Computational Systems Biology
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Lecture – 06
Fundamentals of Mathematical Modelling

In today's video, let us fix the fundamentals of mathematical modelling by looking at a very motivating example, the SIR model for the spread of infectious diseases. This is a very popular model and when I teach this course in class, I usually have a very lively discussion about the various improvements one can make to this model and so on. And it starts fixating several of the ideas in terms of what are the most important assumptions or what are the most important enhancements, one might want to do the model and so on.

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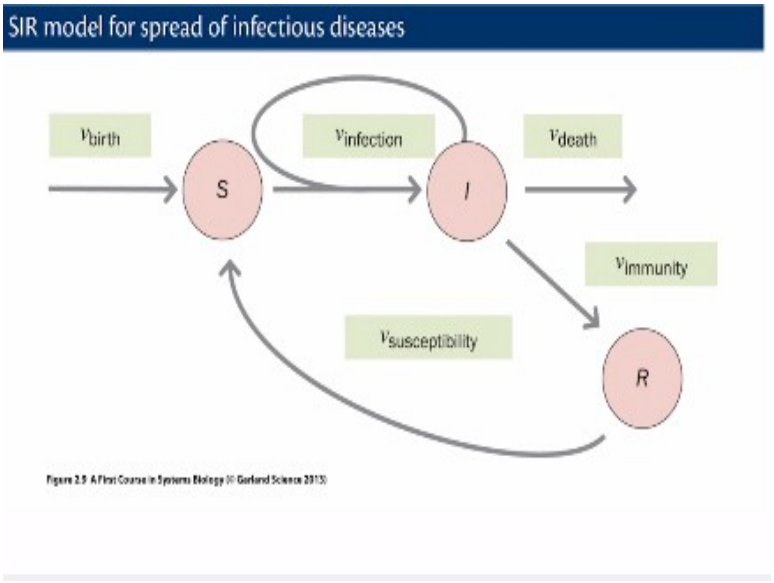

A very motivating example that we talked about yesterday. So, this is the model for spread of infectious diseases. So, as we said earlier, there are three kinds of subpopulations you want to worry about: What fraction of people are susceptible? What fraction of people are infected? And what fraction of people are recovering from a disease? And we typically write this out as SIR and so it's called the SIR model of infectious diseases.

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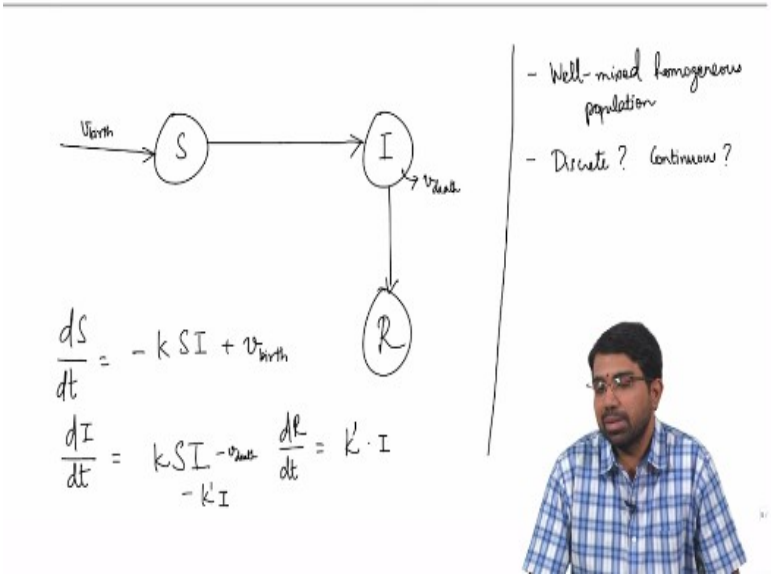

So, given this, let's just step aside. What are all the things that you need to worry about? Think of this like your standard chemical reaction where SIR or like species, even before this you may want to state certain assumptions. What I am trying to do here? I want to find out the number of the fraction of infected people at time t. Is that fraction going be very high? Then, I need to alert my hospital authorities or whatever.

