Modeling Epidemics
For Neural Network Students

Wulfram Gerstner

EPFL, Lausanne, Switzerland

1. Neural Networks and Epidemics
2. The Problem with COVID19
3. The SIR model
4. Intervention strategies
5. Quiz

https://www.worldometers.info/coronavirus/

https://labblog.uofmhealth.org/rounds/how-scientists-quantify-intensity-of-an-outbreak-like-covid-19

https://en.wikipedia.org/wiki/Compartmental_models_in_epidemiology

https://www.youtube.com/watch?v=Xmun0ZqpQeg

https://en.wikipedia.org/wiki/List_of_countries_by_hospital_beds

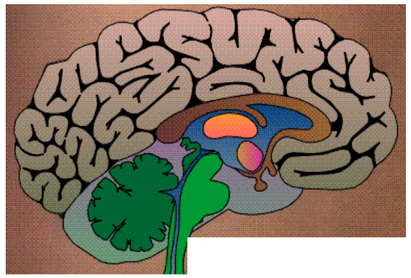
https://www.medrxiv.org/content/10.1101/2020.03.05.20031815v1

Comments to previous slide

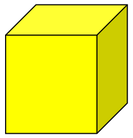
Special session for the students in my Neural Network Classes at EPFL.

This is a class on Neural Networks, but given the special situation I would like to talk today about how to model an epidemics such as COVID19.

6.0. Neural Review: Brain information processing

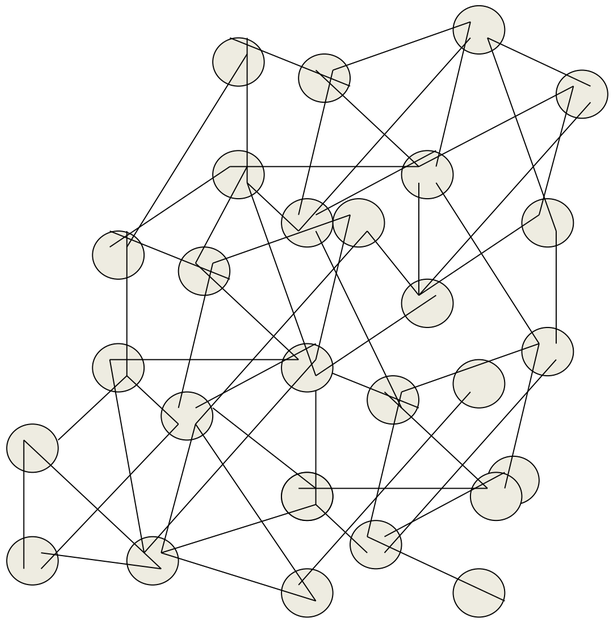


Brain



1mm

10 000 neurons
3 km of wire
many connections



Billions of neurons

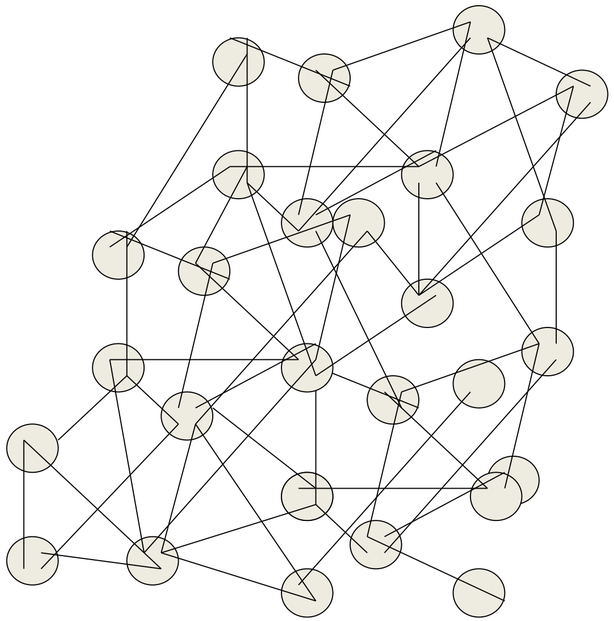
Comments to previous slide

Comments previous slide:

In the brain there are billions of neurons that are highly connected with each other: Each neuron makes several thousand connections to other neurons and neuronal activity spreads from one group of neurons to the next.

6.0. Epidemics: Interacting people

Same type of math that we apply to recurrent neural networks can be applied to spreading of an infection



- Equations for activation
- Spreading of activation
- Network analysis: average dynamics

Comments to previous slide

Comments previous slide:

The same type of math that we use to analyze recurrent neural networks can also be used to analyze network activity.

