Bistability in biochemical signaling models

Part 3

Icahn School of Medicine at Mount Sinai

SBCNY

Outline: Part 3

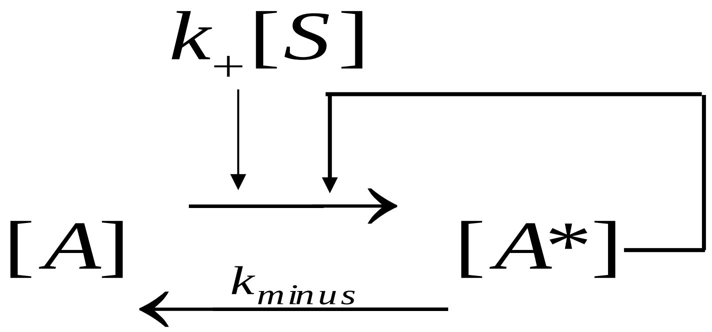
How to predict if bistability will be present?

Rate-balance plots

Examples of rate-balance plots in MATLAB

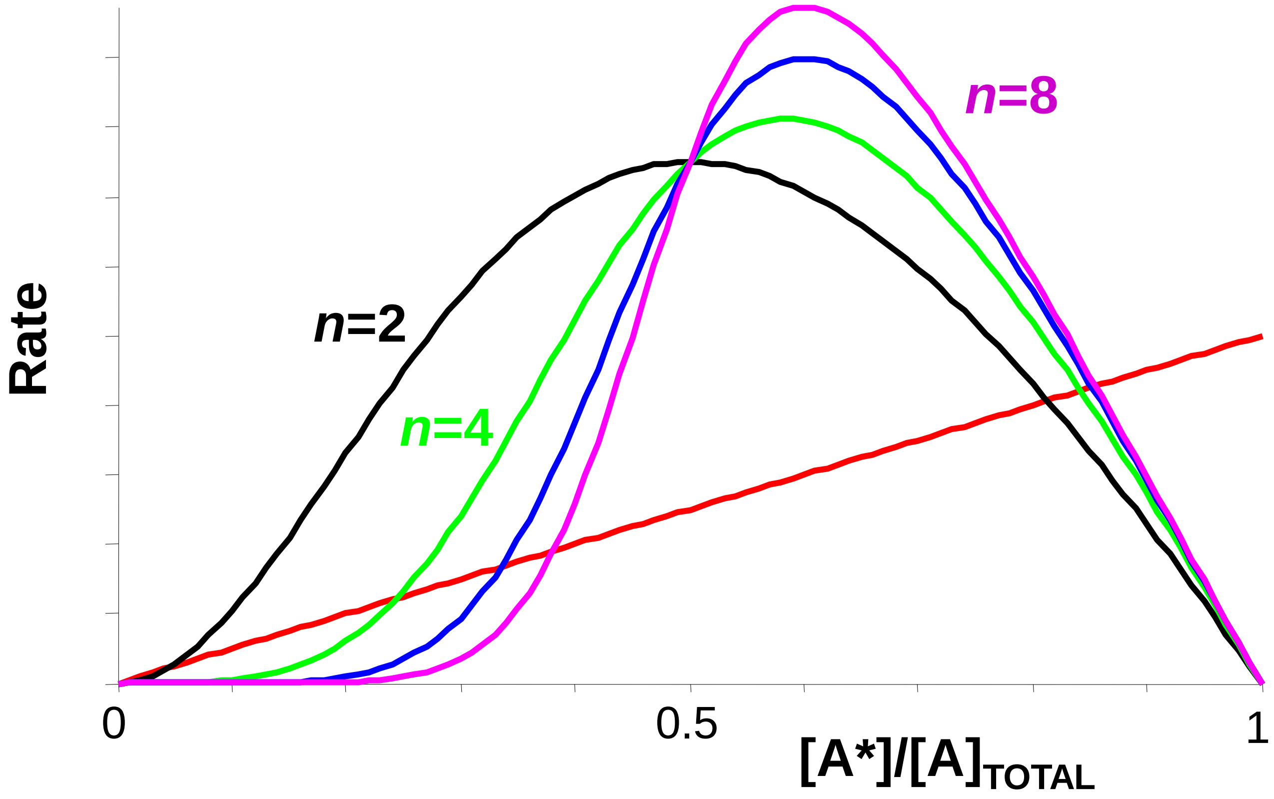
Rate balance plots

3) Michaelian system with ultrasensitive feedback



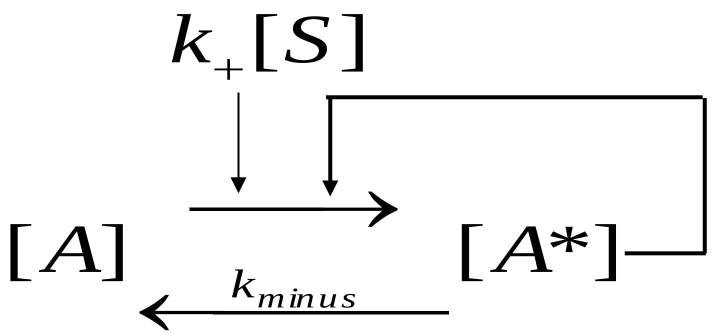
$$FR = \left(k_+[S] + k_f \frac{[A^*]^n}{[A^*]^n + K_{mf}^n} \right) \left([A]_{TOTAL} - [A^*] \right)$$

