Introduction to Dynamical Models in Biology
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Module 1
Lecture No 3
Modeling the spread of Infectious Disease

Hello, welcome to Module 3, week 1 of our course on Introduction to Dynamical models in Biology. Here in this module we will try to make a simplified model, dynamical model to understand spread of infectious diseases, remember that there is many type of infectious diseases and some of them are very complex, how they spread for example take malaria, for spread of malaria is a vector-borne disease for spread of that you require the vector mosquito and through mosquito it spreads among human being. Whereas, common cold is a very simple infection and it spreads from one person to another person without any vector like mosquito or fly or something like that, so in this module we will try to model that type of simple spread of infection, like spread of infection of common cold from one infected person to the other.

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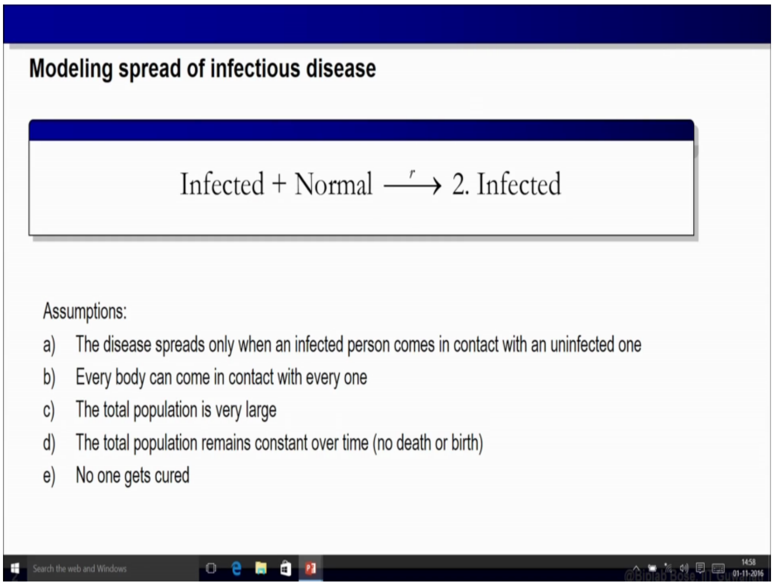

Modeling spread of infectious disease

$$\text{Infected} + \text{Normal} \xrightarrow{r} 2.\ \text{Infected}$$

Assumptions:
a) The disease spreads only when an infected person comes in contact with an uninfected one
b) Every body can come in contact with every one
c) The total population is very large
d) The total population remains constant over time (no death or birth)
e) No one gets cured

So if you remember in the second module we discussed that we have to always simplify the problem and we have to make the simplest model possible and to do that we have to make certain assumptions. So here we do not really have a complete graphical model, but rather I can write like this, that for spread of infection like common cold you have a infected person, that person comes in contact with the normal person, which is not infected and that normal person become infected so you get 2 infected person. And we want to model this process, so from an infected person to a normal person the infection is spreading suppose with the rate constant ‘r’. So we want to create a dynamical model ODE based dynamical model for this system, so let us look into the assumption that we will make before we jump into right in the ODE and creating the model and analyzing it.

The first assumption is that we have made a simplified model, so you are assuming that the disease spread only when an infected person comes in contact with uninfected person, the second assumption is very important, we assume that everybody in the population come in contact with everyone. That means we are not quarantining we are not separating the infected people from uninfected people, so everybody mingles with everyone hence when I meet a infected person with common infected with common cold as I come in contact with that person I get infected, remember these criteria is important because to create a ODE based model you have assume the system is well-mixed or homogenous that means within a city, within a campus, within a school everybody can mingle with each other. So every person can mingle with each other, so it is a well-stirred system well-mixed system or a homogenous system.

So that requirement, that assumptions we have made because that is one critical requirement to make an ordinary differential equation based model. The second one is also coming from that requirement of for a particular ODE based model that the total population should be very large, if you remember in module 2 video we discussed that when the number of elements, number of molecules, number of people involved in the process are small in number then even a single change will cause a abrupt change in the process, so we cannot use ODE based model there. To use ODEs to model our process we have to assume number of molecule, number of people, number of elements, and number of components of the process are very large in number, so in these case as we are modeling the spread of infection from one person to another so we have to assume the number of people in the system is very large.

