Toggle Switch is one dimensional (why toggle switch)

- Simple transcriptional model for P.

\[ \frac{dP}{dt} = \beta - \alpha P \]

\[
\begin{align*}
\text{production term} & \quad \text{degradation term} \\
\beta & \quad \alpha P
\end{align*}
\]

Steady state of the system

We can find steady states by solving

\[ \frac{dP}{dt} = 0 \Rightarrow 0 = \beta - \alpha P \]

\[ \Rightarrow P_{st} = \frac{\beta}{\alpha} \]

(Aside: This model obeys exponential kinetics (it's linear in P)

\[ P(t) = \frac{\beta}{\alpha} (1 - e^{-\alpha t}) + P_0 e^{-\alpha t} \]

Graphical way to find steady state (aka "fixed points")

Analyzing stability of fixed points, arrows show direction of derivation.

Stable fixed point
Positive feedback

Production term can be function of $P$.
- Increasing function of $P$: “positive feedback”
- Decreasing function of $P$: “negative feedback”

Let’s consider first case

- Production term saturates
- Hyperbolic production term produces only one stable fixed point

Sigmoidal production term

- Can have 2 stable fixed points = bistability
- Which one reached depends on when system starts
  “System has memory”
Let's consider a system where the production term is a sum of a sigmoidal function and a constant function of $P$:

![Graph showing a sigmoidal function and a constant function](image)

- $\beta < \beta_{\text{crit}}$
- $\beta = \beta_k$
- $\beta > \beta_u$

At exactly right value of $\beta$, curve touches x-axis.

This is called a bifurcation point - a pair of fixed points.

Keep going, and lower fixed points merge & disappear!

Bifurcation diagram summarizes fixed point behavior:
- Upper FP (stable)
- Lower FP (stable)
- Unstable FP

![Bifurcation diagram](image)
Toggle switch

System exhibits memory in bistable region
Hard to turn ON when it starts in OFF state.
Hard to turn OFF when it starts in ON state.

If $\beta$ is a signal, switch is robust to noise up to a threshold level, but once it's ON, doesn't require high level to maintain ON state.

This type of bifurcation is called a "saddle node" bifurcation.

So-called "canonical" form is intersection of parabola with x-axis:

$$\frac{dx}{dt} = \lambda - x^2$$

(Briefly)

A 2D toggle switch

$\begin{align*}
X &\rightarrow Y \quad \text{mutual inhibition; either } X \text{ or } Y. \\
\frac{dx}{dt} &= \frac{Z}{1+y^n} - x \\
\frac{dy}{dt} &= \frac{Z}{1+x^n} - y
\end{align*}$

Can find and analyze fixed points in x-y plane.
Method: Plot the "nullclines."

\[ x_{nc} : \quad \frac{dx}{dt} = \frac{2}{1+xy} = x = 0 \]
\[ \Rightarrow x_{nc} : \quad x = \frac{2}{1+y} \]

\[ y_{nc} : \quad \frac{dy}{dt} = \frac{2}{1+xy} - y = 0 \]
\[ \Rightarrow y_{nc} : \quad y = \frac{2}{1+x} \]

Fixed points from intersections of nullclines.