110231 Nonlinear Dynamics Lab

Exercise Sheet

'Simple models of biochemical switches and oscillators'

Motivated by graph theory and nonlinear dynamics, an influential trend in Systems Biology at the moment is to explore small regulatory devices. Examples are circuits of negative feedback loops as oscillators, feedforward loops as noise filtering devices in gene regulation and interlinked feedback loops acting on different time scales for achieving a balance between robustness and rapid reaction to a stimulus. Here we will explore seven 'small devices' described by Tyson et al. (2003). In addition to learning, how certain types of dynamics can be 'implemented' with simple ODE systems, this exploration will also put to use the set of tools for analyzing ODE systems, which we have accumulated so far.
Please make sure that you understand, how the wiring diagrams are related to the differential equations in each of the cases.

Exercise 1: Reproduce the rate curves and the signal-response curve for the 'linear response' case (1a) from Tyson et al. (2003).

Exercise 2: Reproduce the rate curves and the signal-response curve for the 'hyperbolic response' case (1b) from Tyson et al. (2003).
Why can this two-dimensional system (with $R(t)$ and $R_p(t)$ being the dynamical variables) be represented by a single ODE?

Exercise 3: Reproduce the rate curves and the signal-response curve for the 'sigmoidal response' case (1c) from Tyson et al. (2003).
Confirm that the Goldbeter-Koshland function describes the steady-state concentration of the response R_p as a function of the signal S.

Exercise 4: Reproduce the rate curves and the time course for the 'adaptation' device (1d) from Tyson et al. (2003). Why is the signal-response curve not helpful here?

Exercise 5: Reproduce the rate curves and the signal-response curve for the 'irreversible switch' case (1e) from Tyson et al. (2003), which arises from mutual activation.

Exercise 6: Reproduce the rate curves and the signal-response curve for the 'homeostatic response' case (1g) from Tyson et al. (2003).

Exercise 7: Reproduce the phase portrait and the bifurcation diagram for the activator-inhibitor device (2b) from Tyson et al. (2003).

Reference: Tyson, J.J., Chen, K.C. and Novak, B. (2003) *Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell.* Current Opinion in Cell Biology 15, 221–231.