RNA Biology
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Lecture - 02
Introduction to RNA Biology and RNA World-Evidences

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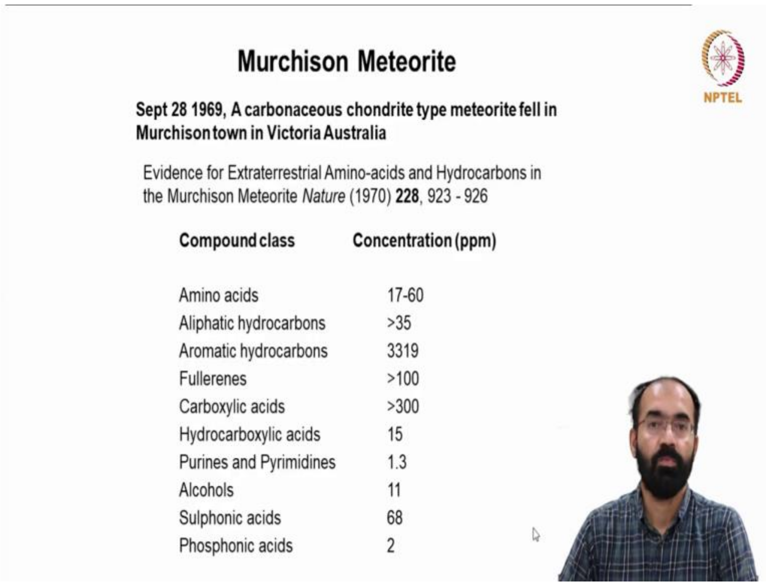

Welcome you all for another session of RNA Biology. Today, we will resume where we left in the previous class, and this was the last slide which we were discussing that is about the Murchison Meteorite which was discovered in the Australia Queensland, Australia, so Victoria Australia in fact.

And different compounds are measured using various chemical techniques. And there is a relevance, why this was compared to Murchison Meteorite.

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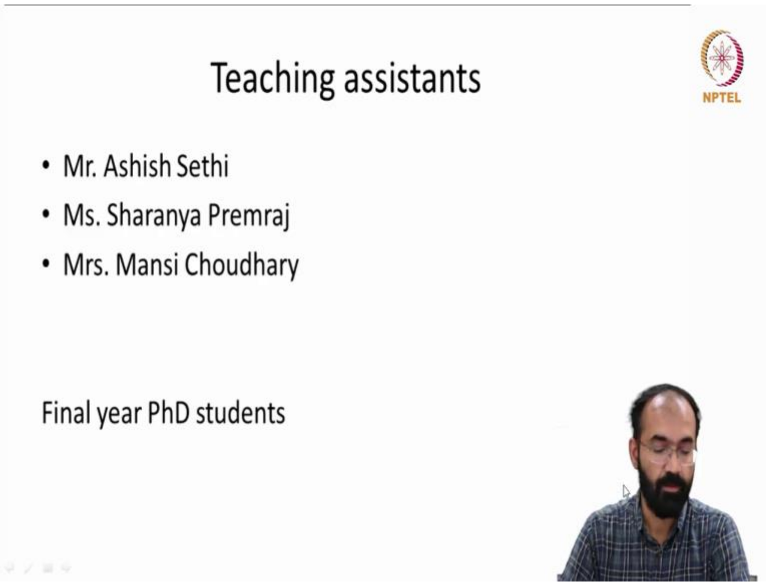

So, before going into the details I would like to introduce, they are teaching assistants, would be assisting me in carrying out this lecture series is Mister Ashish Sethi, Miss Sharanya Premraj and also Misses Mansi Choudhary. So, these are final year, PhD students who would be part of conducting this lecture.

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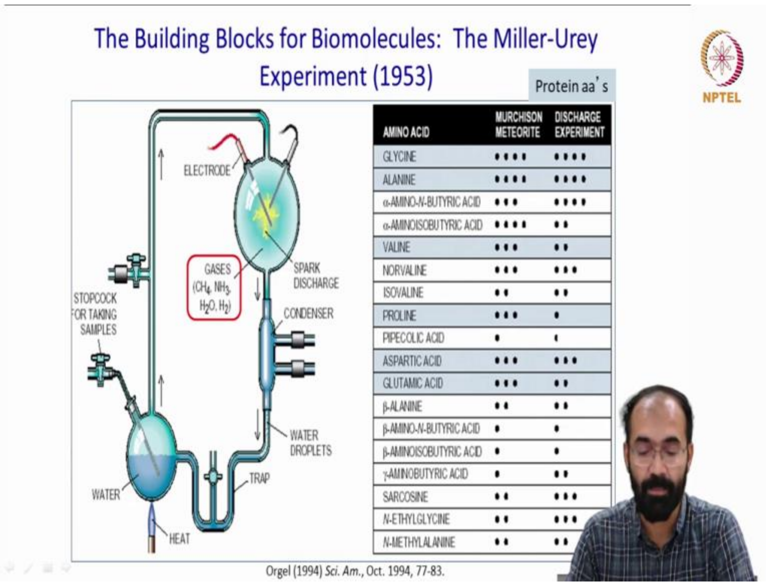

So, now in the previous class, we had discussed about Urey-Miller experiment, one of the major finding of RNA biology research. So, in 1953, at university of Chicago, they conducted a very simple experiment as you can see here in a big a glass container where you have water vapor and also you have given two electrodes. And also different gases such as methane, ammonia and water vapor and hydrogen, they are there.