I am neither a virologist nor an epidemiologist.
But, for more than 20 years, I have used mathematical models to describe biological phenomena in neural networks.

Using this type of math we can analyse a standard model of epidemics.

Spread of COVID19 infections: where is the problem?

1. Switzerland has 4.5 hospital beds per 1000 people

   this includes: accidents, cancer, neurology, …

Suppose half of them can be made free for an epidemics.

2. 80% of Covid19 patients have no or weak symptoms.
   Suppose that 5% of Covid19 patients have complications:

   pneumonia with breathing difficulties that need to be hospitalized

3. If 10% of the population are simultaneously infected:
   - then this does not sound like a lot
   - but there are not enough beds for patients w. complications

Spread of infections: where is the problem?

Comments previous slide:
Newspapers talk a lot about the number of deaths and mortality. However, the mortality depends on the treatment. A good treatment of pneumoina with breathing problems requires a hospital. Therefore we need hospital beds.

The example on the previous slide is a based on the actual number of hospital beds in Switzerland. All the other numbers are estimations.

However, there is a common misconception that for an epidemics you have 50 percent of people being sick at the same time. This is WRONG. Already with 10 percent of people who are simultaneously sick, we run into a real problem in Switzerland – and this is exactly the problem that Italy has experienced during the last two weeks and is still suffering from.
There will not be enough beds to treat the serious cases with complications in a hospital!!

Problems of COVID19

- Patients that could normally be treated cannot go to hospital:
  ‘overload of healthcare system’

- Covid19 Epidemics is difficult to stop because
  - people with mild (or no) symptoms are infectious
  - estimation: each infected person infects on average
    (at least) 2-3 others

→ We need to control the number of SIMULTANEOUS infections
→ Stay at home

Comments to previous slide

Comments previous slide:

The specific case of COVID19 is particularly difficult, since people that do not feel sick (because they have no symptoms or only weak symptoms) can spread the disease. Thus, the simple rule: ‘stay at home when you have a fever’ does not work! In a village in Italy where the whole population has been tested, 50 percent of the infected people reported feeling ‘not sick’.

Infected people, even if they feel not sick, can infect others.
Therefore everybody has to stay at home – otherwise the number of simultaneously infected people goes above the fraction that hospitals can manage.

Model of how infections spread:

N = Total population, split into three groups: S+I+R

S = Susceptible: persons that can get the disease

I = Infectious: can infect others

R = Recovered: are now immune.

In Δt = 1day, number of infectious people increases by

$$\Delta I = \frac{\beta}{N}\Delta t \cdot S \cdot I(t) - \gamma \Delta t \cdot I(\mathrm{t}) \longrightarrow I(t+\Delta t) = \Delta I + I(t)$$

number of people infected by a single person in 1 day

rate of recovery

Comments to previous slide

Suppose that we have a population of N people with closed borders. Some of them are infectious (number I). These people can infect those other people that are still susceptible (number S) since they have not yet had the disease. The factor of spreading is beta (with a normalization constant N).

The number of infectious people increases because new people can get infected. It decreases because some people recover. The decay factor is gamma.

Beta times Δt (divided by N) is the probability that a single infectious person infects one other person in. We can think of it as the probability that an infectious person meets another person time the probability that the infection is transmitted during the encounter. The factor N has no deep meaning: it is a convention to scale beta with N so that the total size of the population is less relevant when we compare countries of different size. However the scaling with Δt is important: if I choose Δt=1hour instead of Δt=1day the increase in ΔI is proportionally smaller.

The increase ΔI is proportional to the number of encounters S*I between susceptible and infectious people; the decrease is due to recovery from infection.

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https://www.youtube.com/watch?v=Xmun0ZqpQeg

Comments to previous slide

The previous considerations lead to the famous SIR model.

Spread of infections: SIR model

S = Susceptible: can get the desease

I = Infectious: can infect others

R = Recovered: are now immune.

N = Total population. $N=S+I+R$

$$\frac{dI}{dt} = \frac{\beta}{N} S \cdot I - \gamma I$$

$$\frac{dS}{dt} = -\frac{\beta}{N} S \cdot I$$

Comments to previous slide

To model spreading of infections, a famous mathematical model is the SIR model. SIR stands Susceptible-Infected-Recovered.

We make the time step Δt smaller and small which then leads to a differential equation for the number of infectious people.
The number S of susceptible people decreases because they get infected.

