Corona, Mathematical Epidemiology, Herd Immunity, and Data

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1 Introduction

This paper is meant as a contribution to the discussion of what is a suitable response or containment strategy for the Covid-19 epidemy. It grew out of an earlier version, [SL2]. The main part is an explanation of the type of models that have been developed in mathematical epidemiology, the relationship between them, and in particular the notion of an unstable state.
This is of great importance since some politicians seem to suggest that we can reduce the number of active infections to zero and then return to normal life. Mathematics on the other hand suggests, that if you want to return to normal life, without the risk of a restart of the epidemy, you can only do so, if enough people are immunized. And that probably means, that without an effective vaccine there is no way to keep the total number of infected below a natural threshold - the so called herd immunity.

In the simplest mathematical model, whose only variables are the currently infected and currently immunized individuals, this is just a percentage of the total population.

For Covid-19 this model is inappropriate - one has to deal with different subgroups of the population, and I will explain later how this is done. To a large extent the mathematical theory is applicable to any infectious disease. The respective differences lie in the parameters of the model, and they are difficult to determine. These parameters are crucial in order to give an estimate on the damage an epidemy will do. Therefore, I will discuss data to begin with, and especially mortality or infection fatality rate, as this is sometimes called in the literature. Data are basically results of tests, so I will first, in a summary fashion, describe my (incomplete) understanding of tests, the immune system and the process of infection.
The aspect I am not discussing is the destructive effect that the measures against the epidemy have for the economy and the whole fabric of the society.

Further reading: **[Ma]**, **[Zin]**.

2 Generalities about virus (PCR) tests, antibody (serological) tests, and a layman's picture of the course of infection

In a simplified way we think about the process of an infection as a contact process: a person with an active infection or an infectious person meets another, and if this one is susceptible, i.e. not yet immunized, then with a certain probability the infected will pass on the infection. Passing on the infection means realistically passing on a certain, not too small, virus load, which starts to grow exponentially. This will trigger a response of the immune system of the newly infected, and in the cases with a positive outcome eventually the virus will be eliminated. Part of this immune response is the production of very specific blood cells (B cells) which in turn produce antibodies that target the specific antigen (in this case the virus). One does not have this type of cells before the first infection. By type of cell I mean cells with this precise genome. They are 'newly invented' by mutations in a small part of the genome of specific cells - stem cells - in the bone marrow. The PCR tests try to find the virus, for Corona in swabs from throat and nose. The serological tests try to find the antibodies in blood samples. Both tests need minimum levels of virus respectively antibodies.
There is a big difference between SARS-CoV-1 or SARS and SARS-CoV-2, the virus responsible for Covid-19. Like in influenza, infected persons become infectious before or even without ever developing symptoms, as was pointed out e.g. in studies conducted in Guangdong and Vo, [Guang], [Vo]. On the other hand the level of virus associated with PCR detectability can be safely assumed to be somewhat lower than the virus level which is necessary to become infectious. The antibody response, or more specifically the monoclonal antibody response, starts later. There is a London/Liverpool study [Lon] on SARS-CoV-2 which gives a variable delay from the onset of symptoms of 5 - 40 days. 8.5% of the participants of that study never developed antibodies, at least not a detectable amount, or seroconverted as is the jargon. For hospitalized patients of Covid-19, according to this study, the antibody level stays constant for up to 2 months. This is certainly not true for asymptomatic or mildly symptomatic infected, who represent the majority of all SARS-CoV-2 cases. This will be explained in Section 3. But in any case the antibody count will go down when there is no antigen to work on. Recovered persons will no longer be serologically positive but still be immunized against the Covid-19 virus, that means they are able to crank up monoclonal antibody production without the delay of 10 days. See **Figure** 1 for a schematic picture of virus and antibody time evolution.

It should be noted though that **Figure** 1 refers to the dominant type of infection. It has been observed that patients can become PCR negative and PCR positive again, the virus probably attacking different organs. See the graph for patients P and H

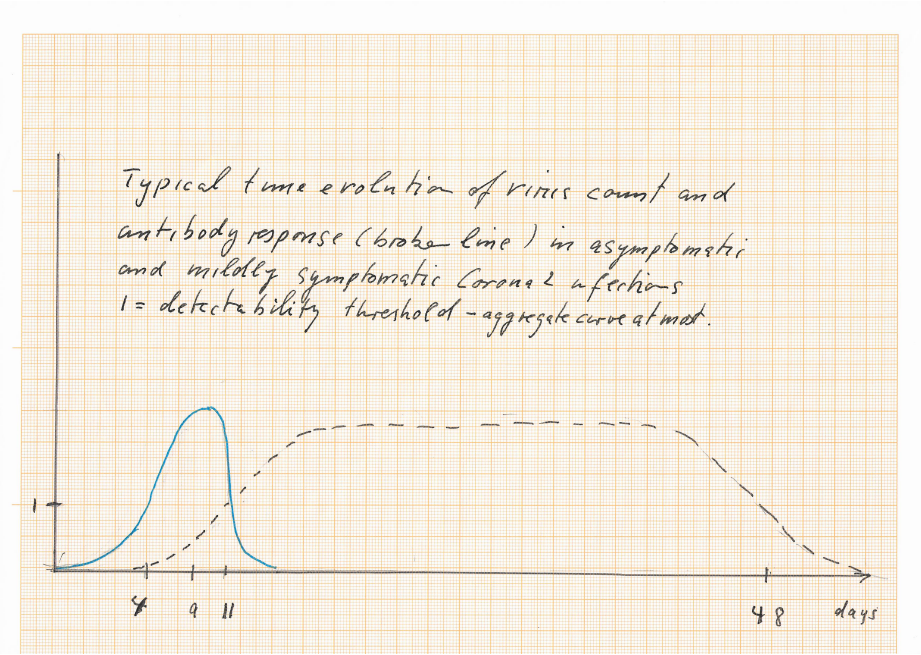

Figure 1*: A schematic view of virus and antibody counts normalized to level* 1 *for detectability. Numbers will be explained in the next section.*

(mother and daughter) in the Guangdong study.

In many respects the SARS-CoV-2 virus infection resembles the flu. The virus passes via aerosol inhalation to the sputum in the throat and nose region and proliferates there. One does not even have to develop a cold before one starts to be infectious. At least 40% of all infected among all age groups never develop symptoms at all, and an overwhelming majority only develops mild symptoms. Under normal conditions, represented e.g. by the 'new cases' in the study [Vo], the ratio of asymptomatic is 60% - the Vo data will be discussed extensively in Section 5.

But whether you are asymptomatic or presymptomatic, you are still infectious [Mu]. If one goes by the mild symptoms on the other hand, these are not specific. In the study [Eng], 90% of the people who crossed one of the symptom boxes in the questionaire, were serologically negative. The characteristic SARS like illness, and that is what Covid-19 meant at the beginning, hits only very few of the infected, namely less than 5% in the age group below 50. On the other hand, there is overwhelming qualitative evidence that whether you develop a mild cold, no symptom at all or the severe illness, depends on the level of exposure to contaminated aerosol. The qualitative picture I have in mind is **Figure 2**. There is evidence that people in Vo got the infection on two different events, the percentage of severely symptomatic lower and the percentage of asymptomatic higher (60%) for the later group.

Unfortunately there are many types of Corona viruses, and viruses are mutating fast. So antibodies for Covid-19 are not 100% effective for Covid-20, and that is bad

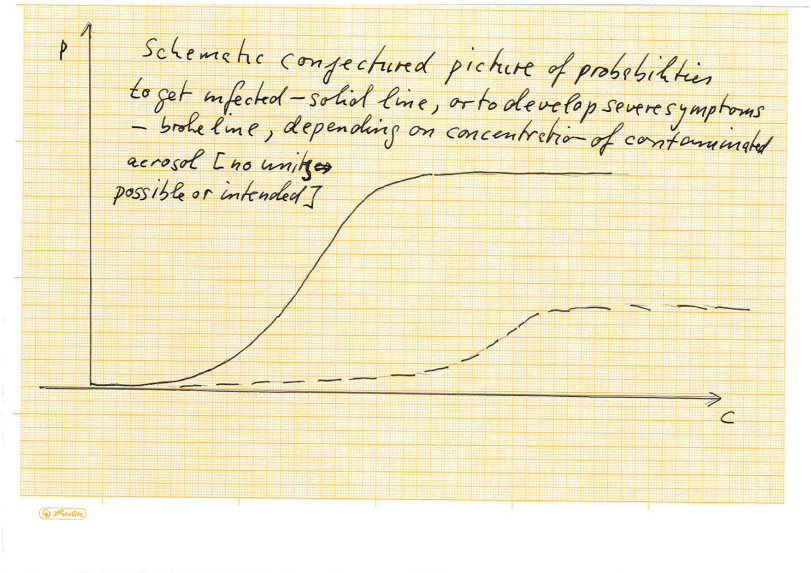

Figure 2*: Conjecture of dependence of the outcome of the infection on aerosol contamination c .*

news. On the other hand antibodies for pre-Covid-19 Corona infections might have some effectiveness for Covid-19. This might be called cross immunization, like the vaccination a la Jenner, using the cowpox antibodies against smallpox. In any case, whether a vaccine will produce antibodies as effective as the natural antibody against Covid-19 or even more effective against Covid-20 remains to be seen. This is especially true since the question whether flu vaccines prevent asymptomatic transmission has not even been asked to my knowledge.

