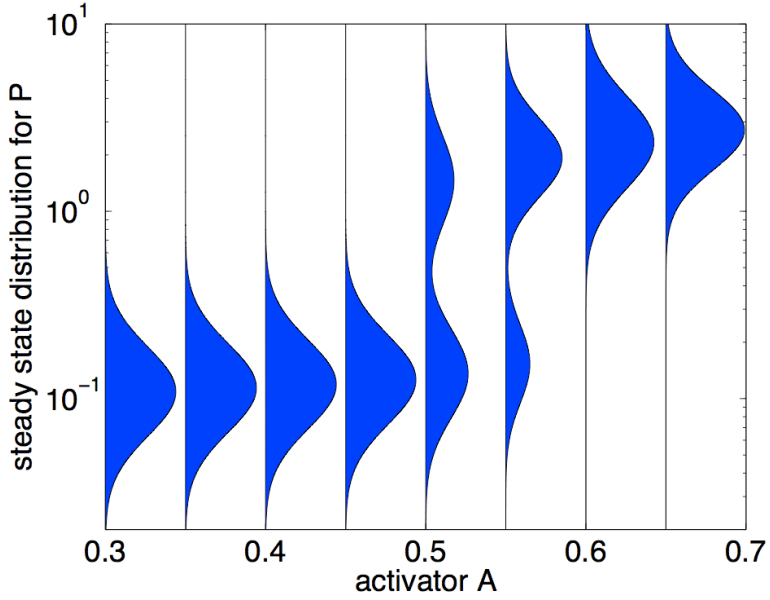


Bifurcation in Biological Systems

Bifurcation

If the variation of a parameter changes the **qualitative behavior** of the steady state(s), we call it bifurcation.

By qualitative behavior, we mean

a) **number of steady states**

b) **stability of the steady states**

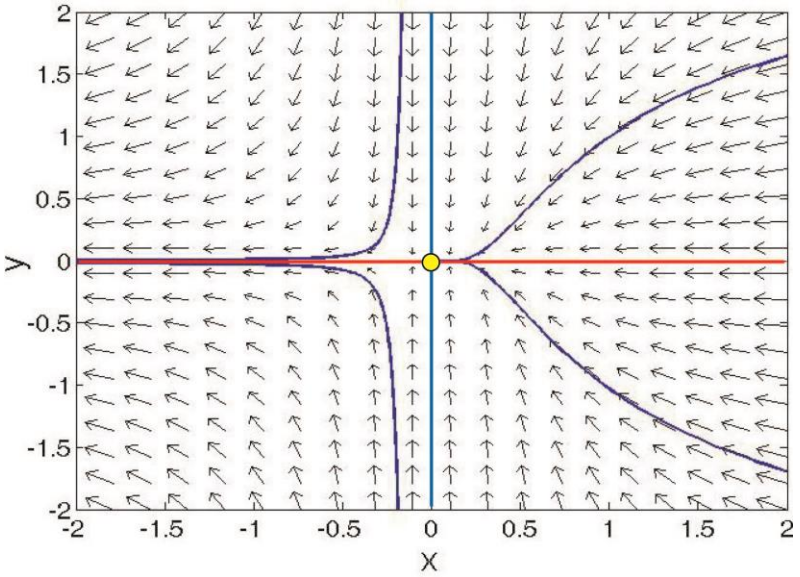
Change in either of these two or both, will change the phase portrait. Therefore, bifurcation in a sense is change in the phase portrait of the system with change in a parameter.

