Introduction to Developmental Biology
Prof. Subramaniam K
Department of Biotechnology
Indian Institute of Technology Madras

Lecture No-01
Introduction

Firstly, a few basics about exams and syllabus. So that is what we will go through so that is coming one after.

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So this is the course content. The course content has two main headings: principles and then early embryonic development. So the main focus within the next 40 lectures also is to master the principles of developmental biology. So these are basic concepts that apply to development in different contexts meaning in diverse organisms, so these are fundamental principles.

So that is our main goal, and then a detour we will also get into an introductory series of lectures on genetics because oftentimes I find some students are really weak in genetics and genetics is a central theme in developmental biology. A whole lot of developmental biology we have learned from genetics. So the second part I am sure we will find enough time to go to the second part, early embryonic development.

So, we are going to focus on the very early part of embryonic development which has a lot of conserved features among organisms. So what we will not cover are the developments of individual organs of a multicellular organism, so that we will probably do one or two examples but we are not going to talk about for example in mammals; How heart develops? How does the brain develops? How the liver develops like that.

We are not going to get into those details that are not possible in an introductory course, so this is the course content.

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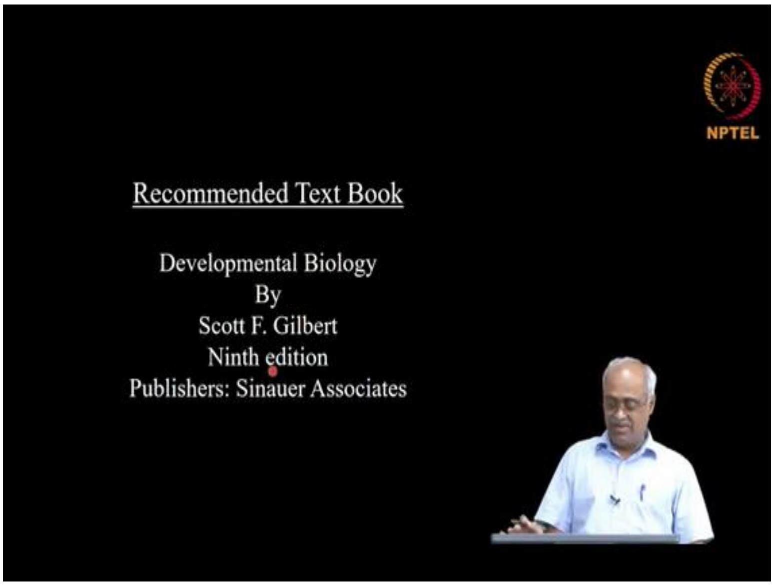

So, now this is the book 9th edition or 10th whatever 9th and, after 9th any of the editions of this developmental biology by Scott Gilbert will be the textbook and reading that one book will be good enough. So not the entire book, whatever we are covering those chapters, so that has pretty much everything I am going to talk about.

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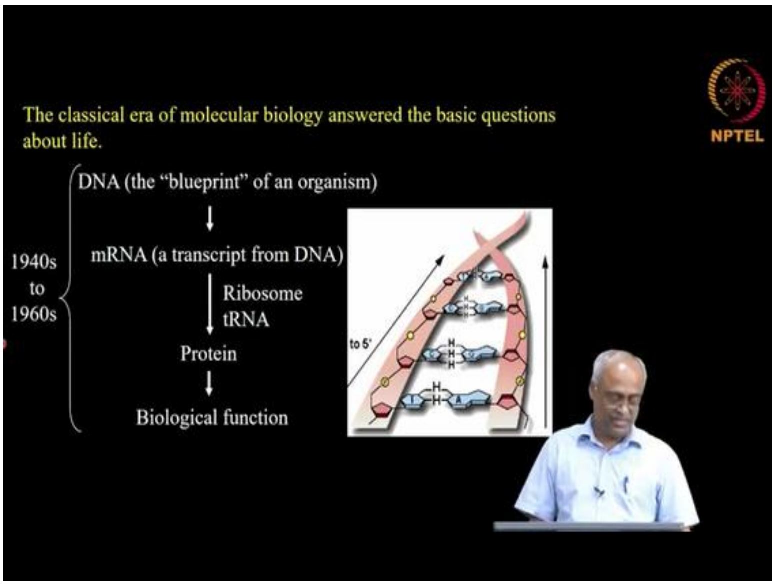

So let us now begin, before we get into developmental biology, so what we are going to do is we are going to look historically how we came to where we are right now. So, if you go back a couple of centuries, people did not even know living things are made up of the same elements that are there in the periodic table. So, therefore Erwin Schrodinger wrote a famous book, “What is life?”

