Bio-Physical Chemistry
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Lecture - 06
Forces in Protein Folding

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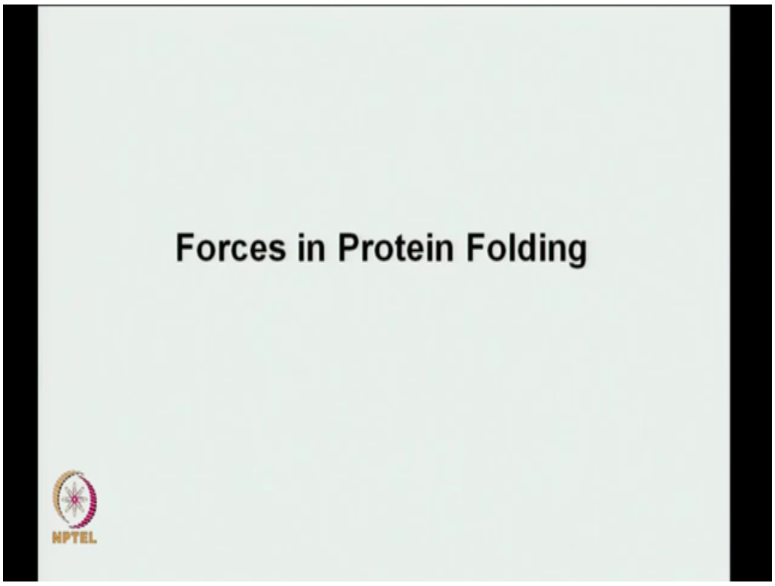

Forces in Protein Folding

Today, the topic we will be starting with this Forces in Protein Folding, ok. Now, the last few lectures just trying to go back to what we have done, we started looking at the birth of a peptide or protein. And then what did we look at? We looked at the development of the secondary structure. Why you need a secondary structure? We looked at the alpha, right, one of the most common structural elements, then we looked at a beta.

And we saw that you know beta if you have to form a beta sheet then you will be having multiple strands, right, which are interconnected through hydrogen bonds. That, one of the major differences between beta and alpha is, in alpha you have these n capping agents, right n cap and c cap, but in beta you at least have two strands which possibly do not have any capping n, so they are free to interact with other moieties. So, that is why beta proteins are so prone to aggregate, ok.

Second, we also looked at, which was the last class which was kind of I went through it a little bit hurriedly what we looked at was mixture, right. That means, we had alpha beta and then we looked at all alpha; that means, alpha elements coming together to form a huge domain or the full protein. And what we saw out there was different orientations of one alpha helix with respect to the other, because it does not have to have to be parallel all the time. It will depend upon the protein, the function, you know and respective interactions some of these which would which would you know come across later.

So, you know before going any further with structure I think that is what we are going to do with respect to the structural aspect. I am not going to go into mixed alpha beta too much or beta because it just takes a lot of time. Whenever you know situation arises or you know we face a situation like that where we have to take an example we will take an example, but otherwise this is what you need to know, ok.

So, today we will look at a very important topic. The topic is you think about this, you start from an unfolded protein essentially you know a linear chain under disordered state of the protein when it comes out and in then it goes to the?

Student: Nation.

Nation or the full it was the nation state and it goes to the full state, it is a native state, right. What are the typical forces, what are the typical forces which act to stabilize the protein against the huge entropy loss which encounter from going towards a very compact configuration starting from a very flexible one because there is indeed a huge loss in entropy.

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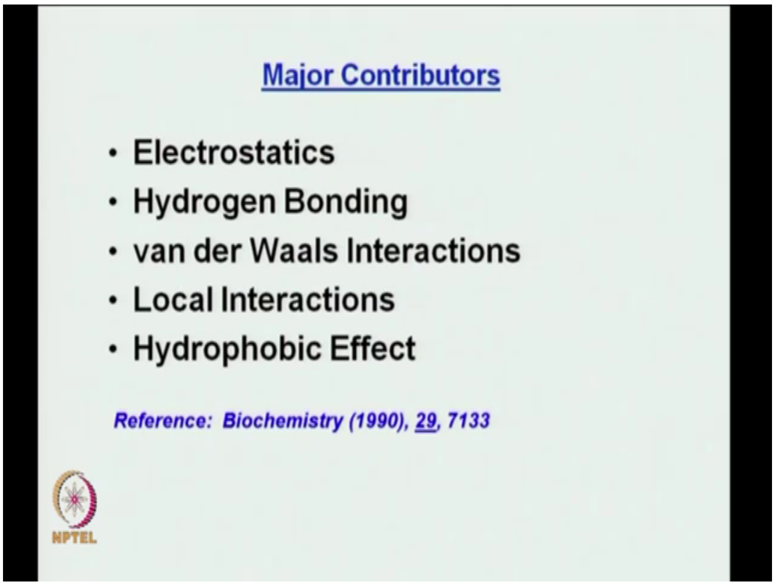

Major Contributors

- Electrostatics
- Hydrogen Bonding
- van der Waals Interactions
- Local Interactions
- Hydrophobic Effect

Reference: Biochemistry (1990), 29, 7133

So, the forces can be classified. These are the major contributors what you can see electrostatics, right, hydrogen bonding, van der Waals interactions, local interactions and hydrophobic effect. Now, all of these individual, you have heard about and some of these you know definitely know a lot about I am sure.

You know what we will do is a we will take each of these one by one, and we will try to look at some mathematical aspects and also their relevance in terms of protein folding and forces, ok. That is what we are going to look at.

