Applied Statistical Modelling (STAT 40510)
Main Project
Task 2: Model Fitting

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TBC

Format of the Project

The main project in PK in STAT 40510 will be made up of several tasks.

- Follow the online lectures independently, attend weekly office hours in Weeks 5-7.
- Over the same time period, complete (in a group) **Tasks 1 and 2** to test your knowledge of what you have learned.
- Again over the same time period, you will be assigned your most challenging task, **Task 3**. You should begin to do background reading to understand what is required here.
- In Week 8, you should present your work to date, the presentation should consist of:
  - The theoretical concepts you have learned in Tasks 1–2;
  - How you will apply these in Task 3.
- The final report (due towards the end of the trimester) will be based entirely on Task 3.

Time (h)	Cp (mg/L)
0.1	7.12
0.2	5.15
0.4	2.88
0.5	2.24
0.7	1.51
1	1.07
1.5	0.88
2	0.84
3	0.8
5	0.74
7	0.68
12	0.56

Table 1: Plasma concentration of a drug at various times after the administration of a 100-mg IV dose

1 The task

A $100 - \mathrm{mg}$ dose of a drug was administered intravenously. Plasma samples were taken at various times after the dose and analyzed for unchanged drug. The data are listed in Table 1. The data indicate that the drug follows two-compartment Pharmacokinetics. Using nonlinear least squares or otherwise, fit the model $Cp(t) = A\mathrm{e}^{-\alpha t} + B\mathrm{e}^{-\beta t}$ to the data and hence:

1. Determine the values of A, B, α, and β.
2. Determine the micro rate constants k_{10}, k_{12}, and k_{21}.
3. Determine the primary PK parameters: Cl, Cld, V_1, V_β, and Vd_{ss}. Take as given the formulae below.

$$\mathrm{Cl} = k_{10}V_1, \tag{1a}$$

$$\mathrm{Cld} = k_{12}V_1, \tag{1b}$$

$$V_\beta = \frac{S \cdot F \cdot D}{\beta \mathrm{AUC}}, \tag{1c}$$

$$Vd_{ss} = V_1\left(\frac{k_{12} + k_{21}}{k_{21}}\right). \tag{1d}$$