive real parts, otherwise it is unstable. (Provided that the Jacobian matrix is nonsingular)

A focus has rotations of state around it. A node has no rotations as indicated by the imaginary part of the eigen values.


Stable Focus
Stable Node


Centre
(Always Stable)


Saddle Point
(Always Unstable)


Unstable Focus
Unstable Node

Example: The Volterra-Lotka Ecosystem Model (Prey-Predator Problem)

Let x = number of members of prey species

y = number of members of predators.

$$\boxed{\begin{aligned} \dot{x} &= (1-y)\,x \\ \dot{y} &= (x-1)\,y \end{aligned}}$$

predators $\uparrow$ $\Rightarrow$ prey $\downarrow$

prey $\uparrow$ $\Rightarrow$ predator $\uparrow$

Jacobian Matrix $= \begin{bmatrix} 1-y & -x \\ y & x-1 \end{bmatrix}$

Singular Points $(0,0)$ and $(1,1)$

at $(0,0)$ $\Rightarrow$ $\underset{\sim}{A} = \begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}$

$$\det(\underset{\sim}{A} - \hat{\lambda}\underset{\sim}{I}) = (1-\hat{\lambda})(-1-\hat{\lambda}) = 0$$

$$\Rightarrow \quad \hat{\lambda}_1 = 1 \quad , \quad \hat{\lambda}_2 = -1$$

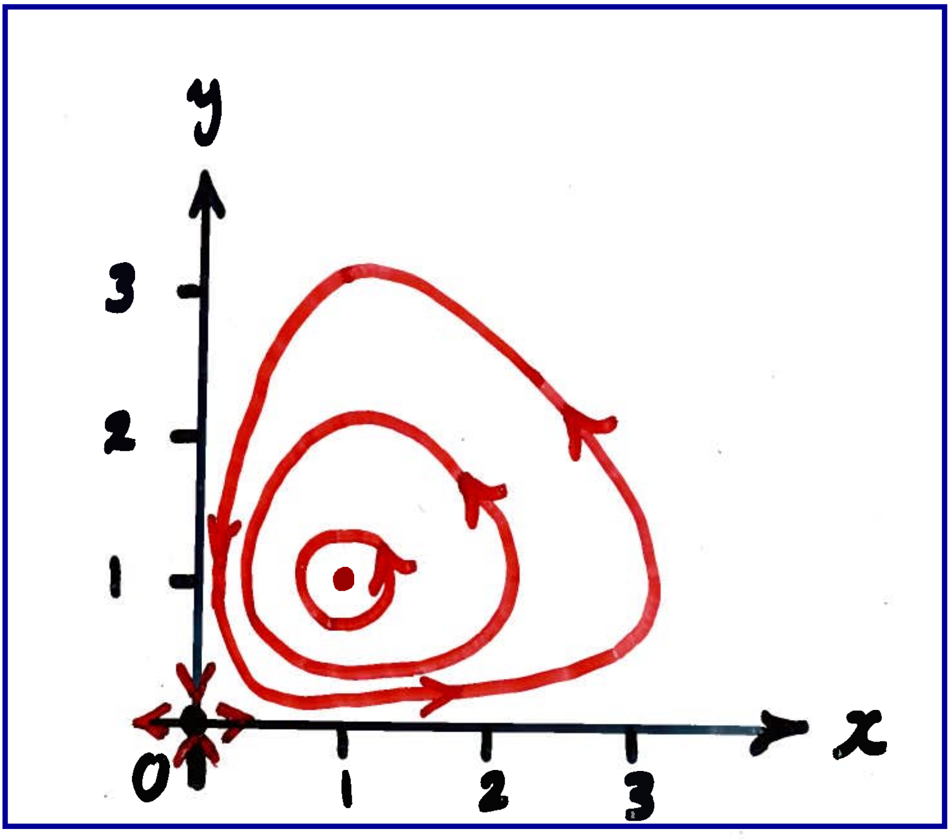
$\Rightarrow$ $\boxed{\text{origin is a saddle point}}$

at $(1,1)$ $\Rightarrow$ $\underset{\sim}{A} = \begin{bmatrix} 0 & -1 \\ 1 & 0 \end{bmatrix}$

$$\det(\underset{\sim}{A} - \hat{\lambda}\underset{\sim}{I}) = \hat{\lambda}^2 + 1 = 0$$

$$\Rightarrow \quad \hat{\lambda}_1 = i \quad , \quad \hat{\lambda}_2 = -i$$

$\Rightarrow$ $\boxed{(1,1) \text{ is a centre}}$



Stability of Limit Sets

* The local behavior of the flow near an equilibrium point is determined by linearizing the vector field at the equilibrium point.