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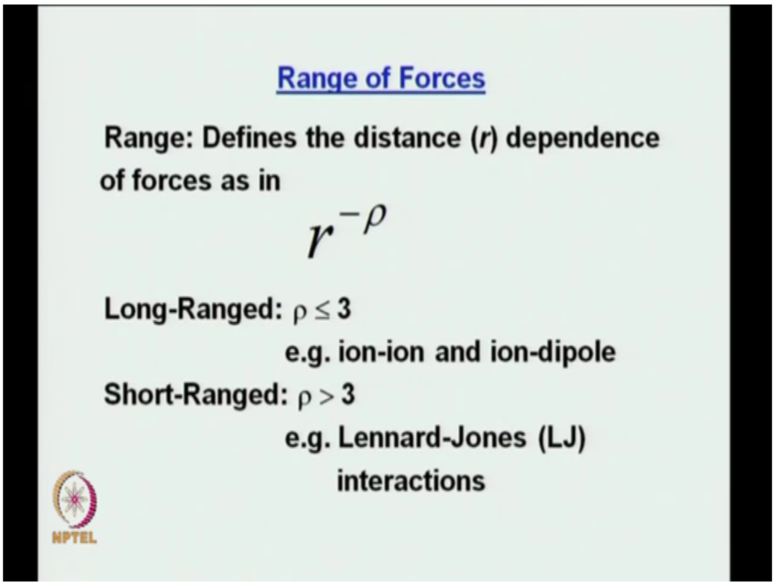

Range of Forces

Range: Defines the distance (*r*) dependence of forces as in

$$r^{-\rho}$$

Long-Ranged: $\rho \leq 3$

e.g. ion-ion and ion-dipole

Short-Ranged: $\rho > 3$

e.g. Lennard-Jones (LJ) interactions

So, the first thing we start with is something refer to as the range of forces. What do you mean by the range? Range defines the distance that your force is depend upon. So, for example, you can see out here it varies as r to power negative of rho, right, now think about your Coulomb interaction, or your Coulomb potential, right. It is an inverse of what? r dependence; that means, here rho would be 1, right, your potential, I mean your Coulomb potential the rho is 1, ok.

So, there are two different ranges; obviously, if you have a long range you will be having a short range. The idea is that both of these forces for example, van der Waals the dispersion forces are typically what? Short or long range. This is short range forces. So, look at the definition of long range and short range. So, long range tells you that the rho is less than equal to 3, right ion, ion dipole and all those things.

The short range is rho greater than 3 which are typically your Lennard Jones interactions, the van der Waals interactions. So, remember r to the power 6, r to the power 12, right and all those things 1 by r to the power 12; that means, r to the power minus 12, r to the power minus 6. So, those are your short ranged forces because the r dependence is huge, ok.

So, these are two things we always have to keep in mind because both of these are very much operative in protein folding, right.

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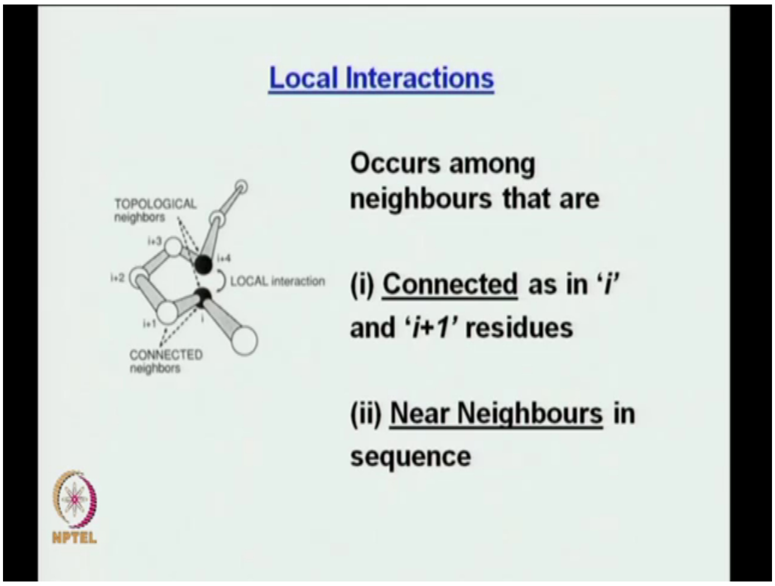

Local Interactions

Occurs among neighbours that are

(i) Connected as in '*i*' and '*i+1*' residues

(ii) Near Neighbours in sequence

And then, we talk about some instructions known as local interactions. What do you mean by local interactions? Obviously, if you have local interactions we will also be having non-local interactions.

So, the way we define local interactions is this. It occurs among neighbors that are connected obviously. If you have a jth residue or an ith residue as shown out here then if it is connected to i plus 1 its neighbor, right, so it is a local interaction. Or if you look at this remain an alpha helix; you have hydrogen bonds between what? i and.

Student: i (Refer Time: 05:41).

i plus 4. So, the same thing happens here. If you can see it out here you have a local interaction between ith and i plus 4th as residue; that means they are pretty near to each other in terms of the sequence, ok. So, these are local interactions. So, one of the local interactions you already know is dominated by hydrogen bonding as in case of an alpha helix, right.

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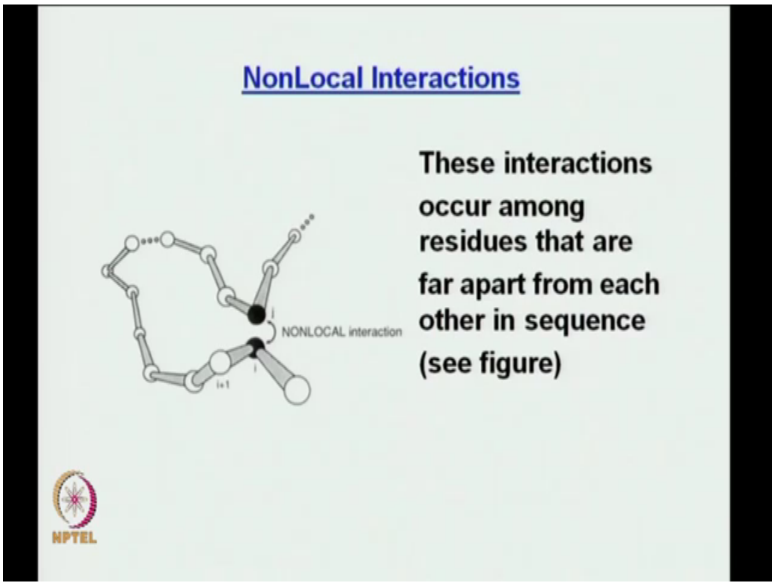

NonLocal Interactions

These interactions occur among residues that are far apart from each other in sequence (see figure)

Now, let us go to the next one which is where the interactions can be non-local. Now, here you can see what happens. Obviously, one here the residues would be far apart from each other; that means, you will not be having residues which are very next to each other that is j j plus 1, i i plus 1 like that.

