Microfluidics
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Lecture - 38
Micro reactors (continued)

Okay so let us talk about microreactors. Microreactors are small size devices where the reaction takes place in a narrow confinement in a channel typically of size less than 100 micron okay. So you know the applications of microreactors can be into production of chemicals and they can also be used for analysis of chemicals okay.

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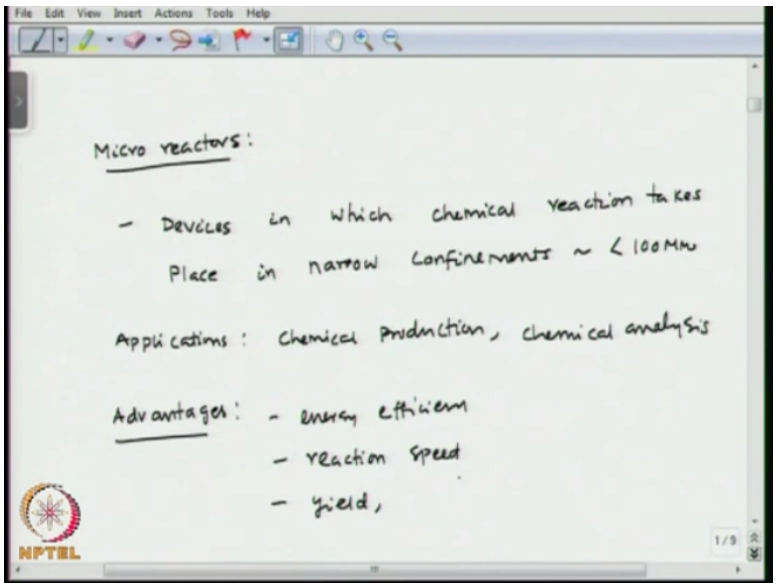

So we are talking about microreactors and these are devices in which chemical reaction takes place in narrow confinements and typically they are of size<100 micron and their applications into chemical production and chemical analysis. Some of the advantages of microreactors, they are energy efficient. The energy efficiency is higher and the reaction speed is faster because of the smaller size.

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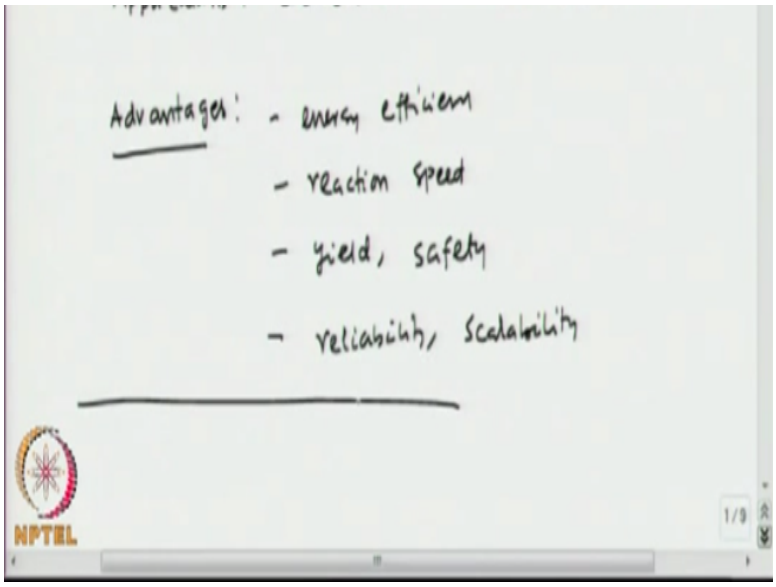

The space time yield as we will be talking about is much higher as compared to conventional reactors and safety is much better and reliability and scalability (()) (02:31) much better in microreactors okay.

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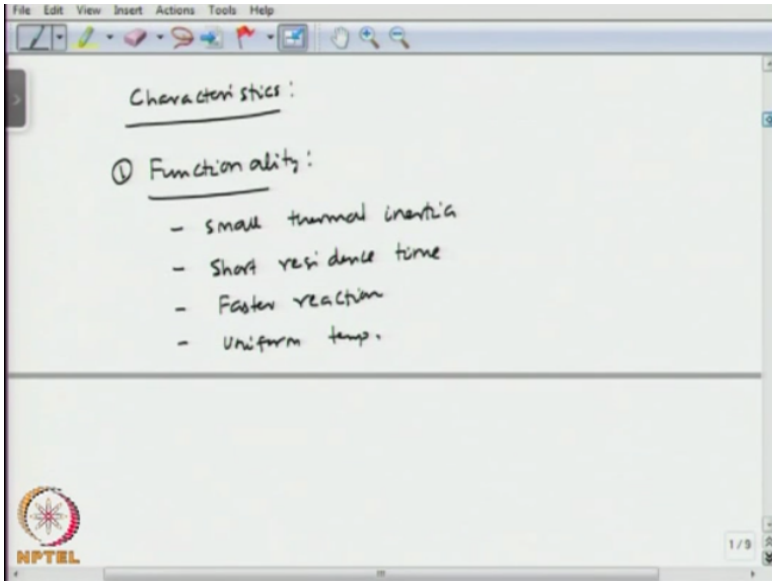

So let us look at few characteristics of microreactors. The microreactors have smaller size okay and larger surface area to volume ratio. So they would benefit in terms of several advantages, 1 will be you know since the surface area to volume ratio is high, the reaction speed is much faster okay. The thermal inertia is much lower and the temperature uniformity is going to be much better okay.

So some of the advantages in terms of the functionality are small thermal inertia, short residence time and faster reaction, uniform temperature okay.

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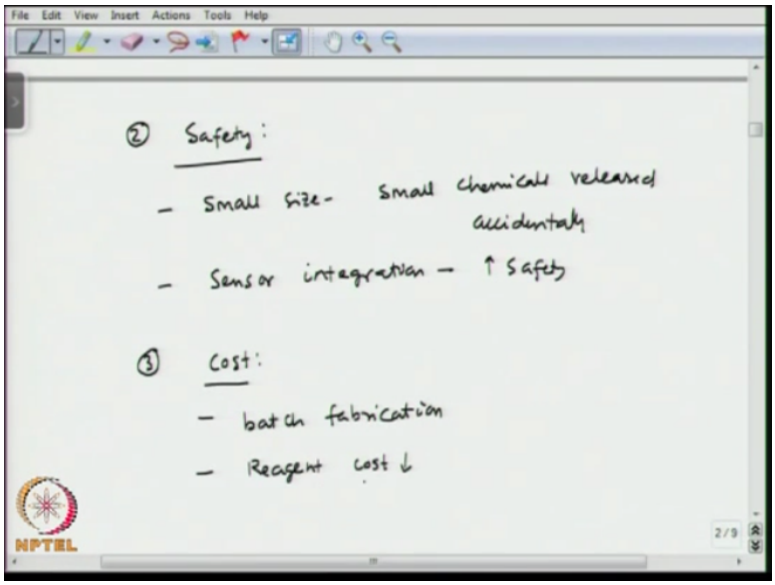

Then there are advantages in terms of safety okay because we are talking about you know small size reactors, if there is any leakage only small volume of reactants will be ejected okay. So the safety aspect is much higher as compared to conventional reactor and also it is possible to integrate sensors within microreactors so that also bring in some additional safety aspects.

So safety aspects because of the small size, small chemicals released accidentally and the sensor integration possible okay so that sensor integration also increases the safety okay and the third aspect is the cost. Since microreactors can be batch fabricated, the cost is less and also the reagent cost is going to be less.

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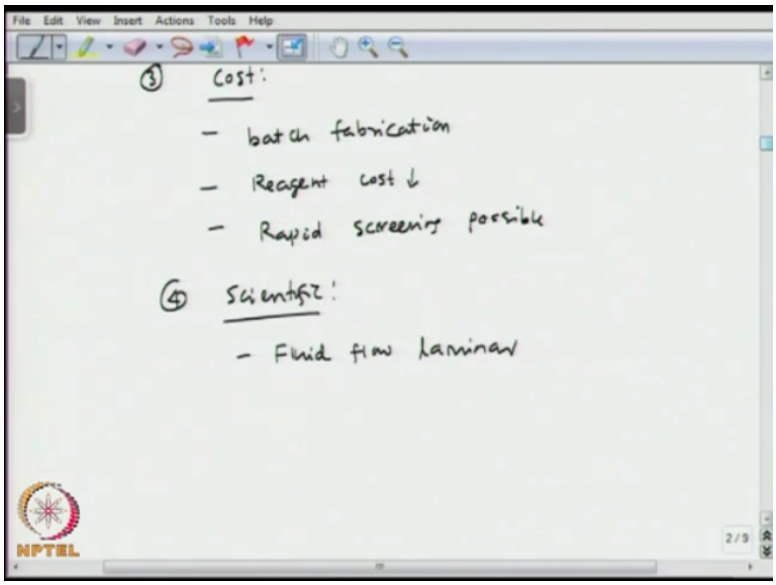

And rapid screening of multiple reactants possible okay. So the rapid screening possible and 1 scientific merit is that in microreactors the flow is laminar because of the lower lens scale and since laminar flow is much better understood you know the microreactors can be easily analyzed. They can be analyzed using you know theoretical models; they can be analyzed using safety codes in a much better way.

So the scientific merit is that the fluid flow is laminar okay. Now let us look at few specifications of microreactors.