The studies quoted in this section are [**Vo**], [**Guang**], [**Mu**], [**Lon**], *and* [**Eng**].

3 Conclusions from the studies in Vo, Gangelt, and Bad Feilnbach, with a view to application to the study in Geneva

The study in the city of Vo, in Veneto is based on massive PCR testing of its ca. 3 000 inhabitants, mainly on the days of February 25, 26, 27, 28, 2020 which was the carnival week, and a second test on March 7, 2020. The study proved that in a small community with two tests about a week apart and strict quarantine rules plus a lockdown of two weeks, February 23 - March 7, 2020 the infection can be eradicated. The study also gives an estimate on the duration of the span of detectability - larger than the time of infectiousness - of a Covid-19 infection: typically around 10 days. I will explain in Section 5 how this is possible. Actually, I think this has to be modified a bit, since, as I mentioned already, there seem to have been two separate infection

waves in Vo.

The study in Gangelt was another carnival outbreak, in this case in the rhine region, and traced back to a festivity on February $15th$. In a community of 12 600 inhabitants randomized PCR and antibody tests were performed on 900 people. 33 of those participating in the test in the week of March 31 - April 6 tested PCR positive. This has to be compared to 48 positive tests in the rest of the population during the same week.

One can not directly compare these numbers, one has to take oversampling into account, i.e. the fact that if you repeat the test every week you will test individuals positive up to 3 times. More precisely, if you know the weekly rate of positive PCR tests in a population as a percentage of the whole population, and you take a large random subset of this population, where you find a percentag p of PCR positive, then there are formulas connecting p, d and α, with α being the percentage of infected that your PCR tests discover, and d being the rate of new infections per day. Disregarding the change over time of p and d one has:

$$\frac{p}{\sum_k f(k)} = \alpha \quad , \quad \frac{\alpha}{7 \cdot d} = \frac{\alpha}{p}\, o \quad , \quad 7 \cdot o = \sum_k f(k) \ .$$

Here $f(k)$ is the probability that an infected stays detectable for at least k days, and o is the oversampling.

Taking the Vo data into account, a rough estimate gives the rate of 0.9 to 1.6 for oversampling and a probability of at most 0.18 for an infection to be discovered by the tests out of the study. Estimating the cumulative number of infected up to March $31st$ with the help of the number of positive antibody tests within the test group, i.e. 105, and comparing with the total of 340 PCR positives in Gangelt up to March $31st$, gives 0.22, which I think is not a huge but significant difference. And as I will explain too in Section 5, this is a conservative estimate.

Moreover the data of Gangelt indicate that about $\frac{1}{3}$ of all infections occured during carnival and of those, after the first week of March only a tiny fraction could be discovered by PCR testing. So the 0.18 is probably too much, which means that after one month the rate of false serologically negatives will be already significant.

Also there is a statement in the study [Gang] that only 16% of those serologically positive and who had participated in the carnival festivities were asymptomatic. But in Vo in exactly the same situation, a carnival outbreak, 45% were asymptomatic. This apparent contradiction is most easily resolved if you assume that the sensitivity of the serological test among the asymptomatic, call it s, is significantly below 1. Solving the linear system

$$0.55 + 0.45 \cdot s = x \ , \ \frac{0.45 \cdot s}{0.55} = \frac{16}{84}$$

gives a global sensitivity $x = 0.55/0.84 \approx 0.65$.

For the serologically positive who had not participated in carnival the Gangelt study gives a rate of 36% asymptomatic. But for the people who had been infected later in the 8th calendar week during the outbreak in Vo, the ratio between asymptomatic and symptomatic is $\approx 60\%/40\%$ (similar to the data from China, which I have only from the FT newspaper). Solving

$$0.4 + 0.6 \cdot s = x \ , \ \frac{0.6 \cdot s}{0.4} = \frac{36}{64}$$

gives $x = 0.4/0.64 \approx 0.63$, so a similar number.

Compare this to the fact sheet published by the RKI on its website, about an antibody test conducted in Bad Feilnbach in the 23rd calendar week. In Bad Feilnbach the outbreak had similarly occured around March 1st. After approximately 9 weeks, 40% of the serologically negative stated on the questionaire to have been positively PCR tested. I will assume they were symptomatic. Only 14.5% of the serologically positive stated they were asymptomatic. The formula as above gives $x = \frac{0.55 \cdot 0.6}{0.85} \approx 0.38$, if one assumes the total percentage of asymptomatic infected to be only 45%, a conservative estimate. So my conjecture on the 'true' sensitivity of the antibody tests is that it differs significantly from the sensitivity tested on hospitalized Covid-19 patients: It starts out below 0.7 and after around 2 months drops to a value less than 0.4.

The large scale study in Geneva was conducted starting on April 6, and the result of the first 4 weeks of antibody tests is published in [Gen]. I think that there the sensitivity should be comparable to Gangelt, [Gang], i.e. less than 0.7, since both studies were conducted at the tail end of the outbreak. With this correction, my guess is that by the beginning of May at least 15% of the population in Geneva had gone through the infection. For Bad Feilnbach I guess a similar percentage, and for Gangelt a percentage close to 20% . More precisely, if you take into account that only 22 individuals who had been tested PCR positive previously showed up for the antibody test in Gangelt, and if you assume 0.65 sensitivity for the antibody test, then the number of infected in the test group would be ca. 170, i.e. about 19% by March 31st. But the sensitivities might also be a bit lower. The calculations I did above, except for the example of Bad Feilnbach, assume a sensitivity close to 1 for all symptomatic. This is probably not true, my estimate is only a conservative estimate.

Going back to the question of oversampling, the corresponding estimate for the oversampling o would be

$$\frac{48}{33 \cdot 13} \ o \cdot 0.19 = \frac{340}{1300} \ , \ \text{ so } \ o = 1.23 \ .$$

These are all estimates which could be checked in larger scale randomized studies. They are 'universal' and not restricted to the studies from which they were obtained. This holds not only for the sensitivity of the antibody tests (0.65% after 1 month, 0.39% after 2 month) but also holds for the oversampling o within PCR tests.

The studies quoted in this section are **[Gen]**, **[Guang]**, *and* **[Vo]**.

4 Data for the Covid-19 epidemy

Here I want to explain my understanding of the data on Covid-19, focussing mainly on mortality. In politics and the media actually covid deaths and new infections are constantly mentioned. Since there is a not explicitly stated but clearly noticeable undercurrent claiming that covid is so much more dangerous than the flu, let me begin with the likely flu mortality. The influenza virus is rapidly mutating and unfortunately it does not seem to have lost virulence lately. The data I use are the total number of monthly death from the federal statistical office in Germany. What I propose to look at, are the months, where the number of deaths is above certain quantiles, the median and the 2/3 quantile, and to use the excess mortality above the median as an upper estimate for the number of victims of the epidemy, and the excess mortality above the 2/3 quantile as a lower estimate respectively. For the 60 months from May 2015 up to April 2020 we have 28 months with more than 76 000 deaths and among those are 20 months with more than 78 500 deaths.
The months with more than 76 000 deaths in the respective periods May - April are:
2015/2016: January - March,
2016/2017: October - March,
2017/2018: December - April,
2018/2019: December - April,
2019/2020: October - April,
and two outliers, namely August 2018, and July 2019.
The months with more than 78 500 deaths in the respective periods May - April are:
2015/2016: January and March,
2016/2017: December - March,
2017/2018: December - April,
2018/2019: December - March,
2019/2020: December - April.
The estimate on the number of deaths from infectious diseases is
$8\,400 - 14\,000$ for the period 2015/2016,
$39\,700 - 50\,700$ for 2016/2017,
$46\,500 - 59\,000$ for 2017/2018, with $28\,600 - 31\,100$ alone in March 2018,
$19\,900 - 31\,600$ for 2018/2019,
and $17\,700 - 33\,500$ in 2019/2020.
The lower estimate for the number of victims of the epidemy in April 2020 is indeed lower than the known number of covid deaths.
My conclusion is, that we had every year a 'flu' epidemy in the winter months, culminating in March. In March 2020 - by the lower estimate - we would estimate 6 400 flu deaths. against 1 800 covid deaths. April 2020, the peak of the covid epidemy, resulted in 5 800 covid dead, still much less than the flu deaths in March 2018. The period 2014/2015 is outside the 60 months considered here, but would have an

estimated $34\,300 - 45\,000$ flu deaths.

The first set of data that I want to compare the above numbers to are the data of swedish covid deaths, because there was no complete lockdown in Sweden, and part of Sweden has probably by now reached a stable state of immunization. That of course does not mean that there are no infections, it only means that the number of infections is a large fixed multiple of the imported infections, as in Iceland.

By the end of September 2020, Sweden had a little bit less than 5 900 covid deaths, i.e. 0.59 *per mille* of its population of about ten million people. Comparing this to the 'flu' epidemies Germany experienced between 2015 and 2020, and especially to the number of people killed by the 'flu' in the single month of March 2018, i.e. at least 0.35 *per mille* of the german population, puts the covid death toll of Sweden into perspective.