I. Complex Eigenvalues

The real part of $\hat{\lambda}_i$ gives the rate of expansion (if $Re\ \hat{\lambda}_i > 0$) or contraction (if $Re\ \hat{\lambda}_i < 0$) of the spiral trajectory; the imaginary part of $\hat{\lambda}_i$ is the frequency of rotation.

II. Characteristic Multipliers

$$m_i = e^{\hat{\lambda}_i T} \quad \text{for any } T > 0$$

If $Re\ \hat{\lambda}_i$ is the rate of contraction or expansion then $|m_i|$ is the amount of contraction or expansion

$$\mathrm{Re}\ \hat{\lambda}_i < 0 \iff |m_i| < 1$$

$$\mathrm{Re}\ \hat{\lambda}_i > 0 \iff |m_i| > 1$$

Definition: An equilibrium point is called **hyperbolic** if $\mathrm{Re}\ \hat{\lambda}_i \neq 0$, or $|m_i| \neq 1$ for all "i".

III. Lyapunov Exponents

$$\lambda_i = \lim_{t\to\infty} \frac{1}{t} \ln |m_i(t)|$$

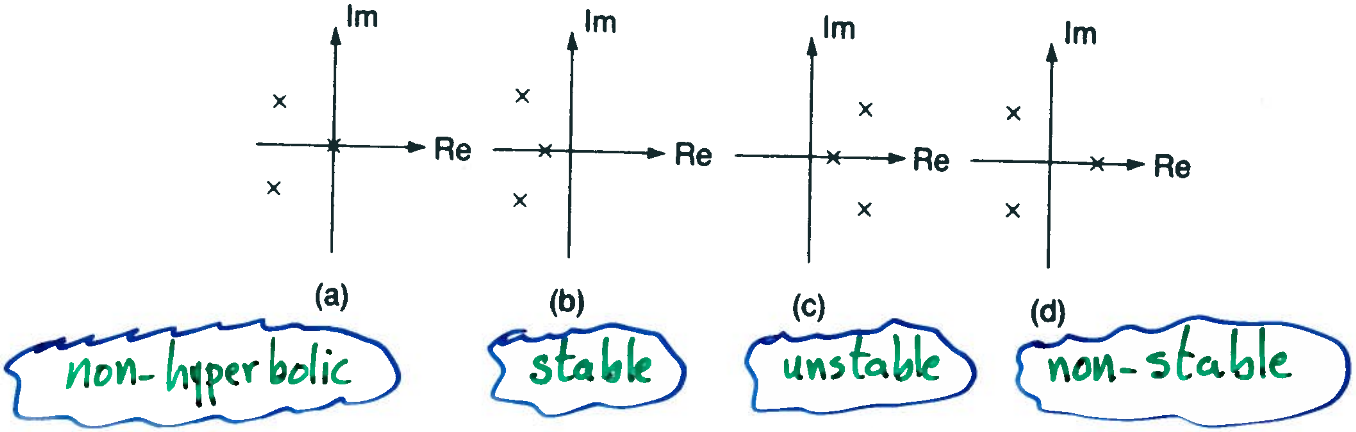
$$= \lim_{t\to\infty} \frac{1}{t} \ln \left| e^{\hat{\lambda}_i t} \right| = \lim_{t\to\infty} \frac{1}{t} \mathrm{Re}\ \hat{\lambda}_i t$$

