Biomicroelectromechanical Systems

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Module No. # 01

Lecture No. 14

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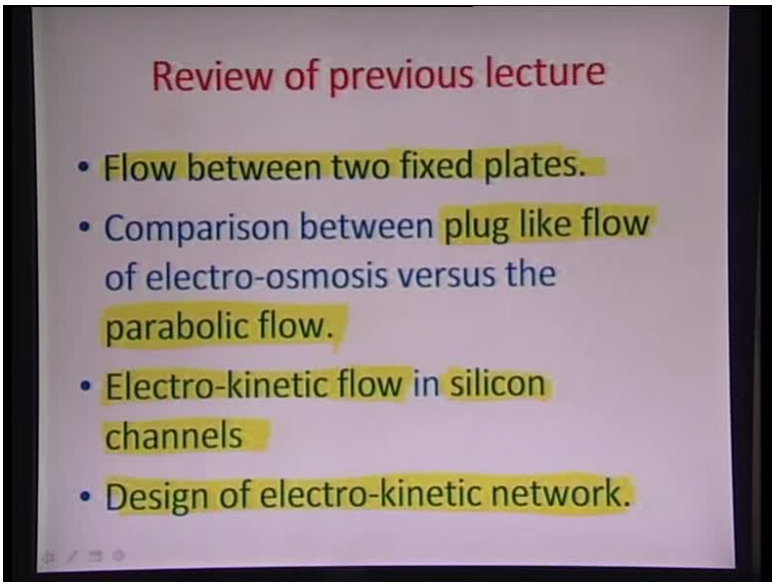

Hello and welcome back to this 14th lecture on Biomicroelectromechanical Systems. Let us do a quick review of what we tried to cover last time. We tried to, kind of look into the equations for flow between two fixed plates; we also compared the profiles that would be generated, the velocity profiles that would be generated between the different kind of flows, electro-kinetic and pressure driven. Also we found out that for the electro-kinetic flows, the flow profile is more like a plug, so it has uniform velocity all through the cross section between the double layers formulated on all the sides of the channel, very close to the surface of the channel.

So, electro-osmosis, electro-kinetic flows, electrophoresis this essentially has a flow which is more like a plug as opposed to the pressure driven flow which is more parabolic in nature. So there is velocity variation from the point of no slip on both sides and

maximizing when you consider the exact center - the work center of the channel. We also tried to investigate why or how was the mechanism of the electro-kinetic flows in silicon channels. So essentially, there is a formulation of Hydroxide, a linkage on the top of the silicon and on contact with a certain pH solution; with the certain pH, it actually formulates, dehydrogenates and forms SiO minus. Essentially, there is a negative charge which is developed on the top of the silicon surface and because of which whenever there is water or any other constituent flow within the micro channel of almost always, there is this diffused layer which is created in the bulk, as it moves by an external voltage applied perpendicular to the cross section of the channel, it drives the fluid along with it and essentially goes to one end from another. So, we also were just about to discuss the design of electro-kinetic networks in such flow applications and I would like to just take this up a little more today.

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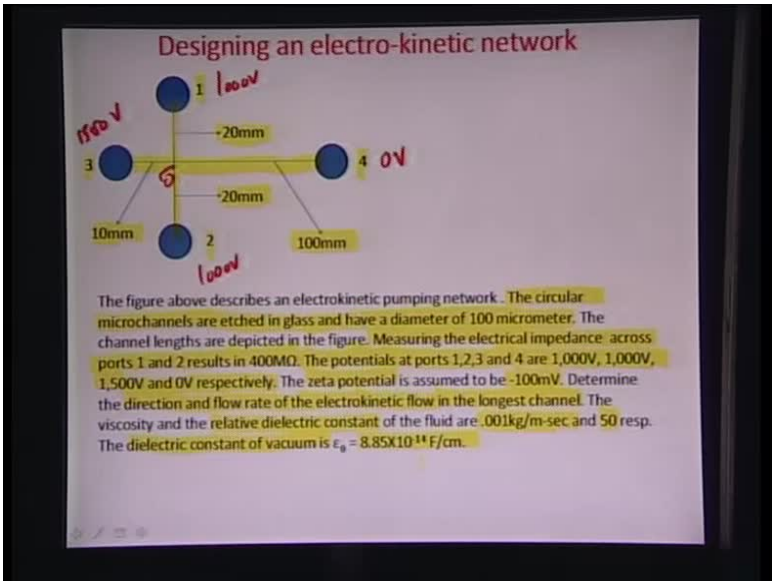

So, the question that we posted last time and which was not in fact solved was that, how do we design really such electro-kinetic networks and these networks are immensely useful for micro pumping, micro scale transportation of fluid. So here in this figure as you see, there is a crisscross architecture of micro channels and there are four reservoirs marked 1, 2, 3 and 4, and length dimensions of these individual channels are given, like for example, if we consider the center to be o - the center of the intersecting network of channels to be o, then 1 o length is 20 millimeters; 2 o is again 20 millimeters; 3 o is about 10 millimeters; 4 o is about 100 millimeters. So we assume that the cross section

of these micro channels are perfect circular, they are etched in glass, they have a diameter of about 100 micrometers. So measuring the electrical impedance across ports 1 and 2 results in 400 mega ohms, and we assume that the fluid filled inside this channel 1, 2 is really responsible for providing the resistance and also that resistance is homogeneous. Therefore if the medium is not altered, there is almost always a uniform resistance per unit length depending on - if the channels are continuously filled.

We assume that in micro flow domains, still continue mechanics holds and there is almost always continuity - a flow continuity. Therefore in this case, we make up presumption that resistance per unit length is constant.

So the potentials that we apply for driving the flow and we have to apply perpendicular potentials, perpendicular to the cross sectional area of the micro channels containing this fluids So ports 1, 2, 3, 4 respectively are 1000 volts, 1000 volts, 1500 volts and 0 volt. So essentially, you are not applying any potential at port 4 - it is 0 volts; you apply 1000, 1000 volts on 1 and 2, and you are applying of 1500 volts in port 3. Then you want to figure out what is a pumping rate? (or) What is the flow rate of such a channel architecture. Some constants and parameters which are given regarding the surface since it is glass - in contact with an aqueous-based solvent. The zeta potential is assumed to be about minus 100 millivolts and you have to determine the direction in the flow rate, if you assume that there is an electro-kinetic flow going on in the longest channel. Some other parameters are that the viscosity of this aqueous medium is about 0.001 kg per meter second and the relative dielectric constant is about 50. We assume that the dielectric constant for vacuum is about 8.85 into 10 to the power of minus 14 fared per centimeter.

Let us design this micro pump and at the outset, we assume that the micro channel system contains continuous and homogeneous fluid. We assume that the micro channel contains a homogeneous and continuous fluid. So therefore, the electrical impedance in each channel is proportional to the length, so it is proportional to the length of the channel.