Effects of changes in hill exponent *n*



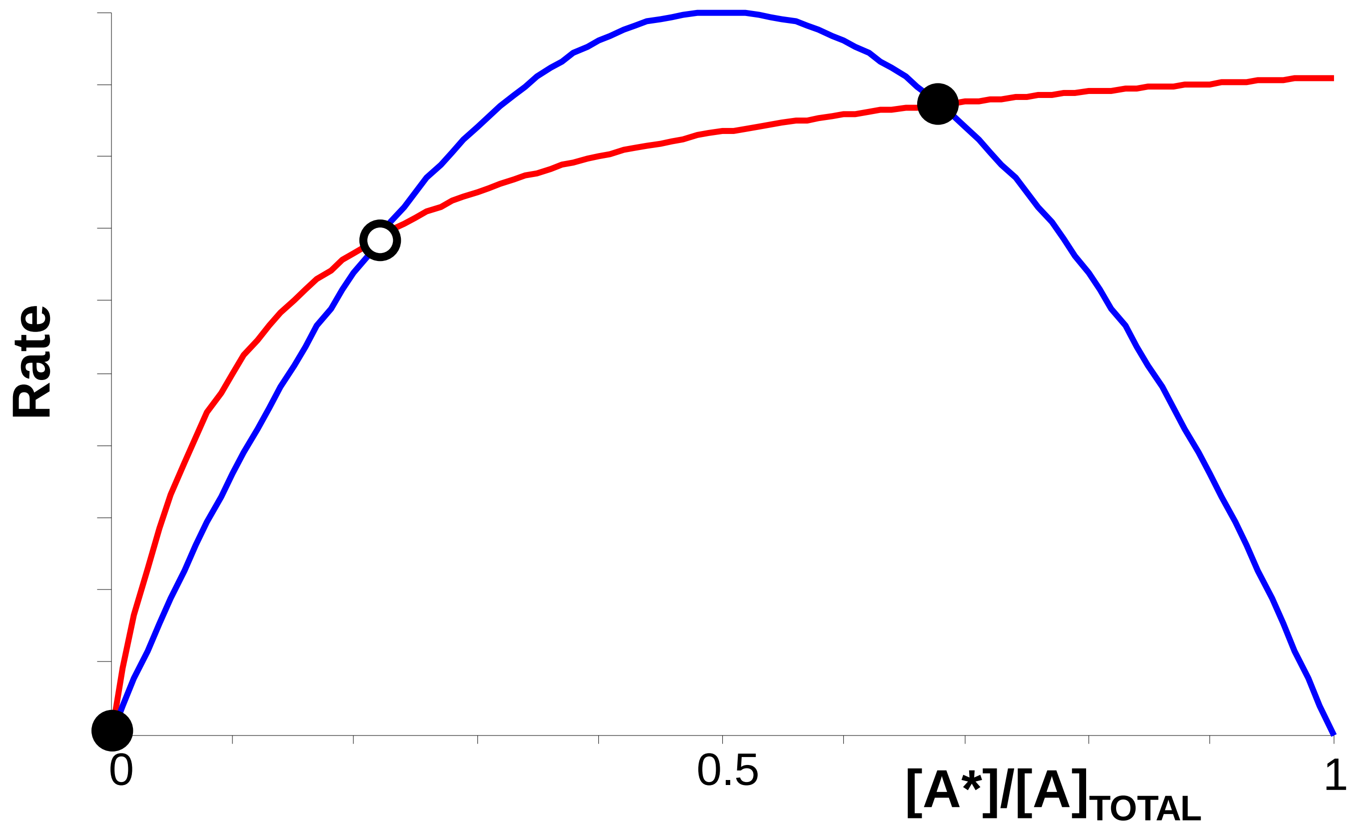
Rate balance plots

4) Linear feedback plus saturating back reaction



$$FR = \left(k_+[S] + k_f[A^*]\right)\left([A]_{TOTAL} - [A^*]\right)$$

