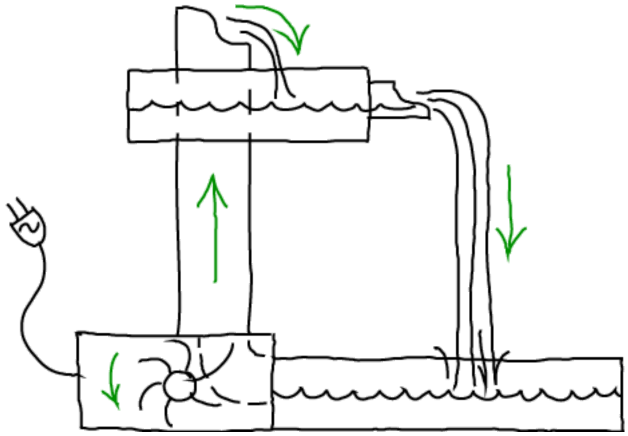
Non-equilibrium: Steady States

The Steady State: A Key Description of Biology



Background

- A steady state is characterized by unchanging probabilities / concentrations, but matter or probability may be flowing.
- Mathematically, all time derivatives are zero.
- Although the cell is not strictly in a steady state, many processes can be modeled reasonably as steady: think "homeostasis".
- Equilibrium is a special steady state in which no net flows of material or probability occur.
- Steady states with flows (i.e., those out of equilibrium) require input of matter or energy. They are not self-sustaining. The "desktop waterfall" shown above must be plugged in for the flow to be maintained.
- Steady states with flows typically are amenable to a simple mathematical treatment. They also are convenient modules for connecting to other parts of a larger system - the sources and sinks of flows.

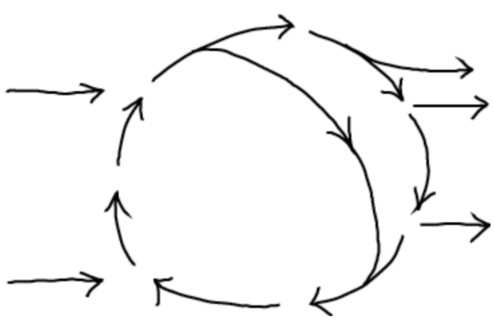
Schematically

A steady state consists of one or more inputs and one or more outputs, with each component unchanging in time.

$$\text{External Source} \longrightarrow A \longrightarrow B \longrightarrow \text{External Sink}$$

$$\frac{d[\mathrm{A}]}{dt} = 0 \qquad \frac{d[\mathrm{B}]}{dt} = 0 \tag{1}$$

A more typical (and complex) case includes multiple inputs/outputs and an internal cycle



Key Biological Examples

- Michaelis-Menten catalytic cycle
- Citric acid cycle
- Molecular locomotion
- Active transport

Steady-state analysis of a Michaelis-Menten (MM) process

A standard MM process models conversion of a substrate (S) to a product (P), catalyzed by an enzyme (E) after formation of a bound-but-uncatalyzed complex (ES).

The simple MM model can also be viewed as a cycle because the enzyme E is re-used. Blue arrows indicate steady net flows.

(The standard MM process here can be contrasted with the corrected MM cycle that allows for reverse events and physical single-step processes.)

A steady state will occur if P is removed at the same rate as S is added. Mathematically, for steady state, we set the time derivative of the ES complex to zero.

$$\frac{d[\mathrm{ES}]}{dt} = [\mathrm{E}][\mathrm{S}]\,k_{\mathrm{on}}^{\mathrm{ES}} - [\mathrm{ES}]\,k_{\mathrm{off}}^{\mathrm{ES}} - [\mathrm{ES}]\,k_{\mathrm{cat}} = 0 \tag{2}$$

The result yields what looks like a dissociation constant in terms of the steady-state (SS) concentrations:

$$\frac{[\mathrm{E}]^{\mathrm{SS}}[\mathrm{S}]^{\mathrm{SS}}}{[\mathrm{ES}]^{\mathrm{SS}}} = \frac{k_{\mathrm{off}}^{\mathrm{ES}} + k_{\mathrm{cat}}}{k_{\mathrm{on}}^{\mathrm{ES}}} \equiv K_M \tag{3}$$

In words, in the steady state, the ratio of concentrations on the left assumes the constant value given by the particular ratio of rate constants in the middle. The effective "equilibrium" constant KM is conventionally defined but not strictly needed.

The basic steady state result (3) can be used to calculate other quantities of interest, such as the overall rate of product production

$$k_{\mathrm{cat}}[\mathrm{ES}]^{\mathrm{SS}} = [\mathrm{E}]^{\mathrm{SS}}[\mathrm{S}]^{\mathrm{SS}}\,\frac{k_{\mathrm{cat}}}{K_M} \tag{4}$$

now given in terms of the steady-state E and S concentrations, which should be known.

The standard MM model is unphysical

All molecular processes are reversible, so any model with a uni-directional arrow is necessarily approximate: see the discussion of cycles. The full MM cycle, allowing for reverse events and permitting only single-step processes, is subjected to a (more complicated) steady-state analysis in an advanced section.