

# MD SIMULATIONS OF LIQUID-LIQUID INTERFACE OF AMINOACID SOLUTIONS.

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## Introduction

It is well known that one of the most important structure formation components in biological systems is biomembranes. They in fact form surfaces that can be treated as interfaces between polar aqueous solutions and non-polar environment of phospholipidic side chains. It is hard to overestimate the role of polarity and non-polarity of phases on the distribution of substances and formation of different structures inside biological systems. Of special interest are the interaction properties of proteins with solvents and interfaces, which contribute to the process of protein folding and its functions as well. That's why our idea was to study the behaviour of amino acid residues, as monomer units of proteins, in an interfacial system.

## Objective

By means of molecular dynamics simulations we intended to study the properties of amino acid residues in a system containing liquid-liquid interface between water and hexane, which we took as a non-polar phase. We intended to determine free energy profiles, free energy of partitioning between two phases and free energy of adsorption at interface. MD simulations can also reveal conformational changes of residue structure in different environment.

## Simulation section

The system consisted of two lamellae (one of water and one of hexane), placed in a simulation with periodic boundary conditions in all three directions. In fact there are two interfaces because of the periodicity. The x and y box sizes are 40 Å. The height of each lamella is approximately 20 Å, but it varies slightly because of the Berendsen barostat algorithm applied along z-axis maintaining pressure of 1 bar. There are 1070 water molecules and 147 hexane molecules in hexane lamella. Hexane phase was initially arranged in 3 layers of hexane molecules,  $7 \times 7 = 49$  molecules in each layer. We make simulations with collision thermostat, maintaining system temperature at 300K. Integration step of 1 fs was chosen. Trajectories up to several nanoseconds were collected.

We used AMBER99 forcefield and TIP3P water model with unconstrained internal degrees of freedom. The amino acid residue, initially settled at the interface, was used in the form as if they were built into protein sequence. We did not do any terminal blocking. In fact they cannot exist in reality, but they reflect the properties of protein monomer units.

As a first step towards modeling the above described system was modeling it without hexane phase, but using a rigid wall potential to prevent water molecules evaporate from the surface.

From the simulations we got residue trajectories, derived probability histograms for residue and for its parts. We built up orientation patterns of residues.

## Results and Discussion

Let us consider at first the results of water-vacuum simulations. We performed them for all main types of residue side chains. But, generally speaking, we can regard side chains as hydrophobic or hydrophilic to some extent.

For purely hydrophobic side chains the residues tended to stay near the interface. We consider an example of phenylalanine (Fig 1). Probability histograms for mass center of backbone and side chain are depicted. The red and green lines are the borders of repulsive potential. We see that PHE adsorbs at the interface. And it is clear that it has a certain conformational and rotational asymmetry. The backbone being a hydrophilic part tends to settle itself deeper in the water layer than the side chain.

The similar behaviour was observed in systems with other residues. But as for residues with strongly hydrophilic side chains, they tended to desorb from the interface into bulk water phase.

Let us now pass to a water-hexane system.

On the Fig 2 we see the density profiles of hexane and water phases. The interface region is about 5 Å wide. On Fig 3 we observe the probability histogram for this system. The residue adsorbs at the interface and again has dominant orientation direction. But the distance between peaks of two curves is about 1.2 Å instead of 2 Å in the water-vacuum case.

We studied analogously other types of residues.

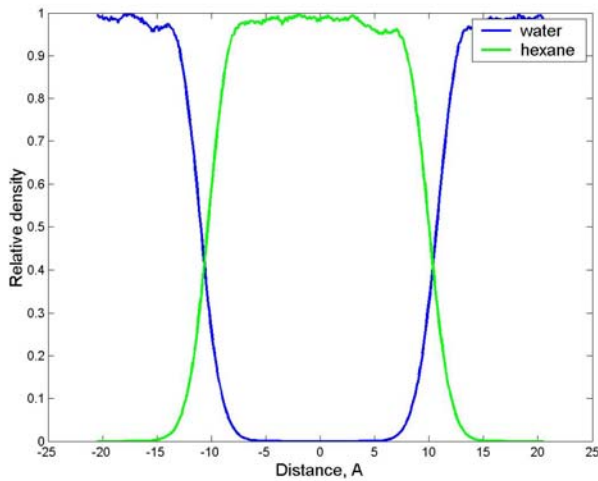


Fig 2.

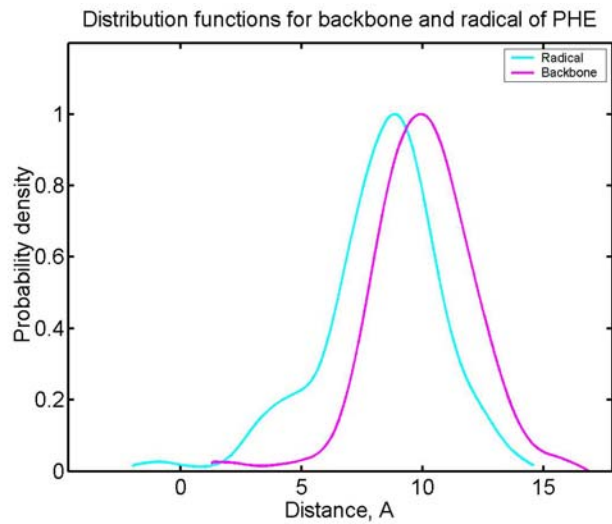
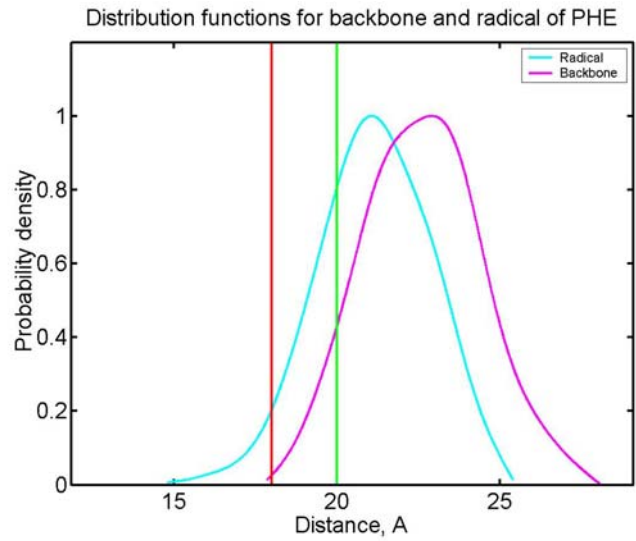


Fig 3.