On build-up of epidemiologic models - development of a SEI^{3}RSD model for the spread of SARS-CoV-2

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Abstract

The present study investigates essential steps in build-up of models for description of the spread of infectious diseases. Combining these modules, a SEI^3RSD model will be developed, which can take into account a possible passive immunisation by vaccination as well as different durations of latent and incubation periods. Besides, infectious persons with and without symptoms can be distinguished. Due to the current world-wide SARS-CoV-2 pandemic (COVID-19 pandemic) models for description of the spread of infectious diseases and their application for forecasts have become into the focus of the scientific community as well as of broad public more than usual. Currently, many papers and studies have appeared and appear dealing with the virus SARS-CoV-2 and the COVID-19 disease caused by it. This occurs under medical, virological, economic, sociological and further aspects as well as under mathematical points of view. Concerning the last-mentioned point, the main focus lies on the application of existing models and their adaptation to data about the course of infection available at the current time. Clearly, the aim is to predict the possible further development, for instance in Germany. It is of particular interest to investigate how will be the influence of political and administrative measures like contact restrictions, closing or rather re-opening of schools, restaurants, hotels etc. on the course of infection. The steps considered here for building up suitable models are well-known for long time. However, understandably they will not be dealt with in an extended way in current application-oriented works. Therefore, it is the aim of this study to present some existing steps of modelling without any pretension of completeness. Thus, on the one hand we give assistance and, on the other hand, we develop a model capable to take already known properties of COVID-19 as well as a later possible passive immunisation by vaccination and a possible loss of immunity of recovered persons into account.

Keywords: Epidemiologic models, SARS-CoV-2 pandemic, mathematical modelling, qualitative, solution behaviour

1 Introduction

1.1 About the COVID-19 pandemic

At first, in December 2019 several cases of a serious lung disease occurred in the Chinese city Wuhan. Shortly after, a new virus of the corona family was identified and its complete genome sequence was published, see Wikipedia (2020), e.g. Afterwards, the virus has spread in almost all countries. On 11 Mart 2020 the WHO classified this new disease as pandemic. The virus was officially nominated as SARS-CoV-2, the triggered disease as COVID-19.

Meanwhile, the SARS-CoV-2 pandemic has become a serious challenge for the whole world, its social, economic, political and first of all medical consequences hardly can be estimated. Studies show that the virus primarily is quickly spread via droplet infection and by aerosols, especially, if persons get in near and longer contact. Without any pretension of reasonable completeness we refer to Wikipedia (2020), *Robert Koch-Institut: COVID-19 in Deutschland* (2020) for overview and current information as well as to Adam (2020), Streeck et al. (2020), Groß et al. (2020), Merlot (2020), Lednicky et al. (2020) and the references cited therein. Besides, we refer to *TU Berlin: SARS-CoV-2 blog, Hermann Rietschel Institut* (2020) for fluidic investigations concerning the spread of SARS-CoV-2 in air. In Ahlawat et al. (2020), the role of relative humidity in airborne transmission of SARS-CoV-2 in indoor environments has been discussed. In Mitze et al. (2020), the possible protection of masks, including simple ones, against infection has been studied, see also Chu et al. (2020) for a corresponding meta-analysis. In some meat-processing plants in Germany and other countries, super-spreading events occurred promoted by special climatic working conditions, see Günther et al. (2020). Concerning the risk of an infection in trains we refer to Hu et al. (2020). The spread of infection is promoted by a wide absence of immunity within the population as well as by not yet existing vaccine and medicines. The initial hope of immunity after a survived infection could not been strengthened, see Schultheiß et al. (2020). At many laboratories all over the world, scientist are intensively searching for an adequate vaccine. Scientists of very different disciplines investigate virus, disease, possible vaccines and medicines, economic, political, social, psychological and other consequences.

Current data concerning the course of infection are collected and provided by the Johns Hopkins University in Baltimore, USA, and in Germany by the Robert Koch-Institut (RKI) *Robert Koch-Institut: COVID-19 in Deutschland* (2020). The serious situation in many countries caused by the pandemic has not only challenged the policy but also the scientific community. In some countries the spread of SARS-CoV-2 could be decelerated by partially deep cuts into the social and economic life. However, the proceedings of infection locally and temporally differ remarkably in various countries and regions. After the Chinese region around Wuhan, the virus came to western Europe, at first to Italy, then to

other European countries, to the USA, Brazil, Russia, India, South Africa and nearly to all countries. Unfortunately, after a successful deceleration the number of new infections is growing again in many countries. Now, in August 2020, considering the whole world, the SARS-CoV-2 pandemic goes on and a point of culmination is not yet reached.

1.2 About modelling of the spread of infectious diseases

Due to the SARS-CoV-2 pandemic, suddenly models describing the spread of infectious diseases are not only object of research at specialised institutions and of comparatively few scientists, but they have come highly into the focus of many medics, virologists, economists and mathematicians.

There is a long tradition of investigation of infectious diseases, of their spread within human community as well as of a corresponding development of mathematical models for description. Exemplarily we refer to Hethcote et al. (1981), Hethcote (2000), Busenberg and Cooke (1993), to Schuster (2013) for introduction to biomathematics and modelling in biology and epidemiology, to Krämer and Reintjes (2013) for medical and epidemiological background as well as to Vynnycky and White (2010) for comprehensive modelling of infectious diseases.

It is impossible to appreciate here in an adequate manner all these mathematical or highly mathematically oriented works concerning the pandemic and its possible consequences which have been published last time. A small overview can be found in Adam (2020). Moreover, we refer to Grimm et al. (2020). Contrary to standard models, there the individual groups of persons like susceptible and infective ones are further subdivided to address specific moments in their behaviour. The arising complex model is strongly tailored to the COVID-19 epidemic in Germany. In Dehning et al. (2020) the authors investigate several possible scenarios after easing existing restrictions of public life. In Hartl and Weber (2020), the effects of several measures for containment performed in Germany are investigated a posteriori. In Quaas (2020), some aspects of parameter exploitation from available data are considered, particularly concerning the reproduction number. Moreover, we refer to Prakash (2020) and Ansumali and Prakash (2020) for results of a strong lock down to the course of infection. In Bacaër (2020), a mathematical model has been developed which describes the begin of the SARS-CoV-2 epidemic in France.

1.3 Aims and content of this study

This study is an revised and updated version of the former papers Wolff (2020c), Wolff (2020b). It is the aim to provide systematically some general components for building-up deterministic models for the spread of infectious diseases. The approaches summarised here are well-known. However, they could be an assistance for interested colleagues who do not deal with mathematical modelling every day. In this study, modelling means building-up models, i.e., the derivation of mathematical descriptions for real processes, here the spread of infectious diseases, starting with some basic assumptions confirmed by empirical findings.

Outline of the remaining paper:

(i) In section 2, we investigate some general aspects of modelling the spread of infectious diseases in human communities. Although this work is also a consequence of the COVID-19 pandemic, our presentation is not to closely oriented to known specifics of SARS-CoV-2. At the end of this section, we get a SEI^3RSD model, which can take essential items of COVID-19 known today into account. I^3 means, that there are distinguished three classes of infectious persons. Contrary to Grimm et al. (2020) we only subdivide classes of population with respect to the course of infection and disease, but not with respect to age or social behaviour. However, the mentioned modular design principle allows to extend the model in case of necessity.

(ii) In section 4 we deal with some mathematical questions arising from the developed models. In particular, we investigate some solution behaviour of the corresponding mathematical problems like unique global solvability and non-negativity of each solution component. Besides this, some aspects of dimensional analysis and its application to the models are treated.

2 On general models for the spread of infectious diseases

Here we present in short some items of deterministic models for courses of infections in human communities. We are geared to the review paper by Hethcote (2000) as well as to the books by Vynnycky and White (2010) and by Schuster (2013), Ch. 5. Concerning epidemiological issues, we only go into details,

if this seems to be necessary for general understanding. At some places, we refer to current findings related to SARS-CoV-2. This allows a reasonable selection of modelling steps in order to develop a basic model for the spread of SARS-CoV-2 in section 3.

2.1 Basic notations and assumptions

We provide some useful definitions and explications, other ones will be introduced later. Thus, misunderstandings can be excluded, and we can limit the frame of our study. We follow approximately Vynnycky and White (2010), pp. xxi - xxvi, and Ch. 1.

2.1.1 Infection and transmission ways

An *infection* is understood as the invasion of one organism by a smaller one (infecting organism). If the latter is not harmful, it is called pathogenic agent or *pathogen* and can cause an *infectious disease*. We only consider microscopic pathogens (viruses, bacteria, protozoa) as well as infections in human communities.

The majority of pathogens effecting humans live only in humans or vertebrate animals, their *transmission* from one to another host occurs in a variety of ways:

(i) by direct contact (leprosy, e.g.),

(ii) via the respiratory route (influenza, SARS-CoV-2, e.g.),

(iii) via the faecal-oral route (dysentery, e.g.),

(iv) by sexual contact (HIV, gonorrhoea, e.g.)

(v) by contacts with insects (vector-borne infection) (malaria, e.g.)

We note that sexually transmitted diseases require a special modelling, since not all parts of the population have nearly the same sexual activity. This is not in the focus here. Moreover, the modelling of HIV/AIDS contains special features, we refer to Vynnycky and White (2010), Ch. 8 and 9.4-9.6, to Weyer and Eggers (1990) and to the references cited therein.

2.1.2 Adequate contacts and reproduction numbers

In order to model the spread of infectious diseases the term *contact* needs more explication. Clearly, each contact between two individuals is a singular event. A pathogen can be transmitted or not. Moreover, depending on the individuals, a formally equal contact can lead to a transmission or not.

Thus, for a suitable modelling generalisation and averaging are required. For this reason, the concepts of an adequate contact, contact and reproduction numbers were introduced.

Definition 2.1. (**Adequate contacts, reproduction and contact numbers**)

(i) A contact is called *adequate* (also *effective*), if it leads to a transmission of the pathogen from an infectious person to another one, and, if the affected individual is susceptible, then an infection is provoked.

(ii) The *basic reproduction number* ρ_0 is the average number of adequate contacts of an infectious individual during its infectiousness, if it is introduced into a host population where everyone is susceptible.

(iii) The *contact number* σ is the average number of adequate contacts of a typical infectious person during its infectiousness with all persons.

(iv) The *replacement number* ρ (also called *reproduction number*) is the average number of adequate contacts of an infectious individual during its infectiousness with only susceptible persons.

Here we use the letter ρ instead of R like in Vynnycky and White (2010), Hethcote (2000), to avoid confusion with the number of recovered persons R (see paragraph 2.1.5). In other words, during an adequate contact the pathogen is transmitted with the probability one (Weyer and Eggers (1990), p. 66). Sometimes, the result of an adequate contact of an infectious with a susceptible person is called *secondary infection*. Thus, one can say that ρ is the number of secondary infections produced by an infectious person during its infectiousness. Thus, ρ takes into account, that not each adequate contact produces an infection, because the fraction of susceptible persons generally shrinks in the course of infection. Therefore, ρ is time-dependent. The basic reproduction number ρ_0 is constant, it is related

to the beginning of an infection course. The contact number σ may be time-dependent. This is the case, if infectious persons change their contact behaviour voluntarily or due to restrictions mandated by authorities. Thus, at the beginning, σ equals to ρ_0 and ρ. Summarising these thoughts, there holds in almost all cases

$$\rho_0 = \rho(0) = \sigma(0), \qquad \rho(t) \leq \sigma(t) \leq \rho_0 \qquad \text{for } t \geq 0. \tag{2.1}$$

In the case of concrete models one uses generally contact and replacement numbers, σ and ρ, which reflect the *current* infection behaviour. Moreover, these current numbers can be related to other quantities describing the model in a natural way. We return to this in paragraph 2.2.2. As we will see later, ρ_0, σ and ρ are dimensionless quantities, i.e., they do not have any units.

Finally, we note that an adequate contact and hence the contact number are infection-dependent. A physically equal contact is adequate for one pathogen but not for another one. Clearly, the contact number depends on the mean duration of infectiousness.

The concept of the contact number averages the different and random behaviour of individuals.

2.1.3 Assumptions concerning population dynamics

When investigating the spread of infectious diseases, generally *two* mutually influencing processes have to be considered: The development of the infection itself and the dynamics of the population in which the infection extends, see Hethcote (2000). The assumptions listed up consecutively must be chosen in accordance with real proceedings of infections. Moreover, these assumptions should be supported by as much as possible empirical and medical findings. In Hethcote (2000), many cases of infections occurred in earlier time or recently are discussed in detail.

(i) (**Closed-population model**) An assumed *constant* number of community members (see remark 2.2) seems to be justified, if the infection spreads quickly, approximately within a year, and/or, if there is a balance between births, migration and non-disease-related deaths. In connection with disease modelling, these deaths are often referred to as "natural deaths". The deaths caused by infection can be listed as an extra class, or, they can be included into the group of (immune) recovered persons.

(ii) (**Dynamic-population model**) A *variable* number of community members should be taken into account, if the infection leads to many deaths, or, if a big growth of population and/or an essential migration substantially influence the population balance. Now, it is necessary to consider an additional equation for the population development, either with given rates of births, deaths and migration or as a logistic equation (see paragraph 2.2.1.3).

Generally, in the case of constant population the model which has to be developed becomes easier as for variable population. For a better overview, at first we deal with a constant number of community members, in subsection 2.3.3, a variable population is considered in short. In accordance with current findings about SARS-CoV-2 and with the demographical development at least in Germany, an assumed constant population seems to be justified.

2.1.4 Assumptions concerning the course of infection

(i) The whole population is divided in several *disjoint classes* w.r.t. the course of infection. The temporal development of each class and its interaction with others is described by an own equation. In the simplest case there are two classes: Persons who are susceptible for the infection and infected individuals. This approach leads to *compartment models*.
In section 2.1.5, we deal with this item in detail.

(ii) The *specifics of an infection process* are taken into account like mean duration of infectiousness of an individual, delay of infectiousness by a newly infected person (latent period), mean duration of acquired immunity after an overcome infection.
Detailed explications are given in section 2.2.

(iii) *Outer influences* on the infection process are considered like vaccinations and their temporal delay after the begin of infection (see paragraph 3.3), available capacities of intensive care or political measures to contain further infections, see for instance Grimm et al. (2020), Dehning et al. (2020).

We note, that for modelling one assumes homogeneity within the separate classes of population with respect to contact behaviour and course of infection. Otherwise, a further subdivision is necessary. In the

same manner, the durations mentioned above are averaged quantities. The real existing heterogeneity even within the same class is averaged based on the large number of individuals.

2.1.5 Infection-relevant classes of the population

Depending on specific characteristics of infection the population is divided into disjoint subsets (classes, compartments) (see remarks 2.2 concerning terms like 'number' and 'fraction').

(i) The number of persons *susceptible* for an infection is mostly abbreviated by S. The fraction of S w.r.t. the whole population is abbreviated by s. This class is also named *vulnerable*, its members are potentially at risk by the infection.

(ii) The number of *infected* persons is named by I, the fraction by ι (Greek iota). (Using i, there arise difficulties with the dot indicating the time derivation.)
If the model is to be to take a *latent period* into account, the class of infected is divided into subclasses in the following way.

(A) The number of *exposed* persons which had an adequate contact with an infectious infected individual is abbreviated by E and e, respectively. That means, these persons already have the pathogen of infection, but *cannot yet* transmit it to further persons. The mean duration of disposition in this class is referred to as *latent period*.

(B) The number of *infectious* persons is abbreviated by I and ι, respectively. This class contains former exposed persons which have become infectious after ending of latent period. Via an adequate contact they can infect susceptible persons. The mean time duration between infection and first appearance of symptoms is named *incubation period*. The latent period can be shorter as the incubation one. Besides, the infectious stage can end before the symptoms disappear.
Depending on concrete circumstances, the class I can be further divided, with regard to time and/or in parallel. A splitting with respect to time can be done into

(a) a class I_1 of infectious persons without symptoms, i.e., before ending the incubation period.

