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. kel = 0.2 hr^{-1} use t = 5 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. kel = 0.1 — 0.3 hr^{-1} use t = 10 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

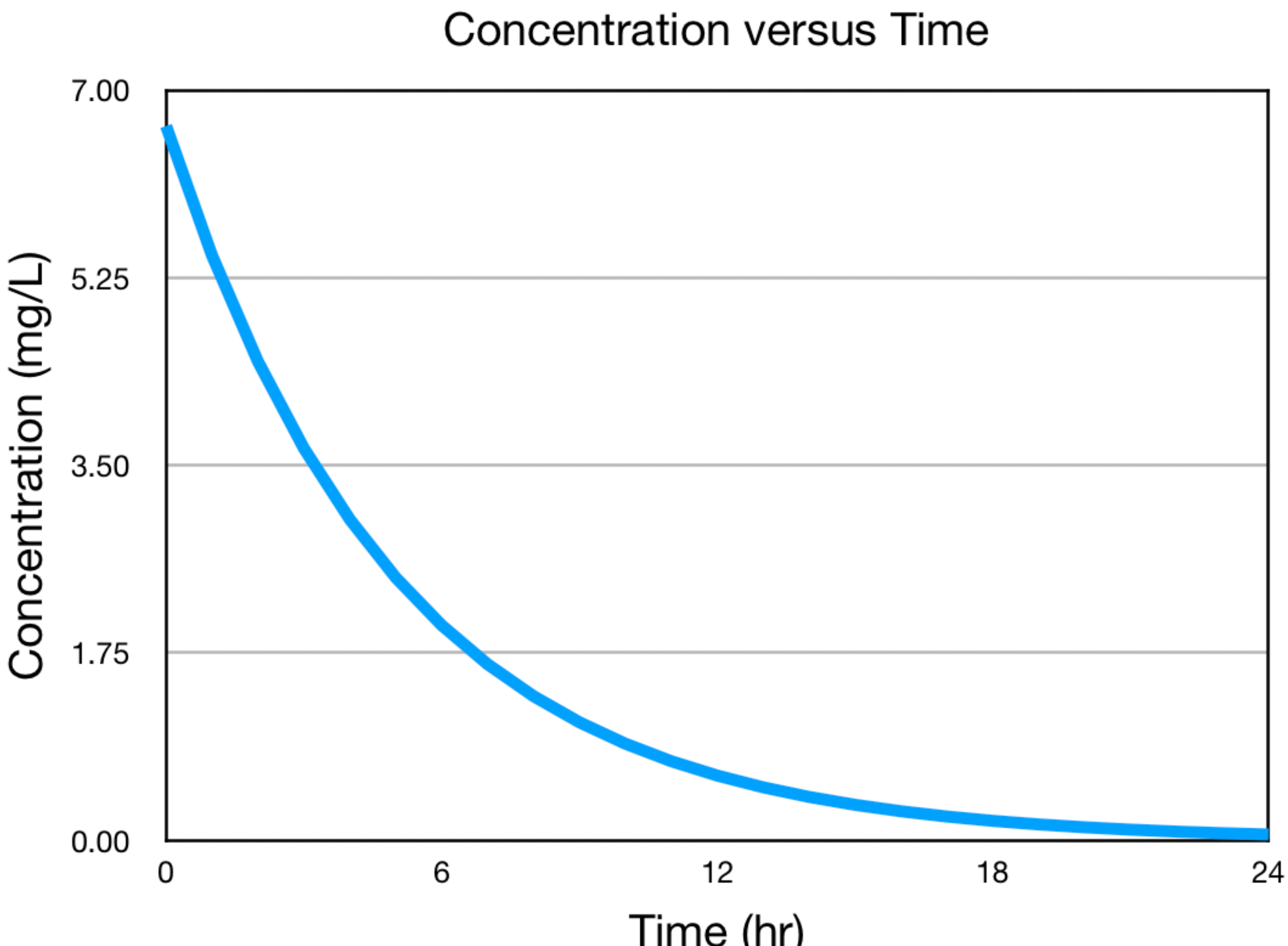
$$Cp = \frac{Dose}{V} \bullet e^{-kel \bullet t}$$

