EXCELing with Mathematical Modelling
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Week – 07
Lecture – 32 (Tumour Models 1)

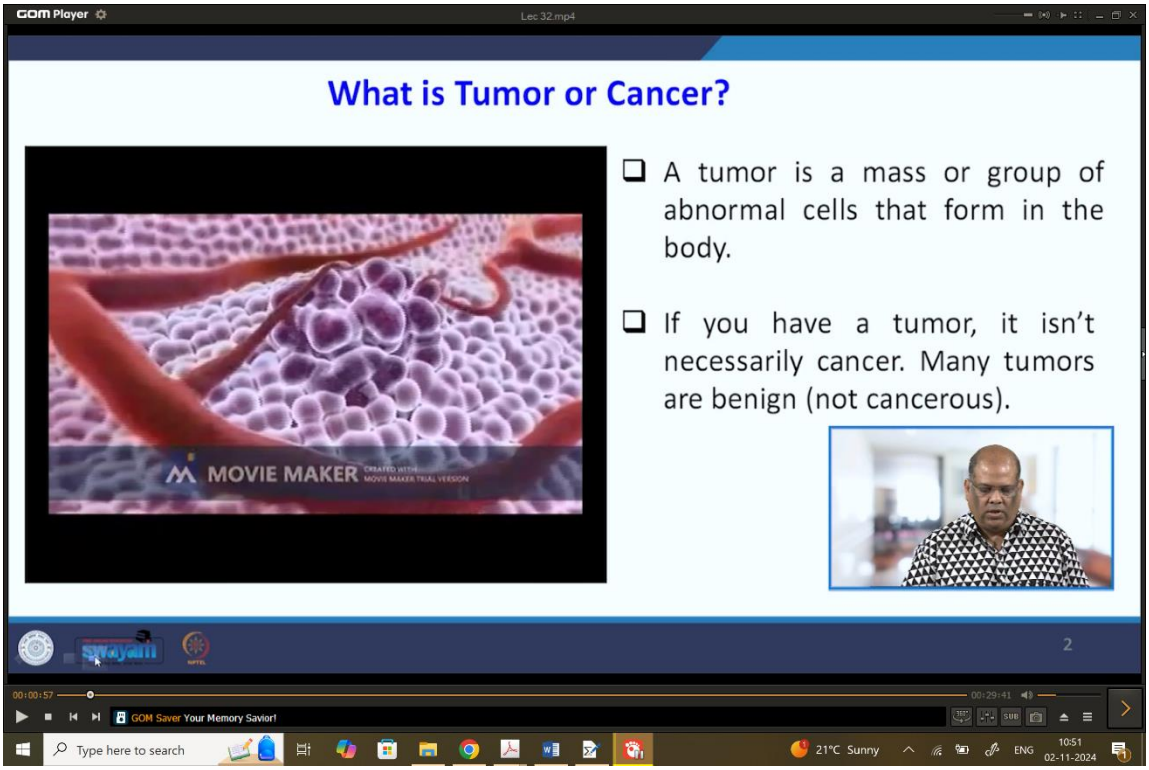
Hello, welcome to the course EXCELing with Mathematical Modelling.

Today we will be discussing about the models which represents tumour growth.

So let us see, what is a tumour?

So basically a tumour is a mass or group of abnormal cells that forms in the body and that takes place because of some problem with the DNA structure whose reason actually is not known.

So as you can see the cells in the video they are growing so fast. So that is what the tumour is and they try to connect with the blood vessels. So either they generate it or they try to connect it with the blood vessels through which they send the malignant tumour cell and which affects the other parts of the body. So that is how your tumour works.



However, not all the tumours are malignant that is cancerous, some of them are benign and the word is benign and not cancerous.

So, scientists have used this mathematical modelling to assess the growth of the tumour and we have many mathematical functions that gives somewhat good results and they can represent the growth of a tumour.

So to start with, we have this linear tumour growth model. So the first equation here, it says

$$\frac{dT}{dt} = k$$

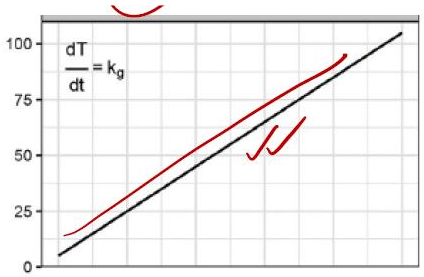
where T is the tumour and this is the time.