And that quest that is there eternally in the human mind got largely answered during this period in the 1940s to 60s, the classical era of molecular biology. By the time the biochemists have already shown that living cells are made up of the same elements from the periodic table and we obey the laws of thermodynamics everything; the soul, mind, those ideas died.

And we learned that living things can be investigated the way we have investigated non-living parts of the world and this classical era of molecular biology answered some of the central questions that are like, what is the genetic material? We know it is the DNA and we know how that gets copied for replication purpose and then that information is copied into mRNA and then translated into protein and proteins do the function.

So this is largely answering biology at the cellular level quite satisfactorily and that is why it is called the golden era or classical era. So once this is done then to address that question what is life, what is left after this?

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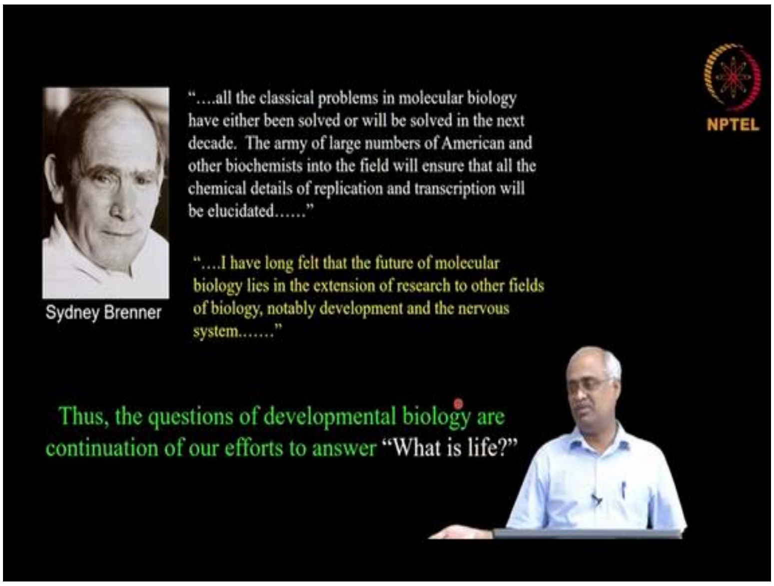

And that is where, one of the main players during the Classical era, Sydney Brenner in a letter to the MRC chairman Medical Research Council Chairman he proposed what to do now? We have solved this DNA to protein, genetic code, translation, tRNA, ribosome, all those that all figured out. So then he came up with this, read this patiently, “All the classical problems in molecular biology have either been solved or will be solved in the next decade”, this is in the 1960s okay 63, I believe, Then you have the sentence “the army of large numbers of American and other biochemists will fill up the details” not major concepts, he thought those are all details. “They will handle all of that the chemical basis of whatever I showed you in the previous slide, so what is the big question for him in the continuation of answering what is life? I have long felt that the future of molecular biology lies in the extension of research to other fields of biology notably development and the nervous system”.

The point is what I showed you in the previous slide are at a cellular level; now how different cells interact among themselves in a multicellular context. So, that is what development is. So he thought that is the natural extension of following the central question of biology so in that sense the questions of developmental biology or continuation of our efforts to answer what is life?

So in that sense I view developmental biology is the center of learning biology, it is a continuation of learning biology,and not surprisingly most of the advances in cell biology techniques like imaging and molecular biology techniques are often developed to address the questions of developmental biology, So, that is what gave rise to all those advancements in technology.