We end up with two differential equations, and two parameters gamma and beta.

Basic Reproduction number in the SIR model

basic reproduction number

$$R_0 = \frac{\beta}{\gamma}$$

Increase of infections if

$$\frac{S}{N} > \frac{1}{R_0}$$

I = Infectious

$$\frac{dI}{dt} = \frac{\beta}{N} S \cdot I - \gamma I \longrightarrow \frac{1}{\beta}\frac{dI}{dt} = \left(\frac{S}{N} - \frac{\gamma}{\beta}\right) I$$

S = Susceptible:

$$\frac{dS}{dt} = -\frac{\beta}{N} S \cdot I \longrightarrow \frac{1}{\beta}\frac{dS}{dt} = -\frac{1}{N} S \cdot I$$

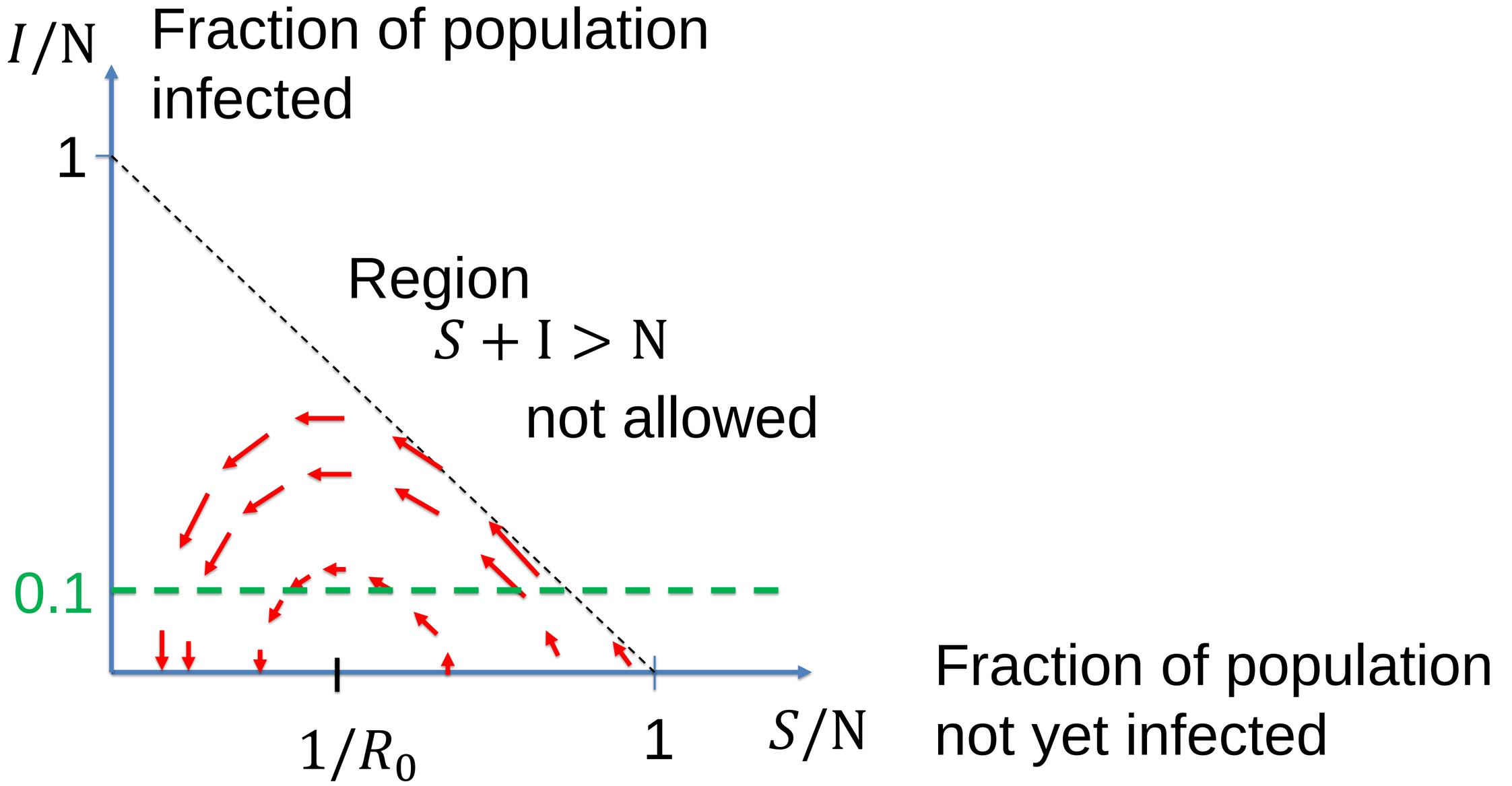
Comments to previous slide

We can think of ‘1 over beta’ as a time scale of infection. In case of COVID probably a few days. If we rewrite the equations with that time scale we see that the relevant term is a comparison of the FRACTION S/N of susceptible people with a ratio (gamma/beta). The inverse of this ratio defines the basic reproduction number:

