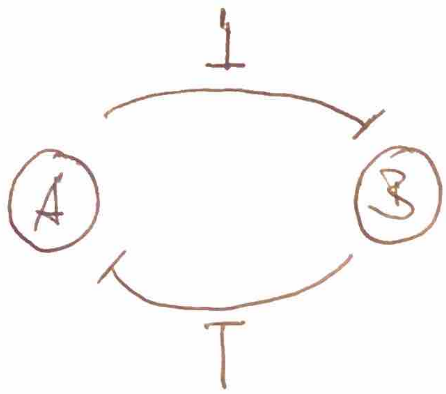
Bistability and the toggle switch

We would like to design a biochemical device which has two stable states and one can switch between them



mutual inhibition

$$\boxed{\dot{A} = \frac{\alpha_1}{1+B^n} - A \qquad \dot{B} = \frac{\alpha_2}{1+A^n} - B}$$

A and B bind to the promoter of ~~the~~ each other and inhibit expression

Steady state: $A = \dfrac{\alpha_1}{1+B^n}$; $B = \dfrac{\alpha_2}{1+A^n}$

Plot the nullclines: $\cancel{A = \alpha_1}$

$$\boxed{B = \frac{\alpha_2}{1+A^n} \quad (\dot{B}=0) \qquad B = \left(\frac{\alpha_1}{A} - 1\right)^{1/n} \quad (\dot{A}=0)}$$

The first one ($\dot{B}=0$) is easy

$B'(A=0)=0$ for $n>1$

$B(A=0)=\alpha_2$; $B(A\to\infty)=0$; $\frac{dB}{dA}=-\frac{\alpha_2}{(1+A^n)^2}\, n A^{n-1}$

