Thermodynamics for Biological Systems:
Classical and Statistical Aspects
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Lecture – 86
Analysis of MD Trajectory

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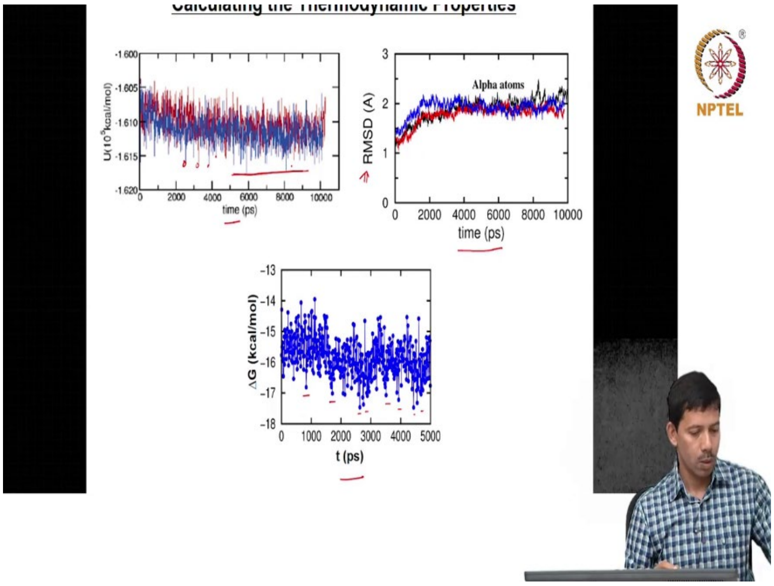

After you generate so many microstates and you plot them this is what you will be seeing. So, here I am just showing a couple of properties of my molecule of interest. my molecule is a biomolecule, a protein. So, if I plot the potential energy of my system over time, so, this data generated from molecular dynamics simulations and therefore there is a time involved, so if I plot over time I see how my potential energy of the system is varying.

So, the potential energy was minus 1.605 into 10 to the power of 5 kcal/mol and over time you can see the potential energy is decreasing. So that means the system is stabilizing farther when I run, when I generate more and more confirmations. Here I am showing the free energy of binding of a small ligand into the protein and I generate different confirmations of the complex and calculating Delta G over time.

Here I am showing basically something called root-mean-square displacement what is the deviation of my new confirmations compared to my starting conformation. So, I started from confirmation let us say unfolded protein and now I am trying to see the protein folding and when

I get the new confirmations, I can compare those new confirmations, with respect to my starting confirmed conformation and I see how much I have deviated from the starting structure.

And this RMSD is basically showing how the molecule has evolved over time. So, if you brought them up over time you basically see every microstructure, so here each point it is more easily visible. so here, each point is basically showing the structure of the protein ligand complex. Now if you want to get the average over all these energy values, or you want to get the average potential energy of the system, you can go back to your definition of ensemble average or time average and you get those properties calculated.

So we will do that now. So, like how you calculate the average property we have discussed, how we calculate average property, so, I just take a couple of examples. you simulated your system and you generated several microstates and now I am asking you to calculate the average potential energy of the system.

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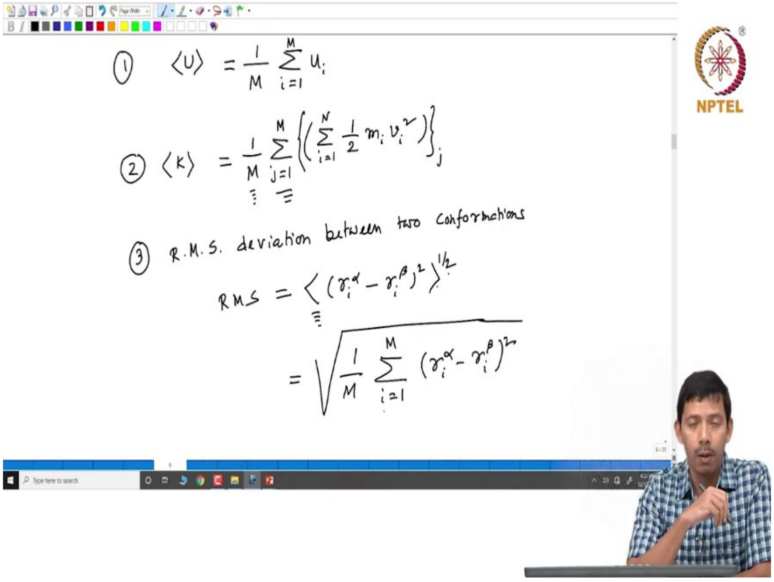

① $\langle U \rangle = \frac{1}{M} \sum_{i=1}^{M} u_i$

② $\langle K \rangle = \frac{1}{M} \sum_{j=1}^{M} \left\{ \left(\sum_{i=1}^{N} \frac{1}{2} m_i v_i^2 \right) \right\}_j$

③ R.M.S. deviation between two conformations

$$RMS = \langle (r_i^\alpha - r_i^\beta)^2 \rangle^{1/2}$$

$$= \sqrt{\frac{1}{M} \sum_{i=1}^{M} (r_i^\alpha - r_i^\beta)^2}$$

So, how will you calculate you can calculate the ensemble average and so ensemble average of that would be, since I am taking the time average, so m is the number of microstates I have generated and i is equal to 1 to n and Ui, so Ui is basically energy of ith microstate. So, if I take the average over all the microstates generated, I can do ensemble average

$$< U > = \frac{1}{M} \sum_{i=1}^{M} u_i$$

if I have to calculate the ensemble average of the kinetic energy. Let us say K is my kinetic energy so how am I going to get that? so, again I will take the time average so my m is number of microstates generated

$$< K > = \frac{1}{M}\sum_{j=1}^{M}\{ (\sum_{i=1}^{N}\frac{1}{2}m_i v_i^2)\}_j$$

Here M is the number of microstates and N is number of particles present in the box. This is the ensemble average of the kinetic energy of my system. So here I have summed over all the microstates and then divided by number of microstates and that is the average value. And here I summed over all the N particles present in my box in each microstates. So, that is how you can calculate the average kinetic energy.

You also can calculate the RMS deviation between two structures. So what is the Root Means Square Deviation between two configurations? Let us say my confirmations are alpha and beta and so I am talking about root mean square. So, RMS is taking the average, so alpha is my state and beta is my another state and I want to get the root mean square. So, if I have to get it I again have to make use of my time average.

$$RMS = < (r_i^{\alpha} - r_i^{\beta})^2 >^{1/2}$$

$$\sqrt{\frac{1}{M}\sum_{i=1}^{M}(r_i^{\alpha} - r_i^{\beta})^2}$$

And again M is my number of microstates. My Mean is my ensemble average so root mean square displacement between two states alpha and beta can be obtained from your set of microstates generated from molecular dynamics or Monte Carlo okay. Then next thing, okay let us take one example one test case, how my ensemble average values compare with the experimental data.