Section 11.2 Prescribing Drug Dosage

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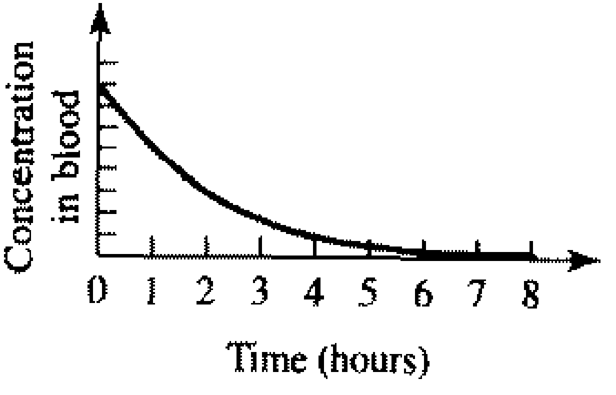
Motivation

- We are interested in what happens to the concentration of the drug in the blood as doses are given at regular intervals.
- Let $C(t)$ be the concentration of the drug at any time t (in hours).



Motivation

The evolution of concentration $C(t)$ in a body is governed by

$$\frac{dC}{dt} = -kC$$

with initial condition $C(0) = C_0$. The solution of the differential equation

$$C(t) = C_0 e^{-kT}$$

gives the concentration over time.

Dosing Schedules

Let's look at ways in which the drug can be administered. Let us define the following:

- H = highest safe level of drug concentration,
- L = lowest effective level of drug concentration,
- C_0 = initial dose,
- T = interval of time between doses.

Case 1: T is large (Long intervals between doses)

The residual R_n can be calculated by

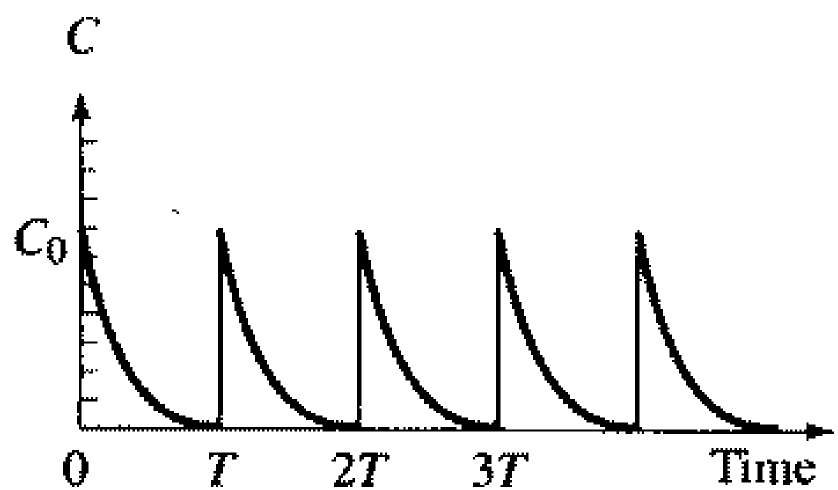
$$R_n = \frac{C_0 e^{-kT}\left(1 - e^{-nkT}\right)}{1 - e^{-kT}}$$

The sequence of R_n's have a limiting value, in which we call R.

$$R = \lim_{n\to\infty} R_n = \frac{C_0 e^{-kT}}{1 - e^{-kT}} = \frac{C_0}{e^{kT} - 1}$$

Case 1: T is large (Long intervals between doses)

Now for large T, the residual concentration for each dose approaches 0, so the various administrations of the drug are independent.



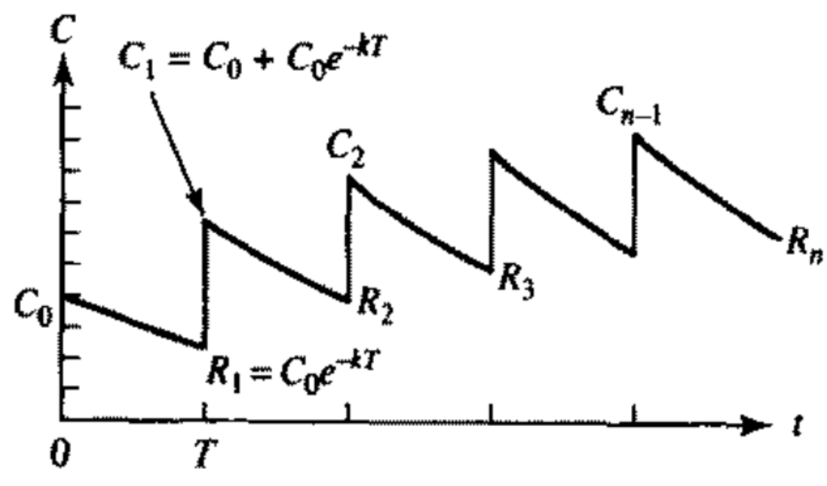
Note: $C(T) = C(2T) = C(3T) = 0.$

Case 2: T is shorter (shorter intervals between doses)

Let R_n be the residual concentration at time t after the initial dosage C_0. Then

$$R_n = C_0 e^{-kT}(1 + r + \cdots + r^{n-1})$$

$$C_{n-1} = C_0 + R_{n-1}$$



Case 2: T is shorter (shorter intervals between doses)

