2BrNO $\rightarrow$ 2NO + Br$_2$

Molecules must collide
Collision must occur at the favorable arrangement (steric effects)
Molecules should carry $E > E_a$
Arrhenius equation:

\[ k(T) = Ae^{\frac{E_a}{RT}} \]

- **A**: preexponential factor ~ collision frequency x fraction of collisions that are effective due to steric effects, etc.
- **\( E_a \) (Joule/mol)**: activation energy needed to surmount a barrier from reactants to products
- **R=8.314 Joule/(mol*K)**: the gas constant
- **T (K)**: temperature
\[ k(T) = Ae^{\frac{-E_a}{RT}} \]

\[ \ln k = \ln A - \frac{E_a}{RT} \]

straight line: \( \ln(k) \) vs \( 1/T \)
- slope = \( \frac{E_a}{R} \)
- intercept = \( \ln A \)
The rate constant for a first-order rxn with an activation energy \( E_a = 123 \text{ kJ/mol} \) at 311 K is \( k(311K) = 0.200 \text{ s}^{-1} \). At what temperature the rxn rate doubles, i.e., \( k(T) = 2^*k(311K) \)?

\[
\ln k_1 = \ln A - \frac{E_a}{RT_1} \quad \ln k_2 = \ln A - \frac{E_a}{RT_2}
\]

\[
\ln k_2 - \ln k_1 = \ln \frac{k_2}{k_1} = \ln A - \frac{E_a}{RT_2} - \left( \ln A - \frac{E_a}{RT_1} \right) = -\frac{E_a}{R} \left( \frac{1}{T_2} - \frac{1}{T_1} \right)
\]

\[
\ln \frac{k_2}{k_1} = -\frac{E_a}{R} \left( \frac{1}{T_2} - \frac{1}{T_1} \right)
\]

\[
\frac{1}{T_2} = \frac{1}{T_1} - \frac{R}{E_a} \ln \frac{k_2}{k_1} = \frac{1}{311} - \frac{8.314 \cdot \ln 2}{123,000} = 3.168 \cdot 10^{-3}
\]

\[
T_2 = 315.5K
\]

\[
T_2 - T_1 = 315.5K - 311K = 4.5K
\]
Catalysis

Catalyst: consumed and regenerated in a course of a reaction.

What does a catalyst do?

   Speeds up a chemical reaction.

How does it work???

   Lowers the reaction barrier ($E_a$).
   Changes pre-exponential ($A$).

Does it affect exo-/endothermicity?

   No.
Homogeneous catalysis: same phase
   Enzymes, ozone decomposition, etc...

Heterogeneous catalysis: different phases
   Pt catalytic converter, many organic syntheses, etc
Enzyme catalysis:
Example from Prof. Arieh Warshel research (UCS)
Cell differentiation is controlled by chemical switch:

- **GTP (on)**
- **GDP (off)**

GTP: guanin tri phosphate
GDP: guanin di phosphate

No differentiation
Chemistry of cell differentiation:

\[ \text{GTP} + \text{H}_2\text{O} \rightarrow \text{Phosphate (P}_i\text{)} + \text{GDP} \]

very slow reaction

Can be catalyzed by the enzyme called RAS - but still is too slow

Working combination: \( \text{RAS+GAP} \)

Certain mutations in RAS: cancer
GTPase rxn: the Energetics

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Calc</th>
<th>Exp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>27.9</td>
<td>(27.5)</td>
</tr>
<tr>
<td>Ras</td>
<td>23.2</td>
<td>23.1, 22.2</td>
</tr>
<tr>
<td>RasGap</td>
<td>16.1</td>
<td>15.9</td>
</tr>
</tbody>
</table>

![Diagram showing the energetics of the GTPase reaction](image)

- **Rectants**: $\text{H}_2\text{O} + \text{GDP}$
- **Intermediate**: $\text{GDP}$
- **Products**: $\text{P}_{\text{ox}} + \text{GDP}$
Mutations in positions 12, 13 and 61 of Ras were found in 30% of human tumors. They were found to impair the GTPase reaction:

\[
\text{GTP} \rightarrow \text{GDP} + P_i
\]
Arieh Warshel:
How does it work and why mutations affect RAS's catalytic properties?

Approach: Use computers to model the chemistry of enzyme catalysis.
Close Proximity of Gln 61, Water and GTP in the active site
Inverse GTPase rxn: \[ \text{GDP} + P_i \rightarrow \text{GTP} + \text{H}_2\text{O} \]
Effects of mutations in the RAS position 61:

<table>
<thead>
<tr>
<th></th>
<th>Reaction Rate (sec$^{-1}$)</th>
<th>Barrier (kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ras</td>
<td>$4.7 \times 10^{-4}$</td>
<td>23.1</td>
</tr>
<tr>
<td>RasGAP</td>
<td>19.1</td>
<td>15.9</td>
</tr>
<tr>
<td>RasGAP Q61L</td>
<td>$10^{-3}-10^{-6}$</td>
<td>22-26</td>
</tr>
<tr>
<td>Ras Q61L</td>
<td>$7.4 \times 10^{-6}$</td>
<td>25.5</td>
</tr>
</tbody>
</table>

GAP accelerates by $\sim$5 orders of magnitude!
Q61L reduces intrinsic rate by $\sim$1-2 orders of magnitude!
Q61L reduces rate with GAP by $\sim$4-7 orders of magnitude!
Heterogeneous catalysis: molecular view

\[ \text{C}_2\text{H}_4 + \text{H}_2 \rightarrow \text{C}_2\text{H}_6 \]
Catalytic converter (Pt, Rd, Pd on Al₂O₃)

\[ \text{CO} + \text{O}_2 \rightarrow \text{CO}_2 \quad \text{(Pt+Pd)} \]
\[ \text{NO, NO}_2 \rightarrow \text{N}_2 + \text{O}_2 \quad \text{(Pt+Rd)} \]