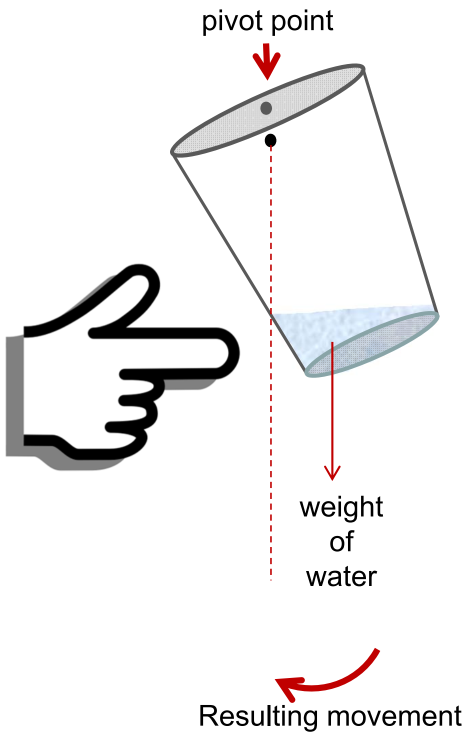
Negative feedback and biological oscillators

Negative feedback can generate oscillations

Negative feedback is process where an effect diminishes itself.

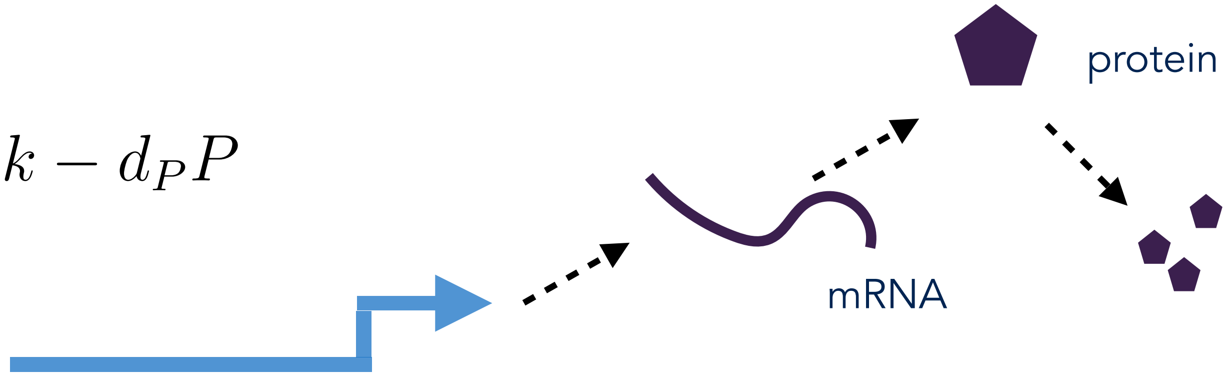


If an increase in the output causes the system to act to decrease that output, then the system has negative feedback.

Degradation is stabilising

Consider constitutive expression

$$\frac{dP}{dt} = k - d_P P$$



At steady state

$$k = d_P P^*$$

synthesis rate is constant, but
degradation rate is not

For a fluctuation **above** steady state

$$d_P P > d_P P^*$$

degradation **increases**

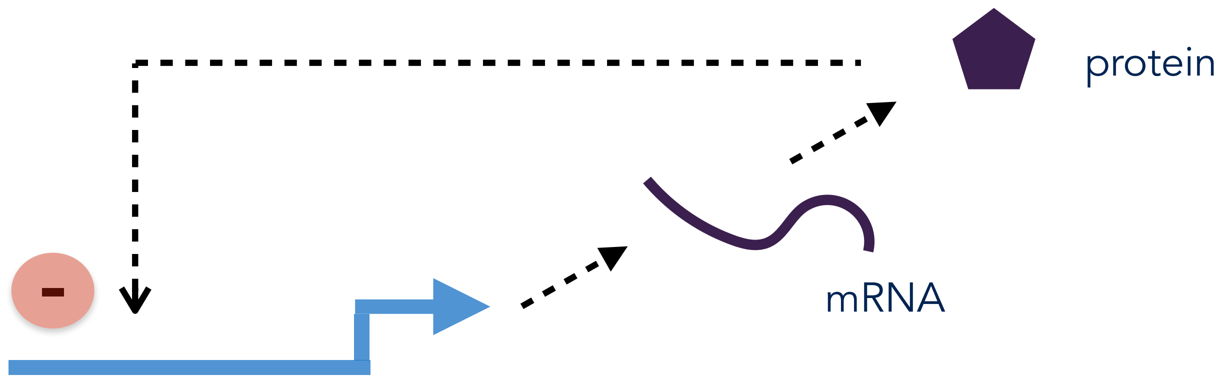
For a fluctuation **below** steady state