An example in a system of ODEs

$$\frac{dx}{dt} = m - x^2 \qquad \frac{dy}{dt} = -y$$

m < 0; No real steady state

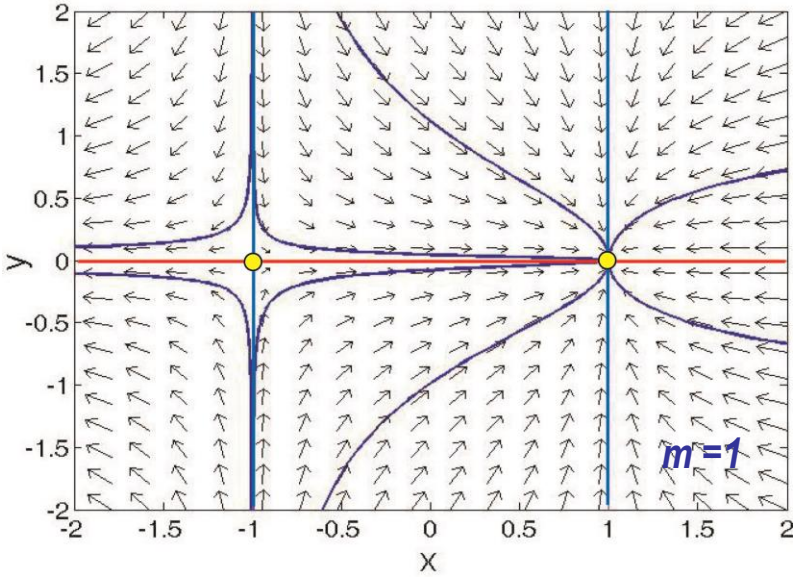
m = 0; steady state at (0,0) → Saddle-node type



m > 0;

Steady state at $(-\sqrt{m}, 0)$ → Saddle point

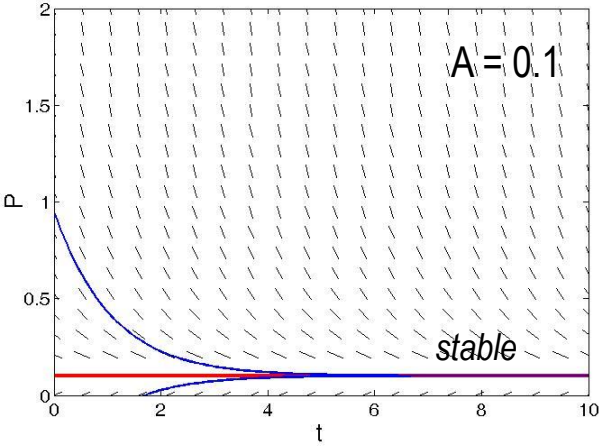
Steady state at $(+\sqrt{m}, 0)$ → Stable node/sink

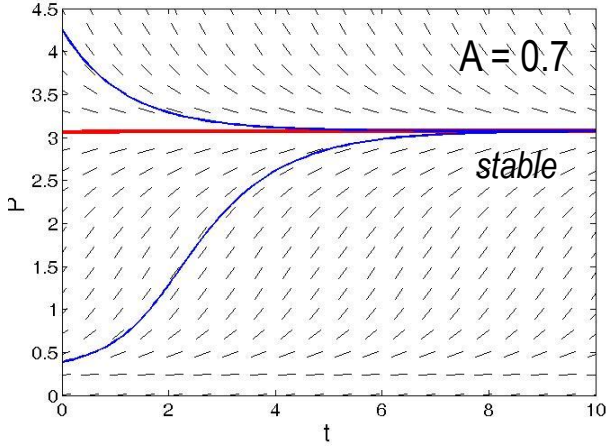


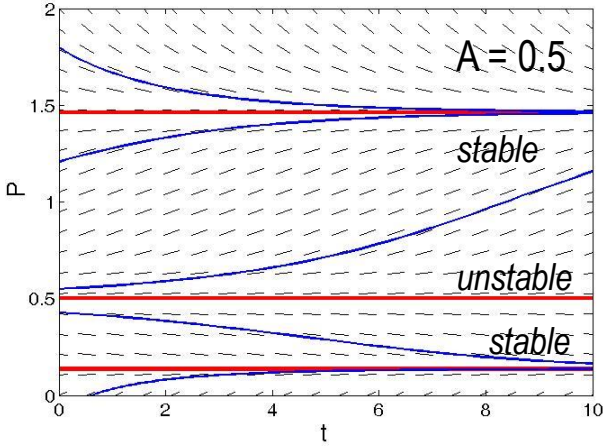
From Bifurcation to cellular heterogeneity

A signal A controls expression of a protein P & P also controls its own expression

