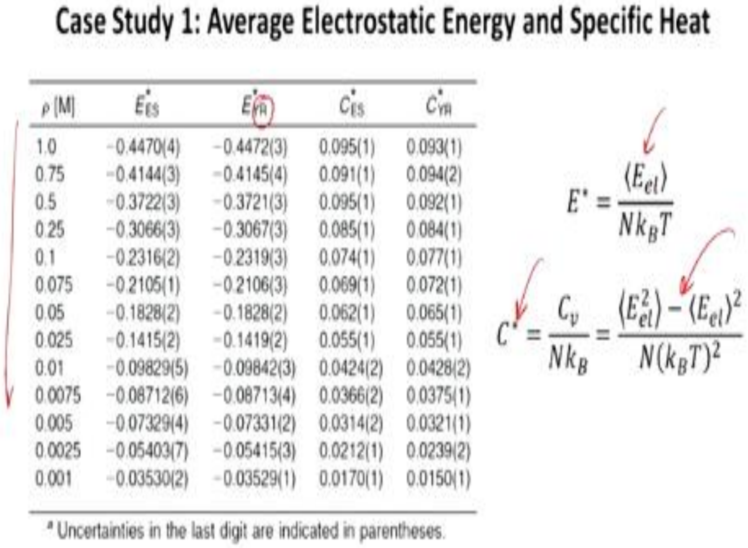
Advanced Thermodynamics and Molecular Simulations

Prof. Prateek Kumar Jha
Department of Chemical Engineering
Indian Institute of Technology, Roorkee

Lecture - 49
MD Simulations – Case Studies II

Hello all of you, so in the last class we have been discussing this example of MD Simulations of Electrolytes. We already have defined what the system is? What the interactions are? And how we have done the benchmark studies, so today I will directly proceed to the results of these particular simulations.

(Refer Slide Time: 01:03)



Case Study 1: Average Electrostatic Energy and Specific Heat

ρ [M]	E^*_{ES}	E^*_{YR}	C^*_{ES}	C^*_{YR}
1.0	−0.4470(4)	−0.4472(3)	0.095(1)	0.093(1)
0.75	−0.4144(3)	−0.4145(4)	0.091(1)	0.094(2)
0.5	−0.3722(3)	−0.3721(3)	0.095(1)	0.092(1)
0.25	−0.3066(3)	−0.3067(3)	0.085(1)	0.084(1)
0.1	−0.2316(2)	−0.2319(3)	0.074(1)	0.077(1)
0.075	−0.2105(1)	−0.2106(3)	0.069(1)	0.072(1)
0.05	−0.1828(2)	−0.1828(2)	0.062(1)	0.065(1)
0.025	−0.1415(2)	−0.1419(2)	0.055(1)	0.055(1)
0.01	−0.09829(5)	−0.09842(3)	0.0424(2)	0.0428(2)
0.0075	−0.08712(6)	−0.08713(4)	0.0366(2)	0.0375(1)
0.005	−0.07329(4)	−0.07331(2)	0.0314(2)	0.0321(1)
0.0025	−0.05403(7)	−0.05415(3)	0.0212(1)	0.0239(2)
0.001	−0.03530(2)	−0.03529(1)	0.0170(1)	0.0150(1)

[a] Uncertainties in the last digit are indicated in parentheses.

$$E^* = \frac{\langle E_{el} \rangle}{N k_B T}$$

$$C^* = \frac{C_v}{N k_B} = \frac{\langle E_{el}^2 \rangle - \langle E_{el} \rangle^2}{N (k_B T)^2}$$

So, the first thing that we computed is we computed the average Electrostatic Energy of the system so we leave aside the repulsive Lennard Jones part we only compute the electrostatic energy and take an average over many, many trajectories as we do as we have discussed earlier. So, this quantity E* is therefore the average of the electrostatic energy of the entire system divided by the thermal energy $k_B T$ and the number of particles in the system.

$$E^* = \frac{\langle E_{el} \rangle}{N k_B T}$$

And we also compute the specific heat that is defined as the fluctuation in the electrostatic energy and we again put that into dimensionless units like C_v by Nk_B and defined as the squared of el average minus average el square divided by the number of particles and k_B T square.