Also, the another difference is if you look at the figure that is drawn out here, right. In the figure you can see what you mean by non-local. You can have an ith amino acid out here; you can have another ith amino acid you know from say another helix chain or from the same helix chain. What is the difference? The difference is non-local is because in terms of the number of residues or in terms of the sequence of the total protein they are much much far apart from each other, ok.

So, why is this relevant? You think about this when a protein force you have seen it in last class and even you know the previous the class before the last one, that if you have 8 helices it is not necessary that helix 1 always has to interact with helix 2. If you have helix 1 you can have by geometry, by you know whatever you know this structure we have a helix can helix 8 can come and talk to helix 1 because it depends upon how they fold. So, these are essentially your non-local interactions.

And because you know final native state you find a lot of these non-local interactions present you would definitely assume the non-local interactions can also play an important role in protein folding, ok.

So, before going into the specifics of you know they are major contributors. So, what we did just learn about two things, one was ranges which depends upon the distance and the other one is local and non-local which depends upon something known as topology something we have come across before, right.

So, this is the difference, range, distance, this one is more of topology which is these are called topological neighbors or topological non-neighbors, right.

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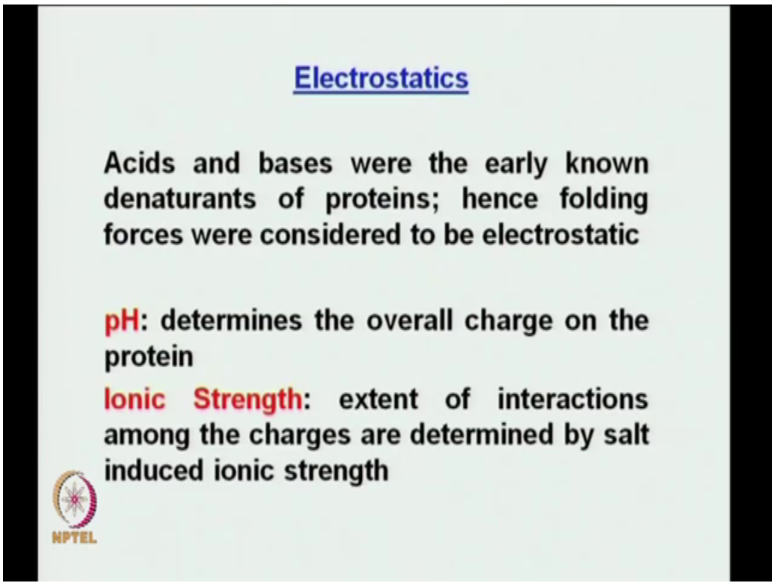

Electrostatics

Acids and bases were the early known denaturants of proteins; hence folding forces were considered to be electrostatic

pH: determines the overall charge on the protein

Ionic Strength: extent of interactions among the charges are determined by salt induced ionic strength

So, let us start with the electrostatics. This is the first topic or the first major contribute. Now, why do we care about electrostatics? You know it is very simple. Electrostatics is all about you know attractions, repulsions, attractive forces, repulsive forces, how you can increase them; how you can decrease them, right how you can modulate them. But the reason it is so important was actually very straightforward. You think about this.

You take a protein, right a protein which is very stable and it is very well folded in a buffer solution normal temperature, right, say pH is equal to 7, at room temperature. Now, what people saw was if there would decrease the pH or increase the pH what would happen is your proteins would become destabilized. See, if the moment you are increasing or decreasing a pH what are you playing with?

You are playing with hydrogen hydroxyl ions; that means you are playing with charges. So, obviously, if a variation of charge like this; that means a concentration of hydrogen or hydroxyl can affect the protein folding or the structure of the protein it just means that electrostatics do play a very important role in maintaining the native structure, ok. So, that was the first defining point where people show that electrostatics have to play a role. And hence we have to know what the electrostatics.

What we will do or try to do in this classes in this classes, subsequent classes, go a little bit more into what electrostatics is all about, give you some flavors of we know, if people would talk about electrostatics what typical mathematical equations, mathematical tools they would use, what you know specific things you were try to keep in mind, ok.

So, as out you know shown out you rather pH what does it show? It shows that determines the overall charge on the protein obviously, because you start varying increasing or decreasing pH accordingly your protonate deprotonate residues its charges will vary; then also the ionic strength. Now, remember if you have an attraction or repulsion if you two charges.

Now, if you put in salts what will happen? The salts can actually come in between those solved the respective charges an actually screen those interactions. So, that is why not only pH you have heard about you know these two word, right salting in or salting out. So, this is essential in happens because of this ionic strength that is what you doing. You are modulating or changing the ionic strength, right, ok.

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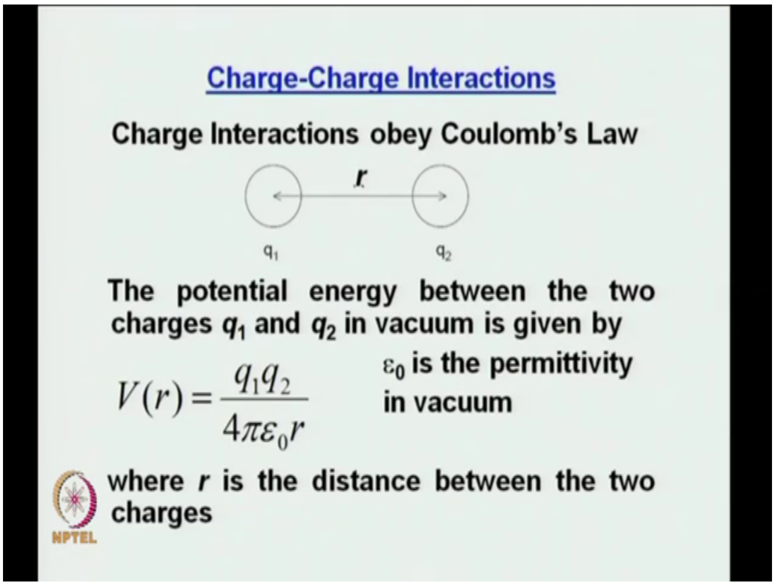