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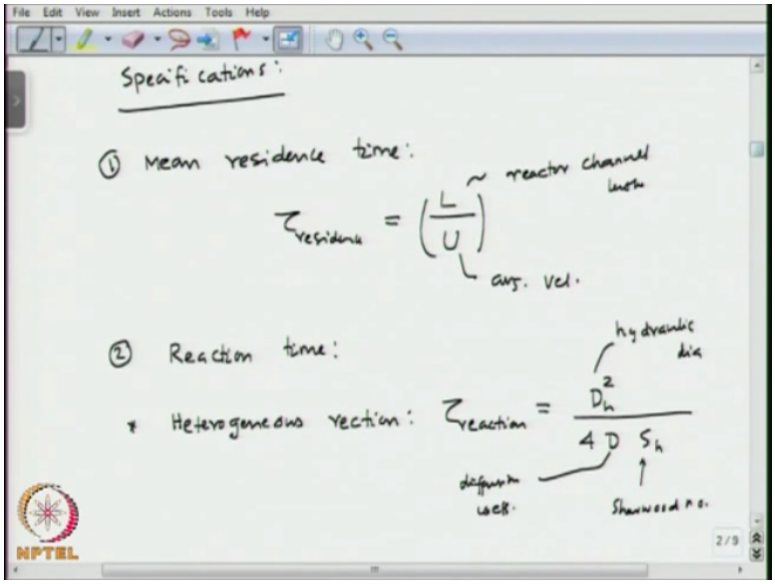

We will look at specifications okay. One important specification is that this microreactors work on continuous flow basics meaning the reactants flow as they react okay. So what it requires is that there should be enough resident time for the reactants to react with each other okay. So the residence time is an important specification in case of microreactors. So 1 important specification is the mean residence time.

So tau residence is going to be L/U, so this is the reactor channel length and this is the average velocity okay. We can find out the reaction time depending on how the reaction is happening. The reaction time is if it is because of heterogeneous reaction then the tau reaction is going to be Dh square/4D*Sh.

This is the hydraulic dia and this is diffusion coefficient and this is called Sherwood number okay.

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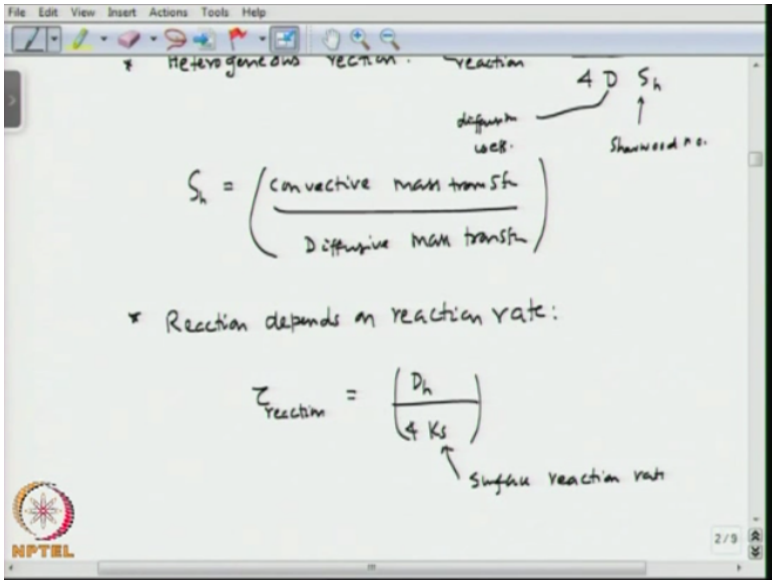

And the Sherwood number is defined as this is the subscript is convective mass transfer/diffusive mass transfer okay. Now in case of a case where the reaction depends on reaction rate then in that case we can write down the expression for tau reaction as Dh/4*Ks okay and Ks is the surface reaction rate okay.

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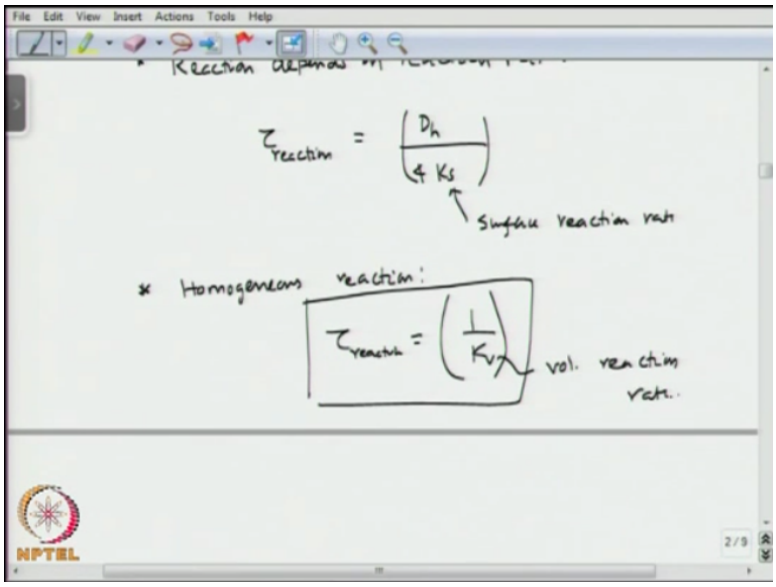

Now in case of homogeneous reaction, tau reaction is going to be 1/Kv and Kv is the volumetric reaction rate okay.

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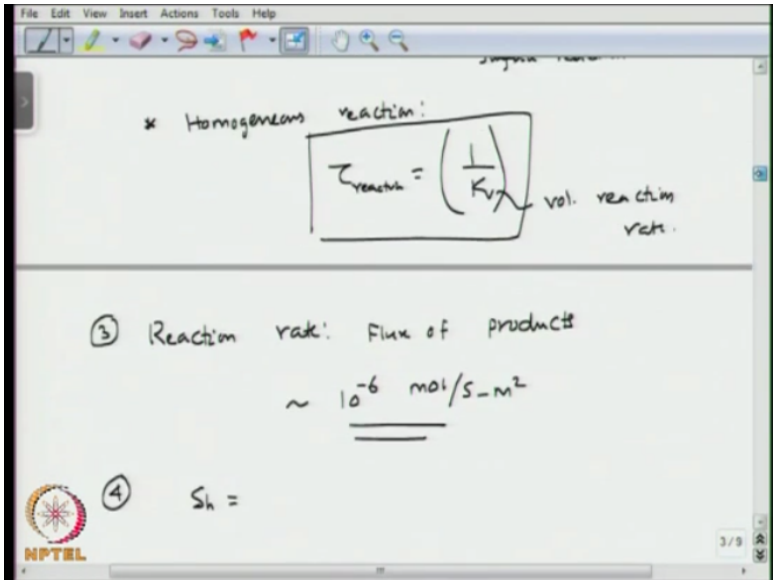

The other specification is the reaction rate so this basically determines the flux of products okay and typically in microreactors, the reaction rate is 10 to the power -6 mole per second meter square okay and the Sherwood number basically convective you know as you have defined is the convective mass transfer/diffusive mass transfer.

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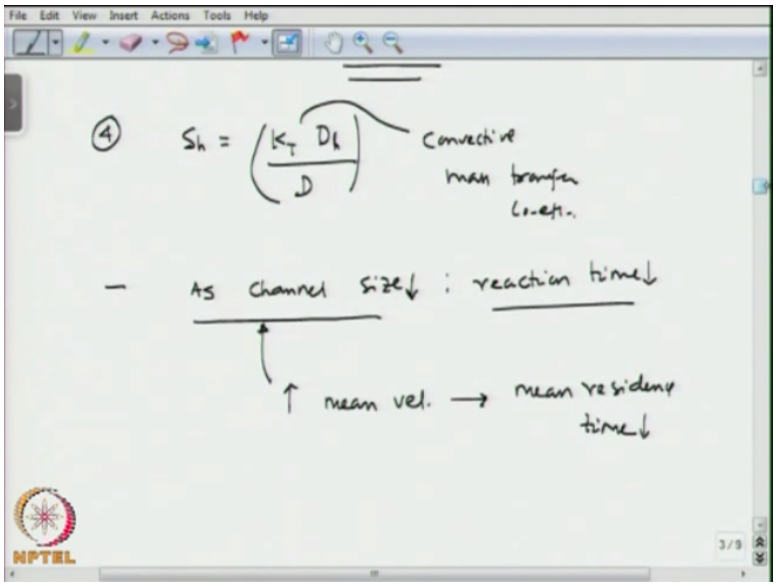

So it is KT*Dh hydraulic dia/diffusion coefficient and here KT is the convective mass transfer coefficient okay. Now as you can see as the channel size decreases if you look at the reaction time, a channel size decreases, the reaction time is going to reduce okay. So if you are talking about smaller and smaller microchannel, the reaction time is going to reduce but at the same time as the channel size reduces.

And we are trying to maintain the same throughput, the flow velocity will be increasing and if the flow velocity increases, the residence time is going to reduce okay. So what ideal you would need is parallel multiple channels. So that the throughput can be you know coming from all those smaller channels. At the same time, it provides enough residence time inside and the reaction time is also reduced okay.

So our channel size is reducing, the reaction time is reducing but the reduction in channel size also is to increase in mean velocity and with increase in mean velocity, we get the mean residence time reduces okay.

So a characteristic of a good reactor will be that the reaction time is reduced but at the same time the mean residence time is to be maintained to a minimum okay so that the reactants get enough time to mix with each other.