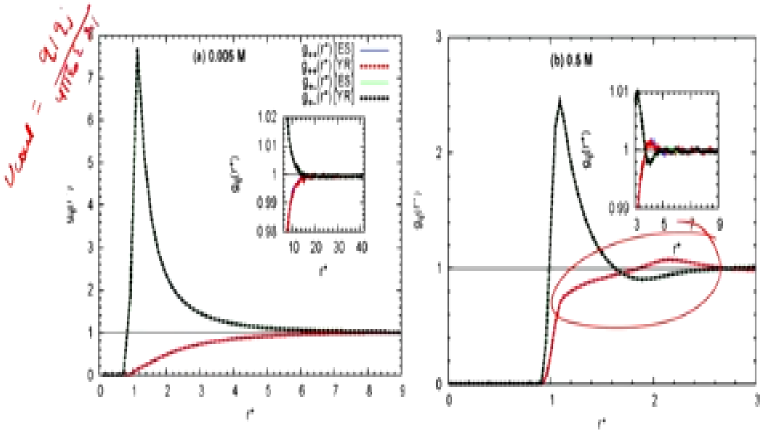
$$C^* = \frac{C_v}{Nk_B} = \frac{\langle E_{el}^2\rangle - \langle E_{el}\rangle^2}{N(k_BT)^2}$$

And we have done it for a whole range of concentrations of Electrolytes where concentration is defined as in molars of the salt and since the objective of the work was to compare the performance of and accuracy of the Ewald Summation and the Yakub Ranchi scheme particularly the YR scheme that was being implemented, we had compared the values between these two simulations and we found reasonable agreement over a range of the ρ values.

So, this gives me a confidence that the method is capturing the Energetics pretty well whatever approximation we have made in the YR method is not resulting in significant departures from the energy we obtain or specific heat we obtain in the Ewald summation method and in fact it is a very good test because on one hand the energy is an average measure but a specific heat is a measure of the fluctuations. So, if a method is able to capture both the average and fluctuations pretty well we can rest assured that the method will be worth working with because this is the quantity that we are typically interested in we are interested in the average and interested in the fluctuation of the energy values.

(Refer Slide Time: 03:28)

Case Study 1: Liquid Structure for 2:2 electrolyte using Radial Distribution Functions



So, the next thing that we do we started analyzing the structure of the electrolyte solutions using the radial distribution function. Now since we have two species that is plus and minus we have four possible pairs of the radial distribution function. We can have g_{++} we can have a g_{+-} these two pairs and two for the two schemes so in total we have four combinations two each for each of these schemes. And what we can see pretty much is you can pretty much see no difference between the results of Ewald Summation and Yakub Ranchi scheme and more importantly what you see is the like charges which are represented by the red thing here expose a repulsion and why do we say it is a repulsion because the g values are less than 1.

On the other hand the unlike charges that is the black thing here shows an attraction because the g values happen to exceed 1, g equal to 1 is the case when we have an ideal gas. So, anything higher than that roughly speaking is an attraction anything less than that roughly speaking is the repulsion the reason why I say roughly speaking is not completely true and we discuss some cases later when I discuss atomistic simulations but it is generally valid that whenever the g of r exceeds 1 or whenever we have a peak in g of r we can see that there is some attraction going on. If there is no peak and if the values are always less than 1 that means simply repulsion between the particles.

