Compartmental PK Models

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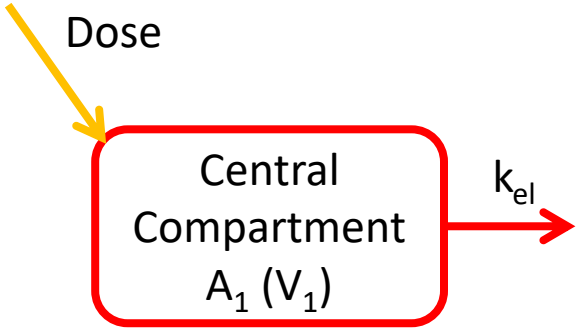
Combining differential equations into PK models

Now that we know the building blocks (differential equations), we can combine them into more complex models.

In this lecture we will see some examples of compartmental PK models.

1 compartment - IV

1-compartment disposition model with IV administration



$$\frac{dA_1}{dt} = -k_{el} \cdot A_1$$

First-order process

$$A_1(0) = Dose$$

$$k_{el} = \frac{CL}{V_1}$$

$$C = \frac{A_1}{V_1}$$

The dose is injected as an instantaneous bolus into the central compartment (A_1).

The amount of drug in the central compartment disappears with a first-order process (exponential decrease) with rate constant k_{el}

The "observed" drug concentration is the amount in compartment 1 divided by the volume

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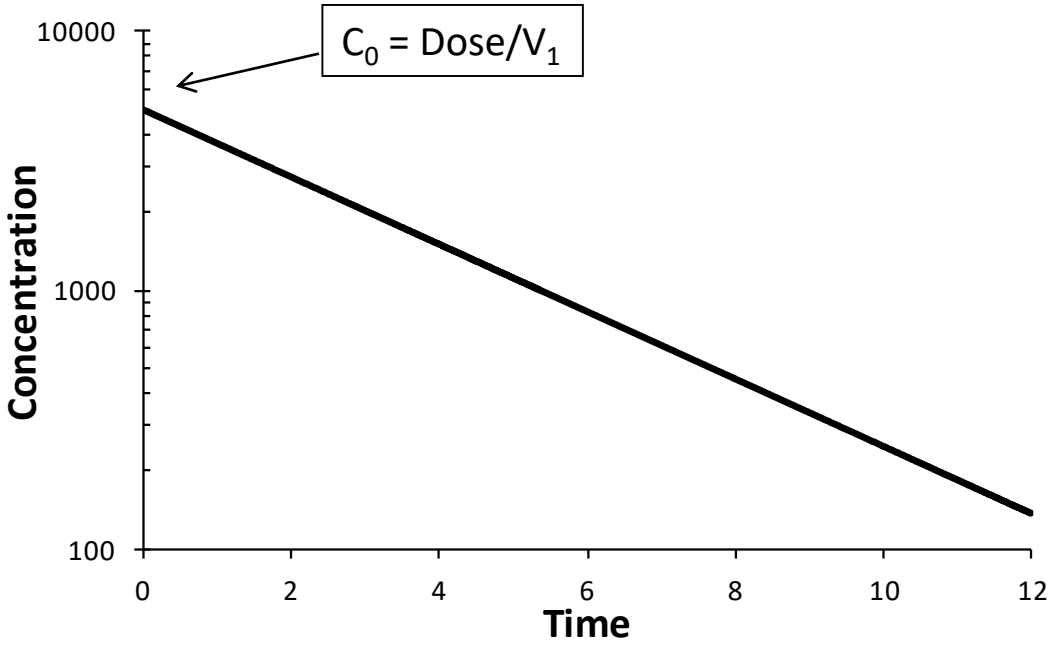
1 compartment - IV

