9.9 *Application:* More Pharmacokinetics

Section 9.9, *Pharmacokinetics* merely scratches the surface of a complex field of biological modelling. More realistic models recognize that to understand the passage of a drug through the body, more than one location must be considered. In the language of pharmacokinetics, these locations are called "compartments."

Consider the situation in which a dose of some prescription drug is administered by injection. The drug is then located at one point in the body from which it moves eventually to the target organ, and then is eliminated.

Example: A single dose.

There are two compartments, the place where the drug is injected and the target organ. The equations modelling the drug level at the place of injection is the same as in the one compartment model in the text. Let I be the level of the drug at the place of injection. Then

$$I' = -k_I I$$

models the diffusion of the drug from the point of injection (and the absorption of the drug by the target organ). The solution to this is

$$I = Ae^{-k_I t}.$$

If we take I_0 to be the size of the dose, then the solution is

$$I = I_0 e^{-k_I t}.$$

To model the drug level in the second compartment, let D be the level of the drug in the target organ. Then D is a solution to

$$D' = -I' - k_D D = k_I I_0 e^{-k_I t} - k_D D.$$

The first term represents absorption of the drug into the organ (equal to the amount leaving the injection site) and the second represents elimination of the drug from the body.

This differential equation is not easy to solve. The method of separation of variables (which you probably used to solve problem 2 in the laboratory in the text) doesn't work here. Instead, a lucky guess is required. Since we see both $I_0 e^{-k_I t}$ and $-k_D D$, we might guess that the solution involves both $e^{-k_I t}$ and $e^{-k_D t}$. Our lucky guess is that the solution looks like:

$$D = Be^{-k_I t} + Ce^{-k_D t}.$$

To see if this is so, and to find the constants B and C, we substitute the expression for D into the differential equation:

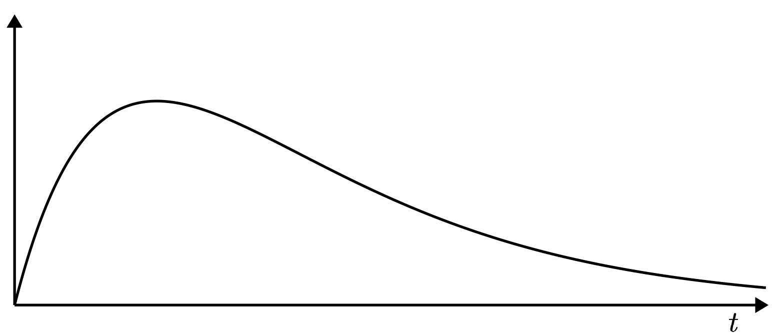
$$\begin{aligned}
D' &= k_I I_0 e^{-k_I t} - k_D D \\
\left(Be^{-k_I t} + Ce^{-k_D t}\right)' &= k_I I_0 e^{-k_I t} - k_D(Be^{-k_I t} + Ce^{-k_D t}) \\
-k_I Be^{-k_I t} - k_D Ce^{-k_D t} &= k_I I_0 e^{-k_I t} - k_D Be^{-k_I t} - k_D Ce^{-k_D t} \\
-k_I Be^{-k_I t} &= k_I I_0 e^{-k_I t} - k_D Be^{-k_I t} \\
-k_I B &= k_I I_0 - k_D B \\
B &= \tfrac{k_I I_0}{k_D - k_I}.
\end{aligned}$$

With this value of B, we have a solution to the equation. We then choose C so that $D(0) = 0$ (at the time of the injection, there is no drug in the organ).

$$\begin{aligned}
0 &= \tfrac{k_I I_0}{k_D - k_I} e^{-k_I \cdot 0} + Ce^{-k_D \cdot 0} \\
0 &= \tfrac{k_I I_0}{k_D - k_I} + C \\
C &= -\tfrac{k_I I_0}{k_D - k_I}.
\end{aligned}$$

Our solution, then, is

$$D = \frac{k_I I_0}{k_D - k_I}\left(e^{-k_I t} - e^{-k_D t}\right).$$



Laboratory: Two Compartment Models

As in the text, you're the doctor. This time, your patients have two compartments.

1. Let's say that you want the level of a certain drug in the body to be at least m and no more than M. We're using the model of the previous example. What should the initial injection be so that eventually the level of drug in the organ reaches M?

   Hint: First find the value of t where $D = \frac{k_I I_0}{k_D - k_I}\left(e^{-k_I t} - e^{-k_D t}\right)$ reaches its maximum. Substitute this into the expression for D to find the maximum value of D. It looks messy, but it will simplify.

2. Your patient is in the hospital and you can drip the drug into the bloodstream at a constant rate r. What should that rate be in order to come close to an ideal drug level of L? Again, assume that the drug leaves the body according to the model in the example above.

   Hint:

   You'll need the solution to the model in the second problem in the lab in the text. It's $D = \frac{r}{k}\left(1 - e^{-kt}\right)$. Thus, you can assume the level of drug at the point of injection is

   $$I = \frac{r}{k_I}\left(1 - e^{-k_I t}\right)$$

   and the differential equation for the level of drug at the organ is:

   $$D' = k_I I - k_D D = r(1 - e^{-k_I t}) - k_D D.$$

   You'll need a lucky guess (essentially the same as the lucky guess above). Compute D' from this and substitute it and D into the equation $D' = r(1 - e^{-k_I t}) - k_D D$ to find the values of B and C. Sketch your solution. What should r be so that D approaches L?