

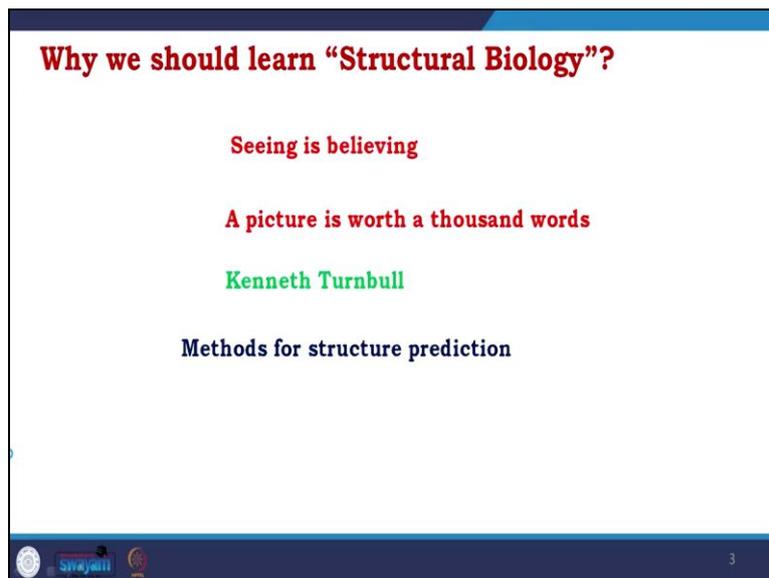
Structural Biology
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Indian Institute of Technology – Roorkee

Lecture 01
Introduction: Why to Study Structural Biology

Hi everyone. Welcome to the course of structural biology. I am Doctor Saugata Hazra from the Department of Biotechnology, IIT, Roorkee. And I am your guide to take to this course. My idea to develop the Structural Biology course is very introductory to explain what is happening as a whole around structural biology, not only about structural Biology techniques. I am trying to give you a comprehensive idea of this journey, starting from how Biology is developed. It is a historical tour of how biotechnology is developing how the biotechnology research starts recorded, and further going through the biological macromolecules, and how they have to be readout, how that reading would be utilized towards developing structures; the structural Biology techniques and then how to read the 3D coordinates.

How to use them for visualization? How to look at this process the static structure which we are solving towards dynamics and then some applicative measures where you could see how we use Structural Biotechnology or Structural Biology techniques towards the development of science, towards applications.

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Why we should learn “Structural Biology”?

Seeing is believing

A picture is worth a thousand words

Kenneth Turnbull

Methods for structure prediction

swayam

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The one-line answer is seeing is believing, so, through Structural Biology, we could see the molecules, and as Kenneth Turnbull told, a picture is worth a thousand words. So we want to make a visualization. We want to take pictures to visualize what is happening in Biology.

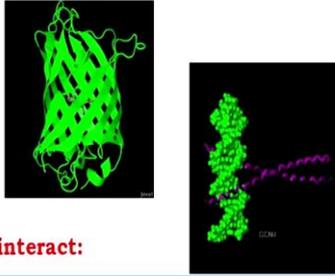
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Structural Biology: Introduction

Structural biology is the study of how biological molecules are built.

Using a variety of imaging and spectroscopic techniques, scientists view molecules in three dimensions to see,

a) How the architecture is:



b) How the macro-molecules interact:

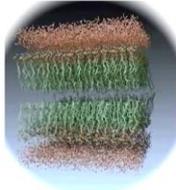
The slide features a blue header with the title 'Structural Biology: Introduction' in red. Below the title, there is a definition of structural biology and a statement about the use of imaging and spectroscopic techniques. Two sub-points are listed: 'a) How the architecture is:' and 'b) How the macro-molecules interact:'. Under point 'a', there are two 3D molecular models: a green ribbon structure of a protein and a purple and green ribbon structure of a DNA-protein complex. At the bottom of the slide, there are logos for 'Swayam' and 'IIT Bombay'.

Structural Biology is the study of how biological macromolecules are built. Scientists use various imaging and spectroscopic techniques to view molecules in three dimensions to see different functions. One how the architecture is? How do the macromolecules interact? The interaction of macromolecules means communicating one of the most critical things in Biology. As you see here, there are different DNA protein interactions. There are different transcription factors, which have different motifs. We will talk about motifs.

