STABILITY ANALYSIS

Principles of Synthetic Biology | Fall 2011 | Midterm Review

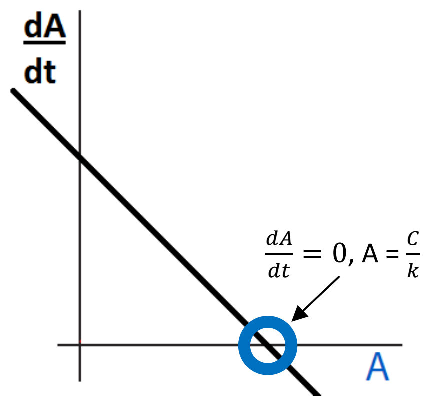
Single-Species Transient Stability Analysis

Let's start simple, first-order feedback where A represses translation of A:

⃠ -> A (constitutive promoter)
A -> ⃠ (degradation, k)

Simplified ODE: $\frac{dA}{dt} = -k * A + C$

where C is an A-independent generation term. Therefore the plot can be represented by a straight line with slope –k and positive intercept C.

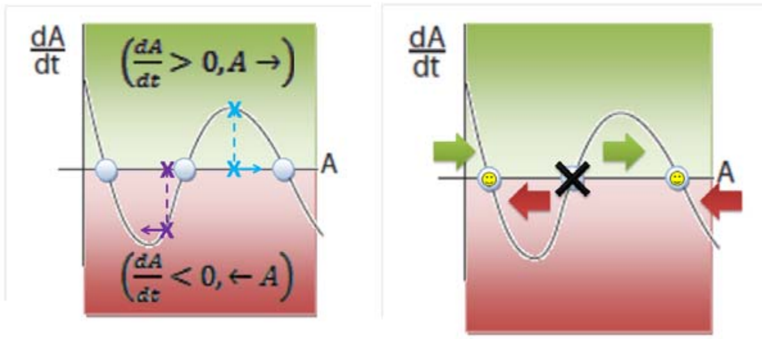


Stability occurs in steady-state where: $\frac{dA}{dt} = 0$. In this simple system, there is only one intersection point.

We can test the stability of this point by demonstrating decrease in concentration of A triggers a positive $\frac{dA}{dt}$ for the consequent time-step, returning back towards stability. Likewise, and increase in concentration of A results in a negative $\frac{dA}{dt}$, also returning in the direction of stability.

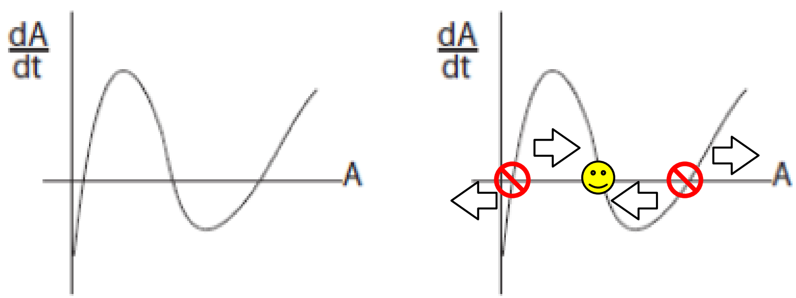
First-order feedback systems must have negative feedback for stability. Intuitively, this means a system with unregulated production of A would not have stability. Think of other first-order cases examples where stability is not possible (ex. Functions without positive intersections with the x-axis.) These anomalies extrapolate to higher order systems.

Now let us consider the first problem on the last year's midterm:



- Critical points of stability occur when $\frac{dA}{dt} = 0$. Marked below with circles in the figure on the left.
- For any given transient concentration of A, $\frac{dA}{dt}$ will correlate to whether the system is currently consuming A $\left(\frac{dA}{dt} < 0, \leftarrow A\right)$ or generating A $\left(\frac{dA}{dt} > 0, A \rightarrow\right)$.
- From $\frac{dA}{dt}\, vs.\, A$, we are able, for any given transient concentration of A, determine what stable steady-state concentration it will tend towards.

Similarly:



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Dual Species Steady State Stability Analysis

Nullcline: The function representing the *steady state concentration of Y* as a function of the concentration of X.

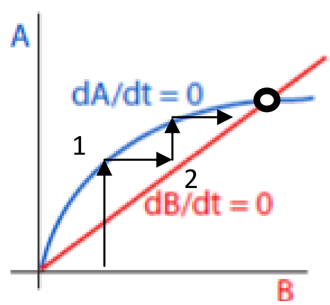
Stable combination pairs of X and Y may be derived from an overlayed XY plot comprising of

- *Steady state concentration of Y* as a function of *X concentration*, overlayed with the
- *Steady state concentration of X* as a function of the concentration of Y.

Assume dA/dt is negative for large A and dB/dt is negative for large B.

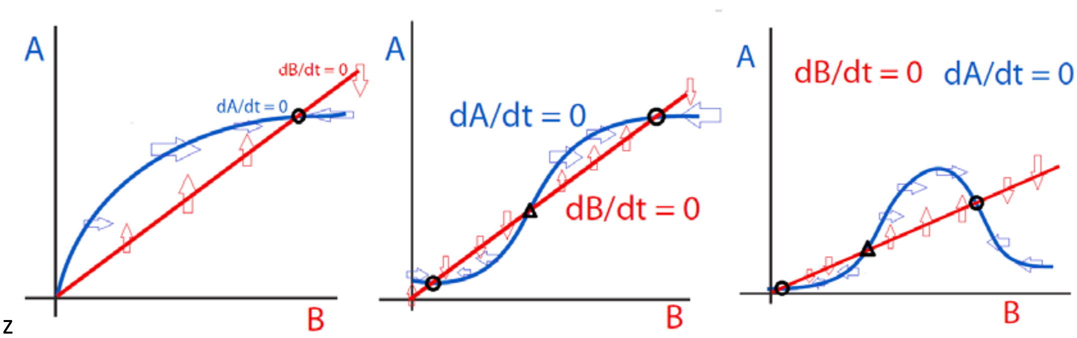
1. Using this plot, for any given concentration of species B, you are able to determine the steady state concentration that species A should approach.
2. Continuing this analysis, if the concentration of A reaches that value, you can then find the correlated steady state concentration of species B by mapping to the dB/dt = 0 curve.

Using this dynamic analysis, we can determine a stable critical point where dA/dt = dB/dt = 0.



With the additional information that dA/dt is negative for large A and dB/dt is negative for large B, we are able to label the outer regions of the plot for large [A] and large [B] with flux arrows pointing in the negative direction. As flux switches direction at each intersection or critical point, we are then able to quickly label all segments on the plot with the direction of the species flux and visually identify stable intersection points.

Fall 2011 Midterm Q1:



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