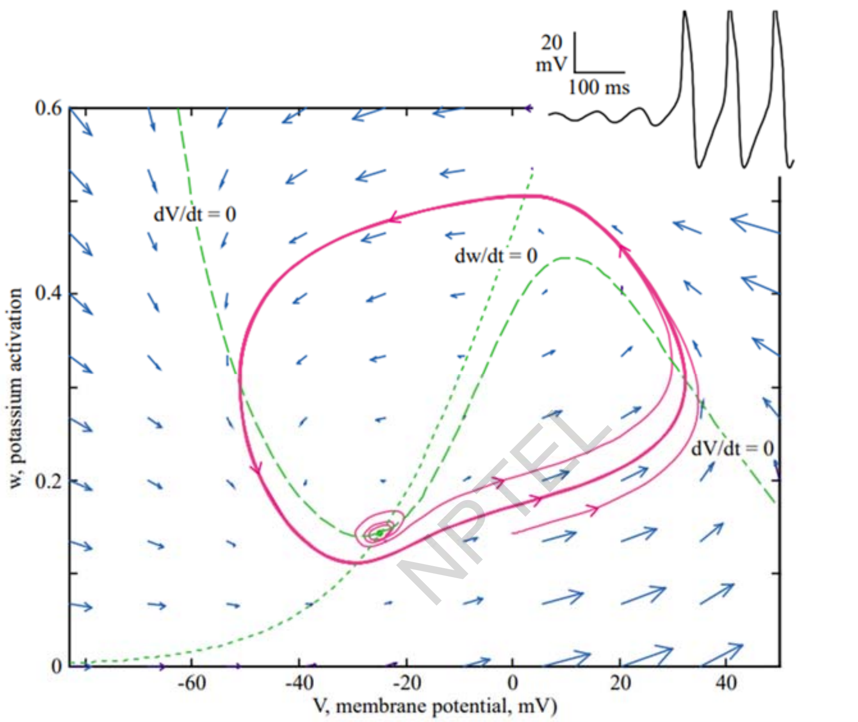
Week 04 Lecture 16

<u>LIMIT CYLCE</u>

- Consider an external current is applied
- The below fig shows the phase plane and, in the insert at top right, the membrane potential versus time, when an external current (Iext) of 95 $\mu A/cm^2$ is applied.



– the membrane potential oscillates with an increasing amplitude and then breaks into a large oscillation which is repeated exactly from cycle to cycle. This oscillation is called a limit cycle.
-A limit cycle is a second feature of nonlinear systems which is not observed in linear systems.
–In a nonlinear system the limit cycles have a fixed amplitude, which is a characteristic of the system itself, and is not determined by the initial values. In a linear system, the oscillation can have any size, depending on the initial values.
–a nonlinear system can have more than one limit cycle, but each limit cycle will be an isolated curve like the one shown in Fig.

– The corresponding trajectory in the phase plane spirals around the equilibrium point with an increasing amplitude and then meets the limit cycle, which is the large closed curve in the plane.

Compute a linear approximation to the nonlinear system in the vicinity of an equilibrium point.

– let X is the system's n-dimensional state vector.Then ,

$$\dot{\vec{X}} = \begin{bmatrix} \dot{X}_1 \\ \dot{X}_2 \\ \cdot \\ \cdot \\ \dot{X}_n \end{bmatrix} = \begin{bmatrix} f_1(\vec{X}) \\ f_2(\vec{X}) \\ \cdot \\ \cdot \\ f_n(\vec{X}) \end{bmatrix}$$

The functions $f_i(\vec{X})$ can be expanded in a Taylor series around any point $\vec{X}_0$

If $\vec{X}_0$ is is an equilibrium point, then $f_i(\vec{X}_0)=0$ for all i from the definition of an equilibrium point.

