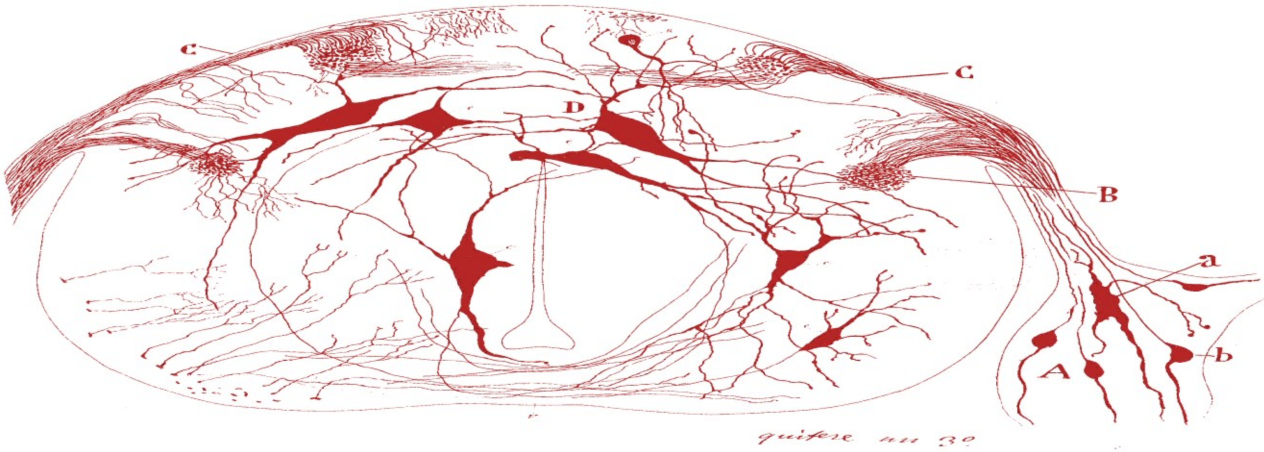

Modeling for Neuroscience: A Primer

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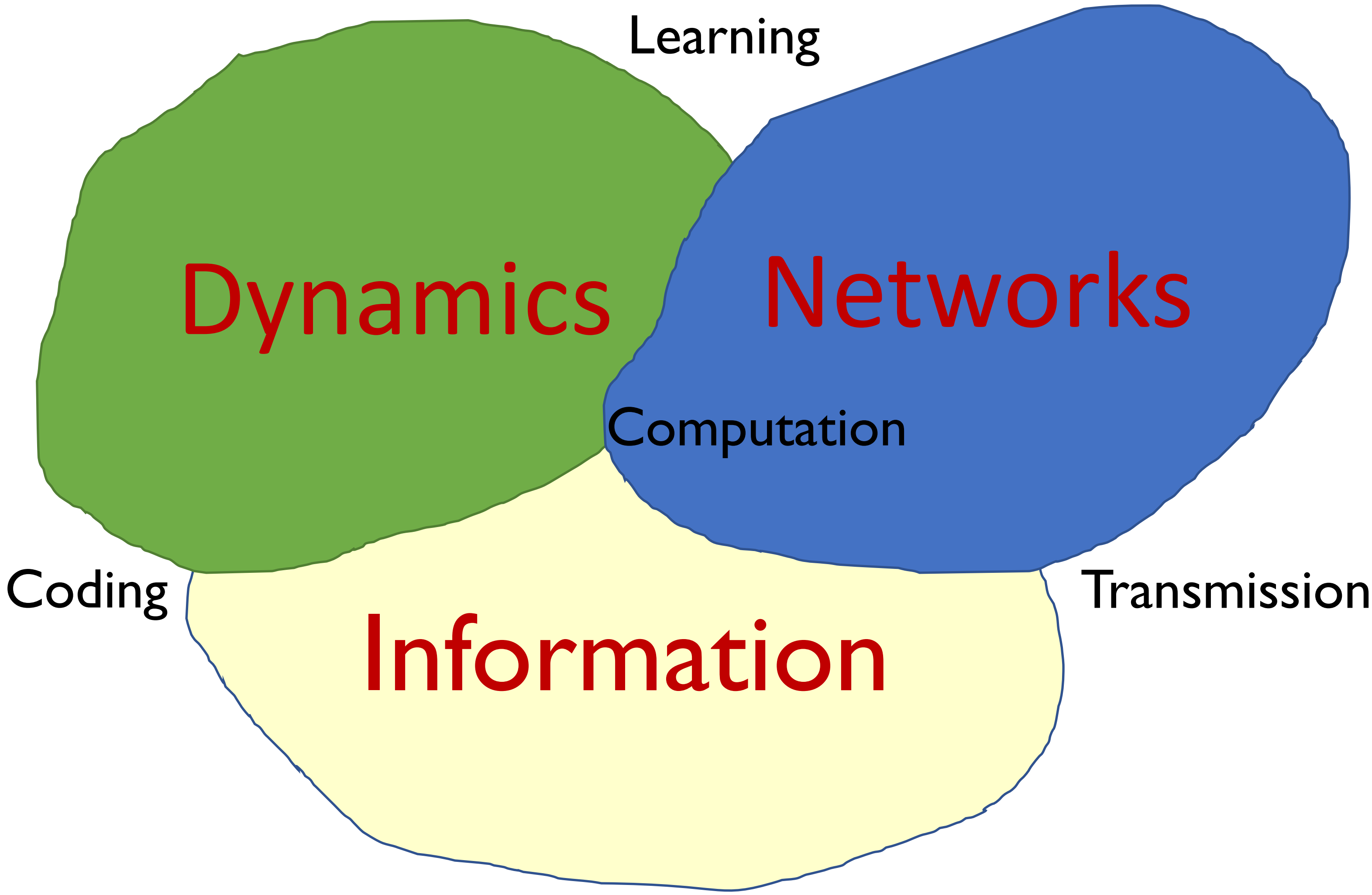

Learning
Dynamics
Networks
Computation
Coding
Information
Transmission

Modeling

Mechanistic

"Black box"

Modeling a neuron

Imge: www.dana.org/article/how-does-the-brain-work/

In the spirit of the Spherical Cow...