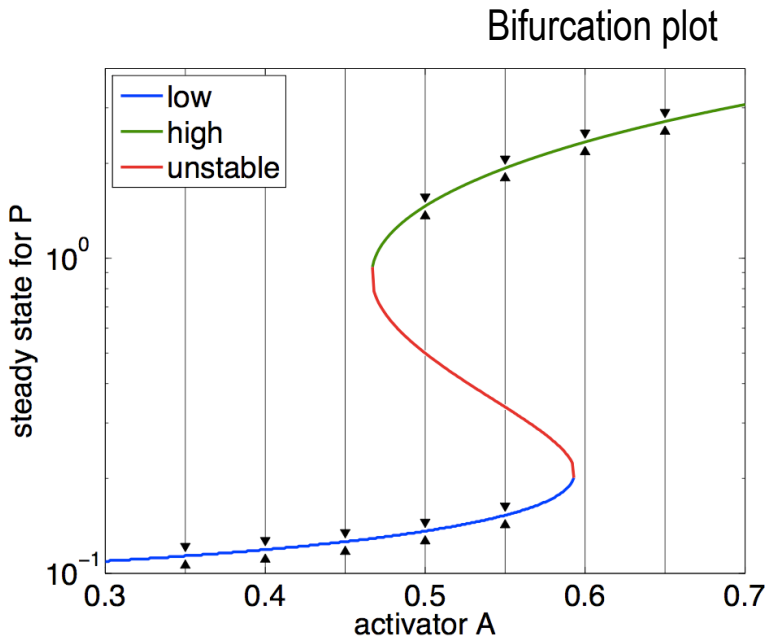
$$\frac{dP}{dt} = 0.1 + 10.\frac{A^2}{1+A^2}.\frac{P^2}{1+P^2} - P$$