Let me first estimate mortality, or as the technical term is IFR (infection fatality rate) for the different age groups in Germany, and use this together with the swedish data to get an estimate on the number of infected, i.e. immunized, in the swedish poplation of the $20-49$ years old. I am using the German data from the RKI for the PCR positive in the calender weeks $27-39$, 2020 (July - end of September) and the covid deaths up to October 6th, in order to account for delays, to calculate a CFR (case fatality rate) and compare with the weeks $10-22$. These weeks are chosen since mass testing was introduced during June. The result is in *per mille* for the CFR of the respective age groups:
$20-29$ years old: 0.08 , down from 0.3 in the calender weeks 10 - 22,
$30-39$ years old: 0.43 , down from 0.85,
$40-49$ years old: 1.2 , down from 2.25,
$50-59$ years old: 6.0 , down from 9.3,
$60-69$ years old: 25 , down from 41 ,
and the $70-79$ years old: 91, down from 138 in the calender weeks 10 -22.

The ratio of confirmed covid cases in these age groups, also given in *per mille*, are:
2.3, 1.5, 1.35, 0.85, 0.45, and 0.35.
Probably the older age groups get tested less frequently.
In the calender weeks 10 - 22 these numbers were
2.9, 2.4, 2.6, 2.4, 1.8, and 1.6.
These last ratios *per mille* are in good agreement with the observation in the Geneva study [Gen], that the rate of infected is roughly constant in the population of the $20-49$ years old, and drops by a factor of 0.7 in the age group of the $50-65$ years old.

So it seems that by increasing test capacities since June, we have quadrupled the discovery rate of Corona infections in the age group $20-29$, doubled the discovery rate in the age group $30-49$, but increased it only by 50% in the other age groups. We

have to take into account that Geneva was a hotspot for Switzerland. The discovery rate in hotspots is always higher than elsewhere, and nevertheless the discovery rate was at most 10% in Geneva. We can be sure that the discovery rate in the whole of Germany was not more than 5%, and probably even less before the end of May. That gives us an estimated IFR of

- 0.02 *per mille* for the $20-29$ years old
- 0.04 for $30-39$
- 0.12 for $40-49$
- 0.5 for $50-59$
- 2.0 for $60-69$ and
- 7.0 *per mille* for the $70-79$ years old.

These are the numbers under the conditions of the epidemy in Germany in the months of March to May 2020. If we assume the same IFR for Sweden, this would mean that ca. 0.5 million people have been Corona infected among the $30-39$ years old swedes by the end of September, 0.35 million among the $40-49$ years old, and ca. 0.32 million among the $50-59$ years old. That means roughly one third of the swedish population in the age group $40-59$ and two thirds in the age group below 40 have gone through the infection. And that might correspond to the required level for stable immunization during the summer months. The last number is not very reliable because the number of Corona deaths is - luckily - so small in that age group. But you can compare the total death toll of Corona in Sweden up to the end of September and the estimated death toll of the flu epidemy January to March 2018 in Germany. The swedish and german percentages in the different age groups are comparable. Actually the swedish percentages are a bit less than the german ones.

Next I want to discuss - but only briefly - the antibody tests that have been conducted in many of the Corona hotspots, apart from Geneva also Ischgl in Tyrolia, the province of Bergamo in Lombardy, Greater London etc. All of them gave a huge discrepancy between the PCR confirmed cases and the serologically proved cases. This reduced the total IFR across all age groups, bringing them in line with the CFR observed in Iceland, which is 0.5%.

For instance for Greater London where 17% of all tested persons were serologically positive, one arrives at 0.6%. But as I pointed out already, the serological tests do not give the true number of infected, most likely also not for Geneva, London and Gangelt. Only $\frac{1}{2}$ to $\frac{2}{3}$ of the total number of infected were discovered by the antibody tests. The ratio is certainly much lower for the antibody tests among blood donors,

on the other hand it should be closer to one in Lombardy, because of the higher percentage of severe cases.

Finally in this section I want to comment on an obvious fact.
Corona is not only more dangerous for the older people, but Corona is also disproportionally dangerous for the elderly, who are living in nursing homes. The rate of deaths occuring in nursing homes in Germany as a proportion of all covid deaths has gone down from 40% to 23%, but it is still huge and could be avoided, as the study in Vo has shown, by testing all staff working in nursing homes or ambulant care weekly. The percentage of the elderly in ambulant care among the covid deaths is not available for Germany. But among those elderly who are in need of care according to the legal definition, only one fourth live in nursing homes, another fourth receives professional care at home, and half are still cared for by family members. The latter ones obviously have a vastly lower risk of being infected by the Corona virus or any other infectious disease. The ones getting professional care at home have an intermediate risk. It would be important for the statistics to know how high their risk is.

Some of the websites providing data are:
destatis.de (esp. 'Sonderauswertung monatlicher Sterbedaten')
rki.de (data per age group of covid cases only on the Tuesday updates)
socialstyrelsen.se
folkhalsomyndigheten.se (latest data only in swedish)
bag.admin.ch
gov.uk
and *london.gov.uk*

5 Remarks on statistics and the data from Vo

When we speak about statistics we mean two different things: descriptive statistics like the data of the RKI or the monthly death numbers of the national statistical office, and predictive statistics. For instance, saying that a male person of age 65 has a probability of 98.5% to reach the age of 66, is of the second kind, as are all the precentages/*per mille* given in the previous paragraph for total immunization of populations based on randomized antibody tests. One should keep in mind that predictive statistics is always based on the law of large numbers. Confidence intervals are calculated based on probabilities for a test to give a false positive or false negative answer for given values of the quantity you want to estimate. This is, in a way, completely illogical in itself, but can be made rigorous if one assumes a probability for the quantity you want to estimate, sometimes called a Bayesian prior. In this example of the 65 year old man, e.g. there is as I explained a huge variation of frequency of deaths from month to month, which is connected to infectious diseases. The year on

year variation is much lower for Germany, and below 4% even in extreme flu years like 2018. We always explain that by using the law of large numbers. This law can be seen as an hypothesis or as a theorem derived under certain assumptions - again on probabilities. For applications probabilities mean nothing else than relative frequencies of observable or non-observable data. So predictive statistics is impossible without modelling assumptions. It is always based on the existence of a large number limit of relative frequencies, and one should not place too much confidence in confidence intervals.

One can distinguish two approaches to the teaching of mathematical statistics.
The first is usually called the Bayesian approach. It starts from a set of particular e.g. Gaussian probability distributions (but there are many others). These are distributions jointly of the quantities you don't observe but want to predict and on the other hand on the observed quantities. Based on these distributions you calculate e.g. confidence intervals for estimators, that is prediction algorithms whose input are the observed quantities and whose output are the predictions.
The second approach goes under the title of nonparametric statistics. In this approach one tries to replace the assumption on the specific formula for the joint distribution by more general qualitative (independence) and quantitative (tightness) assumptions. What one never can avoid, is the assumption that the joint distribution is well approximated by one determined by finitely many alternatives, and that the observations are (conditionally) independent.

I will now explain all this a bit more precisely with the example of the anonymized public data of the Vo study [Vo], which is available as an Excel file on the web. Let me first tell the story of the events in Vo, as you can reconstruct them from that file, using also the Guangdong data, [Guang].
In the week before carnival, February $16-22nd$, there were already a number of covid infected in Vo, and among them the individual who was to become the first covid dead in Italy. It was probably known that covid had arrived in Italy, but not that it had arrived in Vo. So there were carnival celebrations. On Friday, February $21st$, the first covid death occured. The team in the University hospital of Padova found the same day a second PCR positive. The team immediately swung into action, testing 40, probably contacts, on Saturday and about 60 on Sunday. In retrospect one has to say that they hit on a chance correlation, because they found a large number of people who had been infected on a single event in the week before. In any case they had already discovered 21 infected individuals by Sunday, of which 5 did not show any symptoms. So they were able to persuade the authorities to declare a lock down of 14 days for Vo on Sunday, and started to test everyone in Vo, trying to find as many of the infectious as early as possible. So about 200 people were tested on Monday, February $24th$, about 470 on Tuesday, about 410 on Wednesday, about 490 on Thursday, about 920 on Friday, and finally about 40 on Saturday, February $29th$.

At the end of the lockdown on March 7th almost everyone was tested again. Eight new infections were discovered.

How can one conclude the dates or probable dates of the infection from this Excel file? Apart from the first and the second test results, there are two more hard data. The first is, whether a positively tested individual got severely ill - if I counted correctly, these are 7 out of 79, excluding the person who was dead on Friday, February $21st$. The second is, whether a person who tested positive with no symptoms did develop symptoms later. Of these presymptomatic cases there were 10. Now these presymptomatic individuals are clustering: One of them was discovered on Saturday, 4 of them on Sunday, 4 on Thursday and one on Friday. The only way to explain this is, that a person is presymptomatic with overwhelming probability only for one day; moreover, a majority of the discovered individuals got infected on two separate occasions; and finally, that the incubation time, that is the time from infection to the first day, when one is PCR detectable, is almost deterministic for a typical case. To obtain this almost deterministic incubation time, one can use the anecdotical evidence collected in the Guangdong, [Guang] and Munich, [Mu] studies. My guess is that you become presymptomatic on the $3rd$ or $4th$ day after infectious contact (latin numbering), so that the presymptomatic discovered on February $27th$ were infected on February $24th$ or February $25th$. This was some children's carnival celebration most likely. And similarly the presymptomatic of February $23rd$ were infected on what was probably a more adult celebration on February $20th$ or $21st$. I am telling this also as a story to show, how easily seemingly anonymized data can be used with a little bit of additional information e.g. as a starting point for a police investigation into unruly behavior.