Charge-Charge Interactions

Charge Interactions obey Coulomb's Law

The potential energy between the two charges q_1 and q_2 in vacuum is given by

$$V(r) = \frac{q_1 q_2}{4\pi\varepsilon_0 r}$$

ε_0 is the permittivity in vacuum

where r is the distance between the two charges

So, let us quickly look at the charge interactions. The charge interactions they obey the Coulomb's law you know the potential energy. So, here are two charges q 1 and q 2 shown by space and the potential energy in vacuum, remember in vacuum is given by V of r is equal to q 1 q 2 by 4 pi epsilon 0 r, right. What is the epsilon 0? This is the permittivity in vacuum, right. What is r?

Student: Distance.

The distance between the two charges, ok. Now, this is in vacuum so, that means, you have nothing else. What happens or what will happen to this charge interaction if I take these two charges and put it in a liquid or a solvent where obviously, it is no longer vacuum and that solvent might be having its own what?

Student: (Refer Time: 11:15).

Dielectric constant, right; that means epsilon value.

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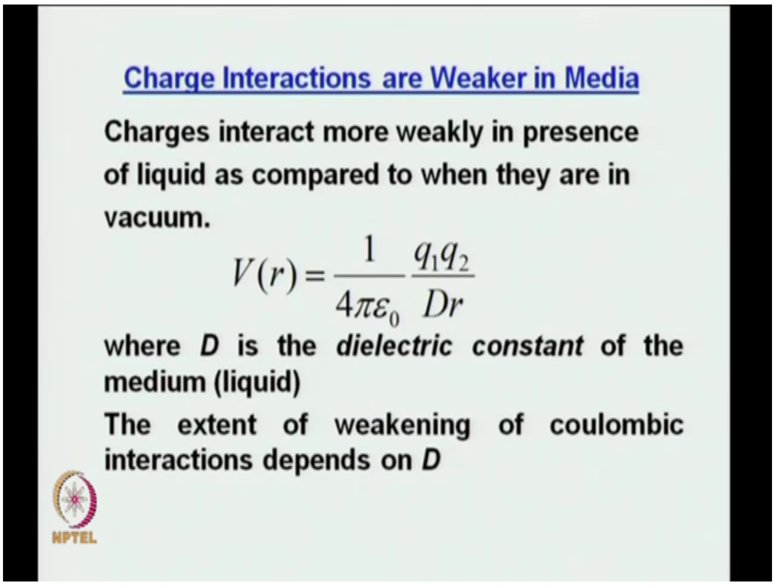

Charge Interactions are Weaker in Media

Charges interact more weakly in presence of liquid as compared to when they are in vacuum.

$$V(r)=\frac{1}{4\pi\varepsilon_0}\frac{q_1q_2}{Dr}$$

where *D* is the *dielectric constant* of the medium (liquid)

The extent of weakening of coulombic interactions depends on *D*

So, that is what this slides now says. Charge interactions are weaker in media. To what extent? The weak the in presence of a liquid of a certain dialectic constant D, they interact in form of this equation where V of r is equal to 1 by 4 pi epsilon 0, this is the constant which we encounter in the previous equation too. q 1 q 2 the product of the two charges, it is in the in the numerator. r again it is the distance. But now we have another term, what is that? It is D. It is the.

Student: Dielectric.

Dielectric constant of that respective liquid or solvent. That means, now this D is actually trying to do something in terms of modulating the extent of interaction between these two charges, ok. So, hence as we just said this extent of weakening of this Coulombic interactions will depend upon the dielectric constant.

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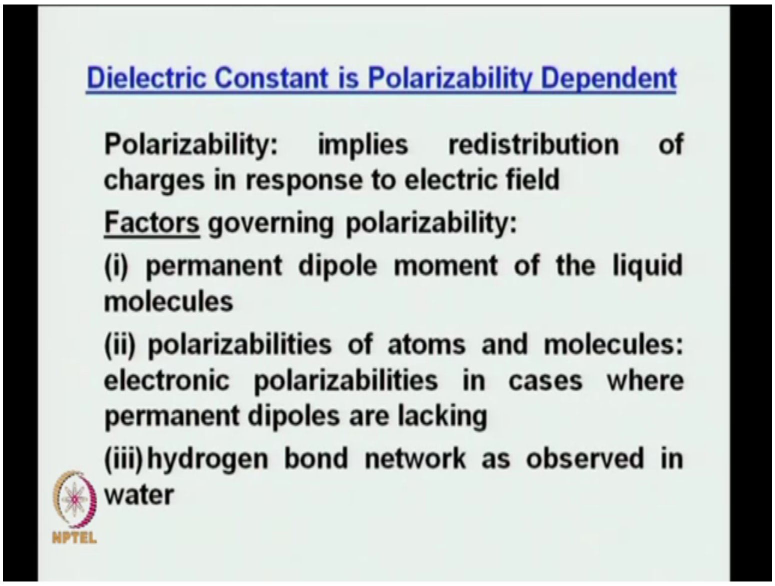

Dielectric Constant is Polarizability Dependent

Polarizability: implies redistribution of charges in response to electric field

Factors governing polarizability:

(i) permanent dipole moment of the liquid molecules

(ii) polarizabilities of atoms and molecules: electronic polarizabilities in cases where permanent dipoles are lacking

(iii) hydrogen bond network as observed in water

So, what is dielectric constant really depend upon? You know depends upon the polarizability. Now, what do you mean by polarizability? So, for those of you who have you know you know keep interest in our chemistry, there is something there are set of rules you have learn before known as a Fajan's rules, right. In Fajan's rules deals with the polarizability of the electron cloud. So, that is what polarizability is all about.

So, if you have something which is a polarizable medium, if you would take two charges, you put the two charges in, now according to the charge according to the charge based on the polarizability of that medium of that liquid those molecules of the liquid would reorient themselves, right.

