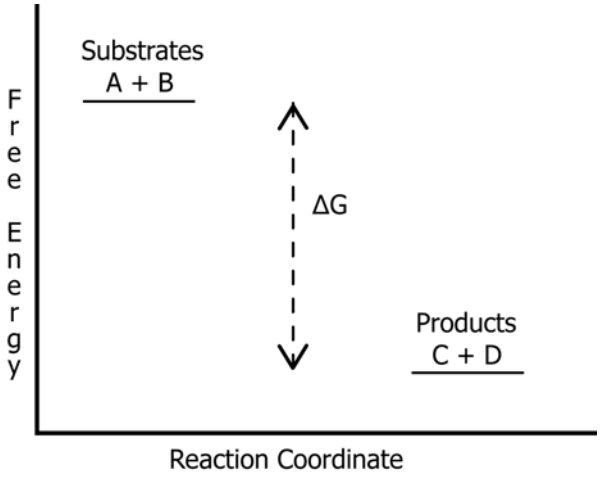
5.60 for 7.05 in a Nutshell

Thermodynamics of Reactions

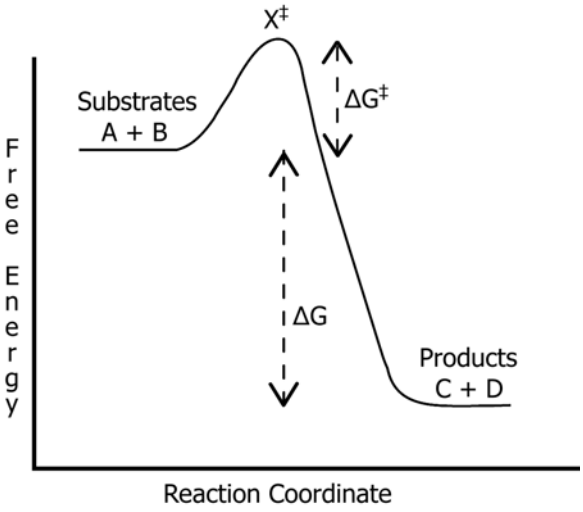
$$\mathbf{A + B \rightleftharpoons C + D}$$



ΔG defines if a reaction will be spontaneous, non-spontaneous, or in equilibrium
G ≡ Gibbs Free Energy (Top graph)
$\Delta G = G_{products} - G_{substates}$

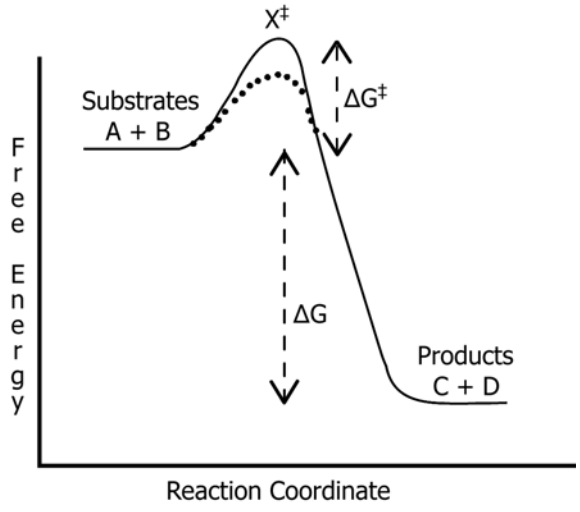
ΔG > 0	➜	Non-spontaneous Reaction
ΔG = 0	➜	Reaction in Equilibrium
ΔG < 0	➜	Spontaneous Reaction

ΔG° ≡ "standard free energy change" at T=25 °C (298 K), P= 1 atm, and concentration of both substrates and products of 1M
ΔG°' ≡ "standard free energy change" as above but, in addition, at pH = 7



R ≡ ideal gas constant
T needs to be in degrees Kelvin
$\Delta G = \Delta G° + RT \ln ([C][D]/[A][B])$
$K_{eq} \equiv ([C][D]/[A][B])$
Therefore $\Delta G = \Delta G° + RT \ln (K_{eq})$