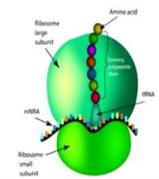
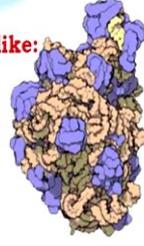
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Structural Biology: Introduction

c) How the membranes are built of:



d) How the protein synthesis machinery looks like:

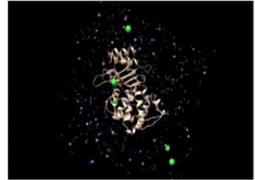
Swayam

How are the membranes built? We know that the organelles in the cells are divided by membrane, and membranes have a critical role in making in and out for many molecules. So how the membranes are constructed, and how it makes differentiation, all these things would be part of structural Biology. What did the protein synthesis machinery look like?

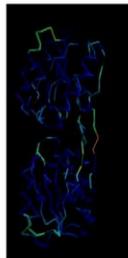
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Structural Biology: Introduction

e) How protein interact with solvents:



f) How protein adopt alternative conformations:

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How do proteins interact with solvent? In the physiological system, proteins interact with water, and proteins interact with ions and all. So, their interaction takes an important role that also we are going to look at. How protein adopt alternative conformations, as we say in if you think about the cell or biological system, you will see that it works like a factory. The only difference is that no operator is standing there to switch on and off.

This type of conformational changes what you see in the protein here helps switch on and off and make the biological process go smoothly. As we all say in biology, enzyme work is good, especially for enzymes. Enzyme not work is not bad. But enzyme overwork is always bad. It could create a lot of diseases if the enzyme could not switch on and off in the proper time.

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Structural Biology: Introduction

All those information has helped researchers understand how the thousands of different molecules in each of our cells work together to keep us healthy

Structural studies have also shown how misshapen molecules make us sick, and as a result, these studies have prompted new treatments for many diseases

"The eye doesn't see. The brain sees. The eye just transmits. So what we see isn't only determined by what comes through the eyes. What we see is affected by our memories, our feelings, and by what we've seen before."
– Brandon Stanton

Evolution

Structure

Function

All those information has helped researchers understand how the thousands of different molecules in each of our cells work together to keep us healthy. Structural studies have also shown how miss happened molecule makes us sick, and as a result, the studies were prompted new treatments for many diseases. And by getting structure, we understand how it binds to the ligand and substrate. So the first and foremost application of Structural Biology is to utilize the sequences and help us get the function. But that is not the end. Structure helps us in many things like evolution. If you look at the changes of domain structure organization confirmation, help us track the evolution happening in this world.

So we started talking that seeing is believing, but there is something more than that. As Brandon Stanton told the eye does not see. The brain sees. The eye transmits. So what we see is not determined by what comes through the eyes. What we see is affected by our memories, feelings, and what we have seen before. So yes, structural Biology could be your eye, but it could be of the brain by taking it carefully.

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Observation:

It's said that: "Seeing is believing"

Biology, as we all know, is the study of living organisms and their vital processes

It began as natural history which aimed to understand the whole organism in context

Natural history, which is essentially the study of plants and animals, was based on observational methods. It can be found from the earliest recorded history of biology that the Babylonians, Egyptians, Chinese, and Indians made innumerable observations in the course of their agricultural and medical practices



I will go to start with the observation; the first thing I talked about seeing is believing. As we all know, biology is the study of living organisms and their vital processes. And it began as natural history, which aims to understand the whole organism in context.

Natural history, which is essentially the study of plants and animals, was based on the observational method. It can be found from the earliest recorded history of Biology that the Babylonians, the Egyptians, Chinese and Indian made innumerable observations in the course of their agricultural and medical practices.

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Observation through Eyes or by Merit:

People have learned a lot in those era about life but unable to learn things which would lead to any rational concept or hypothesis.

Rapid progress started to be made with the advent of Greek civilization

Greek civilization produced legendary personalities who, by virtue of their astounding insight, examined the phenomena of the natural world and made seminal contributions to natural philosophy

Observation through eyes or by merit: People have learned a lot in this era about life. But there are no learning things that would lead to any rational concept of hypothesis. Rapid progress started to be made with the advent of Greek civilization. Greek civilization produced

legendary personalities who, by virtue of their astounding insight, examine the natural world's phenomenon and made a seminal contribution to natural philosophy.