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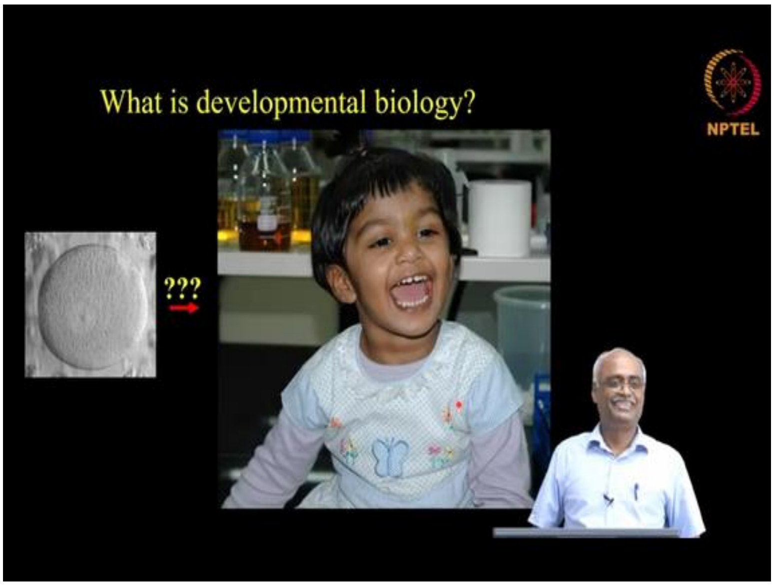

So this kind of set the stage to be attracted to developmental biology, now let us think what is developmental biology? Extremely simple you do not even need a word to define images that will be enough. So this is a human oocyte, a symmetrical cell the cytoplasmic contents are uniform, there is not any gradient of molecules from one place to another place you cannot even tell which is top and bottom, which is dorsal or ventral; it is a symmetrical sphere and from there you get to this baby. Is not it very wonderful, this is the most wonderful thing on earth. This complex transformation that happens and that answering these questions is what is developmental biology. So, now let us move on. So, what are the central questions that one wants to understand in this process? they are here so that is the primary focus of today we are not going to get into very specific topics in developmental biology because today's introduction I do not want to speed up very quickly.

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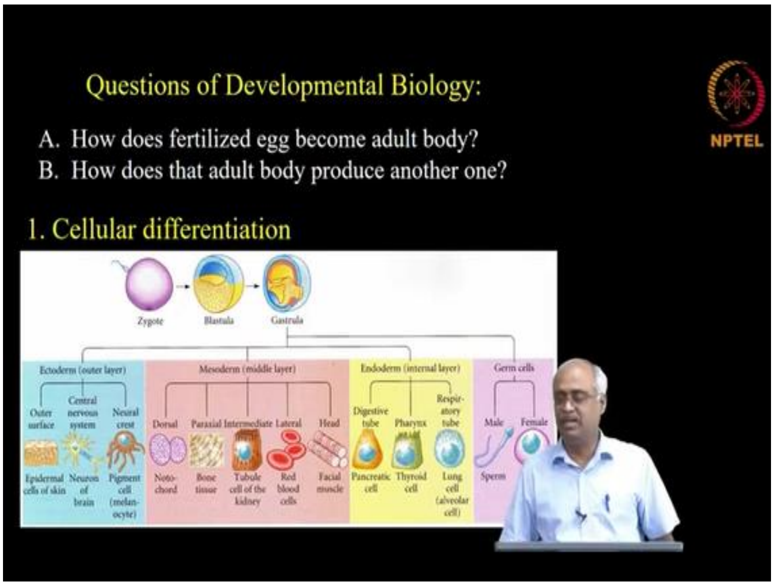

First, there are two broader questions; then within that, we have sub-questions, so the broader question is the first thing. The egg that we saw how does that become the adult body?. So, that is one broader big question of developmental biology. Second, how does that adult body make another adult body? So, these are the two big questions of developmental biology.

And now, let us break it down to addressable levels the first one is cellular differentiation. So, you might think I understand mitosis I have learned how that works in cell biology class, so the embryo undergoes divisions and makes a lot of cells but will a lump of cells make you, you? No right? So, you are not a lump of cells, you have a lump of different kinds of cells right and how cells that are identical become different kinds of cells?

So that is the process of cellular differentiation, so what are the kinds if you are wondering it is given in this picture. Yeah So, you can see at the left end you have epidermal cells your skin cells, nervous system neurons, these two do not look alike and so on if you go, the pigment cells are very different then notochord that will come in the embryo that is a transient structure. Bone cells are very different from the nephrons of the kidney right? Red blood cells have no resemblance to any of the other ones we saw, muscle cells and digestive tube cells, the intestinal mucosa, if you look at the gland cells the thyroid cell for example and the lung alveoli so, and then the gametes the most important of all: sperm and egg.
So these are different kinds of cells and how cells differentiate? That is one of the most fundamental questions in developmental biology.

