CALIFORNIA STATE SCIENCE FAIR
2009 PROJECT SUMMARY

Name(s)
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Project Number
S0423

Project Title
TSEs: Analyzing Copper 2+ Binding in the Octarepeat Region of the Infectious Prion Protein

Abstract

Objectives/Goals
By modeling the interactions between Cu2+ and the octarepeat region of the infectious prion protein and then analyzing the effects of temperature on the bonds, new insights can be made into the question of why prions do not denature under normal temperatures.

Methods/Materials
Computer Programs: NAMD (NAnoscale Molecular Dynamics); VMD (Visual Molecular Dynamics).
Molecular models and data: prion octarepeat region protein model (pdb); organic component submolecular mass, energy and Van Der Waals force data for all atoms in octarepeat region; atomic mass, energy and Van Der Waals force data for Cu2+.
Model preparation: Using the VMD and prp21, remove water and create two octarepeat region models: one with copper and a second without. Combine the two pdb models with atomic property data to create two psfs (protein structure file). Use NAMD energy program to generate the .xsc file. Run practice tests determining number of steps required for stable results.
Temperature Simulation: Perform steps for both models at many temperatures. Run NAMD simulation for 440 steps to generate .dcd (trajectory file) for octarepeat region. Use RMSD script to extract residue values for both models at each temperature. Visually evaluate simulation of physical movement of molecule.

Results
The graphs show the RMSD values at different temperatures for the five residues. Each of the residues is a different amino acid: histidine imidazole, two glycine amides, glycine carbonyl, and trp indole. The values indicate the variability in the distance between the amino acids and the protein strand in Angstroms. A lower distance means the distance is more tightly regulated. Each RMSD simulation generates an animated graphical display of the backbone of the protein. Less flexibility means there is probably some force or bond holding the residue in place.

Conclusions/Discussion
This simulation shows that Cu2+ makes the octarepeat region stiffer. Thus providing further evidence that the presence of Cu2+ may be a required aspect fora misfolded prions to be more easily transferred. It provides insight that the Cu2+ changes the octarepeat region of the prion protein in such a way that denaturing it will be more difficult. By understanding why diseased prion proteins are resistant to denaturing, a solution can be found to destroy these proteins once they have been created.

Summary Statement
It is difficult to render diseased prion proteins harmless; this experiment suggests that the Cu2+ plays a role in making the infected prion harder to denature, and this may vary with temperature.

Help Received
Darrell Steely helped get me started, Dr. Glenn Millhauser gave me the coordinates needed and reviewed my completed project.