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The Greek Contribution:

The most distinguished of them was **Aristotle** (384–322 BC) whose interests spanned all branches of knowledge including biology



He was first to undertake a systematic classification of animals based on specific principles, some of which remain valid even today

His student, **Theophrastus**, who is said to have done for botany what Aristotle did for zoology



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The most distinguished of them was Aristotle, whose interest spans all branches of knowledge, including Biology. He was first to undertake a systematic classification of animals based on specific principles that are even valued today. Theophrastus, his student, did that for plants.

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Greek scientists were not confined themselves only in classification and categorization

They speculated about the nature of matter and formulated hypotheses

Concept of Atoms:

Democritus (470–380 BC) proposed that all matter consisted of tiny particles which were further indivisible



The early “atomists” thought that the infinite universe consisted of atamos (or atoms) and void space

Earliest Greek philosophers, **Thales of Miletus**, held the view that the universe contained a creative “force” which he called physis

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Greek scientists could not even find themselves only in the classification and categorization of animals and plants. They speculated about the nature of matter and formulated hypotheses. Democritus, another legendary scientist, proposed that all matter consisted of tiny particles which were further indivisible. So if you look at it with the modern eye, you can understand

that you have already reached the concept of the atom. Democratic early atomists thought that the infinite universe consisted of the atom and void spaces. Early Greek philosopher Thales of Miletus believed that the universe contained a creative force, which he called Physis.

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Elements: Water, Air, Fire, Earth

Thales thought that the basic element of matter was **water**



Anaximenes believed that it was **air**



Heraclitus maintained that it was **fire**



Empedocles combined the ideas of Thales, Anaximenes, and Heraclitus and added one of his own— **earth**



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Thales thought that the basic element of material was water. Anaximenes believed that it was not water. It was air. Heraclitus maintained that it was the fire. Empedocles combines water, air and fire and improves his own Earth.

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Humors:

Accordingly, the notion emerged that all matter was made of differing amounts of fire, air, water, and earth held together by “forces” of attraction and repulsion



Physis as the creative force was accepted also by **Hippocrates**, the eminent Greek physician

However, members of the Hippocratic school gave little importance to the roles thought to be played by fire, air, water, and earth.

Instead, they believed that all living bodies were made up of **four humors** (Latin meaning: liquid or fluid)—blood, phlegm, choler (yellow bile), and melancholy (black bile)

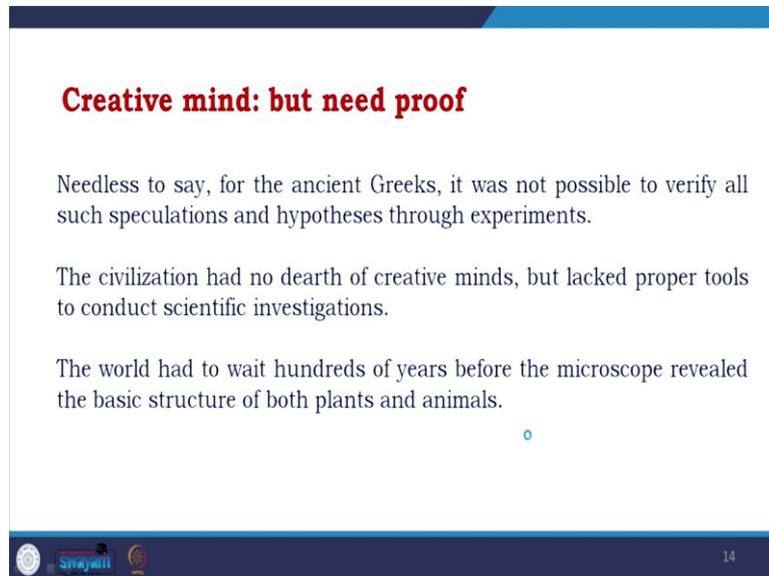
| HUMOR | CHARACTERISTICS | ELEMENT |
|-------------|-----------------------------|---------|
| blood | Sanguine socially useful | air |
| yellow bile | Choleric ruling | fire |
| phlegm | Phlegmatic getting | water |
| black bile | Melancholic avoiding | earth |

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Accordingly, the notion emerged that all matter is made up of differing amounts of fire, air, water and earth held together by forces of attraction and repulsion. Physis as the creative force was also accepted by Hippocrates the eminent great physician, but the member of

Hippocratic school they do not give importance to roles of fire, air, water and Earth. But they believed that the living bodies are made up of four humors (liquid or fluid) blood, Phelgm, Choler (yellow bile), and melancholy (black bile).