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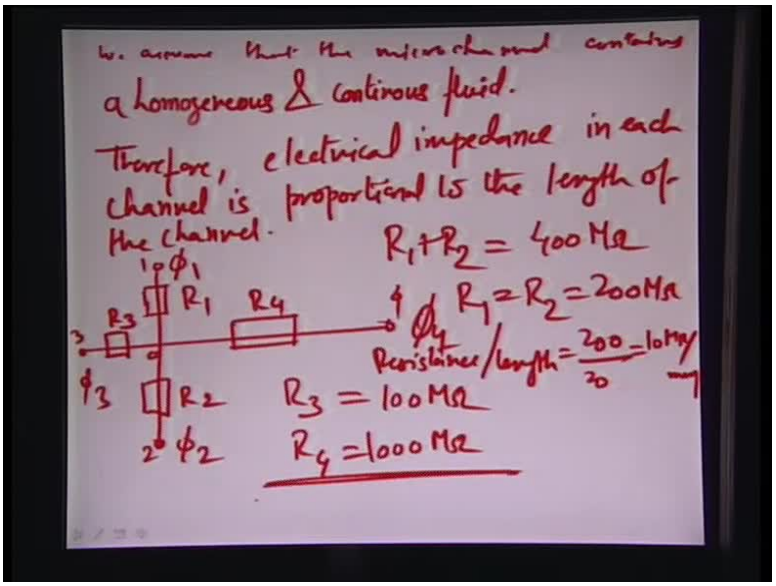

So, let us now draw this network again here and we assume resistances R1, R2, R3 and R4 as an equivalent, to show the resistance of the total channel. We also assume these potentials phi 1, phi 2, phi 4, phi 3 which have earlier been defined in the question. So, we will try to find out what R1, R2, R3 and R4 are. So we know from the question, R1 plus R2, there is cumulative resistance across ports 1 and 2 is about 400 mega ohms. So, this is given, we also know that the lengths between 1, 0 and 2 and 0. So, this is port 1, this is port 2, this port 3, and this is port 4. So, the lengths - the channel lengths between 1, 0 and 2, 0 are same, equal to about 20 millimeters each. Therefore, if we assume fixed resistance per unit length, then really R1 becomes equal to R2 equals to 200 mega ohms, and the resistance per unit length in that case becomes 200 by 20 mega ohm per millimeter, so it is around 10 mega ohms per millimeter. R3 and R4 in this case can automatically be calculated accordingly, so the length of R3 is about 10 millimeters which means resistance is about 100 mega ohms and length of R4 about 100 millimeters which means the resistance is about 1000 mega ohms. So essentially R4 being the longest channel, also has the highest resistance.

So all set and done, we need to somehow solve this problem using some circuit theory approaches. So one approach that we would use here because it is considering a flow of current across a network of channels, or network of resistances. So, the electrical equivalent can be easily found out by the Kirchhoff's law.

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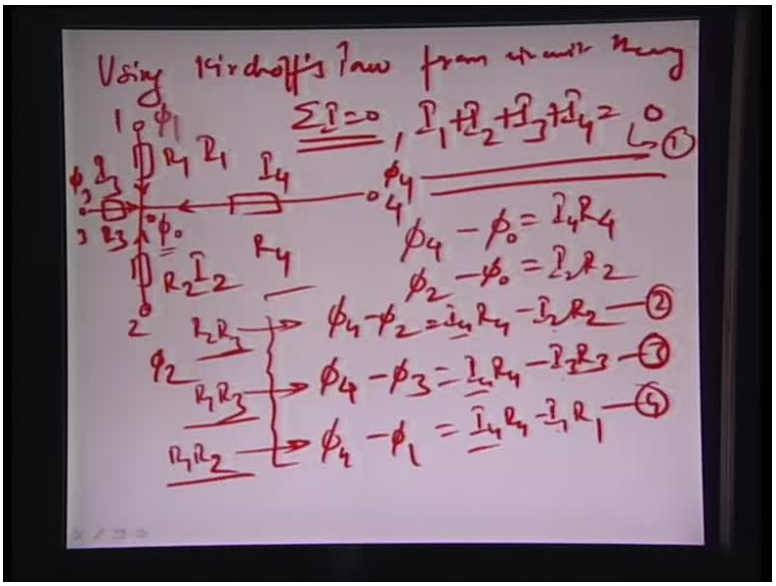

So we use Kirchhoff's law from circuit theory here and what this also says is, there if you are to be assumed that there were several currents here - I1 to I4 and let us draw this network again for convenience. So, we have 1, 2, 3, 4 and resistances R1, R2, R3, R4 and also potentials phi 1, phi 2, phi 3, phi 4.

So if you assume that all these arms correspond to a current value of I1, I2, I3, and I4 - notationally and we also assume that all these currents are converging to this nodal point o, then essentially, all these currents would converge out to be 0, that is what the Kirchhoff's law is right? The sigma I at a node is 0 and this based also on the principle of conservation of energy because we assume that in a circuit, any junction or any point does not produce current by itself, where will it get the energy from? Therefore any current which is converging to a node, or diverging out of a node in all the converging to node from all the directions, is essentially - in summation of that - is essentially 0, is no energy is generated.

So the inflow in a node is exactly equal to the outflow of the current. There is nothing which is contained or nothing which is generated at this particular node of interest. Therefore, let us call this equation 1; we also try to figure out what the differences in potential would be, so if you look at let us say just the arm 4 to 2 and 4 to 1.

So phi 4 minus, let us assume that there is potential phi 0 and this particular node here. So, we can also write this as phi 4 minus phi 0 is essentially the drop in potential by

assuming there I4 passes across the resistance R4, is essentially I4 R4. Similarly, phi 2 minus phi 0 - the potential across these two points here, 2 and 0 is also equal to I2 R2 and therefore phi 4 minus phi 2 is nothing but I4 R4 minus I2 R2. We also assume in identical manner, phi 4 minus phi 3 and phi 4 minus phi 1 to be I4 R4 minus I3 R3 and I4 R4 minus I1 R1. Let us call these equations 2, 3 and 4 respectively. Now, we have to play a little bit trickier because we need to somehow solve these equations and try to figure out a way, so that we can get relationship between essentially, all the you know - all the resistances and all the potentials.

So here, if you multiply equation 2 by let us say R2 R3, and equation 3 by R1 R3, equation 4 by R1 R2 and sum all these things up; let us see what the final form of the equation would really look like. So we have this multiplied by R2 R3, this multiplied by R1 R3, this multiplied by R1 R2. We are just trying to solve because essentially, then we will have this I4 term here coming out and also we have this I1 plus I2 plus I3 term coming out of the resistance domain. So this you can bracket these, I will just show in the next step .

