

**INDIAN INSTITUTE OF TECHNOLOGY ROORKEE**

**NPTEL**

**NPTEL ONLINE CERTIFICATION COURSE**

**Biomedical Nanotechnology**

**Lec - 06**

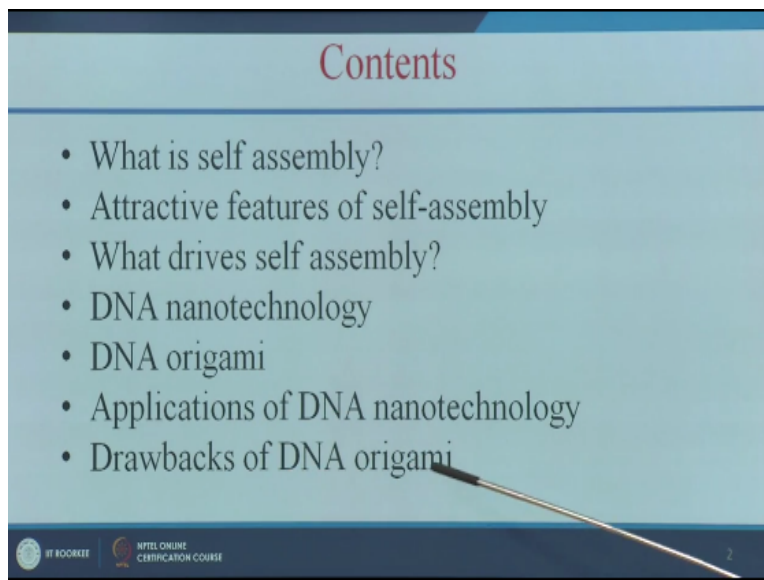
**DNA Nanotechnology**

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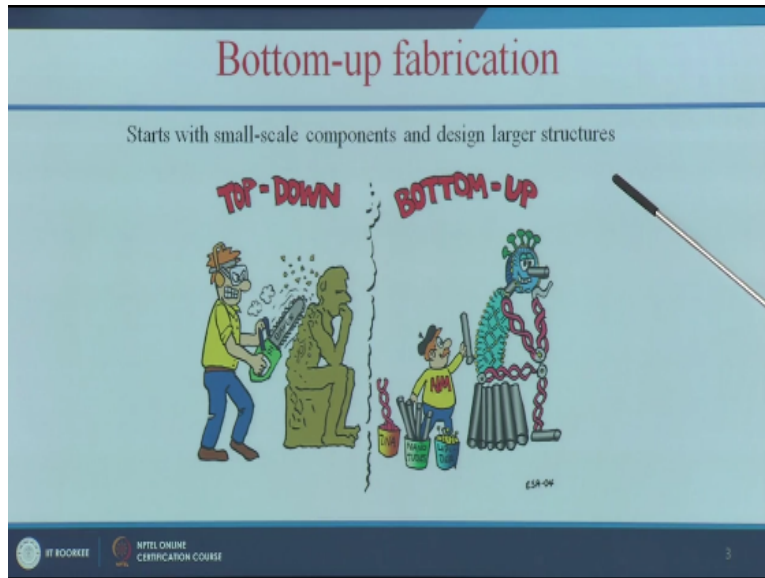
Hello everyone I welcome you all to the 6<sup>th</sup> lecture of this course that is DNA nanotechnology.

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In this lecture we are going to learn what is self assembly and what are the attractive features of self assembly and what drives self assembly and we are also going to learn what is DNA nanotechnology and applications of nanotechnology and we are also going to learn what is DNA origami and what are the drawbacks of DNA origami.

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So here the self assembly is a bottom up fabrication okay so in my first lecture I told you what is top down approach and bottom up approach top down means from bulk to nanostructures and bottom up approach means from atomic scale to nano scale okay so here we start with the small scale components and design the larger structures.

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## Self assembly

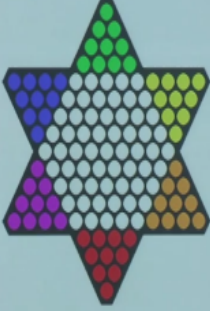
- Self-Assembly (SA) is the spontaneous organization of molecules or objects into well-defined aggregates via noncovalent interactions (or forces)
- Building Blocks: molecules and objects with coded information for self-assembly
- Processing: mix, shake, and form product

So what is self assembly self assembly is a spontaneous organization of molecules or objects into well defined aggregates via non covalent interactions or forces okay so here the building blocks is your molecules are any objects with the coded information for self assembly and here the process is mix and shake and it will form the product okay for example, here if you are losing the DNA molecule it have the coded information so the DNA as A it can form bond with T and G forms bond with C okay.

So that means the molecule is already having the coded information, so when you put in a solution so the DNA easily forms bonds okay so let us see a simple example to understand what is self assembly.


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## Example of self-assembly



Balls could be organized into triangles by an external agent, a player

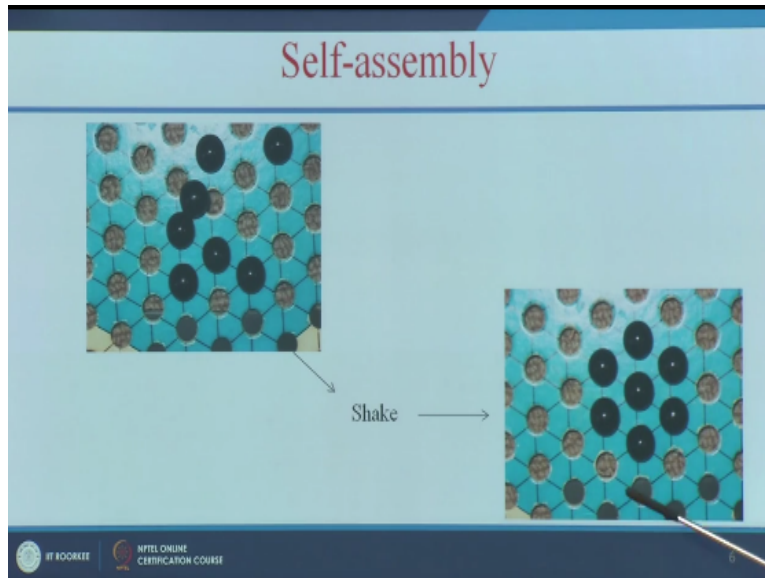
Or: punch holes in desired pattern, roll a stream of balls over the board.



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So this you might have played in your childhood okay so here the balls could be organized into triangles by an external agent or a player okay or what you can do is you can punch holes in the desired pattern and you can role a stream of balls over the board.

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So here you can make a holes in this board okay and put the balls and shake it so it will automatically go and assemble so this is a simple example to understand what is self assembly.

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# Molecular self-assembly

## Molecular Self-Assembly

- One of the most important types of self-assembly in nanoscience is molecular self-assembly.
- A group of molecules spontaneously rearrange their positions in order to form the most stable structure.
- Which arrangement is most stable and why?

The one that has the lowest interaction energy



So let us see what is molecular self assembly so one of the most important types of self assembly in nano science is molecular self assembly so here the group of molecules spontaneously rearrange their positions in order to form the most stable structure okay, so which arrangement is more stable and why, so here the one which has the lowest interaction energy is the more stable, so usually the nature favors which request low interaction energy and also high stable structure okay.

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## Molecular self-assembly

How do molecules move to form most stable structure?

- At room temperature, molecules constantly move around in space and change shape due to heat (or thermal energy) in sample.
- If collection of molecules is not in most favorable configuration (lowest energy), they will move toward most favorable configuration using thermal energy to move.



The formation of the most stable structure in self-assembly is analogous to the tendency of water to flow from a mountain side to a valley.



So how the molecules move to form most stable structure so at room temperatures the molecules constantly move around in space and change shapes due to heat or thermal energy in the sample okay so if a collection of molecules is not in the most favorable configuration that means not in the lowest energy form so they will move towards most favorable configuration using thermal energy to move to the highly stable structure.

So the nature always as I told you earlier it also save as the which request low energy and highly stable structure okay so the simple example is the tendency of water to flow from mountain side to valley okay.

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## Attractive features of self-assembly

- Self-assembly proceeds spontaneously
- The self-assembled structure is often at or close to thermodynamic equilibrium
- Self-assembly tends to reject defects and also has self-healing capability
- Self-assembly is one of the few practical strategies for making ensembles of nanostructures

So what are the attractive features of self assembly? The self assembly proceeds spontaneously and it is often close to thermodynamic equilibrium okay and again it rejects the defects and also it has a self capability and self assembly is one of the few practical strategies for making the nano structures okay.