So, for example, if you have a positive and negative charge and if say you consider liquid molecule which has itself a positive and negative end. So, if you have a negative charge then this positive end would.

Student: (Refer Time: 13:05).

Get attracted to that, solved that. If you have a positive charge, right, the negative end of the dipole would go there and vice versa. That means, they would try to solve it your solved or surround your existing charges which are q 1 and q 2. But what is polarizable depend upon? Because you know that not all molecules will be having a very high dipole moment, ok.

One obviously, you can see the first one. And the first one is the permanent dipole moment of the liquid molecules that is what we know. Why? Because if we have a permanent dipole moment you would be having a positive or negative end. And they would orient themselves with respect to their attractions repulsions as given by the two charges q 1 and q 2 whatever the charges are.

But suppose if you do not have a very huge dipole moment; that means, it typically take out what? Organic systems, organic liquids, right, hexane, heptane and all these things. Now, their dielectric constant I will show you a table in the next slide. Their dielectric constants are very low.

But what do they have? The dielectric constant might be low, but they have electron clouds and hence this electron clouds can be polarizable depending upon the intrinsic polarizability, right and they can also impose their dielectric constant D through this interaction.

That means, they do not have to have a well-defined dipole moment all the time. The dipole moment is small, obviously, then D would be small, but then even if you have a small D its electrons would still reorient based on whatever q 1 and q 2 you have.

That means, respond to the charges you have put in the solution, right. The last one is actually quite important. The last one is hydrogen bond network. In hydrogen bond network you know what water is full of this hydrogen bond network. So, what it means is if you would be putting in two charges in a liquid like water, what do you doing is you are also destructing the hydrogen bond network of the water.

But because you know water is your solvent you have so many hydrogen bonds, so it will not be too much of an energetic penalty, if some of the hydrogen bonds have to break and reorient according to the charges you are putting in because you have a extensive hydrogen bonding network.

It is not that you have just localize hydrogen bonding. If you had been localize hydrogen bonding then you would be disrupting those bonds and that would be a huge penalty. But in case of water that is not true, right. Throughout, uniformly you have an extensive hydrogen bond network.

And typically, when this charges you take you know the concentration of water is always very high and the charges is typically low. So, you know in that case still you have extensive hydrogen bond network which is not disrupted or even though disrupted they are self-compensated by combining with the respective charges, ok.

So, that is why hydrogen bond network is very important because it allows the solvent to kind of talk to the charges put in and also self-compensate whatever disruptions those which are as I putting in or you are putting in once you put them in the solution in water, ok.

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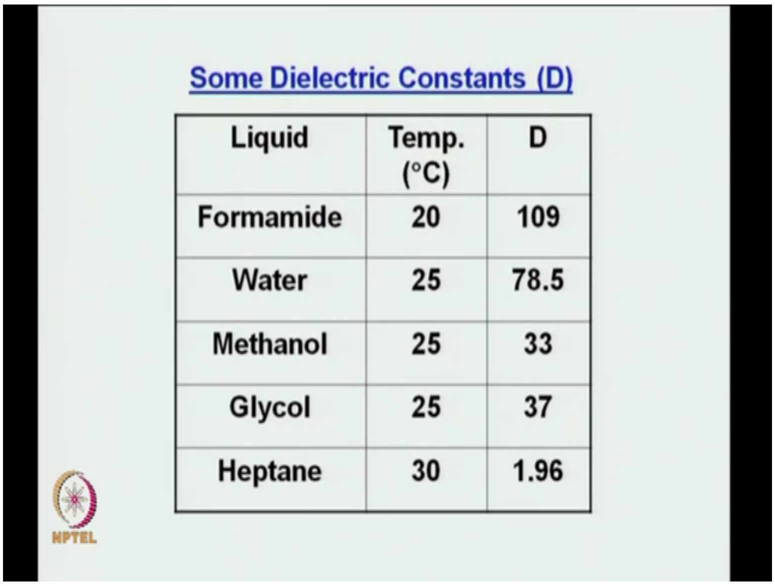

Some Dielectric Constants (D)

Liquid	Temp. (°C)	D
Formamide	20	109
Water	25	78.5
Methanol	25	33
Glycol	25	37
Heptane	30	1.96

So, this is some dielectric constants. Just take a look at this the highest dielectric constants are of formamide, ok. Did you guys know this? You guys knew this, ok. So, water obviously, comes next, and then you can see when we come down methanol is 33 the dielectric constant heptane is barely 2. So, obviously, you can understand that heptane will not be able to separate the charges; that means, the D would be very small, right.

So, what is a dielectric constant do essentially? The molecules come in between the charges and with respect to the dielectric constant they try to shield one charges respect to the other, essentially they screen it, ok. Same thing happens when you put salts in, right they screen it.

Now, do you know why formamide has more dipole moment than water? See water is extensive hydrogen bonding that is given. But, how would you rationalize? One of the way is doing it is that formamide has a pretty high dipole moment, right. And formamide like any other organic system also has extensive electronic polarizability. And these two in combination with some of the other things give formamide, this exclusive place in the dielectric constant list of being more than that of water.

But, guys generally we do not use formamide. What we do is whatever protein chemistry we do mostly it is always in water. So, that is what you are going to focus on mostly, ok.

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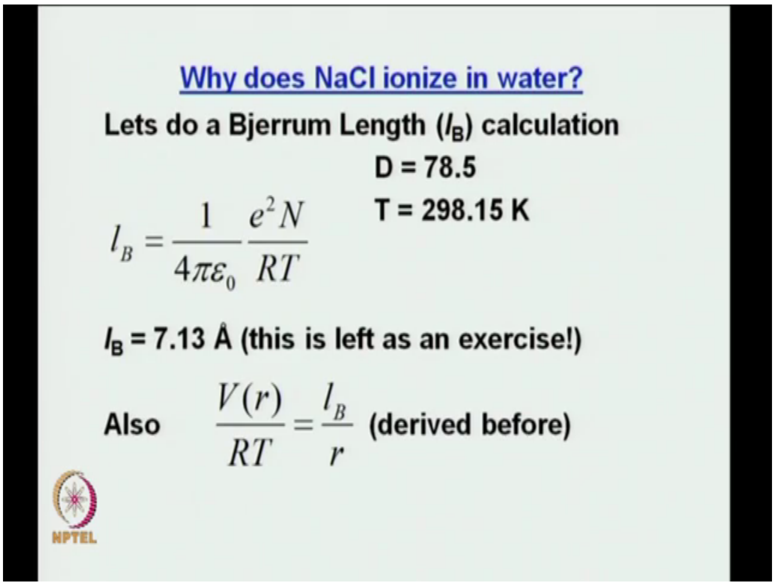

Why does NaCl ionize in water?

