5.0 Introduction
- Frontier Molecular Orbital theory (FMO) describes reactivity of reactions

5.1 Frontier Molecular Orbital theory (FMO) Theory
- The closer the energy (smaller ΔE) of the HOMO (highest occupied molecular orbital) is to the LUMO (lowest unoccupied molecular orbital), the more stable the reaction (better mixing)

- The HOMO behaves as an electron pair donor to the LUMO which acts as an acceptor

5.3A Application of FMO Theory

\[
\text{CH}_3\text{Br} + \text{OH}^- \rightarrow \text{CH}_3\text{OH} + \text{Br}^-
\]

- Substitution reactions are those in which a nucleophile replaces a leaving group
  - The lowest ΔE is the most favorable reaction, determining which HOMO and LUMO will be used
- Nucleophiles: molecules/atoms with “electron-rich centers” (lone pairs)
- Electrophiles: molecules/atoms with “electron-poor centers”

5.3B Properties that impact reactivity for substitution reactions
Rate of substitution reaction
- **Nucleophilicity**: measure of a nucleophile’s strength; the more reactive the Nu, the quicker the reaction.

- **Electrophile structure**: the more accessible the electrophile site, the faster the reaction. Hydrocarbons (the line structures coming from atoms in a molecule) are nonreactive structures that physically block interactions between Nu and E.

- **Leaving Groups**: leaving group efficiency is reliant on the ability for the LG to stabilize a negative charge. This ability is based on:
  - **Size**: larger atoms are better LGs
  - **Electronegativity**: more electronegative atoms are better LGs

5.4 Another representation of reaction mechanisms
2. **Loss of a leaving group**

\[
\begin{array}{c}
\text{Br}^- \\
\text{H} \\
\text{H}
\end{array} \rightarrow \begin{array}{c}
\text{Br}^- \\
\text{H} \\
\text{H}
\end{array} \quad + \quad \begin{array}{c}
\text{Br}^- \\
\text{H} \\
\text{H}
\end{array}
\]

3. **Proton transfers**

**Protonation of a carbonyl oxygen**

\[
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{C}
\end{array} + \begin{array}{c}
\text{H} \\
\text{O} \\
\text{H}
\end{array} \rightarrow \begin{array}{c}
\text{O} \\
\text{H} \\
\text{C}
\end{array} + \begin{array}{c}
\text{H} \\
\text{O} \\
\text{H}
\end{array}
\]

**Base** + **Acid**

**Deprotonation of an oxonium ion**

\[
\begin{array}{c}
\text{H} \\
\text{O} \\
\text{C}
\end{array} + \begin{array}{c}
\text{O}^- \\
\text{H} \\
\text{H}
\end{array} \rightarrow \begin{array}{c}
\text{H} \\
\text{O} \\
\text{C}
\end{array} + \begin{array}{c}
\text{O}^- \\
\text{H} \\
\text{H}
\end{array}
\]

**Acid** + **Base**