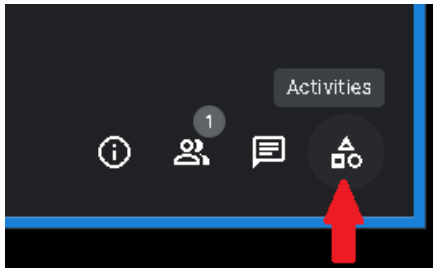
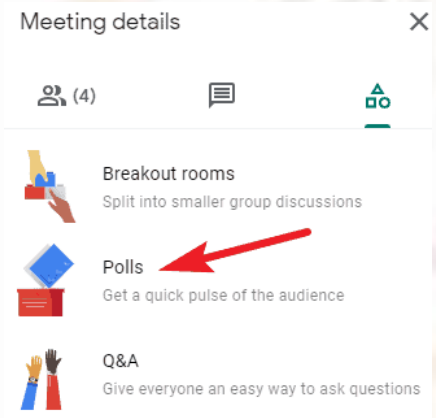
STRUCTURAL BIOLOGY

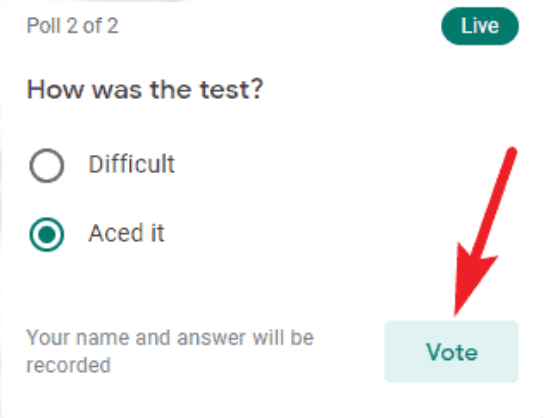
Live Session- Week 1
1 Feb, 2022

About the session

1. The session is going to be interactive and students have to respond using the Google Meet polls. Instructions to access polls was given below.
2. Students were also requested to used Q&A option to post their questions.
3. **2** Questions were already posted, Try to answer them.







Contents

Summary

1. In the initial part of the session, I will provide summary of the previous week lectures.

Sample Problems

1. Sample problems will be displayed using Slides and Google Meet polls.
2. Students can answer the questions using the Google Meet polls.
3. Explanation of problem will be done using Slides and One note.

Questions (from portal)

1. If time permits I will discuss about the questions posted on swayam portal.
2. This can be done using slides or One note

Questions (from students)

1. Finally I will take up Questions from the live audience.
2. The students can ask their questions using Google Meet Q&A or Chat

Summary

Week_1_Lecture_1: Focuses on basic things required to understand this course and on history of biological inventions.

1. Structural biology is the study of how biological molecules are built and considers Microscope (Glass sphere) as the first invention.
2. The earlier inventions of microscopes has a problem of chromatic aberration (It is a failure of lens to focus all the colors to the same points)
3. Microscope helped to study the cell and the principles of cell theory were laid on.
4. Next, the lecture has explanation of several experiments that helps in understanding DNA as the active genetic principle .
5. Study of structural biology provides answers to questions related to architecture of molecules, about the interactions between them and with the solvent, ions…
6. Theory of natural selection states which are better adjusted to their environment will most likely to survive and can transmit their traits to the next generation.

Summary

Week_1_Lecture_2: This lecture is about Biological macro-molecules.

1. Understanding the composition and structure helps to study of macro molecules of life.
2. Chemical properties of various biological macro molecules was explained followed by the explanation of the 3C of covalent bonds.
3. Carbohydrates are sugars and polymers of sugars. They are classified based on the location of carbonyl group and based on number of carbons.
4. Fats have two components, Glycerol and fatty acids joined by a ester linkage to form fats. The single/double bond defines the nature of fats.
5. DNA/RNA is the polymer of nucleotides, which are in turn divided into nucleosides (Nitrogen based & sugar) and phosphate group.
6. Proteins are polymers of amino acids joined by a peptide linkage between the carboxyl group of one amino acid with the amino group of other amino acid.
7. The 3C's are Configuration (spatial arrangement of atoms), Conformation (rotation across the bonds) and Chirality.

