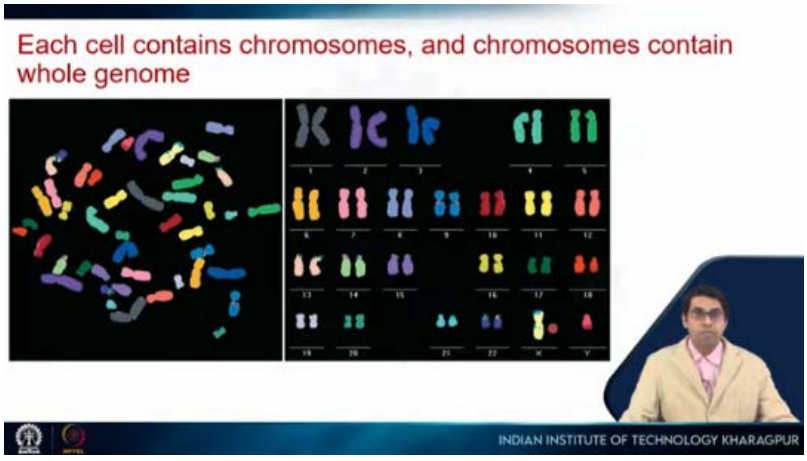
Introduction to Complex Biological Systems
Professor Dibyendu Samanta and Professor Soumya De
Department of Bioscience and Biotechnology
Indian Institute of Technology, Kharagpur
Lecture 23
Cell division cycle

Welcome to the third lecture of week 5. Today, I am going to talk about cell cycle division. As discussed in the last lecture, we saw that eukaryotic cells, or our cells, contain chromosomes. DNA is not a single molecule; rather, it is divided into multiple molecules.

These are chromosomes. Normally, they are scattered like this. We normally arrange them according to their size. The longest one is chromosome 1, and the smallest is 22; then, the sex chromosomes are named X and Y. In the case of cell cycle division or the cell division cycle, we will see that segregating these different molecules, DNA molecules, or chromosomes into the two daughter cells very effectively is one of the most important challenges.

We are going to spend quite some time understanding how cells achieve this fantastic feat. So, let's look at these chromosomes once again. We have 46 chromosomes. We have 23 chromosomes, 1 to 22, and then the sex chromosome X or Y. Now, there are pairs of each. So, there are two copies of 1, two copies of 2, two copies of 22, and then X and Y. So, the total is 46.

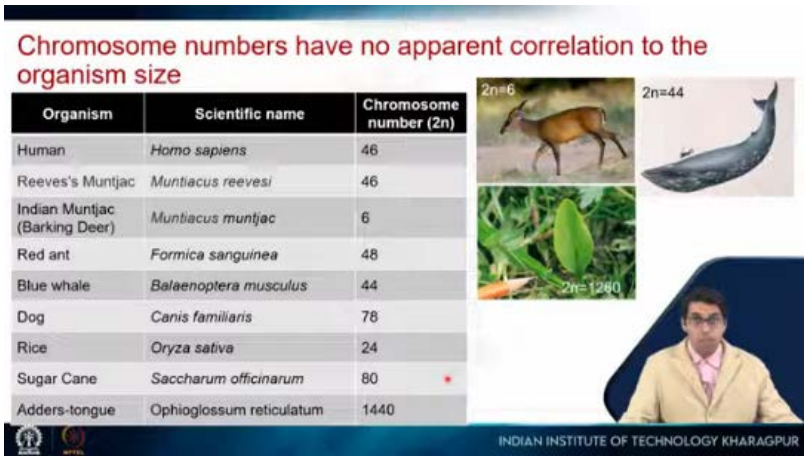


So this is called diploid. Now it turns out that chromosome numbers have no apparent correlation to the organism's size. So this is us, this is Reeves's Muntjac, so it's basically a

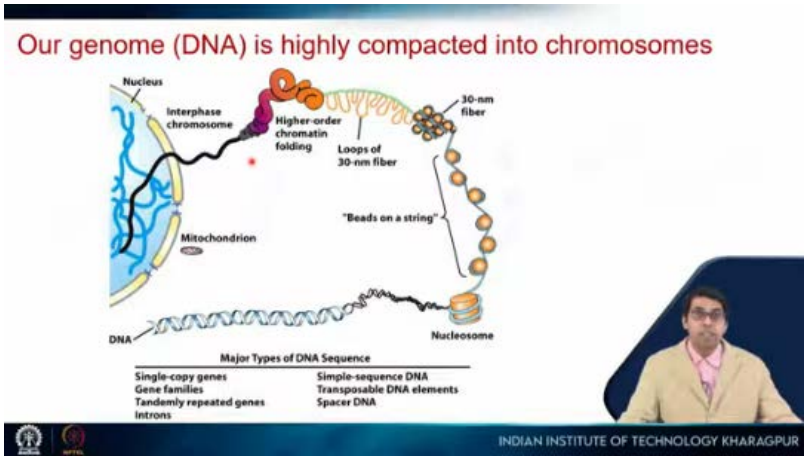
deer, and it has exactly the same number of chromosomes. But then this other deer, the Indian Muntjac, has only six chromosomes. The red ant, which is much smaller, has 48 chromosomes, more than us.

On the other hand, the blue whale, which is much bigger, has 44 chromosomes, so two less than us, dogs have 78, and so on and so forth, as you can see. This one, the Adders-tongue, is most probably the organism with the largest number of chromosomes. So the number of chromosomes reported for the Adders-tongue is 1,440.

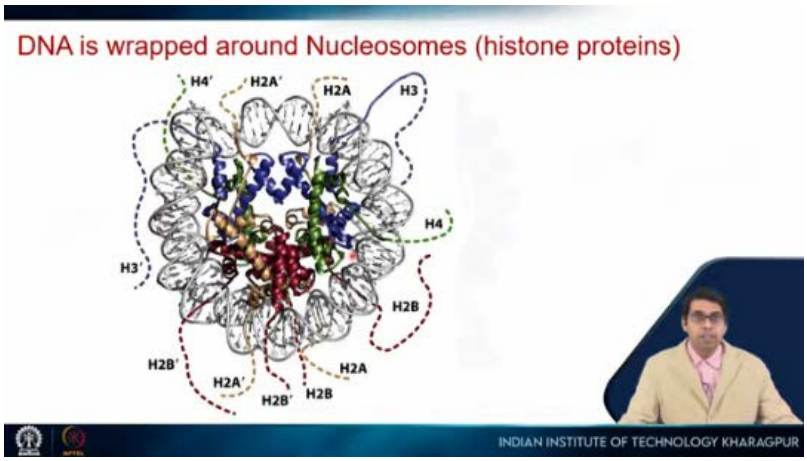
You can imagine that when a cell has to divide, these chromosomes will be replicated. So this 1,440 will become 2,880 right. and each of those chromosomes will have to be separated or segregated into the two cells.



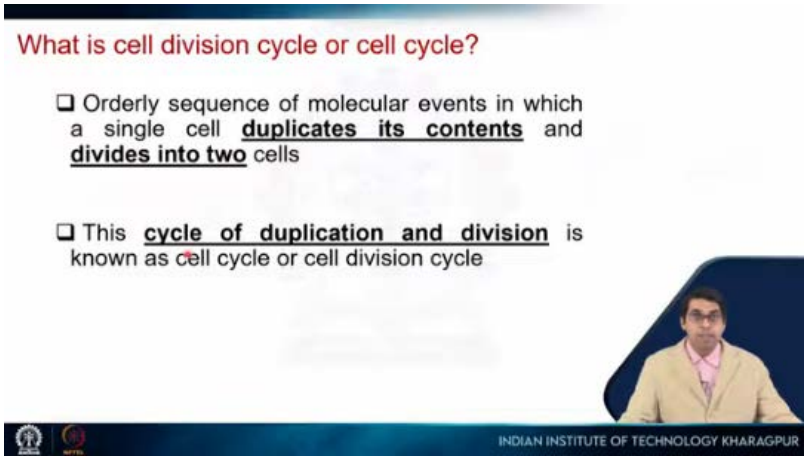
So that's a fantastic task that is achieved by our cells every second. So here is the structure of the chromosome. This is DNA and the DNA is wrapped around histone proteins to form the nucleosome, and then it is packed further to form the chromosome.



Now we will see that normally this chromosome is something like this in the interphase. When it goes into the M phase, it will become much more condensed. So the pictures and diagrams that I showed you in the two slides back are normally in the M phase.