Another interesting assumption that we make is that we are not considering any death or birth, these assumption although you all know that in a population there will be certain death without a infection, death is a normal process and there will be also some birth so population will increase. But what we have done we have considered that there is no death and no birth, that means total population is constant that helps us to reduce the complexity in the equations that we make. This type of assumption is usually fare enough if we are considering the time period in which the population of the city or the school or the region you are modeling remains constant over time, it does not change appropriately too much and these type of assumption to simplify the equations we make very often in other biological processes also.

Suppose you are modeling some processes involving 10 different proteins, you will assume that there is no production of new protein molecules there is no degradation of the old protein molecules, so total number of proteins in the system is constant, and usually this type of assumption is fare enough if you are dealing with a small interval of time, another assumption the last assumption that I will make here to model this process is that no one get cured. Yes, if I get common cold even without any drug maybe in 3-4 day I will get cured, but if I assume that, my equations will be bit complicated. As you are starting the modeling we will initially make assumption to make the modeling simplified so the equation remains simple as we progress we may add complexity to the model. So with these 5 assumptions let us start making the mathematical model of this.

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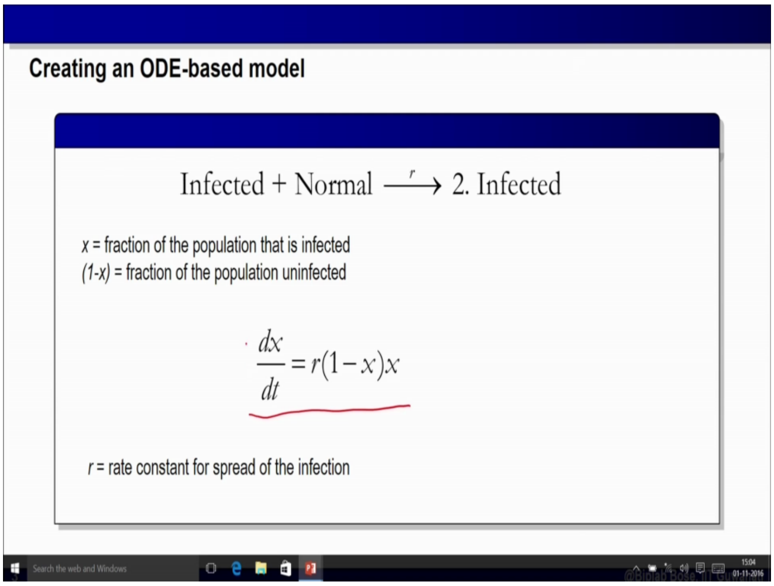

Creating an ODE-based model

Infected + Normal $\xrightarrow{r}$ 2. Infected

x = fraction of the population that is infected
$(1-x)$ = fraction of the population uninfected

$$\frac{dx}{dt}=r(1-x)x$$

r = rate constant for spread of the infection

Remember in case of dynamical models, we will use ordinary differential equation to model our process and if you remember, a differential equation represent the rate of change of something or rate of the process. Here the process is spread of infection, so we want to know the rate of spread of infection, so we represent the rate of spread of infection by a ordinary differential equation and that equation I have written it here $\frac{dx}{dt}=r.(1-x).x$ Let us look into each of this term, 'x' represent fraction of the population that is infected with the disease right now. For example, may be 2% of the population is infected with common cold right now in my institute. Then $(1-x)$ is a fraction of people who are uninfected and 'r' is the rate constant of spread of infection.

So $\frac{dx}{dt}$, the derivative of 'x' with respect to time is the rate of spread of the infection that is, it is showing the rate of change in population of infected person. It is rate of change of 'x', obviously it depends upon how many infected person is there and how many uninfected person are there, that is why it is equal to or proportional to $r.(1-x).x$

So in this ODE, 'x' is the depended variable. Time 't' is independent and 'r' is a constant and we call it parameter of the equation of the model. Let us see our equation, $\frac{dx}{dt}=r.(1-x).x$. If I expand this, $(1-x).x=x-x^2$. That means the highest power of 'x' in this equation is 2.So it is not a linear ODE, it is non-linear ODE. Now, once you have this ODE we will try to use this as a model and try to answer some basic questions, so what are the questions that I can ask here? I can ask two types of question.