I need to figure out various things, right? So, how does a disease spread, a communicable disease? Interaction between susceptible people and infected people. You basically have an edge here. Some sort of collision. If I have to say something like, ds by dt is something, what would my assumptions be? So, people are well mixed in a reactor, it is the equivalent of that.

The people are, very likely to interact. Everybody is equally likely to interact with everybody else. There is some sort of uniform probability of interaction between the people. So, this is one thing. What kind of other things you need to worry about? Maybe some birth rates and yes, so there are simplifications such that you can do, if a disease spreads quickly, you can ignore these.

If you are looking at a one-month window, you are assuming that there not significantly larger number of births and deaths except of course, a disease that is going to affect infants and so on. So, immediately you will start seeing, right? There are certain assumptions which are valid in

certain scenarios but will be fundamentally defeated in other scenarios. So, you need to always be cautious about these and infected people can recover.

So, how would you write out these interactions? What is ds/dt going to be? Some –kSI, right?

$$\frac{dS}{dt} = -kSI$$

Everybody agrees? There will be some S_0, so you are, I mean, this is just the rate of change. You will have an initial population of susceptibles from which these changes will happen but we have to assume other edges. So, if you want to consider v_{birth}, you will have,

$$\frac{dS}{dt} = -kSI + v_{birth}$$

You may have to consider a v_{death} .You will have a different v_{death} here (in I) and a different v_{death} here (in R).

Or for simplicity, we will just leave out the death rates currently. Or we can just assume this death (in I) because this may be more significant than other deaths (in R). So, wait for a moment, let's write out what is dI/dt.

What is the rate at which people get infected? It will depend upon the interaction between susceptible and infected people, right? So, it is going to be proportional to S and proportional to I, connected by some constant (k). It will also have $-v_{death}$ and so on.

$$\frac{dI}{dt} = kSI - v_{death}$$

Yeah, so let's first write out what is dR/dt.

$$\frac{dR}{dt} = k'I$$

This will again come here in dI/dT

$$\frac{dI}{dt} = kSI - v_{death} - k'I$$

There is some sort of a mass balance, right? So, in fact that people become recovered or you know, susceptible people become infected, recovered people could become susceptible again, let's not worry about all those complexities at the moment. So, there are different kinds of interactions that can happen essentially.

We will try to look at this model in greater depth as we go on but it is just to kind of, attract you to modelling because it's very easily understandable model and we can immediately suggest a lot of improvements, right. So, let's see if we have got the modelling right in a very basic fashion.

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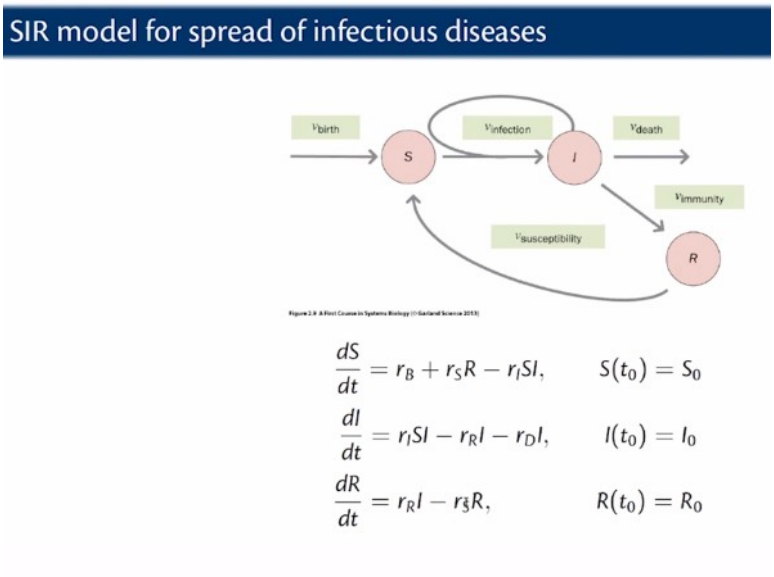

So, this is very similar to what we started off with, so

dS/dt = v_{birth} + some recovered people coming in - some rate of infection that connects S and I and takes them to infected.

dI/dt= Some rate of infection that connects S and I and takes them to infected - some death rate which can actually be linked to the population - some recovery rate,

dR/dt = Some rate of how the infected people recover - how the recovered people actually become susceptible again.

