Optimal Sampling

Determining the ‘Best’ Time to Collect Samples
Objectives

• Understand the Idea of Optimal Sampling
• Understand the Graphical, Numerical and Analytical Methods of Determining Optimal Sampling Times
Why Optimal Sampling

- **Samples Scarce**
  - Needle stick - pain
  - Indwelling cannula - Patient sick
  - Blood loss

- **Assay**
  - Cost
  - Time required

- **With Limited Data we want the Best Estimates of Parameter Values**
Optimal Sampling

• Gives a Single Time per Parameter
  – Based on Known Model and Parameter Values
    e.g. \( k_{el} = 0.2 \text{ hr}^{-1} \) use \( t = 5 \text{ hr} \)
    [IV Bolus - One compartment]

• Use a Range of Parameter Values
  – When Values not Exact Use a Range of Sample Times -
    Choose Extreme of Range for More Points
    e.g. \( 0.1 \rightarrow 0.3 \text{ hr}^{-1} \) use \( t = 10 \text{ and 3.3 hr} \)
      as well as 5 hr
    [IV Bolus - One compartment]
Optimal Sampling

• How did I get the time values in the previous slide

• A number of approaches
  – Graphical
  – Analytical
  – Numerical
Graphical Approach

- One Compartment Model - IV Bolus

\[ Cp = \frac{Dose}{V} \cdot e^{-kel\cdot t} \]

- Time for Best Values for kel and V
Graphical Approach

• Simulate Data using Known Model and Model Parameters

• Adjust One Parameters (at a time) by a Small Amount (± 1, 5, 10%) in Both Directions

• Plot ($\Delta C_p / \Delta \text{Parameter}$) versus Time to Determine Time of Maximum Change, Maximum Sensitivity
Graphical Approach

Concentration versus Time

- Y-axis: Concentration (mg/L)
- X-axis: Time (hr)

The graph shows the concentration of a substance decreasing over time, following a exponential decay pattern.
Graphical Approach

Vary $k_e l$ (with Constant Value of $V$)
Graphical Approach

Vary $k_{el}$ (with Constant Value of $V$)

$\frac{dC_p}{dk_{el}}$

Time (hr)

$kel = 0.2 \text{ hr}^{-1}$
Graphical Approach

Vary V (with Constant Value of kel)
Graphical Approach

Vary V (with Constant Value of kel)

\[ V = 15 \text{ L} \]
Analytical Approach

- Differentiate $C_p$ versus Parameter, $P_i$, to Determine $dC_p/dP_i$
- Differentiate $dC_p/dP_i$ versus Time to Determine $d^2C_p/dt.P_i$
- Set $d^2C_p/dt.P_i$ equal to 0 to Find the Time for the Maximum Value of $dC_p/dP_i$
- Solve for Time
Analytical Approach

One Compartment - IV Bolus Dose

\[ Cp = \frac{Dose}{V} \cdot e^{-kel \cdot t} \]

\[ \frac{dCp}{dkel} = - \frac{t \cdot Dose}{V} \cdot e^{-kel \cdot t} \]

\[ \frac{d^2Cp}{dkel \cdot dt} = (t \cdot kel - 1) \cdot \frac{Dose}{kel} \cdot e^{-kel \cdot t} = 0 \]

\[ t = \frac{1}{kel} = \frac{1}{0.2} = 5 \text{ hr} \]
Analytical Approach

One Compartment - IV Bolus Dose

\[ Cp = \frac{Dose}{V} \cdot e^{-kel\cdot t} \]

\[ \frac{dCp}{dV} = - \frac{Dose}{V^2} \cdot e^{-kel\cdot t} \]

\[ \frac{d^2Cp}{dV \cdot dt} = \frac{Dose}{V^2 \cdot kel} \cdot e^{-kel\cdot t} = 0 \]

\[ t \Rightarrow -\infty \ hr \]

Practical Limit \( t = 0 \)
Numerical Approach

• Use ADAPT II, Sample Module
  – Define the Model
  – Enter the Parameter Values
  – Review Output
Optimal Sampling for Model Selection

- Use the Program DESIGN
- Define both Models
- Run the Program
- Output Gives the Best Time to Distinguish Between Models
DESIGN

• Output Plot
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