Bioengineering: An Interface with Biology and Medicine
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Lecture – 16
Genetics-I

Welcome to MOOC-NPTEL on bioengineering, an interface with biology and medicine.

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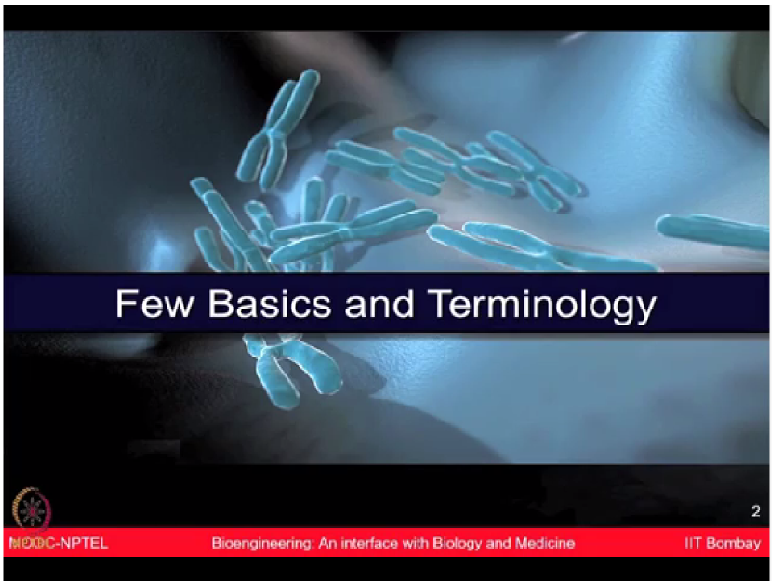

Let us kind of first start with some basics, some terminology.

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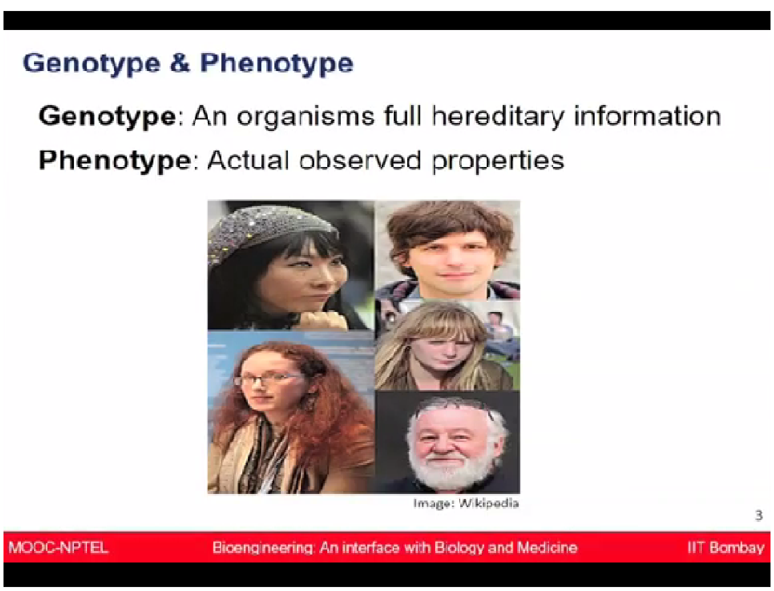

When we say genotype, it means all the genetic contents of a given individual, all the genetic information and phenotype, how actual individual looks like, their morphology, their phenotype characteristics.

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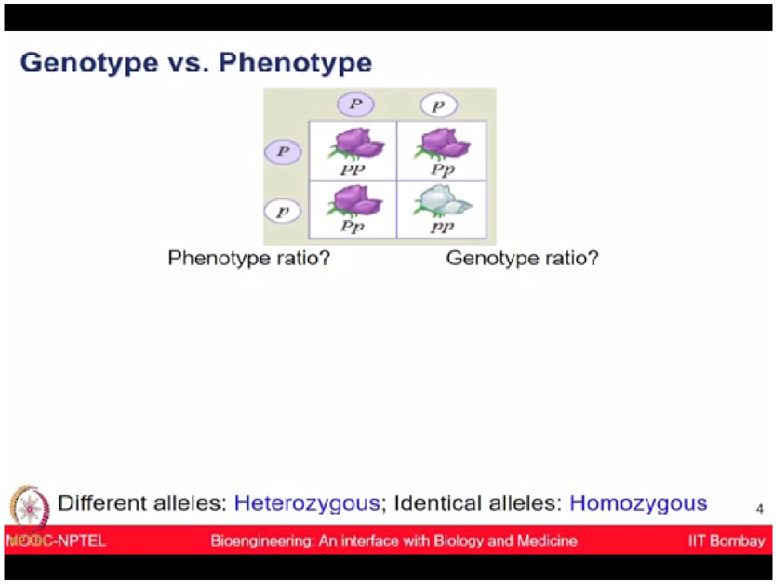

Now let us kind of discuss this part in context of Mendel's experiment. So Gregor Mendel, he was the scientist who did genetics experiment on the pea plant, on the garden pea and while he was looking at pea plants, he observed there are many contrasting characteristics present in the pea plant and he thought that those are some sort of characters which transmit from one to next generation and for the same, now we say those heritable factors or gene.

So for the same factors, there might be different alleles which are present there. So one gene might be having different allele forms. So let us say this is a plant, a flower which is shown here, is the purple coloured flower. Now if a gene course for it, but she is having dominant entry. So let us say P. Now a resistive form of that will be a p, right. So first I want to make you familiar with the terminology. Dominant, recessive, homozygous, heterozygous. So let us kind of do one Punnett square cross and try to understand these terminologies.

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By the way in genetics, it will be good idea that you can open your own notebooks and as we go along, there will be certain problems for you to also try out. It looks very easy but you know, when you do it, you will be more confident. So both from the sperm and the ova from the male and female parts, let us say now you have these gametes. So it is very straightforward but let me kind of now ask you some terminologies here.

So let us ask how many homozygous recessive are here, homozygous recessive? Somebody rightly mentioned 1. So a p is the recessive characteristic, right. Dominant is the P. So many we have homozygous dominant here? 1, PP. How many are heterozygotes? Which are 50%, right, 50% are heterozygous. Now what will be the genotype here? Genotype means genetic contents of this.

"Professor - student conversation starts" 1:2:1. Everybody agrees to him. And what are its phenotype? 3:1. Why 3. 1 character is dominant. Because 1 is dominant, right. P, P is dominant. **"Professor - student conversation ends."** So I am sure now you already know yourself all the terminologies.

So in this case here, the genotypic ratio will become 1:2:1 and phenotypic ratio, all those which are dominant, which is purple in colour, is the phenotypic ratio as compared to the white which is recessive colour, right. So this is how I think is a good idea for us to learn the terminologies and this is what, you know, Mendel was looking at it.

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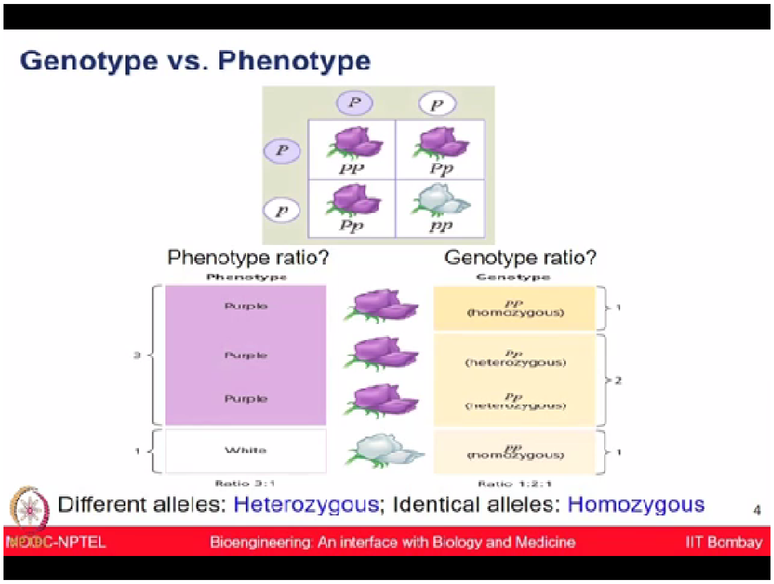

But before I come to Mendel's experiment, I thought to make you familiar with the properties and these terminologies. So in this case, we got 3 purple and 1 white, ratio was 3:1 which is phenotypic ratio and we have 1:2:1 which is the genotypic ratio. Again it kind of, you know, go back and think about at the cell level. We have already talked about it. And from the individuals, we have billions of cells. Each cell contains those nucleus but in those, we have the DNA contents, chromosomes.

