Molecular dynamics study of the aqueous solubility and early-stage aggregation of the Trp-cage miniprotein (TC5b) using GROMACS

Understanding the solubility of proteins in aqueous environments is a central theme in modern biophysics. Protein solubility influences nearly every aspect of biological and industrial system from maintaining proper cellular function to ensuring the stability of protein-based therapeutics. In **biomedical science**, protein aggregation resulting from poor solubility underlies several neurodegenerative diseases such as **Alzheimer's**, **Parkinson's**, and **Huntington's disease**. Studying the molecular factors that control protein–water interactions, therefore, provides critical insight into disease mechanisms and aids in the rational design of therapeutic interventions. From an **industrial and biotechnological perspective**, protein solubility determines the success of enzyme production, formulation of biopharmaceuticals, and long-term storage stability of vaccines and protein-based drugs. Molecular dynamics (MD) simulations using tools like **GROMACS** allow us to explore the atomic-level mechanisms that govern solubility, hydration, and aggregation—bridging the gap between theory and experiment. By modeling small, well-characterized proteins such as the **Trp-cage miniprotein**, we can develop principles that extend to larger and more complex systems relevant to health, biotechnology, and materials science.

Objective

Quantify how TC5b interacts with water and how concentration, ionic strength, and temperature influence its solubility or aggregation propensity. Use single-molecule simulations to characterize hydration and stability, and multi-copy simulations plus umbrella sampling to estimate the free energy of dimerization.