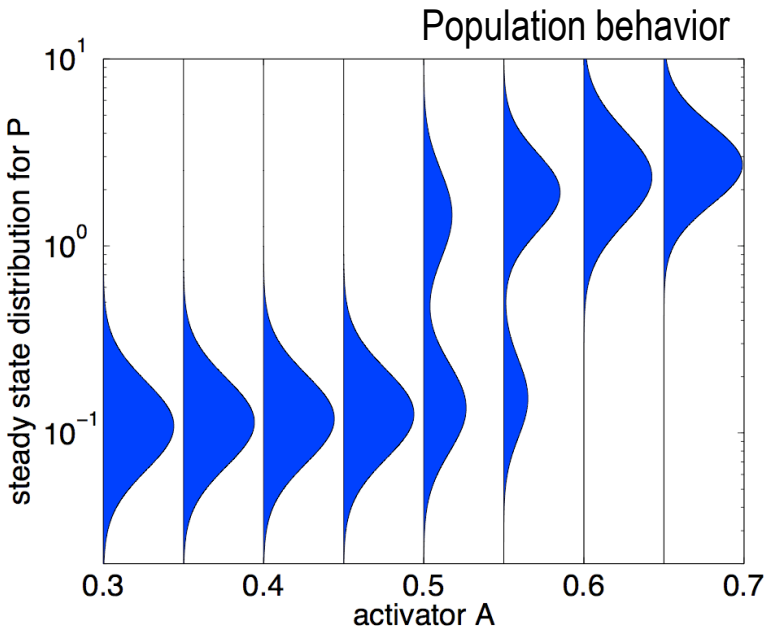






From Bifurcation to cellular heterogeneity



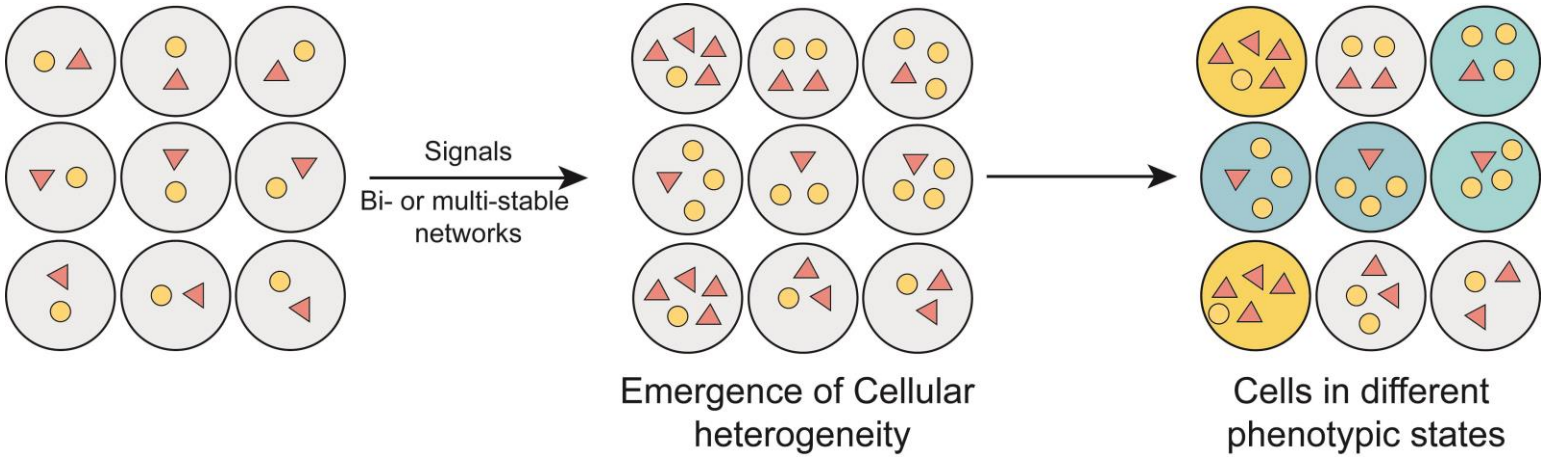


Bistable system → Bi-modal population distribution

Ref: PLOS Computational Biology

Bifurcation in Developmental Biology

One single cell type → Multiple cell type

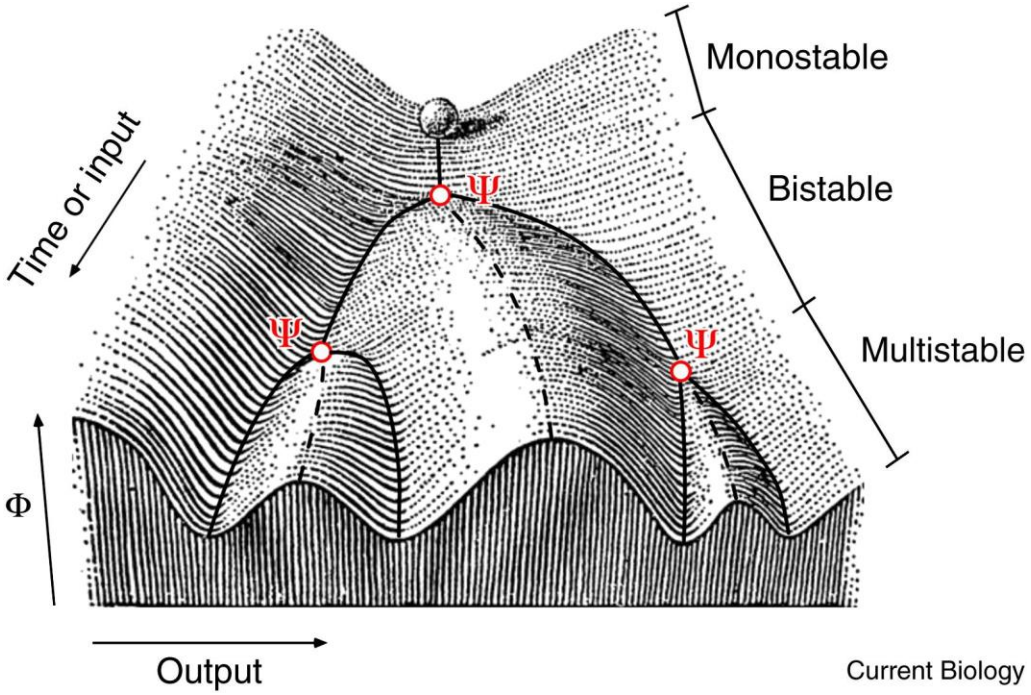


Key molecules of embryonic development like NANOG shows bistability

Bifurcation in Developmental Biology

One single cell type → Multiple cell type

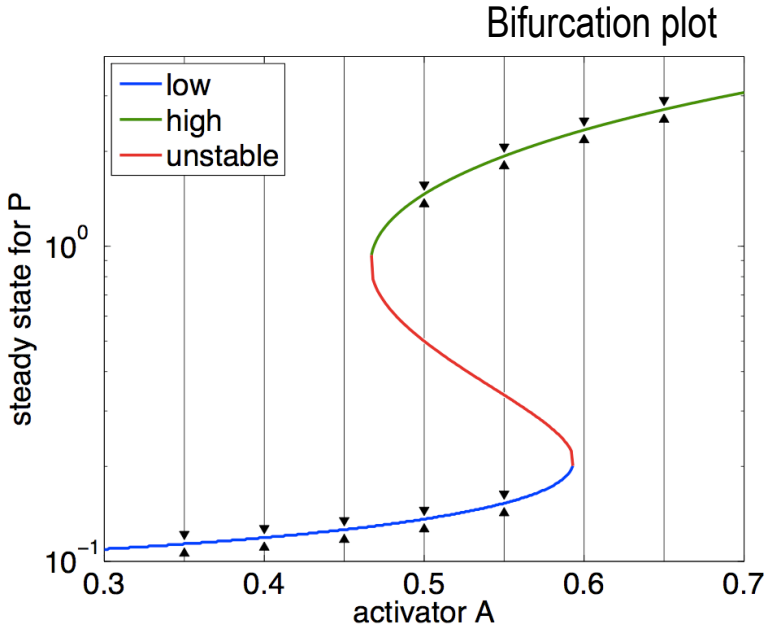
Waddington's landscape



From Bifurcation to Hysteresis

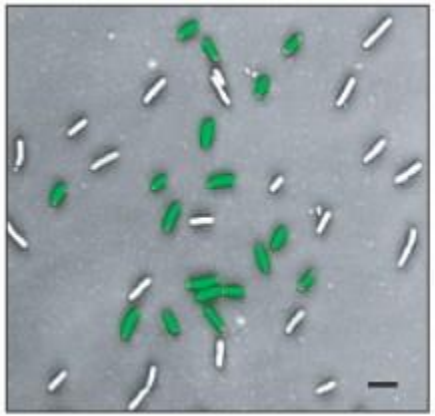
Hysteresis: The future steady state is chosen based upon the past steady state