So rate of change of time is a constant and we say it is a linear tumour growth.

Obviously they are quite easy to solve and if you just want to solve it will be some

$$T = kt + \text{constant}$$

and since this is a linear equation, the tumour growth is called a linear, as you can see it is a straight line and hence the graph which you get is also a straight line. So the tumour grows like this.



Now sometimes it happens that the cells, they also kill themselves, so it is called the natural decay of the cells or the natural death of the cells.

In that particular case you have the growth constant and this is the natural decay or death of the cell and hence we get something like this.

In that particular case you have the curve like this and if you want to generate this curve with the help of Microsoft Excel, for this case the value of k = 2 but d = 0.01.

So, if you plug these values in this difference equation differential equation and solve it you will going to get this kind of curves.

The question is then why we are having so many differential equations to represent the tumour growth that is because tumour growth is varies from person to person and there are so many kinds of tumour and it has been noticed that say in case of brain tumour this particular kind of function matches and in case of say tumour in the lungs this particular kind of function matches the data and hence we have several kinds of growth as far as this tumour growth is concerned.

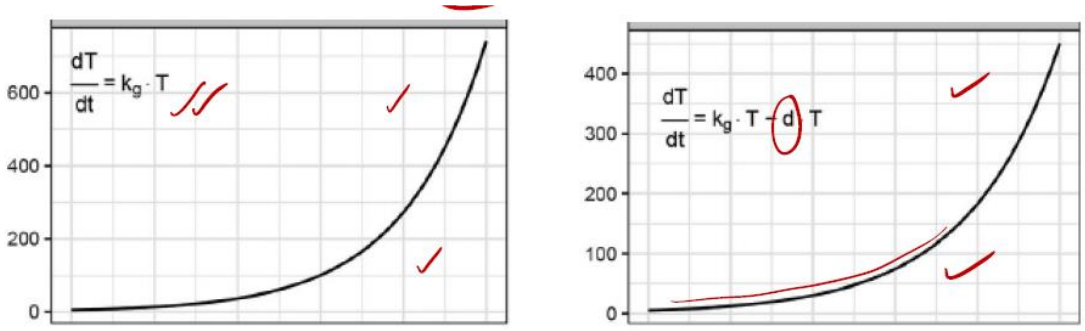
So our second kind will be the exponential tumour growth and the exponential tumour growth is

$$\frac{dT}{dt} = kT \Longrightarrow \frac{dT}{T} = kdt$$

$$\Longrightarrow \ln T = kt + \text{constant} \Longrightarrow T = e^{kt+\text{constant}}$$

So that's why it is called the exponential tumour growth model and with the same logic I say that there is some natural death of tumour cells and hence this (– dT) comes here but again I can just take $(k - d)T$ replace this by certain constant and you get the solution seen as like this.

So, this is the two graphs that you will get for tumour growth model and in this particular case we take the value of k to be 0.1 and d as 0.01. This particular thing also known as shrinkage. But, it is easy way to remember that this is caused by the natural death of the tumour cells.



And, if you notice and compare both the graphs you will see that here the growth is a bit sharp whereas here it is a bit flat and then going again up both are exponential but due to this component the growth of the tumour cell is somewhat a bit less because it is given a negative sign whereas this grows totally exponentially without any shrinkage or very natural death of the cell.

The next one is the Logistic and Gompertzian tumour growth model. We have done the Logistic and Gompertzian growth, So, once again if we recall those, the rate of change of tumour is

