Advanced Thermodynamics and Molecular Simulations

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Lecture – 58
Case Studies

Hello all of you. So, in the last lecture we discussed the mesoscale simulation methods, which are the methods aimed at working with longer length and time scales than typically possible in standard molecular dynamics or Monte Carlo simulations particularly for atomic systems and today I will discuss some of the case studies of the mesoscale methods, that has taken from my own research of course, you can find many more elaborate studies on these methods but I picked the ones that I have worked with.

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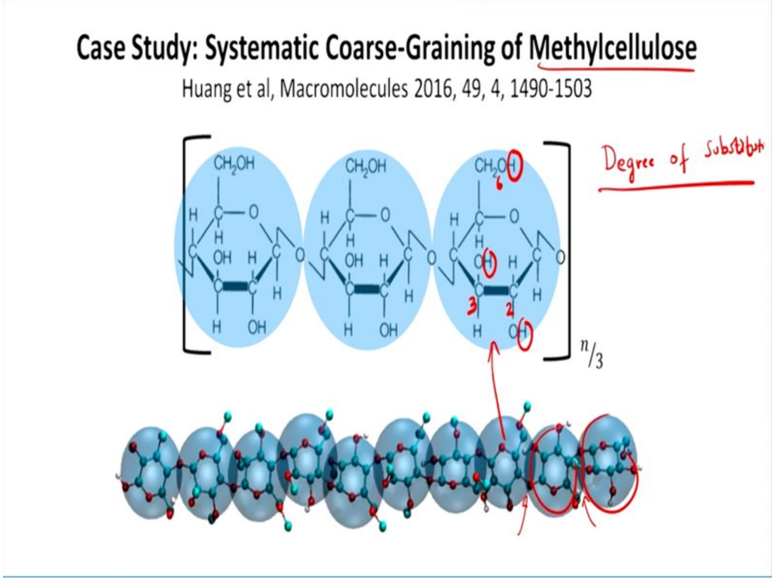

Case Study: Systematic Coarse-Graining of Methylcellulose

Huang et al, Macromolecules 2016, 49, 4, 1490-1503

So, the first study I will discuss is for systematic coarse graining of the methylcellulose molecule and the reason why we wanted to do a systematic coarse grain simulation in this case, is because we of course did atomistic simulations but they were limited to very small molecular weights. The polymers that we wanted to simulate were having much larger molecular weights than compared to the ones we were simulating and the second thing is that we wanted to simulate the aggregation behavior of these molecules because the methylcellulose tends to form gels at higher temperature we were interested in trying to capture that not only at a qualitative level, but also at a quantitative level because we wanted to predict the behaviour of methylcellulose molecules.

So in particular we are interested in what role the amount of the methyl groups on the polymer chain has on the aggregation behavior and look at the amine amount of the methyl group. There is a characteristic called the degree of substitution. So, every repeat unit of the methylcellulose contains three positions where a methyl group can come in. So, what I am showing here is the backbone of cellulose molecule as drawn and there are three sides where the hydrogen can be replaced by a methyl group. So, this is referred as 2, 3 and 6 sides so clearly the six is outside the ring and two and three are attached to the ring.

Now the degree of substitution is defined as the number of the methyl group per repeat unit. So, clearly for every repeat unit, you can have zero methyl group, one methyl group, two or three in the case of three your occupying all the sides. In the case of two you can have two three methylcellulose that will occupy second and third side or 3 6 or 2 6 or you can have a single occupation in that case will have a two-methyl cellulose, three methyl cellulose, six methyl cellulose.

In general, we are not interested in the situation at a particular repeat unit, but an average value that is defined over all the repeat units and that is how the classification of methyl cellulose is typically done. So, the average substitution can vary from again from zero to three and what we are interested in is knowing that whether substitution at any particular side whether it is two three or six has a behaviour different from that on the other side, that is the first part and how much substitution has the; characteristics of giving me the aggregation behavior or gelation behaviour that we demand or as opposite of that what is the gelation behaviour coming from what is the corresponding degree of substitution or in the there.

So, we can want to predict the relation between the degree of substitution of the polymer chain with their gelation behaviour and aggregation behaviour and of course, you want to look at the behaviour of polymer molecules themselves. So, the way we did that since the objective was to really simulate as long polymers as possible, we did somewhat aggressive coarse graining and we said we will represent every repeat unit as one coarse grain entity.

So, we have around 20 atoms in every repeat unit and that becomes one coarse grain entity in our simulation of course, the coarse grain entities are mutually exclusive there are no atoms in common although I have drawn in here as them overlapping but there are no atoms in common. So, these are basically my repeat units which are represented using one coarse grain unit so, you basically perform both atomistic simulations and coarse grain simulations.