R0 is the typical number of people a single patient can infect during the duration of his or her infection. This is the number people talk about in the papers.
To understand this statement consider the following:
(1/gamma) is the time an infectious person has to infect other people. Hence Beta times (1/gamma) is the total number of infections a single infectious person can cause during the infectious periode.

Infections start to DECREASE if the fraction of susceptible people falls below 1/R0.

SIR Model: Phase Plane Analysis



Comments to previous slide

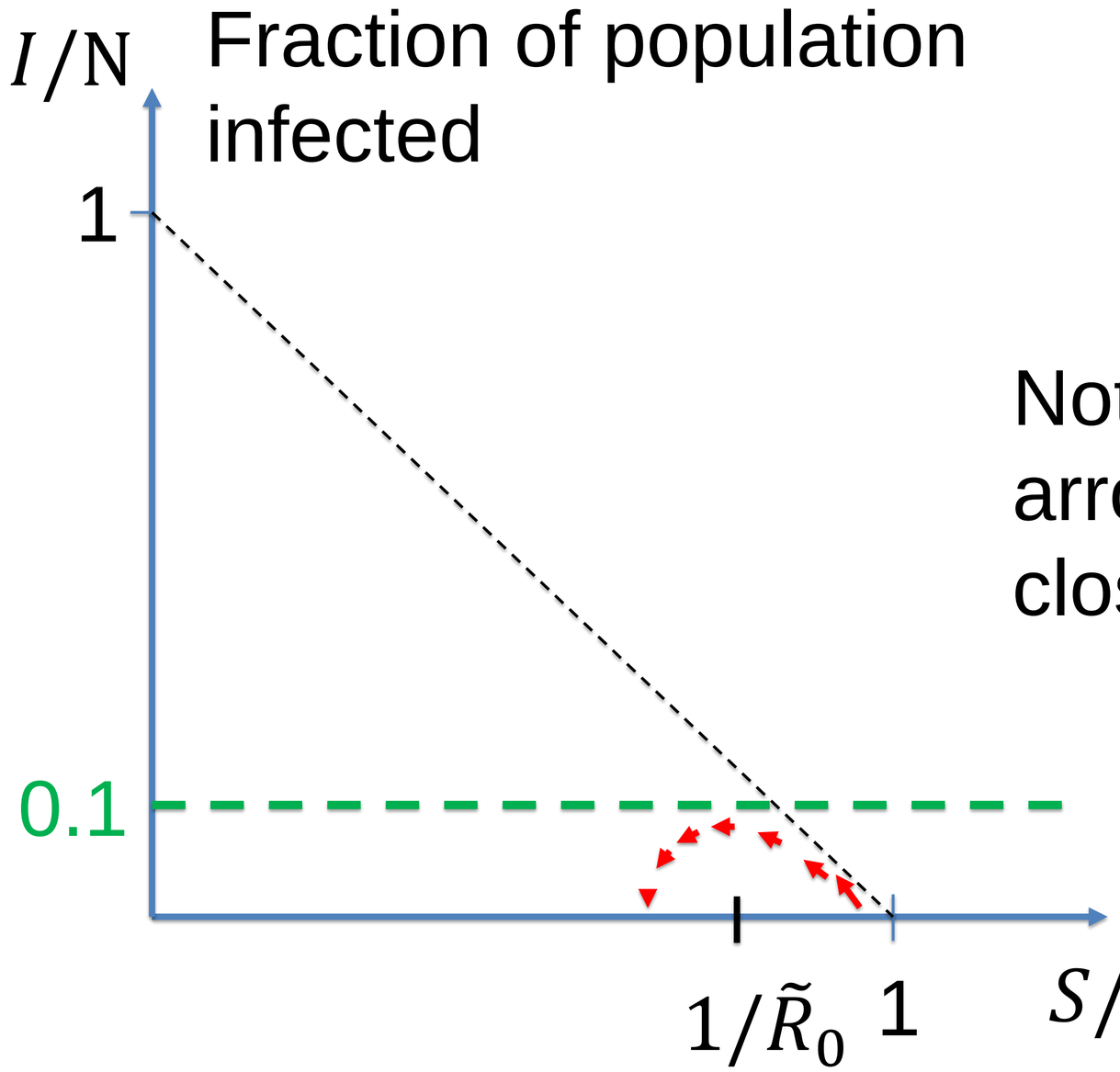
We now use phase plane analysis to study this 2-dimensional system.
I did not plot the nullclines, but you will do this in the exercises.
The system is somewhat special because we do not have one or two or three fixed points, but a whole line of fixed points along the x-axis.

