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DISSERTATION

Aggregation and optimisation in epidemiological models of heterogeneous populations

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Abstract

This thesis is concerned with the analysis of models of heterogeneous populations in infectious disease epidemiology. Special considerations are made with respect to variables arising from the aggregation of heterogeneous variables. We analyse the asymptotic behaviour, steady states, and stability of simple heterogeneous SI-, SIS-, and SIR-models with parametric heterogeneity, which are described by an infinite dimensional system of ODEs. As for homogeneous models, we are able to define a basic reproduction number which can be used as an indicator for the existence of endemic steady states and stability of disease free steady states. In some cases a finite dimensional ODE system for the aggregated variables can be formulated, which simplifies both analysis and practical calculations.

For SIS-models we also consider the influence of heterogeneity on early warning signs for critical transitions. We develop a stochastic model to incorporate fluctuation effects and the random import of the disease into the population. We analyse the influence of heterogeneity on warning signs for critical transitions. This theory shows that one may be able to anticipate whether a bifurcation point is close before it happens. Using numerical simulations, we show that known scaling laws for early warning signs no longer hold true for heterogeneous models. We identify various different ways in which heterogeneity can influence these scaling laws. This is of importance if one wants to interpret potential warning signs for disease outbreaks.

One obstacle to applying heterogeneous models in practice is that in order for the equations to be well defined it is necessary to have knowledge of the initial conditions for the distributed heterogeneous variables. This information is in many cases not available. However, the variables of interest are often not the heterogeneous variables, but their aggregated counterparts. We therefore develop set-membership estimation techniques for these aggregated variables under the assumption that the initial conditions for the heterogeneous variables are only partially known. By numerically solving certain optimisation problems we are able to calculate these estimations.

Furthermore, we consider optimal control problems for heterogeneous systems. For models with parametric heterogeneity, we show by example how aggregation techniques can in certain cases be used to reduce the infinite dimensional problem to a finite dimensional one, for which the well developed standard optimal control theory can be applied. We also develop a version of Pontryagin's maximum principle for heterogeneous systems that include aggregated variables. We do this not in the framework of parametric heterogeneity, but more generally for size structured PDEs.

Contents

Introduction

Infectious diseases are a great concern even in our modern times. Some life threatening maladies such as acquired immunodeficiency syndrome (AIDS), malaria, schistosomiasis, and cholera are endemic in many parts of the world, particularly developing countries. The effects of these diseases are not only in an increased mortality, but also put a significant strain on the economies of the afflicted countries. The same is true for less threatening infectious diseases which are more prevalent in the western world. For example, the estimated total economic burden of annual influenza epidemics in the US is 87 billion dollars ([87]). Even if a disease only affects animals, such as foot and mouth disease, the impact on the livelihood of people and whole economies can be considerable. Combating and preventing these infections, whether they are long time epidemics such as AIDS or short disease outburst as seen in the Ebola virus, is therefore not only important for the people directly afflicted, but for whole societies. To do so more effectively, infectious diseases need to be well understood.

As all health-related events, infectious diseases are studied in the field of epidemiology. One of the goals of this field as applied to infectious diseases is to trace factors that contribute or are responsible for the transmission of an infectious agent from one individual to another and to control these factors to prevent its spreading. The role of mathematical epidemiology in this process can be broadly categorized into three stages ([29]). First, one must formulate a model by translating assumptions about behaviour, demography, immunity, etc. into mathematical notation. The next step is to analyse these mathematical models and study the dependencies of the dynamics on various factors. Finally, we can draw conclusions and formulate policies by translating the mathematical results back to give them biological meaning. In this thesis we focus on the second of these steps. However, we endeavour not to loose sight of the biological origins and consequences of our considerations.

The ways in which epidemiological transmission process are modelled are manifold. Different biological situations give rise to different mathematical models. These variations are due to distinct transmission mechanics (e.g. transmission via sexual contact or by the bite of a mosquito), nature of the infection (e.g. viral or parasitic), possibility of recovery or immunity from the disease, social behaviour of the population, and many more differences that characterise various situations. Furthermore, all of these elements may influence each other in intricate ways.

It is then easy to see that models that capture every aspect which could influence disease transmission would be exceedingly complex. They are therefore a poor starting point when trying to gain understanding of infectious disease dynamics. Hence, one common way to approach this problem is to start with very simple models that only capture a few basic features of disease transmission and can be easily analysed ([18, 29]). As these models are understood, we can consider additional aspects of interest in the transmission process and in this way successively increase the complexity of the models that are fully understood. Furthermore, not only are these simple models easier to analyse, but are sometimes already good approximations of the real processes and very useful in practical applications.

In epidemiology, the most widely used way to formulate dynamics of infectious diseases are so-called compartmental models, dating back to Kermack and McKendrick in 1927 ([66]). In these models the population is divided into a certain number of sup-populations (called compartments) which are assumed to be important in the disease transmission. The dynamics are based on the transition of individuals from one compartment into another. We will illustrate this by a simple example.

We consider a population consisting at time t of $N(t)$ individuals, and divide it into two compartments, susceptible (denoted by $S(t)$) and infected ($I(t)$). We assume that there are two transmission processes. First, a transmission from the susceptible to the infected population which models the infection process and for which a transmission rate is given. Second, a transmission out of the infected population which models mortality due to the disease and for which a constant mortality rate μ is given. Under the assumption that contacts between individuals are uniformly distributed and that a fraction σ of contacts leads to an infection, one reasonable transmission rate is the mass-action law $\sigma\frac{I(t)S(t)}{N(t)}$ ([82]). Using this, the dynamics of the susceptible population are $\dot{S}(t) = -\sigma\frac{I(t)S(t)}{N(t)}$, since the susceptible population decreases with exactly that rate. Conversely, the infected population increases with the inflow of newly infecteds at rate $\sigma\frac{I(t)S(t)}{N(t)}$ and decreases with rate $\mu I(t)$ due to mortality, so that $\dot{I}(t) = \sigma\frac{I(t)S(t)}{N(t)} - \mu I(t)$. Since $N(t) = S(t) + I(t)$ these two equations completely describe the disease dynamics once initial conditions are given.

This simple model, known as an SI-model (for Susceptible-Infected), can easily be extended. If, for example, the disease is not fatal but individuals recover with rate γ from the infection and are afterwards immune towards the disease, we can introduce a new compartment of recovered individuals, $R(t)$. The dynamics of $R(t)$ are given by $\dot{R}(t) = \gamma I(t)$. The dynamics for $S(t)$ and $I(t)$ are the same once γ is substituted for μ. Also, we now have $N(t) = S(t) + I(t) + R(t)$. The resulting model is known as an Susceptible-Infected-Recovered-model, or SIR-model for short. In a similar way we could define an SIS-model (Susceptible-Infected-Susceptible), where an infected individual is upon recovery transmitted back into the susceptible population. By introducing more and more compartments and increasing the possibilities of transmission between compartments, these models can be extended to an arbitrary level of complexity. More in-depth discussion of these models as well as further derivations from basic principles can be found in numerous textbooks on mathematical epidemiology, e.g. [18, 19, 29, 64].

This kind of models assume that the individuals in each compartment are homogeneous, i.e. there is no distinction between any two of them. There are however situations in which such a distinction plays an important role in the transmission of the disease. For example, we might want to keep track of how long an individual has been infected for (also known as the infection-age), since this can greatly influence the probability of transmitting the disease. Creating a compartment for each infection-age would make the resulting model infeasibly large. It is more practical to consider a heterogeneous model.

In heterogeneous models we follow [29] and assign each individual in one or more compartments a certain *state*. These states describe the chosen characteristics (those, that are deemed of importance for the transmission of the disease) of each individual. They may contain information about the individual (like age, social behaviour, or immune status) or about the disease (e.g. viral load or time since infection). If the state changes with time we call it a dynamic state, otherwise we call it static or parametric state. It may take continuous or discrete values. Mathematically, the resulting models are in the form of infinite dimensional systems of ordinary differential equations (ODEs) or the form of partial differential equations (PDEs), depending the underlying assumptions.

The need for heterogeneous systems has been realised early in the development of mathematical models for infectious diseases. Even Kermack and McKendrick's original work dealt with an age-structured system. One hindrance in their advancement was of mathematical nature: heterogeneous models are analytically as well as computationally more difficult to handle. Particularly advances in computing have however helped to overcome some of these difficulties and have led to good understanding of certain heterogeneous models. But a second problem with these models lies in their practical application. To utilise them, the distribution of the state among the population needs to be known. This information is in many cases not available. Furthermore, while the modelling of the heterogeneity may be necessary to mathematically describe the dynamics of the disease transmission, the values of interest are often not the heterogeneous variables, but their aggregated equivalent.

This will be the starting point for this thesis.

In Chapter 1 we consider an SI-model with parametric heterogeneity, described by an infinite dimensional ODE system. We reduce this to a finite dimensional system of ODEs, describing the dynamics of the aggregated variables. The asymptotics of this system can be described in full. We discuss how they differ from the asymptotics of a homogeneous model. Our analysis also allows us to describe what information about the heterogeneous variables is necessary to determine the behaviour of the aggregated variables. We also introduce the notion of the basic reproduction number for the heterogeneous system and compare how its value as an indicator for the asymptotic behaviour changes with regard to the homogeneous system.

In Chapter 2 we continue the discussion of SI-models and focus on aggregation. We show that for a class of heterogeneous SI-models it is always possible to derive a finite dimensional ODE system describing its aggregated variables. We apply this approach to an existing model in the literature to illustrate two points. First, we show how estimation of the unknown distribution of the heterogeneity among the population can be included into the model. The resulting equations depend on only a few parameters which can then be determined from data. Second, we look at an optimal control problem whose state equations are given by the heterogeneous model. We demonstrate how the aggregated system is analytically simpler to study.

In Chapter 3 we analyse a heterogeneous SIS-system. The focus here is on early warning signs for the emergence of a disease outbreak. For this purpose we consider a system containing both variables that change on different time scales as well as stochastic perturbations. In such systems certain characteristics, such as the variance of the process, change their behaviour close to critical points at which the dynamics undergo a qualitative alteration. For homogeneous models this change in behaviour is well understood, and the characteristics follow certain scaling laws that are known and can be used to predict dynamical regime changes ahead of time. We show that in heterogeneous systems the aggregated variables no longer follow these known scaling laws and detect different ways in which they are influenced by heterogeneity.

In Chapter 4 we further analyse the steady states and their stability of SIS- and SIR-models with parametric heterogeneity. We are able to identify the basic reproduction number, which plays a crucial role in this investigation. As we will see, the derivations become very technical even for these comparatively simple models. Results for the aggregated variables can be derived from the knowledge of the behaviour of the heterogeneous system.

In the Chapters 5 and 6 we consider the problem, which we mentioned before, that in practice we often do not have detailed information about the distribution of the heterogeneity among the population. We propose a set-membership estimation technique which allows us to gain information about the possible trajectories of the system under the assumption that our knowledge of the initial conditions is incomplete or imprecise. These estimations can be calculated by solving certain optimisation problems for the heterogeneous system, for which we also present a numerical procedure. In Chapter 5 we do so for systems with parametric heterogeneity and also demonstrate how this technique can be used to compare different intervention scenarios. In Chapter 6 we consider size-structured systems. We show how set-membership estimation can be used in the analysis of such models.

Finally, in Chapter 7 we consider optimal control problems containing size-structured systems such as those presented in Chapter 6. We present a version of Pontryagin's maximum principle for first order PDEs that contain aggregated variables and allow for control in the aggregation. The result is of a very general nature and may be specified to fit numerous applications.

Furthermore we present the context of our work with respect to the existing literature as well as outlooks and suggestions for possible future directions of research. We do so in the individual chapters.

Even though only one smart part of mathematical epidemiology, the study of heterogeneous models for the transmission of infectious diseases is nonetheless a vast field with ongoing research in many different directions. We can here only offer a glimpse at a small section of this field. We nevertheless hope that our contribution will be of help in gaining understanding in this important area of study.

Chapter 1

Aggregation and asymptotic behaviour of an *SI*-epidemic model for heterogeneous populations[1]

1.1 Introduction

In this paper we consider a heterogeneous version of a simple epidemiologic model of a population consisting of a non-infected (potentially susceptible) sub-population and an infected sub-population (SI-model). It is well recognized that modelling the population as homogeneous (with equal susceptibility/infectivity of all individuals) may give a rather distorted picture of the evolution of the disease, compared with the one that appears if the heterogeneity of the population is taken into account. The main goal is to quantitatively describe the differences (and similarities) in the asymptotic behaviour of the disease when modelling the population as heterogeneous, versus homogeneous.

In principle, it is well known that the heterogeneity plays an important role in epidemiologic models, therefore the issue of heterogeneity is introduced and investigated in this subject area in a large number of papers (see e.g. [26, 32, 47, 48, 91, 92, 107]). The main contribution of the present paper is that the asymptotic behaviour of the disease in a heterogeneous population (within an SI framework) is completely and explicitly described, and compared with the one resulting from the homogeneous version of the model. The proofs are rather technical, but not routine. Although the analysis is restricted to a very simple model, it can be useful as a benchmark case for more enhanced investigations of the influence of heterogeneity on the evolution of infectious diseases. Such are indicated in Section 1.6.

A crucial drawback of the heterogeneous models is that they require information about the distribution of the population along the space of heterogeneity, which is usually not available. As a by-product

[1]This chapter has been published in the journal Mathematical Medicine and Biology [109].

of our analysis, it becomes clear what information about the heterogeneity is actually essential for determining the ultimate epidemic state. The required information is (in generic cases) substantially less than the overall distribution.

The paper is organized as follows. In Section 1.2 we present the homogeneous and the heterogeneous versions of the considered SI-model. The aggregation of the heterogeneous model to an ODE model is done in Section 1.3. Section 1.4 is devoted to the asymptotic analysis of the disease, where a comparison between the results for the homogeneous and the heterogeneous model is also presented, as well as some illustrating numerical examples. The concept of reproduction number is adapted to the heterogeneous model and discussed in Section 1.5. Some concluding remarks and perspectives for further investigations of more complex epidemic models are given in Section 1.6. The more technical proofs are given in the appendix.

1.2 The *SI*-model

First we recall the standard SI-model for a population with a variable size, depending on fertility and mortality (natural, and such caused by the disease). Then, in the second subsection, we present a heterogeneous version of the same model.

1.2.1 The homogeneous model

The dynamics of the disease is given by the following equations, in which $S(t)$ and $I(t)$ denote the size of the susceptible and of the infected sub-populations at time $t \geq 0$:

$$\dot{S}(t) = -\sigma y(t)S(t) + \lambda S(t), \quad S(0) = S_0, \tag{1.1}$$

$$\dot{I}(t) = \sigma y(t)S(t) - \delta I(t), \quad I(0) = I_0, \tag{1.2}$$

where

$$y(t) = \frac{I(t)}{S(t) + I(t)} \tag{1.3}$$

is the prevalence. The meaning of the appearing parameters is as usual: λ (positive or negative) is the net inflow rate of susceptible individuals (i.e. the difference between birth and mortality rate), similarly δ is the net mortality rate of infected individuals, and σ is the infectiousness of the disease (strength of infection). Clearly, there is no recovery from the considered disease. In addition, it will be assumed that $\delta > 0$, that is, the infected individuals die at a higher rate than they reproduce. The initial data S_0 and I_0 are both positive.

SI-models are amongst the most basic epidemiological models and therefore an analysis of such models can be found in introductory texts on epidemiology, such as [18, 19, 29]. Here we will derive some of the results anew in order to make the considerations self-contained and to draw parallels between this homogeneous model and the heterogeneous model described below.

Closely related to SI-models are SIR-models where $R(t)$ stands for removed individuals and follows the dynamics

$$\dot{R}(t) = \delta I(t).$$

This population influences the dynamics of $S(t)$ and $I(t)$ because $y(t)$ now has to be defined as $y(t) = \frac{I(t)}{S(t)+I(t)+R(t)}$. However, if the removed no longer participate in infectious contacts, e.g. because the removal is due to quarantine, then the SI and SIR-models are equivalent.

1.2.2 The heterogeneous model

We introduce a heterogeneity into the above SI-model by differentiating the population according to some traits, such as genetic markers, natural resistance towards a disease, or social behaviour, that influence the spreading of the disease. We therefore assume that every individual has a certain h-state (heterogeneity-state) ω. We restrict ourselves to traits that are time invariant, i.e. an individual that has h-state ω stays in that state for all of its lifespan. Denote by Ω the space of all h-states. It will be assumed that Ω is a Borel measurable space with a finite measure μ. This allows Ω to be a continuous or discrete space, as well as a product space involving different traits. Previous works that use this or a similar notion of h-state include [26, 31, 32, 48, 91, 107].

We assume that the h-state ω influences the risk of an individual to become infected by a factor $p(\omega)$. More precisely, we denote by $\bar{S}(t,\omega)$ and $\bar{I}(t,\omega)$ the size of the susceptible and infected sub-populations of h-state ω and assume that the sub-population of each h-state develops similarly as in the homogeneous S-I-model:

$$\dot{\bar{S}}(t,\omega) = -\sigma z(t)\, p(\omega)\, \bar{S}(t,\omega) + \lambda \bar{S}(t,\omega), \quad \bar{S}(0,\omega) = S_0(\omega), \tag{1.4}$$

$$\dot{\bar{I}}(t,\omega) = \sigma z(t)\, p(\omega)\, \bar{S}(t,\omega) - \delta \bar{I}(t,\omega), \qquad \bar{I}(0,\omega) = I_0(\omega). \tag{1.5}$$

Here the "dot" means differentiation with respect to t (for every fixed ω). The difference is that now the infectivity of the environment of the susceptible individuals is represented by the *weighted prevalence* $z(t)$ defined as

$$z(t) = \frac{J(t)}{K(t) + J(t)}, \tag{1.6}$$

where

$$K(t) = \int_\Omega p(\omega)\, \bar{S}(t,\omega)\, \mathrm{d}\omega, \tag{1.7}$$

$$J(t) = \int_\Omega p(\omega)\, \bar{I}(t,\omega)\, \mathrm{d}\omega. \tag{1.8}$$

Notice that not only the individual risk factor $p(\omega)$ is a carrier of heterogeneity in the above model, but also the weighted prevalence $z(t)$, which depends on the current (heterogeneous) distribution of the infected and susceptible individuals. A discussion about the model is given after the assumptions below.

Further, we will use the notations

$$S(t) = \int_\Omega \bar{S}(t,\omega)\,\mathrm{d}\omega, \quad I(t) = \int_\Omega \bar{I}(t,\omega)\,\mathrm{d}\omega. \tag{1.9}$$

for the aggregated states. It is easy to see that in the particular case of $\mu(\Omega) = 1$ and $p(\omega) \equiv 1$, the aggregated states $S(t)$ and $I(t)$ follow the dynamics of the homogeneous model (1.1)–(1.3). Thus the homogeneous model is a special case of the heterogeneous one. Another way to embed the homogeneous model into the heterogeneous one is to consider a set Ω which is a singleton with an unit atomic measure μ.

Below we formulate the assumptions needed for the subsequent analysis.

Assumptions (A). Ω is a complete Borel measurable space (that is, a Lebesgue space) with a nonnegative measure $\mu \geq 0$ with $\mu(\Omega) = 1$. The initial population is normalized: $S(0) + I(0) = 1$. The function $p : \Omega \to [0, \infty)$ is measurable, bounded, almost everywhere strictly positive, and also normalized: $\int_\Omega p(\omega)\,\mathrm{d}\omega = 1$. The initial data $S_0(\cdot)$ and $I_0(\cdot)$ are non-negative and measurable, both are strictly positive on a set of positive measure, and $I_0(\omega) = 0$ wherever $S_0(\omega) = 0$. The parameters $\sigma > 0$, $\delta > 0$, and λ are real numbers.

Everywhere measurability and integration in ω is meant with respect to the measure μ. The differential equations (1.4), (1.5) are considered as ODEs for every ω separately. From Theorem 1 in [108] it follows that given a bounded continuous function $z(t)$, the functions $\bar{S}(t,\cdot)$, $\bar{I}(t,\cdot)$ resulting from the ODE family (1.4), (1.5) are measurable for a.e. $t \geq 0$. Moreover, wherever it appears in the sequel, changing the order of integration in t and ω is justified by Fubini's Theorem (Theorem 2.1 in Chapter V of [33]), while changing the order of differentiation in t and integration in ω is justified due to a variant of Lebesgue's Dominated Convergence Theorem, namely Theorem 5.7 in Chapter IV of [33]. Below we shall perform these manipulations without further references.

Remark 1. Notice, that due to (1.4), if $S_0(\omega) > 0$ for some ω, then $\bar{S}(t,\omega) > 0$ for all $t > 0$. The same also applies to $\bar{I}$. Then, according to (A), we have $S(t) > 0$, $I(t) > 0$ for all $t > 0$, hence $y(t) > 0$. Consequently, also $K(t) > 0$, $J(t) > 0$, $z(t) > 0$ for all $t \geq 0$.

Obviously, the normalization assumptions in (A) are made only for convenience and do not restrict the generality. The same is valid to all positivity assumptions in (A). The assumption that $I_0(\omega) = 0$ wherever $S_0(\omega) = 0$ is natural if the same model is assumed to be also valid before time $t = 0$.

On the other hand, the structure of the model (1.4)–(1.8) is somewhat restrictive. First, the definition of the weighted prevalence (resulting from a proportional mixing scenario, in principle) implicitly implies certain restrictions for the interpretation of the h-states. The model can be derived by considering a heterogeneous social contact network (see [92]), which is an often discussed way to model diseases [9, 10, 83, 84]. Other restrictions are due to the encapsulated assumptions of no-recovery and no-fertility (or fertility with infected off-springs only) of the infected population. Moreover, the off-springs of the susceptible individuals "statistically" inherit the h-state distribution of the current susceptible population. All this is the price to pay for the possibility to perform a detailed analytic investigation of the long run evolution of the disease.

While the homogeneous model only consists of a 2-dimensional ODE-system, the dynamics of the heterogeneous system form a generally infinite dimensional system. This makes its analysis more difficult. Another issue with this heterogeneous model is that the initial distributions $S_0(\omega)$ and $I_0(\omega)$ are either partially or completely unknown. Further, it is often difficult or impossible to measure the quantities $\bar{S}(t,\omega)$ or $\bar{I}(t,\omega)$. Therefore, it is desirable to represent the evolution of the aggregated states S and I by ODEs, if possible. It was shown in [107] even for a more general class of models that the evolution of S and I in the expansion phase of the disease is exactly described by a system like (1.1)–(1.3) where, however, the incidence rate $\sigma y(t)$ is replaced with an (implicitly defined) nonlinear function of the prevalence y. In the next section we obtain an explicit representation of the dynamics of S and I valid in the time horizon $[0,\infty)$. The approach is similar to that in [59, 60, 61, 91, 92, 107] but the result is more explicit due to the specific features of the model considered here.

1.3 Aggregation of the heterogeneous model

In this section we obtain an ODE system that describes the evolution of the aggregated states $S(t)$ and $I(t)$ in (1.9). For shortness we abbreviate $M(t) := K(t) + J(t)$.

Proposition 1. *Let F be the solution of the initial value problem*

$$\dot{F}(t) = 1 - \frac{1}{M(0)} \int_\Omega p(\omega)\, e^{F(t)(\lambda+\delta-\sigma p(\omega))}\, S_0(\omega)\, \mathrm{d}\omega, \quad F(0) = 0, \tag{1.10}$$

and let us define

$$\rho(t) = \dot{F}(t)\, \frac{\int_\Omega p(\omega) e^{-\sigma F(t)\, p(\omega)} S_0(\omega)\, \mathrm{d}\omega}{\int_\Omega e^{-\sigma F(t)\, p(\omega)} S_0(\omega)\, \mathrm{d}\omega}. \tag{1.11}$$

Then the aggregated states S and I of system (1.4)–(1.8) satisfy the equations

$$\dot{S}(t) = -\sigma\rho(t)\, S(t) + \lambda S(t), \quad S(0) = S_0, \tag{1.12}$$

$$\dot{I}(t) = \sigma\rho(t)\, S(t) - \delta I(t), \qquad I(0) = I_0. \tag{1.13}$$

Moreover, the weighted prevalence z in (1.6) is given by $z(t) = \dot{F}(t)$.

In [59] and [60] G. Karev gives a way to reduce equations of a similar form as equations (1.4)-(1.8) to a system of ODEs. However, he deals only with a single population and not, as is done in this paper, with two interacting ones. A. Novozhilov applies Karev's approach to epidemiological models in [91] and [92], but with different equations than discussed here. In [92] he encounters a special case of model (1.4)-(1.8) and acknowledges that Karev's approach is not applicable to it. The proof given here is inspired by the method of Karev, but takes into account specific features of equations (1.4)-(1.8) that allow a reduction to an ODE system.

Proof For the proof we first define $F(t) := \int_0^t z(\tau)\,\mathrm{d}\tau$ (which will be shown below to satisfy (1.10)). We begin with deriving some preliminary relations.

Integrating (1.4) we obtain

$$\begin{aligned}\dot{S}(t) &= \int_\Omega \dot{\bar{S}}(t,\omega)\,\mathrm{d}\omega = -\sigma z(t)\int_\Omega p(\omega)\bar{S}(t,\omega)\,\mathrm{d}\omega + \lambda\int_\Omega \bar{S}(t,\omega)\,\mathrm{d}\omega \\ &= -\sigma z(t)\,K(t) + \lambda S(t).\end{aligned} \tag{1.14}$$

Similarly we get

$$\dot{I}(t) = \sigma z(t)\,K(t) - \delta I(t). \tag{1.15}$$

Differentiating (1.7) yields

$$\begin{aligned}\dot{K}(t) &= \int_\Omega p(\omega)\dot{\bar{S}}(t,\omega)\,\mathrm{d}\omega \\ &= -\sigma z(t)\int_\Omega p(\omega)^2\bar{S}(t,\omega)\,\mathrm{d}\omega + \lambda\int_\Omega p(\omega)\,\bar{S}(t,\omega)\,\mathrm{d}\omega \\ &= \lambda K(t) - \sigma z(t)\int_\Omega p(\omega)^2\bar{S}(t,\omega)\,\mathrm{d}\omega.\end{aligned} \tag{1.16}$$

Similarly,

$$\dot{J}(t) = -\delta J(t) + \sigma z(t)\int_\Omega p(\omega)^2\bar{S}(t,\omega)\,\mathrm{d}\omega. \tag{1.17}$$

Then using the Cauchy formula for equation (1.16) gives

$$\begin{aligned}K(t) &= e^{\lambda t}\left(K(0) - \sigma\int_0^t z(s)\int_\Omega p(\omega)^2\,e^{-\sigma F(s)p(\omega)}S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}s\right) \\ &= e^{\lambda t}\left(K(0) + \int_\Omega p(\omega)\int_0^t \frac{\mathrm{d}}{\mathrm{d}s}e^{-\sigma F(s)p(\omega)}S_0(\omega)\,\mathrm{d}s\,\mathrm{d}\omega\right) \\ &= e^{\lambda t}\int_\Omega p(\omega)\,e^{-\sigma F(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega.\end{aligned} \tag{1.18}$$

Since from (1.4)

$$\bar{S}(t,\omega) = S_0(\omega)\,e^{-\sigma\int_0^t z(\tau)\,\mathrm{d}\tau p(\omega)+\lambda t},$$

we obtain that

$$S(t) = e^{\lambda t} \int_\Omega e^{-\sigma F(t) p(\omega)} S_0(\omega)\, \mathrm{d}\omega. \tag{1.19}$$

For $M(t) := K(t) + J(t)$ we have from (1.16), (1.17) that

$$\dot{M}(t) = \lambda K(t) - \delta J(t).$$

From here one can represent

$$\begin{aligned} \dot{M}(t) &= \lambda K(t) - \delta J(t) = \lambda(1 - z(t))\, M(t) - \delta z(t)\, M(t) \\ &= M(t)\left(\lambda - \lambda z(t) - \delta z(t)\right). \end{aligned}$$

(This equality is easy to check starting from the last expression upwards.) Solving the above equation we obtain that

$$M(t) = M(0)\, e^{\int_0^t (\lambda - \lambda z(\tau) - \delta z(\tau))\, \mathrm{d}\tau} = M(0)\, e^{\lambda t - (\lambda+\delta) F(t)}. \tag{1.20}$$

Having relations (1.14)–(1.20) at hand, we may finalize the proof as follows.

Let us define

$$\rho(t) := z(t)\frac{K(t)}{S(t)} = \frac{J(t)}{M(t)}\frac{K(t)}{S(t)} = \left(1 - \frac{K(t)}{M(t)}\right)\frac{K(t)}{S(t)}.$$

From (1.14) and (1.15) it is evident that S and I satisfy (1.12), (1.13) with this function ρ. On the other hand, substituting the expressions (1.18)–(1.20) for K, S, and $K + J$, we obtain for ρ the representation (1.11). To complete the proof it remains to observe that

$$\dot{F}(t) = z(t) = \frac{J(t)}{M(t)} = 1 - \frac{K(t)}{M(t)},$$

and inserting the expressions (1.18), (1.20) results in (1.10). □

Equations (1.12), (1.13) for $S(t)$ and $I(t)$ have the same form as for the homogeneous system. The only difference is that in place of the incidence function $y(t)$ we use the function $\rho(t)$. Thus, the whole influence of the heterogeneity in this model is encapsulated in the *aggregated prevalence* $\rho(t)$ defined in (1.11) through the solution F of (1.10).

1.4 Asymptotics

1.4.1 The homogeneous system

Before we investigate the asymptotics of the heterogeneous system we analyze the homogeneous system (1.1), (1.3) in order to see later how the heterogeneity influences the asymptotic behavior.

Lemma 1. *If the number $\kappa := \sigma - \delta - \lambda$ is nonzero, then the solution of system (1.1), (1.3) is given by*

$$S(t) = S(0)\left(1 - y(0) + y(0)\,e^{\kappa t}\right)^{-\frac{\sigma}{\kappa}} e^{\lambda t}, \tag{1.21}$$

$$I(t) = I(0)\left(1 - y(0) + y(0)\,e^{\kappa t}\right)^{-\frac{\sigma}{\kappa}} e^{(\sigma-\delta)t}, \tag{1.22}$$

$$y(t) = \left(e^{-\kappa t}\left(y(0)^{-1} - 1\right) + 1\right)^{-1}. \tag{1.23}$$

The last equality is valid also for $\kappa = 0$.

The proof is routine but for completeness it is given in the appendix. Notice that $y(0)^{-1} - 1$ is well defined and positive due to Remark 1.

We split the analysis of the asymptotic behavior of system (1.1), (1.3) in 3 cases.

1. First, we consider the special case $\sigma = \lambda + \delta$. Then from Lemma 1, $y(t) \equiv y(0)$.

The solution $S(t)$ of (1.1) is

$$S(t) = S(0)\,e^{(\lambda - \sigma y(0))t}.$$

Thus, if $\lambda < \sigma y(0)$ both $S(t)$ and $I(t)$ converge to 0 when $t \to \infty$. If $\lambda > \sigma y(0)$ both tend to infinity, and if $\lambda = \sigma y(0)$ then $S(t) = S(0)$ and $I(t) = I(0)$ are constant. Notice that in the last case $I(0) = y(0) = \frac{\lambda}{\sigma}$. Thus

$$\frac{I(0)}{S(0)} = \frac{\frac{\lambda}{\sigma}}{1 - \frac{\lambda}{\sigma}} = \frac{\frac{\lambda}{\sigma}}{\frac{\sigma-\lambda}{\sigma}} = \frac{\lambda}{\delta}$$

and $I(0) = \frac{\lambda}{\delta} S(0)$.

2. Next, consider the case $\sigma > \delta + \lambda$. We have $\lambda - \sigma < -\delta < 0$. Then passing to the limit in (1.21) and (1.22) we obtain that both $S(t)$ and $I(t)$ converge to 0. According to (1.23) the prevalence $y(t)$ converges to 1.

3. Finally, let $\sigma < \delta + \lambda$. Using (1.21) and (1.22), we consider the following cases. If $\lambda < 0$ then $S(t) \to 0$ and $I(t) \to 0$ (since $\sigma - \delta < \lambda < 0$). If $\lambda = 0$ then $S(t) \to S^* := S(0)\,(1 - y(0))^{-\frac{\sigma}{\sigma-\delta}} = S(0)^{1-\frac{\sigma}{\sigma-\delta}} = S(0)^{\frac{\delta}{\delta-\sigma}}$, while $I(t) \to 0$. If $\lambda > 0$ then $S(t) \to \infty$, while the behaviour of $I(t)$ depends on $\sigma - \delta$. In this case, if $\sigma > \delta$ then $I(t) \to \infty$, if $\sigma < \delta$ then $I(t) \to 0$, and if $\sigma = \delta$ then $I(t) \to I^* := I(0)\,(1 - y(0))^{\frac{\sigma}{\lambda}} = I(0)\,(1 - I(0))^{\frac{\sigma}{\lambda}} = I(0)S(0)^{\frac{\sigma}{\lambda}}$. In all of these cases the prevalence $y(t)$ converges to 0 due to (1.23).

We summarize these results in Table 1.1, where we give the steady state to which $(S(t), I(t))$ and the prevalence $y(t)$ converge, depending on the parameter. Conventionally, we consider also ∞ as a steady state.

Case	Subcases	Asymptotics of (S, I)	Prevalence
$\lambda + \delta = \sigma$	$\lambda < \sigma y(0)$	$(0, 0)$	$y(0)$
	$\lambda = \sigma y(0)$	$\big(S(0), \frac{\lambda}{\delta} S(0)\big)$	
	$\lambda > \sigma y(0)$	(∞, ∞)	
$\lambda + \delta < \sigma$	—	$(0, 0)$	1
$\lambda + \delta > \sigma$	$\lambda < 0$	$(0, 0)$	0
	$\lambda = 0$	$(S^*, 0)$	
	$\lambda > 0, \frac{\sigma}{\delta} < 1$	$(\infty, 0)$	
	$\lambda > 0, \frac{\sigma}{\delta} = 1$	(∞, I^*)	
	$\lambda > 0, \frac{\sigma}{\delta} > 1$	(∞, ∞)	

Table 1.1: Asymptotic behaviour of the homogeneous system.

A few remarks follow. If $\lambda + \delta = \sigma$ the prevalence is constant, which is particularly interesting in the case where both $S(t)$ and $I(t)$ tend to infinity.

If $\lambda + \delta < \sigma$, then the prevalence tends to 1, which means that the susceptible individuals become infected "faster" than the infected ones die.

On the other hand, if $\lambda+\delta > \sigma$, then the prevalence goes to zero. This is again particularly interesting in the case where both $S(t)$ and $I(t)$ tend to infinity. In this case, although the total number of infected individuals is unbounded, they eventually make up only a negligible fraction of the total population.

1.4.2 The heterogeneous system

Now, we investigate the asymptotics of the aggregated states $S(t)$ and $I(t)$ of the heterogeneous system (1.4), (1.5), making use of Proposition 1. Also the asymptotics of the weighted prevalence $z(t)$ and the prevalence $y(t)$ will be obtained.

Notice that due to Remark 1 we have $z(t) > 0$, which implies that $F(t) = \int_0^t z(\tau)\,\mathrm{d}\tau$ is strictly increasing.

Define the following sets and numbers:

$$\Omega_+ := \{w \in \Omega : \lambda + \delta > \sigma p(\omega)\}, \qquad S^+(0) := \int_{\Omega_+} S_0(\omega)\,\mathrm{d}\omega,$$

$$\Omega_- := \{w \in \Omega : \lambda + \delta < \sigma p(\omega)\}, \qquad S^-(0) := \int_{\Omega_-} S_0(\omega)\,\mathrm{d}\omega,$$

$$\Omega_0 := \{w \in \Omega : \lambda + \delta = \sigma p(\omega)\}, \qquad S^0(0) := \int_{\Omega_0} S_0(\omega)\,\mathrm{d}\omega.$$

Let us abbreviate $\varphi(t,\omega) := e^{F(t)(\lambda+\delta-\sigma p(\omega))}$. According to Proposition 1 we have

$$\dot{F}(t) \,=\, 1 - \frac{1}{M(0)}\left[\int_{\Omega+} p(\omega)\,\varphi(t,\omega)\,S_0(\omega)\,\mathrm{d}\omega \right. \\ \left. + \int_{\Omega-} p(\omega)\,\varphi(t,\omega)\,S_0(\omega)\,\mathrm{d}\omega + K^0(0)\right], \tag{1.24}$$

where

$$K^0(0) := \int_{\Omega_0} p(\omega)\,S_0(\omega)\,\mathrm{d}\omega.$$

Again from Proposition 1 we have

$$\rho(t) = z(t)\,\psi(F(t)), \quad \text{where } \ \psi(x) := \frac{\int_\Omega p(\omega)e^{-\sigma x\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega e^{-\sigma x\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}. \tag{1.25}$$

A remarkable property of the function ψ is that it is monotonically decreasing, which consequently also applies to $\psi(F(t))$. Indeed, if for any fixed $x \geq 0$ we denote $\Phi(\omega) := e^{-\sigma x\,p(\omega)}S_0(\omega)$, we can represent

$$\psi'(x) = -\sigma\frac{\int_\Omega (p(\omega))^2\,\Phi(\omega)\,\mathrm{d}\omega\,\int_\Omega \Phi(\omega)\,\mathrm{d}\omega - \left(\int_\Omega p(\omega)\,\Phi(\omega)\,\mathrm{d}\omega\right)^2}{\left(\int_\Omega \Phi(\omega)\,\mathrm{d}\omega\right)^2} \,\leq\, 0,$$

where we use the known inequality $\int p^2\,\Phi\,\int\Phi \geq \left(\int p\Phi\right)^2$ for the integral moments of Φ. As a consequence, $\psi^* := \lim_{t\to\infty}\psi(F(t))$ exists and

$$\lim_{t\to\infty}\rho(t) = \lim_{t\to\infty} z(t)\,\psi^*, \tag{1.26}$$

provided that $\lim_{t\to\infty} z(t)$ does exist.

Another preliminary assertion is that the prevalence $y(t) = \frac{I(t)}{S(t)+I(t)}$ satisfies the equation

$$\begin{aligned} \dot{y}(t) \,&=\, \frac{\dot{I}(t)S(t) - I(t)\dot{S}(t)}{(S(t)+I(t))^2} = \frac{\sigma\rho(t)S(t)^2 - \delta I(t)S(t) - (\lambda - \sigma\rho(t))S(t)I(t)}{(S(t)+I(t))^2} \\ &= \sigma\,\rho(t)\,(1-y(t))^2 - (\lambda+\delta-\sigma\rho(t))\,y(t)\,(1-y(t)) \\ &= (1-y(t))\,(\sigma\rho(t) - (\lambda+\delta)\,y(t))\,. \end{aligned} \tag{1.27}$$

We split the analysis of the asymptotic behavior of the heterogeneous system in four basic cases determined by the numbers $S^+(0)$, $S^-(0)$, and $S^0(0)$.

Case 1. $S^+(0) = S^-(0) = 0$.

In this case $S_0(\omega) = 0$ for almost every $\omega \in \Omega_+ \cup \Omega_-$, therefore $p(\omega) = (\lambda+\delta)/\sigma$ for almost every ω for which $S_0(\omega)$ is not zero. Thus, without restricting the generality we can assume that $p(\omega) = (\lambda+\delta)/\sigma$ is constant everywhere, as changing $p(\omega)$ for those ω where $S_0(\omega)$ (and thus $I_0(\omega)$) is zero does not influence the system. This turns the heterogeneous system into a homogeneous one, where σ is replaced by $\tilde{\sigma} := \sigma p(\omega) = \sigma(\lambda+\delta)/\sigma = \lambda+\delta$. The asymptotics in case 1 is presented in the first group of cases in Table 1.1.

Next we consider the following two cases:

Case 2. $S^+(0) = 0$, $S^-(0) > 0$, $S^0(0) > 0$,
Case 3. $S^+(0) = 0$, $S^-(0) > 0$, $S^0(0) = 0$.

In both cases we have from (1.24)

$$\dot{F}(t) = 1 - \frac{1}{M(0)} \left(\int_{\Omega_-} p(\omega)\, \varphi(t,\omega)\, S_0(\omega)\, \mathrm{d}\omega + K^0(0) \right). \tag{1.28}$$

If we assume that $F(\cdot)$ is bounded, then due to its monotonicity it would have a limit, $F_* \geq 0$. Then, having in mind the definition of φ, we obtain that

$$0 = \lim_{t\to\infty} \dot{F}(t) = 1 - \frac{1}{M(0)} \left(\int_{\Omega_-} p(\omega)\, e^{F_*(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\, \mathrm{d}\omega + K^0(0) \right).$$

Since the exponent does not exceed 1, we have

$$0 \geq 1 - \frac{1}{M(0)} \left(\int_{\Omega_-} p(\omega)\, S_0(\omega)\, \mathrm{d}\omega + K^0(0) \right) = 1 - \frac{K(0)}{M(0)} = \frac{J(0)}{M(0)},$$

which is a contradiction (see Remark 1). Thus $F(t) \to \infty$.

Using this last fact we obtain that $\varphi(t,\omega) \to 0$ for $\omega \in \Omega_-$, which implies that the integral in (1.28) converges to zero for $t \to \infty$. Therefore,

$$\lim_{t\to\infty} z(t) = \lim_{t\to\infty} \dot{F}(t) = 1 - \frac{K^0(0)}{M(0)}. \tag{1.29}$$

Here we split the analysis of the two cases. We deal with Case 2 first.
In order to find the limit of $\rho(t)$ we use that $S_0(\omega) = 0$ for almost every $\omega \in \Omega_+$ and that $p(\omega) = (\lambda+\delta)/\sigma$ on Ω_0. Then

$$\begin{aligned} \psi^* &= \lim_{t\to\infty} \frac{\int_{\Omega_-} p(\omega) e^{-\sigma F(t)\, p(\omega)} S_0(\omega)\, \mathrm{d}\omega + \frac{\lambda+\delta}{\sigma} e^{-(\lambda+\delta)F(t)}\, S^0(0)}{\int_{\Omega_-} e^{-\sigma F(t)\, p(\omega)} S_0(\omega)\, \mathrm{d}\omega + e^{-(\lambda+\delta)F(t)}\, S^0(0)} \\ &= \lim_{x\to\infty} \frac{\int_{\Omega_-} p(\omega) e^{(\lambda+\delta-\sigma p(\omega))x}\, S_0(\omega)\, \mathrm{d}\omega + \frac{\lambda+\delta}{\sigma} S^0(0)}{\int_{\Omega_-} e^{(\lambda+\delta-\sigma p(\omega))x}\, S_0(\omega)\, \mathrm{d}\omega + S^0(0)}. \end{aligned}$$

Since $\lambda + \delta - \sigma p(\omega) < 0$ on Ω_-, the two integrals in the last expression converge to zero. We therefore have $\psi^* = (\lambda + \delta)/\sigma$, and due to (1.26) and (1.29)

$$\rho^* := \lim_{t\to\infty} \rho(t) = \left(1 - \frac{K^0(0)}{M(0)}\right) \frac{\lambda + \delta}{\sigma} > 0, \tag{1.30}$$

where the last inequality follows from the fact that $S^-(0) > 0$.

In order to investigate the asymptotics of S we use equation (1.12) to get

$$\begin{aligned} S(t) &= e^{\int_0^t (\lambda - \sigma\rho(\tau))\,\mathrm{d}\tau} S(0) = e^{t\left(\lambda - \frac{\sigma}{t}\int_0^t \rho(\tau)\,\mathrm{d}\tau\right)} S(0) \\ &= e^{t\left(\lambda - \sigma\rho^* + \frac{\sigma}{t}\int_0^t (\rho^* - \rho(\tau))\,\mathrm{d}\tau\right)} S(0). \end{aligned}$$

Since $\frac{\sigma}{t}\int_0^t (\rho^* - \rho(\tau))\,\mathrm{d}\tau$ converges to zero when $t \to \infty$, we obtain that

$$\lim_{t\to\infty} S(t) = \begin{cases} 0 & \text{if } \lambda < \sigma\rho^*, \\ \infty & \text{if } \lambda > \sigma\rho^*. \end{cases}$$

It is obvious from (1.13) that $I(t) \to 0$ for $\lambda < \sigma\rho^*$ and $I(t) \to \infty$ for $\lambda > \sigma\rho^*$. The "critical" case $\lambda = \sigma\rho^*$ requires an additional consideration. We state the result in the following lemma. The proof is given in the appendix.

Lemma 2. *If $\lambda = \sigma\rho^*$ in Case 2, then $S(t)$ converges to some $S^* > 0$ if $\Lambda := \int_{\Omega_-} \frac{S_0(\omega)}{\sigma p(\omega) - \lambda - \delta}\,\mathrm{d}\omega < \infty$. Otherwise $S(t) \to \infty$.*

If Λ is finite then we can use $\rho(t)S(t) \to \rho^* S^*$ and (1.13) to show that $I(t) \to \frac{\sigma\rho^*}{\delta} S^* = \frac{\lambda}{\delta} S^*$. If $\Lambda = \infty$ then $\rho(t)S(t) \to \infty$ and thus also $I(t) \to \infty$.

To analyse the prevalence we first consider the case $\lambda + \delta \leq 0$. Here it is clear from (1.27) that $y(t) \to 1$ due to $\rho^* > 0$. If $\lambda + \delta > 0$ we can rewrite (1.27) as

$$\dot{y}(t) = (\lambda + \delta)(1 - y(t)) \left(\frac{\sigma\rho(t)}{\lambda + \delta} - y(t)\right).$$

If $\lambda + \delta < \sigma\rho^*$ then $\frac{\sigma\rho(t)}{\lambda+\delta} > 1$ for large enough t. Then obviously $y(t) \to 1$. If, on the other hand, $\lambda + \delta \geq \sigma\rho^*$, then $\dot{y}(t)$ is positive if $y(t)$ is smaller than $\frac{\sigma\rho(t)}{\lambda+\delta}$ and negative if it is bigger than that value. From this it is easy to see that $y(t) \to \frac{\sigma\rho^*}{\lambda+\delta}$. Note that these results can be summarised by the formula $y(t) \to \max\left\{\frac{\lambda+\delta}{\sigma\rho^*}, 1\right\}^{-1}$.

We now come to analyzing Case 3.
Here we easily obtain (using (1.29) and $K^0(0) = 0$) that $\sigma\rho^* = \sigma\psi^* \geq \sigma \inf_{\omega\in\Omega_-} p(\omega) \geq \lambda + \delta$. As above we use equation (1.12) to get

$$S(t) = e^{\int_0^t (\lambda - \sigma\rho(\tau))\,\mathrm{d}\tau} S(0) = e^{t\left(\lambda - \sigma\rho^* + \frac{\sigma}{t}\int_0^t (\rho^* - \rho(\tau))\,\mathrm{d}\tau\right)} S(0)$$

where $\frac{\sigma}{t}\int_0^t(\rho^* - \rho(\tau))\,\mathrm{d}\tau$ converges to zero. Because of $\lambda < \lambda + \delta \le \sigma\rho^*$ we get $S(t) \to 0$ and consequently also $I(t) \to 0$.

When analysing the prevalence we again see that for $\lambda + \delta < 0$ we can use (1.27) to get $y(t) \to 1$. If $\lambda + \delta = 0$ an additional argument is needed, which is given in the appendix.

Lemma 3. *If $\lambda + \delta = 0$ in Case 3 then $y(t) \to 1$.*

For $\lambda + \delta > 0$ we can again use the same reasoning as in Case 2 above. Then, due to $\lambda + \delta \le \sigma\rho^*$ we always have $y(t) \to 1$.

Case 4. $S^+(0) > 0$.

If we assume that $F(t) \to \infty$, then the second integral in (1.24) converges to zero, while the first integral converges to $+\infty$. Since $\dot{F}(t) = z(t) \ge 0$, this is a contradiction. Thus $F(t)$ is bounded, and since it is monotonically increasing and strictly positive it has a limit $F^* > 0$. In particular,

$$\lim_{t\to\infty} z(t) = \lim_{t\to\infty} \dot{F}(t) = 0.$$

Then according to (1.26)

$$\lim_{t\to\infty} \rho(t) = \lim_{t\to\infty} z(t)\,\psi^* = 0.$$

Now we investigate the limit F^* of $F(t)$. Passing to the limit in (1.10) we obtain that F^* satisfies the equation

$$\frac{1}{M(0)}\int_\Omega p(\omega)\, e^{F^*(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega = 1. \tag{1.31}$$

The next lemma sates that this equation uniquely determines the value F^*.

Lemma 4. *Equation (1.31) has a unique positive solution.*

Proof. The existence of a solution was obtained above.

Consider the function

$$g(x) := \frac{1}{K(0)+J(0)}\int_\Omega p(\omega)\, e^{x(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega, \quad x \ge 0.$$

Since the function $x \mapsto e^{ax}$ is strictly convex for any $a \ne 0$ and is convex for $a = 0$, and since $p(\omega)\, S_0(\omega) \ge 0$ and the inequality is strict on a subset (of Ω_+) of positive measure, we have that g is strictly convex. Since $g(0) = K(0)/(K(0)+J(0)) < 1$, we conclude that F^* is the unique positive solution of (1.31). □

Now, we investigate the asymptotics. For $S(t)$ this is done easily enough. Using (1.12) and $\rho(t) \to 0$ we have $S(t) \to 0$ for $\lambda < 0$ and $S(t) \to \infty$ for $\lambda > 0$. If $\lambda = 0$ we get from (1.19)

$$S(t) = \int_\Omega e^{-\sigma F(t) p(\omega)} S_0(\omega)\, \mathrm{d}\omega \to \int_\Omega e^{-\sigma F^* p(\omega)} S_0(\omega)\, \mathrm{d}\omega =: S^\star. \tag{1.32}$$

So we have for $\lambda \leq 0$ that $S(t)$ converges to a finite value. Thus, $\rho(t)S(t) \to 0$ which implies $I(t) \to 0$. If $\lambda > 0$, deriving the asymptotics requires additional work. We state the results in the following lemma and refer to the appendix for the proof.

Lemma 5. *Let $\lambda > 0$ in Case 4. Define*

$$\Theta = \frac{M(0)}{\int_\Omega (p(\omega))^2 e^{F^*(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\, \mathrm{d}\omega}.$$

Then

$$\lim_{t\to\infty} I(t) = \begin{cases} 0 & \text{if } \frac{\sigma}{\delta} < \Theta, \\ I^\star & \text{if } \frac{\sigma}{\delta} = \Theta, \\ \infty & \text{if } \frac{\sigma}{\delta} > \Theta, \end{cases}$$

with $I^\star > 0$.

For the prevalence note that in the considered case Ω_+ has a positive measure. From $\lambda + \delta > \sigma p(\omega) > 0$ a.e. on Ω_+ we obtain that $\lambda + \delta > 0$. Since $\rho(t) \to 0$, we see from equation (1.27) that $y(t) \to 0$.

1.4.3 Summary and comparison

Table 1.2 gives for all cases and parameter configurations the asymptotic state (finite or infinite) to which the aggregated solution $(S(t), I(t))$ of the heterogeneous system (1.4), (1.5) and the corresponding prevalence $y(t)$ converge. We also use ρ^* defined by (1.30), S^* and Λ as given in Lemma 2, $S^\star$ as defined in (1.32), and $I^\star$ and Θ referred to in Lemma 5.

We see some obvious similarities between Table 1.1 and Table 1.2. Case 1 is of course itself a homogeneous system with $\lambda + \delta = \sigma$, but Case 2 is also very similar to the same homogeneous system. Once the initial incidence $y(0)$ is replaced by the final aggregated prevalence ρ^* in the differentiation of the sub-cases, the asymptotics are nearly the same. The difference only is that in the critical case $\lambda = \sigma\rho^*$ the heterogeneous system does not necessarily converge to a finite state. Also different is the asymptotic prevalence, which is constant in the homogeneous case, but may take different values in the heterogeneous model.

The cases $\lambda + \delta < \sigma$ and $\lambda + \delta > \sigma$ can be compared to the Cases 3 and 4 respectively. Note that while $S^+(0) = S^0(0) = 0$ implies that $\lambda + \delta < \sigma p(\omega)$ for a.e. ω for which $S_0(\omega) \neq 0$ and the comparison with

Case	Subcases	Asymptotics of (S, I)	Prevalence
$S^+(0) = S^-(0) = 0$: homogeneous case with $\lambda + \delta = \sigma$		see Table 1.1	see Table 1.1
$S^+(0) = 0,\ S^-(0) > 0,\ S^0(0) > 0$	$\lambda < \sigma\rho^*$	$(0, 0)$	$\frac{1}{\max\left\{\frac{\lambda+\delta}{\sigma\rho^*}, 1\right\}}$
	$\lambda = \sigma\rho^*$, $\Lambda < \infty$	$\left(S^*, \frac{\lambda}{\delta}S^*\right)$	
	$\lambda = \sigma\rho^*$, $\Lambda = \infty$	(∞, ∞)	
	$\lambda > \sigma\rho^*$	(∞, ∞)	
$S^+(0) = 0,\ S^-(0) > 0,\ S^0(0) = 0$	—	$(0, 0)$	1
$S^+(0) > 0$	$\lambda < 0$	$(0, 0)$	0
	$\lambda = 0$	$(S^\star, 0)$	
	$\lambda > 0, \frac{\sigma}{\delta} < \Theta$	$(\infty, 0)$	
	$\lambda > 0, \frac{\sigma}{\delta} = \Theta$	$(\infty, I^\star)$	
	$\lambda > 0, \frac{\sigma}{\delta} > \Theta$	(∞, ∞)	

Table 1.2: Asymptotic behaviour of the heterogeneous system

the case $\lambda + \delta < \sigma$ of the homogeneous system is obvious, in Case 4 the inequality $\lambda + \delta < \sigma p(\omega)$ may still hold for a large portion of $\omega \in \Omega$ as $\mu(\Omega_+)$ can be arbitrarily small. Comparing the subcases of Case 4 with those of $\lambda + \delta > \sigma$ of the homogeneous system on the other hand shows a very close connection. The only difference here is that the threshold value for $\frac{\sigma}{\delta}$ that determines whether the infected population dies out or not is changed from 1 to Θ.

The main difference is however that once the parameters λ, σ, δ, and for the heterogeneous system $p(\omega)$, and the initial conditions $S(0)$ and $I(0)$ are fixed, the asymptotic behaviour of the homogeneous system is completely determined. In the heterogeneous system, however, the initial distribution $S_0(\omega)$ can still greatly influence the behaviour. Not only is $S_0(\omega)$ crucial in the definition of the values $S^+(0)$, $S^-(0)$, and $S^0(0)$ and thus in determining which case is at hand, but it (along with $I_0(\omega)$) also plays a role in the definition of ρ^* and Θ, so a difference in the initial distributions may result in a different asymptotic behaviour even though the different initial distributions stay within the same case.

One further aspect that is of interest is the question whether it makes a difference if the disease has a long history at time $t = 0$ (at which the data are given) when comparing the results of the homogeneous and heterogeneous systems. From (1.4) we get

$$\bar{S}(t, \omega) = S_0(\omega)\, e^{-\sigma \int_0^t z(\tau)\, \mathrm{d}\tau p(\omega) + \lambda t} = S_0(\omega)\, e^{-\sigma F(t) p(\omega) + \lambda t}.$$

Thus the proportion between the population sizes of two different h-states is given by

$$\frac{\bar{S}(t, \omega_1)}{\bar{S}(t, \omega_2)} = \frac{S_0(\omega_1)}{S_0(\omega_2)} e^{\sigma F(t)(p(\omega_2) - p(\omega_1))}.$$

We see that in the case $S^+(0) > 0$, where we have $F(t) \to F^*$, this proportion converges to some constant. This shows that the population retains a certain level of heterogeneity for all time.

In the cases where $S^+(0) = 0$ and $S^-(0) > 0$ however we have that $F(t) \to \infty$. Thus this proportion goes to zero whenever $p(\omega_1) > p(\omega_2)$. This implies that asymptotically only the h-state with the lowest value of $p(\omega)$ survives. Thus, in a sense, the population becomes more homogeneous. This, however, does not mean that it can be more closely described by the original homogeneous system. It is more appropriate to say that the homogeneous system more closely resembles the heterogeneous one if σ is changed to σp^* where p^* is the infimum of $p(\omega)$ on Ω or, if this infimum is zero, to a sufficiently small number.

We emphasize that the above results show what information is needed to determine the ultimate state of the system. In particular we see that the final state can in some cases be determined without full knowledge of the initial distribution. For example, if $S^+(0) = S^0(0) = 0$ and $S^-(0) > 0$ then we know that $(S(t), I(t))$ will converge to $(0, 0)$ and the prevalence converges to 1. But this condition is just another way of saying that the set of $\omega \in \Omega$ where both $\lambda + \delta \geq \sigma p(\omega)$ and $S_0(\omega) > 0$ has measure zero. The only information about the function $S_0(\omega)$ that is needed here is its support. And even this information might not be needed in detail (e.g. in the simple case where $\lambda + \delta < \sigma p(\omega)$ for all $\omega \in \Omega$).

In some cases all information about $S_0(\omega)$ is needed. For example, in the case $S^+(0) > 0$, $\lambda > 0$, and $\sigma/\delta = \Theta$ the value Θ can only be calculated with full knowledge of $S_0(\omega)$, and $I^\star$ is only calculable with knowledge of $F(t)$ for all t, for which again $S_0(\omega)$ is needed in detail. However, to verify inequalities like $\sigma/\delta < \Theta$, incomplete information might in some cases suffice.

1.4.4 Numerical examples

The homogeneous SI-model is amongst the simplest epidemiological models. Consequently it is used only as a well understood starting point for the analysis of more complex models. For example, early attempts to understand the transmission of HIV started out by using simple SI-models (see e.g. [23, 81]). Some more recent models for HIV are still recognisable as SI-model, albeit more sophisticated ones using age-structured populations (e.g. [78]) or multiple stages of infection (e.g. [41]). Some diseases in animals have also been modelled using variants of SI-models (e.g. [12, 50]).