So this is again the histone protein, and the DNA is wrapped around this histone protein like this. So what is the cell division cycle, or in short, the cell cycle? The cell division cycle is an orderly sequence of molecular events in which a single cell duplicates its contents and divides into two cells. So one cell will divide into two cells, and it has to distribute all its material correctly into the two daughter cells. This cell cycle of duplication and division is known as the cell cycle or cell division cycle. So what are the important features of the eukaryotic cell division cycle? So here I am going to discuss the eukaryotic cell division cycle because eukaryotic cells are much more complex, and they undergo lots of checks and balances.



So the first important feature is that there is a delicate balance between cell growth and division. So if a cell continuously divides, then it will become smaller and smaller and smaller. So if it becomes too small, then it will not be able to perform its task. So after division, the two smaller cells will have to grow to a certain size before they can divide. So there is this delicate balance between cell growth and division.

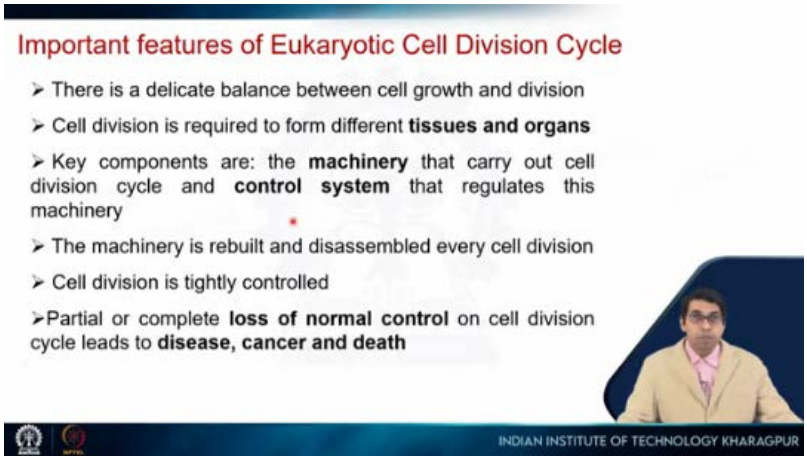
Cell division is required to form different tissues and organs. So we are multicellular organisms, and if you typically think, there are all these different organs like your heart, lungs, liver and each of these organs is made up of multiple cell types. So roughly, there are 200 broadly categorized cell types, but there are many more. So these cells have to divide in order to maintain these tissues and organs.

So, one example that I can give you, and we will talk about this in more detail in next week's lecture. So, for example, if you think about your red blood cells, our red blood cells have a lifespan of around 120 days, which is around four months so, in four months, a red blood cell will die. So, some will die earlier, some will die later, but that's the average time. So these red blood cells have to be replenished, and we have a huge amount of red blood cells. So it turns out that our body makes two to three million red blood cells every second. So that's the huge amount of cell division that goes on every second, producing two to three million red blood cells and that is needed to maintain a constant level of blood in our body and that is true for most organs. Red blood cells are the most dramatic example. I will talk about our intestine in the next lecture, and you will see that when we eat food, our intestine is responsible for digesting that food and absorbing it. So it also undergoes mechanical

wear and tear. Thus, the lining of our intestine has to be replaced, and those cells divide every day. If you think about other cells, they do not divide that much. Now, for cell division, there are two key components. The first one is the machinery which carries out the cell division cycle, and the second one is a control system.

So this control system regulates whether it is a good time to divide, and then it goes through different phases. Whether the first phase is done, can it proceed to the second phase, and so on. So there is this decision-making process that is done by the control system, and the actual division is carried out by a set of machinery. We will look at this in detail. This machinery, we will see, includes microtubules, kinetochores, and other things. These are rebuilt and disassembled every cell division cycle.

So, once the cell cycle is complete, they are disassembled, and when a particular cell commits to go into cell division again, these will be rebuilt and, of course, cell division is tightly controlled by this control system. Because if this control system is lost, it can create diseases such as cancer. So the fundamental event in the cell division cycle of living systems is common. So, whatever cell type we think of, these are the common features.

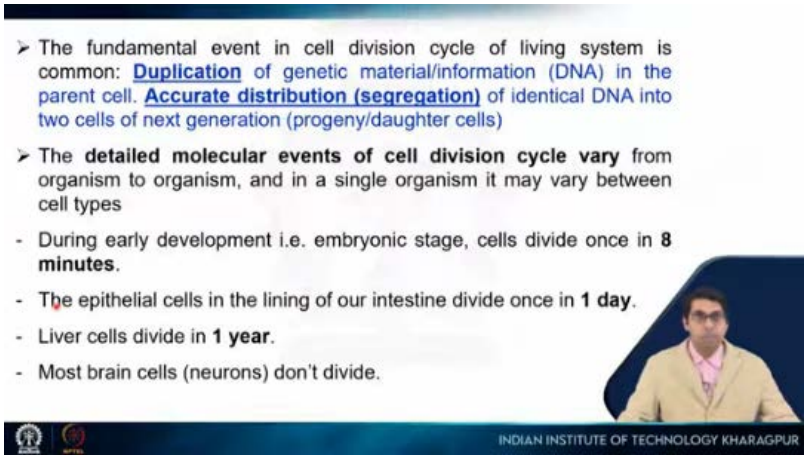


Duplication of the genetic material is the most important part of the cell division cycle and accurate distribution of the identical DNA into the two daughter cells. So, first is the duplication of the DNA. So, all the DNA has to be duplicated. We have 46 chromosomes that will get duplicated to 92 chromosomes and then each pair will have to be transported into the two daughter cells.

So, for example, if chromosome one. has two parts, one from the paternal side and one from the maternal side, and then there will be two copies of paternal chromosome one. So, one copy will go to one daughter cell, and the other copy will go to the other daughter cell. Both cannot go to the same daughter cell. So, this type of accurate distribution has to happen. The detailed molecular events of the cell division cycle vary from organism to organism. Again, in a particular organism, depending on the cell type, it will also vary according to the stage of the organism.

So, embryonic cells will divide in a certain way versus the adult cells. But the overall features are common, and that is what we are going to discuss. So, during early development, that is in the embryonic stage, cells divide once in eight minutes. So, they divide very fast and in that case, what actually happens is we start with a large cell, and then it becomes smaller and smaller and smaller and that is why you will see that these egg cells are so big because they have to contain enough nutrients and enough material so that multiple rounds of cell division can happen.

The epithelial cells in the lining of our intestine divide once in one day. Similarly, liver cells divide once in a year, and our brain cells, the neurons in our brain, do not divide. But this does not mean that the liver cells take one year to divide so it means that their division is less frequent.



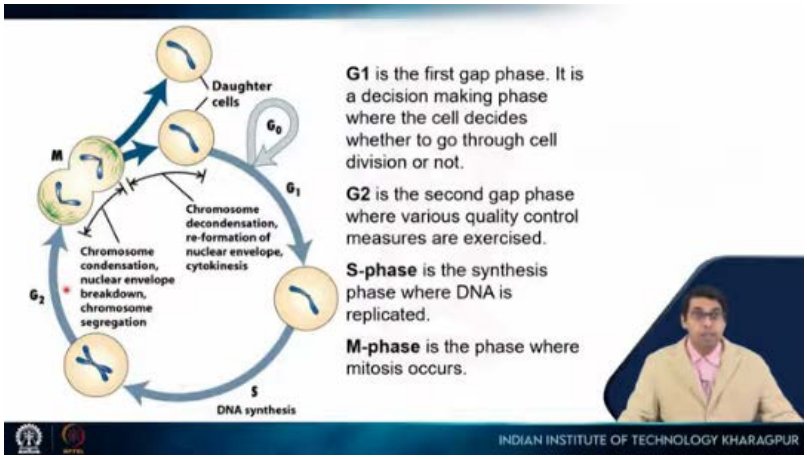
These cells most likely take around 24 hours to divide. So it will be very similar to these cells, but their frequency is much less. So this is the overall schematic of a cell division cycle. So there are two important phases in a cell division cycle. One is the S phase.

Here S stands for synthesis. In this phase, DNA synthesis happens, and the other one is the *M* phase. M stands for mitosis. This is where the segregation of the replicated DNA happens into the two daughter cells.

So these are the two important phases, and they are separated by two gap phases. The first one is called G_1, and the second one is called G_2. So G_1, *S*, G_2, *M*, these are the four standard or important stages of cell division. So G_1 is the first gap phase. It is a decision-making phase where the cells decide whether to go through cell division or not.

So they will decide whether they have enough material to replicate DNA and so on and so forth. So once that is done, it will enter the *S* phase, and in the *S* phase, DNA synthesis happens. So in our case, 46 chromosomes will become 92 chromosomes. Then the G_2 phase is the second gap phase, where various quality control measures are exercised. So all the microtubules and all this machinery are assembled in this phase, and it ensures that the DNA synthesis has happened properly.