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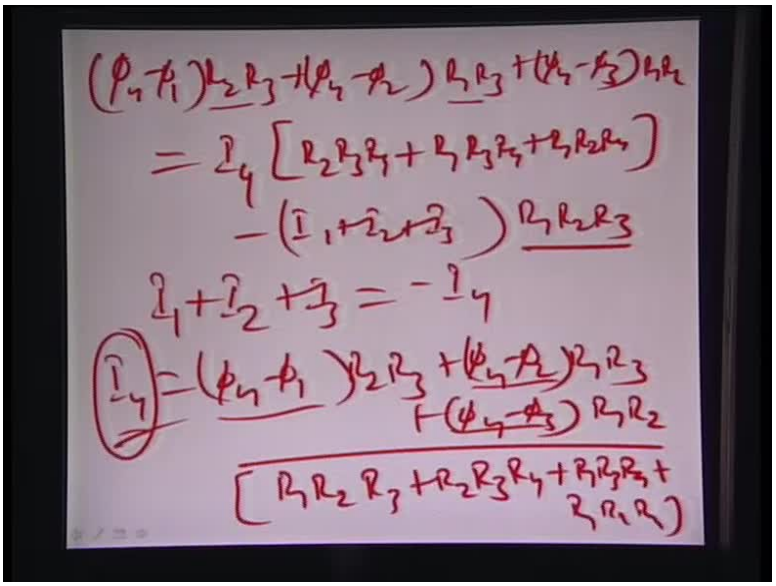

So essentially, let us multiply and add. So we have phi 4 minus phi 1 times of R2 R3, plus phi 4 minus phi 2 times of R1 R3, plus phi 4 minus phi 3 times of R1 R2 is equal to your I4 times of R2 R3 R4, plus R1 R3 R4, plus R1 R2 R4, minus I1 plus I2 plus I3, this whole term comes out in the bracket into R1 R2 R3. So essentially, we multiplied

intentionally these 2, 3 and 4 equations in a manner, so that this R1 R2 R3 can be like a common coefficient for all the different current values in the second terms of this equation with a minus - a negative coefficient.

So, the idea is that we can easily solve this particular equation by assuming that from the first equation, we have a summation of I1 plus I2 plus I3 is minus I4. So, we can easily take out I4 here and I4 comes out to be equal to phi 4 minus phi 1 into R2 R3, plus phi 4 minus phi 2 into R1 R3, plus phi 4 minus phi 3 into R1 R2, divided by R1 R2 R3, plus R2 R3 R4, plus R1 R3 R4, plus R1 R2 R4. So essentially, we have made these equations independent of the current, which we do not know - we do not know the the I1, I2s, I3s and I4s values, we have just made presumptions. However, we do know what these different potentials are, we also know what these resistance are, and the whole idea is to make this equation independent of the I's, so that we can find out from the other terms which we know already - what would be the values of the different I's.

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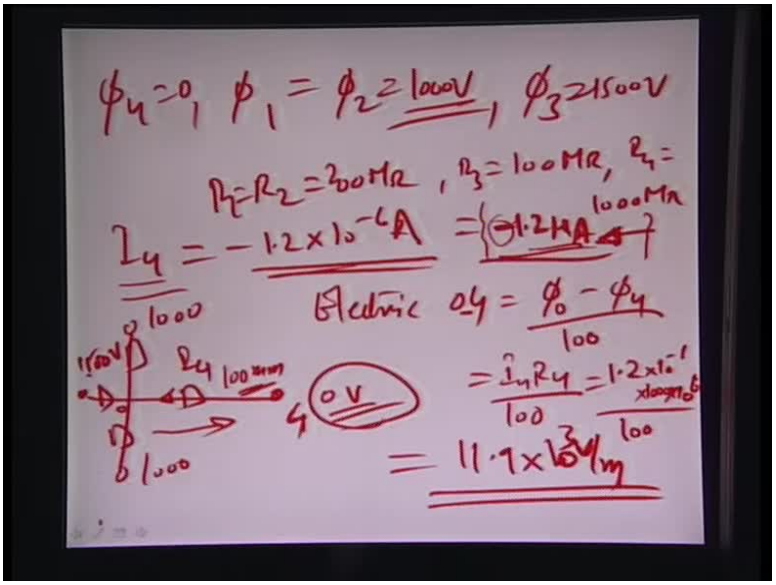

So in this particular case, if you apply phi 4 equals 0, phi 1 is equal to phi 2 is 1000 volts, and these are all mentioned in the problem statement; phi 3 is about 1500 volts, and you have R1 equals R2 is about 200 Mega ohms, R3 is about 100 Mega ohms, R4 is about 1000 Mega ohms. The I4 value comes out to be equal minus 1.2 into 10 to the power of minus 6 ampere or minus 1.2 micro amp. I would just urge you to look towards the dimensions or the magnitude of the current really. So we are really talking about a very

small amount of current minus 1.2 micro amps. That is one aspect, that in electro-kinetic flows, with a very large amount of voltage of the order of 1000 of volts across the capillary, you really get a very small current in the terms of minus 1.2 micro amps. The term minus here also suggests that the intended direction of I4 is really the opposite than what it was assumed. So, if you assume that this network of flows had currents, all converging into the node, I4 was assume to be from 4 to o. Essentially, it is in the other direction, which makes sense because you have applied a 0 volt potential here and you can assume that all the other potentials 1000s of volts on both ends here, 1500 volts here - would be essentially putting or pushing the fluid, towards the junction 4. So, the flow of fluid also determines and defines the direction of the current, as the current is essentially flow finds in the channel. Therefore, the minus sign indicates that the current is flowing out word in an outwardly manner towards the reservoir 4 from the junction o.

That is what one issue about this electro-kinetic circuits, another issue is we also need to determine - what is the electric field in the longest channel? Few may recall the longest channel also, is the one from o and 4 and it is about 100 millimeters in length.

So the electric field between o and 4 is also the voltage between o and 4, which is phi 0 minus phi 4 divided by the length 100 millimeters and - give me a minute here - we can calculate the phi 0 value easily, or phi 0 minus phi 4 value easily as I4 R4, it is the drop in potential, so I4 we know is about 1.2 into 10 to the power minus 6 amps, resistance R4 is about 1000 Mega ohms. So, you have 1000 into 10 to the power 6 and you have the distance as about 100 millimeters and therefore, if we reconvert all this and calculate, it comes out to be 11.9 into 10 to the power 3 volts per meter.

So really there is an intense amount of field which is needed for current - which is about 1.2 micro amperes. Let us calculate the velocity of flow in the particular micro channel based on all these assumptions, and so the first thing that I would like to see here is to determine - what is the mobility of the ions per unit electric field?

So, if you remember the equations that be derived on electro-osmosis flow on the mobility is also the velocity of the ion in an unity electric field are in an unit electric field.