(b) a class I_2 of infectious persons with symptoms, i.e., after ending the incubation period.
If necessary, the last class I_2 can be divided in parallel into

(α) infectious persons I_{21} showing only weak or no symptoms. These individuals are not aware of their disease and danger of infection for others. Therefore, they do not reduce their contact behaviour, at least not more than it is currently usual.

(β) infectious persons I_{22} exhibiting distinct symptoms. Thus, they are aware of their disease and, therefore, they strongly change their contact behaviour or they are hospitalised. Sometimes, a further subdivision in parallel is performed, for instance, infectious persons (without symptoms) in quarantine can be considered, see Grimm et al. (2020).

(iii) The number of *recovered* persons is usually abbreviated by R and r, respectively. Depending on the concrete disease, recovered individuals may be temporarily or permanently immune or immediately susceptible again, see Hethcote (2000) and Vynnycky and White (2010) for examples, e.g.

(iv) The number of *immune* persons is often named by M and m, respectively. Often immune individuals are included into the class of recovered ones, in particular, if their acquired immunity is permanent. Persons can be immune via vaccination (passive immunisation) or by birth (or after survived disease) temporarily or permanently (active immunisation), see Hethcote (2000).

(v) The number of *dead* persons is usually abbreviated by D and d, respectively. Sometimes, to simplify the model, this class is included into the recovered or recovered immune persons, because they are not involved in the further course of infection. However, to get a complete result, dead individuals should constitute an extra class. This is particularly the case, if the lethality is influenced by outer circumstances like availability of intensive-care units in hospitals, see Grimm et al. (2020).

A further subdivision of the classes defined above by attributes like age, danger, social state or sex is discussed in detail in Hethcote (2000) and Vynnycky and White (2010). Moreover, in Grimm et al. (2020), pursuing this way, the authors develop a suitable as possible specific model for the description of SARS-CoV-2 epidemic in Germany.

How many classes have to be considered for a concrete model depends on virological and medical findings, and on how far the models sufficiently well represent the course of infection as well as for which

purpose they are intended. In Hethcote (2000) and Vynnycky and White (2010) many examples are discussed.

Concerning the virus SARS-CoV-2, up to now it seems to be assured, that infected persons are already infectious *before* showing symptoms. Therefore, the latent period is essentially shorter than the incubation one. Moreover, there are infected persons showing after the incubation period no or only weak symptoms and being nevertheless infectious. We refer to Wikipedia (2020), *Robert Koch-Institut: COVID-19 in Deutschland* (2020), Streeck et al. (2020), Adam (2020) and the references cited therein. A permanent immunity after survived disease is not yet assured. Some studies indicate only a temporary immunity, see Schultheiß et al. (2020) and Wikipedia (2020). Insofar a model for the spread of SARS-CoV-2 should take the classes S, E, I_1, I_{21}, I_{21}, R and D into account. In section 3 we discuss this and present a corresponding $\mathrm{SEI}^3\mathrm{RSD}$ model. If future findings show an essential difference between the durations of immunity obtained after surviving the infection and by vaccination, then an additional class of immune individuals has to be considered.

Based on a division into classes, different models have been investigated. Usually, they are abbreviated by SI, SIS, SIR, SEIR etc. Sometimes, there are additions like "with delay" or with notes to population dynamics. We refer to Hethcote (2000), Hethcote et al. (1981), Hethcote and van den Driessche (1995), Hethcote and van den Driessche (2000), Busenberg and Cooke (1993), Schuster (2013), Vynnycky and White (2010) and the references cited therein.

Remarks 2.2. (**Numbers and fractions**)

(i) The *number* of individuals in classes like S, I etc. are quantities equipped with the dimension *persons*, measured for instance by units like *one person* or *thousand persons*. However, we note that the term *number* is often used for *dimensionless* quantities in physics and natural sciences. An important example is the Reynolds number in fluid mechanics. Thus, there may be a source of confusion. In sections 2.2.2 and 4.1, we deal with these questions in the framework of dimensional analysis.

(ii) Generally, a *fraction* is the ratio of two quantities with the same dimension, and thus, it is dimensionless like mass or volume fractions in physics and chemistry. Again, we refer to section 4.1 for details.

2.2 Modelling of infection and equations for the infected

Now let us come to concrete steps in modelling. At first, it is important to model the infection mechanism of susceptible persons by infectious infected individuals. Clearly, the medical and virological details of infection processes are beyond this study, see for instance Vynnycky and White (2010), Ch. 1, and the references cited therein.

A mathematical modelling can be performed in a discrete manner using difference equations, or in a continuous way using differential or integral equations. Here, we only pursue the second way. However, many basic ideas of modelling are the same. Besides the approach with ordinary differential equations (ODE), in subsection 2.2.3, we deal in short with an alternative approach using an integral equation. An advantage of differential-equation models is the availability of broadly developed theoretical results and numerical procedures. For difference-equation models and further aspects of modelling we refer to Vynnycky and White (2010), Ch. 2.

2.2.1 Approach for I with a differential equation

At first we suppose that infected persons are infectious from the beginning of their infection and that they remain permanently infectious. Moreover, we assume that there are only susceptible S and infected I, leading to an SI model.

2.2.1.1 Preparation - exponential growth Like for other comparable growth processes (bacterial culture, non-controlled chain reaction in nuclear fission) it seems to be plausible assuming an *exponential growth*, at least for the beginning, see Heuser (1995), e.g. Let the increment of infected $\triangle I(t)$ (this is the number of newly infected persons) during a time period $\triangle t$ be proportional to the number of already existing infected $I(t)$ as well as to the considered time period:

$$\triangle I(t) = I(t+\triangle t) - I(t) = k\, I(t) \triangle t. \tag{2.2}$$

$k > 0$ is the (generally time-dependent) factor of proportionality (see remark 2.3 for time dependence). If there were $I(t)$ infected individuals at time t, so there are already $I(t) + k\, I(t)\triangle t$ at time $t + \triangle t$. As

it is usual, after division by $\triangle t$ and performing a limit process for $\triangle t \to 0$, from (2.2) one obtains the well-known differential equation

$$\frac{\mathrm{d}I}{\mathrm{d}t}(t) = \dot{I}(t) = k\, I(t) \qquad \text{for } t \in [0, \infty[\tag{2.3}$$

This equation is completed by the initial condition

$$I(0) = I_0 \tag{2.4}$$

with $0 \leq I_0 \leq N(0)$, and $N = N(t)$ is the generally time-dependent number of population members.

It is well-known that for *constant* k the unique global solution of the initial-value problem (2.3), (2.4) is given by the exponential function

$$I(t) = I_0 \exp(k\, t) \qquad \text{for } t \in [0, \infty[\tag{2.5}$$

See remark 2.4 for further comments.

Clearly, the initial-value problem (2.3), (2.4) has also a unique global solution for a variable continuous $k = k(t)$, see Heuser (1995), Walter (2000). This solution is given by

$$I(t) = I_0 \, \exp\big(\int_0^t k(\tau)\, \mathrm{d}\tau \big) \qquad \text{for } t \in [0, \infty[. \tag{2.6}$$

Due to (2.5), a constant k is not realistic after some time for real processes. Thus, there remains the task to find out the detailed structure of k for an infection process. We return to this in the next paragraph 2.2.1.2.

Remark 2.3. (**Time dependence and continuity of parameter functions**)

(i) In empirical sciences parameters are calculated from measured data, or in some cases, they are determined by direct measurements. As a rule, one gets discrete values, for instance the maximum air temperature for each day measured at one chosen place. For further mathematical treatment often a parameter function is constructed using the obtained discrete values. A simple way to do this consists in building a step function. The drawback is that step functions are not continuous at all arguments. The way out is an interpolation to a piece-wise linear continuous function or to functions exhibiting differentiability of some order.

(ii) For convenience, in this study we assume continuity of arising parameter functions. However, some mathematical results remain valid under slightly changed conditions for step functions, see remark 4.6 (i). This point plays some role in section 4.

Remarks 2.4. (**Exponential growth and decay**)

(i) For $k < 0$ the equation (2.3) describes an exponential decay, for instance radioactive decay.

(ii) Typical issues of exponential growth and decay (with constant k) are *doubling time* and *half-value time* (or half time), respectively. These quantities mean the time duration, during which a growing quantity reduplicates and a shrinking quantity is divided in half, respectively. Suppose, a growing quantity reduplicates during the time interval t_1, t_2 with $0 \leq t_1 < t_2 < \infty$. Then the doubling time t_{dop} fulfils $t_{dop} := t_2 - t_1 = {}^1\!/_k \ln(2)$ and is *only* determined by the length $t_2 - t_1$ of the interval and not by its position on the real line. An analogous assertion holds for $k < 0$: The half-value time t_{half} is given by $t_{half} := t_2 - t_1 = -{}^1\!/_k \ln(2)$. If the half-value time is over, a half of the initially existing radioactive substance has decayed. Moreover, the half-value time is also the mean "life span" of a radioactive atom. The value $\exp(k\, t)$ (with $k < 0$) can be interpreted as the probability, that a radioactive atom is not yet decayed at t. This last thought plays an important role later on when dealing with latent and incubation periods.

2.2.1.2 Limited growth - non-linear equation for I In real applications, an unlimited exponential growth predicted by equation (2.5) is no longer observed after some time. Concerning infectious diseases, after some time an infectious person has also adequate contacts (see definition 2.1 (i)) to already infected ones. These contacts do not produce new infected individuals. Therefore, a constant proportionality factor k in (2.3) is *not* realistic. We change this equation in the following way.

$$\frac{\mathrm{d}I}{\mathrm{d}t}(t) = \dot{I}(t) = \beta(t)\, \frac{S(t)}{N(t)}\, I(t) \qquad \text{für } t \in [0, \infty[, \tag{2.7}$$

Instead of k there is the expression $\beta(t)^{S(t)}/_{N(t)}$ with a positive continuous β. It expresses how many adequate contacts one infectious individual has during a time unit *in the middle* with *all persons* of the population. Hence, β is also named *contact coefficient* or *contact rate*. We prefer the first name. In paragraph 2.2.2, we discuss the relations of β with the mentioned above contact and reproduction number (see definition 2.1 (ii)-(iv)). Due to Hethcote (2000), β does not essentially depend on the size of human population, contrary to infections spread among animals. But there is generally a density dependence of β, see Vynnycky and White (2010), p.31. That means, if more people live on the same place, the mean number of contacts grows. Thus, in applications, β is related to the territory considered, for instance for whole Germany, or only for its capital Berlin.

Here, β has the unit *per time* like in Hethcote (2000). Contrary to this, in Vynnycky and White (2010), p. xxi, and Ch. 2, β has the unit *per person*, due to the difference-equation approach.

The factor $^{S(t)}/_{N(t)} = s(t)$ is the fraction of susceptible persons within the whole population. It expresses the probability to meet an individual of the class S at time t. Even though β is constant, the expression $\beta\, ^{S(t)}/_{N(t)}$ decreases due to a shrinking class S in favour of I. Thus, $\beta(t)^{S(t)}/_{N(t)}$ is also named *effective contact coefficient* or *effective contact rate*. From the viewpoint of I it can be spoken about an active effective infection rate. The whole expression on the right-hand side of (2.7) is often named *standard incidence*. It states how many cases of infection occur in a time unit.

The equation (2.7) means that for $S \approx N$, also at the begin with only some few infective individuals, the fraction $^{S}/_{N}$ approximately equals to one. Thus, at this time, exponential growth occurs else. If I grows, this fraction becomes smaller, and the growth of I essentially decelerates. The effective contact rate in (2.7) tends to zero, at least for constant β and N.

The realistic assumption $^{S}/_{N} \approx 1$ for the begin can be applied to linearise the equation (2.7) as well as the equations (2.8) and (2.39), (2.40) below. Based on this, qualitative investigations can be performed, see Bacaër (2020) and the references therein.

We note that the contact coefficient β is a parameter of infection course being strongly influenced from "outside". It depends on the pathogen's properties as well as on social behaviour, namely on contact manner within a considered population. β can be considerably reduced, voluntarily and by means of administrative measures. During the COVID-19 pandemic political authorities in many countries have ordered strong rules concerning limitations of contacts, distances to foreign persons, closings of schools and universities, churches, restaurants etc. As a result one observes a decreasing β and an end of exponential growth of accumulated cases in some countries, for instance in Germany. However, an easing of mandated measures and more carelessness may lead to an increasing β and to essentially more cases, like in Israel or Australia in July, and now, in August 2020 in some European countries.

The equation (2.7) describes the special situation that all susceptible individuals will be infected in the course of time, and they will remain infectious (see (2.11)). If a convalescence has to be taken into account, than this equation has to be changed by

$$\dot{I}(t) = \beta(t)\,\frac{S(t)}{N(t)}\,I(t) - \gamma\,I(t) \qquad \text{for } t \in [0,\infty[, \tag{2.8}$$

That means, in a time unit the class I loses $\gamma\,I(t)$ individuals due to recovery (and loss of infectiousness). The coefficient $\gamma > 0$ is the reciprocal value of the mean infection duration t_{inf}, e.i., $t_{inf} = {}^{1}/_{\gamma}$. Since the average duration of infectiousness is disease-specific, an assumed constant t_{inf} (and thus a constant γ) seems to be plausible. The value $\exp(-\gamma\,t)$ can be interpreted as the probability that an infected person is still infectious at time t (see remark 2.4 (ii) and paragraph 2.2.3). And, otherwise, $1 - \exp(-\gamma\,t)$ is the probability that an infected loses its infectiousness at time t. If infectiousness and disease have very different mean durations, the model could be extended.

If the models are more complex, in (2.7) and (2.8), respectively, one has to divide by $N - D$ instead of N, where D is the number of persons died by infection, see paragraph 2.3.2.2.

In accordance with our assumption at the beginning of paragraph 2.2.1 there holds

$$N(t) = I(t) + S(t) \qquad \text{for } t \in [0,\infty[. \tag{2.9}$$

Contrary to (2.7), in the case of equation (2.8), due to the "outflow" $\gamma\,I(t)$ the evolution of S and I is more complex. There will be an equilibrium, see paragraph 4.3.1.

For constant N the equation (2.8) can be divided by N. This yields an equation for the population fractions $\iota(t) := {}^{I(t)}/_{N}$ and $s(t) := {}^{S(t)}/_{N}$:

$$\frac{\mathrm{d}\iota}{\mathrm{d}t}(t) = \dot{\iota}(t) = \beta(t)\,s(t)\,\iota(t) - \gamma\,\iota(t) \qquad \text{for } t \in [0,\infty[, \tag{2.10}$$

Since the fractions s and ι lie between zero and one, they can be also interpreted as probabilities to meet a susceptible and an infectious person, respectively, see Hethcote (2000) e.g. We return to fractions in connection with dimensional analyse in paragraphs 4.1 and 4.3.1.

2.2.1.3 Relation to the logistic equation

Substituting S by $N - I$ in (2.7), one gets

$$\dot{I}(t) = \beta(t) I(t) - \frac{\beta(t)}{N(t)}\, I^2(t) \qquad \text{for } t \in [0, \infty[. \tag{2.11}$$

For constant β and N, this is the (classical) *logistic equation*. For an initial value $0 < I_0 < N$ its solution grows asymptotically to N. This equation is detailed discussed in many textbooks on ordinary differential equations and on biomathematics, see for instance Heuser (1995), Walter (2000), Schuster (2013).

2.2.2 Relations to contact and reproduction numbers

In definition 2.1 (ii)-(iv), contact and reproduction numbers are defined independently of concrete infection models. Generally, theses numbers play an important role in epidemiology.

Now, it is the aim to find out concrete expressions for ρ_0, ρ, σ in the case of models with equation (2.8) for the infectious infected persons. In doing so, there arise some modifications compared with definition 2.1.