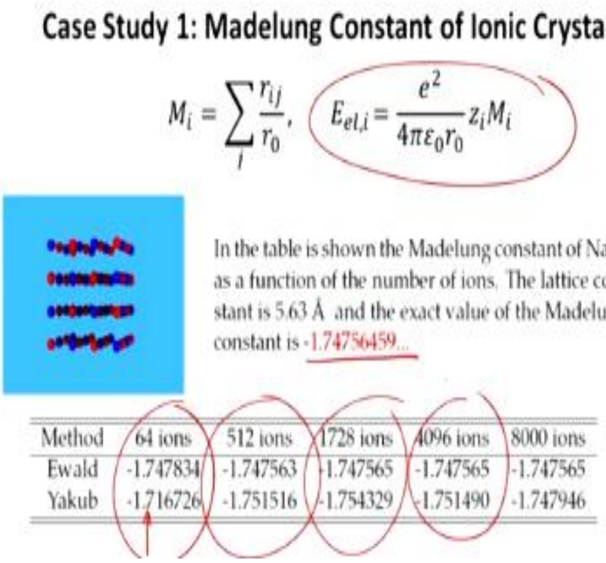
Then we also look at the effect of the concentration. So, clearly you may expect as we increase the concentration of the salt the structure is going to be different because the dilute solution of salt and dense solution of salt will have to have some signature of the density of the solute. And that signature comes in the g of r because g of r is a measure of liquid structure and you can see that coming in this part of the picture first of all you have a small peak now. When I am doing at high concentration and that small peak appears because the concentration is high so some like charge species have to be close to each other because the concentration is high so simply because you have larger number of particles of both plus in the system.

So, you see a small peak but that peak is anyway lesser in magnitude to the unlike charge peak but then what you see somewhere over here is a very interesting phenomena and I will not go in details here what I want you to focus on is the difference between this picture and this picture. In theory of charge system, there is a theory of double layers and this can be explained by that I will not go in details here, but the key point I want to emphasize is that there are significant effects of concentration that are seen when I look at the g of r of the system.

Similarly I can look at the effect of valency so you can see for example repeat the same stuff for a 2 is to 2 electrolyte that is when the valency of both plus and minus is 2 as opposed to both being 1 in this case and now if I compare these cases they will have different structure than compared to the ones to one case especially at higher concentrations. So, as we go to higher concentrations as we increase the valency there are significant changes in structure simply because there is a stronger interaction once we have a two is two electrolyte because my Columbic Interaction is given as-

$$U_{coloumb} = \frac{q_i q_j}{4\pi\varepsilon_0 \varepsilon\, r_{ij}}$$

(Refer Slide Time: 08:29)



Case Study 1: Madelung Constant of Ionic Crystal

$$M_i = \sum_j \frac{r_{ij}}{r_0}, \quad \boxed{E_{el,i} = \frac{e^2}{4\pi\varepsilon_0 r_0} z_i M_i}$$

In the table is shown the Madelung constant of NaCl as a function of the number of ions. The lattice constant is 5.63 Å and the exact value of the Madelung constant is -1.74756459...

Method	64 ions	512 ions	1728 ions	4096 ions	8000 ions
Ewald	-1.747834	-1.747563	-1.747565	-1.747565	-1.747565
Yakub	-1.716726	-1.751516	-1.754329	-1.751490	-1.747946

So, the next thing that we did is there is something called a Madelung Constant that is defined for an Ionic Crystal and the Madelung Constant can be used to define the energy of an Ionic Crystal. So, what we did we prepared an Ionic Crystal so now we are not doing the liquid phase as I have been doing earlier, now you prepare a crystal of the plus and minus ions and we compute the energy and using the energy that is the electrostatic part of the energy I can compute the Madelung constant that is defined using this particular relation and there are values in literature of the Madelung Constant and this is the particular value.

$$M_i = \sum_j \frac{r_{ij}}{r_0}$$

$$E_{el,i} = \frac{e^2}{4\pi\varepsilon_0 r_0} z_i M_i$$

So, the next thing that we did is there is something called a Madelung Constant that is defined for an Ionic Crystal and the Madelung Constant can be used to define the energy of an Ionic Crystal. So, what we did we prepared an Ionic Crystal so now we are not doing the liquid phase