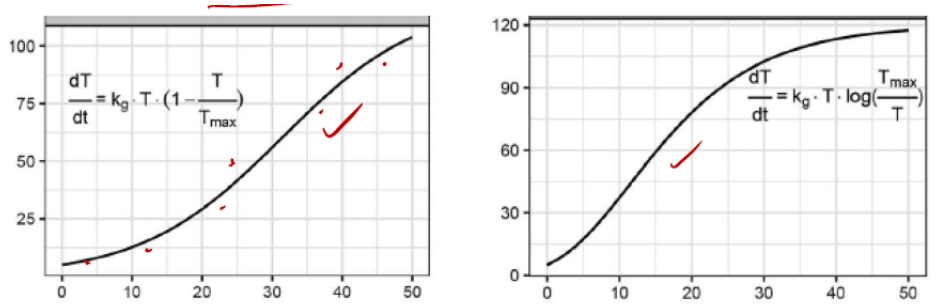
$$\frac{dT}{dt} = kT\left(1 - \frac{T}{T_{max}}\right)$$

where this k is called intrinsic growth rate and this T_{max} is called the carrying capacity. So, the carrying capacity is the maximum resources that the environment can sustain. So, in this particular case the tumour gets its resources from the body. So, the maximum tumour cell that your body can sustain and this k is the growth rate if you plot them with the values k equal to 0.1 and D equal to 0.01 and your T_{max} is equal to 120, you will be able to generate this figure. So, this is your logistic growth.

In the Gompertzian growth, you have the equation of the form the

$$\frac{dT}{dt} = kT\ln\left(\frac{T_{max}}{T}\right)$$

So, in this case again the k is intrinsic growth rate and this T_{max} is the carrying capacity which we have explained before with the same numerical values you will be able to plot a graph like this.



Now, again the question is where you will use the logistic growth and where you will use the Gompertz growth.

So, in tumour models, you get the data, the data is that with respect to time how the tumour is growing directly from the patients, you can, we will be able to measure that and once you measure that, you are going to plot those data and then try to fit one of these functions in that particular data.

And the function which matches most with the data is the function that we take to represent that particular kind of tumour.

So that is why we are learning so many forms of tumour growths so that for a particular tumour we just able to see that which particular functions actually fits the data.

Obviously you can do the equilibrium points and stability analysis of all these models, which I keep them for you, as we have done lots on a single differential equation.

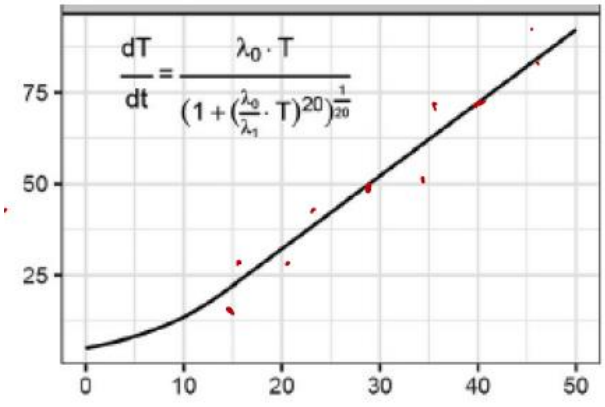
So, here only we discuss about the different growth models of tumour. So, the next one is the combined exponential and linear tumour growth model. So, here it is,

$$\frac{dT}{dt} = \frac{\lambda_0 T}{\left[1 + \left(\frac{\lambda_0}{\lambda_1} T\right)^{20}\right]^{\frac{1}{20}}}$$

So obvious question is what is your λ_0 and what is your λ_1? So this λ_0 is the rate that represents this exponential growth and λ_1 is the rate that gives the linear growth.

Now the question is how this 20 suddenly pop up in this particular function.

Well, it did not start with 20, it can start with some n, but then scientists have taken various values of n and ultimately zeroed it down to 20 because they saw that the kind of graph they are getting it matches a particular kind of data and 20 gives a that is a very good match for those kinds of data.



So, that is why this particular function has been discovered and this proved to be a quite a good fit for some kind of tumour growth model.

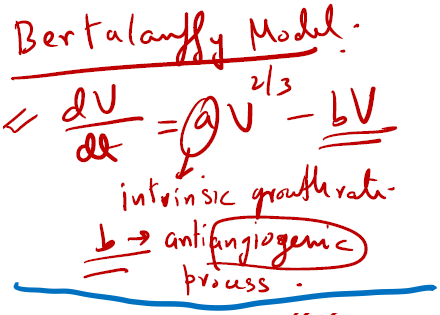
There is another model which is called Bertalanffy model. In this particular model, the volume of the tumour is measured as

$$\frac{dV}{dt} = aV^{\frac{2}{3}} - bV$$

So, a is again the intrinsic growth rate and b is called the rate of antiangiogenic process.