The matrix J of partial derivatives is called the Jacobian matrix of the system.

$$\dot{\vec{X}} \approx \begin{bmatrix} f_1(\vec{X}_0) + \left.\frac{\partial f_1}{\partial X_1}\right|_{\vec{X}_0}(X_1 - X_{01}) + \left.\frac{\partial f_1}{\partial X_2}\right|_{\vec{X}_0}(X_2 - X_{02}) + \cdots + \left.\frac{\partial f_1}{\partial X_n}\right|_{\vec{X}_0}(X_n - X_{0n}) \\ f_2(\vec{X}_0) + \left.\frac{\partial f_2}{\partial X_1}\right|_{\vec{X}_0}(X_1 - X_{01}) + \left.\frac{\partial f_2}{\partial X_2}\right|_{\vec{X}_0}(X_2 - X_{02}) + \cdots + \left.\frac{\partial f_2}{\partial X_n}\right|_{\vec{X}_0}(X_n - X_{0n}) \\ \cdot \\ \cdot \\ f_n(\vec{X}_0) + \left.\frac{\partial f_n}{\partial X_1}\right|_{\vec{X}_0}(X_1 - X_{01}) + \left.\frac{\partial f_n}{\partial X_2}\right|_{\vec{X}_0}(X_2 - X_{02}) + \cdots + \left.\frac{\partial f_n}{\partial X_n}\right|_{\vec{X}_0}(X_n - X_{0n}) \end{bmatrix}$$

$$\dot{\vec{X}} \approx \begin{bmatrix} \left.\frac{\partial f_1}{\partial X_1}\right|_{\vec{X}_0} & \left.\frac{\partial f_1}{\partial X_2}\right|_{\vec{X}_0} & \cdots & \left.\frac{\partial f_1}{\partial X_n}\right|_{\vec{X}_0} \\ \left.\frac{\partial f_2}{\partial X_1}\right|_{\vec{X}_0} & \left.\frac{\partial f_2}{\partial X_2}\right|_{\vec{X}_0} & \cdots & \left.\frac{\partial f_2}{\partial X_n}\right|_{\vec{X}_0} \\ & & \cdot & \\ \left.\frac{\partial f_n}{\partial X_1}\right|_{\vec{X}_0} & \left.\frac{\partial f_n}{\partial X_2}\right|_{\vec{X}_0} & \cdots & \left.\frac{\partial f_n}{\partial X_n}\right|_{\vec{X}_0} \end{bmatrix} \cdot \begin{bmatrix} (X_1 - X_{01}) \\ (X_2 - X_{02}) \\ \cdot \\ (X_n - X_{0n}) \end{bmatrix} = \mathbf{J}\vec{x}$$

$$\vec{x} = \left[(X_1 - X_{01}),\ (X_2 - X_{02}),\ \cdots\ ,(X_n - X_{0n})\right]^T$$

$\dot{\vec{X}} = \dot{\vec{x}}$, because the time derivative of the constant terms in $\vec{x}$ are zero.

$$\dot{\vec{x}} = \mathbf{J}\vec{x} \quad \text{for} \quad \vec{x} = \vec{X} - \vec{X}_0$$

Week 04 Lecture 17

– teh properties of the linear system($\dot{\vec{x}} = \mathbf{J}\vec{x} \quad \text{for} \quad \vec{x} = \vec{X} - \vec{X}_0$) can be determined by observing the trajectories in the vicinity of the equilibrium point

–if the state vector is moved slightly away from the equilibrium point, the properties of such a system are determined by the eigenvalues.

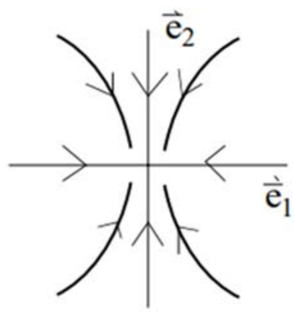
$$\vec{x}(t) = A\, e^{\lambda_1 t}\, \vec{e}_1 + B\, e^{\lambda_2 t}\, \vec{e}_2$$

–Where, e λ1 and λ2 are the eigenvalues of J and $\overrightarrow{e1} and\ \overrightarrow{e2}$ are the eigenvectors of J.