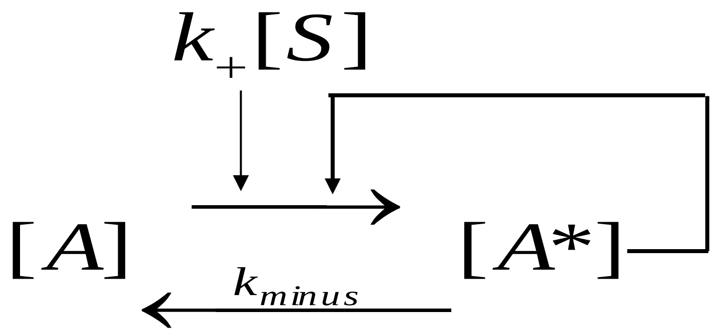
$$BR = k_{minus}\left(\frac{[A^*]}{[A^*] + K_{mb}}\right)$$



Rate balance plots

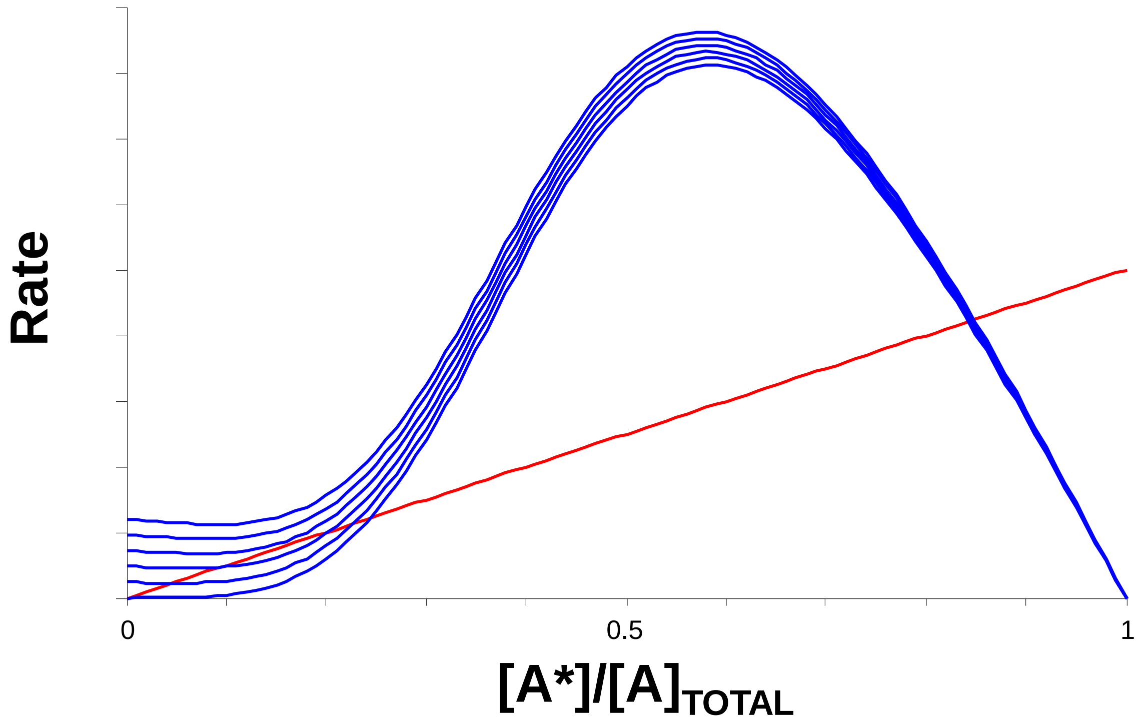
How can the cell change states?