Image source: visav.phys.uvic.ca/~babul

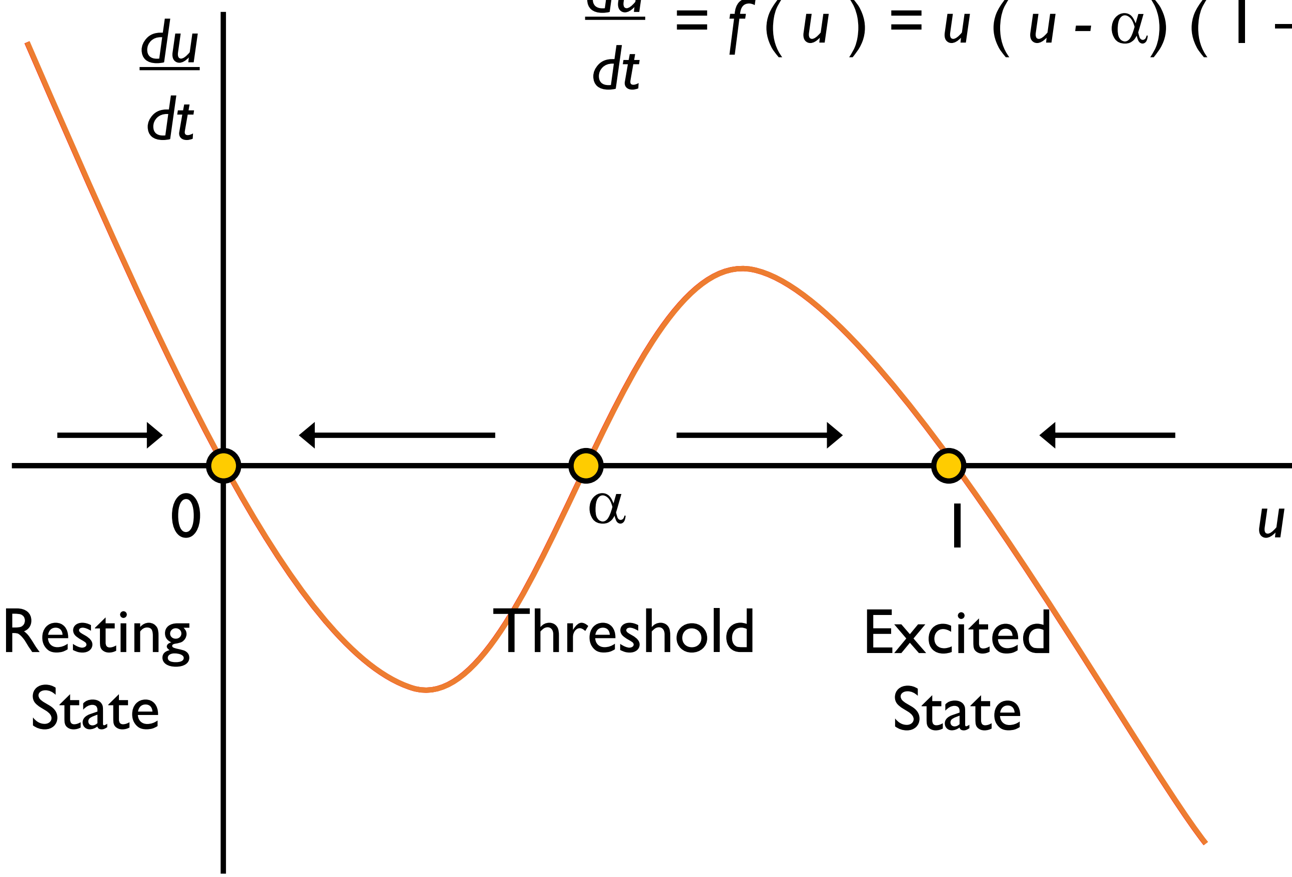
Excitable systems

Each element

- can be either in Resting State or Excited State
- Goes from resting to excited state if stimulation exceeds a threshold
- After excitation, cannot be re-excited for a resting (refractory) period

