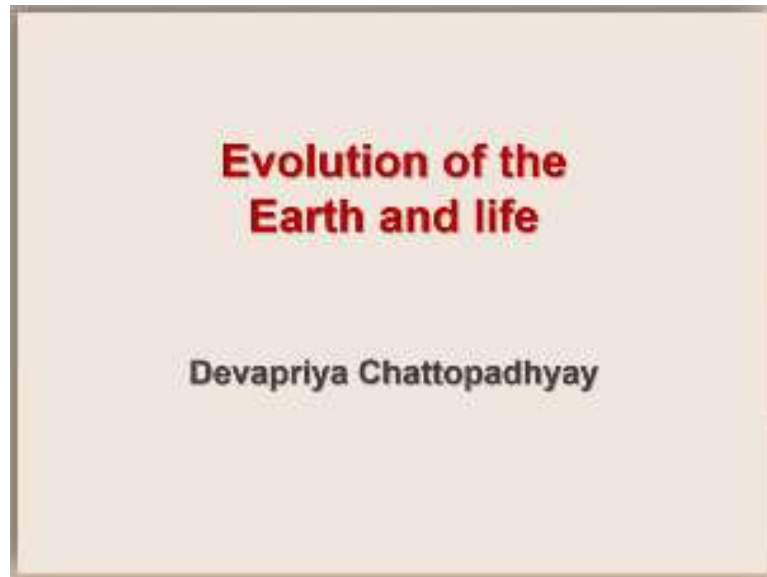


Evolution of The Earth and Life
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Origin of Life: Which Biomolecules Came First?

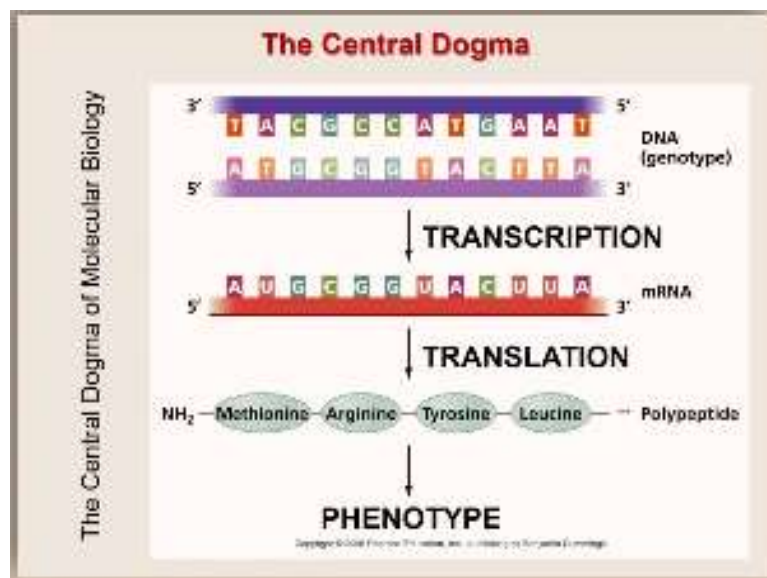
Welcome to the course of Evolution of the Earth and Life.

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Today, we are going to talk about some of the ideas for the development of first genetic material and cells.

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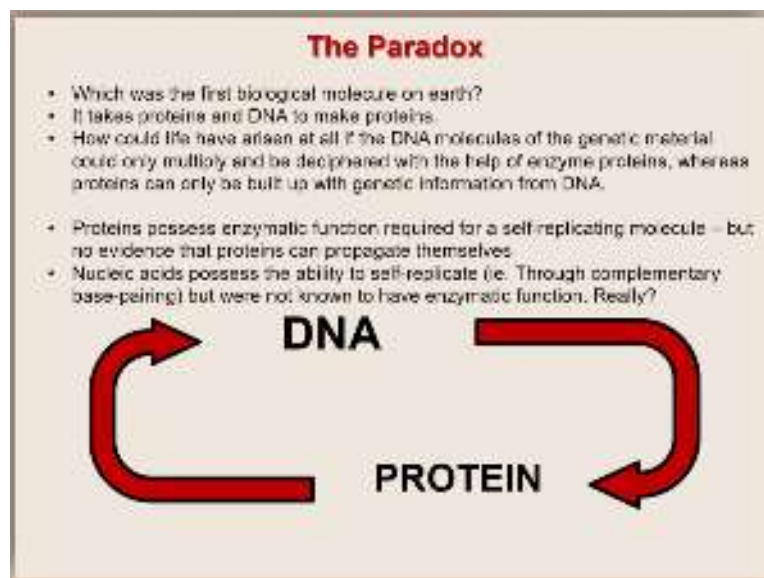
So, we know that one of the major things about life is all of the life are made up of cells. It can be a single cell, it can be multiple cells. And all the cells they have some genetic material and the common genetic material that we know about are DNA and RNA.