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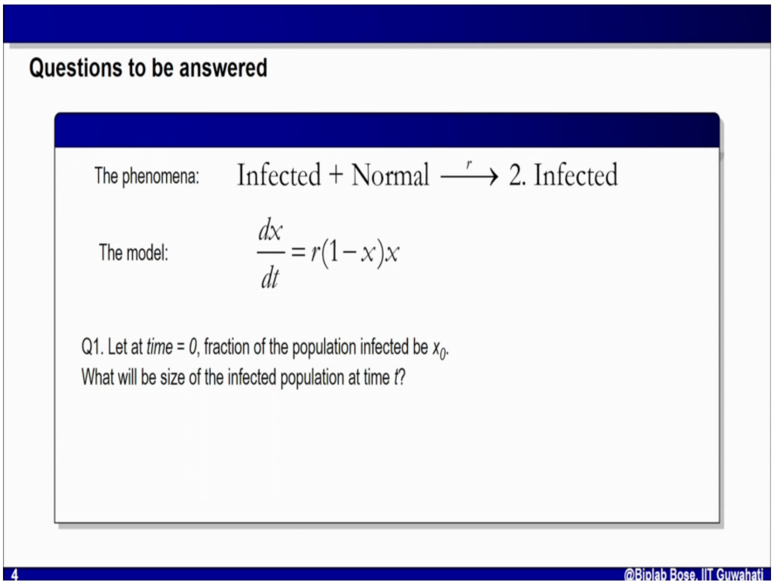

Questions to be answered

The phenomena: $\text{Infected} + \text{Normal} \xrightarrow{r} 2.\ \text{Infected}$

The model: $\frac{dx}{dt} = r(1-x)x$

Q1. Let at *time* = *0*, fraction of the population infected be x_0.
What will be size of the infected population at time *t*?

For example I can ask like this. Right now we have 2% population is infected with common cold and I know the rate constant for spread of the infection that may be 0.5 per day, then how many people will be infected after 1 week? So the question can be written in generalized form that at time = 0, suppose the fraction of population infected is 'x_0' then what will be the size of the infected population at time 't'? This can be one question and you can ask this question and try to answer this question using this ODE. You can ask more generalized questions, you may ask that I want to know the overall dynamics of the spread of infection, that means I want to plot something like this that I have time in horizontal axis and the fraction of people infected in vertical axis and then I want to know how ‘x’ is changing with time. Is it changing linearly, non-linearly, how it is changing? The time ‘t’ maybe from 0 to 30 days something like this so these type of question can also be asked and answered using this ODE based model.

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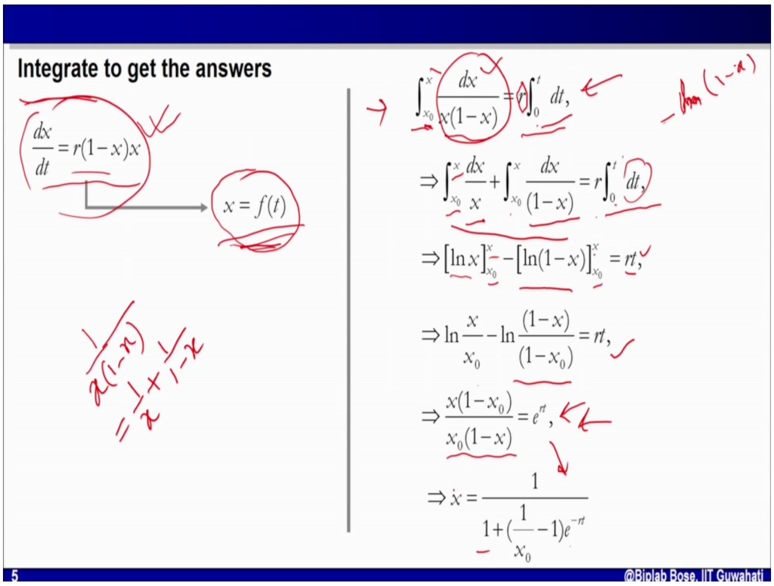