At equilibrium, ΔG = 0
Therefore $0 = \Delta G° + RT \ln (K_{eq})$
Therefore $\Delta G° = -RT \ln (K_{eq})$ and $K_{eq} = e^{-\Delta G°/RT}$



Activation Energy
As the reaction traverses from the substrates to the products, the value of G does not just decrease. Note that the highest free energy point is considered the transition state $X^{‡}$, defined as an "activated complex" in which bonds are both breaking & forming. To move from the substrates to $X^{‡}$, energy must be added; this is the "activation energy" of the reaction, quantified as $\Delta G^{‡}$ (middle graph). Enzymes reduce the amount of activation energy needed, $\Delta G^{‡}$ (bottom graph). The solid line in the dotted graph shows the energy needed without an enzyme; the dotted line shows the energy needed with an enzyme. **Note that the total ΔG does not change with an**

enzyme!

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Transition State, $X^{\ddagger}$ - "Activated Complex" in which bonds are both breaking & forming

$$A + B \overset{k_1}{\rightleftharpoons} X^{\ddagger} \overset{k'}{\rightarrow} P$$ where rate of change of product is $dP/dt = k_1[A][B] = k'[X^{\ddagger}]$

Assumption 1: Equilibrium is reached quickly for $A + B \rightleftharpoons X^{\ddagger}$
Therefore $K_{eq}^{\ddagger} = [X^{\ddagger}]/[A][B]$ or, rewritten, $[X^{\ddagger}] = [A][B]K_{eq}^{\ddagger}$
Going back to the thermo...
$\Delta G^{\ddagger} = -RT \ln (K_{eq}^{\ddagger})$ which, using algebra, becomes $K_{eq}^{\ddagger} = e^{-\Delta G^{\ddagger}/RT}$
Recall that $dP/dt = k'[X^{\ddagger}]$ and, plugging in for $[X^{\ddagger}]$ from above ...
$dP/dt = k'[A][B]K_{eq}^{\ddagger}$ and, plugging in $K_{eq}^{\ddagger}$ from above...
$dP/dt = k'[A][B]e^{-\Delta G^{\ddagger}/RT}$

Assumption 2: $X^{\ddagger}$ is very unstable and falls apart with the first molecular vibration
Now playing with physics a bit to find k'...
$k' = K\nu$ where $\nu \equiv$ frequency of bond vibration
and $K \equiv$ transmission coefficient (between 0.5 and 1.0)
We need to find ν. To do so, use Planck's Law...
$E = h\nu = k_b T$ where h = Planck's constant
k_b is Boltzmann's constant
and E is energy of a photon
$\nu = k_b T/h$
Since $X^{\ddagger}$ is falls apart with the first molecular vibration, $k' = \nu$
$k' = k_b T/h$

Recall that $dP/dt = k'[A][B]e^{-\Delta G^{\ddagger}/RT}$ so substitution gives
$dP/dt = (k_b T/h)[A][B]e^{-\Delta G^{\ddagger}/RT}$

The **take home message**, from the above equation:
To speed up a reaction, either the temperature must increase, or $\Delta G^{\ddagger}$ must decrease

Note: k' is so fast relative to k_1 that it can essentially be neglected when desired.
Therefore, in essence, the reaction becomes
$$A + B \overset{k_1}{\rightleftharpoons} P$$
Therefore $dP/dt = k_1[A][B]$
If we then reconsider the $X^{\ddagger}$ and recall that $dP/dt = k'[A][B]e^{-\Delta G^{\ddagger}/RT}$ then
$k_1 = k'e^{-\Delta G^{\ddagger}/RT}$