$$d_P P < d_P P^*$$

degradation **decreases**

Negative feedback is stabilising

Consider negative autoregulation



The rate equation is

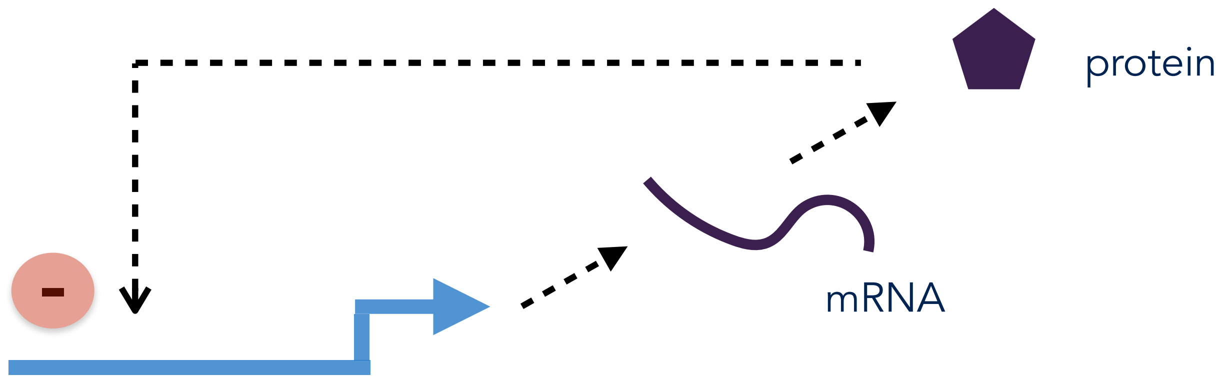
$$\frac{dP}{dt} = \frac{k}{1 + (P/K)^n} - d_P P$$