All the chromosomes are present. There are no breakdowns or damages in the DNA or the chromosomes. Once all those checks and balances are found to be okay, then the cell commits itself to the M phase. So we will see, as I have already alluded to, that there are actually several checkpoints which ensure that everything is fine and the cell can proceed to the next stage. In many books, you will see that the cell cycle is shown like this, where the cell cycle is divided into two phases.

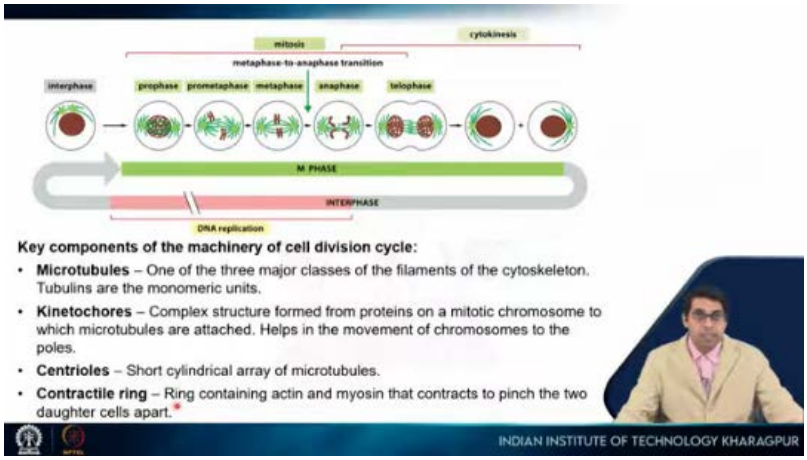


One is the *M* phase, and the other one is the interphase. So G_1, *S* phase, and G_2, these three are combined as the interphase because, in this, the most important event that happens is DNA replication and the other phase where a lot of action happens is the *M* phase. So we are going to go through this *M* phase in more detail now because we have already covered DNA replication in an earlier lecture. The key components of the machinery of the cell division cycle are as follows.

The first one is microtubules. We have already seen microtubules, which are polymers of proteins. So we have seen that tubulins are the monomers of microtubules. A tubulin dimer forms this hollow tube of microtubules, which is a part of the cytoskeleton. The next one is kinetochores.

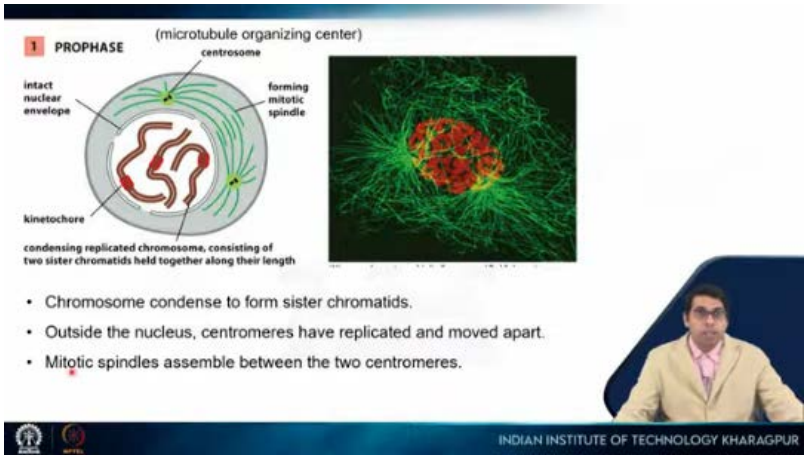
These are complex structures formed from proteins on a mitotic chromosome to which microtubules are attached. So these microtubules get attached to these kinetochores, and they help in the movement of the chromosome to the two poles. Like so, you can see that chromosome movement is shown here. Then there are centrioles. These are short cylindrical arrays of microtubules.

These centrioles are at the two ends of the cell. So they form the two poles, and then there is a contractile ring. So this ring contains actin and myosin, and they contract to pinch the two dot cells apart. So this pinching that happens is because of this actin and myosin cytoskeleton proteins. So let's look at the different phases of the *M* phase or mitosis. The first one is prophase. So in this case, the chromosomes condense to form sister chromatids. So you can see that there are two chromatids. They are connected together. Now, remember, DNA replication has already happened, so these two are exactly the same chromosomes. There are two copies of that.



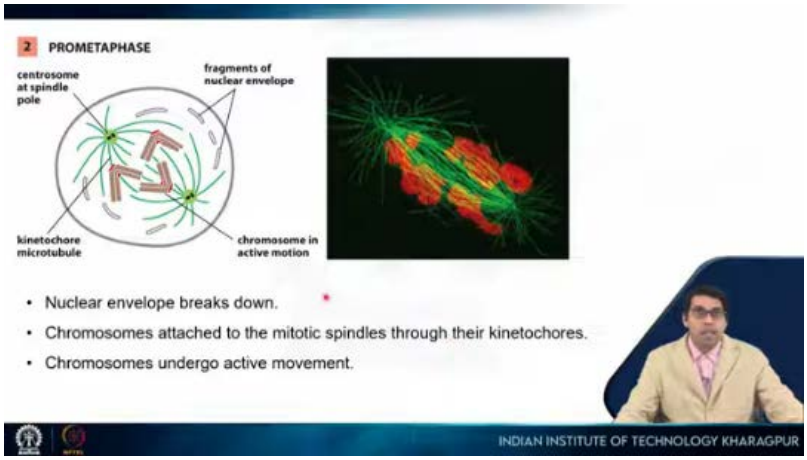
So this is inside the nucleus. Outside the nucleus, centromeres have replicated and moved apart. So initially, there was one centromere. They have replicated, and now they are moving apart. So they are moving apart, and these green lines that you see are microtubules. So they push each other, and that results in these two centromeres or centrosomes moving apart.

This is an actual fluorescence image. In this case, the DNA is colored red. So that's a red dye, and the microtubules are colored green because they are bound to green dye. So we will see these two images for all the different stages. Now, mitotic spindles assemble between the two centromeres.

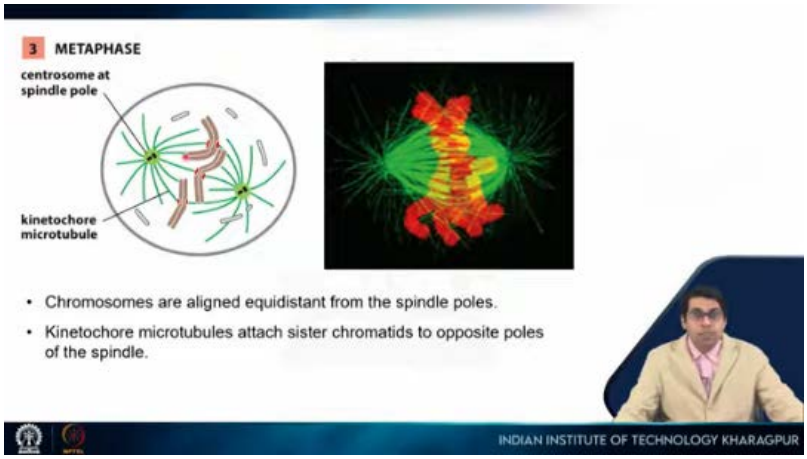


So these are the mitotic spindles. In the next phase, which is the prometaphase, the nuclear envelope disintegrates. The envelope is gone. Now the chromosomes are exposed and they can get attached to these mitotic spindles. So they get attached to the mitotic spindles through their kinetochores and now the chromosomes undergo active movement. So they

will get pulled and pushed around inside the cell. In metaphase, the chromosomes are aligned equidistant from the spindle poles.



So this is something that is very important because the cell has to ensure that these two sister chromatids, one goes to this side and the other one goes to that side. So to ensure that all the sister chromatids are arranged at this plate at the center of the cell. Kinetochore microtubules attach the sister chromatids to the opposite poles of the spindle. This sister chromatid is attached to this, and this sister chromatid is attached to that. So they will grow and shrink. So this push and pull will happen, and that will ensure that all the sister chromatids are at the center of the cell.