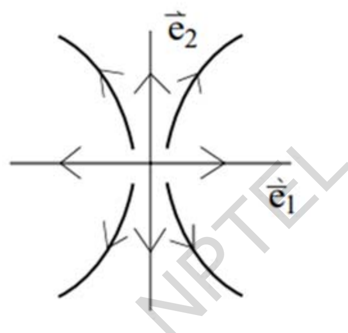
There are five different cases

1) Stable node: λ1 and λ2 both real and negative. Trajectories move smoothly and exponentially toward the equilibrium point. Such an equilibrium point is an

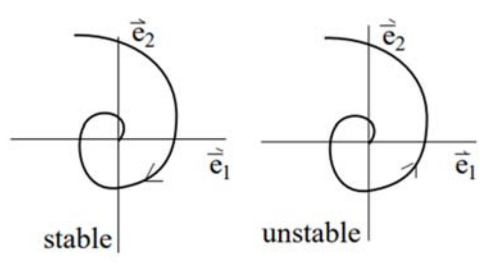
attractor for trajectories in its vicinity and may be an attractor for a large part of the phase plane



2) Unstable node: λ1 and λ2 both real and positive. Trajectories move away from the equilibrium point. The system is stable if placed exactly on such an equilibrium point, but any error will lead to a trajectory that moves away from the equilibrium point

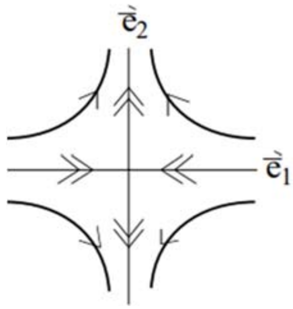


3) Stable and unstable spiral: λ1 and λ2 both complex; complex eigenvalues must occur in complex conjugate pairs. There are two cases, a stable spiral occurs when the eigenvalues have a negative real part and an unstable spiral occurs when the eigenvalues have a positive real part.



4) Saddle node: one real positive eigenvalue and one real negative eigenvalue.One decays exponentially, the other grows exponentially

λ1 is negative, so the trajectories decay toward the equilibrium point along the direction of $\overrightarrow{e_1}$; λ2 is positive, so the trajectories move away from the equilibrium point along $\overrightarrow{e_2}$. Most trajectories follow a hyperbolic path, as sketched for the four trajectories shown with a single arrowhead. However, there are four trajectories which follow the directions of the eigenvectors $\overrightarrow{e1} and\ \overrightarrow{e2}$ and in the vicinity of the equilibrium point. These are indicated by the double arrowheads in the sketch. These trajectories are produced by initial conditions exactly on one of the eigenvectors



<u>V-m reduced HH system</u>

replace the full HH system with a reduced system consisting only of two state variables, V and m and hold h and n constant at their resting values. Then the system becomes

$$C\frac{dV}{dt} = I_{ext} - \overline{G}_{Na}\, m^3\, h_\infty(V_R)(V - E_{Na}) - \overline{G}_K\, n_\infty^4(V_R)(V - E_K) - G_L(V - E_L)$$

$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)}$$

–Consider the behavior of the reduced system starting from the resting potential, -60 mV.

– The below Fig shows a phase plane for the (V, m) system with h=h∞(-60)=0.596 and n=n∞(-60)=0.318.

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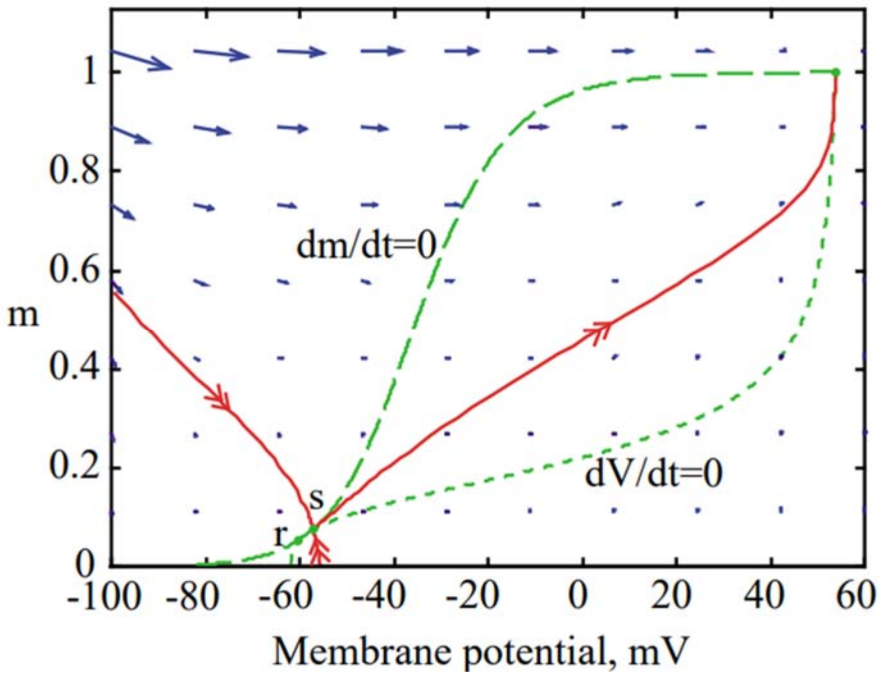