But here I want to use these data for an estimate of $f(k)$, the probability to be detectable by PCR tests for at least k days. As I said before, the use of nonparametric statistics requires a model for a probability distribution, jointly for the quantity you want to estimate and the observations.

I will try to estimate the number of infected in the group of people who were tested on February $26/27th$. The data I will use are the number of asymptomatic (7/8), presymptomatic (0/4), newly discovered (2/2), positively tested (11/16), and individuals in the respective groups (410/490). I will assume that every infected person was detectable first on either February $23rd$ or February $27th$, which is in the end only an assumption on the probability distribution of the first date of detectability, and as usual there will be a lot of hidden independence assumptions.

Calling α the expected ratio of asymptomatic to symptomatic, n_{23}, n_{27} the expected number of infected which were detectable first on February $23rd$, respectively on February $27th$, we derive empirical error functions, assuming already that $\alpha = \frac{1}{2}$, $f(4) = 1$, and that infected are assigned with probability 4.1/9, i.e. $410/(410 + 490)$, to Wednesday and 4.9/9 to Thursday. That means independent assignment. These

error functions are

$$e_1 = n_{23}\,\frac{4.1}{9}\,f(4) - 9 \tag{5.1}$$

$$e_2 = n_{27}\,\frac{4.1}{9}\,f(10) - 2 \tag{5.2}$$

$$e_3 = n_{27}\,\frac{4.9}{9}\,f(1) - 10 \tag{5.3}$$

$$e_4 = n_{23}\,\frac{4.9}{9}\,f(5) + n_{27}\,\frac{4.9}{9}\,f(1) - 16\ . \tag{5.4}$$

$$\tag{5.5}$$

By linear regression, i.e. by minimizing $\sum_j e_j^2$ we get the rough estimate

$$f(5) \approx 0.56\ ,\ f(10) \approx 0.24\ .$$

I would not give confidence intervals for these numbers. But the estimate on $\sum_k f(k)$ one can infer from the data in [Guang] is $\sum_k f(k) < 7$.

If that holds true finally for the study in Gangelt, the oversampling o would be no oversampling but $o = \frac{1}{7}\sum f(k) < 1$. And correspondingly the sensitivity of the serological tests should be even considerably lower than the 0.65 after one month and 0.39 after three months under normal conditions. In order to explain what is a normal condition, it is useful to recall what I conclude from the Vo data. There were two different events in the period February $16 - 25th$, when many got infected. The first event produced, as far as I could make out, 5 presymptomatic individuals and 4 severely symptomatic. It also apparently produced among the asymptomatic individuals around 50% which were detectable for at least 2 weeks. The second event at the end of the week, as far as I could make out, produced no severely symptomatic, again 5 presymptomatic and apparently a proportion of 60% asymptomatic. These numbers are of course far too small to give anything like a confidence interval. But they provide a picture which is more or less in agreement with the data for 4 locally infected individuals in the study of Guangdong.

There are two distiguishable courses the infection may take. If the infection is an aerosol infection, a majority, ca. 2/3 if you believe my estimator, is detectable on the $3rd$ or $4th$ day after infection, and stays detectable for not more than 5 days. That means probably, that the virus does not progress to a significant extent from the respiratory system to other organs. For the remaining 1/3 there is more than one virus peak and probably a sequence of infections of several organs. Looking at the Guangdong data for patients P and H, i.e. mother and daughter, one expects a strong hereditary determinacy, whether you belong to the first or the second group. But whether the infection produces the disease or remains asymptomatic, and if it is symptomatic becomes severe, depends crucially on the virus load.

What I also infer from the two sets of data [Vo] and [Guang], is that the fact that one becomes detectable and contagious about one day before symptom onset is typical

only for the aerosol infection. For other infection categories associated with close contact, see patients E and L, husband and wife, the picture is different. Again this makes sense. The virus has already proliferated, say in the intestines, before reaching large concentrations in the sputum.

The studies quoted in this section are [**Guang**] *and* [**Vo**].
The Vo data are available under *github.com/ncov-ic/SEIR_Covid_Vo*
Further reading: [**Sil**].

6 Basic results from mathematical epidemiology

Mathematical epidemiology is part of mathematical population dynamics. It tries to predict the outcome of an epidemy. There are stochastic models of contact process type and deterministic models, describing the evolution of the percentage of infected individuals in a population with a differential equation. The stochastic models converge in the limit of large numbers to deterministic ones. Nowadays often people assume that the stochastic models are closer to reality. This is not necessarily the case, since the notion of probability itself, if not seen as an abstract concept, relies on the law of large number limit. If a probability is given for an individual to be infectious for a period between times t_1 and t_2 after infection, that is a prediction of the relative frequeny of observing that period, and more precisely to oberserve t_1 and t_2 with a margin of error. The more 'realistic' a stochastic model becomes, the more data are needed to estimate its parameters. If one does not have a huge amount of data, one has to work with assumed probability distributions of specific forms, which have little to do with the underlying real process. In such cases one is better off using deterministic models, which give a better picture of the underlying process in terms of what we know about the ensemble behavior.

There are on the other hand questions that can be phrased only in terms of stochastic models. One example is what happens, when one infectious individual is introduced into a large population with previously no infection. Another example is, how long do you have to wait in a population of finite size, till there are no more active infections. The answers will then be phrased in terms of probabilities.

In epidemiology the oldest useful model is the SIR model. S stands for susceptibles, I for currently infected, and R for removed, either dead, immunized, or quarantined individuals. The model works with the assumption that individuals who have undergone the infection will not be susceptible again on the time scale of the epidemy. This is an idealization which will be true only approximately. In its simplest form the model does not take the course of the infection, the incubation time etc. into account. The duration of the infection just appears as a scaling of time. Also the population is considered to be homogeneous. But this is not crucial. I will explain

how to modify the SIR model to a model with many more parameters. The variables of this 'state of the art' deterministic model are $n_j, s_j(t), i_j(t,a), r_j(t)$ where the index $j = 1, ..., k$ denotes subpopulations, t denotes time, and a the time which has passed since infection for an infected individual.

- n_j is the percentage of individuals in the jth subpopulation, not depending on time t,
- $s_j(t)$ is the percentage of susceptibles, i.e. of individuals who have not yet been infected in the subpopulation j,
- $i_j(t,a)$ is the percentage of infectious individuals who have been infected at time $t-a$ in the subpopulation j,
- $r_j(t)$ is the percentage of removed, i.e. those who are immune, dead, or in quarantine in the subpopulation j,

We say that this model is of meanfield type. The probability of a not yet infected individual to become infected depends on which subpopulation the indvidual belongs to, and the percentages of infectious individuals of given time since infection in all the different subpopulations. But it depends on nothing else.

For most of my exposition this probability will depend linearly on said percentages, a 'mass action' type law. For these models you have invariants - the equivalent of energy and momentum in physics - that determine the outcome of the infection in the population depending on the current state of its course, without the need to solve the differential equations. These invariants have the form

$$\log s_j(t) - \sum_{l=1}^{k} A_{jl}\ s_l(t) - \sum_{l=1}^{k} \int_0^d B_{jl}(a)\ i_l(t,a)\ da\ .$$

Here the A_{jl} represent effective cross infection rates, and the integrals represent current infection levels. Their form will be derived in Section 8. In Section 9, I will discuss modificiations which may become important when the number of currently infected becomes large.

But also for these non mass action type models the crucial obervation is still valid. It depends on the percentages of immunized in the subpopulations r_j whether a state with zero infections is stable or not. To be precise, there still is a matrix with entries A_{jl} as above, such that the question whether the state $s_j(t) = \sigma_j$, $i_j(t,a) = 0$ is stable or unstable is equivalent to the statement that the matrix with entries $\sigma_j A_{jl} = A(\sigma)_{jl}$ has a spectral radius $R(A(\sigma))$ smaller or larger than 1. Or in other words whether all iterates of the simple recursive system

$$x_j(m+1) = \sum_l A(\sigma)_{jl}\ x_l(m)\ . \tag{6.1}$$

are exponentially decaying or whether there exists an exponentially growing solution. If the state $s_j = \sigma_j$, $i_j = 0$ is unstable then there exists a socalled heteroclinic trajetory, starting at that state and leading to a stable state. For the deterministic system any small introduction of infectious will lead to an epidemy following that trajectory.

For the corresponding stochastic system the result can be phrased as follows:
introducing one infectious individual in a population where the percentage of susceptibles is in an unstable state will, with a maybe small but positive probability, result in the epidemy following the heterochlinic trajectory of the deterministic limit system. It should be noted though that the quantity $R(A(\sigma))$ which is sometimes called the reproductive factor of the virus does not determine the initial exponential growth factor of the epidemy - sometimes described with socalled doubling times. The latter is given by a more involved 'eigenvalue' equation (8.6).

Trying to eradicate the infection by temporary measures is not having any effect before you have reached a state of stable immunizations $1 - s_j$. In the case of one homogeneous population, where s is a simple parameter, not a vector, that means

$$1 - s > 1 - \bar{\sigma} \ ,$$

where $1 - \bar{\sigma}$ is the socalled herd immunity.

