Homework Assignment 10: Solutions

1. The units that I will use for the heights of the rectangles are μg/ml and the units that I will use for the widths of the rectangles are hours. In particular, this means that the width of each rectangle will be 0.5 hours. As there are 12 hours to consider and each rectangle will be 0.5 hours "wide," there will be 24 rectangles in total.

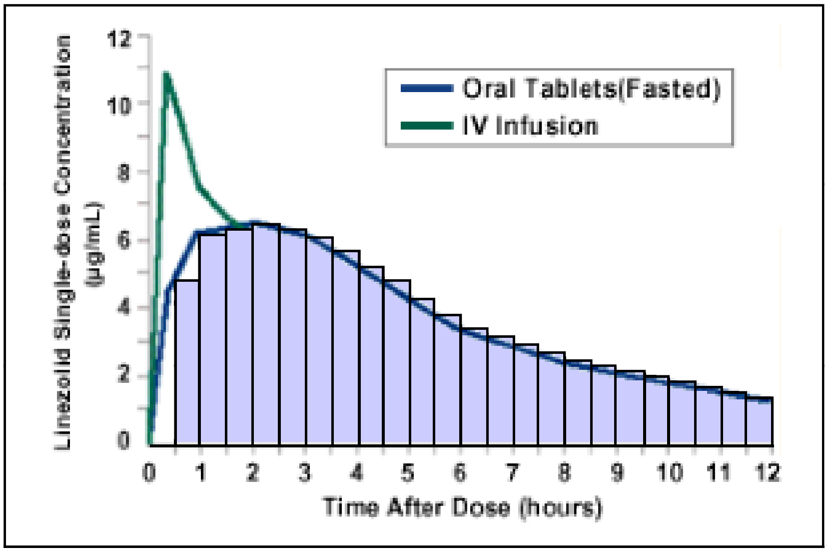
The heights that I measured (by reading values off the blue plasma concentration curve provided) for each of the 24 rectangles are given in the table below.

Rectangle	Height	Rectangle	Height	Rectangle	Height
1	0	9	5.1	17	2.3
2	5.2	10	4.6	18	2.1
3	6.2	11	4.2	19	2.0
4	6.3	12	3.8	20	2.0
5	6.6	13	3.4	21	1.8
6	6.3	14	3.1	22	1.7
7	6.2	15	2.9	23	1.6
8	5.7	16	2.7	24	1.3

Using these heights and a constant width of 0.5 hours, the total area of all 24 rectangles is:

$$\textit{Approximate area under Plasma concentration curve} = 43.55 \ \frac{(\mu g)\cdot(hours)}{ml}$$

The graph of plasma concentration for a patient who received Zyvox™ orally (with the 24 rectangles drawn in) is shown below.



2. To approximate the area under the curve:

$$P(T) = 0.024238 \cdot T^3 - 0.58732 \cdot T^2 + 3.5477795 \cdot T + 0.5$$

(where T = number of hours since Zyvox™ was administered and $P(T)$ = plasma concentration in µg/ml) between $T = 0$ and $T = 12$ using 100 rectangles, the width of each rectangle (call this ΔT) would have to be:

$$\Delta T = \frac{(12 - 0)}{100} = 0.12.$$

The appropriate calculator commands to approximate the area under the plasma concentration curve would be:

```
0.12 [STO⇨] W

y1 = 0.024238*X^3 - 0.58732*X^2 + 3.5477795*X + 0.5

sum(seq(Y1(K*W)*W, K, 0, 99))
```

Performing these commands on a TI-83 gave the approximate area under the plasma concentration curve as:

$$\text{Approximate area under Plasma concentration curve} = 48.79629388 \; \frac{(\mu g)\cdot(hours)}{ml}$$

3. The units that I will use for the heights of the rectangles are μg/ml and the units that I will use for the widths of the rectangles are hours. In particular, this means that the width of each rectangle will be 0.5 hours. As there are 12 hours to consider and each rectangle will be 0.5 hours "wide," there will be 24 rectangles in total.