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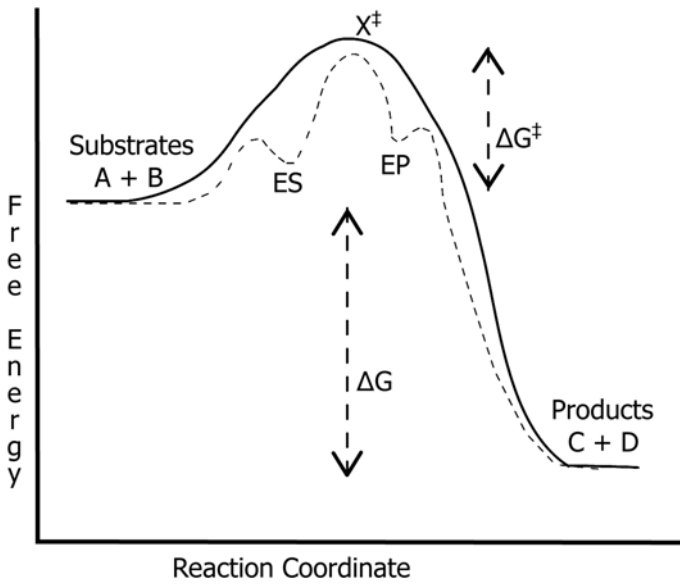
A typical enzyme mechanism for only one product is given by the following equation, where E is the enzyme, S is the substrate, and P is the product:

$$\mathbf{E + S \rightleftharpoons ES \rightleftharpoons EP \rightleftharpoons E + P}$$

The enzyme first forms a complex with the substrate, catalyzes the change in the substrate to the product while still in complex, then separates from the product.

Looking closely at the free energy vs. reaction coordinate graph, there is the uncatalyzed reaction in the solid line, and the catalyzed reaction in the dotted line. There is only one $X^{\ddagger}$ in the uncatalyzed reaction, whereas there are two transition states in the catalyzed reaction: one before ES and one before EP. Note the relative energy wells once either ES or EP have formed.



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Michaelis-Menton Model - Holds for many but not all enzymes. Use reaction:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} E + P$$

Three assumptions:
1. Reaction is monomolecular
2. At early times, [P] is low so can ignore k_{-2}
3. [S] >> [E]

Definition of terms:
$[E]_T \equiv$ concentration of total enzyme
$[E] \equiv$ concentration of free enzyme
$[ES] \equiv$ concentration of enzyme-substrate complex
$[S] \equiv$ concentration of free substrate

Rate of formation of ES = $k_1[E][S]$
Rate of disappearance of ES = $k_{-1}[ES] + k_2[ES]$
At steady state, formation of ES = disappearance of ES, so
$k_1[E][S] = k_{-1}[ES] + k_2[ES]$ which can be rewritten as
$[E][S]/[ES] = (k\text{-}1 + k2)/k1 \equiv K_M$ called the Michaelis Constant

Since $[E] = [E]_T - [ES]$, plug into above equation and get
$K_M = (([E]_T - [ES])[S])/[ES]$ multiply through by [ES] to get
$K_M[ES] = [E]_T[S] - [ES][S]$ do arithmetic to get
$K_M[ES] + [ES][S] = [E]_T[S]$ do algebra to get
$[ES] = ([E]_T[S])/(K_M + [S])$

We know $V_0 \equiv k_2[ES]$ plug into above equation to get
$V_0 \equiv k_2[ES] = k_2([E]_T[S])/(K_M + [S])$
We also know $V_{max} = k_2[E]_T$ which can be rewritten as $k_2 = V_{max}[E]_T$ so plug in to above
$V_0 = V_{max}[S]/(K_M + [S])$ Michaelis-Menten Equation

Look at following situations:
$[S] << K_M$ then $V_0 = V_{max}[S]/K_M$
$[S] >> K_M$ then $V_0 = V_{max}$
$[S] = K_M$ then $V_0 = V_{max}/2$ **Define K_M as the conc. of substrate where $V_0 = ½ V_{max}$**

Define fraction of filled sites on enzyme as $f \equiv [S]/([S] + K_M)$ (Just accept this!)

Define $k_{cat} \equiv k_2 = V_{max}/[E]_T$ = "turnover number" also...
k_{cat} = # of substrate molecules that go to product / # of enzyme molecules
$1/k_{cat}$ = time for one reaction to occur