Introduction to Dynamical Systems

Part 3

Icahn School of Medicine at Mount Sinai

SBCNY

Outline

Analyzing stability of ODE systems

What we mean by stability in general

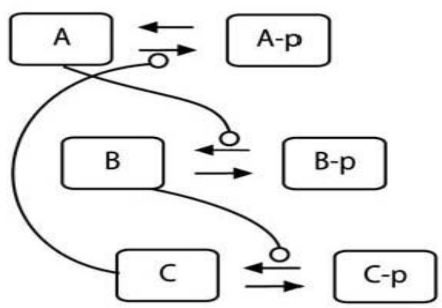
One-dimensional examples

Phase-plane techniques for two-dimensional systems

Example: a mathematical model of yeast glycolytic oscillations

Analyzing stability of ODE systems

Example: a generic three-component repressive network



Mogilner et al., *Developmental Cell* 11:279–287, 2006

The scheme implies a set of differential equations

$$\frac{d[A]}{dt} = \frac{k_{p1}([A]_T - [A])}{[A]_T - [A] + K_{p1}} - \frac{k_{k1}[A][C]}{[A] + K_{k1}}$$

$$\frac{d[B]}{dt} = \frac{k_{p2}([B]_T - [B])[A]}{[B]_T - [B] + K_{p2}} - \frac{k_{k2}[B]}{[B] + K_{k2}}$$

$$\frac{d[C]}{dt} = \frac{k_{p3}([C]_T - [C])[B]}{[C]_T - [C] + K_{p3}} - \frac{k_{k3}[C]}{[C] + K_{k3}}$$

Model parameters:

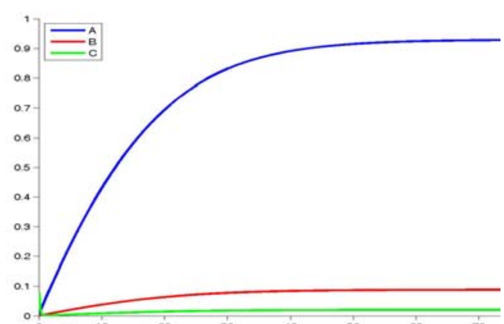
- k_{cat}'s and K_m's for phosphorylation reactions
- k_{cat}'s and K_m's for dephosphorylations
- total amounts of [A], [B], and [C]

The equations are solved using standard numerical techniques

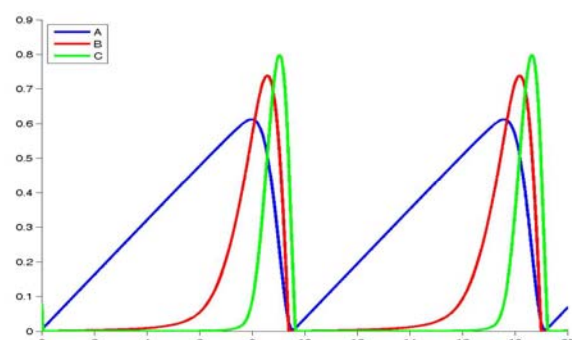
ODE models

Two solutions to this system

Parameter set 1



Parameter set 2



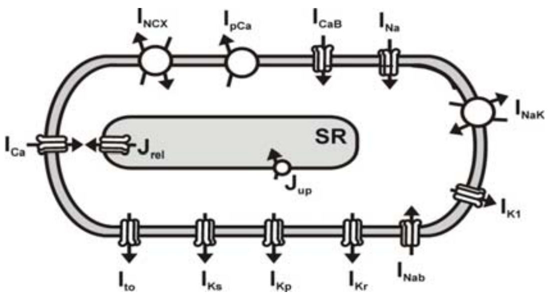
Parameter values greatly influence system behavior