Cell achieves molecular memory



From Bifurcation to Hysteresis

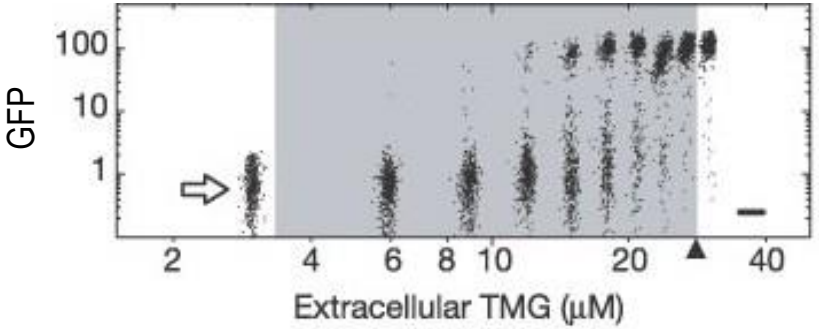
GFP under control of lac operon
Induced by TMG
Has bistability



Ref: Nature

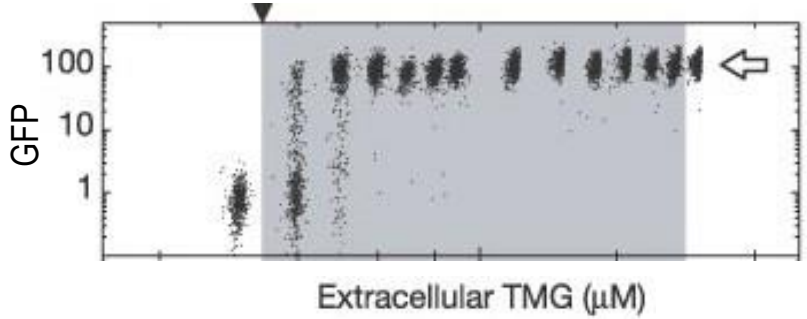
(Increasing TMG with time)

Starting population: Uninduced



(Decreasing TMG with time)

Starting population: With maximum induction



Key points:

1. Bifurcation explains various biological phenomena, from population behavior to cell differentiation
2. Bifurcation with bi-stability / multi-stability gives rise to:
    1. Cellular heterogeniety
    2. Bimodal / multimodal cell population
3. Bifurcation can give rise to hysteresis, thereby creating molecular memory.