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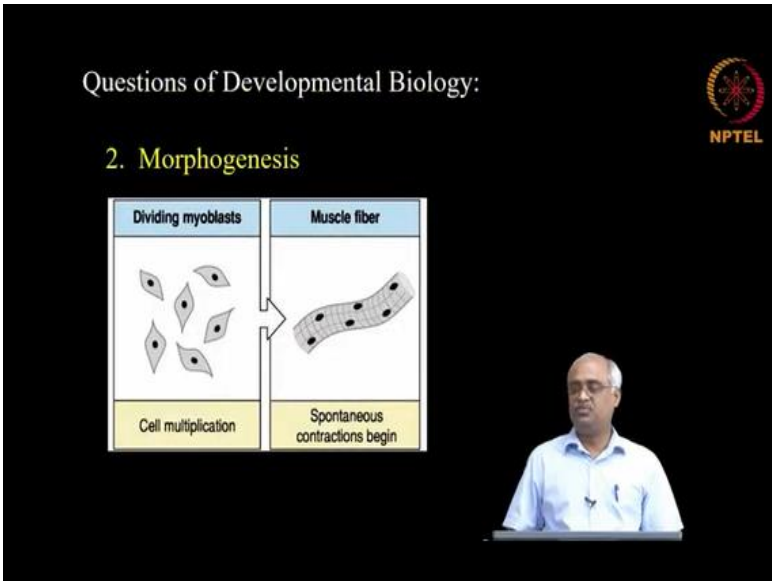

And second, morphogenesis, so okay fine I know how to make neurons okay I made a lot of neurons will they become brain will they become spinal cord? No, so they have to organize and take specific shapes like for example here myoblast, the muscle cells, lump of muscle cells will not become muscle fiber that is not going to help you to have contraction and relaxation. So they have to arrange and take a shape of the muscle fiber and that shape formation is what morphogenesis is. How does that happen? So that is another important question in developmental biology. So going through these questions helps you to get an idea of what is the scope of this course, what am I going to learn at the end of it.

So, I am talking as if these are the outstanding research questions but at the same time, this gives you an idea of what you are going to learn in this course.

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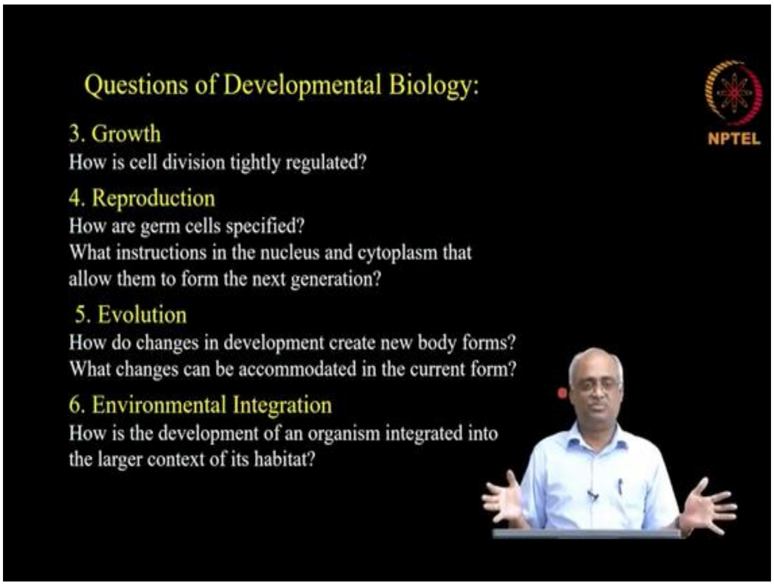

And, the third is growth, so growth does not think okay, I eat every day and I am growing. You pour water and fertilizer the plant grows, what is big deal about growth? But if you think about growth, you will realize it has to be highly coordinated. For example, if you stretch your hand, you will find up to the tip of the longest finger exactly both hands are the same size. They are identical; you can try like none of you will find one hand is a little bigger than the other hand and your face, imagine that to make your face from your infantile stage a lot of cell divisions must have happened right, so one more extra division big deal? 100 times it divided, 101 will it be very different? But yes that will be double the size of your current face. Just imagine one more division you would be a Frankenstein monster you will not be what you are.

And just imagine these were not coordinated in different parts of the body, suppose your nose cells divided double the time and your ears, one ear was one division less what will happen? Your body will not be proportional and there will be no functionality, so growth is highly coordinated. So, how does this coordination happens? So that is an important question. So the next is, I find this most interesting because without which evolution is not possible we would not be existing here. So that is reproduction, only a homo sapiens can give rise to a homo sapiens nothing else, none of the other organisms the wide diversity that exists none can produce, same is the case for any other species, so how the reproduction happens? So how are the reproductive cells specified? How do they remain different from the rest of the body? So these cells are the germ cells, they are the ones involved in reproduction.

