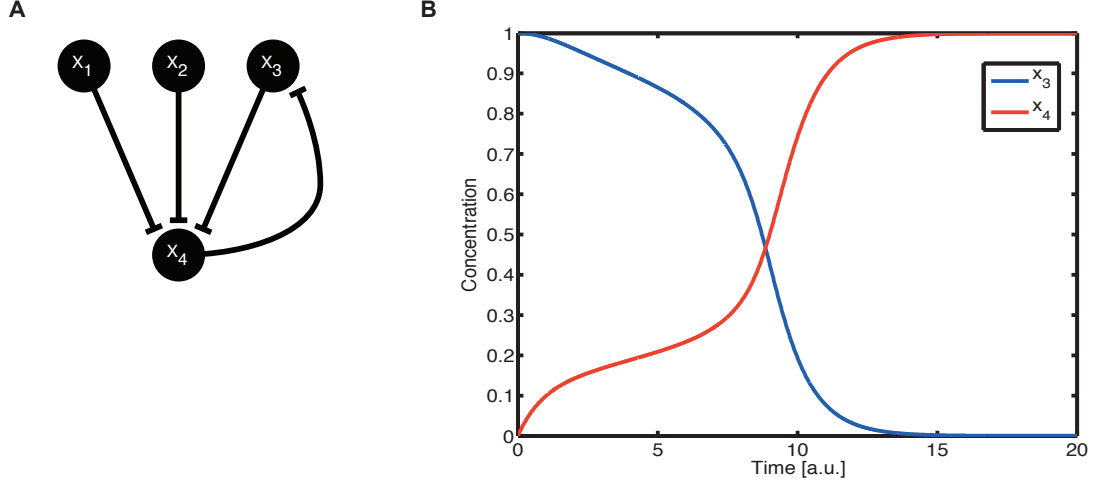


Steady states in discrete and continuous models



We consider the regulatory network between the species X_1, X_2, X_3, X_4 from Figure A, where multiple inputs at a node are linked by an AND gate. Note that this is not the hypergraph representation of the sum-of-product form. The corresponding update functions for species X_3 and X_4

$$B_3(x_4) = \neg x_4 \quad \text{and} \\ B_4(x_1, x_2, x_3) = \neg(x_1 \vee x_2 \vee x_3)$$

are chosen to belong to the limited set of Boolean functions allowed in [1]. The state vector $x_1 = 0, x_2 = 0, x_3 = 1, x_4 = 0$ is a steady state of the Boolean model. The presence of one of its inhibitors (X_3) is enough to repress X_4 . X_3 in turn is active since its only inhibitor (X_4) is off. Note that this is exactly the kind of logic used in [1]. We can now build a continuous model using the transformation method introduced in [1]. The inputs to nodes X_3 and X_4 are

$$\omega_3(\bar{x}_4) = 1 - 2 \frac{\bar{x}_4}{1 + \bar{x}_4} \quad \text{and} \\ \omega_4(\bar{x}_1, \bar{x}_2, \bar{x}_3) = 1 - \frac{4}{3} \frac{\bar{x}_1 + \bar{x}_2 + \bar{x}_3}{1 + \bar{x}_1 + \bar{x}_2 + \bar{x}_3}.$$

We have $\omega_3(0) = 1$ and $\omega_3(1) = 0$, as expected. However, the input to node X_4 is only minimal (0) iff $\bar{x}_1 = \bar{x}_2 = \bar{x}_3 = 1$, which does not agree with the Boolean logic. Here, $B_4(x_1, x_2, x_3) = 0$ iff at least one inhibitor is active.

We now run a numeric simulation of the continuous model starting at the Boolean steady state $\bar{x}_1 = 0, \bar{x}_2 = 0, \bar{x}_3 = 1, \bar{x}_4 = 0$, cf. Figure B. While node X_4 should be completely repressed in this steady state, it still receives an input of $\omega_4 = 1/3$ in the ODE model, which is too high to permanently inhibit its activation. Consequently, we observe a switching of X_3 and X_4 and the model ultimately comes to a rest in the steady state $\bar{x}_1 = 0, \bar{x}_2 = 0, \bar{x}_3 = 0, \bar{x}_4 = 1$.

References

- [1] Luis Mendoza and Ioannis Xenarios. A method for the generation of standardized qualitative dynamical systems of regulatory networks. *Theoretical Biology and Medical Modelling*, 3(13), 2006.