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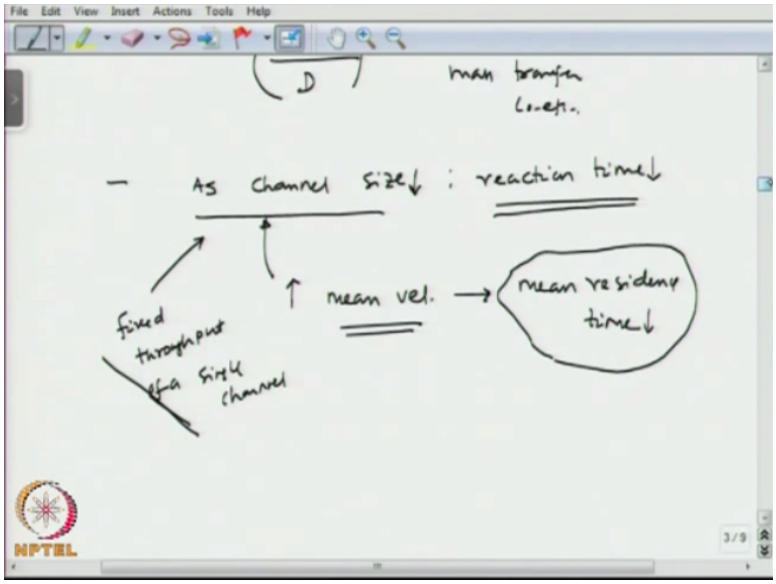

So that is at a fixed throughput okay fixed throughput of a single channel. Now if you divide this channel into multiple parallel channels, so that the reaction time reduces but at the same time the mean velocity remains the same because we have divided the total flow rate into different sub channels then we can reduce reaction time at the same time we can have some minimum residence time.

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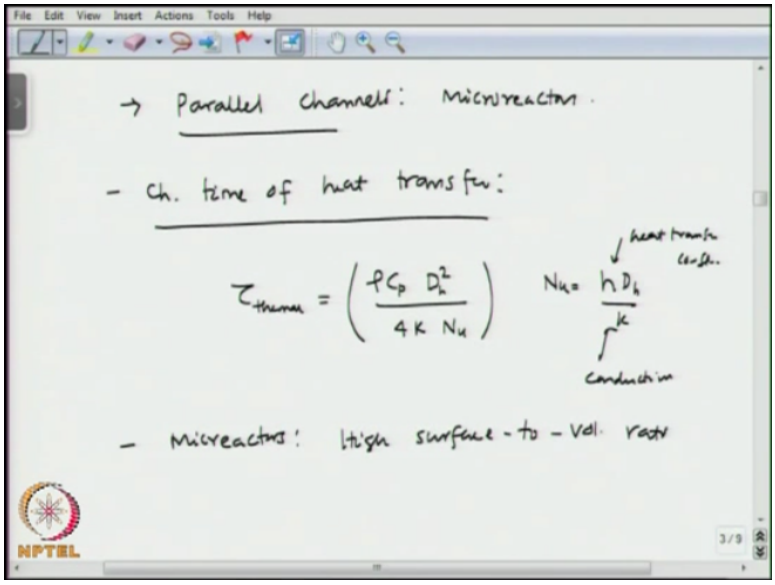

So one approach to do that is to use parallel channels okay, parallel channels in microreactor okay and for that reason, the typical microreactors will have many such parallel channels to get a significant amount of throughput at the same time with the reduced reaction time and some minimum residence time that is required okay. So the next parameter that we define is the characteristic time of heat transfer okay.

So the characteristic time of heat transfer, which can be defined as so tau thermal is going to be rho Cp*Dh square/4*thermal conductive*Nusselt number okay where Nusselt number is h Dh/k, k is conductivity and this is heat transfer coefficient okay. Now here since we are talking about microreactors, the surface area to volume ratio is going to be high so the heat transfer is going to be much better okay.

And you know if the heat transfer time scale is going to be larger than the reaction time scale then there could be chances of explosion okay. So you know we are talking about microreactors, so we are talking about high surface to volume ratio okay.

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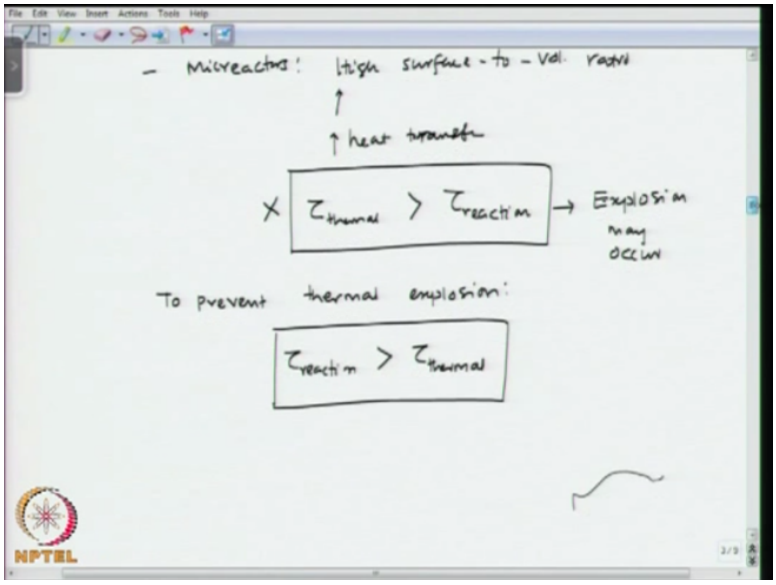

So that means increased heat transfer okay. Now if you have the tau thermal>tau reaction then there is a chance that explosion may occur okay. So we should take care such that you know to prevent thermal explosion the tau reaction must be>tau thermal okay.

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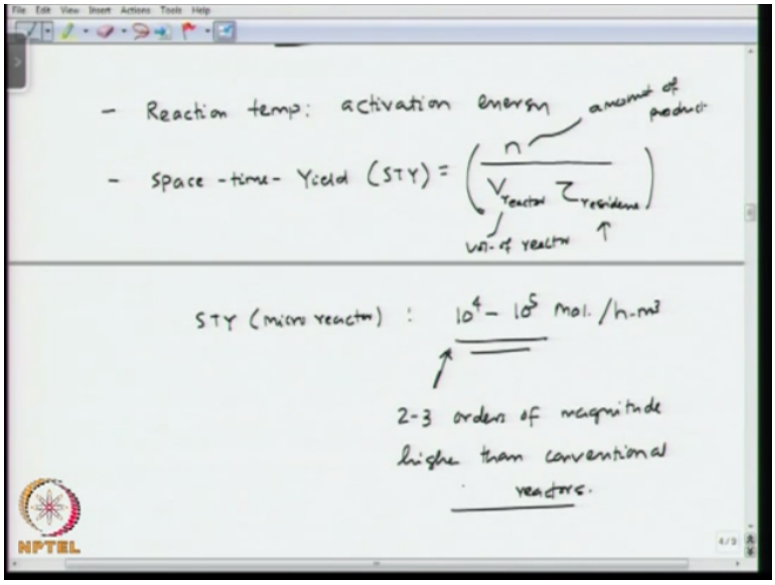

Now the other important parameter to specify is the reaction temperature and the reaction temperature is dictated by the activation energy of the reaction okay. So it depends on the activation energy. Now the other parameter is the space-time-yield. The space-time-yield is defined as the amount of product n/the volume of the reactor okay/the residence time okay. So this is the amount of product.

This is volume of reactor and this is residence time. The typical space-time-yield of microreactors is about 10 to the power 4 to 10 to the power 5 mole per hour meter cube okay

and the space-time-yield of microreactor is about 2 to 3 orders of magnitude higher than the conventional reactors okay. So this is about 2 to 3 orders of magnitude higher than conventional reactors okay.

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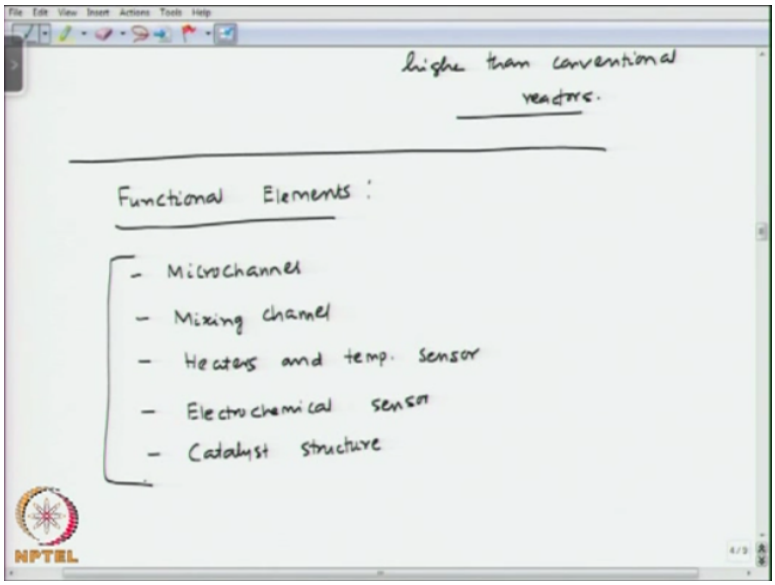

Now let us look at some of the important functional components of a microreactor. So now let us look at the functional elements of a microreactor so the different functional elements so we will have a microchannel okay and we would have a mixing channel where the reactants will mix and will have heaters and temperature sensors. Then we will also have electrochemical sensor to monitor the reaction.

And we would have catalyst, which will initiate the reaction. So these are some important elements of a typical microreactor.