Summary

Week_1_Lecture_3: Focuses on decoding biological macromolecules.

1. In Carbohydrates, the monomer to polymer transition is through the glycosidic linkage. This linkage joins Carbohydrates to Carbohydrates/Other molecules.
2. Protein sequencing is determining the amino acid sequence and uses combination of proteases (break peptide bonds) to sequence the protein.
3. Protein sequencing methods such as Mass Spectrometry gives the residue wise details and Edman degradation is used for N-terminal characterization.
4. The Central dogma is explanation of the flow of genetic information within the organisms and includes a. Replication of DNA, b. Transcription of DNA into RNA and c. Translation of RNA into protein.
5. The study of DNA, RNA and proteins is important to understand life.
6. In DNA sequencing, sanger method states the use of ddNTP's to sequence the DNA, The ddNTP's here lack the bond forming capability and terminate the chain synthesis reaction.

Summary

Week_1_Lecture_4: Lecture 4 is about journey from gene to genome.

1. Reading of all genes is important to understand life, so genome sequencing is preferred.
2. The whole genome of an organisms include a. Chromosomal DNA, b. Mitochondrial DNA and c. Chloroplast DNA (Plants).
3. To Overcome the size limitations in sanger methods, next generation sequencing was introduced.
4. After genome sequencing, we got many genes i.e., we now have many proteins sequences. Now the problem is to know the structure of protein.

Summary

Week_1_Lecture_5: Lecture 5 is about Post Genomic Era

1. Post Genomic Era starts after completing the Human Genome Project and pushes our journey from sequence understanding to functional understanding.
2. In this era, Proteins are considered as major functional elements and have more diverse structures, making the study complex.

Challenges to be dealt in Structural Biology:

1. Constructing the 3D structure of biomolecules.
2. Understanding the folding mechanisms of protein structure.
3. How to reduce cost and time to solve 3D structure.

Question : 1

The cell theory comprises of

1. Cells are basic unit of life
2. All cells have basic chemical composition
3. Hereditary information is passed from cell
4. All of the above

Answer the question on Google meet poll

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Solution:

1. With continual improvements made to microscopes over time, the study of cell was possible and the principles of cell theory were based on these studies.

2. The generally accepted principles of modern cell theory include:

   - All known living things are made up of one or more cells
   - All living cells arise from pre-existing cells by division.
   - The cell is the fundamental unit of structure and function in all living organisms.
   - The activity of an organism depends on the total activity of independent cells.
   - Energy flow (metabolism and biochemistry) occurs within cells.
   - All cells are basically the same in chemical composition in organisms of similar species.

Final Answer : **All of the above**

Question : 2

According to **Avery–MacLeod–McCarty experiment,** what is termed as active genetic principle ?

1. DNA
2. RNA
3. Proteins
4. Lipids

Answer the question on Google meet poll

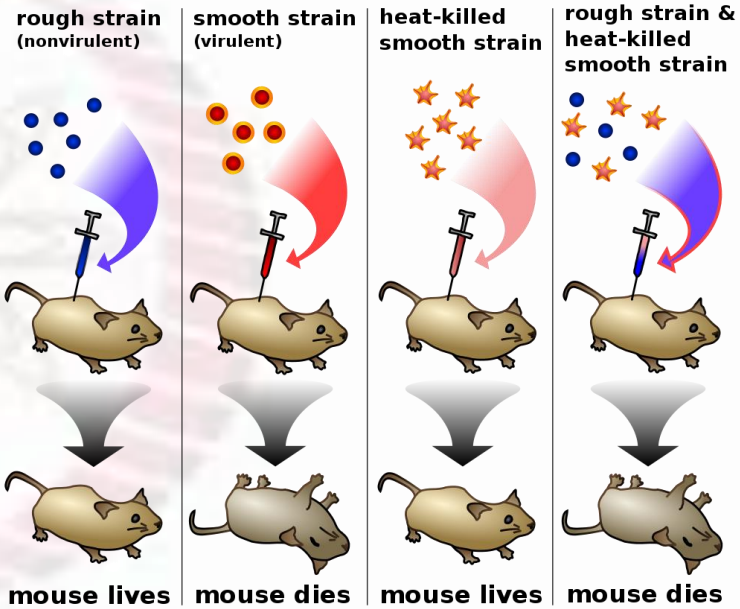
Solution:

