8

Feedback Circuits

8.1 Small Regulatory Sub-networks

8.2 Negative Feedback

8.2.1 *If total concentration of a transcriptional regulator R is partitioned between the part that is free, R_{free}, and the part that is bound to a metabolite, then argue for conditions where $R_{\text{free}} = R/(1 + (s/K_{\text{s}})^h)$, and identify the meaning of h and K_{s}.*

Answer Assume that the metabolite concentration $s << R$, where R is total concentration of regulator:

$$R = R_{\text{free}} + [Rs_h]$$

where Rs_h is the regulator R binding h molecules. The concentration of R with attached s is:

$$K_s^h = \frac{R_{\text{free}} \cdot (s - [Rs_h])^h}{[Rs_h]} \sim \frac{R_{\text{free}} \cdot s^h}{[Rs_h]} = \frac{R_{\text{free}} \cdot s^h}{R - R_{\text{free}}} \Rightarrow$$
$$K_s^h \cdot (R - R_{\text{free}}) = R_{\text{free}} \cdot s^h \Rightarrow$$
$$R_{\text{free}} = \frac{K_s^h \cdot R}{K_s^h + s^h} = \frac{R}{1 + (s/K_s)^h}$$

where h is the number of s molecules that bind simultaneously to R, and K_s^h is the binding constant for the $h+1$ order reaction (K_s is in units of molar).

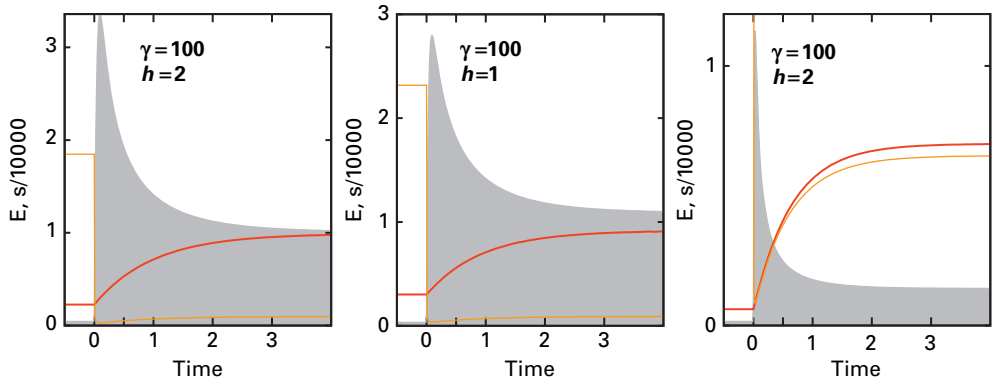

Figure 8.1 Feedback that aims to stabilize the internal concentration of a metabolite. The orange curve shows the concentration of free R.

8.2.2 *Simulate Eqs. (8.2) and (8.3) with* $\gamma = 100$, $K_s = 100$ $h = 2$, $R = 10$ *and "source" changing from* 10 000 *to* 1 000 000 *per time unit (parameters for which* $s >> R$*). Hint: start by simulating the equations until steady state is reached, then change "source" and follow the time development of* E *and* s*. Repeat the simulation for* $h = 1$*, and* $\gamma = 1000$*.*

Answer The equations read:

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{1}{1+R_{\mathrm{free}}^2} - E$$
$$\frac{\mathrm{d}s}{\mathrm{d}t} = \mathrm{source} - \gamma \cdot E \cdot s$$
$$R_{\mathrm{free}} = \frac{R}{1+s/K_s}$$

The equations start at $E = 1$ and $s = 100$ at $t = -10$, and simulated in time-steps of $\mathrm{d}t = 0.001$ until time $t = 0$, where the source is increased to 1 000 000 per time unit. Results for the various options is shown in Fig. 8.1. Notice that the flux through the system in all steady states is constant, given by $\mathrm{d}s/\mathrm{d}t = 0 \Rightarrow \mathrm{flux} = \mathrm{source}$.

8.2.3 *Simulate the repressilator:* $dA/dt = \epsilon + 1/(1+(C/0.2)^h) - A$, $dB/dt = \epsilon + 1/(1+(A/0.2)^h) - B$, $dA/dt = \epsilon + 1/(1+(B/0.2)^h) - C$ *with* $h = 3$, $\epsilon = 0.01$ *and using simple integration with* $dt = 0.005$*.*

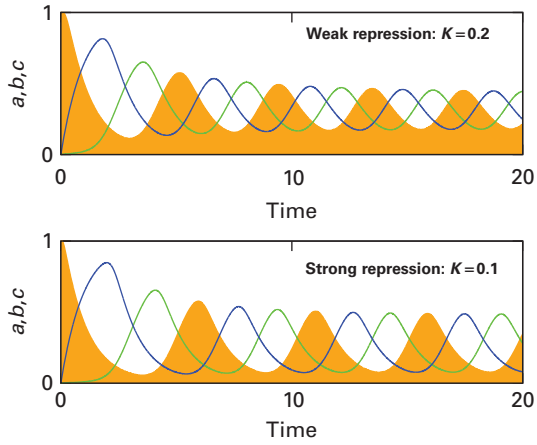

Figure 8.2 Repressilator simulations with binding constant to operators $K = 0.2$. The lower panel compares to stronger binding case.

Answer Start simulation at $a = 1$, $b = 0$ and $c = 0$. Results are shown in Fig. 8.2, where we also investigate the effect of stronger binding, where oscillations show higher contrast.

8.2.4 *Simulate the above repressilator using event-based simulation (Gillespie algorithm), updating A, B, C in units of $u = 1/N$ with $N = 100$, according to production and decay events for each protein type, i.e. for A according to $A \to A + u$ with rate $r = (\epsilon + 1/(1 + (C/0.2)^h)) \times N$, and $A \to A - u$ with rate $r = A \times N$. Study the obtained oscillations for other N values.*

Answer The standard Gillespie algorithm with six different moves: a changing up or down, b changing up or down and c changing up or the down. Rates are calculated on the basis of the values of a, b, c, potential updating times are selected and the system updated. Notice that one should always secure that none of the variables can become < 0. Results can be seen in Fig. 8.4. As N is increased the system approaches the deterministic behavior shown in Figure 8.2, upper panel.

8.2.5 *Simulate the idealized Goodwin model [361, 365]: $dm/dt = 1/(1+r^9) - k_m \cdot m$, $dp/dt = m - k_m \cdot p$ and $dr/dt = p - k_r \cdot r$ using $k_m = k_p = k_c = 0.5$ a degradation rates of mRNA, protein and the regulator, respectively. The regulator r represses production of m, closing the negative feedback loop.*

Answer Start the simulation at $t = -50$ with $m = 1, p = 0, r = 0$ and simulate with time steps $dt = 0.05$. Dynamics for the time window $t \in [0 : 35]$ is shown in Fig. 8.5.