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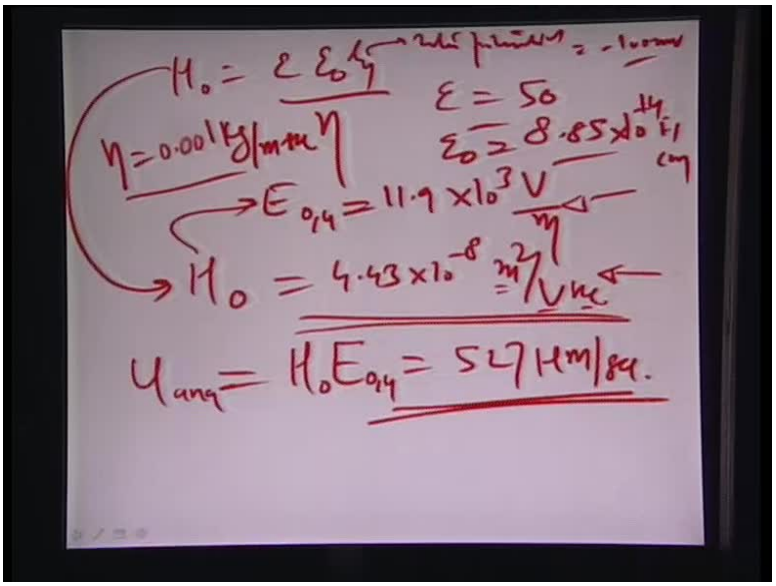

So here, the mobility can also be defined as mu 0 equals epsilon, epsilon 0, zeta by eta. Zeta is given, zeta potential of the surface as about minus 100 millivolts. So, zeta is minus 100 millivolts and the dielectric constant - epsilon - has been given as 50, that of vacuum - permittivity of vacuum has been given as 8.85 into 10 to the power of minus 14 farad per centimeter. We already know from our previous experience with electric field in the arm length 4, that the electric field E here between 0 and 4 is essentially 11.9 into 10 to the power of minus in 3 volts per meter.

We assume the viscosity here, as has been given here in this question of aqueous fluid to be 0.001 kg per meter second. The mobility with all this values comes out to be equal to about 4.4 into 10 to the power minus 8 meter square per volt second. Be careful about the units here again and again, because all these units are differently classified - this is farad per centimeter, this is again kg per meter second, this again volt per meter. So, essentially, you have to convert wherever you feel appropriate. And this is millivolts - so in order to get meter square per volt second, you have to make some conversions and the mobility of this particular flow process comes out be 4.43 into 10 to the power minus 8 so, multiply that with electric field here to calculate the flow velocity. The flow velocity of the analyte, here, is essentially mu 0 times of E between 0 and 4 and if you apply these different values of mu 0 and E, this comes out to be about 527 micrometers per second.

So very interesting, because this is only half a millimeter per second. If you apply such a high potential about 1000 volts, 1500 volts, of the order of 1000s of volts of potential, you are getting a current which is almost in the range of micro amps which again causes of flow, which is essentially, only, half a millimeter per second. Therefore this really is not a very high-yield process, in terms of applied energy and the output - it may not be a very highly efficient process. However, the advantage that electro-kinetic flow has to offer in many situations - we do need flowing mechanisms without any mechanically active components in the device.

There are several micro pumping models and will be doing - a covering - on some of them in the latter half of this course where we can use mechanical motion to generate flows like this with the micro scale architecture. In some other instances, we probably do away with the mechanical motion because of the softness of the material that we are dealing, especially, if you are talking about biological entities like cells, proteins or molecules, there would be a rapid confirmation change - particularly in proteins, as you flow them through micro channels to do some diagnostics, to do something important and useful, and there what would be important is to carry the molecule of the entity using an alternate mechanism, without using a non-mechanical method; there is no active components in the circuit.

So, electro-kinetic flow definitely is one such mechanism and although the process may be - not a very high throughput, high yield one, still it is preferable because it is probably one of the few modes available, where you can transport fluids by just rapidly applying an electric field, and also it is more integrable to microelectronics because you can apply these high voltages through screen printed electrodes across both ends of the channel, very easily. So even though, the velocity is only half a millimeter per second, it sometimes works out to be a better process in comparison to the other conventional counterparts which are available.

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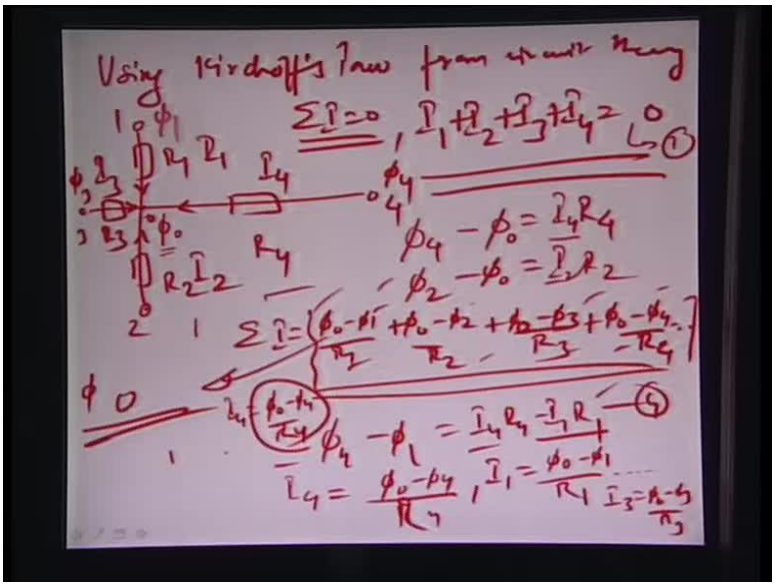

We have another simpler method of solving this whole problem and this again is based on the Kirchhoff's law here. So, let me just go ahead and show you quickly, what we can do. So essentially as we know here, the I4 comes out to be phi 0 minus phi 4 divided by R4, and similarly, the I1 comes out to be phi 0 minus phi 1 divided by R1, and so on so forth, and I3 comes out to be phi 0 minus phi 3 divided by R3.

So, whatever we have done in this, can be more simplified by just putting this various I values in the first equation of the Kirchhoff's law and being able to tell - what or how it will behave. So, sigma I essentially here, would mean phi 0 minus phi 1 by R1, plus phi 0 minus phi 2 by R2, plus phi 0 minus phi 3 by R3, plus phi 0 minus phi 4 by R4 and as we know, summation of this - is essentially 0. So, this actually brings us to the same equation as we have talked about here, when we were trying to calculate what I4 is.

So this is another very simpler method of finding out - what the - so from here, you can find out the phi 0 which is unknown actually, because you have only one variable and one equation, other parameters - phi 1 to 4 and R1 to 4 are all known, and then from phi 0, you could easily find out what I4 is, just by calculating phi 0 minus phi 4 by R4. So, it is a much simpler method of mathematical estimation, in comparison to the other method which was demonstrated. So there in a nutshell, is how you can design electro-kinetic pumping mechanisms and what I would be interested to do next with you is, essentially finding out of flow rates in terms of volume discharge.