And the electrodes are kept such a way that they can be given a powerful electric shock. And what happens is because the water vapor etcetera are present after this discharge experiment, then you have a condenser below where you have a cooling option. And the condense water of this electric discharge and also when this inorganic gases and water vapor, hydrogen etcetera.

The reason, there is a reason why these molecules are selected because the prebiotic world is mainly supposed to contain these molecules abundantly, unlike modern times oxygen etcetera. So, after this solid discharge going on what you end up getting is the products that are formed because of this very high temperature and also very high you know electric electric pulses.

And then they are conducted in the bottom and needless to say that there is a source of water vapor which is there below which is heated and which is water molecule which is boiled and the vapor will be discharged into this chamber. So, now, they analyze the component with that of the Murchison Meteorite. So, that is something very interesting. If you look into the amino acid composition, like glycine, alanine etcetera, you can see they are equivalent in amount.

That is 4 dots means abundant, 3 dot means reasonably abundant, 2 dot means present, and 1 dot means very scarcely present. So, this is the density or the intensity representation of individual components. And I will not go into the details of each and every component. So, whenever you compare the components what that were present in this Urey-Miller experiment and to that of the Murchison Meteorite, they find there is a reasonable similarity between the components.

So, what it says that the meteorite when it is entering the atmosphere, that is of course, coming from a a outer space and this very high temperature and interaction with the various gases etcetera can naturally allow the formation of these components. So, what we should understand the nature did not choose a specific compound or a specific chemical for the life to originate.

Rather, it used the chemicals available then and the product that are formed because of the prebiotic conditions and then a life is originated. So, that is what this similarity indicates.

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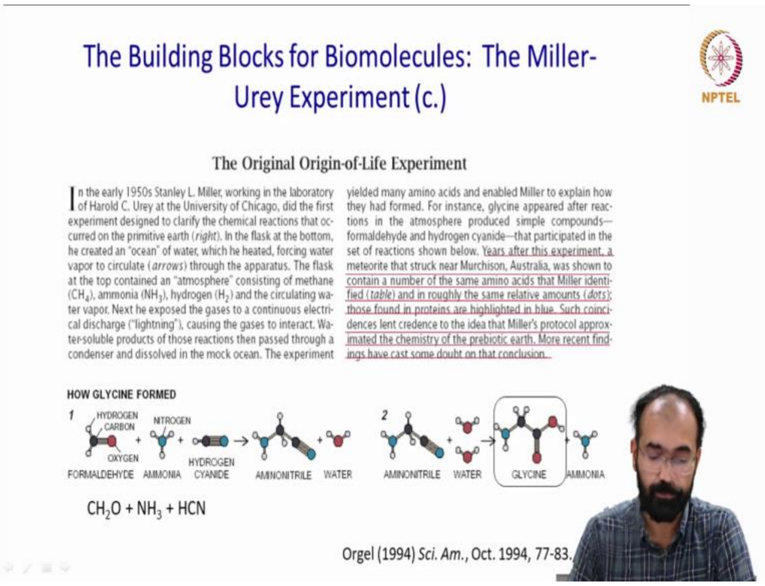

So, now if you look back into the building blocks of life that is various biomolecules and especially from the Urey-Miller or Miller-Urey experiment. And we can see a lot of compounds that such as how glycine is formed, how formaldehyde is formed from ammonia because various components can combine together in presence of water. It can give rise to several biomolecules.

Biomolecule is little bit premature to say right now because life has not originated there. But eventually these molecules end up being part of various life system. So, several years after the discovery people find out that what are the conditions and situations through which these molecules got a upper hand for being part of living organism. We will see them one by one.

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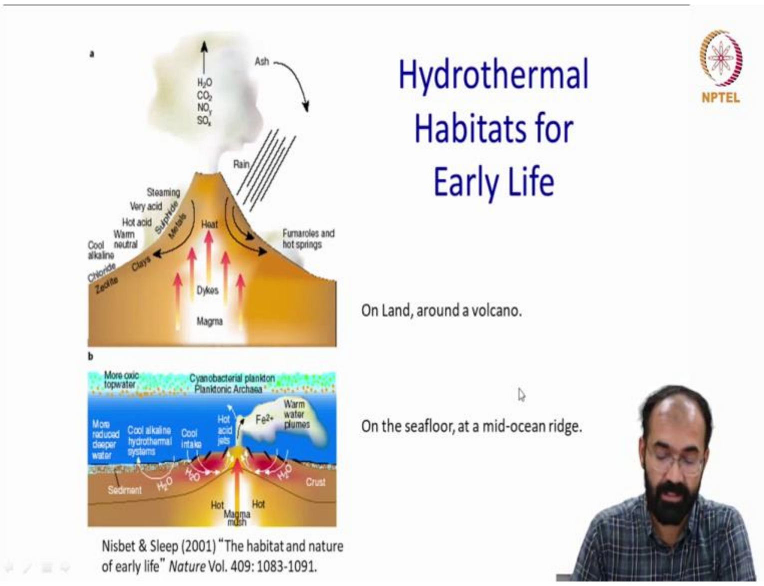

So, one more point which we discussed was the hydrothermal vents. So, what are hydrothermal vents? We know under the planet surface, there is very high temperature is there, and where the planets crust is thinner; there is a chance that this high temperature beneath the planet earth surface will be exposed to the atmospheric. You all know about volcanic eruption, explosion etcetera.