Now, there is something called a central dogma of biology of molecular biology. And that is that DNA or deoxyribonucleic acid converts to mRNA or RNA and this process is called a transcription. And then this RNA or messenger RNA basically goes through a change and forms things like proteins. And this is also called a translation and that is what impacts how the body is actually going to look like.

Now, with this idea it becomes very important to think about that what was the first molecule and how do you take it to form a cell. So, the idea of how life originated on the earth starts from this abiogenesis where a biological material can lead to the formation of organic molecules. But, only formation of organic molecules are not enough to form something what we know as life.

So, life has to be a self-replicating mechanism and therefore it is important to know how that assembly took place. But as I am saying that there is a major problem because what was the original organic molecule that started this process. And it is not a very simple question.

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So, again this is something of a paradox, the question is which was the first biological molecule on the Earth? Why is it important to know? It is important to know because now we know that it takes both proteins and DNA to make proteins. So, DNA stores information and proteins are basically important to create further development of information and to create DNA. So, it is a loop.

And the question is when the loop was not there at the beginning where do you start from do you start from DNA or do you start from protein. So, the question is the first biological

molecule on Earth was it a DNA or was it a protein. Because, that is what we know about the central dogma of molecular biology.

And it becomes even more complex because if we ask this question that how could life have arisen at all, if the DNA molecules of the genetic material could only multiply and be deciphered with the help of enzyme enzyme proteins. Whereas, proteins can also only be built up with genetic information from DNA.

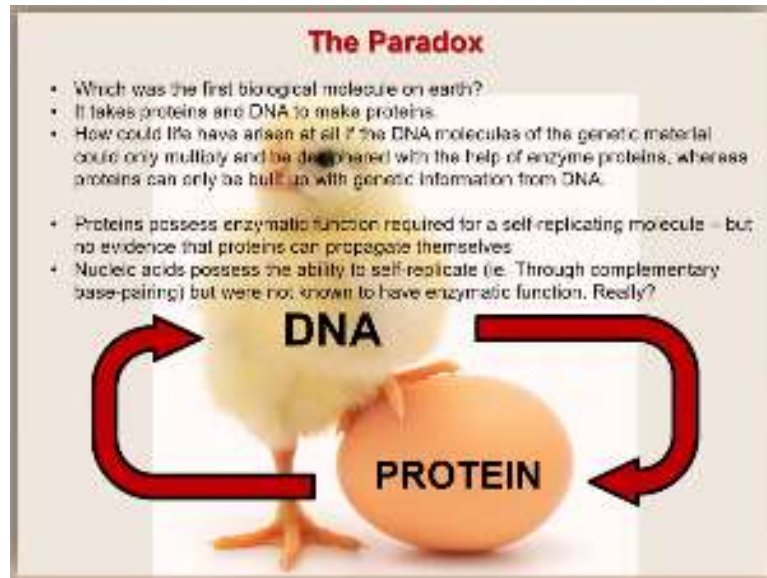
So, you need the proteins to develop and create these DNA molecules but, at the same time the proteins can only be formed with the genetic information from DNA. So, it is kind of tied together very very neatly and it is difficult to break it and predict which one was the first one. Now, can it be possible that one of them actually operate as or can function as the other one too.

So, that is the idea that the scientists started to explore, that is it possible that proteins which possess enzymatic functions that can propagate themselves and then they realize that yes protein possesses enzymatic functions which required for the self-replicating molecules.

But there is no evidence that proteins can propagate themselves so proteins cannot really pass on this kind of an information thing and also replicate themselves. So, therefore it is not really a viable idea that the proteins are working both as a protein as well as a something equivalent to a DNA of genetic material.

