

PREFACE

21st century will be the century of life science. Life material and life phenomena will be the prominent research objectives for scientists. Biology will not be only a science based on observations and experiments, but also a science based on Quantum Theory. As Walter Gilbert said: "The new paradigm, now emerging, is that all the genes will be known (in the sense of being resident in databases available electronically), and that the starting point of a biological investigation will be theoretical. An individual scientist will begin with a theoretical conjecture, only then turn to experiments to follow up or test that hypothesis."

After completing the Human Genome Project, the main research trend now turns to proteins. In studying proteins, besides using the traditional experimental tools and theoretical methods, large scale computer simulations have indispensably become the third approach.

Computer simulation allows researchers the ability to observe the processes of protein changes in as short as 1 fs and structural changes versus temperature or versus time. Also, new protein structures can be easily obtained by using the Knock-Out Method. Additionally, directions for further biological experiments can be readily identified, saving significant amount of time, especially for difficult experiments. We can say that computer simulation has become an important tool in the study of the functioning of proteins and their structures. It is also an excellent supplementary tool for biological experiments.

Scientific researches have already touched the realm of highly sophisticated systems. There have been different physics at different times. Nano-material and proteins are the two main research directions for physicists in the present time. But, in order to study these two materials numerically, we have to attain the level of 100 ~ 1000 Tflops ($10^{12}/s$) computer simulation speed. For example, for nano-material:

- To simulate two nano-particles (diameter 5 nm or less), consisting about 1000 atoms, 50 Tflops is needed.
- To simulate the interaction between two nano-particle groups, 250 Tflops is needed.

- To simulate a complete nano-structure, 1000 Tflops is needed.
- For protein macro-molecule;
- To simulate 1 nanosecond, 50 Tflops is needed.
- To simulate the action of enzyme, 250 Tflops is needed.
- To simulate the fold of protein, 1000 Tflops is needed.

To reach such computer simulation speed level, we typically use two kinds of high performance computers: supercomputers and cluster computers. Supercomputers are too expensive. Now most researchers use cluster computers. This textbook will use the cluster system to perform simulations as well;

Cluster + Linux + Parallel Calculation

A protein can complete its fold in micro-seconds (10^{-6} second). But to simulate one nano-second of protein activities, current computers may take up to one whole day. For this reason, we may need to use up to 10000 computers to complete just a folding simulation. To search a medicine that cures the variola illness, we may potentially have to test 35 million medicine molecules. This means we shall need to use about 2 million computers running together to form a virtual supercomputer capable of 1100 Tflops. This is not very practical. For such a scale of simulation, as the next best choice, researchers are trying to use Grid Computing techniques. It is basically distributed computing, using internet to connect many computers into a huge "virtual supercomputer".

In this textbook, we shall only discuss two basic questions of protein simulation: Molecular Dynamics (MD) of Protein and Full Electronic Structure (FES) of Protein. We shall not discuss the basic knowledge of protein and Linux. Students who already have the knowledge can directly skip to Chapter 6 for study. Also, we shall not discuss the research topics of protein either. We believe students will be able to pick up their research topics of protein simulation after they have studied the two simulations in this textbook.

The goal of this textbook is to show students how to run simulation programs in detail without introducing the corresponding theories. So, we shall only simply list some necessary knowledge in this textbook. Student can refer to other related books in this field.

For molecular dynamics of proteins, we shall refer to NAMD program as an example (<http://www.ks.uiuc.edu/Research/namd/>).

For full electronic structure of protein, we shall use the ODA

program as example (Ladik, J. et al., Chem. Phys., 108:203(1986) and Jiang, Y. Ye, Y. J., and Chen, R. S., Biophys. Chem., 59:95-105(1996)).

This textbook is a course for science major students who want to study computer protein simulation. Its manuscripts have been lectured for six years to graduate students in the Department of Physics, Fudan University.

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