Molecular Dynamics: The Knot Protein Project
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Background

Overview of Molecular Dynamics

Hypothesis 1 is supported. We were able to replicate the process of protein folding using molecular dynamics simulations.

Hypothesis 2 was not supported by the results of my simulation. The results above did not support the hypothesis as the protein did not form a knot.

Overview of Molecular Dynamics

- Utilized various commands to set up my computer and install various types of software
- Ran a series of task simulations to learn how to use computer software to complete scientific simulations
- Learned how to analyze data collected from the simulations

Molecular Dynamics Simulation Process

- All simulations throughout this course were done in the terminal of the Ubuntu software
- Ubuntu is a desktop operating system utilized for various purposes, however for this class we used the system to complete our simulations
- The terminal (which is a command line interface) was used to enter commands to set up and run our simulations
- Various programs were used within the terminal to complete and analyze our simulation data (Gromacs, VMD, & SMOG 2.2)

Example Simulation Data: Folding and Unfolding of a Protein

- Step 1. Unfolding (high temp)
- Step 2. Refolding (low temp)

Simulations:

Simulation A:
- 1o6d at 137K
- The purpose of this simulation was to determine a baseline to compare to our future simulations
- In this protein we can see that a knot is present as the red strand threads through the yellow and forms a knot

Simulation B:
- 1o6d at 165K
- In this simulation, the protein was placed into a higher temperature, which forced the protein into an unfolded state

Simulation C:
- 1o6d at 137K
- In this simulation, the unfolded protein from simulation B was placed back into a colder temperature to determine if it would flip back to the folded position
- The red strand did not thread through the yellow strand indicating that a knot was not formed

Results

Significance

Proteins are very complex macromolecules that are responsible for many processes within an organism. With all the processes that proteins are accountable for, it is important to understand how they function and what causes them to become dysfunctional. In order to function properly, proteins must fold into the correct shape, however this does not always occur, and misfolded proteins cause various diseases to transpire.

Big Picture Question:
- Is the occurrence of misfolded proteins related to a protein’s energy state?

Objective:

1. Make protein models where the folded state is the lowest energy (native topology model).
2. Fold it (or unfold it) with simulations.
3. Compare the results with experiments.

The Project (Testing Hypotheses)

The protein of interest for this simulation was 1o6d (a slow folding protein) that could possibly be altered in order to increase its folding efficiency.

1o6d.pdb (MTT - Minimally-Tied Trefoil Thermatoga maritima methyltransferase)

Hypothesis 1: Can the process of protein folding within a simulation replicate real life protein folding?

Hypothesis 2: Are knock out mutations in a protein responsible for creating stable proteins that can withstand any condition?

The Approach

- All-atom structure (reality)
- Simple Cα model (on computer)
- All-atom structure is stripped down to only the Cα atom “skeleton”.

Methods

- Step 1. Unfolding (high temp)
- Step 2. Refolding (low temp)

All-atom structure

References: