

Advanced Process Dynamics
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Lecture 36
Analysis of infectious disease dynamics

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NPTEL ONLINE CERTIFICATION COURSE

Kermack–McKendrick (*SIR*) model

Model assumptions:

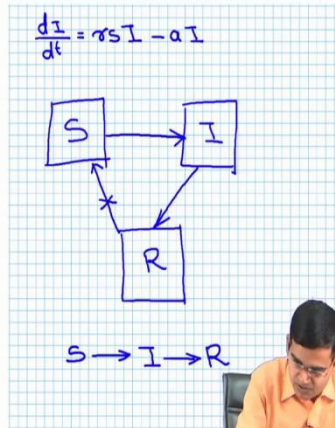
- The total population is constant
- The population is divided into three compartments
 - susceptibles, S , who can catch the disease
 - infectives, I , who have the disease and can transmit it
 - removed class, R , namely, those who have either had the disease, or are recovered, immune or isolated until recovered
- Recovery confers immunity to the individual
- Incubation period is zero
- The population is well-mixed

 [Murray, *Mathematical biology: I. An introduction*]

Kermack-McKendrick (SIR) model

Model assumptions:

- The gain in the infective class is at a rate proportional to the number of infectives and susceptibles, that is, rSI , where $r > 0$ is a constant parameter
- The rate of removal of infectives to the removed class is proportional to the number of infectives, that is, aI where $a > 0$ is a constant parameter



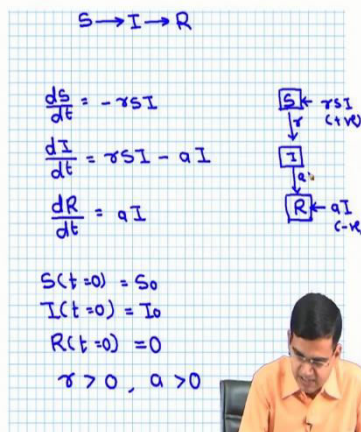
[Murray, *Mathematical biology: I. An introduction*]

Kermack-McKendrick (SIR) model

$$\begin{aligned} \frac{dS}{dt} &= -rSI & (1) \\ \frac{dI}{dt} &= rSI - aI & (2) \\ \frac{dR}{dt} &= aI & (3) \end{aligned}$$

r : infection rate (> 0)
 a : removal rate (> 0)
 Initial conditions:
 $S(0) = S_0, I(0) = I_0, R(0) = 0$

[Murray, *Mathematical biology: I. An introduction*]



Kermack-McKendrick (SIR) model

Key questions?

- Given r, a, S_0 and the initial number of infectives I_0 , whether the infection will spread or not?
- If the infection does spread, how does it develop with time?
- When will it start to decline?
- When do you declare the spread of an infectious disease an "epidemic"?

Hello, and welcome back. In the last week, we started off with analysis of nonlinear dynamical systems in higher order.

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Now, we saw the underlying mathematical formulation and also took up very interesting case of diabetic operation, diabetic transient operation of a CSTR. As I have mentioned before, we will take up more physical examples. And in this week, we will take two more examples. Today, we will start with an interesting case of analysis of infectious disease dynamics. So, since the beginning of 2020, the world has been experiencing the pandemic caused by COVID-19.

Not only has the disease devastated the entire world, but it has also invoked certain interesting discussions among the community, both scientific as well as people at large. that how to make predictions about the evolution of infectious disease. Or when can we say that it would result into an epidemic, or in today's case, as the conditions prevail in the world, whether it would result in a pandemic or not.

There has also been a lot of discussion on the mathematical models which predict such a phenomenon and whether or not these models are applicable, whether or not this model would be successful and why under certain cases they are not proving to be correct in making predictions and so on. So, today, what we will do is we will try to understand some basics of the mathematical methods, which go for modeling the dynamics of infectious diseases.

In fact, we can understand that there are a lot of agencies worldwide as well as in India, which maintaining the data of the people which are getting infected, which are getting recovered, which unfortunately succumbing to death and so on. So, we understand that the population under a certain category. For example, the population of the recovered persons is changing with time.

The population of infected ones is changing with time, the population of confirmed cases is changing with time. So, therefore, one can understand that we are actually dealing with a dynamical system, where certain category of population is changing with time the number is changing with time and therefore, it makes the system a dynamical system and therefore, one may expect that we can analyze the dynamical behavior of the system.

And that would, in principle put us in a position to predict the future cause of the pandemic. So, in principle, we must be in a position to tell whether, in future the pandemic would

prevail or not, when it is going to die out and similar questions may be answered. So, let us look into the first and the simplest model and the model assumptions here in front of us.