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# Self assembly

Polar ends are attracted to water      e.g. of two-ended molecules in water  
Molecules spontaneously organize themselves into a pattern

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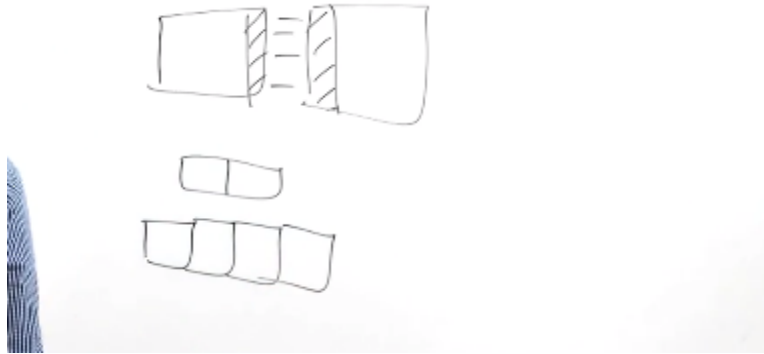
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So let see some other examples suppose you are having a molecules two ended molecules in the water for example this kind of molecules which have the polar head that means water liking or hydrophilic molecule and it is having none polar riles that is hydrophobic so when you put this gram molecules in the water what happens although hydrophilic heads will be facing the water and all the hydrophobic tails will away from the water okay.

So you will get this kind of milieus structure a simple example is if you put a drop of oil in a water you will get a circular ring kind of structure right so the another example is we can make nano particle then this case they made a sliver nano cubes okay and they coded with a hydrophobic linger only one side of this cube so you will get this get kind of assembly and when you code on the both the sides you will get this kind of line kind of structure and when you cote it on the 4 sides all the 4 sides will get this kind of assembly and when you mix the 4 side coated nano cubes with the 1 side coated nano cubes I will get this kind of assembly.

And when you place a like a 6 sided coated you will get this kind of assembly, so I will explain in detail like.

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So this is your nano cubes and this coated with the hydrophobic ligand okay so it will join together it forms this kind of structure if your coating this nano cubes are only one side okay and if your coating this nano cubes on both the sides it will form this kind of assembly so you can understand from this picture.

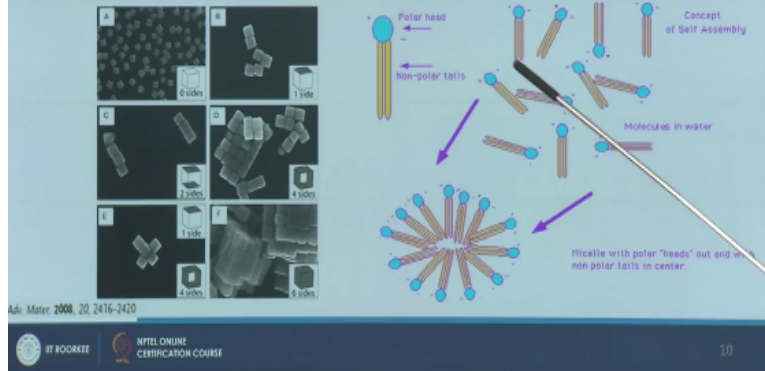
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# Self assembly

Polar ends are attracted to water

e.g. of two-ended molecules in water

Molecules spontaneously organize themselves into a pattern



So if you are coating it on only one side you will get this kind of assembly and if you are coating on both the sides you will get this kind of assembly.

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## Organization at the nanoscale

- In recent years, the synthesis of diverse nanoparticles is well developed. However, the most important and challenging part is their organization at the nanoscale.
- The multi-dimensional assembly of nanoparticles with controlled morphology in highly ordered arrays is important for realizing their novel applications.
- Organized or self-assembled nanostructures show remarkable collective properties, useful for engineering nanoarchitectures.
- For example, physical properties such as the optical and electronic properties of silver and the magnetic properties of cobalt superlattices are different compared to individual particles.

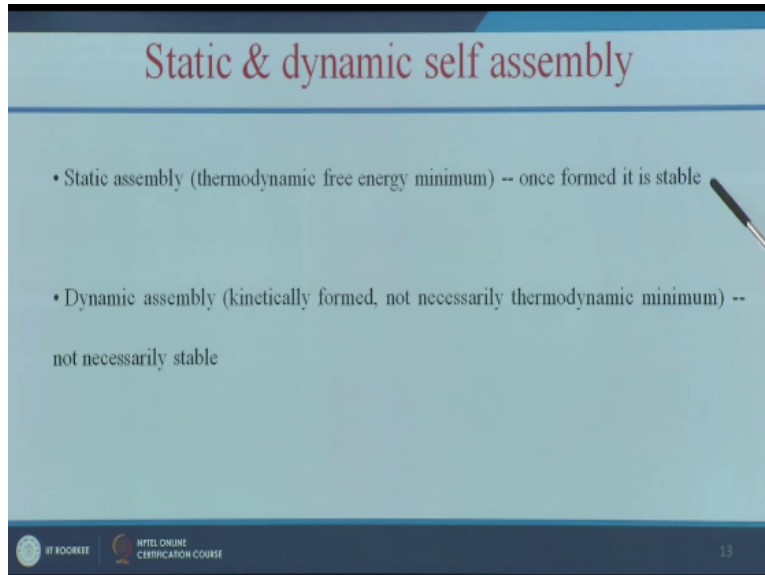
So why we need organization at the nano scale okay so the synthesis of dividers nano particle is well developed we are developed various methods to syntheses nano particles but the challenging task is how to arrange this nano particles okay challenging part is their organization at the nano scale okay so the multi dimensional assembly of nano particles with controlled morphology is very important for realizing their novel applications okay so the organized or self assembly nano structures it will show a remarkable collective properties which will be useful for engineering nano architectures.

A simple example is so if this all the alphabets are scatted you do not get any meaning so this alphabet should be arranged in a proper way to get the meaning for the word nano scale so similarly if the nano particles are disposed are scatted you do not get any meaning so you have to arrange in a proper structure okay so then only you can get various novel properties for example the physical properties and optical properties of the silver and magnetic materials is different okay when compare to the individual properties and another thing is it is a key to successful application of nano particles based devices and in this self assembly we wil get a defect free order nano structure okay.

So we can create periodic assemble nano structures to different and novel and innovative procedures so which has a various application by using self assembly we can arrange this nano particles and we can make it various nano structures which will have lot of application okay and how do we can do it we can do this nano organization by using top down approach like

lithography but in this lecture we are going to learn how we can use this bottom up approach for self assembly.

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Okay again this self assembly is divide into two types the static assembly and dynamic assembly so the static assembly is thermodynamic free energy minimum okay. So once it is formed it is stable and dynamic assembly it is kinetically formed it is not necessarily thermodynamic minimum and not necessarily stable, okay.

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## What drives self assembly?

- Forces of chemical bonding
  - non-covalent, ionic, van derWaals, hydrogen
- Other forces (magnetic, electrostatic, fluidic, ...)
- Polar/Nonpolar (hydrophobicity)
- Shape (configurational)
- Templates (guided self assembly)

So what are the forces driving this self assembly, so we can see that these are the forces of chemical bonding for example non-covalent interactions, ionic, Van Der Waals and hydrogen and other forces such as magnetic as well as hydrofluoric or hydrophobic and these are some of the forces which play a major role in driving this self assembly.

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## Chemical interactions

Different types of chemical interactions

- Relatively weak interactions desired.
- Most common weak interactions:
  - **Hydrogen Bond:** Special type of attractive molecular interaction between electro negative atoms (such as oxygen) and a hydrogen atom that is directly bonded to another electro negative atom.
  - **Electrostatic or Coulomb Attraction:** Between positive or negatively charged atoms in molecules.

And let us say what are the chemical interactions play a role in this self assembly so mainly the weak interactions play a major role in this self assembly, okay. So let us say example hydrogen bond, it is a special type of attractive molecular interaction between electro negative atom such as oxygen and hydrogen atom that is directly bonded to another electro negative atom and you know what is electrostatic or Coulomb attraction.

That means so it is forming between the positively or negatively charged atoms in a molecule that is called as electrostatic attraction.