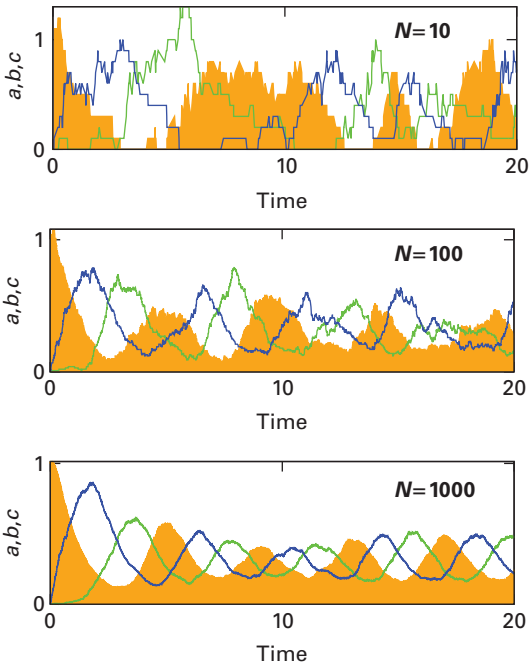

Figure 8.3 Repressilator simulations with binding constant to operators $K = 0.2$, using a random update with changes in a,b,c of size $1/N$.

8.2.6 *Simulate the simple time-delay equation:*

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -x(t-\tau)$$

and convince yourself that it either gives exponentially damped, or exponentially amplified oscillations.

Answer The simulation requires that one remembers x for a window τ in the past. Set $\mathrm{d}t = 0.01$, and define $x(i)$, for $i \in [-\tau/\mathrm{d}t, 100/\mathrm{d}t]$, set $x(i) = -i/\tau$ for $i \in [-\tau/\mathrm{d}t, 0]$. Update for $j > i$, $x(j) = x(j-1) - x(j-\tau/\mathrm{d}t) \cdot \mathrm{d}t$ for $j = 1, 2, ...100/\mathrm{d}t$. Dynamics for the time window $t \in [0:35]$ are shown in Fig. 8.6. One observes damped oscillations for $\tau < 1.5$, whereas larger τ leads to oscillations and exponential amplification.

8.2.7 *Simulate the time-delay equation:*

$$\frac{\mathrm{d}p}{\mathrm{d}t} = \frac{1}{1 + (p(t-\tau)/0.1)^2} - p(t)$$

for $\tau = 1$, $\tau = 2$ and $\tau = 5$.

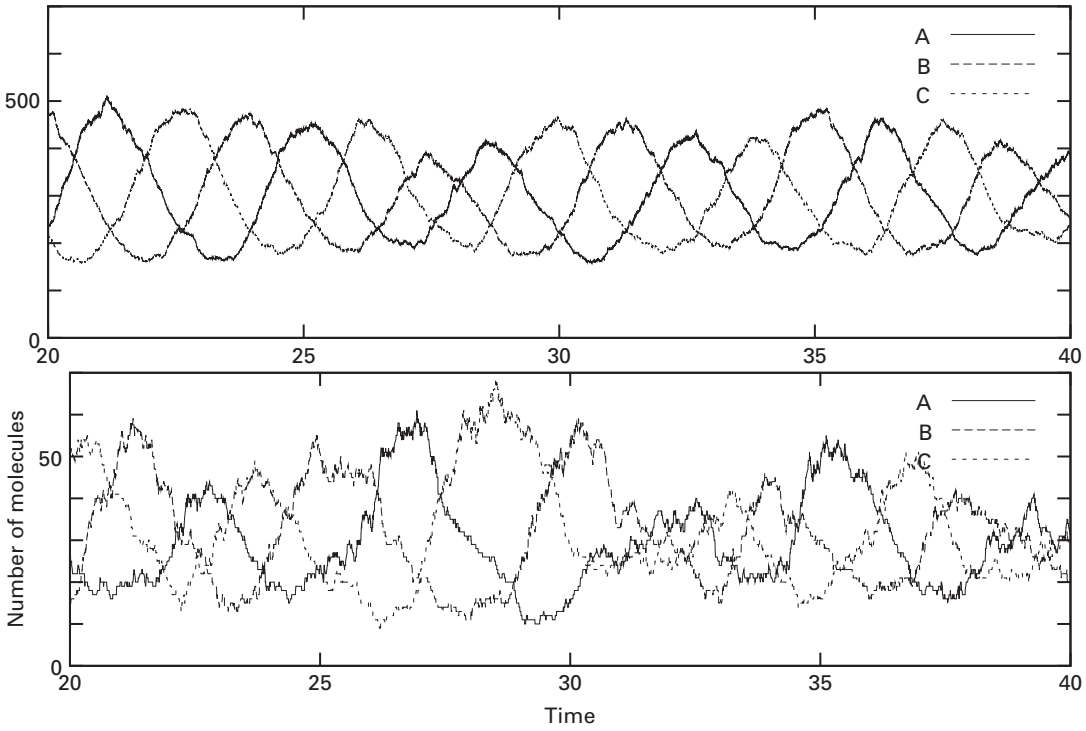

Figure 8.4 Repressilator with $N = 1000$ (upper panel) and $N = 100$ transcripts (lower panel). The repressilator was introduced by Elowitz and Leiblers, which engineered CI from λ, LacI and TetR in one low-copy plasmid and inserted in *E. coli*. TeTR also repressed a promoter for the reporter gene GFP in a high copy number plasmid.

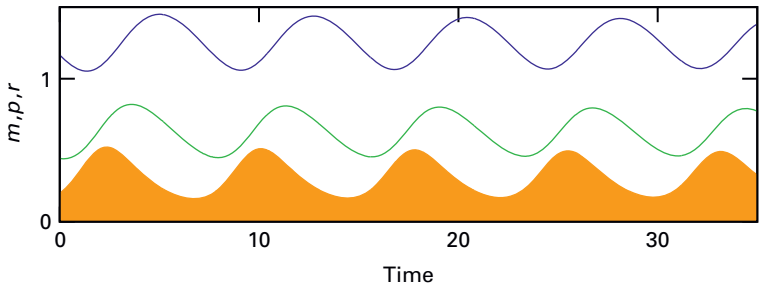

Figure 8.5 Goodwin oscillator, with the shaded region being the mRNA.

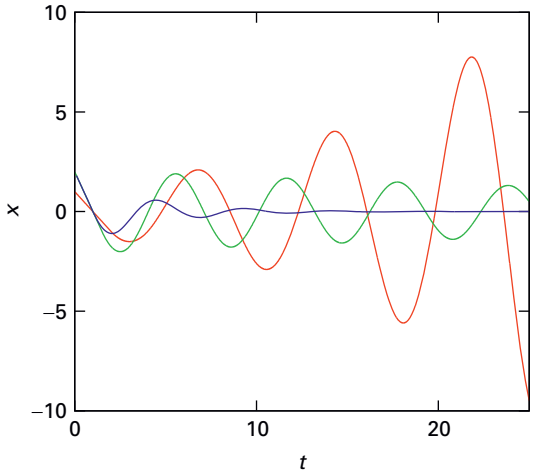

Figure 8.6 Time delay simulated for $\tau = 1$, $\tau = 1.5$ and $\tau = 2$.