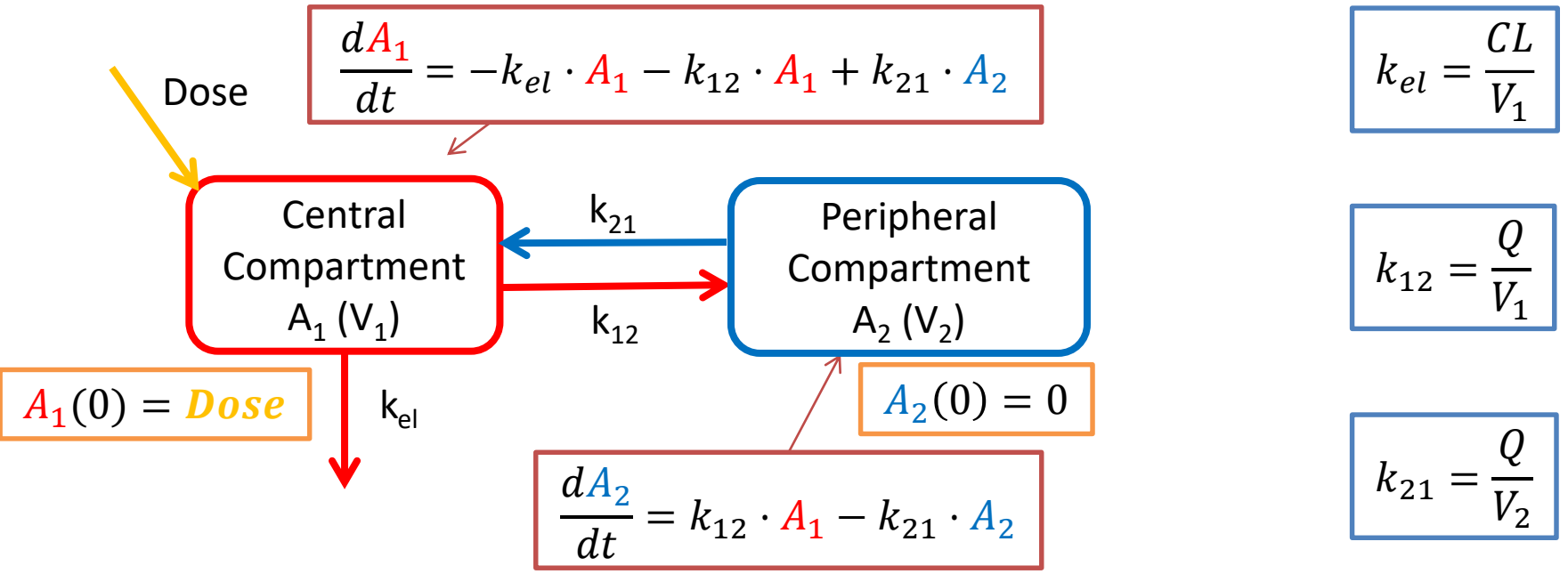
When plotted on a semi-log chart, the concentration declines like a straight line with slope $-k_{el}$