In the cases of low molecular weight when we can do both we use atomistic simulations to train the coarse grain model or parameterize the coarse grain model and in cases where we cannot do atomistic simulations, we use the already trained coarse grain model to simulate the behaviour for longer molecular weights.

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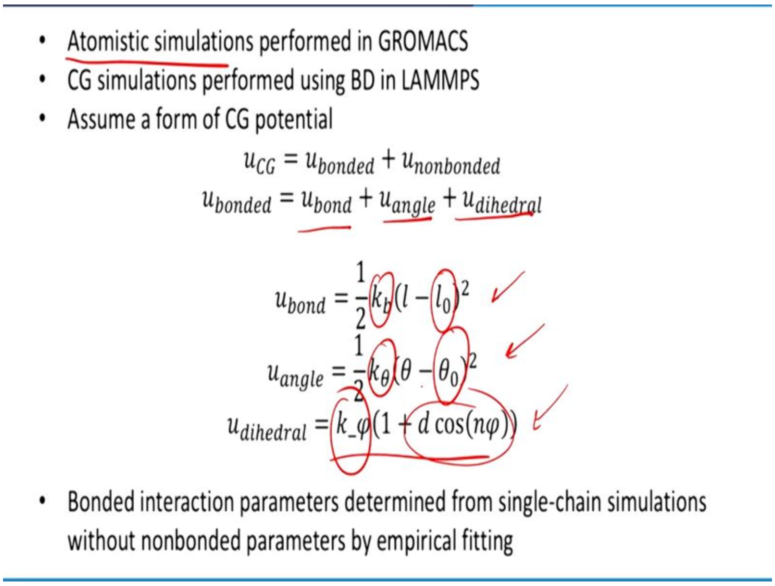

- Atomistic simulations performed in GROMACS
- CG simulations performed using BD in LAMMPS
- Assume a form of CG potential

$$u_{CG} = u_{bonded} + u_{nonbonded}$$
$$u_{bonded} = u_{bond} + u_{angle} + u_{dihedral}$$

$$u_{bond} = \frac{1}{2}k_b(l - l_0)^2$$
$$u_{angle} = \frac{1}{2}k_\theta(\theta - \theta_0)^2$$
$$u_{dihedral} = k\_\varphi(1 + d\cos(n\varphi))$$

- Bonded interaction parameters determined from single-chain simulations without nonbonded parameters by empirical fitting

So, with this kind of a motivation what we did was the atomistic simulation was performed in Gromacs. I will not go in details of the force fields and all that they are in the paper that is effort to hear. The coarse grain simulations of performing dynamics in labs. We start with assuming a form of the coarse grain potential that includes a bonded interaction and unbonded interaction. The bonded part is comprised of a bond interaction and angle interaction and dihedral interaction and we assume some very simple form of these interactions-

$$u_{bond} = \frac{1}{2}k_b(l - l_0)^2$$

$$u_{angle} = \frac{1}{2}k_\theta(\theta - \theta_0)^2$$

k_b and k_θ are the strength of the bond and angle respectively, l_0 and θ_0 are the equilibrium bond distance and the equilibrium angle in the system. Similarly, we have a dihedral interaction where k_Φ is a measure of the strength and this term represents the phase of the dihedral.

$$u_{dihedral} = k_\phi(1 + d\cos(n\phi))$$

So, for the bounded interaction part we perform the single chain simulations both in atomistic and coarse grain simulation and basically, we fit the coarse grain simulation to atomistic simulation by performing a variation of parameters in the coarse grain simulation. I want to emphasize here that since our model is very simplistic, we have actually used fewer number of CG units because every 20 atom that we have roughly in every repeat unit is considered as one CG unit. The stimulation in CG model is pretty quick and therefore we can perform many-many of these simulations in relatively less time and that is how we can basically fit atomistic results by performing many coarse grains simulations, but fewer atomistic simulations.