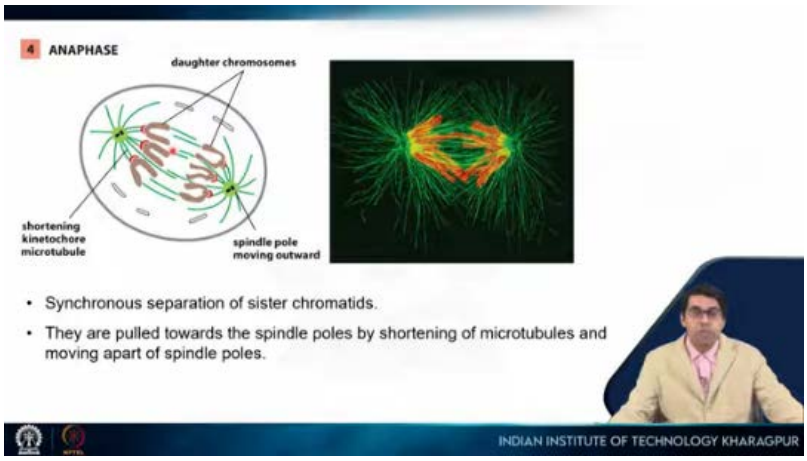


The fourth stage, which is the anaphase, triggers suddenly, and that happens when these two sister chromatids are separated. So how does this happen? This happens because the sister chromatids are connected together by certain proteins called cohesins. So you can

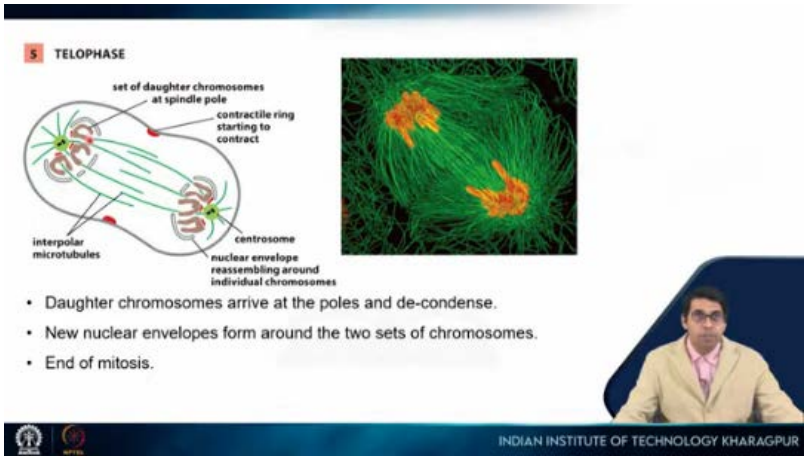
think of them as glue so these cohesin proteins form a complex that attaches these two sister chromatids together.

The change or the beginning of the anaphase is triggered by the degradation of these cohesin molecules or cohesin proteins. So there are proteases that will get activated at this cell at this phase of the cell cycle, and they will degrade the cohesin. Once that happens, this glue is gone, and the two sister chromatids are separated. Now these microtubules start shortening. So the shortening of these microtubules results in the movement of the sister chromatids towards the two poles. So 46 chromosomes will move in this direction, and the remaining 46 chromosomes will move in this direction.

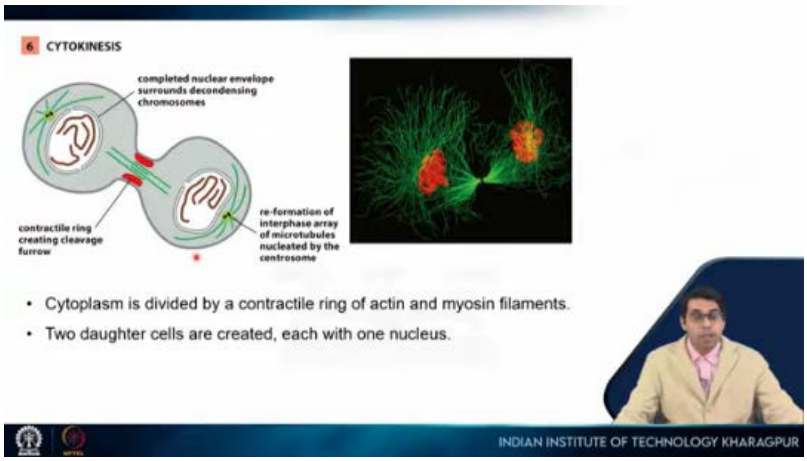
This ensures that an exact distribution happens. So the two paternal chromosome ones, one will go here, and the other one will go here. The two paternal or the two maternal chromosome ones, one will go here, and the other one will go here, so like that. So in the last phase, the daughter chromosomes arrive at the poles.



So they are here. Now they will start decondensing. A new nuclear envelope starts building. You can see that the nuclear envelope is building. So there will be two nuclei and that marks the end of mitosis. Now what remains is the division of the cell. So that is cytokinesis. So the cell membrane will start invaginating like this, and that is triggered by the contractile ring that is formed by actin and myosin filaments. So we already saw microtubule filaments here; actin and myosin filaments become active.



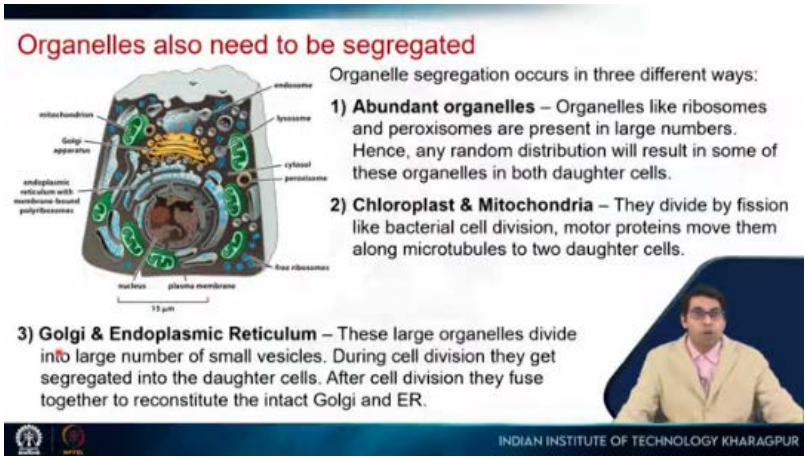
So they start forming a ring. here, and they will start contracting so that will pinch the cell membrane and finally result in the formation of two daughter cells. And you can see there are microtubules, and each will have one centriole each. So that is the cell division. Now remember that what we have done here so far is we have looked at the division of the genetic material or the segregation of the genetic material.



But there are other cellular organelles which are also present, and they also have to be efficiently divided into the two daughter cells. So that is done by these three different mechanisms. The first one is for abundant organelles. Organelles like ribosomes and peroxisomes, which are present in large numbers. So ribosomes will be scattered throughout the cell.

Now, if the cell divides like this, you will have enough ribosomes in the two daughter cells. So it's just by sheer number that they are distributed into the two daughter cells. Chloroplasts and mitochondria are very important organelles. So, to ensure that both cells

get enough of these organelles, they divide by fission, just like bacterial cell division. And they are transported by motor proteins along the microtubules to the two daughter cells.

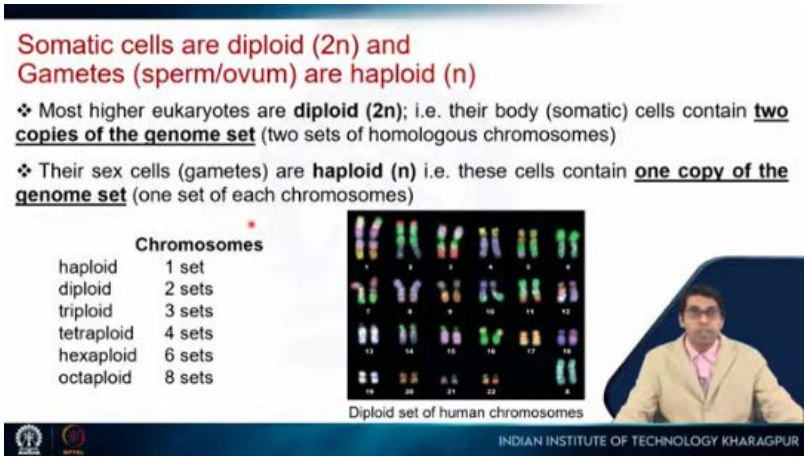


So they sort of hitchhike on these microtubules along the two poles. That ensures that enough chloroplasts and mitochondria will be present in the two daughter cells if it divides like this. Golgi and endoplasmic reticulum divide into smaller vesicles, and then during cell division, they are segregated into the two daughter cells. After the division is complete, they fuse together to reconstitute the intact Golgi and endoplasmic reticulum. So this is a recapitulation of what we have done so far that we have 46 sets of chromosomes. It becomes 92, and then it gets divided into two cells, which is 46 and 46. So, this type of division happens in cells which are called somatic cells, which are diploid because they have two copies of each chromosome, one from each parent. There are other types of cells that we have, which are the sex cells or the gametes. So, sperm and ovum, these are haploid.