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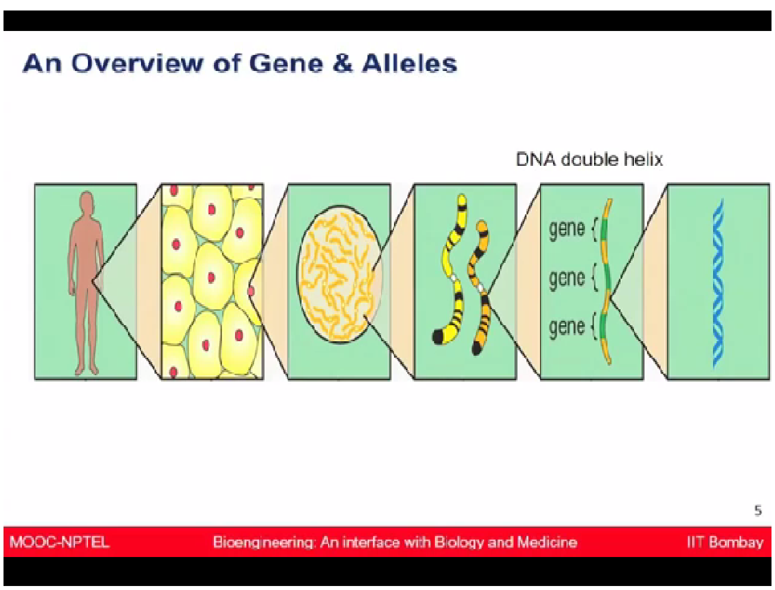

From those, we have the genes.

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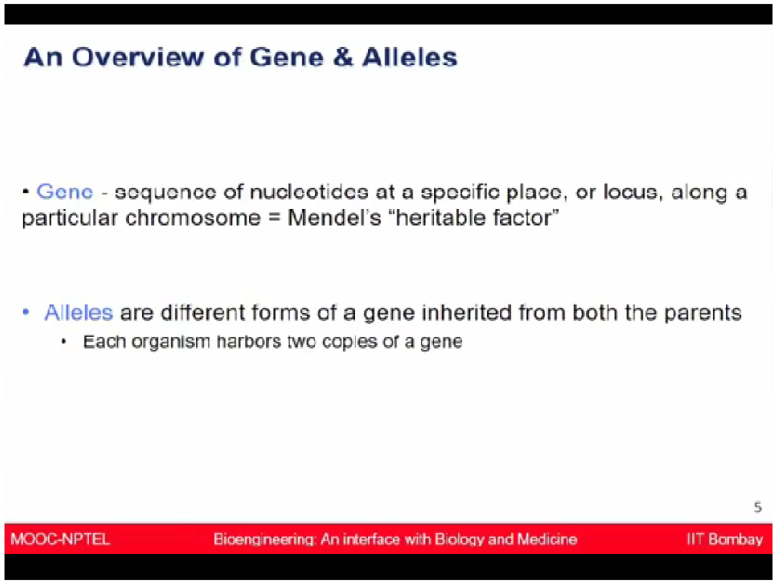

What Mendel was thinking that these genes what we think now is the sequence of nucleotides at a specific place which contains some of the heritable factors, which contains some information which could inherit from one to next generation. Later on people realized that this could be termed as a gene.

So now what we think is gene is what Mendel already thought that time as the heritable factors which can transmit from one to the next generation. And there could be different alleles of a given gene which are having one copy from each parents. So in this case, let us say we say the P and p, right. Those are for the same characteristic, purple or the white. So these are the 2 alleles of a given gene which are inherited from the parents.

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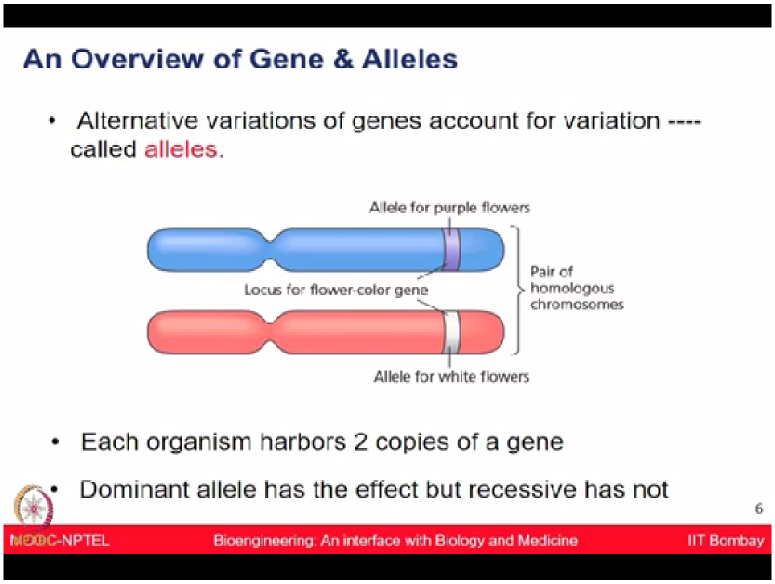

So as you can see here the alternative variations of these genes are known as alleles for purple flower on this chromosome or the white flower here, these are the pair of homologous chromosomes. So each organism harbours 2 copies of a given gene. A dominant allele has the effect but recessive does not show an effect and that is the dominated, known as dominant characteristic which is going to show its properties.

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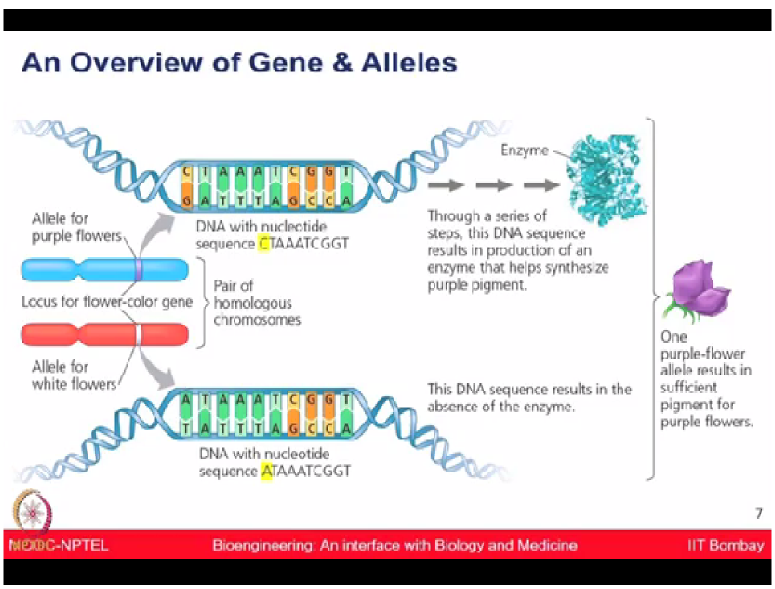

Now in this context of purple versus white colour, if you look at this sequence of the gene which course for the purple colour versus the sequence of this gene which is for the white colour, it is exactly same, just 1 base pair change from C to A. That is the only change here. But because of that one change, so when we talk about the sequences, we are talking about only, you know, some letters of ATGCs, they have to be in a defined manner.

And sometime, you know, just by that 1 change of 1 base, can result into lot of mis-regression, lot of deformities and many times in the cancer patients, people find out lot of mutations happens. Sometimes some thing gets shift, some base pair shifts and therefore the entire protein coding sequences can be changed. So in this case, it is very interesting example here.

You can see that, you know, because of 1 base pair change, this is going to make enzyme which is required to give the purple colour whereas this one has deficiency. It cannot make the enzyme for purple colour. It only shows the white pattern. So same gene sequence just with 1 base pair change, this is why the alleles of that given gene and it is going to show you the 2 different properties of purple versus white colour.

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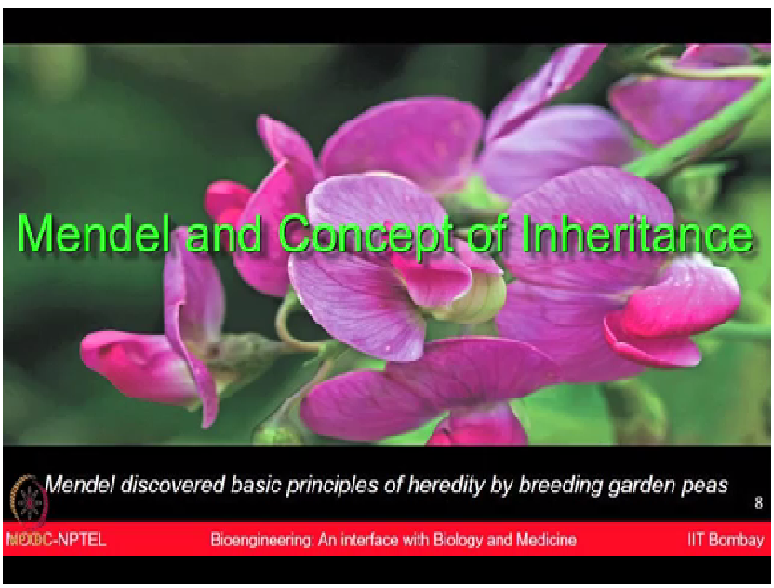

So now let us come and talk about Mendel, what he did and his experiment on the inheritance concept.