The triangle below the black-dashed line indicates the allowed region (because $S+I+R=N \rightarrow S+I<N$ (or $=N$).

Based on the tools we discussed in class two weeks ago, we can qualitatively construct the arrows in all regions.
Trajectories depend on the initial condition.
For COVID19, the initial condition is very close to S=N and I=0, so say S=N-epsilon and I=epsilon. This means that the trajectory makes a large excursion.

HOWEVER, the fraction of simultaneously infected people should stay below 0.1 (green line). THIS IS WHERE THE PROBLEM COMES FROM!

SIR Model: Influence of R_0



Note:
arrows are smaller close to x-axis

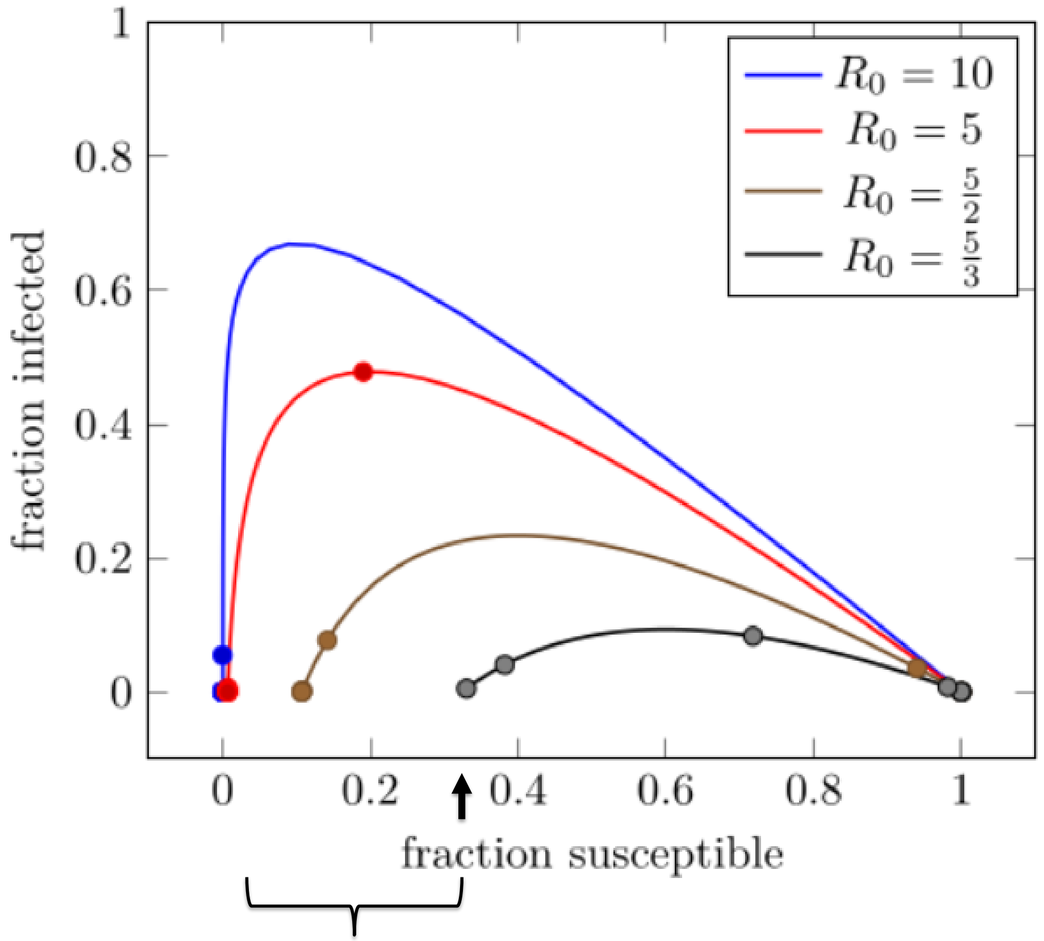
Comments to previous slide

We now change R0 to a new value tilde-R0.