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## Chemical interactions

- **Metal Ligand Interaction:** Certain types of metals, such as iron, form weak bonds with specific atoms in molecules.
- **Van der Waals Interactions:** Weak attraction between non-polar molecules, such as those present in automotive oils.
- **Hydrophilic Interactions:** Tendency for charged groups in molecules to be attracted to water when used as a solvent.
- **Hydrophobic Interactions:** Tendency of nonpolar substances to aggregate in aqueous solution and exclude water molecules.

The third one is, metal ligand interaction so here the certain types of metals such as iron form a big bonds with the specific atom in the molecules and Van der Waals interactions so here the weak attraction between the non polar molecules such as those present in the automatic oils and hydrophilic interaction that means the tendency for charged groups in molecules to be attracted to water when use as a solvent.

The last one is the hydrophobic interactions that means the tendency of non polar substance to aggregate in aqueous solution and exclude the water molecules, okay.

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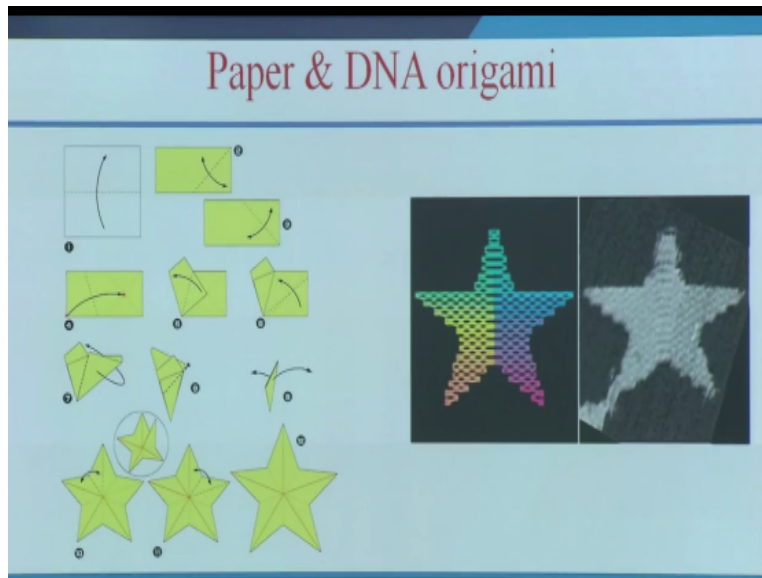
## DNA nanotechnology

- DNA nanotechnology is an area of current research that uses the bottom-up, self-assembly approach for nanotechnological goals.
- DNA nanotechnology uses the unique molecular recognition properties of DNA and other nucleic acids to create self-assembling branched DNA complexes with useful properties.
- DNA is thus used as a structural material rather than as a carrier of biological information, to make structures such as two-dimensional periodic lattices both tile-based as well as using the "DNA origami" method.
- DNA origami is the nanoscale folding of DNA to create arbitrary two and three dimensional shapes at the nanoscale.

So let us see what is DNA nanotechnology, so DNA nanotechnology uses the bottom of that is self assembly approach for making DNA base nano structures, so here the DNA nano technology uses unique molecular recognition properties of DNA and it create the self assembly branched DNA complex with useful properties, okay. So here DNA is used as a structural material so usually the DNA are genetic material which carries a biological information.

But here the DNA will be used as a structural material for making different nano structure, so that is called as DNA origami method, so the DNA origami is that nano scale folding up DNA to create arbitrary two or three dimensional shapes at the nano scale.

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So you know what is paper origami so using a paper we can make a different kind of structures, okay. So similarly we can use the DNA to make different kind of structures, so this is the paper origami you can use the paper and we can make different kind of shapes or structures and if you are trying to mimic the similar kind of things you thing DNA that is called as DNA origami.

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# Nucleic acid

Nucleic acid contains linear polymer of nucleotides

## Nucleotides:

Sugar + base + phosphate



nucleoside

DNA and RNA both have five carbon sugars called pentoses.

DNA contains 2-deoxy-D-ribose

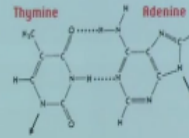
RNA contains D-ribose

So let us see some basics okay, so the nucleic acid contains linear polymer of nucleotides, so what is nucleotide, what is nucleoside? So the DNA contains sugar, base and phosphate so the sugar + base is nucleoside and the combination of sugar base and phosphate is nucleotide in case of DNA will have 2-deoxy –D-ribose sugar in case of RNA it contains D-ribose sugar okay. So here the base is in simple you can 80 GC that is your adenine thymine, guanine and cytosine okay.

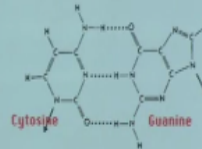
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## Chargaff's rule of base pairing

**A with T:** the purine **adenine (A)** always pairs with the pyrimidine **thymine (T)**



**C with G:** the pyrimidine **cytosine (C)** always pairs with the purine **guanine (G)**



And we have to understand what is Chargaff rules that is very important in this DNA nano technology, okay. So this A always form bond with T, okay you can see here this adenine always form bond with thymine using two hydrogen bonds and other thing is the cytosine bonds with guanine with 3 hydrogen bonds, okay. So this is the Chargaff rules and where A always bonds with T and G always pair with the C.

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## DNA nanotechnology

- The specificity of the interactions between complementary base pairs make DNA a useful construction material through design of its base sequences and three-dimensional structures in the shapes of polyhedral.
- These DNA structures have also been used to template the assembly of other molecules (Example. gold nanoparticles).

So this specific interaction between the complementary base pairs that means like A how it forms bond with T and G forms with C so that makes the DNA as attractive material attractive construction material, so using the property we can make different kind of nano structures, okay.

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## Thermal annealing

- For **experimental** synthesis of the DNA nanostructure, the oligonucleotides with designated sequences can be **synthesized** by a DNA synthesizer, **purified** via electrophoresis or chromatography, **mixed** together at the stoichiometric molar ratio in a near-neutral buffer containing divalent cations (usually  $Mg^{2+}$ ), **heated** to denature, and then gradually **cooled** to allow the ssDNA molecules to find their correct partners and adopt the most **energy favorable** conformation (i.e., self-assembly).

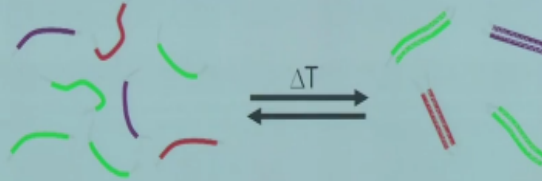
So for experimental synthesis of DNA nano structure we need more amount of DNA so how we can synthesize with DNA, so this oligonucleotides can be synthesized by DNA synthesizer and it can be purified by techniques like electrophoresis or chromatography and it can be mixed together at the stoichiometric molar ratio in a near neutral buffer containing divalent cations, okay.

And if you want to denature the DNA it can heat the DNA that will break the hydrogen bond and it will denature the DNA and if you want to make it re-nature it can be cooled so that the single strand DNA combine and forms a double strand DNA, okay. And these are the very good example for the self assembly.

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## DNA basics

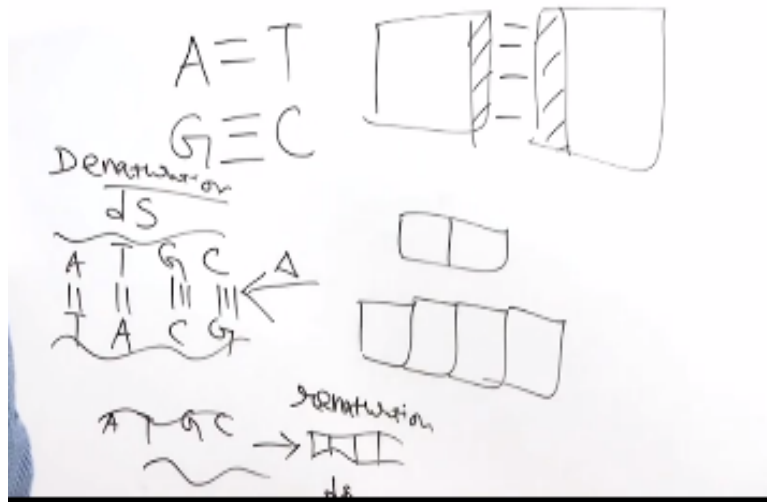
- DNA hybridization is the process that forms the double helix
- Random diffusion: power of self-assembly
- Sequence and temperature controls the hybridization event



- Reverse process called melting
  - Melting temperature ( $T_m$ ) is sequence dependent
  - G-C pairs  $\sim 2x$  as strong as A-T pairs

So let us see what is DNA hybridization.