So, in this picture, you can see two situations one is a volcanic depiction and another is hydrothermal vent. Basically, volcano and the hydrothermal vents are one and the same, except that volcano is on the terrestrial surface that is the dry land whereas, the at the sea floor the same volcano when it comes that is acting as a hydrothermal vent.

In both cases, in prebiotic world, there are lots of inorganic substance, and this heat at intensive heat both you see in the volcanic surface and also in the hydrothermal vent will provide a catalyst or a accelerating agent for a biological reaction to happen. And we know even now when a volcanic eruption takes place lot of gases, you know inorganic substance come out.

And because of the high temperature it has the potential it has the power to give rise to various biomolecules eventually, and it keeps happening. Even now you can do produce various biomolecules in laboratory condition. So, note the point that volcanic environment and also the hydrothermal vents could also trigger similar to what you saw in the case of Murchison Meteorite.

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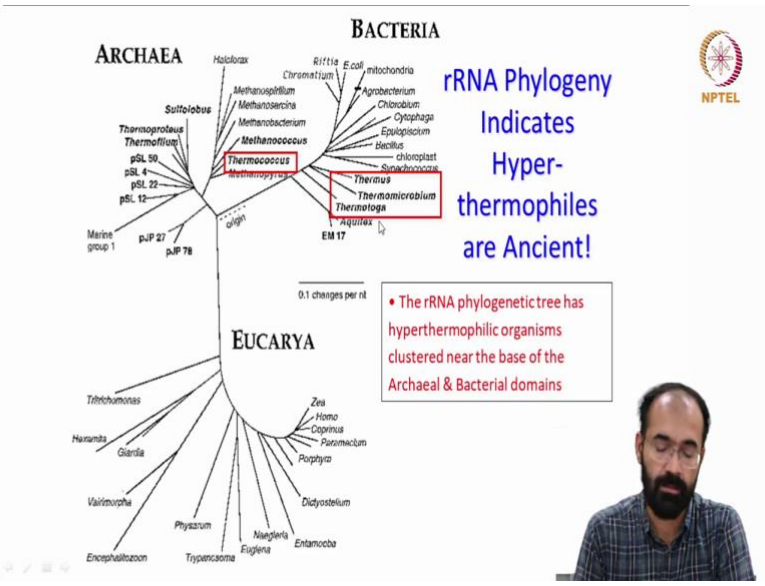

So, now do we have other evidence that is what we are looking for, ok. We are saying that you know these molecules could have been formed near the hydrothermal vents, volcanic environment etcetera. But do we have any evidence? One such evidence what we can get from, ribosomal RNA phylogeny.

So, you know prokaryotes are the primitive life forms, broadly the living organisms are classified into two, prokaryotes and eukaryotes. So, we will not go into the details right now, but understand the prokaryotes are more primitive in terms of their organism complexity compared to eukaryotes. Hence, they are considered to be evolved much earlier on this planet.

So, now, when you compare different types of bacteria, bacteria can be broadly classified into 3 group, archaea which is much primitive than bacteria then the bacteria which is actual bacteria, and then you have the advanced category that we call them as eucarya. So, our interest is mainly the branch between the archaea and the bacteria.

So, in archaea group you have one group called thermococcus, which is circle circled in red box, and then you have bacterial group that is thermus and thermomicrobium and thermotoga. So, these 3 groups when you try to compare them at RNA phylogeny level, RNA ribosomal, RNA is basically used for comparing different organisms and their relatedness. Even it is used as, modern days it is used as a very powerful tool for comparing the interrelationships.

So, if you looked at ribosomal RNA phylogeny reveal that the high temperature organism that the thermococcus and thermos, these animals, this bacteria, they leave or they prefer a very high temperature environment. And in this situation, it seems that they are more related, they have more genetic similarity compared to rest of the bacteria.

So, what it says that the organisms that high temperature organism, the organism which prefers high temperature even today, they have more relatedness compared to the rest of the bacterial group that is the mesophilic or psychrophilic bacterial group. Mesophilic means normal temperature, psychrophilic cold loving bacteria. The thermophilic bacteria are more related and they are more primitive also.

So, this suggests that these organisms could have originated much much early in the life origin of life on the planet earth.