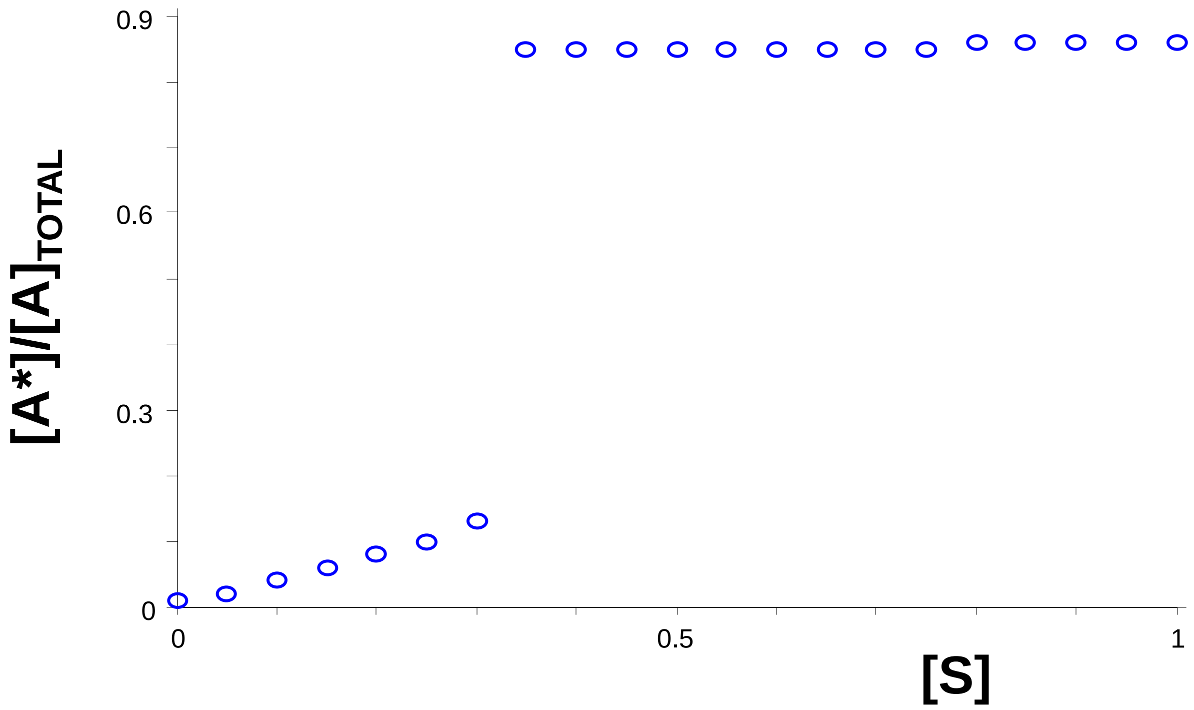
Vary the amount of stimulus [S]