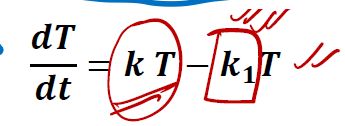
Now what is angiogenic process?

So what happens is as you have shown as you have seen in the video that this aim of this tumour to connect them with the blood vessels either they grow of their own which is called the angiogenesis or they try to, the cells try to go and connect with the blood vessels of the body so that they can circulate all the malignant tumour cells throughout the body and that is how a person gets infected very fast.

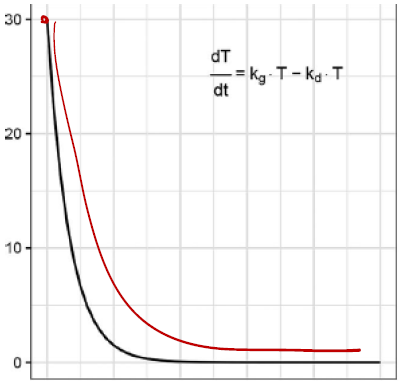


So, antigenic process means that there will be some drugs which will stop the growth of this blood vessels. So, this particular b is take care of that it kills or it does not allow the tumour to grow by its anti-angiogenic property. So, this is one kind of tumour growth model and Bertalanffy model.

Now, let us take what happens with treatment.

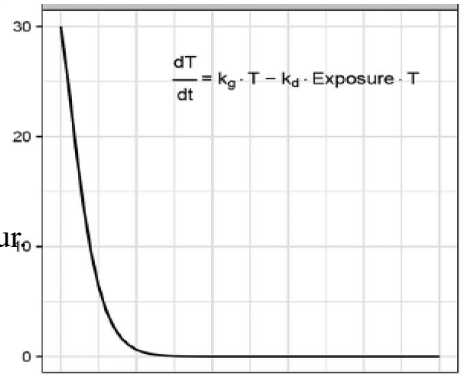


So, here you see that it is growing exponentially and we have minus some k_1T. So, due to drug effect, whatever it is, it is killing the tumour at the rate k_1. So, in this particular case and the one we have done where I have shown the model is something like $kT - dT$, this was the natural death. But here due to some drug, this particular tumour is getting eradicated or getting changed, this is exponential.



And so your curve, it starts with some initial value of the tumour it is growing with due to this term but the drug is killing the tumour cells and hence it is going down and ultimately coming back to coming go down to zero.

Now this is an exposure dependent treatment effect. Now what does it mean? That again it is doing exponential growth and this exposure is due to drugs.



So what does this exposure means is that there is a time, a time interval or the time span during which your drug is going to work and various doses of drugs are going to be applied inside the body of the person suffering from this tumour.

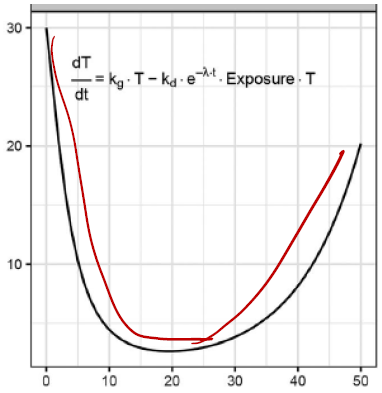
So, this exposure is due to the drugs at which helps in killing the tumour cells at a rate k_1. So, that is why $(-k_1)$ times some exposure which is going to be a function which can be a function of time and generally people use what is called Hill's function.

I am not going to do that. It is a very complicated function not needed for this particular course, it is kind of research level thing, but anyway the idea is that you can use a functional form of time to ensure that the drugs are applied inside the body and the people get cured.

So, this kind of model is also applicable.

Special form of exposure is that, okay, you have a function, then you multiply it again with respect to some exponential factor of time that with time the effect of drug slowly goes off.

So, here it is an exposure development treatment but with resistance.



So, what happens is that there is a person suffering from tumour, he is having an exponential growth of tumour and then the drug is given but then with time that the effect or efficacy of the drugs that goes out and due to which you see that the okay that there is a tumour which is going down but the moment the effect of the drugs goes up the tumour also relapse and this is very known case scenario, which happens in many patients.