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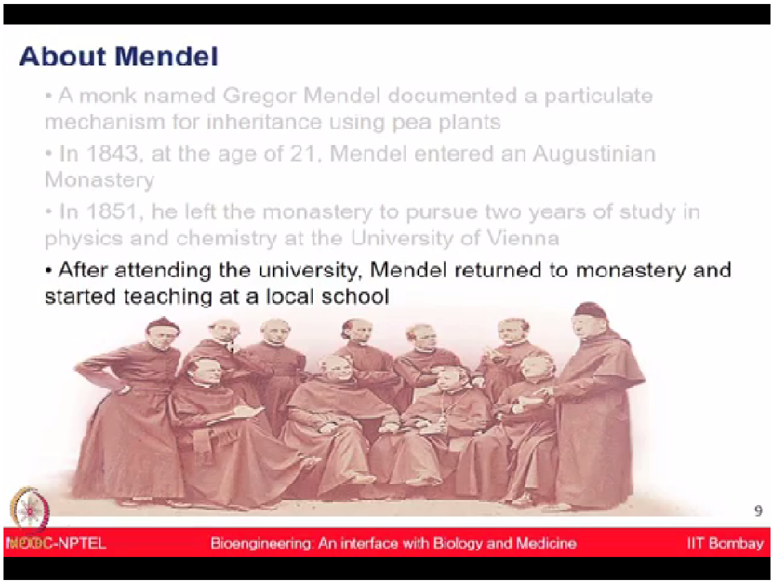

So Mendel was doing the experiments not for a job, not for the sake of the profession. He was doing these things out of his interest and he was actually a monk who was, you know, studying the pea plant by growing them in his own backyard. And at the age of 21, he joined this Augustinian Monastery but he did not like that too much and then he felt that he should do more advanced study in physicals and chemistry.

So in fact, he was much more interested to study physics, chemistry, maths, not biology. Sometime, you know, you may not like a subject but you might be able to still make an original contribution to the field that you will be remembered for that contribution. So after he returned back from the university, then he again joined that Monastery and started teaching in a local school.

And he was just growing the garden peas in the garden and then he was making very close observation, very meticulous notes of what is happening from one general to the next generation. So each time when he do a cross, he will count that, you know, what is the properties he is looking at, how many seeds he is growing, how many pea plants made out of it, what are their each characteristics.

And because he was doing it so meticulously, he was able to come with certain mathematical numbers and he was very astonished himself that there are many properties which are showing similar kind of, you know, patterns. So then he was able to formulate certain rules and certain laws which became Mendelian laws of genetics.

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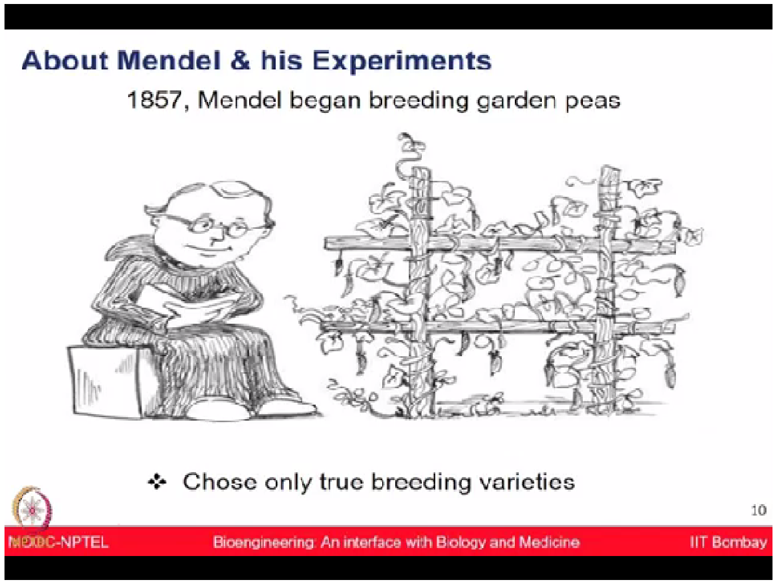

So he chose only true breeding varieties. Now it does not make any sense, you know, what is the true breeding variety and why he need to chose the true breeding variety. So Mendel chose only true breeding varieties, in the statement for his experiments which he did on the pea plants. What could be true breeding means? **"Professor - student conversation starts"** It does not contain (()) (10:01).

Somebody tried saying that no mutation. Any better explanation. Homozygous. Homozygous. Homozygous. **"Professor - student conversation ends."** So you are ensuring that if it was purple colour coming, purple colour can come out of either, you know, it can be Pp or PP. So you are ensuring that they are going to contain the same characteristics from one to next generation.

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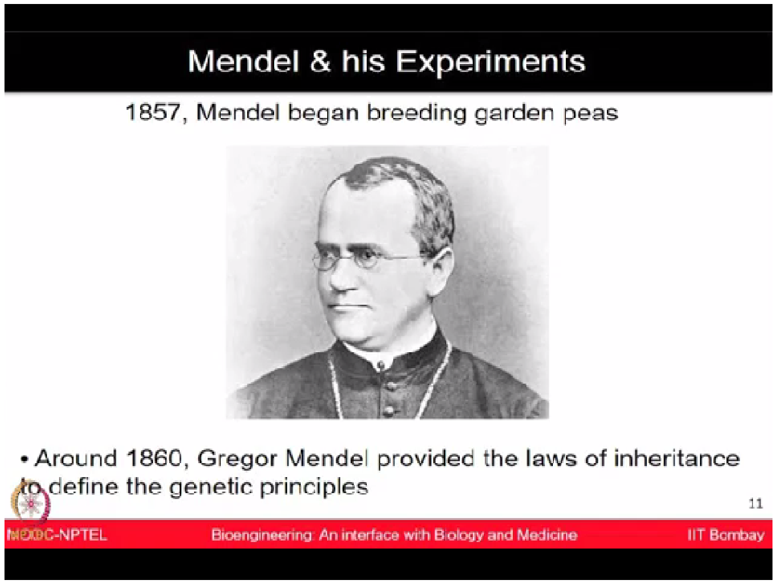

So therefore, he was choosing those characteristics and those plants, the true breeding. Till 1860, he was able to come up with the law of inheritance to define the genetic principles. So what are these heritable traits.

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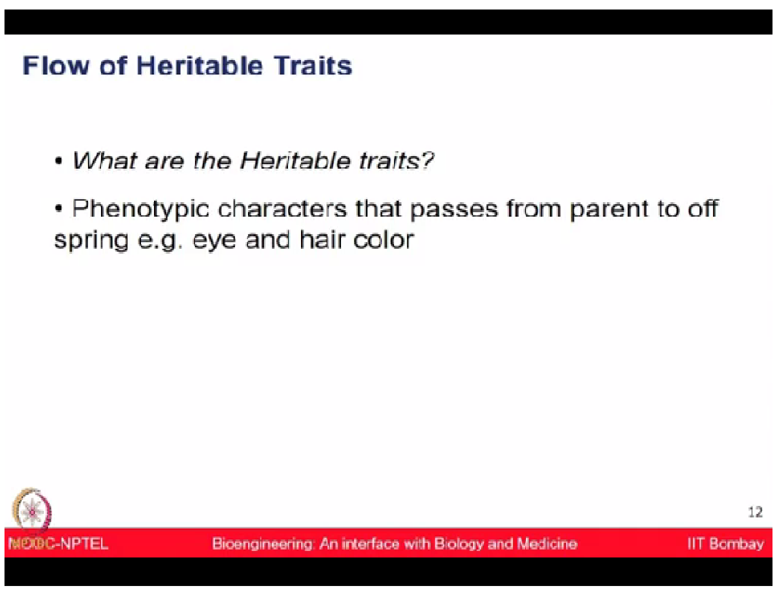

These heritable traits are many characteristics like some type of eye colours, sometimes hair, different type of hair patterns are there, different type of eye colours. Yes? **"Professor - student conversation starts"** What are exactly due to true breeding varieties. So ideally if you are crossing a purple coloured one with purple coloured one and you are still getting the progeny's purple coloured.

You are ensuring that you are doing one to next generation those crosses and still you are getting purple coloured, you are not segregating, it means those are true breeding. Does that answer to your question as well? **"Professor - student conversation ends."** So what are the genetic principles which accounts for the transmission of these traits?

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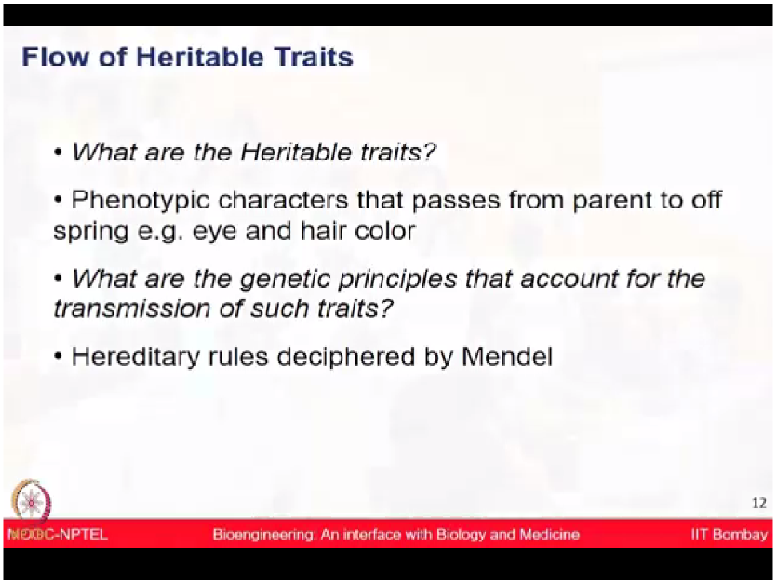

Well, many of the rules which were deciphered by Mendel as hereditary rules.