At first, we assume a *constant* contact coefficient β. As described after equation (2.8), let t_{inf} be the average duration of infectiousness with $t_{inf} = 1/\gamma$. Based on definition 2.1 and (2.1), one gets

$$\rho_0 = \sigma = \beta\, t_{inf} = \frac{\beta}{\gamma}, \tag{2.12}$$

Thus, for constant β the numbers ρ_0 and σ coincide. For a generally variable $\beta = \beta(t)$, it is useful to define the quantities ρ_0, $\sigma = \sigma(t)$ and $\rho = \rho(t)$ in the following way, bearing (2.12) and (2.8) in mind.

$$\rho_0 = \beta(0)\, t_{inf} = \frac{\beta(0)}{\gamma}, \quad \sigma(t) = \beta(t)\, t_{inf} = \frac{\beta(t)}{\gamma}, \quad \rho(t) = \beta(t)\, t_{inf}\, \frac{S(t)}{N} = \frac{\beta(t)}{\gamma}\, \frac{S(t)}{N} = \sigma(t)\, \frac{S(t)}{N}. \tag{2.13}$$

As already stated, ρ_0 remains constant in either case. The factor $S(t)/N$ takes into account that the replacement number ρ counts only adequate contacts with susceptible persons (during the period of infectiousness). This is the difference to σ, cf. definition 2.1 (iii), (iv).

A detailed inspection shows, that some explanation needs concerning σ and ρ. $\sigma(t)$ and $\rho(t)$ are indeed *current* contact and replacement number, respectively. They explain the average number of adequate contacts (with all persons and with susceptible ones, respectively) of a *new* infectious person, assuming that $\beta(t)$ (and $S(t)/N$) remain constant during its infectiousness. Thus, in some sense, $\sigma(t)$ and $\rho(t)$ are *virtual* contact and replacement number, respectively, describing a frozen state. However, just these numbers play an important role, see paragraphs 4.3.1 and 4.3.2.

Based on definition 2.1, the individual (real) contact and replacement number, σ_p and ρ_p, respectively, of an individual p (still with an averaged contact behaviour) can be calculated by

$$\sigma_p = \int_{\tau_0(p)}^{\tau_0(p)+t_{inf}} \beta(\tau)\, \mathrm{d}\tau, \qquad \rho_p = \int_{\tau_0(p)}^{\tau_0(p)+t_{inf}} \beta(\tau)\, \frac{S(\tau)}{N}\, \mathrm{d}\tau. \tag{2.14}$$

Here, the mean duration of infectiousness t_{inf} is used, and $\tau_0(p)$ is the begin of infectiousness of the individual p. It is thinkable to use an individual $t_{inf}(p)$. At least in this study, these numbers do not play any role. Even for constant β, the replacement number ρ depends on time.

Equation (2.13) confirms the assertion mentioned above, that the quantities ρ, σ and ρ_0 are *dimensionless*. In other words, they are numbers in the sense of remark 2.2 (i). Note that for more complex models the expressions for σ and ρ generally differ from (2.13), see remark 3.1 and section 4.3.1.

Equation (2.8) and the last relation in (2.13) allow the following interpretation. The current replacement number $\rho(t)$ is the ratio of *inflow* $\beta\, S/N\, I$ and *outflow* $\gamma\, I$ of infectious persons, see Quaas (2020), also for an application of this idea. Thus, the meaning of replacement number can be well explained.

In accordance with many deterministic epidemiologic models an infection within a completely susceptible population can start if and only if there holds

$$\rho_0 > 1 \tag{2.15}$$

For further discussion and for the question how to determine ρ with the help of available data we refer to Hethcote (2000), Vynnycky and White (2010) and, especially concerning SARS-CoV-2, to Quaas (2020), *Robert Koch-Institut: COVID-19 in Deutschland* (2020), Mikut et al. (2020) and to the references therein. In connection with dimensional analysis we return to ρ in paragraphs 4.3.1 and 4.3.2.

We close this paragraph with remarks concerning the use of some terms,

Remarks 2.5. (On parameters, numbers and rates)

(i) A *parameter* and a *coefficient* are understood as additional quantities in equations or as quantities formed by them. Parameters can be provided with units, than they have a dimension. If they occur without units, they are called dimensionless. In the last case, they are also called *(characteristic) numbers* or *ratios*.
As an example, the contact coefficient β in (2.3) has the dimension 'reciprocal time', e.i. $1/T$. (T stands for the dimension time.)
The basic reproduction number ρ_0, the replacement number ρ and the contact number σ are dimensionless and thus (characteristic) numbers. Note, that in current discussions about the SARS-CoV-2 pandemic sometimes the terms reproduction rate and infection rate are used incorrectly. This may lead to confusion in the broad public.

(ii) A *rate* is often understood as a quantity which dimension has the time in the denominator. For instance, the contact coefficient β is a rate. Moreover, the whole right-hand side $\beta(t)\, I(t)\, S(t)/N(t)$ of (2.7) is a rate, the total contact rate.

2.2.3 Supplement: Approach for I with an integral equation

The derivations of differential equations (2.3) and (2.7) have been performed under the assumption that each infected person is infectious from the begin and for all time. Generally, this is not the case. Equation (2.8) models a finite infectiousness, assuming an exponential decay, cf. remark 2.4 (ii), which does not need to be the case. Thus, there were developed general approaches containing explicitly stochastic moments and leading to integral equations for I. In a special case, this is equivalent to differential equations. We explain this in short and follow Hethcote and van den Driessche (1995), Hethcote and van den Driessche (2000). Since models with differential equations are in the focus of this study, we do not want to apply this approach to more complex models like SEIRD ones.

For $t \geq 0$ we note by $p_I(t)$ the probability that an infected is infectious until time t. We assume:

(i) The infectiousness begins immediately after an adequate contact.

(ii) There are no death cases, neither infection-related nor other ones.

These two assumption are made to focus on essential items. If necessary, the model can be suitably extended (see remark 2.7 (i), (ii)). Let be p_I a (Lebesgue-measurable) function fulfilling

$$p_I(0^+) := \lim_{t \to 0,\, t>0} p_I(t) = 1, \qquad p_I \text{ not increasing on } [0,\infty[, \qquad p_I(t) \geq 0 \text{ for } t \in [0,\infty[, \tag{2.16}$$

$$\int_0^\infty p_I(u)\,\mathrm{d}u = \omega := t_{inf} < \infty. \tag{2.17}$$

Again, $0 < \omega = t_{inf} < \infty$ is the average duration of infectiousness (see remark 2.4 (ii) as well as the explications after (2.8)). For the case $\omega = \infty$ we refer to Hethcote and van den Driessche (2000).

We follow Hethcote and van den Driessche (2000) with small changes, allowing furthermore a continuous $\beta = \beta(t)$. The approach for infected persons is given by

$$I(t) = I_0 p_I(t) + \int_0^t \beta(\tau) I(\tau)\, \frac{S(\tau)}{N(\tau)}\, p_I(t-\tau)\,\mathrm{d}\tau. \tag{2.18}$$

$I_0 p_I(t)$ means the (probable) number of initially infected persons being still infectious at time t. The integral is the sum of persons infected at t, being (probable) still infectious.

Remark 2.6. Contrary to (2.8), the approach in (2.18) contains explicitly a stochastic moment. However, let us remark, that the approach in (2.8) contains indirectly a stochastic moment via the concept of adequate contacts, which is averaged by a generally large number of individuals.

Now we consider two special cases for p.

2.2.3.1 Exponentially decaying infectiousness Now we assume

$$p_I(t) = \exp(-\gamma t) \quad \text{with } \gamma = const. > 0. \tag{2.19}$$

From condition (2.17) there follows

$$\gamma = \frac{1}{\omega} = \frac{1}{t_{inf}}. \tag{2.20}$$

As it has been mentioned above, γ is the reciprocal mean duration of infectiousness $t_{inf} = \omega$.

In Hethcote et al. (1981), it was proved that under assumption (2.19) the integral approach in (2.18) is equivalent to the one with differential equation (2.8). A probability p_I tending to zero causes a decay of infective individuals.

2.2.3.2 Infectivity of equal duration Now it is assumed that the common duration of infectiousness for all infective persons amounts to $0 < \omega < \infty$. This corresponds to the function p_I referred to

$$p_I(t) := \begin{cases} 1 & \text{for } t \in [0, \omega], \\ 0 & \text{for } t > \omega. \end{cases} \tag{2.21}$$

Thus, p_I fulfils the conditions (2.16), (2.17). However, it is *not* continuous at $t = \omega$. This may lead to a non-continuous function I. Inserting (2.21) into (2.18), one gets the following slightly cumbersome expression.

$$I(t) := \begin{cases} I_0 + \int_0^t \beta(\tau)\, I(\tau)\, \frac{S(\tau)}{N(\tau)}\, \mathrm{d}\tau & \text{for } 0 \le t \le \omega, \\ \int_{t-\omega}^t \beta(\tau)\, I(\tau)\, \frac{S(\tau)}{N(\tau)}\, \mathrm{d}\tau & \text{for } t > \omega. \end{cases} \tag{2.22}$$

These two integral equations are equivalent to an initial-value problem for a differential equation as well as to an initial-value problem for a differential equation with delay, more preciously to the problem

$$\dot{I}(t) = \beta I(t)\, \frac{S(t)}{N(t)} \qquad \text{for } t \in [0, \omega[, \qquad\qquad I(0) = I_0, \tag{2.23}$$

as well as to the problem

$$\dot{I}(t) = \beta(t) I(t)\, \frac{S(t)}{N(t)} - \beta(t-\omega) I(t-\omega)\, \frac{S(t-\omega)}{N(t-\omega)} \qquad \text{für } t \ge \omega, \tag{2.24}$$

$$I(\tau) = I_\omega(\tau) \qquad \text{for } \tau \in [0, \omega] \tag{2.25}$$

Here, I_ω is the solution of problem (2.23). In order to avoid a jump function regularisations can be used (see remark 2.7 (iii)). If $I_0 = 0$, than I is also continuous in $t = \omega$, however, it is identically zero. We close this paragraph with additional remarks.

Remarks 2.7. (i) The case of a delayed infectiousness of infected persons has not been considered in this paragraph. Two possibilities may be offered. At first, one can introduce a further class E of already infected persons who cannot yet infect others (see paragraph 2.1.5). The further procedure is analogous, a probability has to be defined which determines how long an individual in E is not yet infectious. Another possibility would be to continue with the class I as before and define the function p_I differently from (2.16), setting it zero at some initial time interval. Of course, this violates the monotony condition in (2.16). Moreover, it is not clear, whether the mathematical results in Hethcote and van den Driessche (1995), Hethcote and van den Driessche (2000) can be extended to this case.

(ii) Cases of death caused by disease or not can be taken into account by additional exponential terms within the integral equations for I, see Hethcote and van den Driessche (1995), Hethcote and van den Driessche (2000).

(iii) The function p_I in (2.21) generally has a jump. This could complicate mathematical investigations and numerical calculations. A resort could be a regularisation, substituting the jump function by a piece-wise linear and continuous one. Such approach could be

$$p_I(t) := \begin{cases} 1 & \text{for } 0 \le t \le \omega - \xi, \\ -\frac{1}{2\xi}\,(t - (\omega - \xi)) & \text{for } \omega - \xi \le t \le \omega + \xi, \\ 0 & \text{für } t > \omega + \xi. \end{cases} \tag{2.26}$$

with some $0 < \xi < \omega$. Up to $t = \omega - \xi$ all infected individuals are infectious, from $t = \omega + \xi$ nobody is else infectious. Between these points in time, there is a linear decay of infectiousness.

(iv) In Hethcote and van den Driessche (2000), the presentation is more general as here, and mathematical results are presented.

2.3 Completion of models

After dealing with equations for the class I of infectious infected persons, it is now the aim to add further equations for remaining classes like S, E and R. As a result, we get complete models suitable for several kinds of infection courses. In this section 2.3, the focus lies on development and reasoning of models. In connection with mathematical investigations in section 4 the needed equations will be presented in a compact way as well as completed with initial and other conditions.

2.3.1 SI and SIS models with constant population number

In this paragraph we consider only models described with the two classes S and I. Either the infected persons remain in I for all time (SI model), or they return to S after survived disease (SIS model). Therefore, we need a suitable equation for S. We distinguish two basic cases oriented to paragraphs 2.2.1 and 2.2.3.

2.3.1.1 Modelling with differential equations Let us suppose that the evolution of I is given by the differential equation (2.8). Clearly, the growth rate for I is the loss rate for S. Therefore, it yields

$$\dot{S}(t) = -\beta(t)\,\frac{I(t)}{N(t)}\,S(t) + \gamma\,I(t) \qquad \text{for } t \in [0,\infty[. \tag{2.27}$$

(Again with a continuous time-dependent β). Contrary to (2.8), now I is in the numerator instead of S. Of course, there is no mathematical change. However, it is a question of interpretation. The term ahead S, e.i., $-\beta(t)\,{}^{I(t)}\!/_{N(t)}$, can be regarded as effective infection rate from the viewpoint of S. Moreover, besides the sign, it is generally different from the effective contact rate $\beta(t)\,\frac{S(t)}{N(t)}$ from the viewpoint of I (see equation (2.8)).

Neglecting birth and death rates as well as migration, e.i., setting $N(t) = N_0 = const.$, or assuming $N = N(t)$ as given, we get a closed simple SIS model formed by (2.8) and (2.27) together with initial conditions for S and I. Clearly, for $\gamma \equiv 0$ it turns into an SI model. For mathematical and numerical investigations it is mostly sufficient to solve only one equation, after substituting in (2.27) I by $N - S$, for instance.

2.3.1.2 Supplement: Modelling with integral equations As explained in paragraphs 2.2.3 and 2.2.3.1, the approach with a differential equation for I can be regarded as a special case corresponding to an exponentially decaying infectiousness. Let us repeat equation (2.18) again.

$$I(t) = I_0 p(t) + \int_0^t \beta(\tau) I(\tau)\,\frac{S(\tau)}{N(\tau)}\,p(t-\tau)\,\mathrm{d}\tau. \tag{2.28}$$

Since there are only the classes S and I, due to $N(t) = S(t) + I(t)$ it yields

$$S(t) = N(t) - N(0) + S_0(1 - p(t)) - \int_0^t \beta(\tau) I(\tau)\,\frac{S(\tau)}{N(\tau)}\,p(t-\tau)\,\mathrm{d}\tau. \tag{2.29}$$

For $p \equiv 1$ (corresponds to permanent infectiousness and $\gamma \equiv 0$) and $N(t) = N_0 = const.$ the well-known SI model (2.8) and (2.27) for $\gamma \equiv 0$ easily follows by taking the time derivative. In this simple case, as a rule, the formulation with differential equations is more convenient.

2.3.2 SIRD, SIRSD, SEIRD and SEIRSD models with constant population number

The following models contain more than two classes. In SIRD and SIRSD models, the class I loses members to the class R of recovered persons as well as to the class D of infection-died individuals. In SEIRD and SEIRSD models, there occurs a special class E of already infected, but not yet infectious persons.

2.3.2.1 SIRD and SIRSD models The SIRD model is sometimes called classical epidemiological model (CEM) and widespread. Assuming that all recovered persons remain permanently immune, the equation for S is given by (cf. (2.27))

$$\dot{S}(t) = -\beta(t)\,\frac{I(t)}{N(t)-D(t)}\,S(t) \qquad \text{for } t \in [0,\infty[. \tag{2.30}$$

As a new issue, N in the denominator is substituted by $N-D$, since died persons do not have any contacts. The numbers of individuals in R will *not* be subtracted from N. Persons from R have furthermore adequate contacts with I individuals, but these contacts do not lead to infections.