Answer The simulation requires that one remembers x for a window τ in the past. Set $\mathrm{d}t = 0.01$, and define $p(i)$, for $i \in [-\tau/\mathrm{d}t, 100/dt]$ set $p(i) = -i/\tau$ for $i \in [-\tau/\mathrm{d}t, 0]$. Update for $j > i$:

$$p(j) = p(j-1) + \left(\frac{1}{1 + (p(j - \tau/dt)/0.1)^2} - p(j) \right) \cdot \mathrm{d}t$$

for $j = 1, 2, ...100/\mathrm{d}t$ Dynamics for the time window $t \in [0 : 35]$ are shown in Fig. 8.7. One observes damped oscillations for $\tau < 2$, whereas larger τ leads to stable oscillations.

8.2.8 *Simulate the time-delay equation:*

$$\frac{\mathrm{d}p}{\mathrm{d}t} = \frac{1}{1 + (p_{\mathrm{old}}/0.1)^2} - p(t)$$

where p_{old} *at time* t *is the proteins produced from time* $t' \in [t - 3 \cdot \tau, t - \tau]$ *weighted by* $w \propto \exp(-(t-t')/\tau)$*, i.e. production takes at least* τ *to contribute, but after this time the delivery time is smeared out with a characteristic time* τ*. The time-delay equation should be simulated for* $\tau = 1$, 2 and 5.

Answer The simulation requires that one remembers x for a window τ in the past. Set $\mathrm{d}t = 0.01$, and define $p(i)$, for $i \in [-3\tau/\mathrm{d}t, 100/\mathrm{d}t]$ set $p(i) = -i/(3\tau)$ for $i \in [-3\tau/\mathrm{d}t, 0]$ (arbitrary start conditions). Update for $j > i$:

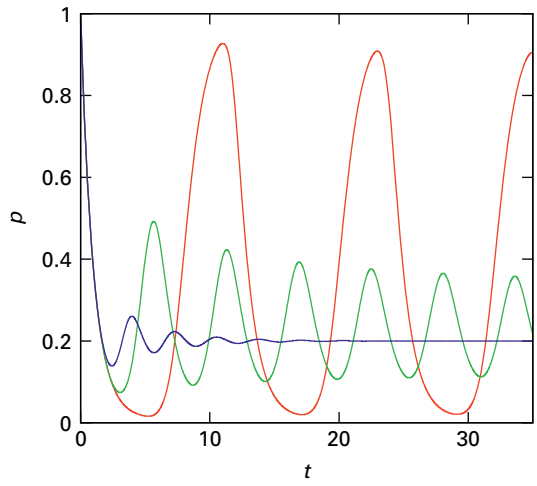

Figure 8.7 Time delay for feedback to protein production, simulated for $\tau = 1$, $\tau = 2$ and $\tau = 5$.

$$p(j) = p(j-1) + \left(\frac{1}{1 + (p_{\rm old}/0.1)^2} - p(j) \right) \cdot {\rm d}t$$

$$p_{\rm old}(j) = \frac{\sum_{i=j-\tau/{\rm d}t}^{j-3\tau/{\rm d}t} p(i) {\rm e}^{-(j-i)/({\rm d}t \cdot \tau)}}{\sum_{i=j-\tau/{\rm d}t}^{j-3\tau/{\rm d}t} {\rm e}^{-(j-i)/({\rm d}t \cdot \tau)}}$$

for $j = 1, 2, ...100/{\rm d}t$. Notice that the last equation represents a normalized sum of contributions from the past, stretching out to three times the decay time τ. Dynamics for the time window $t \in [0:35]$ are shown in Fig. 8.8. One observes damped oscillations for small τ, whereas larger τ leads to stable oscillations.

8.2.9 *Maintenance of homeostasis is essential for health, and degenerative processes associated with diseases should be be counteracted by cellular repair. An example may be Parkinson's disease [30] where growth of fibrils F may be counteracted by cellular (protease) proteins P:*

$$\frac{{\rm d}F}{{\rm d}t} = \frac{m}{1+P} - P \cdot F \tag{8.1}$$

$$\frac{{\rm d}C}{{\rm d}t} = P \cdot F - \nu \cdot C \tag{8.2}$$

$$\frac{{\rm d}P}{{\rm d}t} = 1 - P - P \cdot F + \nu \cdot C \tag{8.3}$$

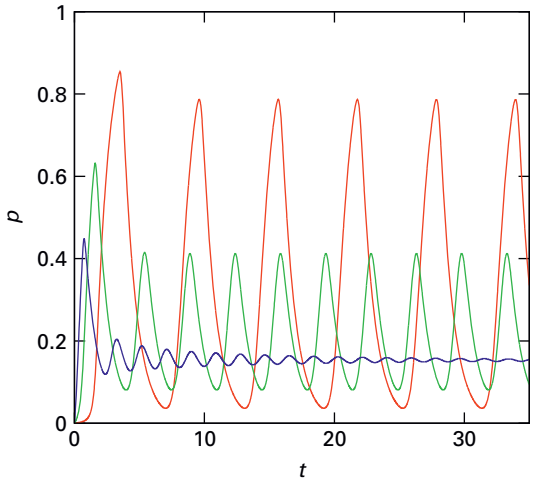

Figure 8.8 Time delay for feedback to protein production, simulated for $\tau = 5$, starting from $t = \tau_b$ in the past, with $\tau_b = 0.5$, $= 1$ and $= 2$ (red and most oscillating).

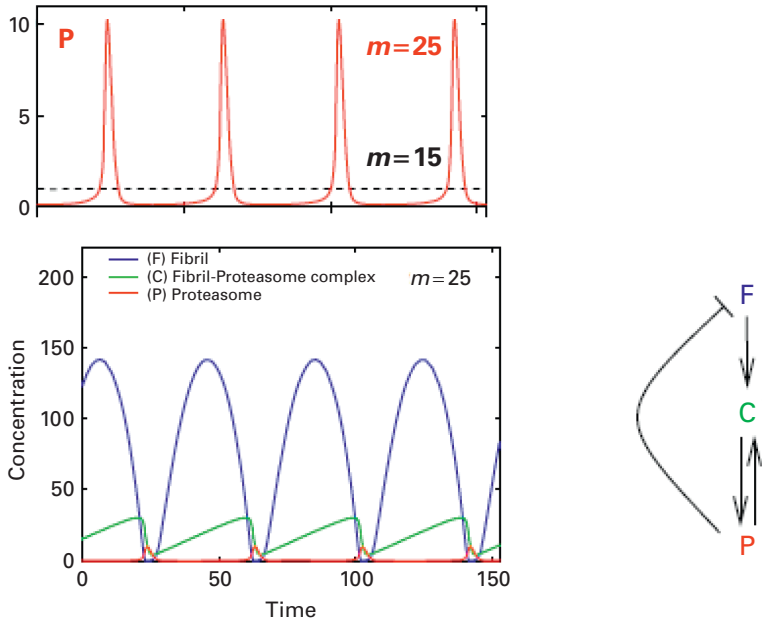

Figure 8.9 Simulation of free proteasome concentration in idealized model of Parkinson's disease.

Here m parameterizes the influx of new potential fibrils, an influx that is partially repressed by P. $1/\nu$ is the lifetime of the complex between mature fibrils and the cellular repair machinery P. Draw the implied network, and identify positive and a negative feedback. Simulate the equations for $\nu = 1$ and $m = 10$, and $m = 25$, respectively.