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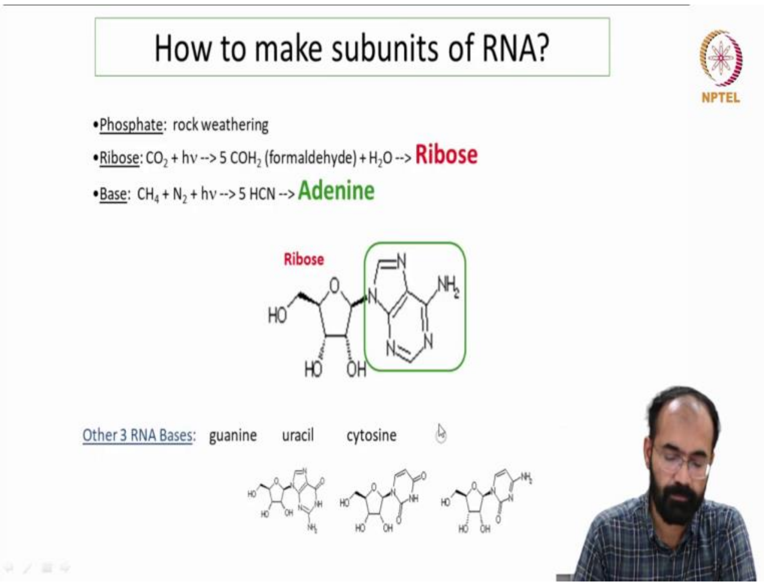

So, now let us think, can we make various subunits or components of RNA. We are all discussing about the RNA world hypothesis. So, RNA have got 3 major components, one is a phosphate, that is a acting as a back bone of the RNA, and then a ribose, a pentose sugar and a nitrogenous base.

So, phosphate can come from rock weathering because there are many phosphate containing rocks are there, and they can be you know during rain and other environmental condition, they can provide adequate quantity of phosphate. And the ribose sugar you can have carbon dioxide, energy together, 5 COH2 molecule that is basically formaldehyde molecules combined with water can give rise to ribose sugar. We will come to that more in detail, name of that reaction etcetera.

And the nitrogenous base methane and ammonia, nitrogen methane and nitrogen along with the heat can give rise to hydrogen cyanide. It is also called as hydro cyanic acid, and 5 hydrogen cyanide molecule can give rise to adenine. So, what we should understand; that the phosphate can come from the rocks, ribose can come from chemical reaction, and adenine also can come from the chemical reaction.

Remember, adenine is one of the nitrogen base. There is RNA has got adenine, uracil, cytosine and guanosine. So, there are 4 bases are there and in DNA the uracil is replaced by thymine which we will see later on what is the difference etcetera. So, you can see the ribose sugar usually combined with the nitrogenous base and which in turn make use of a phosphate backbone to give rise to one monomer of the RNA.

And the other bases, 3 RNA bases are guanine, uracil and cytosine whose molecular structure is being given here and they also can be form spontaneously. Means, what we should understand, without any enzymes or any other new intervention, purely from the inorganic material you can get this organic molecule such as ribose sugar and nitrogenous bases, which can eventually participate in the formation of the RNA.

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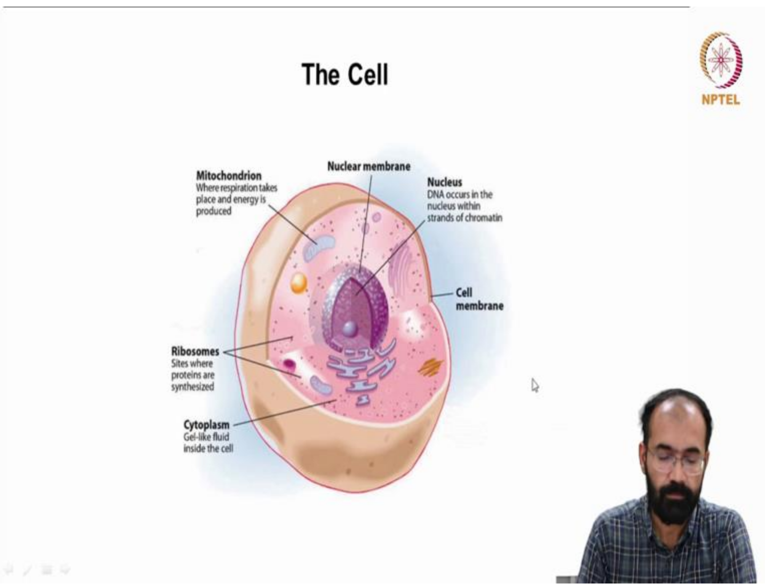

Now, this is a typical structure of the cell, and we know that cell is circled by a plasma membrane and also a nucleus where the genetic material is situated. So, this is a typical building block.