$$= \mathrm{Re}\ \hat{\lambda}_i$$

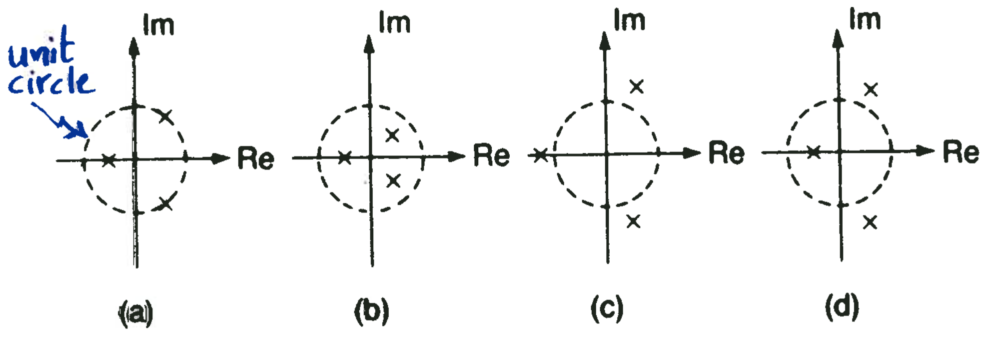
The Lyapunov exponents indicate the rate of contraction (if $\lambda_i < 0$) or expansion (if $\lambda_i > 0$) near the equilibrium point. Every point in the basin of attraction has the same λ_i as the attractor

