School of Mathematics & Applied Statistics

MATH111: Mathematics Applied Mathematical Modelling 1

Assignment Week 8 Solutions

Spring 2007

1. The model discussed in this section is analysed in Kubota and Maibach (1992).

   A drug delivery vehicle, such as a skin patch, is attached to a patient. The amount of drug per unit area (X) in the skin is described by the following differential equation

$$\frac{\mathrm{d}X}{\mathrm{d}t} = -\left(k_{12} + k_{1B}\right) X + k_{21} A_0, \quad X\left(0\right) = 0. \tag{1}$$

   In this equation A_0 is the concentration of drug per unit area in the delivery device, which is maintained at a constant level. The parameters k_{12} and k_{21} are the rate at which drug enters the vehicle from the skin and the skin from the vehicle respectively. The parameter k_{1B} is the rate at which drug leaves the skin and enters the blood stream.

   (a) Solve equation (1) to find the amount of drug per unit area in the skin as a function of time. What is the medical significance of your answer?

   (b) The cumulative amount of drug per unit area excreted from the skin (Ae_s) is expressed by

$$Ae_s = \int k_{1B} X \,\mathrm{d}t, \quad Ae_s\left(0\right) = 0.$$

   Determine Ae_s.

   K. Kubota and H.I. Maibach. A compartment model for percutaneous absorption: Compatibility of lag time and steady-state flux with diffusion model. *Journal of Pharmaceutical Sciences*, **81**(9):863–865, 1992.

   Solution

   (a) The differential equation can be written in the form of a first-order linear differential equation and can therefore be solved by finding an itegrating factor.

$$\frac{\mathrm{d}X}{\mathrm{d}t} + \left(k_{12} + k_{1B}\right) X = k_{21} A_0,$$

$$R = \exp\left[\int \left(k_{12} + k_{1B}\right) \mathrm{d}t\right],$$

$$= \exp\left[\left(k_{12} + k_{1B}\right) t\right]. \Rightarrow \frac{\mathrm{d}}{\mathrm{d}t}\left\{\exp\left[\left(k_{12} + k_{1B}\right) t\right] X\right\} \quad = k_{21} A_0 \exp\left[\left(k_{12} + k_{1B}\right) t\right],$$

$$\Rightarrow \exp\left[\left(k_{12} + k_{1B}\right) t\right] X = \frac{k_{21} A_0}{k_{12} + k_{1B}} \exp\left[\left(k_{12} + k_{1B}\right) t\right] + c,$$

   where c is an aritrary condition. Applying the initial condition $X\left(0\right) = 0$ we obtain $c = -k_{21} A_0$. Thus

$$X\left(t\right) = \frac{k_{21} A_0}{k_{12} + k_{1B}} \left\{1 - \exp\left[-\left(k_{12} + k_{1B}\right) t\right]\right\}$$

   (b)

$$Ae_s = k_{1B} \int X\left(t\right) \mathrm{d}t,$$

$$= k_{1B} \int \frac{k_{21} A_0}{k_{12} + k_{1B}} \left\{1 - \exp\left[-\left(k_{12} + k_{1B}\right) t\right]\right\} \mathrm{d}t,$$

$$= \frac{1_{1B} k_{21} A_0}{k_{12} + k_{1B}} \left\{t + \frac{1}{k_{12} + k_{1B}} \exp\left[-\left(k_{12} + k_{1B}\right) t\right]\right\},$$

where c is an arbitrary. Applying the initial condition $Ae_s(0) = 0$ we obtain $c = -\frac{1_{1B}k_{21}A_0}{k_{12}+k_{1B}}$. Thus

$$Ae_s(t) = \frac{1_{1B}k_{21}A_0}{k_{12}+k_{1B}}\left\{t + \frac{1}{k_{12}+k_{1B}}\exp\left[-\left(k_{12}+k_{1B}\right)t\right] - \frac{1}{k_{12}+k_{1B}}\right\}.$$

2. After irradiation, the number of unavailable binding sites in the spleen for injected CFU decreases according to the differential equation

$$\frac{\mathrm{d}U}{\mathrm{d}t} = -\lambda_1 U, \qquad U(0) = U_0. \tag{2}$$

The number F of available binding sites in the spleen changes according to

$$\frac{\mathrm{d}F}{\mathrm{d}t} = \lambda_1 U - \lambda_2 F, \quad F(0) = 0, \tag{3}$$

where the term $\lambda_2 F$ represents the decay of available sites due to radiation damage.