The class I loses members to R and to D. Thus, the equation (2.8) must be changed:

$$\dot{I}(t) = \beta(t)\,\frac{S(t)}{N(t)-D(t)}\,I(t) - \gamma\,I(t) - \delta\,I(t) \qquad \text{for } t \in [0,\infty[. \tag{2.31}$$

Again, $\gamma > 0$, and $t_{inf} = 1/\gamma$ is the mean duration of infectiousness. In this approach, the last one ends with the disease, or, the patient is regarded as recovered after his or her infectious period. The term $-\gamma\,I(t)$ describes that infected persons leave class I. Here, a permanent immunity is assumed. $\delta > 0$ is the infection-specific lethality coefficient, $1/\delta$ is the mean life span of infected people related to the infection. (A general life span is taken into account in paragraph 2.3.3.) Hence, $-\delta\,I(t)$ is the lethality rate, it describes how many individuals of I die in a time unit caused by infection. The equations for R and D, respectively, are

$$\dot{R}(t) = \gamma\,I(t) \qquad \text{for } t \in [0,\infty[, \tag{2.32}$$

$$\dot{D}(t) = \delta\,I(t) \qquad \text{for } t \in [0,\infty[. \tag{2.33}$$

In summary, the differential equations (2.30) - (2.33) (together with corresponding initial conditions - see subsection 3.2) describe a SIRD model for an assumed constant population. Thus, it yields

$$N_0 = N(t) = S(t) + E(t) + I(t) + R(t) + D(t), \qquad \text{for } t \in [0,\infty[. \tag{2.34}$$

This leads to

$$N(t) - D(t) = S(t) + E(t) + I(t) + R(t), \qquad \text{for } t \in [0,\infty[. \tag{2.35}$$

Therefore, if necessary, the denominator in (2.30) and (2.31) can be substituted.

Remark 2.8. Summing up the equations (2.31) - (2.33), one obtains an equation for the sum $I+R+D$.

$$\dot{I}(t) + \dot{R}(t) + \dot{D}(t) = \beta(t)\,\frac{S(t)}{N(t)-D(t)}\,I(t) \qquad \text{for } t \in [0,\infty[. \tag{2.36}$$

The sum $I+R+D$ represents the whole number of infected individuals, currently and formerly (accumulated cases). Furthermore, via $S = N - I - R - D$, S can be excluded on the right-hand side. In applications, equation (2.36) can be used for determining β from measured data, or more precisely from daily reported numbers of newly infected, recovered and died persons.

(SIRSD **model**) A *loss of immunity* of recovered persons can be integrated in the following way. Assuming a mean duration of immunity t_{imm} and setting $\mu := 1/t_{imm}$, the term $-\mu\,R(t)$ is the rate of loss for R and of benefit for S. Thus, there must be added $-\mu\,R(t)$ on the right-hand side of (2.32), and $\mu\,R(t)$ on the right-hand side of (2.30). Therefore, equations (2.30) and (2.32) are replaced by the following ones.

$$\dot{S}(t) = -\beta(t)\,\frac{I(t)}{N(t)-D(t)}\,S(t) + \mu\,R \qquad \text{for } t \in [0,\infty[, \tag{2.37}$$

$$\dot{R}(t) = \gamma\,I(t) - \mu\,R \qquad \text{for } t \in [0,\infty[. \tag{2.38}$$

2.3.2.2 SEIRD and SEIRSD models Now we consider a more general case. The class S directly loses members to the class E consisting of infected persons who are not yet infectious. After expiration of latent period the individuals of E become infectious. Then they belong to an I class. Besides this, we assume that after overcome infection former infected persons go into class R of recovered individuals.

Either they remain there being permanently immune or they become susceptible again after some time. Finally, individuals from I may die by the infection-caused disease.

The equation for S is given by (2.30), assuming a permanent immunity in R.

The special feature of class E is expressed in modelling, too. Individuals from E cannot be (newly) infected, and they cannot infect others. Thus, E can only grow, if there are adequate contacts between persons from S and I. Based on (2.8) we can write:

$$\dot{E}(t) = \beta(t)\,\frac{S(t)}{N(t) - D(t)}\,I(t) - \epsilon\,E(t) \qquad \text{for } t \in [0, \infty[. \tag{2.39}$$

Here, $\epsilon > 0$ is a parameter which can be referred to the reciprocal value of the latent period, e.i., $t_{lat} = 1/\epsilon$, see Grimm et al. (2020). The term $-\epsilon\,E(t)$ describes the loss of E to I. This loss is the benefit for I. Therefore, we can write

$$\dot{I}(t) = \epsilon\,E(t) - \gamma\,I(t) - \delta\,I(t) \qquad \text{for } t \in [0, \infty[. \tag{2.40}$$

Again, $\gamma > 0$, and $t_{inf} = 1/\gamma$ is the mean duration of infectiousness. Contrary to the situation in subsection 2.2 and in paragraph 2.3.2.1, now the infectiousness begins only after the end of latent period. The term $-\gamma\,I(t)$ describes that infected persons leave class I. As above in the previous paragraph, $\delta > 0$ is the infection-specific lethality coefficient. The equations for R and D are the same ones as in (2.32) and (2.33).

Finally, the differential equations (2.30), (2.32), (2.33), (2.39), (2.40) (together with corresponding initial conditions - see subsection 3.2) describe a SEIRD model for an assumed constant population.

(SEIRSD **model**) The difference between SEIRD and SEIRSD models is that recovered persons loss their immunity. Again, as a consequence, equations (2.30) and (2.32) must be replaced by (2.37) and (2.38).

2.3.3 Consideration of population development

Now, we want to discuss in short how a variable population number can be taken into account within the models presented above. There are two possible approaches, see Hethcote and van den Driessche (2000):

(i) The population development is controlled by rates for births, migration and deaths non-caused by the infection under consideration.

(ii) A modified logistic equation is used.

Here, we only consider the first case in more detail, for the second one more complex we refer to Hethcote and van den Driessche (2000) and to the references cited therein.

In the case of a variable population number, $N = N(t)$, died persons are *not* included into N, independently of the death reason. The classes of died individuals can be calculated a posteriori.

The temporal course of N is described by a differential equation along with an initial condition.

$$\dot{N}(t) = b\,N(t) - \delta_{nat}\,N(t) - \delta_{inf} I(t) + r_{mig}(t) \qquad \text{for } t \in [0, \infty[, \tag{2.41}$$

$$N(0) = N_0 > 0. \tag{2.42}$$

Here are $b \geq 0$, $\delta_{nat} \geq 0$ birth and death coefficients related to the whole population, the death coefficient $\delta_{inf} \geq 0$ is related to infected persons, r_{mig} is the migration rate. All these quantities may be time-dependent continuous functions. The migration rate can be regarded as difference of immigration and emigration rate:

$$r_{mig}(t) = r_{immi}(t) - r_{emi}(t) \qquad \text{for } t \in [0, \infty[, \tag{2.43}$$

with $r_{immi}(t) \geq 0$ and $r_{emi}(t) \geq 0$. Since individuals of all classes may migrate, one can set (see remark 2.9):

$$r_{immi}(t) = r^S_{immi}(t) + r^E_{immi}(t) + r^I_{immi}(t) + r^R_{immi}(t), \tag{2.44}$$

$$r_{emi}(t) = r^S_{emi}(t) + r^E_{emi}(t) + r^I_{emi}(t) + r^R_{emi}(t). \tag{2.45}$$

Now we complete the equations for S, E, I and R from SEIRD and SEIRSD models in paragraph 2.3.2.2.

$$\dot{S}(t) = -\beta(t)\,\frac{I(t)}{N(t)}\,S(t) + b\,N(t) + \mu\,R(t) - \delta_{nat}\,S(t) + r^S_{immi}(t) - r^S_{emi}(t) \qquad \text{for } t \in [0,\infty[, \tag{2.46}$$

$$\dot{E}(t) = \beta(t)\,I(t)\,\frac{S(t)}{N(t)} - \epsilon\,E(t) - \delta_{nat}\,E(t) + r^E_{immi}(t) - r^E_{emi}(t) \qquad \text{for } t \in [0,\infty[, \tag{2.47}$$

$$\dot{I}(t) = \epsilon\,E(t) - \gamma\,I(t) - (\delta_{nat} + \delta_{inf})\,I(t) + r^I_{immi}(t) - r^I_{emi}(t) \qquad \text{for } t \in [0,\infty[, \tag{2.48}$$

$$\dot{R}(t) = \gamma\,I(t) - \mu\,R(t) - \delta_{nat}\,R(t) + r^R_{immi}(t) - r^R_{emi}(t) \qquad \text{for } t \in [0,\infty[. \tag{2.49}$$

Here, it has been supposed that all newborns are susceptible (otherwise, an additional class is needed), and that only infectious infected can die caused by infection.

The initial values S_0, E_0, I_0 and R_0 should be meaningfully between 0 and N_0 fulfilling the condition

$$N_0 = S_0 + E_0 + I_0 + R_0. \tag{2.50}$$

It is easy to see that the right-hand side of (2.41) for N can be obtained after addition of the right-hand sides of (2.46) - (2.49). Hence, die condition (2.50) ensures that for an existing unique solution there holds for all t

$$N(t) = S(t) + E(t) + I(t) + R(t). \tag{2.51}$$

Therefore, in the equations (2.46) and (2.47), N can be substituted reducing the whole system of equations. Via

$$D(t) = D_0 + \int_0^t \delta_{inf}\,I(\tau)\,\mathrm{d}\tau + \int_0^t \delta_{nat}\,N(\tau)\,\mathrm{d}\tau \tag{2.52}$$

the number of died persons can be calculated a posteriori.

Remark 2.9. The numbers N, S etc. are all non-negative. Thus, the model allows an unlimited immigration, but *not* a suchlike emigration. Strictly speaking, all emigration rates r_{emi}, r^S_{emi} etc. must be equipped with switch-off functions, which prevent negative values for N, S etc. We drop this here, because in paragraph 3 there arise an analogous problem connected with the vaccination rate. There, a suitable switch-off function will be constructed.

3 A SEI^{3}RSD model with possible vaccination for the description of the spread of SARS-CoV-2

Now it is the aim to develop a model which is better adjusted to so far known findings about SARS-CoV-2, without aspiring the elaborateness in Grimm et al. (2020). In particular, we do not divide the classes S, E, R into further subclasses in accordance with social or other aspects.

Some findings relevant for modelling are: Latent and incubation periods differ, infected persons are infectious after the end of incubation period and there exist infectious infected persons without or only with light symptoms, see Wikipedia (2020), *Robert Koch-Institut: COVID-19 in Deutschland* (2020), e.g. Thus, we introduce the class E and subdivide the class I. Additionally, we take into account that recovered persons lose their acquired immunity and that susceptible individuals become temporarily immune via vaccination.

For a better overview we assume a constant population number $N = N_0$. The considerations concerning a variable N in paragraph 2.3.3 can be included without any difficulties, if needed.

3.1 Partition of the class of infectious infected persons

A specific feature of the present model is that the class of infectious infected individuals I is subdivided (see also paragraph 2.1.5).

(i) The class E (of infected, but not infectious persons) loses to the class I_1 consisting of individuals who are already infectious, but they do not have any disease symptoms. The mean length of stay in I_1 equals to the difference between incubation and latent period, t_{inc} and t_{lat}, respectively.

(ii) After the end of incubation period the class I_1 loses parallelly to two further classes, more precisely to

(a) I_{21} consisting of furthermore infectious infected persons without or with only weak symptoms. Thus, the affected are not aware to their illness. The loss of infectiousness is assumed to be the beginning of recovery after a mean 'disease duration' $t_{inf,1} - t_{inc}$;

(b) I_{22} consisting of furthermore infectious infected persons exhibiting stronger symptoms and feeling ill. Thus, the affected are either in home isolation or in a hospital. Their recovery also starts with the loss of infectiousness after a mean 'disease duration' $t_{inf,2} - t_{inc}$.

If the start of recovery and the end of infectiousness do not coincide, then, when indicated, the classes I_{21} and I_{22} have to be subdivided further. We drop this here. However, the model allows different lengths of disease periods.

The partition into I_{21} and I_{22} is hence relevant, because it is plausible that the individuals certainly exhibit different contact behaviour. People with remarkable disease symptoms generally behave more carefully or are even hospitalised. In both cases one can assume that they infect essentially less susceptible persons.

3.2 Equations and initial conditions for all classes

Summarising the considerations above, now we write down all equations. For S we present a modified version of (2.37).

$$\dot{S}(t) = -\Big(\beta_1(t)\,\frac{I_1(t)+I_{21}(t)}{N(t)-D(t)} + \beta_{22}(t)\,\frac{I_{22}(t)}{N(t)-D(t)}\Big)\,S(t) + \mu\,R(t) - q\,\varphi(S) \qquad \text{for } t \in [0,\infty[. \tag{3.1}$$

Individuals from I_1 and I_{21} are supposed to have the same contact behaviour. This one of I_{22} members essentially differs. From the description of classes I_1, I_{21} and I_{22} follows the suggestion

$$\beta_{22} < \beta_1. \tag{3.2}$$

Clearly, this is not required for mathematical reason. The function $q\,\varphi(S)$ is the *vaccination rate* consisting of the actual rate q and the control function $\varphi(S)$. In order to focus here on the equations, we provide more information in paragraph 3.3.

The modified equation for E is given by (cf. (2.39))

$$\dot{E}(t) = \Big(\beta_1(t)\,\frac{I_1(t)+I_{21}(t)}{N(t)-D(t)} + \beta_{22}(t)\,\frac{I_{22}(t)}{N(t)-D(t)}\Big)\,S(t) - \epsilon\,E(t) \qquad \text{for } t \in [0,\infty[. \tag{3.3}$$

As explained above, there holds $t_{lat} = 1/\epsilon$.

The equation for I_1 must indicate that I_1 gets growth from E and loses to I_{21} and I_{22}. This loss happens in parallel, and so it is only seen in the equations for I_{21} and I_{22}. Contrary to (2.40) we assume that individuals from I_1 do not die due to infection.

$$\dot{I}_1(t) = \epsilon\,E(t) - \gamma_1\,I_1(t) \qquad \text{for } t \in [0,\infty[. \tag{3.4}$$

There hold $\gamma_1 > 0$ and $1/\gamma_1 = t_{inc} - t_{lat}$. For the classes I_{21} and I_{22} the following equations hold.

$$\dot{I}_{21}(t) = (1-\alpha)\gamma_1\,I_1(t) - \gamma_{21}\,I_{21}(t) \qquad \text{for } t \in [0,\infty[, \tag{3.5}$$

$$\dot{I}_{22}(t) = \alpha\gamma_1\,I_1(t) - \gamma_{22}\,I_{22}(t) - \delta\,I_{22}(t) \qquad \text{for } t \in [0,\infty[, \tag{3.6}$$

The parameter α fulfils

$$0 < \alpha < 1. \tag{3.7}$$

.

$1-\alpha$ and α reflect the partition of infectious infected individuals from I_1 to I_{21} and I_{22} after the end of incubation period. α is also called manifestation index, since it characterises the fraction of ill persons with remarkable symptoms. The time duration $t_{inf,1} - t_{inc}$ is the reciprocal value of γ_{21}, $t_{inf,2} - t_{inc}$ correspondingly to γ_{22}. $t_{inf,1}$ is the point of time of recovery ever since of infection for I_1 and $t_{inf,2}$ correspondingly for I_2. The relation $t_{inf,2} > t_{inf,1}$ seems to be plausible, but it has no mathematical relevance. $\delta > 0$ is the lethality coefficient, the model approach is, that only heavily diseased persons die caused by infection.

Now, the class R consists of individuals stemming from I_{21} and I_{22} as well as of persons immunised by vaccination. If recovered lose their immunity, they return to S. Thus, the equations for R and D are

$$\dot{R}(t) = \gamma_{21}\, I_{21}(t) + \gamma_{22}\, I_{22}(t) - \mu\, R + q\, \varphi(S) \qquad \text{for } t \in [0, \infty[, \tag{3.8}$$

$$\dot{D}(t) = \delta\, I_{22}(t). \qquad \text{for } t \in [0, \infty[, \tag{3.9}$$

From the mathematical point of view the parameter β_1, β_{22}, μ, ϵ, α, γ_1, γ_{21}, γ_{22}, δ can be time-dependent and continuous (see (4.1) and (4.2) for more explication). The initial conditions are chosen as follows.

$$S(0) = S_0 \qquad \text{with } 0 < S_0 < N_0, \tag{3.10}$$

$$E(0) = E_0 \qquad \text{with } 0 \le E_0 < N_0, \tag{3.11}$$

$$I_1(0) = I_{10} \qquad \text{with } 0 \le I_{10} < N_0, \tag{3.12}$$

$$I_{21}(0) = I_{210} \qquad \text{with } 0 \le I_{210} < N_0, \tag{3.13}$$

$$I_{22}(0) = I_{220} \qquad \text{with } 0 \le I_{220} < N_0, \tag{3.14}$$

$$R(0) = R_0 \qquad \text{with } 0 \le R_0 < N_0, \tag{3.15}$$

$$D(0) = D_0 \qquad \text{with } 0 \le D_0 < N_0. \tag{3.16}$$

Mostly, one chooses $D_0 = 0$, but this is not mathematically required. The initial values should be consistent with N_0, therefore, we assume

$$N_0 = S_0 + E_0 + I_{10} + I_{210} + I_{220} + R_0 + D_0. \tag{3.17}$$

For the start of an infection there must hold as minimal requirement

$$E_0 + I_{10} + I_{210} + I_{220} > 0 \tag{3.18}$$

Again, this is not an actual mathematical assumption, but a vanishing sum in (3.18) very simplifies the problem.