Answer See simulation result in Fig. 8.9. For discussion, references and variations of the model, the reader may consult Kim Sneppen *et al. Phys. Biol.* **6**, 036005 (2009).

8.3 Positive Feedback

8.3.1 *Model the sequestering switch between two proteins A and B produced according to $dA/dt = P_{\rm A}/(1 + B_{\rm f}^2) - A$, $dB/dt = P_{\rm B} - B$, and where A and B form a complex with binding constant $K = 0.01 = A_{\rm f}B_{\rm f}/[AB]$. Here free concentrations are $A_{\rm f} = A - [AB]$ and $B_{\rm f} = B - [AB]$ binding to each other with $K_{\rm AB} = 0.01$, whereas basal production rates are, respectively, $P_{\rm A} = 10$ and $P_{\rm B} = 5$. Show that the system is bistable, by starting the simulation from two different initial conditions (one may also perform 100 simulations, starting at points where both A and B are between 0 and 10).*

Answer The two equations are simulated in discrete time steps $\mathrm{d}t = 0.01$, at each point calculating the complex concentration:

$$[AB] = \frac{1}{2}(A + B - K_{\rm AB}) - \sqrt{0.25 \cdot (A + B + K_{\rm AB})^2 - A \cdot B}$$

where $K_{AB} = 0.01$. $B_f = B - [AB]$ is inserted into

$$A(t + dt) = A(t) + dt \cdot \left(\frac{P_{\rm A}}{1 + B_f^2} - A \right)$$

whereas $B = P_{\rm B} = 5$ is kept at a fixed value. Results is shown in Fig. 8.10. The left panel highlight that concentration in free b is very different between two fixed points.

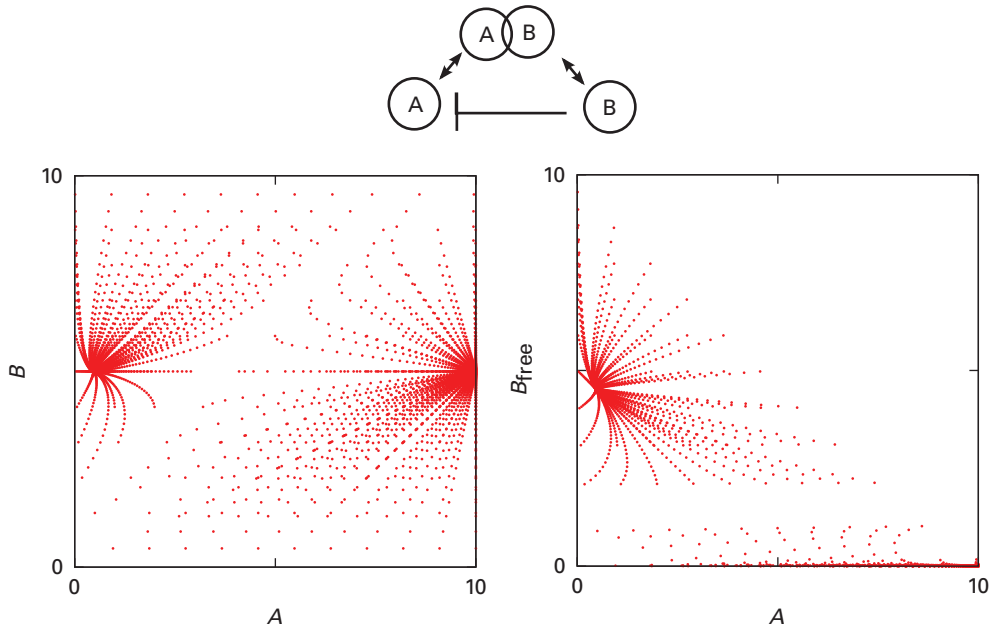

Figure 8.10 Trajectories starting from various points with $A = 0, 1, 1...10$ and $B = 0, 1, 2...10$ and showing values of A and B at 0.1 time unit intervals.

8.4 Combining Feedback in small molecule regulation

8.4.1 *Simulate the "consumer motif" where the small molecule activates the regulator. The concentration of the complex* $[Rs]$ *is given by:*

$$K^h = \frac{(R^{\rm tot} - [Rs]) \cdot (s - h[Rs])^h}{[Rs]} = \frac{(R^{\rm tot} - [Rs])s^h}{[Rs]} \Rightarrow [Rs] = \frac{R^{\rm tot} \cdot (s/K)}{1 + (s/K)}$$

for $h = 1$*, where we use* $R = R^{\rm tot}$ *as the total* R*, and assume* R *to be much smaller than* s*.* K_s *sets the binding strength of the* $\{\mathrm{Rs}\}$ *complex.*[1]

[1]If multiple s bind to R, the concentration of free R (not sequestered by s) is $R_{\rm free} = R^{\rm tot} - h_s[Rs_{h_s}] = R^{\rm tot}(1 + (1 - h_s)(s/K)^{h_s})/(1 + (s/K)^{h_s})$.

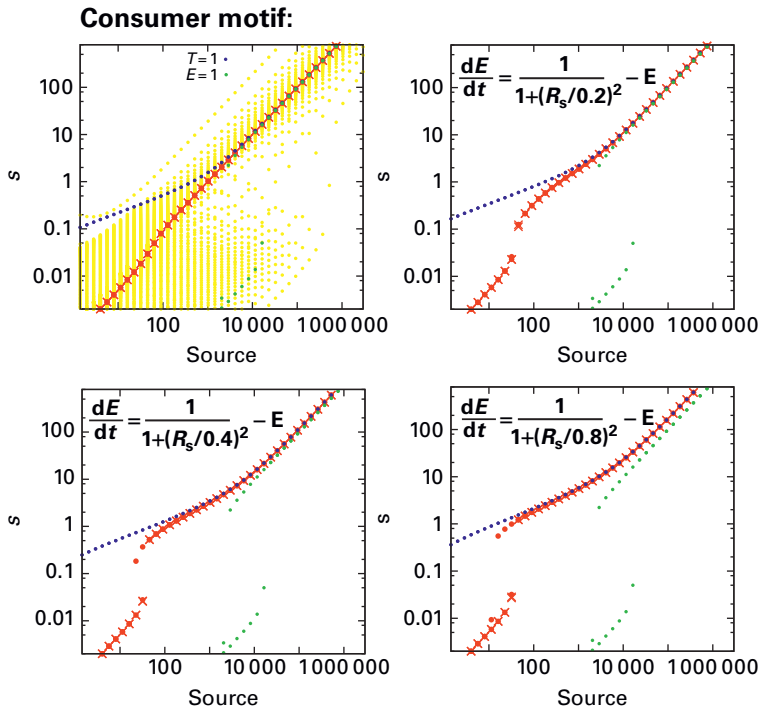

Figure 8.11 Internal metabolite as a function of external resource. In the upper-left panel we show the standard case with equal regulation of T and E, the other panels have a weaker regulated E. In each case we also investigate behavior where either $E = 1$ is fixed, or $T = 1$ is fixed. The yellow dots in the upper left-hand panel also shows the trajectory until a steady state is reached.