We use tools of "dynamical systems" to understand different behaviors

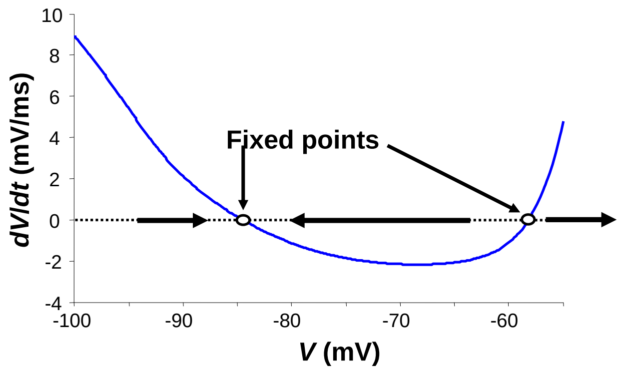
Stability analysis of ODE systems

A one-dimensional example

Isolated cardiac myocyte



$$\frac{dV}{dt} = \frac{-I_{ion}}{C_m}$$



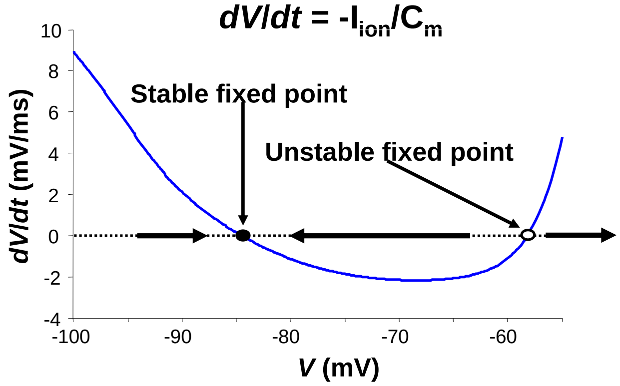
Beginning with a myocyte at rest (-85 mV), simulate instantaneous change in voltage, resulting I_{ion}, then resulting dV/dt

Change to < -85 → positive dV/dt
Change to ~-70 → negative dV/dt
Change to >~-58 → positive dV/dt

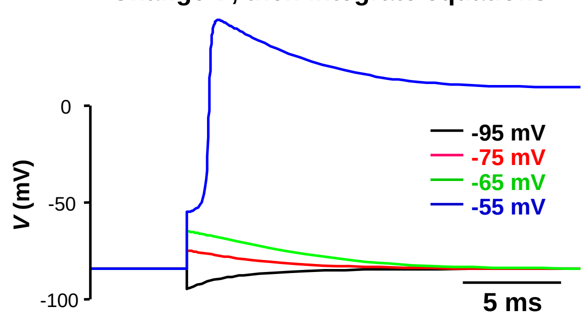
Stability analysis of ODE systems

Instantaneous changes in membrane potential

$dV/dt = -I_{ion}/C_m$



Change *V*, then integrate equations

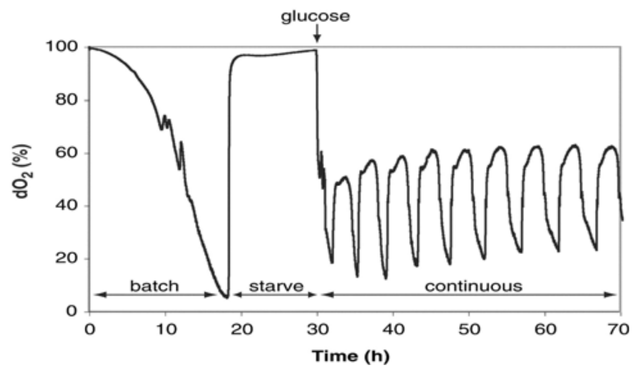


Deviations below -85 mV or between -85 and ~-58 mV result in a return to the resting state.
This is a stable fixed point
Small deviations from -58 mV cause action potentials or return to the resting state.
This is an unstable fixed point

We will learn to analyze these more rigorously

Stability analysis of ODE systems

A two-dimensional example: Yeast glycolytic oscillations



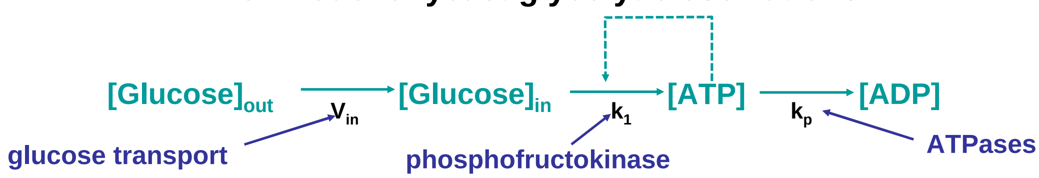
Tu *et al*., *Science* 310:1152-1158, 2005