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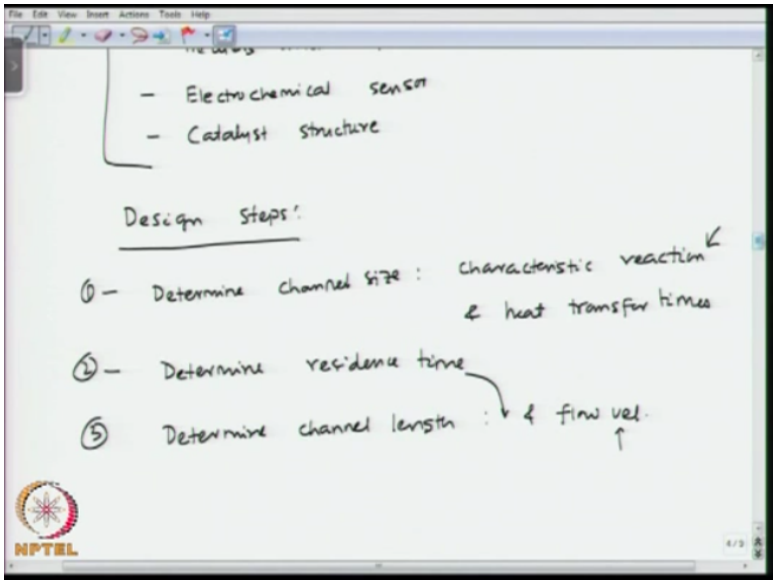

Now let us talk about the design steps, how we approach and design a reactor. The first step is to determine the channel size and this can be done by using the characteristic reaction and heat transfer times okay. So we ensure that the reaction time is>the heat transfer time and determine the channel size and from the channel size we determine the residence time okay.

So after we determine the residence time, the third step would be to determine the channel length accordingly to determine the channel length from the residence time and the flow velocity, which will come from the throughput okay.

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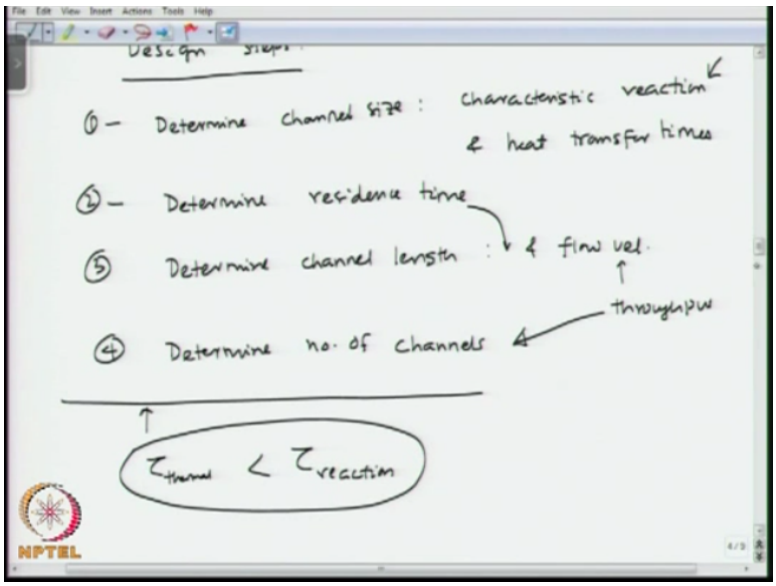

Then the next step would be to determine number of channels, which will also come from the throughput okay. Now one important parameters in the design is that the tau thermal has to be<tau reaction as we discussed earlier to prevent explosion.

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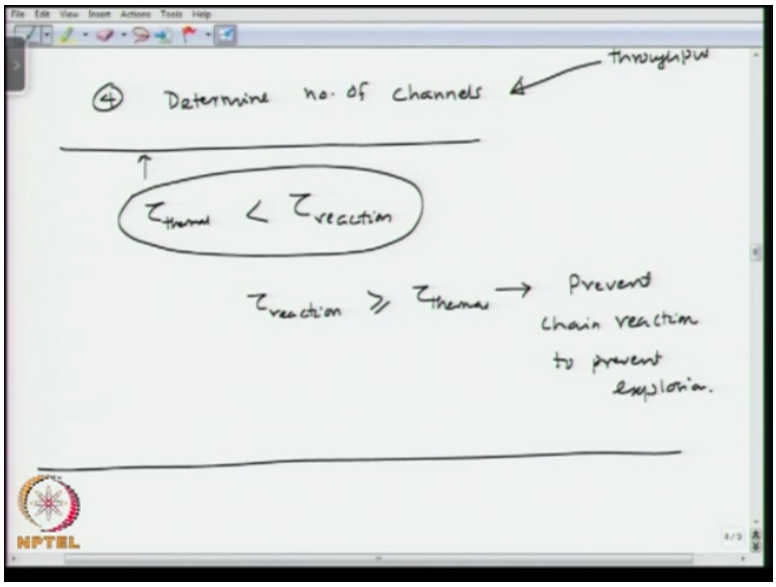

Or in the limiting sense the tau reaction can be>=tau thermal and this is to prevent chain reaction to prevent thermal explosion okay. So with that let us move on and talk about micro fuel cell okay. A fuel cell as we know it is a device that converts chemical energy into electrical energy okay and a fuel cell does that at room temperature okay and micro fuel cells are miniaturized versions of fuel cells and with maximum power capacity less than 5 watt okay.

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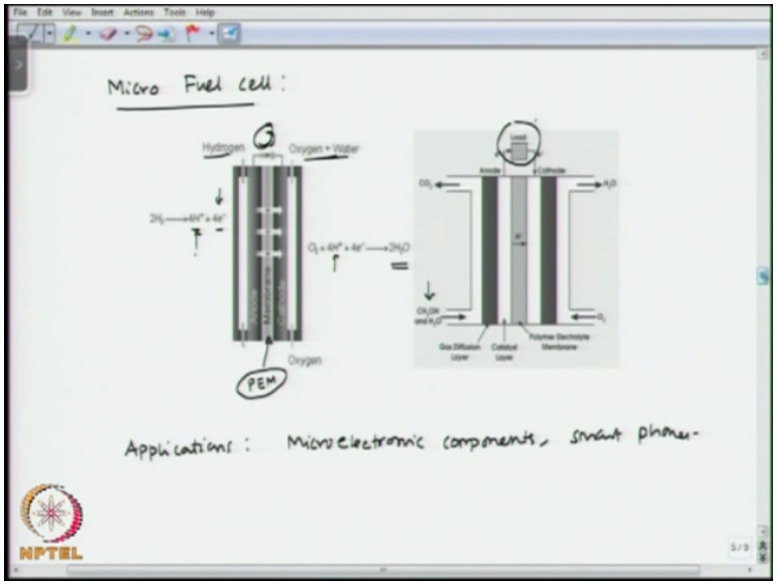

If you look at here this talks about a typical fuel cell what happens in a fuel cell. Here the hydrogen is the fuel, which comes in to the anode side and the hydrogen at the anode breaks into H+ protons and electrons okay and these anodes are porous. They are porous electrodes

so the protons are easily created of the anode and then here there is a membrane which is proton exchange membrane okay.

They can be polymer electrolyte membrane, so this proton exchange membrane basically allows the proton to pass through and the proton pass through the membrane and at the cathode side, we have oxygen coming and at the cathode the proton combines with oxygen to give water okay. So that is what happens at the cathode side. Alternatively, methanol has also been used as fuel.

So here methanol and water go in and methanol will break into carbon dioxide and proton. Proton will pass through the membrane and on the other side it will combine with oxygen to produce water okay. So you know we talk about fuel cell, we talk about micro fuel cell and the principle of operation of micro fuel cells are similar to that of a fuel cell and the applications are into different areas.

For example, for microelectronic components and into smart phones okay. So here as you said the proton passes through the membrane but what about the electron? The electron goes through the external circuit to produce electricity okay. So any load can be taken using the electron that is flowing through the external circuit okay.

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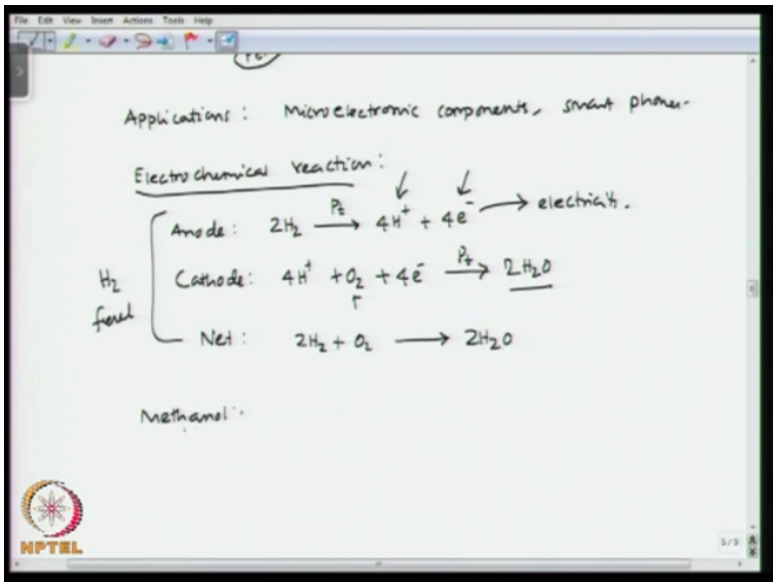

So if you look at the electrochemical reaction, so at the anode we have the hydrogen breaking into proton and electron in presence of a catalyst and at the cathode side you would have the proton combined with oxygen and that would give 2H2O okay. So the net reaction would be

2H2+O2 giving rise to water okay. So this proton goes through the membrane, combines with oxygen and gives water.