Slide courtesy of Joel Tarning

2 compartment - IV

2-compartment disposition model with IV administration

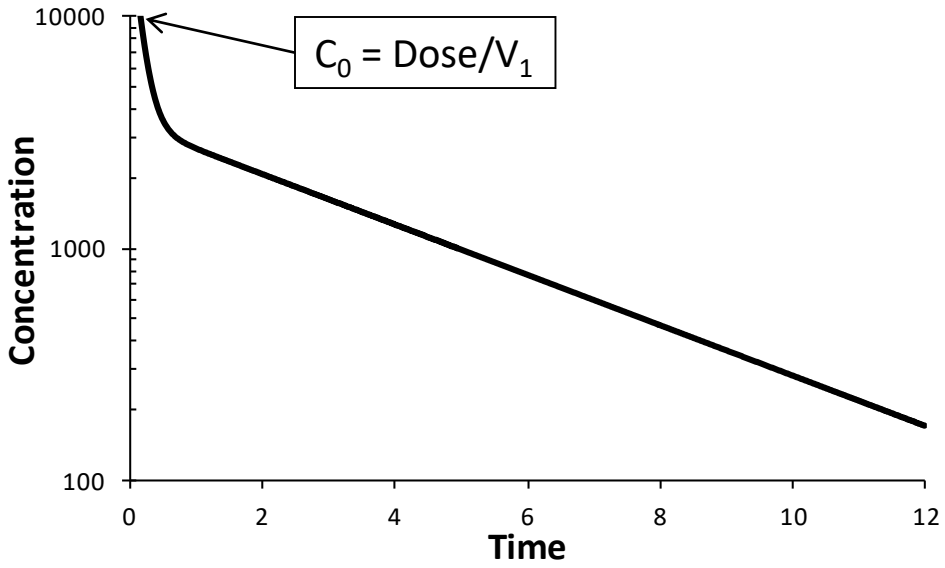


As with the 1 compartment model, the dose is injected as an instantaneous bolus into the central compartment (A_1), from where it is eliminated with rate k_{el}

A peripheral compartment (A_2) is appended to the central compartment and it fills up or empties based on the difference in concentration.

2 compartment - IV

When plotted on a semi-log scale, the concentration in the central compartment declines in a bi-phasic fashion (bi-exponential).

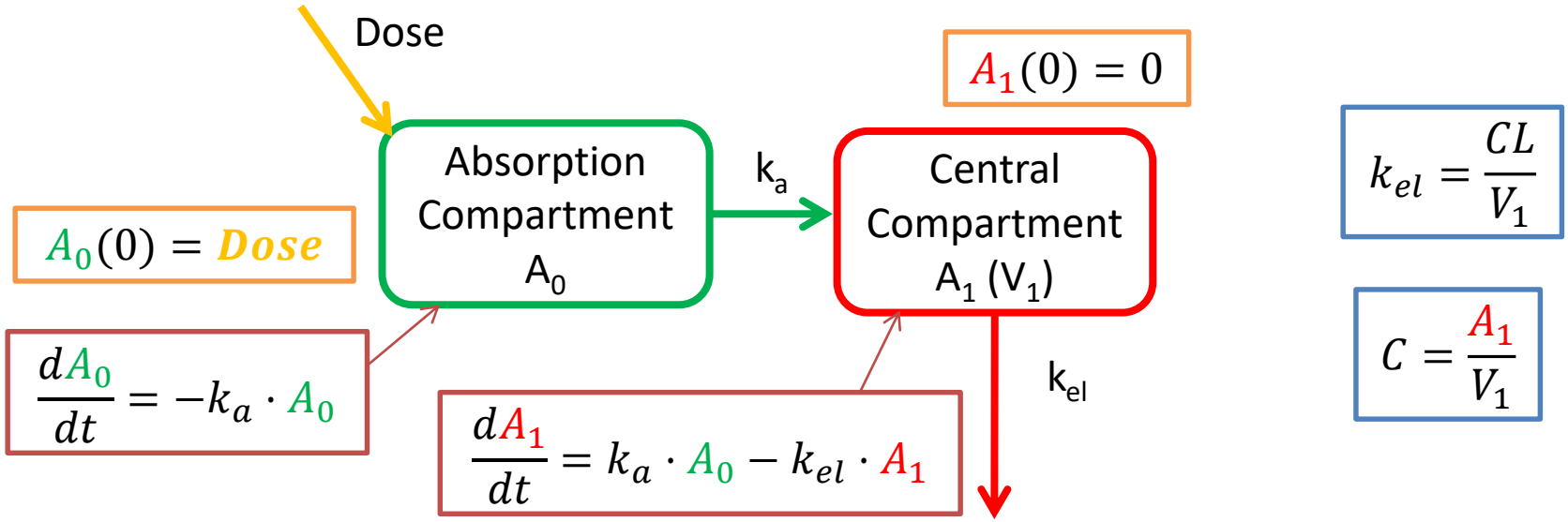


During the rapid disappearance phase (called alpha), the drug is both being eliminated and distributed into the peripheral compartment.