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Creative mind: but need proof

Needless to say, for the ancient Greeks, it was not possible to verify all such speculations and hypotheses through experiments.

The civilization had no dearth of creative minds, but lacked proper tools to conduct scientific investigations.

The world had to wait hundreds of years before the microscope revealed the basic structure of both plants and animals.

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So they did a lot of initial observations made a hypothesis, and some of them, as I told still valid. But they couldn't verify all such speculation and hypothesis through experiments. The civilization had no dearth of creative minds, but lacked proper tools to conduct scientific investigations. The world had to wait hundreds of years before the microscope revealed the basic structure of both plants and animals.

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History of instrument for visualization:

The magnifying power of segments of a glass sphere was known for nearly 2000 years.

During the first century AD, glass was invented by the Romans



End of 16th century, two Dutch spectacle-makers, **Hans Jensen** and his son **Zacharias**, invented the compound microscope by putting several lenses in a tube.



Zacharias Jensen microscope 1600

However, their instruments were of little practical utility since the magnification was only around 9X and the images were blurred

In the late 17th century, another Dutchman, **Antonie van Leeuwenhoek**, became the first man to make and use a real microscope, using single lenses magnifications up to 270X



So let us come to the history of instruments for visualization. The magnifying power of a segment of a glass sphere was known for nearly 2,000 years. During the first century AD, glass was invented by the Romans. End of the 16th century, two Dutch spectacle makers Hans Jensen and his son Zacharias, invented the compound microscope by putting several lenses in a tube. However, that instrument was of little practical utility since the magnification was only around 9X, blurred images. The real breakthrough came true in the 17th century when another Dutchman Anthony Van leeuwenhoek became the first man to use a real microscope using single lenses magnification of 270X.

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When it came into that stage, the improvement of microscopy facilitated the introduction of a new concept in the internal structure of living organisms, which is called the cell. The cell's credit of the first description goes to Robert Hooke an English physicist and microscopist. Hooke found an air-filled compartment and introduced the term cell, published in 1665 in micrographia.

Chromatic aberration created problems with earlier microscopes, resulting in the compromise of the resolution for resolving power. The introduction of achromatic microscopes satisfactorily addressed the problem.

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Cell Theory:

In 1838, German botanist **Mathias Jacob Schleiden** postulated that every structural element of plants is composed of cells or their products



Subsequently, in the following year, German zoologist **Theodor Schwann** extended the proposition to include animals. **Biological science saw a rapprochement between botany and zoology**



The conclusions of Schleiden and Schwann together formed the **cell theory**—a gigantic advance in the study of living organisms.



Added to this in the 1850s was **Rudolf Virchow's** aphorism *omnis cellula a cellula* (every cell from a preexisting cell).

In 1838, German botanist Mathew Jacob Sheldon postulated that plants' structural elements are composed of cells or their product. Subsequently, the following year German zoologist Theodor Schwann extended the proposition to include animals. Biological science saw a rapprochement between botany and zoology when Aristotle first came up, which is prudent, and he had given the classification and categorization.

The conclusion of Schleiden and Schwann together formed the cell theory, a gigantic advance in the study of living organisms. In the 1850, Rudolf Virchow's aphorism *Omnis cellula a cellula* (every cell from a pre-existing cell).

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The diagram illustrates the six postulates of Cell Theory. On the left, the words 'C e l l' and 'T h e o r y' are stacked vertically. The postulates are arranged in two rows of three:

- 1. All living organisms are made of cells (Illustrated with a snake).
- 2. Cells are the basic unit of life (Illustrated with a grid of cells).
- 3. Cells arise from pre-existing cells (Illustrated with a single cell).
- 4. Hereditary information is passed from cell (Illustrated with a chain of cells).
- 5. All cells have the basic chemical composition (Illustrated with a chain of hexagons).
- 6. Energy flow occurs within cells (Illustrated with a wavy line).