Since SI-models are mostly used as baseline models, we will not attempt to capture the exact dynamics of a specific disease. Rather we give some numerical examples to illustrate the effect that different initial distributions $(S_0(\omega), I_0(\omega))$ can have on the asymptotics, although we choose distributions that yield the same cumulative values, i.e. the initial conditions for the aggregated system (1.12)-(1.13) stay the same. Although the parameters used here are of a magnitude suitable for modelling HIV[2], the specific

[2] The force of infection has been studied for example in [17], while parameters for population growth or mortality rates can be found in the internet data repository of the World Health Organisation at `www.who.int`

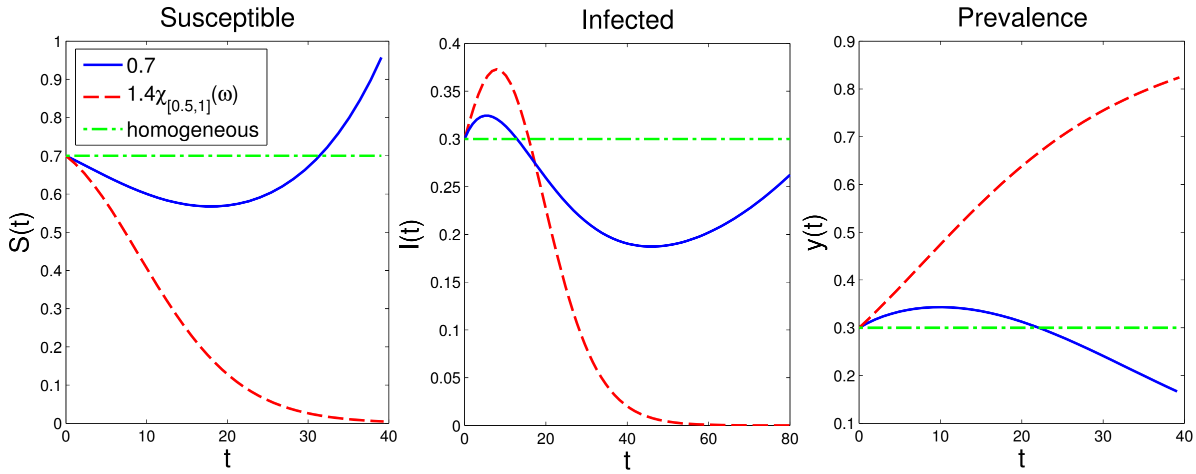

Figure 1.1: Comparison of the trajectories of the system for different choices of $S_0(\omega)$ and the homogeneous system. The solid lines show the results for a constant initial distribution $S_0(\omega) = 0.7$, the dashed lines for $S_0(\omega) = 1.4\chi_{[0.5,1]}(\omega)$. The dash-dotted line represents the solution for the homogeneous system.

values have been chosen to highlight the differences in behaviour due to different choices of the initial conditions.

We first want to show how a different choice of $S_0(\omega)$ can influence the system. As Ω we take the interval $[0, 1]$ and for μ the Lebesgue measure. We set $I_0(\omega) = 0.6\chi_{[0.5,1]}$ where $\chi_{[0.5,1]}$ is the indicator function of the interval $[0.5, 1]$. Further we set $p(\omega) = \frac{1}{2} + \omega$, $\sigma = 0.3$, $\delta = 0.21$, and $\lambda = 0.09$. Note that $\lambda + \delta = \sigma$ and $\lambda = \sigma y(0)$, which means that if the population were homogeneous both $S(t)$ and $I(t)$ would be constant. It is easy to see that with our choice of parameters $\Omega_+ = [0, 0.5)$ and $\Omega_- = (0.5, 1]$. The set Ω_0 consists only of one point and, since $p(\omega)$ is strictly monotonically increasing, is a μ-null set.

Now we look at two different initial distributions $S_0(\omega)$. On the one hand, we consider $S_0(\omega) = 0.7$, on the other $S_0(\omega) = 1.4\chi_{[0.5,1]}(\omega)$. Obviously both cases yield $S(0) = 0.7$. But in the first case $S^+(0) > 0$ while in the second case $S^+(0) = 0$. The results can be seen in Figure 1.1. When $S^+(0) > 0$ the number $S(t)$ of susceptible individuals goes to infinity and since $\frac{\sigma}{\delta} > \Theta$ for our choice of parameters ($\Theta \approx 1.3091$, while $\frac{\sigma}{\delta} \approx 1.4286$), so does $I(t)$. The prevalence, however, still goes to zero. When, on the other hand, we take $S_0(\omega) = 1.4\chi_{[0.5,1]}(\omega)$, we see that both the populations of susceptible and infected individuals go to 0, while the prevalence increases towards 1. As mentioned above, both $S(t)$ and $I(t)$ are constant for the homogeneous system.

A second aspect we want to raise, is the influence of the choice of $I_0(\omega)$. Since $S(0)+I(0) = 1$, the value of $I(0)$ is fixed once $S_0(\omega)$ is chosen. However, the choice of $I_0(\omega)$ still influences $J(0)$. To illustrate the effects different values of $J(0)$ can have on the system we consider the following parameters: Ω, μ,

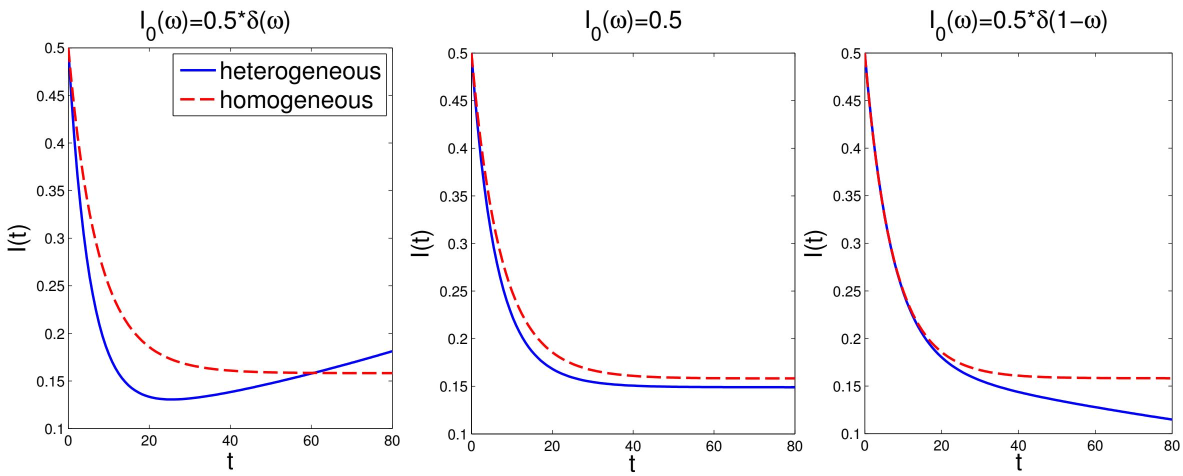

Figure 1.2: Comparison between the trajectories of $I(t)$ for different choices of $I_0(\omega)$ and the homogeneous system. The solution to the heterogeneous system is given by the solid line while the solution for the homogeneous system is represented by the dashed line.

and $p(\omega)$, are chosen as above, while we set $\sigma = 0.2$ and $\delta = 0.2$. We take $S_0(\omega) = 0.5$ to be constant. Thus we are in the case $S^+(0) > 0$ and $S(t)$ always goes towards infinity as long as λ is positive. We now choose λ such that for $I_0(\omega) = 0.5$ we have $\frac{\sigma}{\delta} = \Theta$, which yields $\lambda \approx 0.1145$. Note that $\lambda + \delta > \sigma$, $\lambda > 0$, and $\sigma = \delta$. Thus, in a homogeneous population the population of susceptibles goes to infinity while the population of infected individuals converges. In our heterogeneous case $I(t)$ also converges. We then change $I_0(\omega)$ while keeping all other parameters fixed. We consider the two choices $I_0(\omega) = \frac{1}{2}\delta(\omega)$ and $I_0(\omega) = \frac{1}{2}\delta(1-\omega)$ where $\delta(x)$ is the Dirac delta distribution. Thus $I(0) = 0.5$ for all of these choices while $J(0) = 0.25$ for $I_0(\omega) = \frac{1}{2}\delta(\omega)$ and $J(0) = 0.75$ for $I_0(\omega) = \frac{1}{2}\delta(1-\omega)$ compared to $J(0) = I(0) = 0.5$ for constant $I_0(\omega)$. The results are shown in Figure 1.2. Since $S(t)$ goes to infinity in all of the cases, we restrict ourselves to giving the results for the infected population only. For $I_0(\omega) = 0.5$ we can see the convergence of $I(t)$. If $I_0(\omega) = \frac{1}{2}\delta(\omega)$ then $\frac{\sigma}{\delta} > \Theta$ and $I(t)$ goes to infinity, while for $I_0(\omega) = \frac{1}{2}\delta(1-\omega)$ we get $\frac{\sigma}{\delta} < \Theta$ and $I(t)$ goes towards 0.

1.5 Basic reproduction number

In this section we consider both the homogeneous and the heterogeneous model assuming that $\lambda = 0$, which means that the population has a fixed size if a disease is not present.

We use the definition of the basic reproduction number R_0 as given in [31] where it is defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. The importance of this number lies in the threshold criterion which says that a disease can invade the population if $R_0 > 1$ and can not invade if $R_0 < 1$.

In the homogeneous model the basic reproduction number R_0^{hom} is given by $\frac{\sigma}{\delta}$ (see for example [29]). This is due to the fact that a single infected individual in an otherwise completely susceptible population has on average σ infectious contacts per unit of time and a life expectancy of $\frac{1}{\delta}$. In order to define a basic reproduction number for the heterogeneous system we use the following result obtained in [31].

Theorem 1. *Let $S(\omega)$ denote the density function of susceptibles describing the steady demographic state in the absence of the disease. Let $A(\tau, \zeta, \omega)$ be the expected infectivity of an individual which was infected τ units of time ago, while having h-state ω towards a susceptible which has h-state ζ. Assume that*

$$\int_0^\infty A(\tau, \zeta, \omega) \, \mathrm{d}\tau = a(\zeta) b(\omega).$$

Then the basic reproduction number R_0 for the heterogeneous system is given by

$$R_0 = \int_\Omega a(\omega) b(\omega) S(\omega) \, \mathrm{d}\omega.$$

In our heterogeneous system the initial condition $S_0(\omega)$ is, in the absence of any infected individuals, a steady state due to $\lambda = 0$. To derive an expression for the infectivity $A(\tau, \zeta, \omega)$ we note that σ denotes the strength of infection. The value $p(\omega)$ influences the number of contacts an individual has. Then the chance of an infectious contact between the infective ω individual and a specific ζ individual is given by $\sigma p(\omega) \frac{p(\zeta)}{\int_\Omega p(\xi) S_0(\xi) \, \mathrm{d}\xi}$. The infectivity of an individual is constant for its whole lifespan. In the absence of susceptible individuals the equation for the infected is given by $\dot{I}(t) = -\delta I(t)$, which suggests that the probability that an infected individual is still alive at time t is given by $e^{-\delta t}$. Thus $A(\tau, \zeta, \omega)$ is given by $\sigma p(\omega) \frac{p(\zeta)}{\int_\Omega p(\xi) S_0(\xi) \, \mathrm{d}\xi} e^{-\delta \tau}$. We have

$$\int_0^\infty A(\tau, \zeta, \omega) \, \mathrm{d}\tau = \int_0^\infty \sigma p(\omega) \frac{p(\zeta)}{\int_\Omega p(\xi) S_0(\xi) \, \mathrm{d}\xi} e^{-\delta \tau} \, \mathrm{d}\tau = \frac{\sigma}{\delta} \frac{p(\zeta)}{\int_\Omega p(\xi) S_0(\xi) \, \mathrm{d}\xi} p(\omega)$$

and thus

$$R_0 = \frac{\sigma}{\delta} \frac{\int_\Omega p(\omega)^2 S_0(\omega) \, \mathrm{d}\omega}{\int_\Omega p(\omega) S_0(\omega) \, \mathrm{d}\omega}.$$

Note that if $p(\omega) \equiv 1$, i.e. we are dealing with the homogeneous system, then $R_0 = \frac{\sigma}{\delta}$ as before.

Assume now that a fraction of the population is already infected. Since $\lambda = 0$, the population of infected individuals dies out in both models. Also, the population of susceptibles is strictly decreasing. An important question is whether the population of susceptible individuals also goes extinct or if some individuals remain uninfected.

For the homogeneous model this question can be answered immediately from Table 1.1.

Proposition 2. *If the basic reproduction number $R_0^{hom} = \frac{\sigma}{\delta}$ of the homogeneous model satisfies the inequality $R_0^{hom} \geq 1$ then the population of susceptible individuals dies out. If $R_0^{hom} < 1$ then a part, $S^* = S(0)^{\frac{\delta}{\delta-\sigma}}$, of the initial population stays uninfected.*

Note that S^* as given here is the same as in Table 1.1.

Similarly we can use Table 1.2 to get the following result for the heterogeneous model.

Proposition 3. *Define*

$$R^* = \frac{\sigma}{\delta} \operatorname*{essinf}_{\omega \in \Gamma} p(\omega) = \frac{\sigma}{\delta} \sup_{\substack{B \subseteq \Gamma \\ \mu(B)=0}} \inf_{\omega \in \Gamma \setminus B} p(\omega),$$

where $\Gamma = \{\omega \in \Omega : S_0(\omega) \neq 0\}$. If $R^* \geq 1$ then the population of susceptible individuals dies out. If $R^* < 1$ then a part, $S^\star = \int_\Omega e^{-\sigma F^* p(\omega)} S_0(\omega)\,\mathrm{d}\omega$, of the initial population stays uninfected, where F^* is the unique positive solution of the equation

$$\int_\Omega p(\omega) e^{F^*(\delta - \sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega = M(0).$$

Proof If $R^* \geq 1$ then $\frac{\sigma}{\delta} p(\omega) \geq 1$ almost everywhere on Γ. This means that $\mu(\Gamma \cap \Omega_+) = 0$ which implies $S^+(0) = 0$. If $R^* < 1$ then there is a set $A \subseteq \Gamma$ with positive measure on which $\frac{\sigma}{\delta} p(\omega) < 1$. Hence, $\mu(\Gamma \cap \Omega_+) > 0$ and $S^+(0) > 0$. Then the conclusions of the proposition in both cases follow from Table 1.2. The statement about F^* is proven in Lemma 4. $\square$

Note that $R_0 = \frac{\sigma}{\delta} \frac{\int_\Omega p(\omega)^2 S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega p(\omega) S_0(\omega)\,\mathrm{d}\omega} \geq \frac{\sigma}{\delta} \operatorname*{essinf}_{\omega \in \Gamma} p(\omega) \frac{\int_\Omega p(\omega) S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega p(\omega) S_0(\omega)\,\mathrm{d}\omega} = R^*$. This also shows that $R_0 = R^*$ if and only if $p(\omega)$ is constant a.e. on Γ.

The above proposition exhibits an important difference between the homogeneous and heterogeneous model, which is that the indicator that determines whether the population dies out or not is in the homogeneous case given by the basic reproduction number R_0^{hom}, while in the heterogeneous case this indicator is R^* which in general is different from R_0.

In the homogeneous model a disease that can invade the population is characterised by $R_0^{hom} > 1$, hence it kills the whole population by Proposition 2. This is no longer necessarily the case in the heterogeneous model. Instead we encounter the following three possibilities:

- $1 \leq R^* \leq R_0$: the disease leads to an outbreak and $S(t) \to 0$,
- $R^* < 1 \leq R_0$: the disease leads to an outbreak and $S(t) \to S^\star$,
- $R^* \leq R_0 < 1$: the disease does not lead to an outbreak and $S(t) \to S^\star$.

1.6 Concluding remarks and perspectives

In this paper we show within a simple 2-dimensional distributed (SI) model how the asymptotic behaviour of a disease in a heterogeneous population depends on the distribution of the population among the space of heterogeneity (the h-distribution). The analysis is based on the fact that for this particular distributed model it is possible to obtain a 3-dimensional ODE model that exactly reproduces the evolution of the aggregated susceptible and infected individuals. The latter model involves only a few averaged characteristics of the h-distribution. We show that the asymptotic behaviour of the disease qualitatively depends on these characteristics and describe it comprehensively.

On the other hand, the information about the h-distribution of the population is usually scarce and uncertain. Moreover, the results in this paper are obtained under restrictive conditions in a model that is simplistic, anyway. As mentioned in the introduction, this analysis should be viewed as a baseline for more complex studies. In particular, we envisage two lines of further research indicated below. Both lines may involve distributed modes of dimension 3 or 4 with much richer structure than the one considered in the present paper.

1. The uncertainty in the h-distribution of the population gives rise to a tube of possible aggregated state-trajectories. The sections of this tube at any given time instant provides a set-membership estimation of the state of the disease, which is independent of the particular realizations of the uncertainties. To obtain numerically such set-estimations is tractable by involvement of known methods in the optimal control theory, and this is our next goal.

2. A second line of ongoing research involves distributed prevention control, which influences the transmission rate of the disease, but is costly. Using the technique of optimal sparse control one may address the following question: to which risk groups (in terms of the h-distribution of the population) should the prevention be allocated and how this allocation evolves with time. The results in [34] suggest that the answer critically depends on the current state of the disease. It turns out that the optimal allocation of prevention (with respect to reasonable intertemporal criteria) might vary from most risky to least risky groups. The necessary numerical analysis is tractable for much more complicated models as the one considered in this paper.

The results in this paper will conveniently serve as a benchmark case for testing the results of each of the investigations mentioned above, since the asymptotics are precisely known in this case.

Appendix

Proof of Lemma 1. Differentiating (1.3) we obtain

$$
\begin{aligned}
y'(t) &= \frac{\mathrm{d}}{\mathrm{d}t}\frac{I(t)}{S(t)+I(t)} = \frac{\dot{I}(t)S(t) - I(t)\dot{S}(t)}{(S(t)+I(t))^2} \\
&= \frac{\sigma y(t)S(t)^2 - \delta I(t)S(t) + \sigma y(t)S(t)I(t) - \lambda S(t)I(t)}{(S(t)+I(t))^2} \\
&= \sigma y(t)(1-y(t))^2 - \delta y(t)(1-y(t)) + \sigma y(t)^2(1-y(t)) - \lambda y(t)(1-y(t)) \\
&= \left(y(t) - y(t)^2\right)(\sigma - \delta - \lambda)\,.
\end{aligned}
$$

This is a Bernoulli equation and its solution is given by (1.23).

From (1.1) we have

$$
S(t) = S(0)e^{-\int_0^t \sigma y(s)\,\mathrm{d}s + \lambda t}.
$$

Simple calculations give that

$$
\int_0^t y(s)ds = t - \frac{\ln(y(t))}{\sigma-\delta-\lambda} + \frac{\ln(y(0))}{\sigma-\delta-\lambda},
$$

thus

$$
e^{\int_0^t -\sigma y(s)ds} = y(0)^{-\frac{\sigma}{\sigma-\delta-\lambda}}\, y(t)^{\frac{\sigma}{\sigma-\delta-\lambda}}\, e^{-\sigma t}.
$$

Then using (1.23) we have

$$
\begin{aligned}
S(t) &= S(0)\, y(0)^{-\frac{\sigma}{\sigma-\delta-\lambda}}\, y(t)^{\frac{\sigma}{\sigma-\delta-\lambda}}\, e^{(\lambda-\sigma)t} \\
&= S(0)\, y(0)^{-\frac{\sigma}{\sigma-\delta-\lambda}} \left(e^{-(\sigma-\delta-\lambda)t}\left(y(0)^{-1}-1\right)+1\right)^{-\frac{\sigma}{\sigma-\delta-\lambda}} e^{(\lambda-\sigma)t} \\
&= S(0)\left(1 - y(0) + y(0)\, e^{(\sigma-\delta-\lambda)t}\right)^{-\frac{\sigma}{\sigma-\delta-\lambda}} e^{\lambda t}.
\end{aligned}
$$

Considering

$$
\begin{aligned}
\frac{I(t)}{S(t)} &= \frac{\frac{I(t)}{S(t)+I(t)}}{\frac{S(t)}{S(t)+I(t)}} = \frac{y(t)}{1-y(t)} = \\
&= \frac{1}{\left(e^{-(\sigma-\delta-\lambda)t}\left(y(0)^{-1}-1\right)+1\right)\left(1 - \frac{1}{e^{-(\sigma-\delta-\lambda)t}(y(0)^{-1}-1)+1}\right)} \\
&= \frac{1}{e^{-(\sigma-\delta-\lambda)t}\left(y(0)^{-1}-1\right)} = \frac{e^{(\sigma-\delta-\lambda)t}}{y(0)^{-1}-1} = e^{(\sigma-\delta-\lambda)t}\frac{y(0)}{1-y(0)} \\
&= e^{(\sigma-\delta-\lambda)t}\frac{I(0)}{S(0)},
\end{aligned}
$$

we get

$$I(t) = S(t)\frac{I(t)}{S(t)} = I(0)y(0)^{-\frac{\sigma}{\sigma-\delta-\lambda}}y(t)^{\frac{\sigma}{\sigma-\delta-\lambda}}e^{-\delta t}$$
$$= I(0)\left(1 + y(0)e^{(\sigma-\delta-\lambda)t} - y(0)\right)^{-\frac{\sigma}{\sigma-\delta-\lambda}} e^{(\sigma-\delta)t}.$$

□

Proof of Lemma 2. On the assumptions of the lemma and in view of (1.12), $S(t)$ is given by

$$S(t) = S(0)\, e^{\int_0^t (\lambda-\sigma\rho(\tau))\,\mathrm{d}\tau} = S(0)\, e^{\sigma\int_0^t (\rho^*-\rho(\tau))\,\mathrm{d}\tau}.$$

We split the integral

$$\int_0^t (\rho^* - \rho(\tau))\,\mathrm{d}\tau = \int_0^t (z^*\psi^* - z(\tau)\psi(F(\tau)))\,\mathrm{d}\tau$$
$$= \int_0^t (z^* - z(\tau))\,\psi^*\,\mathrm{d}\tau + \int_0^t z(\tau)\left(\psi^* - \psi(F(\tau))\right)\,\mathrm{d}\tau$$

in two parts and denote them by $\mathrm{Int}_1(t)$ and $\mathrm{Int}_2(t)$ respectively.

Using (1.28), (1.29) and the definition of φ we have

$$\mathrm{Int}_1(t) = \frac{\psi^*}{M(0)}\int_0^t\int_{\Omega_-} p(\omega)\, e^{F(\tau)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau$$

From this we can see that $\mathrm{Int}_1(t)$ is monotonically increasing. It remains to see whether it is bounded or not. Observe that for $\omega \in \Omega_-$ the function $\varphi(\cdot,\omega)$ is strictly decreasing. Then (1.28) implies that $\dot{F}(t)$ is strictly increasing. Hence, $F(t) > t\dot{F}(0) = tz(0)$ for $t > 0$ and we get

$$\begin{aligned}
\mathrm{Int}_1(t) &= \frac{\psi^*}{M(0)}\int_0^t\int_{\Omega_-} p(\omega)\, e^{F(\tau)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau \\
&< \frac{\psi^*}{M(0)}\int_0^t\int_{\Omega_-} p(\omega)\, e^{z(0)\tau(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau \\
&= \frac{\psi^*}{M(0)z(0)}\int_{\Omega_-} p(\omega)\frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega \\
&\le \frac{\psi^*\sup_{\omega\in\Omega_-} p(\omega)}{M(0)z(0)}\int_{\Omega_-}\frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega.
\end{aligned}$$

Since $\dot{F}(t) = z(t) < 1$, which implies that $F(t) < t$, we have that

$$
\begin{aligned}
\mathrm{Int}_1(t) \geq \mathrm{Int}_1(tz(0)) &= \frac{\psi^*}{M(0)} \int_0^{tz(0)} \int_{\Omega_-} p(\omega)\, e^{F(\tau)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau \\
&> \frac{\psi^*}{M(0)} \int_0^{tz(0)} \int_{\Omega_-} p(\omega)\, e^{\tau(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau \\
&= \frac{\psi^*}{M(0)} \int_{\Omega_-} p(\omega) \frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega \\
&\geq \frac{\psi^* \inf_{\omega\in\Omega_-} p(\omega)}{M(0)} \int_{\Omega_-} \frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega.
\end{aligned}
$$

Notice that $\inf\limits_{\omega\in\Omega_-} p(\omega) > (\lambda+\delta)/\sigma = \rho^* \left(1 - \frac{K^0(0)}{M(0)}\right)^{-1} > 0$. Then the above two inequalities for $\mathrm{Int}_1(t)$ show that $\mathrm{Int}_1(t)$ converges if and only if the integral $\int_{\Omega_-} \frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega$ is bounded in t. Since the exponent under the integral converges to zero when $t \to \infty$, we obviously have

$$
\lim_{t\to\infty} \mathrm{Int}_1(t) < \infty \iff \int_{\Omega_-} \frac{S_0(\omega)}{\sigma p(\omega)-\lambda-\delta}\,\mathrm{d}\omega < \infty.
$$

Now, we investigate $\mathrm{Int}_2(t)$. Since we know that $\psi(\cdot)$ is decreasing and $F(\cdot)$ is increasing, we have that $\psi^* - \psi(F(t)) \leq 0$. Thus $\mathrm{Int}_2(t)$ is monotonically decreasing. In order to prove that it converges we estimate it using that $z(t) \leq 1$, $\psi^* = \frac{\lambda+\delta}{\sigma}$, and the definition of $\psi(\cdot)$ in (1.25):

$$
\begin{aligned}
|\mathrm{Int}_2(t)| &\leq \int_0^t \left| \frac{\lambda+\delta}{\sigma} - \frac{\int_\Omega p(\omega) e^{-\sigma F(\tau)\, p(\omega)} S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega e^{-\sigma F(\tau)\, p(\omega)} S_0(\omega)\,\mathrm{d}\omega} \right| \mathrm{d}\tau \\
&= \int_0^t \left| \frac{\lambda+\delta}{\sigma} - \frac{\int_{\Omega_-} p(\omega) e^{(\lambda+\delta-\sigma p(\omega))F(\tau)}\, S_0(\omega)\,\mathrm{d}\omega + \frac{\lambda+\delta}{\sigma} S^0(0)}{\int_{\Omega_-} e^{(\lambda+\delta-\sigma p(\omega))F(\tau)}\, S_0(\omega)\,\mathrm{d}\omega + S^0(0)} \right| \mathrm{d}\tau \\
&= \int_0^t \left| \frac{\int_{\Omega_-} \left(\frac{\lambda+\delta}{\sigma} - p(\omega)\right) e^{(\lambda+\delta-\sigma p(\omega))F(\tau)}\, S_0(\omega)\,\mathrm{d}\omega}{\int_{\Omega_-} e^{(\lambda+\delta-\sigma p(\omega))F(\tau)}\, S_0(\omega)\,\mathrm{d}\omega + S^0(0)} \right| \mathrm{d}\tau.
\end{aligned}
$$

Using again that $F(t) > \dot{F}(0)t$ we obtain that

$$
\begin{aligned}
|\mathrm{Int}_2(t)| &\leq \frac{1}{S^0(0)} \int_0^t \int_{\Omega_-} \left| \frac{\lambda+\delta}{\sigma} - p(\omega) \right| e^{(\lambda+\delta-\sigma p(\omega))z(0)\tau}\, S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}\tau \\
&= \frac{1}{\sigma z(0) S^0(0)} \int_{\Omega_-} (\sigma p(\omega)-\lambda-\delta) \frac{1-e^{-tz(0)(\sigma p(\omega)-\lambda-\delta)}}{\sigma p(\omega)-\lambda-\delta} S_0(\omega)\,\mathrm{d}\omega \\
&\leq \frac{\int_{\Omega_-} S_0(\omega)\,\mathrm{d}\omega}{\sigma z(0) S^0(0)} = \frac{S^-(0)}{\sigma z(0) S^0(0)}.
\end{aligned}
$$

Thus $\mathrm{Int}_2(t)$ converges. Consequently $\mathrm{Int}_1(t) + \mathrm{Int}_2(t)$ converges if $\mathrm{Int}_1(t)$ converges and we have

$$
S(t) = S(0) e^{\sigma \int_0^t (\rho^* - \rho(\tau))\,\mathrm{d}\tau} \to S^* < \infty, \tag{1.33}
$$

(with some strictly positive number S^*), provided that $\int_{\Omega_-} \frac{S_0(\omega)}{\sigma p(\omega)-\lambda-\delta}\,\mathrm{d}\omega < \infty$. Otherwise $S(t) \to \infty$. $\square$

Proof of Lemma 3 Since $\lambda + \delta = 0$ we have from (1.27)

$$\dot{y}(t) = (1 - y(t))\sigma\rho(t).$$

The solution to this ODE is

$$y(t) = e^{-\sigma \int_0^t \rho(\tau)\,\mathrm{d}\tau}(y(0) - 1) + 1.$$

We see that

$$\lim_{t\to\infty} y(t) = 1 \Longleftrightarrow \int_0^\infty \rho(t)\,\mathrm{d}t = \infty.$$

We remind that due to $S^+(0) = S^0(0) = 0$ and the fact that $\varphi(t,\omega)$ is decreasing on Ω_-, we have from (1.28) that $\dot{F}(t)$ is increasing. Then

$$\rho(t) = \dot{F}(t)\psi(F(t)) \geq \dot{F}(0)\psi(F(t)) = z(0)\psi(F(t)).$$

On the other hand,

$$\rho(t) = \dot{F}(t)\psi(F(t)) = z(t)\psi(F(t)) \leq \psi(F(t)).$$

Then

$$\lim_{t\to\infty} y(t) = 1 \Longleftrightarrow \int_0^\infty \psi(F(t))\,\mathrm{d}t = \infty.$$

Since $\psi(x)$ is decreasing and $F(t) \leq t$, we have $\psi(F(t)) \geq \psi(t)$. Thus

$$\begin{aligned}
\int_0^\infty \psi(F(t))\,\mathrm{d}t \geq \int_0^\infty \psi(t)\,\mathrm{d}t &= \int_0^\infty \frac{\int_\Omega p(\omega)e^{-\sigma t\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega e^{-\sigma t\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}\,\mathrm{d}t \\
&= \int_0^\infty \frac{-\frac{1}{\sigma}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega e^{-\sigma t\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}{\int_\Omega e^{-\sigma t\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega}\,\mathrm{d}t \\
&= -\frac{1}{\sigma}\int_0^\infty \frac{\mathrm{d}}{\mathrm{d}t}\ln\left(\int_\Omega e^{-\sigma t\,p(\omega)}S_0(\omega)\,\mathrm{d}\omega\right)\,\mathrm{d}t \\
&= -\frac{1}{\sigma}\ln(0) + \frac{1}{\sigma}\ln(S(0)) = \infty.
\end{aligned}$$

$\square$

Proof of Lemma 5. In order to obtain the asymptotics of $I(t)$ we shall use equation (1.13). We have to determine the asymptotic behaviour of the term $\rho(t)S(t)$, where we have $\rho(t) \to 0$ and $S(t) \to \infty$. Using (1.11) and (1.19) we get

$$\rho(t)S(t) = \dot{F}(t)e^{\lambda t} \int_\Omega p(\omega)e^{-F(t)\sigma p(\omega)} S_0(\omega)\,\mathrm{d}\omega.$$

Since $\int_\Omega p(\omega)e^{-F(t)\sigma p(\omega)} S_0(\omega)\,\mathrm{d}\omega$ converges, we only need to consider the asymptotic behaviour of the term $\dot{F}(t)e^{\lambda t}$. Differentiating $\dot{F}(t)$ as given in (1.10) and using (1.10) again yields

$$\ddot{F}(t) = (\lambda+\delta)(\dot{F}(t))^2 - \left((\lambda+\delta) - \frac{\sigma}{M(0)} \int_\Omega (p(\omega))^2 e^{F(t)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\right)\dot{F}(t).$$

We now write

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\dot{F}(t)e^{\lambda t}\right) = \ddot{F}(t)e^{\lambda t} + \dot{F}(t)\lambda e^{\lambda t} = \dot{F}(t)e^{\lambda t}\left(\frac{\ddot{F}(t)}{\dot{F}(t)} + \lambda\right).$$

Integrating this equation for $\dot{F}(t)e^{\lambda t}$ and using the above expression for $\ddot{F}(t)$ we obtain that

$$\begin{aligned}
\dot{F}(t)e^{\lambda t} &= \dot{F}(0)e^{\int_0^t \left[(\lambda+\delta)\dot{F}(\tau) - \left((\lambda+\delta) - \frac{\sigma}{M(0)}\int_\Omega (p(\omega))^2 e^{F(\tau)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\right) + \lambda\right]\mathrm{d}\tau} \\
&= \dot{F}(0)e^{(\lambda+\delta)F(t) + \int_0^t \left[\frac{\sigma}{M(0)}\int_\Omega (p(\omega))^2 e^{F(\tau)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega - \delta\right]\mathrm{d}\tau}.
\end{aligned}$$

Since $F(t)$ converges we need to consider only the integral in the exponent. The first term in the integrand converges to $\sigma\Theta^{-1}$. Thus, if $\delta > \sigma\Theta^{-1}$ then $\dot{F}(t)e^{\lambda t}$ converges to zero and consequently $I(t) \to 0$. Analogously, $I(t) \to \infty$ if $\delta < \sigma\Theta^{-1}$. This leaves the case $\delta = \sigma\Theta^{-1}$. Here we have

$$\begin{aligned}
&\int_0^\infty \frac{\sigma}{M(0)}\left[\int_\Omega (p(\omega))^2 e^{F(t)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega - \delta\right]\mathrm{d}t \\
&= \int_0^\infty \left[\frac{\sigma}{M(0)}\int_\Omega (p(\omega))^2 e^{F(t)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega \right. \\
&\qquad \left. - \frac{\sigma}{M(0)}\int_\Omega (p(\omega))^2 e^{F^*(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega\right]\mathrm{d}t \\
&= \frac{\sigma}{M(0)}\int_0^\infty \int_\Omega (p(\omega))^2 e^{F^*(\lambda+\delta-\sigma p(\omega))}\left(e^{(\lambda+\delta-\sigma p(\omega))(F(t)-F^*)} - 1\right) S_0(\omega)\,\mathrm{d}\omega\,\mathrm{d}t \\
&= \frac{\sigma}{M(0)}\int_\Omega (p(\omega))^2 e^{F^*(\lambda+\delta-\sigma p(\omega))}\int_0^\infty \left[e^{(\lambda+\delta-\sigma p(\omega))(F(t)-F^*)} - 1\right]\mathrm{d}t\, S_0(\omega)\,\mathrm{d}\omega.
\end{aligned}$$

Using de l'Hospital's rule we get

$$\begin{aligned}
\lim_{t\to\infty} \frac{\ln(\dot{F}(t))}{-t} &= \lim_{t\to\infty} -\frac{\ddot{F}(t)}{\dot{F}(t)} \\
&= \lim_{t\to\infty} -(\lambda+\delta)\dot{F}(t) \\
&\quad + \left((\lambda+\delta) - \frac{\sigma}{M(0)} \int_\Omega (p(\omega))^2 e^{F(t)(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega \right) \\
&= (\lambda+\delta) - \frac{\sigma}{M(0)} \int_\Omega (p(\omega))^2 e^{F^*(\lambda+\delta-\sigma p(\omega))} S_0(\omega)\,\mathrm{d}\omega \\
&= \lambda+\delta-\sigma\Theta^{-1} = \lambda > 0
\end{aligned}$$

This shows that $\ln(\dot{F}(t))$ declines asymptotically linear. Thus $\dot{F}(t) = e^{\ln(\dot{F}(t))}$ goes to zero faster than e^{-ct} for some $c > 0$. Because of the equation $\lim\limits_{t\to\infty} \frac{\dot{F}(t)}{F(t)-F^*} = \lim\limits_{t\to\infty} \frac{\ddot{F}(t)}{\dot{F}(t)} = -\lambda$ we can therefore conclude that $F(t) - F^*$ goes to zero faster than de^{-ct} for some constants d and c. From this it follows that the integral $\int_0^\infty \left[e^{(\lambda+\delta-\sigma p(\omega))(F(t)-F^*)} - 1\right] \mathrm{d}t$ converges and due to the fact that $p(\omega)$ is bounded the convergence is uniform in ω. Consequently $\rho(t)S(t)$ also converges, which implies $I(t) \to I^\star < \infty$. $\square$

Chapter 2

Aggregation of general *SI*-models

2.1 Introduction

The analysis of the heterogeneous SI-model in Chapter 1 is based on the fact that, due to the specific form of the equations, it is possible to formulate an ODE model for the aggregated variables with the aid of auxiliary functions that can be calculated independently. We will now show that for a class of heterogeneous SI-models with parametric heterogeneity it is always possible to find an equivalent finite dimensional ODE model. Due to their simpler structure these models are more suited for certain tasks.

Since no information gets lost in this transformation between models, the finite dimensional model still contains information about the distributed original state. Furthermore, parameters that depend on the variable of heterogeneity are still present. Since exact knowledge of the initial condition for the heterogeneous system is in practice often not available, they have to be estimated from data. By including this estimation into the model formulation we will for certain systems be able to get rid of the remaining expressions depending on the heterogeneity by introducing scalar parameters to be estimated from data.

In Section 2.2 we present the general model and the ODE model for its aggregated states. In Section 2.3 we consider an existing model from the literature and apply the results from Section 2.2. As mentioned above, in Section 2.4 we will include estimation of initial conditions into the model. Finally, in Section 2.5 we show how the equations for the aggregated states can be used to considerably simplify optimal control problems where the state equations are given by a heterogeneous SI-model.

2.2 General model

We consider SI-models of the following type:

$$\begin{aligned} \dot{\bar{S}}(t,\omega) &= \bar{S}(t,\omega) f_1(t,\omega,G(t),H(t)), \quad \bar{S}(0,\omega) = S_0(\omega), \\ \dot{\bar{I}}(t,\omega) &= \bar{I}(t,\omega) f_2(t,G(t),H(t)) + \bar{S}(t,\omega) f_3(t,\omega,G(t),H(t)), \quad \bar{I}(0,\omega) = I_0(\omega), \end{aligned} \tag{2.1}$$

where the functions f_k are of the form

$$f_k(t,\omega,G(t),H(t)) = \sum_{i=1}^{m_k} u_{ki}(t,G(t),H(t))p_{ki}(\omega),$$

with given functions u_{ki} and p_{ki} ($p_{2i}(\omega) = 1$ for all i), and $G(t) = (G_1(t),\ldots,G_m(t))$ and $H(t) = (H_1(t),\ldots,H_n(t))$ are aggregated variables of the form

$$G_j(t) = \int_\Omega g_j(\omega)\bar{S}(t,\omega)\,\mathrm{d}\omega \quad \text{and} \quad H_j(t) = \int_\Omega h_j(\omega)\bar{I}(t,\omega)\,\mathrm{d}\omega.$$

We will assume that all functions here are integrable and that the system (2.1) has a unique solution that is a.e. measurable.

First note that the solution of the equation for the susceptible population can be written as

$$\bar{S}(t,\omega) = S_0(\omega)e^{\int_0^t f_1(\tau,\omega,G(\tau),H(\tau))\,\mathrm{d}\tau}.$$

Furthermore we get for the variables that are weighted averages of the susceptible population that

$$\begin{aligned}
\dot{G}_j(t) &= \frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega g_j(\omega)\bar{S}(t,\omega)\,\mathrm{d}\omega = \int_\Omega g_j(\omega)\dot{\bar{S}}(t,\omega)\,\mathrm{d}\omega = \int_\Omega g_j(\omega)\bar{S}(t,\omega)f_1(t,\omega,G(t),H(t))\,\mathrm{d}\omega \\
&= \int_\Omega g_j(\omega)\bar{S}(t,\omega)\sum_{i=1}^{m_1} u_{1i}(t,G(t),H(t))p_{1_i}(\omega)\,\mathrm{d}\omega \\
&= \sum_{i=1}^{m_1} u_{1i}(t,G(t),H(t))\int_\Omega g_j(\omega)p_{1i}(\omega)\bar{S}(t,\omega)\,\mathrm{d}\omega \\
&= \sum_{i=1}^{m_1} u_{1i}(t,G(t),H(t))\int_\Omega g_j(\omega)p_{1i}(\omega)S_0(\omega)e^{\int_0^t \sum_{l=1}^{m_1} u_{1l}(\tau,G(\tau),H(\tau))p_{1l}(\omega)\,\mathrm{d}\tau}\,\mathrm{d}\omega \\
&= \sum_{i=1}^{m_1} u_{1i}(t,G(t),H(t))\int_\Omega g_j(\omega)p_{1i}(\omega)S_0(\omega)e^{\sum_{l=1}^{m_1} A_l(t)p_{1l}(\omega)}\,\mathrm{d}\omega,
\end{aligned}$$

where the auxiliary functions A_i are defined through the differential equations

$$\dot{A}_i(t) = u_{1i}(t,G(t),H(t)), \quad A_i(0) = 0.$$

Similarly, for weighted averages of $I(t,\omega)$ we get

$$\begin{aligned}
\dot{H}_j(t) &= \int_\Omega h_j(\omega)\dot{\bar{I}}(t,\omega)\,\mathrm{d}\omega = \int_\Omega h_j(\omega)\bar{I}(t,\omega)f_2(t,G(t),H(t)) + \bar{S}(t,\omega)f_3(t,\omega,G(t),H(t))\,\mathrm{d}\omega \\
&= f_2(t,G(t),H(t))H_j(t) + \sum_{i=1}^{m_3} u_{3_i}(t,G(t),H(t))\int_\Omega h_j(\omega)p_{3_i}(\omega)S_0(\omega)e^{\sum_{l=1}^{m_1} A_l(t)p_{1_l}(\omega)}\,\mathrm{d}\omega.
\end{aligned}$$

Thus, these variables (which w.l.o.g. include $S(t)$ and $I(t)$ by adding the functions $g_j(\omega) = 1$ and $h_j(\omega) = 1$) can be described by a set of ODEs that only depend on other aggregated variables.

Note that the last equation is the reason why $f_2(t, G(t), H(t))$ is not allowed to depend on ω. Since $\bar{I}(t, \omega)$ does not allow a simple representation like $\bar{S}(t, \omega)$, any dependence of f_2 on ω would make it impossible to reformulate the integral term so that it is only dependent on aggregated variables.

We summarise these findings in the following theorem.

Theorem 2. *The aggregated variables of system (2.1) are described by the ODE system*

$$
\begin{aligned}
\dot{G}_r(t) &= \sum_{i=1}^{m_1} u_{1i}(t, G(t), H(t)) \int_\Omega g_r(\omega) p_{1i}(\omega) S_0(\omega) e^{\sum_{l=1}^{m_1} A_l(t) p_{1l}(\omega)} \, \mathrm{d}\omega, \quad G_r(0) = \int_\Omega g_r(\omega) S_0(\omega) \mathrm{d}\omega, \\
\dot{H}_s(t) &= f_2(t, G(t), H(t)) H_s(t) \\
&\quad + \sum_{i=1}^{m_3} u_{3i}(t, G(t), H(t)) \int_\Omega h_s(\omega) p_{3i}(\omega) S_0(\omega) e^{\sum_{l=1}^{m_1} A_l(t) p_{1_l}(\omega)} \, \mathrm{d}\omega, \quad H_s(0) = \int_\Omega h_s(\omega) I_0(\omega) \mathrm{d}\omega, \\
\dot{A}_j(t) &= u_{1j}(t, G(t), H(t)), \qquad A_j(0) = 0.
\end{aligned}
\tag{2.2}
$$

2.3 Example

We now want to apply the result of the previous section to an existing model. The following equations are taken from [107] where they are used to model the spreading of the human immunodeficiency virus (HIV):

$$
\begin{aligned}
\dot{\bar{S}}(t, \omega) &= -\sigma p(\omega) \frac{J(t)}{K(t) + J(t)} \bar{S}(t, \omega) + \lambda(S(t), I(t)) \bar{S}(t, \omega) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)} \bar{S}(t, \omega), \\
\dot{\bar{I}}(t, \omega) &= \sigma p(\omega) \frac{J(t)}{K(t) + J(t)} \bar{S}(t, \omega) - \delta(S(t), I(t)) \bar{I}(t, \omega), \\
S(t) &= \int_\Omega \bar{S}(t, \omega) \, \mathrm{d}\omega, \\
I(t) &= \int_\Omega \bar{I}(t, \omega) \, \mathrm{d}\omega, \\
K(t) &= \int_\Omega p(\omega) \bar{S}(t, \omega) \, \mathrm{d}\omega, \\
J(t) &= \int_\Omega \kappa p(\omega) \bar{I}(t, \omega) \, \mathrm{d}\omega, \\
&\bar{S}(0, \omega) = S_0(\omega), \quad \bar{I}(0, \omega) = I_0(\omega).
\end{aligned}
\tag{2.3}
$$

The meaning of the parameters is as in Chapter 1; the additional parameter γ denotes the inflow rate of susceptible individuals resulting from the infected population, and κ is a positive constant describing the difference in the average risk for infected individuals in contrast to susceptible individuals.

This model clearly is an example of the general system (2.1). We identify

$$
\begin{aligned}
&u_{11}(t, K(t), J(t)) = -\sigma \frac{J(t)}{K(t)+J(t)}, && p_{11} = p(\omega),\\
&u_{12}(t, S(t), I(t)) = \lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)}, && p_{12} = 1,\\
&u_{2}(t, S(t), I(t)) = -\delta(S(t), I(t)), && p_{2} = 1,\\
&u_{3}(t, K(t), J(t)) = \sigma \frac{J(t)}{K(t)+J(t)}, && p_{3} = p(\omega),\\
&g_1(\omega) = 1, \quad g_2(\omega) = p(\omega), &&\\
&h_1(\omega) = 1, \quad h_2(\omega) = \kappa p(\omega). &&
\end{aligned}
$$

Using Theorem 2.2 the equations for the auxiliary variables $A_1(t)$ and $A_2(t)$ become

$$
\begin{aligned}
\dot{A}_1(t) &= -\sigma \frac{J(t)}{K(t)+J(t)},\\
\dot{A}_2(t) &= \lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)}.
\end{aligned}
$$

Note that $\bar{S}(t,\omega)$ can be described by

$$
\bar{S}(t,\omega) = S_0(\omega) e^{\int_0^t -\sigma p(\omega) \frac{J(\tau)}{K(\tau)+J(\tau)} + \lambda(S(\tau), I(\tau)) + \gamma(S(\tau), I(\tau)) \frac{I(\tau)}{S(\tau)} \, \mathrm{d}\tau} = S_0(\omega) e^{A_1(t) p(\omega) + A_2(t)}.
$$

Using this together with Theorem 2.2 the equation for $S(t)$ becomes

$$
\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{K(t)+J(t)} \int_\Omega p(\omega) S_0(\omega) e^{A_1(t) p(\omega) + A_2(t)} \, \mathrm{d}\omega\\
&\quad + \left(\lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)} \right) \int_\Omega S_0(\omega) e^{A_1(t) p(\omega) + A_2(t)} \, \mathrm{d}\omega\\
&= -\sigma \frac{J(t)}{K(t)+J(t)} \int_\Omega p(\omega) \bar{S}(t,\omega) \, \mathrm{d}\omega + \left(\lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)} \right) \int_\Omega \bar{S}(t,\omega) \, \mathrm{d}\omega\\
&= -\sigma \frac{J(t)}{K(t)+J(t)} K(t) + \left(\lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)} \right) S(t).
\end{aligned}
$$

The other three equations can be dealt with in the same way. The final equations are then given by

$$
\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{K(t)+J(t)} K(t) + \lambda(S(t), I(t))S(t) + \gamma(S(t), I(t))I(t), \\
\dot{I}(t) &= \sigma \frac{J(t)}{K(t)+J(t)} K(t) - \delta(S(t), I(t))I(t) \\
\dot{K}(t) &= -\sigma \frac{J(t)}{K(t)+J(t)} e^{A_2(t)} \int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)} S_0(\omega)\mathrm{d}\omega + \left(\lambda(S(t),I(t)) + \gamma(S(t),I(t)) \frac{I(t)}{S(t)}\right) K(t) \\
\dot{J}(t) &= \sigma \frac{J(t)}{K(t)+J(t)} e^{A_2(t)} \kappa \int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)} S_0(\omega)\, \mathrm{d}\omega - \delta(S(t), I(t))J(t), \\
\dot{A}_1(t) &= -\sigma \frac{J(t)}{K(t)+J(t)}, \\
\dot{A}_2(t) &= \lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)},
\end{aligned}
$$

supplemented with the appropriate initial conditions. For A_1 and A_2 this initial conditions are known to be 0. The initial conditions for S and I are the total number of infected and susceptible individuals in the population, a quantity that is reasonably well known in many situations. The quantities $K(0)$ and $J(0)$ can be calculated from the initial conditions of the distributed system. If they are not known, it seems prudent to estimate just these two values instead of the whole distributions. But since $S_0(0, \omega)$ still appears in the equations one cannot help but estimate at least this one initial condition.

2.4 Parametrising initial conditions and removing integration

For the heterogeneous system to be well determined we need to know the initial conditions $S_0(\omega)$ and $I_0(\omega)$. In practice these functions are often not known exactly. One way to deal with this problem is to assume that the initial conditions belong to a family of functions described by a small number of parameters and estimate this parameters by fitting the model to actual data. This problem persists when we deal with the ODE system for the aggregated variables, as they generally include integral terms containing $S_0(\omega)$. However, in some special cases a specific family of parametrised function may be used to get rid of the integral terms in the equations.

We will continue with the example of the previous section under three additional assumptions:

1. $\Omega = [0, \infty)$,
2. $p(\omega) = \omega$,
3. $f(\omega) = \frac{S_0(\omega)}{S(0)}$ is the probability density function of a generalized inverse Gaussian distribution.

ad 1.) The interval choice is necessitated by the family of functions under considerations. Other intervals can be considered for different choices.
ad 2.) We will restrict ourselves to the case $p(\omega) = \omega$ and $q(\omega) = \kappa\omega$ for some $\kappa \in \mathbb{R}$. Letting $p(\omega)$ and $q(\omega)$ take a more general form would only complicate notation. Furthermore, every important aspect of the calculation is already included when considering this easy functional form.
ad 3.) Since the integral over $\frac{S_0(\omega)}{S(0)}$ is 1 we can treat it as a probability density function $f(\omega)$. This can be interpreted as the distribution of the trait ω amongst the initial susceptible population $S(0)$. The generalized inverse Gaussian distribution is a distribution with three parameters $a > 0$, $b > 0$, and $c \in \mathbb{R}$. Its probability density function is

$$f(\omega) = \frac{\left(\frac{a}{b}\right)^{\frac{c}{2}}}{2K_c(\sqrt{ab})}\omega^{c-1}e^{-\frac{a\omega}{2}-\frac{b}{2\omega}}$$

with parameters a, b, and c, where K_c is the modified Bessel function of second kind, i.e.

$$\begin{aligned} I_\alpha(x) =& \sum_{m=0}^{\infty} \frac{1}{m!\Gamma(m+\alpha+1)}\left(\frac{x}{2}\right)^{2m+\alpha}, \\ K_\alpha(x) =& \frac{\pi}{2}\frac{I_{-\alpha}(x) - I_\alpha(x)}{\sin(\alpha\pi)}. \end{aligned}$$

The moments of a generalized inverse Gaussian with parameters a, b, and p are given by

$$\mathbb{E}[\omega^n] = \left(\frac{b}{a}\right)^{\frac{n}{2}} \frac{K_{c+n}(\sqrt{ab})}{K_c(\sqrt{ab})}.$$

The generalized inverse Gaussian is a very general distribution and includes for example the Wald and Gamma distributions as special or limit cases.

Using these two assumptions turns our system into

$$\begin{aligned} \dot{S}(t) &= -\sigma\frac{J(t)}{K(t)+J(t)}K(t) + \lambda(S(t),I(t))S(t) + \gamma(S(t),I(t))I(t), \\ \dot{I}(t) &= \sigma\frac{J(t)}{K(t)+J(t)}K(t) - \delta(S(t),I(t))I(t), \\ \dot{K}(t) &= -\sigma\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}S(0)\int_\Omega \omega^2 e^{A_1(t)\omega}f(\omega)\,\mathrm{d}\omega + \left(\lambda(S(t),I(t)) + \gamma(S(t),I(t))\frac{I(t)}{S(t)}\right)K(t), \\ \dot{J}(t) &= \sigma\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}S(0)\kappa\int_\Omega \omega^2 e^{A_1(t)\omega}f(\omega)\,\mathrm{d}\omega - \delta(S(t),I(t))J(t), \\ \dot{A}_1(t) &= -\sigma\frac{J(t)}{K(t)+J(t)}, \\ \dot{A}_2(t) &= \lambda(S(t),I(t)) + \gamma(S(t),I(t))\frac{I(t)}{S(t)}. \end{aligned}$$

We will look more closely at the integral term. We can rewrite it as

$$
\begin{aligned}
\int_\Omega \omega^2 e^{A_1(t)\omega} f(\omega) d\omega &= \int_\Omega \omega^2 e^{A_1(t)\omega} \frac{\left(\frac{a}{b}\right)^{\frac{c}{2}}}{2K_c(\sqrt{ab})} \omega^{c-1} e^{-\frac{a\omega}{2} - \frac{b}{2\omega}} d\omega \\
&= \int_\Omega \omega^2 \frac{\left(\frac{a}{b}\right)^{\frac{c}{2}}}{2K_c(\sqrt{ab})} \omega^{c-1} e^{\left(A_1(t) - \frac{a}{2}\right)\omega - \frac{b}{2\omega}} d\omega \\
&= \int_\Omega \omega^2 \frac{\left(\frac{a}{b}\right)^{\frac{c}{2}}}{2K_c(\sqrt{ab})} \omega^{c-1} e^{\frac{(2A_1(t) - a)\omega}{2} - \frac{b}{2\omega}} d\omega \\
&= \frac{a^{\frac{c}{2}} 2K_c(\sqrt{(a - 2A_1(t))b})}{(a - 2A_1(t))^{\frac{c}{2}} 2K_c(\sqrt{ab})} \int_\Omega \omega^2 \frac{\left(\frac{a - 2A_1(t)}{b}\right)^{\frac{c}{2}}}{2K_c(\sqrt{(a - 2A_1(t))b})} \omega^{c-1} e^{-\frac{(a - 2A_1(t))\omega}{2} - \frac{b}{2\omega}} d\omega.
\end{aligned}
$$

We now see that the integral in the last term can be interpreted as the second moment of generalized inverse Gaussian distribution with the parameters $a - 2A_1(t)$, b, and c. We therefore get

$$
\begin{aligned}
\int_\Omega \omega^2 e^{A_1(t)\omega} f(\omega) d\omega &= \frac{a^{\frac{c}{2}} 2K_c(\sqrt{(a - 2A_1(t))b})}{(a - 2A_1(t))^{\frac{c}{2}} 2K_c(\sqrt{ab})} \frac{b}{a - 2A_1(t)} \frac{K_{c+2}(\sqrt{(a - 2A_1(t))b})}{K_c(\sqrt{(a - 2A_1(t))b})} \\
&= \frac{a^{\frac{c}{2}} b}{(a - 2A_1(t))^{\frac{c}{2}+1}} \frac{K_{c+2}(\sqrt{(a - 2A_1(t))b})}{K_c(\sqrt{ab})}.
\end{aligned}
$$

Putting this in our model yields the following system

$$
\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{K(t) + J(t)} K(t) + \lambda(S(t), I(t)) S(t) + \gamma(S(t), I(t)) I(t), \\
\dot{I}(t) &= \sigma \frac{J(t)}{K(t) + J(t)} K(t) - \delta(S(t), I(t)) I(t), \\
\dot{K}(t) &= -\sigma \frac{J(t)}{K(t) + J(t)} e^{A_2(t)} S(0) \frac{a^{\frac{c}{2}} b}{(a - 2A_1(t))^{\frac{c}{2}+1}} \frac{K_{c+2}(\sqrt{(a - 2A_1(t))b})}{K_c(\sqrt{ab})}, \\
&\quad + \left(\lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)} \right) K(t), \\
\dot{J}(t) &= \sigma \frac{J(t)}{K(t) + J(t)} e^{A_2(t)} S(0) \kappa \frac{a^{\frac{c}{2}} b}{(a - 2A_1(t))^{\frac{c}{2}+1}} \frac{K_{c+2}(\sqrt{(a - 2A_1(t))b})}{K_c(\sqrt{ab})} - \delta(S(t), I(t)) J(t), \\
\dot{A}_1(t) &= -\sigma \frac{J(t)}{K(t) + J(t)}, \\
\dot{A}_2(t) &= \lambda(S(t), I(t)) + \gamma(S(t), I(t)) \frac{I(t)}{S(t)}.
\end{aligned}
$$

This model now depends on the parameters a, b, and c, as well as $S(0)$, $I(0)$, and $J(0)$ (the value $K(0)$ can be calculated with the knowledge of a, b, c, and $S(0)$), which can be estimated from data.

2.5 Optimal control

In this section we use the aggregation of the SI-model to deal with the following optimal control problem.

$$F(u,v) = \int_0^T h(t, S(t), I(t))dt + g(S(T), I(T)) \to \max \tag{2.4}$$

where

$$\begin{aligned}
\dot{\bar{S}}(t,\omega) &= -\sigma\phi_1(u(t))p(\omega)\frac{J(t)}{K(t)+J(t)}\bar{S}(t,\omega) + \lambda(S(t),I(t))\bar{S}(t,\omega) + \gamma(S(t),I(t))\frac{I(t)}{S(t)}\bar{S}(t,\omega),\\
\dot{\bar{I}}(t,\omega) &= \sigma\phi_1(u(t))p(\omega)\frac{J(t)}{K(t)+J(t)}\bar{S}(t,\omega) - \delta(S(t),I(t))\phi_2(v(t))\bar{I}(t,\omega),\\
S(t) &= \int_\Omega \bar{S}(t,\omega)\,\mathrm{d}\omega,\\
I(t) &= \int_\Omega \bar{I}(t,\omega)\,\mathrm{d}\omega,\\
K(t) &= \int_\Omega p(\omega)\bar{S}(t,\omega)\,\mathrm{d}\omega,\\
J(t) &= \int_\Omega \kappa p(\omega)\bar{I}(t,\omega)\,\mathrm{d}\omega,\\
&\bar{S}(0,\omega) = S_0(\omega), \quad \bar{I}(0,\omega) = I_0(\omega).
\end{aligned} \tag{2.5}$$

The functions $h : [0,T]\times\mathbb{R}_{\geq 0}\times\mathbb{R}_{\geq 0} \to \mathbb{R}$ and $g : \mathbb{R}_{\geq 0}\times\mathbb{R}_{\geq 0} \to \mathbb{R}$ together with the partial derivatives h_I, h_S, g_I, and g_S are Lipschitz continuous in (S,I) and, in the case of h, measurable in t for every (S,I). The functions $\phi_1 : [0,c_1] \to [0,1]$ and $\phi_2 : [0,c_2] \to [0,1]$ are continuously differentiable and strictly monotonically decreasing. As controls $u(t)$ and $v(t)$ we allow measurable functions from $[0,T]$ to $[0,c_1]$ and $[0,c_2]$ respectively.