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So, we have the model assumptions that, this particular model is the famous SIR model. It was put forward by Kermack and Mckendrick as early as in 1927. So, it is nearly, it is around 95 years that this particular model has been around. And since this was the first model that attempted to describe the dynamics of infectious diseases, obviously, this was a simple model, and very elementary in fact.

But even with such an elementary model, we can actually describe the dynamics of infectious diseases very well as long as the underlying assumptions which were made during the development of the model hold true. So, let us see what all are the assumptions. The first assumption is that the total population is constant.

So, this means that you are not considering the cases where there is an exchange of population, which means there is an out flux of the population from the region or there is a continuous influx of the population from the region. So, you consider a fixed, a constant number of members in the community. Let us say that number is N .

And throughout your dynamics, that total N does not change. There would be compartmentalization within this number N . So, these days you can see confirmed cases, infected cases, deaths and so on. So, these are the smaller compartments within this larger population and it has been assumed that the total number N remains constant.

Then the population is divided into three compartments as I said that you would be dividing the entire population N into three compartments, into various compartments in SIR model, there are three compartments. What is the first compartment? Susceptibles, denoted by S . So, all of those members of this population which can potentially catch the disease are referred to as susceptibles.

So, since this is an infectious disease, we are considering a disease which is infectious which means, which would spread from one member to the other member. If you introduce some members which are already infected in the population, then the members which are susceptible to catch this disease would be referred to as S , which means susceptibles.

The second compartment is infectives, I, mind that these are infectives not infected. Infected means the ones which have contracted the infection. Infectives means that not only these members have contracted the infection, they are now the members which can spread infection to others. So, infective means that they have infection and then they can spread infection to other members of the population.

We will denote them by I. And thirdly, the removed class. Often this letter R is confused with recovered. In the Model SIR, R is not recovered, but removed class. What is the meaning of removed? Well, recovered is a subset of this removed class. So, a susceptible population will contract the disease to come to the compartment I, which means, which are infective.

The infective ones would spread the infection potentially and perhaps a part of those infectives may get recovered. So, those that subset of the population I which has been recovered from the population would become, would act as R but we are referring R as removed and recovery is only one of the mechanisms of removing the population from consideration.

Well, the population which undergo death is the population which is no more susceptible, obviously, and they can also not spread further infection. So, they are not infective. So, that population has been removed from consideration and therefore, one of the mechanisms apart from recovery is death, for example. So, all of the mechanisms following which the population is no more susceptible and it is no more infective will be referred to as removed.

So, those who have either had disease or recovered, so, one of the assumptions is that once you have contracted the disease and you have recovered from it, you would no more contract the disease again. So, recovered and further stages are the ones which are considered as removed. Immune, so, a particular group may have a higher level of immunity or certain other conditions which would render them immune.

They may be vaccinated. So, again, that particular class may be considered as removed and are isolated until recovered. So, we are not going into the details of the steps which have been undertaken to make this population insusceptible to further contraction of the disease. We are have lumped all of these cases into one category, which is called R.

Now, the next assumption is that recovery confers immunity to the individual. In case of a COVID-19 for example, you must have heard that once the person recovers, at least for some

period of time after recovery, he is no more susceptible to contracting the infection again. So, once you recover, you have no path from going from R to S again.

So, susceptibles become infected, infected become removed from the population altogether. The removed population can no more become susceptible again. Well, in certain diseases it is possible, in certain diseases, this does not hold true. So, for diseases for which this particular statement holds true, that recovery confirms in confers immunity to the individual, our analysis will hold true.

Then, the incubation period is zero. What is the meaning of the statement that the incubation period is zero? This simply means that there is no period between catching the infection and becoming an infective. Which means that as soon as an individual, a susceptible individual catches infection, he becomes infected. So, there is no period during which there is a doubt whether the person is infective or not, that incubation period has been considered to be zero.

Finally, the population is well mixed. For COVID-19 for example, makes sense that the population is well mixed means that there is an equal probability of every individual to be coming into the contact of the other individuals in the population thereby spreading the disease via infection. So, the population is well mixed. Again, in case of COVID-19, this assumption holds true. There is no reason for not making this assumption.

For certain diseases for example, sexually transmitted diseases, this assumption may not hold true that every single individual has the equal probability of spreading infection to every other individual in the species, in that particular population. So, for diseases like influenza or COVID-19, this particular assumption that the population is well mixed holds true. Now, when we have these assumptions, what mathematical statements can be made? Let us see if we can make some mathematical statements.

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So, the assumptions are now, now, the analysis becomes a little more mathematical that the gain in the infective class I, the gain in the infective class is at a rate proportional to the number of infective as well as susceptibles. Let us see if it makes sense. So, if there are more number of susceptibles, there is a higher probability that you would get infected or the entry to the infective class would be higher, if there are more number of susceptibles.