Lets do a Bjerrum Length (l_B) calculation

D = 78.5

T = 298.15 K

$$l_B = \frac{1}{4\pi\varepsilon_0}\frac{e^2 N}{RT}$$

l_B = 7.13 Å (this is left as an exercise!)

Also $\frac{V(r)}{RT} = \frac{l_B}{r}$ (derived before)

So, let us look at why does NaCl ionize in water. But, before actually going to that with try to introduce something, this is known as Bjerrum length.

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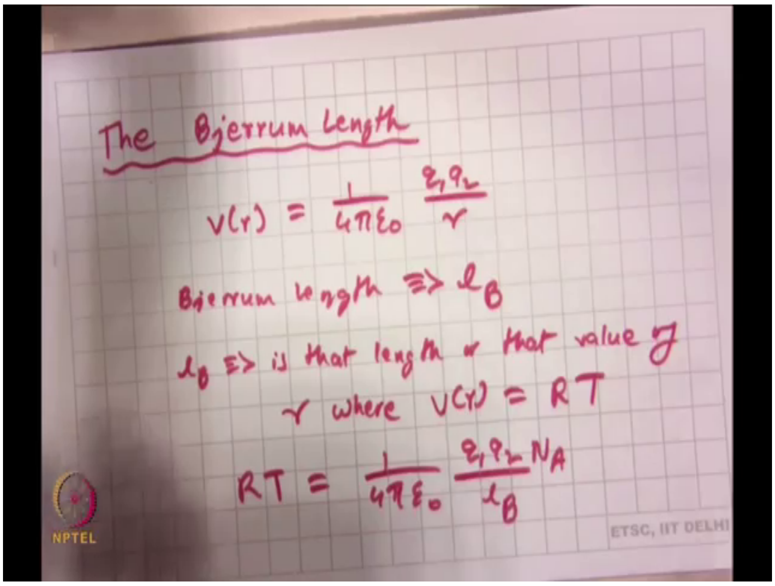

The Bjerrum Length

$$V(r) = \frac{1}{4\pi\epsilon_0}\frac{q_1 q_2}{r}$$

Bjerrum length $\Rightarrow l_B$

$l_B \Rightarrow$ is that length or that value of r where $V(r) = RT$

$$RT = \frac{1}{4\pi\epsilon_0}\frac{q_1 q_2 N_A}{l_B}$$

Have you heard of this before Bjerrum length? So, let us see what it means. So, you already know this, right. So, V of r; so V of r is equal to 1 by 4 pi epsilon 0, q 1 q 2 by r [FL]. We always seen this. Now, what does Bjerrum length say? Bjerrum length says, the Bjerrum length is given by this symbol l B, ok, where B stands for Bjerrum length, right.

So, this Bjerrum length is that length; that means, this l B is that length or that value of r. Where r is what? The difference or the separation between the two charges q 1 and q 2 is that length or that value of r where; this is really important V of r is equal to RT, where V of r is equal to RT. So, that means, when r is equal to l B, when r is equal to l B, V of r will be equal to what? RT.

So, based on this definition what we can write is then RT is equal to 1 by 4 pi epsilon 0 q 1 q 2 by. What do I write instead of r? l B, good. And then, remember when we are doing RT generally what we see? You see is K t, right. But then when there is it become RT?

Student: (Refer Time: 19:41).

Right. So, I can write N out here for Avogadro number of molecules, right, where N is, so this is N A where N A is referred to as the Avogadro number, ok. So, N A is your Avogadro's number.

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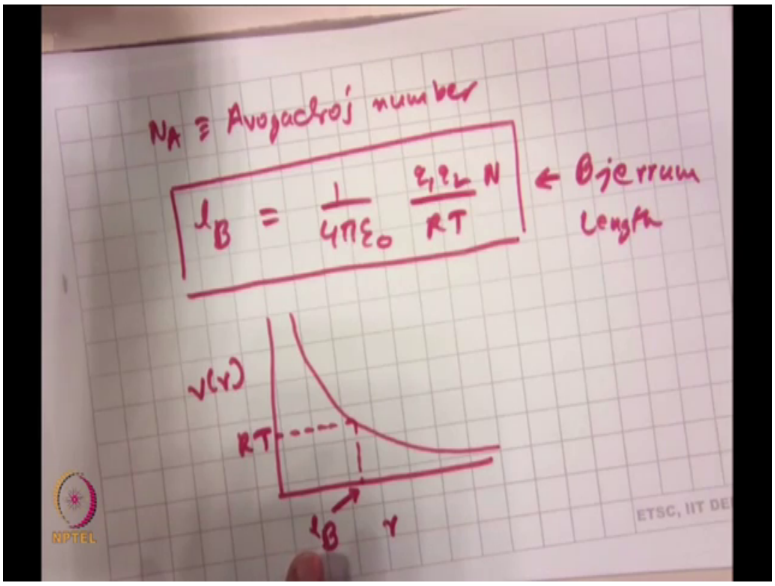

$N_A \equiv$ Avogadro's number

$$\boxed{l_B = \frac{1}{4\pi\varepsilon_0}\frac{q_1 q_2 N}{RT}} \leftarrow \text{Bjerrum Length}$$

Now, what is the significance of this? The significance is this. What does RT correspond to at K T correspond to? K T corresponds your thermal energy, right. Why? Well, you know K is your what Boltzmann constant. It has a certain unit of energy over temperature, you time it by T you get energy, ok.