Integrate to get the answers

$$\frac{dx}{dt} = r(1-x)x \longrightarrow x = f(t)$$

$$\frac{1}{x(1-x)} = \frac{1}{x} + \frac{1}{1-x}$$

$$\int_{x_0}^{x} \frac{dx}{x(1-x)} = r\int_0^t dt,$$

$$-\ln(1-x)$$

$$\Rightarrow \int_{x_0}^{x} \frac{dx}{x} + \int_{x_0}^{x} \frac{dx}{(1-x)} = r\int_0^t dt,$$

$$\Rightarrow [\ln x]_{x_0}^{x} - [\ln(1-x)]_{x_0}^{x} = rt,$$

$$\Rightarrow \ln\frac{x}{x_0} - \ln\frac{(1-x)}{(1-x_0)} = rt,$$

$$\Rightarrow \frac{x(1-x_0)}{x_0(1-x)} = e^{rt},$$

$$\Rightarrow x = \frac{1}{1+(\frac{1}{x_0}-1)e^{-rt}}$$

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So let us start with the first, to answer this question we have to get the original function of ‘x’ with respect to time and how do we get that? We have a ODE to start with and remember a ODE is nothing but the derivative of a function, so from this derivative we have to get the original function and to do that we will do integration as you have done it in your calculus class. So what I have to do I have to integrate this thing so that I can get the function of ‘x’ in terms of function of time, so how we will do the integration? To do the integration you have to separate out ‘t’ and ‘x’. So that is what I have done here. I have separated out ‘t’ and ‘x’.

By separating out, $\int_{x_0}^{x} \frac{dx}{x.(1-x)} = r.\int_0^t dt$

Remember, ‘x_0’ is the initial value of ‘x’ and I have to integrate dt from 0 to ‘t’ and remember ‘r’ is a constant, that is why I have taken that out of the integration sign. This type of integration is very simple. I can do some algebraic rearrangement. Remember,

$\frac{1}{x.(1-x)} = \frac{1}{x} + \frac{1}{(1-x)}$. So, I have separated this one into two terms, $\frac{dx}{x} + \frac{dx}{(1-x)}$, both these terms has to be integrated from 'x_0' to 'x' and the second one has to be integrated from 'x_0' to 'x' and on the right hand side we have, $r.\int_0^t dt$

Move further, using the simple formula of integration we get,

$$\begin{array}{c} x \\ \ln \text{¿} \\ \text{¿} \\ \text{¿} \\ \int_{x_0}^{x} \frac{dx}{x} = \text{¿} \end{array} \; ; \; \begin{array}{c} (1-x) \\ \ln \text{¿} \\ \text{¿} \\ \text{¿} \\ \frac{dx}{(1-x)} = -\text{¿} \\ \int_{x_0}^{x} \text{¿} \end{array} \; ; \; r.\int_0^t dt = r.t \; .$$

If I move further we can rearrange this term and we get,

$$\ln \frac{x}{x_0} - \ln \frac{1-x}{1-x_0} = r.t$$

$$\frac{x(1-x_0)}{x_0.(1-x)} = e^{r.t}$$

Remember, I want to get 'x' as a function of time. So I want to keep 'x' on one side of the equal to sign and rest of the thing on the other side. So I just did a algebraic rearrangement of the whole thing here from these I get,

$$x = \frac{1}{1 + \left(\frac{1}{x_0} - 1\right).e^{-r.t}}$$

Remember, that is what we wanted. I wanted to know 'x' as a function of time, so we have 'x' on the left hand side and time on the right hand side. 'r' here in this exponent is a constant. It is a rate constant. 'x_0' is also a constant because you have decided that at the very beginning that 'x_0' is the initial population size which is infected fraction of the population that is infected.