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So as I told you this A always form bonds with T and G always form bond with C, okay. So when you have the DNA like this and this is your complementary based on the other stand and it forms the hydrogen bond, so when you apply this heat what happen this double standard DNA became a single standard DNA and when you cool it again it forms the double standard DNA, so when you apply heat it will breaks the hydrogen bonds.

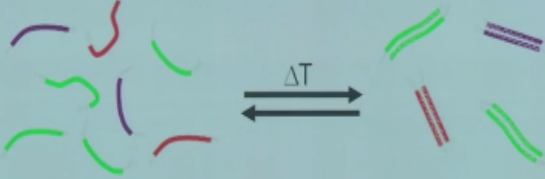
And it will become a single standard DNA and when you reduce the temperature and allow it to cool it will form a again double standard DNA that is called as renaturation, so this is your denaturation and this is called renaturation.

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## DNA basics

- DNA hybridization is the process that forms the double helix
- Random diffusion: power of self-assembly
- Sequence and temperature controls the hybridization event



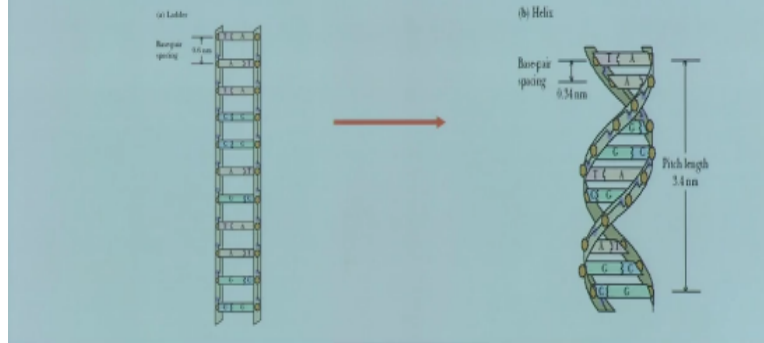
- Reverse process called melting
  - Melting temperature ( $T_m$ ) is sequence dependent
  - G-C pairs  $\sim 2x$  as strong as A-T pairs

So that is called as DNA hybridization so here you can see here simple example so you can use that color code so you can see here this green color DNA bind to green color DNA and red color is binding to red color, so it is like a this sequence are complemented to the other sequence so that is why it is forming a double standard DNA, so when you apply the heat it can be become single standard and when you remove the temperature it can be like a double standard DNA. So using this we are going to make different kind of nano structures.

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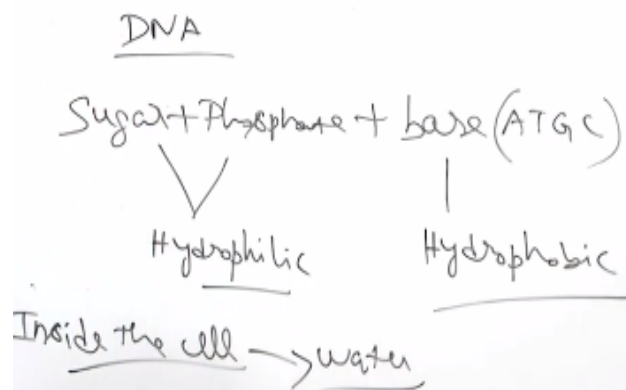
## Why DNA is helical?

DNA has two polynucleotide strands wound together to form a long, slender, helical molecule, the **DNA double helix**.



So next thing is, why the DNA is helical in nature, okay. So usually it can be like a ladder like structure so why it is forming this kind of helical structure.

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As I told you the DNA has 3 main components sugar okay phosphate and base that is your nitrogen base ATGC okay so in this, these two are hydrophilic and this is hydrophobic and inside the cell, cell is full of water right. So what happens is in this if we have a wave length like this like a ladder structure the water molecules can disturbed the structure and this ways has to be escape from the water because this is hydrophobic.

So this base will be inside okay, and your sugar and phosphate will be on the outside, where these are water allowing okay and these base are hydrophobic that is water re plant or. So after that also it can be like this structure even the base can be inside, so then also it can be like a DNA ladder like structure, so why it has to attend like this kind of helical structure.

Yes if we have this kind of space gap again the water molecule can enter inside and it can disturb this structure so that is why it has to attend this kind of helical thinner structure to our the entry of water molecule okay, and another reason is the bonding angle between this A and D and G and C also place measure role in giving this helical structure another simple analogy to understand why it is helical is suppose you are cloth is wet, so what you do you twist your cloth to remove the water right.

The same principle here also, so the base is hydrophobic so it has to be produced so it is forming a helical like structure.

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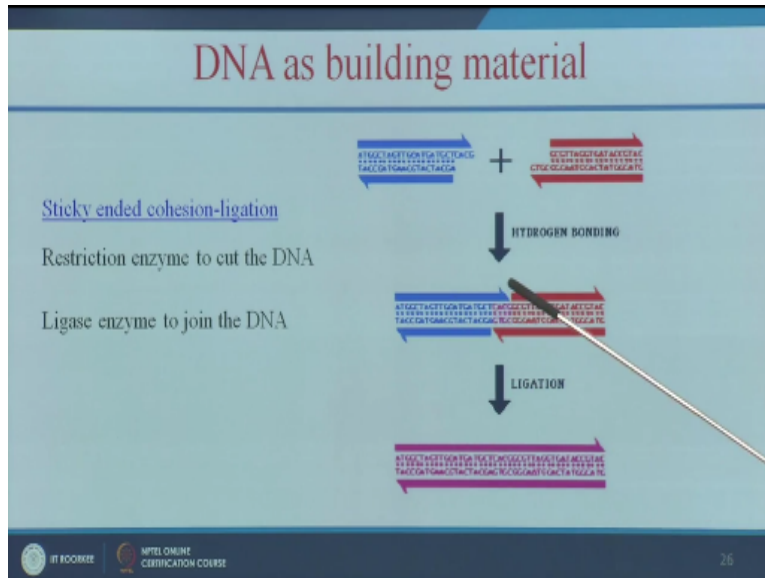
## Why DNA?

- DNA is appropriate for nanotechnological methods for several reasons:
  - It is a (relatively) stable chemical, which exists in different forms (nucleotides, nucleic acids)
  - As a polymer it can form very long molecules
  - It has a well defined, repetitive structure
  - “Rules” for determining the structure are simple and well-understood
  - Within the molecule many atoms are available to form useful interactions/modifications
  - DNA is a biocompatible material

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And why we have to select DNA for making this nano structures okay, so where the DNA is a appropriate nanotechnological method for several reasons, so first one is this relatively stable chemical and which exists in different forms okay and again as a polymer it can form a very long molecules and it has a well defined and repetitive structure, and again the rules for determine the structure or simple and well understood okay and within the molecule many atoms are available to form useful interaction and modification and by in the DNA is a again biocompatible material okay, so that is why we are using DNA as a structural material for constructing various nano structures.

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So we can use the DNA as a building material so here two important enzyme play a major role the first one is restriction enzyme okay, so this enzyme is also called as molecular scissor so it can cut the DNA at specific site okay when another enzyme is ligase enzyme so it can join the two DNS fragments.

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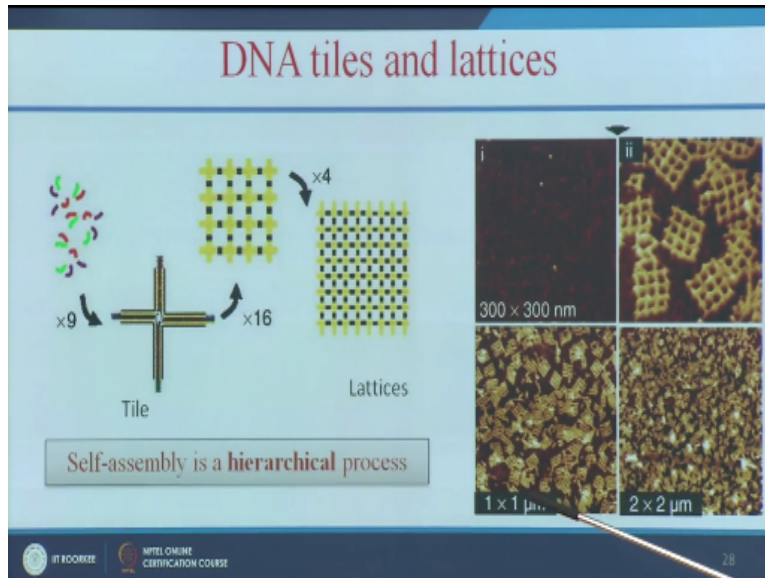
# DNA as building material

Assembly of branched junctions into a 2-d lattice

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So using this self assembly principle we can make a different kind of nano structures and we can reach even two dimensional lattice.