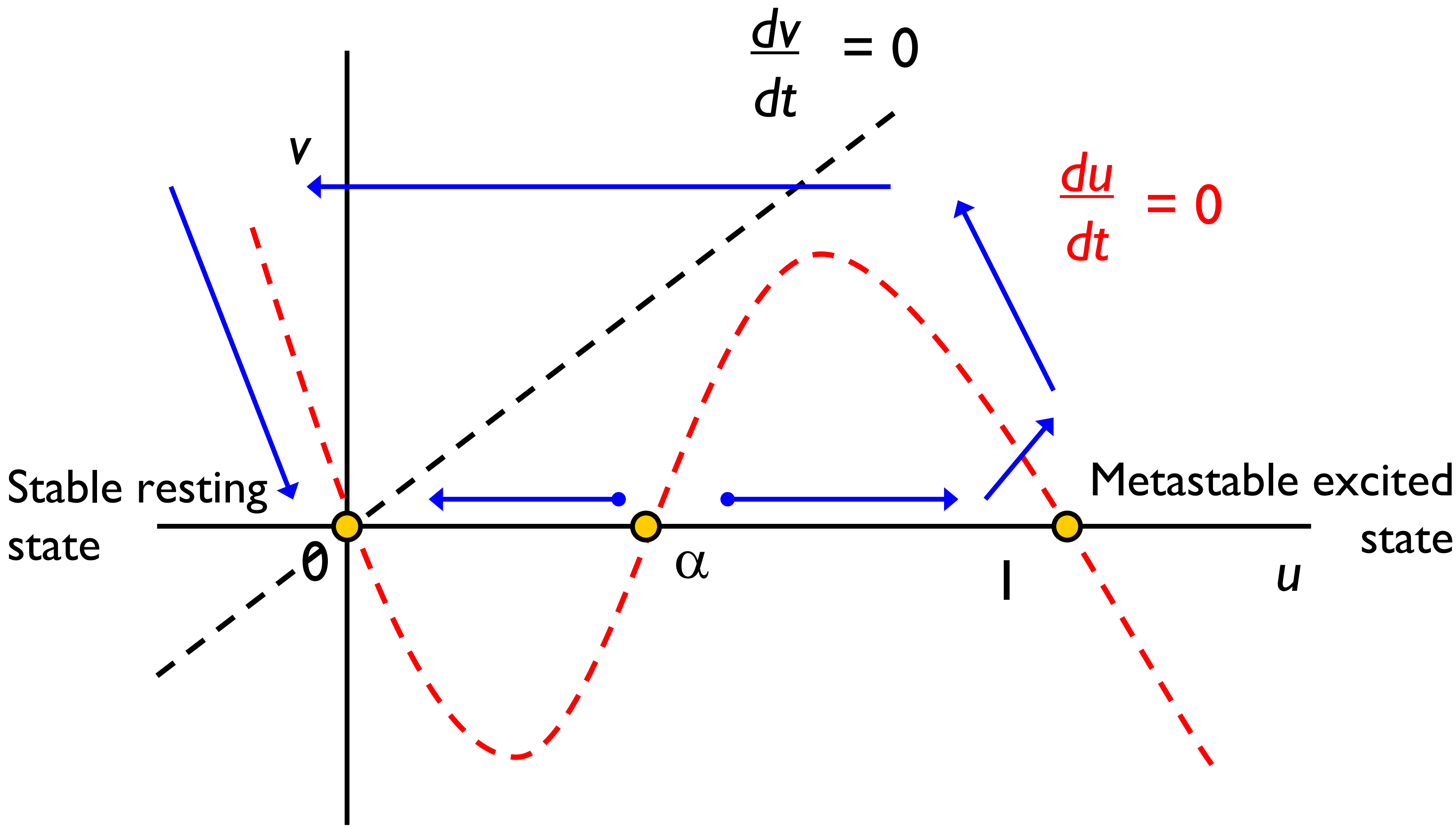
A simple model

$$\frac{du}{dt} = f(u) = u(u - \alpha)(1 - u) - v$$



$$\frac{dv}{dt} = \varepsilon\,(k\,u - v)$$

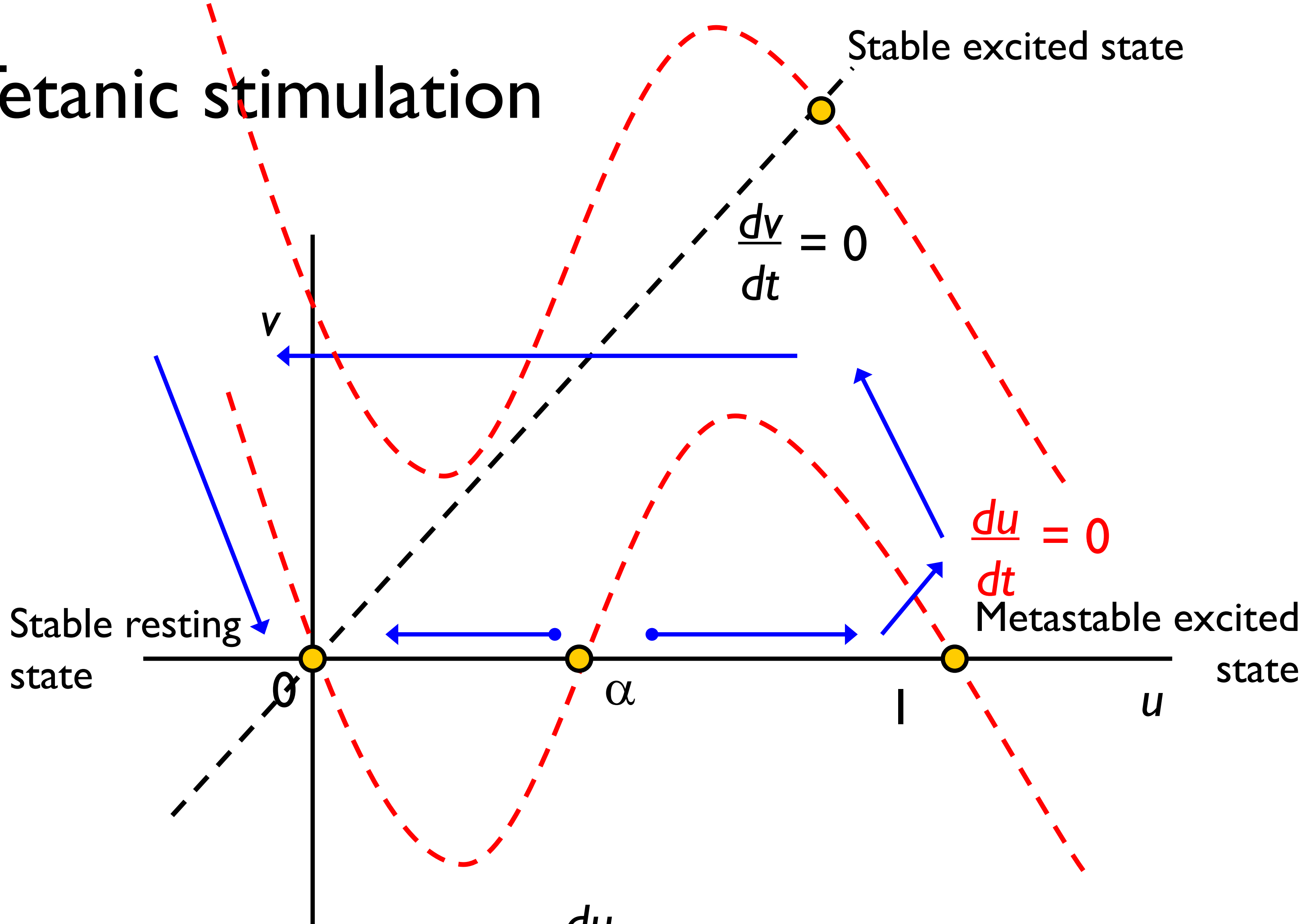
Phase plane dynamics of the simple model