The system (2.5) is the same as (2.3) except for the two functions ϕ_1 and ϕ_2. The function $\phi_1(u)$ is attached to the strength of infection σ. It measures to what fraction of σ the strength of infection is reduced to if an effort u is taken. That ϕ_1 is strictly monotonically decreasing reflects that an increased effort u leads to a decrease in σ. The function $\phi_2(v)$ has a similar interpretation with respect to the mortality rate $\delta(S,I)$.

If the cost function h depended on the distributed variables $\bar{S}(t,\omega)$ and $\bar{I}(t,\omega)$, then we would have to deal with the infinite dimensional system (2.5). However, since we assume that h depends only on the aggregated states $S(t)$ and $I(t)$ we can calculate these states using the finite dimensional set of ODEs for the aggregated states. The presence of the two functions ϕ_1 and ϕ_2 does not influence the derivations of the aggregated system in section 2.3, so these equations are

$$
\begin{aligned}
\dot{S}(t) &= -\sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}K(t) + \lambda(S(t),I(t))S(t) + \gamma(S(t),I(t))I(t),\\
\dot{I}(t) &= \sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}K(t) - \delta(S(t),I(t))\phi_2(v(t))I(t),\\
\dot{K}(t) &= -\sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega,\\
&\quad + \left(\lambda(S(t),I(t)) + \gamma(S(t),I(t))\frac{I(t)}{S(t)}\right)K(t),\\
\dot{J}(t) &= \sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\kappa\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega - \delta(S(t),I(t))\phi_2(v(t))J(t),\\
\dot{A}_1(t) &= -\sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)},\\
\dot{A}_2(t) &= \lambda(S(t),I(t)) + \gamma(S(t),I(t))\frac{I(t)}{S(t)},
\end{aligned}
\tag{2.6}
$$

together with the initial conditions

$$
\begin{aligned}
S(0) &= \int_\Omega S_0(\omega)\,\mathrm{d}\omega, & I(0) &= \int_\Omega I_0(\omega)\,\mathrm{d}\omega,\\
K(0) &= \int_\Omega p(\omega)S_0(\omega)\,\mathrm{d}\omega, & J(0) &= \int_\Omega \kappa p(\omega)I_0(\omega)\,\mathrm{d}\omega,\\
A_1(0) &= 0, & A_2(0) &= 0.
\end{aligned}
$$

The resulting problem (2.4), (2.6) is a standard optimal control system. There is a large amount of literature for such problems (e.g. [67]). With the short notation $x(t) = (S(t), I(t), R(t), J(t), L(t), K(t))$ and $f(t, x(t), u(t), v(t)) = \dot{x}(t)$, the Hamiltonian for this problem is

$$H(t, x, \eta, u) = \langle \eta, f(x, u, t)\rangle + h(t, x).$$

According to Pontryagin's Maximum Principle, a necessary condition for $(x^*(t), v^*(t), u^*(t))$ to be optimal is the existence of an absolutely continuous function $\eta(t)$ such that

$$
\begin{aligned}
H'_x(t, x^*(t), \eta(t), u^*(t), v^*(t)) &= -\dot{\eta}(t), \quad \eta(T) = g_x(x^*(T)),\\
\max_{(u,v)\in[0,c_1]\times[0,c_2]} H(t, x^*(t), \eta(t), u, v) &= H(t, x^*(t), \eta(t), u^*(t), v^*(t)).
\end{aligned}
$$

For writing out the adjoint equations we assume that λ, γ and δ are constant and not dependent on $S(t)$ or $I(t)$. These assumptions significantly simplifies the equations for η_1 and η_2. In this case the adjoint equations become

$$
\begin{aligned}
\dot{\eta}_1(t) &= \eta_1(t)\lambda - \eta_3(t)\gamma\frac{I(t)}{S(t)^2}K(t) - \eta_6(t)\gamma\frac{I(t)}{S(t)^2} + h'_S(t,x(t)),\\
\dot{\eta}_2(t) &= \eta_1(t)\gamma - \eta_2(t)\delta\phi_2(v(t)) + \eta_3(t)\gamma\frac{K(t)}{S(t)} + \eta_6(t)\gamma\frac{1}{S(t)} + h'_I(t,x(t)),\\
\dot{\eta}_3(t) &= \sigma\phi_1(u(t))\frac{J(t)}{(K(t)+J(t))^2}\Bigg(-\eta_1(t)J(t) + \eta_2(t)J(t)\\
&\qquad +(\eta_3(t)-\eta_4(t)\kappa)e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega + \eta_5(t)\Bigg) + \eta_3(t)\left(\lambda + \gamma\frac{I(t)}{S(t)}\right),\\
\dot{\eta}_4(t) &= \sigma\phi_1(u(t))\frac{K(t)}{(K(t)+J(t))^2}\Bigg(-\eta_1(t)K(t) + \eta_2(t)K(t)\\
&\qquad -(\eta_3(t)-\eta_4(t)\kappa)e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega - \eta_5(t)\Bigg) - \eta_4(t)\delta\phi_2(v(t)),\\
\dot{\eta}_5(t) &= -\left(\eta_3(t)-\eta_4(t)\kappa\right)\sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\int_\Omega p(\omega)^3 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega,\\
\dot{\eta}_6(t) &= -\left(\eta_3(t)-\eta_4(t)\kappa\right)\sigma\phi_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)\,\mathrm{d}\omega.
\end{aligned}
$$

In the following we want to identify $u^*(t)$ and $v^*(t)$. Note that here we again allow the parameters λ, γ, and δ to be dependent on $S(t)$ and $I(t)$. We calculate

$$
\begin{aligned}
H'_u(t,x(t),\eta(t),u(t),v(t)) =& -\eta_1(t)\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}K(t) + \eta_2(t)\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}K(t)\\
& - \eta_3(t)\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)d\omega\\
& + \eta_4(t)\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}e^{A_2(t)}\int_\Omega \kappa p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)d\omega\\
& - \eta_5(t)\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}\\
=& \;\sigma\phi'_1(u(t))\frac{J(t)}{K(t)+J(t)}\Bigg(-\eta_1(t)K(t) + \eta_2(t)K(t)\\
& -(\eta_3(t)-\eta_4(t)\kappa)e^{A_2(t)}\int_\Omega p(\omega)^2 e^{A_1(t)p(\omega)}S_0(\omega)d\omega - \eta_5\Bigg),
\end{aligned}
$$

and then define a function $\theta_1(t,x(t),\eta(t))$ by $H'_u(t,x(t),\eta(t),u(t)) = \phi'_1(u(t))\theta_1(t,x(t),\eta(t))$. Similarly we calculate

$$
H'_v(t,x(t),\eta(t),u(t),v(t)) = -\phi'_2(v(t))\delta(S,I)\left(\eta_2(t)I(t) + \eta_4(t)J(t)\right)
$$

and define a function $\theta_2(t,x(t),\eta(t))$ by $H'_v(t,x(t),\eta(t),u(t)) = \phi'_2(u(t))\theta_2(t,x(t),\eta(t))$. Assuming that neither $\theta_1(t,x(t),\eta(t))$ nor $\theta_2(t,x(t),\eta(t))$ is equal to 0 on an interval of positive length, we see that due to the fact that $\phi_1'(t)$ and $\phi_2'(t)$ are never zero the optimal control is of Bang-Bang type and given by

$$(u^*(t), v^*(t)) = \begin{cases} (0,0) & \theta_1(t,x(t),\eta(t)),\ \theta_2(t,x(t),\eta(t)) > 0, \\ (c_1,0) & \theta_1(t,x(t),\eta(t)) < 0,\ \theta_2(t,x(t),\eta(t)) > 0, \\ (0,c_2) & \theta_1(t,x(t),\eta(t)) > 0,\ \theta_2(t,x(t),\eta(t)) < 0, \\ (c_1,c_2) & \theta_1(t,x(t),\eta(t)),\ \theta_2(t,x(t),\eta(t)) < 0. \end{cases}$$

To find out whether there are any singular arcs, i.e. one of the functions θ_1 or θ_2 becomes zero on an interval of positive length, one would need to further study the adjoint equations. Due to the complex nature of these equations we will not do this.

We will consider the same model again with a small change in the control constraints. We assume that $c_1 = c_2$ and add the constraint that $u(t) + v(t) \le c$. In particular the two controls cannot be chosen independently of each other. One possible interpretation for such a constraint is that u and v are allocations to prevention and treatment of the disease out of a common budget.

The control constraints can be summarised as

$$g(u(t), v(t)) \ge 0, \quad \text{where} \quad g(u,v) = (u, v, c - u - v).$$

In this case, additionally to the necessary conditions above, a further necessary condition for an optimal control is the existence of a function $\mu(t) = (\mu_1(t), \mu_2(t), \mu_3(t))$ which satisfies

$$\begin{aligned} H_u'(t,x(t),\eta(t),u(t),v(t)) + \langle \mu(t), g_u(t)\rangle &= 0, \\ H_v'(t,x(t),\eta(t),u(t),v(t)) + \langle \mu(t), g_v(t)\rangle &= 0, \\ \mu_1(t), \mu_2(t), \mu_3(t) &\ge 0, \\ \langle \mu(t), g(t)\rangle &= 0. \end{aligned}$$

This means

$$\begin{aligned} H_u'(t,x(t),\eta(t),u(t),v(t)) + \mu_1(t) - \mu_3(t) &= 0, \\ H_v'(t,x(t),\eta(t),u(t),v(t)) + \mu_2(t) - \mu_3(t) &= 0, \\ \mu_1(t)u(t) &= 0, \\ \mu_2(t)v(t) &= 0, \\ \mu_3(t)(c - u(t) - v(t)) &= 0. \end{aligned}$$

We now want to give $(u^*(t), v^*(t))$ again as a function dependent on $x(t)$ and $\eta(t)$. We fix a $t \in [0,T]$ and suppress the dependence of the functions on the variables to simplify notation. First, we assume that $u^* + v^* < c$. Then $\mu_3 = 0$. Since H_u' and H_v' are never zero μ_1 and μ_2 must be non-zero too, which

means that $(u^*, v^*) = (0, 0)$. Furthermore μ_1 is non-negative. So for $H'_u + \mu_1$ to be zero, H'_u must be negative, i.e. $\theta_1 > 0$. Similarly we get $\theta_2 > 0$. Now conversely consider the case that both θ_1 and θ_2 are positive. Assume that $u^* > 0$. Then $\mu_1 = 0$ and we have $H'_u = \mu_3$. But because of $\theta_1 > 0$ we have $H'_u < 0$ while $\mu_3 \geq 0$. Thus u^* cannot be positive. Analogous reasoning shows that v^* must also be zero. Thus, the three statements $u^* + v^* < c$, $(u^*, v^*) = (0, 0)$, and $\theta_1, \theta_2 > 0$ are equivalent.
Next, consider the case $\theta_1 < 0$ and $\theta_2 > 0$. We know that $u^* + v^* = c$. Assume that $v^* > 0$. Then $\mu_2 = 0$ and $H'_v = \mu_3$. Since H'_v is negative this is a contradiction. We get that $(u^*, v^*) = (c, 0)$. The case $\theta_1 > 0$ with $\theta_2 <$ can be dealt with similarly and yields $(u^*, v^*) = (0, c)$.
So far we have

$$(u^*(t), v^*(t)) = \begin{cases} (0,0) & \theta_1(t, x(t), \eta(t)), \theta_2(t, x(t), \eta(t)) > 0, \\ (c,0) & \theta_1(t, x(t), \eta(t)) < 0, \theta_2(t, x(t), \eta(t)) > 0, \\ (0,c) & \theta_1(t, x(t), \eta(t)) > 0, \theta_2(t, x(t), \eta(t)) < 0. \end{cases}$$

It remains to determine $(u^*(t), v^*(t))$ in the case $\theta_1(t, x(t), \eta(t)), \theta_2(t, x(t), \eta(t)) < 0$. The values $(u^*, v^*) = (0, c)$ or $= (c, 0)$ are possible candidates. If u^* and v^* are both greater than 0, we get $\mu_1 = \mu_2 = 0$ and thus

$$H'_u = \mu_3,$$
$$H'_v = \mu_3,$$

which implies

$$H'_u = H'_v.$$

So possible candidates for $(u^*(t), v^*(t))$ are $(0, c)$, $(c, 0)$, and all positive solutions of the system

$$\begin{aligned} \phi'_1(u(t))\theta_1(t, x(t), \eta(t)) &= \phi'_2(v(t))\theta_2(t, x(t), \eta(t)), \\ u + v &= c. \end{aligned} \tag{2.7}$$

The actual value of $(u^*(t), v^*(t))$ is the candidate that gives the biggest value for the Hamiltonian. We define

$$\tilde{H}(t, x, \eta, u, v) = \phi_1(u)\theta_1(t, x, \eta) + \phi_2(v)\theta_2(t, x, \eta),$$

which contains all terms of the Hamiltonian that depend on the controls u and v. Thus maximising H with respect to u and v is equivalent to maximising $\tilde{H}$ with respect to u and v. To decide between the two candidate values $(0, c)$ and $(c, 0)$ we can reformulate the condition to maximise the Hamiltonian as follows:

$$\begin{aligned} & \tilde{H}(t, x, \eta, c, 0) > \tilde{H}(t, x, \eta, 0, c) \\ \Leftrightarrow \quad & \phi_1(c)\theta_1(t, x, \eta) + \phi_2(0)\theta_2(t, x, \eta) > \phi_1(0)\theta_1(t, x, \eta) + \phi_2(c)\theta_2(t, x, \eta) \\ \Leftrightarrow \quad & \theta_1(t, x, \eta)\left(\phi_1(c) - \phi_1(0)\right) > \theta_2(t, x, \eta)\left(\phi_2(c) - \phi_2(0)\right) \\ \Leftrightarrow \quad & \frac{\theta_1(t, x, \eta)}{\theta_2(t, x, \eta)} > \frac{\phi_2(c) - \phi_2(0)}{\phi_1(c) - \phi_1(0)}. \end{aligned}$$

The larger one of these two values then has to be compared to any possible solution of (2.7). We now mention two cases where this comparison can be done analytically. We assume that ϕ_1 and ϕ_2 are both twice continuously differentiable and concave, at least one of them strictly concave. Using the relation $u + v = c$ we can write $\tilde{H}$ as dependent on only one of the control variables,

$$\tilde{H}(t, x, \eta, u) = \phi_1(u)\theta_1(t, x, \eta) + \phi_2(c - u)\theta_2(t, x, \eta).$$

Then

$$\begin{aligned} \frac{d}{du}\tilde{H} &= \phi_1'(u)\theta_1(t, x, \lambda) - \phi_2'(c - u)\theta_2(t, x, \lambda), \\ \frac{d^2}{du^2}\tilde{H} &= \phi_1''(u)\theta_1(t, x, \lambda) + \phi_2''(c - u)\theta_2(t, x, \lambda). \end{aligned}$$

We see that the solutions of 2.7 are the extremals of $\tilde{H}$ with respect to u. But due to the concavity of ϕ_1 and ϕ_2 the second derivative is positive, and any solution of (2.7) therefore minimises the Hamiltonian. The optimal control is therefore given by one of the values $(c, 0)$ or $(0, c)$.

For the second case assume that ϕ_1 and ϕ_2 are both twice continuously differentiable and convex, at least one of them strictly convex. The same argument as before shows now that any solution of (2.7) maximises the Hamiltonian. It is also easy to see that $\tilde{H}$ is strictly concave in u, so any solution is unique and the Hamiltonian at this point bigger than at the boundaries. If (2.7) has a solution, this solution also gives the optimal control value. If there is no solution to control is given by one of the boundary values $(c, 0)$ or $(0, c)$.

We conclude that by exchanging the infinite dimensional optimal control problem (2.4), (2.5) with the finite dimensional problem (2.4), (2.6) we can identify the optimal control (u, v) as a function of x and η which are given by a finite dimensional system of ODEs. Solving the optimal control problem then reduces to solving the boundary value problem given by the state and adjoint equations. We see that the key advantages of taking this approach are twofold: firstly, using the aggregated system allows us to apply Pontryagin's maximum principle in its standard form without deriving it for an infinite dimensional ODE system; and secondly the resulting finite dimensional ODE system is numerically easier to handle than the infinite dimensional system (finding the solution analytically will in general not be possible).

2.6 Conclusions

We have shown that for a large class of SI-models with parametric heterogeneity the dynamics of the aggregated states can be described by a finite dimensional ODE system. The information about the initial conditions of the heterogeneous system is still necessary, however under some assumptions the system can be described by a finite number of parameters which can then be estimated from data.

The ODE system can also be useful if the model is to be used in context with other considerations, as we have shown for the case where the heterogeneous system forms the state equations in an optimal control problem. Furthermore, this system is easier to handle for numerical procedures since standard methods for solving ODEs can be used.

Given these advantages, it would be of interest to develop similar aggregation techniques for more complex models. Since we relied in our derivation on the simple structure of SI-models, we cannot expect such result for general classes of complex dynamics. However, in special cases such aggregation techniques might be applicable.

Chapter 3

Heterogeneous Population Dynamics and Scaling Laws near Epidemic Outbreaks[1]

3.1 Introduction

Infectious diseases have a big influence on the livelihood (and indeed lives) of individual people as well as the performance of whole economies [94]. The development and understanding of mathematical models that can explain and especially predict the spreading of such diseases is therefore of enormous importance. A seminal work in this area was provided by Kermack and McKendrick in 1927 [66]. Up to this day their model is used as basis for analysis, although it has of course been extended in numerous ways. One such way is to consider heterogeneous populations. This is due to the realisation that individual people differ in their genetics, biology and social behaviour in ways that influence the spreading of infectious diseases. One type of model treats these individual traits as a static parameter [26, 48, 91]. Since these parameters have a certain distribution amongst the population some information may be gained by studying the moments of this distribution [32, 107]. Other models deal with time varying heterogeneities like age or duration of the infection [1, 34, 56]. For a more complete overview of different ways to model heterogeneity in this context we refer to textbooks on mathematical epidemiology such as [19, 29, 64].

In this paper we will exclusively deal with susceptible-infected-susceptible, in short SIS, models. These models assume that an individual is either infected or susceptible, and furthermore that an infected individual recovers from the infection with no lasting immunity and immediately becomes susceptible again. One of the main applications of SIS models are sexually transmitted diseases [21, 37, 55, 115], but other bacterial infections can also be modelled this way [45]. There are also applications of this model outside of biology, for example in the study of spreading of computer viruses [65, 113] or social

[1] This chapter has been accepted for publication in the journal Mathematical Biosciences and Engineering.

contagions [52]. Heterogeneous versions of this model also have a long history, see for example [77].

One feature that is present in most of these models is the existence of a threshold that fundamentally influences the behaviour of the system. This threshold is usually given in terms of the basic reproduction number R_0. If this number is smaller than one, then a disease can not lead to an outbreak and usually a disease free population rests, mathematically speaking, in a stable steady state. If R_0 is however bigger than one, then a disease can become endemic in a population. In many diseases this number is not constant but is susceptible to seasonal or other environmental changes [5, 64]. Hence, it is important to provide rigorous mathematical analysis, how R_0 has to be viewed for heterogeneous populations [24].

Once we understand this influence of heterogeneity, then it is of great interest to analyse possible warning sings that indicate the approach of R_0 to the critical value, when R_0 depends upon parameters. One approach to model this setup is to consider epidemic dynamics as a multiple time scale system where the population dynamics, including infection and recovery, are fast while parameters influencing R_0 drift slowly, so that R_0 increases from the sub-threshold regime $R_0 < 1$ to the critical value $R_0 = 1$. Considering also stochastic perturbations, it has been shown in various epidemic models [69, 93] that there exist warning signs for the upcoming critical value when recoding time series from the sub-threshold regime $R_0 < 1$. We follow in this vein and study how incorporating heterogeneity into a stochastic SIS model influences the warning sings of an impending critical transition.

In this paper we will study in particular the influence of heterogeneity on scaling laws. Knowing the exact nature of scaling laws is necessary if they are to be used to predict epidemic outbreaks. Only if they are known is it possible to match the theoretical warning signs to data and consequently anticipate significant changes in the progression of a disease. See [72] for an example where prediction from a data measles data set [39] is realised. Furthermore, knowledge of scaling laws give information about the stochastic stability of the progression of the disease. In particular it tells us with which rate the stability decreases, which has important real world effects as this can result in (short-lived) increases of the prevalence of the disease.

Our two main results for dynamics and warning signs for heterogeneous SIS models can be summarized on a non-technical level as follows:

(R1) We prove a theorem, how the global dynamical structure of the deterministic (i.e. no noise) homogeneous population model is preserved when the homogeneous population is replaced by a heterogeneous one. In particular, the result shows that upon very reasonable modelling assumptions on the heterogeneity, the homogeneous and heterogeneous models have the same basic bifurcation structure with an epidemic threshold at $R_0 = 1$.

(R2) We extend the heterogeneous SIS model by stochastic perturbations as well as by slow parameter dynamics. We use numerical simulations to investigate warning signs for epidemic outbreaks based upon scaling laws of the variance in the sub-threshold regime. We show that the rate of variance can change below the epidemic threshold when

(a) a cut-off for the heterogeneities is considered,

(b) a discretise distribution of heterogeneities is considered,

(c) if the system interacts with the upper and lower level population boundaries,

(d) if the transmission rate cannot be separated into a product of parametric drift and contribution from heterogeneity.

We also provide first steps to explain (a)-(d) on a non-rigorous level via formal calculations and considering the influences of various terms in the model.

The main implications for prediction and management of epidemic outbreaks are twofold. First, an epidemic threshold still exists for heterogeneous populations. It may shift due to the distribution of types in the heterogeneous population considered but we still have a tipping point or critical transitions towards an endemic state. This shows that there is a need to develop warning signs that can be applied before the outbreak. However, warning signs from homogeneous population models do not directly generalize to the heterogeneous situation. In particular, the functional form at which the warning sign of variance rises, does depend crucially on many additional factors, which are not predicted by simple homogeneous SIS-models.

The paper is structured as follows. In Section 3.2 we briefly review a homogeneous SIS-model as a baseline for our considerations. We state some known results about this model that are relevant to our analysis. In Section 3.3 we introduce the heterogeneous model we wish to study. In Section 3.4 we state, prove, and interpret the first main result (R1). In Section 3.5 we explain, why we extend the model by a slow parameter drift and by a noise term. Furthermore, we explain some background from the theory of warning signs for stochastic multiscale SIS models with homogeneous populations. In Section 3.6, we numerically analyse the influence that heterogeneity has on the behaviour of the system near bifurcation point by looking at the variance as warning sign. In Section 3.7, we provide a few first steps to explain the numerical observations. In particular, Sections 3.6-3.7 provide the details for our second main result (R2). We conclude in Section 3.8 with an outlook of future problems for epidemic models with heterogeneous populations which arose during our analysis.

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3.2 The homogeneous model

Basic SIS-models are well understood and an in-depth discussion of them can be found in introductory books about mathematical epidemiology (e.g. [18, 19, 64]). As a baseline homogeneous model we use

$$\begin{aligned} \dot{S}(t) &= -\beta \frac{I(t)}{S(t)+I(t)} S(t) - \eta S(t) + \gamma I(t), \quad S(0) = S_0 \geq 0, \\ \dot{I}(t) &= \beta \frac{I(t)}{S(t)+I(t)} S(t) + \eta S(t) - \gamma I(t), \quad I(0) = I_0 \geq 0, \end{aligned} \tag{3.1}$$

where $\frac{\mathrm{d}}{\mathrm{d}t} = \dot{}$ denotes the time derivative, $\beta > 0$ is the transmission rate and $\gamma > 0$ the recovery rate. The parameter η models the propagation of the disease due to imported cases of the infection. Such import can, for example, be explained by brief contacts with individuals outside of the population (see [64, 93]). The parameter η has also been used with different interpretations. In [52] and [53] η denotes spontaneous self-infection in the transmission of social contagions. In [102] and [114] η is a time dependent function modelling an infective medium. Furthermore, in [4] the mean field approximation of the $\epsilon-$SIS model introduced in [106] is presented. It too is an (heterogeneous) SIS-model with positive η. The general model with $\eta > 0$ will be used in the analysis of the steady states and bifurcation of the deterministic heterogeneous model. For the analysis of the stochastic model it will be included in the noise term.

Note that the positive quadrant is invariant for (3.1) so our choice of initial conditions ensures that the population sizes of infected and susceptibles remain non-negative. We shall only consider $(I(t), S(t)) \in [0, +\infty) \times [0, +\infty)$ for $t \geq 0$ from now on.

By adding the two equations in (3.1), it is easy to see that $S(t) + I(t)$ is constant in this model. Because of the structure of (3.1) we can assume without loss of generality that $S(t) + I(t) = 1$, since re-scaling both variables $S(t)$ and $I(t)$ by the inverse of the population size yields a total population of size 1. By substituting $S(t) = 1 - I(t)$ into the equation for $I(t)$ we can describe the system by the single equation

$$\dot{I}(t) = \beta(1 - I(t))I(t) + \eta(1 - I(t)) - \gamma I(t), \quad I(0) = I_0. \tag{3.2}$$

If $\eta = 0$ then we define $R_0 = \frac{\beta}{\gamma}$, known as the basic reproduction number. If $R_0 \leq 1$ then (3.2) has single steady state, $I^* \equiv 0$, that is globally asymptotically stable. If $R_0 > 1$ then (3.2) has two steady states. The steady state $I^* \equiv 0$ remains but is now unstable. The second steady state is $I^{**} \equiv \frac{\beta-\gamma}{\beta}$ and is globally asymptotically stable with the exception of $I_0 = 0$. From a mathematical perspective, this exchange-of-stability happens at a transcritical bifurcation when $(I, R_0) = (0, 1)$. If $\eta > 0$ then (3.2) always has one steady state. It is globally asymptotically stable, i.e., all non-negative initial conditions yield trajectories that are attracted in forward time to the steady state.

3.3 The heterogeneous model

We now modify the baseline model (3.1) by dividing the population according to some trait that is relevant to the spreading of the disease. This can indicate social behaviour like contact rates or biological traits like natural resistance towards the disease (for a detailed interpretation of heterogeneity we refer to introductory works in epidemiology, e.g. [29]). Each individual is assigned a heterogeneity state (h-state) ω which lies in some set Ω. This ω can of course also be a vector carrying information about more than one trait.

We assume that the disease spreads amongst the population of each h-state according to the dynamics

$$
\begin{aligned}
\dot{S}(t,\omega) &= -\beta(\omega)\frac{J(t)}{T(t)+J(t)}S(t,\omega) - \eta(\omega)S(t,\omega) + \gamma(\omega)I(t,\omega), \quad S(0,\omega) = S_0(\omega) \\
\dot{I}(t,\omega) &= \beta(\omega)\frac{J(t)}{T(t)+J(t)}S(t,\omega) + \eta(\omega)S(t,\omega) - \gamma(\omega)I(t,\omega), \quad I(0,\omega) = I_0(\omega),
\end{aligned}
\tag{3.3}
$$

where we use the definitions

$$
T(t) := \int_\Omega q(\omega)S(t,\omega)\,\mathrm{d}\omega \qquad J(t) := \int_\Omega q(\omega)I(t,\omega)\,\mathrm{d}\omega.
$$

Here we consider the following variables:

- $q(\omega)$ is the intensity of participation in risky interactions of an individual with h-state ω,
- $\beta(\omega) = \rho(\omega)q(\omega)$ where $\rho(\omega)$ is the force of infection of the disease towards an individual with h-state ω,
- $\gamma(\omega)$ is the recovery rate for an individual with h-state ω,
- $\eta(\omega)$ is the h-state dependent fraction of individuals that become infected through the import of the infection from outside the population.

Of course, $\eta(\omega)$ can also take any of the different interpretations mentioned in section 3.2. Note that if all these variables are constant then the heterogeneous system (3.3) is equivalent to the homogeneous system (3.1).

We want to make a short note about two aspects of this model. One is that for each ω the population $S(t,\omega) + I(t,\omega)$ is obviously constant. This implies that ω itself is not influenced by the disease and an individual that has h-state ω at the beginning remains in that h-state for the duration of our consideration. The second aspect is the transmission function $\frac{J(t)}{T(t)+J(t)}$. Transmission functions of this type have been used before [32, 34, 107]. Such a transmission function can for example be derived by assuming a population with a heterogeneous social contact network [91]. Models with such populations are at the centre of intensive current research (see e.g. [9, 10, 28, 63]).

We now formulate the mathematical assumptions for the heterogeneous population epidemic model used in our subsequent analysis. The set Ω is a complete Borel measurable space with a nonnegative measure μ and $\int_\Omega \mathrm{d}\mu(\omega) = 1$. All integration with respect to ω is taken to be with respect to that measure. All functions and parameters are assumed to be nonnegative and measurable with respect to μ. Since $S(t,\omega) + I(t,\omega)$ is constant we can introduce a density function $f(\omega) := S(t,\omega) + I(t,\omega)$. We can assume without loss of generality that $\int_\Omega f(\omega)\,\mathrm{d}\omega = 1$. The function $q(\omega)$ is taken to be positive almost everywhere on Ω, i.e. there is always some probability for risky interaction for each h-state. We have

$$T(t) + J(t) = \int_\Omega q(\omega)(S(t,\omega) + I(t,\omega))\,\mathrm{d}\omega = \int_\Omega q(\omega) f(\omega)\,\mathrm{d}\omega = C$$

for some constant $C > 0$. By using $\frac{q(\omega)}{C}$ instead of $q(\omega)$, we can assume without loss of generality that $T(t) + J(t) = 1$. We also assume that the three functions $\beta(\omega)$, $\gamma(\omega)$ and $\eta(\omega)$ are bounded, which makes sense from a modelling viewpoint. Furthermore, we assume there exists an $\varepsilon > 0$ such that

$$\inf_{\omega\in\Omega} \beta(\omega) \geq \varepsilon \quad \text{and} \quad \inf_{\omega\in\Omega} \gamma(\omega) \geq \varepsilon.$$

These assumptions just mean that the transmission probability is never equal to zero when infected and susceptible individuals meet and that there is always at least some positive, albeit potentially very long, time after which any infected individual recovers from the disease. An important consequence of these assumptions is that the functions $S(t,\cdot)$, $I(t,\cdot)$ are measurable for every $t \geq 0$ (see Theorem 1 in [108]). For $\eta(\omega)$ we consider two cases. First the case that there exist a set $A \subseteq \Omega$ with positive measure such that $\eta(\omega)f(\omega) > 0$ for $\omega \in A$. We denote this case by $\eta > 0$. The second case where such a set does not exist will be denoted by $\eta = 0$.

Using $S(t,\omega) = f(\omega) - I(t,\omega)$ and $T(t) + J(t) = 1$ we can describe the system (3.3) by

$$\begin{aligned} \dot{I}(t,\omega) &= (\beta(\omega)J(t) + \eta(\omega))f(\omega) - (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))I(t,\omega), \quad I(0,\omega) = I_0(\omega), \\ J(t) &= \int_\Omega q(\omega) I(t,\omega)\,\mathrm{d}\omega. \end{aligned} \tag{3.4}$$

It is now a natural question to ask which dynamical features are shared by the homogeneous population ordinary differential equation (ODE) given by (3.2) and the heterogeneous population differential-integral equation (3.4).

3.4 Persistence of Dynamical Structure

In this section we show that in terms of steady state solutions and their stability properties the system (3.4) exhibits the same behaviour as the system (3.2).

Theorem 3. *If $\eta > 0$ then the system (3.4) has a unique steady state solution. This solution is globally asymptotically stable. If $\eta = 0$ we define the basic reproduction number*

$$R_0 = \int_\Omega q(\omega) f(\omega) \frac{\beta(\omega)}{\gamma(\omega)} \,\mathrm{d}\omega. \tag{3.5}$$

If $R_0 \leq 1$ then (3.4) has the unique steady state solution $I(t,\omega) = 0$. This solution is globally asymptotically stable. If $R_0 > 1$ then (3.4) has exactly two steady state solutions, one of which is $I(t,\omega) = 0$. In this case, the solution $I(t,\omega) = 0$ is an unstable steady state solution while the second steady state solution is globally asymptotically stable with the exception of $I_0(\omega) = 0$ a.e. on Ω.

Proof. We first show that the system does indeed have the number of steady states we claim it has. Let $\hat{I}(\omega)$ be a steady state of (3.4) and $\hat{J} = \int_\Omega q(\omega)\hat{I}(\omega)\,\mathrm{d}\omega$. As a steady state of (3.4) $\hat{I}(\omega)$ is characterised by the equation

$$\hat{I}(\omega) = f(\omega) \frac{\beta(\omega)\hat{J} + \eta(\omega)}{\beta(\omega)\hat{J} + \eta(\omega) + \gamma(\omega)}. \tag{3.6}$$

Plugging this into the equation for $\hat{J}$ yields

$$\hat{J} = \int_\Omega q(\omega) f(\omega) \frac{\beta(\omega)\hat{J} + \eta(\omega)}{\beta(\omega)\hat{J} + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega. \tag{3.7}$$

Every solution $\hat{J}$ to (3.7) yields a steady state of (3.4) by putting it into equation (3.6). Thus, we are searching for the roots of the function

$$g(x) = \int_\Omega q(\omega) f(\omega) \frac{\beta(\omega)x + \eta(\omega)}{\beta(\omega)x + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega - x$$

in the interval $[0,1]$. We have

$$g(0) = \int_\Omega q(\omega) f(\omega) \frac{\eta(\omega)}{\eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega$$

and

$$g(1) = \int_\Omega q(\omega) f(\omega) \frac{\beta(\omega) + \eta(\omega)}{\beta(\omega) + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega - 1 < \int_\Omega q(\omega) f(\omega) \,\mathrm{d}\omega - 1 = T(t) + J(t) - 1 = 0.$$

A simple calculation yields

$$\begin{aligned} g'(x) &= \int_\Omega q(\omega) f(\omega) \frac{\beta(\omega)\gamma(\omega)}{(\beta(\omega)x + \eta(\omega) + \gamma(\omega))^2} \,\mathrm{d}\omega - 1, \\ g''(x) &= \int_\Omega q(\omega) f(\omega) \frac{-\beta(\omega)\gamma(\omega) 2(\beta(\omega)x + \eta(\omega) + \gamma(\omega))\beta(\omega)}{(\beta(\omega)x + \eta(\omega) + \gamma(\omega))^4} \,\mathrm{d}\omega. \end{aligned}$$

Note that the second derivative is always negative. We consider the case $\eta > 0$ first. We know that $g(x) = 0$ has a solution since $g(0) > 0$ and $g(1) < 0$. Since $g(x)$ is concave this solution is unique.

Consider now the case $\eta = 0$. In this case $g(0) = 0$, so 0 is a solution. If $g'(0) \leq 0$ then $g(x)$ negative on the whole interval $[0, 1]$ due to the concavity of $g(x)$. If however $g'(0) > 0$ then $g(x)$ is positive for small enough x. Using same reasoning as in the case $\eta > 0$ we see that there exists a unique positive solution to $g(x) = 0$. We therefore need to determine whether $g'(0) > 0$. Since $\eta = 0$ this is given by

$$g'(0) = \int_{\Omega} q(\omega) f(\omega) \frac{\beta(\omega)}{\gamma(\omega)} \, \mathrm{d}\omega - 1 = R_0 - 1.$$

We see that if $R_0 \leq 1$ then $g'(0) \leq 0$ and 0 is the only solution to $g(x) = 0$, if $R_0 > 1$ then $g'(0) > 0$ and there exists a unique solution in of $g(x) = 0$ in $(0, 1)$ alongside the solution 0.

Now we want to show that the system converges to a steady state. In order to do this, we first need to show that $J(t)$ converges. In particular, we want to prove:

Lemma 6. *The limit $J^* = \lim_{t \to +\infty} J(t)$ exists. Furthermore,*

$$\dot{I}(t, \omega) \lesseqgtr 0 \Leftrightarrow I(t, \omega) \gtreqless \frac{f(\omega)(\beta(\omega) J(t) + \eta(\omega))}{\beta(\omega) J(t) + \eta(\omega) + \gamma(\omega)}. \tag{3.8}$$

The proof of Lemma 6 is one major difficulty in this proof. However, the argument is quite lengthy and technical; hence we include it in Appendix 3.8.

Now that we know that $J(t)$ converges it remains to show that if $\eta = 0$ and $R_0 > 1$ then $J(t)$ converges a positive value and not to 0 unless $I_0(\omega) = 0$ a.e. on Ω. Consider the inequality

$$\sup_{\zeta \in \Omega} \left(\frac{\beta(\zeta)}{\gamma(\zeta)} \right) J(t) = \int_{\Omega} q(\omega) \sup_{\zeta \in \Omega} \left(\frac{\beta(\zeta)}{\gamma(\zeta)} \right) I(t, \omega) \, \mathrm{d}\omega \geq \int_{\Omega} q(\omega) \frac{\beta(\omega)}{\gamma(\omega)} I(t, \omega) \, \mathrm{d}\omega.$$

Thus, if $J(t)$ is positive and sufficiently small we have

$$\begin{aligned}
& R_0 - 1 > \int_{\Omega} q(\omega) \frac{\beta(\omega)}{\gamma(\omega)} I(t, \omega) \, \mathrm{d}\omega \\
\Leftrightarrow \quad & J(t) R_0 - J(t) > \int_{\Omega} q(\omega) \frac{\beta(\omega)}{\gamma(\omega)} J(t) I(t, \omega) \, \mathrm{d}\omega \\
\Leftrightarrow \quad & J(t) \int_{\Omega} q(\omega) f(\omega) \frac{\beta(\omega)}{\gamma(\omega)} \, \mathrm{d}\omega - \int_{\Omega} q(\omega) I(t, \omega) \, \mathrm{d}\omega > \int_{\Omega} q(\omega) \frac{\beta(\omega)}{\gamma(\omega)} J(t) I(t, \omega) \, \mathrm{d}\omega \\
\Leftrightarrow \quad & \int_{\Omega} \frac{q(\omega)}{\gamma(\omega)} \left(f(\omega) \beta(\omega) J(t) - \gamma(\omega) I(t, \omega) - \beta(\omega) J(t) I(t, \omega) \right) \, \mathrm{d}\omega > 0 \\
\Leftrightarrow \quad & \int_{\Omega} \frac{q(\omega)}{\gamma(\omega)} \dot{I}(t, \omega) \, \mathrm{d}\omega > 0.
\end{aligned}$$

This shows that the term $\int_\Omega \frac{q(\omega)}{\gamma(\omega)} I(t,\omega)\,\mathrm{d}\omega$ is monotonically increasing. But since

$$\int_\Omega \frac{q(\omega)}{\gamma(\omega)} I(t,\omega)\,\mathrm{d}\omega \le \frac{1}{\inf\limits_{\omega\in\Omega}\gamma(\omega)} J(t),$$

we see that $J(t)$ is bounded below by a positive, monotonically increasing function. Therefore it can not converge to 0. Since $I_0(\omega) > 0$ on a set of positive measure we have that $J(0) > 0$. Thus, $J(t)$ converges to a positive value.
Conversely, if $I_0(\omega) = 0$ a.e. on Ω then $J(0) = 0$. Directly from (3.4) we see that in this case $\dot{I}(t,\omega) = 0$ for a.e. $\omega \in \Omega$ and thus $J(t) = 0$ for all $t \ge 0$.

Since $J(t)$ converges, the convergence of $I(t,\omega)$ follows immediately from (3.8). Obviously the limit of $I(t,\omega)$ is one of the steady states we identified above. We have also shown that if there are two steady states then $I(t,\omega)$ converges to the positive one, unless $I_0(\omega) = 0$ a.e. on Ω. Since in all other cases the convergence of $I(t,\omega)$ is independent of the initial data, the claim about asymptotic stability is proven. $\square$

In the case $\eta = 0$ the value R_0 acts as a threshold value that determines whether there exists an endemic steady state or not. So far R_0 has only this mathematical meaning. The basic reproduction number is however a biological concept. Using the definition given in [31], the basic reproduction number is defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. We now want to show that the value R_0 as we defined it coincides with this definition. Also in [31] the following result was obtained.

Proposition 4. *Let $S(\omega)$ denote the density function of susceptibles describing the steady demographic state in the absence of the disease. Let $A(\tau,\zeta,\omega)$ be the expected infectivity of an individual which was infected τ units of time ago, while having h-state ω towards a susceptible which has h-state ζ. Assume that*

$$\int_0^\infty A(\tau,\zeta,\omega)\,\mathrm{d}\tau = a(\zeta)b(\omega).$$

Then the basic reproduction number R_0 for the system is given by

$$R_0 = \int_\Omega a(\omega)b(\omega)S(\omega)\,\mathrm{d}\omega.$$

In our case the function $f(\omega)$ describes a steady state, provided that there are no infected individuals. The value $\beta(\omega)$ denotes the strength of infection for an individual with h-state ω. The value $q(\omega)$ indicates the number of infectious contacts an infected individual with h-state ω has. On the other hand $\beta(\zeta) =$

$\rho(\zeta)q(\zeta)$ is the average amount of risky contacts that would lead to an infection that an individual with h-state ζ has. The chance of an infectious contact between the infective ω individual and a specific ζ individual is therefore given by $q(\omega)\frac{\beta(\zeta)}{\int_\Omega q(\xi)f(\xi)\,\mathrm{d}\xi} = q(\omega)\beta(\zeta)$. In the absence of susceptible individuals the equation for the infected is given by $\dot{I}(t) = -\gamma(\omega)I(t)$, which suggests that the probability that an infected individual is still infected at time t is given by $e^{-\gamma(\omega)t}$. Since the infectivity of an individual is in our case independent of how long ago the individual was infected, we can conclude that the expected infectivity $A(\tau, \zeta, \omega)$ is given by $q(\omega)\beta(\zeta)e^{-\gamma(\omega)\tau}$. Since

$$\int_0^\infty A(\tau, \zeta, \omega)\,\mathrm{d}\tau = \int_0^\infty q(\omega)\beta(\zeta)e^{-\gamma(\omega)\tau}\,\mathrm{d}\tau = \beta(\zeta)\frac{q(\omega)}{\gamma(\omega)},$$

we can use Proposition 4 and get

$$R_0 = \int_\Omega \beta(\omega)\frac{q(\omega)}{\gamma(\omega)}f(\omega)\,\mathrm{d}\omega.$$

This is exactly the basic reproduction number as defined in Theorem 3.

3.5 Extending the Model

Although the heterogeneous population SIS model (3.4) does capture additional realistic features of populations, there are several effects, which it cannot account for at all, or does not account for very well. In particular, finite-size effects and small fluctuations are not included. Furthermore, most realistic heterogeneous parameter distributions, e.g. the transmission rate, are not fixed in time but could be considered as additional dynamical variables. In this section, we extend the model (3.4) to include these effects.

3.5.1 Noise

In Section 3.2 we introduced several interpretations of the parameter η. Although it is modeled as a deterministic influence on the disease, the effect η is supposed to describe on the other hand is seemingly of a random nature. Furthermore, even in a situation where we don't want to model any of these effects (i.e we set $\eta = 0$) we can still expect there to be some random deviations from the transmission of the disease as predicted by the deterministic model. In fact, the validity of deterministic epidemiological models is usually argued by viewing them as the average transmission and recovery rate of individual random contacts in a sufficiently large population. It is therefore justified to expect to see some remaining randomness in the actual progression of the disease [20, 54, 76, 90].

We therefore want to model these random effects by exchanging the term containing η with a term containing a stochastic process. A natural starting point for the case when the functional form and properties of the stochastic process are not known is to consider white noise $\xi = \xi(t)$ with mean zero $\mathbb{E}[\xi(t)] = 0$ and δ-correlation $\mathbb{E}[\xi(t) - \xi(s)] = \delta(t - s)$, i.e. ξ is a generalized stochastic process, so-called white noise, as discussed in [8]. We also want to consider the case when the noise depends upon the heterogenity and write $\xi = \xi(t, \omega)$ with the caveat that $\omega \in \Omega$ still denotes the variable measuring the heterogeneity distribution, while we suppress the underlying probability space for the stochastic process ξ in the notation.

Putting $\xi(t, \omega)$ into equation (3.3) yields

$$\begin{aligned} \dot{S}(t,\omega) &= -\beta(\omega)\frac{J(t)}{T(t)+J(t)}S(t,\omega) + \gamma(\omega)I(t,\omega) - \sigma(\omega)\xi(t,\omega), \quad S(0,\omega) = S_0(\omega) \\ \dot{I}(t,\omega) &= \beta(\omega)\frac{J(t)}{T(t)+J(t)}S(t,\omega) - \gamma(\omega)I(t,\omega) + \sigma(\omega)\xi(t,\omega), \quad I(0,\omega) = I_0(\omega). \end{aligned} \tag{3.9}$$

The function $\sigma(\omega) : \Omega \to [0, +\infty)$ is assumed to be bounded and basically provides the noise level for a specific ω. Note that for every ω, the sum $S(t, \omega) + I(t, \omega)$ is still constant. We can therefore again describe the system (3.9) by the smaller system

$$\begin{aligned} \dot{I}(t,\omega) &= \beta(\omega)J(t)f(\omega) - (\beta(\omega)J(t) + \gamma(\omega))I(t,\omega) + \sigma(\omega)\xi(t,\omega), \\ J(t) &= \int_\Omega q(\omega)I(t,\omega)\,\mathrm{d}\omega. \end{aligned} \tag{3.10}$$

One problem with using an additive noise term is that $I(t, \omega)$ always has to be positive. But in this model it would be possible for $I(t, \omega)$ to become negative. To disallow this we will use

$$\dot{I}(t,\omega) = \max\{0, \beta(\omega)J(t)f(\omega) + \sigma(\omega)\xi(t,\omega)\} \quad \text{if} \quad I(t,\omega) = 0.$$

Similarly, since $I(t, \omega)$ has to be smaller than $f(\omega)$, we use

$$\dot{I}(t,\omega) = \min\{0, -\gamma(\omega)f(\omega) + \sigma(\omega)\xi(t,\omega)\} \quad \text{if} \quad I(t,\omega) = f(\omega).$$

In the following considerations we restrict ourselves to models using additive noise. However, we want to indicate another commonly encountered modelling possibility, which is using a multiplicative noise term instead of an additive one. That is, to use

$$\begin{aligned} \dot{I}(t,\omega) &= \beta(\omega)J(t)f(\omega) - (\beta(\omega)J(t) + \gamma(\omega))I(t,\omega) + g(I(t,\omega),\omega)\xi(t,\omega), \\ J(t) &= \int_\Omega q(\omega)I(t,\omega)\,\mathrm{d}\omega, \end{aligned} \tag{3.11}$$

where $g : \mathbb{R} \times \Omega \to [0, +\infty)$ is bounded. Imposing the conditions $g(0, \omega) = 0$ and $g(1, \omega) = 0$ can now ensure that it is never possible for $I(t, \omega)$ to become negative or larger than $f(\omega)$. Usually, one also assumes that $g(\cdot, \omega)$ does not vanish between zero and one.

Which of these two options is chosen will depend on what kind of random influences are to be considered. If the random fluctuations are meant to offset fluctuations in the transmission and recovery of the infection, then the multiplicative noise term might be more appropriate. First of all, if no infected individuals are present then the disease does not spread at all, which is captured by this model. Also, if nearly no one (or nearly everyone) is infected then the inaccuracies of the deterministic model should be small, so the noise term should also be small. Again, the multiplicative noise exhibits this behaviour.

The model with additive noise, which we will use in the following, is however not without merit. It allows us to model a population that has contact with an outside source that can import the disease into the population. This source can be, as mentioned above, another population which imports the disease. Alternatively, there might be factors in the environment that import the infection. For a population of animals it could for example model the possibility to become infected through one of its food sources. Also for human populations this allows us to assume that there are vermin or insects in their environment, which are carriers of the disease and are able to transmit it to humans. In these situations there is a chance to become infected even in a population that consists entirely of susceptible individuals, which is not captured in models using multiplicative noise.

Also, it should be noted that if both effects are present, i.e. internal fluctuations as well as external fluctuations, and we assume that both noise terms act as summands in the model, then the noise term is

$$[\sigma(\omega) + g(I(t,\omega),\omega)]\xi(t,\omega). \tag{3.12}$$

Near the two states $I(t,\omega) \equiv 0$ and $I(t,\omega) \equiv f(\omega)$, we have that $g(I(t,\omega),\omega)$ is a higher-order term in comparison to the constant term as long as the constant term does not vanish and we are mainly interested in the regimes near the the two states $I(t,\omega) \equiv 0$ and $I(t,\omega) \equiv f(\omega)$ in the remaining part of this work. Also note that a multiplicative noise term $g(I(t,\omega),\omega)\xi(t,\omega)$ with $g(0,\omega) > 0$ can always be written as

$$g(I(t,\omega),\omega)\xi(t,\omega) = \left[g(0,\omega) + \big(g(I(t,\omega),\omega) - g(0,\omega)\big)\right]\xi(t,\omega),$$

which is near $I(t,\omega) = 0$ again the sum of an additive noise term and a term of higher order. Based on these arguments, we proceed with additive noise but it could definitely be interesting to investigate the purely multiplicative noise in future work.

3.5.2 Multiple time scales

As a final extension of our model we now introduce a slow variable into the system. Making certain model parameters slow dynamic variables is a very natural extension used in virtually all areas of research in mathematical biology [43, 70]. The main reason is that it is usually not correct to assume that all system parameters are fixed but most system parameters are going to change slowly over time, so a parametric model should rather be viewed as a partially frozen state for a model with multiple time scales.

In the context of epidemiology, many diseases have seasonal cycles or are latent for a longer period before it comes to an outbreak. In both cases we assume that the basic reproduction number R_0 was smaller than 1 until some time, which means the stable steady state of the deterministic system is 0, and bigger than 1 afterwards, which means that a stable endemic steady state exists. In order to capture this in our model we assume that $\beta(\omega)$ slowly changes over time. In fact, there are many different possibilities that may lead to a slowly changing transmission rate, including seasonal changes, evolutionary processes, socio-economic influences, and so on. Furthermore, if we would keep the transmission rate fixed as a parameter, then we would either observe a disease-free state or an endemic state in the SIS model but not the transition between the two cases. It is precisely the *dynamic* transition regime which we are interested in.

We assume that the time dependence of the function $\beta(t,\omega)$ is such that R_0 is increasing in t. For example, assume that $\beta(t,\omega)$ is separable, i.e. there exists a function $\beta_0(t)$ such that $\beta(t,\omega) = \beta_0(t)\beta(\omega)$, and that this function $\beta_0(t)$ evolves according to the equation $\dot{\beta}_0(t) = \varepsilon$ for $0 < \varepsilon \ll 1$. In this case we would have

$$R_0(t) = \int_\Omega q(\omega)f(\omega)\frac{\beta_0(t)\beta(\omega)}{\gamma(\omega)}\,\mathrm{d}\omega = \beta_0(t)\int_\Omega q(\omega)f(\omega)\frac{\beta(\omega)}{\gamma(\omega)}\,\mathrm{d}\omega.$$

Thus, $R_0(t)$ is strictly increasing and, if $\beta_0(0)$ is small enough, $R_0(0) < 1$. This is exactly the situation we want to capture. This effect can of course also be achieved with a $\beta(t,\omega)$ which is not factorisable. We are therefore looking at the system

$$\begin{aligned} \dot{I}(t,\omega) &= \beta(t,\omega)J(t)(f(\omega) - I(t,\omega)) - \gamma(\omega)I(t,\omega) + \sigma(\omega)\xi(t,\omega), \\ \dot{\beta}(t,\omega) &= \varepsilon h(t,\omega), \\ J(t) &= \int_\Omega q(\omega)I(t,\omega)\,\mathrm{d}\omega, \end{aligned} \tag{3.13}$$

with an appropriate function $h(t,\omega)$.

3.5.3 Warning-Signs for the Homogeneous Fast-Slow Stochastic Model

In this section, we briefly recall some techniques for fast-slow systems and warning signs for stochastic fast-slow systems. For reviewing this material, we consider a simple homogeneous version of (3.13) to simplify the exposition

$$\begin{aligned} \dot{I}(t) &= \beta(t)I(t)(1 - I(t)) - \gamma I(t) + \sigma\xi(t), \\ \dot{\beta}(t) &= \varepsilon, \end{aligned} \tag{3.14}$$

where $I = I(t)$ is the fast variable and $\beta = \beta(t)$ the slow variable. For $\sigma = 0$, $\varepsilon = 0$, the set $\mathcal{C}_0 = \{(I,\beta) \in [0,+\infty) \times [0,+\infty) : I(\beta - \gamma - \beta I) = 0\}$ is called the critical manifold [58] and consists of steady states for the fast subsystem, which is obtained by setting $\varepsilon = 0$ in (3.14). The transcritical bifurcation discussed in Section 3.2 separates $\mathcal{C}_0$ into three parts in the positive quadrant

$$\mathcal{C}_0^a = \mathcal{C}_0 \cap \{R_0 \leq 1\}, \quad \mathcal{C}_0^r = \mathcal{C}_0 \cap \{R_0 > 1, I = 0\}, \quad \mathcal{C}_0^e = \mathcal{C}_0 \cap \{I > 0\}.$$

Then $\mathcal{C}_0^a$ and $\mathcal{C}_0^e$ consist of attracting steady states for the fast subsystem, while $\mathcal{C}_0^r$ is repelling. The stability is exchanged at the transcritical bifurcation point with $\beta = \gamma$, i.e. at $R_0 = 1$. The deterministic fast-slow systems analysis of the dynamic transcritical bifurcation with $0 < \varepsilon \ll 1$ can be found in [68, 98], where one key point is that one can extend a perturbation $\mathcal{C}_\varepsilon^a$, a so-called attracting slow manifold, of $\mathcal{C}_0^a$ up to a region of size $I \sim \mathcal{O}(\varepsilon^{1/2})$ and $\beta - \gamma \sim \mathcal{O}(\varepsilon^{1/2})$ as $\varepsilon \to 0$ near the transcritical bifurcation point. The relevant conclusion for us here is that a linearisation analysis is expected to be valid up to this region, excluding a small ball of size $\mathcal{O}(\varepsilon^{1/2})$.

It can be shown that sample paths of the stochastic system with $0 < \varepsilon \ll 1$, $0 < \sigma \ll 1$ also track with high-probability the attracting manifold inside a neighbourhood of order $\mathcal{O}(\varepsilon)$ plus a probabilistic correction term [13]. However, as the transcritical bifurcation point $(I, \beta) = (0, \gamma)$ is slowly approached from below $\beta \nearrow \gamma$, the probabilistic correction term starts to grow. Indeed, there is a simple intuitive explanation for this behaviour due to an effect also called "critical slowing down". To understand this effect, Taylor expand the drift and diffusion terms of the I-component of the stochastic differential equation (3.14) around $\mathcal{C}_0^a$ and keep the linear terms, which yields

$$\dot{\mathcal{I}}(t) = [\beta - \gamma]\mathcal{I}(t) + \sigma\xi(t), \tag{3.15}$$

where we view β as a parameter for now and use $\mathcal{I}$ to emphasize that we work on the level of the linearization. Then (3.15) is just an Ornstein-Uhlenbeck (OU) process [36]. Consider the regime $\beta \leq \gamma$, then the variance of the OU process increases if β increases and it is an explicit calculation [69] to see that

$$\lim_{t \to +\infty} \text{Var}(\mathcal{I}(t)) \sim \frac{\sigma^2}{\gamma - \beta} \qquad \text{as } \beta \nearrow \gamma, \tag{3.16}$$

so the variance increases rapidly as we start to approach the bifurcation point by changing the parameter β more towards γ. This makes sense intuitively as the deterministic stabilizing effect from the drift term $[\beta - \gamma]\mathcal{I}(t)$ pushing towards a region near $\mathcal{C}_0^a$ is diminished ("critical slowing down") and hence the noisy fluctuations increase. It is known that the effect of critical slowing-down in combination with noise can be exploited to predict bifurcation points in certain situations (see e.g. the ground-breaking work [112]). The idea has been also suggested in the context of ecology [22] and then applied in many other circumstances [99]. In fact, one may prove that we indeed have for the full nonlinear stochastic fast-slow system (3.14), under suitable smallness assumptions on a fixed noise level and staying $\mathcal{O}(\varepsilon^{1/2})$ away from the region of the deterministic bifurcation point, that

$$\text{Var}(I(t)) \sim \frac{A}{(t_{crit} - t)^\alpha} + \text{higher-order terms}, \quad \text{as } t \nearrow t_c, \tag{3.17}$$

where $\alpha = 1$, $A = \sigma^2$, $\beta(t_{crit}) = \gamma$ with $\beta(0) < t_{crit}$; the details can be found in [69] using moment expansion methods, and in [14] using martingale methods and/or explicit OU-process results. The main practical conclusion is that there is a leading-order scaling law of the variance as the value of R_0 is approached by letting the transmission rate slowly drift in time. This scaling law can be used for prediction as the scaling exponent $\alpha = 1$ is universal for a non-degenerate transcritical bifurcation. In fact, a calculation of the leading-order covariance scaling laws for all bifurcations up to codimension-two in stochastic fast-slow systems has been carried out [69], which builds a mathematical framework for generic systems.

However, this theory simply does not apply to the heterogeneous population model (3.13) we consider here. In particular, the influence of heterogeneity on early-warning signs has not been investigated much to the best of our knowledge (for examples see [62, 99]). Since it is a key effect in realistic models of disease spreading, it is natural to ask, how it influences the scaling law (3.17).