Most plots have assumed [S]=0

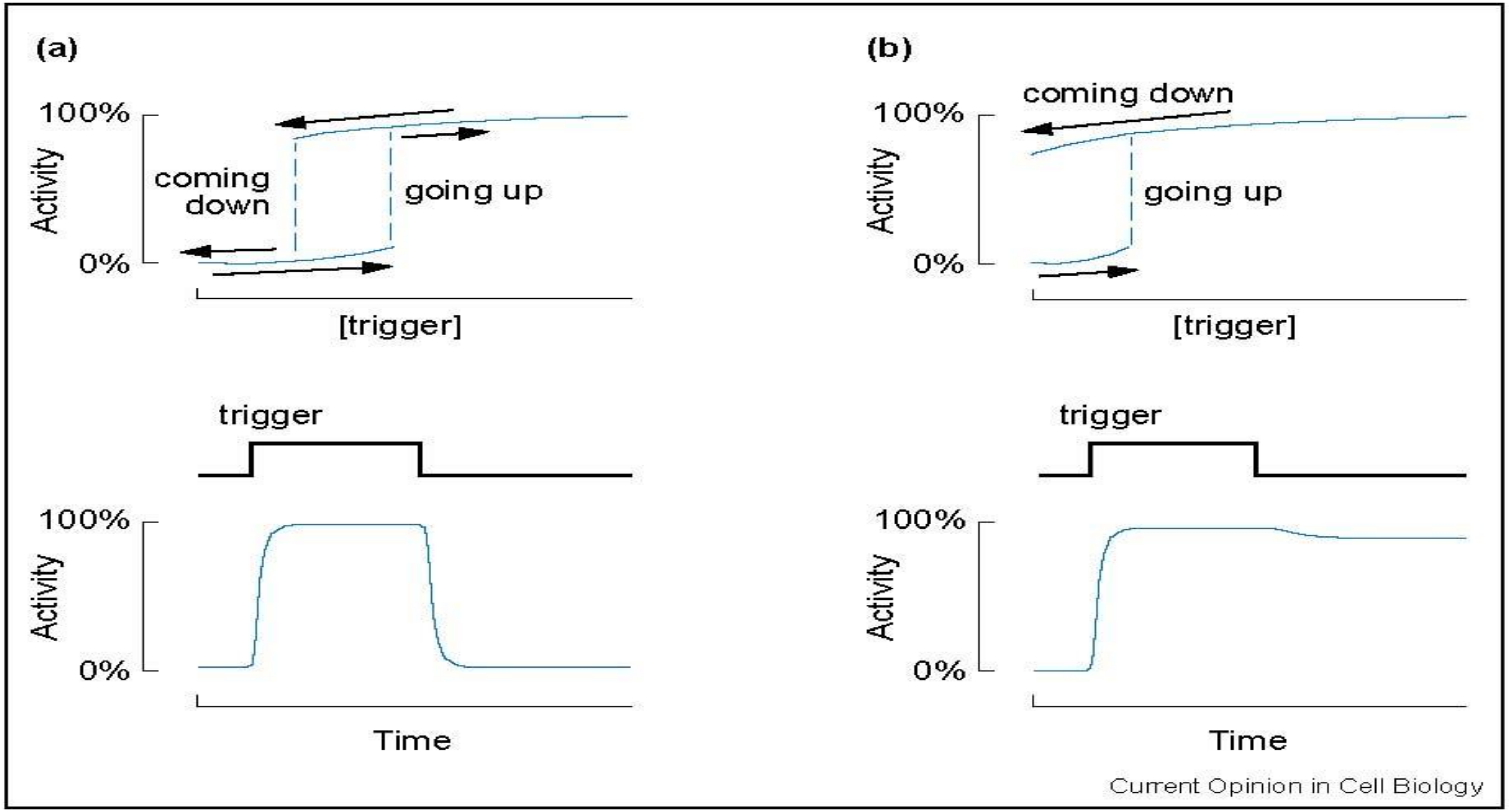
$$FR = \left(k_+[S] + k_f \frac{[A^*]^n}{[A^*]^n + K_{mf}^n} \right) \left([A]_{TOTAL} - [A^*] \right)$$