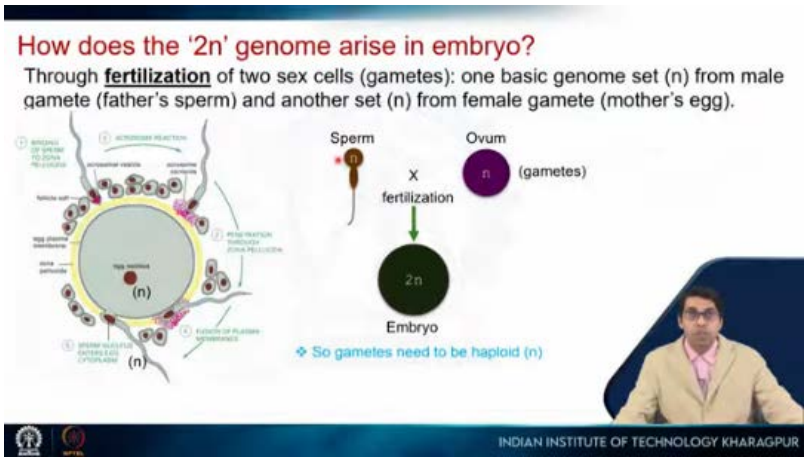
So, they have only one copy of the genome. The sperm and the ovum will have only 23 chromosomes. So, how does this happen? So, how do we get these cells? What division is responsible for that?

We will see that it is done by a different type of division, which is called meiosis. So, this is just for your information that if there is one set of chromosomes, it's called haploid. If there are two sets of chromosomes, it's diploid. We can have three, four, six, and eight cells. So, strawberries are an example of octoploid, where they have eight sets of each chromosome. Strawberries have 77 chromosomes, and there will be eight sets for each of those chromosomes. So, seven times eight, 56 chromosomes are present in a strawberry. I

will come to how these haploid cells are generated, but the fertilization of two haploid cells, the sperm and ovum, will result in each having 23 chromosomes.



In our case, this will have 23 chromosomes, and this will have 23 chromosomes. When they come together, fertilization occurs, and then the embryo will have two sets of chromosomes because 23 comes from here, and 23 comes from here. So that is a total of 46. Right. So how do we get these haploid gametes in a diploid organism?

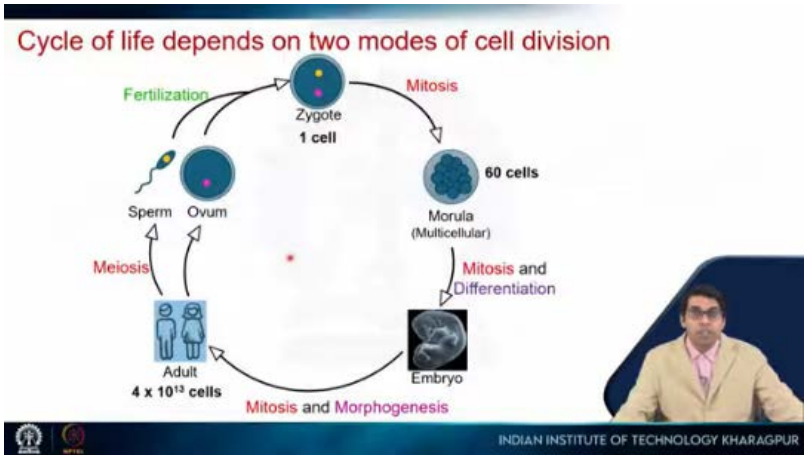


Before I go into that, this is just an overview of the life cycle of an organism like us. Life starts as a single cell. It is a zygote. It is diploid. There are two sets of chromosomes.

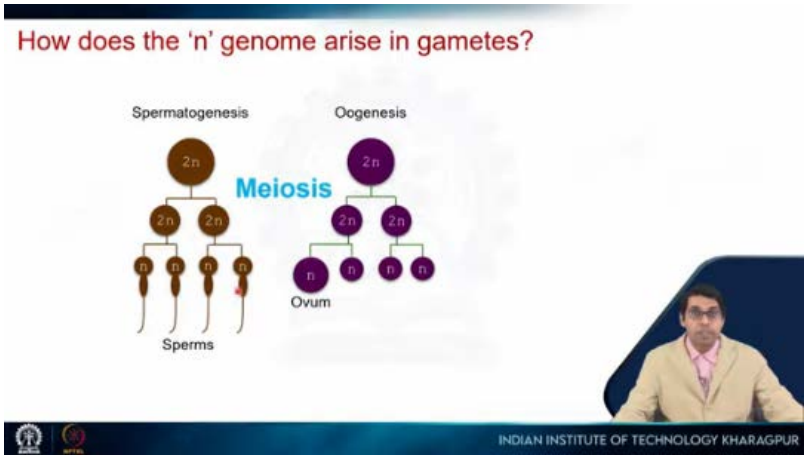
Now mitosis will happen. This is the normal cell division that we have seen and all these different cells will be generated. Each of them will have $2n$ copies of DNA. Then something interesting happens, which we will discuss in the next lectures: differentiation.

So the cells, these cells are most probably all very similar to this, but then the cells will differentiate. So there will be skin cells, there will be different organs that will develop, there will be bones. So all these different cells are generated, and that is also called morphogenesis. So the body plan happens, and the body is developing.

So we will have almost 200 different types of cells. Now all of these are mitosis. So mitosis will actually generate different types of cells. And then we also have to generate the sperm and ovum, which are generated by meiosis. So in this case, $2n$ is maintained during mitosis, and meiosis will result in the formation of n. So 23 chromosomes here, 23 chromosomes here.

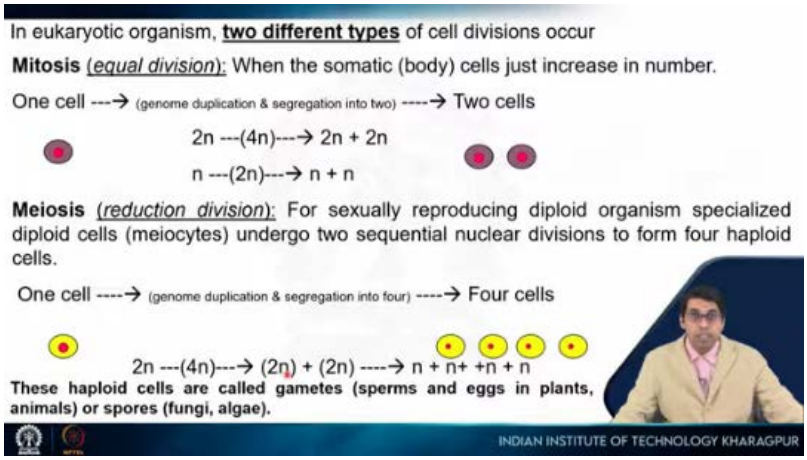


Now these two combine together to form again a new life, which is a $2n$ cell. So, meiosis undergoes two divisions. So, this is a $2n$ cell. DNA replication happens. So, it will be $4n$, and then it undergoes the first division.



So, this is $2n$ and $2n$, and then it will undergo another division. So, each of these will be n. So, from one cell, we get four gamete cells. So, it can be sperm or ovum, and we end up with cells which are n or haploid. So, the same thing is shown here. So, mitosis is equal division, $2n$ goes to $4n$, and then from $4n$, we get two daughter cells, $2n$ and $2n$. So, this is for diploid. If an organism is not diploid, but again mitosis happens, then it will be n goes to $2n$, and then it becomes n and n. Meiosis is reduction division. So, in this case, the number of chromosomes will decrease.

So, $2n$ becomes $4n$. The first division will result in 2 cells. Each will be $2n$ and $2n$ and then the second division will result in 4 cells. Each of them will be n, n, n, and n. So, here is a comparison.



This is mitosis. We have already seen this. So let's focus on meiosis. So in this case, we have taken a very simple cell which has only one chromosome. So one chromosome.

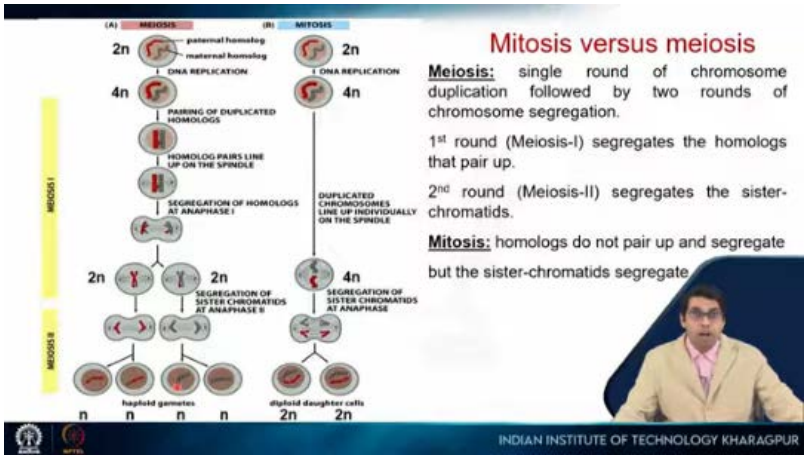
Now there will be two copies, one from the father and one from the mother. So paternal and maternal. So the first step is DNA replication. So now there are two paternal chromosomes. You can see two red chromosomes here and two maternal chromosomes, two gray chromosomes here.