So with that we come across a lot of models which gives you an idea of the growth of the tumour cells and the corresponding effect of drugs on the tumour cells.

Before going to the numerical solution, we just check the equilibrium points and the stability of two such growth models. You have to do with all the models. I just take the example of two of them.

So to start with, we take the logistic growth, where we have denoted the equation as

$$\frac{dT}{dt} = kT\left(1 - \frac{T}{T_{max}}\right)$$

where T is the tumour, k is the intrinsic growth rate and T_{max} is the carrying capacity. So to find the equilibrium point, we put

$$kT\left(1 - \frac{T}{T_{max}}\right) = 0 \Longrightarrow\ T = 0\ and\ T = T_{max}.$$

Now to find the stability, you write

$$f(T) = kT\left(1 - \frac{T}{T_{max}}\right) \Longrightarrow\ f'(T) = k - \frac{2kT}{T_{max}}.$$

Now at $T = 0$, $f'(0) = k > 0$, which implies the system is unstable about the equilibrium point $T = 0$. Also,

$$f'(T_{max}) = k - \frac{2kT_{max}}{T_{max}} = k - 2k = -k < 0.$$

So, this implies that at $T = T_{max}$, the system is asymptotically stable. So, this is the equilibrium point and the stability analysis for the logistic growth.

Let us take one more where we have taken Gompertzian growth. So, there the equation with which we represent is

$$\frac{dT}{dt} = kT \ln\left(\frac{T_{max}}{T}\right),$$

and if you want to find the equilibrium point, I have to put

$$kT \ln\left(\frac{T_{max}}{T}\right) = 0 \Longrightarrow T = 0 \text{ and } \ln\left(\frac{T_{max}}{T}\right) = 0,$$

and this will give me

$$T = 0 \text{ and } \ln\left(\frac{T_{max}}{T}\right) = 0 \Longrightarrow \frac{T_{max}}{T} = e^0 = 1 \Longrightarrow T = T_{max}.$$

Let

$$g(T) = kT \ln\left(\frac{T_{max}}{T}\right) = kT(\ln T_{max} - \ln T)$$

$$\Longrightarrow g'(T) = k \ln\left(\frac{T_{max}}{T}\right) + kT\left(\frac{-1}{T}\right) = k \ln\left(\frac{T_{max}}{T}\right) - k$$

So, if you want to check what is $g'(0)$, you will see that your $\ln\left(\frac{T_{max}}{T}\right)$ is undefined.

And this implies that here T = 0 is a singular point and we cannot conduct the stability analysis for this point T = 0.

So, we stick to only $T = T_{max}$ and you see that

$$g'(T) = k \ln\left(\frac{T_{max}}{T_{max}}\right) - k = -k < 0.$$

And hence, here also, the system is asymptotically stable about the equilibrium point $T = T_{max}$

Now, let us see how you will generate the numerical solutions with Microsoft Excel.

So, I already have filled it up because there are so many equations and it will be so time consuming.

