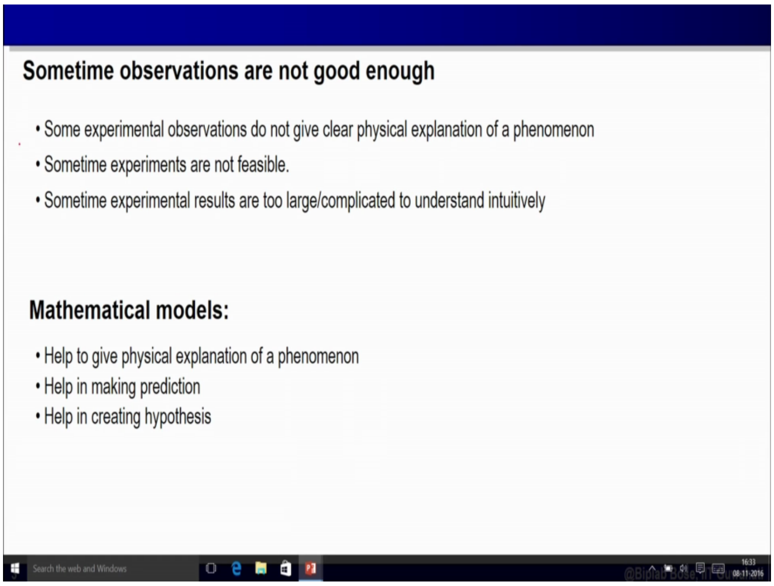
**Introduction to Dynamical Models in Biology**
**Professor Biplab Bose**
**Department of Biosciences and Bioengineering**
**Indian Institute of Technology Guwahati**
**Module 1**
**Lecture No 1**
**Mathematical Modeling in Biology**

Hello, welcome to our course on Introduction to Dynamical models in Biology. This is week 1 and this is model 1, here we have general discussion on modelling in biology specifically in dynamical models in biology. As a biology student, you must be aware that once upon a time biology used to be just like star gazing. You can look at the star, you can observe the motion, but you cannot actually change its position and do experiment on the star. Biology used to be like that once upon a time; you can observe a bird, you can observe a flower, you can measure the size of a lizard tail, you can note them down but cannot actually change, manipulate that biological form, life form.

But biology has graduated from that observation based science and now we can actually decide what type of experiment we will do based on our hypothesis. Based on our requirement we do interfere with the system, you inject a drug in an animal and then study how its blood pressure is changing. If required, we genetically modify a bacteria introduce a new genes in that to see what will be the effect of that genes on the bacterial metabolism or bacterial survival. You create a whole new organism a transgenic mouse to do your study, to understand the effect of the gene on the physiological development of the mouse, these are very common. And we have graduated from the days of measuring tail length, and colour of flower, now we have a diverse type of data. We have genomic data sequences of genes, AMRE sequence, genomic sequence, sequences of micro aranais. You have large amount of proteomic data, which tells about which protein is expressed in how much amount in different types of cells in human body.

We have data on structure proteins; we have network maps showing interaction between different molecules. So we have huge amount of data now in our hand and everyday thousands of scientists are generating different forms of data in different biological systems. These observations is key in understanding how life works and that is how we have made progress tremendous progress rather in understanding living systems. But sometimes these data or observations or experimental observation rather has some limitations and that is where the mathematical models come into play. For example, suppose you have treated someone with a drug and you are doing a dose dependent experiment; you are treating yourselves with different doses of drug. You observe that particular phenomena happen only when you are using a higher amount of the drug.

(Refer Slide Time: 4:17)