So these are the sister chromatids, and they are connected together by the cohesin molecules. Now, something interesting happens. So, in the case of mitosis, these chromosomes are arranged like this and each of these will be connected to the two poles on different sides so that they can be distributed like this. Here, they are arranged side by

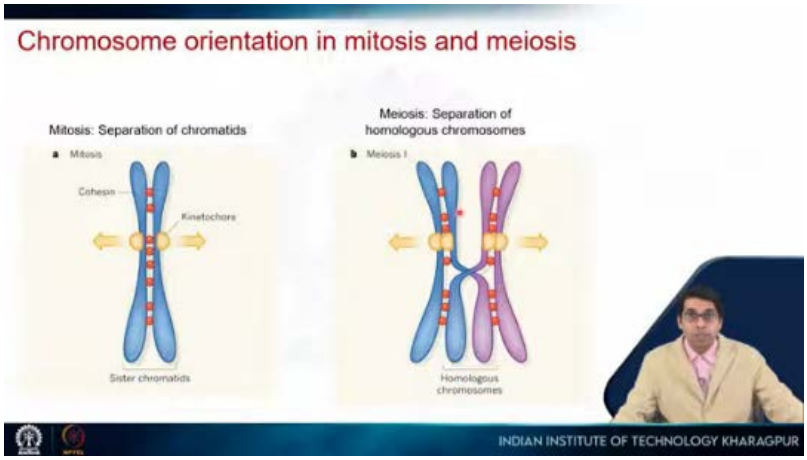
side and there is something that is called crossing over. So, you see that this is chromosome 1. So, the red one is from the father, and the gray one is from the mother.

Now, there is a connection between them. We will see this picture in more detail in the next slide. In the first division, what happens is this is $2n$, but both sister chromatids have gone into this, and both sister chromatids have gone into this cell. So, these two cells are not similar to these two cells.

Now, another division happens, which is similar to this, and the two sister chromatids go into two different cells. So, we end up with four cells, and each of these will have only one chromosome one, and that can be from the paternal side or that can be from the maternal side. However, there is some mixing that has also happened, which is called crossing over, because you will see that a small bit of red has come here and a small bit of gray has come here. So, this is something that is called crossing over, and that results in genetic diversity. So, in the case of mitosis, the two sister chromatids are attached like this by the cohesin molecules or cohesin proteins.

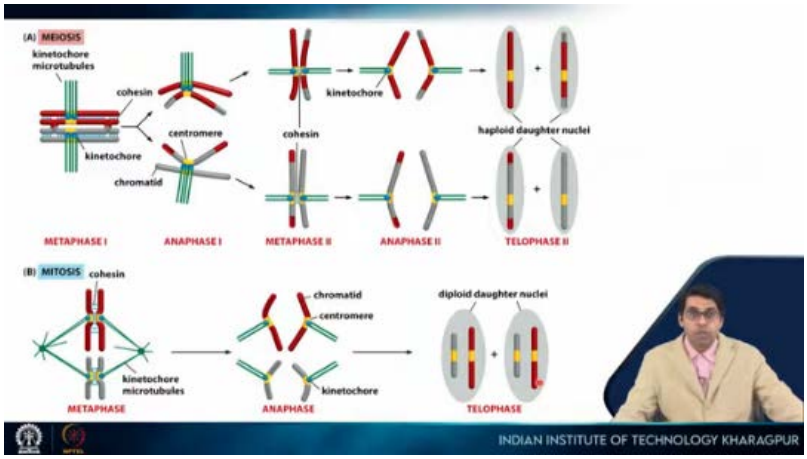


Kinetochores are here, and they are connected to the two poles. In two directions, so they will get separated here, so one will go here, and the other one will go in this direction. In the case of meiosis, the two sister chromatids are present side by side. So, this is from the paternal, this is from the maternal, and both are connected on one side, and here both are connected on the other side, and here crossing over happens. So, some part of this chromosome will go here, and some part of this chromosome will go here.



So, the same thing is shown here in more detail. So, you can pause the video and just go through this yourself. So, in this case, what you will see is the first division results in these two. So, both maternal chromosomes are in one cell, both paternal chromosomes are in the other cell, and then the second division will result in four daughter cells, each being haploid, and you will see that some bits and pieces of the maternal chromosome are with the paternal chromosome, and here the paternal chromosome is with the maternal chromosome.

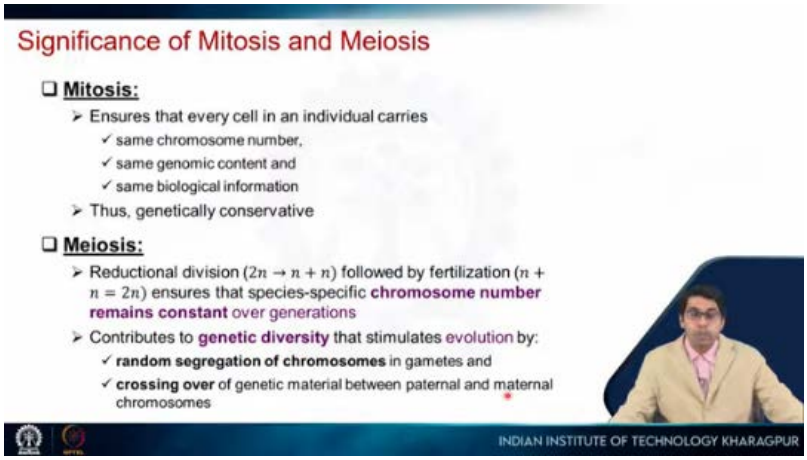
So, this DNA is not exactly the same as this DNA. So, this is genetic mixing. But nothing like that happens in meiosis. So, whatever is here is exactly what you get here. So, no mixing of DNA happens.



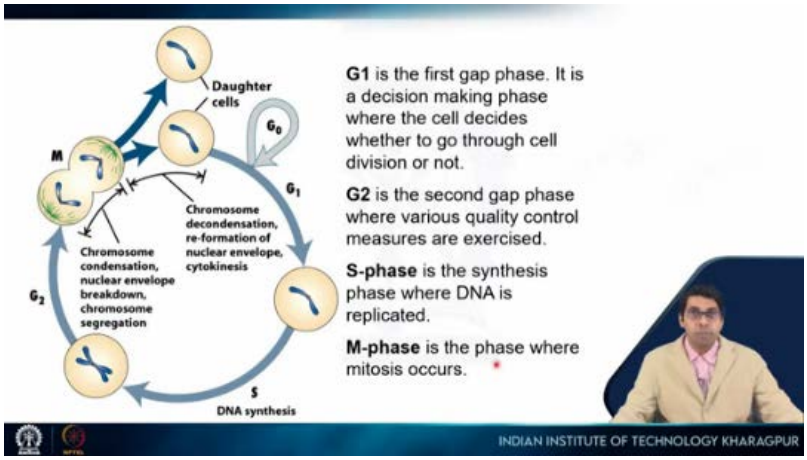
Mitosis ensures that every cell in an individual carries the same chromosome number, same genomic content, and same biological information. So, mitosis is genetically conservative. On the other hand, meiosis is reduction division. So, it ensures that the species-specific

chromosome number remains constant over generations. Because reduction division happens, and then the sperm and ovum will combine.

So it will again give rise to $2n$. It also contributes to genetic diversity that stimulates evolution. So this is a very important part that it plays because the random segregation of chromosomes in the gametes and crossing over results in the exchange of material between the paternal and maternal chromosomes. So a child will always have some genetic material that comes from the father and some genetic material that comes from the mother.



So we have seen how cell division happens and how the machinery plays an important role. Now we are going to focus on the control of the cell cycle, the cell division cycle. So this is just a recapitulation of what we have seen: G_1, S, G_2, and M, right? So these are the four phases. So a very elegant experiment was done almost 50 years back by Rao and Johnson, where they figured out that this cell goes through these different phases and there are checkpoints.



So what did they do? They took two eukaryotic cells and fused them. So I'm not going to go through the technology, but let's see what the outcome is. So one cell was in the *S* phase, meaning it is replicating DNA. The other one is in the G_2 phase, which is after the *S* phase.

So when they fuse them together, this one cell will have two nuclei. Now the question was, can they exchange material between each other, and can they influence each other? So you would expect that, okay, this is in the *S* phase, this is already done, so it can proceed to the *M* phase, but that is not what happened. This somehow retarded the progression of *G2* into the M phase. Once this is done, DNA replication is completed, and it goes into the *G2* phase.