Below threshold → decays to resting state

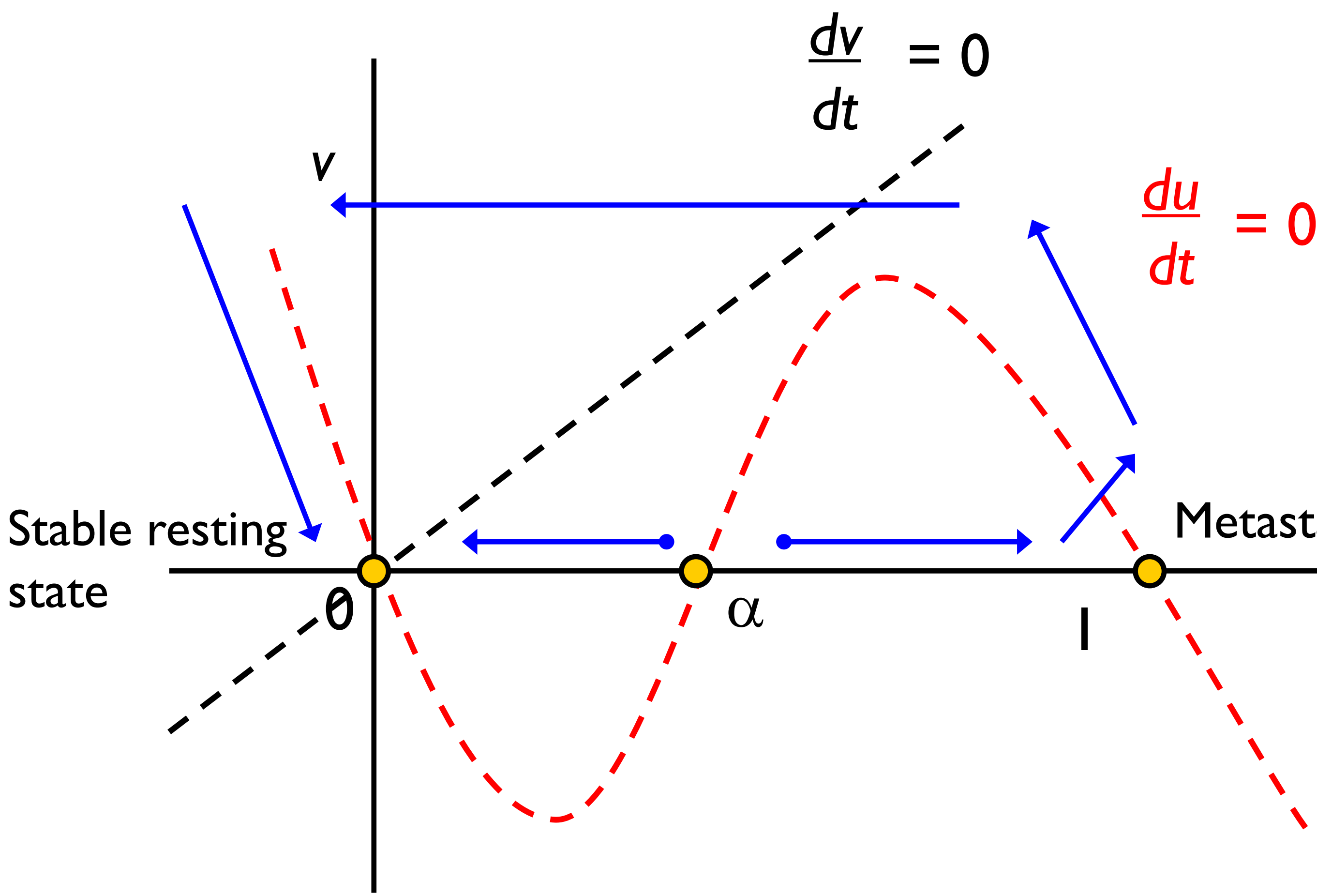
Above threshold → excitation (large excursion from stable resting state).