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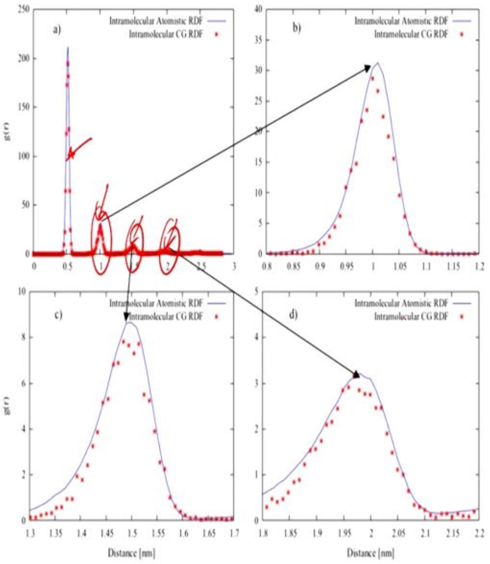

So, this is one example of the property that we computed to compare against. So, we are here comparing the radial distribution function of the atomistic and coarse grain simulation what you see is that the blue line is coming from the atomistic simulation and the red dots are coming from the coarse grain simulation. And you see that agreement is pretty good it is capturing not only the height of the peak, but almost every peak that we have in the simulation. These peaks which are rather small here are also zoomed in and you can see the agreement is pretty good over all the peaks that we care about, more importantly I would like to emphasize here that it is not that we started with this model to begin with because whenever you have any coarse grain problem, you do not have any starting point for the interaction model unless you are getting it from potential of mean force.

So, one has to think the other way around and start with the model containing minimum possible number of parameters and try to see how much of the physics that we have gained and if further details are needed then only more terms are added. So, first, for example, we had only bond parameters and then we saw how the radial distribution function is being matched then on the basis of that you figured that maybe we also need an angle interaction. Once we have done the angle part then we thought that something else is still lacking and we can add the dihedral and so on.

So, at every step of the coarse graining procedure or the model building the coarse grain model we have to, as a rule always think that what is the minimum set of parameters that we have will have the same representation of the behaviour that we really want, we are not really concerned on building a coarse grain model. That can exactly reproduce every possible result in atomistic simulation because that would be as I was telling the last class will be same as the atomistic model that is every atom which is CG unit.

So, clearly the goal is not to have something that is more accurate, but the goal is to have something that is reasonably accurate yet efficient and that was the I would say the objective behind our coarse grain simulation because we wanted to really extend it to longer molecular weight change to something that would not only capture the behaviour of atomistic simulations, but can also be applied to long chain simulations.

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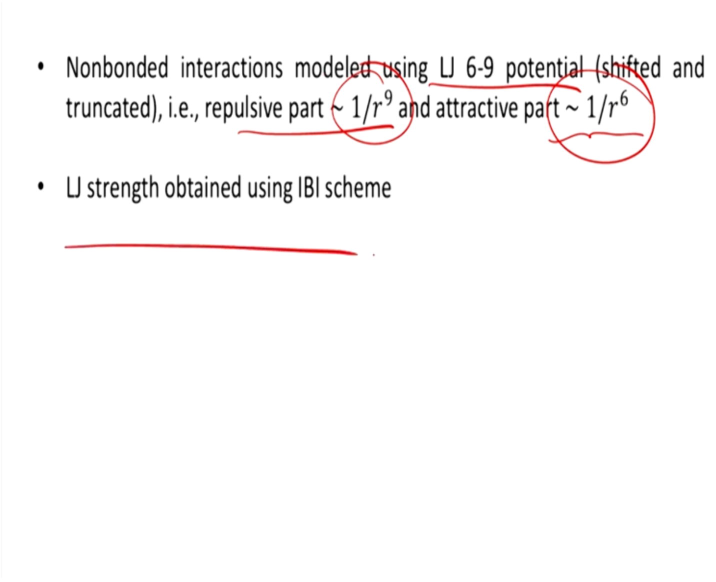

- Nonbonded interactions modeled using LJ 6-9 potential (shifted and truncated), i.e., repulsive part ~ $1/r^9$ and attractive part ~ $1/r^6$
- LJ strength obtained using IBI scheme

So, next we move to looking at the Non-bonded interactions. So, we model that using the Lennard Jones 6-9 potential. That contains the repulsive part going like one over r^9. What we had discussed earlier had the repulsive part like 1 over r^{12}, of course we had tried that, but we figured that maybe this will be better than that in terms of accuracy. The attractive part is the same as earlier so as I have been telling you earlier, this has really a physical meaning it comes from the theory of the of the Vander Waal interaction.

And this point part is kind of arbitrary what basically it characterizes the softness of the particles in the picture. The higher powers we go it becomes more and more hard but we figure that keeping it nine gave us the fit that was desired. Again, there is no particular reason why we cannot think of any other portable fit so there is no unique mapping when we think of a coarse grain model, it is only one of the possible coarse grain model that we could have built.

And finally, the strength of the Lennard Jones interaction while obtained using that iterative Boltzmann involves a scheme. That is, we took the atomistic simulation RDF as the target and we varied the parameters in this case the Lennard Jones parameter to fit the atomistic solution RDF but in this case, we are looking at the radial distribution function of the multiple chain system as opposed to the single chain system, because for single chain system we have already used that to get the bonded parameters.