3.6 Numerical results

Here we present numerical simulations of the homogeneous and heterogeneous system to see the influence of the heterogeneity. We have chosen to consider the variance as the early warning sign. We assume that the variance behaves like $\frac{A}{(t_{crit}-t)^\alpha}$ for appropriate A and α, where t_{crit} is the time at which $R_0(t) = 1$. The main difficulty lies in correctly determining α. We will calculate it by fitting the reference curve $\frac{A}{(t_{crit}-t)^\alpha}$ to the time series of our simulation using the least squares method. To smoothen the time series we will average the variance over 100 simulations. However, since the reference curve goes to infinity at t_{crit} we do not fit the curve over the whole interval, which also takes into account the theory, which excludes a small ε-dependent ball near $R_0(t) = 1$ as discussed in Section 3.5.3. We therefore calculate the best fit over 80% or 90% of the considered time interval. Generally, fitting over 90% gives better results. In the cases we consider only 80% of the interval, fitting over a larger part would not yield reasonable results as the solution goes to $-\infty$. These are cases in which the sample path drops below the negative unstable branch of the transcritical bifurcation (see Figure 3.9). Since different choices in the size of the considered interval lead to slightly different values for α we cannot claim to calculate the exact α that the variance of $I(t)$ follows. We will however be able to detect changes in the level of α that are due to influences of the heterogeneity.

One further aspect we fix for all our considerations is the order in which we aggregate the system and calculate the variance. We could calculate the variance of $I(t,\omega)$ and then aggregate these variances, or first calculate $I(t) = \int_\Omega I(t,\omega)\,\mathrm{d}\omega$ and calculate the variance of $I(t)$. We choose the latter option since in applications it is more feasible to be able to track the changes of the prevalence of the disease in the whole population rather than being able to track it for each h-state, as would be required by the first method.

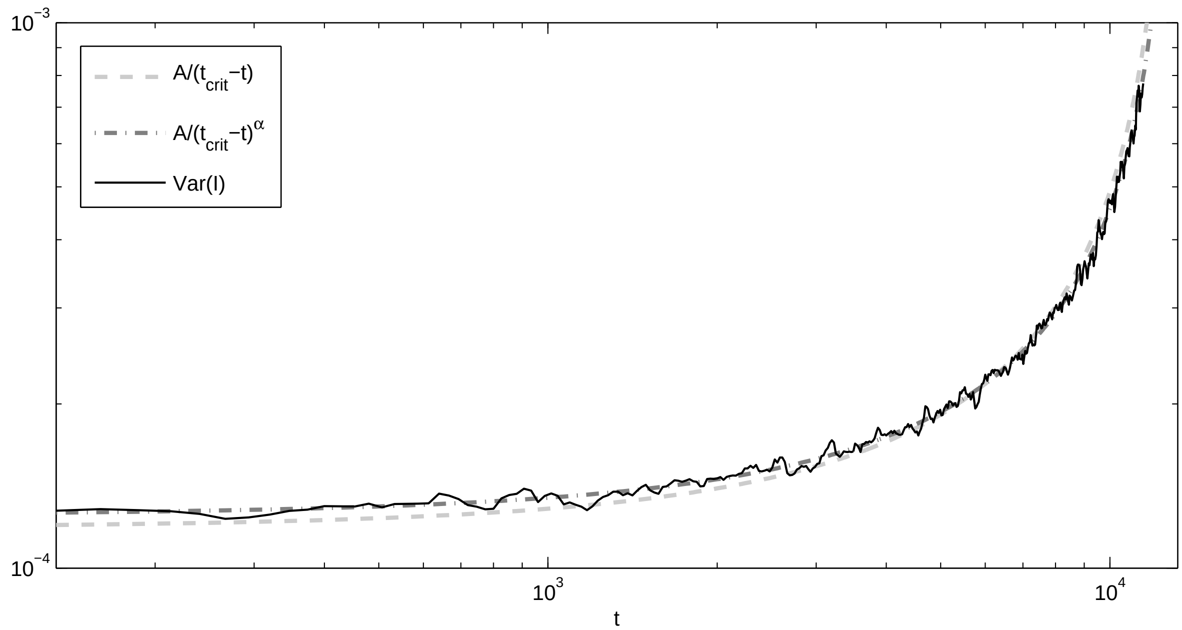

Figure 3.1: Here we see the variance of the aggregated variable $I(t)$. As a reference we show the curve $A/(t_{crit} - t)^{\alpha}$ with both the expected theoretical exponent $\alpha = 1$ and with the exponent $\alpha = 0.9125$ provided by the best fit over 80% of the considered time interval.

In this section, we shall only consider the numerical simulations make observations about the results. A more detailed discussion *why* certain effects may occur is then given in Section 3.7.

First we consider the homogeneous system with additive noise and a very simple multiplicative time dependency of β:

$$\begin{aligned} \dot{I}(t) &= \beta\, \beta_0(t)(1 - I(t))I(t) - \gamma I(t) + \sigma\xi(t), \\ \dot{\beta_0}(t) &= \varepsilon. \end{aligned}$$

As initial conditions we choose $I(0) = 0$ and $\beta_0(0) = 0$. The parameters are chosen as $\beta = 0.3$, $\gamma = 0.4$, and $\sigma = 0.01$. The time scale separation parameter ε for the slow variable drift is set to $\varepsilon = 0.0001$. If we allow $I(t)$ to become negative then we know that the variance of $I(t)$ should behave as $\frac{A}{t_{crit}-t}$. In Figure 3.1 we show the variance of $I(t)$, averaged over 100 simulations, and the reference curve with both the theoretical exponent $\alpha = 1$ and with the exponent provided by the best fit over 80% of the time interval. The measured exponent is reasonably close to the theoretically predicted value $\alpha = 1$; this slight underestimate is expected as a transcritical bifurcation splits into two saddle bifurcations upon generic perturbations and for saddle-nodes the exponent is $\alpha = \frac{1}{2}$; see also [69] for more details, which exponents may occur in the generic cases.

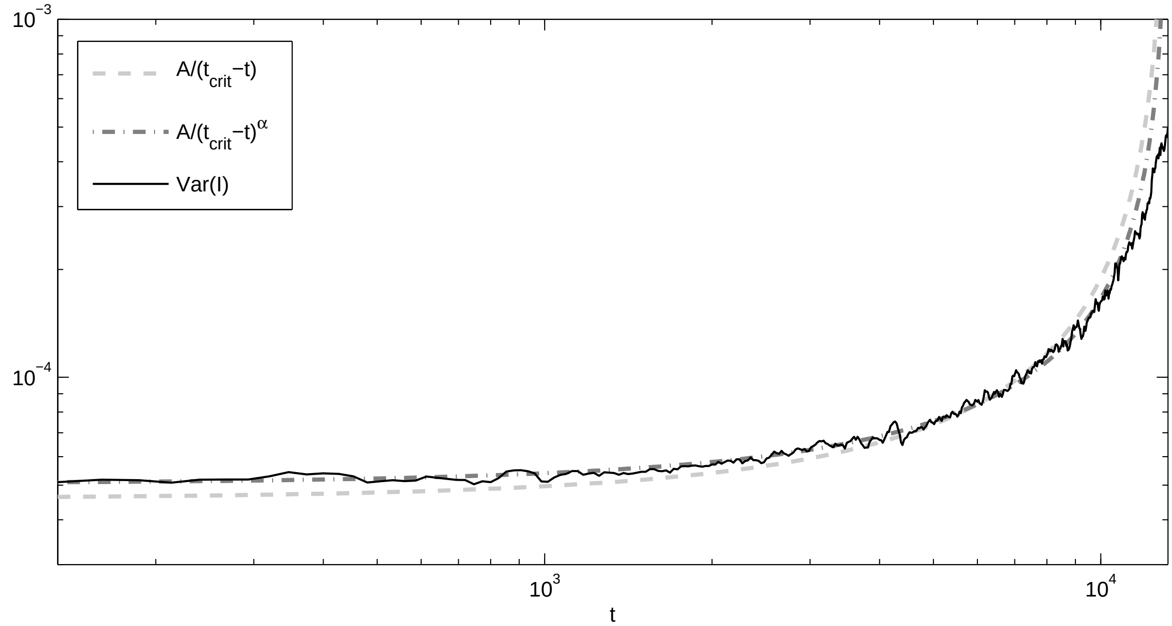

Figure 3.2: Here we see the variance of the aggregated variable $I(t)$. As a reference we show the curve $A/(t_{crit} - t)^{\alpha}$ with both the expected theoretical exponent $\alpha = 1$ and with the exponent $\alpha = 0.8414$ provided by the best fit over 90% of the considered time interval. Note that as we approach the critical moment the curve for the variance is noticeable below the curve with $\alpha = 1$.

Figure 3.2 shows the result of this calculations if we cut off $I(t)$ at 0, i.e. we use the rule

$$\dot{I}(t) = \max\{\sigma\xi(t), 0\}, \quad \text{if} \quad I(t) = 0$$

for the discrete-time numerical scheme; for an introduction to numerical schemes for stochastic ordinary differential equations see [49]. The results show that the key exponent α decreases in comparison to the system without cut-off.

Next, we consider the heterogeneous system. We are going to consider situations in which the white noises $\xi(t,\omega)$ are dependent on each other for different $\omega \in \Omega$, or where the space of h-states is discrete to understand, which implications these assumptions have on the model. Note that both assumptions have a direct modelling motivation. Usually, we may group or cluster different parts of a heterogeneous population into different classes, e.g. all parts with a different trait. Secondly, $\xi(t,\omega)$ models all stochastic internal and external effects and one natural assumption would be that all classes of the heterogeneous population are subject to the same external fluctuations, which would lead to the case $\xi(t,\omega) = \xi(t)$, i.e. the same white noise acts on all h-states. Note that for the aggregated variable $I(t)$ we have

$$\dot{I}(t) = \int_{\Omega} \beta(t,\omega)J(t)(f(\omega) - I(t,\omega)) - \gamma(\omega)I(t,\omega)\,\mathrm{d}\omega + \int_{\Omega} \sigma(\omega)\xi(t,\omega)\,\mathrm{d}\omega.$$

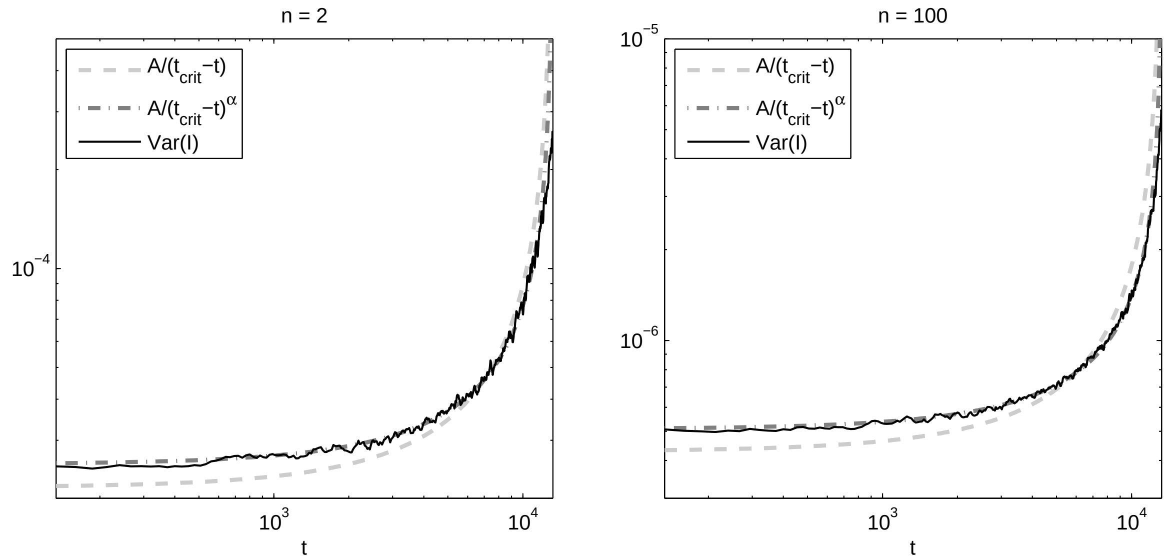

Figure 3.3: The results for the discrete heterogeneous system for two different values of n. For $n = 2$ the best fit results in $A = 0.0432$ and $\alpha = 0.7842$, for $n = 100$ in $A = 0.0004$ and $\alpha = 0.7135$. Note that both values decrease for bigger n.

If Ω is continuous and the $\xi(t,\omega)$ are independent of each other, then $\int_\Omega \sigma(\omega)\xi(t,\omega)\,\mathrm{d}\omega = 0$ and the influence of the noise is reduced to indirect effects. We therefore consider either continuous Ω with dependent $\xi(t,\omega)$ or a discrete Ω with independent $\xi(t,\omega)$.

We start with the discrete h-state scenario. For an integer $n > 1$ we set

$$\Omega = \left\{ \frac{i}{n-1} : i = 0, \cdots, n-1 \right\}.$$

As measure μ we choose the counting measure normed to 1 over Ω

$$\int_\Omega \phi(\omega)\,\mathrm{d}\omega = \frac{1}{n}\sum_{i=1}^{n} \phi(\omega_i).$$

We assume that $\beta(t,\omega) = \beta_0(t)\beta(\omega)$ and $\dot{\beta_0}(t) = \varepsilon$. As in the homogeneous case we choose $I(0) = 0$ and $\beta_0(0) = 0$ as initial conditions and $\beta = 0.3$, $\gamma = 0.4$, and $\sigma = 0.01$ for the parameters. The time scale separation parameter ε for the slow variable is again set at $\varepsilon = 0.0001$. Here the heterogeneity influences the number of elements in Ω and the distribution $f(\omega)$. Furthermore, $\xi(t,\omega)$ are chosen as n independent identically distributed random variables. We will both now and for continuous Ω later consider the distribution

$$f(\omega) = \frac{\frac{1}{\sqrt{2\pi}\theta} e^{-\frac{(\omega-0.5)^2}{2\theta^2}}}{\int_\Omega \frac{1}{\sqrt{2\pi}\theta} e^{-\frac{(\zeta-0.5)^2}{2\theta^2}}\,\mathrm{d}\zeta}.$$

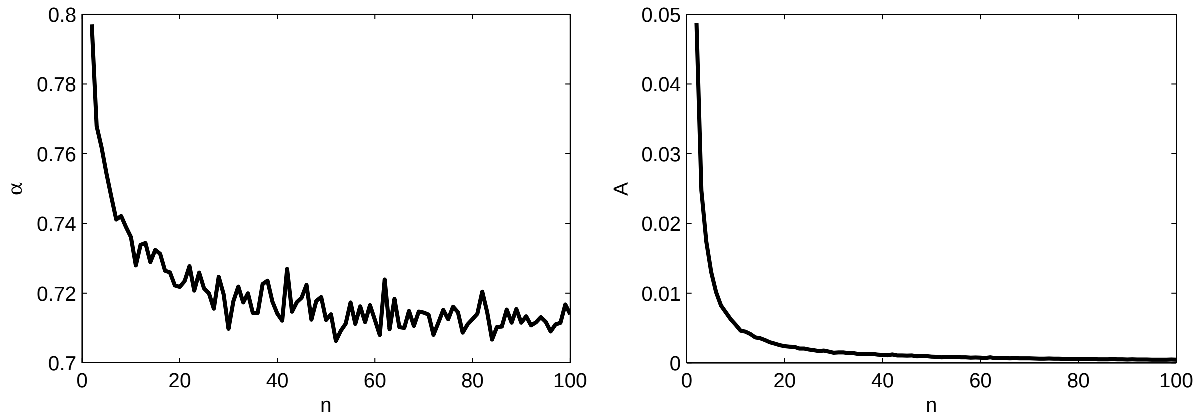

Figure 3.4: We see the influence of n on the on the parameters for the best fit, calculated over 90% of the time interval. Both α and A decrease as n increases. The decrease is steep for small n and approaches a constant level as n becomes large.

This is simply a normal distribution with mean 0.5 truncated to Ω. Figure 3.5 shows $f(\omega)$ for different values of p. The parameter θ is the standard deviation of this distribution. Note that as θ goes towards 0, the function $f(\omega)$ converges to the delta-distribution $\delta(\omega - 0.5)$. Hence, the the heterogeneous system starts to approximate the homogeneous one as $\theta \to 0$. On the other hand, if $\theta \to +\infty$ then $f(\omega)$ converges to the constant function $f(\omega) = 1$. We will therefore parametrise $f(\omega)$ with $\theta = \frac{1}{(2p-2)^2} - \frac{1}{4}$ for $p \in (0, 1)$. In the discrete case which we consider first, this yields approximately a binomial-type distribution. In Figure 3.3 we show the result for $p = 0.5$ and two different choices of n. Figure 3.4 shows how both α and A in the best fit curve change with increasing n. A clear trend is observed showing that α (and A) decrease as n is increased.

For the heterogeneous system with continuous Ω we choose $\Omega = [0, 1]$ with μ as the Lebesgue measure. At first we again restrict the influence of the heterogeneity to the function $f(\omega)$. The choice of the other parameters in unchanged from the discrete system. What has to be changed however, is the noise term in the equation. As mentioned above we want the noise for different h-states to be dependent on each other. We do this by using the first natural approximation of using the same white noise for all h-states, i.e. $\xi(t, \omega) = \xi(t)$ independent of ω. In Figure 3.6 we show the variance of $I(t)$ against the reference curves for two different values of the parameter p. In Figure 3.7 we show, how p influences both A and α. The results show that upon increasing p, we first see α increase and A decrease until they stabilize for larger p. We observe that the stabilization approximately happens when the distribution $f(\omega)$ starts to have full support on $[0, 1]$.

The last case we are interested in here is to consider a system where $\beta(t, \omega)$ is not separable in the sense that it cannot be factored into a product of functions depending only on t and ω. From the

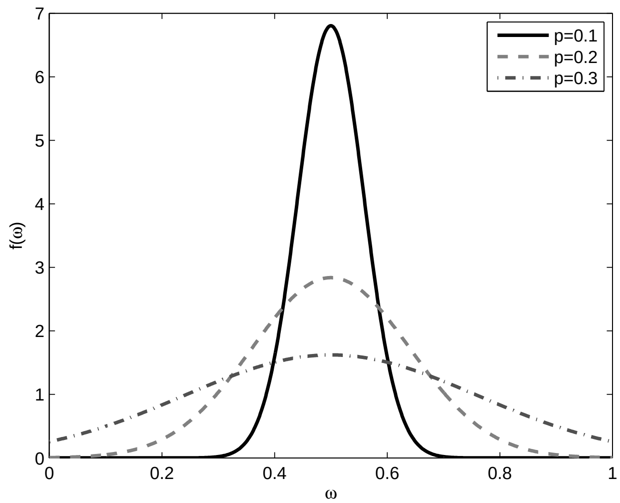

Figure 3.5: Plot of $f(\omega)$ for different values of p. For small p the function $f(\omega)$ approaches a δ-Distribution at 0.5. For larger p the function becomes more flat. Note that for small p the support of $f(\omega)$ increases with p.

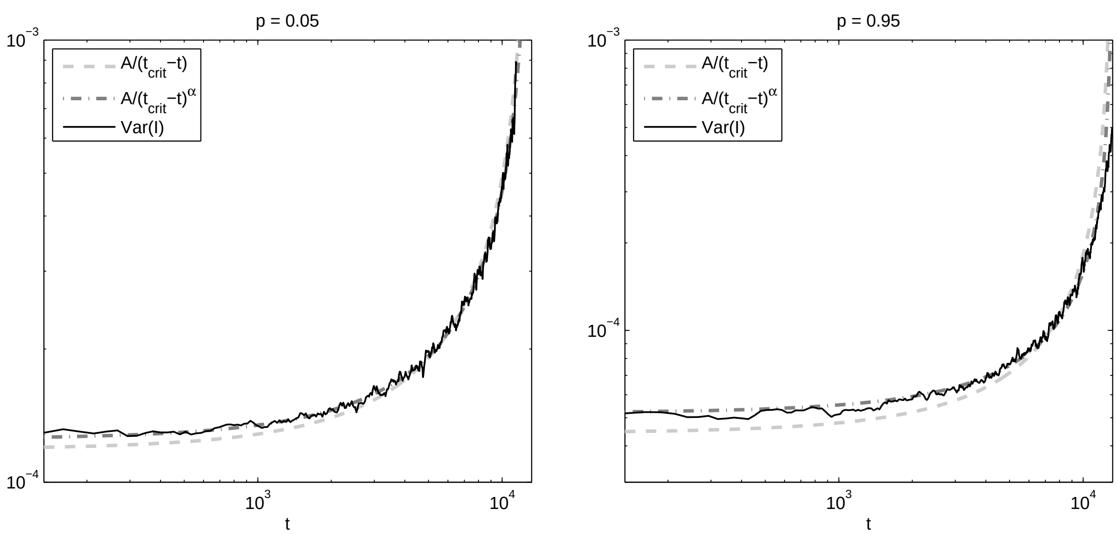

Figure 3.6: Results for the continuous heterogeneous system for two different values of p. For $p = 0.05$ the best fit over 90% of the time interval was calculated as $\alpha = 0.8587$ and $A = 0.0074$. For $p = 0.95$ these values were $\alpha = 0.7885$ and $A = 0.0923$. We can see that for $p = 0.95$ the variance is visibly below the reference curve with $\alpha = 1$ while for $p = 0.05$ it still follows this curve quite closely.

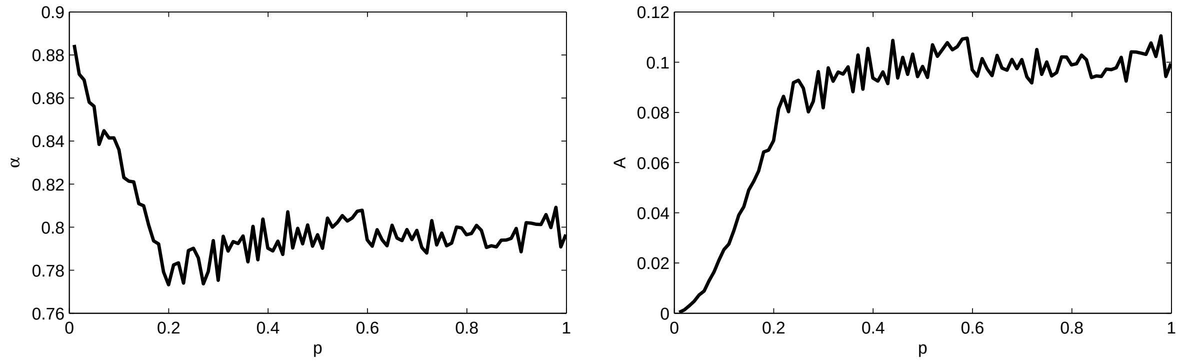

Figure 3.7: This shows the influence of the parameter p on the values α and A of the best fit, calculated over 90% of the time interval. In α we see initially a steady decrease until it reaches a constant level. In A we see an initial increase until the values reach a fixed level. Note that the levelling out both α and A occur for the same values of p. Furthermore, by comparing with Figure 3.5 we see that this coincides with those values of p for which the support of $f(\omega)$ becomes the whole of Ω.

modelling standpoint, this means that the evolution of the transmission rate and the heterogeneity in the population interact in a non-trivial way, for example, one may consider the situation when a certain population trait amplifies the change in the transmission rate, while another trait decreases it. As a first benchmark mathematical example, we simply set

$$\dot{\beta}(t,\omega) = \varepsilon(\omega + 0.5)t^{\omega - 0.5},$$

which is solved by $\beta(t,\omega) = \varepsilon t^{\omega+0.5}$. We restrict any further influence of ω to $f(\omega)$. However, we choose $f(\omega)$ slightly differently than before. We set

$$f(\omega) = \frac{\frac{1}{\sqrt{2\pi}0.1} e^{-\frac{(\omega-\mu)^2}{2*0.1^2}}}{\displaystyle\int_0^1 \frac{1}{\sqrt{2\pi}0.1} e^{-\frac{(\zeta-\mu)^2}{2*0.1^2}} \,\mathrm{d}\zeta},$$

i.e. a normal distribution with mean μ and a standard deviation of 0.1. We let μ vary in $[0,1]$. All other parameters are the same as before. Figure 3.8 shows, how μ influences A and α as calculated from an aggregation of 100 simulations and fitted over 90% of the time interval. We observe a very strong trend in the crucial exponent α, which decreases as the mean μ of $f(\omega)$ is increased.

3.7 Explanations

In this section we give some explanations, formal or heuristic, for the effect that are observable in our simulations

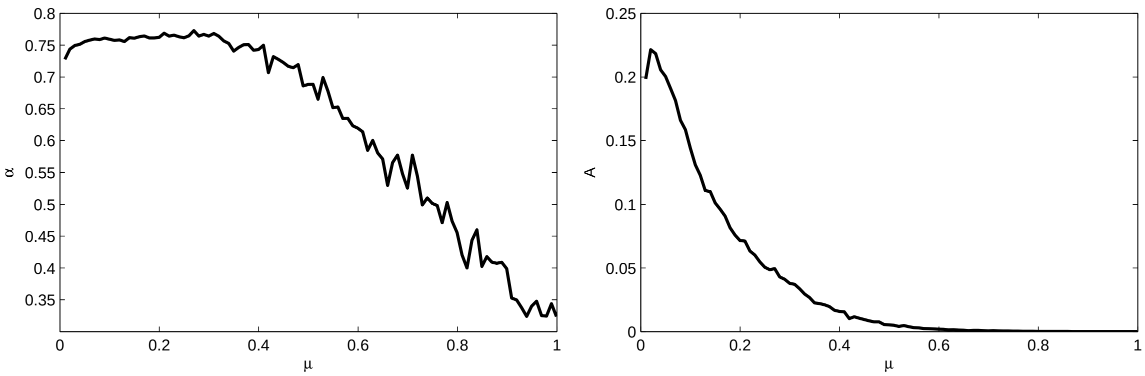

Figure 3.8: We see the influence of the parameter μ on the values α and A of the best fit, calculated over 90% of the time interval. With increasing μ both α and A decrease significantly.

3.7.1 Homogeneous system

The first effect we want to explain is the influence of the cut off on the homogeneous system. Since the steady state solution $I(t) = 0$ is asymptotically stable and the added white noise always has an expected value of 0, in the system without cut off $I(t)$ fluctuates around 0. Once we introduce the cut off $I(t)$ can no longer fluctuate freely. This introduces a bias in the positive direction. That is, a sample path $I(t)$ is free to change upwards but we stop it when it changes too far downwards. This results in the averaged path being strictly positive (see Figure 3.9). Another effect is that because we restrict the fluctuations of the white noise we decrease the variance of the resulting stochastic process $I(t)$. This can be seen by comparing Figures 3.1 and 3.2. Finally, in the system without cut off the variance increases at a certain rate. In the system with cut off this increase is still present, but we also have a second effect at work. Due to the fact that the averaged path also increases, each individual sample path has, as it were, more space to fluctuate in, as a downwards deviation from the average path can now be bigger than before without hitting 0. Thus in addition to the usual increase in the variance there is also a decrease of the restriction we place on the variance. Therefore, the increase of the variance is steeper in the system with cut off. This steeper increase is translated into a decrease of α.

3.7.2 Discrete heterogeneous system

We now want to analyse the observed changes in the heterogeneous system. We first look at the case where Ω is discrete. Recall that we used

$$f(\omega) = \frac{1}{\sqrt{2\pi}\theta} e^{-\frac{(\omega-0.5)^2}{2\theta^2}} \frac{1}{C}.$$

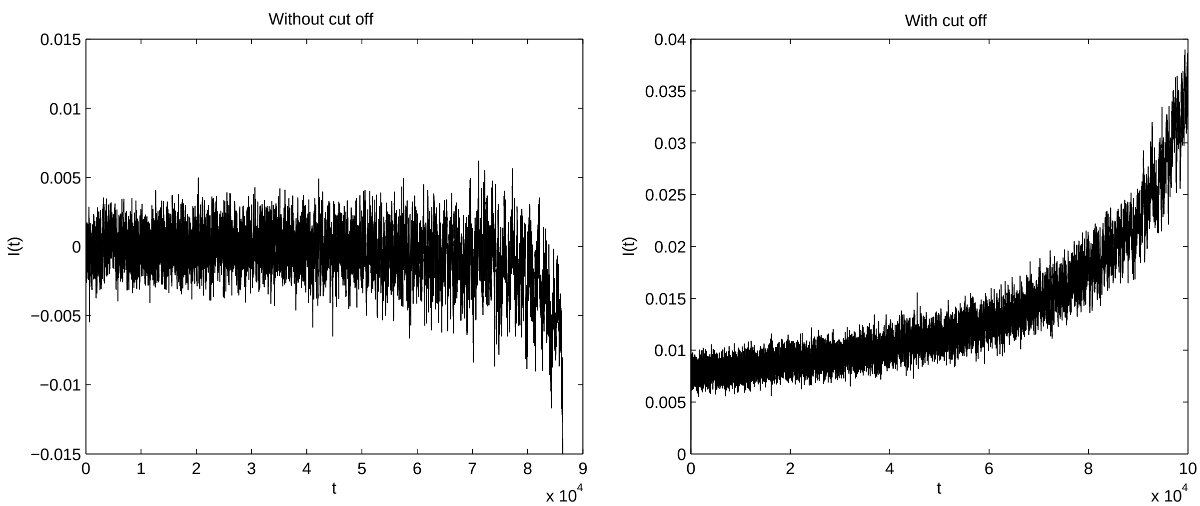

Figure 3.9: Averaged path of the homogeneous system, averaged over 100 simulation, both with and without cut off. The path without cut off eventually tends towards $-\infty$ as it drops below the unstable branch of the transcritical bifurcation.

with

$$C = \frac{1}{n}\sum_{i=1}^{n} \frac{1}{\sqrt{2\pi}\theta} e^{-\frac{\left(\frac{i}{n-1}-0.5\right)^2}{2\theta^2}}.$$

In Figure 3.10 we show, how this normalisation constant C changes with n. Since C is increasing in n we have that, heuristically, for a fixed $\omega \in \Omega$ the value $f(\omega)$ decreases. A more rigorous way to state this is to say that if ω is in Ω for a discretisation level n_1 and for a level n_2 with $n_1 < n_2$, then $f(\omega)$ is smaller for n_2. Now note that due to the fact that we have chosen most of our parameters independent of ω, the linearisation of $\dot{I}(t,\omega)$ is given by

$$\dot{\mathcal{I}}(t,\omega) = \beta(t)f(\omega)\mathcal{I}(t) - \gamma\mathcal{I}(t,\omega) + \sigma\xi(t,\omega).$$

Thus, if $f(\omega)$ becomes smaller then $I(t,\omega)$ becomes more "rigid", i.e. it fluctuates less, which results in smaller value of A. But this in turn also means that as R_0 approaches 1 the additional freedom to fluctuate increases. This results in a bigger increase in the variance of $I(t)$ and thus a smaller value of α. Both of these effects are visible in Figure 3.4. Furthermore, by comparing Figures 3.4 and 3.10 we see that the levelling out of α and A coincides with the levelling out of C.

3.7.3 Continuous heterogeneous system

For the heterogeneous system with continuous Ω we note that by definition we always have $I(t,\omega) \in [0, f(\omega)]$. If the parameter p is big enough then $f(\omega)$ is large enough for all ω so that the upper bound

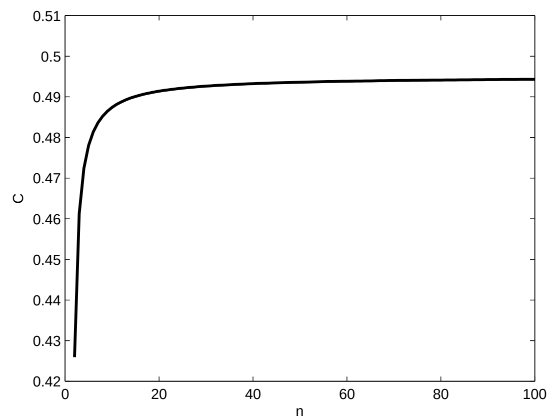

Figure 3.10: The normalisation constant C for $n = 2, \dots, 100$.

is not important due to the fact that it is never reached. If p is small however, then $f(\omega)$ also becomes small for some ω. Thus we not only have a cut off at 0 but also at $f(\omega)$. Thus, for small p the variance is even more restricted. Also for these ω a rise of the average path will not result in more freedom in its fluctuation due to the restriction above by $f(\omega)$. Only when p increases and the upper bound $f(\omega)$ becomes less and less important, then the increase of the variation is aided by a increased freedom to fluctuate, which leads to lower values of α. In Figure 3.7 we see exactly this behaviour. Since these changes in A and α depend solely on these cut off effects we expect that they vanish if we make the same simulations for the system without cut off. The results of such a simulation can be seen in Figure 3.11, where indeed p has no discernible influence on A or α.

3.7.4 Non-separable $\beta(t, \omega)$

In order to explain our observations of the system where $\beta(t, \omega)$ is not separable we first look at the linearisation of the equations. We assume that all functions in our equations are in $L^2(\Omega)$. We can write for the deterministic system (3.4)

$$\dot{I}(t, \omega) = F(I(t, \omega))$$

with

$$F(I(t, \omega)) = \beta(\omega) \int_\Omega q(\omega) I(t, \omega) \, \mathrm{d}\omega (f(\omega) - I(t, \omega)) - \gamma(\omega) I(t, \omega)$$

The Fréchet-derivative of F, evaluated at I^* and applied to $\zeta(\omega)$, is given by

$$\left[\frac{\mathrm{d}F}{\mathrm{d}I}(I^*) \right] \zeta(\omega) = \beta(\omega) \int_\Omega q(\omega) \zeta(\omega) \, \mathrm{d}\omega \; (f(\omega) - I^*) - \beta(\omega) \int_\Omega q(\omega) I^* \, \mathrm{d}\omega \; \zeta(\omega) - \gamma(\omega) \zeta(\omega).$$

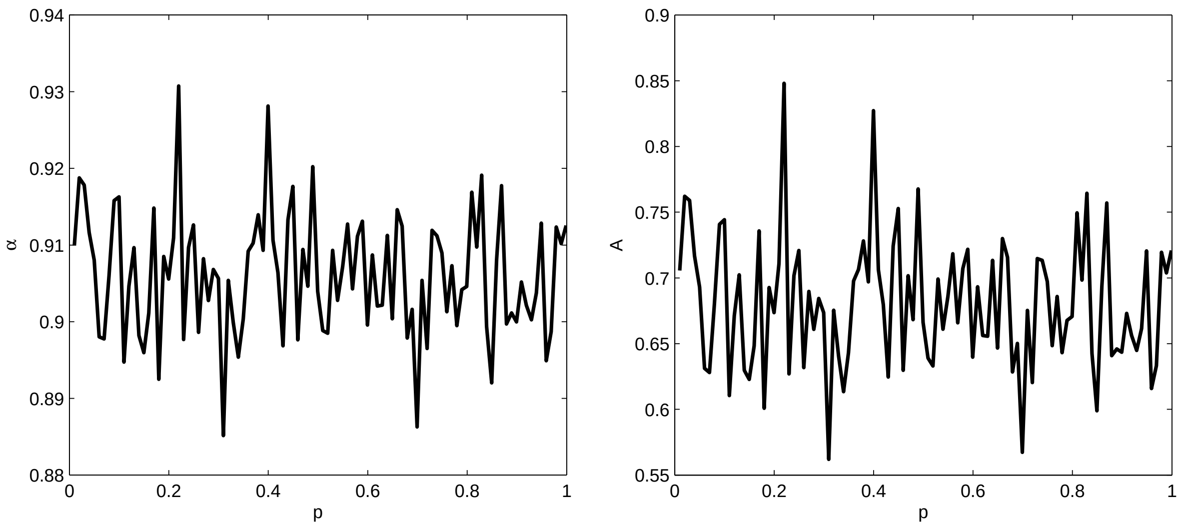

Figure 3.11: We show, dependent on p, the change in the values α and A of the best fit, calculated over 80% of the time interval, for the heterogeneous system without cut off. There is no discernible influence of p present.

We define a linear operator T by $T\mathcal{I}(t,\omega) = \left[\frac{\mathrm{d}F}{\mathrm{d}I}(0)\right]\mathcal{I}(t,\omega)$. In particular, the equation linearised at 0 reads as

$$\dot{\mathcal{I}}(t,\omega) = T\mathcal{I}(t,\omega) = f(\omega)\beta(\omega)\int_{\Omega} q(\omega)\mathcal{I}(t,\omega)\,\mathrm{d}\omega - \gamma(\omega)\mathcal{I}(t,\omega).$$

We are interested in the spectrum of the operator T. We consider this operator on the space $X = \{\zeta \in L^2(\Omega) : \zeta(\omega) \in [0, f(\omega)]\}$, i.e. the subset of $L^2(\Omega)$ that consists of the points which are possible states of our system. A point $\lambda \in \mathbb{C}$ is an eigenvalue of T if and only if there exists an eigenvector $\zeta \in X$ such that $T\zeta - \lambda\zeta = 0$. This equation in its longer form is

$$f(\omega)\beta(\omega)\int_{\Omega} q(\omega)\zeta(\omega)\,\mathrm{d}\omega - \gamma(\omega)\zeta(\omega) - \lambda\zeta(\omega) = 0.$$

We can rearrange this to get

$$\zeta(\omega) = f(\omega)\frac{\beta(\omega)}{\gamma(\omega)+\lambda}\int_{\Omega} q(\omega)\zeta(\omega)\,\mathrm{d}\omega.$$

Plugging this into the above equation yields

$$\begin{aligned} 0 &= f(\omega)\beta(\omega)\int_{\Omega} q(\omega)f(\omega)\frac{\beta(\omega)}{\gamma(\omega)+\lambda}\,\mathrm{d}\omega \int_{\Omega} q(\omega)\zeta(\omega)\,\mathrm{d}\omega - f(\omega)\beta(\omega)\int_{\Omega} q(\omega)\zeta(\omega)\,\mathrm{d}\omega \\ &= f(\omega)\beta(\omega)\int_{\Omega} q(\omega)\zeta(\omega)\,\mathrm{d}\omega \left(\int_{\Omega} q(\omega)f(\omega)\frac{\beta(\omega)}{\gamma(\omega)+\lambda}\,\mathrm{d}\omega - 1\right) \end{aligned}$$

An eigenvalue λ of T must therefore satisfy

$$\int_\Omega q(\omega)f(\omega)\frac{\beta(\omega)}{\gamma(\omega)+\lambda}\,\mathrm{d}\omega = 1. \tag{3.18}$$

or

$$(\gamma(\omega)+\lambda)\zeta(\omega) = 0 \quad \text{and} \quad \int_\Omega q(\omega)\zeta(\omega)\,\mathrm{d}\omega = 0. \tag{3.19}$$

Note that any λ that satisfies the first equation in (3.19) is negative as $\gamma(\omega)$ is strictly positive. Furthermore, due to $q(\omega)$ being a positive function, any eigenvector to fulfil the second equation in (3.19) has to be negative somewhere. The domain X which we consider for T does therefore not contain any eigenvectors satisfying this equation. For these reasons we consider only equation (3.18) to be relevant for our considerations. This equation has a unique solution. Note that for $\lambda = 0$ the left hand side is exactly R_0. In particular, λ is positive if $R_0 > 1$ and negative if $R_0 < 1$. Note that if we assume in our calculations that $\gamma(\omega)$ is independent of ω then we can rearrange the equation (3.18) to identify λ as[2]

$$\lambda = \int_\Omega q(\omega)f(\omega)\beta(\omega)\,\mathrm{d}\omega - \gamma.$$

If we now assume that $\beta(t,\omega)$ is a time dependent slow variable, then we can expect that this equation approximately describes the evolution of λ. In particular, if $\beta(t,\omega)$ is separable, $\beta(t,\omega) = \beta_0(t)\beta(\omega)$, then $\int_\Omega q(\omega)f(\omega)\beta(\omega)\,\mathrm{d}\omega$ is a constant κ and we get

$$\lambda(t) = \beta_0(t)\kappa - \gamma.$$

We know that $\lambda(t)$ is the exponential rate with, which the quasi-stationary system ($\varepsilon = 0$) would go to 0. Hence, for negative $\lambda(t)$, the smaller it is the more "rigid" the system is. If $\beta_0(t)$, and thus $\lambda(t)$, is increasing fast near the critical point then it is tightly locked to 0 until shortly before t_{crit}. Therefore, we expect a sharp increase in the variation close to t_{crit} and thus a low α. We show this effect for the homogeneous system in Figure 3.12.

In our simulation for the heterogeneous system we achieve the same effect by changing the distribution $f(\omega)$. Recall that we used $\beta(t,\omega) = \varepsilon t^{\omega+0.5}$. Thus, for $\omega = 0$ the increase is as the square root of t while for $\omega = 1$ it is polynomial. With the parameter μ we can control, which increase is dominant. If μ is small then $f(\omega)$ is concentrated on those ω for which $\beta(t,\omega) \approx \varepsilon t^{0.5}$. Thus it grows slowly and we expect a higher α. Also the system is less "rigid" and allows for a higher overall variance in $I(t)$ and thus larger A. As μ increases, so does the derivative of $\lambda(t)$ and we expect a more rigid system (hence smaller A) and a faster increase of the variance near the critical point (smaller α). Both of these behaviours can be seen in Figure 3.8. In Figure 3.13 we show how $\lambda(t)$ behaves for different choices of μ.

[2] This is an example why we only consider equation (3.18): if $\gamma(\omega)$ is constant then (3.19) has exactly one solution $\lambda_2 = -\gamma$. This eigenvalue is always smaller than λ and does therefore not concern us.

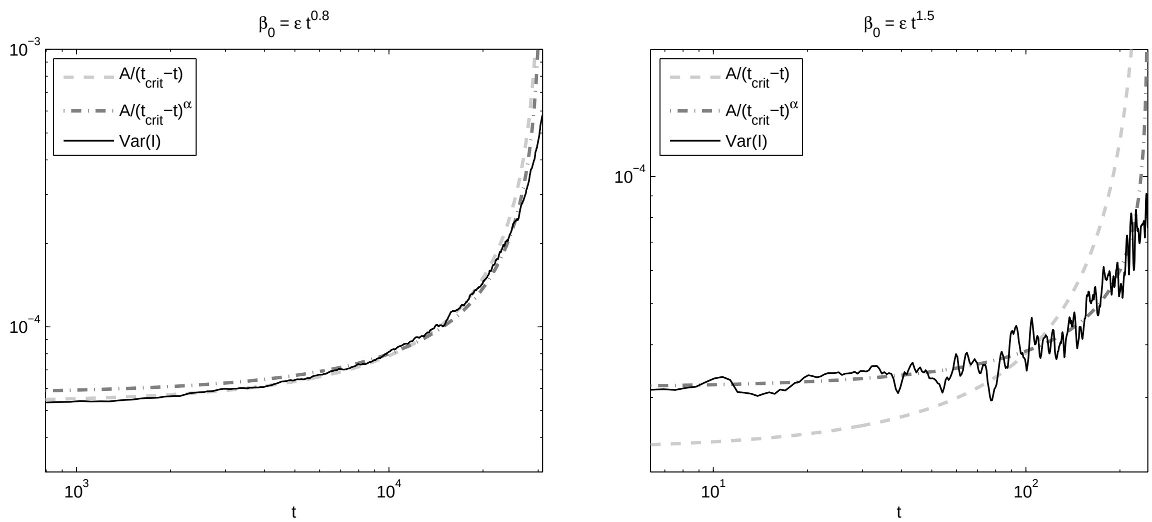

Figure 3.12: The homogeneous system for different $\beta_0(t)$, with best fit over 90% of the time interval. While for $\beta_0(t) = \varepsilon t^{0.8}$ the variance is still in the vicinity of the reference curve with the theoretical exponent $\alpha = 1$ (although visibly below it), for $\beta_0(t) = \varepsilon t^{1.5}$ these curves are markedly different. This can also be seen in the value α of the best fit. In the former case it is $\alpha = 0.8435$ while for the latter we get $\alpha = 0.3795$.

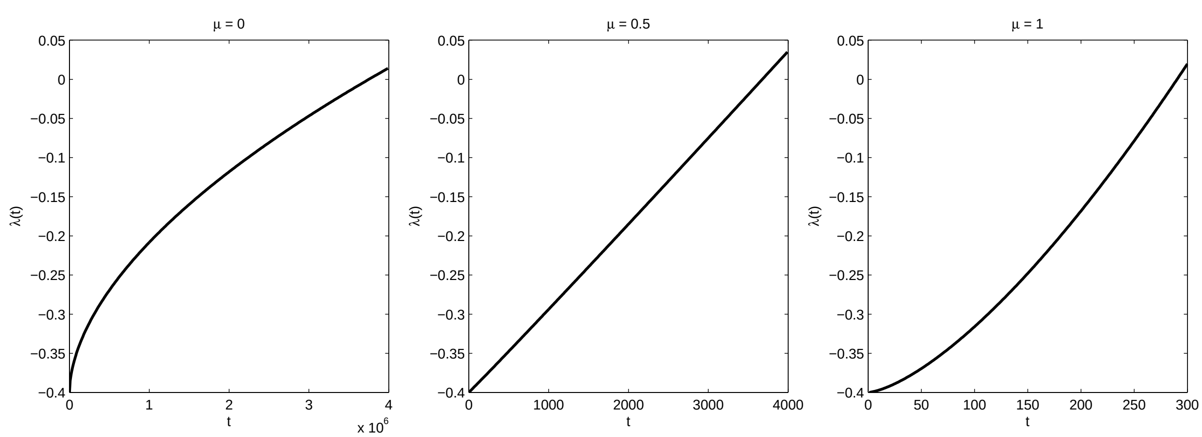

Figure 3.13: The function $\lambda(t)$ for different choices of μ. We can see that for $\mu = 0$ the function $\lambda(t)$ is concave and for $\mu = 1$ it is convex. For the intermediate value $\mu = 0.5$ it is approximately linear. Furthermore we see a significant difference in the time it takes for $\lambda(t)$ to reach 0.

3.8 Outlook

In this paper we have provided new insights on qualitative persistence and quantitative non-persistence of various dynamical phenomena in an SIS-model with heterogeneous populations. The main conclusions are that one can expect a generic dynamical structure of a disease-free and endemic state, separated by a transition at R_0, to persist. However, the classical warning signs for tipping points have to be re-considered carefully in heterogeneous epidemic models. In particular, we observed that the scaling law exponent for the inverse power-law increase of the variance decreases and in many cases lies below the theoretically predicted values of the homogeneous population system. This means that using an extrapolation procedure with fixed exponent to predict the region, where the practical R_0-value lies, may not give the correct epidemic threshold.

Since, this work is one of the first investigations of warning signs in heterogeneous population models, it is clear that many open questions remain. Here we shall just mention a few of these. From a mathematical perspective, it would be natural to ask for a full analytical description of phenomena arising near bifurcation points for heterogeneous stochastic fast-slow systems. There are basically no results in this direction available yet, although recent significant progress in mathematical multiscale dynamics may suggest that a (partial) analysis should be possible [69]. From a biological and epidemic-modelling perspective, it would be interesting to compare different classes of models to the fast-slow heterogeneous stochastic SIS model we considered with a view towards heterogeneity, epidemic thresholds and warning signs for critical transitions. For example, this could include SIR models [51, 92], adaptive network dynamics [40, 88, 101], and stochastic partial differential equations [3, 71].

Of course, many other extensions of the model, for example demographic changes, could also influence the behaviour. A focus on quantitative scaling laws could shed new light on which models are most appropriate for certain disease outbreaks, when results are compared with data.

Of course, our study here only carries out a few important baseline steps to achieve these future goals. Nevertheless, it provides clear evidence for the need to further investigate the interplay between various effects such as parameter drift, noise, and heterogeneity in the context of biological models, which exhibit bifurcation phenomena of high practical and social relevance.

Appendix: The convergence in mean

Here we prove the auxillary result Lemma 6, which shows that for the deterministic heterogenous SIS model we study, a suitable weighted mean of the infected population $J(t) := \int_\Omega q(\omega)I(t,\omega)\ \mathrm{d}\omega$ has a well-defined limit.

Proof of Lemma 6. We employ the same notation as in the proof of Theorem 3. In addition, define

$J^* = \limsup J(t)$ and $J_* = \liminf J(t)$. Assume that $J(t)$ does not converge, then $J^* - J_* > 0$. In the following five steps we lead this assumption to a contradiction.

Step 1: Define

$$h(J(t), \omega) = \frac{f(\omega)(\beta(\omega)J(t) + \eta(\omega))}{\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega)}.$$

We get this function by setting $\dot{I}(t, \omega) = 0$ in (3.4) and solving for $I(t, \omega)$. Further define $\Omega_f = \{\omega \in \Omega : f(\omega) > 0\}$. Obviously $\Omega \backslash \Omega_f$ is of no interest as $I(t, \omega) = 0$ there. Note that $\frac{\partial}{\partial J(t)} h(J(t), \omega) = \frac{f(\omega)\beta(\omega)\gamma(\omega)}{(b(\omega)J(t)+\eta(\omega)+\gamma(\omega))^2} > 0$ on Ω_f such that $\frac{\mathrm{d}}{\mathrm{d}t} h(J(t), \omega) \gtrless 0 \Leftrightarrow \dot{J}(t) \gtrless 0$. This also shows that $h(J(t), \omega)$ is monotone in $J(t)$. We have

$$\begin{aligned} \dot{I}(t, \omega) &= (\beta(\omega)J(t) + \eta(\omega))f(\omega) - (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))I(t, \omega) \\ &= (\beta(\omega)J(t) + \eta(\omega))f(\omega) - (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))\left(h(J(t), \omega) + I(t, \omega) - h(J(t), \omega)\right) \\ &= (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))\left(h(J(t), \omega) - I(t, \omega)\right) \end{aligned} \tag{3.20}$$

Note that we get

$$\dot{I}(t, \omega) \lesseqgtr 0 \Longleftrightarrow I(t, \omega) \gtreqless h(J(t), \omega). \tag{3.21}$$

This proves one of the claims in Lemma 6. Using (3.20) we get

$$\begin{aligned} \left| \frac{\mathrm{d}}{\mathrm{d}t} h(J(t), \omega) \right| &= \left| \frac{\partial}{\partial J(t)} h(J(t), \omega) \dot{J}(t) \right| = \left| \frac{\partial}{\partial J(t)} h(J(t), \omega) \int_\Omega q(\omega) \dot{I}(t, \omega) \, \mathrm{d}\omega \right| \\ &= \left| \frac{f(\omega)\beta(\omega)\gamma(\omega)}{(b(\omega)J(t) + \eta(\omega) + \gamma(\omega))^2} \int_\Omega q(\omega)(\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))\left(h(J(t), \omega) - I(t, \omega)\right) \mathrm{d}\omega \right| \\ &\leq \frac{f(\omega)\beta(\omega)\gamma(\omega)}{(b(\omega)J(t) + \eta(\omega) + \gamma(\omega))^2} \int_\Omega q(\omega)(\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega)) \left| h(J(t), \omega) - I(t, \omega) \right| \mathrm{d}\omega \\ &\leq f(\omega) \frac{\beta(\omega)\gamma(\omega)}{(\eta(\omega) + \gamma(\omega))^2} C \int_\Omega q(\omega) f(\omega) \, \mathrm{d}\omega \\ &= f(\omega) \frac{\beta(\omega)\gamma(\omega)}{(\eta(\omega) + \gamma(\omega))^2} C, \end{aligned} \tag{3.22}$$

where $C = \sup_{\omega \in \Omega_f} (\beta(\omega) + \eta(\omega) + \gamma(\omega))$.

Step 2: Define

$$\begin{aligned} \delta(\omega) = h(J^*, \omega) - h(J_*, \omega) &= f(\omega) \left(\frac{(\beta(\omega)J^* + \eta(\omega))}{\beta(\omega)J^* + \eta(\omega) + \gamma(\omega)} - \frac{(\beta(\omega)J_* + \eta(\omega))}{\beta(\omega)J_* + \eta(\omega) + \gamma(\omega)} \right) \\ &= f(\omega) \frac{\beta(\omega)\gamma(\omega)\left(J^* - J_*\right)}{(\beta(\omega)J^* + \eta(\omega) + \gamma(\omega))\left(\beta(\omega)J_* + \eta(\omega) + \gamma(\omega)\right)}. \end{aligned}$$

For all $\varepsilon > 0$ there exist arbitrarily large t^* such that $J(t^*) < J_* + \varepsilon$. We want to give an estimate for $t(\omega)$ such that $h(J(t),\omega) \leq \delta(\omega)/3 + h(J_* + \varepsilon, \omega)$ for $t \in (t^*, t(\omega))$. Because of (3.22) we get

$$\begin{aligned}
t(\omega) &\geq \frac{\delta(\omega)}{3f(\omega)\frac{\beta(\omega)\gamma(\omega)}{(\eta(\omega)+\gamma(\omega))^2}C} = \frac{f(\omega)\frac{\beta(\omega)\gamma(\omega)(J^*-J_*)}{(\beta(\omega)J^*+\eta(\omega)+\gamma(\omega))(\beta(\omega)J_*+\eta(\omega)+\gamma(\omega))}}{3f(\omega)\frac{\beta(\omega)\gamma(\omega)}{(\eta(\omega)+\gamma(\omega))^2}C} \\
&= \frac{(J^* - J_*)}{(\beta(\omega)J^* + \eta(\omega) + \gamma(\omega))\,(\beta(\omega)J_* + \eta(\omega) + \gamma(\omega))} \frac{(\eta(\omega)+\gamma(\omega))^2}{3C} \\
&\geq \frac{\inf_{\omega\in\Omega_f}\left((\eta(\omega)+\gamma(\omega))^2\right)(J^* - J_*)}{3C^3} =: \kappa.
\end{aligned}$$

Note that $\kappa > 0$ and is independent of ω.

Step 3: Because of

$$\delta(\omega) \geq f(\omega) \frac{\inf_{\omega\in\Omega_f}(\beta(\omega)\gamma(\omega))\,(J^* - J_*)}{C^2}$$

we have for every $\varepsilon > 0$ a t_ε such that $h(J(t),\omega) < h(J^*,\omega) + \varepsilon\delta(\omega)/2$ for all $t > t_\varepsilon$. Assume now that $I(t,\omega) > h(J^*,\omega) + \varepsilon\delta(\omega)$. Then using (3.20) we see that

$$\begin{aligned}
\left|\dot{I}(t,\omega)\right| &= (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))\,|h(J(t),\omega) - I(t,\omega)| \\
&\geq \inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega))\frac{\varepsilon}{2}\delta(\omega) \geq \frac{\varepsilon}{2} f(\omega) \inf_{\omega\in\Omega_f}\left(\frac{\delta(\omega)}{f(\omega)}\right) \inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega)).
\end{aligned}$$

From this and (3.21) we get that for t large enough we have $I(t,\omega) \leq h(J^*,\omega) + \varepsilon\delta(\omega)$ for all $\omega \in \Omega_f$.

Step 4: Choose $\varepsilon > 0$ small enough such that the two inequalities

$$h(J^*,\omega) - \varepsilon\frac{\delta(\omega)}{3} \geq h(J_* + \varepsilon, \omega) + \frac{2}{3}\delta(\omega), \quad 2\varepsilon \leq \frac{\kappa}{3} \inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega)) \tag{3.23}$$

hold true. Now choose a t^* such that $J(t^*) < J_* + \varepsilon$. Let t^* also be large enough such that for all $t \geq t^*$ we have

$$I(t,\omega) \leq h(J^*,\omega) + \varepsilon\frac{\delta(\omega)}{3}. \tag{3.24}$$

For every $\omega \in \Omega_f$ and for $t \in (t^*, t^* + \kappa)$ where $I(t,\omega) \geq h(J^*,\omega) - \varepsilon\delta(\omega)/3$ we have because of the first inequality in (3.23) that $|I(t,\omega) - h(J(t),\omega)| \geq \delta(\omega)/3$. Thus, using the second inequality in (3.23), we get

$$\begin{aligned}
\left|\dot{I}(t,\omega)\right| &= (\beta(\omega)J(t) + \eta(\omega) + \gamma(\omega))\,|h(J(t),\omega) - I(t,\omega)| \\
&\geq \frac{\delta(\omega)}{3} \inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega)) \geq \frac{2\delta(\omega)\varepsilon}{3\kappa}.
\end{aligned}$$

Combining this with (3.24) and using (3.21) yields

$$I(t^* + \kappa, \omega) \leq h(J^*, \omega) - \varepsilon \frac{\delta(\omega)}{3}, \quad \omega \in \Omega_f.$$

Step 5: Let $\tau > t^* + \kappa$ be such that $h(J(\tau), \omega) \geq h(J^*, \omega) - \varepsilon\delta(\omega)/3$ for all $\omega \in \Omega_f$ and $J(\tau) > J(t)$ for $t \in (t^* + \kappa, \tau)$. Since $I(t, \omega)$ is increasing if and only if $h(J(t), \omega) > I(t, \omega)$ we have for all $\omega \in \Omega_f$ that $I(\tau, \omega) \leq h(J(\tau), \omega)$. Thus $\dot{I}(\tau, \omega) \geq 0$ for all $\omega \in \Omega_f$ and consequently $\dot{J}(\tau) = \int_{\Omega_f} q(\omega)\dot{I}(\tau, \omega)\,\mathrm{d}\omega \geq 0$. Therefore, if $I(t, \omega) = h(J(t), \omega)$ for any $t \geq \tau$, we have that $\dot{I}(t, \omega) = 0$ while $\dot{J}(t) \geq 0$ and consequently $\frac{\mathrm{d}}{\mathrm{d}t} h(J(t), \omega) \geq 0$. Hence, $I(t, \omega) \leq h(J(t), \omega)$ for all $t > \tau$ and all $\omega \in \Omega_f$. This in turn implies that $J(t)$ is monotonically increasing for $t > \tau$. Thus, $J(t)$ converges in contradiction to our assumption.