Griffith's experiment suggests that bacteria are capable of transferring genetic information through a process known as transformation.

Griffith used a virulent, and a nonvirulent strains of pneumococcus bacteria which infect mice –. The Virulent strain developed a capsule that protected itself from the host's immune system and resulting in the death of the host, while the nonvirulent strain did not have that protective capsule and was affected by the host's immune system.

In the same experiment, heat killed virulent and nonvirulent was able to kill the mice. While neither alone harmed the mice, but the combination was able to kill its host.

Griffith was also able to isolate both virulent and nonvirulent strains of pneumococcus from the blood of these dead mice. From this, Griffith concluded that nonvirulent had been "transformed" into the lethal virulent strain by a "transforming principle".



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According to **Avery–MacLeod–McCarty experiment,** what is termed as active genetic principle ?

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Solution:

- From Griffith observation lets assume, the DNA had survived the heating process and was taken up by the nonvirulent strain.
- Further the exact nature of the transforming principle was verified in the experiments done by Avery, McLeod and McCarty and by Hershey and Chase.
- Chemical analysis of the active part, showed that the proportions of carbon, hydrogen, nitrogen, and phosphorus in this active portion were consistent with the chemical composition of DNA.
- They also found that the enzymes that break apart proteins or RNA (trypsin, chymotrypsin and ribonuclease) did not affect the active part, but an enzyme "deoxyribonucleodepolymerase" (which break down DNA) destroyed the active part.

Final Answer **: DNA**

Question : 3

Which bond is formed in the polymer of nucleic acids?

1. Peptide bond
2. Phosphodiester bond
3. Glycosidic bond
4. None of the above

Answer the question on Google meet poll

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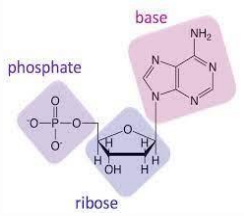
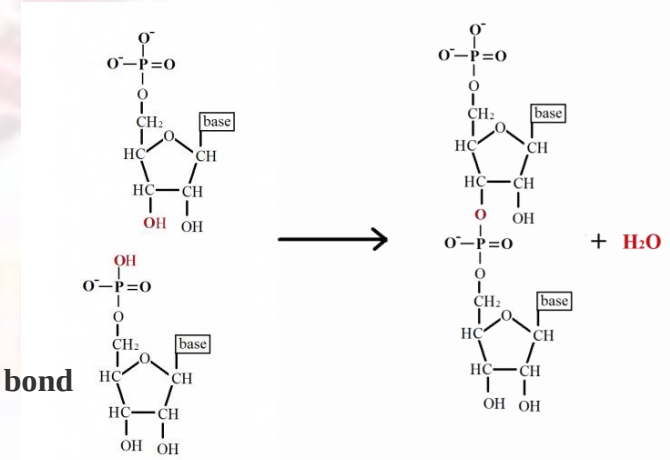
Solution:

- Nucleic acids are composed of nucleotides, which are made of three components: a 5-carbon sugar, a phosphate group and a nitrogenous base.



- The two main classes of nucleic acids are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). If the sugar is ribose, the polymer is RNA; if the sugar is the ribose derivative deoxyribose, the polymer is DNA.
- When two nucleic acids are brought together, the hydroxyl groups of phosphate and sugar reacts to form two ester bond. (The "bond" involves this linkage C-O-PO_2^--O-C.)