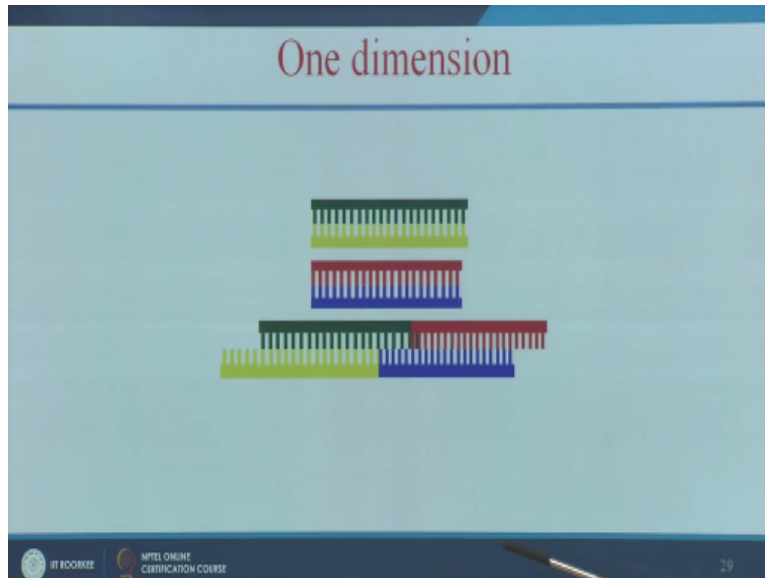
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Here you can see here this is a DNA style okay, and the time will be arranged and formed the lattice like structure these are called a DNA tiles and DNS lattice.

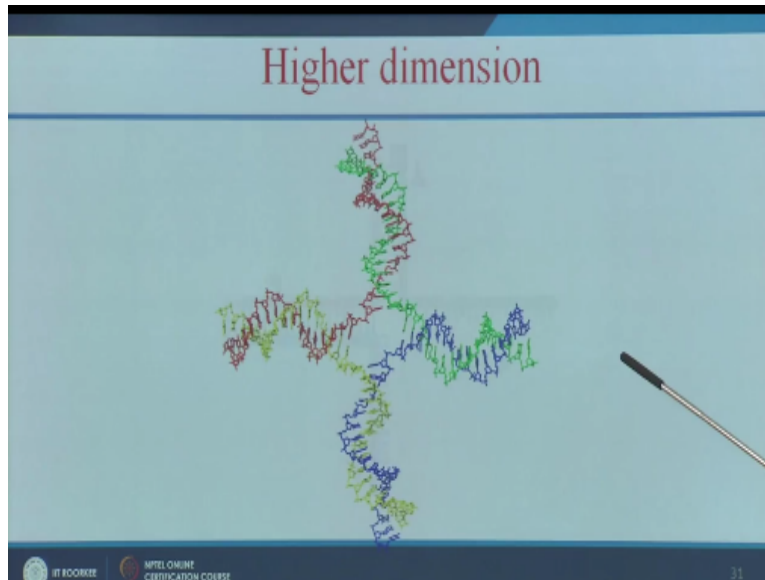
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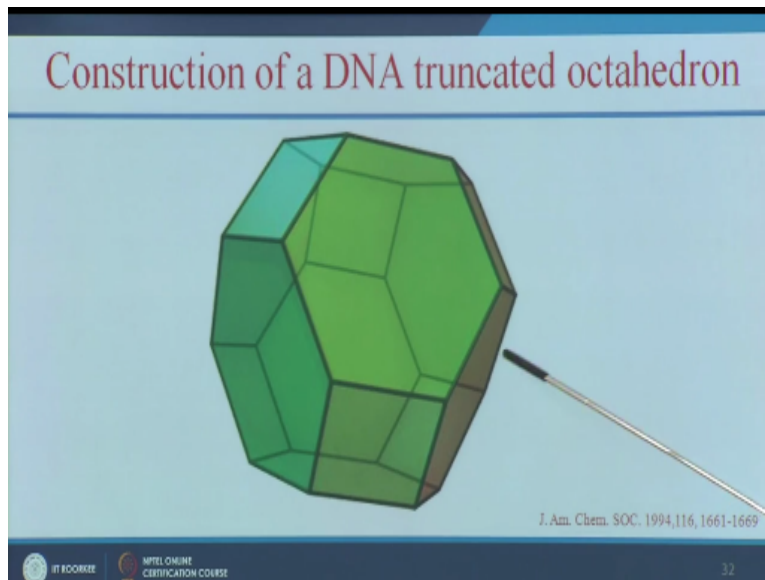
So using this self assembly and the complementary base pairing.

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We can make one dimension and we can also achieve this kind of higher dimension structures.

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And we can also make a DNA truncated octahedron structures okay.

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## DNA nanotechnology

**A**

**B**

- About 8 bases must be paired for a double helix to be stable at room temperature.
- A DNA-based four-way crossover structures producing a rigid planar tile. The distance between adjacent tile is 20nm.
- The structure, imaged by AFM, is produced by spontaneous self-assembly of the individual crossovers.

**A**

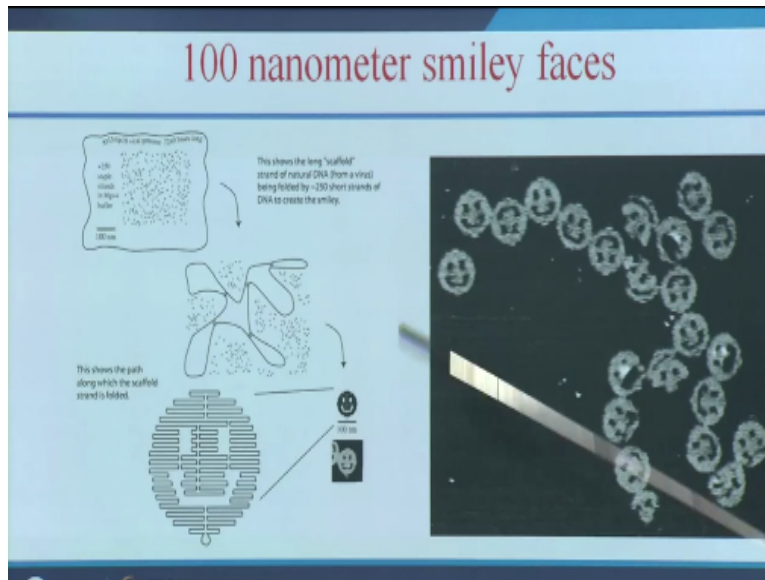
**B**

**C**

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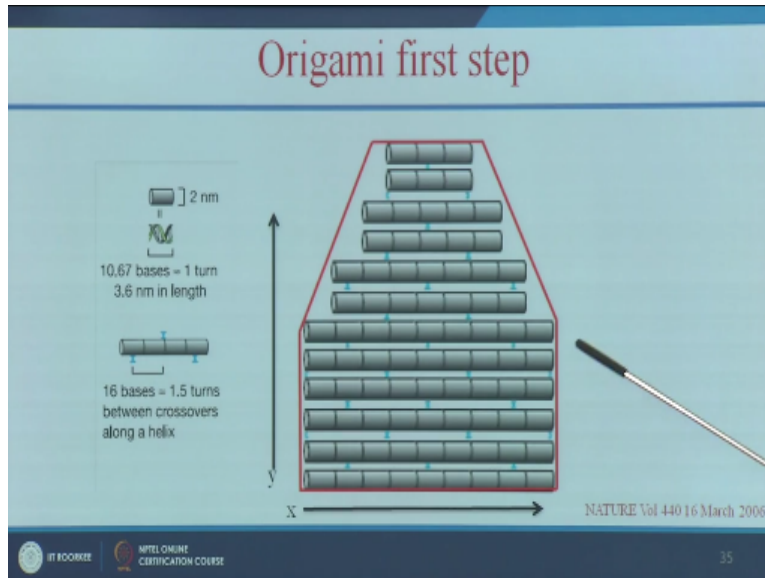
And here it need about a eight basis must be paired for a double helix to be stable at room temperature and this DNA based four way cross over structures producing a rigid plan a tile okay and the distance between the adjust and tile is 20 nano meter and as i told you in the previous lecture for a biological molecule like DNA are put in we have to use the enzyme first understanding the structure, so this is a from picture and we can see here, how it forms a beautiful lattice structure.