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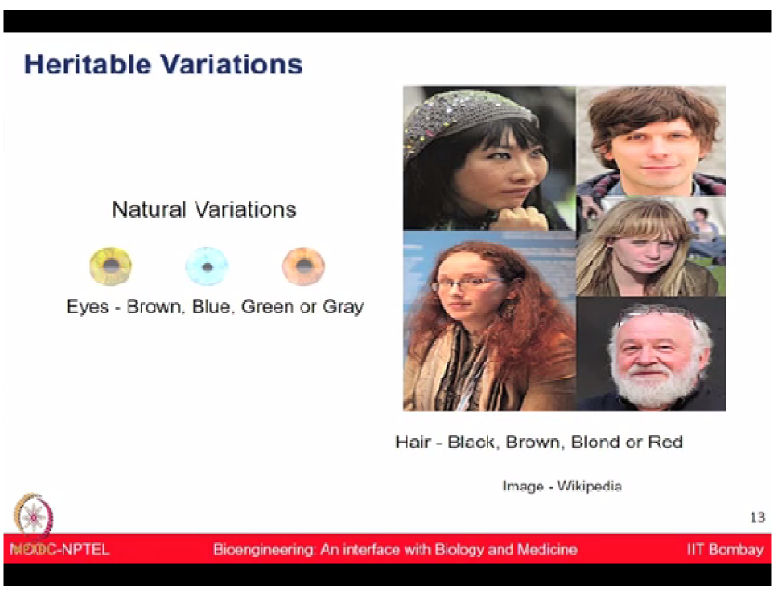

So I am sure you can, you know, observe different patterns of hair, different colours, different type of eye colours. All of these are natural variations which are there and they still keep, you know, passing from one to next generations and we do see that these are heritable characters, heritable variations.

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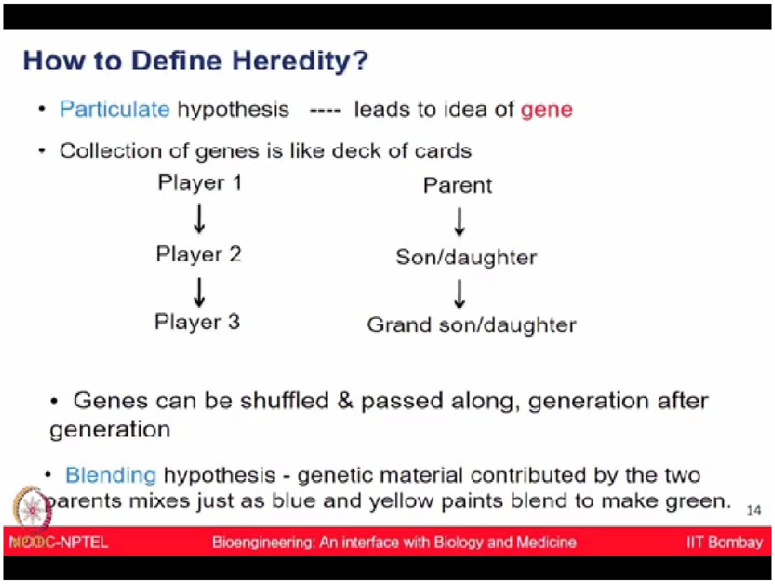

So how to define heredity? People have tried to come up with different hypothesis that how to define heredity. One hypothesis is known as particulate hypothesis which is essentially you are playing the cards, you are shuffling the cards and while shuffling the cards from, you know, while distribution, it is always random, right. You have no idea that how these cards are going to be distributed to different players, from one to second to third player.

Genes are like that, from one to second to the third generation, probably you are shuffling the cards and that is known as particulate hypothesis which became more popular. So here, you know, genes can be shuffled and passed around from the one to next generation. Another hypothesis was blending hypothesis.

It means from the 2 parents, genes are coming and they are blended like paint. So like paint colour and they are going to give rise to a different colour like from the blue and the yellow paints if they get blend, they will make the green colour. So this hypothesis is not as popular but these are again some hypothesis to explain how to define heredity.

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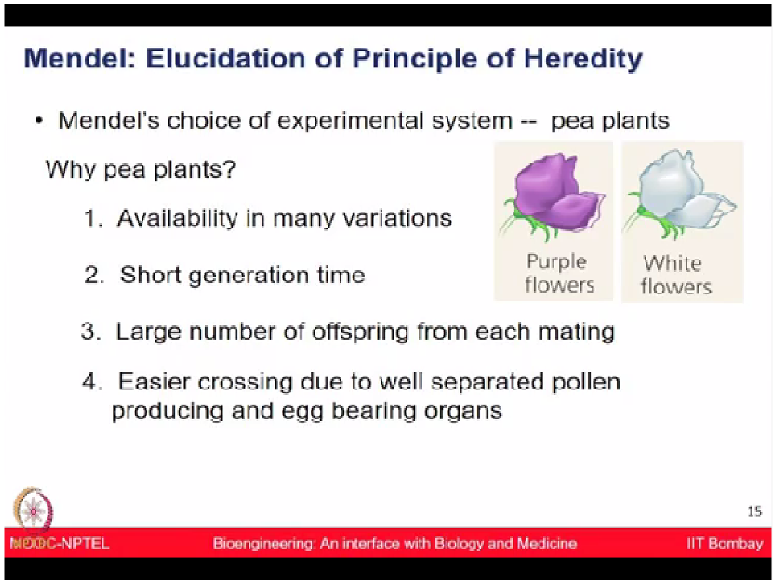

So Mendel chose peal plant. Of course, because of availability of pea in the garden what he was, you know, where he was in that monastery. He felt that, you know, these are the experimental system which can be done very fast, very short generation timing and it has many characteristics, at least 7 he observed which are derived looking from the, you know, same gene having different allelic forms.

Then, you know, you can generate large number of seeds and you can make those countings in any of the biological experiment, statistics become very important because you have to ensure that you have enough N to prove or disapprove your hypothesis and that it was again good system here.

Because if you think about doing experiments with the animal system, if you would have chosen mouse or, you know, any other animal model, then it may not have been so easy for him to grow that many number of model system to do statistics and you cannot grow them so fast either. He was also having full control about doing the self pollination or the cross pollination of the pea plants for the breeding purpose. So as a result, all of these things were quite helpful for Mendel to think about doing genetic experiments.

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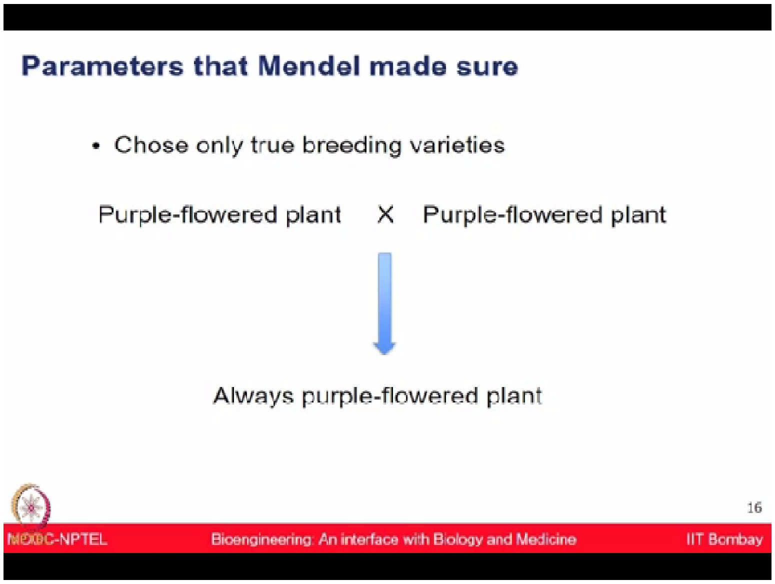

As he talk, he chose only true breeding varieties. He was crossing them to multiple generations only selecting those which were showing the same pattern.

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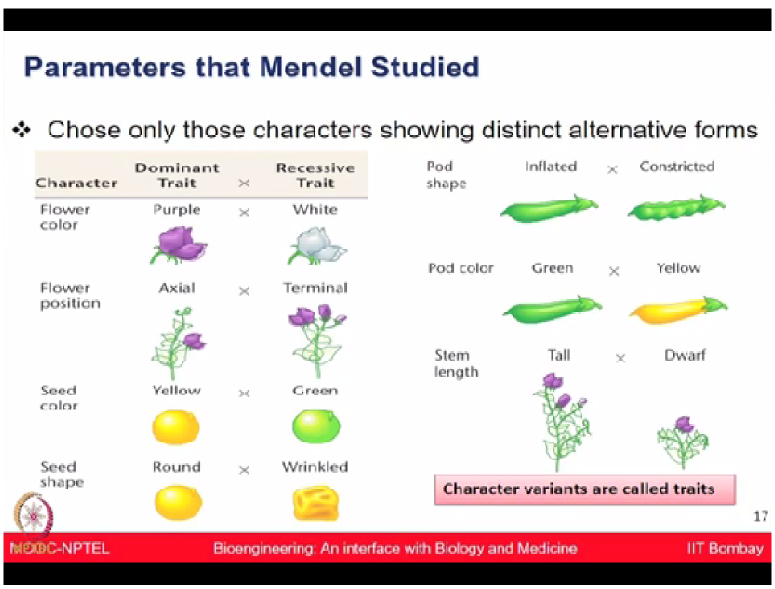

And he selected only one characteristics at a time for his studies which are having distinctive alternative forms. So for example, purple versus white colour of the flower that is one characteristic he has tried to study. We already talked about some part of that. Flower positions, whether it is axial or terminal. Seed colour, a lit yellow colour or green coloured seed. Seed shape, it can be round or wrinkle shaped.