So in cell theory, they have made some postulates. All living organisms are made of cells. Cells are the basic unit of life. Cells arise from pre-existing cells. Hereditary information is

passed from cells. All cells have a basic chemical composition. Energy flow occurs within the cell.

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Post Cell Theory:

Now, the attention of the scientific world shifted to the “living” processes inside the cell

Together with the cell theory, two other landmark developments during the second half of the 19th century made the study of intracellular components all-the-more compelling

These developments were associated with two legendary individuals—**Charles Darwin** and **Gregor Mendel**



Now, when preliminary cell work was established, the scientific world's attention shifted to the living process inside the cell. The cell theory to other landmark development during the second half of the 19th Century, makes the study of intracellular components all the more compelling. This development was associated with two legendary individuals, Charles Darwin and Gregor Mendel.

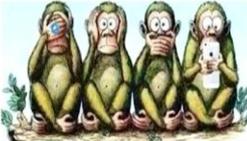
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Theory of natural selection:

In 1858, Charles Darwin published his theory of natural selection in “**On the Origin of Species by Means of Natural Selection**”

The crux of the theory is as follows: In the randomly varying nature, some variations are more advantageous than others

There is always a struggle for existence and those organisms which are better adjusted to their environment, even slightly, will most likely survive and transmit their advantageous traits to the next generation



Theory of natural selection by Charles Darwin in 1858: Charles Darwin published the theory of natural selection on the origin of species through natural selection. The Crux of the theory was as follows. In the randomly varying nature, some variations are more advantageous than

others. There is always a struggle for existence. Those organisms better adjusted to the environment even slightly will most likely survive and transmit their advantageous traits to the next generation.

So, according to his; own language. It is not the strongest species that survive nor the most intelligent but the most responsive to change. This is called adaptation

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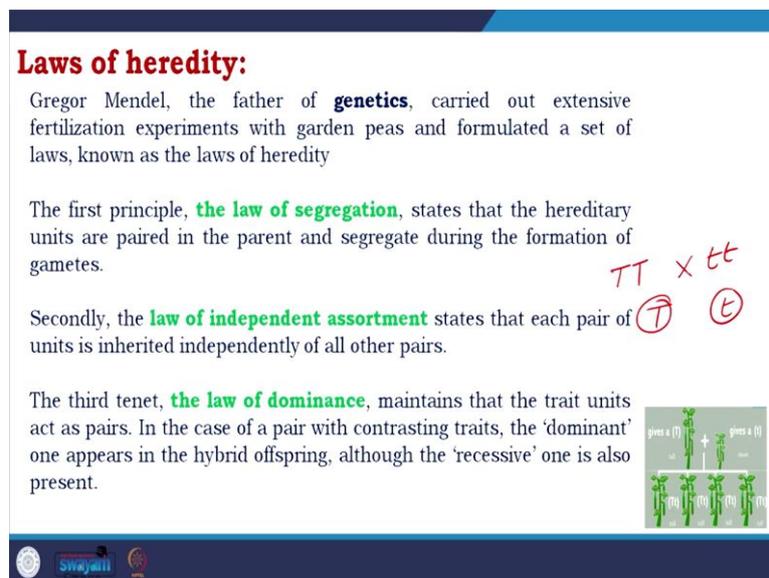
Laws of heredity:

Gregor Mendel, the father of **genetics**, carried out extensive fertilization experiments with garden peas and formulated a set of laws, known as the laws of heredity

The first principle, **the law of segregation**, states that the hereditary units are paired in the parent and segregate during the formation of gametes.

Secondly, the **law of independent assortment** states that each pair of units is inherited independently of all other pairs.

The third tenet, **the law of dominance**, maintains that the trait units act as pairs. In the case of a pair with contrasting traits, the 'dominant' one appears in the hybrid offspring, although the 'recessive' one is also present.



In two laws of heredity, Gregor Mendel, the father of genetics, carried out extensive fertilization experiments with garden peas and formulated a set of laws known as laws of heredity. The first principle, the law of segregation, states that the hereditary units appeared in the parent and were segregated during the formation of gametes. So their pair, suppose there TT and tt when it cross becomes T from here and t from here.