Assume that Rs is the concentration of the active form of R. Consider the consumer motif:

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \epsilon + \frac{[Rs]^2}{[Rs]^2 + K_E^2} - E \;\; ; \;\; \frac{\mathrm{d}T}{\mathrm{d}t} = \epsilon + \frac{[Rs]^2}{[Rs]^2 + K_T^2} - T$$

with $R = 1$, $\gamma = 1000$, $\epsilon = 0.001$, $K = 10$ *and* $K_E = K_T = 0.1$. *Simulate the system until steady state is reached for a range of values of the source* σ *between 1 and 1 000 000 (i.e. set* $\sigma = 2^i$, $i = 0, 1, 2 \ldots 20$*). For each value of* E *and* T, s *is determined from the flux Eq. (8.14).*

Answer For each value of σ we start simulations at four different initial values of $E, T = (1,1), (0,1), (1,0)$ and $(0,0)$ and set $s = \sigma \cdot T/(\gamma \cdot E + 1)$

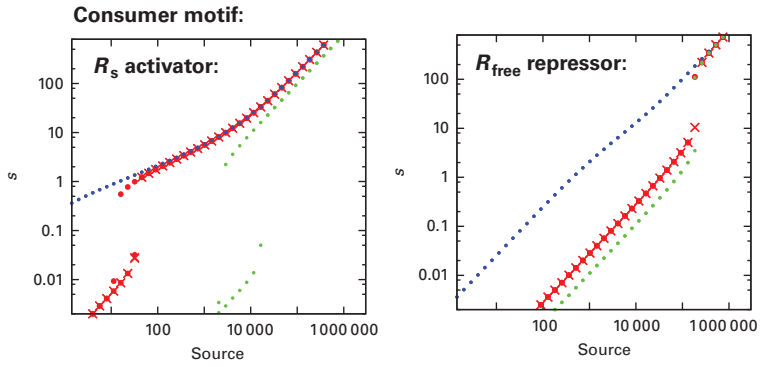

Figure 8.12 Internal metabolite as a function of external source, with $R_{\rm s}$ as an activator, and $R_{\rm free}$ as a repressor.

initially. Simulate equations in small timesteps $\mathrm{d}t = 0.001$ (small because γ is large, and thus the fastest change very fast). Simulate until steady state E, T and s are reached. Plot s as function of σ. Results are shown in Fig. 8.11.

Notice that in the figure, s is sometimes smaller than $R = 1$, which in principle requires a better treatment of the complex formation that we use here. However, if both s and K is rescaled by the same factor, all the above results is repeated.

Notice in particular that as we remove negative feedback by maintaining a constant high metabolism of the metabolite ($E = 1$), there are two stable fixed points, signalling bistability and hysteresis. Also notice that if E is more weakly regulated than T, the s versus σ curve exhibits ultra-sensitive behavior and even bi-stability.

8.4.2 *Simulate the "consumer motif" above, but using* $\mathrm{R}_{\rm free}$ *as a repressor instead of* Rs *as an activator, and compare the steady-state plot in the two cases. Use* $R = 1$, $\gamma = 1000$, $\epsilon = 0.001$, $K = 10$ *and* $K_T = 0.1$, *but* $K_E = 0.8$. *Simulate the motifs for various values of the source* σ *between 1 and 1 000 000 (i.e. set* $\sigma = 2^i$, $i = 0, 1, 2 \ldots 20$*).*

Answer Same procedure as in the previous question, with results shown in Fig. 8.12.

8.4.3 *Simulate the "consumer motif" above if* Rs *regulates itself as activator and repressor, and compare the steady-state plot in the two cases. Use* $R = 1$, $\gamma = 1000$, $\epsilon = 0.001$, $K = 10$ *and* $K_T = 0.1$, *but* $K_E = 0.8$. *Set* $K_R = 0.1$ *and use the same equation for* R *as for* T. *Simulate the motifs for various values of the source* σ *between 1 and 1 000 000 (i.e. set* $\sigma = 2^i$, $i = 0, 1, 2 \ldots 20$*).*

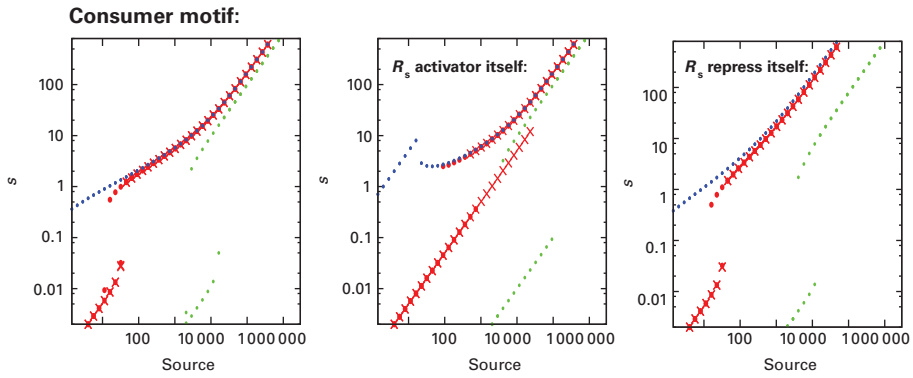

Figure 8.13 Internal metabolite as a function of external resource, with R_s regulating itself in the same way as it regulates T. R is regulated more weakly ($K = E = 0.8$ whereas $K_R = K_T = 0.1$) as a repressor.

Answer Uss the same procedure as in the previous question, with results shown in Fig. 8.13. When R_s activates itself one can see that the regime of bistability is increased. With chosen parameters, there is not much effect from R_s self-repression.

8.4.4 *Simulate the "fashion motif" for steady-state values of both internal s and the flux* $= \sigma \cdot T$ *through the system. Use* $R = 1$, $\gamma = 1000$, $\epsilon = 0.001$, $K = 10$ *and* $K_T = K_E = 0.1$ *and let Rs act as a repressor. Simulate the motifs for various values of the source* σ *between 50 and 1 000 000 (i.e. set* $\sigma = 2^i$, $i = 0, 1, 2 \ldots 20$*).*

Answer Use the same procedure as in the previous questions, with results shown in Fig. 8.14. One can see that the flux drops or remains near constant for a large range of external sources.