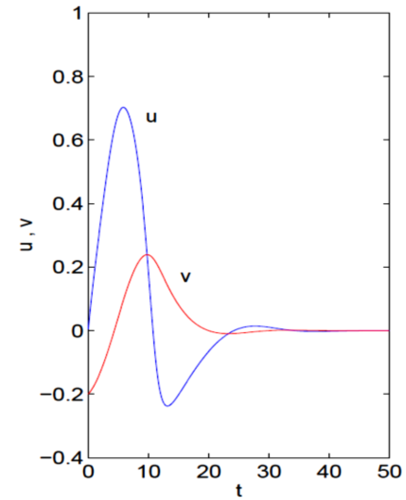
Tetanic stimulation



$$\frac{du}{dt} = f(u) = u\,(u - \alpha)\,(1 - u) \;\; - v + I_{ext}$$

Phase plane dynamics of the simple model

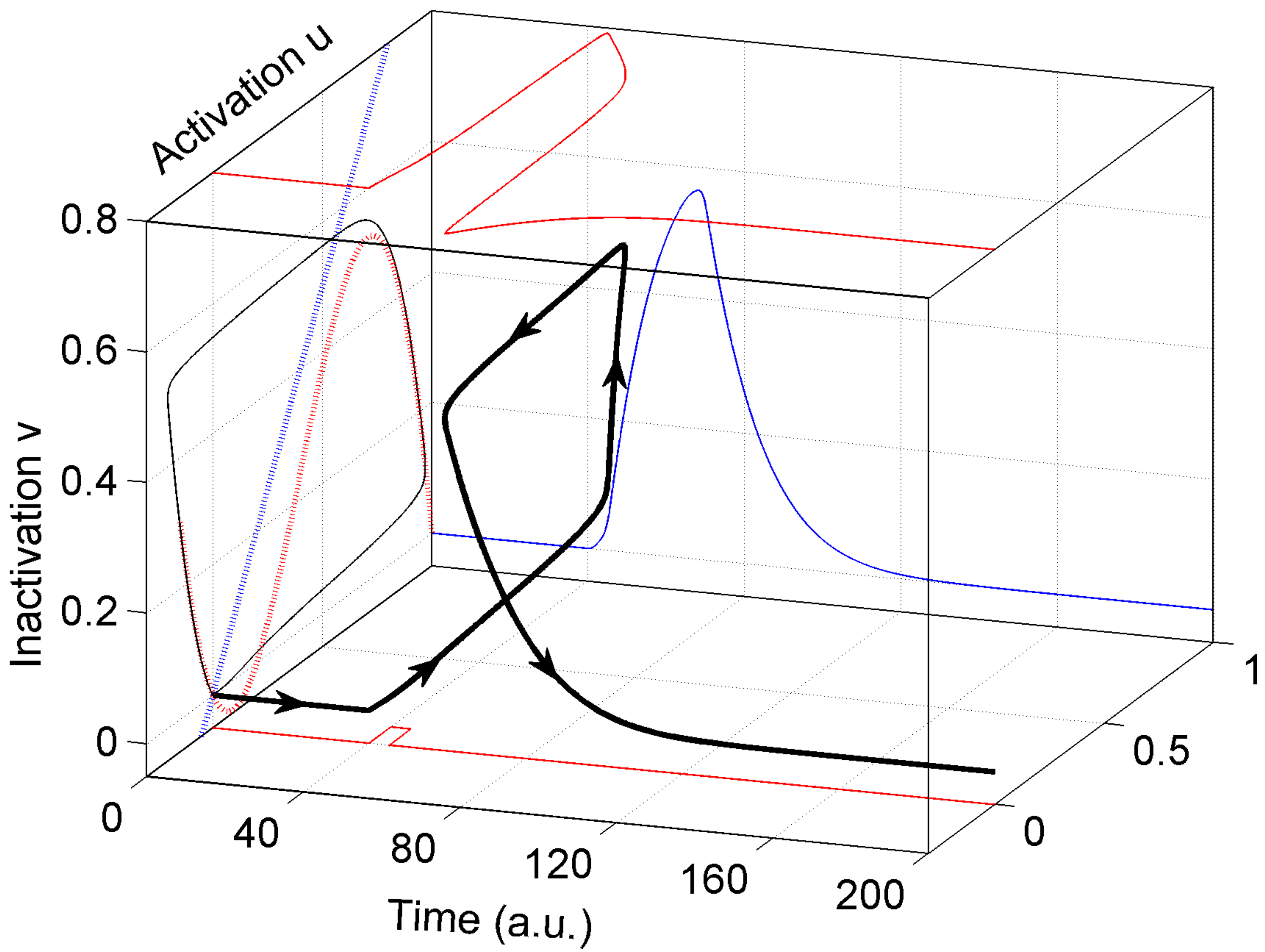




Below threshold → decays to resting state

Above threshold → excitation (large excursion from stable resting state).

Time-evolution of the simple model



On application of supra-threshold stimulus the FHN model exhibits an action potential. Projection of the phase plane trajectory along u and v planes are shown.

Image: Sinha and Sridhar, Patterns in Excitable Media (CRC Press)

What we have developed is actually the

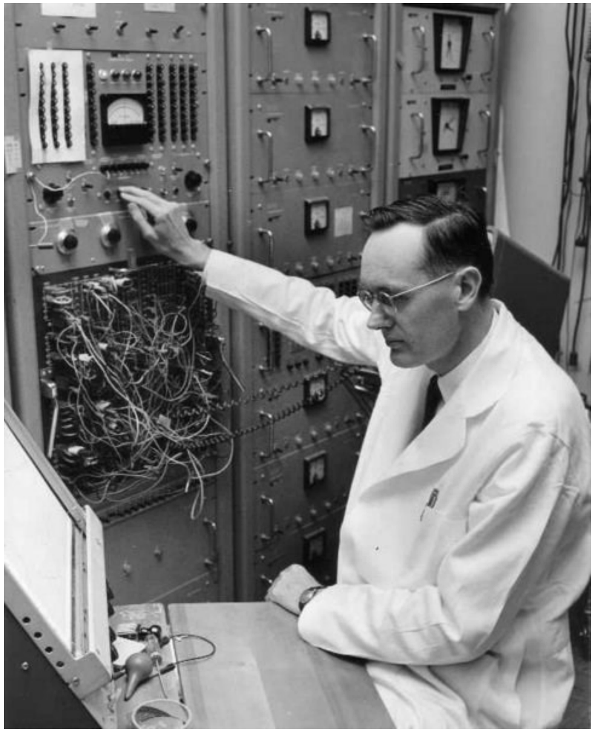
Fitzhugh-Nagumo model

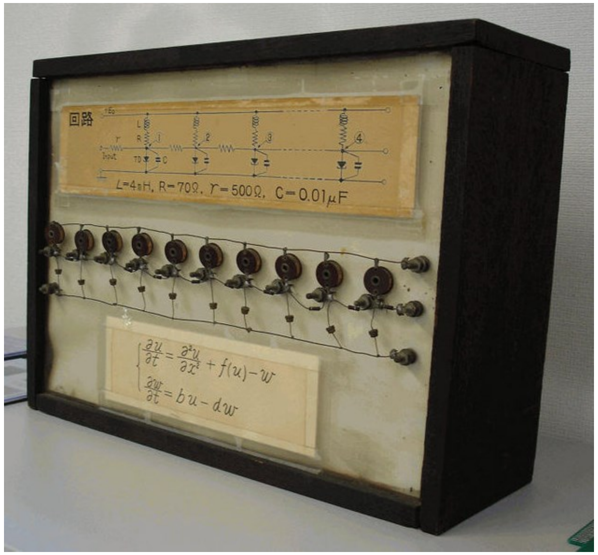
$$\frac{du_e}{dt} = F_e(u_e, v) = Au_e(u_e - \alpha)(1 - u_e) - v,$$
$$\frac{dv}{dt} = \epsilon(u_e - v),$$

Developed independently by R Fitzhugh (1961) [who called it the Bonhoeffer-Van der Pol model] and J Nagumo (1962) to isolate the essential concepts of excitation propagation

Richard Fitzhugh: Simplified the Hodgkin-Huxley equations describing spike generation in squid giant axon

Jin-ichi Nagumo: built monostable multivibrator electronic circuit using tunnel (Esaki) diodes
Esaki diodes have cubic I-V curve similar to that used in Fitzhugh's eqn





Tutorial

Numerical solution of Fitzhugh-Nagumo differential equations

Using Euler method (simple but not recommended for serious work)

