Thermodynamics for Biological Systems:
Classical and Statistical Aspects
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Lecture – 78
Computer Simulations Tricks

Now we will be talking about the different boundary conditions. So before we go to the different boundary conditions

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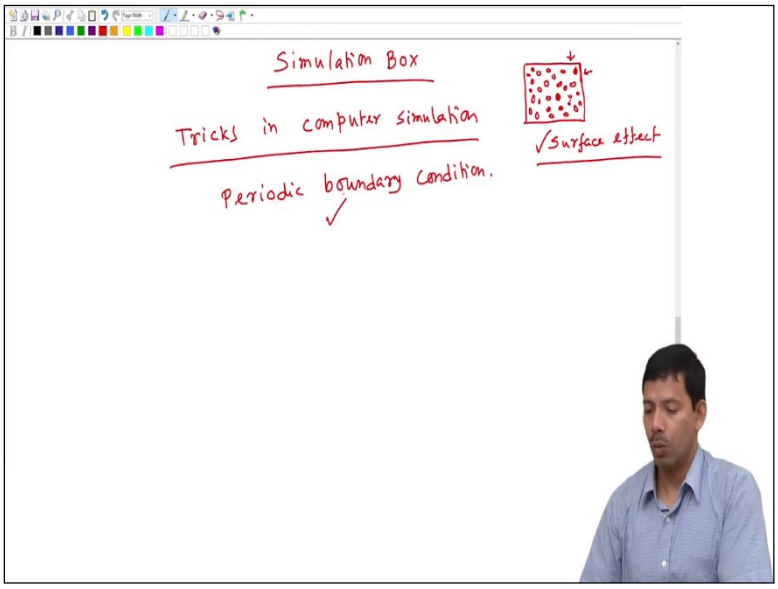

As I said that we need to put our molecules or the protein in a box that we call a solution box, is basically a box where you put that protein at the center of. So this is my protein I put of my protein at the center off. The simulation box could be of different shape the most conventional simulation box is cubic, there are examples of truncated octahedron to rectangular boxes the as a simulation box the most common is a cubic box to simulate a protein. As truncated octahedron, they are more of a spherical shape. So, if you want simulator, a liquid drop then truncated octahedron is better option than the cubic box. If we take this box solution box and I am simulating liquid argon for example then give me of course is not a lattices random distribution. So, in this distribution you will see something different for this molecule here versus this molecule here. The differences are this molecule feels the presence of all the neighbouring molecules around it; this molecule has no neighbour in this direction or that direction.

Therefore the force experienced by the molecular at the centre will be very different than the force experienced by this molecule at the edge or at the surface and that is a problem if you are trying to simulate for example bulk water or if you are trying to simulate even a protein. A Protein in a cellular environment or in in-vitro experiment it is having lots of water molecules or the buffer solution around it.

So, those water, water solution protein in vitro test tube you have all similar properties this would so this will exhibit the similar properties and therefore this water and this water should not have different properties. Here they so different properties because force exerted on them by other particles a different. And that problem is called the surface effect. So, surface effect is basically the limitation where the surface molecules experience different force due to the neighbours compared to the particles which are in the bulk phase.

So we need to remove we need to come out of this surface effect we need to remove the surface effect and in that context trick. So, now we be talking about so we have discussed our solution box now we will be talking about tricks some tricks in computer simulation. We employ a trick which is called periodic boundary condition. So, by this periodic boundary condition we will remove the surface.

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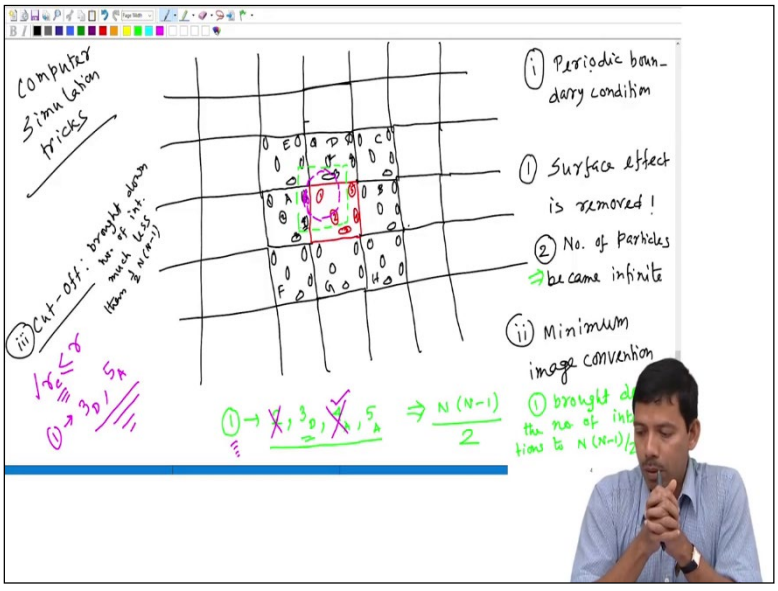

So, let me draw a summation box, a cubic summation box and here I draw just so the molecule here 1 here 2 here 3 here ,4 here and 5 where molecule 2 at the centre and molecule 5 at the edge. So, the first experience by two and five be different we now 1 and 2 employ a trick of periodic

on a commission by which we remove the surface area where 5 and 2 both of them all the molecules in the box will experience similar force on them.

So, in this periodic boundary condition what you do will replicate this central simulation box along x, y and z direction infinitely, so what I am doing I am now replicating the central simulation box in all x, y and z direction infinitely. So here I have particle 1, 2, 3, 4, and 5. So, basically my replication I mean I am just taking that same distribution of the particles and just replicating along its x, y and z direction. So, therefore this is 2, 3, 4, 5, 1, 2, 3, 4, 5 so you continue this.