They are the only ones that can go from diploid state to haploid state and by fusion in fertilization can restore the diploid. How are they specified and how come they remain different from the rest and what are the instructions in their nucleus and cytoplasm? Remember the oocyte cytoplasm brings a lot of things for the embryonic development, so what are they in these two cellular structures that help them to form the next generation?

So these are the questions of reproduction and the fifth is evolution, so nothing in biology makes sense except in the light of evolution. So do not forget this sentence you just cannot understand biology without really understanding the evolutionary cause and the functional consequence of any of the processes you are looking at.

And now in the developmental biology context, there is an important thing, the changes that are necessitated by the adaptational requirement to the environment must be possible within the existing body structure. When you are trying a new change for fitting into a new environment the existing organisms should not be dying. So, the modifications that are required will have to be permitted by the existing developmental plan, the body plan.

So, therefore the development constraints the possible routes of adaptation, and in that sense, you need to consider what is possible in the current developmental plan to see what adaptations are possible, so in that sense evolution and development are very intricately linked, so changes in development is what gives rise to adaptation and that is what gets selected during natural selection.

So evolution is a central question in developmental biology. So how do changes in development create new body forms and what changes can be accommodated without compromising the survival of the organism, so that is important. So a dinosaur becoming a bird cannot happen in one step, without endangering its current ability to exist as a dinosaur, so that is just to give you an example; then we cannot forget the environment because an organism adapts to a given environment and as we just saw that has to be accommodated in the current development. So to give you an example which is there in the book as you may have already heard many reptiles their sex determination, whether it is going to be male or female is dependent on the temperature, and sometimes chemicals in the environment also influence an organism's ability to develop.

So therefore in the larger habitat, habitat means in the place and community and the ecosystem in which an organism survives how does the developmental plan fits into it, like for example a succulent plant is better fit to live in a desert environment, So you cannot go and grow paddy there, so the developmental plan of paddy or the developmental plan of a cactus is integrated into the environment, the habitat where they grow.

So in that sense, we need to look at the environmental aspect as well, so these are the major questions in developmental biology. So, it pretty much touches all areas of biology.

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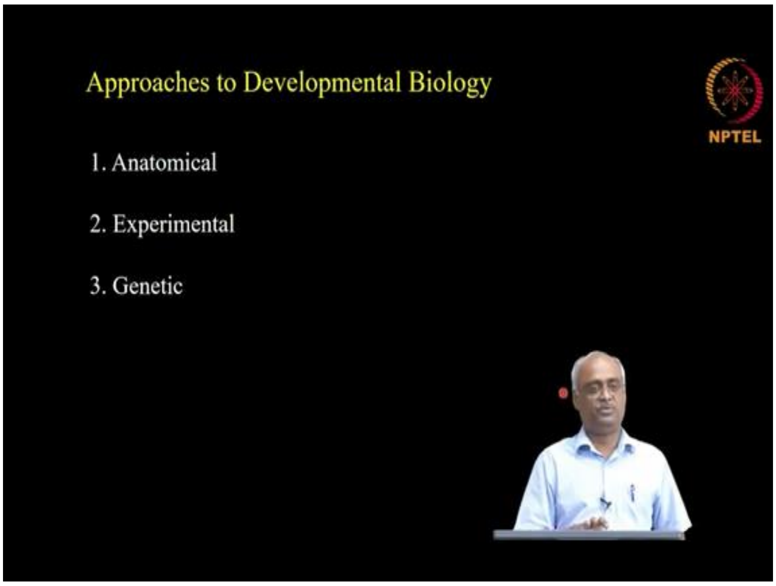

So we move on, so how do we study the development of an organism? So people over the period time they have used to different approaches, initially, when the tools were very primitive or non-existing they simply did the observation of embryos. So essentially anatomical approaches we call them anatomical. You simply look at the anatomy of an embryo of a particular species and compare it with another one and so on.

And then you come up with the common themes for example the things give birth to a baby directly are viviparous and some lay eggs and the eggs hatch, they are oviparous,and so on. They made classifications and they saw certain general themes and principles. So, that is the anatomical approach this does not mean I am talking the only history, currently, also it is very important.