8.4.5 *The fashion motif is so named so one may view s as a product, T as producer, and E as consumer. The positive feedback around E reflects the tendency of consumers to want what is scarce. Adding the additional positive feedback of R being activated by itself (Rs) may then reflect a tendency of consumers to communicate and enhance their common fashions. Simulate the "fashion motif" with Rs activating production included. Plot state values of both interval s and the flux* $= \sigma \cdot T$ *through the system. Use* $R = 1, \gamma = 1000, \epsilon = 0.001, K = 10, K_T = K_E = K_R = 0.1$ *and let Rs act as a repressor, except for itself. Simulate the motifs for various values of the source* σ *between 50 and 1 000 000 (i.e. set* $\sigma = 2^i, i = 0, 1, 2 \ldots 20$*).*

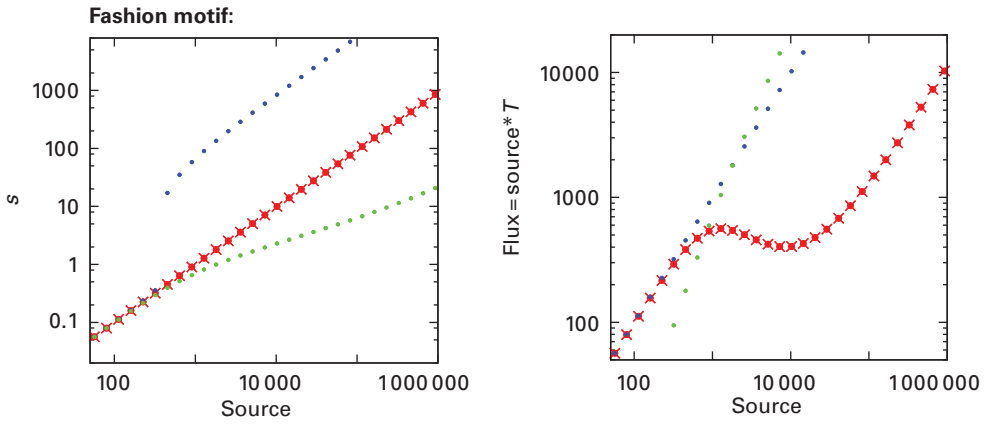

Figure 8.14 Fashion motif, internal metabolite and flux as function of external resource.

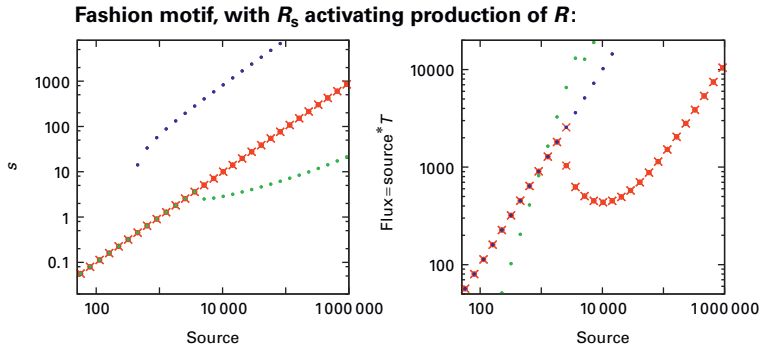

Figure 8.15 Fashion motif with R_s activating production of R.

Answer Same procedure as in the previous question, with results shown in Fig. 8.15. When R_s activates itself one can see that a small region of bistability, reflecting the potential for a market to collapse when production exceeds a certain threshold.

8.5 Combining Feedback & Spatial order

8.5.1 *Simulate the model in Fig. 8.13, that is, update the following equations by using a timestep* $\mathrm{d}t = 0.001$*, for* $x = 1, 2, 3 \ldots 100$*:*

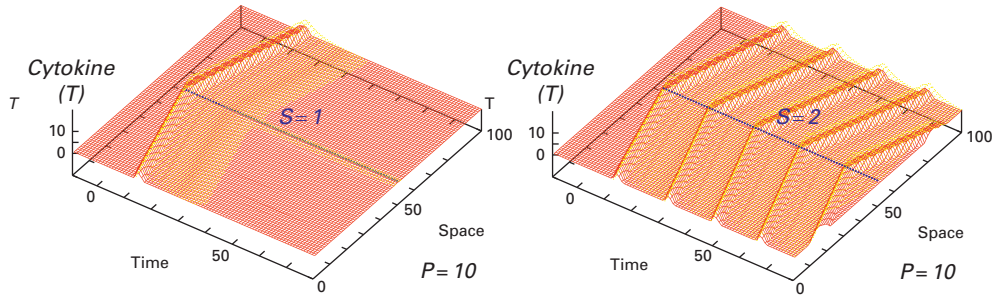

Figure 8.16 Simulation with low and high levels of stress, $S = 1, S = 2$, respectively. In both cases using positive feedback strength $P = 10$. The red surface marks the cytokine T, whereas the yellow surface is the level of the repressor R. The blue line marks $S > 0$ excitation.

$$\begin{aligned}\Delta_T(x) &= S(x) + \frac{p \cdot T(x)^2}{1 + T(x)^2} - \frac{R(x) \cdot T(x)}{0.1 + T(x)} - T(x) \\ &\quad + D \cdot (T(x-1) + T(x+1) - 2T(x)) \\ \Delta_R(x) &= T(x) - R(x)/\tau \\ T(x) &= T(x) + \Delta_T(x) \cdot \mathrm{d}t \quad \text{and} \quad R(x) = R(x) + \Delta_R(x) \cdot \mathrm{d}t\end{aligned}$$

where one should remember to update all Δ_T and Δ_R before finally updating T and R. The inflammation is introduced through a persistent $S = 1$ at position $x = 50$, whereas $S = 0$ otherwise. Use parameters $p = 10$, $D = 1$, $\tau = 5$. Explore the behavior for other values of S.

Answer The equations are simulated by simple integration in time steps $\mathrm{d}t = 0.001$ in Fig. 8.16. One can see that increasing inflammation S increases response from one wave to a sequence of waves, initiated at regular intervals.

8.5.2 *Simulate the model from Question 8.5.1 for various values for the strength of the positive feedback p.*

Answer The equations are simulated by simple integration in timesteps $\mathrm{d}t = 0.001$ in Fig. 8.17. One can see that increasing positive feedback P, the system is first non-responsive to inflammation, then responsive, finally settling in the fully excited state that cannot transmit any information.

8.5.3 *Simulate the model in the previous questions for parameters $p = 50$ and $S = 1$ at $x = 0$, for different values of the degradation time of R, $\tau = 5$ to $\tau = 20$.*

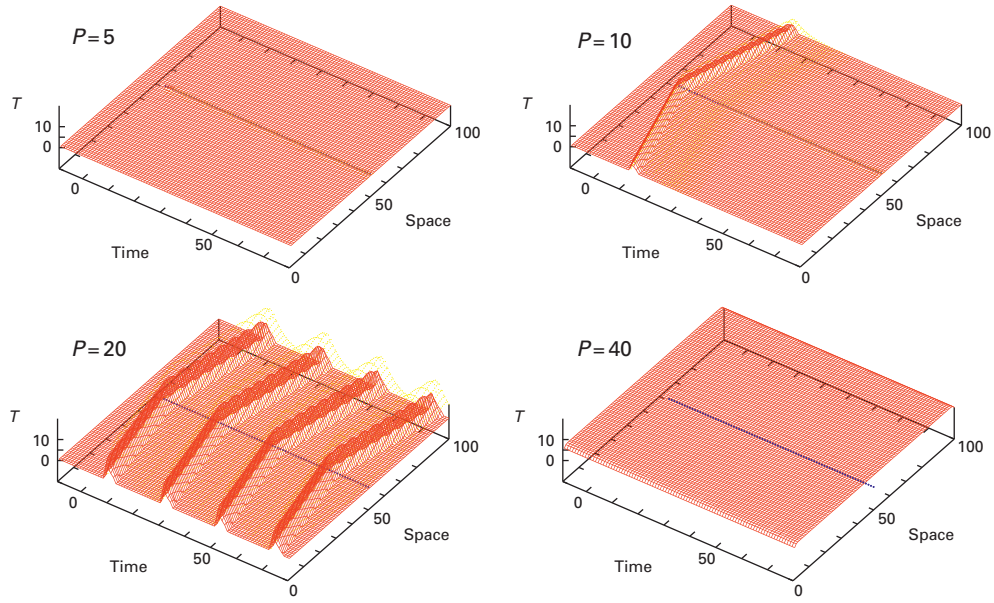

Figure 8.17 Simulation with fixed $S = 1$, varying positive feedback strength $P = 5$ to $P = 40$. The red surface marks the cytokine T, whereas the yellow surface is the level of the repressor R. The blue line marks $S > 0$ excitation.