So, therefore, the gain in infective class is at a rate proportional to the number of N susceptible, now what about the number of infectives, if there are more number of infected

persons, they would spread more disease, and therefore, the rate of change of infectives would depend upon the number of infectives itself. So, the gain in infective class is at a rate which is proportional to the number of infectives and susceptibles both.

Which means, we will have $\frac{dI}{dt} = rSI$, where r is a constant in fact, it is a positive constant.

So, I can write here $\frac{dI}{dt} = rSI$, where r is a positive constant. Now, this is the rate at which the population would enter the compartment of I , larger number of infectives will result in more number of people coming in the compartment of I , larger number of susceptibles will result in more number of people coming to I .

Now, as more number of infectives are present, since infectives will subsequently result into the removed ones, by recovery, by death or by any other mechanism, now, you can say that the out flux from the compartment I would be directly proportional to the number of members in I itself. So, the rate of removal of infectives to the removed class, I to R , would be proportional to the number of infectives and now, the constant associated constant is a . So, therefore, I can write this as minus aI .

So, now I have an equation which is given as $\frac{dI}{dt} = rSI - aI$, but then if I look into the three compartments, I have a compartment S , I have a compartment I and I have a compartment R , how can I represent various flows which means the movement or transfer of population from one compartment to the other compartment if I have these three compartments?

I know that susceptibles are the ones which would become infected. So, therefore S will have an arrow directed towards I . Now, infectives would ultimately get recovered or removed. So, therefore, I can draw an arrow which is like this. Can I have any more arrow? For example, can I have R going to S . No. Following our previous assumption that infection confers immunity, the recovered ones cannot go to the susceptible class. So, therefore, my flow for this particular system can be written as S going to I going to R .

This is the trend for my flow of population among different compartments. Now, in my case, the number of susceptibles is changing with time, the number of infectives is changing with time, so is the number of removed but I have only one equation here, which is $\frac{dI}{dt} = rSI - aI$.

I should be in principle in a position to write the corresponding dynamical equations for S and R as well. Let us see what those equations are.

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So, if I have the equation for I given as $\frac{dI}{dt} = rSI - aI$, equation number 2 on the left hand side, then if I know that my flow is S going to I going to R then it is not very difficult to see that for I, I have two fluxes. So, for I, I have an influx which is coming from S and I have an outflux which is going to R. What is the relative contribution?

This contribution is aI and this contribution is rSI . aI would be negative because I is going to R and rSI would be positive, because S is going to I. So, if these are the only flows in the system, then it is not very difficult to see that I can write dS/dt is equal to what, S is going to I, so, this quantity which is positive for the arrow going from S to I would become negative for S, so it would become $-rSI$.

I am simply following the arrows and writing the equations. Then, similarly, I can write dR/dt is equal to now for the arrow from I to R for I, I had minus aI and that exact same population would enter the compartment R. So, therefore, for R I will have aI plus. And therefore, I have three dynamical equations here. Since I have three dynamical equations, I should have corresponding initial conditions as well.

So, how does typically physically this whole constitution of epidemic or pandemic work? You have a population and in that population you introduce some infected members. So, in the current situation what happened in the world, the infection is set to have started from Wuhan and then people started flying from Wuhan to different parts of the world.

So, therefore, you started introducing infected members in different parts, geographical locations of the world. Now, those members, which have been infected, which were introduced to the population, if you have paid attention are called patient zeros. So, the first patient which would get infected would be called Patient one, because that will be the first person who is getting infected.

So, that is the secondary infection which is resulting into basically the spread of infection. Otherwise, the person which originally had the infection and which was introduced to the population is called patient zero. So, now, there is no reason for having exactly one person to be introduced in the population.

So, if initial number of members which had infection, which are introduced to the population is I_0 . So, at time t is equal to 0, I will have I_0 , the initial number of members, which had

infection, which were introduced to the population. At the moment you introduce the infected members to the population, the rest of the population becomes susceptible, assuming well mixed population.

Now, you can remove you may not consider some of the populations members of the population based upon other criteria. Otherwise, the rest of the population is now susceptible. So, therefore, S at $t = 0$ will become S_0 , some natural number, I also, some natural number.

Now, at the beginning of the pandemic or the epidemic of the spread of infection, you do not have anyone who is recovered or removed or died or had any kind of other mechanism for removal. So, therefore, you say that R at $t = 0$, fair assumption is 0. You start with 0 and there is no one which is removed, because you are beginning the spread of the infection.

So, therefore, we introduce $R(0)$, number of members which are infected and the susceptible population at the beginning is zero. Finally, we are looking at how the population growth in various compartments takes place. Therefore, I have r which is greater than 0 and I have λ which is greater than 0.

I have $r > 0$ and I have $\lambda > 0$. r is called the infection rate, the rate at which infection spreads because that would be the rate you see here in this box. This would be this would be, this would correspond to the rate at which S goes to I . And removal rate, the infective are going to be removed so, this would correspond to the location here.