Like for example; when you are going to define a particular developmental defect at a single-cell resolution you are expanding that anatomical observation, so it is there inter-twinned with the modern-day approaches. Then once they did that, they try to disturb the embryo and see what happens, if a perfectly spherical embryo divides if it has certain planes of cell division if I just compress will that change and what kind of changes happen and as a result what kind of cells form?

So they started experimenting, which is called experimental approaches. Then when genetic tools became available people started using genetic approaches, for example trying to find mutations in which a particular development does not happen, when you find that is inheritable you have identified a gene that is responsible for the development, so that is the genetic approach.

So you might think, that is the approach that is predominating now but the other two are also intertwined with this, all three are being pursued as of now, but they are sort of historical Initially it is anatomical that gave rise to experimental then later genetics and now it is a combination of all three, so these are the major approaches used to understand development.

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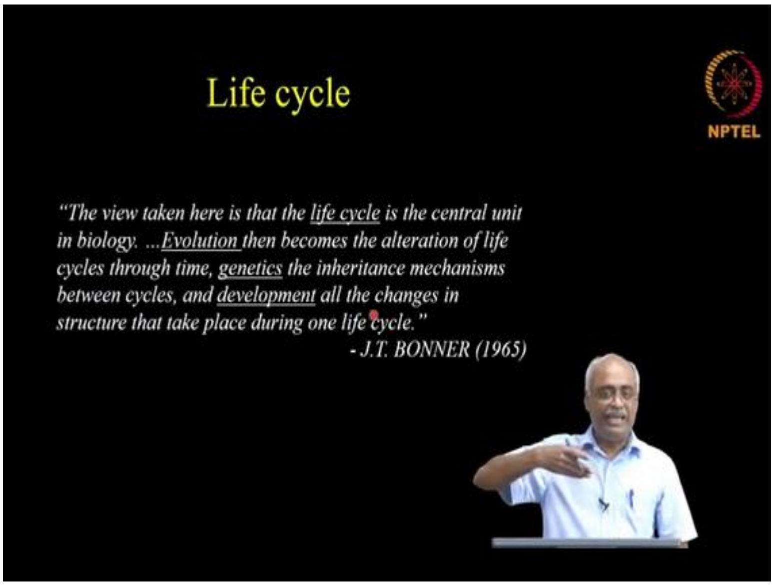

So now before we go further these anatomical and experimental approaches that were there early on, and gave rise I told you certain general themes and one of them is a generalizable lifecycle of multiple organisms, so multiple-meaning I mean diversity of organisms. So you might find organisms extremely diverse but actually if you look at their development from fertilized egg to either hatching or coming out of the mother's womb which is called embryology. So that is the old name for developmental biology.

So embryonic development is what we call developmental biology and now we have learned that development happens even after birth it is not merely growth to give you an idea like every time a differentiated cell dies for example your skin epithelium falls of new skin cells develop. So, development is a continuous process in that sense but earlier people thought that development is only from fertilized embryo egg to hatching.

That is what people thought and that is why it was called embryology, so that period came up with a generalizable life cycle. So, therefore it is appropriate to start our understanding of development by starting with a life cycle, a generalized life cycle that breaks down development into subtopics and therefore we can focus on each one of them.

So, this is a famous quote which is there in the book and I liked it very much and that is why I got this because this actually in five lines defines some four fields very, very clearly. The view taken here is that the life cycle is the central unit of biology starting from fertilization to becoming a sexually mature adult. So that is a central thing here and evolution then becomes the alteration in the life cycle through time from one style of the life cycle to another style. So that alteration is evolution.

It is now easy to understand you know is the process of change that transforms the life cycle and genetics is the inheritance mechanism between cycles, how do I go from one adult body to another body and that is genetics, how that information goes? What are the principles that govern the biological information flow from one generation to another generation and the development of all the changes in one life cycle?

Classically people call it phylogeny and ontogeny; ontogeny means all the changes that happen in one generation, phylogeny means changes over the period of evolution meaning from among multiple life cycles is this clear. So with this quote, we will look at a generalized life cycle but the pictures shown here in the cartoon are that of the frog.

