Thermodynamics for Biological Systems:
Classical and Statistical Aspects
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Lecture – 87
Case Study (Water)

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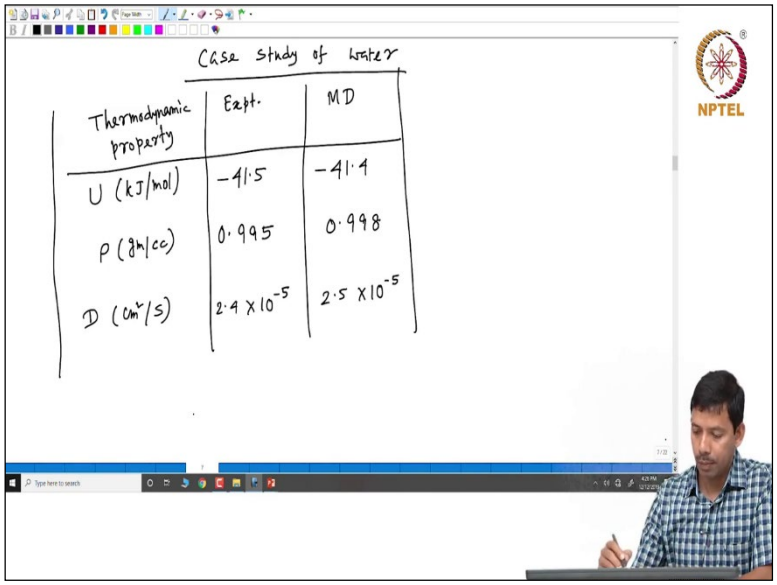

A case study of water. so these are thermodynamic properties of water we are interested to compare, thermodynamic property then result from experiment and result from molecular dynamics. After generating so many confirmations and then taking down ensemble average over them ensemble or time average. So, the thermodynamic property the first one is the potential energy of water in kilojoules per mole.

So, the experimentally measured value of U is -41.5 from MD the measured value is -41.4 so you just can see how reliable or how accurate the simulation can be. The next property is the density gram per CC. The experimentally measured is 0.995 and from MD we get 0.998 diffusivity the diffusion coefficient in centimeter square per second of water experimental value is 2.4 into 10 to the power -5 and what you obtain from MD is 2.5 into 10 to the power -5.

So, as you can see we can reproduce the experimental data very well by choosing the right force field parameters. So, this shows the robustness of MD simulation technique to generate the microstates and after we generate the microstates we take the ensemble average or the time average to get the properties for which experimental data are available. So, the advantage of the

computer simulation technique is that we not only calculating the thermodynamic properties and match them with the external data,

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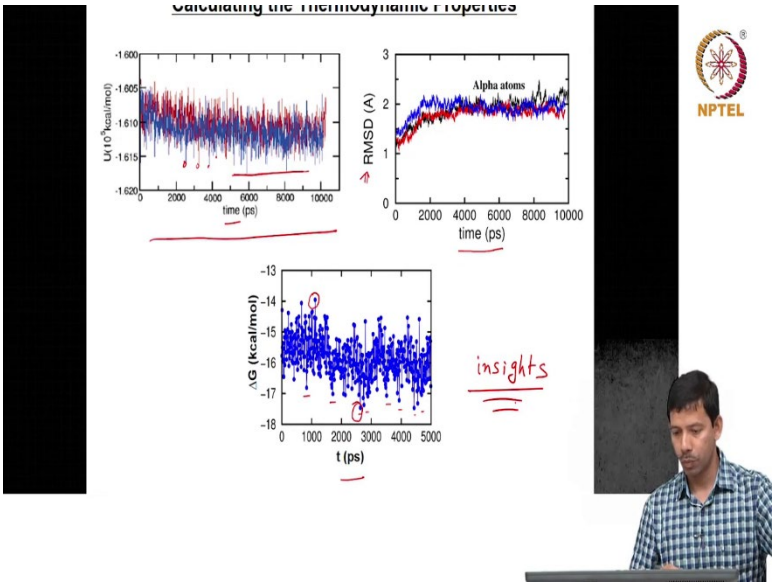

We can always go back to our microstates and pick up each and every microstate and see what transitions had happened. When you take the ensemble average we just get a single ensemble average or time average value that does not give the microstructural information or the transitions happened into the system that we are tackling. But those information are available in my computer simulation data. I can always go back to my time evolution information and from here I can get that, this is the structure of my protein ligand complex where the binding was the strongest versus the one where the binding was the least.