So, now we perform simulations of a multiple chains and look at intermolecular radial distribution function. And we fit that using the iterative Boltzmann inverse on the scheme and get the fitting parameter as the Lennard Jones interaction strength and this is what it looks like.

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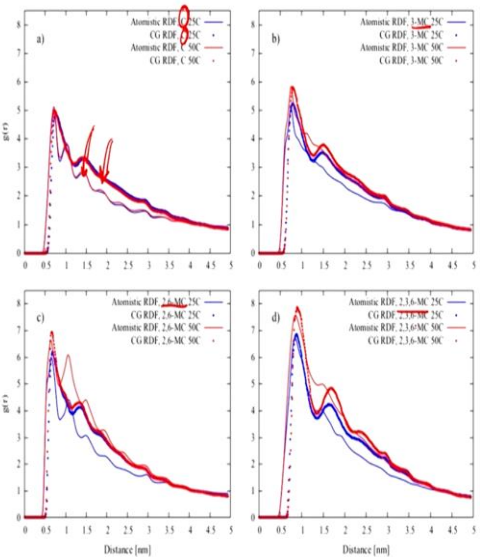

And I am doing it for two different temperatures again because I was interested in the aggregation behaviour and gelation behaviour. And in this case the behaviour is different at different temperature. So, therefore, it performs simulations at two different temperatures. And clearly you cannot you see this red and blue lines are basically data from atomistic simulations and coarse grain simulations so these are for two different temperatures that is 25 degrees Celsius and 50 degree Celsius. We have done it for a variety of chemistries, so C refers to cellulose, 3 MC is 3 methyl cellulose with methyl being at three positions. 2 6 is for 2 6 position and it is a homo polymer containing the same repeat units. And 2 3 6 where all the; positions are occupied by the methyl group and agreement across all the chemistry is quite reasonable between the atomistic and coarse grain model so we can be confident that the aggregation behaviour will be captured by the coarse grain model that we built.

This also can be seen by looking at this snapshot of atomistic and coarse grain simulations for the systems for which we can do both atomistic and coarse grain simulates, that means smaller molecular weight polymers and you see from the snapshots that the aggregation behaviour is quite similar between different chemistries that we had simulated.

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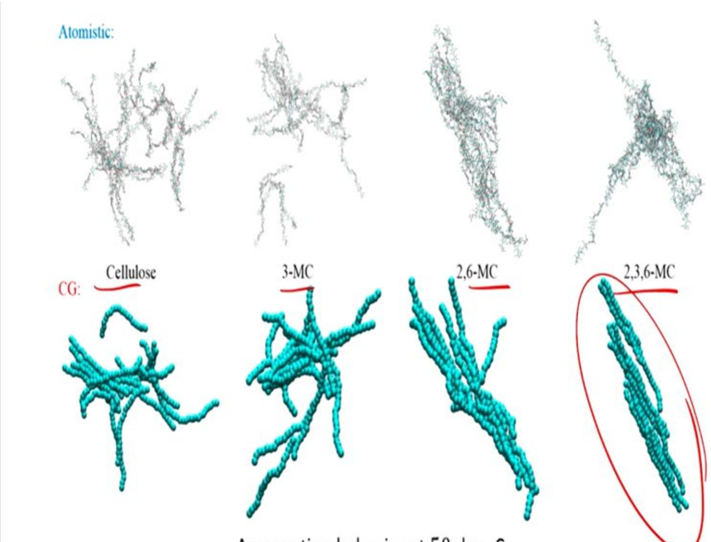

Aggregation behavior at 50 deg. C

Let us say when we go from cellulose to 3 methyl cellulose to 2, 6 and 2, 3, 6 clearly as we increase the methyl groups the aggregation should enhance because the polymer becomes more and more hydrophobic and eventually it should form kind of formation of I would say tight aggregates or packed aggregates and this is what is indeed scene both in atomistic simulations and coarse grains.