- Final Answer **: Phosphodiester bond**

Question : 4

PCR technique is useful for?

1. Unzipping of DNA
2. Amplification of DNA
3. Transcription process
4. None of the above

Answer the question on Google meet poll

PCR technique is useful for?

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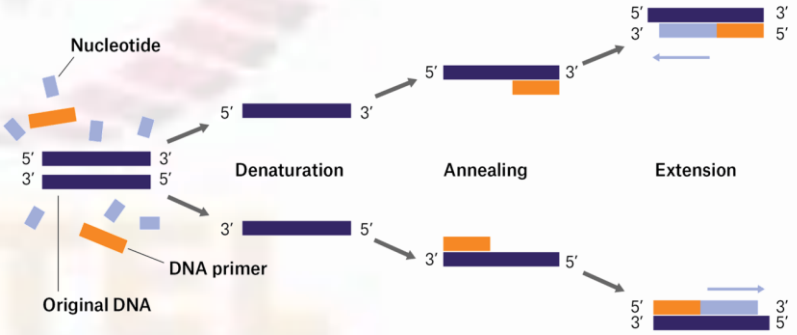
Solution:

- **Polymerase chain reaction** (**PCR**) is a method widely used to rapidly make millions to billions of copies of a specific DNA sample.
- The first step of PCR is **nucleic acid denaturation**, where the two strands of the DNA double helix are physically separated at a high temperature.
- The second step of PCR is Annealing, where the primers bind to the complementary sequences of DNA. During the Extension step, two DNA strands are used as templates by DNA polymerase to enzymatically assemble a new DNA strand from free nucleotides, the building blocks of DNA.
- As PCR progresses, the DNA generated is again used as a template for next cycle, forming a chain reaction in which the original DNA template is exponentially amplified.



- Final Answer :**Amplification of DNA**

Question : 5

What is the key feature of the sanger sequencing method?

1. It is a Chemical Breakdown Method
2. It is a Dideoxy or chain termination method
3. Amino acid sequencing
4. Unzip DNA

Answer the question on Google meet poll

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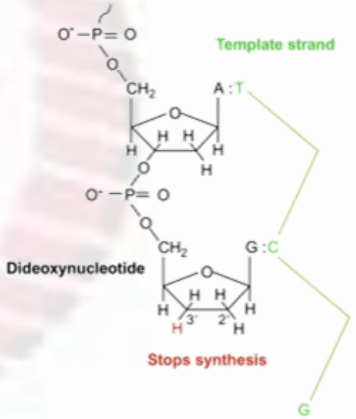
Solution:

- **Sanger sequencing** is a method of DNA sequencing that involves random incorporation of chain-terminating dideoxy nucleotides by DNA polymerase during in vitro DNA replication.
- The chain-termination method requires a DNA template, a primer, a DNA polymerase, dNTPs, and modified di-deoxynucleotide triphosphates (ddNTPs), which terminate DNA strand elongation.



- These chain-terminating nucleotides lack a 3'-OH group required for the formation of a phosphodiester bond between two nucleotides, causing DNA polymerase to cease extension of DNA when a modified ddNTP is incorporated. The ddNTPs may be radioactively or fluorescently labelled for detection.
- Final Answer :**It is a Dideoxy or chain termination method**

Question : 6

What is Chargaff Rule?

1. A+G=T+C
2. %A = %T and %G = %C
3. Both A & B

Answer the question on Google meet poll

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3. Both A & B

Solution:

- **Chargaff's rules** state that DNA from any species of any organism should have a 1:1 stoichiometric ratio of purine and pyrimidine bases (i.e., A+G=T+C).
- More specifically, that the amount of guanine should be equal to cytosine and the amount of adenine should be equal to thymine.
- This pattern is found in both strands of the DNA.

