336: Systems and Control

System States

Version 1.0

Contents

1 System States

In this short chapter we will briefly go over the basic states that a given system can display. We will use examples from systems biology to illustrates the main points. The states a system can exhibit can fall into three groups: (Thermodynamic) equilibrium, steady state, and transients. In the literature the terms equilibrium and steady state are often incorrectly used interchangeably. In this chapter however a strict difference between the two terms will be maintained.

2 Equilibrium

Thermodynamic equilibrium, or simply equilibrium, refers to the state of a system when all forces are balanced. In chemistry, thermodynamic equilibrium is when all forward and reverse rates are equal. This also means that the concentration of chemical species is also unchanging and all net flows are zero. Equilibrium is easily achieved in a closed system. For example, consider the simple chemical isomerization:

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \tag{1}$$

Let the net forward rate of the reaction, v, be equal to $v = k_1 A - k_2 B$. The rates of change of A and B are given by:

$$\frac{dA}{dt} = -v \qquad \frac{dB}{dt} = v$$

At equilibrium $v = 0$, therefore dA/dt and dB/dt both equal zero. The analytical solution to the chemical isomerization can be derived as follows. Given that the system is closed we know that the total mass in the system, $A + B$ is constant. This constant is given by the sum of the initial concentrations of A and B which we will define as $A_o + B_o$. We assume that the volume is constant and set to unit volume, this allows us to state that the sum of the concentrations is conserved. The differential equation for A is given by:

$$\frac{dA}{dt} = k_2 B - k_1 A$$

Rather than solve this equation, let us replace B by the term $A_o + B_o - A$. This yields:

$$\frac{dA}{dt} = k_2 A_o + k_2 B_o - k_2 A - k_1 A = k_2(A_o + B_o) - A(k_1 + k_2)$$

The easiest way to solve this equation is to use Mathematica or Maxima. The Mathematica command is `DSolve[A'[t] == k2 (Ao + Bo) - A[t] (k1 + k2), A[0] == Ao, A[t], t]`, where `A[0] == Ao` sets the initial condition for the concentration of A to be A_o. By implication, the initial condition for B_o is $(A_o + B_o) - A_o = B_o$. The result of applying Mathematica yields the following solution:

$$A(t) = \frac{(A_o + B_o)k_2}{k_1 + k_2} + \frac{e^{-(k_1+k_2)t} v_{\text{initial}}}{k_1 + k_2}$$

The first term in this solution is the equilibrium concentration of A. The second term is an adjustment to the equilibrium concentration over time which tends to zero at infinite time. At $t = 0$, the second term is equal to $v_{\text{initial}}/(k_1 + k_2)$ where v_{initial} is the net reaction rate of the reversible reaction at the initial conditions, that is $k_1 A_o - k_2 B_o$. At $t = 0$, the value of the second term must be the difference between the initial concentration A_o and the equilibrium concentration, A_{eq}. The second term also has an exponential component which approaches zero as time goes to infinity. At this point

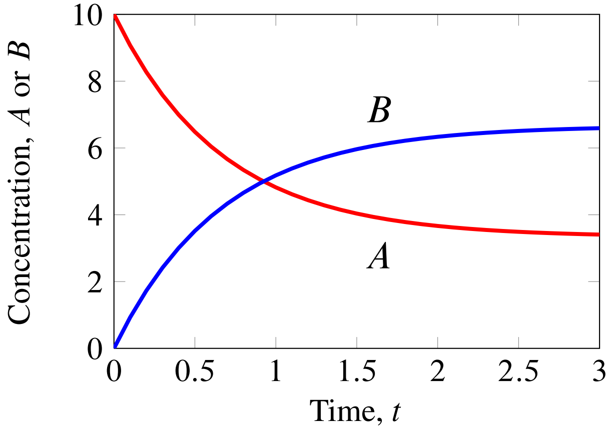

Figure 1: Time course for equilibration of the reversible reaction, $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$ where $k_1 = 1, k_2 = 0.5$, $A_o = 10$, $B_o = 0$. The ratio of the equilibrium concentration is given by k_1/k_2.

we are left with the first term which equals the concentration of A when $dA/dt = dB/dt = 0$.

At equilibrium the reaction rate can be computed by substituting the equilibrium concentration of A and B into the reaction rate, $v = k_2 B - k_1 A$. The equilibrium concentration of A is given by:

$$A_{eq} = \frac{(A_o + B_o)k_2}{k_1 + k_2}$$

The equilibrium concentration of B can be obtained by subtracting A_{eq} from $A_o + B_o$. When the A_{eq} and B_{eq} relations are substituted into v, the result is:

$$v = 0$$

From this somewhat long winded analysis, it has been determined for the closed reversible system, at infinite time, the concentrations of A and B reach some constant values and that the net rate, v is zero. The system is therefore at thermodynamic equilibrium.

In biochemical models it is often assumed that when the forward and reverse rates for a particular reaction are very fast compared to the surrounding reactions that the reaction is assumed to be in **quasi-equilibrium**. That is although the entire system may be out of equilibrium there may be parts of the system that can be approximated as though they were in equilibrium. This is often done to simplify the modeling process. Living organisms are not themselves at thermodynamic equilibrium, if they were then they would technically be dead. Living systems are open so that there is a continual flow of mass and energy across the system's boundaries.