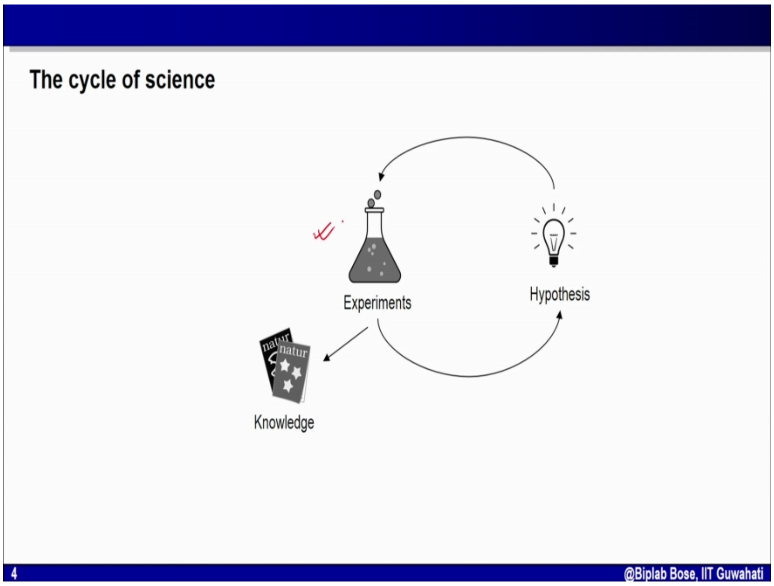



So through experiment you have seen the phenomena, you may measure changes in some molecules as you are treating the cells with the drug and you may have seen that also has a dose dependent behaviour. Now the question comes, why do we have a dose dependent behaviour? Your experimental observation many a time may not give you a clear clue. Rather you can make multiple hypothesis, create mathematical models for them and then taste those models using models and identify which hypothesis is correct and then go back and design the experiment to check whether whatever your mathematical model is telling is correct or not. So in a sense, I can have limitations of my experiment where my experiments cannot give a clear physical explanation of phenomena. But take another case; in that case you actually cannot design experiment.

For example, I am studying suppose the evolution of the gene P53 which is present in human. So I want to know step by step how the P53 gene has evolved. I can know the sequence of P53 right now in different organisms, but the sequences P53 in those organisms which were our ancestors and already disappeared from earth I have no option to know those sequences. So I cannot design experiment to know, what the sequence of P53 in those organisms was. We all know that we draw a phylogenetic tree to understand the evolution of sequences, nucleotides and amino type sequences. In those cases to understand the ancestor and the evolutionary process of the gene you cannot actually do the experiment. In some cases, you can do experiment and you are actually doing experiment but the amount of data generated is huge.

For example, you are doing genome skill study, you are doing proteome skills study; you are screening drugs using proteomics and genomics too. You are generating a huge amount of data and to distil out of that data and to understand that data intuitively is very difficult for us human being. In this case also, building a mathematical model may help you to distil out the observation and to create new hypothesis or make new predictions. So in a sense as I have said and written down here, is the mathematical models are nothing but complementation to your experimental observations. They may help you to give physical explanation to phenomena, a mathematical model may help you to make predictions and most of the time a mathematical model helps you to make new hypothesis that you can go back in your bench and taste by experiments. Now let us look into how a mathematical model fits into as the whole scientific endeavour we are in.

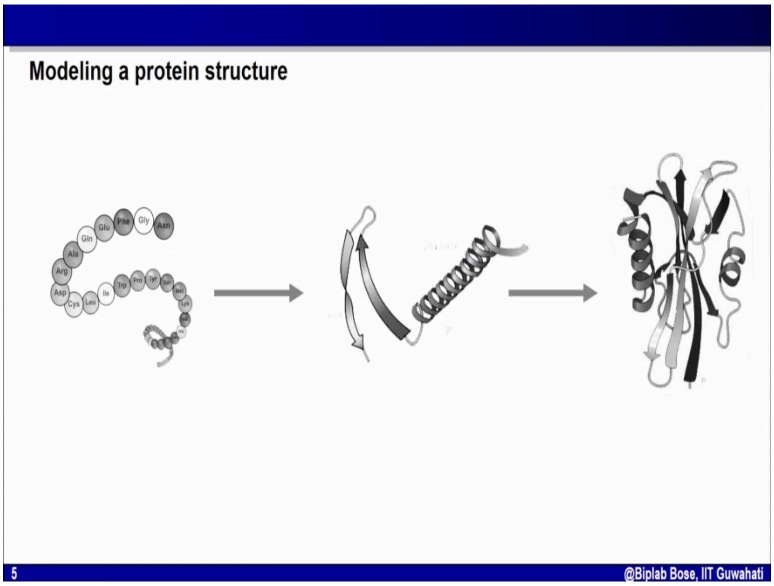
(Refer Slide Time: 6:52)




So in general science has a cycle, it starts with the experiment, you design a experiment in a ideal condition. For example you grow cells in a plate and then you treat them with a particular drug that is your experiment, from this experiment you major some observable and then using that observed behaviour you create a hypothesis. Now, once you have treated the hypothesis, you go back again to the experiment design a new experiment to test this hypothesis. This cycle from experiment to hypothesis, experiment to hypothesis keep on happening and eventually what we get eventually we get is knowledge about the system. So this is a cyclic process of scientific endeavour, mathematical model fits just there. As I said in some cases, experimental observation may not be good enough to understand phenomena or they may be so huge that you cannot actually intuitively understand the implication of that and make meaning out of it or distil out the essence of that observations.