Fig 1.lec17

– there are three equilibrium points in this system (green dots)

– a stable point (labelled as r)
– one saddle node (labelled as s)
– the Fig 2.lec17 shows the expanded view the structure of the phase plane near the resting potential and the saddle node.

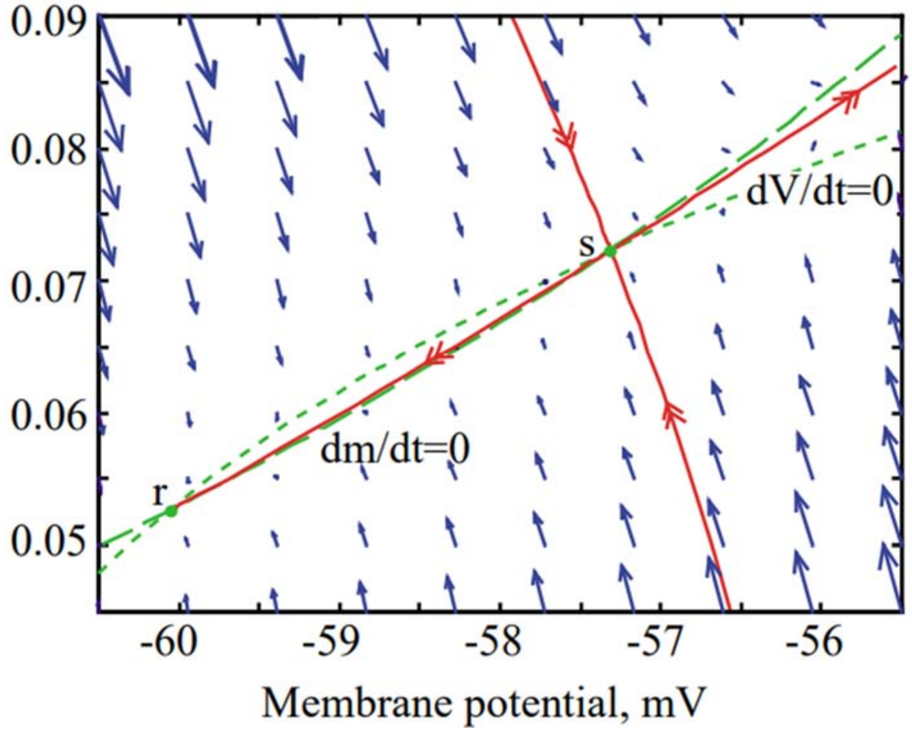


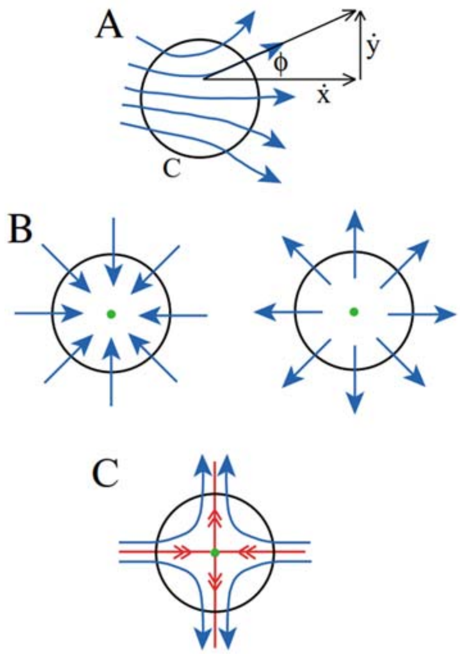
Fig 2.lec17

Week 04 Lecture 18

<u>Conditions for a limit cycle</u>

– In order to have a limit cycle, it is clear that the direction of the arrows in the phase plane must point in a circular flow.
– The index of a closed curve C in the phase plane is the cumulative change in the angle φ = $tan^{-1}(\frac{\dot{y}}{\dot{x}})$ through one counterclockwise orbit of the curve. The index also provides information about any fixed points that might happen to lie inside the curve,

– index for different cases



A) Index =0; because φ starts at an angle near 45˚, fluctuates in the positive and negative direction through the orbit, but returns to its original angle without making a complete turn in either direction.