If the new value is close to one (say R0 =1.2) then the excursions are rather small (below the green line) and slow (arrows are small).

SIR Model: Influence of R_0

Fraction of population infected



distance between dots: 1 time unit T (e.g. 1 months)

Fraction of population not yet infected

Fraction of people who did not get ill (R_0=5/3)

Comments to previous slide

So far we discussed qualitative features of the SIR model.
Real simulations give curves like the one in this graph.

The only free parameter of the curve is the parameter value R0. To indicate the speed, we simulate for a fixed period T, put a dot, and then simulate for another period T.

We don’t know the T for the COVID19, but it is probably 1-3 months.

Thus the disease stops more rapidly for R0=10 than for R0 = 5/3. You pay for this by the big excursion.

Not that for R0=5/2 and R0=5/3 the disease stops well before everybody has had it.

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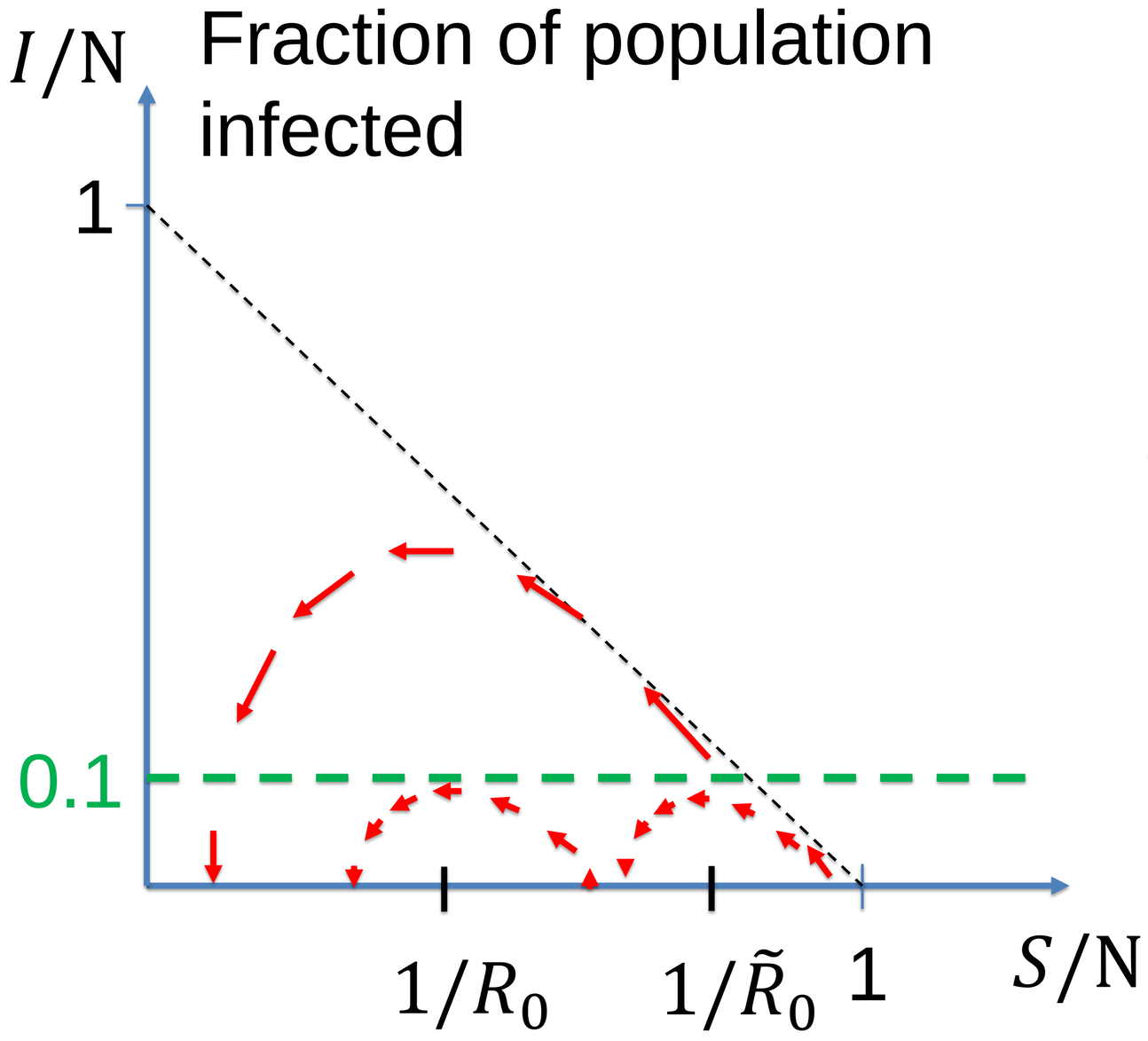
Comments to previous slide

The previous insights can be used to design intervention strategies.