Pod shape, it can be inflated or constricted. Pod colour, green or yellow or stem length, tall or dwarf. So many people say that Mendel was actually very lucky because, you know, in the same system, he was able to get for the same gene, different allelic forms and many properties which usually not present in many other plants or many other animal systems. So he was pretty lucky to, you know, randomly selected pea plant as an experimental system and he did all the experiment which became very reputable and you know, now we have very strong foundation for those laws. So these characteristics variants are called traits.

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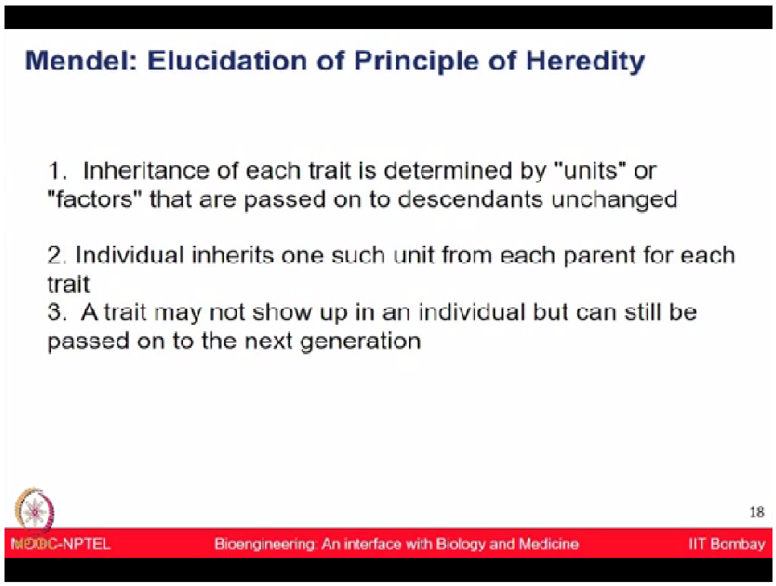

So to elucidate principles of heredity, inheritance of each trait is determined by the units or the factors which we now say and know as a gene which are passed on to descendants which remain unchanged. Individuals inherit one such unit from each parents and then they transmit from the one to the next generation.

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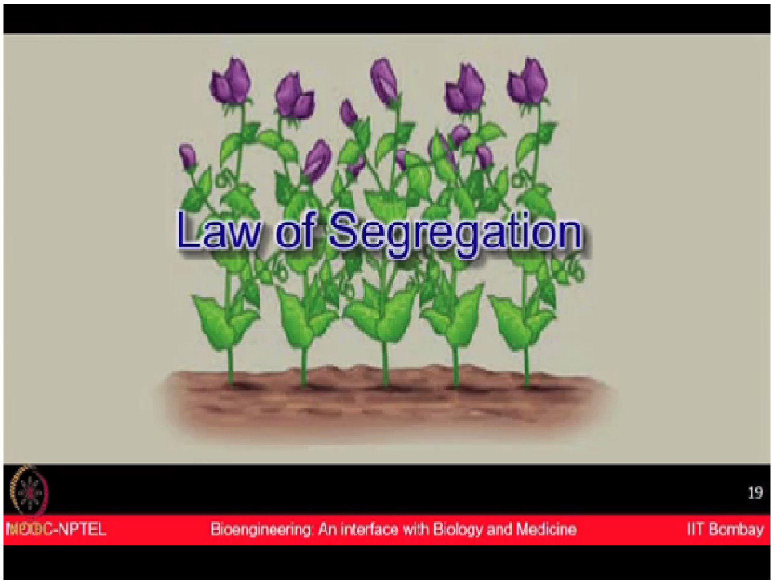

So now back to the Mendel's first law which is law of segregation.

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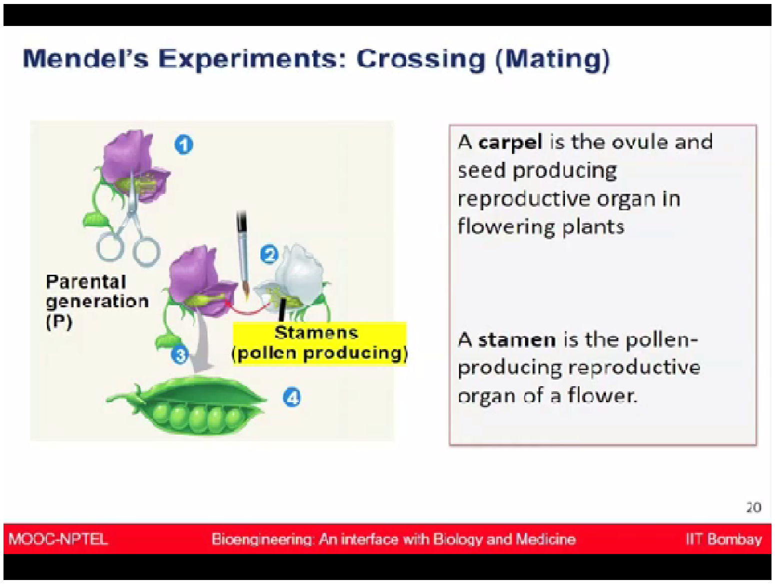

So just to, you know, kind of brief you this is the stamen or the male part of this flower, pollen producing organ.

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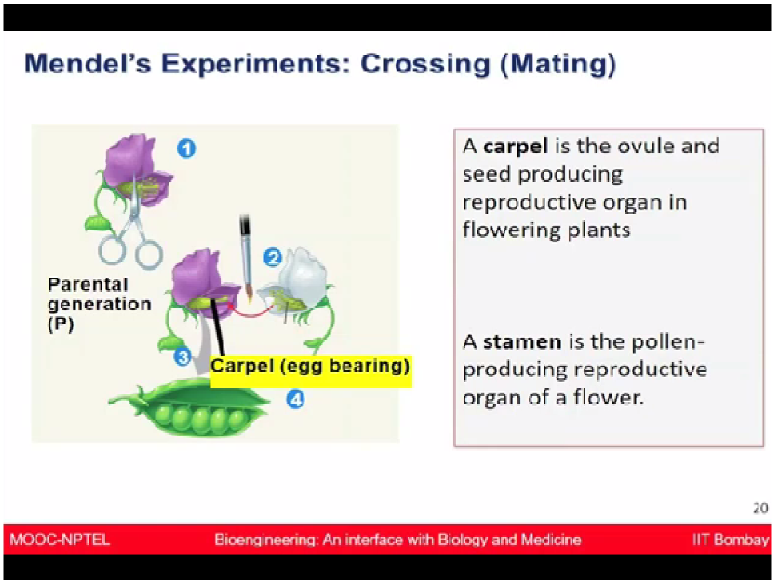

This is the carpel or the female part which is egg bearing part of the flower. So for doing this experiment, he was ensuring that, you know, for doing the crosses, it has to be very well under the control condition just so that it is no cross pollination from one to other different flower and different characteristics. Whatever you want to study, only those pollination you wanted to do that.

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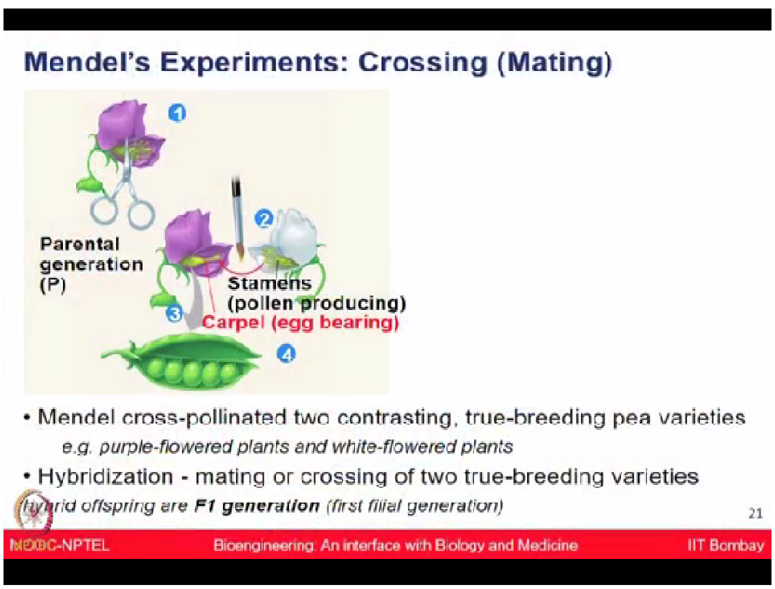

So he cross-pollinated only 2 contrasting and true breeding pea varieties. So, you know, purple versus white for example or long versus short or looking at the yellow versus green, seed shape, etc. **"Professor - student conversation starts"** Purple and white and purple is dominating. **"Professor - student conversation ends."** So his doubt and question is that, you know, what is, is that dominant or recessive we are looking at over there or not.

So all you want to ensure here is you are only studding the homozygous kind of characteristics because, you know, PP or Pp, both are possibility for purple colour. But can you choose only PP and keep growing them further for your experiment because then only, you know, that you are only talking about PP versus pp. So then you have the good experiment to be done. **“Professor - student conversation starts”** Plants were true (()) (17:40) how do you make sure that the peas were true. Right. **“Professor - student conversation ends.”**

So lot of interesting ideas of course, how, you know, he was ensuring these things as I showed you, he was doing these pollination experiments in a very controlled condition so that there is no cross pollination happens from the neighbouring plants which can influence these characteristics. So if he is only growing the purple coloured one and then he is growing white coloured ones separately, then only he will do the cross of those 2 to ensure that only the true breeding varieties, cross can happen.