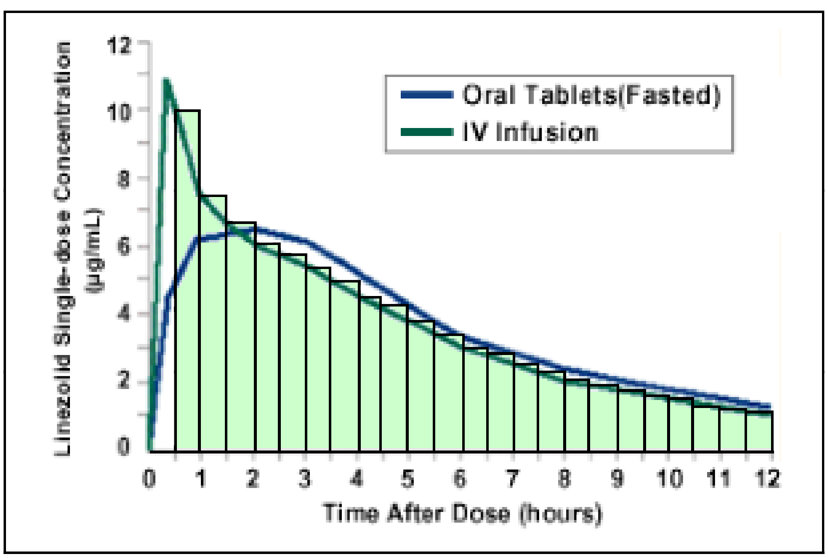
The heights that I measured (by reading values off the green plasma concentration curve provided) for each of the 24 rectangles are given in the table below.

Rectangle	Height	Rectangle	Height	Rectangle	Height
1	0	9	4.6	17	2.0
2	9.8	10	4.1	18	1.9
3	7.6	11	3.8	19	1.8
4	6.7	12	3.3	20	1.7
5	6.0	13	3.0	21	1.6
6	5.7	14	2.8	22	1.3
7	5.3	15	2.4	23	1.2
8	4.9	16	2.2	24	1.1

Using these heights and a constant width of 0.5 hours, the total area of all 24 rectangles is:

$$\textit{Approximate area under Plasma concentration curve} = 42.4 \frac{(\mu g)\cdot(hours)}{ml}$$

The graph of plasma concentration for a patient who received Zyvox™ intravenously (with the 24 rectangles drawn in) is shown below.



4. To approximate the area under the curve: $C(T) = 9.4 \cdot (0.85)^T$

(where T = number of hours since Zyvox™ was administered and $P(T)$ = plasma concentration in μg/ml) between $T = 0$ and $T = 12$ using 500 rectangles, the width of each rectangle (call this ΔT) would have to be:

$$\Delta T = \frac{(12 - 0)}{500} = 0.024.$$

The appropriate calculator commands to approximate the area under the plasma concentration curve would be:

```
0.024 [STO⇨] W

y1 = 9.4*(0.85)^X

sum(seq(Y1(K*W)*W, K, 0, 499))
```

Performing these commands on a TI-83 gave the approximate area under the plasma concentration curve as:

$$\textit{Approximate area under Plasma concentration curve} = 49.70905402 \ \frac{(\mu g) \cdot (hours)}{ml}$$

5. The bioavailability of Zyvox™ is given by:

$$Bioavailability = \frac{AUC_{ORAL}}{AUC_{INTRAVENOUS}} \cdot 100\%.$$

Using the area obtained in Question 2 for AUC_{ORAL} and the area obtained in Question 4 for $AUC_{INTRAVENOUS}$ gives a bioavailability of:

$$Bioavailability = \frac{48.79629388}{49.70905402} \cdot 100\% = 98.164\%.$$

This is not precisely equal to 100% bioavailability as claimed by Pharmacia Corporation. However, it is very, very close. When you further consider that:

(a) The AUC's used in this calculations are just approximations of the "true" areas under the plasma concentration curves, and,
(b) The measurements (of plasma concentration) that these calculations are based on will involve some amount of experimental error,

Pharmacia Corporation would probably be on very strong grounds in claiming that the bioavailability was not statistically significantly different from100%.