Where the system switches between 3 and 1 steady-states is a bifurcation

Switching can be reversible or irreversible



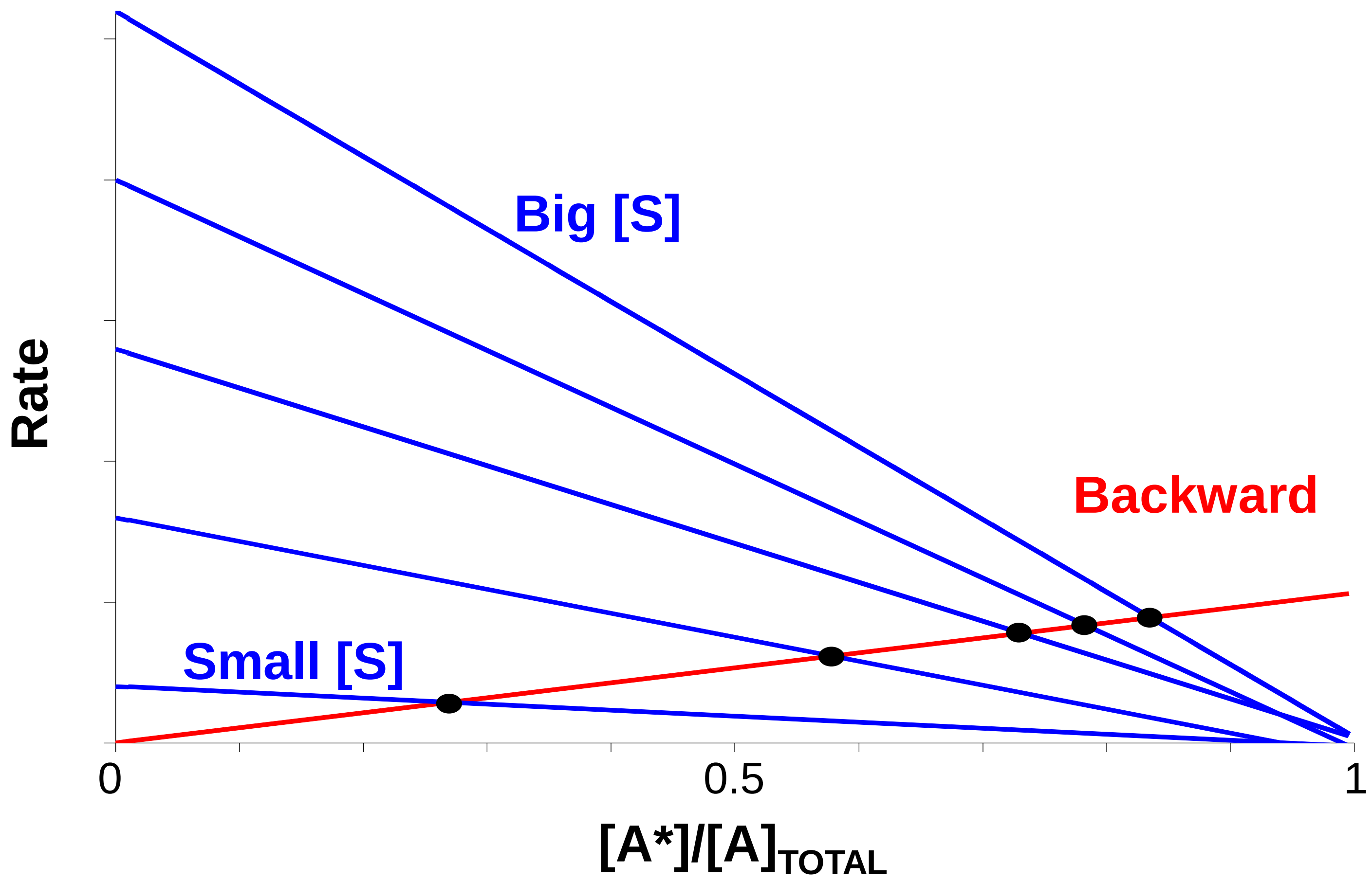
Ferrell (2002) *Curr. Op. Cell Biol.* 14:140–148.