7 Classes of models

The oldest type of models in population dynamics are recursive sequences. Formula (6.1) is an example, but probably the most famous are the Fibonacci numbers proposed by Leonardo of Pisa around 1200 to model the unchecked growth of a rabbit population. (Actually he was most probably not primarily interested in rabbits but in continued fractions). In formulas these models are

$$n_{k+l+1} = f(n_k, n_{k+1}, \cdots, n_{k+l}) \ ,$$

for an algorithm f having as input the number of individuals in the preceding l generations and as output the number of individuals in the current generation, i.e. the rabbits of the l previous generations "produce" the new generation. The recursive system (6.1) is of this type. Generational models are still popular but mostly in the form of stochastic processes in discrete time. There the final formula is

$$n_{k+l+1} = f(n_k, n_{k+1}, \cdots, n_{k+l}, \omega) \ .$$

This is shorthand for an f that has as output not a number but probabilities. Mostly the examples are of just three conditional probabilities, birth, death or keeping the

status quo

$$p_i(n_k, \cdots, n_{k+l}) = P\left(n_{k+l+1} = n_{k+l} + i \mid n_k, \cdots, n_{k+l}\right) \ ,$$

where $i = 1, 0$, or -1 and $\sum_{i=-1}^{1} p_i = 1$. As an algorithm that means that the output is no longer one number but three positive real numbers. As a dynamical system that is initialized with l natural numbers, it produces likewise a sequence not of numbers but of probabilities to observe a natural number, i.e. a sequence of sequences of length $n_k + l$ of positive real numbers.

The problem with generational models is that generations are not synchronized. Even in humans it is not so rare to find e.g. an uncle who is younger than his niece. The second problem is that time is continuous and not discrete. The simplest type of stochastic model that avoids these types of shortcomings are mean field processes in continuous time.

In order not to waste too many paragraphs I will switch now to the stochastic model for the spread of an infectious disease of the SIR type for one homogeneous population. That means we have a population of size N, $S(t)$ is the number of individuals that have not yet been infected at time t, $I(t, a)$ is the number of individuals that have been infected at time $t - a$, and $R(t)$ is the number of removed individuals, i.e. dead, immune, or quarantined.

From the point of view of an individual in the population the process or course of the illness looks as follows. The individual is in the set of susceptibles up to a random time t_1, when it gets infected, then the virus starts to multiply within the individual. When the virus count reaches a certain value, the infected becomes infectious with infectivity $\alpha(a)$ at time $t = t_1 + a$, and after a certain time length d, the function α will become zero. Between t_1 and $t_1 + d$ the infected individual will be removed at a time $t_1 + a_2$, which again is random. The usual way to model these random times is as independently exponentially distributed, that is

$$\frac{P(t_1 > t) - P(t_1 > t + h)}{hP(t_1 > t)} \approx \frac{1}{N}\rho(t) \quad , \quad \frac{P(a_2 > a) - P(a_2 > a + h)}{hP(a_2 > a)} \approx \delta(a) \ .$$

Here $\rho(t)$ stand for infection rate, and $\delta(a)$ for removal rate. The mean field assumption is that

$$\rho(t) = \alpha_0 \sum_{t=t_1+a;\ a<a_2} \alpha(a) \ ,$$

where α_0 is the contact rate in the population. In words, this assumption means that the probability of two individual meeting is independently identically distributed (i.i.d.) - the magic notion in stochastics.

Historically the deterministic SIR model preceeds the stochastic model. It is around 100 years old and does not take effects like the incubation time of the disease into

account. It is of the type of equations describing mass action kinetics in chemical reactions, i.e. a simple system of O(*rdinary*) D(*ifferential*) E(*quations*). The simple SIR model for one homogeneous population reads

$$\begin{aligned} \partial_t s &= -\alpha i s \\ \partial_t i &= \alpha i s - \beta i \\ \partial_t r &= \beta i \,. \end{aligned} \tag{7.1}$$

The meaning is: s, i, r are the percentages of susceptibles, infected, and removed in the population, α is the infection rate, and β is proportional to $1/d$, where d is the duration of the infection. The graphs that are usually shown on the web, namely the

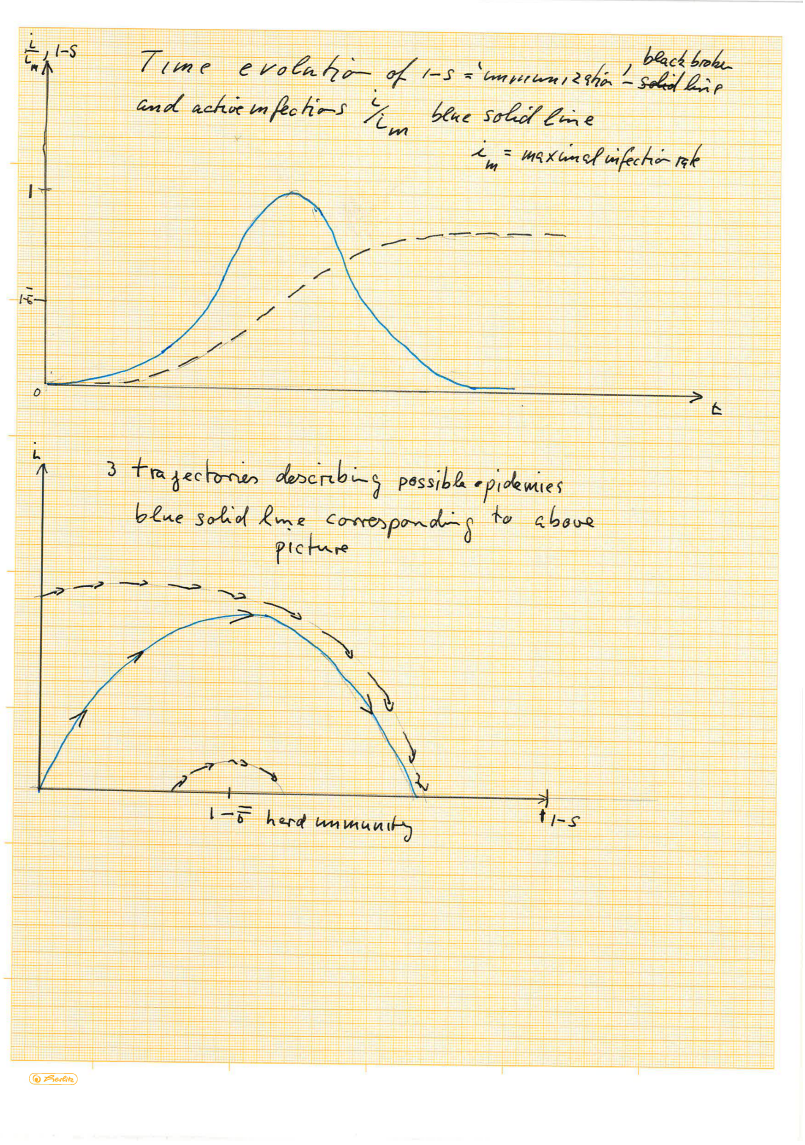

Figure 3*: Schematic picture of the solution curves.*

time evolution of new and cumulative infections, roughly correspond to the solution

curves $i(t), r(t)$, see **Figure** 3.

The connection between the stochastic SIR model and this deterministic SIR model is indirect. This will be discussed in Section 8. Here I will just point out that it is easy to show that in the large N-limit the stochastic SIR model will become deterministic. The limit is not a simple ODE, since it keeps the information of the time a since infection for the infected. Formally the equations are P(*artial*) D(*ifferential*) E(*quations*) in t, a, albeit of the simplest type

$$\begin{aligned} \partial_t s(t) &= -\alpha_0 \left[\int_0^d \alpha(a)\ i(t,a)\ da \right] s(t) = -i(t,0) \\ \partial_t i(t,a) + \partial_a i(t,a) &= -\delta(a)\ i(t,a) \\ \partial_t r(t) &= i(t,d) + \int_0^d \delta(a)\ i(t,a)\ da\ . \end{aligned} \tag{7.2}$$

Models of this type have been extensively studied. They are called delay differential equations, integro-differential equations or (age)structured models. They define a dynamical system but in the (infinite dimensional) space of functions $i(t,\cdot)$ in the interval $[0,d]$. So they are difficult to observe, e.g. by a virus test, which will be negative during incubation and when the individual has ceased to produce the virus, and which never will be so precise as to give you the a at the time of the test.

Further reading: [**HRT**] *for general deterministic population dynamics and epidemiology,* [**EP**] *for stochastic populations dynamics, and* [**DHB**] *for epidemiology.*

8 Qualitative behavior of the SIR models (7.1), (7.2), herd immunity.

I will start the discussion with the simplest SIR model (7.1) for a homogeneous population and then move on to the 'state of the art' SIR-systems.

The simple model is almost explicitly solvable. If you use the method of separation of variables, which most science students will remember from their calculus class, the equations become

$$\partial_t(s+i+r) = 0 \quad , \quad \partial_t(\log s + \frac{\alpha}{\beta} r) = 0 \quad , \quad \partial_t i = \alpha i s - \beta i\ .$$

So we have not one invariant or integral, but two:

$$i + s + r = 1 \quad \text{and} \quad \partial_t \left(\log s - \frac{\alpha}{\beta} s - \frac{\alpha}{\beta} i \right) = 0\ ,$$

and as a consequence everything reduces to the equation

$$\partial_t s = \beta\ \gamma(0)\ s - \beta\ s \log s + \alpha\ s^2\ ,\ \text{where } \beta\ \gamma(0) = \beta \log s(0) - \alpha\ s(0) - \alpha\ i(0)\ ,$$

and the asymptotic limit for large times, i.e. ∞, will be given just by the identities

$$i(\infty) = 0 \text{ and } \beta \log s(\infty) - \alpha\, s(\infty) = \beta\, \log s(0) - \alpha\, s(0) - \alpha\, i(0)\ ,$$

with the additional information $\partial_s \left(\log s - \frac{\alpha}{\beta} s\right)(\infty) \geq 0$, since s and i will both eventually decrease. So the discussion of the simple curve $\beta \log s - \alpha s$ tells everything about the final outcome of the epidemy.

