GSTDMB 2010
Dynamical Modelling for Biology and Medicine:

SOLUTIONS: Introduction to MATLAB / Qualitative and quantitative model analysis

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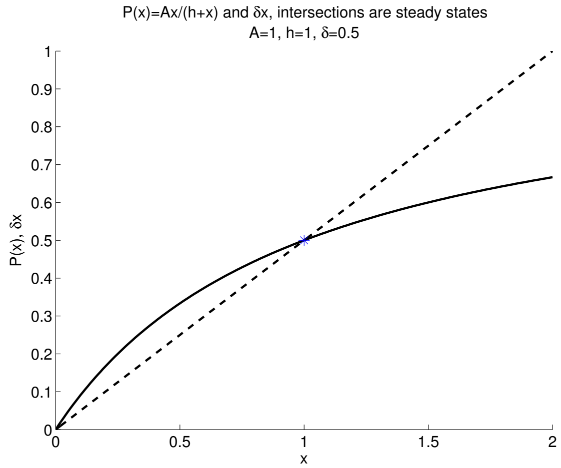
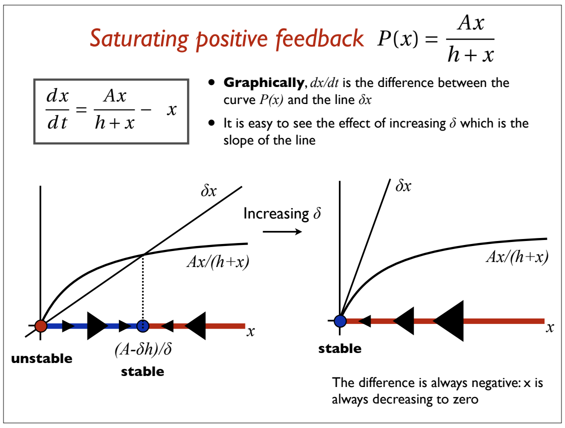
4 Solutions to Exercises

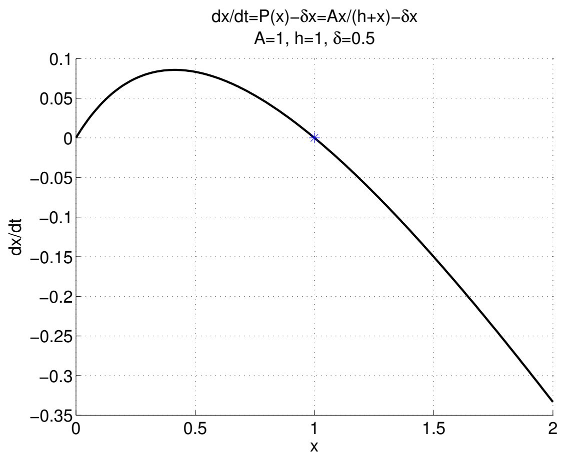
4.1 Positive feedback: $P(x) = \frac{Ax}{h+x}$

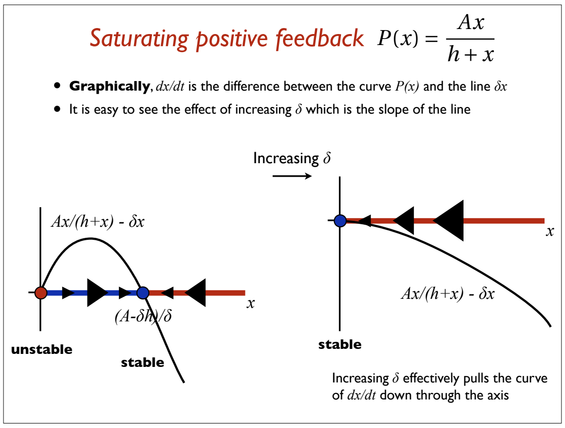
1. Yes, for $\delta = 0.5$ the generated plots in Figure 1 agree with those from the left side of slide 21, reproduced below.