- Final Answer **: Both A & B**

Question : 7

The range of biological macro molecules is

1. 100 – 10 μm
2. 10 – 1 μm
3. 1 – 10 nm
4. 10 – 0.1 nm

Answer the question on Google meet poll

Question : 8

Which biological macro molecules has no polymer form ?

1. Carbohydrates
2. Amino acids
3. Lipids
4. Nucleic Acid

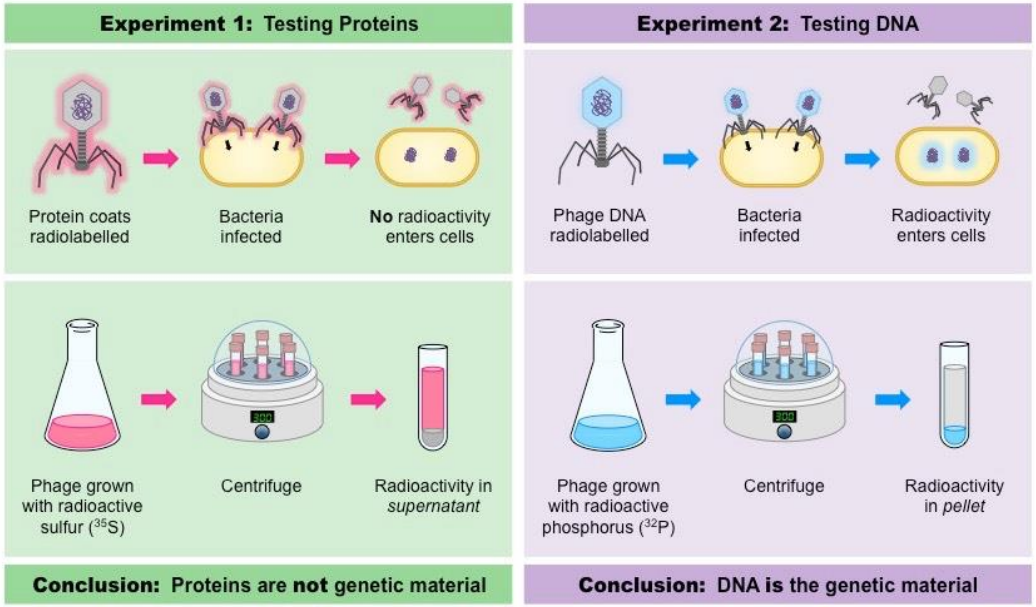
Answer the question on Google meet poll

Question : 9

Based on central dogma, what are key biomolecules to understand life ?

1. Carbohydrates and Proteins
2. Amino acids and Lipids
3. Lipids and DNA
4. Protein and DNA

Answer the question on Google meet poll



Hershey Chase Experiment ?

1. Viruses composed of a protein shell and DNA, so they can be labelled with a different elemental isotope.
2. Radioactive phosphorus-32 was used to label the DNA (phosphorus is present in DNA but not amino acids). Radioactive sulfur-35 was used to label the protein (sulfur is contained in protein but not DNA).
3. When the bacteriophages infected the bacteria, the progeny contained the radioactive isotopes in their structures.
4. The Hershey–Chase experiment helped to confirm that DNA, not protein, is the genetic material.

Nuclear Magnetic Resonance (NMR) ?

1. NMR exploits the idea of proton spin and the proton can behave as magnet to understand the spatial arrangement of atoms.
2. NMR can give idea about how other atoms are placed w.r.t., to their positions. In general the molecules are present in any orientation.
3. When a external magnetic field is applied, the molecules have a quick spin to match the spin of magnetic field (get a stable state).
4. This shift/spin is called as alpha-spin. Apply some energy so that we can turn alpha-spin to opposite direction of magnetic field.
5. EM waves provide the sufficient energy to reverse the alpha-spin to get beta-spin.
6. Based on the position of surrounding atom, the magnet may face shielding effect and have reduced effect of external magnetic field.
7. The amount of energy required to get the beta-spin differs based on the magnetic effect