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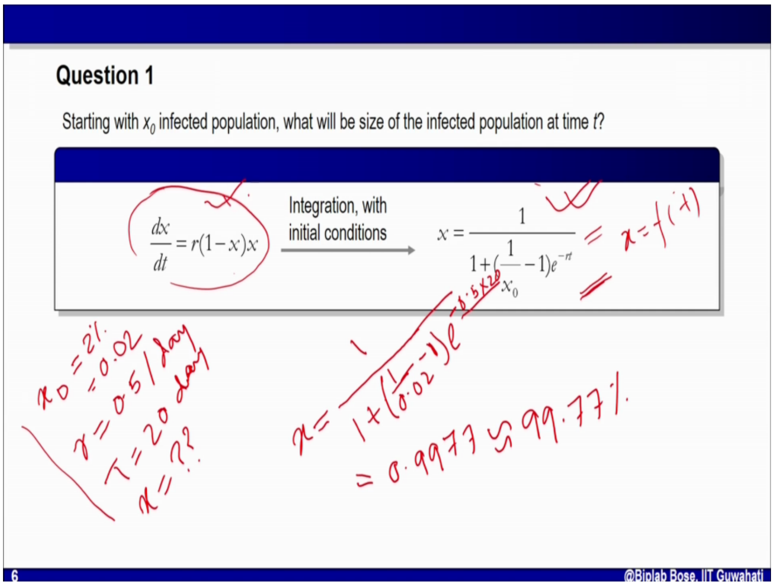

Question 1

Starting with x_0 infected population, what will be size of the infected population at time t?

$$\frac{dx}{dt} = r(1-x)x \xrightarrow{\text{Integration, with initial conditions}} x = \frac{1}{1+(\frac{1}{x_0}-1)e^{-rt}} = x = f(t)$$

$x_0 = 2\% = 0.02$

$r = 0.5/\text{day}$

$t = 20$ day

$x = ??$

$$x = \frac{1}{1+(\frac{1}{0.02}-1)e^{-0.5\times 20}} = 0.9977 \simeq 99.77\%$$

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So once I have these one, that means once I have a ODE, that is my model I have integrated that with initial conditions, remember this my initial condition that t = 0, 'x_0' is my value of fraction of a population infected, so I have integrated this ODE and I have got this one. This function 'x' as a function of time. Now this function is all I need to answer the questions that I have raised.

So let us try with the first question, the first question was that if I have suppose initial population infected 'x_0' is equal to, suppose 2% infected. So that means it is equal to 0.02. Suppose 'r', the rate constant for spread of the disease is 0.5 per day, then my question is after 20 days what fraction of people will be infected? So what fraction of people will be infected that is my question. I can simply answer this question using this function. So, in this case it will be ,

$$x = \frac{1}{1+\left(\frac{1}{0.02}-1\right).e^{-0.5\times 20}}$$

This will give me around value like 0.9977 that is approximately 99.77%, so what I have done, I have taken the numerical value given here and plug them in these function that I have got from the integration of the ODE based model. By plugging this value of 'x_0', r, t, I get the final value of 'x' and that is 0.9977 which is equivalent to 99.77%, that means my model is saying if at initial time point I have 2% of the population infected then after 20 days 99.77% of the population will be infected, so first type of question is answered.

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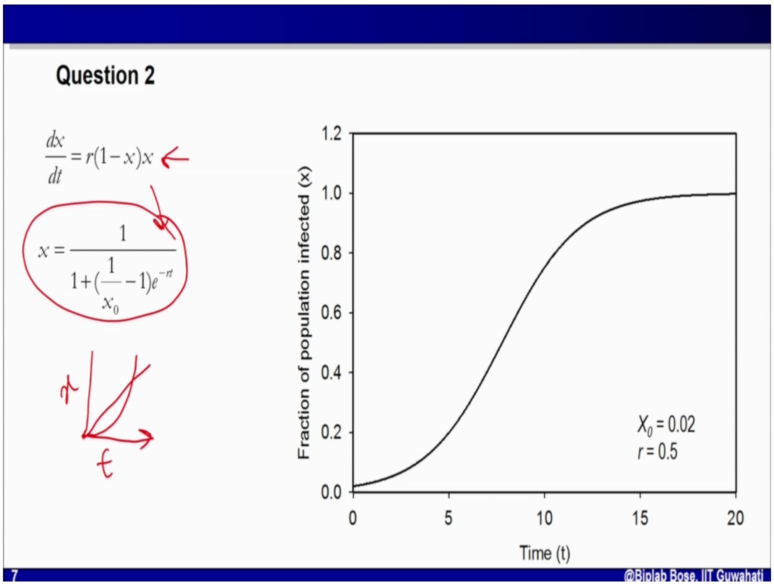

Question 2

$$\frac{dx}{dt} = r(1-x)x$$

$$x = \frac{1}{1+(\frac{1}{x_0}-1)e^{-rt}}$$

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Now look into the second type of question means I want to know the overall dynamics of ‘x’ with the respected time, I want to know how the size of the infected population is changing, is it linear or it is nonlinear. Whatever it is, so I want to know how can I do it, remember this derivative this ODE is my model and integrating it I have got this function. So essentially I have to plot this function with respect to time. So that is what I have done here, if you can see, I have ‘t’ in the horizontal axis, ‘x’ in the vertical axis and I have just simply taken different values of ‘t’ for a fixed value of ‘x_0’ and ‘r’ and I have generated this curve. This curve is initially increasing slowly because obviously initially only 2% of the population is infected.