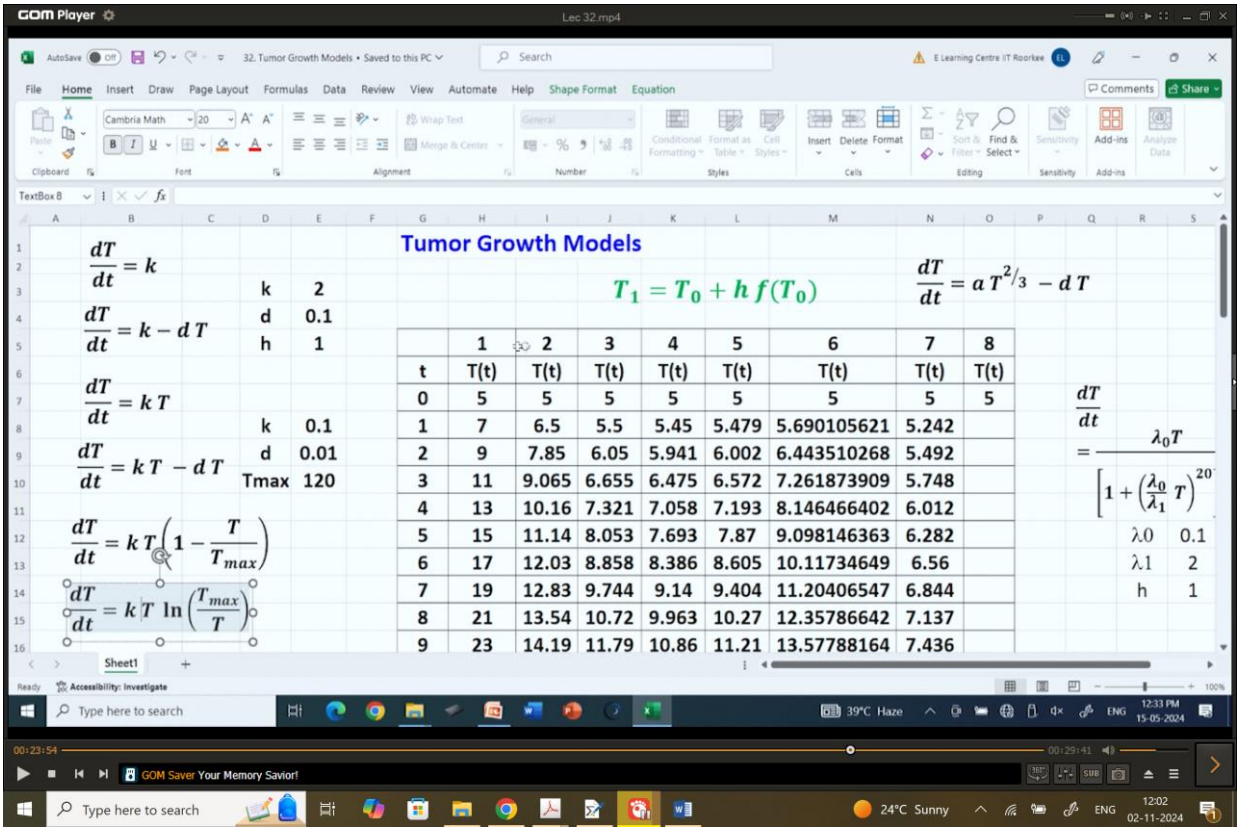
So the first is the linear one, this two, then we have the exponential one, this and this, then we have the logistic one and the Gompertzian one.

I also this equation which depends on volume.

So basically 1, 2, 3, 4, 5, 6, 7. So here also 1, 2, 3, 4, 5, 6 and this 7. The one which I left is this one which I will just do it now.

So this is so we use Euler's method which is this one and this is equal to P0 which is this value plus H which I have taken to be 1 and it is a constant value multiplied by this particular function λ_0 which is 0.1 multiplied by T0 which is this value and this whole thing has to be divided by 1

plus again a bracket open so lambda 0 this one divided by lambda 1 this one again this is a constant lambda 0 divided by λ_1 this goes in a bracket multiplied by T which is T0 and then whole thing goes to the power, and then this whole thing goes towards 1 by 20. So, from 1 again till this one to the power 1 by 20. So, we get here 5.5 and then we drag this till say 50 values and I get this values.



t	1 T(t)	2 T(t)	3 T(t)	4 T(t)	5 T(t)	6 T(t)	7 T(t)	8 T(t)
0	5	5	5	5	5	5	5	5
1	7	6.5	5.5	5.45	5.479	5.690105621	5.242	
2	9	7.85	6.05	5.941	6.002	6.443510268	5.492	
3	11	9.065	6.655	6.475	6.572	7.261873909	5.748	
4	13	10.16	7.321	7.058	7.193	8.146466402	6.012	
5	15	11.14	8.053	7.693	7.87	9.098146363	6.282	
6	17	12.03	8.858	8.386	8.605	10.11734649	6.56	
7	19	12.83	9.744	9.14	9.404	11.20406547	6.844	
8	21	13.54	10.72	9.963	10.27	12.35786642	7.137	
9	23	14.19	11.79	10.86	11.21	13.57788164	7.436	

Now what we do is we plot all of them in the same graph.

So, all the 50 values I go to insert, I go to this and I plot this.

So, now the question is what we get with this.

So you can solve them individually and you can get the individual graph.