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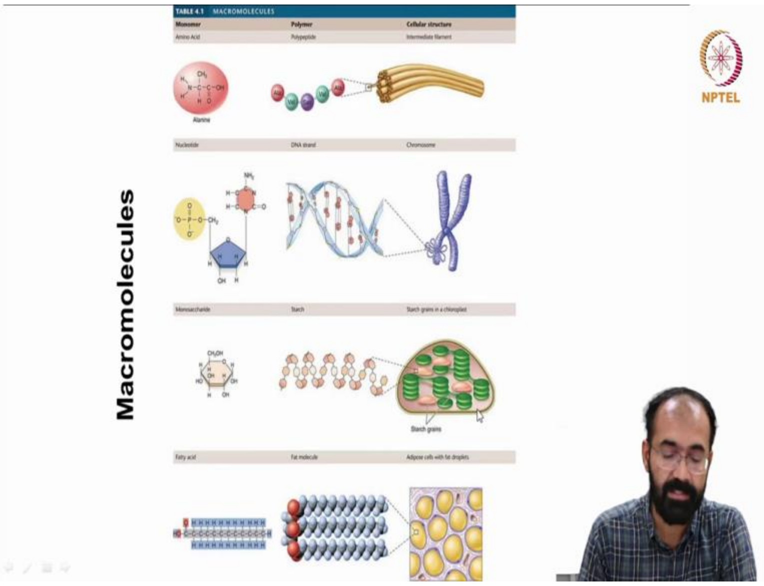

But if you look further, we can understand that they are formed from various monomers and we call them as macro molecules. Like, nucleotides are monomers for the nucleic acid. And mean, every molecule of the DNA or the RNA, they can assemble together, usually the DNA can assemble together and it can give rise to chromosome.

And same way there are many carbohydrates, carbohydrate monomers can group together and can form polysaccharides. Polysaccharides can contribute to the structure and also it can contribute to the energy yielding reactions also. And then comes the fatty acids. Fatty acids are also spontaneously formed.

We will not go into the details of that because this topic is about the RNA biology. And they also can assemble and they can act like a protective cover that is the plasma membrane, and so we have amino acids, we have carbohydrates, and we have nucleic acid and we also have the lipids formed spontaneously which can now assemble and to act like a miniature version of the cell.

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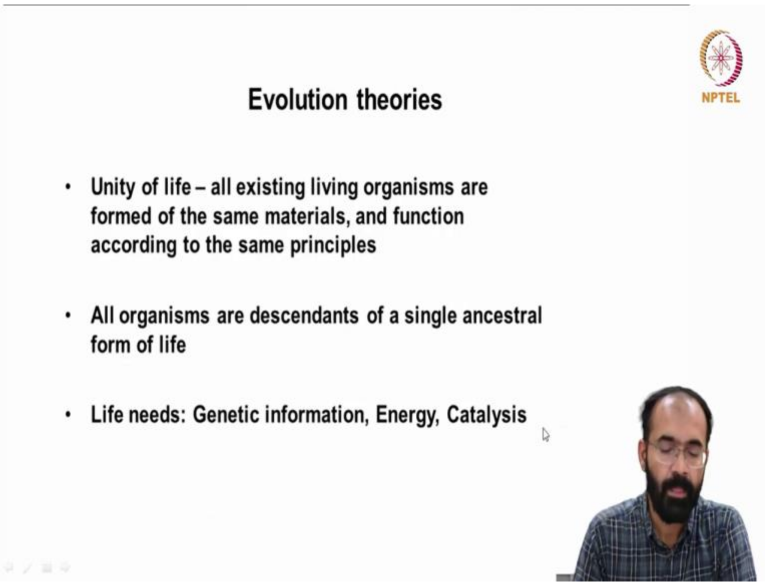

Now, we have to bring in the evolution theory because evolution we kind of discussed in the previous class. That means, any change can technically be called as an evolution, provided that change is adapted, that is welcome into the community or into a society or into a environment, then that will have a tendency to be selected, that will have an affinity to be preferred.

Like I gave you example of you know a mobile phone, evolving mobile phone different features etcetera. If it is adapted for the environment, then it will be selected and then we can call it evolved. So, we can think various similar examples. So, we have to bring in evolution theories every now and then. So, let us bring evolution theory.

So, the unity of life on existing living forms can be formed only from the pre-existing form. This is a non fact. However, it make use of the materials available in the environment. Say for example, if you have a bacteria and bacteria simply cannot make a copy of itself from nothing. It has all the information all the resources for making another bacteria.

However, the resources has to come from the environment. So, it formed from, a bacteria is formed from the same material and it functioned according to the pre-existing bacteria or pre-existing cell. And all organisms are descendants from a single ancestral form of life. This Darwin also says and various evolution theories also says, there is no way every organisms are formed independently.

Of course, they are evolved independently, but the so-called life form must have originated in one form. And what are the need of life? The life always needs a genetic information, then energy and catalysis. So, these are the 3 fundamental steps for the propagation of life.

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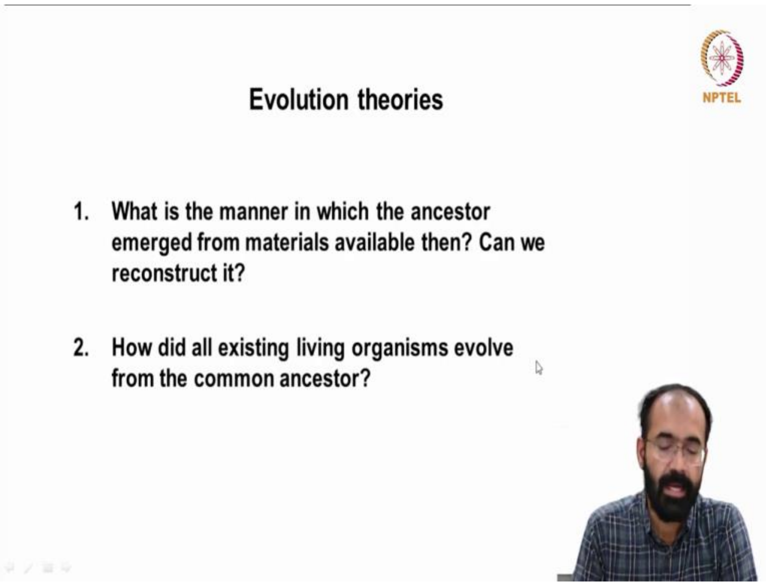