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So, if this be the case what can be done? Now, if I have these three equations in front of me, what can be done is that I can ask several questions. So, the first question can be that given r , λ , S_0 , the removal rate, the infection rate and the initial number of susceptible population, members of the population and you introduced some number of incentives in the infected members in the population, whether the infection would spread or not?

What is the guarantee that there would be an epidemic? What is the guarantee that the infection would spread? We need to know this. Then, if the infection does spread, what will be the dynamics? Would it spread fast? Would it spread slowly? How would it happen? Third, well, if it does spread, when would it start to decline?

And finally, when can you declare that yes, we are having a epidemic or in today's situation, we are going to have a pandemic, when do you declare that the situation is really terrible, that

we need to be vigilant and we need to watch our own behavior so that the pandemic does not spread and result into a disaster.

All of these questions would be answered potentially by analyzing the dynamical behavior of our system. So, let us see, we can always solve the, try to solve the equation, well, I cannot comment whether we can always solve the equation, but we can try to solve the equation but can we have some at least qualitative idea about these, the system which we are currently considering.

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So, we have three equations, we have $\frac{dS}{dt} = -rSI$, I have the $\frac{dI}{dt} = rSI - aI$, and I have $\frac{dR}{dt} = aI$. So, equation 1, equation 2 and equation 3. So, now, before I try to answer any of the questions, my first question would be is this a dynamical system?

The answer is yes, I have three first order ODEs in time, which describes the evolution of my system. So, therefore, in fact, I am dealing with a dynamical system. And what is the dynamical variable? So, my dynamical variable is S, I, R transpose, what is the order of my system, again not very difficult to see the order of the system is 3. I have higher order system.

Linear or nonlinear? This is a nonlinear system I am leaving this as an exercise for you to assure yourself that we are in fact dealing with a nonlinear system, not very difficult to see from here, anyway. And finally, this is also what you can assess, that this is an autonomous system.

Since, this is a nonlinear system, we might have difficulty actually solving this explicitly. We would in fact try to do that but let us first see if we can have some qualitative idea. So, I have $\frac{dS}{dt} = -rSI$. And therefore, I can write dS/dt at $t = 0$ is equal to $-r S_0 I_0$.

What would this give me? This would give me an idea whether the number of susceptibles in my system at least during the early stages of the pandemic would increase or decrease with time. So, this is S, this is t and I know that $r > 0$, S_0 is a population greater than 0, I_0 population greater than 0 which means dS/dt , at $t = 0$ is always less than 0.

Which means that my gradient during the initial stages of the pandemic or epidemic would be negative, number of susceptibles would come down. But if I see dS/dt at any point of time,

then what I see is R is a constant always positive, S is a population of susceptibles always positive, I is population of infective, always positive.

So, therefore, my slope irrespective of time is always going to be negative. So, therefore, this is going to continue, S the population of S will always decrease with time. Can I say the same thing about I ? So, I have dI/dt , at $t = 0$ is equal to what? $rS_0I_0 - aI_0$ from where I can write this as $rS_0 - aI_0$.

Now, the product has to be either positive, greater than 0 or less than 0, I cannot say anything about them at this point of time. I know that I_0 is always positive. So, therefore, if $rS_0 - a$ is greater than 0, my dI/dt at $t = 0$ would be greater than 0. And what is the meaning of this?

The meaning of this is that if the condition $rS_0 - a > 0$, is satisfied during the initial stages of your pandemic, then you would expect an increase in the infected persons or infectives in the population with time. The infectives will not die down, they will increase with time.

And can I quantify this further, so, I can write this as S , $rS_0 - a$ must be greater than a , or in other words rS_0 / a must be greater than 1. So, I have a number rS_0 / a and if this number is greater than 1, then you can say right at the beginning of the pandemic itself if you know S_0 , if you know I , if you know a that pandemic is going to happen.

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And what is the name that we have given to this quantity $rS_0 - a$, if you have been following news, I am sure, it is not very difficult to for you to recall that this number is called reproduction number R_0 . All of these days you must be coming across this term R_0 , reproduction number and it is nothing but rS_0 / a .

It is a number of secondary infections induced by one primary infection in this wholly susceptible population, which means during the beginning of your pandemic or epidemic, if this quantity $R_0 > 1$, then every individual which is infected is infecting more than one individual in the population and therefore, there would be an, there would be a growth in the infection, and this is the popular R_0 factor, which we have seen.

Similarly, at any point of time t , you may define R_t , which would be rS at any point of time t multiplied by a . So, we have in fact, just after having a look into the equation, come up with the popular R_0 parameter, which will tell us, which will give us an idea of whether the

infections would spread or not. We will look into more details of this particular system in the lecture to follow. Till then, goodbye.