□

Chapter 4

Steady states and stability of heterogeneous *SIS*- and *SIR*-models

4.1 Introduction

In Chapter 1 we analysed the asymptotic behaviour of a general SI-model. As mentioned there, SI-models are amongst the simplest models used in epidemiology to describe infectious diseases. In this chapter we analyse the steady states and their stability for more complicated models. In SI-models we consider only the transmission of the disease from the susceptible to the infected population. The next level of complexity is to add one further process, namely the recovery of an infected individual. There are two possibilities. Either, an infected individual may upon recovery return into the population of susceptibles, or it may transfer to a third sub-population of recovered individuals. The first variant of models is known as an SIS-model, the second one as an SIR-model. Thus, these two types of models represent in some sense the next level of complexity from the basic SI-model. We will assume in this chapter that the total population under consideration remains constant. This assumption is often reasonable since for many diseases the duration of the infection is short compared to any demographical changes and the mortality of infected individuals is low. Even in instances where this assumption is not met, it sometimes gives a good approximation to the evolution of the disease while being easier to handle analytically.

We have already dealt to some extent with SIS-models in the previous chapter. In Section 4.2 we will consider a more general version of it. In Section 4.3 we turn to SIR-models. In both cases we identify under certain parameter conditions the steady states of the system and analyse their stability properties.

4.2 *SIS*-model

We now consider an SIS-model where for each ω the infections spreads according to the dynamics

$$\begin{aligned} \dot{S}(t,\omega) &= -\left(\sigma(\omega)\frac{J(t)}{H(t)} + \eta(\omega)\right) S(t,\omega) + \gamma(\omega) I(t,\omega), \\ \dot{I}(t,\omega) &= \left(\sigma(\omega)\frac{J(t)}{H(t)} + \eta(\omega)\right) S(t,\omega) - \gamma(\omega) I(t,\omega), \end{aligned} \tag{4.1}$$

with

$$\begin{aligned} J(t) &= \int_\Omega q_2(\omega) I(t,\omega)\,\mathrm{d}\omega, \\ H(t) &= \int_\Omega q_1(\omega) S(t,\omega) + q_2(\omega) I(t,\omega)\,\mathrm{d}\omega. \end{aligned}$$

This is the same model as considered in Chapter 3, except that we allow the weights for $S(t,\omega)$ and $I(t,\omega)$ to be different from each other. We however assume that $q_1(\omega) < q_2(\omega)\left(1 + \frac{\sigma(\omega)}{\gamma(\omega)}\right)$ holds for all $\omega \in \Omega$ (below we will explain how different assumptions can be used). We will use the same interpretations and assumptions about the parameter functions as in Chapter 3. In particular the distinction between the cases $\eta = 0$ and $\eta > 0$ is the same, the function $f(\omega)$ is defined by $f(\omega) = S(0,\omega) + I(0,\omega)$ and assumed to fulfil $\int_\Omega f(\omega)\,\mathrm{d}\omega = 1$. Using $S(t,\omega) = f(\omega) - I(t,\omega)$ turns (4.1) into

$$\dot{I}(t,\omega) = \left(\sigma(\omega)\frac{J(t)}{H(t)} + \eta(\omega)\right) f(\omega) - \left(\sigma(\omega)\frac{J(t)}{H(t)} + \eta(\omega) + \gamma(\omega)\right) I(t,\omega). \tag{4.2}$$

4.2.1 Steady states

Theorem 4. *If $\eta > 0$ then the system (4.1) has exactly one steady state $\hat{I}(\omega)$ and $\hat{I}(\omega) > 0$ whenever $f(\omega) > 0$. If $\eta = 0$ we define*

$$R_0 = \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)}{\gamma(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega)\,\mathrm{d}\omega}.$$

If $R_0 \leq 1$ then the system (4.1) has the unique steady state $\hat{I}(\omega) \equiv 0$. If $R_0 > 1$ then the system has exactly two steady states, one of them being $\hat{I}(\omega) \equiv 0$, whereas the second steady state is positive whenever $f(\omega) > 0$.

Proof Let $(\hat{S}(\omega), \hat{I}(\omega))$ be a steady state of the system (4.1) and $\hat{J}$ and $\hat{H}$ the aggregated states. From (4.2) we see that $\hat{I}(\omega)$ must fulfil

$$\hat{I}(\omega) = f(\omega) \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \mu(\omega) + \gamma(\omega)}. \tag{4.3}$$

Putting this into the definition of $\frac{J(t)}{H(t)}$ gives us

$$\frac{\hat{J}}{\hat{H}} = \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega)\,\mathrm{d}\omega + \int_\Omega (q_2(\omega) - q_1(\omega)) f(\omega) \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega}. \tag{4.4}$$

Every solution to (4.4) gives a steady state solution of system (4.1) by plugging it into (4.3). We are therefore looking for the solutions of the equation

$$\frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)x + \eta(\omega)}{\sigma(\omega)x + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega)\,\mathrm{d}\omega + \int_\Omega (q_2(\omega) - q_1(\omega)) f(\omega) \frac{\sigma(\omega)x + \eta(\omega)}{\sigma(\omega)x + \eta(\omega) + \gamma(\omega)} \,\mathrm{d}\omega} = x. \tag{4.5}$$

We will denote the left hand side of this equation by $l(x)$ and the right hand side by $r(x)$. We evaluate the first of these functions at 0 and 1. At $x = 0$ we have

$$\begin{aligned} l(0) &= \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\eta(\omega)}{\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega) d\omega + \int_\Omega (q_2(\omega) - q_1(\omega)) f(\omega) \frac{\eta(\omega)}{\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega} \\ &= \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\eta(\omega)}{\eta(\omega)+\gamma(\omega)} d\omega}{\int_\Omega q_1(\omega) f(\omega) \left(1 - \frac{\eta(\omega)}{\eta(\omega)+\gamma(\omega)}\right) \mathrm{d}\omega + \int_\Omega q_2(\omega) f(\omega) \frac{\eta(\omega)}{\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega}. \end{aligned}$$

For $\eta = 0$ this gives $l(0) = 0$ while for $\eta > 0$ we can see that $l(0) > 0$. At $x = 1$ we get

$$\begin{aligned} l(1) &= \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega)\,\mathrm{d}\omega + \int_\Omega (q_2(\omega) - q_1(\omega)) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega} \\ &= \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega) f(\omega) \left(1 - \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)}\right) \mathrm{d}\omega + \int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega} \\ &< \frac{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_2(\omega) f(\omega) \frac{\sigma(\omega)+\eta(\omega)}{\sigma(\omega)+\eta(\omega)+\gamma(\omega)} \,\mathrm{d}\omega} = 1. \end{aligned}$$

Thus $l(0) \geq r(0)$ and $l(1) < r(1)$. In order to show that there is at most one $x \in (0, 1)$ that satisfies equation (4.5) we look at the derivative of $l(x)$ at a point where $l(x) = x$. The derivative of $l(x)$ is given by (in the following we will not explicitly note the dependence of any of the parameter functions on ω)

$$l'(x) = \frac{\int_\Omega q_2 f \frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2} \,\mathrm{d}\omega}{\int_\Omega q_1 f \frac{\gamma}{\sigma x+\eta+\gamma} d\omega + \int_\Omega q_2 f \frac{\sigma x+\eta}{\sigma x+\eta+\gamma} \,\mathrm{d}\omega} - \frac{\int_\Omega q_2 f \frac{\sigma x+\eta}{\sigma x+\eta+\gamma} \,\mathrm{d}\omega \int_\Omega (q_2 - q_1) f \frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2} \,\mathrm{d}\omega}{\left(\int_\Omega q_1 f \frac{\gamma}{\sigma x+\eta+\gamma} \,\mathrm{d}\omega + \int_\Omega q_2 f \frac{\sigma x+\eta}{\sigma x+\eta+\gamma} \,\mathrm{d}\omega\right)^2}.$$

Using the definition of $l(x)$ we get

$$l'(x)=\frac{\int_\Omega q_1 f\frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega}{\int_\Omega q_1 f\frac{\gamma}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega+\int_\Omega q_2 f\frac{\sigma x+\eta}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega}l(x)+\frac{\int_\Omega q_2 f\frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega}{\int_\Omega q_1 f\frac{\gamma}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega+\int_\Omega q_2 f\frac{\sigma x+\eta}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega}(1-l(x))$$
$$=\frac{\int_\Omega q_1 f\frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega}{\int_\Omega q_2 f\frac{\sigma x+\eta}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega}l(x)^2+\frac{\int_\Omega q_2 f\frac{\sigma\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega}{\int_\Omega q_2 f\frac{\sigma x+\eta}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega}(l(x)-l(x)^2).$$

Thus, at a point $x\in(0,1)$ where $l(x)=x$ we have that $l'(x)<1$ is equivalent to

$$\int_\Omega q_1 f\frac{\sigma\gamma x^2}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega+\int_\Omega q_2 f\frac{\sigma\gamma(x-x^2)}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega<\int_\Omega q_2 f\frac{\sigma x+\eta}{\sigma x+\eta+\gamma}\,\mathrm{d}\omega.$$

Elementary manipulations show that this in turn is equivalent to

$$\int_\Omega q_1 f\frac{\sigma\gamma x^2}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega<\int_\Omega q_2 f\frac{\sigma^2x^2+\sigma\gamma x^2+2\sigma\eta x+\eta^2+\eta\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega. \tag{4.6}$$

Due to our assumption that $q_1<q_2\left(1+\frac{\sigma}{\gamma}\right)$ we get

$$\int_\Omega q_1 f\frac{\sigma\gamma x^2}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega<\int_\Omega q_2 f\frac{\sigma^2x^2+\sigma\gamma x^2}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega\leq\int_\Omega q_2 f\frac{\sigma^2x^2+\sigma\gamma x^2+2\sigma\eta x+\eta^2+\eta\gamma}{(\sigma x+\eta+\gamma)^2}\,\mathrm{d}\omega.$$

Thus, if $l(x)=x$ we have that $l(y)>y$ for $y\in(x-\varepsilon_1,x)$ and $l(y)<y$ for $y\in(x,x+\varepsilon_2)$ for sufficiently small $\varepsilon_1,\varepsilon_2>0$. In particular, if $l(x)<x$ for some $x\in(0,1)$, then $l(y)<y$ for all $y>x$.

Now, if $\eta>0$ then $l(0)>r(0)$ and $l(1)<r(1)$. Thus there exists at least one solution to (4.5). By what we have shown this solution is unique. That the resulting steady state is positive whenever $f(\omega)$ is positive can be seen from (4.3). If $\eta=0$ then $x=0$ is a solution. If $l'(0)>1$ then $l(x)>x$ for x sufficiently small and by the same arguments as before $l(x)=x$ has exactly one further solution in $(0,1)$. For the case where $l'(0)<1$ our analysis of $l(x)$ shows that $l(x)=x$ has no solution in $(0,1)$. Finally, if $l'(0)=1$, assume that $l(x)>x$ for some sufficiently small x. If we consider the same system where we exchange $q_1(\omega)$ with $q_1(\omega)+\varepsilon(\omega)$ where $\varepsilon(\omega)>0$ chosen so that all assumptions still hold true. Then for $\|\varepsilon\|$ sufficiently small, $l(x)$ will still be greater than x, but $l'(0)<1$ (see the expression for $l'(0)$ below). This is a contradiction to what we have shown before. Thus if we define

$$R_0=l'(0)=\frac{\int_\Omega q_2(\omega)f(\omega)\frac{\sigma(\omega)\gamma(\omega)}{(\gamma(\omega))^2}\,\mathrm{d}\omega\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}{\left(\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega\right)^2}=\frac{\int_\Omega q_2(\omega)f(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega},$$

we have that if $R_0\leq 1$ then $I(t,\omega)\equiv 0$ is the only steady state of the system, if $R_0>1$ then there are two steady states, one of them is again $I(t,\omega)\equiv 0$.

□

The main point of this proof is to show that equation (4.5) has at most one solution. Our assumption that $q_1(\omega) < q_2(\omega)\left(1+\frac{\sigma(\omega)}{\gamma(\omega)}\right)$ for all $\omega \in \Omega$ is one way to assure this. However this assumption is obviously only necessary and many different assumptions can lead to the same result. For example, if we assume $\eta = 0$ and $q_1(\omega) > q_2(\omega)\left(1+\frac{\sigma(\omega)}{\gamma(\omega)}\right)$ for all $\omega \in \Omega$ then the inequality (4.6) holds with '$>$' instead of '$<$' from which it can be inferred that (4.5) has no solution in $(0,1)$. Furthermore, we were not able to determine whether any assumptions are needed at all and are not aware of any parameter configuration for which equation (4.5) has two or more solutions.

We note that it can be shown the same way as in Chapter 3 that the definition of R_0 as given in Theorem 4 coincides with the definition of R_0 in [31].

4.2.2 Stability

Here we show the asymptotic behaviour of the system (4.1). The proofs here are based on the ones in Chapter 3.

Lemma 7. *The function $\frac{J(t)}{H(t)}$ converges for $t \to \infty$. Furthermore we have*

$$\dot{I}(t,\omega) \lesseqgtr 0 \Longleftrightarrow I(t,\omega) \gtreqless \frac{f(\omega)\left(\sigma(\omega)\frac{J(t)}{H(t)}+\eta(\omega)\right)}{\sigma(\omega)\frac{J(t)}{H(t)}+\eta(\omega)+\gamma(\omega)}. \tag{4.7}$$

Proof We will denote $\frac{J(t)}{H(t)}$ by $K(t)$. Define $K^* = \limsup K(t)$ and $K_* = \liminf K(t)$. Assume that $K(t)$ does not converge, then $K^* - K_* > 0$. In the following five steps we lead this assumption to a contradiction.

Step 1: Define

$$h(K(t),\omega) = \frac{f(\omega)(\sigma(\omega)K(t)+\eta(\omega))}{\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega)}.$$

We get this function by setting $\dot{I}(t,\omega) = 0$ in (4.2) and solving for $I(t,\omega)$. Further define $\Omega_f = \{\omega \in \Omega : f(\omega) > 0\}$. Obviously $\Omega \backslash \Omega_f$ is of no interest as $I(t,\omega) = 0$ there. Note that $\frac{\partial}{\partial K(t)}h(K(t),\omega) = \frac{f(\omega)\sigma(\omega)\gamma(\omega)}{(\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega))^2} > 0$ on Ω_f such that $\frac{\mathrm{d}}{\mathrm{d}t}h(K(t),\omega) \gtreqless 0 \Leftrightarrow \dot{K}(t) \gtreqless 0$. This also shows that $h(K(t),\omega)$ is monotone in $K(t)$. We have

$$\begin{aligned}\dot{I}(t,\omega) &= (\sigma(\omega)K(t)+\eta(\omega))f(\omega) - (\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega))I(t,\omega)\\ &= (\sigma(\omega)K(t)+\eta(\omega))f(\omega) - (\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega))(h(K(t),\omega)+I(t,\omega)-h(K(t),\omega))\\ &= (\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega))\left(h(K(t),\omega)-I(t,\omega)\right)\end{aligned} \tag{4.8}$$

Note that we get

$$\dot{I}(t,\omega) \lesseqgtr 0 \Longleftrightarrow I(t,\omega) \gtreqless h(K(t),\omega). \tag{4.9}$$

This proves the second claim of the lemma. Furthermore, we have

$$\left|\frac{\mathrm{d}}{\mathrm{d}t}h(K(t),\omega)\right| = \left|\frac{\partial}{\partial K(t)}h(K(t),\omega)\dot{K}(t)\right| \leq f(\omega)\frac{\sigma(\omega)\gamma(\omega)}{(\eta(\omega)+\gamma(\omega))^2}C_1, \tag{4.10}$$

where $C_1 = \sup_{t>0}\left|\dot{K}(t)\right|$. It is easy to see that $\dot{K}(t)$ is bounded from which follows that C_1 is finite.

Step 2: Define

$$\begin{aligned}\delta(\omega) = h(K^*,\omega) - h(K_*,\omega) &= f(\omega)\left(\frac{(\sigma(\omega)K^*+\eta(\omega))}{\sigma(\omega)K^*+\eta(\omega)+\gamma(\omega)} - \frac{(\sigma(\omega)K_*+\eta(\omega))}{\sigma(\omega)K_*+\eta(\omega)+\gamma(\omega)}\right)\\ &= f(\omega)\frac{\sigma(\omega)\gamma(\omega)\left(K^*-K_*\right)}{\left(\sigma(\omega)K^*+\eta(\omega)+\gamma(\omega)\right)\left(\sigma(\omega)K_*+\eta(\omega)+\gamma(\omega)\right)}.\end{aligned}$$

For all $\varepsilon > 0$ there exist arbitrarily large t^* such that $K(t^*) < K_* + \varepsilon$. We want to give an estimate for $t(\omega)$ such that $h(K(t),\omega) \leq \delta(\omega)/3 + h(K_*+\varepsilon,\omega)$ for $t \in (t^*, t(\omega))$. Because of (4.10) we get

$$\begin{aligned}t(\omega) &\geq \frac{\delta(\omega)}{3f(\omega)\frac{\sigma(\omega)\gamma(\omega)}{(\eta(\omega)+\gamma(\omega))^2}C_1} = \frac{f(\omega)\frac{\sigma(\omega)\gamma(\omega)(K^*-K_*)}{(\sigma(\omega)K^*+\eta(\omega)+\gamma(\omega))(\sigma(\omega)K_*+\eta(\omega)+\gamma(\omega))}}{3f(\omega)\frac{\sigma(\omega)\gamma(\omega)}{(\eta(\omega)+\gamma(\omega))^2}C_1}\\ &= \frac{(K^*-K_*)}{\left(\sigma(\omega)K^*+\eta(\omega)+\gamma(\omega)\right)\left(\sigma(\omega)K_*+\eta(\omega)+\gamma(\omega)\right)}\frac{(\eta(\omega)+\gamma(\omega))^2}{3C}\\ &\geq \frac{\inf_{\omega\in\Omega_f}\left((\eta(\omega)+\gamma(\omega))^2\right)(K^*-K_*)}{3C_1C_2^2} =: \kappa,\end{aligned}$$

where $C_2 = \sup_{\omega\in\Omega_f}(\sigma(\omega)+\eta(\omega)+\gamma(\omega))$. Note that $\kappa > 0$ and is independent of ω.

Step 3: Because of

$$\delta(\omega) \geq f(\omega)\frac{\inf_{\omega\in\Omega_f}(\sigma(\omega)\gamma(\omega))\left(K^*-K_*\right)}{C_2^2}$$

we have for every $\varepsilon > 0$ a t_ε such that $h(K(t),\omega) < h(K^*,\omega) + \varepsilon\delta(\omega)/2$ for all $t > t_\varepsilon$. Assume now that $I(t,\omega) > h(K^*,\omega) + \varepsilon\delta(\omega)$. Then using (4.8) we see that

$$\begin{aligned}\left|\dot{I}(t,\omega)\right| &= (\sigma(\omega)K(t)+\eta(\omega)+\gamma(\omega))\left|h(K(t),\omega) - I(t,\omega)\right|\\ &\geq \inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega))\frac{\varepsilon}{2}\delta(\omega) \geq \frac{\varepsilon}{2}f(\omega)\inf_{\omega\in\Omega_f}\left(\frac{\delta(\omega)}{f(\omega)}\right)\inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega)).\end{aligned}$$

From this and (4.9) we get that for t large enough we have $I(t,\omega) \leq h(K^*,\omega) + \varepsilon\delta(\omega)$ for all $\omega \in \Omega_f$.

Step 4: Choose $\varepsilon > 0$ small enough such that the two inequalities

$$h(K^*,\omega) - \varepsilon\frac{\delta(\omega)}{3} \geq h(K_*+\varepsilon,\omega) + \frac{2}{3}\delta(\omega), \quad 2\varepsilon \leq \frac{\kappa}{3}\inf_{\omega\in\Omega_f}(\eta(\omega)+\gamma(\omega)) \tag{4.11}$$

hold true. Now choose a t^* such that $K(t^*) < K_* + \varepsilon$. Let t^* also be large enough such that for all $t \geq t^*$ we have

$$I(t,\omega) \leq h(K^*,\omega) + \varepsilon \frac{\delta(\omega)}{3}. \tag{4.12}$$

For every $\omega \in \Omega_f$ and for $t \in (t^*, t^* + \kappa)$ where $I(t,\omega) \geq h(K^*,\omega) - \varepsilon\delta(\omega)/3$ we have because of the first inequality in (4.11) that $|I(t,\omega) - h(K(t),\omega)| \geq \delta(\omega)/3$. Thus, using the second inequality in (4.11), we get

$$\begin{aligned} \left|\dot{I}(t,\omega)\right| &= (\sigma(\omega)K(t) + \eta(\omega) + \gamma(\omega))\,|h(K(t),\omega) - I(t,\omega)| \\ &\geq \frac{\delta(\omega)}{3} \inf_{\omega\in\Omega_f} (\eta(\omega) + \gamma(\omega)) \geq \frac{2\delta(\omega)\varepsilon}{3\kappa}. \end{aligned}$$

Combining this with (4.12) and using (4.9) yields

$$I(t^* + \kappa,\omega) \leq h(K^*,\omega) - \varepsilon \frac{\delta(\omega)}{3}, \quad \omega \in \Omega_f.$$

Step 5: Let $\tau > t^* + \kappa$ be such that $h(K(\tau),\omega) \geq h(K^*,\omega) - \varepsilon\delta(\omega)/3$ for all $\omega \in \Omega_f$ and $K(\tau) > K(t)$ for $t \in (t^* + \kappa, \tau)$. Since $I(t,\omega)$ is increasing if and only if $h(K(t),\omega) > I(t,\omega)$ we have for all $\omega \in \Omega_f$ that $I(\tau,\omega) \leq h(K(\tau),\omega)$. Thus, for all $\omega \in \Omega_f$ we have $\dot{I}(\tau,\omega) \geq 0$ and consequently $\dot{S}(\tau,\omega) \leq 0$. This shows that

$$\dot{K}(\tau) = \frac{\int_{\Omega_f} q_2(\omega)\dot{I}(\tau,\omega)\,\mathrm{d}\omega \int_{\Omega_f} q_1(\omega)S(\tau,\omega)\,\mathrm{d}\omega - \int_{\Omega_f} q_2(\omega)I(\tau,\omega)\,\mathrm{d}\omega \int_{\Omega_f} q_1(\omega)\dot{S}(\tau,\omega)\,\mathrm{d}\omega}{\left(\int_{\Omega_f} q_1(\omega)S(\tau,\omega) + q_2 I(t,\omega)\,\mathrm{d}\omega\right)^2} \geq 0.$$

Therefore, if $I(t,\omega) = h(K(t),\omega)$ for any $t \geq \tau$, we have that $\dot{I}(t,\omega) = 0$ while $\dot{K}(t) \geq 0$ and consequently $\frac{\mathrm{d}}{\mathrm{d}t} h(K(t),\omega) \geq 0$. Hence, $I(t,\omega) \leq h(K(t),\omega)$ for all $t > \tau$ and all $\omega \in \Omega_f$. This in turn implies that $K(t)$ is monotonically increasing for $t > \tau$. Thus, $K(t)$ converges in contradiction to our assumption. □

Theorem 5. *If $\eta > 0$ then the unique steady state of system (4.1) is globally asymptotically stable.*
If $\eta = 0$ then in the case of $R_0 \leq 1$ the unique steady state, which is disease free, is globally asymptotically stable. If $R_0 > 1$ then the disease free steady state is unstable while the second steady state is globally asymptotically stable with the exception of all initial conditions for which $I(0,\omega) = 0$ for almost every $\omega \in \Omega$.

Proof In Lemma 7 we have shown that $K(t) = \frac{J(t)}{H(t)}$ converges. From (4.7) it is then obvious that $I(t,\omega)$ converges. That the limit is one of the steady states is also immediately clear.

It remains to show that if $\eta = 0$ and $R_0 > 1$ then $K(t)$ converges a positive value and not to 0 unless $I_0(\omega) = 0$ a.e. on Ω. Consider the two inequalities

$$\begin{aligned}
\sup_{\tau\in[0,\infty)} H(\tau)\frac{\sup_{\zeta\in\Omega}\left(\frac{\sigma(\zeta)}{\gamma(\zeta)}\right)}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}K(t) &= \frac{\sup_{\tau\in[0,\infty)} H(\tau)\sup_{\zeta\in\Omega}\left(\frac{\sigma(\zeta)}{\gamma(\zeta)}\right)}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}\frac{J(t)}{H(t)} \\
&\geq \frac{\int_\Omega q_2(\omega)\sup_{\zeta\in\Omega}\left(\frac{\sigma(\zeta)}{\gamma(\zeta)}\right)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \geq \frac{\int_\Omega q_2(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}.
\end{aligned}$$

and

$$\frac{\sup_{\tau\in[0,\infty)} H(\tau)}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}K(t) = \frac{\sup_{\tau\in[0,\infty)} H(\tau)}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}\frac{J(t)}{H(t)} \geq \frac{\int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \geq \frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega}.$$

Using them we see that if $K(t)$ is both positive and sufficiently small we have

$$\begin{aligned}
& R_0 - 1 > \frac{\int_\Omega q_2(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} + \frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow\quad & K(t)R_0 - K(t) > \frac{\int_\Omega q_2(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}K(t)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} + K(t)\frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow\quad & K(t)\frac{\int_\Omega q_2(\omega)f(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} - \frac{\int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(f(\omega - I(t,\omega)) + q_2(\omega)I(t,\omega)\,\mathrm{d}\omega} \\
& > \frac{\int_\Omega q_2(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}K(t)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} + K(t)\frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow\quad & \frac{\int_\Omega q_2(\omega)f(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}K(t)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} - \frac{\int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} + K(t)\frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \\
& > \frac{\int_\Omega q_2(\omega)\frac{\sigma(\omega)}{\gamma(\omega)}K(t)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} + K(t)\frac{\int_\Omega (q_2(\omega)-q_1(\omega))I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow\quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)}\left(f(\omega)\sigma(\omega)K(t) - \gamma(\omega)I(t,\omega) - \sigma(\omega)K(t)I(t,\omega)\right)\,\mathrm{d}\omega > 0 \\
\Leftrightarrow\quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)}\dot{I}(t,\omega)\,\mathrm{d}\omega > 0.
\end{aligned}$$

This shows that $\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)}I(t,\omega)\,\mathrm{d}\omega$ is monotonically increasing. But

$$\frac{1}{\sup\limits_{\omega\in\Omega}\gamma(\omega)}J(t) \leq \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)}I(t,\omega)\,\mathrm{d}\omega \leq \frac{1}{\inf\limits_{\omega\in\Omega}\gamma(\omega)}J(t).$$

Thus, if $K(t)$ is positive and sufficiently small, $J(t)$ is bounded below by a positive and monotonically increasing function. But since $K(t) = 0 \Leftrightarrow J(t) = 0$ we see that $K(t)$ cannot converge to 0 if $J(0) > 0$.

If we now assume that $I(0,\omega)$ is positive on a set of positive measure, then $J(0) = \int_\Omega q_2(\omega)I(0,\omega)\,\mathrm{d}\omega > 0$, and consequently $K(t)$ converges to a positive value.

Conversely, if $I(0,\omega) = 0$ almost everywhere on Ω then $J(0) = 0$ and thus $K(0) = 0$. Thus $\dot{I}(t,\omega) \leq 0$ for all $\omega \in \Omega$ and all $t \geq 0$. Consequently $I(t,\omega)$ converges to 0. □

We have carried out the analysis for the distributed heterogeneous system. The corresponding results for the aggregated states follow immediately.

Corollary 1. *If $\eta > 0$ then the aggregated state $I(t) = \int_\Omega I(t,\omega)\,\mathrm{d}\omega$ converges to a positive value I^* which is independent of $I(0)$.*
If $\eta = 0$ and $R_0 \leq 1$ then $I(t)$ converges to 0. If $R_0 > 1$ then $I(t)$ is constant if $I(0) = 0$ and otherwise converges to a positive value I^* which is independent of $I(0)$.

Recall that the positive steady state $\hat{I}(\omega)$ in Theorem 4 can be calculated by computing the unique positive solution of equation (4.4) and plugging it into equation (4.3). To calculate the value I^* in Corollary 1 simply integrate $\hat{I}(\omega)$ over Ω.

The corollary also shows that the qualitative behaviour of the aggregated variables is completely known once the basic reproduction number R_0 is identified.

4.3 *SIR*-model

We look at the heterogeneous SIR-system

$$\begin{aligned}
\dot{S}(t,\omega) &= \mu(\omega)f(\omega)(1-p(\omega)) - \sigma(\omega)\frac{J(t)}{H(t)}S(t,\omega) - \eta(\omega)S(t,\omega) - \mu(\omega)S(t,\omega),\\
\dot{I}(t,\omega) &= \sigma(\omega)\frac{J(t)}{H(t)}S(t,\omega) + \eta(\omega)S(t,\omega) - (\gamma(\omega)+\mu(\omega))I(t,\omega),\\
\dot{R}(t,\omega) &= \mu(\omega)f(\omega)p(\omega) + \gamma(\omega)I(t,\omega) - \mu(\omega)R(t,\omega),
\end{aligned} \tag{4.13}$$

with

$$\begin{aligned}
J(t) &= \int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega,\\
H(t) &= \int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega.
\end{aligned}$$

The new compartment, denoted by $R(t,\omega)$ denotes the number of people in the population with h-state ω that have recovered from the disease and have become immune to further infection The interpretations and assumptions about the parameter functions are the same as in the case of the SIS-model. The parameter $p(\omega)$ is a measurable non-negative function. It denotes the fraction of individuals with h-state ω that are vaccinated or otherwise immunised against the disease at birth. The parameter $\mu(\omega)$

is assumed to be a measurable function that is bounded away from zero similar to $\sigma(\omega)$ and $\gamma(\omega)$. It denotes both the birth and the death rate. We consider them equal so the population size is constant. We define $f(\omega) = S(0,\omega) + I(0,\omega) + R(0,\omega)$ and assume w.l.o.g. $\int_\Omega f(\omega)d\omega = 1$.

4.3.1 Steady states

As with the SIS-system we are only able to prove the following theorem under certain parameter conditions. For the following proof we therefore assume that

$$q_1(\omega)\frac{\gamma(\omega)+\mu(\omega)}{\mu(\omega)} - q_3(\omega)\frac{\gamma(\omega)}{\mu(\omega)} < q_2(\omega)\left(1+\frac{\sigma(\omega)}{\gamma(\omega)}\right) \quad \text{for all } \omega \in \Omega. \tag{4.14}$$

As with the proof of Theorem 4 the results also holds if $\eta = 0$ and the above inequality is fulfilled with '$>$' instead of '$<$'. Again, it is not known whether there are any parameter configurations for which the theorem does not hold true.

Theorem 6. *If $\eta > 0$ then the system (4.13) has exactly one steady state $(\hat{S}(\omega), \hat{I}(\omega), \hat{R}(\omega))$ and $\hat{I}(\omega) > 0$ whenever $f(\omega) > 0$. If $\eta = 0$ we define*

$$R_0 = \frac{\int_\Omega q_2(\omega)f(\omega)(1-p(\omega))\frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega))\,\mathrm{d}\omega + \int_\Omega q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}.$$

If $R_0 \le 1$ then the system (4.13) has a unique steady state that is disease free, i.e. $\hat{I}(\omega) \equiv 0$. If $R_0 > 1$ then the system has exactly two steady states, one of them being disease free.

Proof Let $(\hat{S}(\omega), \hat{I}(\omega), \hat{R}(\omega))$ be a steady state and $\hat{J}$ and $\hat{H}$ the aggregated states. The equation $\dot{S}(t,\omega) = 0$ yields

$$\hat{S}(\omega) = \frac{\mu(\omega)f(\omega)(1-p(\omega))}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \mu(\omega)}. \tag{4.15}$$

Putting this into the equation $\dot{I}(t,\omega) = 0$ leads to

$$\hat{I}(\omega) = \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\gamma(\omega)+\mu(\omega)}\hat{S}(\omega) = \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\gamma(\omega)+\mu(\omega)}\frac{\mu(\omega)f(\omega)(1-p(\omega))}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \mu(\omega)}. \tag{4.16}$$

For $\hat{R}(\omega)$ we get the formula

$$\hat{R}(\omega) = f(\omega)p(\omega) + \frac{\gamma(\omega)}{\mu(\omega)}\hat{I}(\omega) = f(\omega)p(\omega) + \frac{\gamma(\omega)}{\mu(\omega)}\frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega)}{\gamma(\omega)+\mu(\omega)}\frac{\mu(\omega)f(\omega)(1-p(\omega))}{\sigma(\omega)\frac{\hat{J}}{\hat{H}} + \eta(\omega) + \mu(\omega)}. \tag{4.17}$$

Thus, $\frac{\hat{J}}{\hat{H}}$ is given by

$$\frac{\hat{J}}{\hat{H}} = \frac{\int_\Omega q_2(\omega) \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}}+\eta(\omega)}{\sigma(\omega)\frac{\hat{J}}{\hat{H}}+\eta(\omega)+\mu(\omega)} \frac{\mu(\omega)f(\omega)(1-p(\omega))}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega}{\int_\Omega \frac{\mu(\omega)f(\omega)(1-p(\omega))}{\sigma(\omega)\frac{\hat{J}}{\hat{H}}+\eta(\omega)+\mu(\omega)} \left(q_1(\omega) + \frac{\sigma(\omega)\frac{\hat{J}}{\hat{H}}+\eta(\omega)}{\gamma(\omega)+\mu(\omega)} \left(q_2(\omega) + q_3(\omega)\frac{\gamma(\omega)}{\mu(\omega)}\right)\right) \mathrm{d}\omega + \int_\Omega q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}.$$

Every solution of this equation yields a steady state of system (4.13) by plugging it into equations (4.15), (4.16), and (4.17). We are therefore looking for the solutions of

$$\frac{\int_\Omega q_2(\omega) \frac{\sigma(\omega)x+\eta(\omega)}{\sigma(\omega)x+\eta(\omega)+\mu(\omega)} \frac{\mu(\omega)f(\omega)(1-p(\omega))}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega}{\int_\Omega \frac{\mu(\omega)f(\omega)(1-p(\omega))}{\sigma(\omega)x+\eta(\omega)+\mu(\omega)} \left(q_1(\omega) + \frac{\sigma(\omega)x+\eta(\omega)}{\gamma(\omega)+\mu(\omega)} \left(q_2(\omega)+q_3(\omega)\frac{\gamma(\omega)}{\mu(\omega)}\right)\right) \mathrm{d}\omega + \int_\Omega q_3(\omega)f(\omega)p(\omega)\mathrm{d}\omega} = x. \quad (4.18)$$

We denote the left hand side by $l(x)$ and the right hands side by $r(x)$. As in the proof of Theorem 4 it is easy to show that $l(0) = r(0)$ if $\eta = 0$ and $l(0) > r(0)$ if $\eta > 0$, as well as $l(1) < r(1)$. The derivative of $l(x)$ can be written as (we again suppress the ω-dependency of the parameter functions)

$$l'(x) = \frac{\int_\Omega q_2 \frac{\sigma\mu}{(\sigma x+\eta+\mu)^2} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega}{\int_\Omega q_2 \frac{\sigma x+\eta}{\sigma x+\eta+\mu} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega}(l(x) - l(x)^2) + \frac{\int_\Omega \left(q_1 \frac{\gamma+\mu}{\mu} - q_3 \frac{\gamma}{\mu}\right) \frac{\sigma\mu}{(\sigma x+\eta+\mu)^2} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega}{\int_\Omega q_2 \frac{\sigma x+\eta}{\sigma x+\eta+\mu} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega} l(x)^2.$$

At a point $x \in (0, 1)$ where $l(x) = x$ it can then be shown that $l'(x) < 1$ is equivalent to

$$\int_\Omega \left(q_1 \frac{\gamma+\mu}{\mu} - q_3 \frac{\gamma}{\mu} - q_2\right) \frac{\sigma\mu x^2}{(\sigma x+\eta+\mu)^2} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega < \int_\Omega q_2 \frac{\sigma^2 x^2 + 2\sigma\eta + \eta^2 + \eta\mu}{(\sigma x+\eta+\mu)^2} \frac{\mu f(1-p)}{\gamma+\mu} \,\mathrm{d}\omega.$$

Due to our assumption (4.14) this inequality is fulfilled for all $x \in (0, 1)$. The rest of the proof is analogous to the proof of Theorem 4. Note that for $\eta = 0$ we have

$$R_0 = l'(0) = \frac{\int_\Omega q_2(\omega)f(\omega)(1-p(\omega)) \frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega))\,\mathrm{d}\omega + \int_\Omega q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}.$$

□

Here too it can be shown by the same methods as mentioned previously that the definition of the basic reproduction number R_0 coincides with the one given in [31].

4.3.2 Stability

For the SIR-system we will no longer be able to give a complete description of the asymptotic behaviour. We will restrict ourselves therefore to the analysis of the stability of the disease free steady state in the case $\eta = 0$. Note that some of the parameter configurations we consider, such as case 4) and 5) in Theorem 8, imply assumption (4.14).

Theorem 7. *If $\eta = 0$, then the disease free steady state is unstable if $R_0 > 1$.*

Proof Denote $K(t) = \frac{J(t)}{H(t)}$. Let $\|\cdot\|$ denote the L_1 norm on Ω. Furthermore we define a new norm by $\|\|(S(t,\omega), I(t,\omega), R(t,\omega))\|\| = \|S(t,\omega)\| + \|I(t,\omega)\| + \|R(t,\omega)\|$. Let $(S^*(\omega), I^*(\omega), R^*(\omega)) = (f(\omega)(1-p(\omega)), 0, f(\omega)p(\omega))$ be the disease free steady state. Assume the state at time t fulfils $\|\|(S(t,\omega), I(t,\omega), R(t,\omega)) - (S^*(\omega), I^*(\omega), R^*(\omega))\|\| < \varepsilon$ and that $\|I(t,\omega)\| \neq 0$. By choosing ε sufficiently small we can assure that the two terms

$$\frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \text{ and } 1 - \frac{\int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}$$

become arbitrarily small. So for any $\delta > 0$ with $\delta < R_0 - 1$ we have for sufficiently small δ that

$$\begin{aligned}
& R_0 - 1 > \frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad - \left(1 - \frac{\int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}\right) + \delta \\
\Leftrightarrow\quad & K(t)R_0 - K(t) > \frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)K(t)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad - K(t)\left(1 - \frac{H(t)}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}\right) + \delta K(t) \\
\Leftrightarrow\quad & K(t)\frac{\int_\Omega q_2(\omega)f(\omega)(1-p(\omega))\frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} > \\
&\qquad \frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)K(t)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad + \frac{J(t)}{H(t)}\frac{H(t)}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} + \delta K(t) \\
\Leftrightarrow\quad & \frac{\int_\Omega q_2(\omega)f(\omega)(1-p(\omega))\frac{\sigma(\omega)K(t)}{\gamma(\omega)+\mu(\omega)}\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad - \frac{\int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} > \\
&\qquad \frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)K(t)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} + \delta K(t) \\
\Leftrightarrow\quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)K(t)f(\omega)(1-p(\omega))\,\mathrm{d}\omega - \int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega > \\
&\qquad \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)K(t)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\mathrm{d}\omega + \tilde{\delta}K(t) \\
\Leftrightarrow\quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\left(\sigma(\omega)K(t)S(t,\omega) - (\gamma(\omega)+\mu(\omega))I(t,\omega)\right)\mathrm{d}\omega > \tilde{\delta}K(t) \\
\Leftrightarrow\quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\dot{I}(t,\omega)\,\mathrm{d}\omega > \tilde{\delta}K(t),
\end{aligned}$$

where we denote $\tilde{\delta} = \delta \int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega$. Thus for any trajectory with $\|\|(S(t,\omega), I(t,\omega), R(t,\omega)) - (S^*(\omega), I^*(\omega), R^*(\omega))\|\| < \varepsilon$ and $\|I(t,\omega)\| \neq 0$ we have that the term $\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} I(t,\omega)\,\mathrm{d}\omega$ is strictly monotonically increasing. But

$$\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} I(t,\omega)\,\mathrm{d}\omega \le \sup_{\omega\in\Omega} \frac{q_2(\omega)}{(\gamma(\omega)+\mu(\omega))} I(t) = \sup_{\omega\in\Omega} \frac{q_2(\omega)}{(\gamma(\omega)+\mu(\omega))} \|I(t,\omega)\|.$$

Since this in particular implies that $\tilde{\delta}K(t)$ is bounded away from 0, we can conclude that the trajectory of the system leaves the ε-neighbourhood of the disease free steady state in finite time. Thus the disease free steady state is unstable.

□

Theorem 8. *Let $\eta = 0$ and $R_0 < 1$. Define $\Omega_f = \{\omega \in \Omega : f(\omega) \neq 0\}$ and*

$$\Omega_- = \left\{ \omega \in \Omega : q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \le 0 \right\}.$$

Assume that one of the following conditions holds true

(1) $\Omega_- \subseteq \Omega \backslash \Omega_f$,

(2) $\Omega_- \supseteq \Omega_f$,

(3) $\displaystyle\int_{\Omega_-} \left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \right) f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega > 0$,

(4) $p(\omega) = 0$ *and* $q_1(\omega) \le \max\{q_2(\omega), q_3(\omega)\}$ *for all* $\omega \in \Omega_f$,

(5) $q_1(\omega) = q_3(\omega) \le q_2(\omega)$ *for all* $\omega \in \Omega_f$.

Then the disease free steady state is globally asymptotically stable.

Proof In the cases (1)-(3) we will show that the assumption implies the inequality

$$\int_\Omega q_2(\omega)I(t,\omega) + q_3(\omega)R(\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \right) \mathrm{d}\omega > \varepsilon \tag{4.19}$$

for some $\varepsilon > 0$ and all sufficiently large t. This inequality can be used to show

$$\begin{aligned}
& \int_\Omega q_2(\omega) S(t,\omega) \frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega < \int_\Omega q_1(\omega) S(t,\omega) + q_2(\omega) I(t,\omega) + q_3(\omega) R(\omega) \,\mathrm{d}\omega - \varepsilon \\
\Leftrightarrow \quad & \int_\Omega q_2(\omega) S(t,\omega) \frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega K(t) < H(t) K(t) - \varepsilon K(t) \\
\Leftrightarrow \quad & \int_\Omega q_2(\omega) S(t,\omega) \frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \,\mathrm{d}\omega K(t) - J(t) < -\varepsilon K(t) \\
\Leftrightarrow \quad & \int_\Omega q_2(\omega) K(t) S(t,\omega) \frac{\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} - q_2(\omega) I(t,\omega) \,\mathrm{d}\omega < -\varepsilon K(t) \\
\Leftrightarrow \quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} \left(\sigma(\omega) K(t) S(t,\omega) - (\gamma(\omega)+\mu(\omega)) I(t,\omega)\right) \,\mathrm{d}\omega < -\varepsilon K(t) \\
\Leftrightarrow \quad & \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} \dot{I}(t,\omega) \,\mathrm{d}\omega < -\varepsilon K(t)
\end{aligned}$$

This implies that $\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} I(t,\omega)\,\mathrm{d}\omega$ is monotonically decreasing. Since $K(t) = 0 \Leftrightarrow J(t) = 0$ and

$$\frac{1}{\sup\limits_{\omega\in\Omega} \gamma(\omega)+\mu(\omega)} J(t) \le \int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)} I(t,\omega)\,\mathrm{d}\omega$$

we see that $J(t)$ must converge to 0. From this it follows easily that the system converges to the disease free steady state.

We now need to show that (4.19) holds in the first three cases. In case (1) this simply follows from

$$\begin{aligned}
\int_\Omega q_2(\omega) I(t,\omega) + & q_3(\omega) R(\omega) + S(t,\omega) \left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)} \right) \mathrm{d}\omega \\
& \ge \int_\Omega \min \left\{ q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}, q_2(\omega), q_3(\omega) \right\} f(\omega)\,\mathrm{d}\omega =: \varepsilon > 0.
\end{aligned}$$

For the case (2) note that if $S(t,\omega) > f(\omega)(1-p(\omega))$ then

$$\begin{aligned}
\dot{S}(t,\omega) &= \mu(\omega) f(\omega)(1-p(\omega)) - (\sigma(\omega)K(t) + \mu(\omega))\, S(t,\omega) \\
&< \mu(\omega) S(t,\omega) - (\sigma(\omega)K(t) + \mu(\omega))\, S(t,\omega) \\
&= -\sigma(\omega) K(t) S(t,\omega) \le 0
\end{aligned}$$

If $K(t)$ converges to 0 we are done. Otherwise we can assume that for sufficiently large t we have that $S(t,\omega) < f(\omega)(1-p(\omega))$. Similar reasoning shows that we can also assume that for sufficiently large t we have that $R(t,\omega) > f(\omega)p(\omega)$. Define

$$\varepsilon = (1-R_0) \int_\Omega q_1(\omega) f(\omega)(1-p(\omega)) + q_3(\omega) f(\omega) p(\omega)\,\mathrm{d}\omega > 0.$$

Then for sufficiently large t we have

$$\begin{aligned}
&\int_\Omega \left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)(S(t,\omega) - f(\omega)(1-p(\omega))) \\
&\qquad + q_3(\omega)(R(t,\omega) - f(\omega)p(\omega)) + q_2(\omega)I(t,\omega)\,\mathrm{d}\omega > 0 \\
\Leftrightarrow \quad &\int_\Omega q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega \\
&\qquad > \int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega - \int_\Omega \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega \\
\Leftrightarrow \quad &\frac{\int_\Omega q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad > 1 - \frac{\int_\Omega \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow \quad &\frac{\int_\Omega q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&\qquad > R_0 - \frac{\int_\Omega \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega - \varepsilon}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
\Leftrightarrow \quad &\int_\Omega q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega > \varepsilon.
\end{aligned}$$

The last equivalence here follows due to the definition of R_0. For case (3) define $\Omega_+ = \Omega_f \backslash \Omega_-$. Then we have

$$\int_{\Omega_+} q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega > 0$$

which implies

$$\begin{aligned}
&\int_{\Omega_+} q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega) + S(t,\omega)\left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega \\
&\qquad + \int_{\Omega_+} \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega > \int_{\Omega_+} \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega.
\end{aligned} \tag{4.20}$$

Furthermore, with the same reasoning as in case (2), we have for sufficiently large t that

$$\begin{aligned}
&\int_{\Omega_-} \left(q_1(\omega) - \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)(S(t,\omega) - f(\omega)(1-p(\omega))) \\
&\qquad\qquad + q_3(\omega)(R(t,\omega) - f(\omega)p(\omega)) + q_2(\omega)I(t,\omega)\,\mathrm{d}\omega > 0,
\end{aligned}$$

which is equivalent to

$$\int_{\Omega_-} q_2(\omega)I(t,\omega)+q_3(\omega)R(t,\omega)+S(t,\omega)\left(q_1(\omega)-\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega \\ +\int_{\Omega_-}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega > \int_{\Omega_-} q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega. \tag{4.21}$$

Now we choose an ε with

$$0<\varepsilon<\int_{\Omega_-}\left(q_1(\omega)-\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega.$$

For such an ε we have

$$\int_{\Omega_-} q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega>\int_{\Omega_-}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega+\varepsilon \tag{4.22}$$

Adding (4.20) and (4.21) and then using (4.22) we get

$$\begin{aligned}
&\int_{\Omega} q_2(\omega)I(t,\omega)+q_3(\omega)R(t,\omega)+S(t,\omega)\left(q_1(\omega)-\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}\right)\mathrm{d}\omega\\
&\qquad\qquad+\int_{\Omega}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega\\
&>\int_{\Omega_+}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega+\int_{\Omega_-} q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega\\
&>\int_{\Omega_+}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega+\int_{\Omega_-}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega+\varepsilon\\
&=\int_{\Omega}\frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega+\varepsilon.
\end{aligned}$$

Subtracting $\int_\Omega \frac{q_2(\omega)\sigma(\omega)}{\gamma(\omega)+\mu(\omega)}f(\omega)(1-p(\omega))\,\mathrm{d}\omega$ from this inequality results in equation (4.19).

In the cases (4) and (5) we have

$$\begin{aligned}
\int_{\Omega} q_1(\omega)S(t,\omega)+q_2(\omega)I(t,\omega)+q_3(\omega)R(t,\omega)\,\mathrm{d}\omega &\geq \int_{\Omega}\min\{q_1(\omega),q_2(\omega),q_3(\omega)\}\,f(\omega)\\
&=\int_{\Omega} q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega.
\end{aligned}$$

Thus,

$$-\left(1-\frac{\int_\Omega q_1(\omega)S(t,\omega)+q_2(\omega)I(t,\omega)+q_3(\omega)R(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}\right)\geq 0.$$

We again use that for sufficiently large t we have that

$$\frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)\left(f(\omega)(1-p(\omega))-S(t,\omega)\right)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega))+q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}>0.$$

Since $R_0 < 1$ we have for sufficiently large t and a sufficiently small $\delta > 0$ that

$$
\begin{aligned}
R_0 - 1 < &\frac{\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\sigma(\omega)\left(f(\omega)(1-p(\omega)) - S(t,\omega)\right)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega} \\
&- \left(1 - \frac{\int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)f(\omega)(1-p(\omega)) + q_3(\omega)f(\omega)p(\omega)\,\mathrm{d}\omega}\right) - \delta.
\end{aligned}
$$

We encountered this inequality in the proof of Theorem 7 with a '$>$' instead of a '$<$' and a different sign of δ. Taking exactly the same steps as in this proof we get

$$
\int_\Omega \frac{q_2(\omega)}{\gamma(\omega)+\mu(\omega)}\dot{I}(t,\omega)\,\mathrm{d}\omega < -\tilde{\delta}K(t),
$$

from which it follows that the system converges to the disease free steady state as shown above. □

We want to note that in the cases (1) and (3) of the proof of this theorem the fact that $R_0 < 1$ was not used. However, it can be easily shown that this inequality is implied by equation (4.19). The assumptions (1) and (3) are therefore stronger than the condition that $R_0 < 1$. In particular, in case one of these assumptions if fulfilled there is no need to calculate the basic reproduction number in order to know the asymptotic behaviour.

Furthermore, similarly as for the SIS-model it is possible to directly derive results for the aggregated states from the above analysis. In the case $\mu = 0$ we know for $R_0 \leq 1$ that $I(t)$ goes to zero. If $R_0 > 0$ then even a small number of infected individuals will result in the disease being endemic in the population.

4.3.3 *SIR*-model without demography

In this section we look at the SIR-system where $\mu(\omega) = 0$. Consequently the equations are

$$
\begin{aligned}
\dot{S}(t,\omega) &= -\sigma(\omega)\frac{J(t)}{H(t)}S(t,\omega) - \eta(\omega)S(t,\omega), \\
\dot{I}(t,\omega) &= \sigma(\omega)\frac{J(t)}{H(t)}S(t,\omega) + \eta(\omega)S(t,\omega) - \gamma(\omega)I(t,\omega), \\
\dot{R}(t,\omega) &= \gamma(\omega)I(t,\omega),
\end{aligned}
\tag{4.23}
$$

with

$$
\begin{aligned}
J(t) &= \int_\Omega q_2(\omega)I(t,\omega)\,\mathrm{d}\omega, \\
H(t) &= \int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega.
\end{aligned}
$$

Then $R(t,\omega) = R(0,\omega) + \int_0^t \gamma(\omega) I(\tau,\omega)\,\mathrm{d}\tau$. We get

$$\int_0^\infty I(t,\omega)\,\mathrm{d}t = \frac{R^*(\omega) - R(0,\omega)}{\gamma(\omega)},$$

where $R^*(\omega) = \lim_{t\to\infty} R(t,\omega)$. This limit exists since $R(t,\omega)$ is monotonically increasing and bounded above by $f(\omega)$. From this we get

$$\begin{aligned}
\int_0^\infty K(t)\,\mathrm{d}t &= \int_0^\infty \frac{\int_\Omega q_2(\omega) I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega q_1(\omega)S(t,\omega) + q_2(\omega)I(t,\omega) + q_3(\omega)R(t,\omega)\,\mathrm{d}\omega}\,\mathrm{d}t \\
&\leq \int_0^\infty \frac{\int_\Omega q_2(\omega) I(t,\omega)\,\mathrm{d}\omega}{\int_\Omega \min\{q_1(\omega), q_2(\omega), q_3(\omega)\}(S(t,\omega) + I(t,\omega) + R(t,\omega))\,\mathrm{d}\omega}\,\mathrm{d}t \\
&= \frac{1}{\int_\Omega \min\{q_1(\omega), q_2(\omega), q_3(\omega)\} f(\omega)\,\mathrm{d}\omega} \int_\Omega q_2(\omega) \int_0^\infty I(t,\omega)\,\mathrm{d}t\,\mathrm{d}\omega \\
&= \frac{1}{\int_\Omega \min\{q_1(\omega), q_2(\omega), q_3(\omega)\} f(\omega)\,\mathrm{d}\omega} \int_\Omega q_2(\omega) \frac{R^*(\omega) - R(0,\omega)}{\gamma(\omega)}\,\mathrm{d}\omega < \infty.
\end{aligned} \tag{4.24}$$

Using the first equation in (4.23),

$$\dot{S}(t,\omega) = -\left(\sigma(\omega)K(t) + \eta(\omega)\right) S(t,\omega),$$

we see that

$$S(t,\omega) = S(0,\omega) e^{-\sigma(\omega)\int_0^t K(\tau) - \eta(\omega) t\,\mathrm{d}\tau}. \tag{4.25}$$

In particular, for all $\omega \in \Omega$ where both $S(0,\omega) > 0$ and $\eta(\omega) = 0$ hold true we have

$$S^*(\omega) = \lim_{t\to\infty} S(t,\omega) = S(0,\omega) e^{-\sigma(\omega)\int_0^\infty K(t)\,\mathrm{d}t} > 0,$$

while for any ω where either $S(0,\omega) = 0$ or $\eta(\omega) > 0$ the limit is obviously 0. That the function $I(t,\omega)$ converges to 0 is also apparent. We have thus proven the following theorem.

Theorem 9. *In the SIR model (4.23) the disease always dies out, i.e. $I(t,\omega)$ converges to 0 for every $\omega \in \Omega$. Every individual with an h-state ω for which $\eta(\omega) > 0$ becomes infected at some point, i.e. $S(t,\omega)$ converges to 0. For those h-states where $\eta(\omega) = 0$ the fraction $e^{-\sigma(\omega)\int_0^\infty K(t)\,\mathrm{d}t}$ of the initial population $S(0,\omega)$ never becomes infected.*

Note that this result also holds in the case where $\inf_{\omega\in\Omega} \sigma(\omega) = 0$. The function $\gamma(\omega)$ however still has to be bounded away from zero for this result to hold. A second aspect of importance is that $I(0,\omega)$, although it is not present in the formulation of the result or its proof, is still an important factor here, as it has a crucial influence on the value $\int_0^\infty K(t)\,\mathrm{d}t$. Although this value can not be calculated from the initial conditions alone, using (4.24) we can estimate

$$\int_0^\infty K(t)\,\mathrm{d}t \leq \frac{1}{\int_\Omega \min\{q_1(\omega), q_2(\omega), q_3(\omega)\} f(\omega)\,\mathrm{d}\omega} \int_\Omega q_2(\omega) \frac{f(\omega) - R(0,\omega)}{\gamma(\omega)}\,\mathrm{d}\omega,$$

which can be used to give an estimate for $S^*(\omega)$ without calculating the trajectories of the system. A special case where we can give more information on the final state of the system is when the weights $q_1(\omega)$, $q_2(\omega)$, and $q_3(\omega)$ are all equal. In the following theorem χ_A denotes the characteristic function of the set A. Furthermore, we exclude the rather uninteresting case where $\eta = 0$ and $I(t,\omega) = 0$ a.e. in Ω.