And the electron basically goes through the external circuit and provides electricity okay. So this is the case where hydrogen is a fuel okay H2 as the fuel and we can have methanol fuel cells also.

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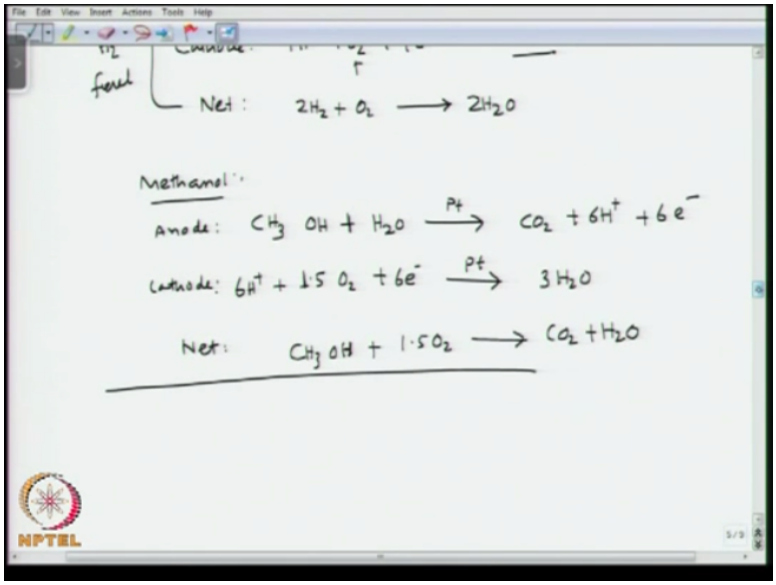

In methanol fuel cell, we would have similar reaction at the anode CH3 OH+H2O will get into carbon dioxide+6H++6e-and the proton will combine with the oxygen to give rise to water okay. So this is at cathode. The net reaction is CH3 OH+1.5 O2 will give CO2+H2O okay. So you know micro fuel cells the principle of operation is you know same as that of the conventional fuel cell.

The only difference is that instead of going for larger channel structures, fuel distribution channels we are going for miniaturized version of the fuel distribution channels and the overall structure of the fuel cell and the maximum power that could be delivered by micro fuel cells are<typically 5 watt.

So here we employ the semiconductor fabrication technology, MEMS technology to fabricate the fuel cells thereby reducing the cost, increasing reliability and increasing the functionality of the device okay.

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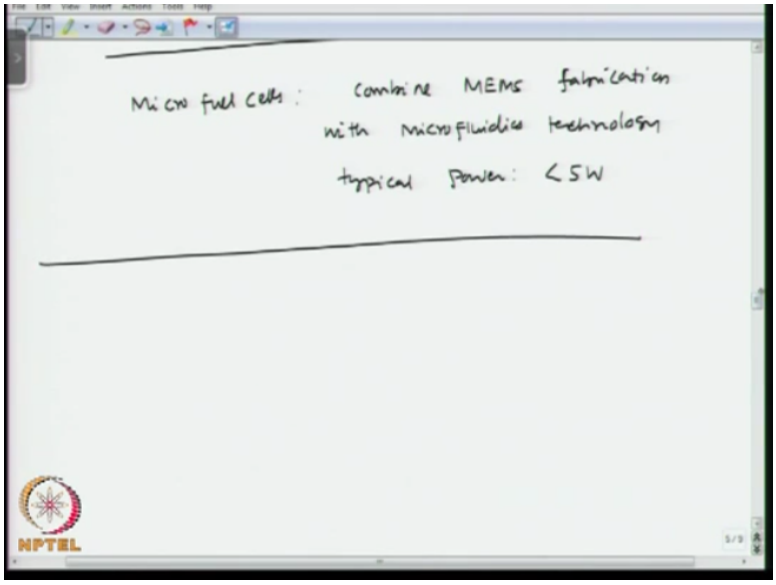

So the micro fuel cells combine MEMS fabrication with micro fluidics technology and the typical power is<5 watts okay. So that is the typical power capacity. So with that let us move on and talk about PCR, polymerized chain reaction. We can fabricate small micro PCRs for analysis of DNAs. So PCRs have different applications. They can be used for you know DNA finger printing to identify the finger prints.

They can be used for diagnosis of diseases. Now before we talk about PCR let us try to understand what DNAs are okay.

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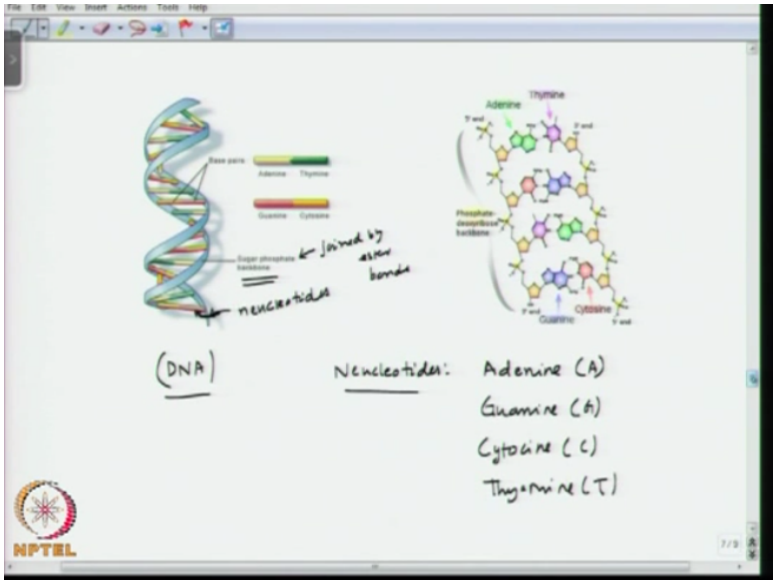

So if you look at here so this is how a typical DNA molecule would look like okay. So this is the structure of a DNA and it has typically 2 long polymers of units called nucleotides okay. So these units 2 long polymers are made out of nucleotides okay and the backbones is made

out of sugar okay. So the sugar phosphate is the backbone and these phosphates are joined by ester bonds okay.

So these are joined by the ester bonds and each sugar is attached to 1 of 4 nucleotides okay. So you know so the 4 nucleotides are adenine, then guanine, cytosine and the thymine AGCT okay.

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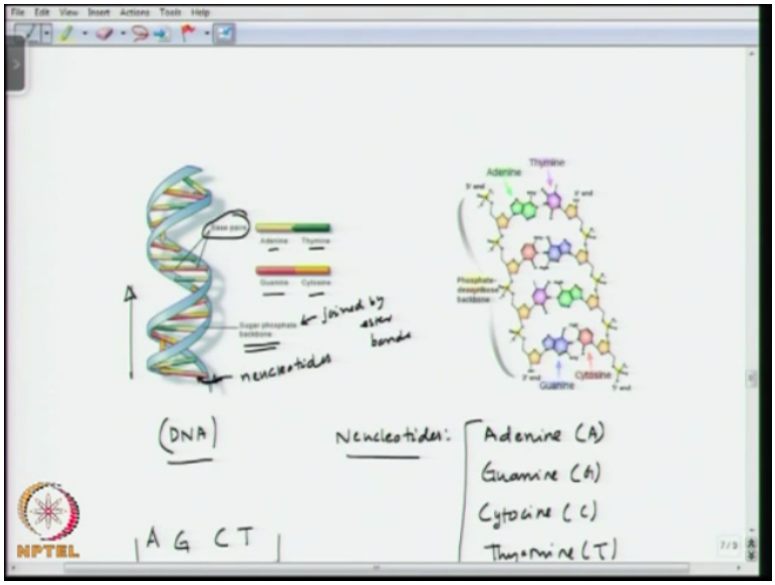

So you know as you can see here so these are the nucleotides base sphere adenine, thymine, guanine cytosine okay. So it is the sequence of these 4 nucleotides along the backbone so AGCT. So these 4 nucleotides they are sequenced along the backbone is what encores the information okay. So the sequence of these 4 nucleotides is unique to a DNA, which is unique to certain individual okay.

So by looking at the nucleotide structure along the backbone of the DNA, we could be predicting which individual it has come from or it can also predict presence of any disease okay. So these sequences can also predict presence of a particular disease okay. So with that understanding let us talk about what you mean by PCR okay.

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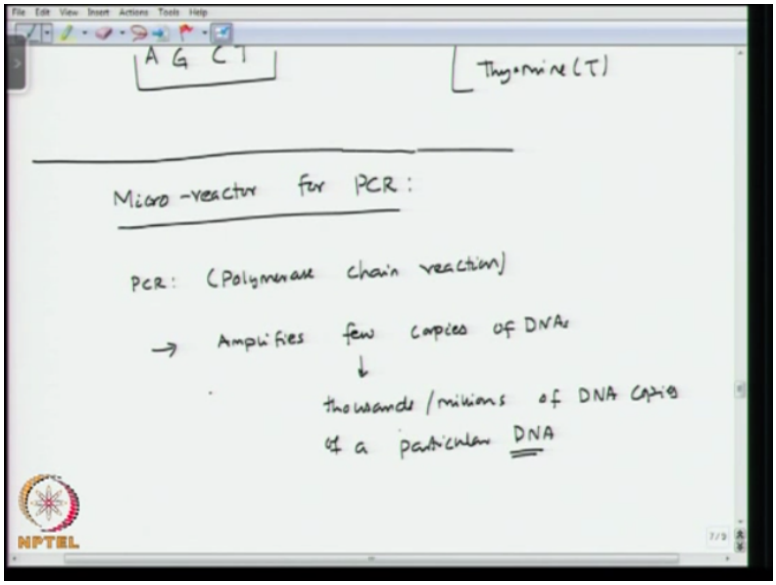

So we talk about the microreactor for polymerized chain reaction or PCR and so the PCR what it does is it takes a you know single strand of DNA or few strands of DNAs and it amplifies to thousands or millions copies of DNA okay. So even if with the a small amount of sample that we have collected will be able to generate enough copies of DNA to be able to detect it okay.