So, what it means is that at this distance r is equal to l B; your potential energy of interaction between these two particles would be typically equal to your thermal energy. That means, whatever energy you are putting in from the you are not putting in essential from the thermal from the surroundings, if you are not heating the system or anything at room temperature then that is the temperature or rather that is the length at l B, where this RT is equal to your V of r, ok.

So, what can we, so what can we write here? So, just to express l B in terms of RT, I can write this again, I can write l of B is equal to 1 by 4 pi epsilon 0 q 1 q 2 over RT, right times N. So, this is a very well known and formal expression of the Bjerrum length.

Graphically, how would we represent or how would we understand this? Say for example, if I am drawing a graph like this, you know the graph is very simple. If I am drawing graph like this and say suppose on my y axis I have V of r, right which is essentially your potential energy. On my x axis I will be having what? r, right because you are plotting a potential V of r against there is you know the distant separation between these two charges.

So, if your potential energy of interactions it goes like this, ok, just random one then if this is your RT if this is your RT; that means, RT is now the potential energy, right. What is the corresponding point on the x coordinate?

Student: (Refer Time: 22:08).

It would be l B x in. So, this one would be now l B. So, the graphically you know some graphs are really helpful to understand things, specially physical aspects, you know mathematical equations. So, you can see in your potential energy curve it is not that your l B is everywhere. When we get the l B? l B is defined as that distance where your V of r is equal to your thermal energy, right.

Student: (Refer Time: 22:31).

I keep repeating this because thermal energy is very important. When you guys did statistical mechanics before you talked about something or I am if you remember it is must have discuss about something known as thermal fluctuations.

Now, fluctuations are always on the order of K T, it is for a molecular RT for n number of molecules. So, think about it. At this length your thermal fluctuation energy is equal to your potential energy of interaction between the two charges, right. This is the underlying significance. Hold on to this thought and I will tell you why this was so significant. We will just take an example.

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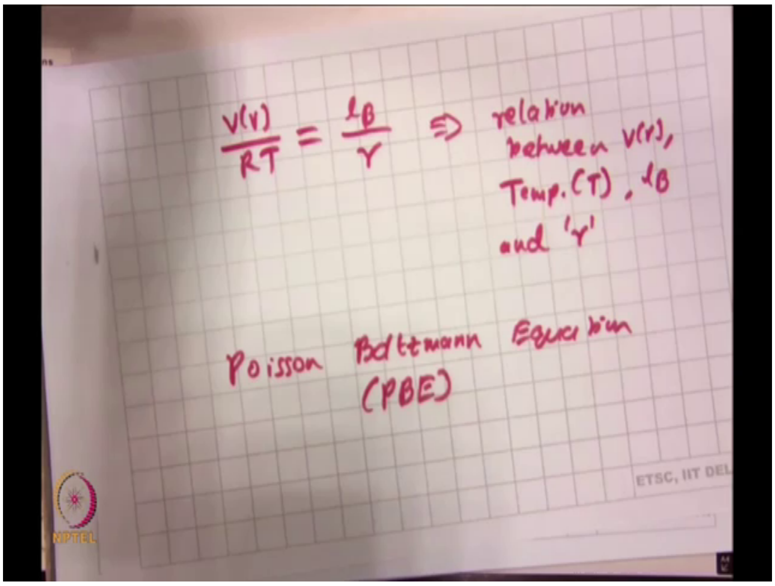


$$\frac{V(r)}{RT} = \frac{l_B}{r} \Rightarrow$$ relation between $V(r)$, Temp. (T), l_B and 'r'

Poisson Boltzmann Equation (PBE)

Before going on further let us just do one more thing. What I can do is I can write if I write say V of r, I will write this again. Say V of r by RT. So, if I write V of r by RT, so what should I get? So, this should be equal to what? Can you tell me?

Student: l B by r.

l B by r. Is everybody with that? Just check. If I take V of r over RT; that means, when I am doing V of r I am keeping r as r. When I am doing RT I am keeping r equal to.

Student: l B.

l B, ok. So, what have you just found out? So, this is an equation. You have found out a relation; you found out a relation between and this is significant V of r temperature which is T, right the Bjerrum length l B and the distance of separation r and the distance of separation r, ok.

So, for example, suppose you know your r, ok, suppose you know your l B. They can easily find at a given temperature the potential energy of interaction. See this potential energy of interaction is very important. We have to know what is the force or what is the energy of interaction between this particles before we take it for further steps or further calculations, right. So, are you guys with this after this point? Right.

Now, let us look at the slide again. We can take a look at the slide. Now, here we doing a calculation, a formal calculation and see the significance of this. We doing a Bjerrum length calculation l of B. What we are doing is we taking sodium chloride. The question we are asking is why does sodium chloride ionize in water? Right.

Now, this you all know now, this you all know. Let us look at it from the thing which is developed from that point of view and you will see what is so significant. So, obviously, D is 78.5 let us take the temperature with 298.15 Kelvin, right.

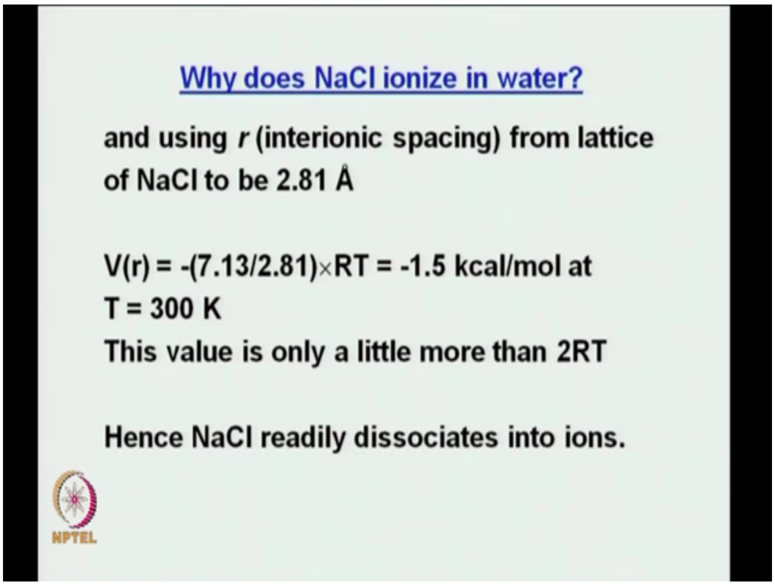
Now, l B is given by that. If you put in all the values, if you put in all the values you know what the permittivity is. You can look this up. You know what the electronic charge is; you know what Avogadro's number is. Even encounter a value of 7.13 angstroms, ok. Now, this you are formally calculating.