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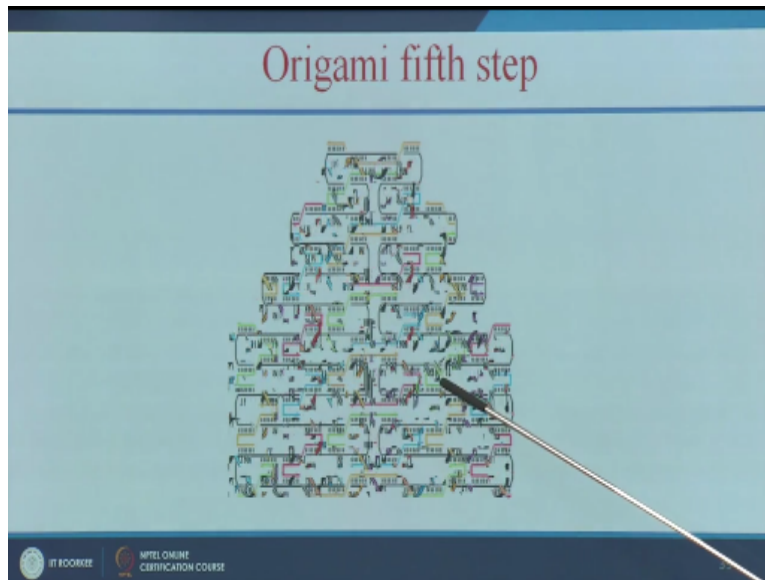
Let us see how to make 100 nanometers smile faces using this DNA okay, so here we can use a viral you know which is off 7000 to 49 basis long okay, and this venuesgance will be made into this kind of smile structures and using a small stands, that means where we going use like more than 250 short stands and we are going to make this kind of smile structure so this short stands are called as also called as staple stands, so for example if you want to staple the bunch of papers in this staple right. Similarly the DNA can be join to whether using this short fragments of DNA that is called as staple stand.

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So if you want to make the smile capacity if face you should have a plan how to make this smile structure okay, so here you can see here the DNA is 2 nano meter diameter and the length is 3.6 nanometer for each helix. So this is a first step to understand how the staple stands you need to connect the 0 to make this smile shape.

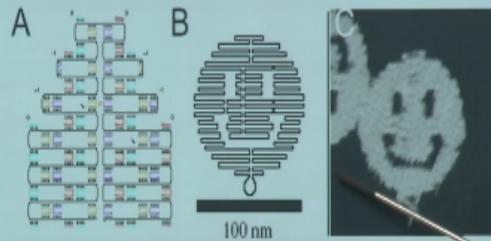
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So once you made the plan so then second step is, so based on plan we have to draw the structure what are what can a smile you are going to make and then you will make the DNA sort fragments sequences so that will bind to this and we can add a some enzymes which will make that complete DNA sequence and finally you will get the complete structure.

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## DNA origami



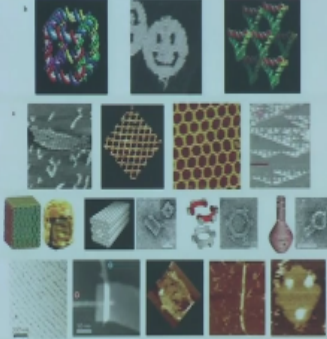
A long template strand is annealed with a number of short strands that either form cross-links at fixed points (loops) or fill regions to form double helices.

So here the long template strand is annealed with the number of short strands okay, so that either form at cross link at fixed points allows and to fill the regions to form the double helix so we will get the 100 nanometer smile face using this DNS.

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## Examples



<https://cando-dna-origami.org/>

<http://cadnano.org/>

<http://cdna.au.dk/software/>

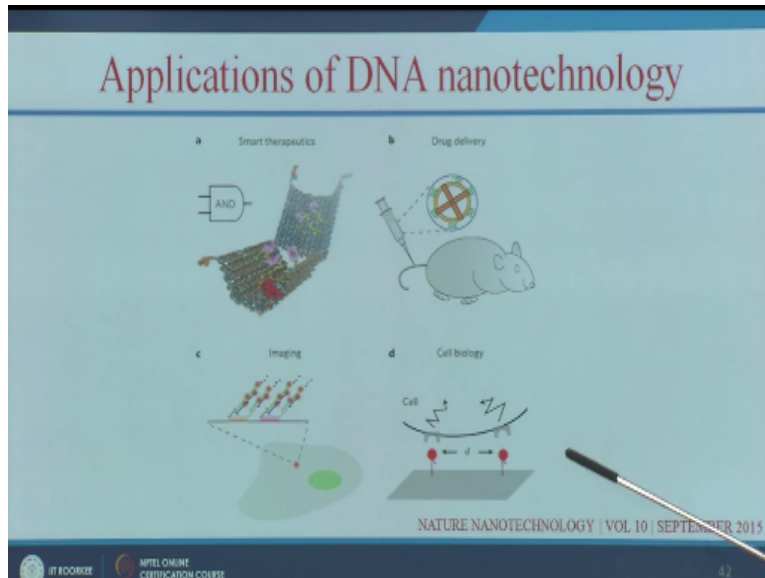
<http://daedalus-dna-origami.org/about/>

*Pinheiro et al., 2011, Nat. Nanotech., 6, 763-772*

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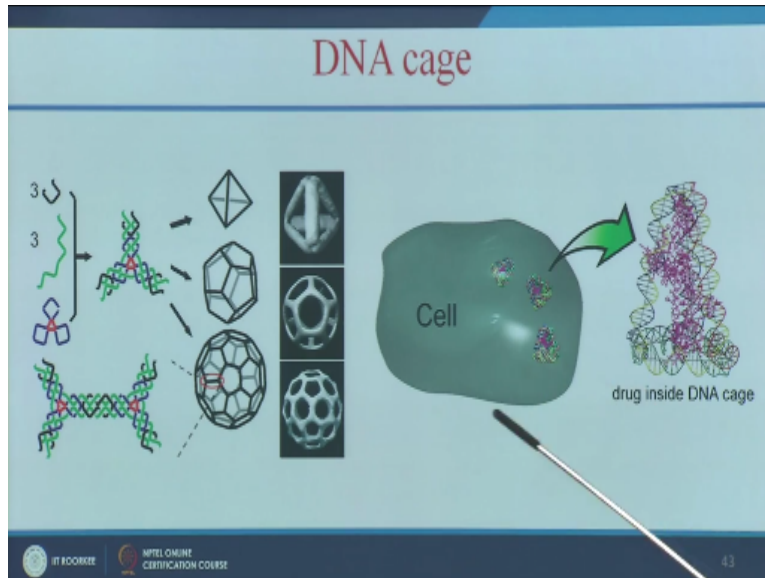
So similarly we can make a different kind of structures okay using this DNA as a construction material and these are the free software's available so design various nano structures using the DNA as a construction material.

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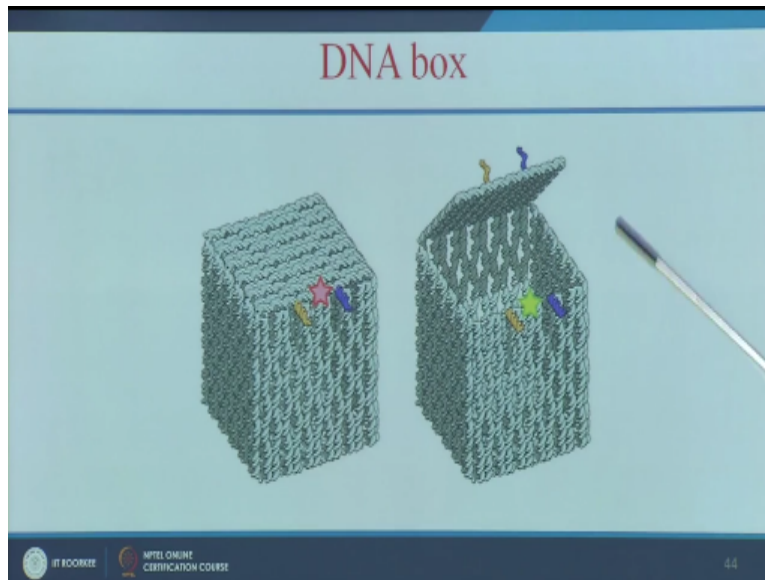
So let us see the applications of DNA nanotechnology so first one is smart therapeutics and the second one is drug delivery, so in the smart therapeutics it will release the drug when there is particular signal is available, and we can also use this kind of nano carrier for drug delivery and we can use this DNA for imaging application for diagnosing various diseases and also we can use it for various cell biology applications.