3 Steady State

The **steady state**, also called the stationary state, is where the rates of change of all species, dS/dt are zero but at the same time the net rates are non-zero, that is $v_i \neq 0$. This situation can only occur in an open system, that is a system that can exchange matter with the surroundings. To convert the simple reversible model described in the last section into an open system we need only add a source reaction and a sink reaction as shown in the following scheme:

$$X_o \xrightarrow{k_o} A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_3}$$

In this case simple mass-action kinetics is assumed for all reactions. It is also assumed that the source reaction, with rate constant, k_o, is irreversible and originates from a boundary species, X_o, that is X_o is fixed. In addition it is assumed that sink reaction, with rate constant, k_3 is also irreversible. For the purpose of making it easier to derive the time course solution, the reverse rate constant, k_2 will be assumed to equal zero and we will set the initial conditions for A

and B to both equal zero. The mathematical solution for the system is given by equation 2:

$$\begin{aligned} A(t) &= v_o \frac{1 - e^{-k_1 t}}{k_1} \\ B(t) &= v_o \frac{k_1 \left(1 - e^{-k_3 t}\right) + k_3 \left(e^{-k_1 t} - 1\right)}{k_3 \left(k_1 - k_3\right)} \end{aligned} \tag{2}$$

As t tends to infinity $A(t)$ tends to v_o/k_1 and $B(t)$ tends to v_o/k_3. The reaction rate through each of the three reaction steps is v_o. This can be confirmed by substituting the solutions for A and B into the reaction rate laws. Given that v_o is greater than zero and that A and B reach constant values given sufficient time, we conclude that this system eventually settles to a steady state rather than thermodynamic equilibrium. The system displays a continuous flow of mass from the sink to the source. This can only continue undisturbed so long as the source material, X_o never runs out and that the sink is continuously unimpeded. Figure 2 shows a simulation of this system.

A topic will discuss in the next chapter is related to the stability of the steady state, that is whether the steady state diverges or restores itself in the face of perturbations to the floating species concentrations, in the above example, A and B.

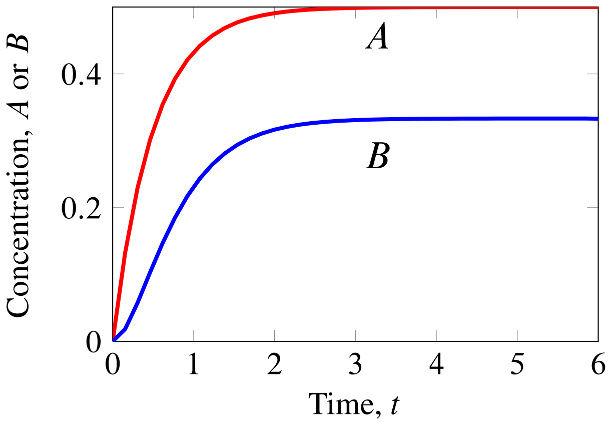

Figure 2: Time course for an open system reaching steady state. $X_o \xrightarrow{k_o} A \xrightarrow{k_1} B \xrightarrow{k_3}$ where $v_o = 1, k_1 = 2, k_3 = 3, A_o = 0, B_o = 0$. X_o is assumed to be fixed.

4 Transients

The final behavior that a system can show is a transient. A transient is usually the change that occurs in the species concentrations as the system moves from one state, often a steady state, to another. Equation 2 shows the solution to a simple system that describes the transient behavior of species A and B. Figure 2 illustrates the transient from an initial condition, in this case from a non-steady state condition to a steady state.

Thermodynamic Equilibrium and Steady State

Thermodynamic equilibrium, or equilibrium for short and the steady state are distinct states of a chemical system. In equilibrium, both the rate of change of species and the net flow of mass through the system is zero. That is:

$$\frac{d\mathbf{s}}{dt} = 0$$

$$\text{for all } i: v_i = 0$$

where v_i is the net reaction rate for the i^{th} reaction step. At equilibrium there is therefore no dissipation of gradients or energy fields. When a biological system is at equilibrium, we say it is dead.

The steady state has some similarities with equilibrium except there is a net flow through the system such that gradients and energy fields are continuously being dissipated. This also means that one or more v_is must be non-zero

The steady state is defined when all dS_i/dt are equal to zero while one or more reaction rates are non-zero:

$$\frac{d\mathbf{s}}{dt} = 0$$

$$v_i \neq 0$$

In some of the literature the terms equilibrium and steady state are confusingly used to mean the same thing, usually steady state. In this book a strict difference between the two will be maintained.

Further Reading

1. Sauro HM (2011) Enzyme Kinetics for Systems Biology. ISBN: 978-0982477311

Exercises

1. Describe the difference between thermodynamic equilibrium and a steady state.

2. If you were given a set of ODEs that described a system. Assuming the system has a steady steady describe two ways you might go about computing the steady state?

3. Using the Laplace transform method, derive the time dependent solutions to the system described in (1).