In either case, transition on the way up is higher than transition on way down

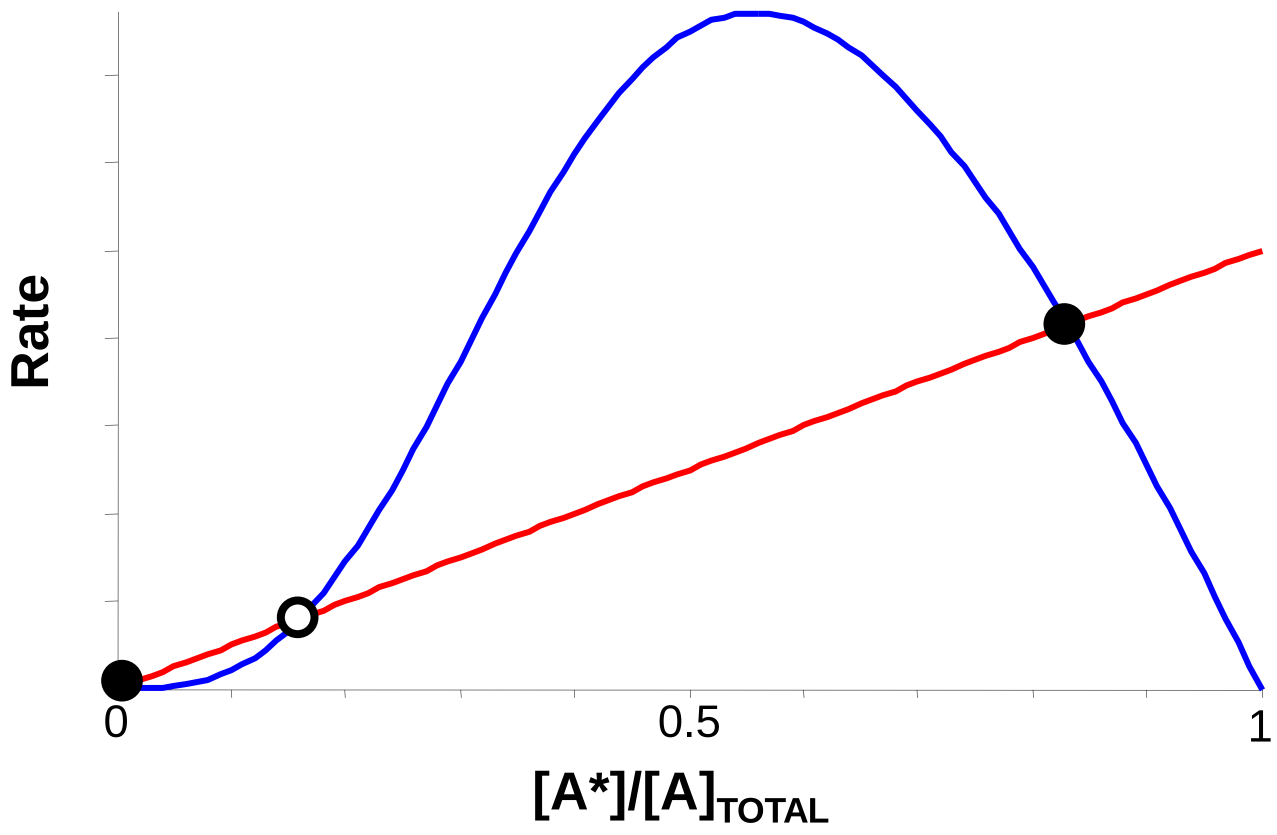
Example: rate-balance plots in MATLAB

We will demonstrate rate-balance plots under two conditions

(1) No feedback



(2) Ultrasensitive positive feedback



Summary

In a one-variable system, bistability can be produced by:

ultrasensitive positive feedback

a back reaction that saturates

Analysis of rate-balance plots can generate a bifurcation diagram showing a transition from monostability to bistability.

Array arithmetic in MATLAB can be used to produce helpful rate balance plots.