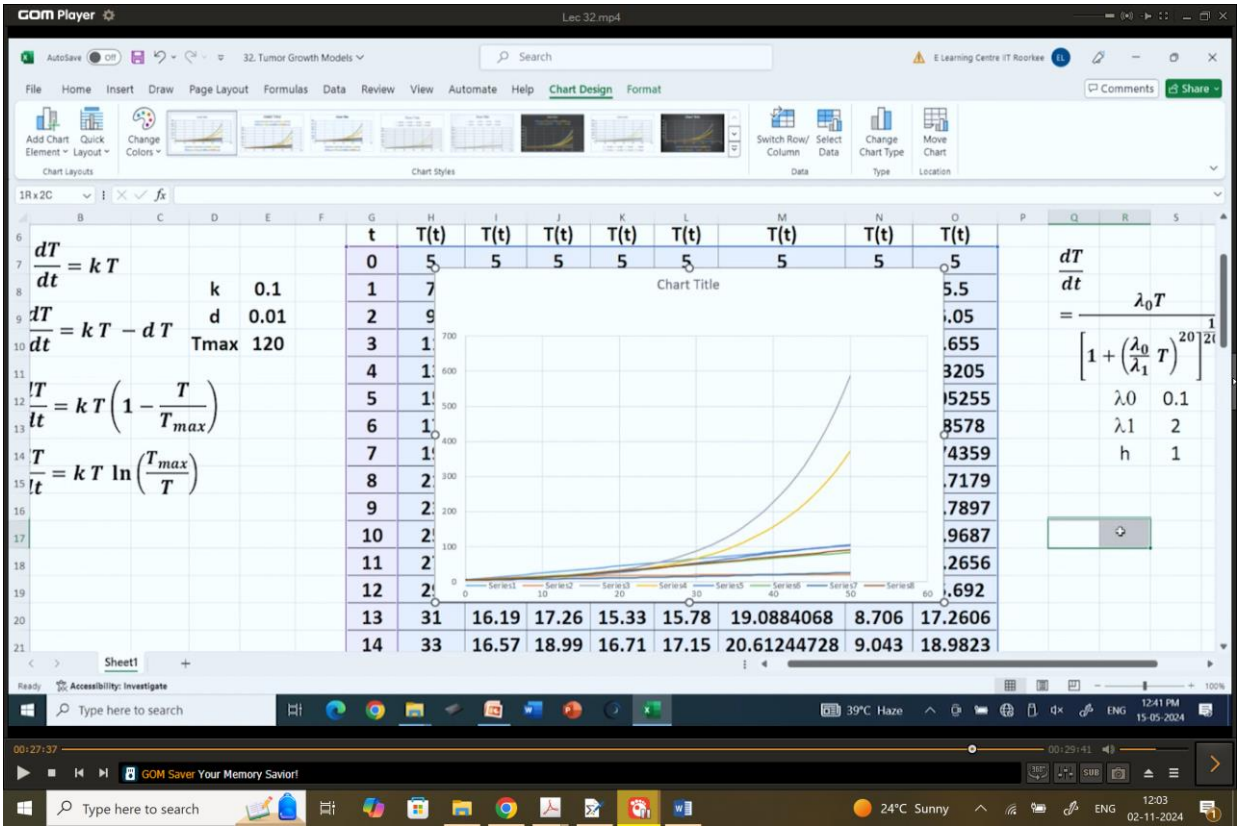
But what I want here is that I want to compare this with various models.

So the idea is that there are so many functions and so many dynamics of the functions.

Now which one to follow?

So what the scientists do is that they get data for a particular kind of tumour. So whether it can be tumour of the brain or whether it can be the tumour of the lungs or whether it can be the tumour in the pancreas. So, all these sort of data once they plot it they look for a function that will match those data.

And so we have so many kinds of function which the researchers have seen that they give a match to these particular tumour growth data.



And that is why we are learning here so many functional mathematical forms. So it depends that what kind of data you get and then you try all these equations, all these kinds of growth to match that particular kind of data and see that which particular function match that particular tumour growth.

So with that, we come to the end of this particular lecture where we have discussed various forms of tumour growth.

In the next lecture, we will be talking about some more interesting models.

Till then, bye-bye.