So the PCR process so it is known as polymerized chain reaction so it amplifies few copies of DNA into thousands or millions of DNA copies okay of a particular DNA okay.

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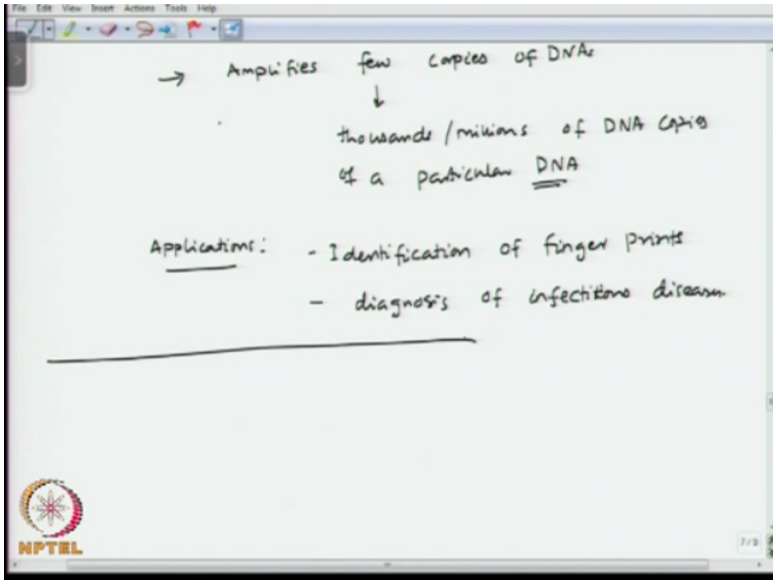

And the applications are into identification of finger prints, which has relevance in forensic application and it can also be used for diagnosis of infectious diseases okay. Now let us look at what are the components and reagents that we need for the PCR process okay.

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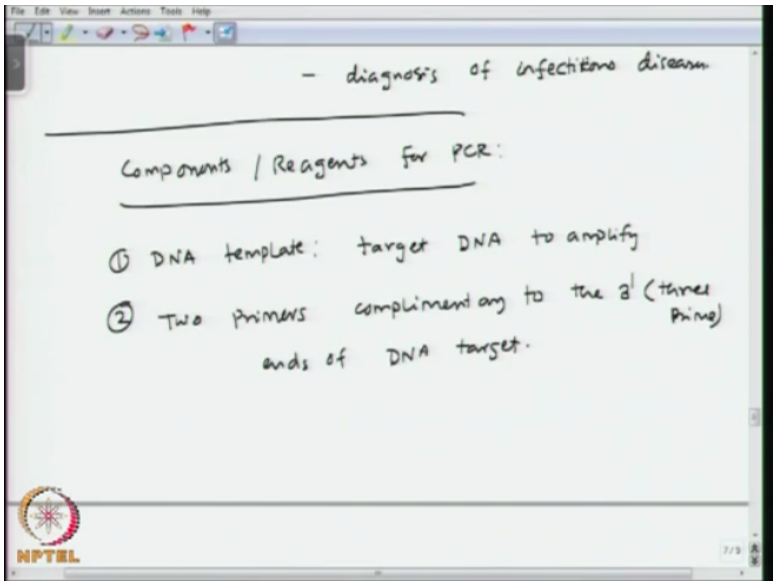

So components and reagents for PCR, we need the DNA template okay. So the DNA template is the target DNA that we are trying to amplify okay. We are going to increase the number. So DNA template is nothing but the target DNA to amplify and the second 1 is 2 primers, which will basically hold the structure. These are complimentary to the 3 prime ends of DNA target okay.

As you know a DNA strand will have a 3 prime and 5 prime ends. So we would need a primer that is equivalent to the 3 prime ends of a DNA strand okay. That is you know complimentary to a 3 prime end of a DNA target okay. So as you can see here the 3 prime end and you have 5 prime end okay. So you need a primer which is complimentary to the 3 prime end of a DNA target okay.

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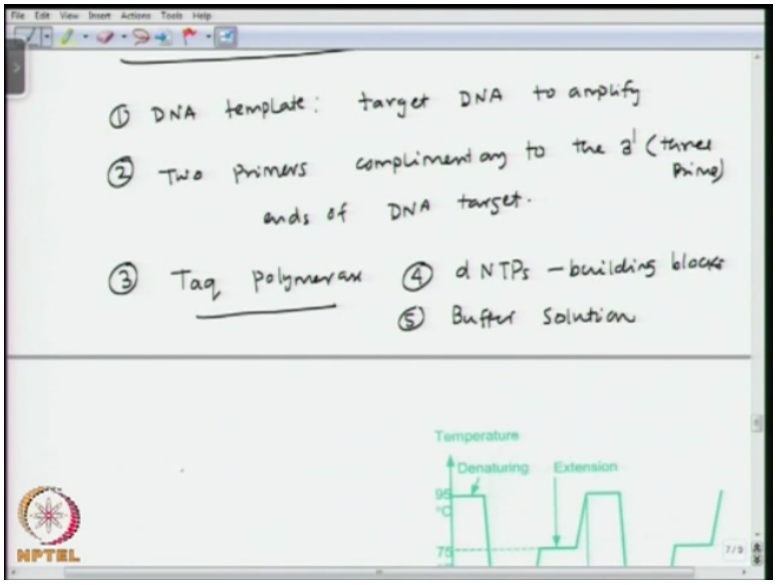

And the third thing we need is a Taq polymerase. So the Taq polymerase is the agent that start to build the complimentary strand equivalent to the single strand DNA using d NTPs okay. So this is the agent and the fourth element that we need are d NTPs okay and these are the building blocks and from these building blocks the complimentary DNA strand is grown and then we need a buffer solution as an environment to do the PCR process okay.

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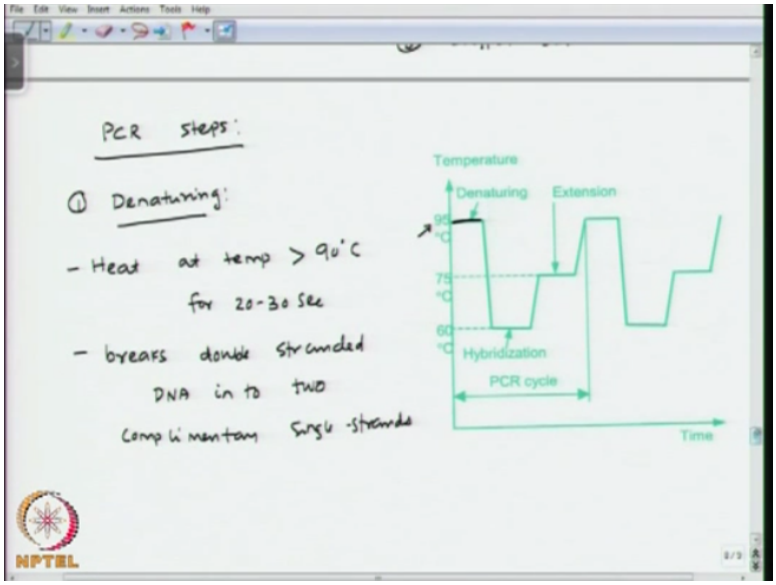

Now what are the different steps of PCR? Will see the PCR steps. First step is called denaturing. During denaturing, the template DNA along with polymerase d NTPs are in a suitable buffer are heated to a temperature about 90 to 95 degrees okay, such that the double stranded DNA separate okay, the 2 strand get separated okay so that is called denaturing where we heat at temperature>90 degree centigrade for 20 to 30 seconds.

And this would break double stranded DNA into 2 complimentary single stranded DNA okay. So this is shown here as we can see this is the denaturing process okay which occurs at about 95 degree centigrade and for 20 to 30 seconds okay.

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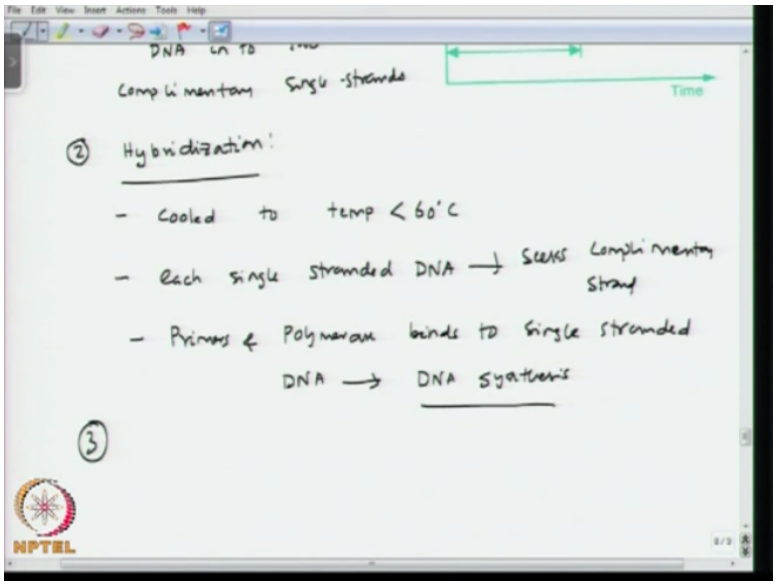

So once the 2 DNA strands separate, the second step would be to do the hybridization and during the hybridization process the PCR elements are cooled to temperature<60 degree centigrade so that each single stranded DNA seeks complimentary strand okay and the primers and the Taq polymerase binds to the single stranded DNA template and the DNA synthesis begins okay.