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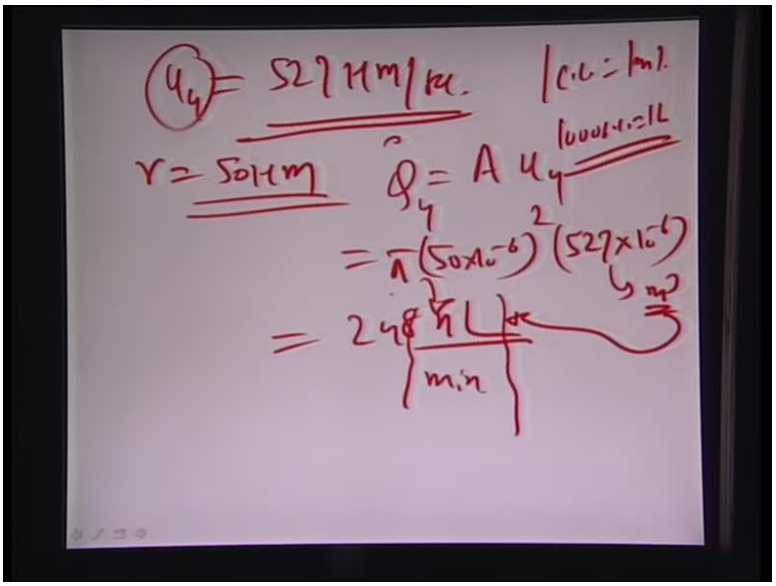

We also know that we have already obtained a flow rate, in the fourth arm, called U4 as 527 micrometers per second; we have been given that the radius of this particular channel - in question - is about 50 micrometers, so the radius is about 50 microns and calculating flow rate here is really not a problem. Essentially, the area of cross section times of U4, and area is pi times of 50 into 10 to the power minus 6 square times of 527 into 10 to the power of minus 6. So this, from calculation, would come out to be about 248 nano litres per minute, this is of course meter cube, so you have to do this conversion - meter cube to nano litre. 1 centimeter cube is essentially 1 ml, so about 1000 ccs make about 1 litre in your talking about 10 to the power of minus 9 litres. So, it is about 10 to the power of minus 6 times of meter cube. So, that is, in nutshell, what the volume flow rate would be? So you again find out, that this volume flow rate of cup of nano litres per minute, is relatively a very small quantity, as is the characteristic of these alternate mechanisms of micro channel flows.

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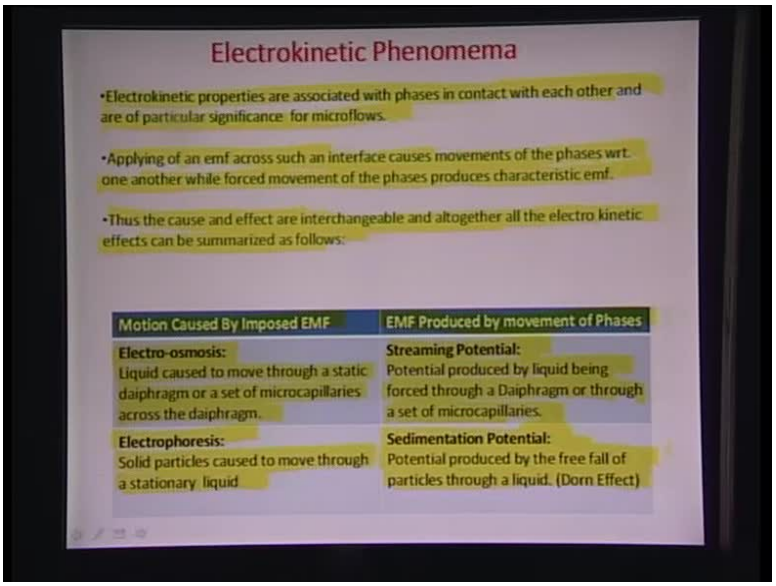

In a nutshell, electro-kinetic properties are associated with the phases in contact with each other, and of particular significance for micro flows. Applying an emf across such an interface causes movement of phases with respect to one other, while force movement of the phases produces characteristic emf.

So, the cause and effect are really interchangeable, and altogether all the electro-kinetic effects can be summarized as are motion caused by imposed emf; all emf produced by the movement of phases. First category as we know already - phenomena like electro-osmosis, electrophoresis where motion is caused by an applied emf. Electro-osmosis is where liquid is cast to move through a static diaphragm containing a set of microcapillaries, or in any case, through micro capillaries in general - by applying an induced emf. Electrophoresis on the other hand, is where the solid particles are cause to move through a stationary liquid by applying an external electric field.

So, for the other mechanism where emf is really produced by the movement of phases, the first property is the streaming potential, which is also the potential produced by the liquid, which is being forced through a diaphragm, or through a set of micro capillaries.

Also, sedimentation potential - the potential produced by the free fall of particles, especially when they are suspended in a medium – a liquid medium, is also known as the Dorn effect. This is also the mechanism in chemical industries to find out a lot of

information about the quality of the colloid, which is present or which is under investigation.

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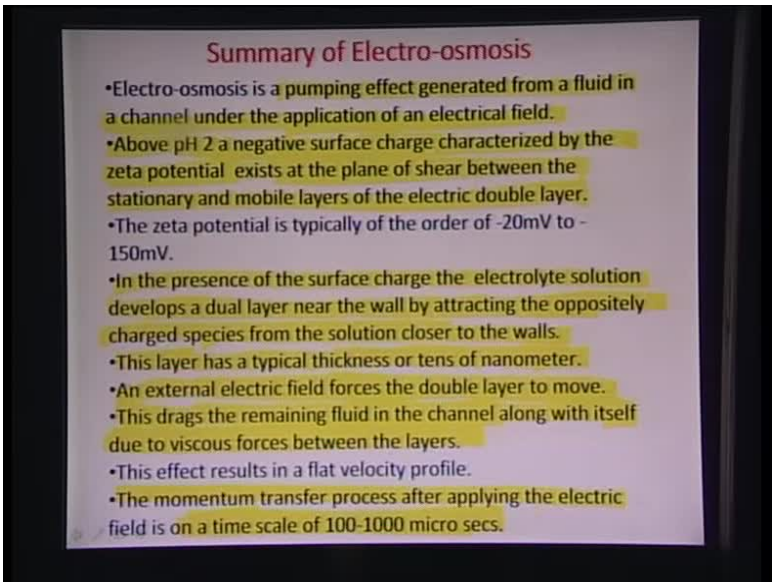

So for electro-osmosis, summarily, we can say that it is a pumping effect, which is generated from a fluid in a channel, under the application of an external electric field, so as you take the pH of the contacting phase (liquid phase) over a surface - to above 2, the surface immediately develops a negative charge, characterized by a zeta potential, and this exists at the plane of shear between the stationary and mobile layers of the electric double layer that is formulated. So, there is a layer of diffused charges through the medium, starting from the double layer, all the way up to way the charge density falls to almost 0. Zeta potential is of the order of a few tens of millivolts to about 100s. So, typically it is about minus 20 millivolts, all the way to about 150 millivolts or so.