(a) Solve equation (2) to find the number of unavailable sites as a function of time, $U(t)$.

(b) Substitute your expression for $U(t)$ into equation (3). Solve the resulting differential equation to find the number of available sites as a function of time, $F(t)$.

(c) Find the value of t, $t_{\max}$, where the number of available sites (F) is maximised (F_{max}).

(d) Determine the maximum number of available sites available. Simplify your expression as far as possible.

This question is based upon Matioli (1976).

G. Matioli. (1976). Consideration of some functional properties of the hemopoietic sources. *Mathematical Biosciences*, **28**, 373–376.

Solution

(a) This equation can be written as a first-order linear differential equation. Its solution can therefore be found by finding an integrating factor. Alternatively, it can be solved by treating it as a separable differential equation.

$$\begin{aligned}\int_{U_0}^{U}\frac{\mathrm{d}U}{U} &= \int_0^t -\lambda_1\mathrm{d}t,\\ \Rightarrow \ln\left|\frac{U}{U_0}\right| &= -\lambda_1 t,\\ \Rightarrow U &= U_0\exp\left[-\lambda_1 t\right].\end{aligned}$$

3. After substituting in the expression for $U(t)$ that we have just calculated the differential equation can be written as a first-order linear differential equation. Its solution can therefore be found by finding an integrating factor.

$$\begin{aligned}\frac{\mathrm{d}F}{\mathrm{d}t} + \lambda_2 F &= U_0\lambda_1\exp\left[-\lambda_1 t\right],\\ R(x) &= \exp\left[\int\lambda_2\mathrm{d}t\right],\\ &= \exp\left[\lambda_2 t\right],\\ \Rightarrow \frac{\mathrm{d}}{\mathrm{d}t}\left\{\exp\left[\lambda_2 t\right]F\right\} &= U_0\lambda_1\exp\left[\left(\lambda_2-\lambda_1\right)t\right],\\ \Rightarrow \exp\left[\lambda_2 t\right]F &= \frac{U_0\lambda_1}{\lambda_2-\lambda_1}\exp\left[\left(\lambda_2-\lambda_1\right)t\right] + c,\end{aligned}$$

where c is an arbitrary constant. Note that in integrating we have assumed that $\lambda_1 \neq \lambda_2$. Applying the initial condition $F(0) = 0$ we obtain $c = -\frac{U_0\lambda_1}{\lambda_2-\lambda_1}$. Thus

$$F = \frac{U_0\lambda_1}{\lambda_2-\lambda_1}\left\{\exp\left[-\lambda_1 t\right] - \exp\left[-\lambda_2 t\right]\right\}.$$

4. The maximum value will occur when $\frac{\mathrm{d}F}{\mathrm{d}t} = 0$. Using the solution to our previous question we obtain

$$\frac{\mathrm{d}F}{\mathrm{d}t} = \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left\{-\lambda_1 \exp\left[-\lambda_1 t\right] + \lambda_2 \exp\left[\lambda_2 t\right]\right\}.$$

After some algebra we find that

$$\begin{aligned}\frac{\mathrm{d}F}{\mathrm{d}t} &= 0,\\ \Rightarrow t_{\max} &= \frac{1}{\lambda_2 - \lambda_1}\ln\left(\frac{\lambda_2}{\lambda_1}\right).\end{aligned}$$