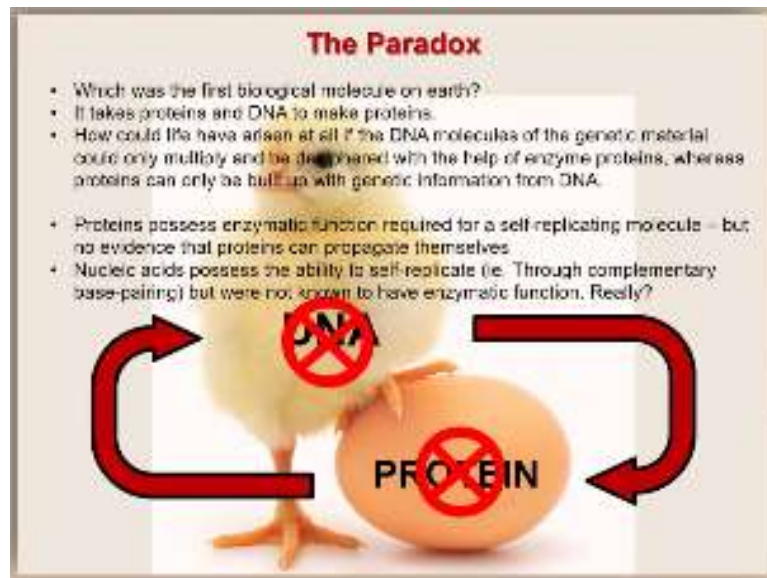
Now, the remaining thing is to look at the DNA. So, nucleic acids which includes both DNA as well as RNA they possess the ability to self-replicate. So, through complementary base pairing but, were not known to have enzymatic functions. So, can they work as proteins so at least 20 years ago it was not known that they can have both of these functions together and something changed around this time.

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So, again at this point it is a chicken and egg problem whether it was the DNA which came first or it was the protein which came first.

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And what eventually scientists realized that it is none of them. It is a third candidate and the third candidate is another nucleic acid what we know as RNA.

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RNA-World

One potential solution to the chicken-and-egg phenomenon was the idea that the original biomolecule was neither DNA or proteins but rather RNA.

Cech's discovery

in *Tetrahymena thermophila*

The RNA molecule is cut up

The ends of the RNA pieces are joined

The piece of RNA that was cut out is now free to give catalytic RNA

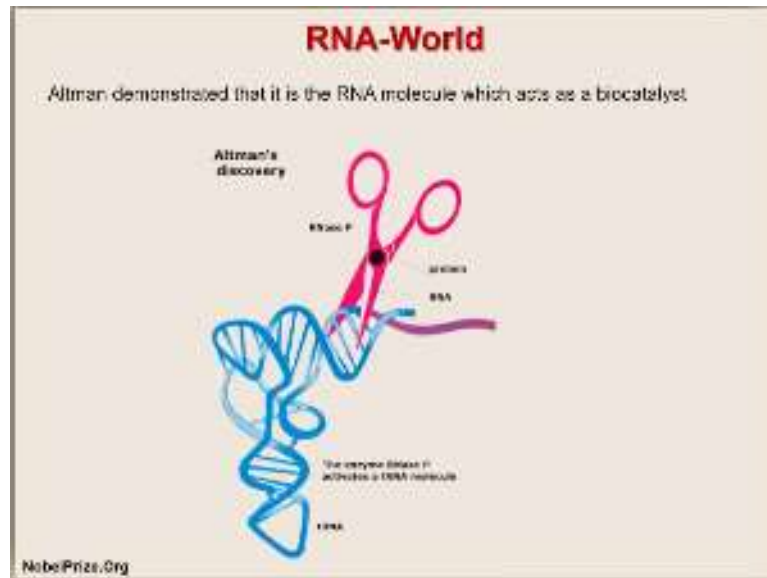
Tetrahymena is a unicellular eukaryote that lives in freshwater.

So, one potential solution to this chicken and egg problem was that the idea that the original biomolecule was neither DNA nor protein but rather RNA. So, RNA is basically ribonucleic acid it is not a double helix pattern it is a single strand.

Now the idea that actually started this was this discovery by Cech is that in some organisms in this case a particular organism called tetrahymena thermophila it is a species of a unicellular eukaryote that lives in fresh water.

There the RNA can be broken down like it basically cuts up. And the ends of the RNAs are joined together and often that piece of RNA is removed to give catalytic RNA. So, basically they are changing some of the reactions and sort of working more like an enzyme or protein. So, that is one of the times when the scientist demonstrated that RNA has this ability to work both as a nucleic acid a genetic material source of information but also as an enzyme or where you are basically I mean expressing some of these information.

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Similarly, another scientist Sydney Altman, he demonstrated that RNA molecules can act as a biocatalyst. So, there were two strands of evidence both of them showed that RNAs have this necessary quality to act both as a source of information and also to implement some of these information into formation of proteins. And that is why the idea was favoured that probably the first material the first organic molecule was neither DNA nor a protein it was something like an RNA.