SIR Model: Intervention strategy: Reduce R_0 initially



Initially we reduce
$R_0 \rightarrow \tilde{R}_0$
then we go back to
R_0

Fraction of population not yet infected

Comments to previous slide

If a disease breaks out, the government must take measures so as to reduce R0 to $\tilde{R}_0$ with a value close to one, or even smaller than one.
At a later time we can go back to the normal value. There might be a second small outbreak but it is not so big because fewer people are susceptible.
Importantly, even AFTER the second outbreak fewer people have had the disease than in a case without intervention.
Intuitively the reason is as follows:
Suppose R0=2. Hence every infected person will (at the beginning of the disease) infect two others by chance encounters.
Suppose we are the moment when 49 percent of the people have not had the disease and are still susceptible. There are now 2 different situations:

(i) The other 51 percent are currently infected and infectious. In that case nearly all the remaining people will also be infected, because half of the chance encounters will be only average with a susceptible person.

(ii) Only 1 percent are currently infected. These will by chance encounters infect another 1 percent, but then the disease rapidly dies out.

Spread of infections in SIR Model

Role of basic reproduction number

- Epidemics stops without excursion (immediate decrease of I) if reproduction number $R_0 < 1$
- Epidemics stops after some time also if $R_0 > 1$ (with finite number of unaffected people S>0 remaining)
- Excursions (maximal number of I/N) are smaller if
  - we start with S < N (i.e., many previously immune people)
  - the reproduction number R_0 is close to 1
- No excursion/immediate return if initially $\frac{S}{N} < 1/R_0$
- ‘Speed’ of spreading remains small if $\frac{I}{N} \ll 1$

Comments to previous slide

There are two important parameters in the model:

The reproduction number R0 and the initial fraction S/N of susceptible people.
The two together determine where there is

- no excursion in the phase plane
- small excursion in the phase plane
- large excursion in the phase plane

By excursion in the phase plan, I loosely refer to the fact that initially the number of infected people grows, before it decays back again.

The two parameters together also determine how many people remain unaffected (have not had the disease and are still susceptible) once the disease has stopped.

Spread of infections

1. Keep basic reproduction number R_0 small:
   → Stay at home!
2. R_0 may grow again thereafter (after many weeks!)
3. Strategy of confinement policy:
   -make peak of *I(t)* smaller, but broader
   → no overload of healthcare system
   -reduce area under peak
   → less people get it in total

https://en.wikipedia.org/wiki/Compartmental_models_in_epidemiology

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Comments to previous slide

Government recommendations are useful:
We must ALL TOGETHER reduce the reproduction number R0 for several weeks.

And this is done best if we stay at home.

Even if R0 is later increased again, the net effect of transient reduction is positive for two important reasons:

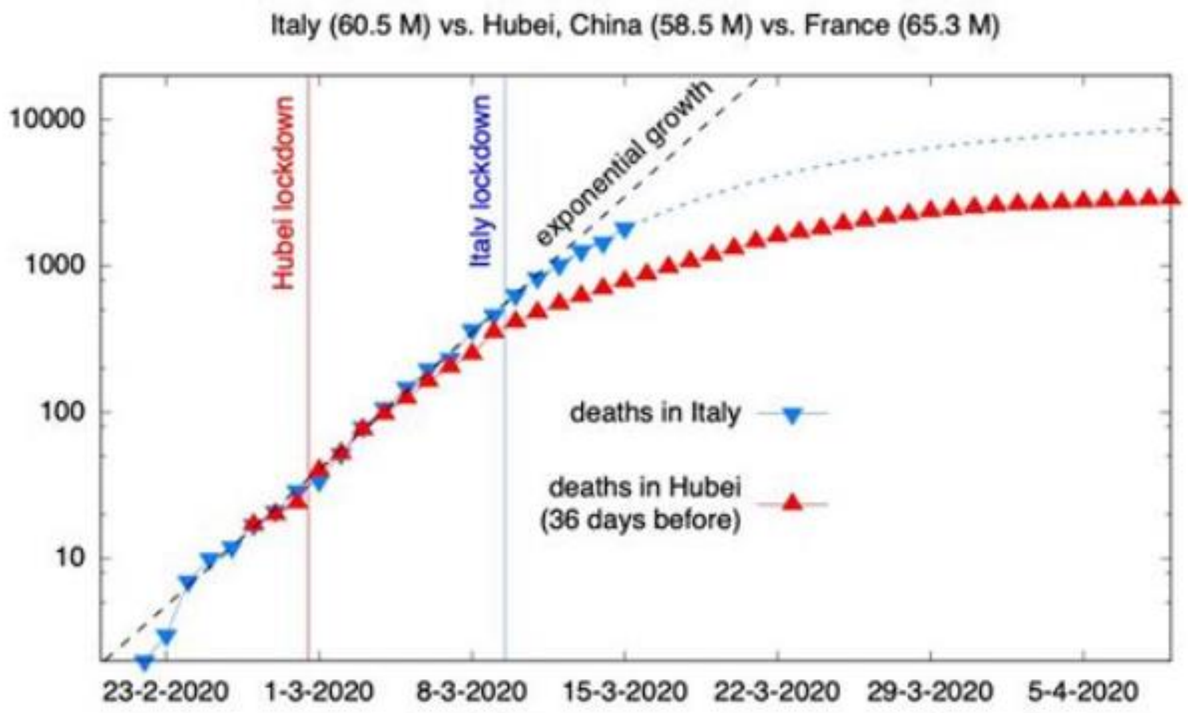
- At no point the number of infected people is so big as to overcharge the hospital system.
- The total number of people who got the disease is smaller.

I do not know for how many weeks the reduction is necessary. But probably 8-15 weeks.

Spread of infections: Intervention strategies work

Federico Ricci-Tersenghi professor of physics in Italy

https://www.facebook.com/federico.riccitersenghi/posts/10158298832728559



Growth has been exponential,
until country started intervention strategy

For all numbers:
https://www.worldometers.info/coronavirus/

Comments to previous slide

All these considerations are independent of whether all the people in the group R have recovered or whether some of them have died.

The main reason to follow the curve of the number of deaths is that this is the most reliable number in the current outbreak of COVID19.
The number of confirmed cases depends critically on the number of tests performed. I estimate that for one confirmed patient 10 other patients have the disease without even tested.

The slide here is mainly to show that intervention strategies work.

Quiz: SIR model

[ ] The reproduction number R_0 can be interpreted as the number of people a single infectious person will infect on average (at the beginning of the disease).

[ ] The outbreak of an infectious disease with $R_0>1$ will stop only once everybody in the population has had the disease.

[ ] The number of people who get the disease before it dies out only depends on R_0

[ ] Intervention strategies try to reduce the value of R_0

[ ] If the intervention strategy ends and people go back to normal behavior (normal R_0), the same number of people will get the disease in the end as if no intervention had taken place

Summary: epidemics with the SIR model

1. Infectious diseases have a threshold for spreading which is set by the basic reproduction number R_0. Diseases spread if
(i) $R_0 > 1$ AND (ii) initial state of susceptible population $S/N > 1/R_0$.
During spreading the initial growth is exponential. Growth slows down because the fraction of susceptible people decreases. For a new disease such as COVID19 the initial fraction is close to one, $S/N=1-\varepsilon$. Hence it spreads for any $R_0 > 1$.

2.The peak number of infected people is reached if $S/N= 1/R_0$.
The final state is NOT the state with S=0, i.e., the epidemics stops BEFORE everybody has had the disease, just because there are no longer enough ‘victims’.

3. By a step-by-step policy (temporary reduction of contact numbers) the fraction of susceptible people can be moved below $1/R_0$.
If the natural R_0 is slightly above 2, that means that in the end 60 percent of the population will have had the disease AFTER the step-by-step policy.
Without temporary reduction of contact numbers about 90 percent would get the disease (because the trajectory in the phase plane makes a much bigger excursion, see curve for R=5/2)

Strengths and Limits of the SIR model

Strengths: - mathematically transparent, easy to interpret
- only two parameters: R_0 and initial value of S

Limits:
- No delay for incubation time
- Infinite immunity for recovered people
- Perfect mixing:
  - everybody interacts with everybody else
  - no group structure (clusters of friends)
  - no age structure

Extensions of model: https://en.wikipedia.org/wiki/Compartmental_models_in_epidemiology