The second, slower phase (called beta) starts once the concentration in the two compartments is in equilibrium, so that the drug is still eliminated from the central compartment, but it then feeds back from the peripheral, which acts as a resevoir

1 compartment - oral

1-compartment disposition model with oral absorption

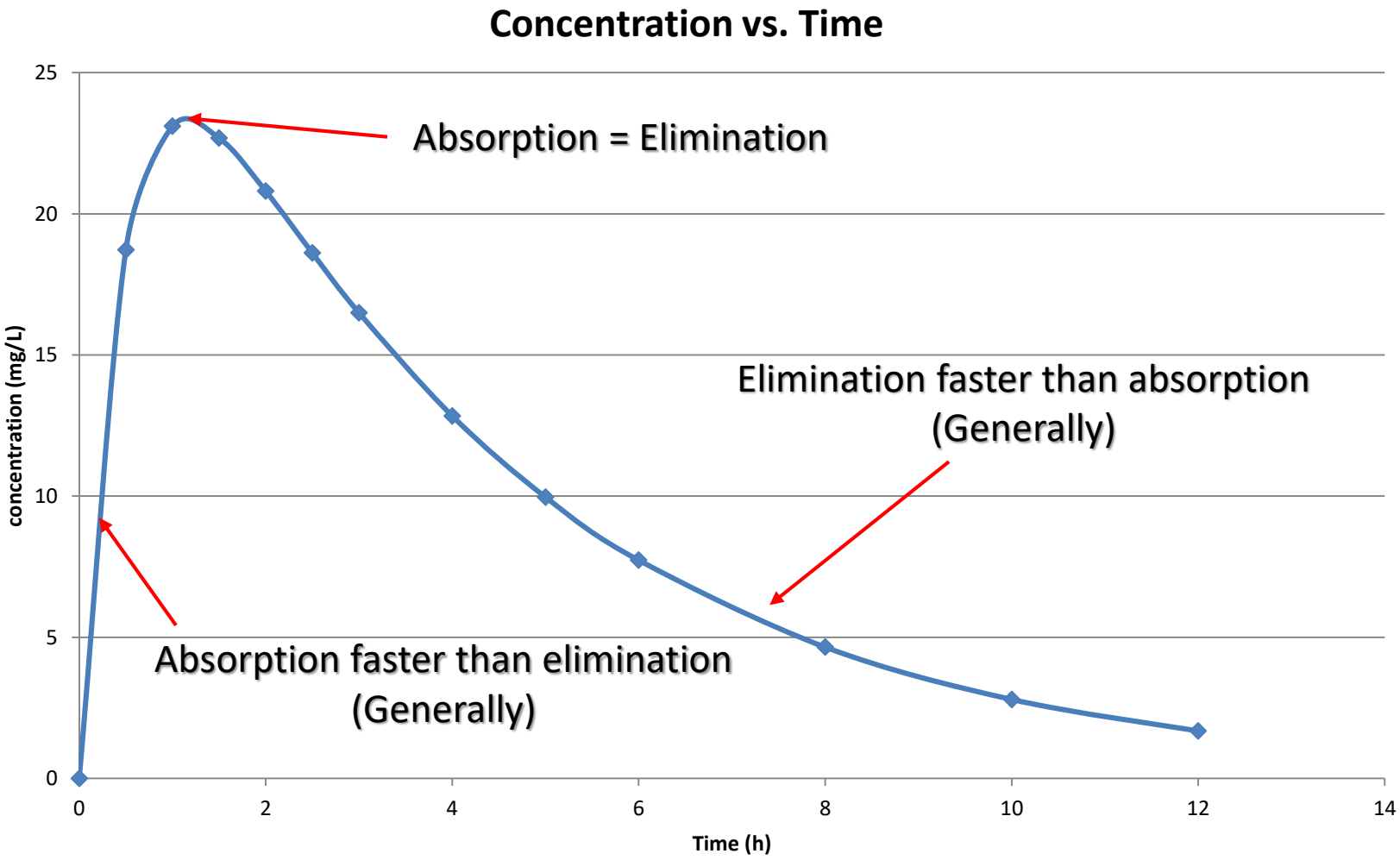


The dose is put in the absorption compartment (A_0), and it then gets absorbed with a first-order process k_a into the central compartment (A_1).