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

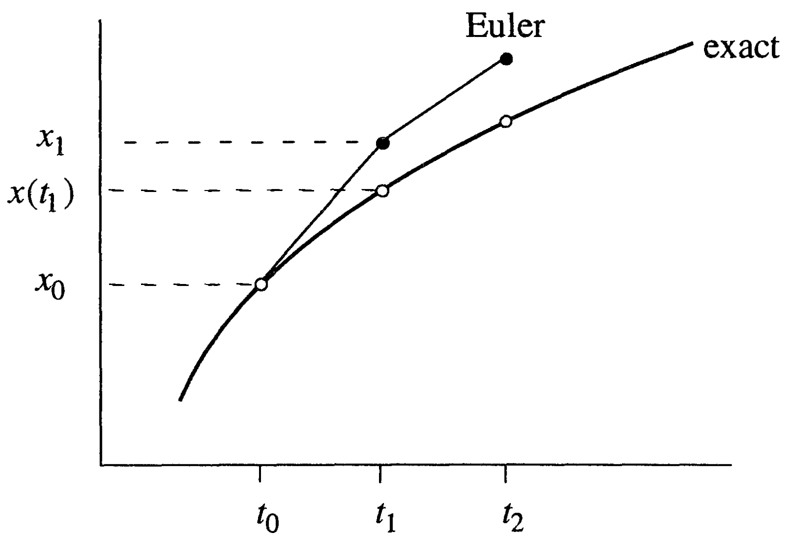
Using $\quad dx/dt \equiv Lt_{\Delta t \to 0} \{x(t + \Delta t) - x(t)\} / \Delta t$

$$\Rightarrow \quad x(t_0 + \Delta t) \approx x_1 = x_0 + f(x_0)\Delta t$$

$$x_2 = x_1 + f(x_1)\Delta t$$

$$x_{n+1} = x_n + f(x_n)\Delta t$$

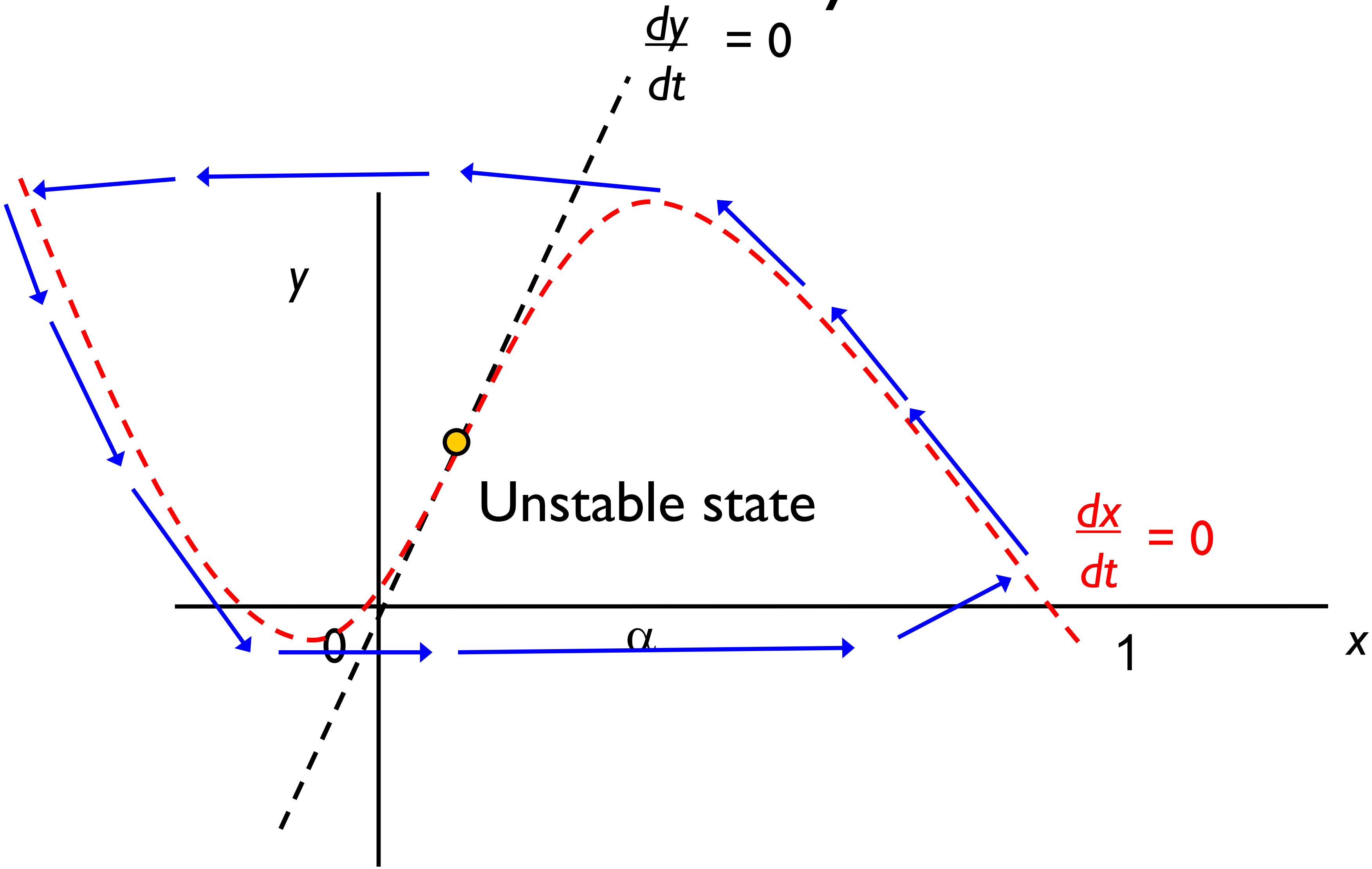
Image: Strogatz, Nonlinear Dynamics and Chaos