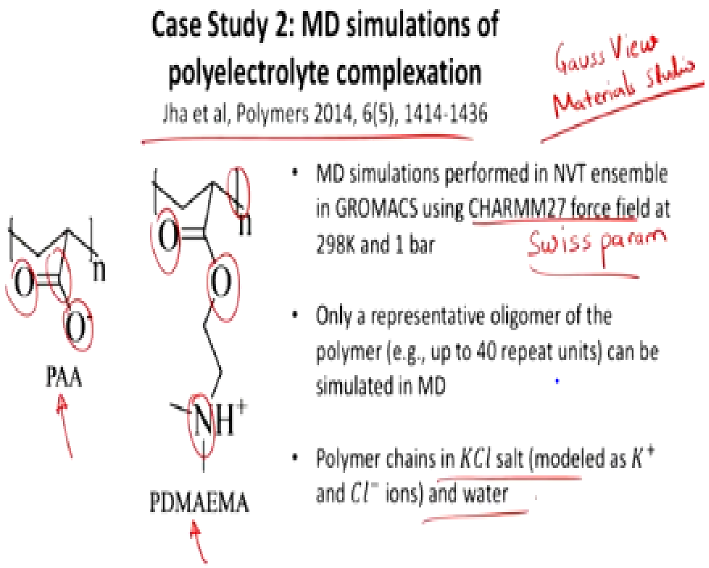
as I have been doing earlier, now you prepare a crystal of the plus and minus ions and we compute the energy and using the energy that is the electrostatic part of the energy I can compute the Madelung constant that is defined using this particular relation and there are values in literature of the Madelung Constant and this is the particular value.

And the goal was that whether I can get or to produce the same value by doing our simulations, because this would be a second check of our method. The first check was we were comparing to the Ewald Summation and the second check is we will be comparing to a literature data that can be coming from some theory.

So, what we find is the agreement is pretty good in fact only with like 64 ions we are getting the first decimal right but the second decimal is not right, if I increase to 512 we get until like two decimals correct and as I go to like 1728 or 4096 we get slightly closer, although the Ewald Summation still remains better than the Yakub Ranchi scheme and the reason why this happens is because of the assumption that we have made in the Yakub Ranchi scheme. So, there are differences when I look at the Madelung Constant so therefore for stimulation of crystals it is not a good scheme and in fact if you look at it using the idea I have been telling you that we are doing an Isotropic Averaging of the long range part that is done in the fourier space so that isotropic averaging is clearly not going to be accurate when we are looking at ionic crystal because the crystal by itself is not isotropic but that difference that it brings in is not really so large to really discard the Yakub scheme even for the case of the ionic crystal.

So, we now proceed to our next example that is a study of poly electrolyte complexion, so in this case we are again working with plus and minus ions but now they are poly ions that are polymers containing a negative charge and polymer containing a positive charge by the way this is a separate paper from the earlier paper.

(Refer Slide Time: 10:34)



Case Study 2: MD simulations of polyelectrolyte complexation

Jha et al, Polymers 2014, 6(5), 1414-1436

Gauss View

Materials Studio

- MD simulations performed in NVT ensemble in GROMACS using CHARMM27 force field at 298K and 1 bar

Swiss param

- Only a representative oligomer of the polymer (e.g., up to 40 repeat units) can be simulated in MD
- Polymer chains in KCl salt (modeled as K^+ and Cl^- ions) and water

So in this case now we are doing atomistic simulations that include all interactions between all the atoms of my positively charged polymer and the negatively charged polymer. And the particular polymers I am simulating is PAA that is Polyacrylic acid and another polymer known as PDMAEMA. So, now you may imagine as I have been discussing the force fields there would be interaction between every atom of both these molecules with every atom of the same molecule and every atom of the other molecules in the system and all of this is given by the force field, this case we are using the charm 27 force field there is actually a very nice automated tool known as Swiss Param it is available on web that can give you the force field files when you input the molecular structures typically you create the molecular structure in some software we use the software in this case we can use for example Gauss View or you can use software's like Materials Studio. We had used Materials Studio in this particular case, so we will upload the coordinate files in the Swiss Param server it is an online server and it gives me back the force field file that I can use. It only has the charm 27 force field when I used it, there are other automated tools out there that can do its job but then the whole range of molecules over which you can use such tools are pretty limited because those tools are developed for particular class of molecules.

So, in case where the tools are not available there are other ways to develop force fields which is again using literature data but then it requires more manual work of writing parameters into a file or borrowing parameters from different libraries. That is still possible but somewhat more complicated, but in this case we use the swiss param online tool.

The next thing that is important is a polymer is a large molecule and clearly such large molecules cannot be simulated in MD. So, polymers can go to like micron size and what we are doing in MD is like simulation boxes of size like 5 to 10 nanometers or 20 nanometers, so all we can do is only a representative oligomer of the polymer chain. So, let us say for example a polymer has 10000 repeat units we can simulate only like 30 or 40 repeat units of the polymer chain that is not quite a polymer it is defined as an oligomer.

