Drug’s with a lower clearance persist for a longer time in the body. Drug’s with a higher clearance persist for a shorter time in the body. The longer a drug resides in the body, then the greater the exposure a patient has to a drug. A measure of drug exposure is the **area under curve (AUC)**. The units on AUC are a very non-intuitive concentration-time. (As with any area, the units are simply the units for the x-axis multiplied by the units of the y-axis.) For this discussion, concentration is specifically mass/vol and not molarity. Molarity is convenient for the coverage of in vitro results and binding studies, but pharmacokinetic data originate from living systems – either animals or humans. $C_p$ data in animals and humans are normally in mass/vol. AUC and clearance are intimately related. In fact, it is through AUC that clearance can be calculated. So, how can one determine AUC for a drug?

AUC can be determined in two ways. Method one involves integrating the $C_p$-time plot of a drug. An idealized $C_p$-time plot for an IV bolus is shown below. The AUC for this plot, when evaluated from $t=0$ to $t=\infty$, is $C_p^0/k_{el}$. Of course, one would first need to know both $C_p^0$ and $k_{el}$. These values could be determined from a ln $C_p$-time plot from the same data.

\[
AUC = \frac{C_p^0}{k_{el}}
\]

Method two for determining AUC for a drug is to crudely estimate the value with the trusty trapezoid rule. Each data point defines a trapezoid shaped region in the curve. The sum of the areas created by each data point gives an approximate AUC. While crude, this method is fairly effective and simple. Because $C_p$-time data points do not stretch to infinity, one needs a method to estimate the AUC from the last $C_p$ data point to infinite time. The remaining area can be estimated as the value of the final $C_p$ point divided by the $k_{el}$ value of the drug.
Regardless of how \( AUC \) is estimated, dividing the amount of drug that the animal or human was dosed by \( AUC \) gives \( CL \). This calculation is the most common method for determining \( CL \) for a drug.

\[
CL = \frac{D_o}{AUC}
\]

Note the units on \( CL \). If dose is a drug mass and \( AUC \) uses mass instead of moles, then the mass units cancel and \( CL \) comes out with the correct units of volume/time.

\[
\frac{\text{volume}}{\text{time}} = \frac{\text{mass}}{\text{mass} \times \text{time}} = \frac{1}{\text{volume}}
\]