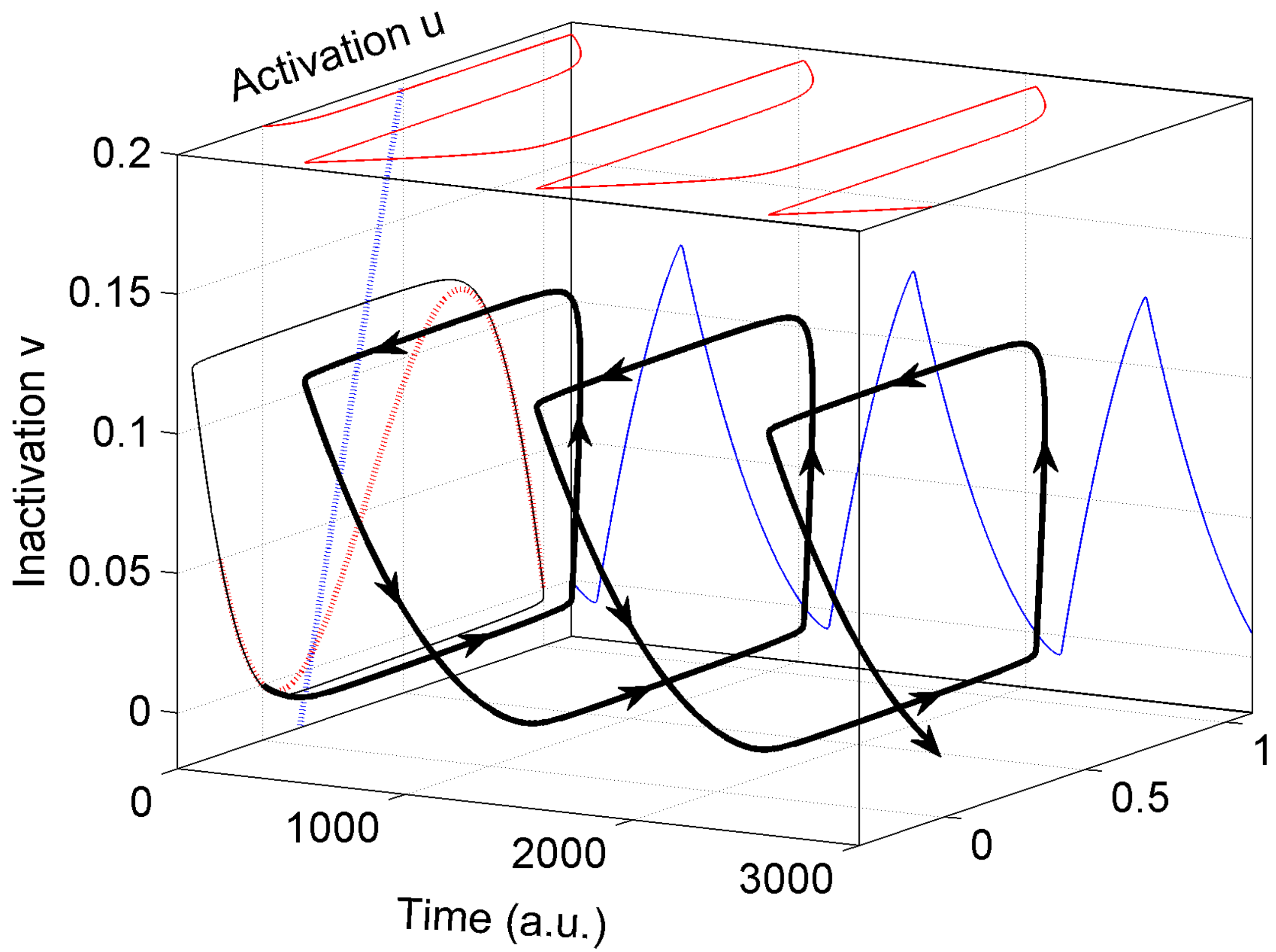
Solving FHN:

Supply u(1),v(1)
Iterate
For i = 1: T,
  u(i+1) = u(i)+del_t*u(i)*(1-u(i))*(u(i)-th)-v(i)+I
  v(i+1) = v(i)+del_t*epsilon*(k*u(i) – v(i))
end

