Molecular Dynamics Research

Harper Sewalls

In this paper I will discuss and explain the methods by which Dr. Edwards and myself have began investigating the conformational changes that certain highly dynamic proteins undergo when they dock with one another. We have been using the Western Kentucky University high precision computing cluster in order to run molecular dynamics simulations with a program called AMBER. AMBER takes data in the form of the coordinates of the atoms in a protein and can then be used to simulate the motion of these molecules at a specified temperature. There are certain things that such research can do that will be helpful to future researchers. Lastly I will talk about where we are now and where we are going.

AMBER works on the Linux command line which was made to be very good at organizing files and data structures. The files that must be manipulated and moved around in our research generally consist of large data files. These files come in a few different forms including prmtop which is a file containing a list of all of the atoms in an in vacuo protein or solvated protein system. Another file type is inpcrd which contains coordinates for the three dimensional location of each atom. Files like this are submitted to the computing cluster to be divided and conquered by many smaller processors. When a file is submitted it is done so along with the help of another input file that contains instructions on what needs to be done to the protein. These instructions specify how much time should be simulated and also how the temperature should change throughout the simulation. Each discrete time step is equal to a femtosecond which is ten to the negative fifteen seconds. The data can then be viewed by importing the inpcrd files onto the device that you are using to interact with the computing cluster. Inpcrd files show change in the protein over time. This data is then plugged into a program called VMD or visual molecular dynamics. The protein then appears represented how you choose. They can be as protein ribbons or as individual atoms linked by molecules. Another viewing scheme shows only the hydrogen bonds as they form and disappear. We are using this software to predict the conformation of proteins that can be very dynamic and hard to pin down with x-ray diffraction. So far we have been heating the proteins to a very high temperature and then cooling them back down in an attempt to see if they will change their shape after a high energy state. I plan to write a step by step guide detailing the steps necessary to make use of AMBER and VMD.

The research that we are conducting consists of using the molecular dynamics program AMBER to simulate the motion of large proteins. The computer simulations are useful because X-ray diffraction is used to determine the shape of such proteins. This method is inadequate for accurate representations of protein shape. Many of the proteins we are using are very dynamic and have a large number of “moving parts”. Oftentimes their function reflects this dynamic nature. For example, one of the proteins is used in the DNA replication of a deep sea vent dwelling organism. The protein’s free movement allows it to withstand the heat of its environment and remain functional and not denaturing. Once we have developed a good formula for predicting conformation then other researchers can more reliably obtain protein data. It is difficult now to obtain structural data about molecules and especially for conformational pairs of proteins. With this computational formula anyone will be able to predict the likelihood of various docking configurations for large proteins. This is the end goal of this phase of the investigation.