5. To find the maximum number of free sites we substitute the expression for $t_{\max}$ into the solution $f(t)$.

$$\begin{aligned}F_{\max} &= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left\{\exp\left[-\frac{\lambda_1}{\lambda_2 - \lambda_1}\ln\left(\frac{\lambda_2}{\lambda_1}\right)\right] - \exp\left[-\frac{\lambda_2}{\lambda_2 - \lambda_1}\ln\left(\frac{\lambda_2}{\lambda_1}\right)\right]\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left\{\exp\left[\ln\left(\frac{\lambda_2}{\lambda_1}\right)^{-\frac{\lambda_1}{\lambda_2-\lambda_1}}\right] - \exp\left[\ln\left(\frac{\lambda_2}{\lambda_1}\right)^{-\frac{\lambda_2}{\lambda_2-\lambda_1}}\right]\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left\{\left(\frac{\lambda_2}{\lambda_1}\right)^{-\frac{\lambda_1}{\lambda_2-\lambda_1}} - \left(\frac{\lambda_2}{\lambda_1}\right)^{-\frac{\lambda_2}{\lambda_2-\lambda_1}}\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left\{\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_1}{\lambda_2-\lambda_1}} - \left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_2}{\lambda_2-\lambda_1}}\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_1}{\lambda_2-\lambda_1}}\left\{1 - \left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_2-\lambda_1}{\lambda_2-\lambda_1}}\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_1}{\lambda_2-\lambda_1}}\left\{1 - \frac{\lambda_1}{\lambda_2}\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2 - \lambda_1}\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_1}{\lambda_2-\lambda_1}}\left\{\frac{\lambda_2 - \lambda_1}{\lambda_2}\right\},\\
&= \frac{U_0\lambda_1}{\lambda_2}\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_1}{\lambda_2-\lambda_1}},\\
&= U_0\left(\frac{\lambda_1}{\lambda_2}\right)^{1+\frac{\lambda_1}{\lambda_2-\lambda_1}},\\
&= U_0\left(\frac{\lambda_1}{\lambda_2}\right)^{\frac{\lambda_2}{\lambda_2-\lambda_1}}.\end{aligned}$$

In the mid-session test and/or the final exam you may be asked a question about Maple.

Your answer should include all maple code that you used to obtain the answer.

3. The Shannon function is defined as

$$H(p) = -\left[p\log_{10}(p) + (1-p)\log_{10}(1-p)\right],$$

where $0 < p < 1$.

(a) Plot the Shannon function.

(b) What value of p maximises the value of the Shannon function?

(c) What is the maximum value of the Shannon function?

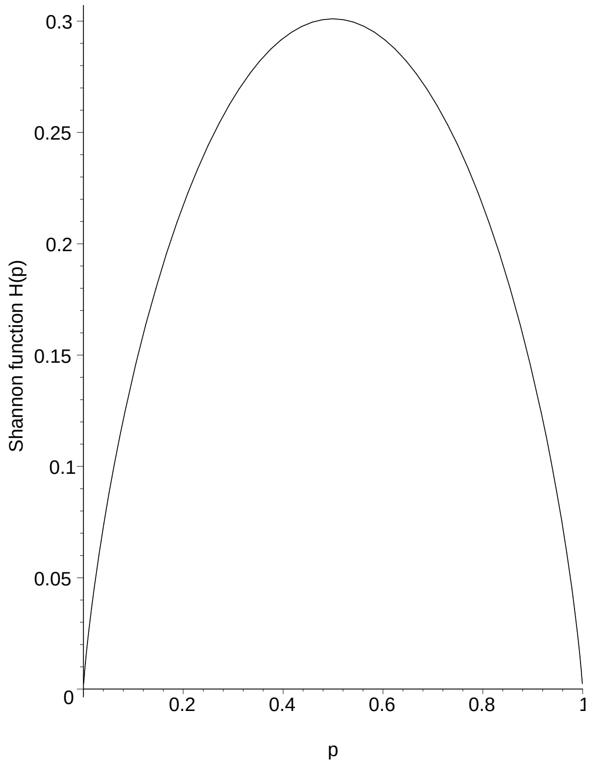

Figure 1: The Shannon function $H(p)$ as function of p

The importance of the Shannon function is described in Bruen & Forcinito (section 9.2, pages 162-164).

A.A. Bruen and M.A. Forcinito. Cryptography, Information Theory, and Error-Correction. Wiley-Interscience, Hoboken, NJ, 2005.

Solution This is a straightforward question. Make sure that you define the Shannon function using `log10` and *not* `log`

Maple code is at the end of the question.

(a) See figure 1.

(b) $p = \frac{1}{2}$.

(c) $\frac{\ln 2}{\ln 10}$.

```
# week8-2007.maple
# 21.09.07
#
#
# NOTE the use of log10 rather than log to define the Shannon function.
H := -(p*log10(p) +(1-p)*log10(1-p));

lprint("Part (a)");
plot(H,p=0..1,color=BLACK,labels=["p","Shannon function H(p)"], \
     labeldirections=[horizontal,vertical]);

lprint("Part (b)");
p := solve(diff(H,p),p);

lprint("Part (c)");
```

```
H;
```