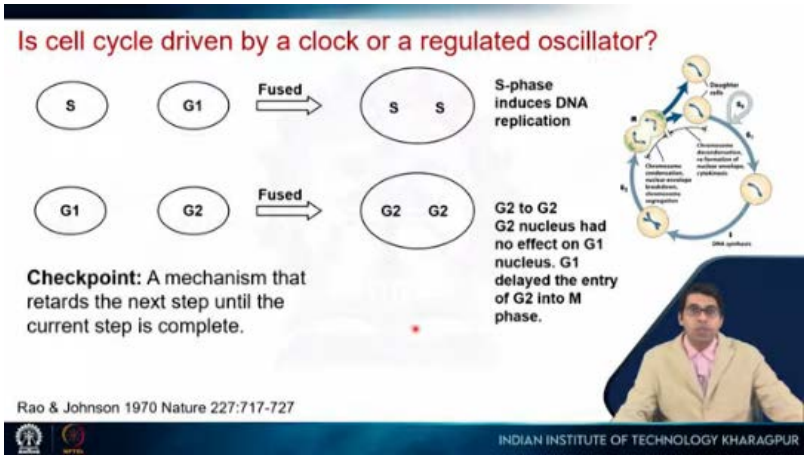
They both together go to the *M* phase. So it means that whatever factors here can diffuse into this nucleus and can inhibit it from going into the *M* phase. So there is some sort of check that once both are in the *G2* phase, all the DNA replication has happened, then only the cell goes into the *M* phase. They did other sets of experiments. So here they fused *S* with *G1*.

So in this case, *S* with *G1*. So what happened is that *G1* did not prevent the *S* phase, but this, the *G1*, went into the *S* phase very quickly. It means that there are factors in this which induced this nucleus to go into the *S* phase quickly. They also fused *G1* with *G2*.

So one cell, one nucleus in this and one nucleus in this. So in this case, the G2 nucleus had no effect on *G1*. So *G2* did not have any effect on *G1*. But *G1* delayed the entry of *G2* into

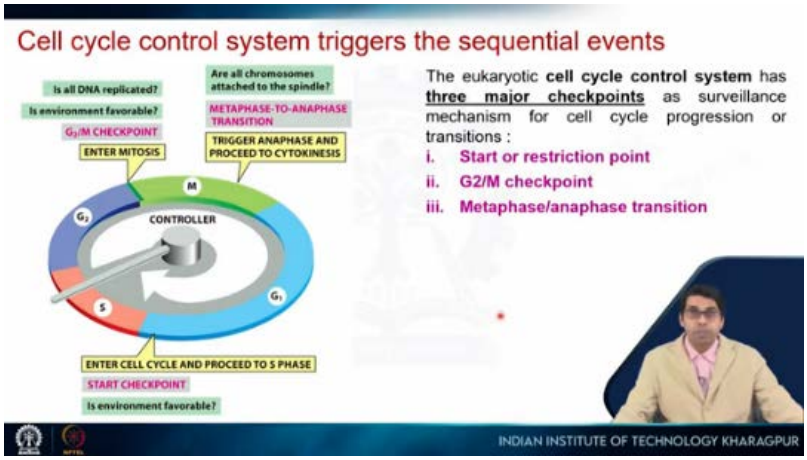
the *M* phase. So only when *G1* got into *G2*, then only they together progressed into the *M* phase.

So this means that there are checks and balances at every phase of the cell cycle, which retards the next step until the current step is completed. So that is the checkpoint of a cell cycle. So it turns out that there are three major checkpoints. The first one is the start or restriction point. So the start or restriction point is here. So after the *G1*, the cell decides if the environment is favorable or they have enough material to replicate DNA because the DNA number will double in the *S* phase.



Then there is the *G2/M* checkpoint. So it is between the *G2* phase and the *M* phase. So the cell has to decide if all the DNA is replicated. Is the environment favorable? Is all the machinery there?

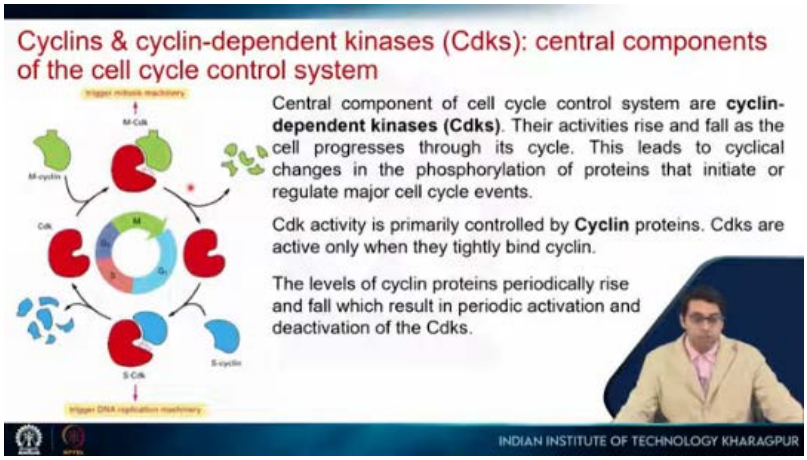
Now it can enter the *M* phase and once it's in the *M* phase, there is a checkpoint between the metaphase and the anaphase. So, at the metaphase, remember that all the sister chromatids are arranged at the center plate. So, they have to be properly arranged at the center plate. Once that is at the center plate, once that is done, then only the anaphase will be triggered because the cohesin molecules will be degraded, and the two sister chromatids will be pulled apart along the two poles.



So, what is the mechanism of these checkpoints? How does this work? There are proteins which are called cyclins and another set of proteins which are called cyclin-dependent kinases, which are the central components of this cell cycle control system. So, you have already seen kinases. So, kinases are enzymes which phosphorylate certain amino acids.

It can be a tyrosine residue; it can be a serine or a threonine residue. So, these kinases will not do that unless the cyclin is present. So, for example, this is a kinase; it will be inactive. Once this cyclin comes in, it will bind this cyclin-dependent kinase, and it will get activated.

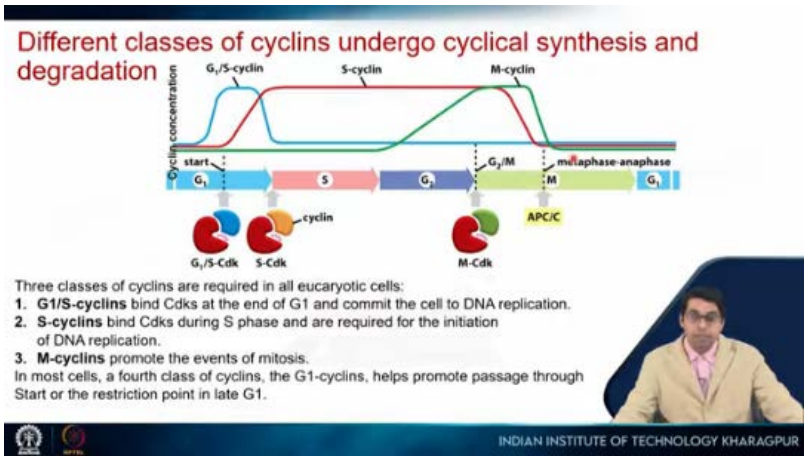
So it will phosphorylate certain proteins that will trigger this set of events. Once its job is done, the cyclin is degraded, which means that the kinase is again inactivated. So different phases of the cell cycle are driven by different cyclins. So we will see that different cyclins are produced at different phases of the cell cycle.



So it is shown here. There are three classes of cyclins that are required in eukaryotic cells. The first one is the G1 to S cyclin, which is shown here in blue. So it binds to the CDKs or the cyclin-dependent kinases. At the end of the G1 phase and commits the cell to DNA replication.

So the cyclin is produced. It will trigger this G1 to S phase. It will trigger the cell to go from G1 to the S phase, and then it gets degraded. Now the second cyclin comes in, which is the S-cyclin. S-cyclin binds to CDKs during the S phase and is required for the initiation of DNA replication.