- Time for Best Values for kel and V

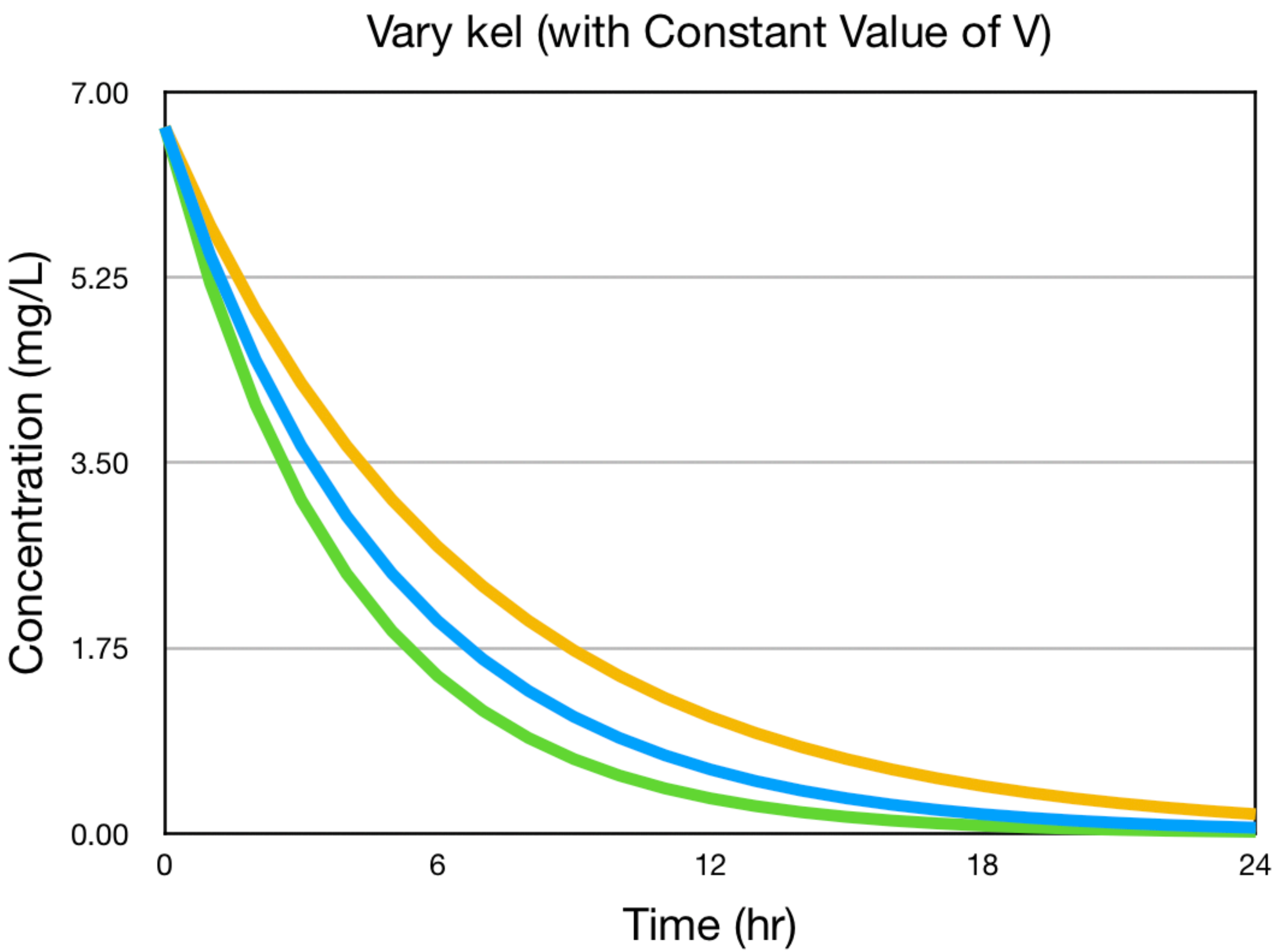
Graphical Approach

- 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 (ΔCp/ΔParameter) versus Time to Determine Time of Maximum Change, Maximum Sensitivity