Answer The equations are simulated by simple integration in time steps $\mathrm{d}t = 0.001$ in Fig. 8.18. One can see that short lifetimes prevent waves. Increasing the lifetime beyond a threshold value initiates traveling excitable waves at time intervals that grow with the lifetime of the repressor (the cell needs to reduce the repressor level before a new wave can propagate).

8.5.4 *We have not described how a cell can chemotax through a series of waves. The main idea is that it should be more sensitive to the positive gradient than the negative. This is obtained by a chemotaxing cell that is sensitive at low concentrations, and insensitive when the concentration is higher. To propagate, the cell should remember extreme positive changes for some time. Make a model for the random walk of a chemotaxing cell, assuming this behavior.*

Answer Model the cytokine waves as in Question 8.5.1, using $P = 20$ and $\tau = 5$. Define a chemotaxing walker as a walker that can be in two states:

In state 1 it does a random walk +1 or -1 with equal probability.

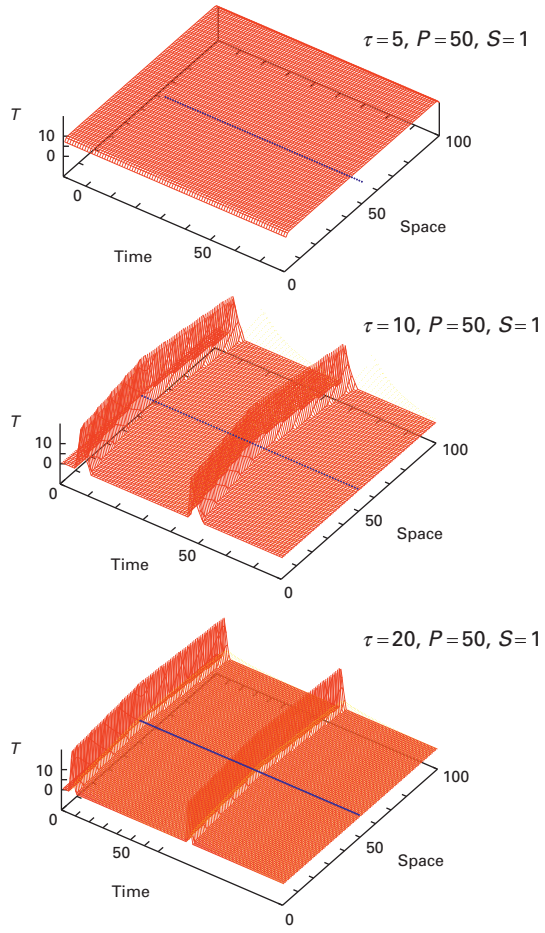

Figure 8.18 Simulation with fixed $S = 1$, positive feedback strength $p = 50$ and increasing value of the lifetime of the repressor.

If the T-field changes to $T > T\text{threshold} = 5$ units, the walker is switched to state 2. It measures the gradient and its direction and remembers this direction.

The walker remembers the state 2 for a time τ, during which it always walk in the remembered direction.

After this relaxation time τ, the walker switches back to state 1.

The result is shown in Fig. 8.19.

8.5.5 *Explore timescales for remembering the large positive changes in T in previous questions.*

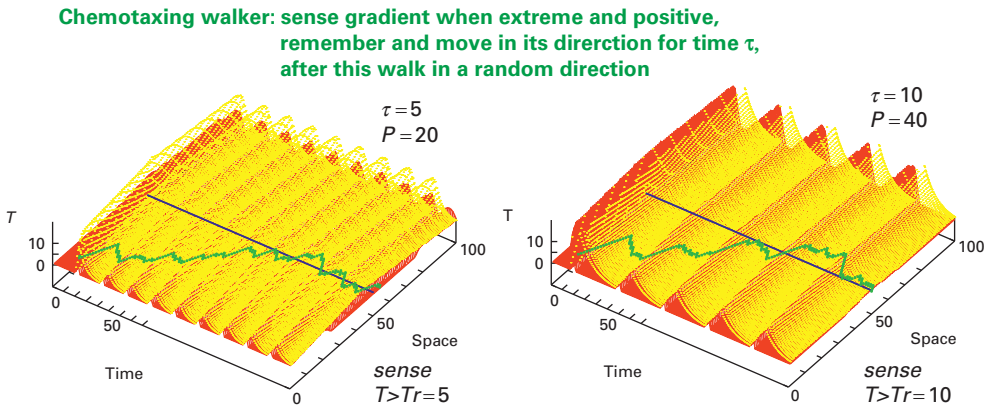

Figure 8.19 Simulation with chemotaxing walker in a field of travelling cytokine waves.

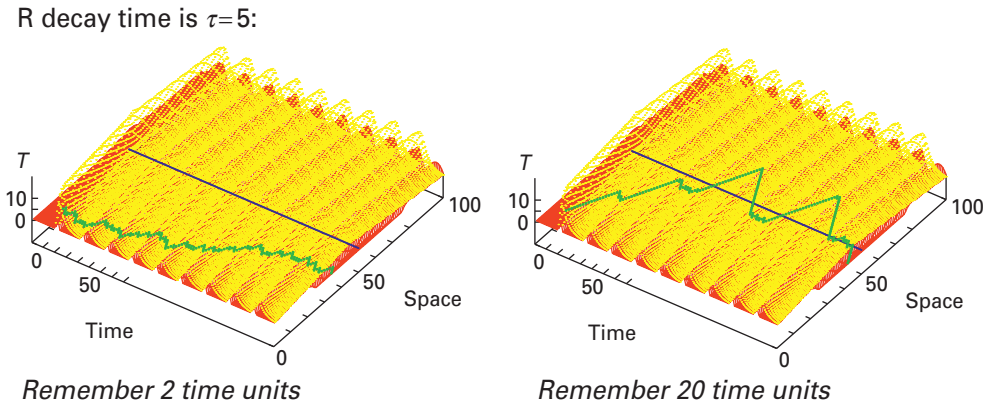

Figure 8.20 Simulation with chemotaxing walker in a field of travelling cytokine waves. The two simulations are for two different values of the memory of chemotaxing cell.

Answer Model cytokine waves as in Question 8.5.1 using $P = 20$ and $\tau = 5$. Define a chemotaxing walker as a walker that can be in two states:

In state 1 it does a random walk $+1$ or -1 with equal probability.