So, this is very similar except you may want to instead of v_{death}, you can use a k_{death}*I and so on. **"Student conversation"** Exactly, right? So, this is where we need to worry

about, right? This is a continuous system or it is discrete? We are not talking about people, we are talking about population or fractions of populations. We are literally treating them as chemical species in a reactor. This is where a lot of chemical engineers actually work in SIR modelling I presume.

But you can also have a completely discrete system, or at the least you could just fractionate the system. You can have, you can group them by age. May be twenty to thirty year olds are relatively more immune to this or sixty to eighty year olds are extremely susceptible to this. So, you can fractionate that population now. Or you can consider many more interventions. So, let us just think about other interventions you may want to make.

What are the other interventions you may want to make here? The improvements to the model? Yeah, so the recovered people can go get infected again. Yes, so that is this. Recovered people become susceptible or you mean they can just a direct relapse of infection? Yes, you can have that too. Infection can directly relapse, so you can have a connection from R to I, back to I straight.

Yeah**,** so the birth rate can itself be a function of disease, yes that is a possibility. Bunch of people who are genetically immune or better still who is not genetically immune to the disease if you have been vaccinated, right? So, can you model vaccinations? If somebody has been vaccinated probability of contracting the disease just drops. So, in fact this should be what, these are actually things that are used by governments to say who to vaccinate.

So, when there was the Ebola outbreak, obvious, you probability didn't need to model to do that but you have to vaccinate the health care workers because they had the maximum risk of contracting and spreading the disease. They had the highest susceptibility. Maybe you want to vaccinate school children because they travel by a school bus, then they go to an evening class, they go to school where they interact with a lot of people so on and so forth.

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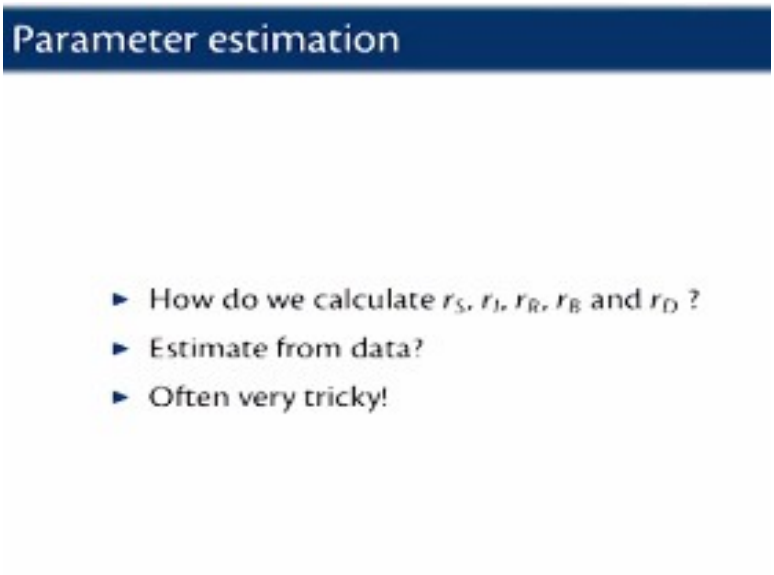

So, you may have to actually model these different populations differently and all the heterogeneities in the population. How do you calculate these different constants that are there, parameters, the rate of susceptibility, the rate of infection, the rate of recovery, the rate of birth, the rate of death and so on. So, we can basically try to fit the model back just like you would get some readings of what are the concentration of my enzyme, rate of my reaction and fit your Michaelis Menten curve.

Similar thing here, obviously a lot more challenging. You want to fit about five parameters from different sets of epidemiological data. You get different data sets from historical records of how this particular infection has spread through a particular city and you use that to make accurate estimations of these but it could be quite tricky.