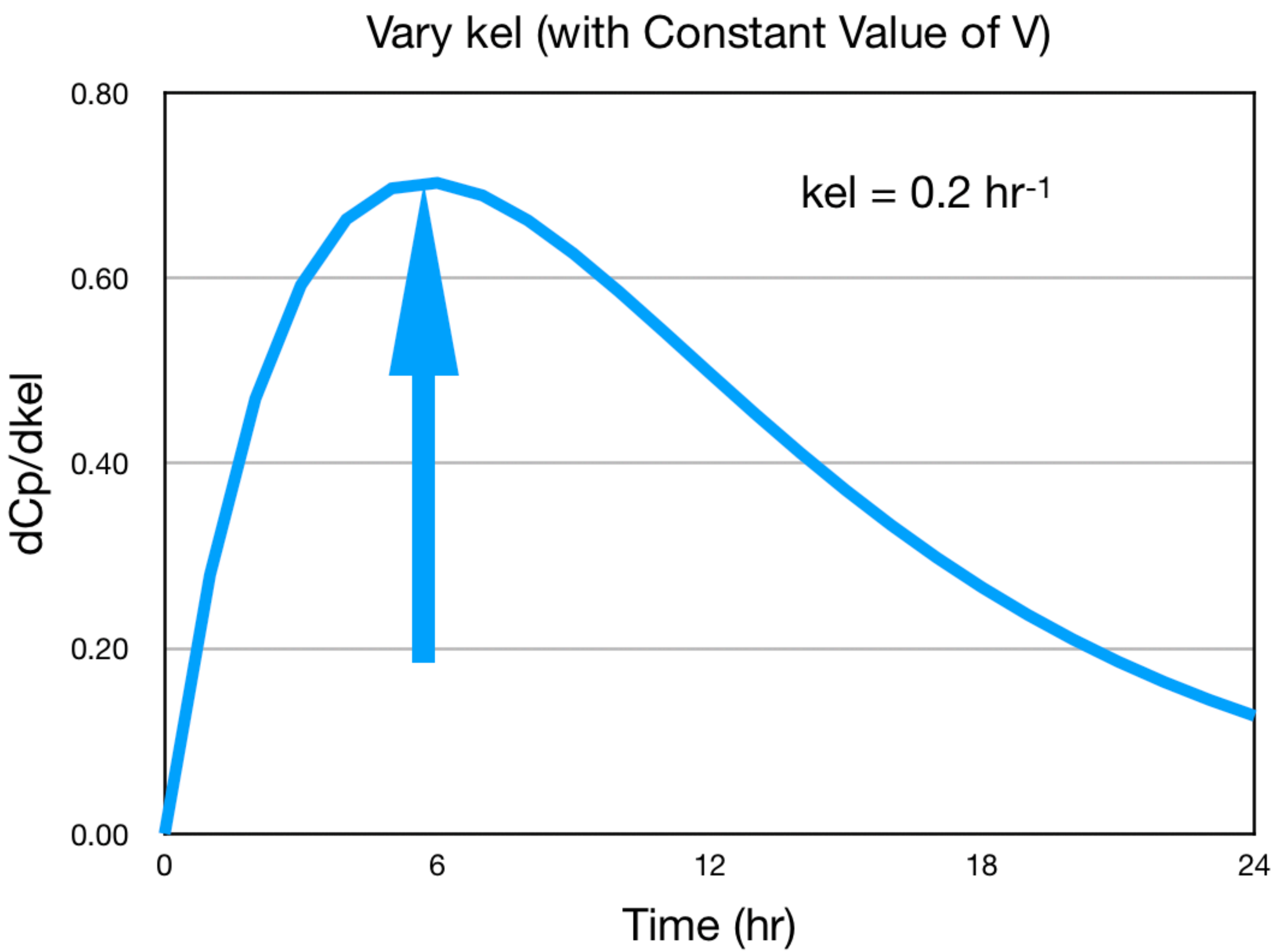
Graphical Approach



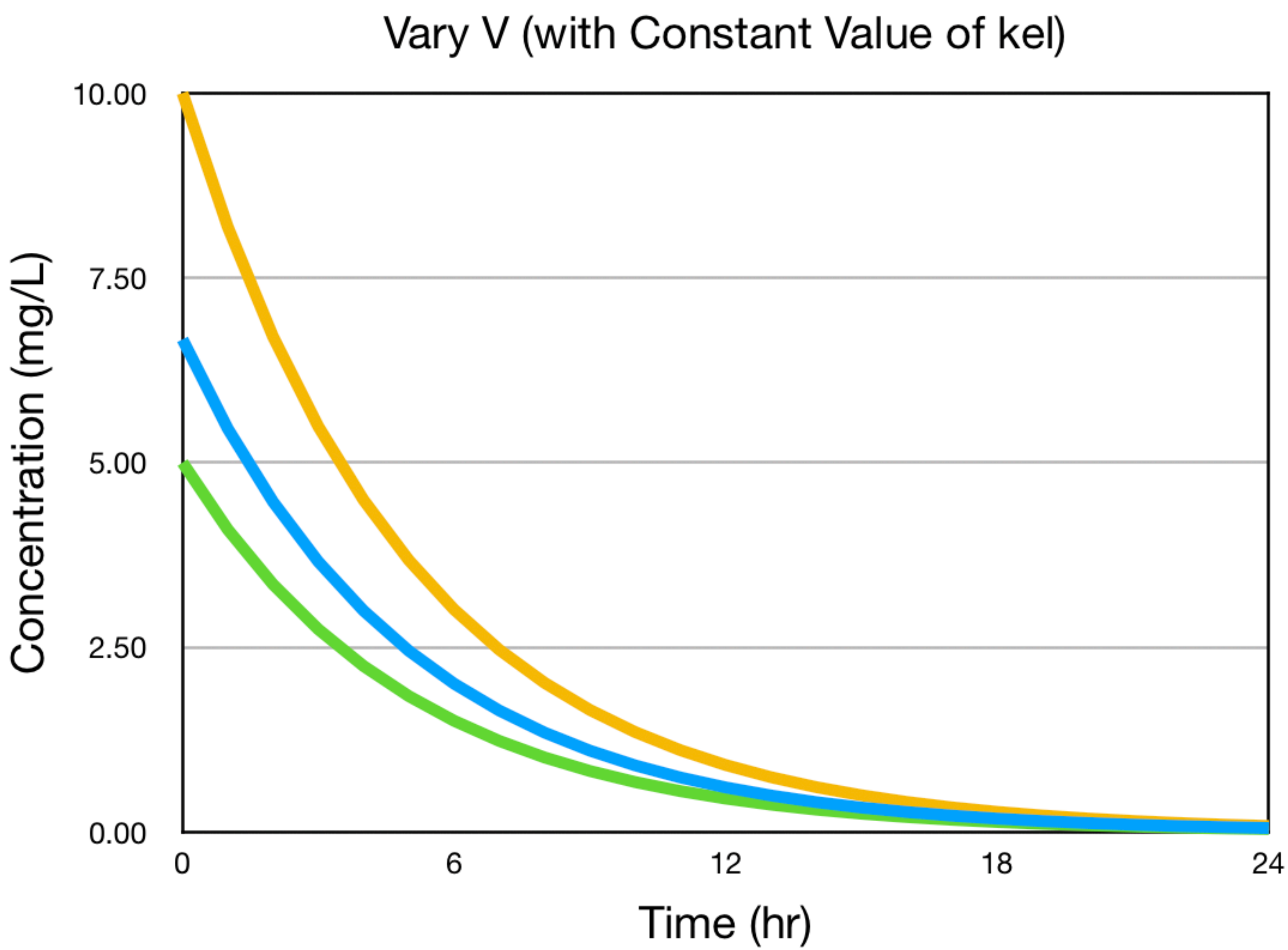
Graphical Approach



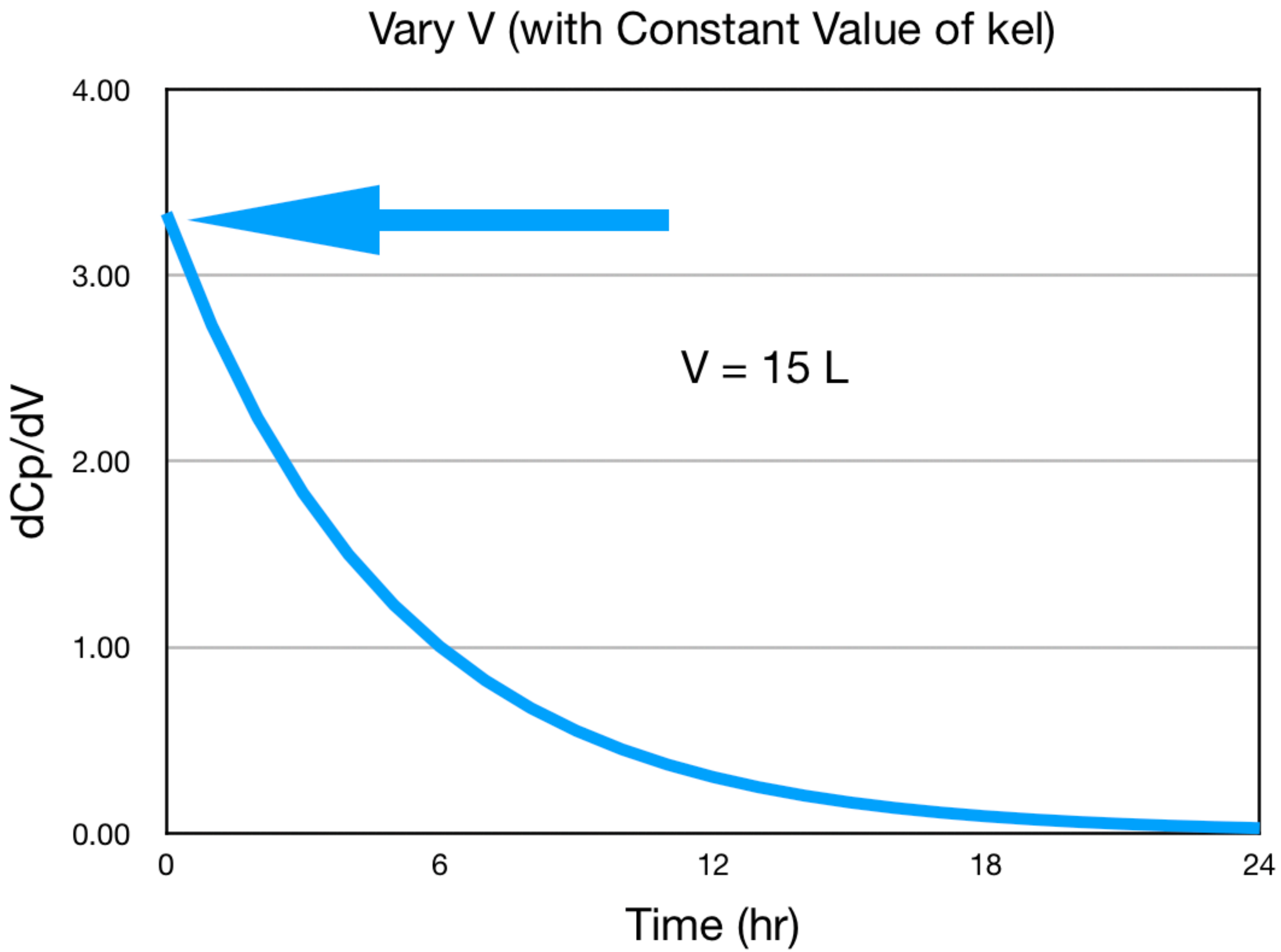
Graphical Approach



Graphical Approach



Graphical Approach



Analytical Approach

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