If the T-field change to $T > T\text{threshold} = 5$ units during one time unit, the walker is switched to state 2. It measures the gradient and its direction and remembers this direction.

The walker remembers the state 2 for a time τ_{chemo}, during which it always walks in the remembered direction.

After this relaxation time τ, the walker switches back to state 1.

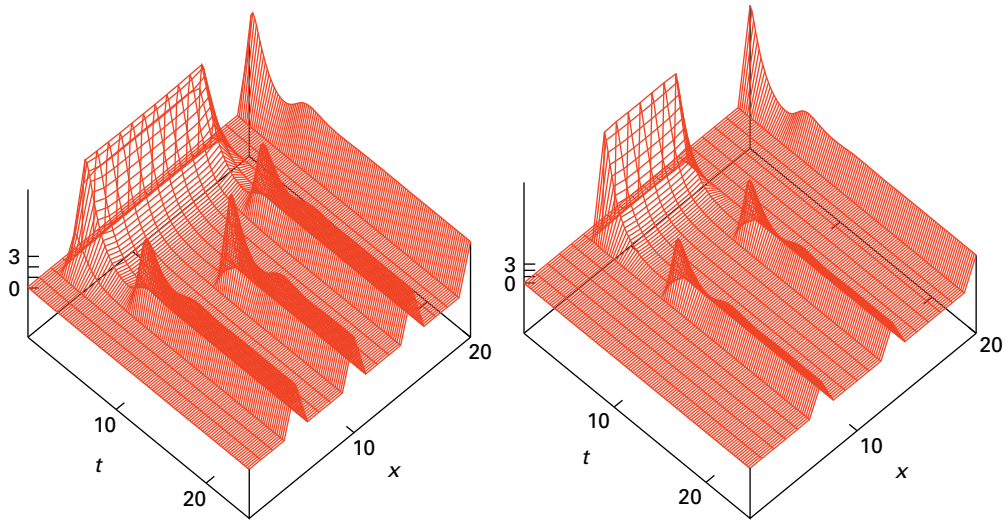

Figure 8.21 Stripe formation with local positive feedback coupled to a diffusing inhibitor. The left-hand panel starts with $a = b = 0.01$; the right-hand panel starts with $a = b = 0.1$, in both cases $a(20) = 1$.

The result is shown in Fig. 8.20, with the left-hand panel showing $\tau_{\text{chemo}} = 2$, whereas the right-hand panel shows for $\tau_{\text{chemo}} = 20$. One can see that small τ_{chemo} gives a smaller drift, whereas a large value can give an overshoot. In practice, the assumed desensitization of the walker to negative gradients may give additional constraints.

8.5.6 *Simulate the model in Fig. 8.15 and Eq. (8.21) on a one-dimensional line (1, 2, 3, . . . , 20) with $D = 1$. First use initial conditions $a = b = 0.01$, except $a(20) = 1$, then use initial conditions $a = b = 0.1$, except $a(20) = 1$.*

Answer The equations reads:

$$\frac{\mathrm{d}a}{\mathrm{d}t} = \frac{a(x)^2}{b(x)} - a(x)$$
$$\frac{\mathrm{d}b}{\mathrm{d}t} = a(x)^2 - b(x) + (b(x+1) - 2 \cdot b(x) + b(x+1))$$

for $x = 1, 2, ...20$ with periodic boundary conditions. It is simulated using time step $\mathrm{d}t = 0.002$ in Fig. 8.21.

8.4.7 *Repeat the previous question for initial conditions $a = b = 0.01$, except $a(20) = 1$, but with half, and then a third of production/decay rates for the dynamics of b.*

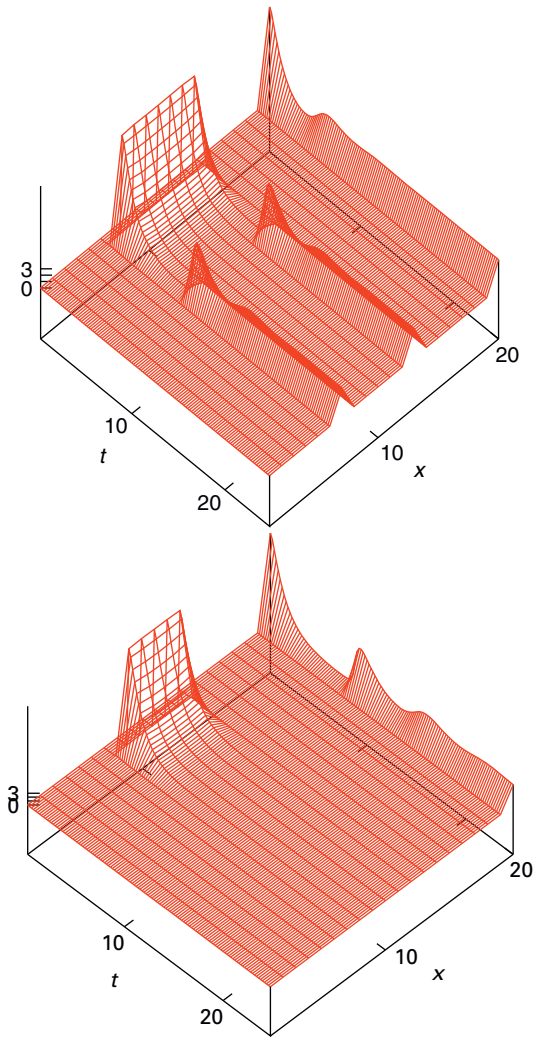

Figure 8.22 Stripe formation simulation using b timescale set by $\tau = 2$ (top panel) and $\tau = 3$ (bottom panel). In both cases one starts with $a = b = 0.01$, and $a(20) = 1$.

Answer The equations read:

$$\frac{\mathrm{d}a}{\mathrm{d}t} = \frac{a(x)^2}{b(x)} - a(x)$$
$$\frac{\mathrm{d}b}{\mathrm{d}t} = \frac{1}{\tau}(a(x)^2 - b(x)) + (b(x+1) - 2 \cdot b(x) + b(x+1))$$

with dynamics for $\tau = 2$ and $\tau = 3.x = 1, 2, ...20$ shown in Fig. 8.22.

8.5.8 *Estimate the wavelength for the fastest-growing wave of the linear part of the KS equation.*

Answer Test the growth of a simple wave $h(x,t) = h_q(t) \cdot \sin(qx)$ with wave number q. Inserting this into the linear part of the KS equation one obtains:

$$\frac{\mathrm{d}h}{\mathrm{d}t} = -\frac{\mathrm{d}^2 h}{\mathrm{d}x^2} - \frac{\mathrm{d}^4 h}{\mathrm{d}x^4} \Rightarrow$$
$$\frac{\mathrm{d}h_q}{\mathrm{d}t} = q^2 \cdot h_q - q^4 h_q = q^2 \cdot (1 - q^2)$$

an equation which has maximal growth at wavenumber $q^2 = 1/2$ or $q = 1/\sqrt{2}$. The corresponding wavelength $\lambda = 2\pi/q = 2\pi\sqrt{2} = 2 \cdot 3.14 \cdot 1.4 \sim 9$, which is indeed close to the lateral extension of the tip-splitting bulges of the front.