B) Curve surrounding a stable or unstable equilibrium point, the index is +1 because in either case, the arrow makes one full counterclockwise revolution as the curve is orbited in the counterclockwise direction.

C) For a saddle node, the index is –1

Properties of Index

1) If teh closed curve C is deformed into C', without touching any equilibrium point as shown in fig 1 lecture 18

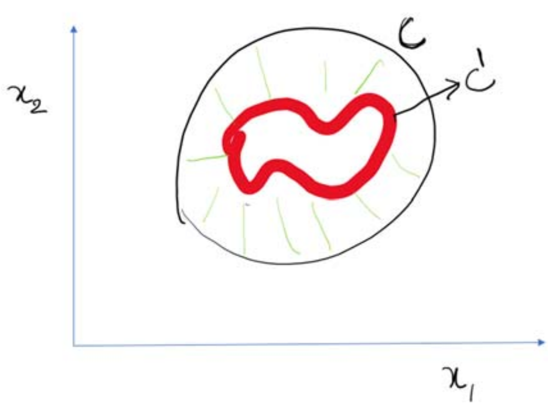


Fig 1:lecture 18

– In a closed curve C, having three equilibrium points , the index will be given as below

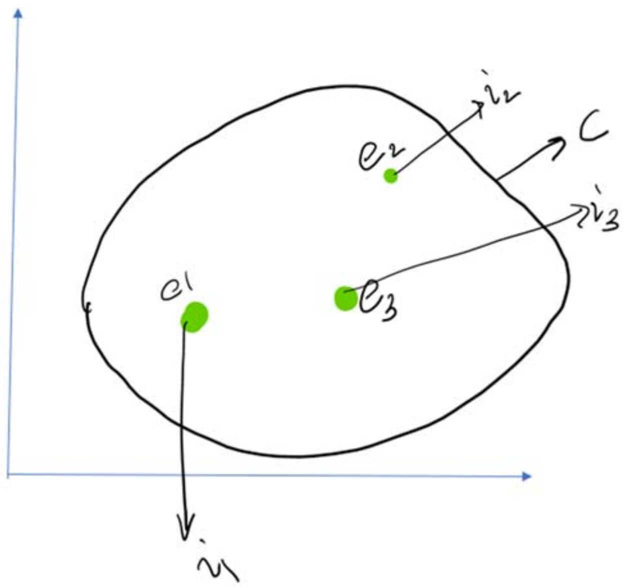


Fig 2:lecture 18

Index= $i_1 + i_2 + i_3$

The index of a curve is equal to the sum of the indices around all the equilibrium points contained within the curve.

2) If C is deformed into C' without crossing an equilibrium point, and therefore without changing its index . The index of C' is equal to the sum of the indices of the small circles around the equilibrium points plus the indices of the straight line segments. Each pair of straight line segments can be brought as close together as possible, so the index accumulated during transit in one direction along a line is exactly compensated by the transit in the other direction. This leaves only the indices of the three equilibrium points.