Many mathematical models of this process have been developed
Bier, Bakker, & Westerhoff published a very simple one (*Biophys. J.* 78:1087-1093, 2000)

We will analyze stability using this example system

Stability analysis of ODE systems

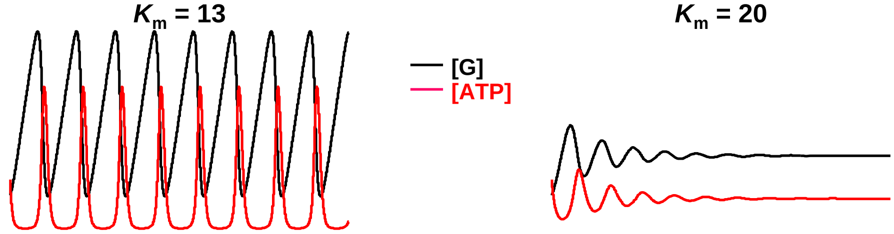
Bier model of yeast glycolytic oscillations



$$\frac{d[ATP]}{dt} = 2k_1[G][ATP] - \frac{k_p[ATP]}{[ATP]+K_m} \qquad \frac{d[G]}{dt} = V_{in} - k_1[G][ATP]$$

Default parameter values: V_{in} = 0.36, k_1 = 0.02, k_p = 6

K_m = 13 **K_m = 20**



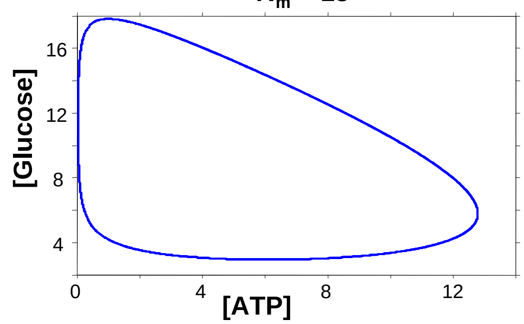
How can we understand the qualitatively different behavior?

Stability analysis of ODE systems

Phase-plane techniques for 2D systems

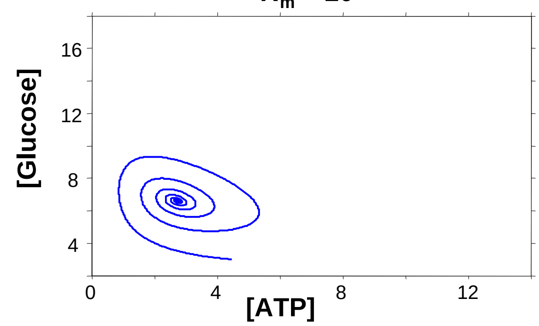
Instead of plotting [G] and [ATP] vs. time, plot [G] vs. [ATP]

$K_m = 13$



[G] and [ATP] oscillate indefinitely in a "stable limit cycle"

$K_m = 20$

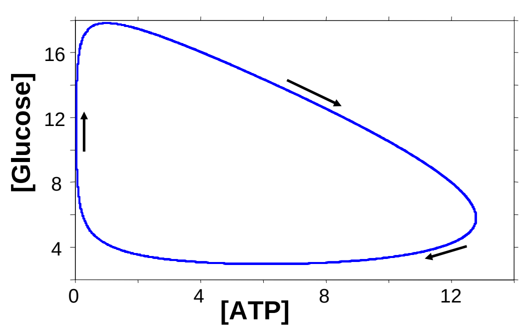


[G] and [ATP] converge to a "stable fixed point"

Stability analysis of ODE systems

In 2D phase plane, direction determined by: $\begin{bmatrix} d[ATP]/dt \\ d[G]/dt \end{bmatrix}$

At any given location, the derivatives define a vector in the phase plane



$$\frac{d[G]}{dt} = V_{in} - k_1[G][ATP]$$

$$\frac{d[ATP]}{dt} = 2k_1[G][ATP] - \frac{k_p[ATP]}{[ATP] + K_m}$$

Summary

A "fixed point" of a dynamical system is a set of variables where all derivatives are equal to zero.

A fixed point can be stable, meaning that after a small perturbation away from the fixed point, the system will return to that fixed point.

With two-variable systems, it can be helpful to plot one variable versus the other, in the "phase-plane."