If you start with any $s(0), i(0) > 0$ for large times, the fraction of removed will approach the unique solution of $\beta \log s - \alpha s = \beta \log s(0) - \alpha s(0) - \alpha\, i(0)$ with $s < \frac{\alpha}{\beta}$. This value, $\frac{\alpha}{\beta}$ is called herd immunity. Actually it has two interpretations. The first is what I just explained: It is the maximal possible ratio of the population, which has escaped the infection during the whole course of the epidemy. The second is: It is the value of the ratio of susceptibles in the population at which the number of infected starts to decrease.

If you believe in this simple model, the message for disease control is equally simple. Suppose the epidemy starts with small $i(0)$ and $s(0) > \frac{\beta}{\alpha}$, and suppose you are able, but only temporarily, to decrease α, how far should you decrease α? Well, you know in any case, that $s(\infty) \leq \frac{\beta}{\alpha}$ eventually. So obviously to get there quickly and not to overshoot the optimal choice is

$$\tilde{\alpha} = \alpha\beta\, \frac{\log \beta - \log \alpha - \log s(0)}{\beta - \alpha[s(0) + i(0)]}\ .$$

If you reduce the contact ratio more, that will get you only to an $s(T), i(T)$ at the time T of lifting the temporary restrictions, which is the starting point of a new epidemy. That is the second wave we are seeing at the moment in Germany.

Let me also briefly discuss what we call a singular perturbation of the simple SIR model. The SIR model is very untypical for an ODE in two variables, s and i, since it has the whole interval $\{(s, i) \mid 0 < s < 1, i = 0\}$ as stationary points. If you perturb it a bit (ε, as usual, means a small number) e.g.

$$\partial_t s = -\alpha i\, s + \varepsilon(1 - s) \quad , \quad \partial_t i = \alpha i s - \beta i\ .$$

the situation changes. The interpretation of the added term is that on a slower time scale either removed individuals lose their immunity or the population changes by the natural birth death process. For this singularly perturbed system there are only two stationary states $(i_0, s_0) = (0, 1)$ and $(i_1, s_1) = \left(\varepsilon\left(\frac{1}{\beta} - \frac{1}{\alpha}\right), \frac{\beta}{\alpha}\right)$, and every solution which starts with positive $i(0)$ will spiral into (i_1, s_1). The behavior of the solutions will be that of socalled relaxation oscillations, they will move fast from unstable $s > \frac{\beta}{\alpha}$ and small i to stable $s < \frac{\beta}{\alpha}$ and small i, but then on the slow time scale, s will increase again, become unstable and so on. But the width of the oscillations will eventually decrease exponentially, see **Figure** 4.

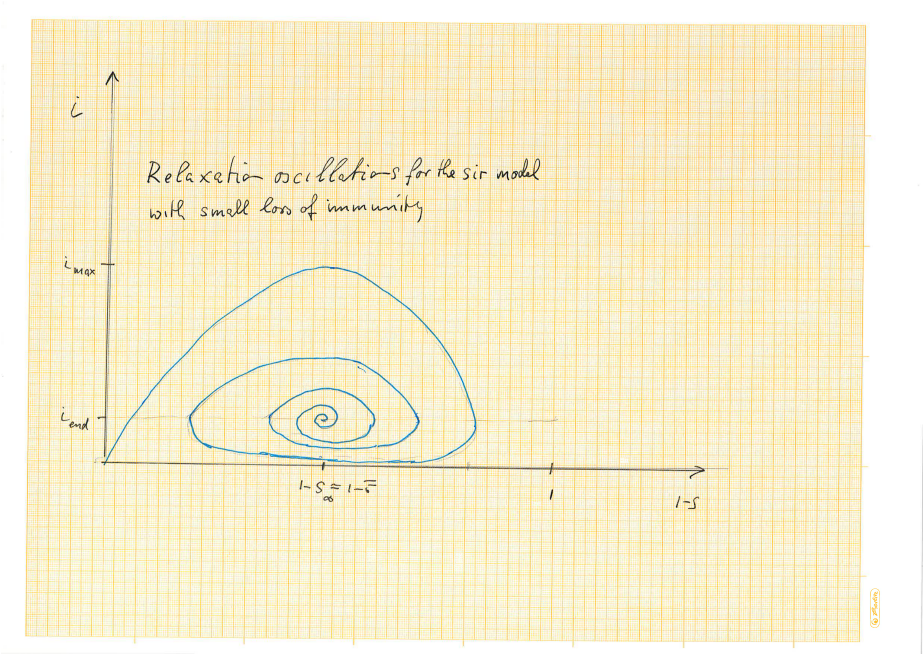

Figure 4: *SIR with loss of immunization.*

Now let us move to the state of the art deterministic s, i, r models. These are age structured models of the type (7.2) discussed in the Section 7, but for several sub-populations: $s_j, i_j, r_j,\ j = 1, \cdots, k$.

The equations read

$$\begin{aligned}
\partial_t s_j(t) &= -i_j(t,0) && (8.1)\\
(\partial_t + \partial_a) i_j(t,a) &= -\delta_j(a) i_j(t,a)\ ,\ 0 < a < d && (8.2)\\
i_j(t,0) &= \left[\int_0^d \sum_{l=1}^k \alpha_{jl}(a)\ i_l(t,a)\ da\right] s_j(t) && (8.3)\\
\partial_t r_j(t) &= i_j(t,d) + \int_0^d \delta_j(a) i_j(t,a)\ da\ . && (8.4)
\end{aligned}$$

Again, there is an almost explicit formula. With $\Delta_j(a) = \int_0^a \delta_j(\sigma)\ d\sigma$, we have

$$\begin{aligned}
\partial_a \left(e^{\Delta_j(a)}\ i_j(t,a)\right) &= -e^{\Delta_j(a)}\ \partial_t i_j(t,a)\ ,\ \text{or}\\
i_j(t,a) &= e^{-\Delta_j(a)}\ i_j(t,0) - \int_0^a e^{\Delta_j(\sigma)-\Delta_j(a)}\ \partial_t i_j(t,\sigma)\ d\sigma\\
&= -\partial_t \left(e^{-\Delta_j(a)} s_j(t) + \int_0^a e^{\Delta_j(\sigma)-\Delta_j(a)}\ i_j(t,\sigma)\ d\sigma\right)\ .
\end{aligned}$$

So apart from the k obvious invariants $n_j(t) = s_j(t) + \int_0^d i_j(t,a)\ da + r_j(t)$, we have

again the k additional invariants of the form

$$\log s_j - \sum_{l=1}^{k} A_{jl}\ s_l - \sum_{l=1}^{k} \left[\int_0^d B_{jl}(a)\ i_l(a)\ da \right] = f_j(s,i) \tag{8.5}$$

$$A_{jl}\ = \int_0^d \alpha_{jl}(a) \exp(-\Delta_l(a))\ da\ ,\ B_{jl}(a) = \exp(\Delta_l(a)) \int_a^d \alpha_{jl}(\sigma) \exp(-\Delta_l(\sigma))\ d\sigma\ .$$

And again we know that all s_j are decreasing. Stability or instability of a point $s_j(0)$ is determined by the matrix $A(s(0))$ with entries $s_j(0)A_{jl}$. If $s_j(0)$ is exponentially unstable, then the linearized system has an exponentially growing solution $\hat{i}$ with positive $\hat{i}_j$, or a solution of the linear system of integral equations

$$\hat{s}_j(0) = s_j(0) \sum_{l=1}^{k} \int_0^d \alpha_{jl}(a) \exp(-\Delta_l(a)) \exp(-\lambda a)\ \hat{s}_l(0)\ da\ , \tag{8.6}$$

with $\lambda > 0$ and all $\hat{s}_l(0)$ of one sign. This is equivalent to $R(A(s(0))) > 1$, where $R(A(\sigma))$ is the spectral radius of the matrix $A(\sigma)$.