In the presence of surface charge, the electrolyte solution develops a dual layer near the wall by attracting the oppositely charged species from the solution, closer to the walls. This layer typically has thickness of about tens of nanometers - very small layer, very close to the surface, and in this situation, if you plant an external electric field, it forces the double layer to start moving so there are these instances, where the ionic forces generated by the external field kind of does away with the holding force, the viscous forces in between the layer and it causes the shear of this fluid, along the double layer. So, there is a static fluid facing the wall of the capillary, and that there is a shearing

across this double layer. Following this, the part of the liquid which is between the two double layer or between the whole, this double layer starts to move with a uniform velocity towards one of the electrons, depending on what the potential - the zeta potential of the surface would be, as a plug like flow, so they have a uniform velocity while it flows. This drags the remaining fluid in the channel because charge motion – and a very small channel would essentially mean a lot of that forces generated across the ions and these are also due to the viscous forces which exist between the charge particle and the fluid. Therefore, due to these viscous forces, the layer start moving, the whole liquid which it is immersed in, or suspended in. So, this effect results in a flat velocity profile which we have seen earlier and the momentum transfer process after applying the electric field is approximately on a time scale of about 100 to 1000 microseconds. So, you have to just about wait for about, close to 1 millisecond, to be able to get any substantial movement effects seen registered within the channel.

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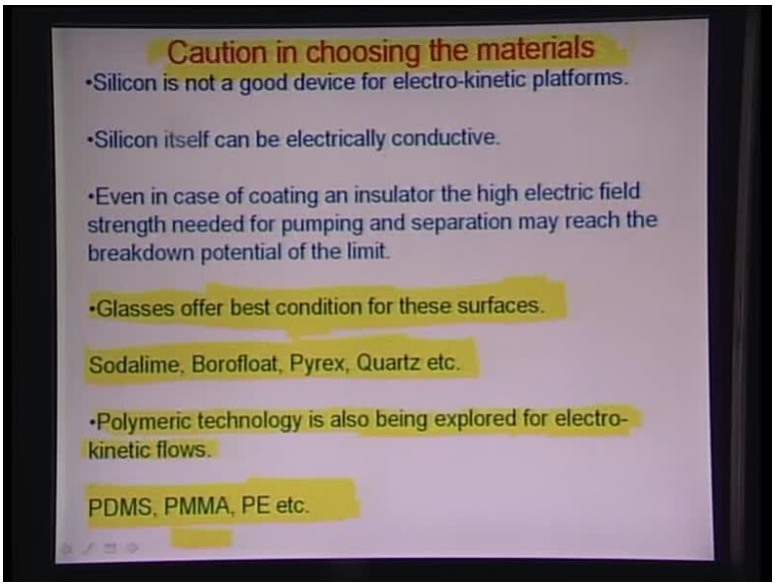

So there has to be a certain caution in choosing materials especially, for the electro-kinetic applications. Silicon, particularly, is not really a good device for electro-kinetic platforms because silicon itself can be electrically conducting depending on, whether it has dope end material.

So, silicon can typically change behavior from being insulating to being conducting, because that is how the semiconductors behave. The band gap that they have is

essentially a function of temperature. It all depends on if there are few electrons which are the valance band, get thermally excited to the conduction band or not, at certain temperature. So, it is really not a very good device for electro-kinetic platforms, and what will happen by the way, if the platform is electrically conducting? The current will rather flow through the silicon and there would not be any registered ion movement because of this. So, it will flow through the silicon in general.

Silicon would be a short circuit in that application. On other hand glasses does offer a pretty good surface for investigating or exploring such kind of flows - you know - different types of glasses - Sodalime, Borofloat, Pyrex, Quartz etcetera. So, glasses do offer a better condition in comparison to silicon. One of the reasons is that, glass is a better insulator than silicon is. Silicon, essential is a semiconductor. It has a very different band gap, structure than what insulators do have to offer, and some of the glasses which are commonly use Sodalime, Borofloat, Pyrex. Quartz is very clean form of glassy material essentially, it has a very clean absorption spectrum one of the purest forms of glasses. It is available as very good for optical detection as well.

So, in electro-kinetic applications, there are lots of research initiatives which have been taken in the area of protein or DNA movement, where fluorescence read outs is one of the ways of detecting, how these molecules translate across these particular chips - right? Therefore, glass also provides this additional advantage, that can have a good transduction mechanism, optical mechanisms can be easily executed and because of the optically transparency of the glassy material.

Of course, if you consider fabrication protocols, silicon has a very well defined protocol of etching - wet or dry, depending on whether the etchant is a gas phase or liquid. A glass, of course, can be etched using mostly wet etching techniques, and depending it has to - you know - the process essentially, has to be done in a clean area and this has to also be, preceded by photolithography step, where very small, thin architectures - really micro - have to be developed. If you recall the example that we showed in the last few slides of designing an electro-kinetic pumping network, the diameter of the capillary in question was only 100 microns. So, you cannot etch a 100 micron feature without doing photolithography step, preceding the etching step. So, whether it is silicon or glass, these techniques are very useful only because of the fact that this microsystems technology, fabrication technology area, has been very well developed.

Polymers, as we know, has also a substantial amount of advantage being bio-friendly and also flexible to amenable fabrication techniques. Polymer technology is also being explored for electro-kinetic flows, especially materials, which can change or get oxidized on exposure to gas plasmas like PDMS, PMMA, Polyethylene and these are some polymeric materials which can form the salon all kind of bonds SiOH bonds on there surface, on exposure to some gas plasma systems. Such surface modifications being explored and exploited for the motion of charged molecules using this concept of electro-kinetic flows. So there has to be definitely some amount of caution in choosing the materials for designing the electro-kinetic flowing systems.

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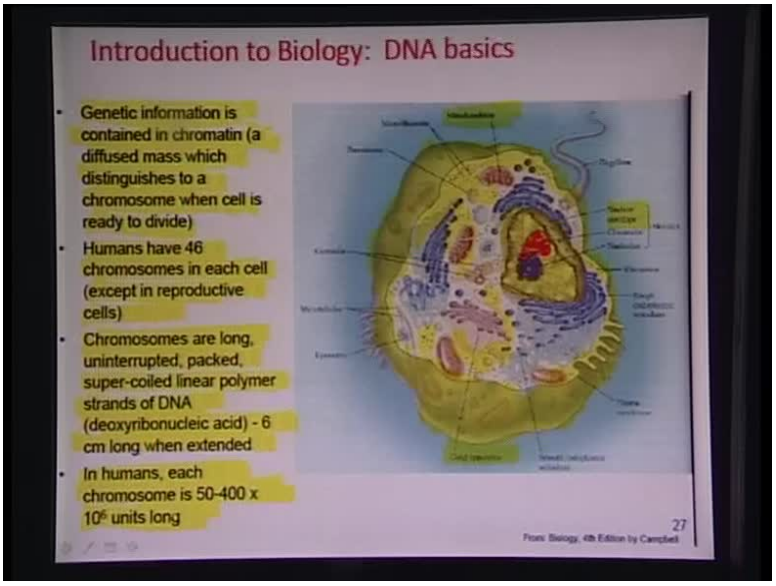

So, let us actually, now, delve into a little bit of why is it really that we need ,these all different techniques of sensing or transport to do analysis, or to do diagnostics. So, I would like to just explore some basics, some preliminary-level topics in biology, as a part of this course, because this would be important for understanding and the utility of these areas as well. So, let us look at one of the most fundamental - you know - building blocks of our own systems - our own human body, the cell.