Analytical Approach

One Compartment - IV Bolus Dose

$$Cp = \frac{Dose}{V} \bullet e^{-kel \bullet t}$$

$$\frac{dCp}{dkel} = -\frac{t \bullet Dose}{V} \bullet e^{-kel \bullet t}$$

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

$$t = \frac{1}{kel} = \frac{1}{0.2} = 5\ hr$$

Analytical Approach

One Compartment - IV Bolus Dose

$$Cp = \frac{Dose}{V} \bullet e^{-kel \bullet t}$$

$$\frac{dCp}{dV} = -\frac{Dose}{V^2} \bullet e^{-kel \bullet t}$$

$$\frac{d^2Cp}{dV \bullet dt} = \frac{Dose}{V^2 \bullet kel} \bullet e^{-kel \bullet t} = 0$$

$$t \Rightarrow -\infty \ hr$$

Practical Limit t = 0

Numerical Approach

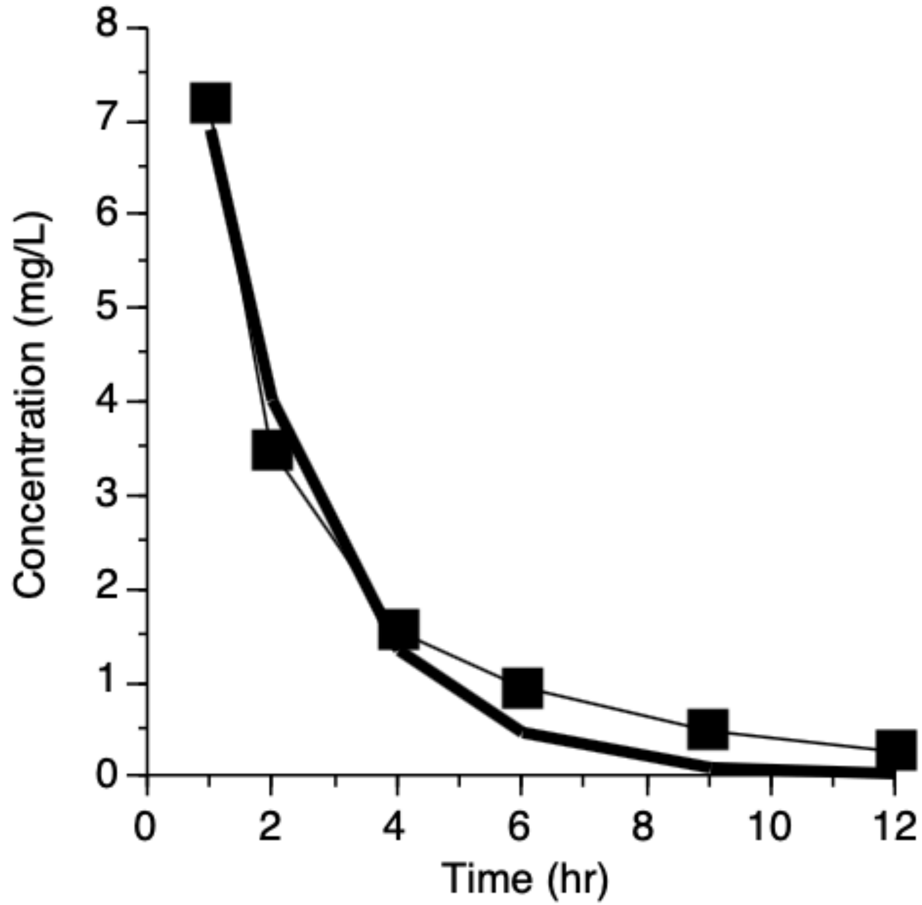
- Use ADAPT II, Sample Module
  - Define the Model
  - Enter the Parameter Values
  - Review Output

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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