

A Molecular Dynamics Study of the Structure of a Tetratricopeptide Repeat Protein

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Kinesin is a motor protein that uses ATP to transport proteins and other molecules intracellularly. It is comprised of stalk, head, and tail regions. The kinesin tail domain is composed of two light chains which each contain six tetratricopeptide repeats (TPR) and are responsible for binding cargo for transport along microtubules. A TPR is a 34-amino acid motif which contains two 14-aa helical regions joined together with a 6-aa loop. The goal of this research is to experimentally and computationally determine the structure of the kinesin light chain TPR regions. Molecular dynamics will be used to provide information about possible conformations and the dynamic behavior of the molecule. In order to verify our computational approach, we initially performed molecular dynamics on a TPR sequence for which 3D structural information is available (2AVP) and tested the energetic and structural effects of end-capping the protein, force field selection, the nature of the metal cofactors, and the dependence of the results on the initial structure. After exhaustive testing of simulation parameters, we are mutating 2AVP into the kinesin TPR and examining the stability of the protein using MD.