$\left.\frac{dB}{dA}\right|_{A=0}=0$

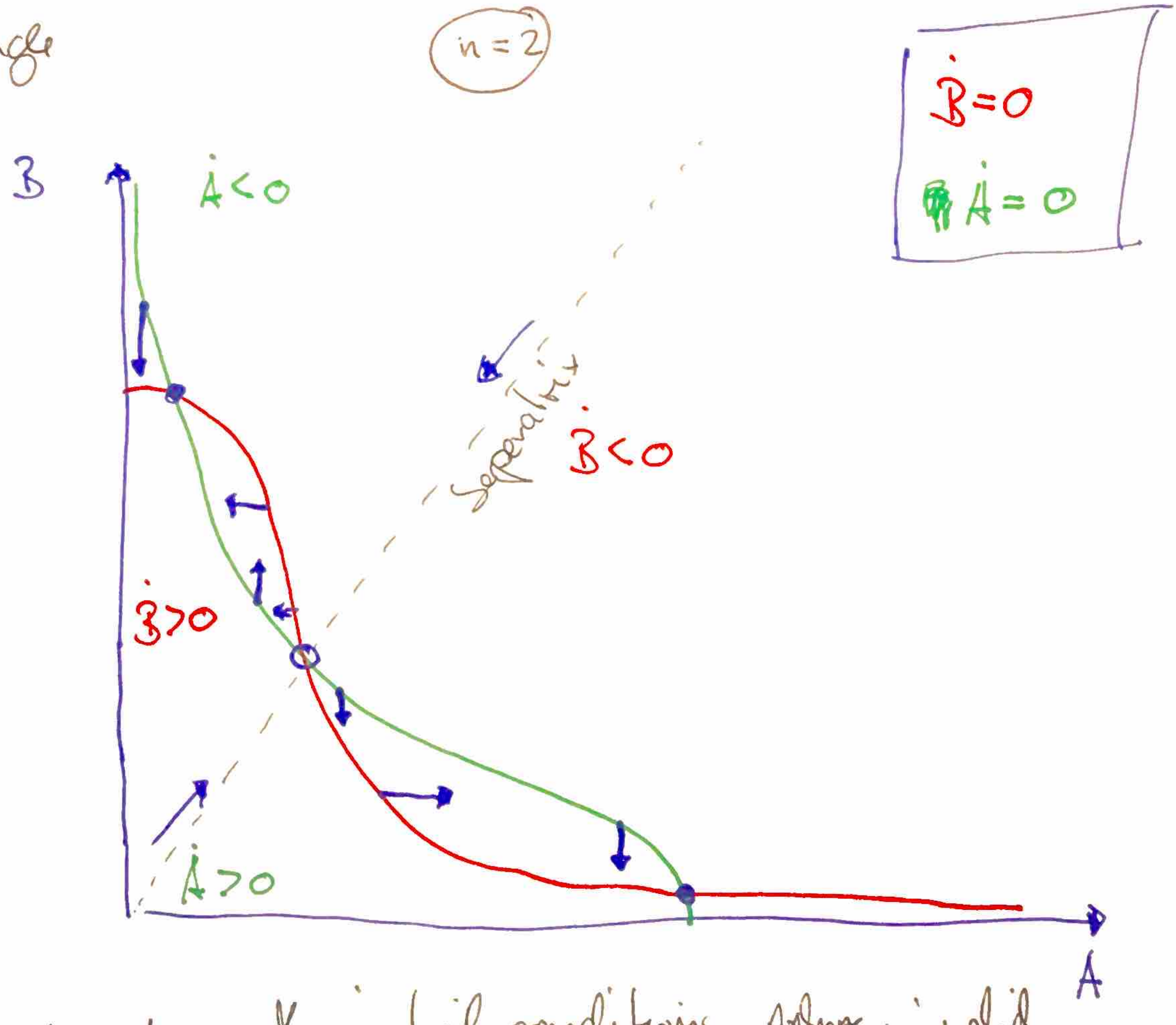
The second one is a bit more difficult

$B(A=0)=\infty$; $B(A\to\alpha_1)=0$; $B(A>\alpha_1)\notin\mathbb{R}$

$$\frac{dB}{dA}=-\left(\frac{\alpha_1}{A}-1\right)^{\frac{1}{n}-1}\frac{\alpha_1}{A^2} \Rightarrow B'(A\to\alpha_1)=-\infty$$

This means the nullcline crosses the A-axis with a right angle

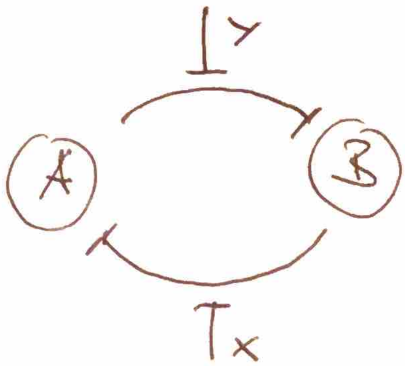
n = 2



It depends on the initial conditions in which fixed point the system ends

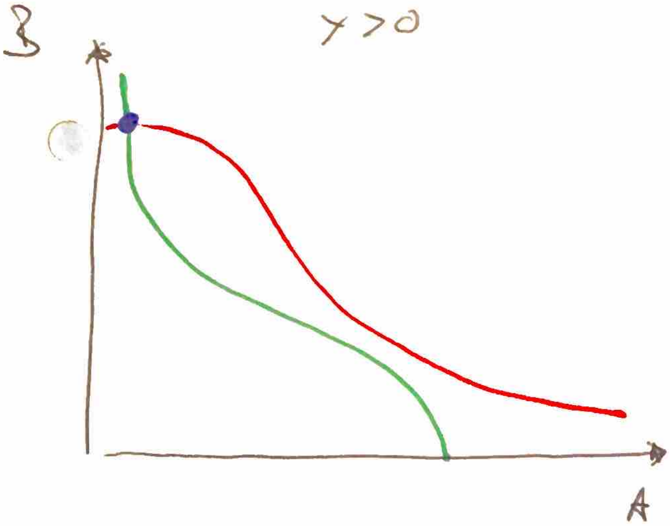
Now consider the inducer

$$\boxed{\dot{A} = \frac{\alpha_1}{1+\frac{B^2}{1+x}} - A \qquad \dot{B} = \frac{\alpha_2}{1+\frac{A^2}{1+y}} - B}$$

