Thermodynamics for Biological Systems:
Classical and Statistical Aspects
Prof. Sanjib Senapati
Department of Biotechnology
Indian institute of Technology - Madras

Lecture – 74
Computer Simulations of Macromolecules

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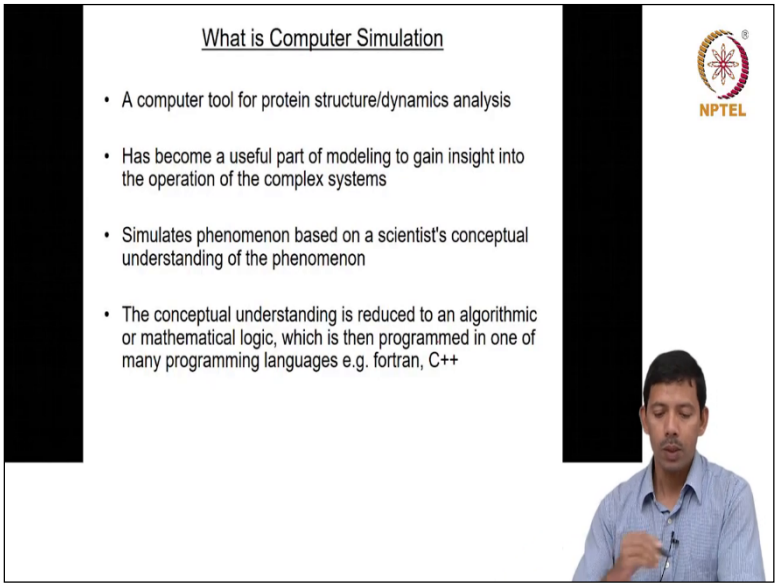

Now what is computer simulation? So computer simulation is a computer tool for analyzing from biomolecular point of view or protein structure and dynamics. So, here protein is you know just an example it could be your liquid molecules, it could be DNA, it could be polymer and whatever material you are interested in. So, this is a computer tool which basically analyze the structure and dynamics of a complex system.

And because of the robustness of computer simulation methods it has become a very useful part in modelling a complex system. And when you model a complex system this simulation method gives you a lot of useful insights which are otherwise very difficult to obtain experimentally. So, that is that is basically the microscopic information versus macroscopic information. So, the macroscopic information you get from experiment but the microscopic information is very difficult to obtain experimentally.

And there we can rely upon computer simulation techniques which basically can give you atomic level description of the system and from there you can gather useful insights about the operation of the complex systems. But the important thing in computer simulation method is that you have

to have a conceptual understanding of your system or the phenomena or the order system you are dealing with. So, what it means is that let us say you are simulating liquid water bulk liquid water so and you are trying to get let us say the diffusivity the diffusion coefficient of the water molecules or you are trying to calculate the density of liquid water.

So when you start the computer simulation of water all you have to know to start with is that this molecule water is composed of 1 oxygen and 2 hydrogen and oxygen here and 2 hydrogen atoms and there is a bond between oxygen and hydrogen 1 there is a bond between oxygen and hydrogen 2, there is an angle between H1 O H2 and so on so forth. Also you have to know that oxygen is having Delta negative charge and these are having Delta positive charge.

So, this conceptual understanding you have to have before you start your simulations and where these information's are required and important that also I will explain you in the coming you next. When it comes to biological system let us say you are simulating a protein and you are trying to get the different microstate of a protein. So, for a protein the microstates are nothing but the different conformations. So, when you are trying to capture different conformations of a protein you start your simulation and the conceptual understanding of the protein you need to know to start with is that this protein is having a sequence of alanine, glycine, lysine and so on so forth.

And then you also have to tell the computer that my alanine is having this connectivity and alanine took lysine there is a peptide bond and so on so forth and another in my carbonyl carbon is positively charged oxygen tentatively charged and so and so forth. so, that information that conceptual understanding basically the protein sequence and having acid sequence in the protein and how the atoms have different charge distribution and what are the bonds who are the angles who are the dihedral present in the in the protein.

Those; information you have to define and that is your conceptual understanding of the system or the phenomena. So, once you have that understanding all you do you basically put that conceptual understanding as an algorithm. So, once you have that algorithm and you write that algorithm by your programming language it could be Fortran it could be C++ and you write those algorithm as a computer program and feed to the computer.

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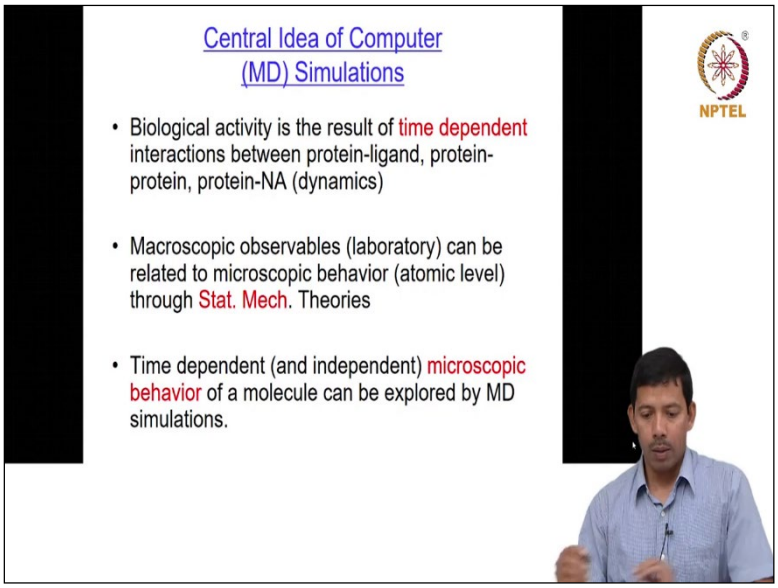

So computer now we will look for the same H and O atoms and wherever it gets H and O it puts off that bond distance value it will put up that HOH angle value whenever it finds that 3 atoms order are coming in a consecutive order. So, your conceptual understanding is now put up as an algorithm which is now fit to the computer.

So, what is the central idea of computer simulations so here I will mostly talk about molecular dynamics simulations. Even though there are many other simulation techniques like Monte Carlo, Brownian dynamics and so on but in this topic I will be covering mostly the molecular dynamics simulation which is by the way perhaps most robust competition is not technique among available techniques. So, the central idea of computer simulations in general is that biological activity is the result of time-dependent interactions.

That means that there is a time-dependent information present in our biological systems and that is easily understandable because none you know none the molecules in our body is static. So, that all the biomolecules protein ligand nucleic acids so they are always moving and whenever they are moving so they do have different interactions if you do in vitro experiments of protein and protein.

So, every moment the proteins are interacting and their interactions are different from time t1 to time t1 plus delta t because their conformations are changing so in they have this conformation the interaction is different than this conformation. So, therefore there is a dynamics involved and what you get in the laboratory which we defined as macroscopic properties or macroscopic

objects they can be obtained by the microscopic information or the atomic level behaviour of the system.

So in other words as we saw in the previous slide that if you know XYZ coordinates of each atom that give you uniform information so those in we can convert to the macroscopic quantity of the thermodynamic quantity by using the statistical mechanical theories which is the ensemble approach. And this microscopic information we can explore by MD simulation and that is what we I have introduced the MD simulation to get the microscopic behaviour or in other words to capture different conformation of a protein or to look at the different distribution of the water molecules if you are interested to simulate about water.