So what happens is after the denaturation, the 2 strands will separate and in hybridization the DNA strands will be cooled to a temperature<60 degree centigrade and each complimentary DNA strand will look for its complimentary the double strand okay. So each strand will look for each complimentary strand so in that case the Taq polymerase and the primers will bind to that individual strand.

And the polymerase will start using the d NTPs to grow the complimentary strand for each of these individual strands okay.

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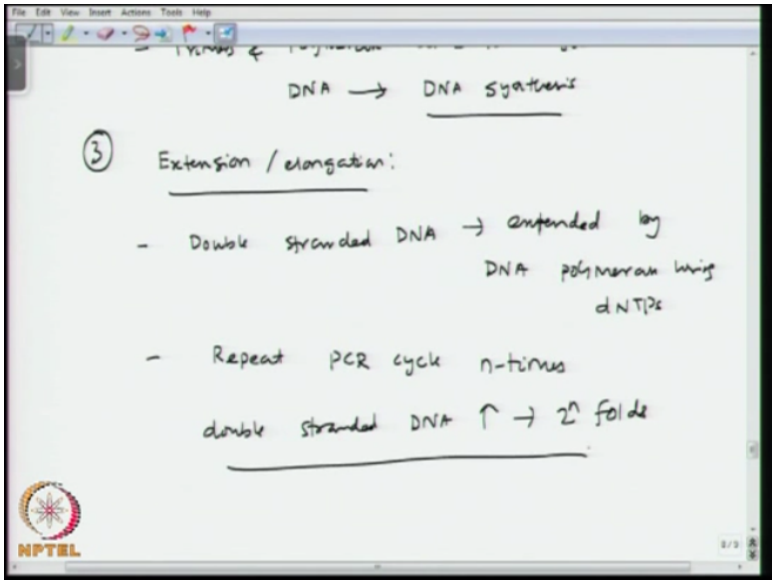

So that is known as DNA synthesis and once the DNA synthesis strands starts we go for what is called extension or elongation. So here in this case, as the polymerase works the double stranded DNAs are formed and it extend okay, extended by DNA polymerase using d NTPs okay and if you repeat the PCR cycle n-times then the double stranded DNA would increase 2 to the power n fold okay.

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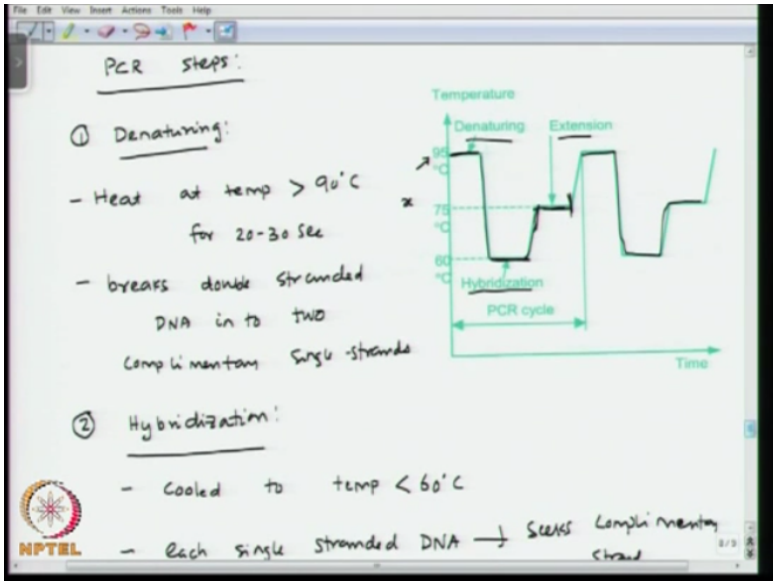

So you know as you can see here so this is denaturing this is suddenly cooling down to 60 degrees so this is the hybridization process. Then increasing back to 70 to 75 degree and then holding it for sometimes is extension phase. So denaturing, hybridization and extension this finishes a cycle okay and if this cycle is continued n-times okay then next we start with you know some number of DNA x.

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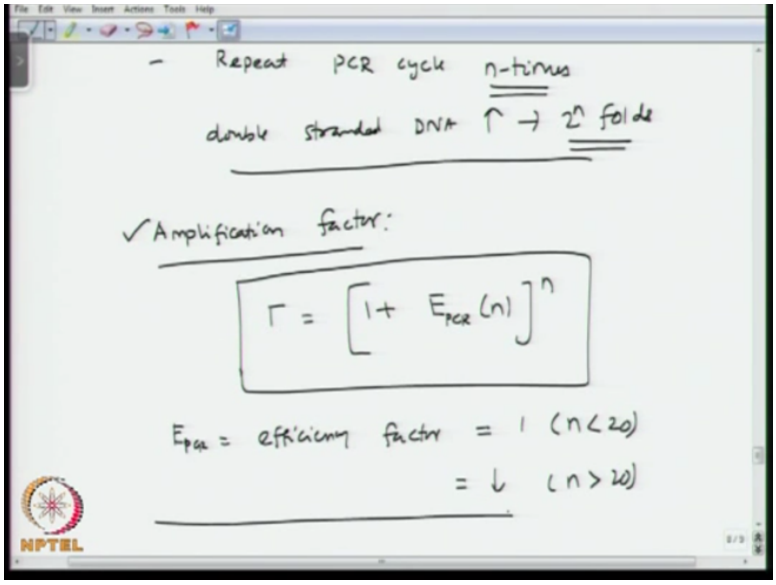

Then by doing n cycles the number will increase 2 to the power n fold okay. So the amplification factor we can define something called an amplification factor and this amplification factor gamma can be 1+efficiency of PCR cycle n to the power n okay. So the DNA gets amplified by n-times okay. So EPCR is the efficiency factor and this is going to 1 if number of cycle < 20 and the value will reduce if n > 20 okay.

So with that understanding now let us take on a design problem where you will you know design a PCR chip okay.

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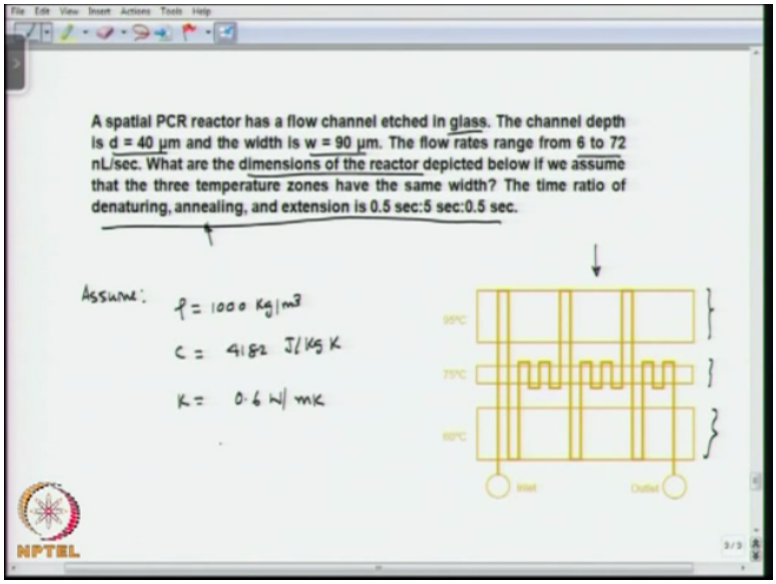

So this is the example that is shown. Here we have a special PCR reactor that has flow channel etched in glass. The channel depth is 40 micron and the width is 90 micron. The flow rates range from 6 to 72 nanoliter per second. Now we are interested to determine the

dimensions of the reactor that is shown below here and we assume that 3 temperature zones of the same width okay.

So these temperature zones have same width and the time ratio of denaturing, annealing and extension is 0.5 second, 5 second and 0.5 second. So annealing is basically the hybridization that we just discussed okay. So the first step you know we can assume that you know liquid the sample has the property as that of water. So we assume that the density is that of water so 1000 kg per meter cube.

And the specific heat is 4182 joule per kg kelvin and conductivity is 0.6 watt per meter kelvin.

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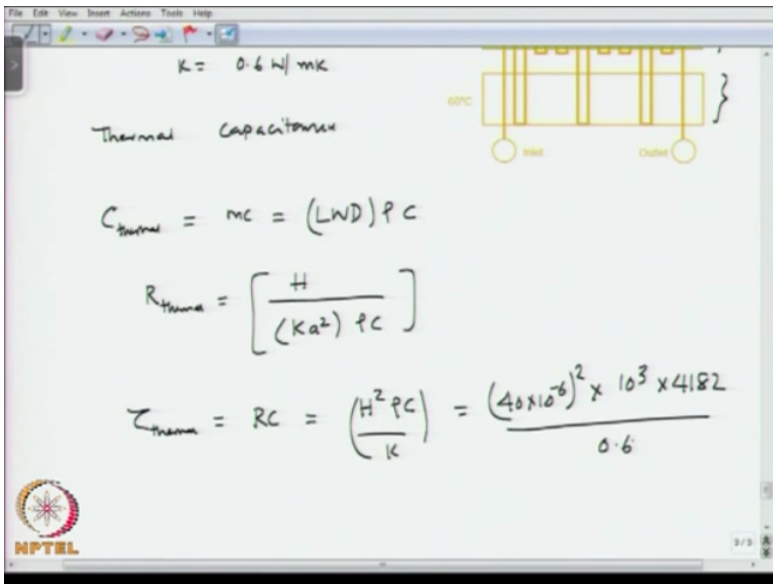

So first we calculate the thermal capacitance. Thermal capacitance, C thermal will be=mc so LWD so that is the volume into density into C. Now from there we can find the thermal resistance and calculate as H/ka square*rho C okay, H is the channel height so from there you can find the thermal time constant, which is RC which is given by H square rho C/k.