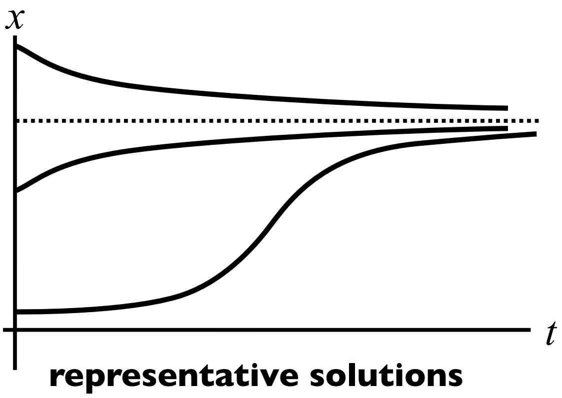


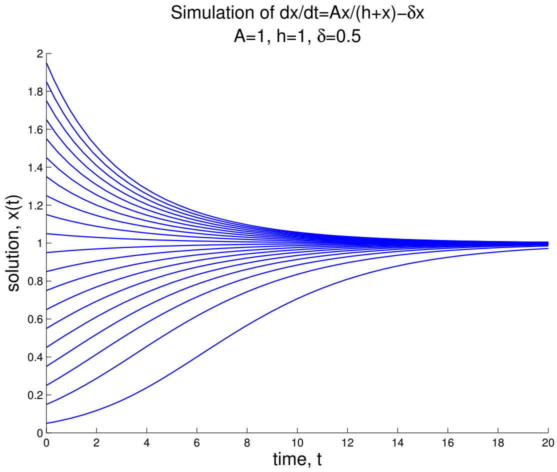
2. For the phase-line diagram, see the left side of slide 22, reproduced below. There is a single stable steady state, and $x = 0$ is unstable.





3. The representative solutions and simulations below do agree:





4. As you increase δ the line moves round until it no longer intersects the curve (at least for positive, and hence biologically relevant, values of x). For these parameter values, the bifurcation is at $\delta = 1$. For $\delta > 1$ the figures agree with those on the right hand sides of slides 21 and 22.

To see the graphs for various values of δ superimposed on single plots, try running "`saturatingmultid.m`".

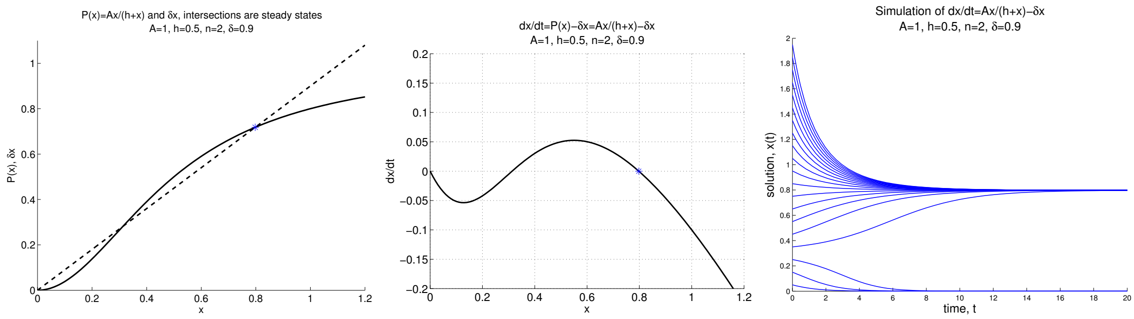
4.2 Positive feedback: $P(x) = \frac{Ax^n}{h^n+x^n}$

For our version of "`hill.m`", see the file "`hillsol.m`".

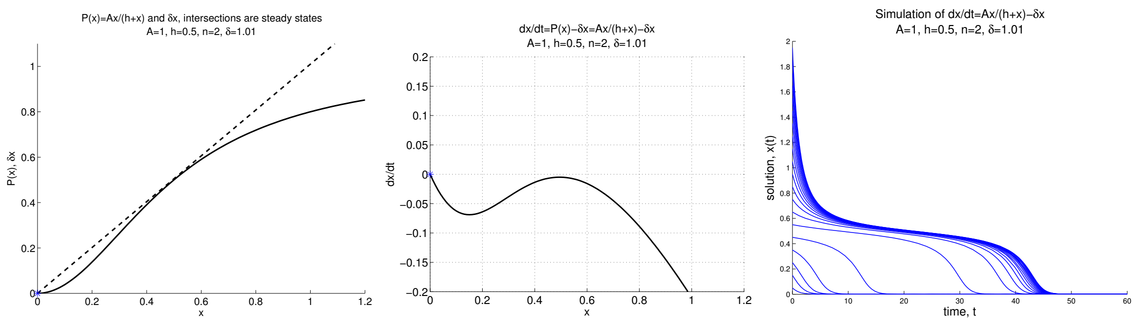
1. $P(x) = \frac{Ax^n}{h^n+x^n}$ with $n = 2$ (compared to that with $n = 1$) has an inflection (it is *sigmoidal* in shape). It starts with zero slope at $x = 0$, then curves upward, before flattening out. For these parameters, there are three intersections of $P(x)$ with δx, suggesting that there will be bistability.