Remarks 3.1. (i) (Different durations of immunity) In the model, it is implemented that recovered and vaccinated susceptible persons have immunity of the *same* mean duration $1/\mu$. If this is not the case, one could consider a further class of "immune after vaccination". Equally, a further class could be convenient, if for instance recovered persons are permanently immune and vaccinated ones only for some time.

(ii) (On contact and replacement number) In paragraph 2.1.2, contact and replacement numbers have been defined. However, for a better handling, in paragraph 2.2.2 current contact and replacement numbers have been introduced for a variable contact coefficient β. Hence, for the model under consideration it seems to be plausible to express σ as follows

$$\begin{aligned} \sigma &= \beta_1(t_{inc} - t_{lat}) + \beta_1(1-\alpha)(t_{inf,1} - t_{inc}) + \beta_{22}\alpha\, \frac{t_{inf,2} - t_{inc}}{1 + \delta\,(t_{inf,2} - t_{inc})} = \\ &= \frac{\beta_1}{\gamma_1} + (1-\alpha)\,\frac{\beta_1}{\gamma_{21}} + \alpha\,\frac{\beta_{22}}{\gamma_{22}+\delta}. \end{aligned} \tag{3.19}$$

The first addend represents the I_1 individuals, the second one I_{21} members, and, finally, the third one is related to I_{22} individuals, taking the infection-related death coefficient δ into account (see remark 4.8 for reasoning). Moreover, after incubation period, an infected individual belongs to I_{22} with the probability α and to I_{21} with the probability $1-\alpha$. Hence, one gets the following (virtual) replacement number (reproduction number), observing (2.12).

$$\rho = \left\{ \frac{\beta_1}{\gamma_1} + (1-\alpha)\,\frac{\beta_1}{\gamma_{21}} + \alpha\,\frac{\beta_{22}}{\gamma_{22}+\delta} \right\} \frac{S}{N-D}. \tag{3.20}$$

3.3 An approach for the vaccination rate

The term $q\varphi(S)$ in (3.1), the vaccination rate, indicates how many persons are vaccinated in a time unit. The part q is the actual vaccination rate. It is justified, if there are sufficiently many persons for vaccination. This is surely the case at begin of a vaccination campaign. The part $\varphi(S)$ is a control

function. If there are no persons to be vaccinated, the vaccination process ends. Otherwise, the function S would be sometime negative for mathematical reason.

For the actual vaccination rate q we propose a piece-wise linear approach:

$$q(t) := \begin{cases} 0, & \text{for } t \in [0, t_1], \\ q_1 \frac{t-t_1}{t_2-t_1}, & \text{for } t \in [t_1, t_2], \\ q_1, & \text{for } t \in [t_2, \infty[. \end{cases} \tag{3.21}$$

with

$$0 \le t_1 < t_2 < \infty, \qquad q_1 = const. > 0. \tag{3.22}$$

The formula (3.21) means that for $t_1 = 0$ the vaccination campaign starts with the begin of infection. In the current case of COVID-19 this is impossible, hence, a begin at $t_1 > 0$ reflects the real situation. After that, q grows linearly up to the final rate q_1, e.i., the limit of capacity is reached. This approach seems to be realistic for a new vaccine which production has to be start-up and its distribution surely has to be improved. Clearly, instead of (3.21) other approaches are possible. The constant q_1 has the dimension $^P/_T$, persons per time.

The control function $\varphi(S)$ ensures that the vaccination campaign ends, if the number of susceptible persons comes up to zero. At first we define a dimensionless cut function φ_ε for an arbitrarily chosen and fixed $\varepsilon > 0$ via

$$\varphi_\varepsilon(\sigma) := \begin{cases} 1, & \text{for } \sigma > \varepsilon, \\ \frac{\sigma}{\varepsilon}, & \text{for } 0 \le \sigma \le \varepsilon, \\ 0, & \text{for } \sigma < 0. \end{cases} \tag{3.23}$$

The slope of φ_ε between zero and one is $^1/_\varepsilon$. If ε tends to zero, φ_ε tends (point-wise, but not uniformly) to a jump function. Due to its non-continuity in the point zero, we want to avoid it for mathematical reasons. Finally, we define the term $q\varphi(S)$ by

$$q(t)\,\varphi(S) := q(t)\,\varphi_\varepsilon(\frac{S}{N_0}). \tag{3.24}$$

For reasons of dimensional homogeneity, $^S/_{N_0}$ has been chosen as argument of φ_1. This will be beneficial later on. From (3.23) and (3.24) we get easily

$$q(t)\,\varphi(S) = q(t) \begin{cases} 1, & \text{for } \frac{S}{N_0} > \varepsilon, \\ \frac{S}{N_0\,\varepsilon}, & \text{for } 0 \le \frac{S}{N_0} \le \varepsilon, \\ 0, & \text{for } S < 0. \end{cases} \tag{3.25}$$

In applications, the threshold value $\varepsilon > 0$ has to be chosen suitably small. Generally, at begin of the infection course, one can expect $^S/_{N_0} \approx 1$. Thus, ε should be small, more precisely $\varepsilon \ll {}^S/_{N_0}$, in order to avoid an essential influence to the model at begin. For mathematical reason the function $\varphi(S)$ is also defined for negative S. Under mild assumptions the non-negativity of S can be proved (see section 4.2). Thus, there is no practical consequence in applications.

3.4 General remarks concerning the model

The SEI^{3}RSD model developed above takes several known findings about SARS-CoV-2 and COVID-19 into account. However, it is less complex than the model developed and numerically investigated in Grimm et al. (2020). If necessary, the modular design principle allows extensions and simplifications of the model described above.

This model is a continuous one, the arising mathematical task is an initial-Value problem for a system of ordinary differential equations (ODE). As an advantage, the extensive mathematical instruments on theory and numerics of ODE are well available. Otherwise, the population is discrete. Therefore, to correspond possibly well to the reality, "sufficiently large" populations must be assumed. An alternative to a continuous model is a discrete one based on difference equations, see Vynnycky and White (2010), e.g. Generally, concerning models of phenomena in empirical sciences, an important task consists in validation and verification in order to decide, under which conditions the applied models yield sufficiently good approximations with the reality. In particular, a typical question is whether a SIRD model can sufficiently well describe a real course of infection, or a SEIRD model must be chosen.

A general drawback of modelling with ODE is the absence of local dependence of the functions looked for, here S, E, I_1, I_{21}, I_{22}, R and D. However, in many countries the spread of SARS-CoV-2 essentially differs from region to region. Therefore, the models discussed here only reflect a mean situation, for instance in Germany or in a single federal land.

A way out with partial differential equations (PDE) containing terms describing local movements of population parts seems theoretically possible. Surely, there will arise large difficulties in determining various parameter functions. Instead of population numbers corresponding density functions have to be used (persons per quadrate kilometre, e.g.). Additionally, there may be non-local effects caused by travelling excelling daily usual movement in the surrounding field. Hence, it is not a surprise that the author did not find corresponding references to PDE. In Hethcote (2000) and in Vynnycky and White (2010), PDE are addressed in short to model a dependence on age.

4 On mathematical investigation of models

Now, it is the aim to investigate the mathematical problem arising from the SEI^{3}RSD model. At first, we formulate in paragraph 4.1 an equivalent problem in dimensionless quantities. This so-called non-dimensionalised form may have some advantages. After that, in paragraph 4.2, we prove existence and uniqueness of a global solution and study its properties. We focus on the SEI^{3}RSD model, although many results can be applied in modified form to less complex models like SIR ones. Finally, in paragraph 4.3, we discuss some issues related to contact and replacement numbers for some models.

4.1 Formulation of the problem in non-dimensionalised form

Now, we want to deal in more detail with the dimensions of functions and parameters involved in problem (3.1), (3.3) - (3.6), (3.8) - (3.16). For lack of space, here we do not repeat all equations and initial conditions, but we write them alike in an equivalent form with dimensionless quantities. This procedure is also called non-dimensionalisation.

An advantage of this procedure is generally a reduction of the number of parameters determining the equivalent problem. Sometimes, there can be an advantage in numerical investigations. Moreover, the influence of parameters and their interplay can be well investigated. For more information we refer exemplarily to Görtler (1975), Hutter (2003), Hutter and Jöhnk (2004), Zlokarnik (2005) as well as to a compact presentation in the lecture Wolff (2018) (Chapter 7).

We record that all numbers of persons, S, E, I_1, I_{21}, I_{22}, R, D and N_0, S_0, I_0, I_{210}, I_{220}, R_0 and D_0 have the dimension *persons*, abbreviated by P, corresponding units may be $e_P = 1\,person$ as well other ones like $100\,persons$. The time derivatives of the functions S, E etc. have the dimension $^P/_T$, T being the dimension *time*. In connection with epidemics the time is often measured by the unit *day*. Bearing in mind these informations, it follows that all parameters β_1, β_{22}, μ, ϵ, γ_1, γ_{21}, γ_{22}, δ have the dimension $^1/_T$. α is dimensionless. Of course, the continuous time t has the dimension T, equally t_{lat}, t_{inc}, $t_{inf,1}$, $t_{inf,2}$.

In accordance with the model under consideration, let the parameter functions fulfil (see remark 2.3)

$$\beta_1,\, \beta_{22}, \delta \in C([0, t_{ex}[), \qquad \beta_1(t) > 0,\, \beta_{22}(t) > 0, \delta(t) > 0 \quad \text{for } t \in [0, t_{ex}], \tag{4.1}$$

$$\mu,\, \epsilon,\, \gamma_1,\, \gamma_{21},\, \gamma_{22},\, \delta = const., \quad \mu \geq 0,\, \epsilon > 0,\, \gamma_1 > 0,\, \gamma_{21} > 0,\, \gamma_{22} > 0. \tag{4.2}$$

Here, let $t_{ex} > 0$ or $t_{ex} = \infty$, the index ex points to 'existence interval'.

The choice in (4.1) and (4.2) is motivated by up to now known findings on SARS-CoV-2. The parameters β_1 and β_{22} strongly depend on human contact behaviour, the lethality coefficient seems to be influenced by the capacities of health systems in divers countries. The constance of remaining parameters is not mathematically predicted. The case $\mu \equiv 0$ means permanent immunity. The continuity requirements in (4.1) allow to deal within the framework of continuously differentiable solutions, see remark 4.6 (i).

The next step is to define a dimensionless time (number) τ (see remark 4.3 (iii)). We choose the approach

$$\tau := t\,\gamma_1, \tag{4.3}$$

and we define the dimensionless functions s, e, ι_1, ι_{21}, ι_{22}, r and d in accordance with

$$s(\tau) := \frac{S(t)}{N_0},\ \iota_1(\tau) := \frac{I_1(t)}{N_0},\ \iota_{21}(\tau) := \frac{I_{21}(t)}{N_0},\ \iota_{22}(\tau) := \frac{I_{22}(t)}{N_0},\ r(\tau) := \frac{R(t)}{N_0},\ d(\tau) := \frac{D(t)}{N_0}. \tag{4.4}$$

Moreover, we define dimensionless parameters and parameter functions:

$$\tilde{\beta}_1(\tau) := \frac{\beta_1(t)}{\gamma_1}, \qquad \tilde{\beta}_{22}(\tau) := \frac{\beta_{22}(t)}{\gamma_1}, \qquad \tilde{\mu} := \frac{\mu}{\gamma_1}, \qquad \tilde{\epsilon} := \frac{\epsilon}{\gamma_1}, \tag{4.5}$$
$$\tilde{\gamma}_{21} := \frac{\gamma_{21}}{\gamma_1}, \qquad \tilde{\gamma}_{22} := \frac{\gamma_{22}}{\gamma_1}, \qquad \tilde{\delta}(\tau) := \frac{\delta(t)}{\gamma_1}.$$

These new parameters also fulfil (4.1) and (4.2). Note, that the formal counterpart to γ_1 becomes one. Therefore, the equations (3.1), (3.3) - (3.6), (3.8), (3.9) are equivalent to

$$\dot{s} = -\frac{\tilde{\beta}_1\,\iota_1 + \tilde{\beta}_1\,\iota_{21} + \tilde{\beta}_{22}\,\iota_{22}}{1-d}\,s + \tilde{\mu}\,r - \tilde{q}\varphi_\varepsilon(s) \qquad \text{on } [0,\infty[\tag{4.6}$$

$$\dot{e} = \frac{\tilde{\beta}_1\,\iota_1 + \tilde{\beta}_1\,\iota_{21} + \tilde{\beta}_{22}\,\iota_{22}}{1-d}\,s - \tilde{\epsilon}\,e \qquad \text{on } [0,\infty[\tag{4.7}$$

$$\dot{\iota}_1 = \tilde{\epsilon}\,e - \iota_1 \qquad \text{on } [0,\infty[\tag{4.8}$$

$$\dot{\iota}_{21} = (1-\alpha)\,\iota_1 - \tilde{\gamma}_{21}\,\iota_{21} \qquad \text{on } [0,\infty[\tag{4.9}$$

$$\dot{\iota}_{22} = \alpha\,\iota_1 - \tilde{\gamma}_{22}\,\iota_{22} - \tilde{\delta}\,\iota_{22} \qquad \text{on } [0,\infty[\tag{4.10}$$

$$\dot{r} = \tilde{\gamma}_{21}\,\iota_{21} + \tilde{\gamma}_{22}\,\iota_{22} - \tilde{\mu}r + \tilde{q}\varphi_\varepsilon(s) \qquad \text{on } [0,\infty[\tag{4.11}$$

$$\dot{d} = \tilde{\delta}\,\iota_{22} \qquad \text{on } [0,\infty[. \tag{4.12}$$

For a better overview we usually do not write the argument τ, derivatives with respect to τ are also indicated by a dot. The dimensionless function $\tilde{q}$ has the following form.

$$\tilde{q}(\tau) := \begin{cases} 0, & \text{for } \tau \in [0,\tau_1], \\ \tilde{q}_1\,\frac{\tau-\tau_1}{\tau_2-\tau_1}, & \text{for } \tau \in [\tau_1,\tau_2], \\ \tilde{q}_1, & \text{for } \tau \in [\tau_2,\infty[. \end{cases} \tag{4.13}$$

Moreover, further dimensionless quantities are given by

$$\tau_1 := \gamma_1\,t_1, \qquad \tau_2 := \gamma_1\,t_2, \qquad \tilde{q}_1 := \frac{q_1}{N_0\gamma_1}. \tag{4.14}$$

Taking (3.23), (4.13) and (4.14) into account, the term $\tilde{q}\varphi_\varepsilon(s)$ is written as

$$\tilde{q}\varphi_\varepsilon(s) = \tilde{q}\begin{cases} 1, & \text{for } s > \varepsilon, \\ \frac{s}{\varepsilon}, & \text{for } 0 \le s \le \varepsilon, \\ 0, & \text{for } s < 0. \end{cases} \tag{4.15}$$

Finally, the complete non-dimensionalised problem includes else the adjusted dimensionless initial conditions resulting from (3.10) - (3.16):

$$s(0) = s_0 := \frac{S_0}{N_0} \qquad \text{with } 0 < s_0 < 1, \tag{4.16}$$

$$e(0) = e_0 := \frac{E_0}{N_0} \qquad \text{with } 0 \le e_0 < 1, \tag{4.17}$$

$$\iota_1(0) = \iota_{10} := \frac{I_1}{N_0} \qquad \text{with } 0 \le \iota_{10} < 1, \tag{4.18}$$

$$\iota_{21}(0) = \iota_{210} := \frac{I_{21}}{N_0} \qquad \text{with } 0 \le \iota_{210} < 1, \tag{4.19}$$

$$\iota_{22}(0) = \iota_{220} := \frac{I_{22}}{N_0} \qquad \text{with } 0 \le \iota_{220} < 1, \tag{4.20}$$

$$r(0) = r_0 := \frac{R_0}{N_0} \qquad \text{with } 0 \le r_0 < 1, \tag{4.21}$$

$$d(0) = d_0 := \frac{D_0}{N_0} \qquad \text{with } 0 \le d_0 < 1. \tag{4.22}$$

with a condition equivalent to (3.17):

$$1 = s_0 + e_0 + \iota_{10} + \iota_{210} + \iota_{220} + r_0 + d_0. \tag{4.23}$$

The additional condition (3.18) necessary for a release of infection leads to its counterpart

$$e_0 + \iota_{10} + \iota_{210} + \iota_{220} > 0. \tag{4.24}$$

The mathematical problem (4.6) - (4.12), (4.16) - (4.22) consists in determining seven dimensionless functions, s, e, ι_1, ι_{21}, ι_{22}, r, d which argument is the dimensionless time (number) τ. This problem is governed by seven (dimensionless) parameter functions in (4.5), by α, by three numbers τ_1, τ_2, $\tilde{q}_1$ and the threshold value ε induced by the vaccination rate as well as by seven dimensionless initial conditions s_0, e_0, ι_{10}, ι_{210}, ι_{220}, r_0, d_0.