So hybridization is the phenomenon which is mating or the crossing of 2 true breeding varieties and which is known as the F1 generation or the filial generation. Just get familiar to the terminology, P means parental generations, parents, F1 is the filial or their progenies. So in the first, when he did the cross, the first generation looked like all purple coloured. So now let us talk about his crossing experiment where he crossed purple versus white 2 of the contrasting traits.

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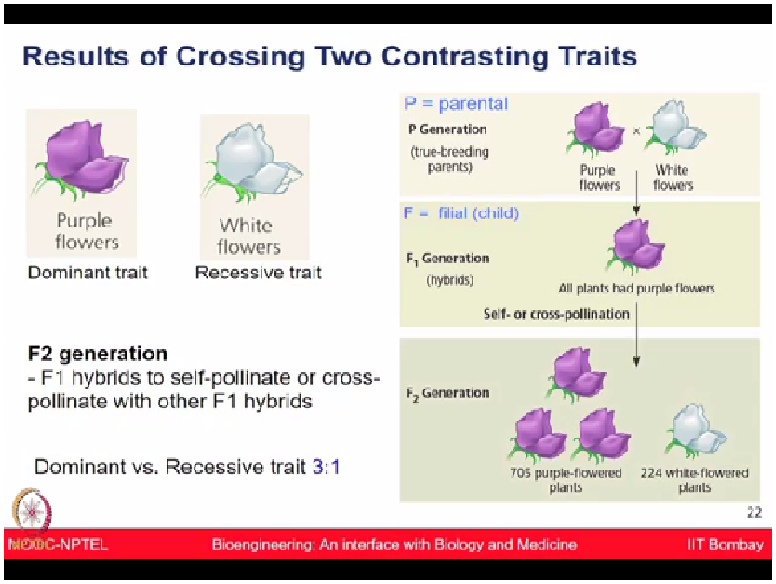

So this is dominant colour trait, the purple coloured versus white as a recessive trait. Now P generation or the parent generations, these are true breeding parents, purple or white. F1, all of them showed purple pattern and when he again crossed them further, it distributed into the purple versus white, 3:1 kind of ratio. And he did this experiment on many other characteristics, not only the purple and white.

Among all of the contrasting characteristics of different pea properties which he was studying and therefore, he was able to come up with some conclusion that looks like, you know, they distribute in a very specific ratio. It is not very random phenomenon. So the F2 generation is when he is doing the F1 hybrid self-pollinating them and then they are resulting into large number of these seeds which he was growing further and then able to come up with these numbers.

So again what you can see the large number of flowers which he was counting. So 700 purple flower with 220 or so of white flower. So this is what then he felt that these are the allelic forms of a given gene or factors which are showing the same property but only one contrasting differences found.

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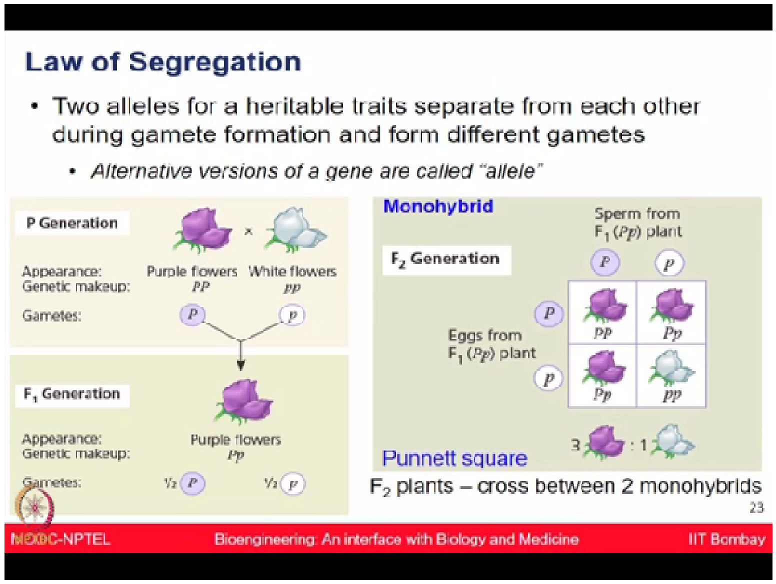

Till now the cross will look like, so we already briefly talked about the Punnett square. So this was the cross, the purple flower versus white flower. These are the gametes. P and p (()) (20:18). In the F1 generation, you will have this hybrid Pp. From the male and the female parts, the egg and the sperm, you are doing this cross and that results into this ratio of 3:1 of the phenotype.

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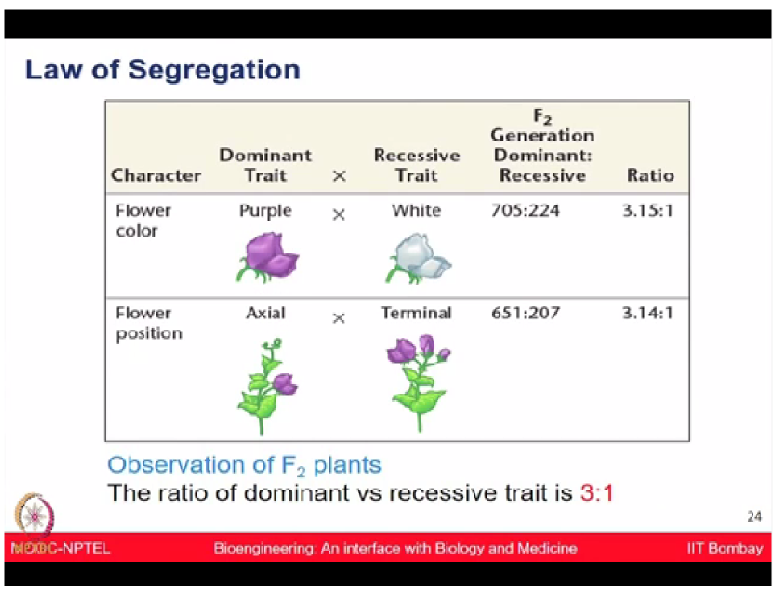

As I mentioned, he did this on many properties, not only the purple and white, also on the flower position. And the ratio was not exactly 3:1, it was, you know, 3.15 or 3.14:1 but he was finding similar kind of patterns, similar numbers in many properties. So the ratio of dominant versus recessive trait was 3:1. Now question is if we have 1 purple flower, how are we going to determine the genotype? Whether the purple flower is PP or Pp, right? If we have purple flower, it can be, 2 properties possible.

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So let us imagine 2 situation.

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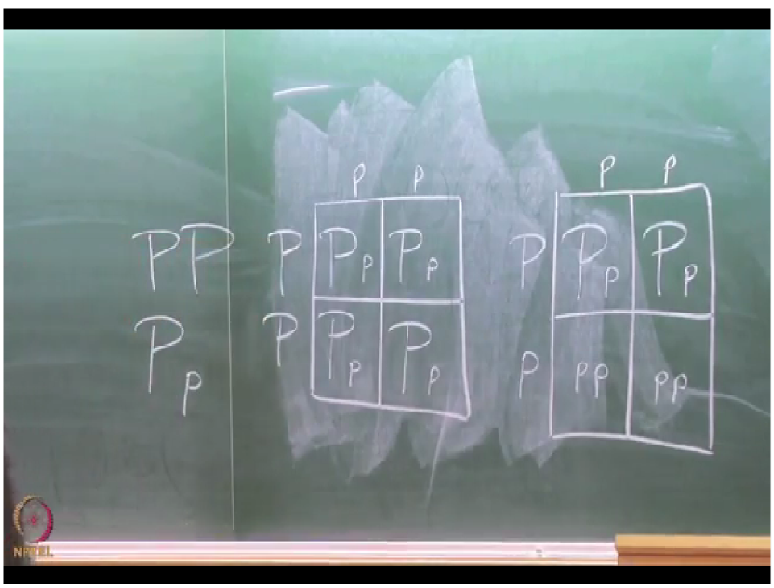

One is PP and second is Pp, both of them are purple flower. If I give you some seeds and I tell you that all the seeds are going to make the flowers which will look like purple, can you determine the genotype or their genetic makeup? Are these PP or Pp? So Mendel was doing these experiments himself. He was doing lot of back crosses and one of the cross which he observed, so please do try yourself as well.

Whatever I do, you should try it out yourself. So we have 2 possibility. One is PP. Second is P and a p. He made a cross of these 2 conditions with homozygous recessive which was pp. With this cross, now if you derive yourself, show what kind of numbers can you get now in terms of ratios? In the second possibility, what is the ratio?

"Professor - student conversation starts" 1:1. So, yes. **"Professor - student conversation ends."** So you have 1:1 or 50% here because these are going to show you the purple colour flowers. These are going to show you white colour flower. So if the genotype or the genetic composition of that was Pp, then you will see 1:1 ratio.