Now, this for you left as an exercise. Please do the calculations and see where you getting it or not. Just to familiarize yourself with how people actually do these calculations and make estimates on the Bjerrum length, right from given conditions.

See conditions are not that you know hard to get, right if you have it in water you know the (Refer Time: 26:12) constant, the temperature is always given to you. If you do not know; if you doing it at room temperature you know what is the temperature is nowadays it is very cold, you can take that temperature, so like that.

Now, this thing we also developed just before, right that V of r over RT is equal to l B over r. We just derived.

(Refer Slide Time: 26:34)



Why does NaCl ionize in water?

and using *r* (interionic spacing) from lattice of NaCl to be 2.81 Å

$V(r) = -(7.13/2.81) \times RT = -1.5$ kcal/mol at $T = 300$ K

This value is only a little more than 2RT

Hence NaCl readily dissociates into ions.

Now, what can we use it for? Let us go the next slide. Here r remember it is a distance between the two charges. So, we take this r from here crystal lattice of sodium chloride we know you know people know how the sodium chloride you know crystal cell is arranged and you can easily read of parameters, right, cell parameters from (Refer Time: 26:55) crystal structures have been solved.

So, here people have said that you can assume the interionic spacing to be 2.81 angstroms, right. Now, given this, given this equation and do a formal calculation you see what I am taking is, in this case I am taking the temperature to with 300 Kelvin, right. The V of r, you understand why it is negative. Why is it negative? The interaction potential why is it negative?

Student: (Refer Time: 27:27).

Attraction.

Student: (Refer Time: 27:28).

Attraction, right because I have a negative charge and a positive charge. That is what I am looking at. Because I am having to ionize, right two charges essentially. It gives me a value of minus 1.5 kilo calories per mol at this given temperature. Now, this value is only a little more than 2 RT, right.

You can do it, it is only little more than 2 RT. Now, what does it tell you? Without even trying to think about the question, think about the system first. It is like this. The interaction energy at this length is minus 1.5 kilo calories per mol. The value is a little more than 2 RT, right. What is RT? RT is essentially is your thermal fluctuation, right.

Student: (Refer Time: 28:19).

Getting 2 RT on fluctuation is not a huge deal. Now, see you add a point where the interaction energy between these two is not their height, right based on what the thermal energy we are putting in.

So, because it is just twice RT if there is any thermal fluctuation, right and these things can always happen you have so many molecules, so many collisions happening out there. You will easily get read of what? Your thermal fluctuations can easily override what? The potential energy of interaction between the sodium and chloride ions. That is what it means.

See this is something we know you have to realize, you have to; what do you actually doing now is you looking at this one from mathematical point of view, you are actually calculating energies now. And you are actually calculating and seeing why sodium chloride does ionized dissociate in water. It has no other choice.

Why? Because based on the Bjerrum length, based on this interionic spacing the interaction energy between this ions is not there high. You put it in water, you have the D coming in, right, that decrease interaction in the lot more.

See the same thing would not be happening in vacuum, right. Why not? Because the D is not there. There is nothing to separate these two from each other. But here the D comes in and this value again is so close to your thermal fluctuation your thermal energy you are putting in that the moment you put it in water it just simply separates out, right. So obviously, if you giving more energy, they going to dissociate more, right.

Now, the sodium chloride almost always fully dissociates in water. Anyway what it means is this is the taken point. The taken point is when you look at Bjerrum length, right, when you look at Bjerrum length, Bjerrum length always tells you that if my potential energy is equal to the energy RT, the potential energy interaction is equal to my energy RT which is the thermal fluctuations that I am putting in; at that point I am very close to what? Easily dissociating or separating the ions from each other.

Now, that is a significance of this Bjerrum length and that is why you know not it is not that we always come across this parameter, but this parameter makes so much of a sense. Now, you can understand why, right. So, this is another way of you know trying to look at how species or salts do dissociate in water, right.

So, what I will do is I will stop here for today, ok. You guys think about this Bjerrum length. Next time what I will do is I will start with a little more of this electrostatic interactions and I will give you a flavor of what people do. I will give you a flavor of what people do.

We will introduce something known as Poisson Boltzmann equation, ok. PBE, this is short form. It is a Poisson Boltzmann equation and this will tell you more about this electrostatic interactions, this charge interactions, what are the things in depends it depends upon and this is very close, so something you guys know or are very familiar with, it starts with the D what is that? In case of ions or ionic charges.

Student: Dielectric constant.

Ha?

Student: Dielectric constant.

No. Dielectric constant is constant.

Student: Debye.

Debye. It starts with the Debye Huckel theory, right. It is very close to that. And Debye Huckel theory actually comes from this. We are going to look at the derivation is essentially of this Debye Huckel theory from here, ok.

So, this is how you are going to frame the next few classes. So, the underlying you know principle is that when you take up each and every interaction the electrostatics, hydrogen bonding, van der Waals, hydrophobic effect, we will go little bit deeper into these effects. If you have seen, it is good. If you have not seen, it is even better. You see it here, right.

You have to know this interaction this not only that this interaction stabilize the proteins, but also what is this interaction is made up off, right? What are the factors that effects this interactions? How can we think about this interactions from mathematical point of view?

Specially, one of the most important things we know in proteins is hydrophobic effect. What exactly is hydrophobic effect? You know what do we what do people mean by these two words, hydrophobic? What do people mean? Hydrophobic effect is a huge effect in protein thermodynamics, right and you know many people say obviously, that it is one of the major forces. So, we have to know hydrophobic effect in a lot more detail.

So, along with that we will also look at importance of hydrogen bonds, involved energetics to what extent they contribute to protein stability, ok.

Thank you.