Theorem 10. *In the SIR model (4.23) where $q_1(\omega) = q_2(\omega) = q_3(\omega) =: q(\omega)$, and where $\eta(\omega)S(0,\omega) = 0$ and $I(t,\omega) = 0$ do not both hold true almost everywhere, the final state of the susceptible population is given by*

$$S^*(\omega) = S(0,\omega)e^{-\frac{\sigma(\omega)}{\int_\Omega q(\omega)f(\omega)\,\mathrm{d}\omega}\left(x - \int_\Omega \frac{q(\omega)}{\gamma(\omega)}R(0,\omega)\,\mathrm{d}\omega\right)}\chi_{\{\omega\in\Omega:\eta(\omega)=0\}}(\omega), \tag{4.26}$$

where x is the unique solution of the equation

$$x = \int_\Omega \frac{q(\omega)}{\gamma(\omega)}f(\omega)\,\mathrm{d}\omega - \int_{\{\omega\in\Omega:\eta(\omega)=0\}} \frac{q(\omega)}{\gamma(\omega)}S(0,\omega)e^{-\frac{\sigma(\omega)}{\int_\Omega q(\zeta)f(\zeta)\,\mathrm{d}\zeta}\left(x - \int_\Omega \frac{q(\zeta)}{\gamma(\zeta)}R(0,\zeta)\,\mathrm{d}\zeta\right)}\,\mathrm{d}\omega \tag{4.27}$$

in the interval $\left(\int_\Omega \frac{q(\omega)}{\gamma(\omega)}R(0,\omega)\,\mathrm{d}\omega, \infty\right)$. The final state of the recovered population is given by

$$R^*(\omega) = f(\omega) - S^*(\omega).$$

Proof Note that because of $q_1(\omega) = q_2(\omega) = q_3(\omega) = q(\omega)$ equality holds in equation (4.24). Thus, combining equations (4.24) and (4.25) we get the representation

$$S^*(\omega) = S(0,\omega)e^{-\frac{\sigma(\omega)}{\int_\Omega q(\omega)f(\omega)\,\mathrm{d}\omega}\int_\Omega q(\omega)\frac{R^*(\omega)-R(0,\omega)}{\gamma(\omega)}\,\mathrm{d}\omega}\chi_{\{\omega\in\Omega:\eta(\omega)=0\}}(\omega). \tag{4.28}$$

According to Theorem 9 $I(t,\omega)$ converges to 0, hence $R^*(\omega)$ fulfils the equation

$$R^*(\omega) = f(\omega) - S^*(\omega) = f(\omega) - S(0,\omega)e^{-\frac{\sigma(\omega)}{\int_\Omega q(\omega)f(\omega)\,\mathrm{d}\omega}\int_\Omega q(\omega)\frac{R^*(\omega)-R(0,\omega)}{\gamma(\omega)}\,\mathrm{d}\omega}\chi_{\{\omega\in\Omega:\eta(\omega)=0\}}(\omega).$$

Multiplying this equation with $\frac{q(\omega)}{\gamma(\omega)}$ and integrating over Ω yields

$$\begin{aligned}\int_\Omega \frac{q(\omega)}{\gamma(\omega)}R^*(\omega)\,\mathrm{d}\omega = &\int_\Omega \frac{q(\omega)}{\gamma(\omega)}f(\omega)\,\mathrm{d}\omega \\ &- \int_{\{\omega\in\Omega:\eta(\omega)=0\}} \frac{q(\omega)}{\gamma(\omega)}S(0,\omega)e^{-\frac{\sigma(\omega)}{\int_\Omega q(\zeta)f(\zeta)\,\mathrm{d}\zeta}\left(\int_\Omega \frac{q(\zeta)}{\gamma(\zeta)}R^*(\zeta)\,\mathrm{d}\zeta - \int_\Omega \frac{q(\zeta)}{\gamma(\zeta)}R(0,\zeta)\,\mathrm{d}\zeta\right)}\,\mathrm{d}\omega.\end{aligned} \tag{4.29}$$

Denoting $\int_\Omega \frac{q(\omega)}{\gamma(\omega)}R^*(\omega)\,\mathrm{d}\omega$ by x in equations (4.28) and (4.29) results in equations (4.26) and (4.27). Note that we necessarily have

$$\int_\Omega \frac{q(\omega)}{\gamma(\omega)}R^*(\omega)\,\mathrm{d}\omega \geq \int_\Omega \frac{q(\omega)}{\gamma(\omega)}R(0,\omega)\,\mathrm{d}\omega,$$

as $R(t,\omega)$ is monotonically increasing. Further note that at $x = \int_\Omega \frac{q(\omega)}{\gamma(\omega)} R(0,\omega)\,\mathrm{d}\omega$ the right hand side of (4.27) is given by

$$\begin{aligned}\int_\Omega \frac{q(\omega)}{\gamma(\omega)} f(\omega)\,\mathrm{d}\omega - \int_{\{\omega\in\Omega:\eta(\omega)=0\}} \frac{q(\omega)}{\gamma(\omega)} S(0,\omega)\,\mathrm{d}\omega &\geq \int_\Omega \frac{q(\omega)}{\gamma(\omega)} f(\omega)\,\mathrm{d}\omega - \int_\Omega \frac{q(\omega)}{\gamma(\omega)} S(0,\omega)\,\mathrm{d}\omega \\ &= \int_\Omega \frac{q(\omega)}{\gamma(\omega)} \left(I(0,\omega) + R(0,\omega)\right)\,\mathrm{d}\omega \\ &\geq \int_\Omega \frac{q(\omega)}{\gamma(\omega)} R(0,\omega)\,\mathrm{d}\omega = x,\end{aligned}$$

where at least one of the inequalities is strict. That the solution to equation (4.27) exists and is unique in the given interval can now be inferred from the fact that the left hand side of (4.27) has constant derivative 1 while the derivative of the right hand side is strictly monotonically decreasing in x and converges to 0.
□

Note that instead of knowing $q(\omega)$, $\gamma(\omega)$, and $f(\omega)$ in Theorem 10 it suffices to know the function $\frac{q(\omega)}{\gamma(\omega)}$ and the values $\int_\Omega q(\omega) f(\omega)\,\mathrm{d}\omega$ and $\int_\Omega \frac{q(\omega)}{\gamma(\omega)} f(\omega)\,\mathrm{d}\omega$. Further note that obviously x has to lie in the interval $\left(\int_\Omega \frac{q(\omega)}{\gamma(\omega)} R(0,\omega)\,\mathrm{d}\omega, \int_\Omega \frac{q(\omega)}{\gamma(\omega)} f(\omega)\,\mathrm{d}\omega\right)$.

4.4 Conclusions

We have identified the steady states and analysed the stability of these steady states for both a SIS- and SIR-model. Due to the complexity of these models, we were only able to carry out this analysis under some additional restrictions on the parameters. Furthermore, other SIS- or SIR-models that do not fall into our framework may be of interest, e.g. models using different transmission functions or without constant population. However, such models or extensions of the models presented here may still be analysed by methods similar to the ones we used.

The results show that for heterogeneous systems the basic reproduction number R_0 can in many circumstances be used as an indicator whether an endemic steady state exists or not. Also, the qualitative behaviour of the system near the disease free steady state can be determined by calculating R_0. We see that the basic reproduction number is still as important a concept as it is for the homogeneous systems.

Chapter 5

Set membership estimations for the evolution of infectious diseases in heterogeneous populations[1]

5.1 Introduction

The role of heterogeneity of a population for the evolution of infectious diseases is well recognized in the existing literature, see e.g. [31, 26, 30]. Various kinds of models have been developed to take into account heterogeneity with respect to immune system, contact rates and other traits, including cellular automata [100], random networks [86, 110] distributed integro-differential systems [91, 31, 92, 107], etc. For a more comprehensive bibliography see the recent paper [48]. A substantial limitation for utilization of most of these models is that they require detailed information about the distribution of the population along the numerical values of the traits, that is, about the h-state (heterogeneous state) of the individuals in the population ([30]). Such detailed information is usually not available. The available information is vague and even reliable statistical characteristics are often not known. One way to overcome this difficulty is to pass to aggregated models that require less information. This approach is stressed in [30] and we mention the papers [32, 59, 107, 91, 60, 92] developing aggregation techniques for certain special classes of heterogeneous models defined by integro-differential systems.

In the present paper we employ an alternative approach, in which the distribution of the population among the h-states is uncertain, but set-membership information is available (possibly together with certain aggregated data). The set-membership information may be given in the form of lower and upper bounds for the number of susceptible, infected, recovered, etc. individuals at each h-state. The aggregated information is typically about the total number of susceptible, infected, etc. individuals at the

[1]This chapter has at the time of writing been submitted for peer review to the Journal of Mathematical Biology.

initial time. This information is used to obtain set-membership estimations (shortly set-estimates) for the evolution of the disease. The set estimations at a given time t contain all aggregated states (total number of susceptible, infected, etc. individuals) that are consistent with the available initial information and the model describing the dynamics of the population system. The set-estimation approach is well known and widely used (see e.g. [15, 85, 73]), but in the present epidemiological context there are important points that had to be developed.

The investigation is carried out for a rather general model of a heterogeneous multi-group population, which consists of a distributed first order differential system complemented with integral relations. This model covers heterogeneous versions of SI, SIR, and many other standard epidemiological models. At this level of generality we present our set-estimation approach. In the set-estimation theory for evolutionary systems one can distinguish two different groups of methods. In the first, set-estimations of Markovian type are sought, where the set-estimation at a given time t determines the future set-estimations (the minimal set-estimation has this property). The advantage is, that it is sometimes possible to obtain infinitesimal (even differential) equations for the evolution of Markovian set-estimations in a prescribed family of sets (polyhedrons, ellipsoids, etc., see [73]). The drawback is, that such estimations are usually too "pessimistic" , that is, too large, compared with the minimal set-estimation. Our approach belongs to the second group: at each time the set-estimation is obtained independently of the previously obtained estimations. Technically, finding such estimations (even minimal ones) can be done by solving families of auxiliary dynamic optimization problems. In our case these optimization problems are non-standard, because they involve constraints in the form of first order distributed differential systems and integral relations. Therefore, the first main goal of the paper is to present a technique for solving such optimization problems.

The second goal of the paper is to show that the set-estimation technique may give useful information about the spread of infectious diseases under uncertainty of data (we focus on uncertainty of the h-state-distribution of the initial population). In many cases the population has certain dissipativity property that makes the set-estimations not much expanding, even shrinking to a point or to a reasonably small set, when the time progresses. Thanks to this, one can perform various kinds of comparative analysis. For example, we investigate the effect of various scenarios of interventions (vaccination or prevention programs) applied prior to the outburst of the disease.

We mention that our previous work [109] allows to determine the exact asymptotics of the aggregated states of a class of heterogeneous SI-models, depending on the initial h-state-distribution of the population. This allows to obtain a set-estimation for the asymptotic state of the disease for this particular SI-model in an alternative way. The comparison with the results obtained by the general approach in the present paper, which turns out to be the same, serves as a verification test.

The plan of the paper is as follows. Section 5.2 explains the aim of this paper in terms of a simple SI model used later as benchmark. The general model, the assumptions, and the formulation of the set-estimation problem are given in Section 5.3. In Section 5.4 we present the set-membership technique and some technicalities needed to adapt it to the present framework. Section 5.5 is devoted to numerical analysis of certain SI and SIR heterogeneous models by the set-estimation techniques. Some conclusions and lines of future research are presented in Section 5.6. The main technical issue of the paper is given in the Appendix.

5.2 A benchmark *SI*-model

To present our main motivation, we introduce below a particular case of the problem we investigate in this paper, which involves a heterogeneous version of the known SI model in mathematical epidemiology. The whole population is divided into two groups – susceptible individuals and infected individuals. The individuals are heterogeneous, in the sense that a scalar $\omega \in \Omega \subset \mathbb{R}$ is associated with each individual, indicating specific traits relevant to the particular disease, e.g. the intensity of risky contacts, the state of the immune system, etc. The parameter ω is called heterogeneous state (shortly h-state) of the individual, see e.g. [26, 31] or textbooks such as [30].

The following model is a particular case of the one in [107]:

$$
\begin{aligned}
\dot{S}(t,\omega) &= -\sigma(\omega)p(\omega)\frac{J(t)}{K(t)+J(t)}S(t,\omega) + \kappa S(t,\omega), \quad S(0,\omega) = u_1(\omega),\\
\dot{I}(t,\omega) &= \sigma(\omega)p(\omega)\frac{J(t)}{K(t)+J(t)}S(t,\omega) - \gamma I(t,\omega), \quad I(0,\omega) = u_2(\omega),\\
K(t) &= \int_\Omega p(\omega)S(t,\omega)\,\mathrm{d}\omega,\\
J(t) &= \int_\Omega q(\omega)I(t,\omega)\,\mathrm{d}\omega.
\end{aligned}
\tag{5.1}
$$

Here $S(t,\omega)$ and $I(t,\omega)$ represent the size of the susceptible and of the infected population with h-state ω at time t, respectively. The parameter κ is the net population growth rate of the susceptible population, γ is the net mortality rate of the infected population, $\sigma(\omega)$ is the force of infection, meaning the probability that a risky interaction between a susceptible and an infected individual results in infection of the susceptible individual (it may incorporate also the immune status of the susceptible individual), and $p(\omega)$ and $q(\omega)$ denote the participation rate of susceptible/infected individuals of h-state ω in risky interactions. The aggregated state variables $K(t)$ and $J(t)$ represent the total amount of susceptible/infected individuals, weighted with their respective risky behaviour, while $J(t)/(K(t)+J(t))$ is the weighted prevalence of the disease at time t (see e.g [107, 109] for more detailed explanations). At the initial time $t=0$, the distribution of the initial susceptible and infected sub-populations along the h-states, $\omega \in \Omega$, is given by the functions $u_1(\omega)$ and $u_2(\omega)$, respectively.

In fact, the main quantities of practical interest are the total size of the susceptible and infected populations:

$$S(t) := \int_\Omega S(t,\omega)\,\mathrm{d}\omega \quad \text{and} \quad I(t) := \int_\Omega I(t,\omega)\,\mathrm{d}\omega. \tag{5.2}$$

Solving system (5.1) is not problematic, provided that all data involved are known. However, in reality the information about the distribution of individuals along the heterogeneous space Ω is vague. That is, the functions u_1 and u_2 are not precisely known. A relatively reliable information about these functions is provided by the aggregated values

$$\int_\Omega u_1(\omega)\,\mathrm{d}\omega = S(0) \quad \text{and} \quad \int_\Omega u_2(\omega)\,\mathrm{d}\omega = I(0), \tag{5.3}$$

since measurements of $S(0)$ and $I(0)$ are feasible. Statistical information for higher integral moments of u_1 and u_2 (in the form of equalities or inequalities) may also be available, and its incorporation in our subsequent considerations is a matter of technical work that we avoid for more transparency. Additional information about u_1 and u_2 may be given in terms of bounds:

$$u_i(\omega) \in [\varphi_0^i(\omega), \varphi_1^i(\omega)], \quad \omega \in \Omega, \quad i = 1,\, 2. \tag{5.4}$$

Any pair of measurable functions (u_1, u_2) satisfying (5.3) and (5.4) (that is, consistent with the available information) will be viewed as possible (sometimes called admissible) realizations of the uncertainty for the h-distribution of the initial population.

Due to the uncertainty of the initial data (u_1, u_2), the issue of obtaining a set-membership estimation, $\mathcal{E}(t)$, of the aggregated state $(S(t), I(t))$ does naturally arise. This means that sets $\mathcal{E}(t),\ t \geq 0$, have to be determined, such that

$$(S(t), I(t)) \in \mathcal{E}(t), \quad t \geq 0, \tag{5.5}$$

whatever the admissible initial functions (u_1, u_2) are, where $(S(t), I(t))$ is the corresponding solution of system (5.1) enhanced with (5.2).

The main goal of this paper is to present a computationally implementable approach for obtaining set-membership estimations as in (5.5). Such an approach is developed in the next section for a general system with a structure similar to (5.1), (5.2).

5.3 Formulation of the problem and preliminaries

Having in mind the set-membership estimation problem in the previous section, below we formulate a more general problem that covers heterogeneous versions of a variety of models in mathematical epidemiology and in other areas.

Let $[0, T]$ be a given time-interval and let Ω be a compact interval in which the parameter of heterogeneity, ω, takes values. Denote $D = [0, T] \times \Omega$. State variables in the model below are functions

$$x : D \to \mathbb{R}^m \quad \text{and} \quad y : [0, T] \to \mathbb{R}^n.$$

The dynamics is given by the equations

$$\dot{x}(t,\omega) = f(t,\omega,x(t,\omega),y(t)), \quad (t,\omega) \in D, \tag{5.6}$$

$$x(0,\omega) = u(\omega), \quad \omega \in \Omega, \tag{5.7}$$

$$y(t) = \int_\Omega g(t,\omega,x(t,\omega))\,\mathrm{d}\omega, \quad t \in [0,T], \tag{5.8}$$

where

$$f : D \times \mathbb{R}^m \times \mathbb{R}^n \to \mathbb{R}^m \quad \text{and} \quad g : D \times \mathbb{R}^m \to \mathbb{R}^n$$

are given functions and the upper "dot" means differentiation with respect to t, so that $\dot{x}(t,\omega) := \partial x(t,\omega)/\partial t$. The initial data $u : \Omega \to \mathbb{R}^n$ is uncertain, and the available information about it is given by the following constraints:

$$u(\omega) \in [\varphi_0(\omega), \varphi_1(\omega)], \quad \omega \in \Omega, \tag{5.9}$$

$$\int_\Omega u(\omega)\,\mathrm{d}\omega = c. \tag{5.10}$$

The inclusion in (5.9) is understood component-wise: $u_i(\omega) \in [\varphi_0^i(\omega), \varphi_1^i(\omega)]$, where $u = (u_1, \ldots, u_m)$, $\varphi_j = (\varphi_j^1, \ldots, \varphi_j^m)$, $j = 0,\ 1$; the vector $c \in \mathbb{R}^m$ and the functions φ_0 and φ_1 are given.

We consider every function from the set

$$\mathcal{U} := \left\{ u \in L_\infty^m(\Omega) : u(\omega) \in [\varphi_0(\omega), \varphi_1(\omega)] \ \text{ for a.e. } \omega \in \Omega,\ \int_\Omega u(\omega)\,\mathrm{d}\omega = c \right\}.$$

as an admissible (possible) realization of the uncertain function u.

Before formulating the estimation problem in the spirit of the previous section, we give the necessary assumptions and clarify the meaning of solution of the above model.

Assumptions:

(i) The function f is measurable in (t,ω), g is continuous in t and measurable in ω, both are locally essentially bounded, differentiable in (x,y) with locally Lipschitz partial derivatives, uniformly with respect to $(t,\omega) \in D$;

(ii) the functions $\varphi_0,\ \varphi_1 : \Omega \to \mathbb{R}^m$ are continuous and satisfy the inequalities $\varphi_0(\omega) \le \varphi_1(\omega)$ and $\int_\Omega \varphi_0(\omega)\,\mathrm{d}\omega < c < \int_\Omega \varphi_1(\omega)\,\mathrm{d}\omega$;

(ii) For every $u \in \mathcal{U}$ the solution $(x(\cdot,\cdot), y(\cdot))$ of (5.6)–(5.8) exists on the whole interval $[0,T]$.

By definition, solution of (5.6)–(5.8) is any pair of measurable and bounded functions $(x(\cdot,\cdot), y(\cdot))$ on D and $[0,T]$ respectively, such that for a.e. $\omega \in \Omega$ the equation

$$x(t,\omega) = u(\omega) + \int_0^t f(s,\omega,x(s,\omega),y(s))\,\mathrm{d}s \tag{5.11}$$

holds on $[0,T]$ and (5.8) holds for a.e. $t \in [0,T]$.

Notice that according to Assumption (i) $x(\cdot,\omega)$ is (uniformly) Lipschitz continuous for a.e. ω and y is continuous.

Every $u \in \mathcal{U}$ generates a solution $(x[u], y[u])$ of (5.6)–(5.8) and similarly as in the proof of [34, Proposition 2] one can prove that the solution is unique. Denote

$$\mathcal{R}(t) := \{y[u](t) : \, u \in \mathcal{U}\}\,, \quad t \in [0,T].$$

That is, $\mathcal{R}(t)$ the set of all aggregated states y that result from some admissible realization of the uncertainty, $u \in \mathcal{U}$. In this sense, $\mathcal{R}(t)$ is the exact (meaning *minimal*) set-membership estimation of the aggregated state at time t. In the next section we present a method of obtaining estimates

$$\mathcal{E}(t) \supset \mathcal{R}(t), \quad t \in [0,T].$$

Even more, the method allows to obtain outer approximations of arbitrary accuracy of the convex hull $\mathrm{co}\mathcal{R}(t)$.

Sometimes not all components of y are of interest (latent components). If $L \subset \mathbb{R}^n$ is a given subspace, we will obtain estimations of the projections of $y(t)$ on L:

$$\mathcal{E}(t) \supset \mathrm{pr}_L(\mathrm{co}\mathcal{R}(t)), \tag{5.12}$$

where pr_L is the projection operator on L.

In the epidemiological problems which serve as prototypes for the above problem (cf. [32, 48, 107, 109]), the dimension m may equal 2 (in SI and SIS models), 3 (in SIR models), etc. The aggregated state y has usually a higher dimension than x. In the benchmark model (5.1), (5.2) considered in Section 5.2 we have $m = 2$ and $n = 4$: $x(t,\omega) = (S(t,\omega), I(t,\omega))$, $y(t) = (K(t), J(t), S(t), I(t))$. However, estimating the pair $(S(t), I(t))$ is of primal interest, thus $L := (0, 0, \mathbb{R}, \mathbb{R})$.

5.4 The set-membership estimation

In this section we focus on the approximation of the exact set-membership estimation $\mathcal{R}(t)$. The procedure described in the first subsection is well known in control theory, while the second subsection is devoted to the main technical tool which is specific for the model presented in the previous section. The numerical scheme is briefly described in the third subsection.

5.4.1 The approach

Let us fix a time $\tau \in (0, T]$ and a unit vector $l \in \mathbb{R}^n$. Consider the optimization problem

$$\max_{u \in \mathcal{U}} \langle l, y(\tau) \rangle \tag{5.13}$$

subject to the constraints (5.6)–(5.10). (Here and below $\langle \cdot, \cdot \rangle$ denotes the scalar product.) If $y_l = y[u_l](\tau)$ is a solution, then $y_l \in \mathcal{R}(\tau)$ and $\langle l, y_l \rangle \geq \langle l, y \rangle$ for every $y \in \mathcal{R}(\tau)$. If we repeat the same for a number of unit vectors, say $\{l_1, \ldots, l_k\} =: \Lambda$ we obtain that

$$Y_\Lambda(\tau) := \{y_{l_1}, \ldots, y_{l_k}\} \subset \mathcal{R}(\tau) \subset \{y \in \mathbb{R}^n : \langle l_i, y - y_{l_i} \rangle \leq 0, \; i = 1, \ldots, k\} =: \mathcal{E}_\Lambda(\tau).$$

Thus, $\mathcal{E}_\Lambda(\tau)$ is a set-membership estimation of $y(\tau)$. It is an easy exercise to show that the Hausdorff distance $H(\mathrm{co} Y_\Lambda(\tau), \mathcal{E}_\Lambda(\tau))$ decreases when the set Λ is enlarged, and converges to zero if the sets Λ provide ε-nets on the unit sphere with ε converging to zero. Thus, we may obtain inner and outer approximations of any accuracy to the convex hull of the exact set-membership estimation $\mathcal{R}(\tau)$.

If only a set-membership estimation on a subspace L is needed (see (5.12)), then it is enough to take collections of unit vectors Λ belonging to the space L (which makes problems of high dimension tractable, provided that the dimension of L is low – 1, 2 or 3).

The approach described above requires multiple solving of problem (5.13), (5.6)–(5.10). This is not an easy task, since we deal with a distributed system with non-local dynamics (due to the presence of the aggregated states y) and constraints on the variable u. We employ a gradient projection method in the space $L_\infty(\Omega)$ for the variable $u \in \mathcal{U}$. This means that the objective function in (5.13) is considered as a functional, $J(u)$ of $u \in \mathcal{U} \subset L_\infty(\Omega)$ with $y(\tau)$ viewed as a function of u: $y(\tau) = y[u](\tau)$. The functional

$$J(u) = \langle l, y[u](\tau) \rangle \tag{5.14}$$

has to be maximized on the set $\mathcal{U}$. Then a standard gradient projection method can be implemented – for more details see Section 5.4.3 below.

However, there is an auxiliary problems that arises: to determine the gradient (meaning the Fréchet derivative) of J. This problem will be addressed in the next subsection.

5.4.2 The gradient in problem (5.13)

Let $u \in \mathcal{U}$ and let (x, y) be the corresponding solution of system (5.6)–(5.8) on $[0, \tau] \times \Omega$, where $\tau \in (0, T]$ is the number fixed in the previous subsection. We shall obtain a representation of the Fréchet derivative of the functional J in (5.14) in the space L_∞.

Let

$$\lambda : D \mapsto \mathbb{R}^m \quad \text{and} \quad \nu : [0, \tau] \mapsto \mathbb{R}^n$$

be a measurable and bounded solution on $[0, \tau] \times \Omega$ of the system

$$-\dot{\lambda}(t,\omega) = (f'_x(t,\omega,x(t,\omega),y(t)))^\top \lambda(t,\omega) + (g'_x(t,\omega,x(t,\omega)))^\top \nu(t), \tag{5.15}$$

$$\lambda(\tau,\omega) = -(g'_x(T,\omega,x(T,\omega)))^\top l, \tag{5.16}$$

$$\nu(t) = \int_\Omega (f'_y(t,\omega,x(t,\omega),y(t)))^\top \lambda(t,\omega)\,\mathrm{d}\omega. \tag{5.17}$$

Here the superscript $\top$ means transposition, and the meaning of solution is similar to that of the initial-value problem (5.6)–(5.8). As in the proof of Proposition 2 in [34] one can show that system (5.15)–(5.17) has unique solution.

Proposition 5. *The functional $J : L_\infty(\Omega) \longrightarrow \mathbb{R}$ is Fréchet differentiable and its derivative at u has a representation in $L_\infty(\Omega)$ given by*

$$J'(u) = -\lambda(0,\cdot), \tag{5.18}$$

where λ is defined by (5.15), complemented with (5.16), (5.17).

The proof of this proposition is given in the Appendix.

5.4.3 Implementation of the gradient projection method

Below we briefly describe (first at conceptual level, not involving the discretisation) the implementation of the gradient projection method for solving problem (5.13), (5.6)–(5.10). We start with an initial guess $u^0(\cdot)$ with $\int_\Omega u^0(\omega)\,\mathrm{d}\omega = c$ and $u^0(\omega) \in [\varphi_0(\omega), \varphi_1(\omega)]$ (see Assumption (ii)). Then we obtain the corresponding to u^0 solution (x^0, y^0) of initial value problem (5.6)–(5.8). With this solution inserted in terminal value problem (5.15)–(5.17) we obtain the corresponding λ^0, which determines the Fréchet derivative $J'(u^0) = -\lambda^0(0,\cdot)$, according to Proposition 5. Then we make a gradient step of size ρ^0 defining $u^1(\cdot) := \mathrm{pr}_\mathcal{U}((u_0(\cdot) - \rho^0\lambda^0(0,\cdot))$ ($\mathrm{pr}_\mathcal{U}$ is the projection on $\mathcal{U} \subset L_\infty(\Omega)$), where ρ^0 is chosen by scalar maximization of $J(\mathrm{pr}_\mathcal{U}(u^0(\cdot) - \rho\lambda^0(0,\cdot)))$ with respect to $\rho \geq 0$. The same procedure is repeated iteratively (staring with u^1 at step 1, etc.) until $\mathrm{pr}_\mathcal{U}(u^k(\cdot) - \lambda^k(0,\cdot)) - u^k(\cdot)$ becomes close to zero, which is an indication for that u^k is close to a (local) maximizer. Making the last statement strict is a matter of additional work that we do not touch in this paper.

Above, we sketched the gradient projection method in the space $L_\infty(\Omega)$. However, in the numerical implementation of the method we pass to a finite-dimensional space. We use a discretisation by a second order Runge-Kutta scheme (the Heun scheme) for the differential equations and the trapezoidal quadrature formula for integration over Ω for obtaining approximate solutions of problems (5.6)–(5.8) and (5.15)–(5.17) (the latter is used for calculation of the gradient). The projection on the admissibility set $\mathcal{U}$ is than replaced by a projection on a polyhedral set of the form

$$U := \left\{ (u^1, \dots u^N) \in \mathbb{R}^{m \times N} : \varphi_0(\omega_i) \leq u^i \leq \varphi_1(\omega_i),\ \sum_{i=1}^N \alpha_i u^i = c \right\},$$

where ω_i are the mesh points in Ω, N is their number, and α_i are the coefficients of the quadrature formula. (Observe that U is non-empty for a sufficiently dense mesh $\{\omega_i\}$ due to Assumption (ii).) There is a huge literature and available software for this kind of projection problems, for both see e.g. [42] and the references therein. For details about the implementation of the gradient projection method (including the choice of the step length ρ) see e.g. [96, Chapter 4].

We remind that to obtain a good approximation $\mathcal{E}(\tau)$ of the minimal convex set-membership estimation $\mathrm{co}\mathcal{R}(\tau)$ for a given τ it is necessary to solve problem (5.13), (5.6)–(5.10) for many unit vectors l in the space of interest, L. Even more, in order to predict the evolution of state $y(t)$ by means of the estimation $\mathcal{E}(t)$ we need to do this for a number of time instances τ. Naturally, the obtained (approximate) maximizer u for given τ and l can be used as initial guess for neighbouring instances τ and vectors l, which makes the overall estimation procedure tractable on a commercial PC.

5.5 Numerical analysis

In this section we present numerical results and analysis of versions of SI and SIR heterogeneous models.

5.5.1 SI-model without population growth

Here we deal with the system (5.1), (5.2) with $\kappa = 0$, that is, the disease-free population has constant size. We consider this special case for the following reason: the asymptotics of the minimal set-membership estimation $\mathcal{R}(t)$, $t \to +\infty$, can be determined in an alternative way, and can be compared with the estimation $\mathcal{E}(t)$ obtained by the approach in the present paper. This is a test for the performance of the set-estimation techniques. Let us briefly describe this alternative way.

From (5.1) it is apparent that $S(t,\omega)$ is monotonically decreasing and positive, and thus convergent. This easily implies that $\dot{S}(t,\omega) \to 0$. Since $\dot{I}(t,\omega) = -\dot{S}(t,\omega) - \gamma I(t,\omega)$, we obtain in a standard way that $I(t,\omega)$ converges to 0, provided that $\gamma > 0$. Thus also $I(t) \to 0$. In our paper [109] it is shown how to determine the asymptotics of $S(t)$ for given initial data $(S(0,\cdot), I(0,\cdot)) = (u_1, u_2)$. There, it is assumed that $p(\omega) = q(\omega) > 0$, $\sigma(\omega) = \sigma > 0$ is constant, and the set of those $\omega \in \Omega$, for which $S(0,\omega) > 0$ and $\gamma > \sigma p(\omega)$, has positive measure. Then [109, Section 4.2] claims that

$$\lim_{t \to +\infty} S(t) := S^*(u_1, u_2) = \int_\Omega e^{-\sigma F^* p(\omega)} u_1(\omega)\,\mathrm{d}\omega, \tag{5.19}$$

where F^* is the unique positive solution of the equation

$$\int_\Omega p(\omega) e^{F^*(\gamma - \sigma p(\omega))} u_1(\omega)\,\mathrm{d}\omega = \int_\Omega p(\omega)(u_1(\omega) + u_2(\omega))\,\mathrm{d}\omega.$$

Hence,

$$\lim_{t \to +\infty} \mathcal{R}(t) = \left[\min_{(u_1,u_2)\in\mathcal{U}} S^*(u_1,u_2),\ \max_{(u_1,u_2)\in\mathcal{U}} S^*(u_1,u_2) \right] \times 0. \tag{5.20}$$

Solving the two optimization problems involved in the last formula again requires a numerical algorithm, but now we deal with a completely static problems (differential equations are not involved). Again a gradient projection method is applied, since the Fréchet derivative of S^* can be analytically represented. We skip the details of this procedure.

The essence of the above paragraph is that now we have two different methods for approximation of the limit of $\mathcal{R}(t)$: by the way mentioned just above, and by using the general technique presented in this paper for approximating $\mathcal{R}(t)$, applied for large t. The comparison is clearly seen in Figs. 5.1 and 5.2, obtained for the data specifications described below.

The initial size of the population is normalized to one: $S(0) + I(0) = 1$. Moreover, $\Omega = [0, 1]$, $\delta = 0.15$ and $\sigma = 0.1$. The weight functions $p(\omega)$ and $q(\omega)$ are linear: $p(\omega) = q(\omega) = 0.5 + \omega$ (the constant term means that all individuals have risky contacts). In order to define the lower and the upper bounds $\varphi_0(\cdot)$ and $\varphi_1(\cdot)$ of $u(\cdot)$ we assume that the initial distribution of trait ω among the susceptible and infected populations is close to a normal distribution $\varphi(\cdot)$ with mean 0.5 and variance 0.3 truncated to the unit interval and normalised there. More precisely, its deviation from φ is at most 20%. This leads to bounds

$$u_1(\omega) \in \left[\frac{4}{5}S(0)\varphi(\omega), \frac{6}{5}S(0)\varphi(\omega)\right], \qquad u_2(\omega) \in \left[\frac{4}{5}I(0)\varphi(\omega), \frac{6}{5}I(0)\varphi(\omega)\right].$$

Fig. 5.1 shows the evolution of the estimation $\mathcal{E}(t)$ obtained by using 20 equidistant unit vectors $l \in \mathbb{R}^2$. It converges to the limit set $\mathcal{R}(+\infty)$ calculated as in (5.20). Thus the two different ways to approximate the limit set-estimation are consistent with each other. This can be seen even better in Fig. 5.2 (left plot), where the dotted lines represent the interval in the right-hand side of (5.20), while the solid lines represent the evolution of $\mathrm{pr}_S(\mathcal{E}(t))$. The convergence of $\mathrm{pr}_I(\mathcal{E}(t))$ to zero is seen on the right plot in Fig. 5.2 (right plot).

5.5.2 SI-model with population growth

We continue do deal with the system (5.1), (5.2), but now consider a growing population. We set $\delta = 0.1$, $\sigma = 0.105$, and $\kappa = 0.004$. Fig. 5.3 shows the set-membership estimation $\mathcal{E}(t)$ of the system (5.1) at $t = 2, 4, \ldots, 40$, obtained by using 20 equidistant unit vectors $l \in \mathbb{R}^2$.

We remind that obtaining a set-estimation $\mathcal{E}(t)$ requires solving the auxiliary problem (5.13) for various unit vectors l (in the present model case $l \in \mathbb{R}^2$). A feasible u that solves this problem is called extremal realization of the uncertainty in the initial data, or merely *extremal*, in direction l. A comprehensive analysis of the structure of the extremal u is a complicated task, seemingly not tractable, in general, although it may give useful information about "worst case" realizations of the uncertainty. Our numerical experiments with the SI model in Section 5.5.1 give evidence that the extremal u has a bang-bang structure. More precisely, for an extremal u there exists a subset $A \subset \Omega$ such that $u(\omega) = \varphi_1(\omega)$ for $\omega \in A$

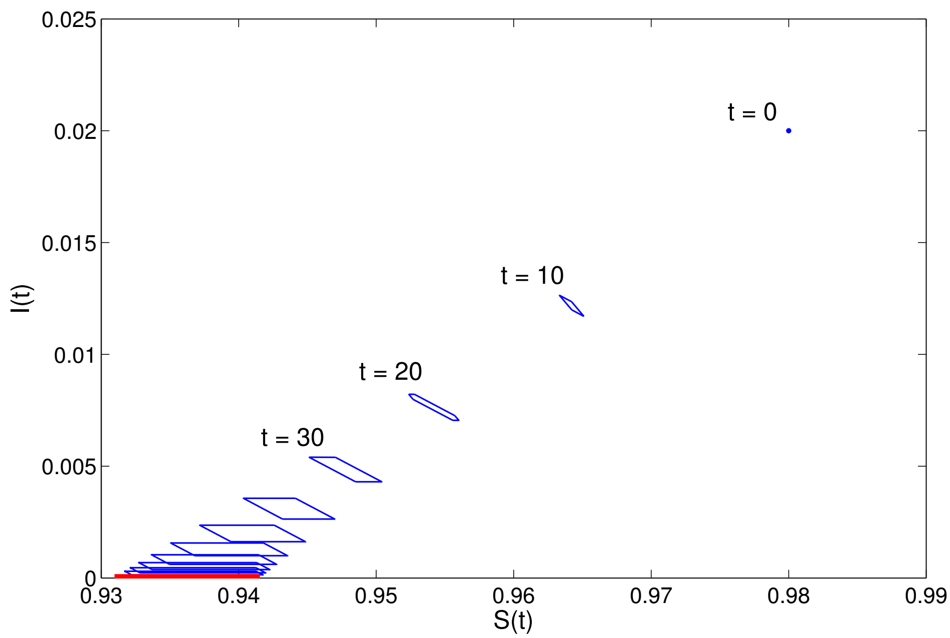

Figure 5.1: Set-membership estimates of system (5.1) with $\kappa = 0$ for various t. The thick line at the bottom left is the exact set-estimation at infinity, $\mathcal{R}(+\infty)$, calculated as in (5.20). For $t < \infty$ the estimation $\mathcal{E}(t)$ is calculated by using 20 equidistant unit vectors $l \in \mathbb{R}^2$.

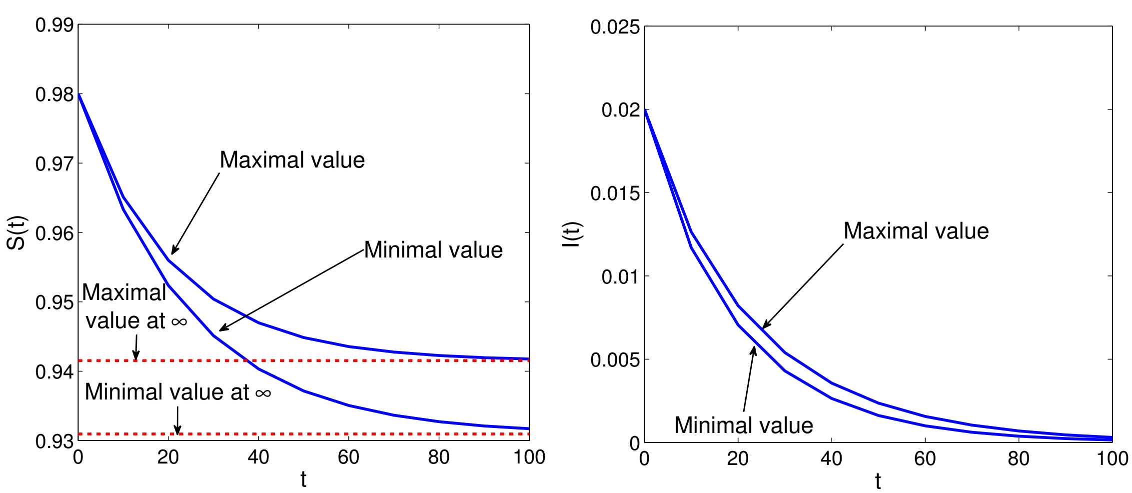

Figure 5.2: Estimates for the maximal and minimal value of S(t) and I(t). For large t these values for $S(t)$ converge to the maximal and minimal value of S^*. For $I(t)$ they converge to 0.

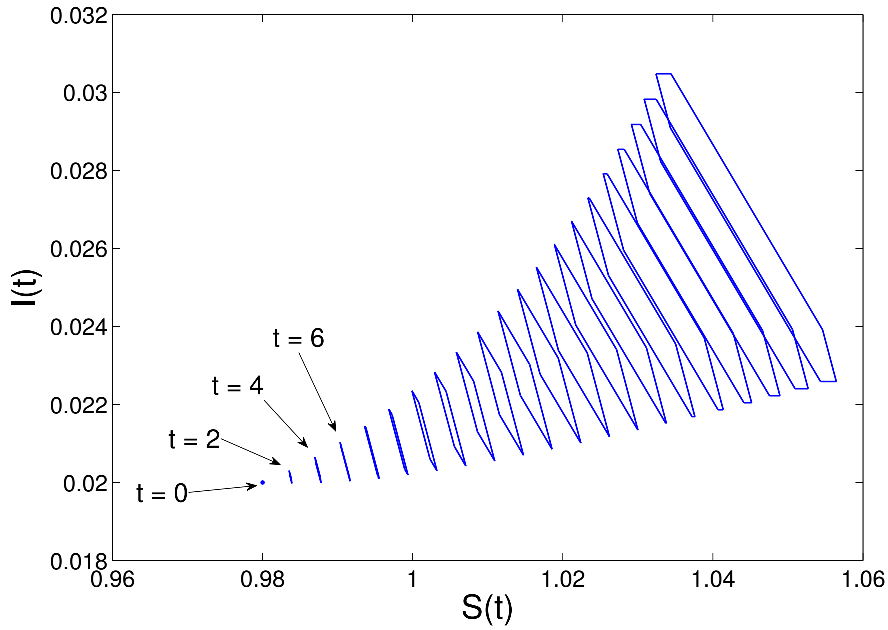

Figure 5.3: Set-membership estimates of system (5.1), (5.2) for various t, obtained by using 20 equidistant unit vectors $l \in \mathbb{R}^2$.

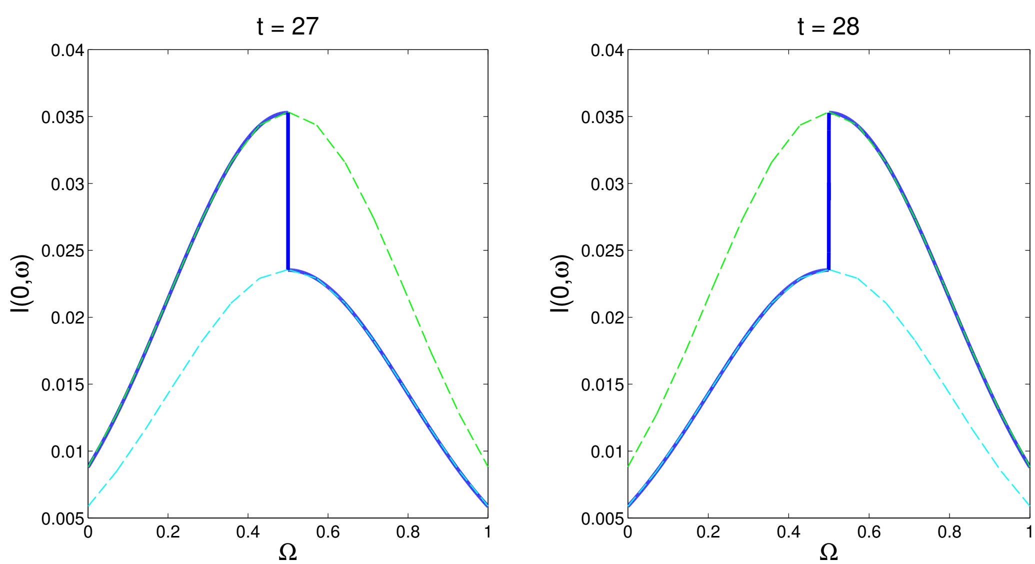

Figure 5.4: The solid lines show the component $u_2(\cdot)$ of the extreme data for direction $l = (\sin(1.4\pi), \cos(1.4\pi))$ and two different values of t. The dashed lines show the lower and upper bounds $\varphi_0^2(\omega)$ and $\varphi_1^2(\omega)$.

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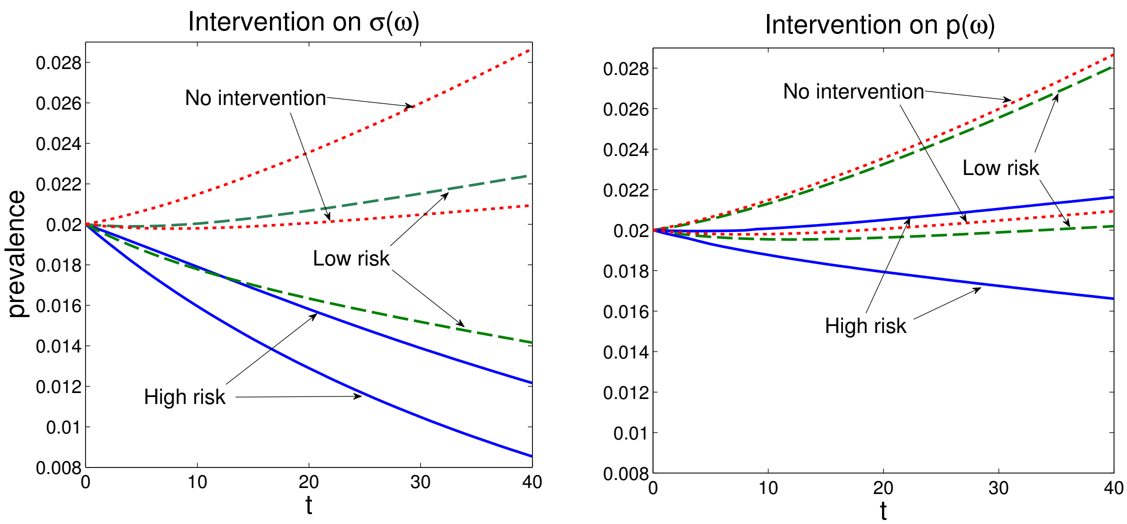

Figure 5.5: Set-estimations of the prevalence, $\mathcal{E}_p(t)$, in case of intervention affecting $\sigma(\omega)$ (left plot) and $p(\omega)$ (right plot). The dotted lines represent $\mathcal{E}_p(t)$ in the case of no intervention, the dashed lines represent $\mathcal{E}_p(t)$ in the case of intervention applied to low risk individuals, and the solid lines – to high risk individuals.

and $u(\omega) = \varphi_0(\omega)$ for $\omega \in \Omega \backslash A$. Of course, the set A depends on u, hence on the estimation time t and the direction l. In the experiments with the present SI-model the set A always consists of a single interval. Fig. 5.4 presents the extremal initial data $u_2(\omega) = I(0, \omega)$ for $l = (\sin(1.4\pi), \cos(1.4\pi))$ and various values of t. For $t = 1, \ldots, 27$ the set A stays the same, $A = [0, 0.5)$, and the corresponding u_2 is depicted on the left plot of Fig. 5.4. For $t = 28, \ldots, 40$ we obtain $A = (0.5, 1]$ and the corresponding u_2 is depicted on the right plot of Fig. 5.4. Thus the structure of the extremal data may abruptly change when the estimation time changes.

In the rest of this subsection we investigate the effect of intervention (prevention) polices implemented prior to or around the outburst of the disease at $t = 0$. Such a policy may influence either the individual susceptibility rate, $\sigma(\omega)$, (say, by vaccination) or the individual contact rate, $p(\omega)$ (by educational or other prevention programs). Assuming that the resource for intervention is limited, the question arises how to allocate it among individuals, regarding their h-state ω. As mentioned in Section 5.2, exact information about the h-state of individuals is not available, therefore a complex intervention policy that targets specific sections of the population with particular h-states cannot be enforced in practice. However, it may be feasible to identify groups of high-level and groups of low-level risk.

In view of the above, we consider two scenarios: applying the intervention to high risk individuals (here we mean those with high values of $p(\omega)$) or applying it to low risk individuals (i.e. those with low values of $p(\omega)$, respectively). Even though this way of modelling of interventions is crude, it qualitatively

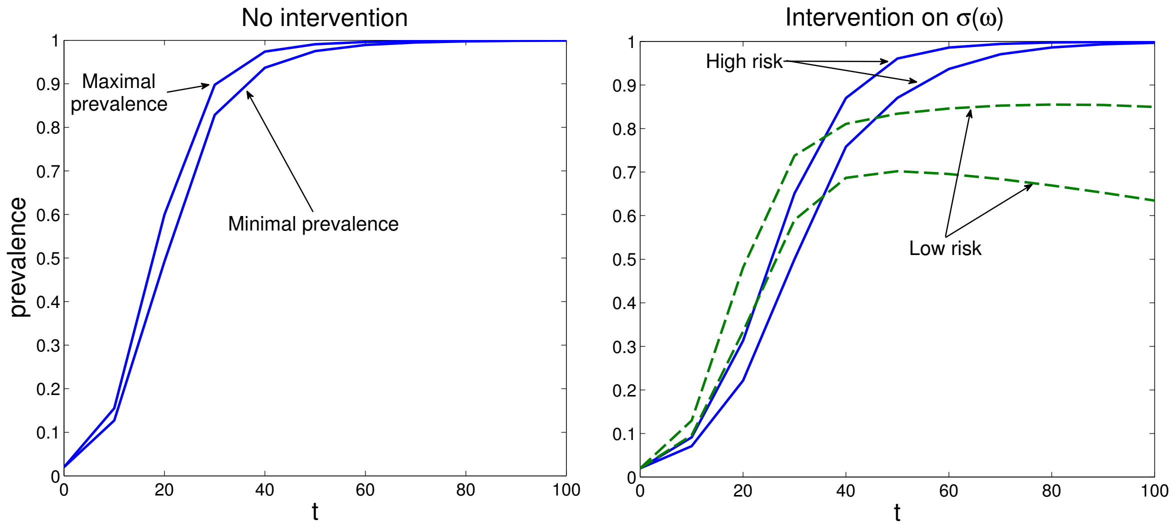

Figure 5.6: The left plot shows the evolution of the set-estimation $\mathcal{E}_p(t)$ of the prevalence in case of no intervention: the whole population becomes (asymptotically) infected. The right plot shows $\mathcal{E}_p(t)$ with the intervention applied to the low risk (dashed lines) and high risk (solid lines) individuals. The intervention targeting the low risk individuals is now significantly more efficient and, in particular, prevents extinction.

answers the question which part of the population (high risk or low risk individuals) should be mainly targeted. As we see below, the answer is not evident.

To be specific, we assume that for a third of the population we can decrease susceptibility rate $\sigma(\omega)$ or the contact rate $p(\omega)$ by 50%. The question is, what will the effect of the intervention be if it is applied to the one third of the population at higher risk versus the same fraction of the population at low risk. The effect of intervention is measured by the set-membership estimation of the prevalence. Let us clarify the last notion. If we have obtained a set-estimation $\mathcal{E}(t)$ for $(S(t), I(t))$, then the corresponding set-estimation for the prevalence $I(t)/(S(t) + I(t))$ is the interval

$$\mathcal{E}_p(t) := \left[\min_{(s,i)\in\mathcal{E}(t)} \frac{i}{s+i}, \max_{(s,i)\in\mathcal{E}(t)} \frac{i}{s+i} \right].$$

In Fig. 5.5 we show the progress of the set-estimation of the prevalence in three scenarios: no intervention (the dotted lines), intervention applied to low risk individuals (dashed lines), and intervention applied to high risk individuals (solid lines). On the left plot the intervention decreases the susceptibility $\sigma(\omega)$ of the treated individuals, while on the right plot – the contact rates, $p(\omega)$. Comparing the figures we see that in both cases interventions are productive and that the intervention applied to high risk individuals is significantly more efficient.

However, it is not always the case that intervention is more efficient if applied to the individuals with highest risk. To show this we consider the above SI model with only the value of $\sigma(\omega)$ increased from 0.105 to 0.3, i.e. we assume higher susceptibility. On the left plot of Fig. 5.6 we see that the prevalence approaches value 1 (and actually the population becomes extinct, asymptotically). We consider again an intervention that reduces $\sigma(\omega)$ by 50%. On the right plot of Fig. 5.6 we see the result of this intervention when applied to the high risk and to low risk individuals, respectively. Again both interventions yield an improvement. However, now the intervention targeting the low risk individuals is more efficient and prevents extinction.

5.5.3 SIR-model

In this subsection we consider the following heterogeneous SIR model:

$$\begin{aligned}
\dot{S}(t,\omega) &= -\sigma p(\omega)J(t)S(t,\omega) + \kappa(I(t,\omega) + R(t,\omega)), \quad S(0,\omega) = u_1(\omega) \\
\dot{I}(t,\omega) &= \sigma p(\omega)J(t)S(t,\omega) - (\gamma+\kappa)I(t,\omega), \quad I(0,\omega) = u_2(\omega) \\
\dot{R}(t,\omega) &= \gamma I(t,\omega) - \kappa R(t,\omega), \quad R(0,\omega) = u_3(\omega)
\end{aligned} \tag{5.21}$$

where

$$J(t) = \int_\Omega p(\omega)I(t,\omega)\,\mathrm{d}\omega.$$

The new variable $R(t,\omega)$ represents the "number" of individuals who have recovered from the infection. Now the parameter γ has to be interpreted as the recovery rate, and κ denotes both the birth rate and the mortality rate. Thus in this model the disease has no influence on the mortality of infected individuals and the size of the population is constant. Furthermore, newborn individuals are assumed to be susceptible and reproduction is not affected by being infected or recovered.

In Fig. 5.7 we show the progress of the set-estimation of $(S(t), I(t))$ for $\sigma = 0.25$, $\kappa = 0.004$, $\gamma = 0.1$, and $p(\omega) = 0.5 + \omega$. We assume that at $t = 0$ there are no recovered individuals, i.e. $u_3(\omega) = 0$, and the bounds on $u_1(\cdot)$ and $u_2(\cdot)$ are the same as in Section 5.5.1. We see that the set-estimation exhibits an oscillatory behaviour, in contrast with the SI-model. The size of the set-estimation varies with time, but remains reasonably small.

It is interesting to mention that the structure of the extremal initial data $(u_1(\omega), u_2(\omega), 0)$ (see Section 5.5.2) in the SIR-model is much more complicated than that in the SI-model. As seen in Fig. 5.8, for a given unit vector $l \in L := \mathbb{R}^2 \times 0$, the extremal initial data $u_2(\omega) = I(0,\omega)$ may change its structure several times when the estimation time progresses: for time instances $t = 20$ and $t = 220$ the lower bound $\varphi_0^2(\omega)$ is active for small ω and the upper bound $\varphi_1^2(\omega)$ is active for large ω, while for time instances $t = 120$ and $t = 320$ the opposite happens.

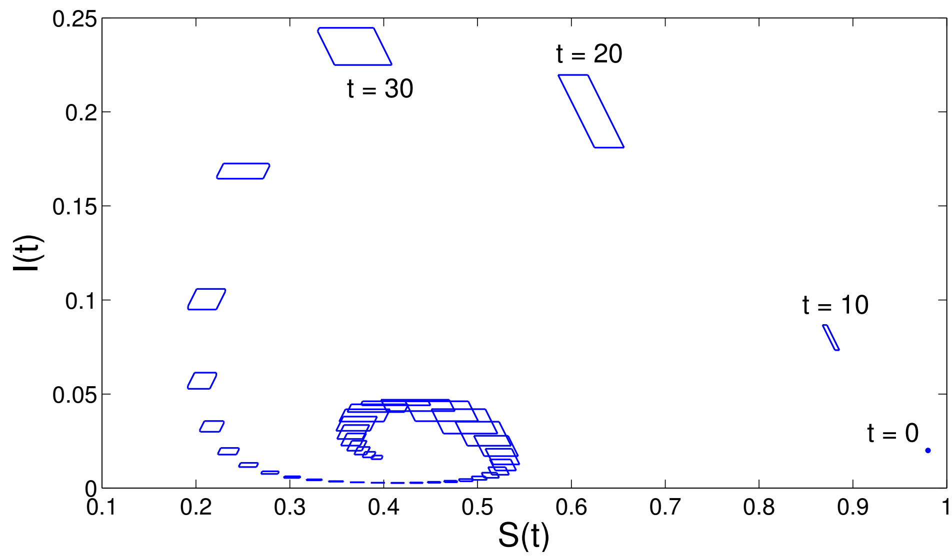

Figure 5.7: Set-membership estimates on the (S, I)-plane of system (5.21) for various times t, obtained by using 8 equidistant unit vectors $l \in \mathbb{R}^2 \times 0$.

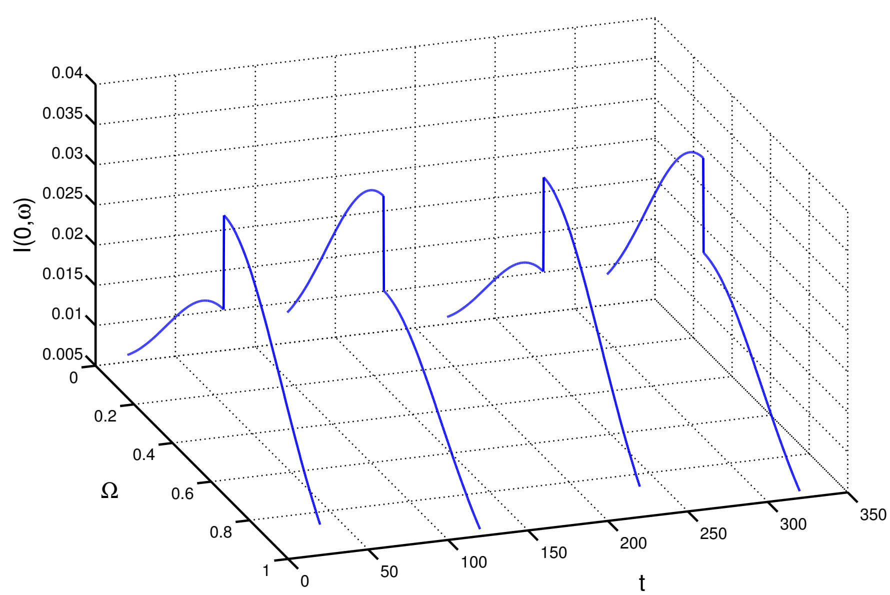

Figure 5.8: Extremal initial data $u_2(\omega) = I(0, \omega)$ corresponding to $l = (0, 1)$ and times $t = 20, 120, 220, 320$.

5.6 Conclusions and perspectives

In this paper we demonstrate the tractability and applicability of the set-membership estimation approach for prediction of the evolution of infectious diseases in heterogeneous populations, using distributed differential models under uncertainty about the individual traits relevant for the disease. The available information is in the form of two-sided bounds for the distribution of the initial population along the space of heterogeneity (the h-states), possibly together with some aggregated data. Although the numerical illustrations of the developed estimation technique involve only SI and SIR heterogeneous models, the technique is applicable to more complex models, provided that the evolution of only 2 or 3 aggregated states (such as the total number of susceptible, infected, recovered, etc. individuals) have to be estimated.

However, the presented general model has the drawback that the individuals do not change their h-state (that is, their individual traits) over time. If the trait comprises the contact rate, this means that individuals keep their contact rate constant, independently of the evolution of the disease. Change of the contact rate may happen only if an individual becomes infected. This assumption is not realistic, and models and corresponding estimation techniques aimed to cope with variable individual traits are a subject of current work.

Another line of research is to involve in the presented model framework *dynamic* intervention policies (not only prevention prior to the outburst of the disease, as in Section 5.5.2 of the present paper). The uncertainty about the h-states of the population brings into consideration the problem to control the evolution of set-membership estimations by prevention or medication policies. This problem is profoundly investigated in other, mainly engineering, contexts (see the recent book [74] and the numerous references therein).

Appendix: Proof of Proposition 5

Let $u(\cdot)$ be an admissible control and $\Delta u(\cdot)$ be such that $u(\cdot)+\Delta u(\cdot)$ is admissible too. We shall denote by $x(\cdot,\cdot)+\Delta x(\cdot,\cdot)$, and by $y(\cdot)+\Delta y(\cdot)$ the state variables corresponding to $u(\cdot)+\Delta u(\cdot)$ and by $J(u)$ the functional $\langle l, y[u](\tau)\rangle$ (we remind that l is a given nonzero vector from $\mathbb{R}^n$). We also introduce the notational convention to skip the arguments x and y. For instance $f(t,\omega) := f(t,\omega,x(t,\omega),y(t))$, $g'_x(t,\omega) := g'_x(t,\omega,x(t,\omega))$, etc.

Let us define the number r as

$$r = J(u+\Delta u) - J(u) + \int_\Omega \langle \lambda(0,\omega), \Delta u(\omega)\rangle \,\mathrm{d}\omega$$

We will show that r fulfils $|r| \leq C||\Delta u(\cdot)||^2_{L_\infty(\Omega)}$ for some positive constant C, from which the proposition follows. First we give a more explicit representation of r.