And continuing the evolution theories in a different angle, we should ask some questions. What is the manner in which the ancestor emerged from materials available then? Can we reconstruct it? This is a million-dollar question. Why? Because, whatever you put effort it is very difficult to recreate a prebiotic world unless you go to a planet where there is no life exist and start doing experiment because, no matter what you create, in the lab condition, they are always the miniature version.

The problem with the miniature version is the area, the volume and the resources are limited. When you talk about a planet you are talking about large scale and the scale sometime is very important. Because scale and time which we cannot create in a laboratory condition. You can do proof of principle, that is why the origin of life on planet earth is not creatable or definable in a laboratory condition.

And then comes the next question, how did all existing living organism evolve from the common ancestor? And we can justify how it originated from the existing common ancestor, but how all these forms are evolved it require billions of years of evolution and lot of luxury of space and resources.

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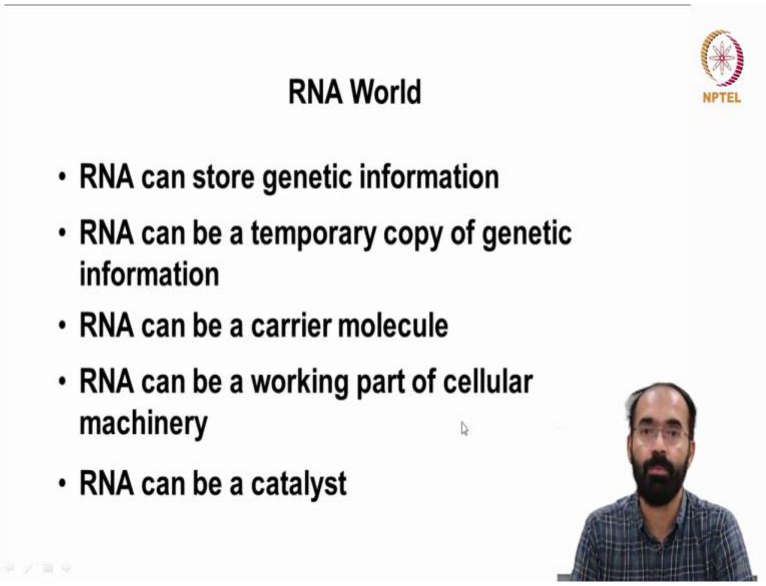

And coming back to the RNA world, we know RNA can store genetic information, from the modern worlds knowledge I am saying this. And RNA can be temporary copy of the genetic information. We know various viruses are there like, influenza virus, even this COVID-virus, these are all having RNA as their genetic material. And RNA can act as a carrier molecule, and also RNA can be a working part of the cellular machinery.

So, these are all existing even in modern day. So, there is no reason to believe that there is no RNA world existed. There is always supporting evidence to suggest that RNA world indeed is a reality. And most importantly RNA can act as a catalyst. Catalyst means capable of carrying out a biological function.

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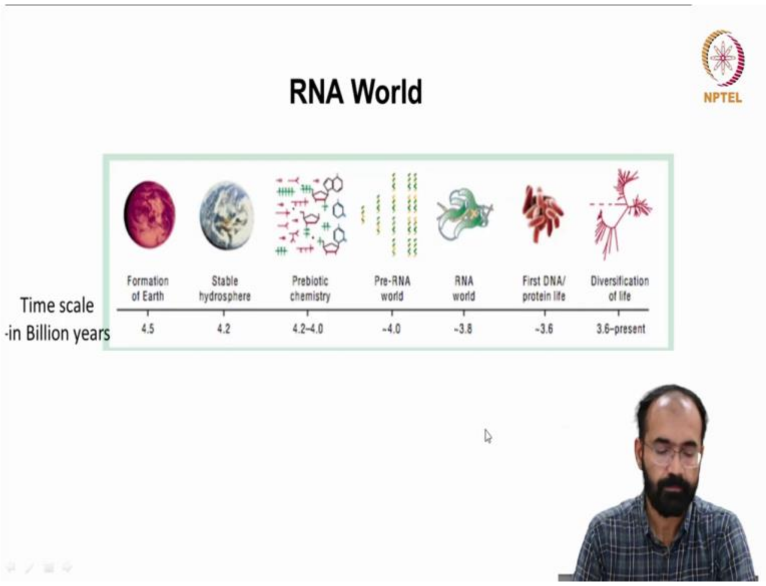

Now, let us look into the RNA world using a time scale. So, around 4.5 billion years ago, you have life on the planet earth that existed which is devoid of any life. And around 4.2 billion years you have the stable hydrosphere. And by around 4.2 to 4 billion years ago you have got pre-biotic chemistry.