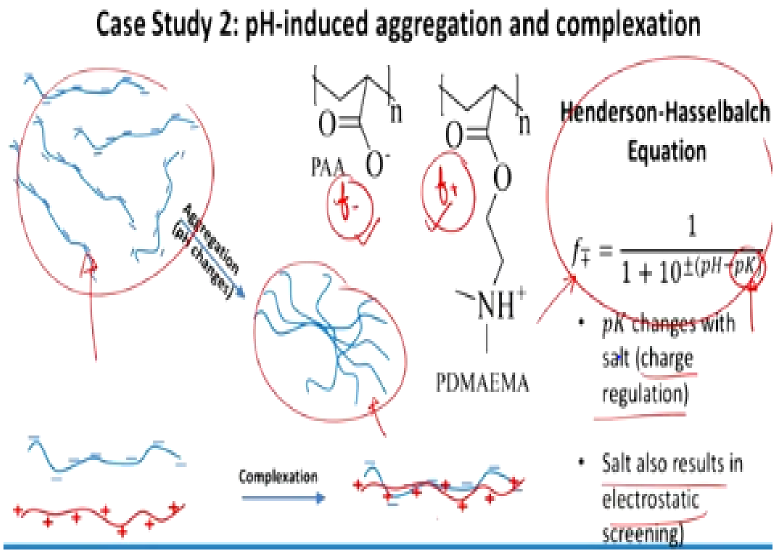
Now clearly that will not have the same molecular structure as the polymer I am trying to simulate but locally speaking it has the same repeat unit and the interaction between atoms as such remains same clearly the conformations of the 40 repeating chain is not going to be the same as a very long chain that is of course more flexible but the local interactions between the atoms are captured pretty well but it remains to be seen how can, we match the results of the 40 repeat units or 20 repeat units or 5 repeat unit's chain to the actual simulations of the longer chains because there is no such study out there because simply it is not possible having said that we can compare our atomistic results to experimental data and although I will not show you the results are not so poor, we do not expect a very good agreement but the qualitative agreement is there and at least the trends are matched quite beautifully.

So, with this kind of outlier this kind of problem in our model we will still simulate Oligomers in this example and the other examples I will discuss but keep in mind that this is a limitation of our MD simulation and we try to do better on that as computers get faster we should be able to do longer polymers and it remains to be seen how the behaviour of the longer polymer simulations would compare with the simulations over a smaller polymer chains.

Now these polymer chains are in a salt solution that is KCl salt, so clearly the salt will be present as potassium ions and chloride ions and in solvent as water. So, the basic physics that happens in this particular problem is the following, so both PAA and PDMAEMA are pH responsive polymers. What this means is the charge on these polymers actually changes as pH changes, in fact there is a equation known as the Henderson Hasselbalch Equation that can be used to find the charge on the polymer as a function of pH and it depends on the strength of the polymer or acidic or basic strength of the polymer that is defined by a quantity called pKA or pKB for the acid or base.

$$Henderson - Hasselbach\ Equation, f+_{-} = \frac{1}{1 + 10+_{-}(pH - pk)}$$

(Refer Slide Time: 15:31)



Case Study 2: pH-induced aggregation and complexation

Henderson-Hasselbalch Equation

$$f_{\mp} = \frac{1}{1 + 10^{\pm(pH - pK)}}$$

- pK changes with salt (charge regulation)
- Salt also results in electrostatic screening)

It turns out that this pKA or pKB that represents the strength of the poly ion in question they change with salt concentration by a phenomena known as charge regulation of course I will not go in details on that as well and in apart from that the presence of salts also results in an screening of electrostatic interactions. Now all of this is not really of too much concern to us because we are doing Atomistic Simulations.

So, simulation should really capture all these effects, having said that doing simulations at constant pH is currently not possible with classical molecular dynamics so therefore what we do is we assume that, the fraction of the negative charges and the fraction of positive charges are constant.