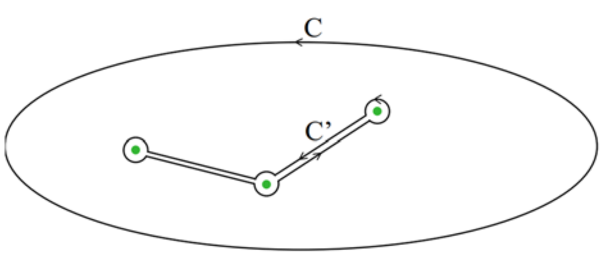


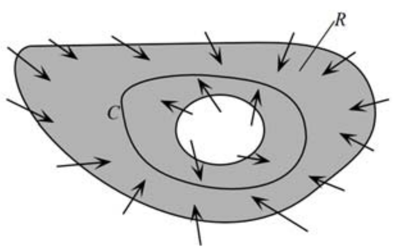
Fig 3:lecture 18

Necesssary condition:- A limit cycle is a closed curve in the phase plane. Its index must be +1, because the velocity vectors must be tangent to the limit cycle at every point (note that it doesn't matter which direction the limit cycle runs, its index still must be +1). As a result, property 2 implies that a limit cycle must contain a number of equilibrium points whose indices sum to +1. That is, a limit cycle must contain an odd number of equilibrium points, with one more stable/unstable point than saddle node; for example two stable or unstable equilibrium points plus a saddle node satisfy the condition.

A **sufficient condition** for a limit cycle for order 2 systems (only) is provided by the Poincaré-Bendixson Theorem.

Suppose that
1. R is a closed, bounded subset of the plane
2. $d\vec{x} / dt = \vec{f}(\vec{x})$ is a continuously differentiable vector field on an open set containing R;
3. R does not contain any equilibrium points

4. There exists a trajectory C that is confined in R, in the sense that it starts in R and stays in R for all time



This theorem imagines a situation in which the trajectory of the system is confined within a space R that is bounded on the outside, but also excludes a region in the inside, so that there can be an equilibrium point inside C to satisfy the index criterion. If conditions can be set up such that the velocity vectors point into the interior of R everywhere on both boundaries, then trajectories that are within R must stay there. Because there are no equilibrium points in R, the trajectory cannot approach a fixed position, which leaves only a limit cycle.

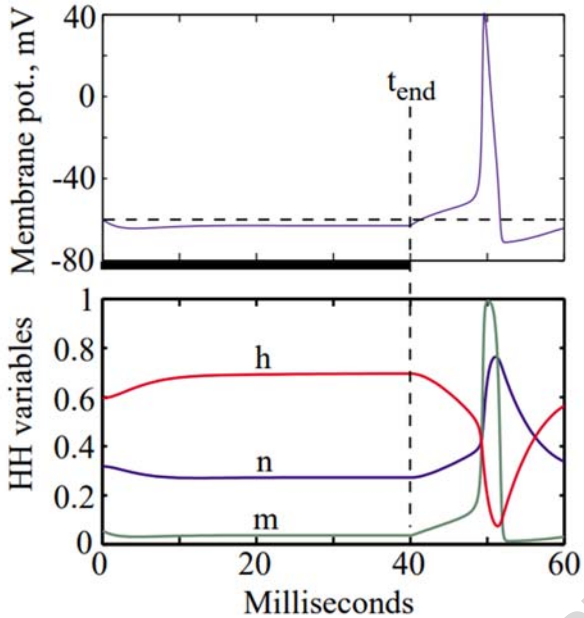
Week 04 Lecture 19

Anode break excitation

When a hyperpolarizing current is applied across a membrane, the electrical potential across the membrane falls (becomes negative of the resting potential); this fall is followed by a drop in the threshold required for action potential (since the threshold is directly linked to the potential across the membrane - they rise and fall together).ABE arises after the hyperpolarizing current is terminated: the potential across the cell rises rapidly with the absence of hyperpolarizing stimulus, but the action potential threshold stays at its lowered value. As a result, the potential is suprathreshold: sufficient to cause an action potential within the cell.
The V-m reduced system provides insight into the phenomenon of anode-break excitation.