So I am replicated my central simulation box along x y and z directions infinitely is goes on, this is my central simulation box and I name this is image A this is image B, C, D, E, F, G, H also okay. So, now if you compare the molecule 2 and molecule 5 none of them are a surface molecule. So, molecule 5 is having all other molecules around it as 4 2 3 1 4, so therefore the surface effect is removed. So by employing the periodic boundary condition we have the surface effect.

Because now note the molecule is in the surface all molecules now find themselves in the bark so the limitation of surface affect removed but in the process we have introduced a problem. The problem is to start with where we had molecule 1 2 3 4 and 5 to consider now we have infinite number of interactions now from 5 we have so many molecules and therefore we have infinite number of interactions.

So, we cannot handle so many interactions if we have to we somehow now have to employ another trick by which we can bring down this number of interactions from infinite to something reasonable number interaction come to consider; so surface effect is removed but number of interact number of particles became infinite, in this is periodic boundary condition. So, in the periodic boundary condition we have the problem of large number of particles.

So, the next trick to bring down the number of interactions to tractable number is minimum image convention, in computer simulation tricks one is the periodic boundary condition and the number two tricks is the minimum image convention. So in minimum image convention what we will do is that will pay attention on one molecule of the center simulation box one at a time. So, let us say we are paying attention on molecule one.

So what I do you will make a box around the central simulation box 1 putting that at the center what I do now I am putting molecule 1 at the center of a box which is having a same dimension as the original simulation box. So, now what I did I kept molecule one at the center of a box which is in green which is having exactly the same dimension as a center simulation box. The same I will apply when I do for 2, 3, 4 and 5.

So, I put 2 at the center and around 2 keeping it at the center I would make a box of same dimension as the original box and then count the number of interactions. So, here if I put one at the center and make the box around one exactly of the same dimensions how original is relation simulation box I should get 4 other molecules in the box because all the boxes got a here are exactly the same.

So, if you draw a box in that 1 dimension you should have another 4 molecule and here like in this case I have so now interaction of 1 in this box is with 2 the original 2, so I need 2 numbers so here is 1, 2, 3, 4 and 5. So here molecule 1 is interacting with 2 it is interacting with molecule 3 in the box D it is interacting with molecule 4 of box A and 5 of box A. So, number interaction remains exactly the same as we had in the central simulation box the same central simulation box 1 particularly attractive 4 other particles since it is 5 particle system.

And by minimum in this convention I brought it down to the same number that one will interact with for 4 such particles no matter whether they are in the central images since so basically now my system is our bulk system. It is a bulk water and my protein is in bulk solvent and all the molecules are behaving similarly therefore it does not matter whether I pick up 3D or I pick up 3C or I pick up 3 from the central simulation box because all the molecules are behaving exactly the same way.

So, now basically number of pair interactions we have brought down again to N into N – 1 by 2 this is the number of pair interactions this will be considering and due to this minimum image convention we brought down the number of interactions from infinity what we had here periodic boundary condition 2 N into N - 1 by 2 pair interactions by minimum image convention we brought down number of interactions to N into N -1 by 2 okay.

So, therefore minimum image convention given us I mean so by periodic boundary class minimum is convention we get rid of a surface effect and therefore we are now making our

solvent more bilk like and but in the process like periodic boundary we introduce many interactions and then by minimum image conventions we brought down the number of interactions to our original 2 into N into N -1 by 2. There is another trick which is called in the cut-off. In this trick some of the interactions that you see in this green box.

Some of the interactions like the 4 here is kind of farthest from 1, so keeping 1 at the center I can draw sphere of radius r c. So, I consider that if the distance R between two particles is less than r c if the distance between particles is less than the value of cut off distance then I ignore those interactions. For example here this molecule which is 4A, 4A is very far away from 1, so the interaction or the influence of 4 on 1 will be very less.

So, I can neglect this interaction so by cut off we have further cutting down the interaction of 1. So, now 1 is interacting 1 so 2 is also gone because the center is away from this distance 1 is not interacting with through 3D and 5A if the cut off, this is coming within the sphere. So, by cut-off we can reduce the number of interactions further them to make our calculation quicker. Now this rc is up to you, so what is the cut-off distance they choose.

So, if you take r c is too small then as you see in my drawing you know many of the interactions are concord that is many good cut-off distance. You should have a compromise of your accuracy and quickness of your simulation. You have to choose r c judiciously so that you cut down number of interactions but you should not compromise with accuracy. So, one has to play in this r c value and see how my thermodynamic properties are he produced well with the experimental data.

So, by cut off you further cut down the number of attractions and this is particularly important for liquid systems or molecule systems where you have millions of atoms and you cut down from millions then few 1000, 10000 of them that makes you a conclusion much, much faster than you have to consider all the possible interaction. So, by cut off you brought down number of interactions further. So, the cut off you brought down number of interactions much less than half into N (N-1), that means your calculation is much faster.

So, these are the composition tricks by which you make your simulation much more practically viable example by making your making your solution more bulk like at the same time you make your calculation faster by cutting down some of the interactions which are which contribute very

vaguely in this example you have practical cases a huge simulation box and some of the molecules far away from protein surface are protein active site.

And those water molecules are very, very less influence on the protein residues and it has been found that neglecting those interactions by those water molecules who are away does not hamper your protein conformations or protein thermodynamic properties so we easily can neglect those water contributions. So, by periodic boundary, minimum image and cut-off distances we made our simulation boxes and simulations system ore tractable and more practical. Now in the next lecture we will see how we generate new confirmation of the protein or how we starting from one distribution of the particles might restrict, how we generate another set of distribution of same particles in the sense how to generate the microstates starting form one microstates to several microstates in the molecular dynamics simulation.