The law of independent assortment states that each pair of units is inherited independently of all other pairs there is no relation in that way. It is independent. And the third one, the most important law of dominance, maintains that the units of the trait act as pairs. In the case of a pair with contrasting traits, the dominant one that appears in the hybrid offspring of the recessive one is also present. Like if you see here, there is a great trait big T, and there is a small t, so they give Tt; all these are tall, so the dominant species is working here.

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Introduction of gene and genetics:

Ironically, Mendel's findings were not recognized during his lifetime. It was only at the turn of the century that his work was rediscovered and a spurt of activities in relation to the laws of heredity ensued thereafter



In 1909, Danish botanist **Wilhelm Johanssen** coined the term "**gene**" as a physical and functional unit of heredity



Earlier, in 1905, British geneticist **William Bateson** had introduced the term "**genetics**"

Now, the question was where in the cell the genes are located?



Ironically Mendel's findings were not recognized during his lifetime. He has done very notable work, but nobody understands that time. It was only at the turn of the century that his work was rediscovered in this part of activities about the laws of heredity ensure. In 1909 Danish botanist Wilhelm Johanssen coined the term gene as a physical and functional unit of heredity. Earlier in 1945, British geneticist William Bateson had introduced the term genetics. So now, when we know about genes and genetics, the question is where the genes are located in the cell.

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Location of genes in the cell:

The cell nucleus and the chromosome it contained were already known by the time gene and genetics were invented and properly named



Between 1825 and 1838, the nucleus was reported by three investigators including **Robert Brown**, who is credited for coining the term "**nucleus**"

Subsequently, German anatomist **Walther Fleming**, who is said to be the **founder of the science of cytogenetics**, was the first to observe and systematically describe the **movement of chromosomes in the cell nucleus during normal cell division**



In 1915, American geneticist **Thomas Morgan** and his students asserted that **genes are the fundamental units of heredity**. Their research confirmed that specific genes are found on specific chromosomes and that genes are indeed physical objects



The chromosome theory of inheritance emerged



The cell nucleus and the chromosome the time gene and genetics already knew its content invented and properly named. Between 1825 and 1838, the nucleus was reported by three investigators, including Robert Brown, who is credited for coining the term nucleus. Subsequently, German anatomist Walter Fleming, who is the founder of science of

cytogenetics, was the first to observe and systematically describe the movement of chromosomes in the cell nucleus during normal cell division.

In 1915 American Geneticist Thomas Morgan and students asserted that genes are the fundamental units of heredity. Their research confirms that specific genes are found on specific chromosomes and that genes are the physical object.

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Introduction of Proteins:

Major advances were already made in the investigation of another kind of important “physical objects” of the cell—the proteins. In 1789, French chemist **Antoine Fourcroy** had recognized several distinct varieties of proteins (though the term was not used then) from animal sources. These were **albumin, fibrin, gelatin, and gluten**



Several years later, in 1837, Dutch chemist **Geradus Johannes Mulder** determined the elemental composition of many of these molecules



The term “**protein**” was subsequently used by Mulder’s associate **Jacob Berzelius** to describe these molecules



The name was derived from the Greek word $\pi\rho\omega\tau\epsilon\iota\omicron\varsigma$ which means “primary,” “in the lead,” or “standing in front”



And when they were focused on genes, the protein was not even neglected. And major advances were already made in investigating another important physical object of the cell, the proteins. In 1789 French chemist Antonie Fourecoy recognized several distinct protein varieties though the term was not used then from animal sources. They have purified studied albumin, fibrin, gelatin, and gluten.

Several years later, in 1937, Dutch chemist Geradus Johannes Mulder determined the elemental composition of many of these protein molecules. Mulder's associate Jacob Berzelius subsequently used the term protein to describe this molecule. The name was derived from the Greek word which means primary in the lead or standing in front.

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Introduction of Enzymes:

One class of proteins are the **enzymes** which **catalyze the biological processes in living organisms**

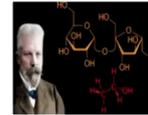
The first enzyme to be discovered was **diastase** (now called **amylase**)



It was extracted from malt solution at a French sugar factory by **Anselme Payne** in 1833

The term "**enzyme**" was coined in 1878 by German physiologist **Wilhelm K€uhne**

In 1897, **Eduard Buchner**, a German chemist and zymologist, fermented sugar with yeast extracts in the absence of live organisms.