And then around 4 billion years ago close to that you have the pre-RNA world. That means the RNA world is not formed, but the components of the RNA have existed. And around 3.8 billion years ago you have RNA world came into existence. And again, after several millions of years, by around 3.6 billion years you have the first DNA and protein molecules that are formed. And, but around 3.6 billion years to modern world is the so-called life existence.

So, around 1 billion years from 4.5 billion years to 3.6 billion years, around 1 billion years this evolution was happening on planet earth. And needless to say, when planet earth was formed, it was too hot for any so-called life forms can exist. So, the cooling process also is very important which took place in over millions of years.

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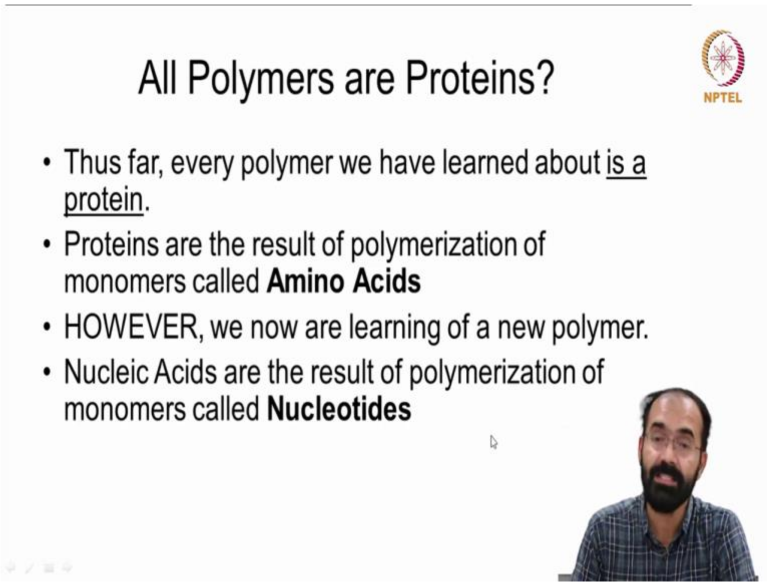

So, let us ask in the modern world or modern life form, you see majority of the polymers are proteins, but can we look little bit more in detail. So far, every polymer that we know is mainly the major component is a protein. But however, proteins are the result of polymerization of individual monomers called amino acids. And we already showed almost all amino acids can be formed from the prebiotic world through inorganic materials.

Now, we are learning, although we know in the modern world the predominant polymer is protein, I am not saying that RNA and DNA are not polymers, they are polymer, but the predominant polymer is the protein. But now we are learning more in detail about a polymer that existed in the RNA world. And nucleic acids are the major polymers then, and they are formed by the polymerization of monomers. And we call them as nucleotides.

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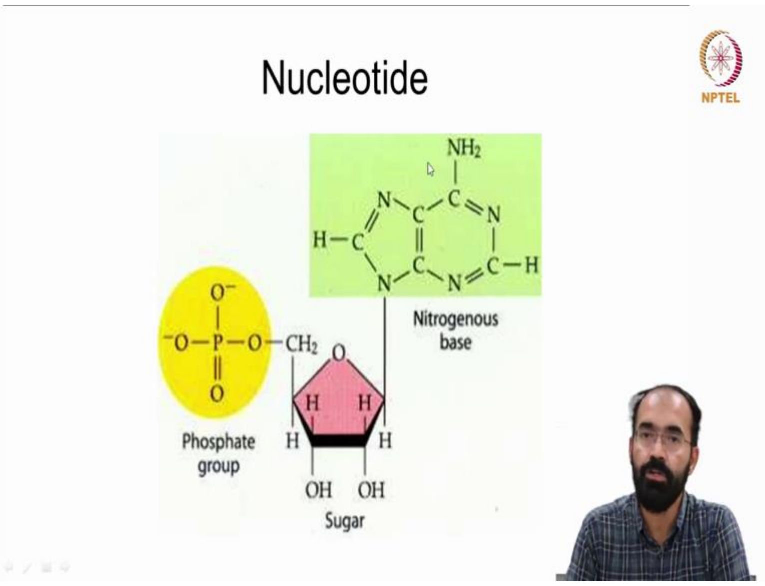

A nucleotide is basically a 3-member component, one is this phosphate group, and then you have a pentose sugar, and then you have got a nitrogenous base. And this pentose sugar has got 5 carbon atoms, and we usually name them as 1 prime, 2 prime, 3 prime, 4 prime and 5 prime. So, you can see here this is 1, 2, 3, 4 and 5 carbon. And this 2 and 3 are very very important and also the 5-prime end. And we will see them when you study more in detail about the RNA.