Distribution in the Complex Plane

Complex Eigenvalues



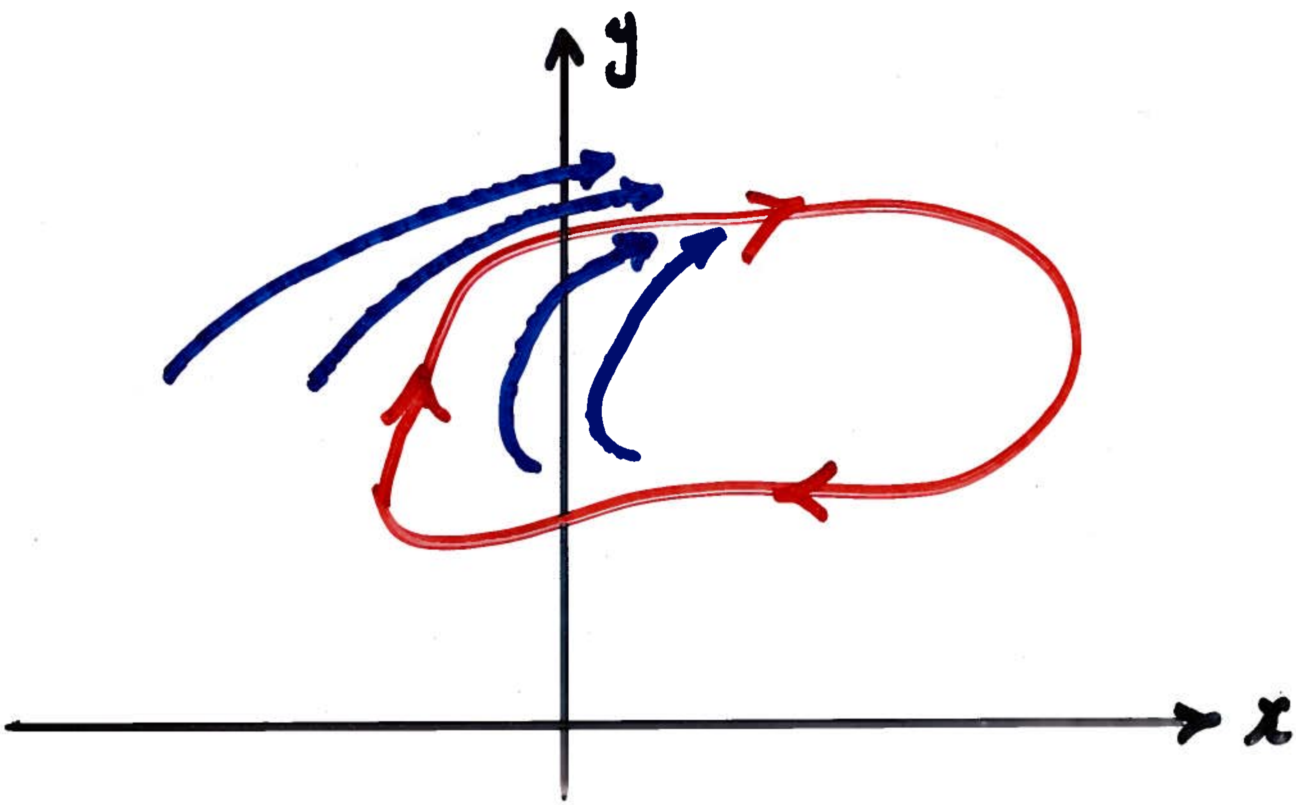
Characteristic Multipliers



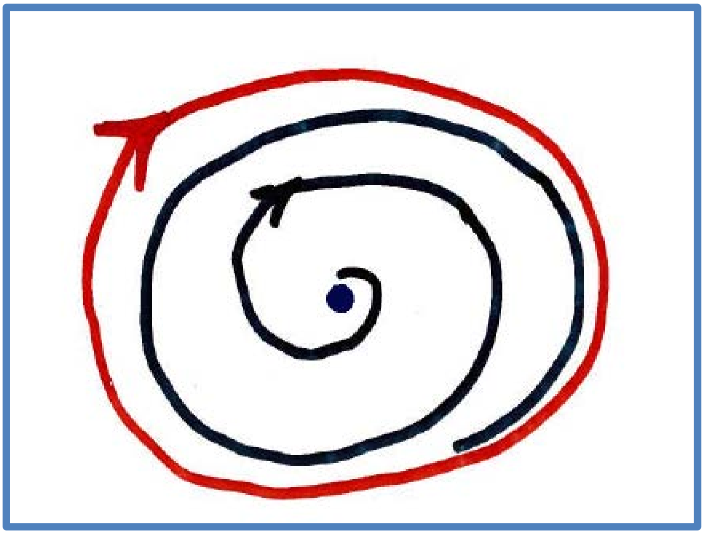
LIMIT CYCLES

Definition

A limit cycle is a closed trajectory such that no trajectory sufficiently near it is also closed. Hence, it is an isolated closed trajectory.



Limit cycle surrounding unstable focus

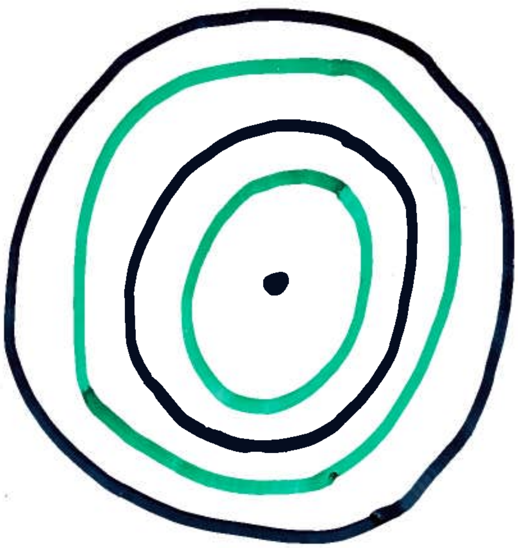


A limit cycle must enclose at least one singular point, and if there is only one, then the singular point cannot be a saddle point.

* A limit cycle is stable if nearby trajectories approach it asymptotically and unstable if they move away.

* If a finite set of periodic trajectories are nested then stable ones must alternate with unstable ones.

