Cell membranes are two-dimensional liquid structures that protect the cell and organelles within those cells. In addition, the cell membranes are responsible for maintaining an electrical and chemical gradient and participate in processes related to cell growth, signal transduction, and immune surveillance. A variety of membrane functions are possible due to the presence of proteins, which contain α-helices or β-barrels in their structure. The functional activity of proteins is influenced by physical factors such as temperature, pH, membrane potential, the presence of allosteric effectors and the lipid composition, To date, thousands of different phospholipids involved in membrane formation have been identified. Membranes with different lipid compositions vary in thickness, packing, curvature, fluidity and phase transition temperature.

Because proteins and lipids vary in length of hydrophobic domains, a so-called 'hydrophobic mismatch' occurs whenever these two lengths differ significantly. Proteins, to reduce the energy penalty due to the hydrophobic mismatch, associate with each other, change their orientation in the membrane or induce conformational changes of the protein or phospholipids present in close contact with the protein. Protein association due to the hydrophobic mismatch is observed for many simple peptides as well as for large proteins such as receptors. It is considered that the hydrophobic mismatch is one of the key mechanisms for protein segregation between cell organelles.

Another parameter affecting the behavior of proteins is lipid packing, which depends on the saturation of bonds in the lipid acyl chains and from the presence of sterols. The varied lipid composition leads to the formation of not miscible domains that vary in lipid packing, fluidity and diffusion coefficient. In some cases, lipid packing promotes protein association as indicated by the results of experimental studies for certain protein complexes. On the other hand, to ensure proper functioning in the membrane, proteins tend to selectively localize in one of the domains with a specific lipid packing.

Experimental and computer studies using biologically active proteins have been conducted for years to determine the effect of hydrophobic mismatch and lipid packing on protein association and partitioning between domains. In addition, simple model WALP proteins were designed to facilitate research into phenomena related to hydrophobic mismatch. However, the presence of specific protein-membrane interactions that result from the amino acid sequence of the protein should be considered in all studies to date.

The goal of our project is to elucidate how hydrophobic mismatch and lipid packing affect the association of proteins and partitioning between membrane domains. The simplified model of the transmembrane helix that we propose excludes the presence of specific interactions with lipids. We intend to use molecular dynamics simulations to determine the energy governing protein association and partitioning depending on the hydrophobic mismatch and lipid packing. We expect that the result of our research will be a simple relationship, how membrane thickness and lipid packing affect protein association and partition between membrane domains. We want to check our predictions both on the WALP model protein and on other biologically active proteins.