So, the cell as we know, is the smallest unit, a repetition of which can make tissue. Our body is comprised of millions of these tissues, and there is an engineering aspect associated with the way the cell behaves. It is wonderful to assume that all our body functionalities are in a level of equilibrium of homeostasis, and any deviation from this

abnormality is like an equilibrium reaction. It would automatically cause and effect, and the effect can lead, or essentially, would lead to taking the equilibrium back to its original position. So, let us see what all constituents are there in cell to begin with.

So, cell essentially has a membrane, this right here - if you see here in this area - is the cell membranes made up lipid bilayer and there are molecules which are floating in this lipid bilayer molecules, like proteins, as if they were moving through jelly. So, essentially, this layer here, is more like a gelatinous membrane, which holds together what is there on the inside of the cell. So, in the inside, we have a thick liquid also known as cytoplasm. You can see this here, essentially, is the liquid which is also passed around, and this is not all to it, because there are certain small organelles, which float around in this liquid and each of this organelle, has a different purpose and goal. Like for example, we have this mitochondria; we have endoplasmic reticulum, which is also the protein warehouse of the cell; we have golgi bodies, and then we have something which is nerve center of any cell, the nucleus.

So, essentially we would be more concerned with what happens in the nucleus, and how the nucleus essentially a programming computer which defines, what the cell has to do at its next step in the life cycle. Therefore, it is very very interesting for an engineer to be able to delve into this, and learn some lessons from what mother nature has to offer as one of the finest pieces of engineering, that it has ever created.

So, in the nucleus most of the genetic information is contained within area called chromatin. It is a diffused mass which distinguishes to a chromosome, when a cell is ready to almost divide. So essentially, the genetic information is somewhere in this particular region here. These are all present as chromosomes, and chromosomes are this double Y-shaped structures - something like this. So, you have two Ys coming out at either ends, and what the chromosome has is essentially a set of a highly, highly-compressed super coiled DNA.

So, if you look into the human system, we normally, all cells in the human system have 46 chromosomes in each of the cells except the reproductive cells, where there are 23, and essentially, the idea is that the two reproductive cells from either sexes, come together to produce the 46. So the chromosome, essentially, is also responsible for replicating a cell into another cell or creating what do you call - life. So, it is a kind of

program or code which has been given by mother nature for the cell to be identically able to duplicate itself into two or more forms, from its own form. So, in a sense, the human system has about (all cells have about) 46 chromosomes, and all except the reproductive cells in the human body, share this number.

As we indicated before, chromosomes are long uninterrupted packed, super-coiled, linear polymeric strands of DNA molecule. Just to add a few surprises for you, the super coiled form of DNA in a chromosome - if you just open up and spread around, it can be as long as about 6 centimeters. So, starting from small molecule or bunch of different molecule, this molecule can extend all the way about 6 centimeters. So can you imagine the kind of compression density that it has? The nucleus could be about - close to a micron size, so you can think about it that how much amount of compression is needed for compressing something which is about 6 centimeters of length, into almost, about a micron cube size volume.So, it is really highly densely packed structure which is available inform of a chromosome.

So, in humans, each chromosome is essentially about 50 to 400 into 10 to the power of 6 units long (by unit, you mean base pairs) so, this is about how much you will have in a one chromosome in terms of the different base pairs on a DNA. So, about 400 into 10 to the power of 6 units are base pairs on 1 chromosome. If you consider the whole DNA, spread it out and see how many base pairs are there, it is as high as 400 into 10 to the power 6. So, this is the kind of number of molecules which you are also essentially packing into the small an area.

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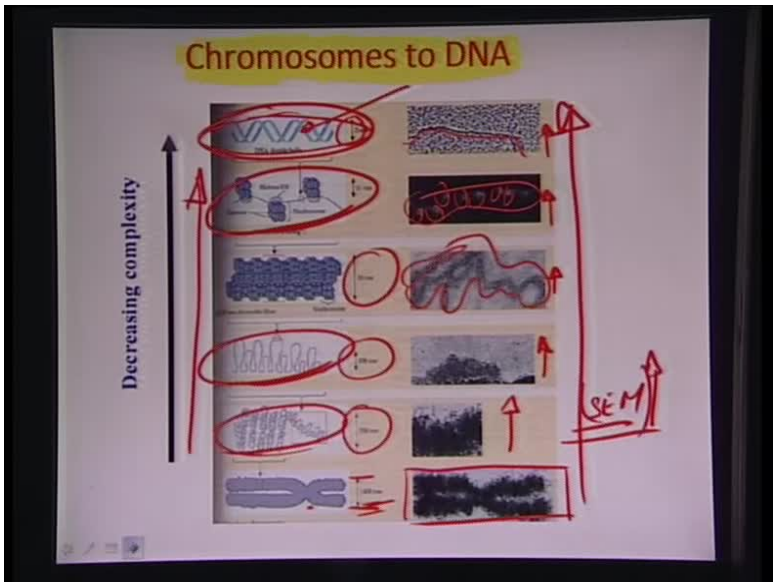

This is a very good illustration here, if you look at - you know - what modern science and physics has to offer, in terms of imaging modalities. So, the left here is essentially an animated sequence of how you can go from a chromosome which is double Y-shaped structure, all the way to a single molecule, a helical molecule of deoxyribonucleic acid. So here it is a super-coiled, super compressed structure in form of a double Y and here if you just keep on opening this in the various steps you were seeing here, it is just about beginning to open this super-coiled structure, step by step, and the new, come finally to form here, which is the DNA molecule.

This is essentially what really happens, if you are using scanning electron micrographs, SEMs, to decipher what is going on here. So, you have case 1 here, which is really what the chromosome looks like. It is this double Y- shaped structure, you blow it up by increasing the mag, or the magnification, and find out that it slowly goes all the way up to the level of a single DNA, which is pretty much like this. So, these are the individual base pairs here - if you see - and this is how the DNA would look like really, and this is the backbone of the DNA. This is a what a coiled, un-coiled DNA is going to somehow look like. So, this is on a real scale that what happens if you look at a chromosome by increase magnification. It is kind of analogous to this image here which is more animated image. So, here the scale is about 100 nanometers; this size, this arrow, is about 100 nanometers - I'm sorry 1000 nanometers and this arrow here, is about 1000 or 1400 nanometers. This arrow on the top here, is about 200 nanometers, 300 and then you have

about 30 nanometers 11 and 2 nanometers finally. So, this is essentially the highest magnification your resolving length which is only 2 nanometers, represented by this arrow here. So, it is decreasing complexity or increasing magnification, that you are looking at. This gives a sequence of what DNA would be from, when extracted from a chromosome.