Now, it is the aim to define a solution to the non-dimensionalised problem (4.6) - (4.12), (4.16) - (4.22) and hence also for the original problem (3.1), (3.3) - (3.6), (3.8) - (3.16). We use mathematical standard notations for spaces of continuous and continuously differentiable functions with values in $\mathbb{R}$ as well as in $\mathbb{R}^n$ ($n \in \mathbb{N}$), see Zeidler and Hunt (2013), e.g. For the theory of ordinary differential equations (ODE) we refer exemplarily to Amann (1995), Heuser (1995), Walter (2000).

Definition 4.1. (**Local and global solution to problem** (4.6) - (4.12), (4.16) - (4.22)
Let the real numbers s_0, e_0, ι_{10}, ι_{210}, ι_{220}, r_0, d_0 fulfil the conditions in (4.16) - (4.22) and (4.23). Besides (3.7), let (4.1), (4.2) and (3.21) - (3.24) hold.

(i) Let $0 < \tau_{ex} < \infty$. A (vector) function $(s, e, \iota_1, \iota_{21}, \iota_{21}, r, d) \in C^1([0, t_{ex}], \mathbb{R}^7)$ is called a *local solution* to problem (4.6) - (4.12), (4.16) - (4.22), if the equations (4.6) - (4.12) are valid on $[0, \tau_{ex}]$, and if the initial conditions (4.16) - (4.22) are fulfilled.

(ii) Let $\tau_{ex} = \infty$. A (vector) function $(s, e, \iota_1, \iota_{21}, \iota_{21}, r, d) \in C^1([0, \infty[, \mathbb{R}^7)$ is called accordingly a *global solution* to this problem, if the equations are valid on $[0, \infty[$, and if the initial conditions are fulfilled.

(iii) The problem (4.6) - (4.12), (4.16) - (4.22) is called uniquely solvable, if two local solutions defined on $[0, \tau_{ex}^{(1)}]$ and $[0, \tau_{ex}^{(2)}]$, respectively, coincide on the interval $[0, \min\{\tau_{ex}^{(1)}, \tau_{ex}^{(2)}\}]$.

The preceding definition contains also assumptions which are not mandatory. However, in doing so, we do not need to repeat them below. For convenience we define local solutions on closed intervals. This is also not mandatory. Analogously, local and global solutions to the original problem (3.1), (3.3) - (3.6), (3.8) - (3.16) can be defined. There holds the following important assertion.

Lemma 4.2. (**Relation between solutions to original and transformed problem**)
If $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d)$ is a solution to the non-dimensionalised problem (4.6) - (4.12), (4.16) - (4.22) on $[0, \tau_{ex}]$, then

$$\begin{aligned} &S(t) = N_0\, s(t\,\gamma_1), && E(t) = N_0\, e(t\,\gamma_1), && I_1(t) = N_0\, \iota_1(t\,\gamma_1), \\ &I_{21}(t) = N_0\, \iota_{21}(t\,\gamma_1), && I_{22}(t) = N_0\, \iota_{22}(t\,\gamma_1), && R(t) = N_0\, r(t\,\gamma_1), \\ &D(t) = N_0\, d(t\,\gamma_1) \end{aligned} \tag{4.25}$$

is a solution to the original problem (3.1), (3.3) - (3.6), (3.8) - (3.16) on $[0, {}^{\tau_{ex}}/_{\gamma_1}]$ and vice versa.

In many cases, the corresponding non-dimensionalised problems are *simplifications* of the equivalent original ones. (Here, the non-dimensionalised problem is governed by only seven parameters instead of eight ones.) As a consequence, theoretical and numerical investigations may be easier, see section 4.3 for examples.

After dealing with the non-dimensionalised problem, the transformation back to the solution of the original problem is performed with the simple scaling in (4.25) for all solution components without a noteworthy effort. We close this paragraph with some remarks.

Remarks 4.3. (i) The choice of a dimensionless time (number), here τ in (4.3), is not unique. Thus, there are different possibilities for various applications. For instance, in Wolff (2020c), the above problem is considered with variable parameters, and τ is chosen by $\tau := t\,\beta_1(0)$.
Another approach uses the latent period t_{lat}, setting $\tau := {}^{t}/_{t_{lat}}$. Again, based on further investigations, a chosen approach can prove to be more or less convenient.

(ii) As it can be seen in (4.5), the behaviour of the solution of the non-dimensionalised problem does not depend on the absolute quantities of the parameters, but only on their ratios. This general finding plays an important role in the model theory, in particular in hydro- and aerodynamics as well as in heat conduction. We refer to Hutter and Jöhnk (2004), Zlokarnik (2005), e.g.

(iii) A great advantage of the dimension analyse is, that characteristics of the dimensionless functions, s, e, ι_1, ι_{21}, ι_{22}, r, d like possible maxima or inflection points of the curves depend only on the dimensionless parameters and (dimensionless) initial values. Based on practical experience, on theoretical considerations as well as on real and numerical experiments, the real influence of the characteristic numbers (dimensionless parameters) can be estimated.

4.2 On solution behaviour of the initial-value problem

Based on the SEI^{3}RSD model developed in paragraph 3, the (original) mathematical problem (3.1), (3.3) - (3.6), (3.8) - (3.16) has arisen. In paragraph 4.1, the corresponding equivalent problem (4.6) - (4.12), (4.16) - (4.22) has been obtained in a form with dimensionless functions depending on a dimensionless argument. Now, it is the aim to prove some assertions about existence of a solution to this last problem. Based on lemma 4.2, the assertions obtained are also ensured for the original problem.

The mathematical theory confirms the nearby conjecture that under not to strong assumptions the problem (4.6) - (4.12), (4.16) - (4.22) obeys a unique global solution which components only take values between zero and one. This is the case under the assumptions formulated in definition 4.1.

At first, from the structure of equations (4.6) - (4.12) an important qualitative property of any possible (local or global) solution follows.

Lemma 4.4. (**Constance of the total population number**)
Under the assumptions formulated in definition 4.1, each local solution $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d) \in C^1([0, \tau_{ex}], \mathbb{R}^7)$ to problem (4.6) - (4.12), (4.16) - (4.22) fulfils

$$s(\tau) + e(\tau) + \iota_1(\tau) + \iota_{21}(\tau) + \iota_{22}(\tau) + r(\tau) + d(\tau) = 1 \qquad \text{for } \tau \in [0, \tau_{ex}]. \tag{4.26}$$

Proof. The addition of equations (4.6) - (4.12) yields the following differential equation for the sum $\sigma := s + e + \iota_1 + \iota_{21} + \iota_{22} + r + d$

$$\dot{\sigma} = 0 \qquad \text{for } \tau \in [0, \tau_{ex}]. \tag{4.27}$$

Condition (4.23) implies

$$\sigma(0) = 1. \tag{4.28}$$

Thus, the theory of ODE implies that $\sigma \equiv 1$ is the unique solution of problem (4.27), (4.28), and, therefore, (4.26) is proven. □

Under condition (4.23) the equations for s and e, e.i. (4.6) and (4.7), can be substituted by the following equivalent ones.

$$\dot{s} = -\frac{\tilde{\beta}_1\,(\iota_1 + \iota_{21}) + \tilde{\beta}_{22}\,\iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r}\, s + \tilde{\mu}\, r - \tilde{q}\, \varphi_\varepsilon(s) \qquad \text{on } [0, \tau_{ex}], \tag{4.29}$$

$$\dot{e}(t) = \frac{\tilde{\beta}_1\,(\iota_1 + \iota_{21}) + \tilde{\beta}_{22}\,\iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r}\, s - \tilde{\epsilon}\, e \qquad \text{on } [0, \tau_{ex}], \tag{4.30}$$

Sometimes, this representations are beneficial. The following theorem confirms what can be expected from the model. There exists exactly one global solution, and, all its components, e.i., the functions s, e etc., are non-negative and located between zero and one.

Theorem 4.5. (**Existence of unique global solution**)
Under the assumptions formulated in definition 4.1 the problem (4.6) - (4.12), (4.16) - (4.22) has exactly one global solution $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d) \in C^1([0, \infty[, \mathbb{R}^7)$ fulfilling (4.26). Let (3.2) be given. For an arbitrarily chosen and fixed $\widehat{\tau} > 0$ we define

$$\tilde{\beta}_1^{\widehat{\tau}} := \max_{\tau \in [0, \widehat{\tau}]} \{\tilde{\beta}_1(\tau)\}, \qquad \tilde{\delta}^{\widehat{\tau}} := \max_{\tau \in [0, \widehat{\tau}]} \{\tilde{\delta}(\tau)\}. \tag{4.31}$$

Then there hold the following inequalities for all $\tau \in [0, \widehat{\tau}]$:

$$0 < s_0 \, \exp\Big(-(\tilde{\beta}_1^{\widehat{\tau}} + \frac{\tilde{q}_1}{\varepsilon})\,\widehat{\tau}\Big) \le s(\tau) \le \max\Big\{1, \Big(s_0 + \widehat{\tau}\,\tilde{\mu}\exp\Big((\tilde{\beta}_1^{\widehat{\tau}} + \frac{\tilde{q}_1}{\varepsilon})\,\widehat{\tau}\Big)\Big)\Big\} \le 1, \tag{4.32}$$

$$0 \le e_0 \, \exp(-\widehat{\tau}\,\tilde{\epsilon}) \le e(\tau) \le \max\Big\{1, e_0 + \widehat{\tau}\,\tilde{\beta}_1^{\widehat{\tau}}\exp(\widehat{\tau}\,\tilde{\epsilon})\Big\} \le 1, \tag{4.33}$$

$$0 \le \iota_{10} \, \exp(-\widehat{\tau}) \le \iota_1(\tau) \le \max\Big\{1, \iota_{10} + \widehat{\tau}\,\tilde{\epsilon}\exp(\widehat{\tau})\Big\} \le 1, \tag{4.34}$$

$$0 \le \iota_{210} \, \exp(-\widehat{\tau}\,\tilde{\gamma}_{21}) \le \iota_{21}(\tau) \le \max\Big\{1, \iota_{210} + (1-\alpha)\,\widehat{\tau}\,\tilde{\gamma}_1\exp(\widehat{\tau}\,\tilde{\gamma}_{21})\Big\} \le 1, \tag{4.35}$$

$$0 \le \iota_{220} \, \exp(-\widehat{\tau}\,(\tilde{\gamma}_{22} + \tilde{\delta}^{\widehat{\tau}})) \le \iota_{22}(\tau) \le \max\Big\{1, \iota_{220} + \alpha\,\widehat{\tau}\,\tilde{\gamma}_1\exp(\widehat{\tau}\,(\tilde{\gamma}_{22} + \tilde{\delta}^{\widehat{\tau}}))\Big\} \le 1, \tag{4.36}$$

$$0 \le r_0 \, \exp(-\widehat{\tau}\,\tilde{\mu}) \le r(\tau) \le \max\Big\{1, r_0 + \big(\widehat{\tau}\,(\tilde{\gamma}_{21} + \tilde{\gamma}_{22}) + \widehat{\tau}\,\tilde{q}_1\big)\exp(\widehat{\tau}\,\tilde{\mu})\Big\} \le 1, \tag{4.37}$$

$$0 \le d_0 \le d(\tau) = d_0 + \int_0^\tau \tilde{\delta}\iota_{22}\,\mathrm{d}\sigma \le \max\Big\{1, d_0 + \widehat{\tau}\,\tilde{\delta}^{\widehat{\tau}}\Big\} Leq1. \tag{4.38}$$

The function d is monotonously increasing.

Proof. The proof consists of several steps. At first, the existence of a unique local solution is proven via a special auxiliary problem. As a result the original problem has exactly one local solution which components are non-negative on the existence interval and their sum is one. Additionally, the inequalities in (4.32) - (4.38) are valid. Finally, a suitable a-priori estimate on an arbitrarily chosen interval $[0, \widehat{\tau}]$ allows the continuation to a unique global solution.