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RNA can do it all!!

Ribonucleic acid (RNA) – the biomolecule which can do it all!!

Thomas Cech
University of Colorado

Sidney Altman
Yale University

DNA is copied into RNA, which is single-stranded and therefore folds into complex shapes.

Nobel Prize in Chemistry, 1989

NobelPrize.Org

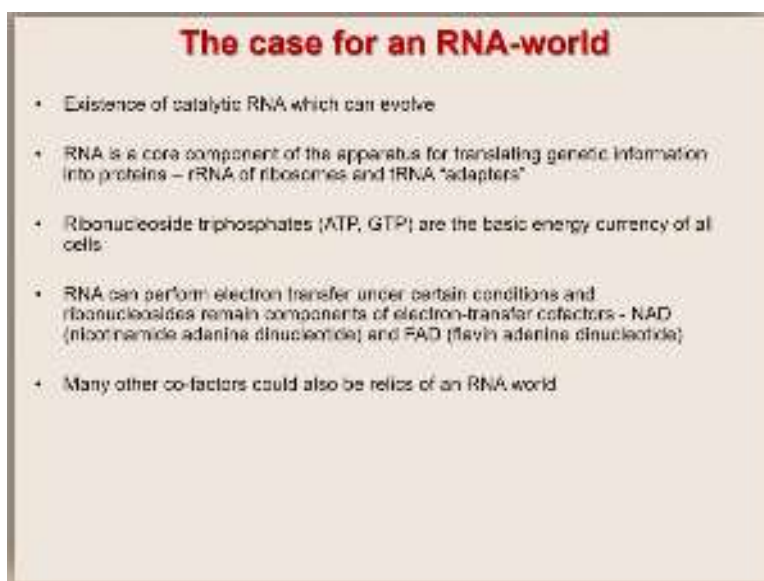
This slide highlights the discovery of RNA's catalytic capabilities. It features two black and white photographs of scientists: Thomas Cech on the left and Sidney Altman on the right. To the right of the photos is a diagram showing a blue double-stranded DNA molecule being transcribed into a single-stranded red RNA molecule, which is shown folding into a complex, three-dimensional shape. The text 'RNA can do it all!!' is at the top, and 'Ribonucleic acid (RNA) – the biomolecule which can do it all!!' is below it. A caption at the bottom right explains that DNA is copied into RNA, which is single-stranded and folds into complex shapes. The Nobel Prize in Chemistry, 1989, is mentioned at the bottom left, accompanied by a small gold medal icon. The source 'NobelPrize.Org' is noted on the right side of the diagram.

And because of this discovery that ribonucleic acid RNA this molecule which can do both of these functions both Thomas Cech and Sidney Altman got the Nobel Prize in Chemistry in 1989.

What they demonstrated that DNA is copied into RNA which is single stranded and therefore, it can fold into complex shapes and this folding finally leads to various kind of functions.

So, it has much more flexibility in terms of performing a function. So, this was quite a new thing to recognize and the initial idea that the world or world of organic molecules of life started with RNA.

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And that is what we meant by the RNA world. That the first formed organic molecules which led to the development of self-replicating system which we call life started with this RNA. There are various evidences which also support this. The first one was this existence of catalytic RNA which can evolve and change and therefore, it can solve some of these initial paradox.

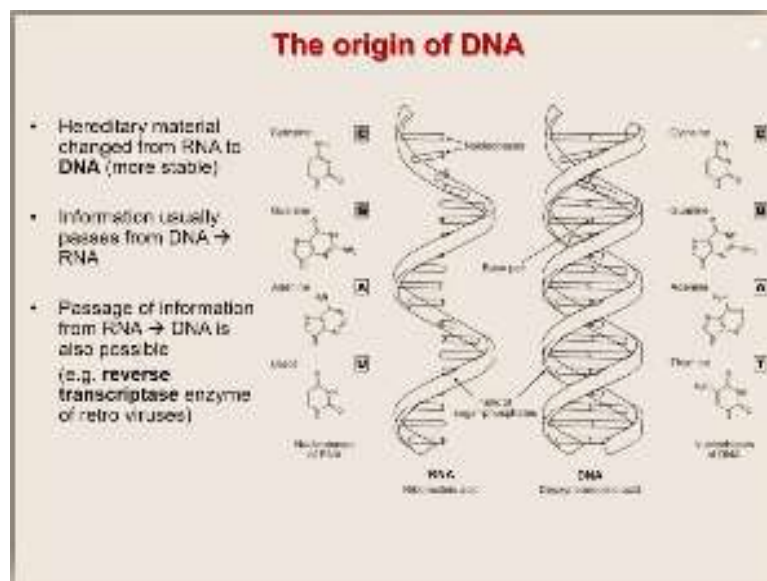
RNA is a core component of the apparatus of translating genetic information into proteins rRNA of ribosome and tRNA they can work as adapters. So, these are all evidences that they are one of the core things in terms of changing genetic or transferring genetic information into proteins. ATP or GTP which are which we know as basic currencies of the cell they are everywhere and we know them.

