In silico studies of the mutant protein causing cystic fibrosis

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Cystic fibrosis (CF), the most frequent inherited monogenic disease with high morbidity and mortality, is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) protein resulting in the lack of functional expression of this chloride channel from the apical membrane of epithelial cells. Most of the mutations abrogate either the expression level or the function of the channel. Serious efforts were made in the last decades to develop a treatment to restore functional CFTR expression, but drug development has been largely confined by the basic understanding of the effect of mutations on protein structure and dynamics. We employ molecular dynamics simulations using GROMACS and other computational methods to learn the effect of mutations of this protein. We found that the most prevalent mutation (deletion of F508) results in global destabilization of the nucleotide domain marked by decreased correlation in motions. The partial GPU utilization of GROMACS and potential application of GPUs in the analysis of molecular dynamics trajectories will be demonstrated.