Modelling Biochemical Reaction Networks

Lecture 20: A genetic toggle switch

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Recommended reading

- Lepzelter et al., J. Phys. Chem. B **111**, 10239 (2007).

Genetic toggle switches

- There are many examples in biology of genes which should not both be transcribed at the same time.
- Various solutions to this problem, including genetic toggle switches, where one gene turns the other off, and vice versa (bistability).
- Synthetic toggle switches have been made.

Model for a genetic toggle switch

$$\mathrm{O}_{\mathrm{A}}^{\mathrm{on}} + 2\mathrm{B} \underset{f_A}{\overset{h_A}{\rightleftharpoons}} \mathrm{O}_{\mathrm{A}}^{\mathrm{off}}$$

$$\mathrm{O}_{\mathrm{B}}^{\mathrm{on}} + 2\mathrm{A} \underset{f_B}{\overset{h_B}{\rightleftharpoons}} \mathrm{O}_{\mathrm{B}}^{\mathrm{off}}$$

$$\mathrm{O}_{\mathrm{A}}^{\mathrm{on}} \xrightarrow{g_A} \mathrm{O}_{\mathrm{A}}^{\mathrm{on}} + b_A\mathrm{A}$$

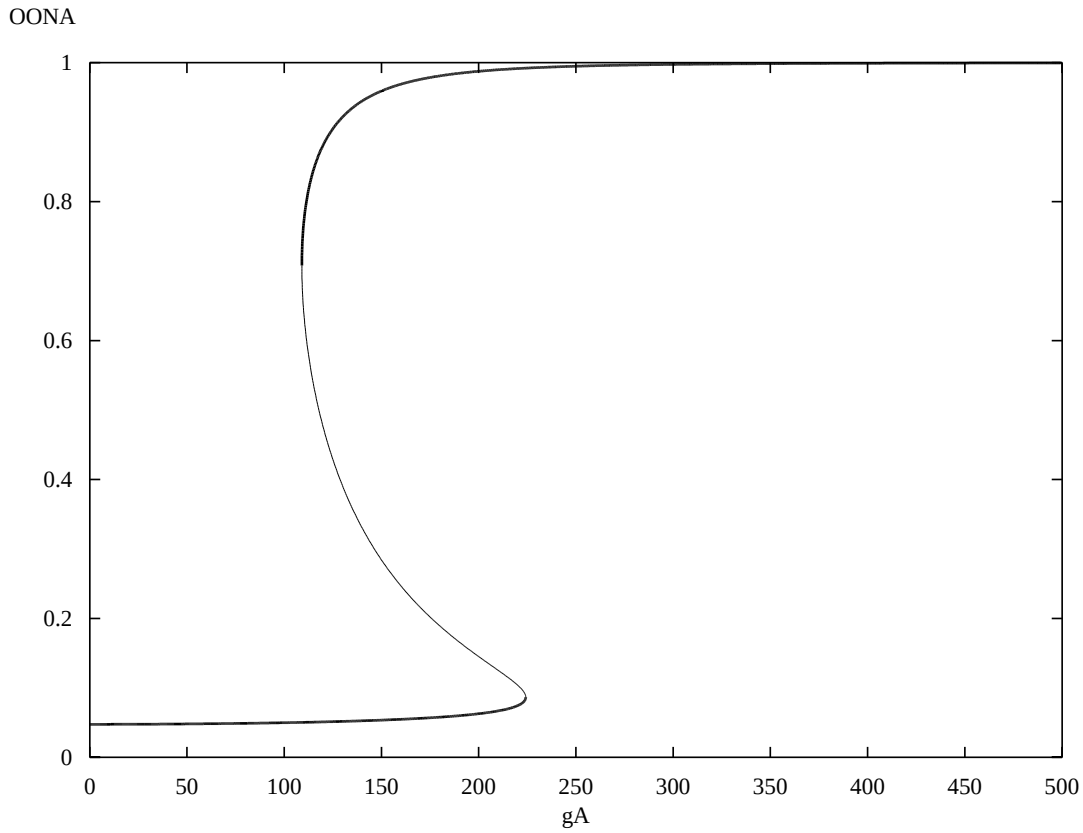
$$\mathrm{O}_{\mathrm{B}}^{\mathrm{on}} \xrightarrow{g_B} \mathrm{O}_{\mathrm{B}}^{\mathrm{on}} + b_B\mathrm{B}$$