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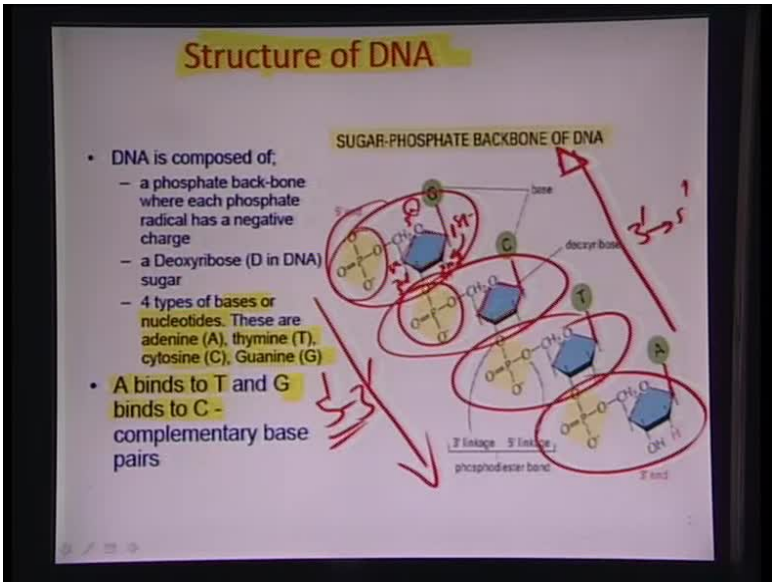

Let us look a little more into what DNA molecule really would look like or behave. So DNA essentially, is like a twisted ladder. You take a ladder, you all know what a ladder is, right? So, in a ladder you have several of these connecting pieces in between two sides – you know - two planks, and this connecting pieces are essentially the steps for ladder. So, if you take a ladder and twist it, and give small, small rotations and try to a twist it, that is how DNA molecule essentially, is made up of. So, the flanks of the ladder, the analogous part in the DNA, is essentially this sugar phosphate backbone. So, you have a 5 Carbon ring here - as you see - and you also have a phosphor diaster linkage between 2 such 5 Carbon rings. This is one ring, this is the second ring; there is a phosphor diaster linkage between both the rings, and there is also a kind of notational representation that all molecules possess. In fact, Biochemistry has been very organized approach of how to grade and number the different positions in a certain molecule of the different atoms. So here, we start with this particular Carbon atom and call it the first Carbon.

We move in a clockwise manner so, this is the second Carbon; this is the third Carbon; this fourth Carbon, and this is essentially, the fifth carbon. So, when we are going from - let us say, bottom to top, we are essentially going from the 3 prime to 5 prime side in going from, on the other direction, we are coming back from the 5 prime to the 3 prime side.

So, also at the first Carbon we have several of these base pair groups, which are covalently bonded to the first Carbon of the sugar molecule, and there are four such groups in DNA - they are Adenine, Thymine, Cytosine and Guanine. So typically, four types of bases or nucleotides, and also very interesting factor, a very fantastic mechanism of this arrangement of molecules is that, these base pairs - Adenine, Thymine, Cytosine, Guanine, only bond to its counterpart; that means, Adenine binds to only Thymine; Guanine only binds to Thymine. We will just see in little bit - why this happens, but then the idea is that Adenine cannot bind to Cytosine, or Guanine cannot bind to Thymine or vice versa. This is a very fascinating event because essentially, there is some kind of orderliness that further nature has automatically provided by ensuring that only specific the bondage between 2 molecules out of all the 4 is allowed. So, if you have a sequence of these base pairs on one side, you will only have their complementary sequence of the base pair on the other side, which is corresponding to the molecule of interest. It has given you a certain kind of a selection probability or it has made your probability of selection of a certain sequence, higher over the other sequence, this is a fascinating approach or thing that mother nature has to offer. This is one of the principles of diagnostics also, that if I can somehow be able to find out what is there on one flank, I should be able to predict what is there on the other flank of the molecule, in terms of the bases. So, let us look into a little more details of the structure of how these bases are realized.

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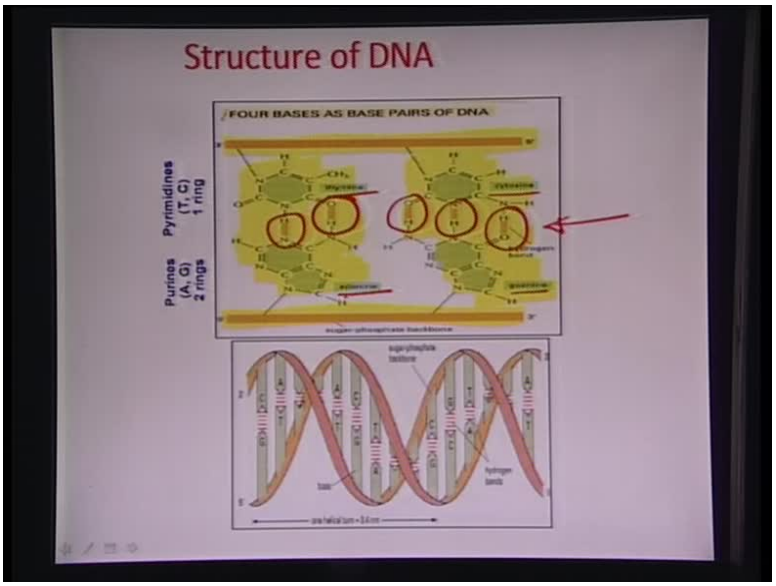

So, if you look at this particular figure here, you have the backbone, the sugar phosphate backbone represented as this orange and thick lines on both sides, and the base pairs here are essentially the connections between these two orange lines. You have Thymine and Cytosine on one side, and Adenine and Guanine on one side. So, the fascinating fact about this is that if you look at really the Thymine and the Adenine bond so, if you are looking at the Thymine and Adenine bond here, we find out that there are only 2 hydrogen bonds between the 2 moieties. So, there are only 2 work centers, 2 bonding centers between the 2 moieties, whereas you look at the Cytosine and the Thymine, the Guanine coupling or pairing you have 3 hydrogen bonds between these 2 moieties. So, one of the reasons why nature offers this unique selectivity of complimentary paring - if you have 3 hydrogen Cytosine bonding to let us say, 2 active side Adenine as vice versa. There is going to be a Thermodynamic problem, it is going to be a unstable structure, or the bonds are not completely filled, and therefore greater probability would be that the molecules with 2 hydrogen bonds, would bond to the molecules only with 2 active sides. Similarly, at the molecules with 3 hydrogen bonds would alternatively bond to molecules with 3 active sides.