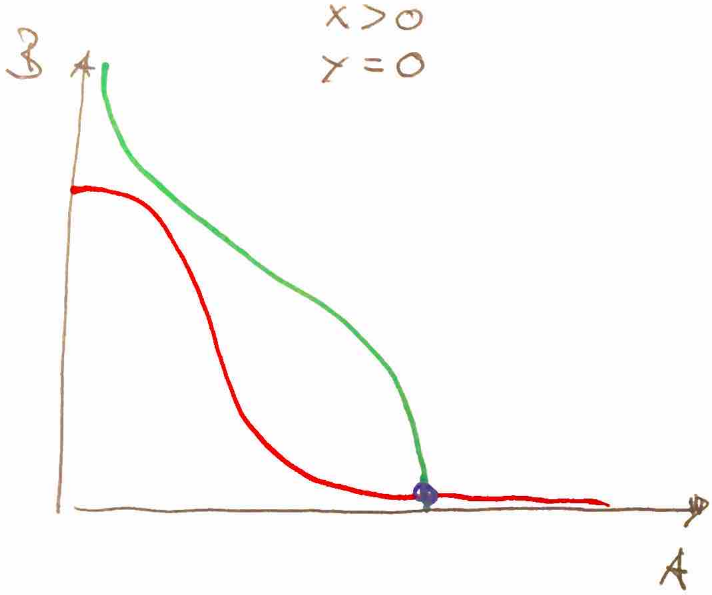


$$\Rightarrow \quad \boxed{\underbrace{B = \frac{\alpha_2}{1+\frac{A^2}{1+y}}}_{\dot{B}=0} \; ; \quad \underbrace{B = \sqrt{1+x}\,\sqrt{\frac{\alpha_1}{A}-1}}_{\dot{A}=0}}$$

$x = 0$
$y > 0$



$x > 0$
$y = 0$

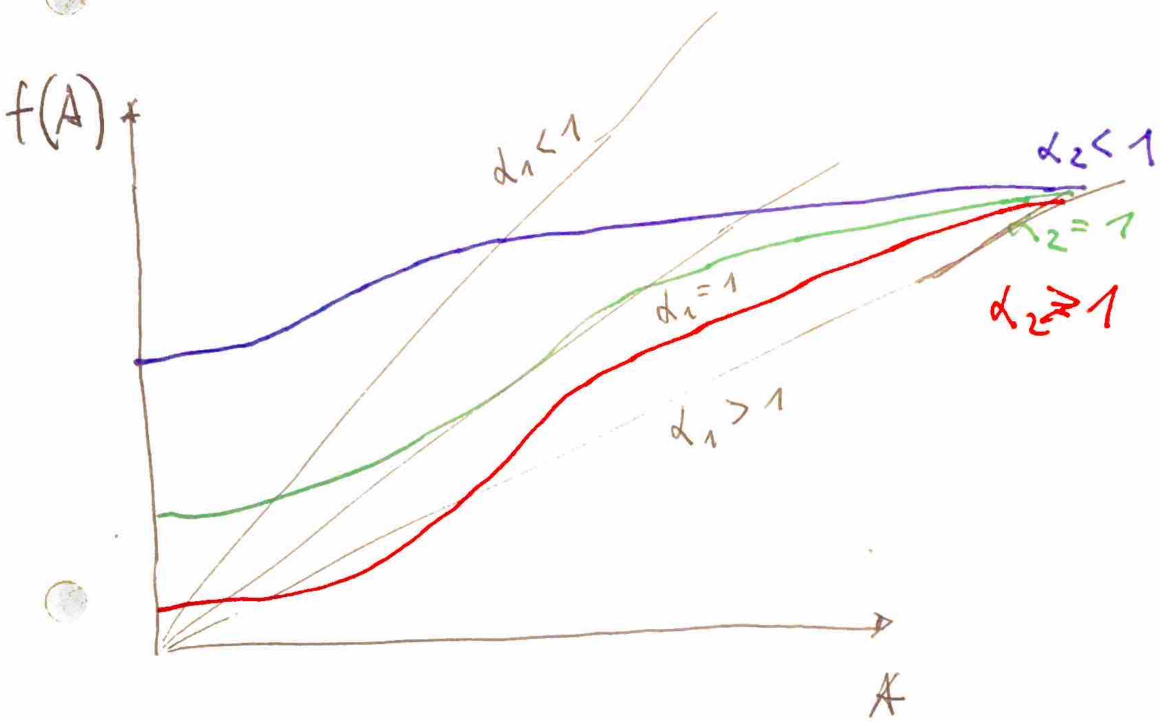


Effect of imbalanced promotor strength

$$A = \frac{\alpha_1}{1+B^2} \quad ; \quad B = \frac{\alpha_2}{1+A^2}$$

plot these as independent functions

$$\Rightarrow A = \frac{\alpha_1}{1+\left(\frac{\alpha_2}{1+A^2}\right)^2} \Leftrightarrow \frac{A}{\alpha_1} = \frac{1}{1+\left(\frac{\alpha_2}{1+A^2}\right)^2}$$



Only if the promotor strength is sufficiently large and the promotors are equally strong bistability occurs.