Steered Molecular Dynamics simulation to study elasticity and rupture of a Contactin protein

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Abstract:
To determine mechanism of injury and the consequent failure, the nature of load transfer to cells and their deformation phenomena as well as their material characteristics and mechanical behavior must be understood
Tissue damage such as Diffuse Axon Injury is directly related to cell injury which can be related to the mechanical failure of the cell under extreme external loading or rapid kinematic motion.
Molecular Dynamics simulation has been implemented here to study the force-displacement relation and debonding of adhesion molecule between axon and ECM.
This molecule is formed of contactin protein, Caspr, NF155 and Necl-1.Here it has been demonstrated how a contactin protein responds to constant forces and how the complex unfolds under dynamic loading.The traction-separation curve, as the constitutive material behavior of the interface, was extracted from MD simulation. Current experimental facilities have been restricted by considerations of infinitesimal size, geometry and biochemical interaction of adhesion. However, Atomic Force Microscopy and optical tweezer experiments measure the extensions of proteins as a function of applied force. Additionally a quantitative and predictive modeling is useful to simulate and study functions of proteins. Recently molecular dynamics approach has been increasingly used as a powerful mean of investigating biomolecular dynamics. In particular, Steered Molecular Dynamics (SMD) is a novel approach to the study of the dynamics of binding/unbinding events in biomolecular systems and of their elastic properties. Using a parallel processing system with 8 nodes, the SMD approach was utilized to apply force on contactin protein and study how it behaves under loading and to evaluate force-displacement relation. The structure of contactin protein was used for simulation from Protein Data Bank (PDB ID 3JXA Ig1-4 fragment). At the first,after removing one chain and generating missed atoms, the energy was minimized for 10,000 cycles. Then the Cα atom of N-terminus was kept to be fixed and by applying a constant force to the central mass along the direction connecting the initial positions of N-terminus and central mass the atomic coordinates of the whole system were recorded. The elongation of molecule was defined as the increase of the end-to-end distance between the termini from that of the native fold. Such elongation was monitored along with the applied force. The force-displacement diagram was outlined. A dynamic force has also been applied with a constant velocity to show the unfolding behavior of protein to analyze interface separation between cell-ECM. The derived force-displacement relation shows the stiffening response of protein under constant applying force and also the constitutive properties of the interface between cell and ECM that can be used in the modeling of upper scale in Cohesive Zone Method to extract the multiscale modeling of white matter of the brain tissue. This research is the developing stage of a research concerning a proper multiscale modeling of the brain tissue to investigate cellular adhesion effects.