In reality there should be a dynamic protonation, deprotonation process going on but we are assuming that there is no such process happening; The protonation or deprotonation is fixed that means the number of negatively charged groups on the polymer chain remains constant throughout my MD simulation they cannot change. In reality they should change because there should be a protonation deprotonation going on in the polymer chain.

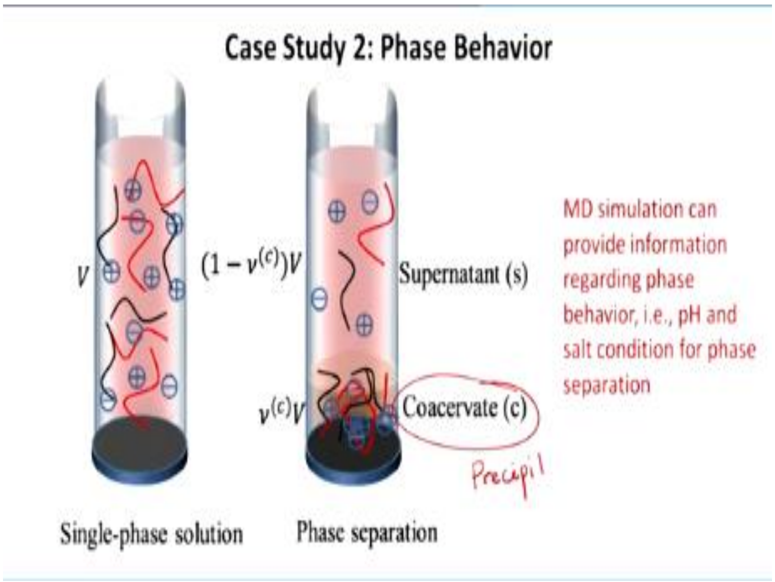
So, having said that we prepare the polymer chains with different charge on them or charge fraction on them that corresponds to the number of negatively charged groups present on the chain or positively charged groups on the chain. And we can do it for different values of these quantities as pH changes and I can evaluate the corresponding value of the fraction using this particular equation, that works great the only problem is that, once we have created certain charge fraction we cannot change that in the course of molecular dynamics you can think of this as since we cannot do chemical reactions we can also not do the protonation deprotonation because that is also kind of a chemical reaction.

So, having said this is what is essentially happening in our simulation is when I am saying I am doing different pH I am simulating with different f - and different f +. Now as that happens the interactions between the polymer chain change because if for example if I am doing in a condition where both the; polymer chains are neutral and compare that to the case when both the polymer chains are charged. So, in one case you will have electrostatic repulsion because the polymer chains are charged if we are looking at the same, charge species between PAA and PAA itself or PDMAEMA and PDMAEMA itself. On the other hand if I look at between PAA and PDMAEMA then in that case there would be an attraction when we work with charge species.

On the other hand when it is neutral there is no electrostatic attraction or repulsion whatsoever. So, therefore we can drive the system from basically a solution like state to some kind of an aggregate with change in pH aggregate will tend to form when we have basically neutral molecules, because they tend if they are Hydrophobic they will come together and form an aggregate. On the other hand solution may form if you have same charge species and they repel each other that is for a system of the same charge. If you have both minus and plus charge species then in that case they can complex together when the fraction of charge in both of them are significantly high because in that case the Coulombic Interaction will dominate and the poly ions will come together of opposite charge.

So, this is the two phenomena that will that can happen here there can be an aggregation at lower pH when the molecules are neutral provided that the molecules are Hydrophobic and there can be a complexation between the molecules of opposite charge provided that both of them are charged that means we are working in the pH where both of them have high value of their fraction of charge. So, this essentially gives rise to the transition of a system from a single phase solution to a phase separated solution.