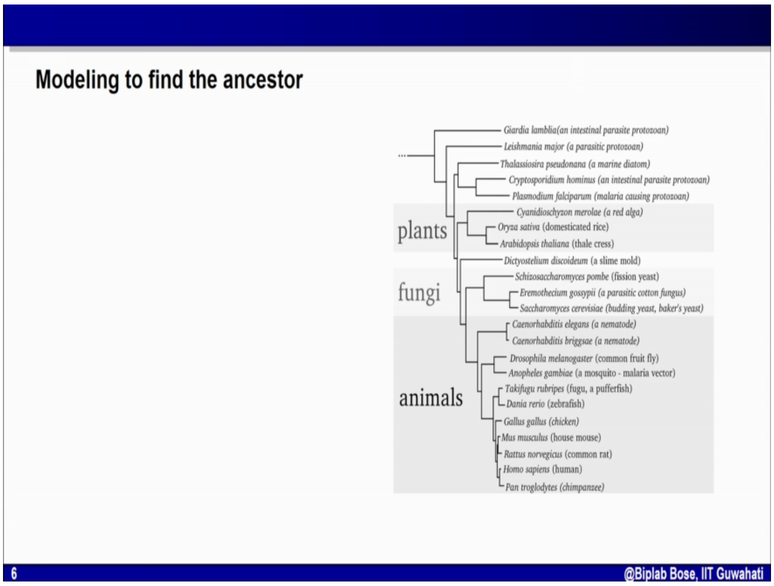
So what you have? You have done the experiment, based on the observation and physical principals that involve you understand you created a mathematical model. That mathematical model helps you to make new hypothesis and from this hypothesis, again you go back to your experiments. So this cycle goes on with experiment, mathematical model, hypothesis building and again experiments and again this way we develop new knowledge. So essentially what I want to say is that mathematical models are actually compliment to your experiments and honestly speaking mathematical models are not new to you. Very frequently structures of protein are predicted by mathematical modelling what you call usually homology model per say.

(Refer Slide Time: 9:11)



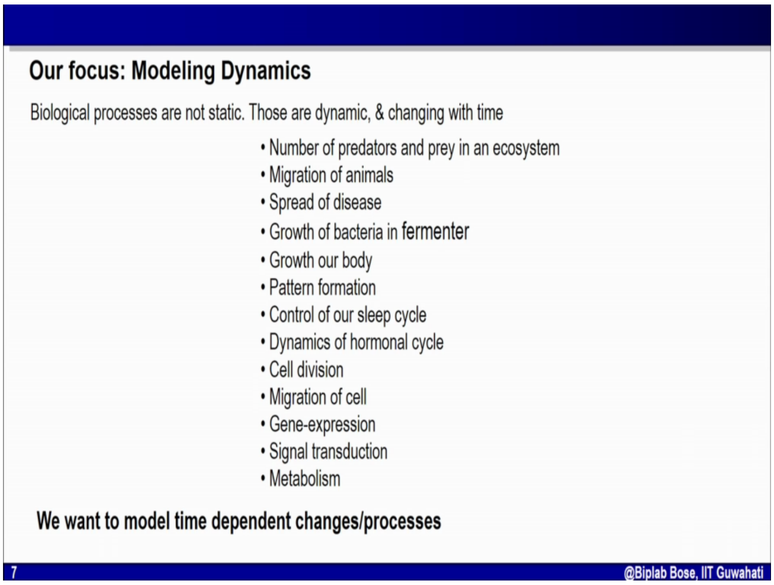

You have a sequence of amino acid sequence of gene, you want to know what type of function it may have, what type of molecule is it, what type of biological function it is related to. As we know, function of a protein depends on a structure so what you do you try to understand the structure of the protein, but if you do not know the real structure of the protein you create a model of that using some mathematical constant and you get a 3D model of the protein, from that you try to understand what may be the function of the protein or you may done the experiment to understand the function, you know what is the function of it. You go back to this 3D model and try to explain that function using the 3D structure and this is very common in biology.

(Refer Slide Time: 9:43)




Another type of model is very common in biology that I mentioned few slides back is Phylogenetic tree. You know the sequence of certain gene right now, you want to know how they have evolved, how they are connected to each other, s you build a mathematical model which you call Phylogenetic tree to understand the evolution of this gene, these types of models are very common in Biology. There is another type of model that is focus of course that is dynamical model.