One class of proteins that enzymes catalyze the biological process in living organisms. The first enzyme discovered was diastase, which is now known as amylase and is still a very industrially relief in protein. This structure was later extracted from malt solution at a French sugar factory by Anselme Payne in 1833. The term enzyme was coined in 1878 by German physiologist Wilhelm Kuhn.

In 1897 Eduard Buchner, a German chemist and zymologist, fermented sugar with yeast extract in the absence of live organisms. This also shows that the enzyme could work without a living organism, so another breakthrough innovation simultaneously.

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Nucleic Acid:

Nucleic acid, was discovered by a Swiss physician **Friedrich Mischer**

Working in the laboratory of biochemist **Felix Hoppe-Seyer** at T€ubingen, Mischer initially intended to study proteins in leucocytes (blood cells containing nuclei)

However, in his experiments he noticed a precipitate of an unknown substance which is neither a protein nor a lipid

Unlike proteins, it contained a large amount of phosphorous. Since the substance was from the cells' nuclei, it was named "**nuclein**"

Later, **Albrecht Kossel**, another scientist in Hoppe-Seyer's laboratory, found that nuclein consisted of four bases and sugar molecules. Kossel provided the present chemical name "**nucleic acid**"

In 1909, a Russian-born American scientist, **Phoebus Levine**, isolated nucleotides, the basic building blocks of ribonucleic acid (RNA)



Swiss physician Frederick Mischer discovered nucleic acid. Frederick was working in the laboratory of Felix Hoppe Sayer, a very famous laboratory of that time in Tuebingen. Mischer initially intended to study protein in leukocytes, a blood cell containing nuclei.

However, in Frederick's experiment, he noticed a precipitate of an unknown substance and established a test showing that this is neither a protein nor a lipid.

Unlike protein, it contained a large amount of phosphorus since the substance they got from the nucleus. They name it nuclein. Later, Albrecht Kossel, working with Frederick Mischer at the same lab of Felix Hoppe-Sayer, found that nuclein consists of four bases and sugar molecules. Kossel provided the present chemical name nucleic acid. In 1909 a Russian-born American scientist, Phobus Levine, isolated nucleotides, the basic building block of ribonucleic acid.

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DNA as genetic material:

All these advances notwithstanding, till the late 1920s, the question regarding the nature of the genetic material remained unanswered

The scenario started changing in 1928 when British bacteriologist **Fred Griffith** carried out an experiment on the pathogenicity of *Streptococcus pneumoniae*. Though not conclusive, the experiment did lay the foundation for later discovery that DNA is the genetic material



The results showed that apparently something in the cell debris of a virulent strain of *Streptococcus* had "transformed" an avirulent strain to become virulent. This something was called the "transforming principle"; it remained unclear what the transforming principle was—RNA, DNA, protein, lipid or carbohydrate.

DNA as genetic material, all these advances not making impact till the late 1920's the question regarding the nature of genetic material remain unanswered. The scenario splattered, changing in 1928 when British bacteriologist Fred Griffith experimented on the pathogenesis of *Streptococcus pneumoniae*. Though not conclusive, the experiment lay the foundation of the later discovery that DNA is the genetic material.

The results show that apparently, something in the cell debris is of a virulent strain of *Streptococcus* had transformed an avirulent strain to become virulent. This something was called the transforming principle at that time. The transforming principle remains unclear: RNA, DNA, protein carbohydrates biological macromolecules.

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DNA as genetic material:

All these adva regarding the :

The scenario **Fred Griffith** Streptococcus did lay the fo material

The results st virulent strai strain to be "transforming principle was-

rough strain (non-virulent) smooth strain (virulent) heat-killed smooth strain rough strain & heat-killed smooth strain

question swered

terio logist genicity of xperiment re genetic

lebris of a avirulent alled the nsforming

mouse lives mouse dies mouse lives mouse dies

This is the description of the experiment. They choose a rough strain that is non-virulent and inject it into the mice. Then they take a smooth strain of Streptococcus which is virulent, and when injected into the mouse, the mouse dies. Then they use heat kills smooth strain the mouse is now not killed. But when the mix-up that heat kills smooth strain with the rough strain, they see that the combination kills the mouse effectively.