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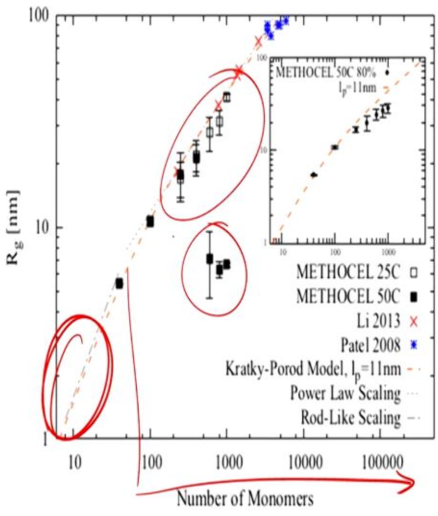

Radius of Gyration

Finally, we looked at the radius of gyration of the individual chains and this is where the strength of the systematic coarse graining starts showing up because I am now probing to much longer chains than we can possibly simulate using atomistic simulation. Atomistic simulation is down here, this is all we can do and under that regime the polymer is what is known as a Kratky Pored polymer that is in the rod like regime. It is something that we should not even call a polymer because it is not flexible enough only when the molecular weights are beyond certain things, certain number of monomers around say 50 or 60 monomers in this case, the flexible nature is start showing up and beyond that point we cannot clearly do the atomistic simulations, but we can always do the coarse grain simulations and the agreement generally was pretty good between the available experimental data and the simulations we conducted of course, there were couple of outliers at higher temperatures and we had attributed this to some sort of a ring formation that we see in our model. But that also has experimental significance again I will not going details here.

The main point is that the systematic coarse graining is able to really push the length and length scales that we can simulate to a level, where we can make quantitative predictions even for much realistic systems and in this case of polymers, I think this is one of the only possible ways to go about because clearly, we cannot simulate very large molecule already long molecular weight

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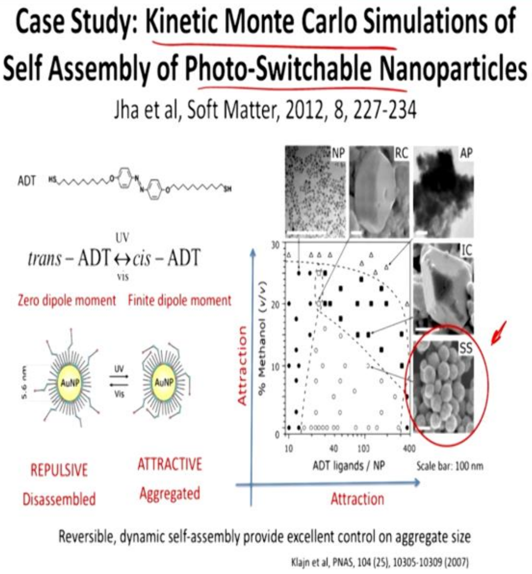

Case Study: Kinetic Monte Carlo Simulations of Self Assembly of Photo-Switchable Nanoparticles

Jha et al, Soft Matter, 2012, 8, 227-234

$trans-\mathrm{ADT}\overset{\mathrm{UV}}{\underset{\mathrm{vis}}{\leftrightarrow}}cis-\mathrm{ADT}$

Reversible, dynamic self-assembly provide excellent control on aggregate size

Klajn et al, PNAS, 104 (25), 10305-10309 (2007)

hts.

The next case study that I will discuss is a kinetic Monte Carlo simulations. As I have said, this is very similar to the Brownian dynamic simulations except that we are doing in the Monte

Carlo fashion and we associate every Monte Carlo step to certain time step. In this case, we are interested in looking at the self-assembly of Photo Switchable Nanoparticles. So, these are fancy nanoparticles which have certain ligands on them which respond to light.

So, when you for example, turn on the UV light the ligands change configuration, and they can become assistors or they can come back to transistors when they are when the light is turned off. So, we can go from a transistor to state by turning on or off the UV light.

Now what is the interesting part of it is when it is in the transistors these ligands on the surface of the nanoparticle have zero dipole movement, dipole movement of the molecule cancels out. So, between the two nanoparticles in the system or anything particle in the system, we have no dipole-dipole attraction because the ligands have no dipole movement.

On the other hand, when they are in the cis state then they have a dipole movement. And therefore, we have an attraction between Nano particles because of the dipole dipole attraction. So, what we can then have is a system containing a nanoparticle whose interactions can be turned on and off or can be tuned by exposing them to light of different view lens. And this is precisely what they have done in this particular study, where they have varied the number of ligands and the nanoparticle, they have varied the solvent and so on, they looked at that how this they nanoparticles self-assemble in response to the light and when do we have the cases where we have a clear reversible transition between aggregate to a dissolved solution.

So, with this kind of motivation again the system was large enough for applicability of any atomistic simulation nanoparticles pretty much have size of the order of like five nanometers. That will have plenty of molecules and we are not looking at one particular nanoparticles of course, they have plenty of ligands on top of them. They contain plenty of atoms and the system itself contains, I would say moles or very large number of the molecules in the system.

