SUMMARY

Recent years have seen significant increase in the ability of theoretical and computational approaches to help us mimic nature and dive into the secrets of structure and function of complex biological systems in cells. At the bases of these approaches we find quantum mechanics , however there is a massive disparity in the time and length scales on which the important cellular events occur and those that are accessible using the quantum-based tools. Larger length scales and longer timescales can be addressed by atomistic treatments, for example by classical molecular dynamics all-atom simulations, based on much simpler molecular mechanical expressions for the energy. Still, there are limitations according the length and time scales we are able to simulate. A solution to that problem could be a coarse-grained approach where groups of atoms are represented by a single bead. A number of different levels of CG models are possible varying in the number of atoms which are represented by a single particle. This method may provide several orders of magnitude of speedup relative to atomistic simulations, thus enabling longer timescales processes for more complex systems to be explored.

CG approaches lack in accuracy relative to all-atom simulations. To overcome this obstacle it is necessary to incorporate knowledge from studies at the small length scales into the more coarse-grained (CG) approaches. Since every method (except for first principles quantum chemistry) depends on parameters to describe the energy of interactions, one can foresee a process by which we can ascend the length scale ladder ,each successive method deployed incorporating parameters taken from the previous one. This approach is already the key to atomistic simulation using MD techniques, as in the widely used parameter sets (force fields), which incorporate data from QM calculations.

In our experiments we tried to use a CG approach that has been already used successfully to describe the dynamics of lipoprotein systems. The model that we used represents a level of coarse-graining where every residue is represented by two CG-beads where each bead represents 10 atoms. Such coarse-graining enables the use of longer timestep (e.g. 20 fs/step) providing several orders of magnitude of speedup. The system we applied the method consist of 2161 atoms which are represented by 261 CG-beads. The system is a two proteins interaction system with dimensions 5x3.8x2.5 nm. The purpose of our experiments was to check the validity of the method and the ability to create a protein-protein interaction complex using this CG approach. The complex we choose was *hTAFII28/hTAFII18* ,one with known 3D structure (PDB code : 1BH9). After the initial removal of the proteins we studied their rapprochement using all-atom and coarse-grained simulations. At the end we compared our final structures with the crystal structure.