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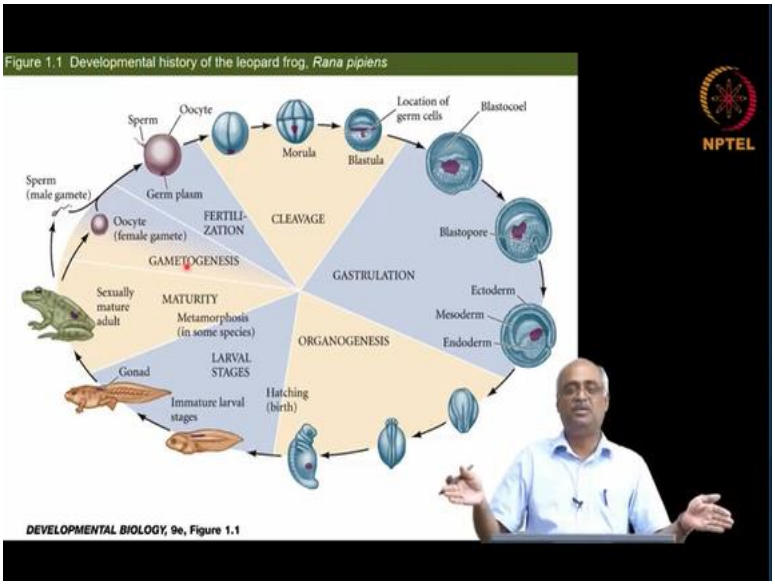

But that applies to most organisms, so the major stages are in the capital letters; fertilization, cleavage, gastrulation, organogenesis, then metamorphosis because there is variation in some organisms, so you have the maturity or larval stages then your gametogenesis. So these 1, 2, 3, 4, 5, 6 stages are the major stages.

So the first is fertilization, so that is a remarkable thing that happens. How many of you know what the cell division stage of the mammalian oocyte is at the time of sperm entry? In most organisms, they are arrested in meiosis one but the stages vary. Some at the end of the prophase one and in some it may be different.

So essentially they are arrested in meiosis one and the sperm entry initiates the oocyte nucleus to complete the meiotic division and then the cellular fusion that the cytoplasmic condense fuse you may think, the entire cytoplasm is from the oocyte and what did the sperm bring? It is the centrioles. The oocyte will not have centrioles the centrioles come from the sperm. So, therefore first to you have the cytoplasmic fusion then once that happens then the nuclei fuse the two pronuclei and you have the diploid genetic material, the entire genetic material is required for the fertilized egg to transform itself into an adult body.

So all of this happens in fertilization, so how each one of these steps triggered and regulated is the question addressed in fertilization and then you have a huge cell comparatively like the oocyte in most organisms is bigger than the other cells of the body and that is then divided into multiple small compartments and that is why you do not say here cell division instead you say cleavage, so basically you are partitioning the cytoplasm into smaller cells.

So this is the fundamental difference between a normal cell division and cleavage in the embryo and each one of those partitioned cells, so meaning you are obviously replicating DNA and therefore you are making multiple nuclei and each nucleic gets smaller portions of the cytoplasm. So that is how it is compartmentalized, so do not think that in this compartmentalization the nucleus is lost in one cell and not in others.

And each one of these new cells formed during cleavage is called the blastomeres and at the end of this cleavage stage you call that embryo a blastula. Then, how this cleavage is regulated? This happens in a certain pattern you just cannot have anything going wrong here. It is like you are done all the rehearsals and backstage arrangements now the concert started now you have to play the music or if it is a dance you have to dance in the right way.

Now you cannot choreograph once it started it just cannot happen and it goes there and no stopping of it just goes on and that has to happen in perfect order no errors, the possible error means death; that is the end of it. So how all that happens? So that is what we learn in the cleavage. So then the next one is these cells now undergo rearrangements, they migrate and rearrange themselves into three major layers we call them germ layers: ectoderm, mesoderm, and endoderm.

So these germ layers are formed by migration and rearrangement of these blastomeres and then that process is called gastrulation. So here you still do not have major differentiations that are going to happen, so you should not get confused with the migrations and differentiation that are going to happen later. So here primarily rearrangement of the cells into three major layers we call germ layers and the end of that you call gastrula.

Then cells of these three layers interact among themselves and undergo further rearrangements and migrations to give rise to specific functional shapes which we call organs and that is the organogenesis. So that is how you have muscle cells making muscles and you know cells from ectoderm for example they make our skin epithelium, they make the neurons, they make the melanocytes the pigment-producing cells that protect us from the UV radiation.