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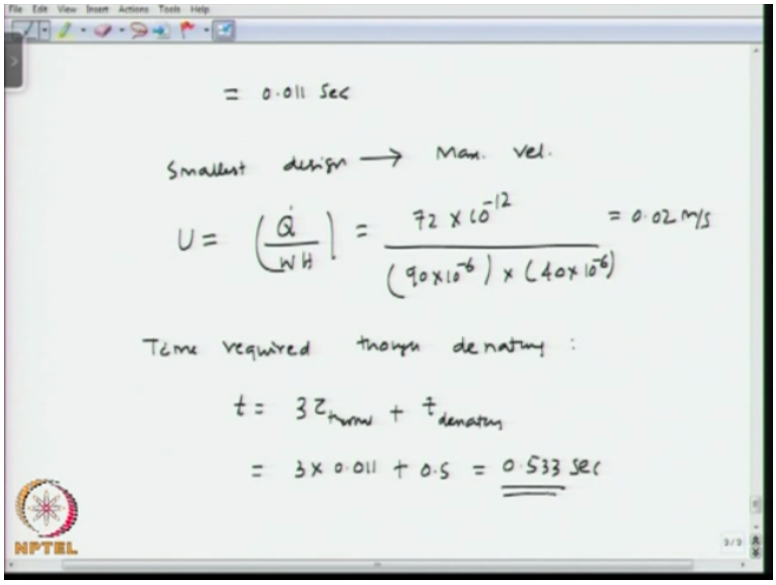

And this will be 40*10 to the power -6 square this is the channel height, 10 to the power 3 is the density, specific it is 4182/0.6, so that will be 0.011 second okay. So the smallest design would consider the maximum velocity okay. So in that case the mean velocity can be Q dot/WH so the flow rate is 72 nanoliter per minute 10 to the power -12/W is 90*10 to the power -6, H is 40*10 to the power -6.

So will have 0.02 meter per second velocity, so the time required through denaturing can be found, so t will be=3 tau thermal+t denaturing. So this will be=3*0.011+0.5 so that will be 0.533 second okay.

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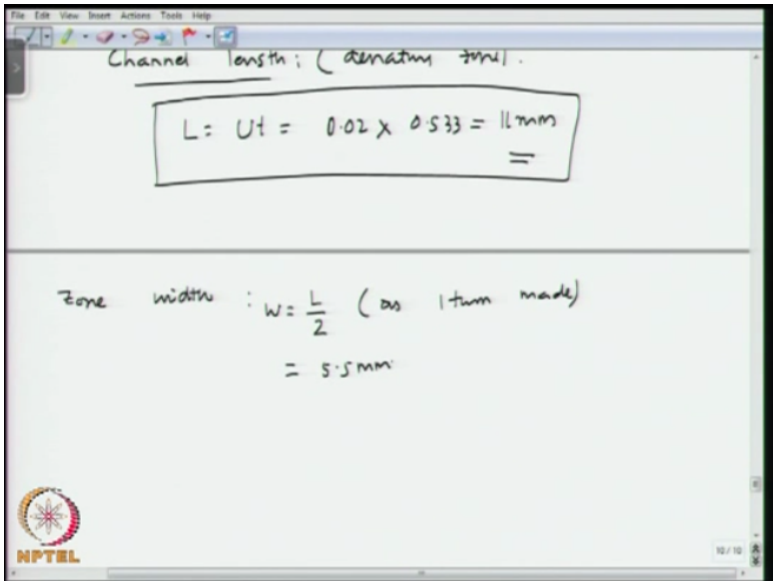

So this is the time required for the denaturing process, so from there we can predict the channel length in the denaturing zone. The channel length L will be U*t, velocity is 0.02

meter per second and time is 0.533 so that will be=11 millimeter, so zone width can be L/2 as 1 turn is made okay. So width=W/2 which will be=5.5 millimeter.

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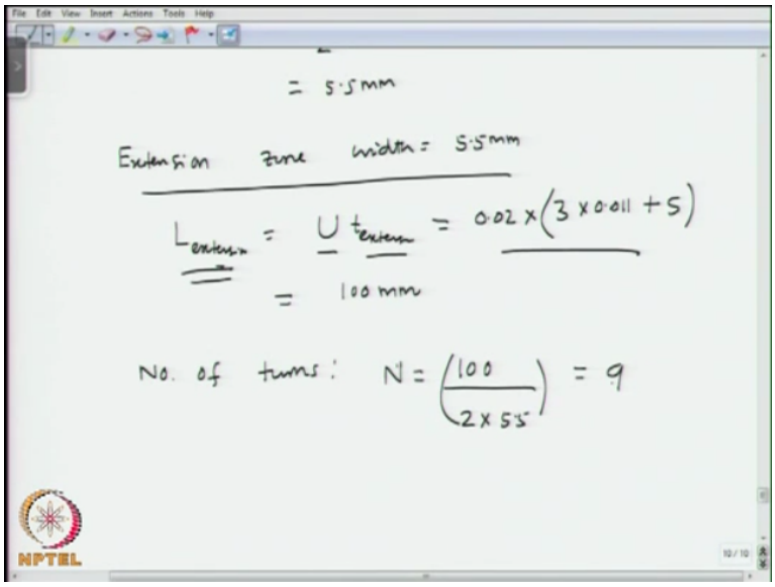

Now the extension zone will have the same width, so extension zone width also be 5.5 millimeter. So the length of the extension zone will be U*t extension, which will be 0.02*the t extension will be 3*0.011+5 so that will be 100 millimeter okay. So the number of turns can be found. Now we know the length of the extension zone because U and t extension zone are known so extension zone width is known.

So number of turns will be N will be 100/2*the width 5.5 so that will be=9 turns.

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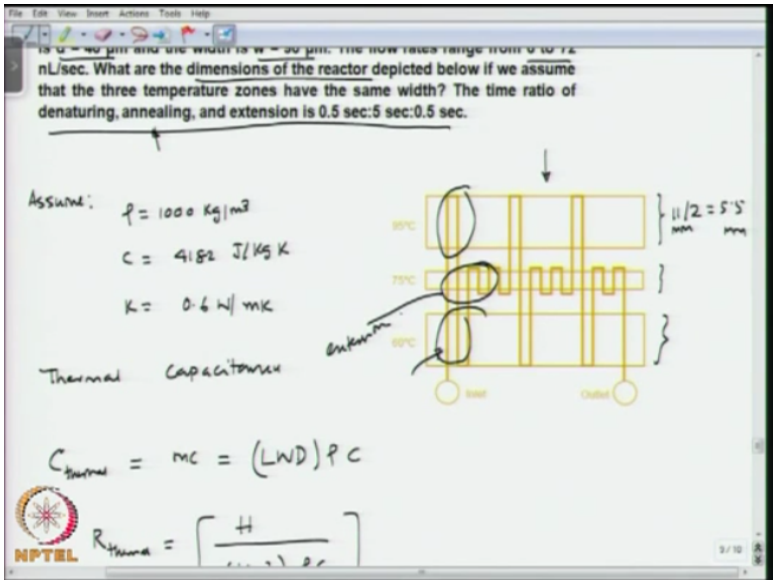

So in the extension zone as you can see here okay so this is the extension zone, this is the hybridization zone, so this is extension zone, the channel will make 9 turns okay.

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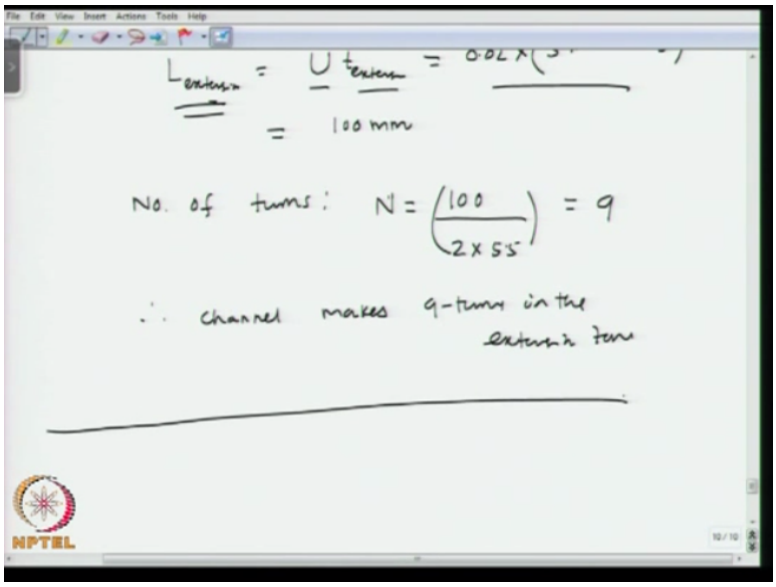

So channel makes 9 turns in the extension zone okay, so that is an example that shows how you can design a micro PCR chip okay so with that let us stop here.