The final one is RNA can perform electron transfer under certain conditions. And some of these ribonucleosides remain components of these electron transfer co-factors. And these co-factors could also have and there are many such co-factors and these co-factors could also be

relics of an RNA world. So, even in today's world there are organisms which show some of these changes and some of these performances showing these multi-functional RNA.

And also that some of the things show how initially it could have worked. But then we also know that majority of the organisms that we find today they are not RNA based only a few virus which are primarily RNA based but then majority of the organisms we see around us are primarily DNA based. Question is why is that so? Why would you have RNA starting the game but then changing it to a more DNA dominated system?

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So, one factor that we understand now is DNA is more stable. And therefore, hereditary material changed from RNA to DNA because of the stability. So, even if the process started with RNA probably there was competition between these organic molecules too. And whichever is more stable will eventually have the higher dominance or higher abundance and therefore, it will be favoured by the natural selection.

We know that DNA eventually transforms to RNA which we called transcription and they then codes to protein. So, it is not DNA can still be the starting point and involvement of RNA can be there just like what we see around us today. But the starting point once the RNA started this mechanism it can eventually convert to a system where primarily DNA dominates.

And once the more stable form is selected for then information usually passes from DNA to RNA. And passage of information from RNA to DNA is also possible. It is also called a Reverse Transcriptase Enzyme in some of the retrovirus but it is not so common.

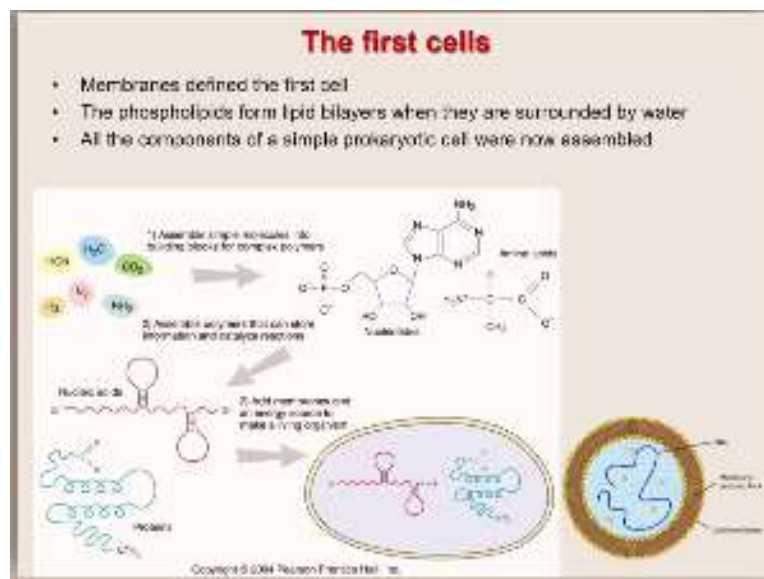
So, therefore the understanding is initial development was from the RNA where it was working as both information carrier of the genetic material but also implementer in some of these development of enzyme like mechanisms.

But, eventually development of DNA led to the system where they were basically selected for because of their stability. Now, these we are talking about only genetic material we still have not explained why there should be a cell?

And there the idea of a development of a cell comes with a membrane. So, as I mentioned that these organic molecules were probably also competing in the sense that whichever organic molecule was better selected they would be selected for.

And this better means in terms of stability, in terms of making them longer probably survive longer things like that. So, you can imagine a scenario where RNA develops a protein which probably stays longer or more stable. But, there is no stopping point for other RNAs to utilize that protein unless there is a barrier. And that barrier comes from a cell membrane.

