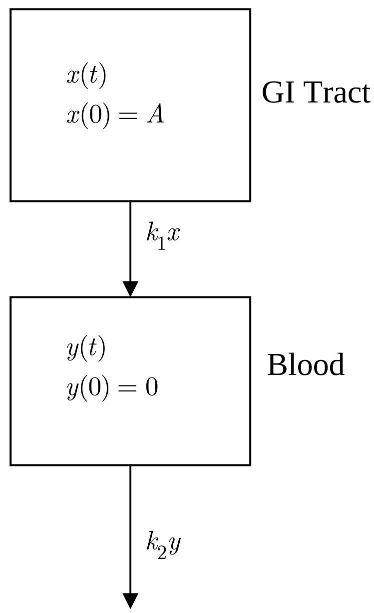
**Name ______________________   Mike Huff Differential Equations**
**Project 2 Modeling the flow of medication through the body**

We will model the flow of a cold medication through the body by using a compartment model. We will treat the parts of the body as compartments, then track the medication as it enters and leaves each compartment.  A typical cold medication leaves one compartment (GI tract) and moves into the next (bloodstream) at a rate proportional to the amount present. The constant of proportionality depends upon the medication, the compartment, and the age and health of the individual.

**Flow of medication**




## A Single Dose of Antihistamine

Suppose there are A units of antihistamine in the GI tract at time 0 and that $x(t)$ is the number of units remaining at any time later *t*. The Balance Law applies:

Net rate = rate in – rate out

Since we start with A units and the medication moves into the blood at a rate proportional to the amount in the GI tract, we have the IVP

$$\frac{dx(t)}{dt} = -k_1 x(t), \quad x(0) = A$$

where $k_1$ is a positive constant. Time is measured in hours and $k_1$ is $hours^{-1}$.

To model the flow in the blood compartment, we assume that this compartment includes the tissues where the medication does its work. The level $y(t)$ of antihistamine in the blood builds up from zero but then falls as the kidneys and liver do the job of clearing substances from the blood. The Balance Law applied to the blood compartment leads to the IVP

$$\frac{dy(t)}{dt} = k_1 x(t) - k_2 y(t), \quad y(0) = 0$$

where time is measured in hours and $k_2$ is $hours^{-1}$.

The result is the **system of linear differential equations:**

$$\begin{aligned} \frac{dx}{dt} &= -k_1 x, & x(0) &= A \\ \frac{dy}{dt} &= k_1 x - k_2 y, & y(0) &= 0 \end{aligned} \tag{1}$$

Although we will develop techniques for solving more general systems later in this course, this particular system is a ***linear cascade*** and its solution is possible with the techniques we've developed so far in this course.

Exercises:

1. Solve the IVP in the first rate equation of system (1). (The top equation)
2. Substitute the resulting formula for $x(t)$ into the second rate equation in system (1).
3. The resulting equation is linear. Find the integrating factor and solve the IVP for $y(t)$. Why must we have $k_1 \neq k_2$ in the model?
4. What happens to the levels of antihistamine in the GI tract over time? What happens to the levels of antihistamine in the blood over time?
5. **Maximum level** Show that after a single dose the antihistamine level in the bloodstream reaches its maximum level when $t = \left(\ln k_1 - \ln k_2\right) / \left(k_1 - k_2\right)$. Hint: when is $y' = 0$?
6. A pharmaceutical company estimates that the values of the rate constants for the antihistamine in the cold pills it makes to be $k_1 = 0.6931(\text{hour})^{-1}$ and $k_2 = 0.0231(\text{hour})^{-1}$. Because $k_2$ is so much smaller than $k_1$, antihistamine stays at a higher level a lot longer in the blood than the GI tract. On a single coordinate grid, graph both the amount of antihistamine in the GI tract and the amount of antihistamine in the blood for a six-hour period assuming A = 1 and with the *k*'s as given here.

7. **Sensitivity to clearance coefficient $k_2$** The clearance coefficient $k_2$ is often much smaller for the old and sick than it is for the young and healthy. This means that for some people medication levels in the blood may become excessively high, even with a standard dosage. Graph the level of antihistamine in the blood using $k_1 = 0.6931(\text{hour})^{-1}$ and $k_2 = 0.231(\text{hour})^{-1}, 0.0731(\text{hour})^{-1}, 0.0231(\text{hour})^{-1}, 0.00731(\text{hour})^{-1}, 0.00231(\text{hour})^{-1}$ Graph the five graphs all on the same coordinate grid. What do you notice?
8. Suppose that A units of antihistamine are present in the GI tract and B units are in the blood at time 0. Solve IVP (1) with the condition $y(0) = 0$ replaced with the condition that $y(0) = B$.
9. **Sensitivity to changes in $k_1$** Let A = 1, keep $k_2 = 0.231(\text{hour})^{-1}$, but let $k_1$ vary.
   a) Graph the level of antihistamine in the blood using $k_2 = 0.231(\text{hour})^{-1}$ and $k_1 = 0.06931,\ 0.11,\ 0.3,\ 0.6931,\ 1,\ 1.5$. Plot the graphs over a 24-hour period. Why do the graphs for larger values of $k_1$ cross the graphs for smaller values?
   b) You need to keep the medication levels within a fixed range so that the medication is both therapeutic and safe. Suppose that the desired range for antihistamine levels in the blood is from 0.2 to 0.8 for a unit dose taken once. With $k_2 = 0.231(\text{hour})^{-1}$, find upper and lower bounds on $k_1$ so that the antihistamine levels in the blood reach 0.2 within 2 hours and stay below 0.8 for 24 hours.