— attractor
— repellor



— stable
— unstable

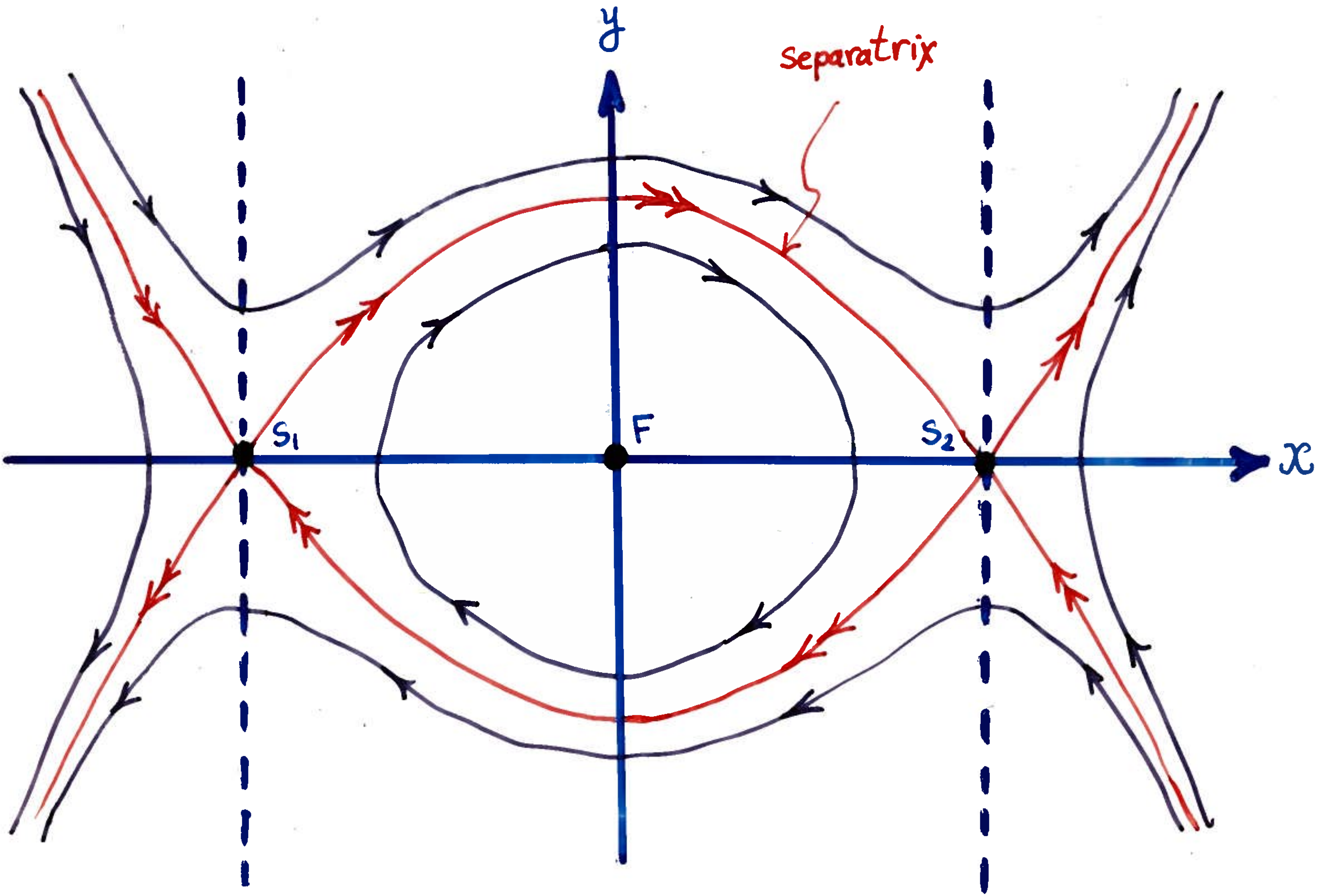
* The set of points from which all originating trajectories tend to a stable limit cycle L (or a point of equilibrium E) is called the region of attraction of L (or E). The boundary of such a region is a separatrix

SEPARATRICES

Definition

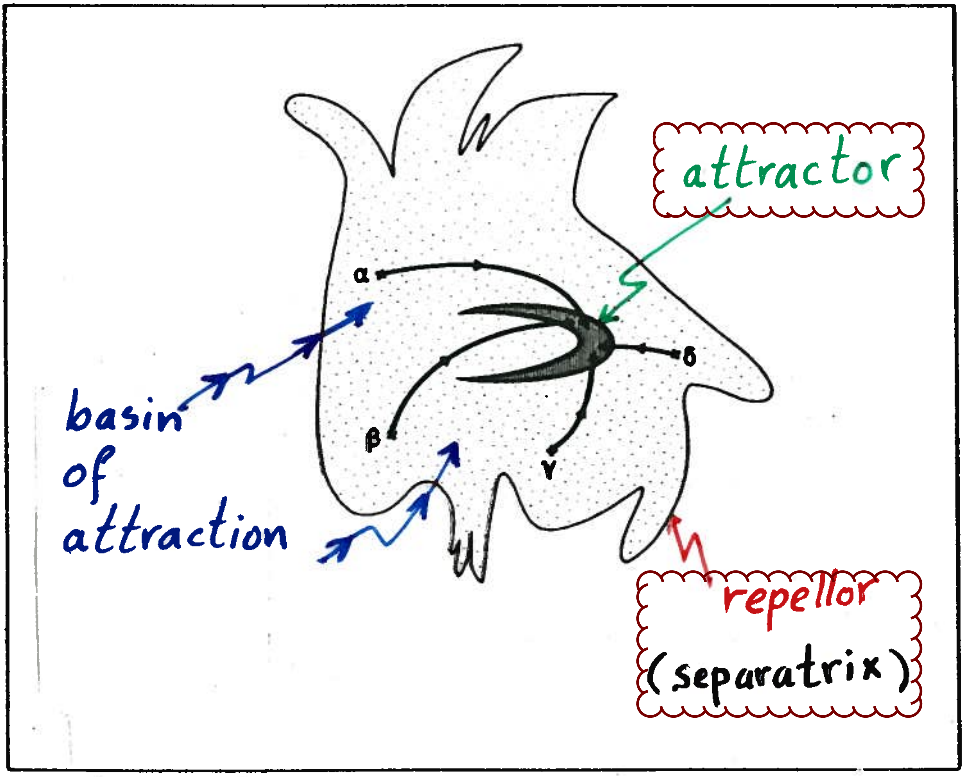
A separatrix is a boundary trajectory of a basin (or region) of attraction. It separates the state plane into regions within each of which the trajectories may show a different type of behavior.