and at steady state

$$\frac{k}{1 + (P^*/K)^n} = d_P P^*$$

Like degradation, negative feedback adjusts its effects to perturbations

$$\frac{k}{1+(P^*/K)^n} = d_P P^*$$



For fluctuations **above** steady state, synthesis **decreases**

$P > P^*$

$$\frac{k}{1+(P/K)^n} < \frac{k}{1+(P^*/K)^n}$$

For fluctuations **below** steady state, synthesis **increases**

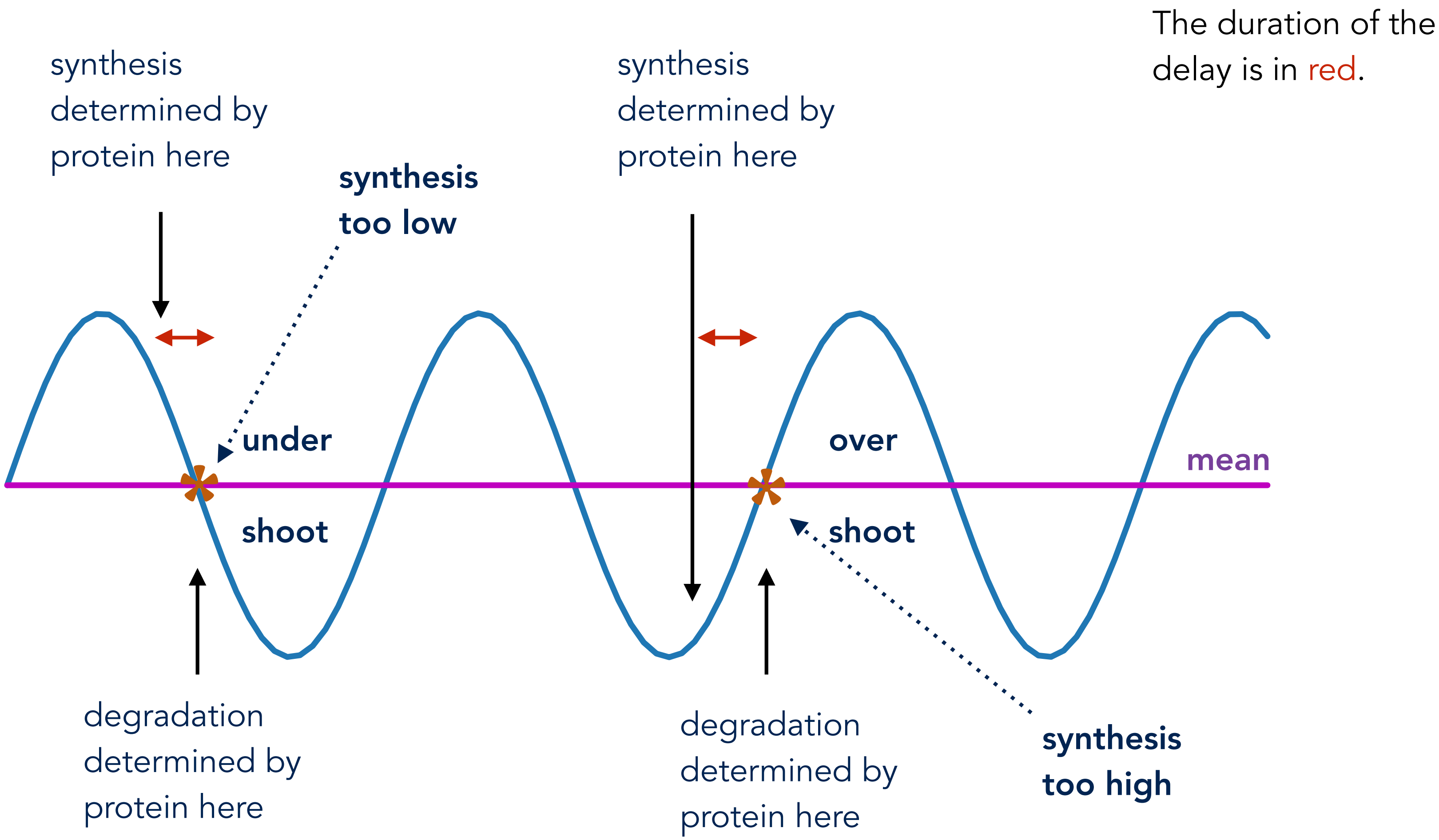
$P < P^*$

$$\frac{k}{1+(P/K)^n} > \frac{k}{1+(P^*/K)^n}$$

Negative feedback on protein synthesis works with degradation

Delayed negative feedback can cause oscillations

The delay causes a mismatch between the strength of synthesis and the strength of degradation.



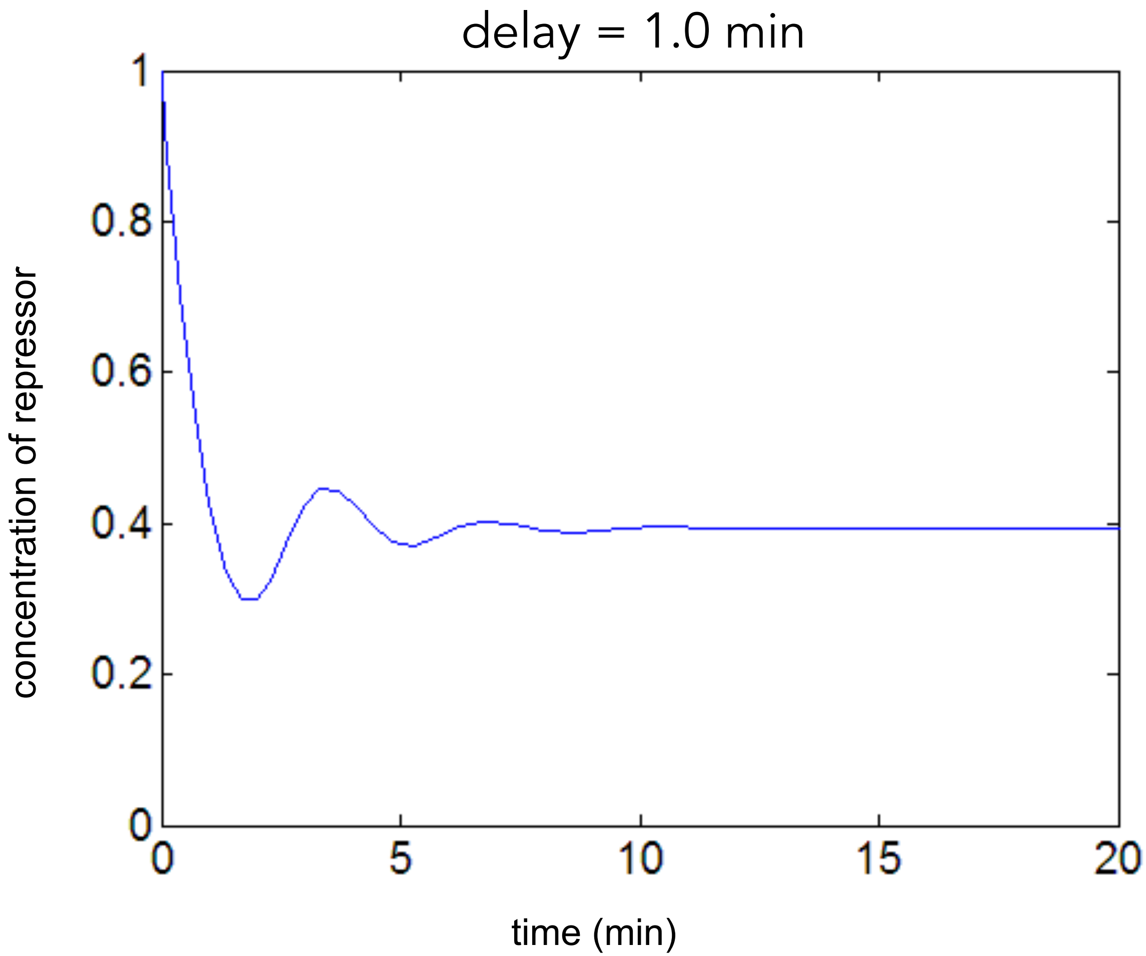
Oscillations are continual overshoots and undershoots because of the mismatch.