On the other hand, if $R(A(s(0))) < 1$ then $s(0)$ is stable. So stability of the age structured system is the same as for the system without age structure. It is also not difficult to show, that if you start a Newton iteration to calculate

$$\log s_j - \sum_{l=1}^{k} A_{jl}\ s_l = \log \sigma_j - \sum_{l=1}^{k} A_{jl}\ \sigma_l + b_j\ ,\ \text{ with } b_j < 0$$

in a stable point σ, this will converge (monotonically in the sense of Krasnozelsky). So you have your choice how to calculate the unique stable solution of

$$\log s_j - \sum_{l=1}^{k} A_{jl}\ s_l = \log s_j(t_0) - \sum_{l=1}^{k} A_{jl}\ s_l(t_0) - \sum_{l=1}^{k} \left[\int_0^d B_{jl}(a)\ i_l(t_0,a)\ da \right]\ .$$

Let me now turn to the calculation of overshooting in a recursive SIR model. The SIR model for k subpopulations without delay is of the form

$$\begin{aligned} \partial_t s_j &= -\sum_{l=1}^{k} A_{jl}\ s_j\ i_l \\ \partial_t i_j &= \sum_{l=1}^{k} A_{jl}\ s_j\ i_l - i_j \end{aligned}$$

where I scaled β to 1 by rescaling time. Examples of A_{jl} are

$$A_{jl} = \alpha_j \alpha_l n_l / \bar{\alpha}\ ,\ \text{ where } \bar{\alpha} = \sum_{l=1}^{k} n_l \alpha_l.$$

Here α_j represents the contact rate of the respective subpopulation and n_j the fraction of that subpopulation. If for $l > j$ one has that $\alpha_l n_l$ is much smaller than $\alpha_j n_j$, the system has nearly a recursive structure. If $A_{jl} = 0$ for $l > j$, then we know that the stable equilibria of the system are $s_j > A_{jj}^{-1}$ for each j. So each subpopulation has its own 'herd immunity'. But the problem is that the invariants are

$$\log s_j - \sum_{l \le j} A_{jl}\, s_l - \sum_{l \le j} A_{jl}\, i_l \ .$$

So even if $s_j(0) < A_{jj}^{-1}$ but $s_l(0) >> A_{ll}^{-1}$ for $l < j$, one will produce a potentially huge overshooting. If you want to avoid this, by temporarily reducing α_j, the only way is, to make sure that the subpopulation l reaches its 'herd immunity' before the epidemy starts again in the subpopulation j.

Figure 5 visualizes this effect. Two strategies are compared for a realistic situation with two subpopulations, think about the older and the younger, more active population. The system is not strictly recursive. If you follow the 'switch on switch off' strategy, in the end more of the older generation have gone through the infection than necessary. The reduction of cases in the younger generation is minimal, if at all.

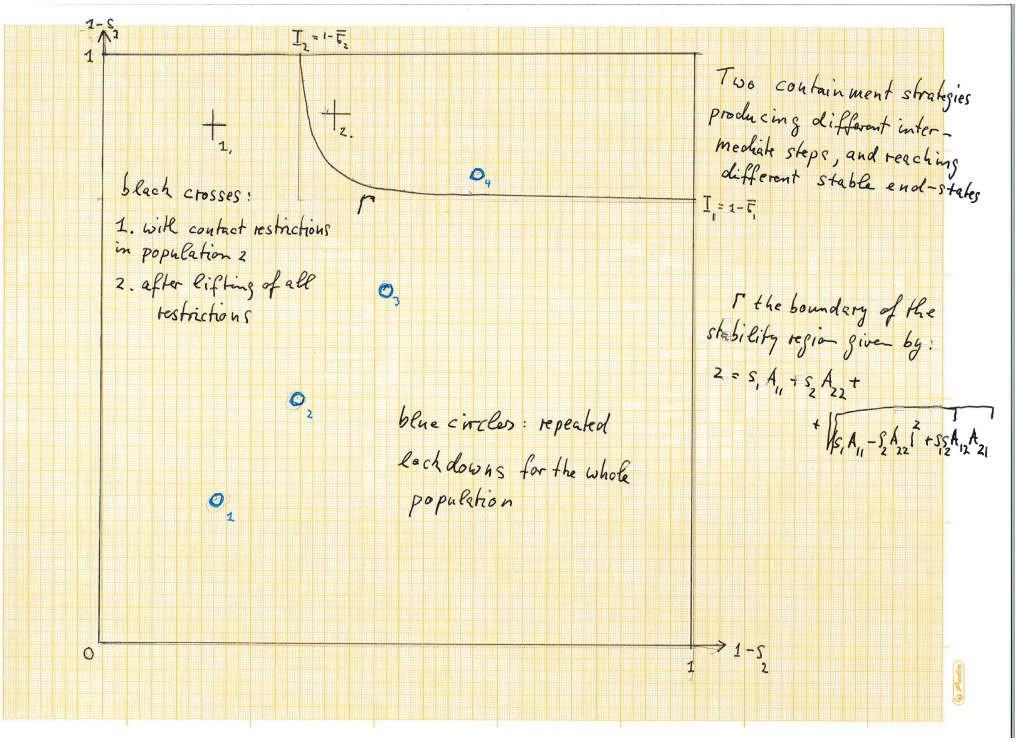

Figure 5*: Two strategies for containment in the case of a nearly recursive structure for two subpopulations. The black crosses represent a two step strategy, where contact between the subpopulations is kept minimal in the first step. The blue circles represent a strategy of repeated lockdowns for the whole populations whenever infection levels have reached a certain value.*

Further reading on system (8.1) - (8.4): [**RR**].

9 Looking more closely at the mechanism of contagion. Superspreading events and non mass action kinetics

The infection by inhalation of contaminated aerosol is for corana as for many other virus infections the dominating mechanism, especially outside family circles. It certainly does not mean that this is the only mechanism, but the one important for the spreading of the epidemy. It is clear that the probability to get infected and moreover also the outcome of the infection depends crucially on the amount of virus contaminated aerosol that is inhaled. Except for heavily symptomatic persons, the amount one individual is exhaling is not so large. Probably this consists of single viroids which then act as a nucleation kernel for a microdroplet formed with condensating exhaled water vapour. Therefore you have to come and stay close to this individual to get infected. Outside - in the summer - it is unlikely that anyone gets infected that way normally. This situation changes when one stays in a forced air ventilation environment. In a turbulent flow the aerosol does not settle down. The situation also changes when staying in a room packed with people. The aerosol concentration of the virus depending on the number of infected can reach levels where basically everyone gets infected (and a large proportion seriously ill). That is what is called a superspreading event. For Corona in Italy and to a limited extent in Germany, this was carnival as I already mentioned in the context of the Vo and the Gangelt data. For Austria it was the skiing season with its apres ski bars. If you think how to model this effect as a stochastic process, you do that as a random walk on a complete graph with contact processes at the nodes. The key change is that the probability to get infected will depend nonlinearly on the number of infections at the respective node. When taking the limit of large numbers, this nonlinear function will be evaluated under a Bernoulli distribution. The point is: also the deterministic limit will be nonlinear. In the system (8.1) - (8.4) the equation (8.3) will change to

$$i_j(t,0) = \sum_{m=1}^{M} f_{jm}\left(\int_0^d \sum_{l=1}^{k} \bar{\alpha}_{ml}(a) i_l(t,a) da\right) s_j(t) \ , \tag{9.1}$$

where M is the number of node types. The system loses its invariants, but all the statements about trajectories and stability of states are still valid. The matrix A of cross infection rates A_{jl} determining the region of stability will just change to

$$A_{jl} = \int_0^d \sum_{m=1}^{M} f'_{jm}(0)\bar{\alpha}_{ml}(a) \exp(-\Delta_l(a)) \ . \tag{9.2}$$

What changes dramatically though, is that a state which is stable, is now stable not under the introduction of an arbitrary amount of infectious, but only under the introduction of a small number of infectious. In the stochastic model that means that the probability that one infectious individual will start an epidemy will be exponentially small in the population number. But the possibility of such an event - or large deviation - is still there. This is what I would call a superspreading event. We say that a stable state becomes metastable.

10 Drawing conclusions for Corona

The first conclusion is a simple one. Epidemiology tells you that without an effective vaccine, indepently how often lockdows are declared, the epidemy will always start again, before you finally have reached a stable state. Herd immunity for a nonhomogeneous population is a region of states, rather than an interval, so one can try to reach the state which has the lowest cost in terms of human lives. If you want to estimate the 'amount of' immunization you need, there is in principle a whole matrix of cross infection rates you have to determine. But if you have few age groups only, with significantly different contact rates, then your system of equations will have a triangular or recursive structure approximately. In that case one knows that one should aim for the state where each subpopulation has its own 'herd immunity'. What an effective strategy would look like was illustrated in **Figure** 5 in Section 8.

Having reached that state though, Corona has still not disappeard. The state itself might be only metastable, and on a longer time scale you will in any case have a loss of immunization and smaller epidemics, as this is the case for influenza.

If you really want to get numbers, then for small epidemics under partial lockdown conditions, you can use the simple SIR model, its invariant, and the relationship $\log s(0)/s(\infty) = \alpha(s(0) - s(\infty))$ to calculate α for the prevailing condition. One has to keep in mind though, that this is an approximation. The approximation is reasonable as long as the maximum number of active infections is small w.r.t. the population size. and $s(0) - s(\infty)$ is not too large. That is because the trajectory stays close to a two dimensional surface, determined by the eigenvalue equation (8.6), which for each $s_j(t)$, $j = 1, ..., k$ has a unique (up to multiplication by a constant) positive solution $\hat{s}_j(t)$.

11 Discussion

The first conclusion one has to draw is: Covid-19, the disease, is rare among the totality of SARS-CoV-2 infected. There is little doubt that in Germany, up to the

end of May at least, only 5% of the SARS-CoV-2 infections were discovered by PCR testing. That means, the C*(ase)* F*(atality)* R*(ate)* has to be divided by 20 to get the I*(nfection)* F*(atality)* R*(ate)*. Up to the age of 70 these IFRs are a fraction of the natural mortality - for the age group $60-69$ it is 2 *per mille* versus 1% or 1.3%, depending on whether you use 2016 or 2018 as reference year. So there is absolutely no justification for lockdow measures decreed by governments. Moreover the data of the large scale antibody tests in Geneva have been published on June $11th$, and it is a scandal that there was no hint of the implication for the ratio IFR versus CFR in official statements or on the RKI website. Moreover there is only hidden information on the CFR per age group, a fact which is tantamount to disinformation of the public.