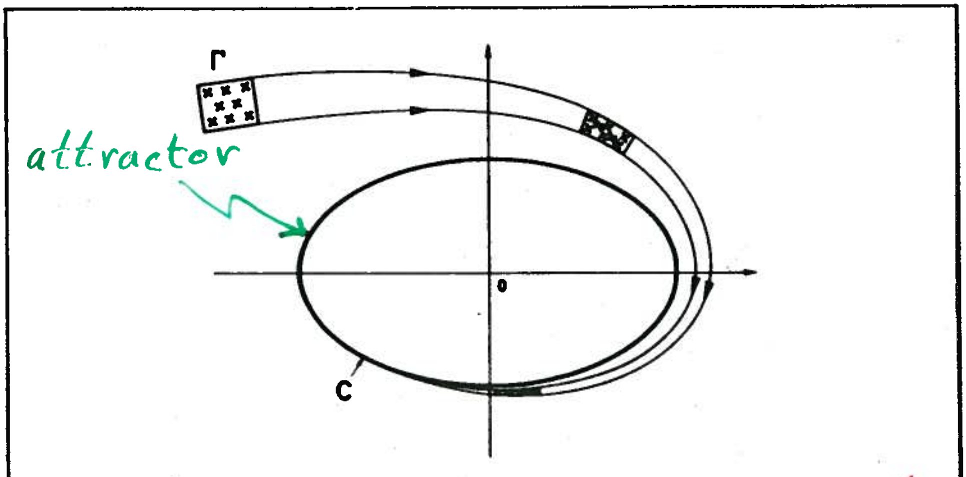
* In general, a separatrix partitions the state space into regions of different qualitative behavior. The motion along any separtrix is asymptotic towards a state of equilibrium.