There are two requirements for a system to oscillate

(i) negative feedback: feedback that acts to reduce deviations of the system away from steady state

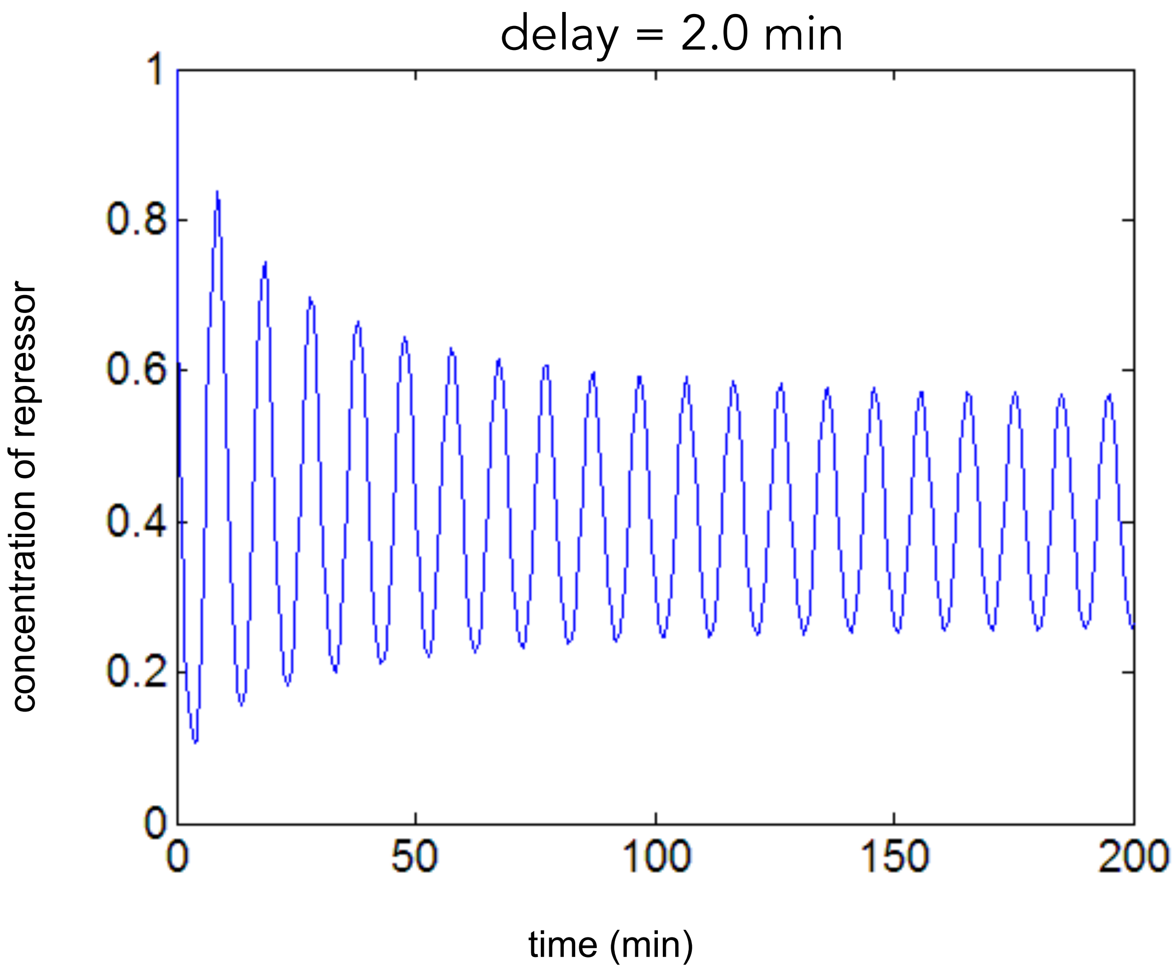
(ii) a delay: a sufficiently long time delay before the feedback acts.

For example: increasing the delay induces oscillations



system tends
to steady state

For example: increasing the delay induces oscillations



system oscillates when the delay is sufficiently long

For example: increasing the delay here increases the amplitude of the oscillations