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Let us see one by one the first one I told you like it can act like a DNA cage and it can carry any kind of drug, so we can load with any kind of anti drug and which can be transfer to the cell and it can kill the cells.

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And we can also made a DNA based box okay, so this box can be loaded with anti drug or any therapeutic molecule and it has a lock this lock is also made by nucleic acid only so when we have the key of nuclei types is this open this box and it will release the drugs.

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## Diagnostics and therapeutics for human health

- Hollow DNA-based box assembled with a lid that could be opened by strand displacement with a specific oligonucleotide key.
- DNA structures can be used to build disease-targeting units for diagnostics and therapeutics (or 'theranostics').
- Hollow structures are designed in a modular fashion, where multiple pharmacologically active species can be caged into different compartments.

*Pinheiro et al., 2011, Nat. Nanotech., 6, 763-772*

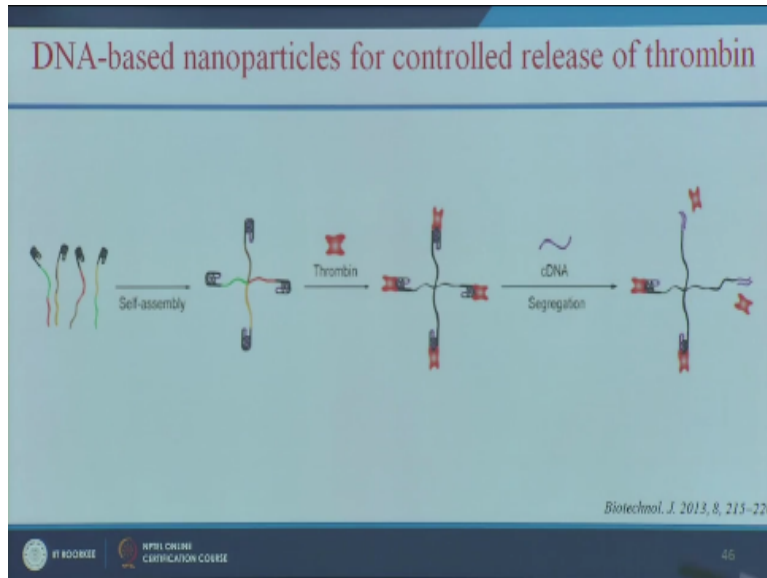
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So we can assemble this DNA base box okay, so this hollow DNA box can be assembled with the lid okay and it could be opened by strand displacement with the specific oligonucleotide key, so this box can be opened with the oligonucleotide key so if we have a DNA sequence that will open this box and you can make this kind of box with the two different kinds of anti drugs or one box with the imaging agent.

So that is called as theranostics nano particle that means so the DNA nano structures which can be used to build disease targeting units for diagnostics as well as therapeutic purpose that means the same nano particle which can diagnosis as well as which can carry the therapeutic agent it is called as theranostic nano particle, okay and again this hollow structures can be designed where multiple pharmacologically active species can be caged into different compartments.

As I told you earlier in case of early stage of cancer if you want to release only this kind of drug, only this box can be opened and the person who is having this advanced stage of cancer if you want to have two different kind of drugs and which can have the very good therapeutic effect in the cancer which is resistance to the drugs, okay.

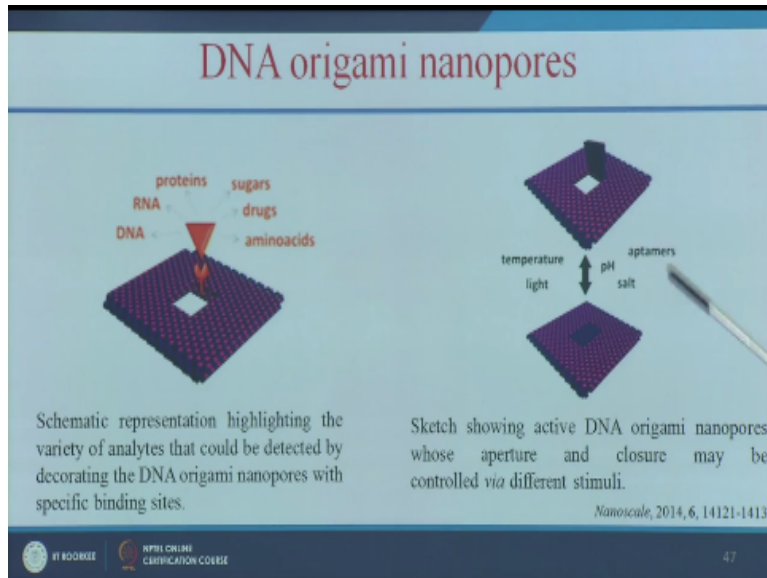
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And also we can use this DNA based nano particles for controlled released of thrombin or any kind of molecules, so here you can see here we are going to use the small fragments have DNA pieces okay, and this DNA is specific for particular protein in this case it is specific for your Thrombin okay. So you can this self assembly process we can make X shape DNA tail and this thrombin will go and mind to this DNA and when you add the cDNA which is specific for this DNA.

What happens is the cDNA go and bind and it will release the thrombin so the thrombin can be released from this DNA. So that is why like we can use the DNA based nano particle for the control is of thrombin, if you have putting only one cDNA it will release only on molecule of thrombin and if you are adding like a four cDNA then it will release all the four thrombin. So similarly we can use that small fragment of DNA as a key to open the DNA based nano particles and it can release the drug according to the, our need.

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And we can also make DNA origami nanopores, so here you can see this example so here the it is a DNA origami nanopores okay, so that could be useful for detecting various compounds. For example, if you are having a receptor in this nanopores when you pass the protein or any passer a sugar or amino acids so it can easily detect and it can uses a kind of good sensor and again this DNA nanopores can be lock and open by using this kind of signals like temperature.

If I apply temperature it can be opened light or pH by using this kind of parameters we can open the pores or we can close the pores and this is also very important role in the control drug release.

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## DNA origami nanopores

(a) Schematic representation of a potential DNA nanopore (in green) embedded in a lipid bilayer (in red) by hydrophobic tags (in blue). In this sketch such nanopores are able to selectively control the passage of ions mimicking e.g. potassium or sodium channels.

(b) Illustration representing a liposome (in red) with DNA origami nanopores (in green) embedded on with hydrophobic tags (in light blue) which are used to release a cargo (small squares in dark blue).

*Nanoscale*, 2014, 6, 1411-14132

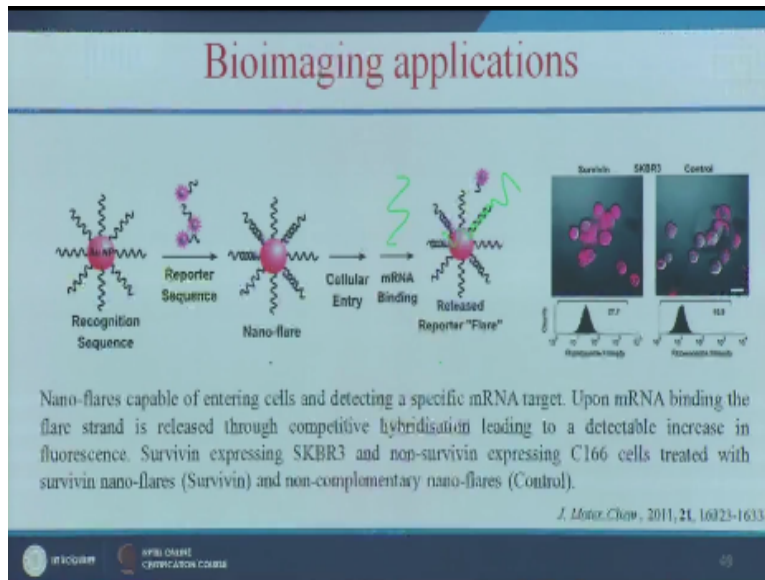
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And next one is this DNA origami nanopores can also mimic like your potassium and sodium channels, so here you can see the example, so this DNA nano pore this is a green color one is a DNA nano pore and this red color is a liquid by a layer, okay and it is selectively acting like the potassium or sodium channels and here this DNA this green color is a DNA origami nanopores and it is emitted in this red color liquid by a layer.