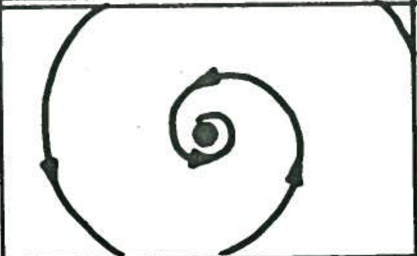
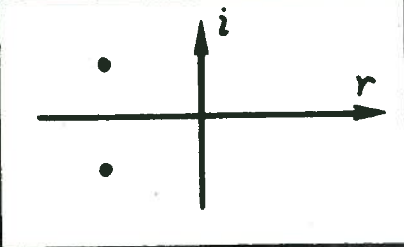
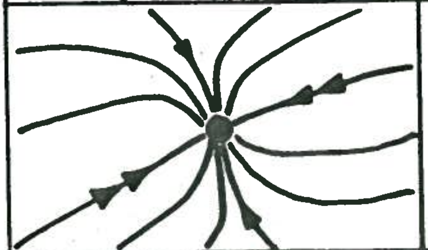
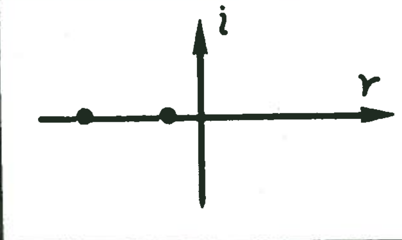
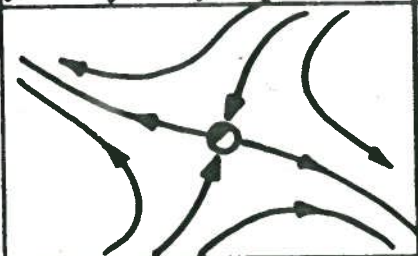
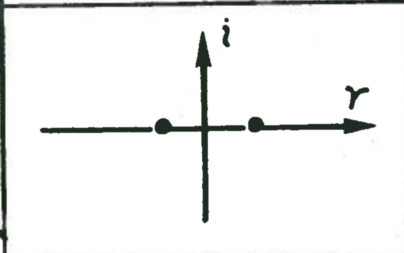
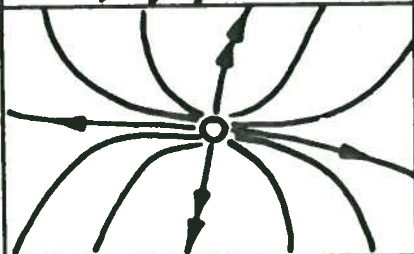
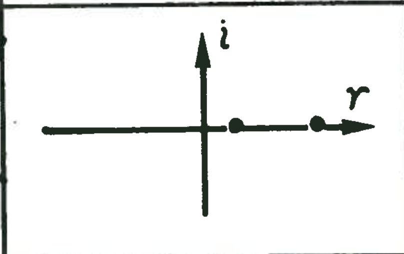
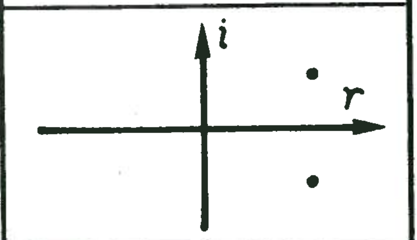
y
separatrix
S1
F
S2
x