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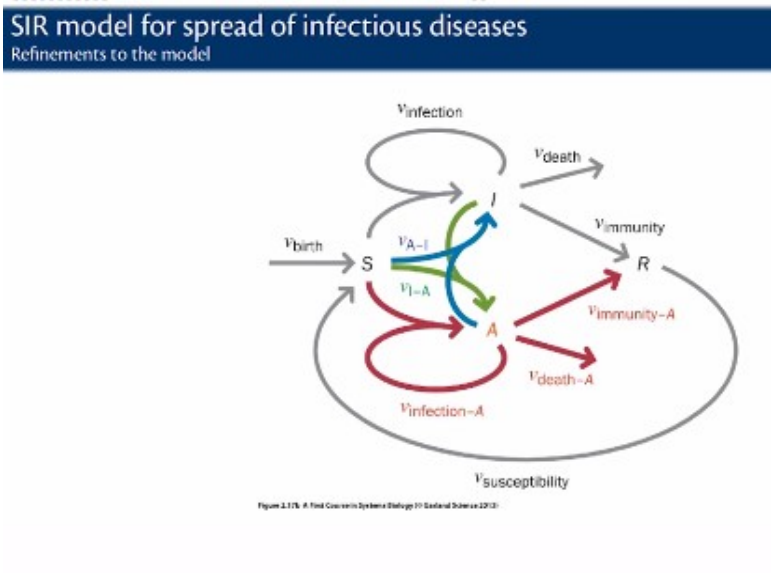

So, you can make several refinements, you can have a different rate at which the infected people recover and so on, whereas there are bunch of immune people who have a different lower death rate and so on, so on and so forth. You can add a lot of edges. And you can actually think of this whole thing as happening on a network. You have a completely discrete model. You take the facebook map of a city and use that to study how the disease flows. You know who is going to interact with whom based on the social network. And then you say only these kinds of people are going to be affected by this, these people are not at risk, these people are at higher risk. So, there are many interesting things that one can do. We will try to look at some of these things in the following classes.

Any questions and many more enhancements to this model you can think about, but yeah, we just focused on a few. You can have, you may want to worry about people immigrating and emigrating from the city for example, right? If those rates are high enough and in fact, you know that's very important when you have a disease that is international in origin. The whole of swine flu, people were worried about who is travelling in from Mexico, who is travelling out to some other part of the world and so on.

And airports became the hub for spreading the disease or containing the disease and so on, **"Student conversation"** Yeah, you mean the birth rates or? **"Student conversation"** Yes, so

$$dS/dt \; \alpha \; S$$

in terms of, usually birth rates are measured in number per thousand of population, so you will say there are three children born per month per thousand people of population or something like that.

So, that's how usually these numbers are estimated. **"Student conversation"** It becomes very challenging. But you will always have some data, right? You would have seen how you would have the last ten days' data, right? So, you will have to quickly build an approximate model based on that. So, this question that you ask is very interesting. This is exactly what's done in, there is a lab which does this called NDSSL, I forget the expansion but this is exactly what they do.

They have a wartime modelling scenario and the peacetime modelling scenario. The wartime modelling scenario is when you have a Zika outbreak and you want to actually handle it. The peacetime is, Zika is done, you have now collected all the data, now how can you prepare for the next outbreak, right? But in war time, you want to still be able to make as good predictions as possible. In fact this is something that Bill Gates has been advocating as a part of the Gates foundation.

But then this modelling can help you answer several questions. Is this going to even become an epidemic? We will look at some of these things in little more detail. **"Student conversation"** Exactly, now that is another steady state for the model, right? Zero. It is the complete steady state but maybe another steady state is that the infected people have become zero, so I=0 is also a steady state and S= I=R=0 is also a steady state for the model as you will see.
So, there is something known as basic reproductive rate, the number of infections per infection kind of thing. If that is too large, then you have a danger of an epidemic. If that can be contained, then you have a good chance of containing the epidemic.
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In today's video, we looked at the example model of SIR which I hope you will agree was a very motivating example. And in the next video, we will start looking at some more examples, different kinds of models which have essentially stemmed from some student assignments and so on.