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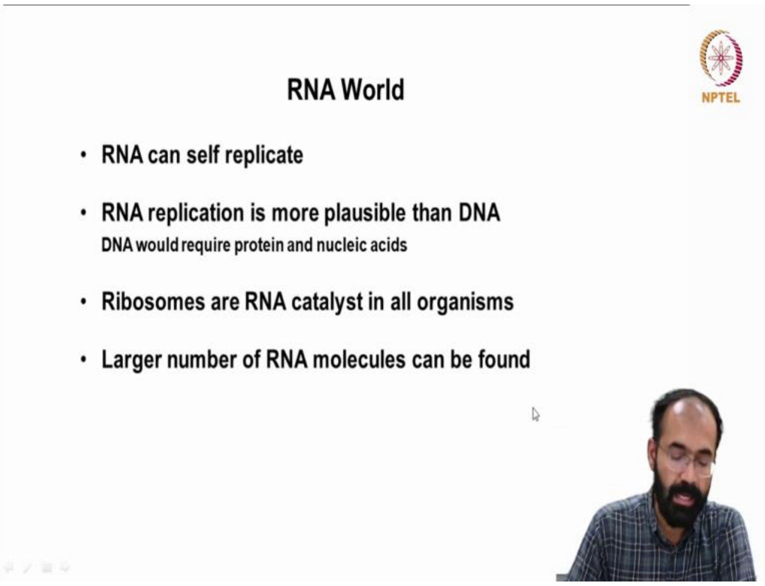

So, in the RNA world we now know that the RNA should be able to self-replicate and RNA replication is more possible than the DNA replication. We will come to that how RNA evolved into DNA, and what was the necessity, etcetera. DNA for some reason because of its structural stability etcetera, it always requires support from other molecules.

So, we have to understand if there was a self-sufficient molecule that should have been RNA. And there are other components such as ribosomes which acts as RNA catalysts in every organism starting from bacteria to human even today. And there are also a large number of RNA molecules that can be found in the modern world even in existing life forms.

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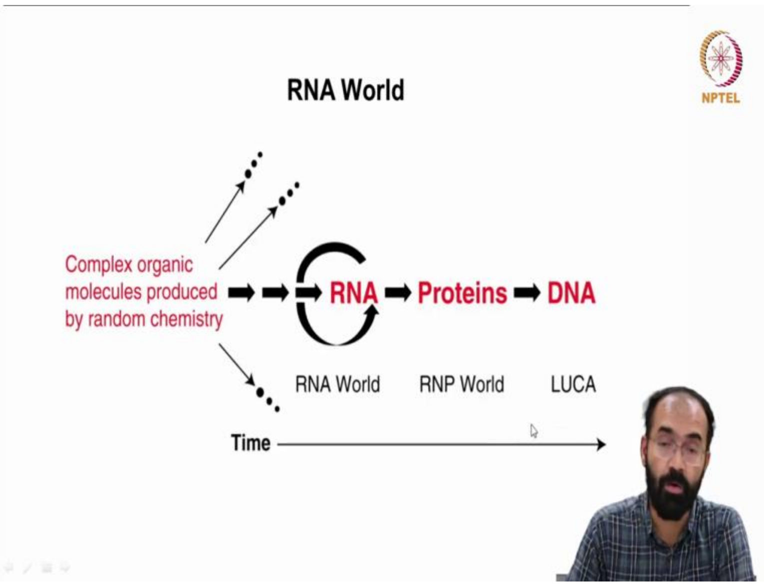

Now, the most important point which we are trying to discuss in the RNA world is that how can we assume that every molecule that are formed must contribute to the RNA or how can we assume the prebiotic world RNA molecule should have been present or it should have been preferred. The answer is no. It is not like that.

Because when you have these various complex organic molecules that are formed by random chemistry, they can evolve in any direction. Direction number 1, direction number 2, direction number 3, direction number 4. But at as the time passed, only one line is preferred.

Say for example; let us assume one family had 4 kids, kid number 1, kid number 2, kid number 3, kid number 4. Kid number 1, did need not marry, then there is less likely that will propagate further. And kid number 2 married had no kids, then second line also stop. Third kid had married and it had kids that person, that organism had kids that person had again kids and that line is continued.

And there is a reason behind it, because that particular molecule or organism is preferred, that organism have the fitness, that have the adaptation or the ability to gel with the environment. Because of all this reason one lineage is preferred and that lineage is what we are having RNA. RNA later was able to make a copy of itself and RNA was able to make later assist in the assembly of amino acid to give rise to proteins.

And this RNA and the protein collaborated together to give rise to DNA. And so that is how that lineage existed. That is why there are different theories where people like NASA, and other organizations will be searching for life on earth. There are various you know organization search for life on extraterrestrial you know planets etcetera.

But what we should understand the life formed on planet is by a chance factor also. It is not that inorganic material if there is a you know methane, ammonia, hydrogen and water vapor is there. Life can form. Of course, can form, but it need not always end up in form.

So, we should understand, it is not just a question of having the raw material for life. You can always end up having a life form. So, it is also a chance factor. So, from this RNA world you end up having an RNP world. RNA world had only RNA. Then, you have got RNA plus protein, we call this RNP, ribo nucleic acid plus protein that is RNP and that eventually give rise to DNA.

And then the LUCA. What is LUCA? Last Unique Common Ancestor and this is the beginning of life in the subsequent generations. Maybe I will stop here. And we will address you in the subsequent class.

Thank you.