ATTRACTORS

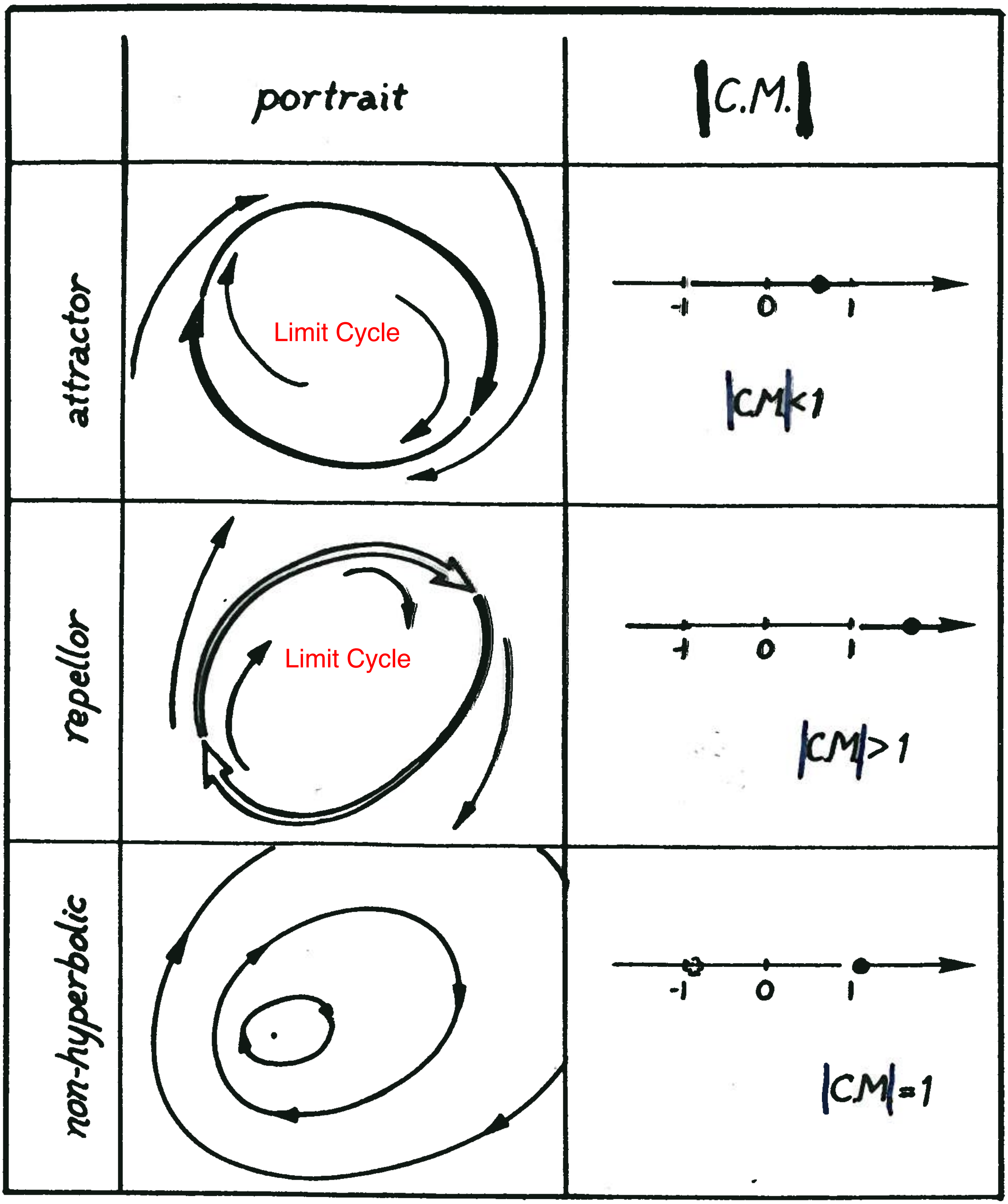




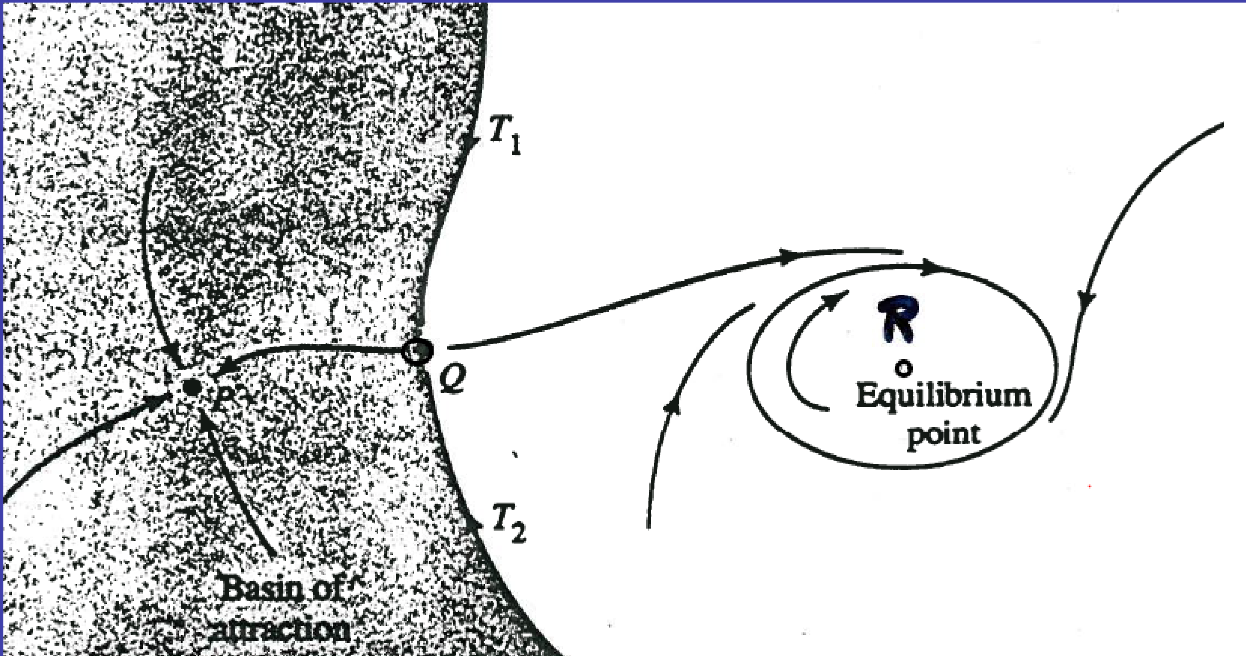
contraction of areas associated with attraction

type	portrait	C.E.
attractors		
		
saddle		
repellors		
		

C.E. = Complex Eigenvalues



|C.M.| = |Characteristic Multipliers|



Q ≙ Saddle Point

P ≙ Stable Equilibrium Point

R ≙ Unstable Equilibrium Point