$$\mathrm{A} \xrightarrow{k}$$

$$\mathrm{B} \xrightarrow{k}$$

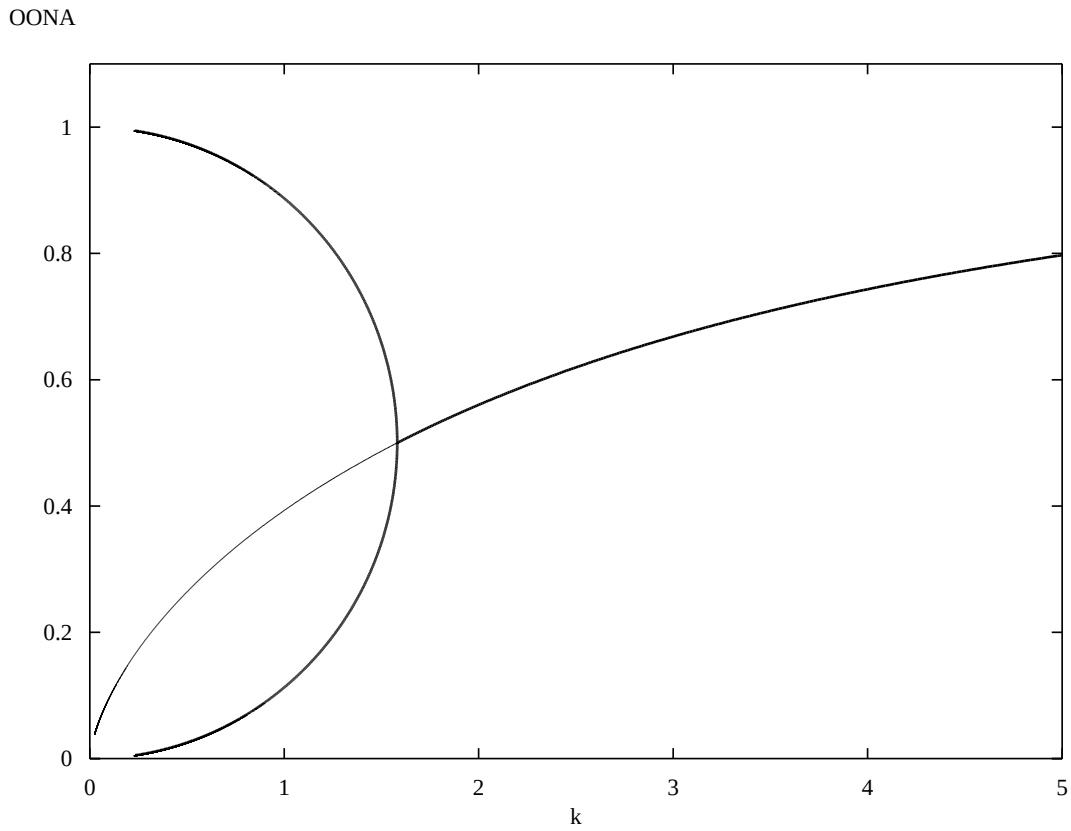
Differential equation model

- Equations and parameters are given in the `xppaut` input file `toggle.ode`.
- Look at what happens when you vary g_A:



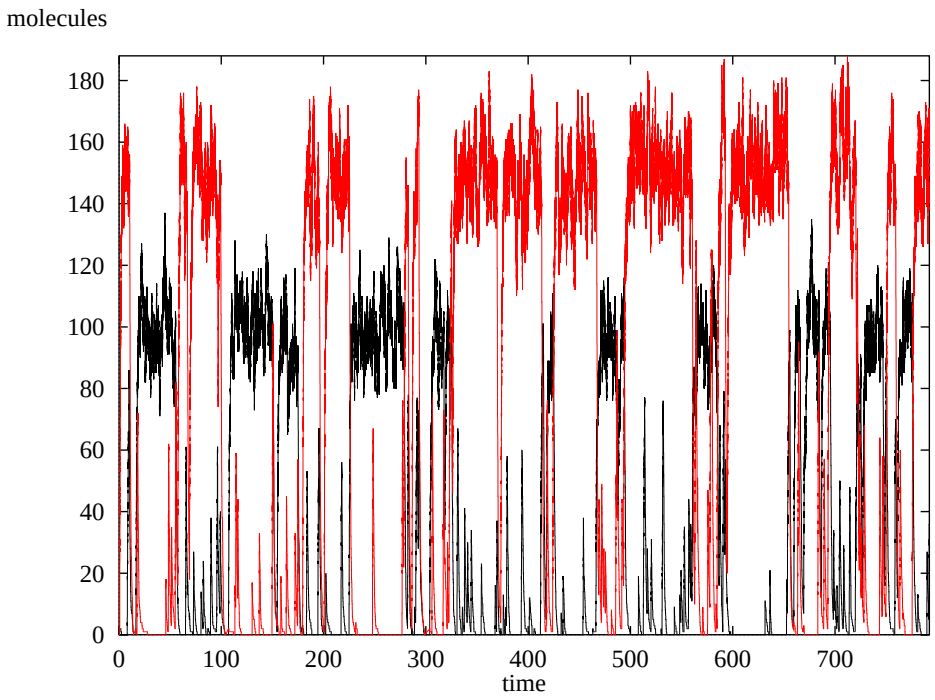
Differential equation model

- Set $h_A = h_B = 0.0005$, $f_A = f_B = 0.5$, $b_A = b_B = 1$, $g_A = g_B = 100$, and obtain the following by varying k:



Stochastic model

- Should in principle calculate stochastic rate constants, but rate constants given above are not in any particular units, so just use them as is.
- File `stoch_toggle.ode`
- Stochastic switching in bistable regime:



Red=A
Black=B