(Refer Slide Time: 20:54)



Case Study 2: Phase Behavior

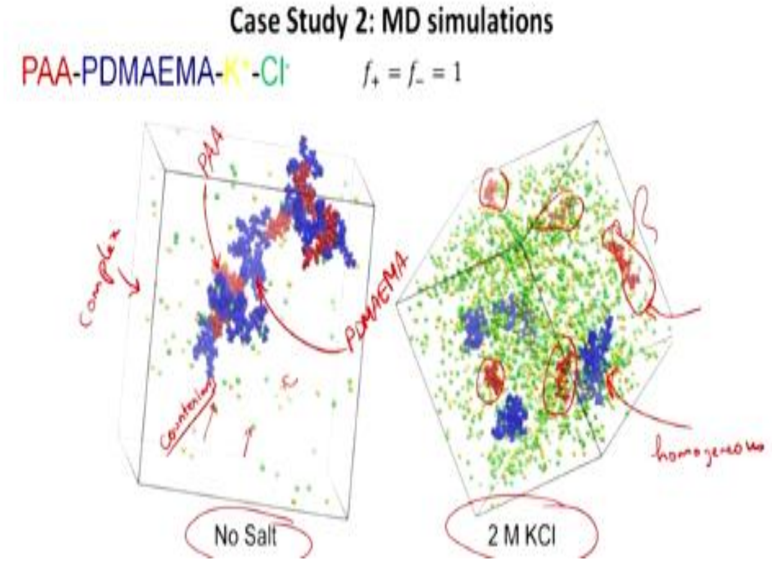
MD simulation can provide information regarding phase behavior, i.e., pH and salt condition for phase separation

So, in cases where the repulsion between the chains are large they will tend to be dissolved on the other hand when the attraction between chains becomes significant they will tend to aggregate and once they tend to aggregate they form a dense phase that separates from solution which is referred as a Coacervate.

Now this may vary in its density in some cases we also form some kind of precipitate when the interactions are even higher then there will be lesser water in that particular phase because there is a stronger interaction between the polymers, again the part of the physics is discussed in the paper you can go through that, but I wanted to set the ground for what we are actually trying to study.

So we want to simulate this particular phase behaviour when will this phase separation happen when will the attraction between the polymers will be such that they will tend to form a phase separated state and how will that change with the pH and salt condition pH I can account for by changing the fraction of chars in the in the beginning of simulation and salt I could incorporate by simply putting in k plus and cl minus ions in the system.

(Refer Slide Time: 22:11)



Case Study 2: MD simulations

PAA-PDMAEMA-K^+-Cl^- $f_+ = f_- = 1$

So, it turns out that it really works pretty well so in this particular case I am simulating a PAA and PDMAEMA west one chain each of them. So, the blue guys in here are my PDMAEMA and you can see it is a polymer chain so there is a long chain of PDMAEMA and the red guys here are the PAA again there is only one chain and these guys are my ionic species Potassium and Chloride ions. There is also solvent in the system actually the number of solvent molecules are huge because we are doing a liquid state but I am not showing the solvent molecules just for the sake of clarity.

So, this is what happens when there is no salt in the system and this is what is happening when you have salt in the system, if you have been careful you can ask that why we have ions when you have no salt and the reason is because the system overall has to be electro neutral. So, if you have negatively charged PAA and positively charged PDMAEMA then it is possible that there is some excess positive or negative charge so we have to compensate that by adding extra ions in the solution this is what is referred as counter ions, because they compensate for the excess charge in the polymeric species.

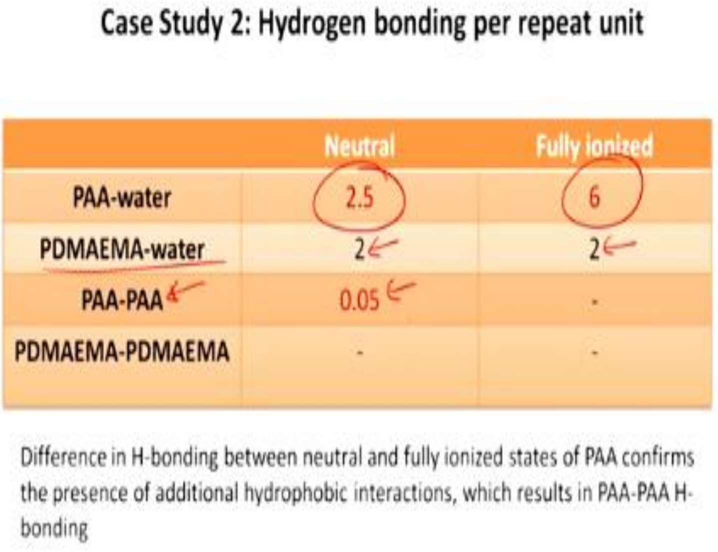
On the other hand in here the counter ions are clearly present but in addition to that you also have salt species because you are adding salt in the system. So, in this particular case I am modeling the counter ions also as k plus and cl minus this need not be the case but it really makes not too much difference if I am looking at different ionic species and what you see here is that for two molar salt this tends to form like a homogeneous solution because this blue guys and the red guys are far from each other so they are pretty much dissolved in the solution on the other hand in the no salt case they tend to form some kind of a complex and therefore this is already representing a phase separation and we are actually doing a small Oligomer as opposed to the long polymer chain, nonetheless we have been able to capture the phase separation behaviour at the molecular signatures of that, because you see on one hand at two molar KCl there is all the polymers are far apart they are tend to be like dissolved in solution on the other hand in the left hand side the polymer come together and therefore this is pretty much representing the case of complexation.