Lemma 8. *The remainder r fulfils*

$$\begin{aligned} r = &-\int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), f_y'(t,\omega) \int_\Omega [g_x'(t,\omega',\tilde{x}(t,\omega')) - g_x'(t,\omega')]\Delta x(t,\omega')\,\mathrm{d}\omega' \right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &+ \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f_x'(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f_x'(t,\omega)]\Delta x(t,\omega) \right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &+ \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f_y'(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f_y'(t,\omega)]\Delta y(t) \right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &+ \int_\Omega \left\langle l, \left[g_x'(\tau,\omega,\tilde{x}(\tau,\omega)) - g_x'(\tau,\omega)\right] \Delta x(\tau,\omega) \right\rangle \mathrm{d}\omega \end{aligned}$$

where $\bar{x}(t,\omega)$ and $\tilde{x}(t,\omega)$ lie between $x(t,\omega)$ and $x(t,\omega)+\Delta x(t,\omega)$ for $(t,\omega) \in D$ and $\bar{y}(t)$ lies between $y(t)$ and $y(t)+\Delta y(t)$ for $t \in [0,\tau]$.

Proof Using (5.6) in the last term in the third row below, we obtain

$$\begin{aligned} &\int_0^\tau \int_\Omega \left\langle \dot{\lambda}(t,\omega), \Delta x(t,\omega) \right\rangle \mathrm{d}\omega\,\mathrm{d}t = \\ &= \int_0^\tau \frac{d}{dt}\left(\int_\Omega \langle \lambda(t,\omega), \Delta x(t,\omega)\rangle\,\mathrm{d}s\right)\mathrm{d}t - \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), \dot{\Delta x}(t,\omega)\right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &= \int_\Omega \langle \lambda(\tau,\omega), \Delta x(\tau,\omega)\rangle\,\mathrm{d}\omega - \int_\Omega \langle \lambda(0,\omega), \Delta x(0,\omega)\rangle\,\mathrm{d}\omega - \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), \dot{\Delta x}(t,\omega)\right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &= \int_\Omega \langle \lambda(\tau,\omega), \Delta x(\tau,\omega)\rangle\,\mathrm{d}\omega - \int_\Omega \langle \lambda(0,\omega), \Delta x(0,\omega)\rangle\,\mathrm{d}\omega \qquad (5.22) \\ &\qquad - \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), f_x'(t,\omega)\Delta x(t,\omega) + f_y'(t,\omega)\Delta y(t)\right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &\qquad + \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f_x'(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f_x'(t,\omega)]\Delta x(t,\omega) \right\rangle \mathrm{d}\omega\,\mathrm{d}t \\ &\qquad + \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f_y'(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f_y'(t,\omega)]\Delta y(t) \right\rangle \mathrm{d}\omega\,\mathrm{d}t, \end{aligned}$$

where $\bar{x}(t,\omega)$ is between $x(t,\omega)$ and $x(t,\omega)+\Delta x(t,\omega)$ for $(t,\omega) \in D$ and $\bar{y}(t)$ is between $y(t)$ and $y(t)+\Delta y(t)$ for $t \in [0,\tau]$. It is standard to prove that $\bar{x}$ and $\bar{y}$ may be chosen measurable. Also, for each $t \in [0,\tau]$ we have

$$\begin{aligned} \Delta y(t) &= \int_\Omega [g(t,\omega,x(t,\omega)+\Delta x(t,\omega)) - g(t,\omega)]\,\mathrm{d}\omega \\ &= \int_\Omega g_x'(t,\omega)\Delta x(t,\omega)\,\mathrm{d}\omega + \int_\Omega [g_x'(t,\omega,\tilde{x}(t,\omega)) - g_x'(t,\omega))]\Delta x(t,\omega)\,\mathrm{d}\omega \qquad (5.23) \end{aligned}$$

where $\tilde{x}(t,\omega)$ is between $x(t,\omega)$ and $x(t,\omega)+\Delta x(t,\omega)$ for $(t,\omega) \in D$, and is also measurable. Substituting $\Delta y(t)$ from (5.23) into the fifth row of (5.22), we obtain

$$\int_0^\tau \int_\Omega \left\langle \dot{\lambda}(t,\omega), \Delta x(t,\omega) \right\rangle \mathrm{d}\omega\,\mathrm{d}t =$$

$$
\begin{aligned}
&= \int_\Omega \langle \lambda(\tau,\omega), \Delta x(\tau,\omega)\rangle \,\mathrm{d}\omega - \int_\Omega \langle \lambda(0,\omega), \Delta x(0,\omega)\rangle \,\mathrm{d}\omega \\
&- \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), f'_x(t,\omega)\Delta x(t,\omega) + f'_y(t,\omega)\int_\Omega g'_x(t,\omega')\Delta x(t,\omega')\,\mathrm{d}\omega' \right\rangle \mathrm{d}\omega\,\mathrm{d}t \\
&- \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), f'_y(t,\omega)\int_\Omega [g'_x(t,\omega',\tilde{x}(t,\omega')) - g'_x(t,\omega')]\Delta x(t,\omega')\,\mathrm{d}\omega' \right\rangle \mathrm{d}\omega\,\mathrm{d}t \quad (5.24)\\
&+ \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f'_x(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f'_x(t,\omega)]\Delta x(t,\omega)\right\rangle \mathrm{d}\omega\,\mathrm{d}t \\
&+ \int_0^\tau \int_\Omega \left\langle \lambda(t,\omega), [f'_y(t,\omega,\bar{x}(t,\omega),\bar{y}(t)) - f'_y(t,\omega)]\Delta y(t)\right\rangle \mathrm{d}\omega\,\mathrm{d}t.
\end{aligned}
$$

Denote the last three terms in (5.24) by $\tilde{r}$. In the first three terms we substitute $\dot{\lambda}(t,\omega)$ and $\Delta x(0,\omega)$ from (5.15) and (5.7), respectively. Using also (5.17), we rewrite the above equality as

$$
0 = \int_\Omega \langle \lambda(\tau,\omega), \Delta x(\tau,\omega)\rangle \,\mathrm{d}\omega - \int_\Omega \langle \lambda(0,\omega), \Delta u(\omega)\rangle \,\mathrm{d}\omega + \tilde{r}. \tag{5.25}
$$

On the other hand we have

$$
\begin{aligned}
J(u+\Delta u) - J(u) &= \langle l, y(\tau) + \Delta y(\tau)\rangle - \langle l, y(\tau)\rangle \\
&= \left\langle l, \int_\Omega [g(\tau,\omega,x(\tau,\omega)+\Delta x(\tau,\omega)) - g(\tau,\omega)]\,\mathrm{d}\omega \right\rangle \\
&= \left\langle l, \int_\Omega g'_x(\tau,\omega)\Delta x(\tau,\omega)\,\mathrm{d}\omega \right\rangle \\
&+ \left\langle l, \int_\Omega [g'_x(\tau,\omega,\tilde{x}(\tau,\omega)) - g'_x(\tau,\omega)]\Delta x(\tau,\omega)\,\mathrm{d}\omega \right\rangle. \qquad (5.26)
\end{aligned}
$$

Adding (5.25) to this equality and taking into account (5.16) we obtain

$$
J(u+\Delta u) - J(u) = -\int_\Omega \langle \lambda(0,\omega), \Delta u(\omega)\rangle \,\mathrm{d}\omega + \tilde{r} + \int_\Omega \left\langle l, [g'_x(\tau,\omega,\tilde{x}(\tau,\omega)) - g'_x(\tau,\omega)]\Delta x(\tau,\omega)\right\rangle \mathrm{d}\omega,
$$

which, in view of the definition of $\tilde{r}$, implies the claim of the lemma. □ □

We next estimate the four terms in the remainder r.

Lemma 9. *The remainder r satisfies the estimate*

$$
|r| \le C||\Delta u(\cdot)||^2_{L_\infty(\Omega)} \tag{5.27}
$$

where C is a positive constant.

Proof As in (5.23) we have

$$
\Delta y(t) = \int_\Omega [g(t,\omega,x(t,\omega)) - g(t,\omega)]\,\mathrm{d}\omega = \int_\Omega g'_x(t,\omega,\tilde{x}(t,\omega))\Delta x(t,\omega)\,\mathrm{d}\omega,
$$

for each $t \in [0,\tau]$. Because of the local essential boundedness of g'_x, we obtain

$$|\Delta y(t)| \leq C_1 \int_\Omega |\Delta x(t,\omega)|\, \mathrm{d}\omega \tag{5.28}$$

for each $t \in [0,\tau]$, where C_1 is some positive constant (as are C_2, C_3, etc., below). Because of (5.11), as in (5.22) we obtain

$$\Delta x(t,\omega) = \Delta u(\omega) + \int_0^t [f'_x(s,\omega,\bar{x}(s,\omega),\bar{y}(s))\Delta x(s,\omega) + f'_y(s,\omega,\bar{x}(s,\omega),\bar{y}(s))\Delta y(s)]\, \mathrm{d}s.$$

for $(t,\omega) \in [0,\tau] \times \Omega' \subset D$ (Ω' being of full Lebesgue measure in Ω). Hence, using (5.28) and the local essential boundedness of f'_x and f'_y, we have

$$|\Delta x(t,\omega)| \leq |\Delta u(\omega)| + C_2 \int_0^t \left[|\Delta x(s,\omega)| + \int_\Omega |\Delta x(s,\omega)|\, \mathrm{d}\omega \right] \mathrm{d}s. \tag{5.29}$$

for $(t,\omega) \in [0,\tau] \times \Omega' \subset D$ (Ω' of full Lebesgue measure in Ω). Integrating the above inequality in ω over Ω and changing the order of integration where necessary, we obtain that the function

$$\delta(t) \stackrel{def}{=} \int_\Omega |\Delta x(t,\omega)|\, \mathrm{d}\omega$$

satisfies

$$\delta(t) \leq ||\Delta u(\cdot)||_{L_1(\Omega)} + C_2(1 + \mathrm{meas}\{\Omega\}) \int_0^t \delta(s)\, \mathrm{d}s$$

and the Gronwall inequality yields

$$\delta(t) \leq C_3 ||\Delta u(\cdot)||_{L_1(\Omega)} \tag{5.30}$$

for all $t \in [0,\tau]$. Substituting (5.30) into (5.29), we obtain

$$\begin{aligned} |\Delta x(t,\omega)| &\leq |\Delta u(\omega)| + C_2 \int_0^t |\Delta x(s,\omega)|\, \mathrm{d}s + C_2 \int_0^t \delta(s)\, \mathrm{d}s \\ &\leq |\Delta u(\omega)| + C_2 C_3 T ||\Delta u(\cdot)||_{L_1(\Omega)} + C_2 \int_0^t |\Delta x(s,\omega)|\, \mathrm{d}s \\ &\leq (1 + C_2 C_3 T\, \mathrm{meas}\{\Omega\}) ||\Delta u(\cdot)||_{L_\infty(\Omega)} + C_2 \int_0^t |\Delta x(s,\omega)|\, \mathrm{d}s \end{aligned}$$

for $(t,\omega) \in [0,\tau] \times \Omega' \subset D$ (Ω' of full Lebesgue measure in Ω). Using again the Gronwall inequality, we obtain

$$|\Delta x(t,\omega)| \leq C_4 ||\Delta u(\cdot)||_{L_\infty(\Omega)} \tag{5.31}$$

for $(t,\omega) \in [0,\tau] \times \Omega' \subset D$ (Ω' of full Lebesgue measure in Ω). From here and from (5.28) we obtain

$$|\Delta y(t)| \leq C_1 C_4\, \mathrm{meas}\{\Omega\} ||\Delta u(\cdot)||_{L_\infty(\Omega)} \tag{5.32}$$

for all $t \in [0,\tau]$. The boundedness of $\lambda(\cdot,\cdot)$, the local essential boundedness of f'_y, the local Lipschitz continuity of f'_x, f'_y and g'_x (cf. Assumption (i)), as well as the inequalities (5.31) and (5.32) allow us to estimate the absolute values of the first three terms in the remainder r from above by $C_5||\Delta u(\cdot)||^2_{L_\infty(\Omega)}$. In the same way, the local Lipschitz continuity of g'_x and (5.31) yield the same estimate from above for the absolute value of the fourth term in the remainder r. $\square$ $\square$

Chapter 6

Modelling and Estimation of infectious diseases in a population with heterogeneous dynamic immunity[1]

6.1 Introduction

Ever since the seminal work by Kermack and McKendrick [66] compartmental models, such as SIR- or SIS-models, play a prominent role in mathematical epidemiology. The idea behind such models is to divide the population into several groups such as susceptibles (S), infectives (I), recovered (R), etc., and to study the interactions between these groups and in particular the transition of individuals from one group into another.

It is obvious that the immune system of individuals plays an important role in this process by counteracting the pathogen inside the body. The exact understanding of how this process works and the modelling of in-host dynamics is the aim of immunology. An introduction to this discipline may be found in [95]. In an epidemiological context immunology is important because the state of the immune system influences, for example, the susceptibility, infectivity, and recovery of individuals. The combination of these two disciplines, sometimes referred to as "immunoepidemiology" ([11, 44, 80]), is therefore a natural consequence. One way to achieve this is to model the within-host dynamics of the pathogen and couple this with an epidemiological model by assuming that the state of within-host dynamics influences the transmission of the pathogen between hosts. This approach has lead to a number of contributions, e.g. [2, 7, 27, 35, 38].

We will instead focus on the influence on the epidemiological dynamics of the waning and boosting of the immune response towards a disease. A short explanation of why the immune response increases

[1]This chapter has at the time of writing been submitted for peer review to the Journal of Biological Dynamics.

and decreases depending on exposure to a pathogen can, for example, be found in [11]. One approach to capture the waning of immunity towards a disease is to introduce additional subclasses of, for example, recovered individuals (e.g. [46, 104]) or individuals with waning immunity from vaccination (e.g. [89, 97]). This approach has the advantage that the dynamics are still described by an ODE model, however these ODE systems can become large if many compartments are added. Another approach is to assume that the recovered population is structured with respect to the immune status of the individuals. This approach retains the low-dimensionality of the equations, however at the cost of introducing a PDE into the system (e.g. [16]). Such systems can also be formulated to include boosting of the immune system for the recovered population as well ([11]). Other approaches to model the boosting of the immune system during the infective period leads to models with multiple structured populations ([80]). We will study dynamical systems in which every sub-population is structured with respect to the host immunity. An example of such a model can be found in [111].

In this paper we present a model for the evolution of the susceptible and infected subpopulations (SIS-model) in which the immunity of individuals has its own dynamics, depending on whether the individual is susceptible of infected. The model involves a system of first order PDEs (of the type of the so-called size-structured systems), which is similar to (but different from) [111]. It could be interpreted in terms of an influenza infection, but similar models may be appropriate to simulate sexually transmitted diseases [18]. In [111] it is argued that this framework can also be used to model microparasite infections.

To numerically simulate heterogeneous models such as the one developed here, the initial distribution of the population along the possible immunity states has to be known. However, precise information about this distribution is not available in practice. Therefore, we develop a method to estimate the dynamics of the disease under uncertain initial conditions, based on available data only. It builds on the general approach of set-membership estimation under deterministic uncertainty (see e.g. [74, 75, 85]).

The paper is organised as follows. In Section 6.2 we introduce a benchmark SIS-model with heterogeneous immunity, which consists of a pair of size-structured first order PDEs. In Section 6.3 we begin the investigation of this model by studying its steady state distributions. In Section 6.4 we present a more general class of models (including SIR-models, for example), and develop the appropriate set-membership estimation technique. This allows us to estimate the evolution of the disease without complete knowledge of its initial state. Finally, in Section 6.5 we apply this technique to the benchmark model to gain additional insights about the steady states found in Section 6.3 and to study how differences in the initial distribution influence the short term and long term behaviour of the disease.

6.2 The heterogeneous *SIS*-model

In the model below we consider a closed population of fixed size, a part of which is infected by influenza. Each individual has an immunity level characterized by a number $\omega \in [0, 1]$: the larger is ω, the higher is the immunity of an individual. The level of immunity has its own dynamics. If an individual is susceptible (that is, not infected, in the present context) in a time interval $[\tau, \theta)$, then her immunity level obeys the equation

$$\dot{\omega}(t) = d(\omega(t)), \quad \omega(\tau) = \omega_\tau, \qquad t \in [\tau, \theta), \tag{6.1}$$

where ω_τ is the immunity level at time τ and $d(\omega)$ is the time-rate of decrease of immunity at immune state ω. Thus, $d : [0, 1] \to (-\infty, 0]$.

Similarly, $e : [0, 1] \to [0, \infty)$ represents the rate of increase of immunity of infected individuals: the dynamics of the immune state of an individual which is infected in $[\theta, \eta)$ is described by the equation

$$\dot{\omega}(t) = e(\omega(t)), \quad \omega(\theta) = \omega_\theta, \qquad t \in [\theta, \eta). \tag{6.2}$$

Of course, if a susceptible individual becomes infected at time θ, then the dynamics of her immune level switches from (6.1) to (6.2), then switches back to (6.1) at the time of recovery. In the long run such switchings may happen several time. Notice that the dynamics of the immune state is not individual-specific – the laws (6.1) and (6.2) apply to each individual.

In order to ensure existence and uniqueness of the solutions of the above ODEs, and invariance of the interval $[0, 1]$ (which is required in order to make the model meaningful) we assume that d and e are continuously differentiable and $d(0) = e(1) = 0$. This resembles the assumption that the interval $[0, 1]$ contains all possible immune states.

Now, we describe the model of the evolution of the susceptible and the infected subpopulations, beginning with some notations. The numbers $S(t, \omega)$ and $I(t, \omega)$ represent the sizes of the susceptible/infected subpopulations of immunity state ω at time t. The susceptibility of a susceptible individual depends on the immunity state and is denoted by $p(\omega) \geq 0$. The infectivity of an infected individual may also depend on the immunity state and is denoted by $q(\omega) \geq 0$. The recovery rate of an infected individual of immunity state ω is denoted by $\delta(\omega) \geq 0$. Finally, $\sigma(t) \geq 0$ is the strength of infection or aggressiveness of the disease. It is reasonably assumed to depend on time in order to capture possible seasonal changes or other time-dependent effects.

Notice that the total population size can be represented as

$$N(t) = \int_0^1 [S(t, \omega) + I(t, \omega)] \, \mathrm{d}\omega.$$

In the model below it will be assumed that the total population size remains constant, therefore one may normalize it to $N(t) = 1$. Then under the assumption of proportional mixing (see e.g. [30]), the incidence rate takes the form

$$\frac{\int_0^1 q(\zeta)I(t,\zeta)\,\mathrm{d}\zeta}{N(t)} = \int_0^1 q(\zeta)I(t,\zeta)\,\mathrm{d}\zeta. \tag{6.3}$$

The evolution of the susceptible/infected individuals, regarding the changes of the immunity state, is described by the equations

$$\begin{aligned} \frac{\partial}{\partial t}S(t,\omega) + \frac{\partial}{\partial \omega}\left(d(\omega)S(t,\omega)\right) &= -\sigma(t)p(\omega)\int_0^1 q(\zeta)I(t,\zeta)\,\mathrm{d}\zeta\, S(t,\omega) + \delta(\omega)I(t,\omega), \\ \frac{\partial}{\partial t}I(t,\omega) + \frac{\partial}{\partial \omega}\left(e(\omega)I(t,\omega)\right) &= \sigma(t)p(\omega)\int_0^1 q(\zeta)I(t,\zeta)\,\mathrm{d}\zeta\, S(t,\omega) - \delta(\omega)I(t,\omega), \end{aligned} \tag{6.4}$$

complemented with the initial conditions

$$S(0,\omega) = S^0(\omega), \quad I(0,\omega) = I^0(\omega), \qquad \omega \in [0,1], \tag{6.5}$$

and the boundary (zero-flux) conditions

$$d(1)S(t,1) = 0, \quad e(0)I(t,0) = 0, \qquad t \geq 0. \tag{6.6}$$

In our case we will fulfil the zero-flux conditions by assuming that $d(1) = e(0) = 0$, which is not principally necessary, but is reasonable and makes the analysis technically simpler (see Remark 4 in Section 6.4.1). For simplicity, the data p, q, δ, σ, S^0, I^0 are assumed to be continuous functions (although this assumption can be easily relaxed – only measurability and boundedness suffice). Also it is reasonably assumed that $d(\omega) < 0$ and $e(\omega) > 0$ for $\omega \in (0,1)$ (strict loss/gain of immunity if not-perfect/missing), and that $p(0) > 0$, $q(0) > 0$. Due to the normalization of the population size we have to assume also that $\int_0^1 [S^0(\omega) + I^0(\omega)]\,\mathrm{d}\omega = 1$.

Equations (6.4) have a clear micro-foundation: they can be derived (like in physics) by calculating what amount of individuals will enter/leave immunity state interval $[\omega, \omega + \Delta\omega]$ in a time horizon $[t, t + \Delta t]$, and then pass to a limit with Δt and $\Delta\omega$. This kind of size-structured systems are widely used in mathematical biology, while in the context of epidemiology we may refer to [80, 111].

The exact definition of the notion of solution of equations (6.4)–(6.6) will be given in Section 6.4.

Remark 2. In the above model we assumed in advance (by taking $N(t) = 1$) that the population has constant size. Notice that equations (6.4) together with the zero-flux conditions (6.6) and the natural condition $d(0) = e(1) = 0$ keep the size of the population constant ($= 1$).

Remark 3. The assumption that there is no in/out flow of population is somewhat restrictive. In fact, in- and out-flows of equal amounts of individuals is implicitly included in the model, provided that the flows have the same ω-distributions as the existing population, hence have no effect on S and I. Moreover, the model (6.4)–(6.6) can be easily enhanced to include out-flows due to mortality (also additional mortality caused by infection) and migration, and in-flows of new-borns and immigrants, having heterogeneous immunity states. This is just a matter of adding new terms in equations (6.4) and replacing the incidence rate with the left term in (6.3) in order to take into account a possible change of the population size.

6.3 Steady states

In this section we investigate the steady states of the benchmark system (6.4) in the case of time-invariant strength of infection $\sigma(t) = \sigma$. Steady states are important in the study of asympototic behaviour and give valuable information, in general. Although we are, due to the complexity of the model, not able to completely describe the steady states or asymptotic behaviour analytically, the calculations here are the basis for a numerical analysis of the steady states which will be carried out in Section 6.5.

We formally drop the time dependence of the functions $S(t,\omega)$ and $I(t,\omega)$. This yields (denoting differentiation with respect to ω by $'$)

$$\begin{aligned} (d(\omega)S(\omega))' &= -\sigma p(\omega) \int_0^1 q(\zeta)I(\zeta)\,\mathrm{d}\zeta\, S(\omega) + \delta(\omega)I(\omega), \\ (e(\omega)I(\omega))' &= \sigma p(\omega) \int_0^1 q(\zeta)I(\zeta)\,\mathrm{d}\zeta\, S(\omega) - \delta(\omega)I(\omega). \end{aligned} \tag{6.7}$$

Note that we have $(d(\omega)S(\omega) + e(\omega)I(\omega))' = 0$ which implies

$$d(\omega)S(\omega) + e(\omega)I(\omega) = \kappa = \text{const.} \tag{6.8}$$

6.3.1 Disease free steady states

First, we look for disease free steady states of (6.7), i.e. solutions with $I(\omega) \equiv 0$. Under this condition (6.8) becomes $d(\omega)S(\omega) = \kappa$. If $\kappa \neq 0$ then $S(\omega) = \frac{\kappa}{d(\omega)}$. Since $\int_0^1 S(\omega)\,\mathrm{d}\omega = 1$ we get that $\kappa = \left(\int_0^1 \frac{1}{d(\omega)}\,\mathrm{d}\omega\right)^{-1}$. This in particular means that $\kappa \neq 0 \Rightarrow \left|\int_0^1 \frac{1}{d(\omega)}\,\mathrm{d}\omega\right| < \infty$. However, note that for $\kappa \neq 0$ the zero-flux condition $d(1)S(1) = 0$ is not fulfilled.

For $\kappa = 0$ we get that $d(\omega)S(\omega) = 0$ which implies $S(\omega) = 0$ for $\omega \in (0,1)$. Since $\int_0^1 S(\omega)\,\mathrm{d}\omega = 1$ we get that $S(\omega) = a\delta_0(\omega) + (1-a)\delta_0(\omega - 1)$ for $a \in [0,1]$ and where $\delta_0(\omega)$ is the Dirac-delta. In particular, the only disease free steady state that fulfils the zero-flux condition $d(1)S(1) = 0$ is $S(\omega) = \delta_0(\omega)$.

6.3.2 Endemic steady states

Now, we consider the solutions of the steady state system (6.7), where $I(\omega)$ is not zero almost everywhere. We furthermore restrict ourselves to solutions where both $S(\omega)$ and $I(\omega)$ are non-negative. For this analysis we fix an $\omega^* \in (0,1)$. Furthermore, for $\kappa, \theta \in (0,\infty)$ we define the three functions

$$g_\kappa(\theta) = \frac{\theta - \int\limits_0^1 \int\limits_{\omega^*}^{\omega} q(\omega) e^{\int_\omega^s \frac{\sigma p(\zeta)\theta}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} \frac{\sigma p(s)\theta}{d(s)e(s)} \kappa \,\mathrm{d}s\,\mathrm{d}\omega}{\int\limits_0^1 q(\omega) e^{-\int_{\omega^*}^{\omega} \frac{\sigma p(\zeta)\theta}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta}\,\mathrm{d}\omega}, \tag{6.9}$$

$$I_{(\kappa,\theta)}(\omega) = g_\kappa(\theta) e^{-\int_{\omega^*}^{\omega} \frac{\sigma p(\zeta)\theta}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} + \int\limits_{\omega^*}^{\omega} e^{\int_\omega^s \frac{\sigma p(\zeta)\theta}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} \frac{\sigma p(s)\theta}{d(s)e(s)} \kappa \,\mathrm{d}s, \tag{6.10}$$

$$S_{(\kappa,\theta)}(\omega) = \frac{\kappa}{d(\omega)} - \frac{e(\omega)}{d(\omega)} I_{(\kappa,\theta)}(\omega). \tag{6.11}$$

First, assume that $(S^*(\omega), I^*(\omega))$ solves (6.7) and is non-negative. Define

$$\theta^* = \int_0^1 q(\omega) I^*(\omega)\,\mathrm{d}\omega, \quad \kappa^* = d(\omega^*)S^*(\omega^*) + e(\omega^*)I^*(\omega^*). \tag{6.12}$$

Using (6.7) and (6.8) it is easy to show for $\omega \in (0,1)$ that $I^*(\omega)$ fulfils

$$I^{*\prime}(\omega) = -\left(\frac{\sigma p(\omega)\theta^*}{d(\omega)} + \frac{\delta(\omega)+e'(\omega)}{e(\omega)}\right) I^*(\omega) + \frac{\sigma p(\omega)\theta^*}{d(\omega)e(\omega)}\kappa^*.$$

From this we see that for $\omega \in (0,1)$ we can write

$$I^*(\omega) = I^*(\omega^*) e^{-\int_{\omega^*}^{\omega} \frac{\sigma p(\zeta)\theta^*}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} + \int\limits_{\omega^*}^{\omega} e^{\int_\omega^s \frac{\sigma p(\zeta)\theta^*}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} \frac{\sigma p(s)\theta^*}{d(s)e(s)} \kappa^* \,\mathrm{d}s. \tag{6.13}$$

Multiplying this equation by $q(\omega)$ and integrating over $(0,1)$ yields

$$\theta^* = I^*(\omega^*) \int\limits_0^1 q(\omega) e^{-\int_{\omega^*}^{\omega} \frac{\sigma p(\zeta)\theta^*}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta}\,\mathrm{d}\omega + \int\limits_0^1 \int\limits_{\omega^*}^{\omega} q(\omega) e^{\int_\omega^s \frac{\sigma p(\zeta)\theta^*}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} \frac{\sigma p(s)\theta^*}{d(s)e(s)} \kappa^* \,\mathrm{d}s\mathrm{d}\omega,$$

which is equivalent to $I^*(\omega^*) = g_{\kappa^*}(\theta^*)$. Plugging this into (6.13) we see that $I^*(\omega) = I_{(\kappa^*,\theta^*)}(\omega)$, and using (6.8) that $S^*(\omega) = S_{(\kappa^*,\theta^*)}(\omega)$. Note that because the solution is assumed to be non-negative and that $I^*(\omega)$ is not identically zero, we get that (κ^*, θ^*) is a pair that fulfils the following conditions:

$$\kappa, \theta, g_\kappa(\theta) \in (0,\infty),\; g_\kappa(\theta) + \kappa \inf_{\omega\in(0,1)} \int\limits_{\omega^*}^{\omega} e^{\int_{\omega^*}^s \frac{\sigma p(\zeta)\theta}{d(\zeta)} + \frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} \frac{\sigma p(s)\theta}{d(s)e(s)} \,\mathrm{d}s \geq 0. \tag{6.14}$$

Now conversely assume that the pair (κ,θ) fulfils (6.14). Then it is obvious that $I_{(\kappa,\theta)}$ and $S_{(\kappa,\theta)}$ are both non-negative. Due to our definition of $g_\kappa(\theta)$ it is easy to see that $\int_0^1 q(\omega)I_{(\kappa,\theta)}(\omega)\,\mathrm{d}\omega = \theta$. Using this, by a simple differentiation of (6.10) we obtain that for $\omega \in (0,1)$

$$I'_{(\kappa,\theta)}(\omega) = \frac{\sigma p(\omega)\int\limits_0^1 q(\zeta)I_{(\kappa,\theta)}(\zeta)\,\mathrm{d}\zeta}{d(\omega)}\left(\frac{\kappa}{e(\omega)} - I_{(\kappa,\theta)}(\omega)\right) - \frac{\delta(\omega)+e'(\omega)}{e(\omega)}I_{(\kappa,\theta)}(\omega). \tag{6.15}$$

Multiplying (6.11) with $\frac{d(\omega)}{e(\omega)}$ and plugging the result into (6.15), then multiplying by $e(\omega)$ yields

$$\big(e(\omega)I_{(\kappa,\theta)}(\omega)\big)' = \sigma p(\omega)\int\limits_0^1 q(\zeta)I_{(\kappa,\theta)}(\zeta)\,\mathrm{d}\zeta S_{(\kappa,\theta)}(\omega) - \delta(\omega)I_{(\kappa,\theta)}(\omega).$$

Consequently, $\big(S_{(\kappa,\theta)}(\omega), I_{(\kappa,\theta)}(\omega)\big)$ solves (6.7) on the open interval $(0,1)$. Thus, we have proven the following theorem.

Theorem 11. *Choose $\omega^* \in (0,1)$. Let $g_\kappa(\theta)$, $I_{(\kappa,\theta)}(\omega)$ and $S_{(\kappa,\theta)}(\omega)$ be defined as in (6.9), (6.10) and (6.11) respectively.*

- *If (κ,θ) fulfils (6.14), then $\big(S_{(\kappa,\theta)}(\omega), I_{(\kappa,\theta)}(\omega)\big)$ solves (6.7) for all $\omega \in (0,1)$.*
- *If $(S^*(\omega), I^*(\omega))$ solves (6.7), define κ^* and θ^* as in (6.12). Then (κ^*,θ^*) fulfils (6.14) and $(S^*(\omega), I^*(\omega)) = \big(S_{(\kappa^*,\theta^*)}(\omega), I_{(\kappa^*,\theta^*)}(\omega)\big)$ for all $\omega \in (0,1)$.*

This theorem shows that there is a one-to-one correspondence between non-negative solutions of (6.7) on $(0,1)$ and pairs (κ,θ) that fulfil (6.14). Note that the solutions that fulfil the zero-flux condition correspond to the pairs $(0,\theta)$ that fulfil (6.14). We look at these solutions more closely. The condition (6.14) reduces in this case to $\theta \in (0,\infty)$ and $g_0(\theta) \in (0,\infty)$. Furthermore, we are looking for solutions for which the total population is constant and equal to 1. Using (6.10) and (6.11) this yields

$$\begin{aligned}
1 &= \int\limits_0^1 I_{(0,\theta)}(\omega) + S_{(0,\theta)}(\omega)\,\mathrm{d}\omega \\
&= \int\limits_0^1 g_0(\theta)e^{-\int_{\omega^*}^{\omega}\frac{\sigma p(\zeta)\theta}{d(\zeta)}+\frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta} - \frac{e(\omega)}{d(\omega)}g_0(\theta)e^{-\int_{\omega^*}^{\omega}\frac{\sigma p(\zeta)\theta}{d(\zeta)}+\frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta}\,\mathrm{d}\omega \\
&= g_0(\theta)\int\limits_0^1 \left(1-\frac{e(\omega)}{d(\omega)}\right)e^{-\int_{\omega^*}^{\omega}\frac{\sigma p(\zeta)\theta}{d(\zeta)}+\frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta}\,\mathrm{d}\omega.
\end{aligned}$$

Using (6.9) we see that for $\theta \in (0,\infty)$ that fulfils $g_0(\theta) \in (0,\infty)$ this is equivalent to

$$0 = \int\limits_0^1 \left(\left(1-\frac{e(\omega)}{d(\omega)}\right)\theta - q(\omega)\right)e^{-\int_{\omega^*}^{\omega}\frac{\sigma p(\zeta)\theta}{d(\zeta)}+\frac{\delta(\zeta)+e'(\zeta)}{e(\zeta)}\,\mathrm{d}\zeta}\,\mathrm{d}\omega.$$

We denote the function on the right-hand side by $r(\theta)$. We see that $r(0) < 0$ (possibly $-\infty$) and $r(\theta) > 0$ (again possibly infinite) for any θ bigger than $\sup_{\omega\in[0,1]} q(\omega) =: Q$. Therefore any solution of the equation $r(\theta) = 0$ must lie in the interval $(0, Q)$. With this notation we arrive at the following corollary.

Corollary 2. *The system (6.7) has a solution that fulfils the zero-flux condition and is non-negative if and only if the function $r(\theta)$ has a root $\theta^* \in (0, Q)$. In this case the solution is given by $(S_{(0,\theta^*)}, I_{(0,\theta^*)})$. This solution is unique if and only if this root is unique.*

We note that one can show that $r(\theta)$ is continuous on any set where it is bounded. The question of the existence of a solution to $r(\theta) = 0$ is therefore closely connected to the question of where $r(\theta)$ is bounded. This however cannot be answered in general and depends on the particular choice of parameter functions. The same applies to the uniqueness.

6.4 Set-membership estimation

In order to calculate a solution of system (6.4) one needs to know the initial distributions of the susceptible and infected subpopulations along the heterogeneity ω, that is, $S(0,\omega)$ and $I(0,\omega)$. However, this information is usually not available in detail. We may assume that the total number of susceptible and infected individuals at time 0, that is, the quantities $S(0) = \int_0^1 S(0,\omega)\,\mathrm{d}\omega$ and $I(0) = \int_0^1 I(0,\omega)\,\mathrm{d}\omega$, are known. We may also have additional information about the initial distributions, for example pointwise constraints of the form $u(\omega) := (S(0,\omega), I(0,\omega)) \in [\phi_1(\omega), \phi_2(\omega)]$ where ϕ_1 and ϕ_2 are known functions. More generally, we summarize the available information about the initial data as $u(\cdot) \in \mathcal{U}$, where $\mathcal{U}$ is a closed, convex and bounded subset of $L_\infty := L_\infty([0,1] \mapsto \mathbb{R}^n_+)$. Below in this section we will formulate the problem of set-membership estimation of the aggregated state of the system, $y(t) := \left(\int_0^1 S(t,\omega)\,\mathrm{d}\omega, \int_0^1 I(t,\omega)\,\mathrm{d}\omega\right)$, based on the information $u(\cdot) \in \mathcal{U}$ about the initial data and the systems dynamics. Moreover, a computational tool for finding (approximating) the set-membership estimation will be provided. This will be done in a more general framework, including other (also higher dimensional) models of interest in epidemiology and beyond.

6.4.1 Formulation of the general model

Below $x : [0,T] \times [0,1] \to \mathbb{R}^n$ will be viewed as a distributed state function and $y : [0,T] \to \mathbb{R}^m$ – as an aggregated state function, with their dynamics given by the equations

$$\frac{\partial}{\partial t}x(t,\omega) + \frac{\partial}{\partial \omega}(A(\omega)x(t,\omega)) = f(t,\omega,x(t,\omega),y(t)), \quad x(0,\omega) = u(\omega), \tag{6.16}$$

$$y(t) = \int_0^1 g(t,\omega,x(t,\omega))\,\mathrm{d}\omega. \tag{6.17}$$

The following assumptions will be standing in this section. The function $f : [0,T] \times [0,1] \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ is differentiable in x and y, the derivatives f_x and f_y and f itself are measurable in (t,ω), locally essentially bounded, and locally Lipschitz continuous in (x,y) uniformly in (t,ω). The function $g : [0,T] \times [0,1] \times \mathbb{R}^n \to \mathbb{R}^m$ is differentiable in x, the derivative g_x and the function g itself are measurable in ω and continuous in t, locally essentially bounded, and locally Lipschitz continuous in x uniformly in (t,ω). Moreover, $f(t,\omega,x,y) \geq -cx$, $g(t,\omega,x) \geq 0$, where $c \geq 0$ is a constant and the inequalities (understood component-wise) hold for every (t,ω) and every $x \geq 0$ and $y \geq 0$. The matrix function $A : [0,1] \to \mathbb{R}^n \times \mathbb{R}^n$ is diagonal with continuously differentiable diagonal elements $a_i(\omega)$, $a_i(0) = a_i(1) = 0$ and $a_i(\omega) \neq 0$ for $\omega \in (0,1)$.

Remark 4. The assumptions about f and g are fulfilled in our model (6.4) with $x = (S, I)$ and $y(t)$ as in the beginning of the present section. Moreover, there we have $A = \operatorname{diag}(d, e)$ and the assumptions about A are fulfilled if d and e are as assumed in Section 6.2. We stress that the additional assumption $d(1) = e(0) = 0$ made there provides one way to satisfy the zero-flux conditions (6.6). In this case equations (6.16), (6.17) require only initial conditions to produce a unique solution (see below). If $d(1) \neq 0$ and/or $e(0) \neq 0$, then the zero-flux conditions must be ensured by adding the boundary conditions $S(t,1) = 0$ and/or $I(t,0) = 0$ (see, e.g., the more general consideration in [6]). The approach below is still applicable, but the calculations become more cumbersome.

As it will be seen below, a solution of (6.16), (6.17) is uniquely defined by the initial condition

$$x(0,\omega) = u(\omega), \quad \omega \in [0,1], \tag{6.18}$$

where $u : [0,1] \mapsto \mathbb{R}^n_+$ is a measurable and bounded function.

The notion of solution of system (6.16)–(6.18) can be defined in several ways, but for the considered problem the method of characteristics seem to be most natural. Let for $i = 1, \dots, n$ the function $\omega_i : [0,T] \times [0,1] \to [0,1]$ be defined as the unique solution of the initial value problem

$$\frac{\partial}{\partial t}\omega_i(t,\rho) = a_i(\omega_i(t,\rho)), \quad \omega_i(0,\rho) = \rho,$$

where ρ is regarded as a parameter for ω_i. Due to the assumptions about $a_i(\omega)$, the mapping $(t,\rho) \mapsto (t, \omega_i((t,\rho))$ is a diffeomorphism of $[0,T] \times [0,1]$ onto itself. Its inverse has the form $(t,\omega) \mapsto (t, \rho_i(t,\omega))$, where ρ_i is continuously differentiable and satisfies $\omega_i(t, \rho_i(t,\omega)) = \omega$ and $\rho_i(t, \omega_i(t,\rho)) = \rho$.

As a motivation for the definition below we assume that x is a continuously differentiable solution of (6.16)–(6.18). Denote $z_i(t,\rho) = x_i(t, \omega_i(t,\rho))$, thus $x_i(t,\omega) = z_i(t, \rho_i(t,\omega))$. Then

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t} z_i(t,\rho) &= \frac{\partial}{\partial t} x_i(t, \omega_i(t,\rho)) + a_i(\omega_i(t,\rho)) \frac{\partial}{\partial \omega} x_i(t, \omega_i(t,\rho)), \\ z_i(0,\rho) &= x_i(0, \omega_i(0,\rho)) = x_i(0,\rho) = u(\rho), \end{aligned}$$

hence

$$\frac{\mathrm{d}}{\mathrm{d}t} z_i(t,\rho) = f_i(t, \omega_i(t,\rho), x(t, \omega_i(t,\rho)), y(t)) - a_i'(\omega_i(t,\rho))\, z_i(t,\rho). \tag{6.19}$$

$$z_i(0,\rho) = u(\rho). \tag{6.20}$$

The above equations motivate the following definition (cf. [6]).

Definition 1. The pair of functions $x : [0,T] \times [0,1] \to \mathbb{R}^n$ and $y[0,T] \to \mathbb{R}^m$ is a solution of system (6.16)–(6.18) if x has the representation $x_i(t, \omega_i(t,\rho)) = z_i(t,\rho)$, $t \in [0,T]$, $\rho \in [0,1]$, where $z_i(t,\rho)$ is measurable in ρ and absolutely continuous in t for a.e. ρ, and (6.19), (6.20), (6.17) are satisfied almost everywhere.

The definition is correct and x is a measurable function due to the measurability of z and the fact that $(t,\rho) \mapsto (t, \omega_i((t,\rho))$ is a diffeomorphism. For the same reason the functions $x_j(t,\omega_i(t,\rho)) = z_j(t, \rho_j(t, \omega_i(t,\rho)))$ in the right-hand side of (6.19) are well defined and measurable. A solution x does not need to be differentiable. It may even be discontinuous in each of the directions t and ω, but x_i is absolutely continuous along almost every characteristic line $(t, \omega_i(t))$.

Lemma 10. *If (x,y) is a solution of (6.16)–(6.18) then the mappings*

$$[0,T] \ni t \mapsto x(t,\cdot) \in L_1(0,1) \quad \textit{and} \quad [0,T] \ni t \mapsto y(t)$$

are continuous.

Proof. The second claim follows from the first due to the Lipschitz continuity of g in x and the boundedness of x. Let us prove the first claim. For every $i = 1, \dots n$ and for a.e. $t,\ \tau \in [0,1]$ we have, by change of the variable $\omega = \omega_i(t,\rho)$

$$\begin{aligned}
&\int_0^1 |x_i(t,\omega) - x_i(\tau,\omega)|\,\mathrm{d}\omega = \int_0^1 |x_i(t,\omega_i(t,\rho)) - x_i(\tau,\omega_i(t,\rho))| \frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho \\
\leq \;& \int_0^1 \left[|x_i(t,\omega_i(t,\rho)) - x_i(\tau,\omega_i(\tau,\rho))| + |x_i(\tau,\omega_i(t,\rho)) - x_i(\tau,\omega_i(\tau,\rho))| \right] \frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho \\
= \;& \int_0^1 |z_i(t,\rho) - z_i(\tau,\rho)| \frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho + \int_0^1 |x_i(\tau,\omega) - x_i(\tau, \omega_i(\tau, \rho_i(t,\omega)))|\,\mathrm{d}\omega \\
&\leq c_1|t-\tau| + \int_0^1 |x_i(\tau,\omega) - x_i(\tau, \omega + \varepsilon(\omega,t,\tau))|\,\mathrm{d}\omega,
\end{aligned}$$

where $|\varepsilon(\omega,t,\tau))| \leq c_2|t-\tau|$ (c_1 and c_2 are appropriate constants). It is a standard fact from the analysis (a consequence from Lousin's theorem, for example) that the second term converges to zero when $t \to \tau$. □

Existence and uniqueness of a solution can be proved by a fixed point argument similarly as in [6]. In fact, the result there is more general, but not directly applicable to our case, since $a_i > 0$ is assumed in [6]. But our assumptions about a_i bring more a simplification rather than complication, since we do not need boundary conditions at $\omega = 0$, resp. $\omega = 1$ (depending on the sign of a_i) – see Remark 4. In addition, the unique solution of (6.16)–(6.18) is proved in [6] to be non-negative, provided that $u(\omega) \geq 0$, $\omega \in [0, 1]$. We also note that the assumptions $f \geq -cx$ and $g \geq 0$ are only needed to ensure non-negativity of the solution.

6.4.2 The set-estimation problem

As explained at the beginning of the section, the initial data $u(\omega)$ is not assumed to be exactly known. Instead, we assume that the only information about $u(\cdot)$ is that $u \in \mathcal{U}$, where $\mathcal{U}$ is a given bounded, closed and convex subset of L_∞. Every element $u \in \mathcal{U}$ will be considered as a possible realization of the uncertainty in the initial data. Let our task be to obtain information about a part of the components of the aggregated state y at a given time, say $t = T$. That is, we wish to estimate the projection $\text{pr}_L y(T)$ on a given subspace $L \subset \mathbb{R}^m$.

Every $u \in \mathcal{U}$ generates a unique solution $(x[u], y[u])$ of (6.16)–(6.18). Denote

$$\mathcal{R}(T) := \{y[u](T) : \, u \in \mathcal{U}\}.$$

That is, $\mathcal{R}(T)$ is the set of all aggregated states $y(T)$ that result from some possible realization of the uncertainty, $u \in \mathcal{U}$. In this sense, $\mathcal{R}(T)$ is the exact (meaning *minimal*) set-membership estimation of the aggregated state at time T. Thus the object of our interest is the set $\mathcal{R}_L(T) := \text{pr}_L \mathcal{R}(T)$. Below we adapt a well-known method for obtaining estimates

$$\mathcal{E}(T) \supset \mathcal{R}_L(T).$$

Even more, the method allows to obtain outer approximations of arbitrary accuracy to the convex hull $\text{co}\mathcal{R}(T)$.

For a fixed $l \in L$ we consider the problem of maximization of

$$J_l(u) := \langle l, y[u](T) \rangle \tag{6.21}$$

on the set $\mathcal{U}$, where $\langle \cdot, \cdot \rangle$ denotes the scalar product in $\mathbb{R}^m$. Notice that J is bounded on $\mathcal{U}$ (see Lemma 11 in the Appendix). Without caring about existence of a solution of problem (6.21), we observe that if (u_l, y_l) is an ε-solution (in the sense that $J_l^\varepsilon := J_l(u_l) \geq \sup_{\mathcal{U}} J_l - \varepsilon$), then

$$\text{co}\mathcal{R}(T) \subset \{y : \, \langle l, y \rangle \leq J_l^\varepsilon + \varepsilon\}.$$

Repeating the same for a mesh $\{l_i\}$ in the unit sphere on L, we obtain the set-membership estimation

$$\mathrm{co}\mathcal{R}_L(T) \subset \mathcal{E}(T) := \bigcap_i \{y : \langle l_i, y\rangle \le J^{\varepsilon}_{l_i} + \varepsilon\},$$

which is the intersection of a finite number of (affine) half-spaces. Furthermore, if ε is small enough and the mesh $\{l_i\}$ is dense enough in the unit sphere in L, the estimation $\mathcal{E}(T)$ provides an arbitrarily fine outer approximation (in Hausdorff sense) to the convex hull of $\mathcal{R}_L(T)$. Notice also that $\mathrm{co}\{y_{l_i}\}$ provides an inner approximation to $\mathrm{co}\mathcal{R}_L(T)$.

The main issue in the above set-estimation approach is to solve problem (6.21). For this, one can apply the standard gradient projection method. In order to implement it, one needs to calculate the derivative of $J(u)$ and perform projections on $\mathcal{U}$. In the next subsection we focus on the first issue, while the implementation of the gradient projection method is standard and will only be briefly discussed.

6.4.3 Solving the set-estimation problem

Recall that f_x, f_y, g_x denote the respective derivatives of f and g. Furthermore, let * denote transposition. Given $u \in \mathcal{U}$ and the corresponding solution $(x, y) := (x[u], y[u])$, consider the following *adjoint system*

$$\begin{aligned}\left(\frac{\partial}{\partial t} + A(\omega)\frac{\partial}{\partial \omega}\right)\lambda(t,\omega) &= -f_x(t,\omega,x(t,\omega),y(t))^*\,\lambda(t,\omega) - g_x(t,\omega,x(t,\omega))^*\,\nu(t)\\ \lambda(T,\omega) &= -g_x(T,\omega,x(T,\omega))^* l,\\ \nu(t) &= \int_0^1 f_y(t,\omega,x(t,\omega),y(t))^*\,\lambda(t,\omega)\,\mathrm{d}\omega\end{aligned} \tag{6.22}$$

with respect to $\lambda : [0,T] \times [0,1] \mapsto \mathbb{R}^n$ and $\nu : [0,T] \mapsto \mathbb{R}^m$. This system has the same structure as (6.16)–(6.18) (and is linear), therefore the solution is understood in the same way, with the same characteristic functions ω_i. Thus a solution of (6.22) exists and is unique.

Theorem 12. *The functional $J_l : L_\infty \mapsto \mathbb{R}$ is Fréchet differentiable. Its derivative has an L_∞ representation, namely for every $u \in \mathcal{U}$*

$$J'_l(u)(\cdot) = -\lambda(0,\cdot),$$

where λ is defined by the adjoint system (6.22) .

The proof of this theorem uses similar arguments as [105, Proposition 1]. However, the latter concerns a system of a form similar to (6.19)–(6.20), but much simpler. There, the characteristic functions $\omega_i(t,\rho)$ are the same for each i, which is a substantial simplification, although mainly technical. Therefore we sketch the proof of Theorem 12 in the Appendix.

Details about the implementation of the gradient projection method for solving problem (6.21) are given in [105]. Here we only mention that in order to obtain a good approximation of the set-membership estimation $\mathcal{E}(T)$ it is necessary to solve problem (6.21) for many unit vectors l in the subspace of interest, L. Moreover, estimations $\mathcal{E}(T_i)$ at a discrete mesh $\{T_i\}$ of time instances may be wished. Naturally, the obtained (approximate) maximizer u for given $T = T_i$ and l can be used as initial guess for neighboring instances T_j and vectors l, which makes the overall estimation procedure tractable on a commercial PC. The critical dimension for the implementability of the method is that of the space L (not the dimensions n and m, which can be much larger). Practically, the number of aggregated states y_j of interest (that is, dim(L)) may vary from 1 to 3.

6.5 Numerical analysis

In this section we apply the results from Section 6.4 to calculate set membership estimations for the benchmark system (6.4). According to Lemma 11 in the Appendix, the mapping $u \to (S[u](t), I([u](t)))$ is continuous in L_∞. Then due to the convexity of $\mathcal{U}$, the exact set-estimation $\mathcal{R}(t)$ is a connected set. Hence, its projection on the I-subspace is an interval, $[I_{\min}(t), I_{\max}(t)]$. Due to the relation $S(t) = 1 - I(t)$ we obtain that

$$\mathcal{R}(t) = \left\{(S, I) \in \mathbb{R}^2 : S = 1 - I,\ I \in [I_{\min}(t), I_{\max}(t)]\right\}. \tag{6.23}$$

Thus, in order to calculate the estimation $\mathcal{R}(t)$ it suffices to solve problem (6.21) for only two vectors l_1 and l_2 given by the positive and negative I-axis.

First, we use the method described at the end of Section 6.4 and demonstrate how this can be used to analyze the steady states of the benchmark system numerically. The actual functional parameters for a given disease are hard to obtain (see discussion in Section 6.6), therefore to illustrate the method we take parameters of simple form (that fulfill all the assumptions), where the force of infection and the recovery rate are of a magnitude appropriate for modeling influenza (see e.g. [48]):

- $\sigma = 2.5$
- $p(\omega) = 1 - \omega$,
- $q(\omega) = 2p(\omega)$,
- $\delta(\omega) = 2\omega$,
- $d(\omega) = -0.015\omega(1 - \omega)$,
- $e(\omega) = 0.15\omega(1 - \omega)$.

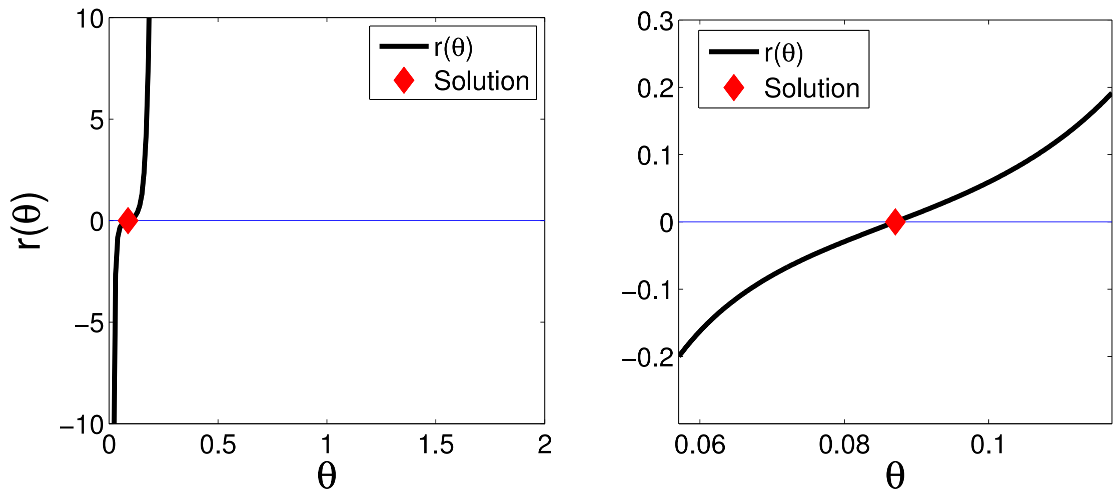

Figure 6.1: On the left we see the function $r(\theta)$ plotted over the interval [0,Q]. Note that the function is not bounded on the whole interval, but is continuous whenever it is bounded. On the right we show the behaviour of $r(\theta)$ near its root. We see that it is strictly monotonically increasing there. In particular, $r(\theta)$ has a unique root given by $\theta^* \approx 0.08707$.

Using these parameters we can calculate the function $r(\theta)$ as described a the end of Section 6.3. In Figure 6.1 we show the function $r(\theta)$ over the interval $[0, Q]$. Note that $Q = 2$ in our case. From this calculations we can conclude that $r(\theta)$ has a unique root. Hence, a steady state exists and it is unique. Having calculated the root θ^* we can then calculate the steady state solution $(S_{(0,\theta^*)}, I_{(0,\theta^*)})$. We show this in Figure 6.2, where we compare the steady state solution with the solution to system (6.4) at $t = 200$, where each component of $u(\omega)$ is given by the function $\omega^4 - 2\omega^3 + \omega^2$, scaled so that $\int_0^1 u(\omega)\,\mathrm{d}\omega = (0.9, 0.1)$.

We will use this steady states to describe the set $\mathcal{U}$ of possible initial distributions. Namely, we set $\phi(\omega) = (S_{(0,\theta^*)}(\omega), I_{(0,\theta^*)}(\omega))$ and define

$$\mathcal{U} = \left\{ u \in L_\infty : \int_0^1 u(\omega)\,\mathrm{d}\omega = \int_0^1 \phi(\omega)\,\mathrm{d}\omega,\ u(\omega) \in [0.5\phi(\omega), 1.5\phi(\omega)] \right\}.$$

Thus, we assume that the prevalence $I(t) = \int_0^1 I(t,\omega)\,\mathrm{d}\omega$ of the disease is initially as we would expect in a steady state, but we allow uncertainty in the actual distribution of the immune level among the population. That the particular initial condition becomes largely irrelevant for t this large can be seen in Figure 6.3. There we use the set-membership estimation technique developed in Section 6.4 to calculate the maximum and minimum value the prevalence $I(t)$ may achieve. We see that the prevalence converges to a single value independent of the initial condition. In Figure 6.4 we show the functions $S(t,\omega)$ and $I(t,\omega)$ for an "extremal" initial condition.

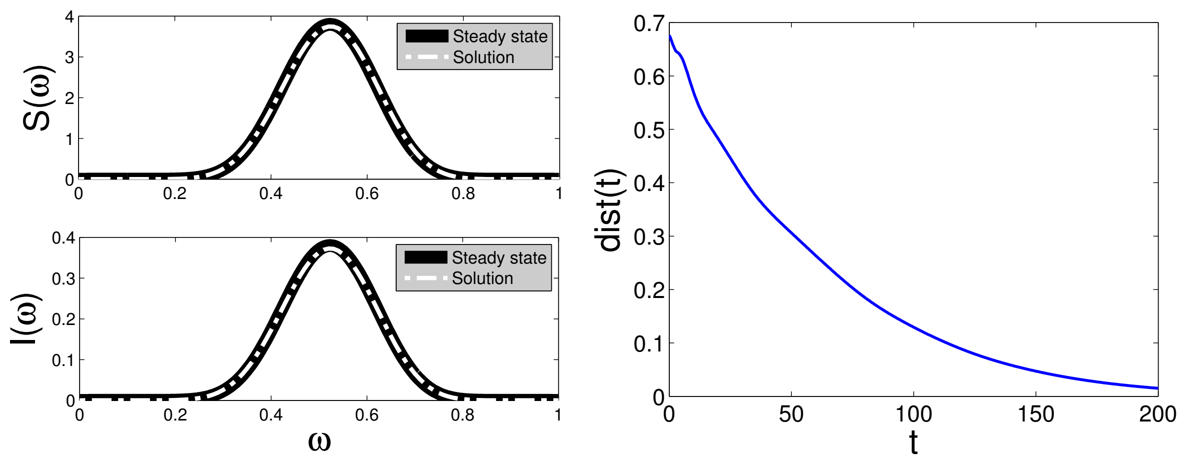

Figure 6.2: We see for both the susceptible and infected population the theoretical steady states $S_{(0,\theta^*)}(\omega)$ and $I_{(0,\theta^*)}(\omega)$ given by the thick black line. The dashed white lines show $S(200,\omega)$ and $I(200,\omega)$ respectively, where S and I were calculated from system (6.4) using a polynomial initial condition. On the right we plot $\operatorname{dist}(t) = \left\|\left(S_{(0,\theta^*)}(\omega), I_{(0,\theta^*)}(\omega)\right) - (S(t,\omega), I(t,\omega))\right\|_{L_1}$ to show that the solution does indeed converge towards the steady state.