So, clearly atomistic simulation is not the way to go accept if we are interested in things happening near the surface of the nanoparticle, if you want to look at the aggregation behaviour, we have to go for the coarse grain model and in this case, we are not interested in actually predicting the experimental data. But we wanted to make qualitative predictions and therefore we used a generic coarse grain model.

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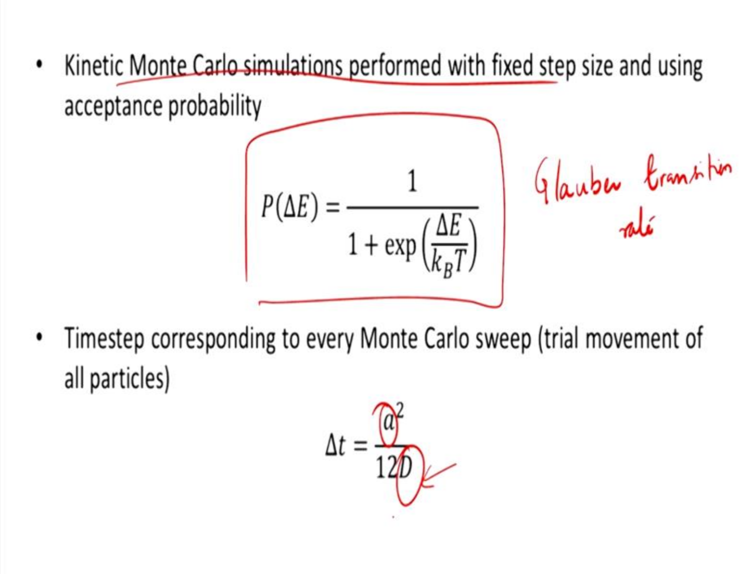

- Kinetic Monte Carlo simulations performed with fixed step size and using acceptance probability

$$\boxed{P(\Delta E) = \frac{1}{1+\exp\left(\frac{\Delta E}{k_B T}\right)}}$$

Glauber transition rate

- Timestep corresponding to every Monte Carlo sweep (trial movement of all particles)

$$\Delta t = \frac{a^2}{12D}$$

So, the kinetic Monte Carlo simulations were performed in a similar manner that we have discussed earlier. We had a fixed step size but we did not use the metropolis criteria we used a slightly different criteria it is referred as the Glauber Transition rate.

$$P(\Delta E) = \frac{1}{1+\exp\left(\frac{\Delta E}{k_B T}\right)}$$

And in fact, we showed that using this particular definition of transition rate we can pretty much recover the diffusion equation or this pretty much is same as solving diffusion equations that is same as bonding dynamics and provides a clear mapping between the bonding dynamics or diffusion equation by doing a Monte Carlo simulation. And the timestep compared to every Monte Carlo sweep that is when I try movement of all the particles in the system is something very given by this-

$$\Delta t = \frac{a^2}{12D}$$

where a is my step size and D is my diffusion coefficient. In here again D is taken constant here one may argue that D need not be constant but in this case the idea was to get more a qualitative behaviour then making any actual quantity predictions and that respect the model was pretty good.

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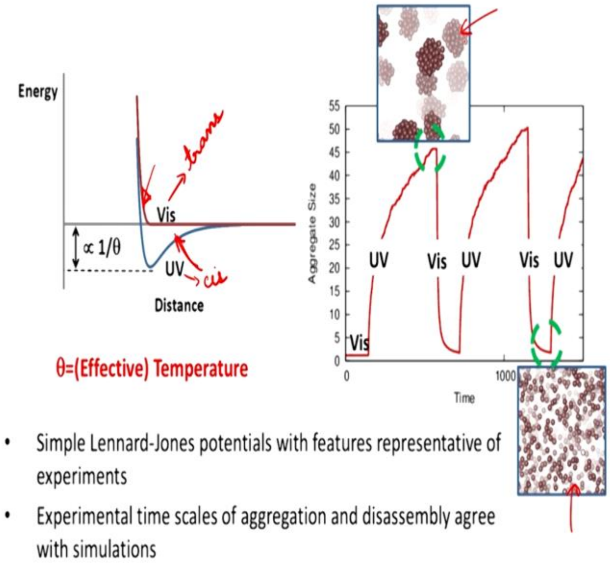

θ=(Effective) Temperature

- Simple Lennard-Jones potentials with features representative of experiments
- Experimental time scales of aggregation and disassembly agree with simulations

So, we looked at variety of things. First of all, we looked at the effect of temperature on the system and we looked at how what will happen when I go from UV state to a visible state and the way we modelled that was using very simple Lennard Jones interaction.