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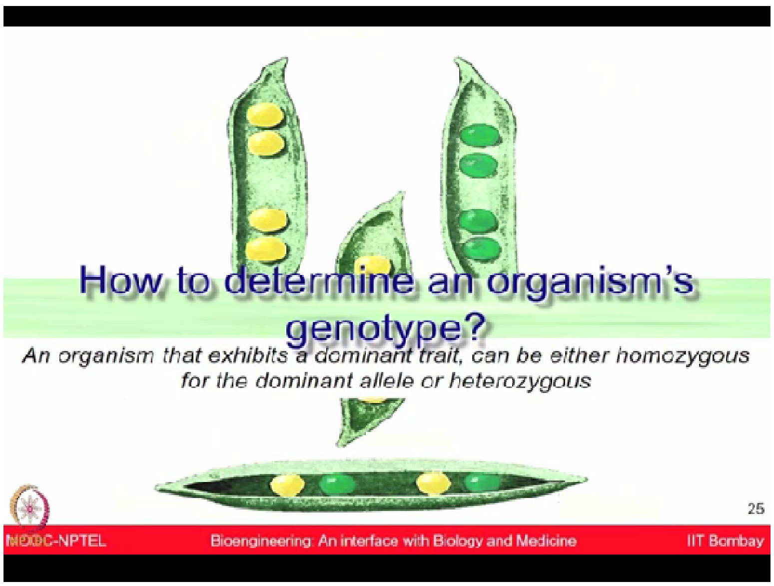

If they were all going to show you purple colour in flower pattern, it means genotype of that seed was PP.

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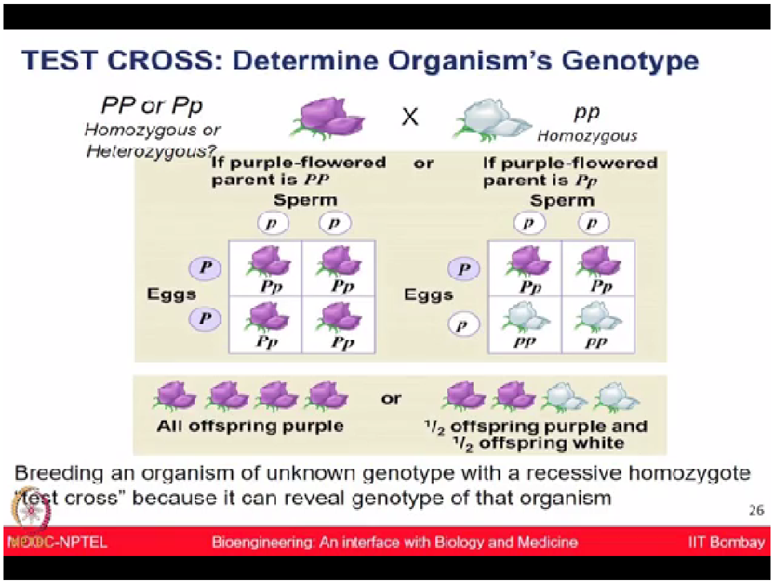

So this is how this kind of test can be done which is known as test cross. And test cross, keep in mind, you are doing always with the homozygous recessive. Test cross always done with the homozygous recessive characteristic. SO in this case where the 2 crosses which we just talked, you have possibility of PP or Pp and you are crossing with the homozygous recessive characteristic of pp, either all offspring were purple colour or 50% of them were purple and 50% of them were white colour.

So I think it is good to be more attentive in genetics lecture. It is not only interesting but also lot of questions are going to come based on that for sure. And as long as, you know, how to make these cross, Punnett squares, you can very easily do these kind of questions. So please make sure that you are trying all of these things yourself.

Whenever we say that make this cross, do try out yourself. It looks very easy some times, but still try to do that. So breeding an organism of unknown genotype with a recessive homozygote is known as test cross which can reveal the genotype or the genetic composition of that particular organism.

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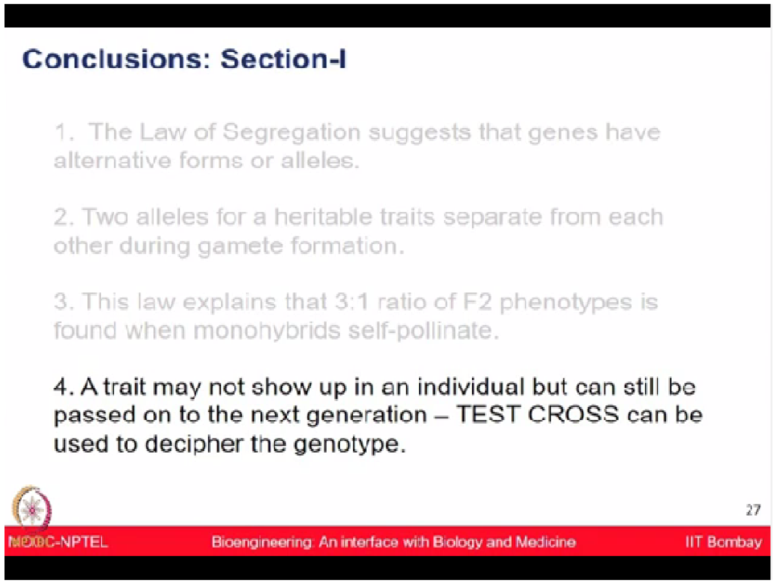

So what we can conclude from this section so far that the law of segregation suggests that genes have alternative forms or the alleles. There are 2 alleles for a given trait which are separable and those can get separated during the gamete formation. It also explains that the ratio is a proximate 3:1 and a trait may not show up in an individual but you can still obtain that information from the test cross which actually can be passed from one to the next generation. That brings us to the second law of Mendel which is law of independent assortment.

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Mendel while he was doing the experiments, of course he did not make the law that time. So he was doing the experiments, he was making those observations. After looking at many experiments giving the same ratios, then only he was able to come up with certain hypothesis that this particular thing is working well and now this can become a rule. So in terms of looking at this now, he started thinking about, you know, earlier we study only one characteristic, one gene and 2 allelic forms of that. Can we now start looking at 2 genes, 2 different properties, different allelic forms.

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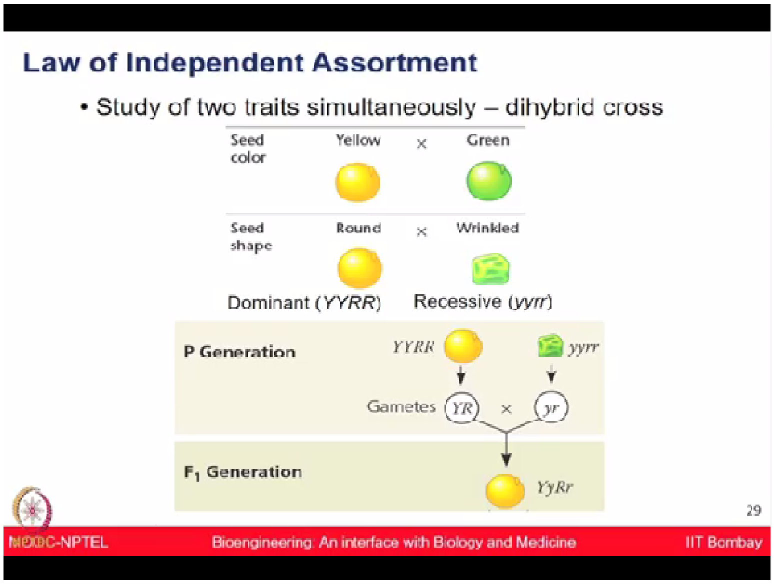

So for example, seed colour and see shape. This is a round seed and yellow colour. So we are looking at 2 properties now, right. And that is known as dihybrid. When we are talking about studying 2 traits simultaneously, that is known as the dihybrids. Or you are talking about a seed which is green in colour but either it is round or it can be wrinkled. So you are looking at 2 different properties here and to denote them, you can say it is YY, RR, or yy, rr.

So although I mentioned to you already that Mendel derived his law as a law of independent assortment. But let us assume the possibilities that what could have been either dependent or independent. So for doing this experiment from the gametes, from the parent generations, resulting in to F1 generation which is this hybrid YyRr. So now let us come, let us assume that Mendel was not sure that what should be hypothesis. Are the 2 properties which we are studying at the same time, they are dependent or they are independent?

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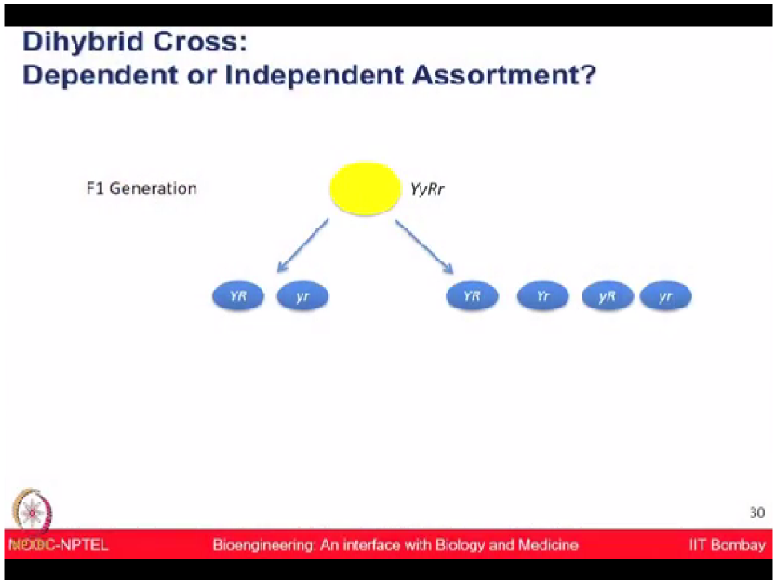

I am sure by now, you know, that the answer it is independent but let us say that, you know, he was not sure that what should be the property. So from this seed which is the hybrid, now we have YyRr, there can be 2 possibilities. Either a gametes which are derived are having the YRyr. Only this kind of characteristics are getting distributed or it can have multiple ways of distribution, YR, yr. Additionally we have Yr and yR.