The second conclusion refers to the comparison between Corona and the flu. This is a useful comparison and not just a point made in the debate. In 2017/2018 we had a terrible flu epidemy in Germany, claiming around 30 000 victims in March 2018 alone. Anybody looking at the data for monthly deaths, separated for the different age groups, will immediately see the effect of this epidemy, down to the age group below 30 but pronounced in the age groups $55-60$ and above. Data are available on the website of the German Federal Statistical Office. The first wave of the epidemy was probably over by May 2018. But one may assume that the two seasonal epidemies of 2018/2019 and 2019/2020 were connected, maybe even caused by the same, if slightly mutated, virus. The second and third wave of the flu claimed less victims, and there was not such a pronounced peak as in March 2018. One should keep in mind that we are told that there is a flu vaccine which we can trust, and still the three waves of the flu epidemic were claiming 84 000 lives by the lower estimate and 124 000 lives by the upper estimate. If you are not an incurable optimist, you have to come to terms with the perspective, that after two and a half more years, the number of Corona dead will be of the same order of magnitude. If I may make a wild guess, the number will be half of the upper estimate above, namely ca. 62 000, and of course not 14 to 26 fold as the journalist J. Müller-Jung claims in the German newspaper FAZ, but still very high compared to the 10 000 victims we have seen so far. Especially it is in my view irresponsible of (almost all) politicians and (some) virologists to promise to the public that they will prevent this flu like outcome.

The third point is about what you can infer for the SARS-CoV-2 infection from the data I quoted. This is partly conjectural because here I am speaking about small data sets, namely [Guang], [Mu], [Gang], [Vo]. Firstly the data indicate that one has to distinguish 2 by 2 types of infection, depending on the type of contagion and the type of susceptible. There are direct contact infections on the one hand - think about sharing food and drink, macroscopic droplet infection, kissing etc., and on the other hand aerosol infections. There are on the one hand individuals where the infection

visits many organs in sequence, and then there are others who get over it in one go. Whether you are one type or the other type of susceptible may be hereditary, but it could also depend on cross immunizations. The data can not give more than hints, it may even be that whether you become the sequential type or not, depends on the type of contact, but I doubt that.

The different types of infection seem to appear with all categories of symptoms. You can be severely symptomatic probably only in conjunction with the sequential type of infection, exactly as it was observed in SARS-CoV-1 patients [Hong], but you can be symptomatic or asymptomatic with all types. And clearly both the ratio of severe cases and the ratio of symptomatic versus asymptomatic crucially depend on the size of virus load you are exposed to. This is particularly striking in the Vo example, where there were two 'superspreading' events. Among those infected in the earlier event, there were at least 4 severe cases and only about a third asymptomatic, whereas among the individuals infected during the later event, 60% were asymptomatic, and as far as I could make out there were no severe cases.

The crucial difference between the aerosol infection and other ways of transmission, is that after being infected by inhaled aerosol, the infected becomes infectious before developing symptoms. But for both types of infection probably there are infectious who never develop symptoms. Among the asymptomatic non-sequentially infections - which represent under the conditions in northern and middle Europe the largest group - and probably also among the mildly symptomatic, there are not so many days, $4-9$, during with they test PCR positive. That translates into a low value of the quantity $\sum_k f(k) = 7 \cdot o$, where $f(k)$ is the probability to be PCR detectable for k or more days. Under the conditions that we had in Vo, but probably also elsewhere, my guess is that $\sum_k f(k)$ will be between 6 and 7. I called it $7 \cdot o$, with o for oversampling, because it relates weekly rates of positive PCR tests and rates of randomized PCR tests, as explained in Section 5.

The third and a half point is about the sensitivity of antibody tests. This depends crucially on the duration and severity of the infection, and on the time elapsed since the infection. In my view it was naive to assume that the RKI study in the hotspot Bad Feilnbach conducted almost 3 months after the peak of the epidemy would show the same sensitivity as the study in Gangelt conducted ca. 2 weeks after the peak there. But generally it holds that the highest percentage of asymptomatic among any collective of seropositives I have seen, are the 36% in the study [Gang] among the non carnivalists, but that percentage should have been 60% . This translates into a sensitivity of 0.63 under normal conditions. And I want to repeat, that means a discovery rate in Geneva, a hot spot for the infection, of $\frac{1}{17}$ for a $20-49$ year old infected individual by PCR tests conducted in April and May, 2020.

The fourth point I want to make is that the models of mathematical epidemiology and in particular those involving differential equations are extremely useful in understanding also the Corona epidemy and its likely outcome. There are many reasons why you cannot expect to directly measure the parameters of the state of the art models, stochastic or deterministic. But you can take the engineering approach of estimating parameters for coarser approximate models. You just have to take into account that there is what we call an order one error, so a safety margin has to be applied to the estimates. I did explain more or less precisely or at least in nearly mathematical terms in which way the simple SIR model, which is about 100 years old, is still a good approximation for the course of the epidemy. The formulas how discovery and quarantining rates - which I called δ - and contact frequencies, levels of aerosol, infectivity, incubation times etc. enter into the final effective cross infection rates among different subpopulations are not that simple, and cannot be. The main useful point is that there is in the end an effective cross infection matrix, and a set of invariants, related to that matrix which for a lot of scenarios determine completely the outcome of an epidemy. In any case the matrix of effective cross infection rates determines whether a state is stable or not.

For those who are not so used to the notion of stability, let me repeat its meaning here in the language of stochastics:
If you have several subpopulations with corresponding rates of immunization and you know the prevailing effective (cross)infection rates for the subpopulations, then there is a formula determining whether this state is in the region of stable states or in the region of unstable states.
If the state is unstable, then with positive probability one infectious individual will start the epidemy - it is like nitroglycerine. Now you never have only one infectious individual, and you could phrase things differently: After having been visited by a finite number of infected - independent of the size of the population, the epidemy will start and infect a positive percentage of the whole population.
If on the other hand you are in a stable state of respective immunizations, the trickle of infected visitors will produce a finite multiple of these infections.
In other words, if you start from a state in the region of instability the outcome is a number of infections proportional to the whole population. If you start from a state in the region of stability the outcome is a number of infections proportional to the number of imported infections.

The fourth and a half point refers to the strategies of containment, that you could and should devise based on the maths for the SIR model with different subpopulations. One should follow a strategy that lets the part of the population with a very low risk reach a state that is far in the stability region for that subpopulation and try to pro-

tect the more vulnerable part of the population during this first unhindered(!) course of the epidemy in the low risk subpopulation. This is going to save lives compared to the (in my mind mindless) switch on switch off control, politics enforces now, see **Figure** 5.

The fifth point: the covid deaths are mainly a nursing home phenomenon and most likely in second place a phenomenon of people cared for by professional providers at home. The rate of deaths in nursing homes has been halved in Germany from 40% up to the end of May, down to at least 23% between the beginning of June and the beginning of October. This probably reflects the fact that many providers are testing their staff regularly. Now there is talk to introduce this for all nursing home providers, and I hope also for the providers of professional care at home. The long delay is in my opinion a scandal. Instead of locking people up in nursing homes, not allowing relatives to visit, staff should have been tested regularly; first everybody for antibodies to see who is immunized, and then everybody not immunized on a weekly basis with the PCR test. The responsibility for the long delay in implementing this kind of measure in Germany lies clearly with our federal health minister and his procrastinations, first starting a long discussion who has to pay for the PCR tests, and then another one, whether it is ethical to let people know via antibody tests, if they are immunized. But also his advisors share part of the responsibility.

The discussion of the IFR, vulgo Covid-mortality is based on German and Swiss data mainly. Test strategies of course vary from country to country. So there was the hope that the antibody tests would allow to discover all individuals who had been infected - at least during the previous two months. I think I could show that this is not the case - and by a wide margin. So tests of larger groups of asymptomatic and mildly symptomatic cases need to be conducted to establish the time profile of the PCR and serological tests for these individuals. The sensitivity I derived by elementary statistics for Gangelt and which is probably true for Geneva as well, might apply also to London, and would bring total mortality in line with the $0.2 - 0.3\%$ you expect if there is no special protection for the elderly. It certainly does not apply to Lombardy. What you see there on a large scale is what you can see in Vo on a small scale. Depending on the virus load you are exposed to, the risk of a severely symptomatic infection increases dramatically. (Such a situation was encountered in carnival celebrations with many infectious participants and in apres ski bars in Tyrolia). But it seems to apply to the outbreaks in London or Geneva. That means taking public transportation increases your chance of getting infected a lot. But it does not increase the conditional probability of a serious illness.

So how can one contain Corona. It is not the number of infections you want to keep

small, especially among the group of young people, but you can inform everybody about the risk he/she runs in their respective age group and with their respective activities honestly. And since the number of infections is now monitored, it is possible to know, where there is a heightened risk of going to a bar, of taking public transportation etc., and then everybody has to decide individually, which risk they want to take.

Waiting for an effective vaccine, which obviously we did not have against the flu in 2018, and going in and out of lockdown is no alternative. Letting a large number of younger people get through the infection more quickly will instead save lives among the older.

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