And here also this blue color square is your anti cancer drug or any other therapeutic molecules, and this carrier can be useful for control delivery or control is of your therapeutical molecule.

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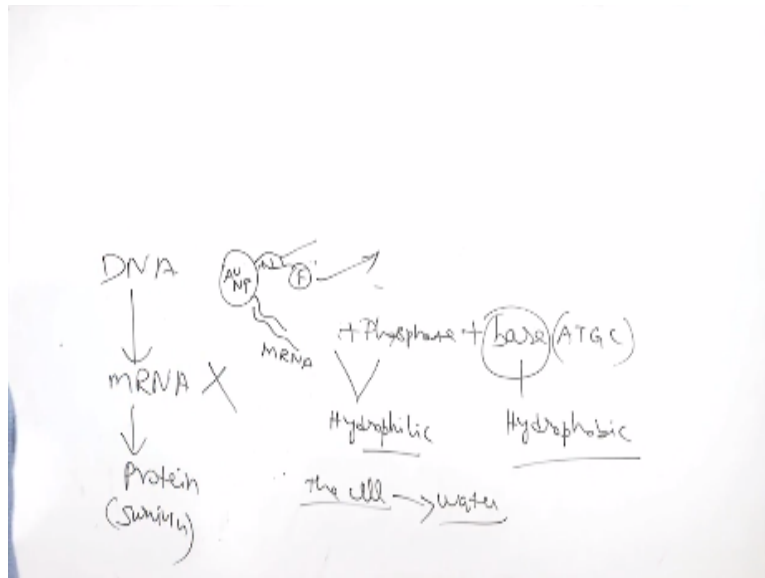




So the next application is we can use it for bioimaging application, here you can see here this grown nano particle it is tagged with a recognition sequence and we can add the reporter sequence, in the reporter sequence is tagged with some kind of fluorescence molecule. So it is binding to this target nano particle and form the nano flare once it enters the cells this sequence will target the mRNA, okay.

So when it binds to sources mRNA what happens is this fluorescence signal will be expressed okay, so it is releasing this reporter flare so it is giving a fluorescence signal. So in the example, so this is survivin is one of the anti-apoptotic proteins that means this kind of protein is mostly expressed in the cancer cells so you target this kind of proteins and it could be useful for cancer therapy, okay. So how do you stop this, we can stop at the protein level or we can stop at the mRNA level.

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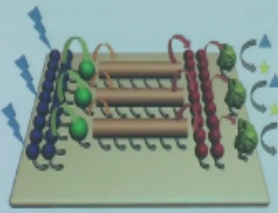


So from DNA we will get the mRNA and from here we will get the protein, so in this example so survivin you have to stop this survivin protein so we can stop at the mRNA level okay, so the sequence which is tagged to goal nano particle so this mRNA will bind to this okay, so what happens is when the mRNA binds the sequence with the fluorescence signal it will be released. So once it is released it will give the fluorescence signal.

So here you can see here the cells which have the more amount of surviving you can see here more amount of fluorescence signal when compared to the control cells where the survivin expression is less or no expression of survivin.

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## Energy transfer and photonics



- DNA nanostructures are intrinsically more rigid than double-stranded DNA and can be used to build longer photonic wires, and further, the unique 2D and 3D spatial arrangements allow the construction of branched paths for energy transfer.
- Light-harvesting complexes can be spatially clustered and aligned, where sequential energy or charge-transfer processes lead to optimized channelling efficiency, to create a new generation of photonic wires, plasmonic or conducting devices (blue, green and red spheres and orange rods represent photonic components that can serve as light-harvesting and energy-transfer materials).

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So we can use this DNA based nano structure for various diagnostic as well as for therapeutic applications, and next application is we can also use this DNA based nano structures for energy transfer and photonics okay, so here the DNA nano-structures are intrinsically more rigid than the double standard DNA so it can be used to build a longer photonic wires, so using this we can harvest light it can act like a light harvesting complex okay, by especially clustered and aligned to create a new generation of photonic wires.

So using, we can use the DNA as a photonic wires and we can also use it for energy transfer as well as photonics.

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## Drawbacks of DNA origami

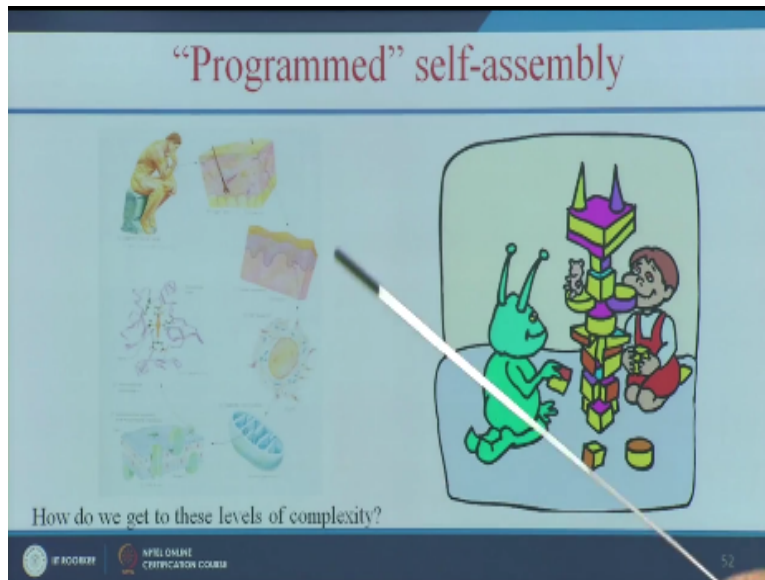
- DNA origamies are not stable in various conditions and require special care. For example, pH has a drastic effect on the structure of DNA nanostructures.
- In low pH solutions the DNA may be de-purinated and in high pH the hydrogen bonding between the DNA strands will be disrupted.
- Heating, many chemicals and some organic solvents denature double-stranded DNA.
- DNase enzymes destroy DNA strands by catalyzing the cleavage of the DNA backbone. Thus handling and storing of samples consisting of DNA structures must be performed carefully.
- The ions present in solution have a strong impact on DNA structures; at low ionic strength the DNA structures will decompose, and high salt concentrations lead to aggregation of the structures.
- Molecular tensions and mechanical forces may have negative effects on structures, particularly on extended structures, too.

So let us see some of the drawbacks of DNA origami, so here the DNA origamies are not stable in various conditions. It required special care for example, pH has a drastic effect on the structure of DNA nano-structures. In low pH the DNA may be de-purinated and in high pH the hydrogen bonding between DNA stands will be disrupted, okay. And also the heating many chemicals and some organic solvents may denature the double standard DNA.

And again the enzymes like DNA enzymes which can destroy the DNA stands and it can also destroy the DNA back bone, okay. So thus, we have to store and handle this samples very carefully and again the ions present in the solutions have a strong impact on the DNA structures, okay. So at low ionic strength the DNA structures will decompose and at high salt concentration which lead to aggregation of the structures.

And also the molecular tensions are mechanical forces also have the negative effects on the structures.

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So we are also example for the program self assembly, so if you see that we also assigned from a simple atoms the atom combines and found the cells and the cells combine and form the tissues and tissues and combine and form the organs and organs combine and form the complete body. So if you understand the self assembly we can also make such kind of complex structures and nano scale devices and everything. But our understanding is of self assembly is still in the elementary level.

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## Summary

- Self-assembly is one of the few practical strategies for making ensembles of nanostructures.
- DNA will be a key player in bottom-up nanotechnology.
- To make more complex DNA structures, more highly developed computer programs are necessary.
- Currently, only a limited number of software programs have been developed to assist with designing complex DNA structures, and to predict the structural properties of the constructs.
- Each of the current programs has its advantages and disadvantages.
- Additionally, sequence optimization is very important and should be performed in concert with structure design.
- DNA nanotechnology and recently DNA origami have opened a novel pathway for addressing many previously impossible challenges.

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And as a summary the self assembly is one of the few practical strategies for making enzymes nano structures and here the DNA will be the keep layer in bottom up nano technology okay, so to make more complex DNA structures you need more highly developed to compute a programs okay, and also we are limited with number of software programs to develop to understand the DNA structures are making the designing the complex DNA structures.

And each of the program has a own advantages and disadvantages and additionally we have to sequence optimization is very, very important okay, and again the DNA nano technology and the DNA origami it has opened a novel pathway for addressing many previously impossible challenges, okay. So I will end my lecture here thank you all for the thing in this lecture I will see you in another lecture.

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