So, we used a Lennard Jones interaction with an attraction part when we were doing the UV light and we used Lennard Jones interaction with no attraction part. The repulsive part is common in both, but attraction was not there when we are doing the visible light. So, UV will correspond to the case when we have Cis ligand and Vis will correspond to the case when we will have the trans ligand.

Now clearly this is done in a manner that we can change the interaction between an, ongoing simulations. So, we can pretty much run cycles of UV and visible light and within a cycle we can have some interaction that is given for that cycle and in the next cycle we can have some other interactions, we run it in cycles.

In the cycle of UV light, we used the Lennard Jones with a fraction part and in the cycle of visible light we used the Lennard Jones with the only the repulsive part and we performed many cycles to look at the effect of the periodic exposure of light to this particular system and clearly, we see that as the UV light is turned on the nanoparticles begin to aggregate and as the UV light is turned off the nanoparticles begin to dissolve and that must be seen.

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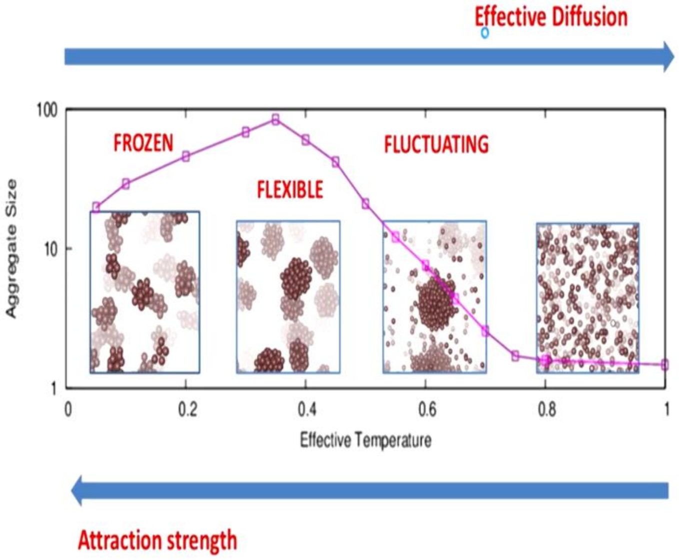

So, this is the condition when the visible light is turned on for some time, because clearly aggregate will take some time to dissolve. So, if we give it enough time, it will become solution. On the other hand, if I keep it in UV light for enough time it will form an aggregate we can also look at this as a function of the density of the non-particle system and clearly, we can have a transition between various possible states.

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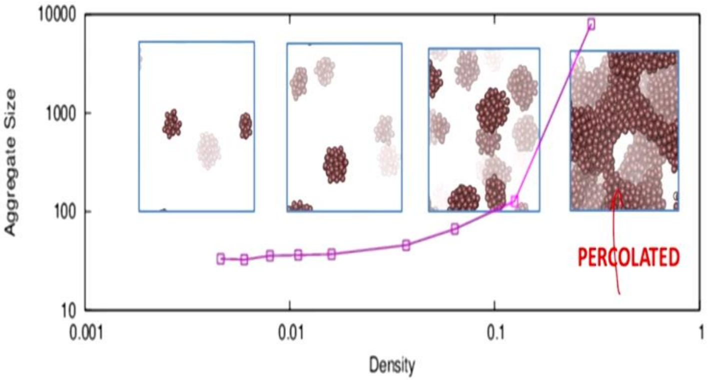

- Aggregate size increases with increase in density
- Percolated "gel" structure at high density

So, this is the effect of intensity here, so as we go to higher density, we can form larger and larger aggregate. And eventually for very large aggregate we can form some kind of percolated structure in the system. So, in general the aggregate size with increased with the increase in density and gel structure will form at higher density in the system we can also characterize the structure in a variety of ways so we can have the measure such as the evidence number density of the particles and the poly dispersity of the entire system and we can see how the aggregate size changes as a function of the parameter.

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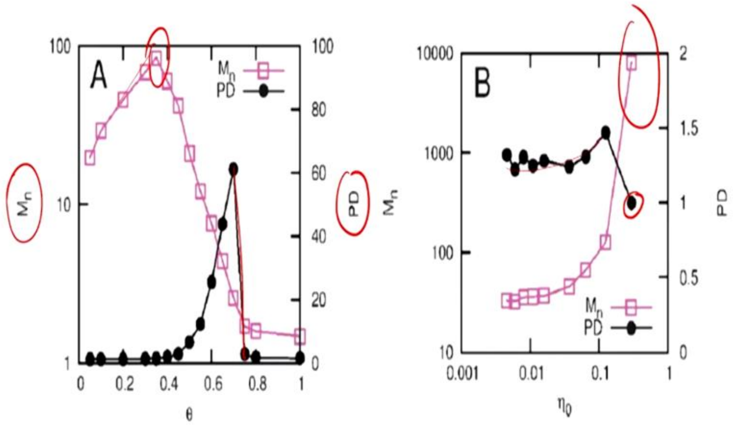

So, for example with increasing θ the aggregate size increases followed by a decrease at large theta value. Now to look at the particular factor we can look at what really happens with θ here.