From excitable to oscillatory

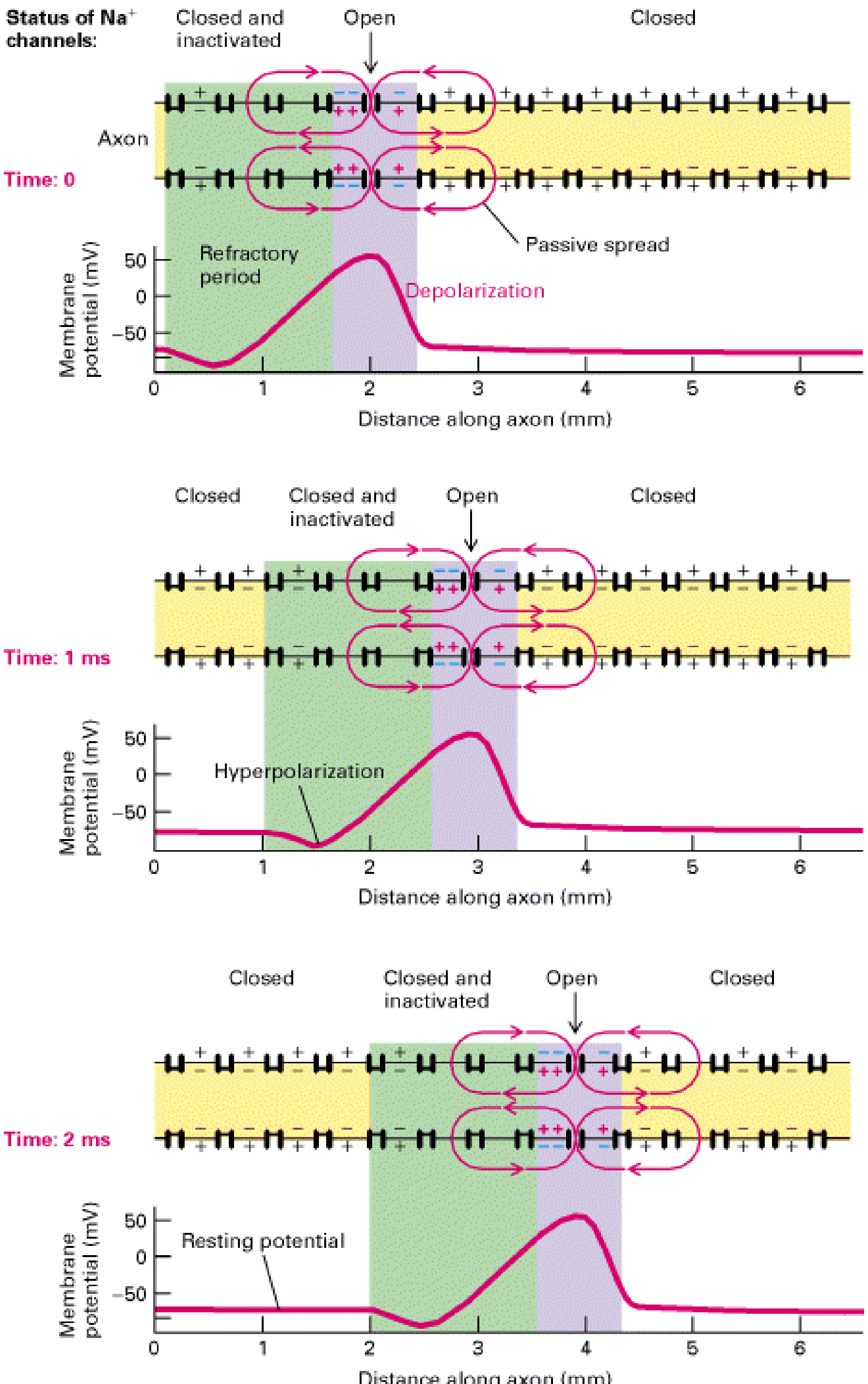


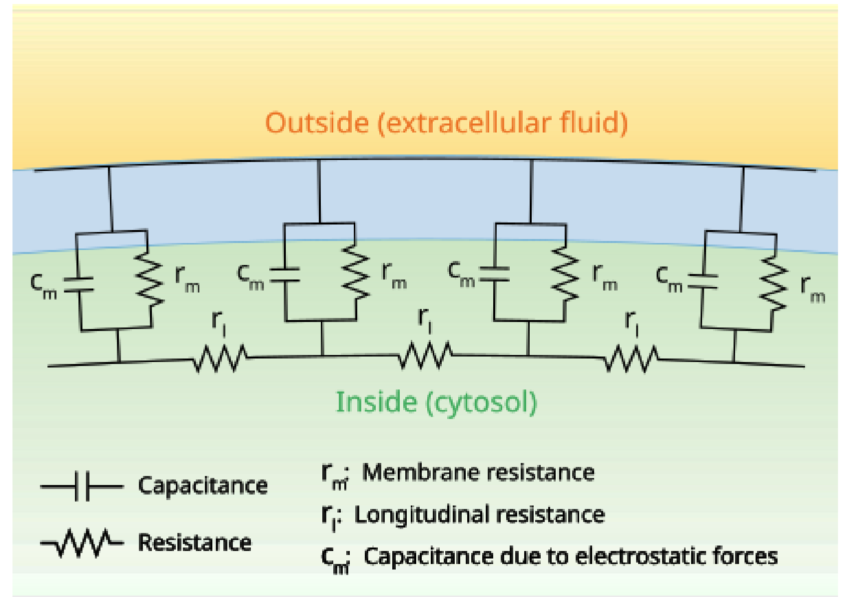
To show oscillatory behavior the single fixed point in the system is made unstable
How ? displace the x-nullcine by *I* (external current)



Images: Sinha and Sridhar, Patterns in Excitable Media (CRC Press)

Propagation along the axon





Introducing Space: The Cable Equation

Hermann von Helmholtz
(1821-1894)

Image: www.lookingoutloud.com

1850: Hermann von Helmholtz showed experimentally that the signal velocity in nerve fibers is finite
Measured it as 27 m/s in the sciatic nerve of the frog

1855: William Thompson (Lord Kelvin) described the propagation of electrical signals in long cables
The problem had become of interest because of the rapid development of long-distance communication by telegraph (first transatlantic cable in 1858).

$$\frac{1}{r_l}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + \frac{V}{r_m}$$

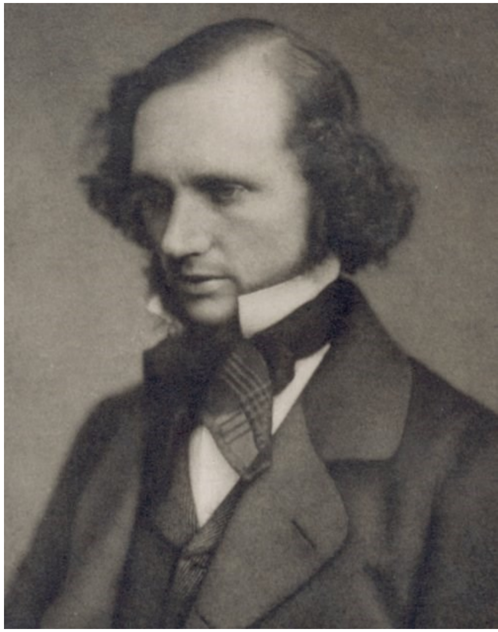


Image:physicsworld.com

William Thomson (Lord Kelvin)
(1824-1907)

From ODEs to PDEs

So how to extend this to a spatially extended oscillatory medium ?

Imagine a continuum of oscillators, neighboring points interacting diffusively

Propagation of activity in a spatial continuum

Mathematically approximated as a **diffusion equation** yielding the partial differential equation

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} - \frac{I_{ion}}{C_m}$$

with diffusion constant

$$D = \frac{G_i}{S_v C_m}$$

G_i: Bulk intracellular conductivity
S_v: Surface to volume ratio of cells
C_m: Membrane capacitance

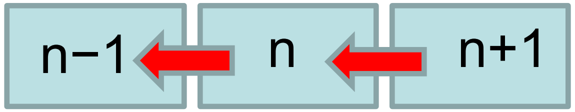
In general, biological tissue is anisotropic $\Rightarrow$ D is a tensor
E.g., activity travels along the direction of fibers much faster than transverse to it

Activity propagation in 1 dimension

Nearest neighbors connected by gap junctions

V_n: transmembrane potential of n-th cell

I_n: current from the n-th to the (n−1)-th cell



The net current that passes through gap junctions of the n-th cell:

$$I_{junction} = I_n - I_{n+1} = g_{gap}(V_n - V_{n-1}) - g_{gap}(V_{n+1} - V_n)$$

where g_{gap}: gap-junction conductance

Using continuum approximation,

$$I_{junction} = -g_{gap}\frac{\partial^2 V}{\partial x^2}$$

yielding PDE describing spatial propagation of activity

$$C_m\frac{\partial V}{\partial t} = -I_{ion} - I_{junction} = g_{gap}\frac{\partial^2 V}{\partial x^2} - I_{ion}$$