Once a large number of population, a considerable number of people get infected, then the rate of spread of the infection increasing further so in the middle we have a sharp rise and then ultimately it saturates at 1, that is 100% .That means slowly by 20 days most of the people in my population is infected. So the population dynamics of the spread of the diseases is not linear. It is a non linear one with a sigmoidal type behavior, S type behavior.

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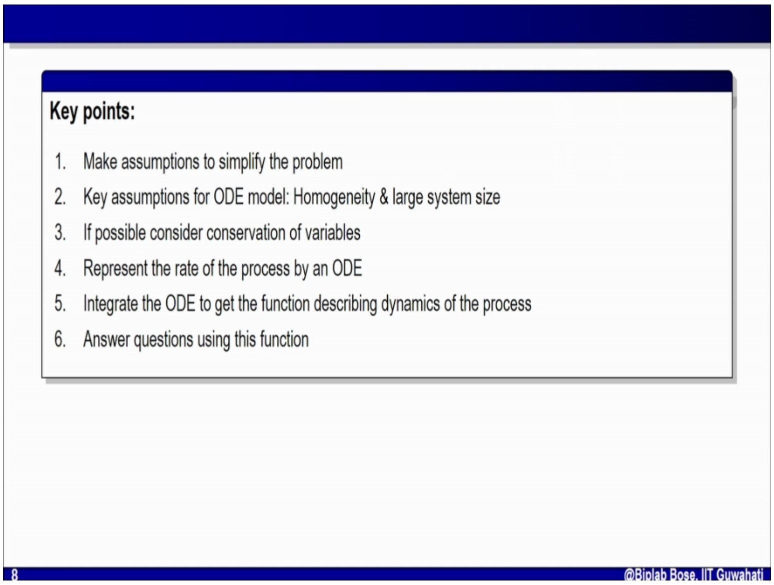

Key points:

1. Make assumptions to simplify the problem
2. Key assumptions for ODE model: Homogeneity & large system size
3. If possible consider conservation of variables
4. Represent the rate of the process by an ODE
5. Integrate the ODE to get the function describing dynamics of the process
6. Answer questions using this function

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So what you have done in this module. To understand the dynamics and spread of the infectious diseases we have created a very simple model. Remember, we are not trying to model the spread of diseases like malaria or dengue which involves vector or something complicated process, we are trying to model simple processes like spread of common cold that happens every year. To simplify this problem we have made some assumptions and we have to make some assumptions, which are required to make this model suitable for ODE based modeling for example we have to make sure that the system is homogeneous or well-mixed that means all people are coming in contact with each other and population size is also very large that means I cannot use the model to model the spread of infection among 5 people or 6 people, I have a large number of population.

And then what we have done we have represented this rate of change in the size of infected people, remember the rate in change in the size of the infected population by a ordinary differential equation. While writing this ordinary differential equation we have made another assumption that the total population of the system is not changing that has help to make our equation a simpler one. We can obviously make a assumption of death and birth, but that will make all equation bit complicated. Then once I have that ODE represent the rate of change in the size of infected population that is my model, I have asked certain questions. For example I have asked if I start with the particular fraction of population infected what will happen after 20 days? I have asked tell me what is the generalized dynamics of the system.

And I have answered these questions by first integrating the differential equation to get the function which represents ‘x’ is function of time which represent ‘x’. ‘x’ is the fraction of population that is infected, so I have got the function by integrating and then I have that function to answer my questions. We will use this type of approach to model something with more complex in future. We will discuss them step by step with the assumptions and how to solve them by integrating the ODE to get the function and then answer these type of questions. Thank you for watching, will build new models in future.