The absorbed amount of drug in the central compartment disappears with a first-order process (exponential decrease) with rate constant k_{el}

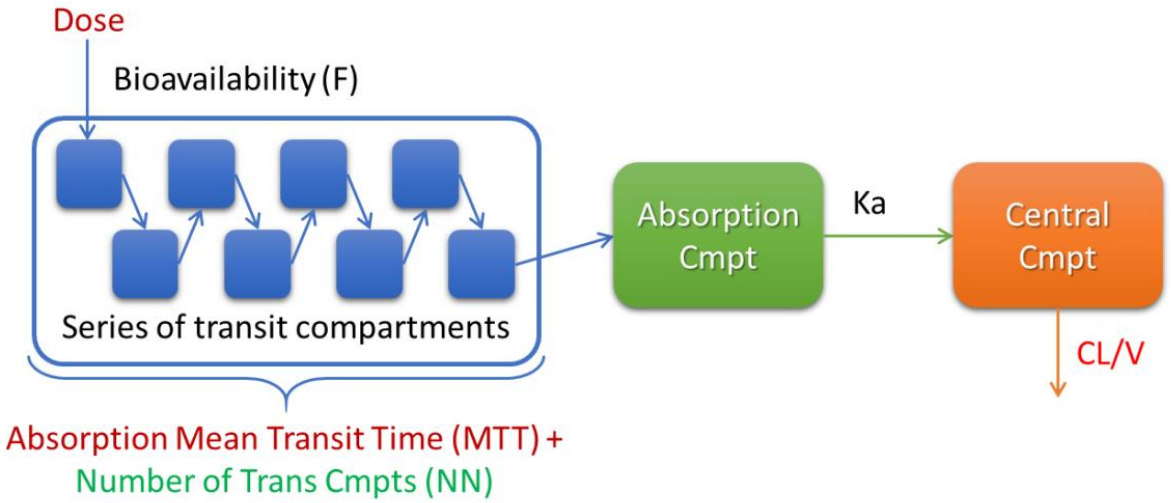
Slide courtesy of Joel Tarning

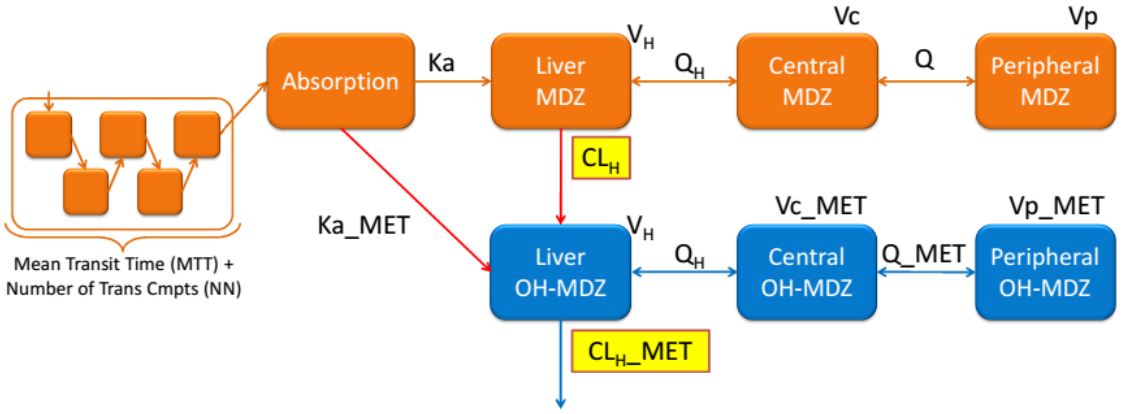
1 compartment - oral



More complex models

Absorption through transit compartments





Parent + metabolite with hepatic extraction