So, with this kind of like kind of like background we can do some more analysis of these systems for example we can look at the hydrogen bonding between the molecules by the way you see some extra red guys here which tend to be like different polymer chains of course we can simulate with multiple chains. But in this case they are simply appearing far apart because of periodic boundary conditions, so this should have been on the other end but you are seeing it as two different species because I am only showing you the atoms inside the box.

So, in reality the polymer chain would have been together but since I am basically correcting for the periodic boundary condition they are appearing as a separate fragment on the other side it is purely artifact of the periodic boundary condition but of course the same thing can be done with multiple polymer chains and you can see the same behavior happening there as well.

So, the next thing we can compute is the hydrogen bonding between the repeat units and hydrogen bonding between the polymer and the water this will tell me what else is happening apart from electrostatic interactions because I told you that the polymer can be Hydrophobic and then it will tend to aggregate together and polymer can be hydrophobic mostly in the neutral state when the electrostatics is not present anyway, so how can we characterize the hydrophobicity of a polymer and the answer lies in that we can compute the hydrogen bonding with water, if it forms more number of hydrogen bonds then it means that the polymer is hydrophilic because the hydrophilic polymer tends to be dissolved in water so tend to form more and more hydrogen bonds with water. On the other hand if the number of hydrogen bonds decrease or is less in that case we can say the polymer is Hydrophobic. Because it is not forming hydrogen bonds with water and therefore it tends to be separated.

(Refer Slide Time: 27:14)



Case Study 2: Hydrogen bonding per repeat unit

	Neutral	Fully ionized
PAA-water	2.5	6
PDMAEMA-water	2	2
PAA-PAA	0.05	-
PDMAEMA-PDMAEMA	-	-

Difference in H-bonding between neutral and fully ionized states of PAA confirms the presence of additional hydrophobic interactions, which results in PAA-PAA H-bonding

So, in this case what we find is PAA forms very few hydrogen bonds with water when it is in neutral state. So, in neutral state it is somewhat Hydrophobic, on the other hand when we go to the fully ionized space then of course now the PAA chains repel each other, so in that kind of a scenario they tend to be somewhat Hydrophilic so, as to speak but clearly there; is something else happening in that fully ionized case because there is electrostatic repulsion between the chains.

For PDMAEMA we really do not find the difference in the hydrogen bonding for neutral case and fully ionized case. We also form the PAA-PAA contacts and that is for the case when we are doing simulations for multiple PAA chains and this is also a significant number that tells me the aggregation of the PAA with itself since we are doing with very few polymer chains that number is small but that does not mean that if I do it for more number of chains we will not have aggregation in fact we will have more aggregation as the number of molecules increase so this pretty much confirms that at least for the case of PAA, there is some Hydrophobicity in addition to electrostatics and that Hydrophobicity particularly is important when it is neutral and that happens at lower values of pH and we showed that if I include that particular Hydrophobicity it is able to explain some of the experimental results that we obtained for this particular system again the details are in the paper I only wanted to tell you what MD can do for this particular system and where else where can we apply molecular dynamics.

So, with that I want to conclude this particular lecture in the next lecture we will take some more examples along these lines, thank you.