(i) (**Construction of an auxiliary problem**) To prove the non-negativeness of the components to a local solutions and to get a good basis for a-priori estimates, we consider a special auxiliary problem. For this purpose we define two functions:

$$f(x) := \begin{cases} x, & \text{for } x \ge 0, \\ 0, & \text{for } x < 0, \end{cases} \qquad \psi_\varepsilon(s) := \begin{cases} 1/s, & \text{for } s > \varepsilon, \\ 1/\varepsilon, & \text{for } s \le \varepsilon. \end{cases} \tag{4.39}$$

We change the equations (4.6) - (4.12) in the following way.

$$\dot{s} = -\frac{\tilde{\beta}_1\,f(\iota_1) + \tilde{\beta}_1\,f(\iota_{21}) + \tilde{\beta}_{22}\,f(\iota_{22})}{f(s) + f(e) + f(\iota_1) + f(\iota_{21}) + f(\iota_{22}) + f(r)}\,s + \tilde{\mu}\,f(r) - \tilde{q}\psi_\varepsilon(s)\,s \qquad \text{on } [0,\infty[\tag{4.40}$$

$$\dot{e} = \frac{\tilde{\beta}_1\,f(\iota_1) + \tilde{\beta}_1\,f(\iota_{21}) + \tilde{\beta}_{22}\,f(\iota_{22})}{f(s) + f(e) + f(\iota_1) + f(\iota_{21}) + f(\iota_{22}) + f(r)}\,f(s) - \tilde{\epsilon}\,e \qquad \text{on } [0,\infty[\tag{4.41}$$

$$\dot{\iota}_1 = \tilde{\epsilon}\,f(e) - \iota_1 \qquad \text{on } [0,\infty[\tag{4.42}$$

$$\dot{\iota}_{21} = (1-\alpha)\,f(\iota_1) - \tilde{\gamma}_{21}\,\iota_{21} \qquad \text{on } [0,\infty[\tag{4.43}$$

$$\dot{\iota}_{22} = \alpha\,f(\iota_1) - \tilde{\gamma}_{22}\,\iota_{22} - \tilde{\delta}\,\iota_{22} \qquad \text{on } [0,\infty[\tag{4.44}$$

$$\dot{r} = \tilde{\gamma}_{21}\,f(\iota_{21}) + \tilde{\gamma}_{22}\,f(\iota_{22}) - \tilde{\mu}r + \tilde{q}\varphi_\varepsilon(s) \qquad \text{on } [0,\infty[\tag{4.45}$$

$$\dot{d} = \tilde{\delta}\,f(\iota_{22}) \qquad \text{on } [0,\infty[. \tag{4.46}$$

The initial conditions (4.16) - (4.22) remain without any change. It is immediately clear, that a solution $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d) \in C^1([0, \tau_{ex}], \mathbb{R}^7)$ to the auxiliary problem (4.40) - (4.46), (4.16) - (4.22) fulfilling the conditions

$$s(\tau) > 0,\ e(\tau) \ge 0,\ \iota_1(\tau) \ge 0,\ \iota_{21}(\tau) \ge 0,\ \iota_{22}(\tau) \ge 0,\ r(\tau) \ge 0,\ d(\tau) \ge 0 \ \text{ on } [0, \tau_{ex}[, \tag{4.47}$$

is also a solution to the following problem

$$\dot{s} = -\frac{\tilde{\beta}_1\,\iota_1 + \tilde{\beta}_1\,\iota_{21} + \tilde{\beta}_{22}\,\iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r}\,s + \tilde{\mu}\,r - \tilde{q}\varphi_\varepsilon(s) \qquad \text{on } [0,\infty[\tag{4.48}$$

$$\dot{e} = \frac{\tilde{\beta}_1\,\iota_1 + \tilde{\beta}_1\,\iota_{21} + \tilde{\beta}_{22}\,\iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r}\,s - \tilde{\epsilon}\,e \qquad \text{on } [0,\infty[\tag{4.49}$$

$$\dot{\iota}_1 = \tilde{\epsilon}\,e - \iota_1 \qquad \text{on } [0,\infty[\tag{4.50}$$

$$\dot{\iota}_{21} = (1-\alpha)\,\iota_1 - \tilde{\gamma}_{21}\,\iota_{21} \qquad \text{on } [0,\infty[\tag{4.51}$$

$$\dot{\iota}_{22} = \alpha\,\iota_1 - \tilde{\gamma}_{22}\,\iota_{22} - \tilde{\delta}\,\iota_{22} \qquad \text{on } [0,\infty[\tag{4.52}$$

$$\dot{r} = \tilde{\gamma}_{21}\,\iota_{21} + \tilde{\gamma}_{22}\,\iota_{22} - \tilde{\mu}r + \tilde{q}\varphi_\varepsilon(s) \qquad \text{on } [0,\infty[\tag{4.53}$$

$$\dot{d} = \tilde{\delta}\,\iota_{22} \qquad \text{on } [0,\infty[. \tag{4.54}$$

To this last problem we can apply lemma 4.4, hence, the equations (4.48) and (4.49) are equivalent to equations (4.6) and (4.7) within the original problem (4.6) - (4.12), (4.16) - (4.22). In other words, a local solution to the auxiliary problem (4.40) - (4.46), (4.16) - (4.22) fulfilling conditions (4.47) is also a local solution to the original problem (4.6) - (4.12), (4.16) - (4.22).
(ii) (**Existence of a local solution to the auxiliary problem**) Based on $0 < s_0 < 1$ and formulated assumptions, the theorem by Picard/Lindelöf ensures a unique local solution $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d) \in C^1([0, \tau_{ex}], \mathbb{R}^7)$ to the auxiliary problem (4.40) - (4.46), (4.16) - (4.22) with $s > 0$ on an existence interval $[0, \tau_{ex}]$ with $\tau_{ex} > 0$.
(ii) (**Properties of the local solution to the auxiliary problem**) Now, we want to prove the assertions in (4.47) for the local solution to the auxiliary problem. These assertions are a consequence of the special structure of equations (4.40) - (4.46). For a better overview we prove this for the function ι_1. (Later on, we prove the stronger assertions (4.32) - (4.38)). From (4.42) one obtains via the representation formula for the solution to a linear differential equation of first order:

$$\iota_1(\tau) = \Big(\iota_{10} + \int_0^\tau \tilde{\epsilon}(x)\, f(e)(x)\, \exp(x)\, \mathrm{d}x\Big) \exp(-\tau) \qquad \text{for } \tau \in [0, \tau_{ex}]. \tag{4.55}$$

Hence, there holds $\iota_1 \geq 0$ on $[0, \tau_{ex}]$. Analogously, the remaining inequalities in (4.47) can be proved. Thus, the solution $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d) \in C^1([0, \tau_{ex}], \mathbb{R}^7)$ to the auxiliary problem (4.40) - (4.46), (4.16) - (4.22) is also a solution to the problem (4.6) - (4.12), (4.16) - (4.22) under consideration.
Due to (4.23) we can apply lemma 4.4, and the assertion (4.26) holds. Based on the non-negativity of the functions s, e, ι_1, ι_{21}, ι_{22}, r, d, they only have values between zero and one.
(iii) (**Proof of the estimates in (4.32) - (4.38) for the local solution**) Now, we want to derive an estimation for the function s, taking into account that the local solution to the auxiliary problem is at once a local solution to the problem under consideration fulfilling (4.47). From (4.48) for s one obtains the representation formula for a solution to a linear differential equation of first order:

$$\begin{aligned} s(\tau) = \Big\{ s_0 + \int_0^\tau \tilde{\mu}\, r(x)\, \exp\Big(\int_0^x \big(\frac{\tilde{\beta}_1\, \iota_1 + \tilde{\beta}_1\, \iota_{21} + \tilde{\beta}_{22}\, \iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r} + \tilde{q}\psi_\varepsilon(s)\big)\, \mathrm{d}y\Big)\, \mathrm{d}x \Big\} \cdot \\ \cdot \exp\Big(- \int_0^\tau \big(\frac{\tilde{\beta}_1\, \iota_1 + \tilde{\beta}_1\, \iota_{21} + \tilde{\beta}_{22}\, \iota_{22}}{s + e + \iota_1 + \iota_{21} + \iota_{22} + r} + \tilde{q}\psi_\varepsilon(s)\big)\, \mathrm{d}y\Big) \qquad \text{for } \tau \in [0, \tau_{ex}]. \end{aligned} \tag{4.56}$$

Taking (4.47), (3.2), $r \leq 1$, (4.13) and (4.15) into account, the assertions in (4.32) follow with t_{ex} instead of $\widehat{t}$. In particular, there holds

$$0 < s_0\, \exp\Big(- (\tilde{\beta}_1^{\tau_{ex}} + \frac{\tilde{q}_1}{\varepsilon})\, \tau_{ex}\Big) \leq s(\tau) \qquad \text{for } \tau \in [0, \tau_{ex}]. \tag{4.57}$$

This estimation is of special importance for the continuation of the local solution. The quantity $\tilde{\beta}_1^{\tau_{ex}}$ is defined analogously to $\tilde{\beta}_1^{\widehat{\tau}}$ via (4.31). The remaining assertions in (4.32) - (4.38) follow in the same manner via corresponding representation formulas, for the present with τ_{ex} instead of $\widehat{\tau}$.
(iv) (**Continuation of the local solution to a global one**) Let $\widehat{t} > t_{ex} > 0$ be arbitrarily chosen and fixed. Due to (4.31) the quantities defined there are monotonously increasing for increasing $\widehat{t}$. Hence, there hold

$$0 < s_0\, \exp\Big(- (\tilde{\beta}_1^{\widehat{t}} + \frac{\tilde{q}_1}{\varepsilon})\, \widehat{t}\Big) \leq s_0\, \exp\Big(- (\tilde{\beta}_1^{\tau_{ex}} + \frac{\tilde{q}_1}{\varepsilon})\, \tau_{ex}\Big). \tag{4.58}$$

We define the number

$$\eta_{\widehat{t}} := \frac{s_0}{2}\, \exp\Big(- (\tilde{\beta}_1^{\widehat{t}} + \frac{\tilde{q}_1}{\varepsilon})\, \widehat{t}\Big). \tag{4.59}$$

The right-hand sides of equations (4.40) - (4.46) form a vector function consisting of seven components depending on $(\tau, s, e, \iota_1, \iota_{21}, \iota_{22}, r, d)$. On the set

$$M := [0, \widehat{t}] \times [\eta_{\widehat{t}}, 1 + \eta_{\widehat{t}}] \times [-\frac{\eta_{\widehat{t}}}{10}, 1 + \eta_{\widehat{t}}] \times \cdots \times [-\frac{\eta_{\widehat{t}}}{10}, 1 + \eta_{\widehat{t}}] \tag{4.60}$$

this vector function is continuous and Lipschitz continuous with respect to $(s, e, \iota_1, \iota_{21}, \iota_{22}, r, d)$, uniformly with respect to $\tau \in [0, \widehat{t}]$. Therefore, the local solution on $[0, \tau_{ex}]$ can be continued in finite steps on $[0, \widehat{t}]$. During this continuation procedure, in each step, the local solution of the auxiliary problem is continued at first. Using the arguments above, this continuation is also a continuation of the original problem. Besides, analogously, the asserted estimations for the continued solution can be shown. Since $\widehat{t} > t_{ex} > 0$ is arbitrarily chosen, a unique global solution to the original problem exists. □

Remarks 4.6. (i) With some small modifications, the results stated in lemma 4.4 and theorem 4.5 can be obtained under the assumption that the parameter functions are Lebesgue-measurable step functions instead of continuous ones. In this case, the functions $s, e, \iota_1, \iota_{21}, \iota_{22}, r, d$ are absolutely continuous, and, hence, only differentiable almost everywhere in the sense of the Lebesgue measure, see Amann (1995), e.g.

(ii) Since s is positive on each finite interval, the remaining functions cannot be equal to one on any finite interval.

(iii) Positive initial values of e, ι_1, ι_{21}, ι_{22}, r, d lead to positive values on finite intervals.

(iv) The essential assertions of theorem 4.5 can also be proven for initial-value problems arising from other models, for instance from a SIRD model Wolff (2020a). In Wolff (2020c), the above problem with variable coefficients has been dealt with. The changes are only technical. Above all one can conjecture, that for more complex models like in Grimm et al. (2020) analogous assertions hold. However, the technical effort would be considerably larger.

4.3 Some remarks on qualitative behaviour

We end the present study with some remarks on qualitative properties of some models considered above. The focus lies on a connection with items of the dimensional analysis. An important question is, where the current contact and replacement number, respectively, occur in the non-dimensionalised equations. Clearly, there is a lot of papers on qualitative behaviour including numerical examples and discussions of former real infection courses. We refer to Hethcote (2000), Vynnycky and White (2010), Bacaër (2020) and to the literature cited therein.

This paragraph is structured as follows. At first, we consider SIRSD and SIRD models. They are of middle complexity. After that, we deal in short with SIR and SIS models. They are special cases in some kind, however, they obey some own features. At the end, we consider SEIRSD and SEI^{3}RD models.

Obviously, under corresponding mild assumptions, lemma 4.4 and theorem 4.5 can be easily applied to the subsequent mathematical problems arising from SIRSD, SIRD, SIR and SIS models. In particular, all solutions components like S, I etc. are non-negative.

4.3.1 SIRSD and SIRD models

We want to return to the role of the replacement number (reproduction number) in the light of dimension analyse, see paragraph 2.2.2. For this reason, we consider a SIRSD model given by

$$\dot{S} = -\beta \frac{I}{N_0 - D} S + \mu R \qquad \text{for } t \in [0, \infty[, \tag{4.61}$$

$$\dot{I} = \beta \frac{S}{N_0 - D} I - \gamma I - \delta I \qquad \text{for } t \in [0, \infty[, \tag{4.62}$$

$$\dot{R} = \gamma I - \mu R \qquad \text{for } t \in [0, \infty[, \tag{4.63}$$

$$\dot{D} = \delta I \qquad \text{for } t \in [0, \infty[. \tag{4.64}$$

We suppose

$$\beta, \delta \in C([0, \infty[), \qquad \beta(t) > 0, \delta(t) \geq 0 \quad \text{for } t \geq 0, \qquad \mu = const. \geq 0, \ \gamma = const. > 0. \tag{4.65}$$

Clearly, for $\mu \equiv 0$ one gets a SIRD model. In analogy with (4.3) we define the dimensionless time (number) τ by

$$\tau := t\,\gamma, \tag{4.66}$$

as well as the dimensionless functions s, ι and r in accordance with (4.4) and the dimensionless parameter functions

$$\tilde{\beta}(\tau) := \frac{\beta(t)}{\gamma}, \qquad \tilde{\mu} := \frac{\mu}{\gamma}, \qquad \tilde{\delta}(\tau) := \frac{\delta(t)}{\gamma}. \tag{4.67}$$

$\tau = 1$ corresponds to a mean duration of infection as a new "time unit". We get the corresponding equations for s, ι and r:

$$\dot{s} = -\tilde{\beta}\,\frac{\iota}{1-d}\,s + \tilde{\mu}\,r \qquad \text{for } \tau \in [0,\infty[, \tag{4.68}$$

$$\dot{\iota} = \tilde{\beta}\,\frac{s}{1-d}\,\iota - \iota - \tilde{\delta}\,\iota \qquad \text{for } \tau \in [0,\infty[, \tag{4.69}$$

$$\dot{r} = \iota - \tilde{\mu}\,r \qquad \text{for } \tau \in [0,\infty[, \tag{4.70}$$

$$\dot{d} = \tilde{\delta}\,\iota \qquad \text{for } \tau \in [0,\infty[, \tag{4.71}$$

The initial conditions remain as before, cf. (4.16) - (4.22):

$$s(0) = s_0, \quad \iota(0) = \iota_0, \quad r(0) = r_0 \qquad \text{with } 0 < s_0, \iota_0, r_0 < 1, \qquad d(0) = d_0 = 1 - s_0 - \iota_0 - r_0. \tag{4.72}$$

Based on lemma 4.4, the denominator $1 - d$ equals to $s + \iota + r$, and, hence equations (4.68) and (4.69) can be reformulated without d. For convenience, we repeat all equations and get the equivalent system:

$$\dot{s} = -\tilde{\beta}\,\frac{\iota}{s+\iota+r}\,s + \tilde{\mu}\,r \qquad \text{for } \tau \in [0,\infty[, \tag{4.73}$$

$$\dot{\iota} = \tilde{\beta}\,\frac{s}{s+\iota+r}\,\iota - \iota - \tilde{\delta}\,\iota \qquad \text{for } \tau \in [0,\infty[, \tag{4.74}$$

$$\dot{r} = \iota - \tilde{\mu}\,r \qquad \text{for } \tau \in [0,\infty[, \tag{4.75}$$

$$\dot{d} = \tilde{\delta}\,\iota \qquad \text{for } \tau \in [0,\infty[, \tag{4.76}$$

As a consequence, the first three equations do not contain d. They can be solved separately, after that, d can be obtained via simple integration. If additionally $\mu \equiv 0$, at first, the subsystem for s and ι can be solved and afterwards r and d can be obtained. This is an advantage for numerical studies.

Now, we want to get the specific expressions for the basic reproduction number ρ_0, contact number σ and replacement number ρ. We remember the ideas in paragraph 2.2.2. An easy way to find ρ consists in taking the ratio of inflow and outflow in (4.74) (or in (4.62)). Thus, we get

$$\rho = \frac{\tilde{\beta}}{1+\tilde{\delta}}\,\frac{s}{s+\iota+r} = \frac{\beta}{\gamma+\delta}\,\frac{S}{S+I+R}. \tag{4.77}$$

Thus, the (current) contact number σ and the basic reproduction number ρ_0 follow in accordance with

$$\sigma = \frac{\tilde{\beta}}{1+\tilde{\delta}} = \frac{\beta}{\gamma+\delta}, \qquad \rho_0 = \sigma(0) = \frac{\tilde{\beta}(0)}{1+\tilde{\delta}(0)} = \frac{\beta(0)}{\gamma+\delta(0)}. \tag{4.78}$$

As already stated, the quantities ρ_0, σ and ρ are dimensionless, ρ_0 is always a constant. The following assertions easily follow.

