

## A simple model for negative feedback

We consider a very simple type of feedback:

$$1) \quad \frac{dx}{dt} = H(x) = F\left(\frac{x}{K}\right) - \gamma x$$

$$2) \quad F(x) = \begin{cases} \beta_H & \text{for } x < 1 \\ \beta_L & \text{for } x \geq 1 \end{cases}$$

Steady state solution:

The steady-state depends on the value of  $\gamma$ :

For  $\gamma > \beta_H/K$  the steady-state is  $x_{st} = \beta_H/\gamma$

For  $\gamma < \beta_L/K$  the steady-state is  $x_{st} = \beta_L/\gamma$

In between there is no solution, but if we assume a rapid slope near  $x=K$ , then the steady state is

$$x_{st} \cong K$$

What about the dynamics? If we start from  $x = 0$ , then if  $\gamma > \beta_H/K$  the system never reaches a high enough level to activate the feedback and the approach to steady-state is:

$$x = \frac{\beta_H}{\gamma} (1 - e^{-\gamma t})$$

If  $\gamma < \beta_L/K$  the system the system has few dynamical phases:

Initial – no feedback:  $x < K$ :  $x = \frac{\beta_H}{\gamma} (1 - e^{-\gamma t})$  for  $t \leq t_0 = -\gamma^{-1} \log\left(1 - \frac{K\gamma}{\beta_H}\right)$  – fast rise to a value  $K$

Later – with feedback:  $x = \frac{\beta_L}{\gamma} + \left(K - \frac{\beta_L}{\gamma}\right) e^{-\gamma(t-t_0)}$

What about a time delay? We consider only the case  $\gamma < \beta_L/K$  for which we find a strong negative feedback?

$$1) \quad \frac{dx}{dt} = F\left(\frac{x(t-\tau)}{K}\right) - \gamma x$$

$$2) \quad F(x) = \begin{cases} \beta_H & \text{for } x < 1 \\ \beta_L & \text{for } x \geq 1 \end{cases}$$

One way by which we can solve such equation is by solving separately for different intervals,  $0 < t < \tau$ ;  $\tau < t < 2\tau$ ; ...;  $n\tau < t < (n+1)\tau$ . We assume that  $x = 0$  for  $t < 0$  and therefore, for the first interval we can solve:

$$\frac{dx}{dt} = F(0) - \gamma x \rightarrow x(t; 0 < t < \tau) = g_1(x)$$

For the next interval we use this solution to solve:

$$\frac{dx}{dt} = F(g_1(t-\tau)) - \gamma x \rightarrow x(t; \tau < t < 2\tau) = g_2(t)$$

And generally:

$$\frac{dx}{dt} = F(g_n(t - \tau)) - \gamma x \rightarrow x(t; n\tau < t < (n + 1)\tau) = g_{n+1}(x)$$

For the step negative feedback function, we can consider two extreme cases:

$\tau \ll t_0$  – small delay – in this case, the function would remain  $F(x(t)) = \beta_H$  for many intervals and the function would simply behave as the non-delayed function:

$$x = \frac{\beta_H}{\gamma} (1 - e^{-\gamma t}), t < (n + 1)\tau; n\tau < t_0 < (n + 1)\tau; n = \frac{t_0}{\tau} \gg 1$$

Then the system will switch to almost the same solution as with the no delay case. Not exactly the same, as this will occur with a delay  $\tau$  which will allow  $x$  to rise a little bit above  $K$ , but not significantly.

$\tau \gg t_0$  – long delay.

In this case, at the first interval, the system will behave as it is in open loop:

$$x = \frac{\beta_H}{\gamma} (1 - e^{-\gamma t})$$

Only at time  $t = \tau + t_0 \gg t_0$  the delayed value of  $x(t - \tau)$  would reach a value of  $K$  and the feedback will kick in, setting the production at  $\beta_L$ . By this time, the value of  $x(\tau + t_0) = \frac{\beta_H}{\gamma} (1 - e^{-\gamma(\tau+t_0)}) \gg K$ . The equation at later stages will therefore be:

$$x(t > \tau + t_0) = x(\tau + t_0) + \left( \frac{\beta_L}{\gamma} - x(\tau + t_0) \right) e^{-\gamma(t-\tau-t_0)}$$