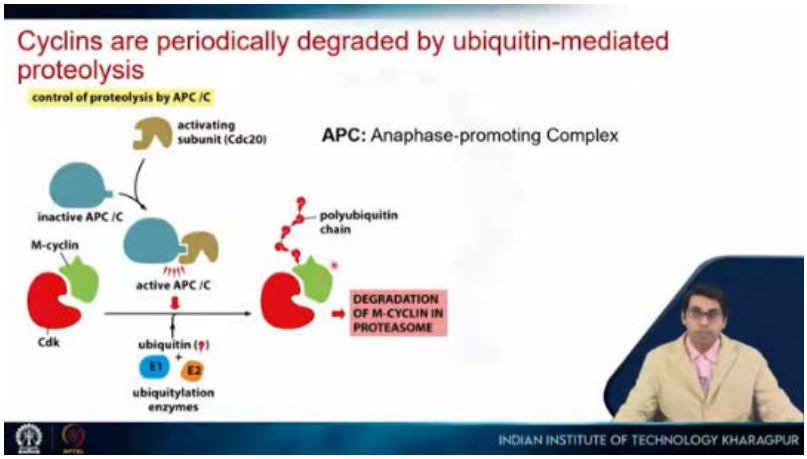
So it will be present throughout this, and then it will get degraded. And then the third one comes in, which is the M-cyclin, which promotes the events of mitosis. So it is produced here, and then again it is degraded. So, these cyclins, their production and degradation, will drive the cell in a particular direction. That is why the cell cycle happens in this unidirectional manner.



So, again, going back to this. We know how cyclins are produced. So we have already gone through this. Gene expression happens, mRNA will be produced, and from that, protein will be produced. So we can control the production of protein by controlling the production of messenger RNA.

Which is transcription. But how do we ensure the protein is degraded once its job is done? Because proteins are quite stable molecules, there are active components inside the cell which degrade proteins. So take, for example, this cyclin, M-cyclin.

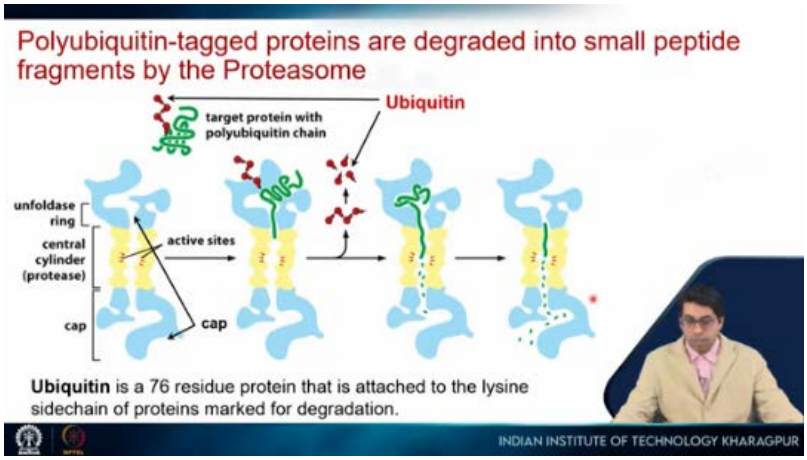
Once its job is done, it will get tagged by certain molecules or certain proteins by a molecule called ubiquitin. So ubiquitin gets tagged onto this, and once that happens, the protein degradation machinery, which is called a proteasome, will know that this protein is marked for degradation. So it will catch that protein and degrade it. So that is shown here.



So this is a protein that is tagged by ubiquitin. So ubiquitin is a very conserved molecule. It consists of 76 amino acids and binds to the lysine of the protein. So the lysine side chain of a protein, which is to be degraded. So on that, ubiquitin is marked.

Now the proteasome will know that this protein has to be degraded. So it will bind that. It will denature it. So using mechanical force, it will denature the protein. It will strip off the ubiquitin because you don't want to degrade that ubiquitin.

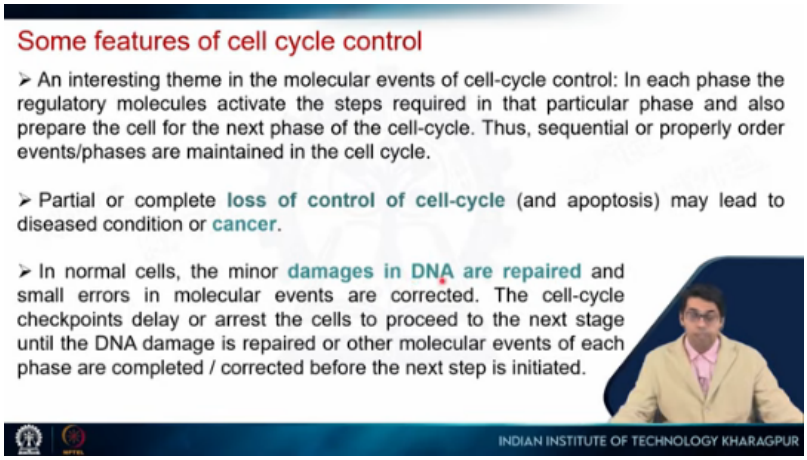
You want to recycle it, and then it will chop up this protein into smaller fragments, smaller peptides and then those peptides will get degraded by other proteases into amino acids. And those amino acids will be recycled to form new proteins. So here are some of the features of cell cycle control.



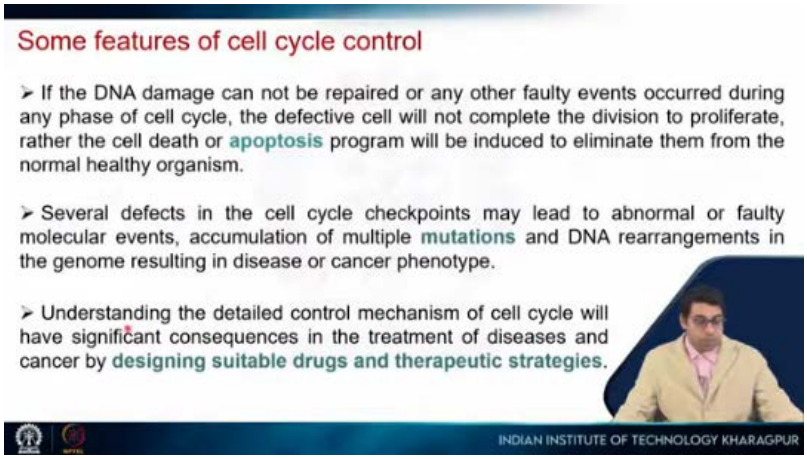
Right. So it's an interesting theme in which molecular events of cell cycle control that we have seen. So here, each phase activates the next step right. and in that particular phase, it also prepares the cell for the next phase of the cell cycle.

So a current phase will prepare the cell for the next step and once everything is favorable, it will move the cell into the next step. So the sequential or properly ordered events are maintained in the cell cycle. Partial or complete loss of this cell cycle can result in disease conditions such as cancer. In normal cells, minor problems such as DNA damage are repaired.

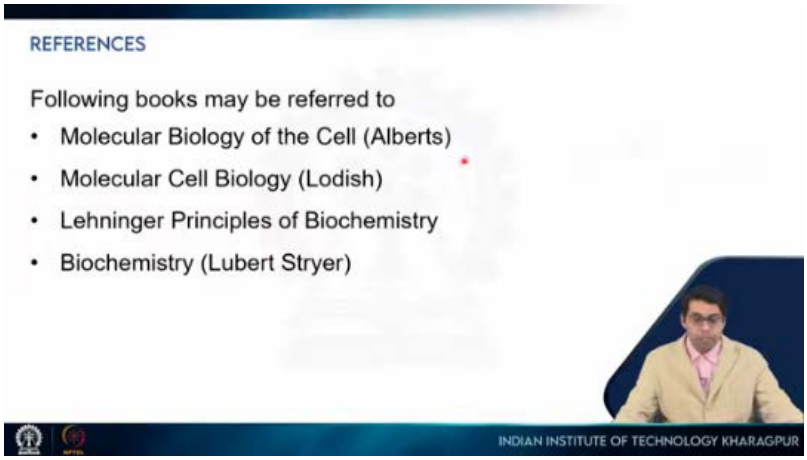
So there are proteins which continuously ensure that there is no DNA damage present. If there is any, then they will repair it and halt the cell in that particular phase. Once all those damages are repaired, the cell will move on to the next step. If the DNA damage cannot be repaired, the cell will trigger a particular event called apoptosis. So it is programmed cell death.



So you don't want that damaged cell to be present in the organ. You want to eliminate it from the organ. Now, several defects in the cell cycle checkpoints may lead to abnormal or faulty molecular events. So the accumulation of multiple mutations and DNA rearrangements in the genome can result in disease phenotypes such as cancer. So understanding the detailed mechanism of this cell cycle control can help us develop treatments for these different diseases.



So these are the books that you can refer to. So the first two is very important. You can go through these books for today's lecture.


REFERENCES
Following books may be referred to
• Molecular Biology of the Cell (Alberts)
• Molecular Cell Biology (Lodish)
• Lehninger Principles of Biochemistry
• Biochemistry (Lubert Stryer)
INDIAN INSTITUTE OF TECHNOLOGY KHARAGPUR

Thank you.