Corollary 4.7. (**Qualitative behaviour of a SIRSD model**)

(i) The six parameters $\tilde{\beta}$, $\tilde{\mu}$, $\tilde{\delta}$, s_0, ι_0 and r_0 determine the solution to problem (4.73) - (4.76). The transition to solution of the original problem S, I, R and D takes place only with dilations or compressions in accordance with lemma 4.2.

(ii) The contact number σ, $\tilde{\mu}$ and the lethality number $\tilde{\delta}$ (or, equivalently, $\tilde{\beta}$, $\tilde{\mu}$ and $\tilde{\delta}$) are the determining dimensionless parameter functions for the problem (4.73) - (4.76).

(iii) A necessary condition for starting a spreading infection is

$$\rho_0 = \sigma(0) > 1. \tag{4.79}$$

A sufficient and necessary condition is given by

$$\rho(0) = \sigma(0)\,\frac{s_0}{s_0+\iota_0+r_0} > 1. \tag{4.80}$$

However, due to $s_0/s_0+\iota_0+r_0 \approx 1$ in many cases, in reality, condition (4.79) is often also sufficient.

(iv) The lethality coefficient δ has only a significant influence, if it has the same magnitude of order as γ. And, if this is the case, then the spread of infection is essentially braked by death cases. This can explain, that the evolution led to pathogens which (as a rule) do not have too high lethality.

(v) The function ι can only grow, so long as the replacement number fulfils $\rho(\tau) > 1$.

(vi) If $\sigma(\tau) < 1$, then also holds $\rho(\tau) < 1$, and ι decreases.

(vii) If $\mu = 0$, then r can only grow, and s can only fall. The case $\mu \neq 0$ is more complex and needs detailed investigations.

(viii) Applying a simple SIRD model (i.e., with $\mu = 0$) to COVID-19 and assuming a realistic $\rho_0 = 3$ and a small lethality coefficient, the function ι grows nearly till 0,66 in the case of a constant β. Thus, if there is no change of contact behaviour, approximately two-thirds of an initially fully susceptible population will be infected.

Remark 4.8. (**Death-adjusted infectious period**)
In simple models like SIS and SIR, the contact number σ fulfils the relation $\sigma(t) = \beta(t)\omega$ (see formula (2.12)), where $t_{inf} = \omega = 1/\gamma$. These models are applied, if infection-related deaths (and generally death cases) do not play a significant role. However, considering a SIRD model as above, the mean effective infectious period ω_{eff} (or the mean death-adjusted infectious period, see Hethcote (2000)) is not $1/\gamma$, but has to be corrected. As a result one obtains

$$\sigma(t) = \beta(t)\,\omega_{eff} = \beta(t)\,\frac{\omega\,\omega_\delta}{\omega + \omega_\delta}. \tag{4.81}$$

Here, $\omega_\delta = 1/\delta$ is the infection-related mean lifetime of an infected person. A reasoning for (4.81) can be obtained as follows. The function

$$\exp(-(\gamma+\delta)t) = \exp(-\gamma\,t)\exp(-\delta\,t) \tag{4.82}$$

can be understood as probability that an initially infected person is infectious and alive at time t. Than the integral

$$\omega_{eff} := \int_0^\infty \exp(-(\gamma+\delta)t)\,\mathrm{d}t = \frac{1}{\gamma+\delta} = \frac{\omega\,\omega_\delta}{\omega+\omega_\delta} \tag{4.83}$$

represents the mean effective infectious period (see formula (2.17)). Thus, besides using the ratio of inflow and outflow, there is an alternative way to obtain relations (4.77) and (4.78) via a mean effective duration of infectiousness.

4.3.2 SIRS and SIR models

Obviously, $SIRS$ and SIR models are special cases of SIRSD and SIRD ones. Thus, the assertions in the preceding paragraph remain valid after slight modifications. However, neglecting the lethality coefficient δ, and thus d, the contact number σ directly occurs in the equations for s and ι. This can be done, if $\delta \ll \gamma$. Therefore, setting $\delta \equiv 0$ and $d \equiv 0$, from (4.77) and (4.78) one obtains

$$\rho = \tilde\beta\,s = \frac{\beta}{\gamma}\,\frac{S}{N_0} = \beta\,\omega\,\frac{S}{N_0}, \qquad \sigma = \tilde\beta = \frac{\beta}{\gamma} = \beta\,\omega, \qquad \rho_0 = \sigma(0) = \tilde\beta(0) = \frac{\beta(0)}{\gamma} = \beta(0)\,\omega. \tag{4.84}$$

Again, we use $t_{inf} = \omega = 1/\gamma$ (ω - mean duration of infectiousness). $\tilde\beta$ and $\tilde\mu$ remain as before. Therefore, and taking $1 = s + \iota + r$ into account, form (4.73) - (4.75) one obtains

$$\dot s = -\sigma\,\iota\,s + \tilde\mu\,r \qquad \text{for } \tau \in [0,\infty[, \tag{4.85}$$

$$\dot\iota = \sigma\,s\,\iota - \iota \qquad \text{for } \tau \in [0,\infty[, \tag{4.86}$$

$$\dot r = \iota - \tilde\mu\,r \qquad \text{for } \tau \in [0,\infty[. \tag{4.87}$$

Now, the contact number σ directly occurs in (4.85) and (4.86), it plays the role of a "dimensionless contact coefficient". Clearly, the assertions (iii), (v) - (vii) of corollary 4.7 remain valid, in (i), (ii), $\tilde\delta$ and D must be removed.

In Schuster (2013), Chapter 5.2, the corresponding system (with $\mu = 0$) is studied for the fractions of S, I and R, named also by s, ι and r, without transforming the time t.

4.3.3 SEIR and SEIRD models

Now, we want to study how important dimensionless numbers influence the infection course in the case of more complex models. In Bacaër (2020), a special $\mathrm{SEIR_1R_2}$ model has been investigated, addressing the begin of the SARS-CoV-2 epidemic in France.

To focus on main items, we deal at first with the following SEIR model.

$$\dot{s} = -\tilde{\beta}\,\iota\,s \qquad \text{on } [0,\infty[\tag{4.88}$$

$$\dot{e} = \tilde{\beta}\,s\,\iota - \tilde{\epsilon}\,e \qquad \text{on } [0,\infty[\tag{4.89}$$

$$\dot{\imath} = \tilde{\epsilon}\,e - \iota \qquad \text{on } [0,\infty[\tag{4.90}$$

$$\dot{r} = \iota \qquad \text{on } [0,\infty[. \tag{4.91}$$

We assume (4.3) and (4.4) (without d) and modify (4.5), defining

$$\tilde{\beta}(\tau) := \frac{\beta(t)}{\gamma}, \qquad \tilde{\epsilon} := \frac{\epsilon}{\gamma}. \tag{4.92}$$

Now, there holds $1/\gamma := t_{inf} - t_{lat}$, and $1/\epsilon := t_{lat}$ remains as before. t_{inf} is the end of infectiousness. Moreover, the contact and replacement numbers are given by

$$\sigma := \frac{\beta}{\gamma} = \tilde{\beta} = \beta\,(t_{inf} - t_{lat}), \qquad \rho = \sigma\,s. \tag{4.93}$$

For a better overview we drop a possible loss of immunity and vaccination. Besides, infection-related deaths are included in r. If necessary, these items can be added without any special effort. Obviously, the system (4.88) - (4.91) is a simplification of (4.6) - (4.12).

We set the initial conditions as in (4.16) - (4.21) and the condition (4.23) with $d_0 = 0$. To avoid trivial cases, we assume

$$e_0 + \iota_0 > 0. \tag{4.94}$$

Due to the special coupling of the equations for e and ι, we add (4.89) and (4.90). Hence, we get a differential equation for the sum $e + \iota$:

$$\dot{e} + \dot{\imath} = \sigma\,s\,\iota - \iota = \big(\sigma\,s - 1\big)\,\iota. \qquad \text{on } [0,\infty[. \tag{4.95}$$

Thus, for

$$\sigma > 1, \qquad e_0 + \iota_0 + r_0 \ll 1, \tag{4.96}$$

the sum $e + \iota$ asymptotically grows up so long as $\rho = \sigma\,s > 1$, or, equivalently $s > s_{min} := 1/\sigma$. The growing sum $e + \iota$ allows three cases: (i) e and ι grow, (ii) e grows, ι decreases, (iii) e decreases, ι grows. These cases are determined by the initial conditions for e and ι.

Let be $\iota_0 > 0$. Then, due to theorem 4.5, $\iota > 0$ for all time. Hence, we can re-write the equations (4.89) and (4.90):

$$\dot{e} = (\sigma\,s - \tilde{\epsilon}\,\frac{e}{\iota})\,\iota \qquad \text{on } [0,\infty[, \tag{4.97}$$

$$\dot{\imath} = (\tilde{\epsilon}\,\frac{e}{\iota} - 1)\,\iota \qquad \text{on } [0,\infty[. \tag{4.98}$$

Due to (4.96) and (4.92) it holds

$$\frac{\gamma}{\epsilon} = \frac{1}{\tilde{\epsilon}} < \frac{\beta}{\epsilon} = \frac{\sigma}{\tilde{\epsilon}}. \tag{4.99}$$

The initial value e_0/ι_0 of the ratio e/ι determines the begin of the evolution of e and ι. If

$$\frac{1}{\tilde{\epsilon}} < \frac{e_0}{\iota_0} < \frac{\beta}{\epsilon}, \tag{4.100}$$

then at least for some time after beginning both functions e and ι grow. The asymptotic value of e/ι is $1/\tilde{\epsilon}$, or, in other words, there holds

$$\frac{e}{\iota} \to \frac{1}{\tilde{\epsilon}} = \frac{\gamma}{\epsilon}. \tag{4.101}$$

The remaining cases

$$\frac{e_0}{\iota_0} < \frac{1}{\tilde{\epsilon}} < \frac{\beta}{\epsilon}, \quad \text{and} \quad \frac{1}{\tilde{\epsilon}} < \frac{\beta}{\epsilon} < \frac{e_0}{\iota_0} \tag{4.102}$$

imply a growing e and a decreasing ι and a decreasing e and a growing ι, respectively, at least for some time. Additionally, for these cases the relation (4.101) remains to hold.

The case $e_0 > 0$ can be dealt with analogously, re-writing (4.89) and (4.90) in the following way.

$$\dot{e} = (\sigma\, s\, \frac{\iota}{e} - \tilde{\epsilon})\, e \qquad \text{on } [0, \infty[, \tag{4.103}$$

$$\dot{\iota} = (\tilde{\epsilon}\, \frac{e}{\iota} - 1)\, \iota \qquad \text{on } [0, \infty[. \tag{4.104}$$

And, finally, the asymptotic behaviour of ι/e is given by

$$\frac{e}{\iota} \to \tilde{\epsilon} = \frac{\epsilon}{\gamma}. \tag{4.105}$$

Clearly, this is equivalent to (4.101).

Obviously, for $\sigma \leq 1$, the sum $e + \iota$ cannot grow, and the infection so does. Depending on initial values e_0 and ι_0, one of these two functions can grow for short time.

Remarks 4.9. (**SEIRD and SEIRSD models**)

(i) Infection-related deaths can be integrated as before in paragraph 4.3.1. The main assertions of this paragraph remain valid with slight modifications.

(ii) A possible loss of immunity and vaccination can be included without difficulties, since the equations for e and ι are not touched by these extensions.

4.3.4 SEI^{3}RSD models

Finally, we want to deal with complex models of SEI^{3}R kind. In order to focus, at first we drop d, loss of immunity and vaccination within the SEI^{3}RSD model presented above in section 3 and paragraph 4.1. Neglecting d and taking $1 = s + e + \iota_1 + \iota_{21} + \iota_{22} + r$ into account, we obtain from (4.6) - (4.11):

$$\dot{s} = -\big(\tilde{\beta}_1\, \iota_1 + \tilde{\beta}_1\, \iota_{21} + \tilde{\beta}_{22}\, \iota_{22}\big)\, s \qquad \text{on } [0, \infty[\tag{4.106}$$

$$\dot{e} = \big(\tilde{\beta}_1\, \iota_1 + \tilde{\beta}_1\, \iota_{21} + \tilde{\beta}_{22}\, \iota_{22}\big)\, s - \tilde{\epsilon}\, e \qquad \text{on } [0, \infty[\tag{4.107}$$

$$i_1 = \tilde{\epsilon}\, e - \iota_1 \qquad \text{on } [0, \infty[\tag{4.108}$$

$$i_{21} = (1 - \alpha)\, \iota_1 - \tilde{\gamma}_{21}\, \iota_{21} \qquad \text{on } [0, \infty[\tag{4.109}$$

$$i_{22} = \alpha\, \iota_1 - \tilde{\gamma}_{22}\, \iota_{22} \qquad \text{on } [0, \infty[\tag{4.110}$$

$$\dot{r} = \tilde{\gamma}_{21}\, \iota_{21} + \tilde{\gamma}_{22}\, \iota_{22} \qquad \text{on } [0, \infty[. \tag{4.111}$$

The definition of parameters as well as the initial conditions (with $d_0 = 0$) are given as in subsection 4.1.

Contrary to the previous models above, it is *not* clear, where in the equations contact and replacement numbers occur. Based on definitions in paragraph 2.2.2 and in remark 3.1, the contact and replacement number are presented for the full problem. Neglecting d and δ, we obtain:

$$\sigma = \frac{\beta_1}{\gamma_1} + (1 - \alpha)\, \frac{\beta_1}{\gamma_{21}} + \alpha\, \frac{\beta_{22}}{\gamma_{22}} = \tilde{\beta}_1 + (1 - \alpha)\, \frac{\tilde{\beta}_1}{\tilde{\gamma}_{21}} + \alpha\, \frac{\tilde{\beta}_{22}}{\tilde{\gamma}_{22}}, \tag{4.112}$$

$$\sigma = \Big\{ \frac{\beta_1}{\gamma_1} + (1 - \alpha)\, \frac{\beta_1}{\gamma_{21}} + \alpha\, \frac{\beta_{22}}{\gamma_{22}} \Big\}\, s = \Big\{ \tilde{\beta}_1 + (1 - \alpha)\, \frac{\tilde{\beta}_1}{\tilde{\gamma}_{21}} + \alpha\, \frac{\tilde{\beta}_{22}}{\tilde{\gamma}_{22}} \Big\}\, s. \tag{4.113}$$

An investigation like for $SEIR$ models before turns out to be more complex. We only sketch some ideas. The addition of equations (4.107) - (4.110) yields an equation for the sum $e + \iota_1 + \iota_{21} + \iota_{22}$:

$$\dot{e} + i_1 + i_{21} + i_{22} = \tilde{\beta}_1\, s\, \iota_1 + (\tilde{\beta}_1\, s - \tilde{\gamma}_{21})\, \iota_{21} + (\tilde{\beta}_{22}\, s - \tilde{\gamma}_{22})\, \iota_{22} \qquad \text{on } [0, \infty[. \tag{4.114}$$

Thus, the sum $e + \iota_1 + \iota_{21} + \iota_{22}$ grows, if

$$\min \Big\{ \frac{\tilde{\beta}_1}{\tilde{\gamma}_{21}}\, s,\ \frac{\tilde{\beta}_{22}}{\tilde{\gamma}_{22}}\, s \Big\} > 1. \tag{4.115}$$

Note that due to theorem 4.5 all functions s, e, etc. are non-negative. Obviously, condition (4.99) is only a coarse sufficient one. The term $\tilde{\beta}_1\, s\, \iota_1$ remains disregarded. A further, more detailed investigation seems to be sophisticated.

Alternatively, the equations for e and ι_1 can be added:

$$\dot{e} + \dot{\iota}_1 = (\tilde{\beta}_1\, s - 1)\, \iota_1 + \tilde{\beta}_1\, s\, \iota_{21} + \tilde{\beta}_{22}\, s\, \iota_{22} \qquad \text{on } [0, \infty[. \tag{4.116}$$

Now, the sum $e + \iota_1$ grows, if

$$\tilde{\beta}_1\, s > 1. \tag{4.117}$$

Again, this is a rough sufficient condition, disregarding the remaining terms in (4.100).

* * *

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