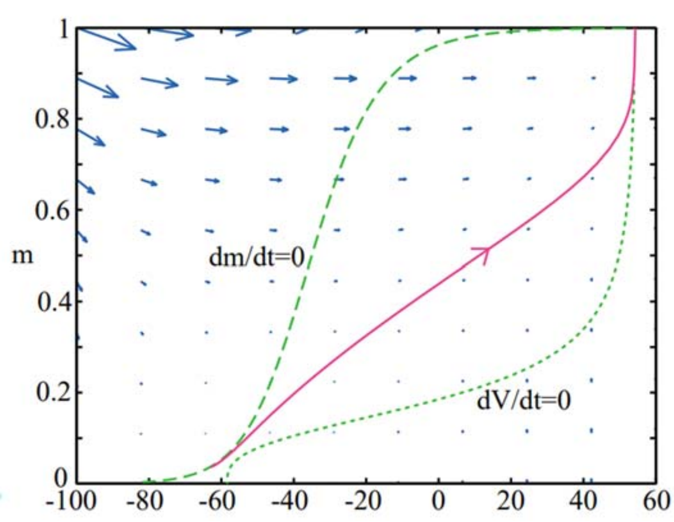
– Refer to the equations of V-m reduced system

Suppose The membrane is hyperpolarized by a –2.8 μA/cm2 current injection over the time period 0 to 40 ms.



When the current is turned off, the membrane potential returns toward rest, but then overshoots the rest potential and fires an action potential.

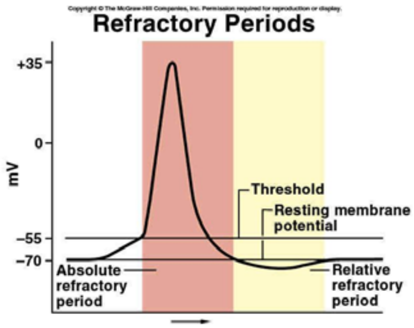
- anode-break effect can be explained by the fact that h increases and n decreases during the maintained current injection, so that the membrane is more excitable at the end of the current (time t_{end}); the increase in h means more sodium channels are available for activation and the decrease in n means that fewer potassium channels are open to stabilize the membrane.



– n decreases and h increases , just at the end of the hyperpolarization.
– (n is 0.272 instead of the resting value of 0.318 and h is 0.695 instead of its resting value of 0.596), In the figure show above.
– The effect of reducing n and increasing h is to move the dV/dt nullcline downward, eliminating the intersection of the nullclines near the rest potential.
– there is now no stable equilibrium point in the reduced system, except near +50 mV.
– the stable equilibrium point at the resting potential is abolished by the changes in n and h so the system undergoes a rapid depolarization which leads to an action potential in the full system.

Week 04 Lecture 20

Refractory period
The depolarization that produces Na+ channel opening also causes delayed activation of K+ channels and Na+ channel inactivation, leading to repolarization of the membrane potential as the action potential sweeps along the length of an axon (see Figure 3.12). In its wake, the action potential leaves the Na+ channels inactivated and K+ channels activated for a brief time. These transitory changes make it harder for the axon to produce subsequent action potentials during this interval, which is called the refractory period. Thus, the refractory period limits the number of action potentials that a given nerve cell can produce per unit time.