So then they understand that there is something in this virulent and non-virulent strain that helped the mouse kill.

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DNA as genetic material: Avery Macleod McCarty Experiment

The conclusive evidence was provided 16 years later, in 1944, by american microbiologists **Oswald Avery, Colin MacLeod, and Maclyn McCarty**

They established that the active genetic principle was DNA since its transforming activity could be destroyed by deoxyribonuclease, an enzyme that specifically degrades DNA

break open + Protease → Mouse dies

break open + DNase → Mouse lives

Rough nonvirulent (type R) Heat-killed smooth virulent (type S)

Avery Macleod McCarty experiment of DNA as genetic material. The conclusive evidence is provided 16 years later, in 1944, by American microbiologist Oswald Avery, Colin Macleod, and Maclyn McCarty. These three people established that the active genetic principle was

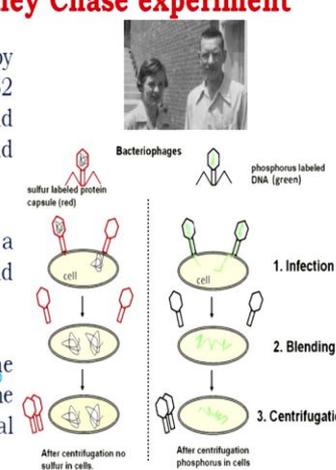
DNA since its transforming activity could be destroyed by deoxyribonuclease, an enzyme that specifically degrades DNA.

They take the rough nonvirulent, and heat kills smooth virulent, which already had taken in the earlier experiment by Fred Griffith. They combine them, and add protease to one and DNAase to another. When they add protease, the mouse dies, they could not kill, the killing ability for killing power of the mixture. Whereas when they add DNAase, the mouse is now survived, which means DNA's make the factor involved in killing ineffective.

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DNA as genetic material: Hershey Chase experiment

A confirmation of the conclusion made by Avery and his colleagues came in 1952 from two scientists, **Alfred Hershey** and **Martha Chase**, who were working at Cold Spring Harbor Laboratory



The protein coat and DNA core of a bacteriophage were labeled with ^{35}S and ^{32}P , respectively

By infecting a bacterial culture with the radiolabeled phage, they showed that the parental DNA, and not the parental protein, was present in the progeny phage

1. Infection
2. Blending
3. Centrifugation

After centrifugation no sulfur in cells
After centrifugation phosphorus in cells

Another very significant experiment was called the Hershey Chase experiment. A confirmation of the conclusion made by Avery and his colleagues came in 1952 from two scientists, Alfred Hershey and Martha Chase, who are working at Cold Spring Harbour laboratory.

A bacteriophage is an organism (virus) that generally kills bacteria. It was used to label with ^{35}S and ^{32}P , respectively. The radioactive Sulphur and radioactive phosphorus. A bacterial culture with the radiolabeled phage showed that the parental DNA, not the parental protein, was present in the progeny phage. So they made this experiment sulfur labeled protein is called Red they go in the cell, and after centrifugation, no sulfur goes inside the cell.

So, it is not the proteins responsible, whereas when they labeled the DNA, which is labeled as green, then make the infection and isolated, they found the radiolabeled DNA in the progeny virus.

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Biology goes molecular:

Undoubtedly, with the discovery of the two most important macromolecules of the living cell—DNA, that carries the blueprint of life, and protein, that executes the plan—biology had turned molecular

In fact, as early as in 1938, **Warren Weaver**, who was the director of the Natural Sciences section of the Rockefeller Foundation at that time, introduced the term **molecular biology**

The cellular processes were now required to be explained in terms of molecular interactions. It became ever more evident that the living system conforms to the laws of physics and chemistry



Undoubtedly the discovery of the two most important macromolecule of the living cell DNA that carries the blueprint of life and protein that executes the plan biology had turned molecular. In fact, in 1938, Warren Weaver was the director of the national science section of the Rockefeller Foundation. At that time introduced the term Molecular Biology. The cellular processes were now required to be explained in molecular interactions.

They want to go deeper than the behavior of DNA or a protein. They want to go for individualistic characterization. It became even more evident that the living system conforms to the laws of Physics and Chemistry. So there is a scenario created before people have done separate things, but now an interdisciplinary platform will be developed.

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