So there are 2 possibilities now, right. Can you please start doing the cross yourself and tell me that what will be the answer from these crosses? So Mendel's law were actually based on the result which he obtained but you know, hypothesis is something when you are making hypothesis, you have no idea that what the results will be. So at that time, you are essentially just, you know, exploring all possibilities. It could be, you know, multiple characteristics might be depending on each other or they might be independent of each other, both are possibilities, right.

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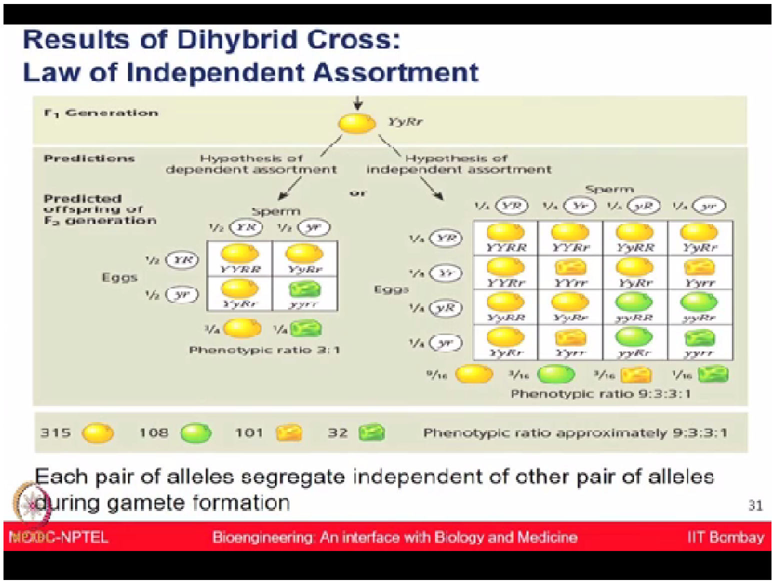

So if these are the characteristics, so now how best you do the crosses and derive the conclusion out of it. If you do the crosses, what will be, if this is the gametes, then what will be the progeny look like? Please do that first. You have to derive all the, no this is not correct. For this one, you have to have all of this gametes. Because of the male and female, both, we have to derive.

So I think, you know, looking at things sometimes, it looks much easier but as you start doing yourself, then you realize that you can make mistakes easily, right. Alright, just to save time, if you do this particular cross here, so male and female gametes which you have YRyr, if that was the case, then the ratio could have been 3:1. But what he found was something different. He found the ratio as 9:3:3:1.

So the round yellow, round green, wrinkled yellow and wrinkled green, they are showing phenotypic ratio as 9:3:3:1 which was different observation then what he was actually assuming. If the characteristics were depending on each other, the ratio could have been 3:1. But because they are independent, they are assorted independently, then the ratio observed was 9:3:3:1. So each pair of alleles segregate independent of other pair of alleles during the gamete formation.

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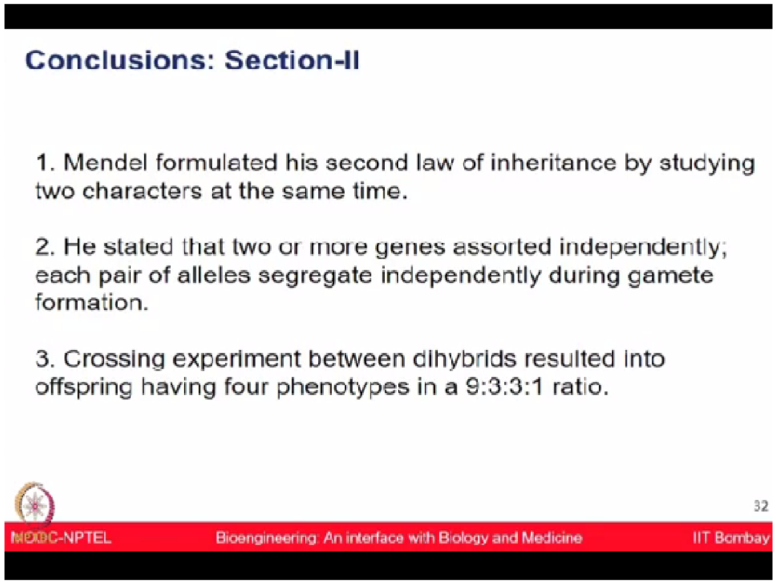

So from this section, we can conclude that the second law of inheritance of Mendel was observed based on these studying 2 characteristics at the time and he stated that 2 or more genes, they can be assorted independently and each pair of these alleles segregate independently during the gamete formation. After crossing the experiment then he observed the ratio which is 9:3:3:1. So Mendel, when he proposed these laws and brought those calculations, those numbers, he published in a small journal.

And that time as I mentioned, he was not doing these things for just doing research for and science from publication point of view, he was doing these things out of his own curiosity and he was not biologist per se. He was just doing these observations based on his interest of observing the nature and the plants. So he was not very popular. Nobody knew about his findings. He published already his results in 1866 but people were not aware of what Mendel did.

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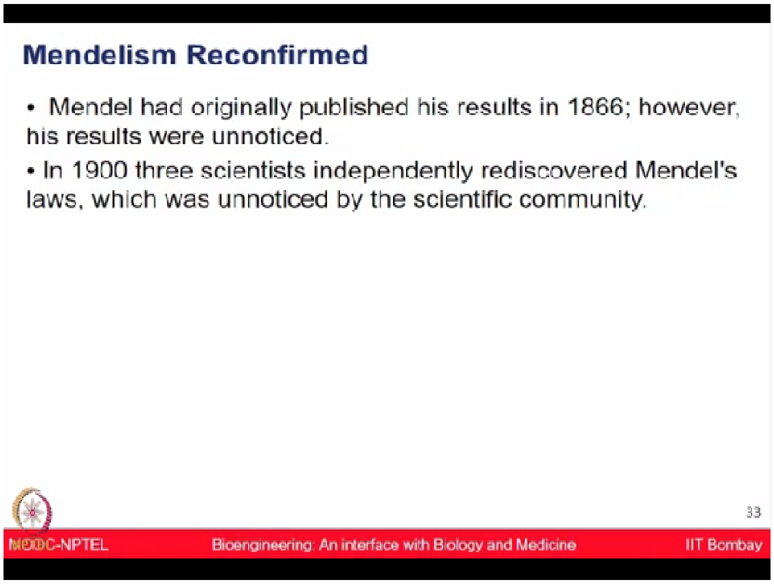

And it just got published in some journal which nobody noticed much about it. Many scientists over the period in 19th century, independently working on different genetic laws. Also they were looking at drosophila or the Fruit fly as a model system to study the inheritance and interestingly they were coming with the conclusions which were exactly same what Mendel already made several years ago.

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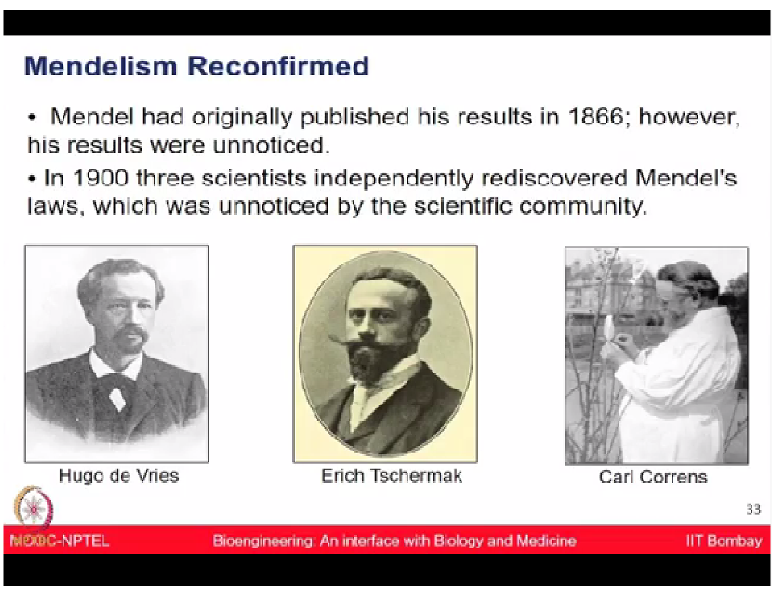

So these 3 scientists, Hugo de Vries, Erich Tschermak and Carl Correns, they made the same conclusions what Mendel already made in 1860s. So then Mendel was kind of, you know, people started recognizing his contribution and in many ways, the Mendelian laws were rediscovered because now people have much more confidence that what Mendel has proposed was very accurate and 3 independent scientist have confirmed their findings, confirmed his findings.

So now everybody started, you know, recognizing and appreciating Mendel's contribution and eventually now he is recognized as the father of genetics. So as I mentioned, let us be open to various observations, the things which we like to do it and irrespective of which discipline you study because you never know you are, you know, training in one area but your observation towards your interest can give rise to certain different output and those will be much more fundamental, much more original contributions for any given field.

So you are now familiar with the 2 main Mendelian laws of segregation and independent assortment. In the next lecture, we will discuss some of the examples of Mendelian genetics. You will see how many human traits follow Mendelian pattern of inheritance and how inheritance pattern are often more complex than predicted by simply Mendelian genetics. Thank you.

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