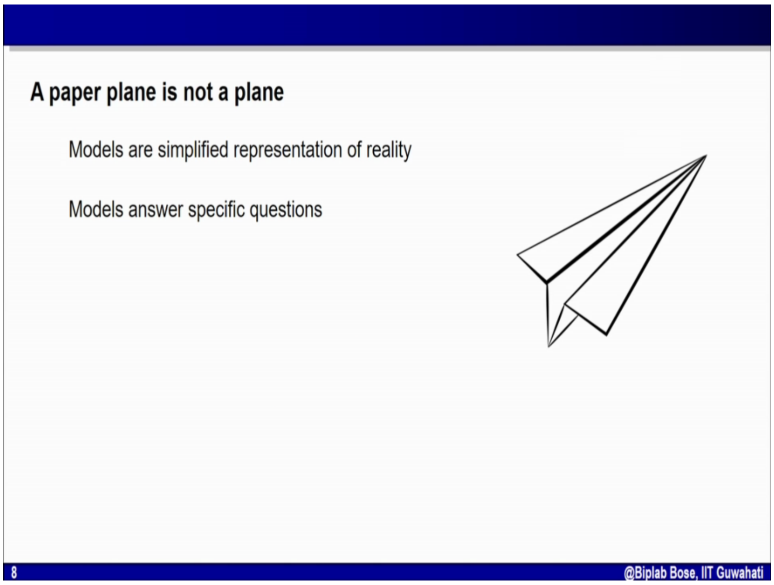
(Refer Slide Time: 10:13)




No living system is static, anything that is living as it processes changes with time which is dynamic. Take the example, growth of a human being, growth of a bacteria in a fermenter or growth of solid tumour in a patient or may be dynamics between a predator and prey in the jungle all these are dynamical system, things are changing with time, take the issue of pattern formation in Zebra or the pattern formation during evolution sorry development of embryo that is changing with time. You can have oscillation in your sleep cycle; you can oscillation and secretion of insulin in your body that is also a dynamic process. If you disturb that oscillatory process your metabolism will get disturbed. If you look at the cellular level the protein production, transcription, gene regulation expression and its regulation all dynamic processes they are changing with time.

Talk about signal transaction, calcium signalling or signalling by the phosphorelay system, these are all dynamic processes. So most of the biological processes from cellular molecular level to population level are actually dynamical processes, and the focus of our course is to how to model these dynamical processes. So we will focus on building model for dynamical processes or systems in biology, and the most interesting thing is that the mathematical formulation, the mathematical techniques that we will use will be the same whether you are using it for a molecular level problem or you are dealing with a population level problem, for example the dynamics between the predator and the prey in a forest. The techniques and the method that we will use will be same.

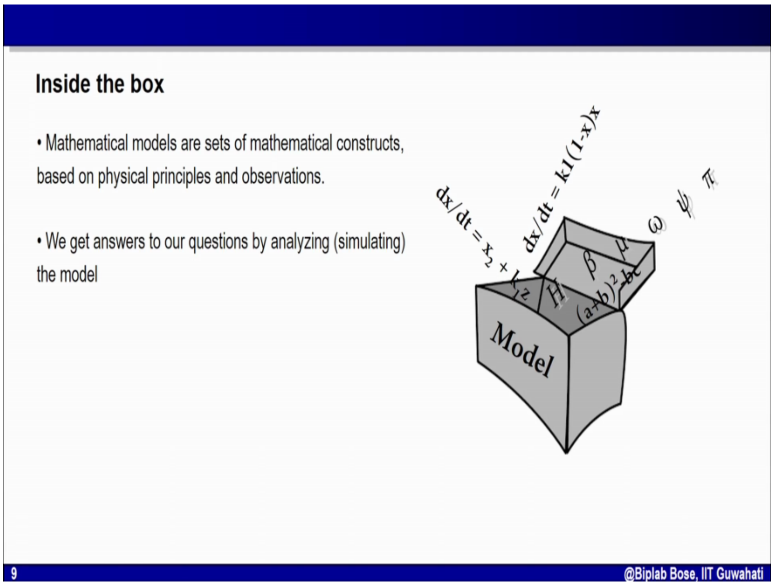
(Refer Slide Time: 12:05)




Before we go further and discuss about it let us understand one key issue, key concept over here. In this course we will build mathematical model for dynamical processes or dynamical models or different models for different biological systems. So we will build models and we have to keep in mind that models are not reality. Let me give you an example; I want to understand flight of a plane, I am designing a new plane or suppose we do not know how plane flies, we want to understand that. I can create a paper plane, that paper plane is a model for a real plane; obviously you understand that this paper plane is not a real plane. But using this paper plane if I fly it I can understand certain behaviour of flight, I can understand how the shape of the plane affects its flight, I can understand the basic phenomena of floating in air, basic phenomena of flying in air.