And you know the inner gut lining by the endoderm and mesoderm making many of the internal organs and some of the organs do have cells from the different layers, it is not that these layers are completely you know independent. So they interact mix as well as induce or get induced by the other cells, all those go on in making organs and then that ends in the birth or hatching. Then once they hatch it is not right away ready, when do you call ready? only when you are a sexually mature adult. So adult by definition is a sexually mature organism of that species. It should be able to reproduce when the life cycle ends. So the life cycle by the way is different from generation time, generation time is the time an individual member of a species exists from birth to death.

Life cycle means from birth to the stage where you can reproduce. So remember these distinctly oftentimes you know some people get confused. So when they come out from the eggshell or come out of the mother's womb they are not right away ready, so they undergo what is called maturity and this maturity in many organisms involves what is called metamorphosis that is because what comes out does not resemble the adult.

As you see in this example you know the tadpole does not look like the frog; the silkworm does not look like the moth; the same goes with butterfly and in many organisms. The adult stage is a fleeting moment of the entire lifecycle. Some of them spend most of the time in the larval stages, in most organisms early forms that are different from the adult form are called the larval stage and these larvae feed and they exist for a longer time in some of the organisms. The bulk of the time of the lifecycle is spent as a larva for example in moths they just come out without having the ability to eat, so whatever the moth ate and stored is what it is going to use to find a mate and lay eggs and die. So do not think each of these stages is constant in terms of relative duration across species.

So we may be living as adults for a very long time but that is not the case in other organisms. So how this maturity is regulated, some people think this is very fascinating; going from the larva that comes out and how that changes into the adult form. People think that is very remarkable and they study metamorphosis in great detail particularly those who study butterflies and moths and of course frog as well.

So this is the summary of the life cycle so basically when we are talking about development we are talking about one of these six processes or a sub-part of one of these processes. For example in our lab we focus on cannot be even called fertilization, it cannot even be called gametogenesis; we focus on a certain aspect of gametogenesis that is what we do.

So each one of them has a lot of interesting specialized questions but this gives you the broader picture; this helps you to map yourself in the broader theme of an organism’s development where does my work or my learning fit. So that is why the life cycle is our starting introduction here.

I will try to tell you some other ways of looking at development. So there is another way of looking at development by comparing to the rest of the non-living world; you just compare an organism development versus a machine building. Can an airplane fly while being built? No right. Can a bicycle be used to go from point A to B while someone is assembling it? No, but organisms while being built are functional; at no point of time, they were dead. So the book goes into telling in very specific details: you breathe while lungs are still forming, you arrange neurons without even having learned to think, and so on. Circulation happens without even building an artery, so all of these things happen. So here it has to function while it's being built, so some people think that is fascinating about development. So like this, you can look at in many, many ways how you know the developmental process is very amazing. So what I find interesting is whatever I have read I have not found anything in the universe where the matter organizes in a more complex way then what happens in development. So when you think of other aspects in the non-living world, what you will find is the scales are enormous but not the complexity or diversity of the process but, here you find that to be extremely complex. You know that first slide where you go from human egg to the baby.

So that is fascinating, you can break down and be interested in metamorphosis or whatever but the end is from this cell to this infant. So that is the big thing. So to further clarify what developmental biology deals with is looking at the way we question different things. Like for example, a geneticist may be interested in how particular genetic information goes from one generation to the next generation.

For example, if you take any gene let us say a gene of an RNA binding protein tries regulating translation. So that is what fascinates me therefore I am picking up that example. So a geneticist may be interested in knowing how this particular gene gets transmitted from one generation to the next generation and a biochemist may be interested in knowing how does this RNA binding protein ends up regulating the translation of this particular mRNA?

But what a developmental biologist asks is why is this particular RNA binding protein produced in these cells but not in those cells? Okay, like for example the genes that we study in our lab why are they expressed only in germ cells and not in my brain or heart or liver, why are they only in germ cells and the other thing is why only at a particular time during development?

Why does NOS-1 protein is produced only from the zygotic primordial germ cells in the embryo but not otherwise? So, this can be summarized in two major things one spatial regulation of gene expression, second temporal regulation of gene expression that is the time. You know why at this stage of development not at other stages, the first one is why in this organ or tissue and not in another organ or tissue.

So this spatial or spatiotemporal regulation of gene expression that is the central thing that we are going to finally come out of this course. So, that is what we are going to finally learn alright with that I end today's lecture.