So, what is happening here is at very small value of θ we have strong interaction between the particles and in that case once the two relevant particles come together, they form an aggregate. But then these aggregates which are formed they move rather slowly and find other aggregates that means many of them moves in the Monte Carlo simulation get rejected as soon as one aggregate is formed, because they are bound to strongly with the other nanoparticle as we increase the temperature the interactions between the non-particles weakens.

Now the aggregate is still form what the aggregate may merge with other aggregate more easily because the bound is not to strong, the particle can move out and form bond with some other aggregator. I am talking about physical bond as opposed to any kind of chemical bond. So; therefore although it is not quite intuitive the largest aggregate size is actually found when we are at intermediate value of temperature not at very low temperature although the strength of the interaction is very strong at low temperature, it does not give me a large aggregate size because once they form these small aggregates, they do not further evolve because they diffuse rather slowly after formation of this that happens because of the strong inter-particle interaction that prevents the movement of the nanoparticles.

At very high temperature as you may expect, you will have a solution because there is no interaction pretty much or very small interaction. In this case the entropy will dominate and the particle would like to be dissolved in the solution this precisely what we see here and this is the behaviour. We also get here that the average aggregate size increases with temperature first followed by a decrease at very last temperature where the interaction is strength becomes much smaller in comparison to the thermal energy of the system you can also characterize the poly dispersity and it is shown in here. And as you may expect poly dispersity is highest at intermediate values of θ. And that happens because that is when we have multiple aggregates in the system and once, we have multiple aggregates that will give rise to higher polydispersity.

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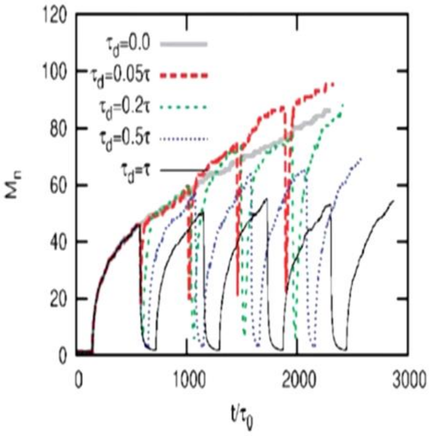

We can also look at the effect of density and again we can see since I was talking about formation of a percolator structure, this is where we see that the aggregate size actually increases significantly at very high density and that is when we have the formation of percolated structure and the same time the poly dispersity actually comes down because once we have the probability structure then we have pretty much a single large aggregate is spanning the entire simulation box and that has a polydispersity of one, because you do not have a aggregates of different size in the system.

The polydispersity in this case represents the variation in the size of the aggregate. Once it forms like a percolated structure, you have only one aggregate in the system and therefore, poly dispersity first increases, but then decrease to one. We also look at other things such as what will happen if I do not turn off the interaction immediately, but we turn off at a certain rate that means the interactions will be slowly brought down to from UV to visible interaction and that was the purpose of this was that the nanoparticles appear to have some memory. So, they will take some time for losing their dipole movement and this effect will also captured in our simulations.

The key idea that I wanted you to take from this example is that we can study a variety of systems using the molecular simulations depending on the requirements, we should become model. If our objective is to understand the physics behind the process, then we can pick a generic course grain model and with other inexpensive simulations we can look at the physics behind it. On the other hand, if we really want to be quantitative if you want to compare to experiments then we have to go to either atomistic simulations where ever possible and systematic coarse grains simulations wherever it is, not possible and then as we had discussed we have methods to tackle the free energy calculations and other methods to look at we are events and so on that can be applied as appropriate.

So, we should not think in terms of the method first and application next what you should think in terms of application first and then choose a method appropriate for the problem that would be computationally feasible with whatever goals that we have in mind and in most cases simpler models are much better than more complicated models because simpler models can be first of all easily run and coded and secondly, they are like able to capture the qualitative behaviour without the need for running over many parameters because simpler models also have fewer number of parameters to work with.

So, it always better to start with simple models and then refine it as a post to starting with the complicated model and get lost with the number of parameters that you have in the system. But there is no hard and fast to do on that but you always should have the application in your mind.

So, with that, I want to conclude todays lecture, thank you.