But obviously using this paper plane you may not ask complicated question like what will happen if there is rain, how navigation system will be there all these complicated questions you may have to answer using this paper plane. So paper plane is a model of a real plane so it is not exactly same of the real plane, it is just a model, it is not a reality. And paper plane can help you to understand only certain unknown things, it cannot tell or answer you all questions about flight of a plane real plane, so all models are like that, all mathematical models whether for a dynamic system or not that we will built are actually a replica, not a exact replica or a reduced replica of a real phenomena that you are dealing with and it can only answer few, certain specific question that we can ask, that we have to keep in mind when we are building models.

(Refer Slide Time: 14:16)

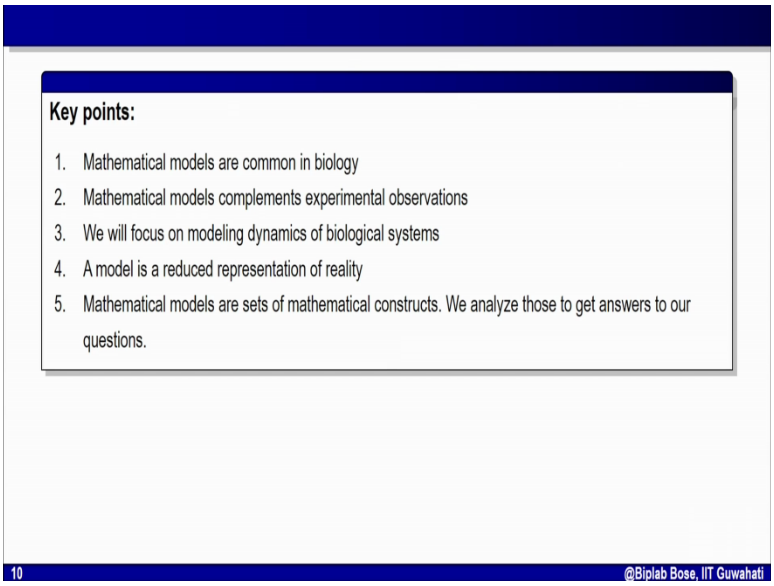



Now the next question comes, then what is a mathematical model, mathematical models are actually nothing but a set of mathematical constants. By mathematical constant I mean it may be a set of equations, for example in the course you will learn how to write ordinary differential equation, set of ordinary differential equations which will create our model, so mathematical model is nothing but a set of mathematical construct which can equations, relation like that. And these equations or relations of mathematical constructs are based on certain physical principal that we believe are playing behind the phenomena that I am studying and based on my observation which is coming from the experiments.

So based on your observation and the physical processes, the physical laws that we know from nature, we build certain mathematical equations and relationship that is our mathematical model. So suppose you want to model the dynamics of P53 in a cell, when you apply your ionisation radiation on the cell, there will be DNA damage and the cell will produce P53 to increase the amount of active P53 and it has been observed that the concentration of P53 oscillates with time, so I want to understand this behaviour. So I will write down certain equation representing these oscillations and those equations will be based on my observation for P53 oscillation of P53 and the physical processes that is going behind this oscillation as I understand. As a whole I will write down some equations or mathematical constant this is my model, now I will ask these questions to this model that means I will analyse these models or sometimes I simulate.

I will use a computer to simulate the behaviour of this model using those equations so that will be simulation. So this analysis or stimulation of the mathematical model will give answer to my questions. So mathematical modelling for example, dynamical modelling in biology will have two part, first part will be to write a right model, write a correct sets of equations and mathematical construct as we believe will represent the process and then you analyse them using the different techniques, some will be using symbolic math using paper and pen, sometimes you will use computer to simulate and analyse the model and that will give you answer to your question that will make prediction what will happen if you do a particular experiment that will help you to create new hypothesis which you can go back and check by experiments.

(Refer Slide Time: 17:16)




So if I jot down mathematical models as I have said is very common in biology, they come in different forms and you have to remember that mathematical models are actually complimentary to experimental observation. They comes in hands in hands and as I have shown from observation of experiments you create a mathematical model that helps you to create a hypothesis again you back to experiment, using this cycle we get knowledge.

And mathematic in our course or modelling, we will focus on dynamical systems and rather we will keep mathematical model to understand the dynamics of different processes. And as I have said models are nothing but a set of mathematical relations, equations, we analyse them to understand the behaviour of the system, the phenomena. We analyse them or simulate them to understand what will happen if we do a particular type of experiment that is prediction. Using these models and by analysing these models we try to make generate some new hypothesis which we can go back and check by experiments.

This is the theme of the whole course, initially we will try to learn the basics of building mathematical model, how to write down those equations, then we will learn how to analyse them and then step by step we will try to build different aspects of mathematical modelling for dynamical systems in biology. Thank you for listening, see you in the next model.