2. There are two stable steady states, separated by one unstable steady state. Initial conditions with small x go to $x = 0$, those with larger x go to the upper stable steady state.

3. Yes, the simulated solutions do agree with the analysis. The superimposed solutions for multiple initial values `x0` show how different initial values go to different stable steady states.



4. As you increase δ, the line moves round anti-clockwise, and the upper two steady states approach one-another. At $\delta = 1$ they coalesce and are lost in a *fold bifurcation* (also known as a *saddle-node* or *blue-sky* bifurcation). This is illustrated on slide 27 of the lectures. If you increase δ just beyond the bifurcation, solutions starting from large x take a long time to reach the remaining steady state at $x = 0$. You can see why from the phase-line diagram for δ just larger than one—although the upper steady states have gone, the dynamics where they were is *very* slow.



5. As δ is decreased, the two upper steady states get further apart. The largest one gets larger and larger, while the intermediate steady state approaches zero, although it is never *lost*. See the sketch on slide 27.

6. As n increases, the switch in $P(x)$ gets steeper. This does not change the qualitative nature of the system, which will be bistable for δ smaller than a bifurcation value which corresponds to δx being tangent to $P(x)$.

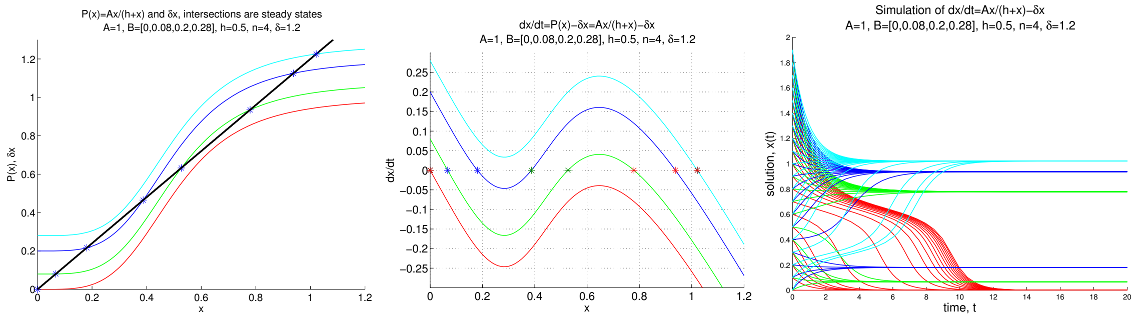
To see the graphs for various values of δ superimposed on single plots, try running "`hillmultid.m`" from the archive you downloaded.

4.3 Positive feedback with constitutive transcription: $P(x) = \frac{Ax^n}{h^n+x^n} + B$

For our version of your "`hillbasal.m`", see the file "`hillbasalsol.m`". To see the graphs for various values of B superimposed on single plots, try running "`hillbasalmultib.m`".

1. With $n = 4$, $A = 1$, $h = 0.5, \delta = 1.2$ and $B = 0$, there is a single stable steady state at $x = 0$. Increasing B first introduces two additional intersections for larger values of x, before the two intersections at lower values are lost.

2. For $B < 0.04$, there is one stable steady state with a small value of x. As B increases further, the graph in the phase-line diagram lifts up until two new crossings appear which correspond to two steady states with larger values of x. Hence, for $0.04 < B < 0.245$ there are two stable steady states, separated by an unstable steady state. Initial values `x0` below (above) the unstable state go to the lower (upper) stable steady state. As B increases further, the graph in the phase-line diagram lifts up until the two crossings corresponding to the lower two steady states disappear. Then all initial conditions go to the only remaining (upper) stable steady state. These ideas can be seen in the figures below, generated by "`hillbasalmultib.m`".



3. The simulated solutions do agree with the analysis.

   For the larger values of B (cyan curves), all solutions converge to a steady state with a high TF level, but those starting from small x do take a long time to reach that remaining steady state because they move very slowly past the *ghost* of the other two steady states. The phase line diagram shows that the rate of change of x is very small there.

4. Sigmoidal feedback plus basal transcription gives the ingredients for a biological switch. Treating B as a switching parameter, for small B all solutions go to a state with low expression of x. Increasing B sufficiently (beyond 0.245) forces a switch to a higher expression level which is robust, since B must be reduced back below 0.04 to switch back to a low expression level. δ can also be seen to act as a switching parameter, so that manipulating mRNA degradation rates could be one way to flip such a *biological switch*.