This leaves us with,

$$R_n = C_0 r \frac{(1 - r^n)}{1 - r}$$

where $r = e^{-kT}$. The series converges only when $|r| < 1$, that is, when

$$e^{-kT} < 1.$$

Case 2: T is shorter (shorter intervals between doses)

Since $R = \frac{C_0}{e^{kT}-1}$ and $C_{n-1} = C_0 + R_{n-1}$, we can find the highest safe level (H) and the lowest effective level (L) of drug concentration:

$$H = \lim_{n\to\infty} C_{n-1} = \lim_{n\to\infty} (C_0 + R_{n-1}) = C_0 + R$$

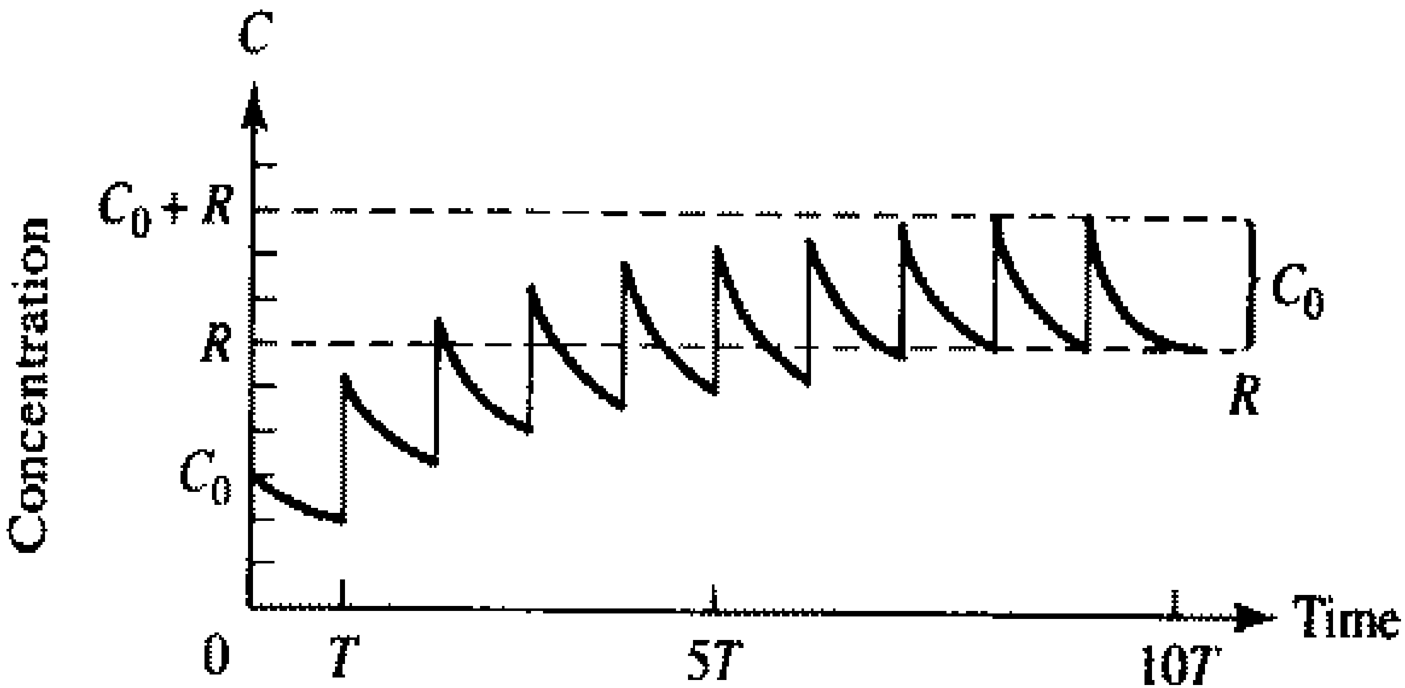
Combining this result with $C_0 = H - L$,

$$C_0 = C_0 + R - L$$

$$\Longrightarrow R = L$$

Case 2: T is shorter

- This shows that the drop in concentration after each dose becomes close to the rise in concentration resulting from each dose.
- In the long run, the loss in concentration will equal the gain in concentration.
- The concentration will eventually oscillate between R and $C_0 + R$.



Case 2: T is shorter

The buildup of drug concentration when the interval between doses is short.

Determining Dose Schedule

Suppose we want to maximize the time between drug doses by setting $R = L$ and $C_0 = H - L$. Then

$$R = L$$

$$\frac{C_0}{e^{kT} - 1} = L$$

$$\frac{H - L}{e^{kT} - 1} = L$$

Determining Dose Schedule

$$\frac{H - L}{L} = e^{kT} - 1$$

$$e^{kT} = \frac{H}{L}$$

$$T = \frac{1}{k} \ln\left(\frac{H}{L}\right)$$

where $C_0 = H - L$.

Conclusion

This model prescribes a safe and effective dosage of drug concentration for every T hours.

$$\begin{cases} C_0 = H - L \\ T = \dfrac{1}{k} \ln\left(\dfrac{H}{L}\right) \end{cases}$$

HW § 11.2: #3,4,5.