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So, the idea is that membranes defined the first cell. And the phospholipid form the lipid bilayer when they are surrounded by water when they are surrounded by water one layer of these phospholipid you know the lipid bilayer is repelling water the other one is basically can be in touch of water. So, basically you have a barrier outside of it is repelling water and inside of it can hold water it is like a bubble and that is the first cell.

And these proteins if there is a beneficial protein that RNA has created. Now, it can be part of this membrane encased area and other RNA outside cannot utilize it. And therefore this

membrane encased protein along with the genetic material will develop more and they will have more abundance and eventually will push will be selected for and this is how the evolution is kind of happening at a cellular scale at the primitive Earth.

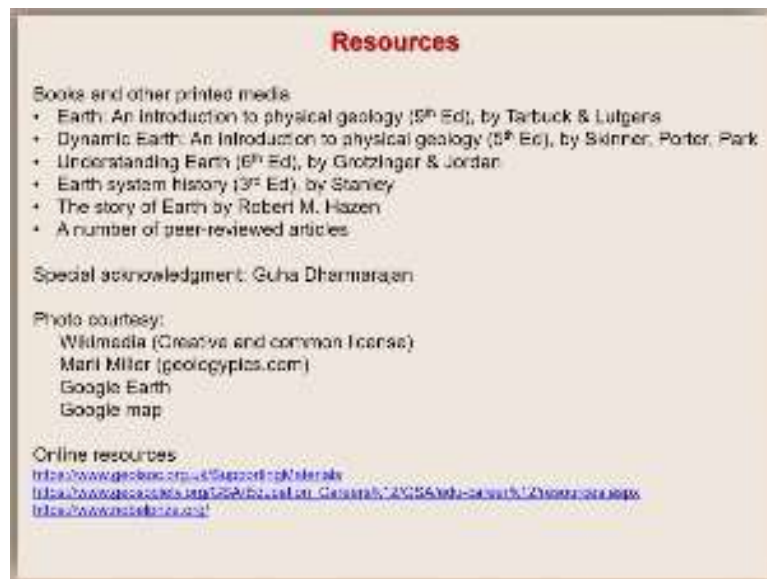
Now, how do we know all of these things? Well part of the information comes from our understanding of molecular biology. Some of it comes from observing some of the very old primitive organisms and part of it comes from theoretical modelling about how each of these molecules behave in a certain condition.

Therefore, there are some uncertainties too so at the best at this point these are some of the more well supported ideas but their ideas nonetheless we do not really have a direct evidence which showed how the first genetic materials behaved? how they were selected for what were the natural selective agents, which were the primary filters because of which certain groups were selected for and others did not. So, there are uncertainties there are some of the things are not very clear but this is based on what evidences we have from these multiple branches that I just explained.

Now, once you have this formation of the first cell what would be the nature of this cell. In today's world we know that there are primarily two major type of cell one is prokaryotic cell the other one is eukaryotic cell. And the first form cells we understand that they resemble a simple prokaryotic cells. Eukaryotic cells contained more advanced organelles which are missing in prokaryotic cells.

And just the mechanism that I explained it is very hard to explain how the organelles would have formed by this process at the very beginning. And therefore, the idea is that the first formed cells must have been prokaryotic in nature they were small they were simple and they primarily had these two components one is the nucleic acid and the other one is protein and probably all of them are encased by the cell membrane.

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So, in today's class we learned what are some of the major paradox in terms of development of first organic molecule connected to life. First biomolecule as we have seen between DNA and protein both of them have this dependence on each other.

And therefore it is hard to explain how the appearance of one at the beginning could have happened. Through the discoveries of Jack and Altman we understood that it is the RNA which has a much more flexible nature and which can operate both as an information source and also as a catalyst and therefore, it is now believed that the initial biomolecules was probably RNA.

And therefore, the world around at that point of time was RNA dominated and that is what RNA world is. But, with time because of the higher stability of DNA, DNA got selected for and therefore, today we see organisms which are primarily DNA dominated. This DNA along with proteins or the new I mean genetic material in the form of RNA along with proteins where at the beginning everywhere and there was no partition.

But, through natural selection probably it was pushed to form this cell membrane and the ones with cell membrane were selected for because they could keep the proteins inside and stop the other RNA to take advantage of those proteins or utilizing those proteins.

And that is probably one of the more strong selective pushes for the development of the cell membrane. And once it is encased in this lipid bilayer cell membrane this is the formation of the preliminary cell. The preliminary cell was very simple and it is by nature was a

prokaryotic cell. This is some of the these are some of the resources that I used for this lecture.

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And here is a question for you to think about. Thank you.