The double-reciprocal (Lineweaver-Burk) plot allows easy calculation of $K_m$ and $V_{\text{max}}$.
Many factors influence the activity of an enzyme

- pH
- Temperature
- Concentration of molecules that bind to enzyme
  - Substrate
  - Reversible inhibitors
  - Irreversible inhibitors (inactivators)
  - Allosteric effectors
- Covalent modification
- Enzyme concentration
Enzymes show maximum activity at their pH optimum
Enzymes can be inhibited by substrate analogs

**Succinate**

\[
\text{COO}^- \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{COO}^- \quad \text{succinate dehydrogenase} \quad \text{C} \quad \text{C} \quad \text{H} \quad \text{COO}^- \quad \text{Fumarate}
\]

**Malonate**

\[
\text{COO}^- \quad \text{CH}_2 \quad \text{COO}^- \quad \text{succinate dehydrogenase} \quad \text{NO REACTION}
\]
Enzymes are greatly inhibited by transition-state analogs

**Adenosine deaminase**

\[ K_m = 3 \times 10^{-5} \]

\[ \text{Adenosine} \rightarrow \text{Ribose} \]

\[ \text{Ribose} + \text{H}_2\text{O} \rightarrow \text{Ribose} + \text{H}_2\text{N} - \text{OH} \]

\[ \text{Ribose} + \text{NH}_3 \rightarrow \text{Ribose} + \text{H}_2\text{N} - \text{C} - \text{N}_2 \]

**Product inhibition:**

\[ K_i = 3 \times 10^{-4} \]

**TS analog:**

\[ K_i = 1.5 \times 10^{-13} \]
Competitive inhibition

\[ E + S \overset{K_i}{\rightleftharpoons} ES \rightarrow E + P \]

\[ EI \leftrightarrow I \]

\[ K_i \]

Figure 6-15a
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Uncompetitive inhibition

\[ E + S \rightleftharpoons ES \rightarrow E + P \]

+ 

\[ \text{I} \]

\[ K_i' \]

ESI

\[ S \]

\[ E + IS\]
Mixed inhibition

\[ E + S \rightleftharpoons ES \rightarrow E + P \]
\[ E + I \rightleftharpoons EI \]
\[ EI + S \rightleftharpoons ESI \]

\[ K_1 \]
\[ K'_1 \]
Competitive inhibition

E + S ⇌ ES → E + P

+ I ⇌ Kᵢ

EI

Figure 6-15a
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\[ \alpha \] is the factor by which \([S]\) must be increased to overcome the presence of inhibitor.
The graph shows the relationship between $1/v_o$ and $1/[S]$ with varying concentrations of inhibitor $[I]$. The slope of the lines is given by $\alpha K_M/V_{max}$, and the equation for $\alpha$ is

$$\alpha = 1 + \frac{[I]}{K_i}$$

where $K_M$ is the Michaelis constant and $V_{max}$ is the maximum velocity. The lines represent different values of $\alpha$: $\alpha = 1$ (no inhibitor), $\alpha = 2$, and $\alpha = 4$. The point $1/V_{max}$ is marked on the y-axis, and $-1/\alpha K_M$ is marked on the x-axis.
Uncompetitive inhibition

\[ E + S \overset{K_i'}{\rightleftharpoons} ES \rightarrow E + P \]

Figure 6-15b
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Mixed inhibition

\[ E + S \rightleftharpoons ES \rightarrow E + P \]

\[ EI + S \rightleftharpoons ESI \]

\[ K_1 \]

\[ K'_1 \]

\[ \text{Figure 6-15c} \]
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Increasing 
[\text{I}]

\[
\alpha = 2.0 \\
\alpha' = 1.5 \\
\alpha = 1.5 \\
\alpha' = 1.25 \\
\alpha = \alpha' = 1 \text{ (no inhibitor)}
\]

\[
\frac{1 - \alpha'}{(\alpha - 1) K_M} + \frac{\alpha - \alpha'}{(\alpha - 1)V_{\text{max}}} \\
- \frac{\alpha'}{\alpha K_M}
\]

Slope = \( \frac{\alpha K_M}{V_{\text{max}}} \)

\[
\alpha = 1 + \frac{[\text{I}]}{K_i} \\
\alpha' = 1 + \frac{[\text{I}]}{K_{i}'}
\]
<table>
<thead>
<tr>
<th>Inhibitor type</th>
<th>Apparent $V_{\text{max}}$</th>
<th>Apparent $K_m$</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>$V_{\text{max}}$</td>
<td>$K_m$</td>
</tr>
<tr>
<td>Competitive</td>
<td>$V_{\text{max}}$</td>
<td>$\alpha K_m$</td>
</tr>
<tr>
<td>Uncompetitive</td>
<td>$V_{\text{max}}/\alpha'$</td>
<td>$K_m/\alpha'$</td>
</tr>
<tr>
<td>Mixed</td>
<td>$V_{\text{max}}/\alpha'$</td>
<td>$\alpha K_m/\alpha'$</td>
</tr>
</tbody>
</table>

Table 6-9
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<table>
<thead>
<tr>
<th>Type of Inhibition</th>
<th>Michaelis–Menten Equation</th>
<th>Lineweaver–Burk Equation</th>
<th>Effect of Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>$v_o = \frac{V_{\text{max}}[S]}{K_M + [S]}$</td>
<td>$\frac{1}{v_o} = \frac{K_M}{V_{\text{max}}}[S] + \frac{1}{V_{\text{max}}}$</td>
<td>None</td>
</tr>
<tr>
<td>Competitive</td>
<td>$v_o = \frac{V_{\text{max}}[S]}{\alpha K_M + [S]}$</td>
<td>$\frac{1}{v_o} = \frac{\alpha K_M}{V_{\text{max}}}[S] + \frac{1}{V_{\text{max}}}$</td>
<td>Increases $K_M^{\text{app}}$</td>
</tr>
<tr>
<td>Uncompetitive</td>
<td>$v_o = \frac{V_{\text{max}}[S]}{K_M + \alpha'[S]} = \frac{(V_{\text{max}}/\alpha') [S]}{K_M/\alpha' + [S]}$</td>
<td>$\frac{1}{v_o} = \frac{K_M}{V_{\text{max}}}[S] + \frac{\alpha'}{V_{\text{max}}}$</td>
<td>Decreases $K_M^{\text{app}}$ and $V_{\text{max}}^{\text{app}}$</td>
</tr>
<tr>
<td>Mixed (noncompetitive)</td>
<td>$v_o = \frac{V_{\text{max}}[S]}{\alpha K_M + \alpha'[S]} = \frac{(V_{\text{max}}/\alpha') [S]}{(\alpha/\alpha') K_M + [S]}$</td>
<td>$\frac{1}{v_o} = \frac{\alpha K_M}{V_{\text{max}}}[S] + \frac{\alpha'}{V_{\text{max}}}$</td>
<td>Decreases $V_{\text{max}}^{\text{app}}$; may increase or decrease $K_M^{\text{app}}$</td>
</tr>
</tbody>
</table>

$\alpha = 1 + \frac{[I]}{K_i}$ and $\alpha' = 1 + \frac{[I]}{K_i'}$