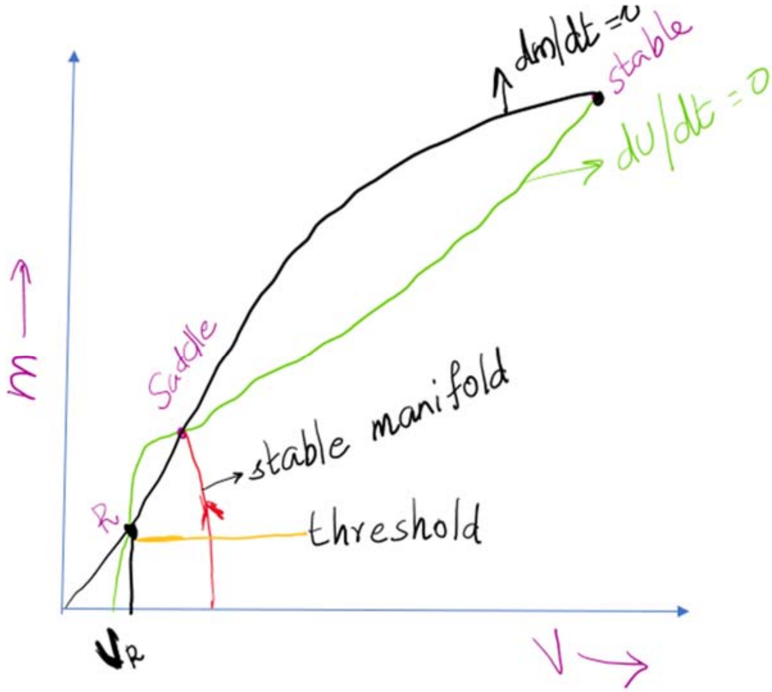
1) Absolute refractory period:- The absolute refractory period is the time interval during which a second action potential is impossible to initiate, regardless of the strength of the stimulus. It ensures that action potentials move in only one direction along an axon. During an action potential, voltage-gated sodium (Na^+) channels open, allowing Na^+ ions to enter the neuron and leading to depolarization.
   Once an action potential is triggered, these Na^+ channels become inactivated and cannot be immediately reopened. This inactivation is responsible for the absolute refractory period.
   The channels remain in this inactivated state until the membrane potential returns to its resting state, after which they reset and can be activated again by a new stimulus.

   . Relative Refractory Period (RRP):

   Immediately following the absolute refractory period, there is a phase called the relative refractory period. During the RRP, a stronger-than-normal stimulus can initiate a new action potential, but it's still difficult because the neuron is in the process of repolarizing (due to the outward flow of potassium ions, K^+).
   The RRP occurs because some sodium channels have reset, while potassium channels are still open. This balance means a greater-than-normal stimulus is required to bring the cell to threshold and initiate an action potential.

<u>Understanding relative refractory period by Phase plane analysis</u>

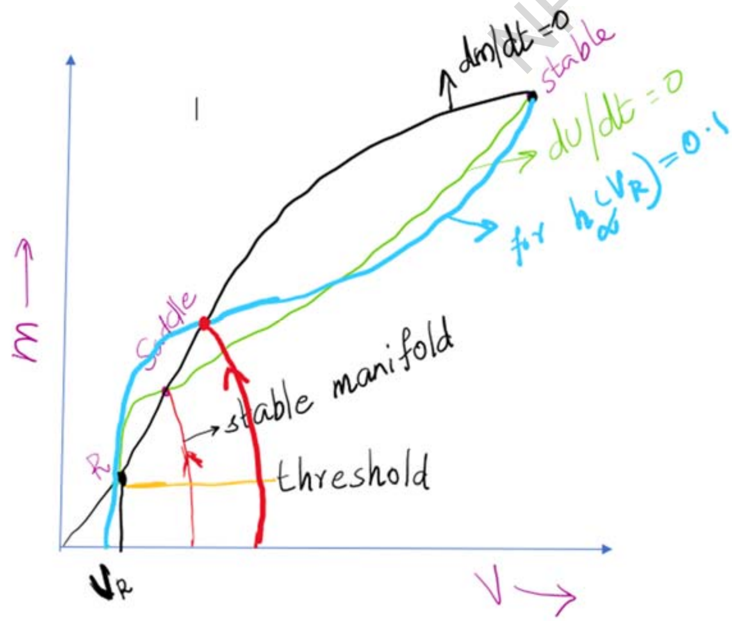
Consider the V-m reduced system with stable node labelled as R , a saddle node and another stable node at m=1.



To teh right side of stable manifold the action potential rises and goes to the stable node at m=1.

At the middle of the action potential $h_{\infty}(V_R)$ goes from to 0.6 to 0.1.

- Then plot teh V nullcline for the new value of h



-The V- nullcline for new value of h (cyan bold trajectory)

– The saddle node gets shifted to a higher voltage (red bold dot)

– The threshold also increases

– the new V value to start the system is much higher now