So, what computer simulation techniques are giving is that they are first getting the confidence that my technique and the models are good enough and therefore I can reproduce experimental data plus it is giving more insights. It is providing more insights about my systems micro structural information. So, I think that is it from statistical thermodynamics part of this course.

So I just want to summarize and if I summarize I would say that we started with the definition of statistical thermodynamics. We said that thermodynamics and statistical thermodynamics they basically can be applied to the same system where thermodynamics the classical thermodynamics gives relations between various thermodynamic quantities. Statistical thermodynamics tells us the magnitude of this thermodynamic quantities in terms of the very constituent of the system.

So statistical thermodynamics assumes that our system is composed of the tiniest particles of atoms and it looks at how these atoms interact with each other and based on those atomic level information it predicts the extent or the magnitude of the thermodynamic properties. So, here thermodynamic properties give the relation among the thermodynamic quantities, statistical thermodynamics tells why the thermodynamic quantities are more in one system versus they are less in another system.

So statistical thermodynamics basically gives the microscopic information of our system whereas thermodynamics gives the information of the macroscopic quantity. So, in the first few lectures I talked about microstates and macrostates I defined the microstates and macrostate in a quantum system to start with a small system and there first we have looked at the Boltzmann distribution law which is a very important distribution law in statistical thermodynamics.

And we have seen that if we can find out a microscopic quantity called partition function that partition function can be related to any thermodynamic quantity. So, we written down some of these relations how partition function is linked to thermodynamic quantities like entropy, enthalpy, Gibbs free energy, Helmholtz free energy and we have shown that once we get the partition function Q then all these thermodynamic quantities can be easily obtained.

But in that context we have seen that the initial formalism had some problem and those problems, one problem in the formalism was the entropy. The entropy was not coming right and Gibbs found that out for the first time and he named it as Gibb's paradox and latter case paradox was resolved by re-formulating the formalism and that was the Boltzmann era. So, until the Boltzmann era people could use the partition functions and get the thermodynamic quantities for small systems.

And in that context you also have looked at the partition function for monatomic gas. But then when we come to a bulk liquid system or our system of interest like biological molecules. And for biological molecules using partition functions in terms of the quantum states is very difficult to use. Because quantum states just for the ground state could be in the order of 10 to the power N for N is number of particles.

And therefore for a classical system like our biological system large systems we had to take a parallel formalism where we basically got the partition function not in terms of the quantum states

we got the partition function in terms of the different distribution of our system. So, when you basically get different distributions of our system just by defining their r and p by defining their positions and momentum we obtain different microstates.

So once we generate different microstates in a classical system and that was ensemble approach by Maxwell Boltzmann particularly by Gibbs. So, Gibbs introduced ensemble approach and in that ensemble approach we can generate different microstates of a system and then we can take their average and we get the ensemble average or the time average and that is the thermodynamic quantity that are measurable experimentally.

So, we defined the ensemble average of a thermodynamic quantity, we defined what ensembles are, we defined what ensemble average is, we defined what time average is, and then we basically wanted to see how we can generate different microstates. So, by definition if we have different microstates we can just take the average over all these microstates and get the ensemble average but then how do you get all these microstates.

So in that context we introduce molecular dynamics simulation which is a computer simulation technique and there by solving Newton's second law we generated different microstates of our system of interest. We found that we could generate as many microstates as you want depending on what kind of computer resources we have. If you have a very, very powerful computer resource we can generate you know millions and billions of microstates.

And if we take average over all these microstates we get the time average and the time average matches very well with the experimental data. We took an example of liquid water the bulk water and we found that for liquid water the MD calculated values match very well with the experimental data. Apart from molecular dynamics simulation we also briefly talked about Monte Carlo simulation technique.

Monte Carlo simulation is another computer simulation technique where we can generate new confirmations of a system using random number generator. While in molecular dynamics we solved Newton's second law, we basically solved differential equations to generate new confirmations. In Monte Carlo we use random number generator to obtain the new confirmations. So, molecular dynamics and Monte Carlo two both are having advantages and disadvantages.

Molecular dynamics simulation advantage is that it has the time information so you can always go back and pick up the particular conformation and find out how that conformation is linked with all other confirmations and therefore molecular dynamic simulation would be much more expensive in terms of computer resources. Whereas Monte Carlo simulation it does not keep the history in a memory, it just looks it just looks at the preceding configuration and generate the new configurations.

So, since it does not have the time information and this Monte Carlo simulation is faster than molecular dynamics. So, these two techniques helped us to generate several micro structures several microstates and once we have the microstates we can calculate the average property of any thermodynamic quantity. That is the whole information I want to give you from statistical thermodynamics aspect of molecules, thank you for listening.