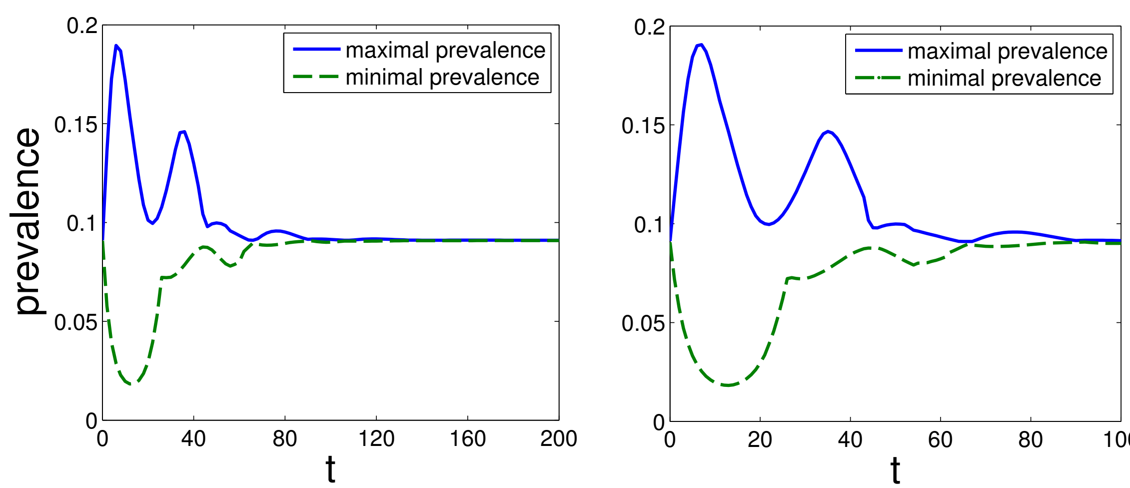

Figure 6.3: Set-membership estimation of the prevalence $I(t)$. Note that while for small t the prevalence can take significantly different values for different initial conditions, for large t both the maximum and the minimum converge to the same value. On the right we show in more detail the interval where the maximum and minimum differ significantly.

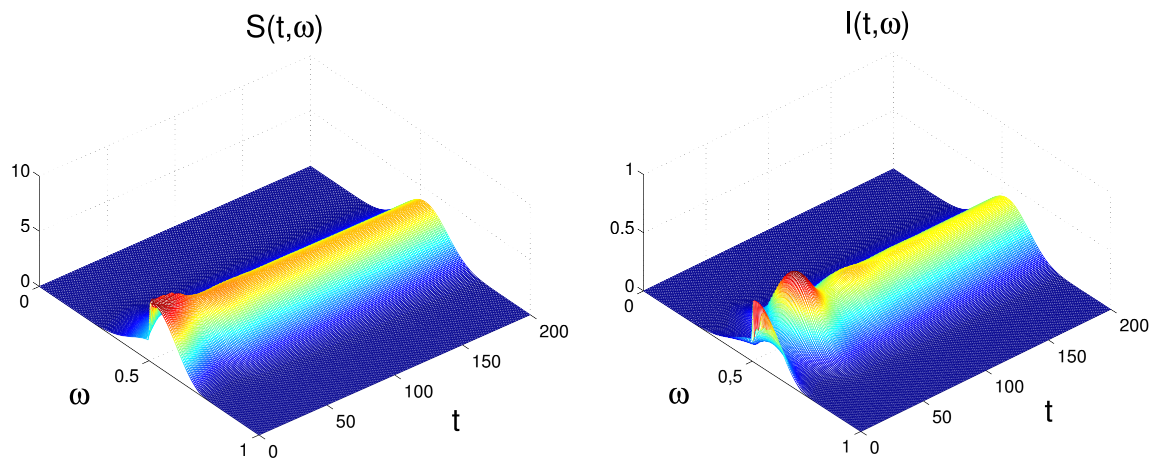

Figure 6.4: The solutions to $S(t, \omega)$ and $I(t, \omega)$ that maximise the prevalence at $t = 200$. It can be seen that both functions converge to fixed shape, which can be shown to coincide with the steady state solution.

We see that with these calculations we can analyse the asymptotic behaviour of the aggregated variables of system (6.4). Using the function $r(\theta)$ we can determine existence and uniqueness of an endemic steady state solution and using the set-membership estimation we can conclude that this steady state is globally asymptotically stable for all initial data $u(\cdot) \in \mathcal{U}$.

If we significantly decrease the force of infection by taking $\sigma = 0.25$, we find that we can no longer find a root of $r(\theta)$. In Figure 6.5 we see that the solution does indeed converge to the disease free steady state we described in Section 6.3.

We now calculate solutions to system (6.4) with periodic $\sigma(t)$. We take all parameters as in the previous subsection, but change σ to $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/100)$. The results can be seen in Figures 6.6 and 6.7. Similar to the case with constant σ the maximal and minimal prevalence converge towards each other. However, they now converge to a periodic solution that oscillates in accordance with the function $\sigma(t)$. In Figures 6.8 and 6.9 we show the results if the sinus term is dampened less and we take $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/10)$. Qualitatively, we see the same behaviour as before, but with more pronounced oscillations. Overall we see that periodic behaviour, which is commonly observed in various diseases, is readily reproduced by this model.

In conclusion, using the techniques developed we are able to estimate the evolution of the disease under uncertain information and to numerically describe the asymptotic behaviour of the system (6.4) for initial conditions $u \in \mathcal{U}$. In particular we see that while the long term behaviour may be independent of the initial condition u, the short term behaviour may change significantly for different u. For example,

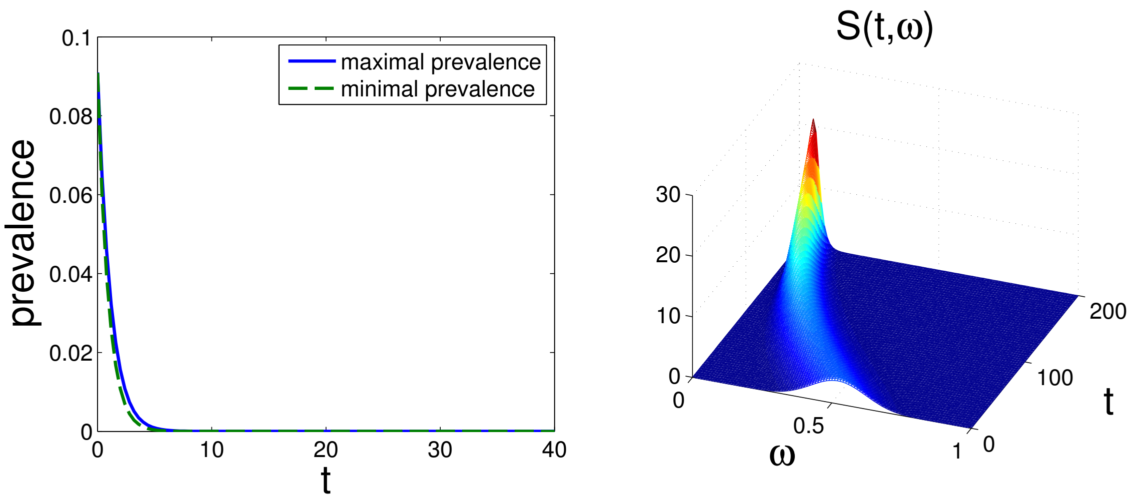

Figure 6.5: On the left we show the set-membership estimation of the prevalence for $\sigma = 0.25$. It can be seen that the disease dies out. On the right we show the solution $S(t, \omega)$ with initial condition $u(\omega) = \phi(\omega)$. We see that the function does indeed tend towards a Dirac delta at $\omega = 0$.

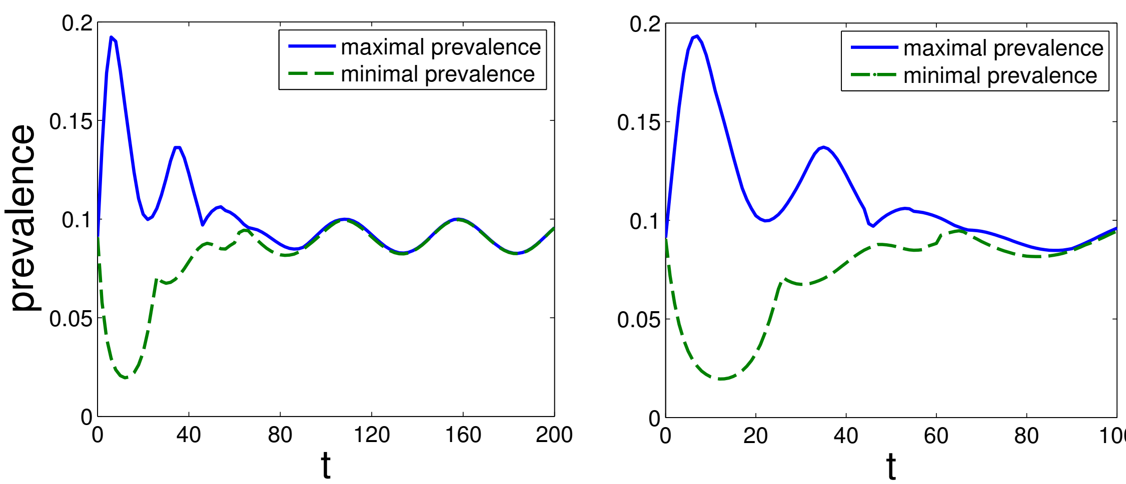

Figure 6.6: Set-estimation of the prevalence for the system with $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/100)$. The prevalence $I(t)$ converges to a periodic solution.

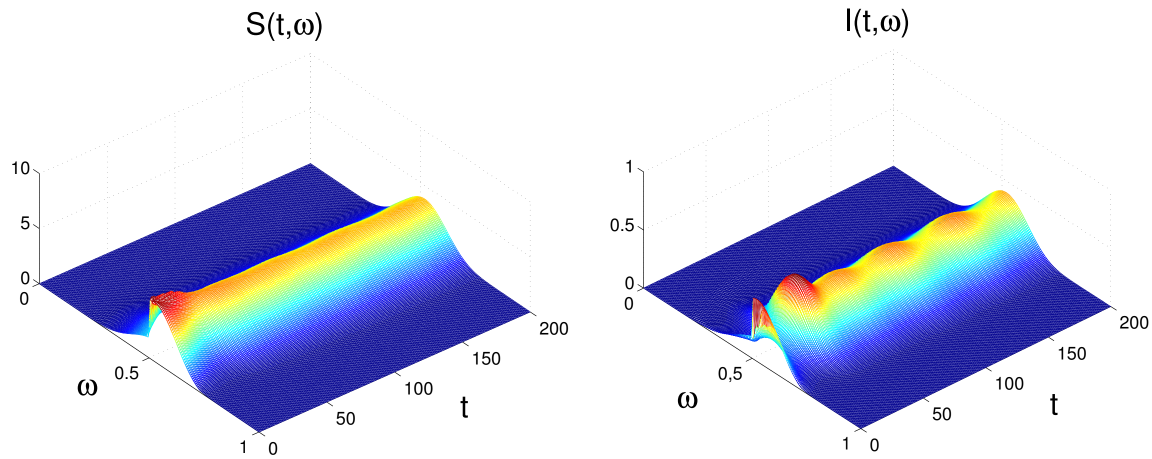

Figure 6.7: Solution $(S(t,\omega), I(t,\omega))$ that maximises the prevalence at $t = 200$ for $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/100)$. Although the solution oscillates the general shape of the solution changes little for large t.

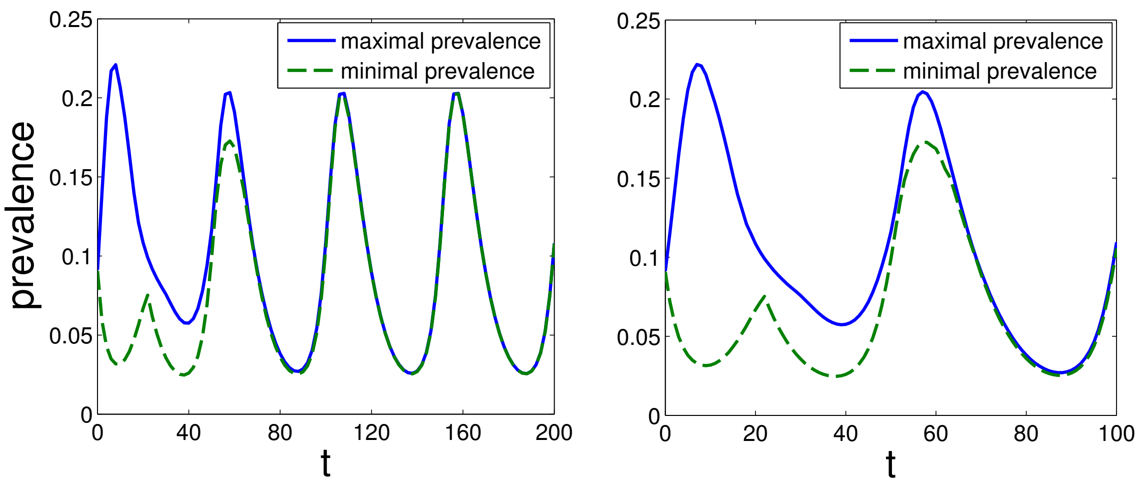

Figure 6.8: Set-estimation of the prevalence for the system with $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/10)$. The prevalence $I(t)$ converges again to a periodic solution, but with more pronounced oscillations.

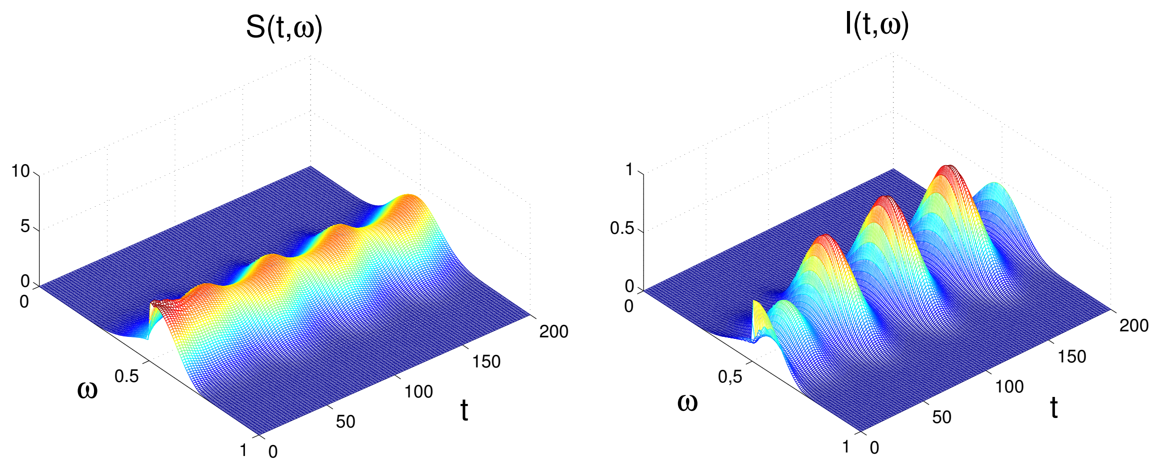

Figure 6.9: Solution $(S(t,\omega), I(t,\omega)$ that maximises the prevalence at $t = 200$ for $\sigma(t) = 2.5(1 + \sin(\frac{4\pi}{100}t)/10)$. Here we can see that between each oscillation the shape of the susceptible population drifts towards lower immunity.

events that decrease the immunity of the population may lead to a temporary outbreak of the disease, or an intervention that is aimed at increasing the immunity will only have temporary benefits. Using set-estimation we can gain information about possible outcomes of such events and actions.

6.6 Conclusions

In this paper we present a model for the evolution of an infectious disease in a population where the individuals have different immunity and their immune states vary with the time according to its own dynamics. We propose a set-membership estimation procedure based on the available information about the initial distribution of the population along the possible immune states. The rest of the parameters of the model are assumed known. However, this is usually not the case: many of the parameters may be uncertain and changing with the time – the rates of loosing/gaining immunity, d and e, the strength of infection, σ, etc. The approach in this paper can be enhanced correspondingly, with the difference that the auxiliary optimization problems that are involved in the set-membership estimations will become more complex, still being tractable by standard methods in the optimal control theory of size structured systems (see e.g. [108]). Such an enhancement could be a topic of further research.

Appendix

Lemma 11. *There exists a constant C such that for every $u_1,\ u_2 \in \mathcal{U}$ and for the corresponding solutions $(x[u_1], y[u_1])$ and $(x[u_2], y[u_2])$ of system (6.16)–(6.18) it holds that*

$$\|x[u_1] - x[u_2]\|_{L_\infty} + \|y[u_1] - y[u_2]\|_C \leq C\|u_1 - u_2\|_{L_\infty}.$$

Proof According to the definition of a solution, $x_i[u_j](t,\omega) = z_i[u_j](t, \rho_i(t,\omega))$, where $z_i[u_j]$ together with $y[u_j]$ satisfy equations (6.19)–(6.20) with $u = u_j$, $j = 1,\ 2$. Then it is straightforward that

$$\|x[u_1] - x[u_2]\|_{L_\infty} = \|\Delta z\|_{L_\infty},$$

where $\Delta z_i(t,\rho) = z_i[u_1](t,\rho) - z_i[u_2](t,\rho)$, $\Delta z = (\Delta z_1, \dots, \Delta_n)$.

Let $\Theta \subset [0,1]$ be of full measure and such that the functions $z_i[u_j](\cdot,\rho)$ are absolutely continuous for every $\rho \in \Theta$. Then

$$\|\Delta z\|_{L_\infty} = \sup_{t\in[0,T]} \overline{\Delta z}(t),$$

where $\overline{\Delta z}(t) := \max_{i=1,\dots,n} \sup_{\rho\in\Theta} |\Delta z_i(t,\rho)|$ is a Lipschitz continuous function due to the uniform Lipschitz continuity of $\Delta z_i(\cdot,\rho)$. From the assumptions about the data of the system, equation (6.17) and equation (6.19), we successively obtain that

$$|y[u_1](t) - y[u_2](t)| \leq c_1\, \overline{\Delta z}(t),$$

$$\begin{aligned}
\overline{\Delta z}(t) &\leq \|u_1 - u_2\|_{L_\infty} + \int_0^t (c_2\overline{\Delta z}(s) + c_3|y[u_1](s) - y[u_2](s)|))\,\mathrm{d}s \\
&\leq \|u_1 - u_2\|_{L_\infty} + \int_0^t c_4\overline{\Delta z}(s)\,\mathrm{d}s,
\end{aligned}$$

where c_1, ..., c_4 are appropriate constants. The claim of the lemma follows from Grönwall's inequality. □

Proof of Theorem 12. Let $u \in \mathcal{U}$ and let $\tilde{u} \in L_\infty(0,1)$. Denote $\varepsilon := \|\tilde{u} - u\|_\infty$, which will be presumably a "small" number. We denote by (x,y) and $(\tilde{x},\tilde{y})$ the corresponding solutions of (6.16)–(6.18). Also we denote by z_i and $\tilde{z}_i$ the corresponding z-functions from the definition of solution, so that $x_i(t,\omega_i(t,\rho)) = z_i(t,\rho)$, similarly for $\tilde{z}_i$. Further, $\Delta u := \tilde{u} - u$, $\Delta x := \tilde{x} - x$, $\Delta y := \tilde{y} - y$, and $\Delta z := \tilde{z} - z$. Then using (6.19), Lemma 11 and some standard calculus we obtain that the following equations are fulfilled:

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\Delta z_i(t,\rho) \;&=\; f_{ix}(t,\omega_i(t,\rho))\,\Delta x(t,\omega_i(t,\rho)) + f_{iy}(t,\omega_i(t,\rho))\,\Delta y(t) - a'(\omega_i(t,\rho))\,\Delta z_i(t,\rho) + o(\varepsilon),\\
\Delta z_i(0,\rho) &= \Delta u_i(\rho),\\
\Delta y(t) \;&=\; \int_0^1 g_x(t,\omega,x(t,\omega))\,\Delta x(t,\omega)\,\mathrm{d}\omega + o(\varepsilon),
\end{aligned}
$$

where the superscripts x and y denote differentiation with respect to x and y, the prime in a' denotes differentiation in ω, the missing arguments of f_{ix} and f_{iy} are obviously $x(t,\omega_i(t,\rho))$, $y(t)$, and $o(\varepsilon)$ is any function of ε (possibly depending on t and ρ), such that $o(\varepsilon)/\varepsilon \to 0$ (uniformly in $t,\ \rho$) when $\varepsilon \to 0$. We mention that the second equation above holds due to $\Delta z_i(0,\rho) = x_i(0,\omega_i(0,\rho)) = x_i(0,\rho) = u_i(\rho)$.

Now we consider the adjoint system (6.22) and denote by $\zeta(t,\rho)$ the corresponding to λ function in Definition 1. Thus

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\zeta_i(t,\rho) \;&=\; -f_{x_i}(t,\omega_i(t,\rho))^*\,\lambda(t,\omega_i(t,\rho)) - g_{x_i}(t,\omega_i(t,\rho),x(t,\omega_i(t,\rho)))^*\,\nu(t),\\
\zeta_i(T,\rho) &= -g_{x_i}(T,\omega_i(T,\rho),x(T,\omega_i(T,\rho)))^* l,\\
\nu(t) \;&=\; \int_0^1 f_y(t,\omega,x(t,\omega),y(t))^*\,\lambda(t,\omega)\,\mathrm{d}\omega.
\end{aligned}
$$

Using the second last equation and changing the variable $\omega = \omega_i(t,\rho)$, we represent

$$
\begin{aligned}
J_l(\tilde{u}) - J_l(u) \;&=\; \langle l, \Delta y(T)\rangle = \int_0^1 \langle l, g_x(T,\omega,x(T,\omega))\,\Delta x(T,\omega)\rangle\,\mathrm{d}\omega + o(\varepsilon)\\
&= \int_0^1 \sum_{i=1}^n \Delta x_i(T,\omega_i(T,\rho))\,g_{x_i}(T,\omega_i(T,\rho),x(T,\omega_i(T,\rho)))^* l\,\frac{\partial}{\partial\rho}\omega_i(T,\rho)\,\mathrm{d}\rho + o(\varepsilon)\\
&= -\sum_{i=1}^n \int_0^1 \Delta z_i(T,\rho)\,\zeta_i(T,\rho)\,\frac{\partial}{\partial\rho}\omega_i(T,\rho)\,\mathrm{d}\rho + o(\varepsilon).
\end{aligned}
\tag{6.24}
$$

Now, we rework the following expression integrating by parts:

$$
\begin{aligned}
&\sum_{i=1}^n \int_0^T\!\!\int_0^1 \frac{\mathrm{d}}{\mathrm{d}t}\,\Delta z_i(t,\rho)\,\zeta_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t\\
&\quad= \sum_{i=1}^n \int_0^1 \Delta z_i(T,\rho)\zeta_i(T,\rho)\frac{\partial}{\partial\rho}\omega_i(T,\rho)\,\mathrm{d}\rho - \sum_{i=1}^n \int_0^1 \Delta z_i(0,\rho)\zeta_i(0,\rho)\frac{\partial}{\partial\rho}\omega_i(0,\rho)\,\mathrm{d}\rho\\
&\qquad- \sum_{i=1}^n \int_0^T\!\!\int_0^1 \Delta z_i(t,\rho)\left[\frac{\mathrm{d}}{\mathrm{d}t}\zeta_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho) + \zeta_i(t,\rho)\frac{\partial}{\partial t}\frac{\partial}{\partial\rho}\omega_i(t,\rho)\right]\mathrm{d}\rho\,\mathrm{d}t.
\end{aligned}
$$

Then we use the relation (6.24) and the identities

$$
\begin{aligned}
&\Delta z_i(0,\rho) = \Delta u_i(\rho), \quad \zeta_i(0,\rho) = \zeta_i(0,\rho_i(0,\rho)) = \lambda_i(0,\rho),\\
&\frac{\partial}{\partial\rho}\omega_i(0,\rho) = 1, \quad \frac{\partial}{\partial t}\frac{\partial}{\partial\rho}\omega_i(t,\rho) = a'(\omega_i(t,\rho))\frac{\partial}{\partial\rho}\omega_i(t,\rho)
\end{aligned}
$$

to obtain the representation

$$J_l(\tilde{u})-J_l(u) = \sum_{i=1}^{n} \int_0^1 \Delta z_i(0,\rho)\,\zeta_i(0,\rho)\,\mathrm{d}\rho+\Delta+o(\varepsilon) = -\int_0^1 \langle \lambda(0,\rho), \Delta u(\rho)\rangle\,\mathrm{d}\rho+\Delta+o(\varepsilon), \quad (6.25)$$

where

$$\begin{aligned}\Delta \;:=\; &-\sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \frac{\mathrm{d}}{\mathrm{d}t}\,\Delta z_i(t,\rho)\,\zeta_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t \\ &-\sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \Delta z_i(t,\rho)\left[\frac{\mathrm{d}}{\mathrm{d}t}\zeta_i(t,\rho)+\zeta_i(t,\rho)\,a'(\omega_i(t,\rho))\right]\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t.\end{aligned}$$

After substituting the expressions for $\frac{\mathrm{d}}{\mathrm{d}t}\Delta z_i(t,\rho)$, $\frac{\mathrm{d}}{\mathrm{d}t}\zeta_i(t,\rho)$, obtained in the beginning of the proof, changing back the variable $\rho = \omega_i(t,\omega)$, and using the equations for Δy and ν, it is a matter of simple algebra to obtain that $\Delta = o(\varepsilon)$. Then from (6.25)

$$J_l(\tilde{u}) - J_l(u) = -\int_0^1 \langle \lambda(0,\omega), \tilde{u}(\omega) - u(\omega)\rangle\,\mathrm{d}\rho + o(\|\tilde{u}-u\|_\infty),$$

which implies the claim of the theorem. □

Chapter 7

Optimal control of size-structured first order partial differential equations

7.1 Introduction

We have seen in the last chapter how size-structured PDEs can arise in epidemiological models of infectious diseases. They also appear in numerous other biological contexts (see [79]). In this chapter we present a theorem on how optimal control problems utilising such size-structured models can be solved. More precisely, we develop a Pontryagin-type maximum principle for the problem. In the problem formulation aggregated variables may appear in the objective function as well as the state equations. We also allow for the control to influence the aggregation itself. In context of the model developed in the previous chapter, this could reflect the possibility to influence the infectivity of the infected sub-population.

In this chapter we consider a general model that puts no restrictions on any of the parameters involved. The usefulness of the presented theorem is therefore not restricted to epidemiological models of disease transmission. It is also closely related to the results from Section 6.4 where we considered optimisation of the initial conditions, while here we focus on control of the dynamics.

7.2 Formulation of the theorem

We consider the optimal control problem

$$\max_{u\in\mathcal{U}} J(u), \tag{7.1}$$

where

$$J(u) = \int_0^T \int_0^1 h(t,\omega,x(t,\omega),y(t),u(t,\omega))\,\mathrm{d}\omega\,\mathrm{d}t + \int_0^1 k(\omega,x(T,\omega),y(T))\,\mathrm{d}\omega, \tag{7.2}$$

with state equations

$$\frac{\partial}{\partial t}x(t,\omega) + \frac{\partial}{\partial \omega}A(t,\omega)x(t,\omega) = f(t,\omega,x(t,\omega),y(t),u(t,\omega)), \tag{7.3}$$

$$y(t) = \int_0^1 g(t,\omega,x(t,\omega),u(t,\omega))\,\mathrm{d}\omega, \tag{7.4}$$

$$x(0,\omega) = x_0(\omega). \tag{7.5}$$

Here $x : [0,T] \times [0,1] \to \mathbb{R}^n$ and $y : [0,T] \to \mathbb{R}^m$. The initial condition x_0 lies in the space $L_\infty([0,1],\mathbb{R}^n)$. For every $t \in [0,T]$ let $\mathcal{U}(t)$ be a bounded and convex subset of $L_\infty\left([0,1],\mathbb{R}^l\right)$. The set $\mathcal{U}$ is then defined as $\mathcal{U} = \{u \in L_\infty\left([0,T] \times [0,1],\mathbb{R}^l\right) : u(t,\cdot) \in \mathcal{U}(t)\}$. We say that the triple (x,y,u) is admissible if it satisfies the state equations (7.3)-(7.5) in the sense as explained in Section 7.3. We say that the triple $(\hat{x},\hat{y},\hat{u})$ is a solution of (7.1) if $(\hat{x},\hat{y},\hat{u})$ is admissible and $J(\hat{u}) \geq J(u)$ for every other admissible triple (x,y,u).

We now formulate the assumptions about the other functions involved. To ease notation, if r is a function of several variables, r'_η we will denote the partial derivative or r with respect to η. The matrix $A : [0,T] \times [0,1] \to \mathbb{R}^{n\times n}$ is diagonal with entries $A_{ii} = a_i(t,\omega)$. The functions $a_i : [0,T] \times [0,1] \to \mathbb{R}$, $f : [0,T] \times [0,1] \times \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R}^l \to \mathbb{R}^n$, $g : [0,T] \times [0,1] \times \mathbb{R}^n \times \mathbb{R}^l \to \mathbb{R}^m$, $h : [0,T] \times [0,1] \times \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R}^l \to \mathbb{R}$, and $k : [0,1] \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}$, as well as the partial derivatives f'_x, f'_y, g'_x, h'_x, h'_y, k'_x, and k'_y are locally bounded, measurable in (t,ω) for every (x,y,u) and locally Lipschitz continuous in (x,y,u). The functions a_i are furthermore absolutely continuous in ω.

In addition we assume that k depends only on components y_i of y for which the corresponding components g_i are independent from u. Finally, let $A(t,0) = A(t,1) = 0$ for almost every $t \in [0,T]$ and for every i let either $a_i(t,\omega) = 0$ for $\omega \in (0,1)$ or $a_i(t,\omega) \neq 0$ for $\omega \in (0,1)$ hold true.

Remark 5. The regularity assumptions about the functions are standard. The restriction that k may only depend on certain components is necessary so that changing the control u at the single time T cannot increase the value of $J(u)$. In fact, this restriction may be weakened to reflect that this independence is only necessary at the final time T. With regards to the assumptions about A we note that allowing a_i to be identically zero can for example be used to model components x_i that do not depend on the structure variable ω. Furthermore, the restriction that $A(t,0) = A(t,1) = 0$ is not strictly necessary and is used only to simplify the proofs (see discussion in Section 7.3).

We will use the notation μ^* for the transpose of the vector (or matrix) μ. For an admissible triple $(x(t,\omega),y(t),u(t,\omega))$ we introduce their adjoint variables $\lambda : [0,T] \times [0,1] \to \mathbb{R}^n$ and $\nu : [0,T] \to \mathbb{R}^m$

via the adjoint equations

$$\begin{aligned}\frac{\partial}{\partial t}\lambda(t,\omega)+A(t,\omega)\frac{\partial}{\partial \omega}\lambda(t,\omega) &= -f'_x(t,\omega,x(t,\omega),y(t),u(t,\omega))^*\lambda(t,\omega)\\ &\quad - h'_x(t,\omega,x(t,\omega),y(t),u(t,\omega)) - g'_x(t,\omega,x(t,\omega),u(t,\omega))^*\nu(t),\end{aligned} \tag{7.6}$$

$$\nu(t)=\int\limits_0^1 f'_y(t,\omega,x(t,\omega),y(t),u(t,\omega))^*\lambda(t,\omega)+h'_y(t,\omega,x(t,\omega),y(t),u(t,\omega))\,\mathrm{d}\omega, \tag{7.7}$$

$$\lambda(T,\omega)=k'_x(\omega,x(T,\omega),y(T))+g'_x(T,s,x(T,\omega),u(T,\omega))^*\int\limits_0^1 k'_y(\sigma,x(T,\sigma),y(T))\,\mathrm{d}\sigma. \tag{7.8}$$

How a solution to this PDE is to be understood will be explained in Section 7.3. Note that the terminal condition (7.8) is well defined, since our assumptions about k assure that the value $u(T,\omega)$ does not influence $\lambda(T,\omega)$.

Theorem 13. *Let $(\hat{x},\hat{y},\hat{u})$ be a solution of (7.1), and let $\hat{\lambda}$ and $\hat{\nu}$ be their adjoint variables. Define the Hamiltonian $\mathcal{H}:[0,T]\times L_\infty([0,1],\mathbb{R}^n)\times\mathbb{R}^m\times L_\infty([0,1],\mathbb{R}^n)\times\mathbb{R}^m\times L_\infty\left([0,1],\mathbb{R}^l\right)\to\mathbb{R}$ as*

$$\begin{aligned}&\mathcal{H}(t,x(\cdot),y,\lambda(\cdot),\nu,u(\cdot))\\ &\quad=\int\limits_0^1 \lambda(\omega)^*f(t,\omega,x(\omega),y,u(\omega))+h(t,\omega,x(\omega),y,u(\omega))+\nu^*(g(t,\omega,x(\omega),u(\omega))-y)\,\mathrm{d}\omega.\end{aligned}$$

Then for $t\in[0,T]$ the equations

$$\begin{aligned}&\frac{\partial}{\partial\lambda}\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),\hat{u}(t,\cdot))=\frac{\partial}{\partial t}\hat{x}(t,\omega)+\frac{\partial}{\partial\omega}A(t,\omega)\hat{x}(t,\omega),\\ &\frac{\partial}{\partial x}\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),\hat{u}(t,\cdot))=-\frac{\partial}{\partial t}\hat{\lambda}(t,\omega)-A(t,\omega)\frac{\partial}{\partial\omega}\hat{\lambda}(t,\omega),\\ &\frac{\partial}{\partial\nu}\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),\hat{u}(t,\cdot))=0,\\ &\frac{\partial}{\partial y}\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),\hat{u}(t,\cdot))=0,\end{aligned} \tag{7.9}$$

with boundary conditions (7.5) and (7.8) hold true, as well as the following maximum principle

$$\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),\hat{u}(t,\cdot))=\max_{u(\cdot)\in\mathcal{U}(t)}\mathcal{H}(t,\hat{x}(t,\cdot),\hat{y}(t),\hat{\lambda}(t,\cdot),\hat{\nu}(t),u(\cdot)). \tag{7.10}$$

How the equations (7.9) are to be interpreted will be explained in Section 7.3.

7.3 Notion of solution

The solutions to the state and adjoint equations are defined via the solutions along the characteristic lines.

Definition 2. *For a given control $u : [0,T] \times [0,1] \to \mathbb{R}^l$, the pair of functions $x : [0,T] \times [0,1] \to \mathbb{R}^n$ and $y : [0,T] \to \mathbb{R}^m$ is a solution to the state equations (7.3)-(7.5) if x has the representation $x_i(t, \omega_i(t,\rho)) = \zeta_i(t,\rho)$, $t \in [0,T]$, $\rho \in [0,1]$, where $\zeta_i(t,\rho)$ is measurable in ρ, absolutely continuous in t for a.e. ρ and fulfils the equations*

$$\frac{\mathrm{d}}{\mathrm{d}t}\zeta_i(t,\rho) = f_i(t, \omega_i(t,\rho), x(t,\omega_i(t,\rho)), y(t), u(t,\omega_i(t,\rho))) - (a_i)'_\omega(t,\omega_i(t,\rho))\,\zeta_i(t,\rho), \tag{7.11}$$

$$y(t) = \int_0^1 g(t,\omega,x(t,\omega),u(t,\omega))\,\mathrm{d}\omega, \tag{7.12}$$

$$\zeta_i(0,\rho) = x_{0_i}(\rho), \tag{7.13}$$

where the characteristic line $\omega_i : [0,T] \times [0,1] \to [0,1]$ is defined as the unique solution of the initial value problem

$$\frac{\partial}{\partial t}\omega_i(t,\rho) = a_i(t,\omega_i(t,\rho)), \quad \omega_i(0,\rho) = \rho. \tag{7.14}$$

This definition is similar to the one presented in Section 6.4. Arguments that show that the system (7.11)-(7.13) is well defined and a motivation for this definition can be found there. We stress that the solution x will generally not be smooth and may even be discontinuous in each of the directions t and x. The component x_i however is absolutely continuous along the characteristic line $\omega_i(t,\omega)$.

Lemma 12. *There exists a constant C such that for all controls $u_1,\ u_2 \in \mathcal{U}$ and for the corresponding solutions $(x[u_1], y[u_1])$ and $(x[u_2], y[u_2])$ of system (7.3)–(7.5) it holds that*

$$\|x[u_1] - x[u_2]\|_{L_\infty} + \|y[u_1] - y[u_2]\|_{L_\infty} \le C\|u_1 - u_2\|_{L_\infty}.$$

Proof According to the definition of a solution, $x_i[u_j](t,\omega) = \zeta_i[u_j](t,\rho_i(t,\omega))$, where $\zeta_i[u_j]$ together with $y[u_j]$ satisfy equations (7.11)–(7.13), $j = 1,\ 2$. Then it is straightforward that

$$\|x[u_1] - x[u_2]\|_{L_\infty} = \|\Delta\zeta\|_{L_\infty},$$

where $\Delta\zeta_i(t,\rho) = \zeta_i[u_1](t,\rho) - \zeta_i[u_2](t,\rho)$, $\Delta\zeta = (\Delta\zeta_1, \ldots, \Delta\zeta_n)$.

Let $\Theta \subset [0,1]$ be of full measure and such that the functions $\zeta_i[u_j](\cdot,\rho)$ are absolutely continuous for every $\rho \in \Theta$. Then

$$\|\Delta\zeta\|_{L_\infty} = \sup_{t\in[0,T]} \overline{\Delta\zeta}(t),$$

where $\overline{\Delta\zeta}(t) := \max_{i=1,\dots,n} \sup_{\rho\in\Theta} |\Delta\zeta_i(t,\rho)|$ is a Lipschitz continuous function due to the uniform Lipschitz continuity of $\Delta\zeta_i(\cdot,\rho)$. From the Lipschitz continuity of g in x and u we get that

$$\begin{aligned}\|y[u_1](t) - y[u_2](t)\|_{L_\infty} &= \left\| \int_0^1 g(t, x[u_1](t,\omega), u_1(t,\omega)) - g(t, x[u_2](t,\omega), u_2(t,\omega))\,\mathrm{d}\omega \right\|_{L_\infty} \\ &\le c_1\,\overline{\Delta z}(t) + c_2\|u_1 - u_2\|_{L_\infty},\end{aligned}$$

where c_1 and c_2 are appropriate constants (as are c_3 and c_4 below). Since

$$\Delta\zeta_i(t,\rho) = \int_0^t \frac{\mathrm{d}}{\mathrm{d}t}\Delta\zeta_i(s,\rho)\,\mathrm{d}s,$$

we can similarly use (7.11) and the Lipschitz continuity of f'_x and $(a_i)'_\omega$ to get

$$\overline{\Delta\zeta}(t) \le c_3\|u_1 - u_2\|_{L_\infty} + \int_0^t c_4\overline{\Delta\zeta}(s)\,\mathrm{d}s,$$

The claim of the lemma follows from Grönwall's inequality. □

A solution of the adjoint equations is defined similarly as that of the state equations.

Definition 3. *The pair of functions $\lambda : [0,T]\times[0,1] \to \mathbb{R}^n$ and $\nu : [0,T] \to \mathbb{R}^m$ are a solution to the adjoint equations (7.6)-(7.8) if λ has the representation $\lambda_i(t,\omega_i(t,\rho)) = \xi_i(t,\rho)$, $t \in [0,T]$, $\rho \in [0,1]$, where $\xi_i(t,\rho)$ is measurable in ρ, absolutely continuous in t for a.e. ρ and fulfils the equations*

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\xi_i(t,\rho) = &-f'_{x_i}(t,\omega_i(t,\rho), x(t,\omega_i(t,\rho)), y(t), u(t,\omega_i(t,\rho)))^*\lambda(t,\omega_i(t,\rho)) \\ &- h'_{x_i}(t,\omega_i(t,\rho), x(t,\omega_i(t,\rho)), y(t), u(t,\omega_i(t,\rho))) \\ &- g'_{x_i}(t,\omega_i(t,\rho), x(t,\omega_i(t,\rho)), u(t,\omega_i(t,\rho)))^*\nu(t),\end{aligned} \tag{7.15}$$

$$\nu(t) = \int_0^1 f'_y(t,\omega,x(t,\omega),y(t),u(t,\omega))^*\lambda(t,\omega) + h'_y(t,\omega,\hat{x}(t,\omega),y(t),u(t,\omega))\,\mathrm{d}\omega, \tag{7.16}$$

$$\begin{aligned}\xi_i(T,\rho) = &k'_{x_i}(\omega_i(t,\rho), x(T,\omega_i(T,\rho)), y(T)) \\ &+ \int_0^1 k'_y(\sigma, x(T,\sigma), y(T))\,\mathrm{d}\sigma\; g'_{x_i}(T,\omega_i(T,\rho), x(T,\omega_i(T,\rho)), u(T,\omega)),\end{aligned} \tag{7.17}$$

where the characteristic line $\omega_i : [0,T] \times [0,1] \to [0,1]$ is defined as the unique solution of the initial value problem

$$\frac{\partial}{\partial t}\omega_i(t,\rho) = a_i(t,\omega_i(t,\rho)), \quad \omega_i(0,\rho) = \rho. \tag{7.18}$$

The same arguments as for the state equations show that the system (7.15)-(7.17) is well defined. The motivation for this definition is again that a smooth solution of this system will be a classical solution of (7.6)-(7.8). We point out the important fact that the characteristic lines for the state equations and the adjoint equations are the same.

Concerning existence and uniqueness of the solution of both the state and adjoint equations we refer to [6]. There, systems of a form even more general than the ones here are considered, but under the assumption that $A(t,\omega) > 0$. However, our assumption that $A(t,0) = A(t,1) = 0$ is a simplification rather than a complication as it dispenses of the need for boundary conditions, hence the proof presented in [6] can be readily adapted to the present problem. Should this assumption not be fulfilled, the approach presented here is still applicable, however the proof of Theorem 13 will become more cumbersome.

Next, we want to explain how equations (7.9) are to be interpreted. First note that if we calculate the Fréchet derivative of $\mathcal{H}$ with respect to λ at a point $(t, \hat{x}(t,\cdot), \hat{y}(t), \hat{\lambda}(t,\cdot), \hat{\nu}(t), \hat{u}(t,\cdot))$ in direction ϕ we get

$$\frac{\partial}{\partial \lambda}\mathcal{H}(t, \hat{x}(t,\cdot), \hat{y}(t), \hat{\lambda}(t,\cdot), \hat{\nu}(t), \hat{u}(t,\cdot))\phi(\cdot) = \int_0^1 f(t,\omega,\hat{x},\hat{y},\hat{u})\phi(\omega)\,\mathrm{d}\omega,$$

so that we can identify $\frac{\partial}{\partial \lambda}\mathcal{H} = f(t,\omega,x(t,\omega),y(t),u(t,\omega))$. Thus the first equation in (7.9) reads

$$f(t,\omega,x(t,\omega),y(t),u(t,\omega)) = \frac{\partial}{\partial t}x(t,\omega) + \frac{\partial}{\partial \omega}A(t,\omega)x(t,\omega),$$

which is the same as equation (7.3). This if course again to interpreted using Definition 2. The second equation is to be interpreted similarly. The third and fourth equations recover the relations (7.4) and (7.7), respectively. Note in particular that any admissible triple together with their adjoint variables will satisfy the equations (7.9).

It is a standard result in optimal control theory that the Hamiltonian is constant along an optimal trajectory, as long the Hamiltonian does not depend explicitly on t ([67]). It is an open question whether the Hamiltonian, as we defined it, has this property. We mention that we include the final term $-\nu^* y$ in the Hamiltonian since it was shown in [103] that for a simpler version of the optimal control problem presented here, where $A = 0$ and g is independent of u, this definition does indeed yield a Hamiltonian that is constant along the optimal trajectory.

7.4 Proof of the theorem

Let the triple $(\hat{x}, \hat{y}, \hat{u})$ be a solution to the optimal control problem, let $\hat{\lambda}(t,\omega)$ and $\hat{\nu}(t)$ be their adjoint variables, and $\hat{\zeta}(t,\omega)$ and $\hat{\xi}(t,\omega)$ the corresponding function according to Definitions 2 and 3. Let for $u \in \mathcal{U}$ the triple (x, y, u) be admissible with adjoint variables $\lambda(t,\omega)$, $\nu(t)$ and corresponding functions $\zeta(t,\omega)$, and $\xi(t,\omega)$. We denote $\Delta x(t,\omega) = x(t,\omega) - \hat{x}(t,\omega)$. A Δ in front of another expression will have a similar definition. Furthermore we use the notation $\Delta_u f(t,\omega,x(t,\omega),y(t)) = f(t,\omega,x(t,\omega),y(t),u(t,\omega)) - f(t,\omega,x(t,\omega),y(t),\hat{u}(t,\omega))$. Again, a Δ_u in front of another function has a similar definition. To further simplify notation we will also skip the state variables and control when they appear as arguments with a "hat", e.g. $f(t,\omega) := f(t,\omega,\hat{x}(t,\omega),\hat{y}(t),\hat{u}(t,\omega))$. We will assume that $\|u - \hat{u}\|_{L_\infty} = \varepsilon$ is small. Using this we get

$$\begin{aligned} J(u) - J(\hat{u}) &= \int_0^T \int_0^1 \Delta h(t,\omega,x(t,\omega),y(t),u(t,\omega))\,\mathrm{d}\omega\,\mathrm{d}t + \int_0^1 \Delta k(\omega,x(T,\omega),y(T))\,\mathrm{d}\omega \\ &= \int_0^T \int_0^1 h_x'(t,\omega)^* \Delta x(t,\omega) + h_y'(t,\omega)^* \Delta y(t) + \Delta_u h(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t \qquad (7.19) \\ &\quad + \int_0^1 k_x'(\omega,\hat{x}(T,\omega),\hat{y}(T))^* \Delta x(T,\omega) + k_y'(\omega,\hat{x}(T,\omega),\hat{y}(T))^* \Delta y(T)\,\mathrm{d}\omega + o(\varepsilon). \end{aligned}$$

To see that the remainder is indeed $o(\varepsilon)$, we consider the term $\Delta h(t,\omega,x(t,\omega),y(t),u(t,\omega))$. For simplicity we assume that h is independent of y (this is only to simplify notation; no additional difficulties arise if h depends on y). We have

$$\begin{aligned} &\int_0^1 h(t,\omega,x(t,\omega),u(t,\omega)) - h(t,\omega,\hat{x}(t,\omega),\hat{u}(t,\omega))\,\mathrm{d}\omega \\ &\quad = \int_0^1 h(t,\omega,x(t,\omega),u(t,\omega)) - h(t,\omega,\hat{x}(t,\omega),u(t,\omega)) + \Delta_u h(t,\omega)\,\mathrm{d}\omega. \end{aligned}$$

The last term is accounted for in (7.19). Using an appropriate $\bar{x}(t,\omega)$ between $x(t,\omega)$ and $\hat{x}(t,\omega)$, the remaining difference can be rewritten as

$$\begin{aligned}
&\int_0^1 h(t,\omega,x(t,\omega),u(t,\omega)) - h(t,\omega,\hat{x}(t,\omega),u(t,\omega))\,\mathrm{d}\omega \\
&\qquad = \int_0^1 h'_x(t,\omega,\bar{x}(t,\omega),u(t,\omega))^*\Delta x(t,\omega)\,\mathrm{d}\omega \\
&\qquad = \int_0^1 h'_x(t,\omega,\hat{x}(t,\omega),\hat{u}(t,\omega))^*\Delta x(t,\omega) \\
&\qquad\qquad + \left(h'_x(t,\omega,\bar{x}(t,\omega),u(t,\omega))^* - h'_x(t,\omega,\hat{x}(t,\omega),\hat{u}(t,\omega))^*\right)\Delta x(t,\omega)\,\mathrm{d}\omega.
\end{aligned}$$

The first term is accounted for in (7.19) while the Lipschitz continuity of h_x in x, y and u together with the fact that $\|\Delta x(t,\omega)\|_{L_\infty}$ and $\|\Delta y(t)\|_{L_\infty}$ can be estimated from above by some constant times ε (see Lemma 12) shows that the remaining term is indeed $o(\varepsilon)$. The same argument can be used for the remaining terms. Similar calculations show up below, where we will not repeat this argument.
Using the representation

$$\begin{aligned}
\Delta y(t) &= \int_0^1 g(t,\omega,x(t,\omega),u(t,\omega)) - g(t,\omega,\hat{x}(t,\omega),\hat{u}(t,\omega))\,\mathrm{d}\omega \\
&= \int_0^1 g'_x(t,\omega)\Delta x(t,\omega) + \Delta_u g(t,\omega)\,\mathrm{d}\omega + o(\varepsilon)
\end{aligned} \tag{7.20}$$

yields

$$\begin{aligned}
J(u)-J(\hat{u}) = &\int_0^T\int_0^1 h'_x(t,\omega)^*\Delta x(t,\omega) + \int_0^1 h'_y(t,\sigma)^*\mathrm{d}\sigma\left(g'_x(t,\omega)\Delta x(t,\omega)+\Delta_u g(t,\omega)\right) + \Delta_u h(t,\omega)\mathrm{d}\omega\mathrm{d}t \\
&+ \int_0^1 k'_x(\omega,\hat{x}(T,\omega),\hat{y}(T))^*\Delta x(T,\omega) + \int_0^1 k'_y(\sigma,\hat{x}(T,\sigma),\hat{y}(T))^*\,\mathrm{d}\sigma\, g'_x(T,\omega)\Delta x(T,\omega)\,\mathrm{d}\omega + o(\varepsilon),
\end{aligned} \tag{7.21}$$

where we also used the fact that due to our assumptions on k the term $\int_0^1 k'_y(\sigma,\hat{x}(T,\sigma),\hat{y}(T))^*\,\mathrm{d}\sigma\Delta_u g(T,\omega)$ is zero.

Now we integrate by parts the following expression

$$
\begin{aligned}
&\sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \hat{\xi}_i(t,\rho)\frac{\mathrm{d}}{\mathrm{d}t}\,\Delta\zeta_i(t,\rho)\,\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t \\
&\qquad = \sum_{i=1}^{n}\int_0^1 \hat{\xi}_i(T,\rho)\Delta\zeta_i(T,\rho)\frac{\partial}{\partial\rho}\omega_i(T,\rho)\,\mathrm{d}\rho - \sum_{i=1}^{n}\int_0^1 \hat{\xi}_i(0,\rho)\Delta\zeta_i(0,\rho)\frac{\partial}{\partial\rho}\omega_i(0,\rho)\,\mathrm{d}\rho \\
&\qquad\quad - \sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \left[\frac{\mathrm{d}}{\mathrm{d}t}\hat{\xi}_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho) + \hat{\xi}_i(t,\rho)\frac{\partial}{\partial t}\frac{\partial}{\partial\rho}\omega_i(t,\rho)\right]\Delta\zeta_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t.
\end{aligned}
\tag{7.22}
$$

We rewrite the term on the left hand side, using $\xi_i(t,\rho) = \lambda_i(t,\omega_i(t,\rho))$, equations (7.11) and (7.20), and a transformation of variables to yield

$$
\begin{aligned}
&\sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \hat{\xi}_i(t,\rho)\frac{\mathrm{d}}{\mathrm{d}t}\,\Delta\zeta_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\mathrm{d}t = \sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \hat{\lambda}_i(t,\omega)\big[\Delta f_i(t,\omega) - (a_i)'_\omega(t,\omega)\Delta x_i(t,\omega)\big]\mathrm{d}\omega\mathrm{d}t \\
&= \int_0^T\!\!\int_0^1 \hat{\lambda}(t,\omega)^*\big[f'_x(t,\omega)\Delta x(t,\omega) + f'_y(t,\omega)\Delta y(t) + \Delta_u f(t,\omega) - A'_\omega(t,\omega)\Delta x(t,\omega)\big]\mathrm{d}\omega\,\mathrm{d}t + o(\varepsilon) \\
&= \int_0^T\!\!\int_0^1 \left(\hat{\lambda}(t,\omega)^* f'_x(t,\omega) + \int_0^1 \hat{\lambda}(t,\sigma)^* f'_y(t,\sigma)\,\mathrm{d}\sigma g'_x(t,\omega) - \hat{\lambda}(t,\omega)^* A'_\omega(t,\omega)\right)\Delta x(t,\omega) \\
&\quad + \int_0^1 \hat{\lambda}(t,\sigma)^* f'_y(t,\sigma)\,\mathrm{d}\sigma\Delta_u g(t,\omega) + \hat{\lambda}(t,\omega)^*\Delta_u f(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t + o(\varepsilon).
\end{aligned}
$$

Using (7.17) it can similarly be shown that the first term on the right hand side of (7.22) is exactly the last line in (7.21). The second term is obviously zero, as $\Delta\zeta_i(0,\rho) = 0$. The remaining term we split in two. By the same method as before we easily get

$$
\begin{aligned}
&-\sum_{i=1}^{n}\int_0^T\!\!\int_0^1 \frac{\mathrm{d}}{\mathrm{d}t}\hat{\xi}_i(t,\rho)\Delta\zeta_i(t,\rho)\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t \\
&\qquad\qquad = -\int_0^T\!\!\int_0^1 \Big(-\hat{\lambda}(t,\omega)^* f'_x(t,\omega) - h'_x(t,\omega)^* - \nu(t)^* g'_x(t,\omega)\Big)\Delta x(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t + o(\varepsilon).
\end{aligned}
$$

For the last term note that

$$
\frac{\partial}{\partial t}\frac{\partial}{\partial\rho}\omega_i(t,\rho) = (a_i)'_\omega(t,\omega_i(t,\rho))\frac{\partial}{\partial\rho}\omega_i(t,\rho).
$$

Consequently we get

$$-\sum_{i=1}^{n}\int_0^T\int_0^1 \hat{\xi}_i(t,\rho)\Delta\zeta_i(t,\rho)\frac{\partial}{\partial t}\frac{\partial}{\partial\rho}\omega_i(t,\rho)\,\mathrm{d}\rho\,\mathrm{d}t = -\int_0^T\int_0^1 \hat{\lambda}(t,\omega)^* A'_\omega(t,\omega)\Delta x(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t.$$

Bringing the right hand side of (7.22) onto the left hand side and using the representations we have derived, we arrive after some cancellation at

$$\begin{aligned}0 = &\int_0^T\int_0^1 \left(\int_0^1 \hat{\lambda}(t,\sigma)^* f'_y(t,\sigma)\,\mathrm{d}\sigma g'_x(t,\omega) - h'_x(t,\omega)^* - \nu(t)^* g'_x(t,\omega)\right)\Delta x(t,\omega)\\ &+\int_0^1 \hat{\lambda}(t,\sigma)^* f'_y(t,\sigma)\,\mathrm{d}\sigma \Delta_u g(t,\omega) + \hat{\lambda}(t,\omega)^*\Delta_u f(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t\\ &-\int_0^1 k'_x(\omega,\hat{x}(T,\omega),\hat{y}(T))^*\Delta x(T,\omega) + \int_0^1 k'_y(\sigma,\hat{x}(T,\sigma),\hat{y}(T))^*\,\mathrm{d}\sigma\, g'_x(T,\omega)\Delta x(T,\omega)\,\mathrm{d}\omega + o(\varepsilon).\end{aligned}$$

Adding this to (7.21) results in

$$J(u) - J(\hat{u}) = \int_0^T\int_0^1 \hat{\lambda}(t,\omega)^*\Delta_u f(t,\omega) + \Delta_u h(t,\omega) + \nu(t)^*\Delta_u g(t,\omega)\,\mathrm{d}\omega\,\mathrm{d}t + o(\varepsilon).$$

We see that a first order condition for $\hat{u}$ to be optimal is that it maximises the Hamiltonian (note that the Hamiltonian has an additional term; this term is independent of u and therefore plays no role in the maximisation). It was already established at the end of Section 7.3 that the first equation in (7.9) is fulfilled . The remaining equations are equally straightforward to prove.

7.5 Conclusions

We have derived a Pontryagin-type maximum principle for an optimal control system using a size-structured PDE as state equation, including aggregated variables depending on the control. We mention that optimal control of size structured systems has been studied before, for example in [108], where the system is one-dimensional. We extend the results there by allowing for arbitrary dimension of the state variables. Optimal control of other heterogeneous systems has been considered for example in [103], where, among others, systems with parametric heterogeneity have been investigated.

One topic we have not touched upon here are additional constraints. Epidemiological models for the transmission of infectious diseases in general ensure non-negativity of the trajectories, and we expect that a meaningful inclusion of a control into these dynamics will retain this property, so that the result presented here is useful in actual applications. However, additional constraints are of course of interest for various other reasons. This includes not only state constraints, but also terminal constraints which could be used to demand that the prevalence of the disease at the terminal time lies beneath some fixed value. Furthermore, problems of the same structure but where the terminal time T is free could be used to calculate control trajectories that eradicate the disease in minimal time.

We see that while the theorem presented here provides a useful extension of previous results in applying optimal control to size-structured models, there are still many ways in which the result may be expanded.

Bibliography

[1] B. Ainseba, M. Iannelli: *Optimal screening in structured SIR epidemics.* Mathematical Modelling of Natural Phenomena 7(03) (2012): pp. 12–27.

[2] S. Alizon, M. van Baalen: *Multiple infections, immune dynamics, and the evolution of virulence.* The American Naturalist 172(4) (2008): E150–E168.

[3] E.J. Allen: *Derivation of stochastic partial differential equations for size-and age-structured populations.* Journal of Biological Dynamics 3(1) (2009): pp. 73–86.

[4] F. Altarelli, A. Braunstein, L. Dall'Asta, J.R. Wakeling, R. Zecchina: *Containing epidemic outbreaks by message-passing techniques.* Physical Review X 4(2) (2014): 021024.

[5] S. Altizer, A. Dobson, P. Hosseini, P. Hudson, M. Pascual, P. Rohani: *Seasonality and the dynamics of infectious diseases.* Ecology Letters 9(4) (2006): pp. 467–484.

[6] L.T.T. An, W. Jäger, M. Neuss-Radu: *Systems of Populations with Multiple Structures: Modeling and Analysis.* Journal of Dynamics and Differential Equations 27(3-4) (2015): pp. 863–877.

[7] J.B. André, J.B. Ferdy, B. Godelle: *Within-host parasite dynamics, emerging trade-off, and evolution of virulence with immune system.* Evolution 57(7) (2003): pp. 1489–1497.

[8] L. Arnold: *Stochastic Differential Equations: Theory and Applications*, Wiley, 1974.

[9] S. Bansal, B.T. Grenfell, L.A. Meyers: *When individual behaviour matters: homogeneous and network models in epidemiology.* Journal of The Royal Society Interface 4(16) (2007): pp. 879–891.

[10] S. Bansal, J. Read, B. Pourbohloul, L.A. Meyers: *The dynamic nature of contact networks in infectious disease epidemiology.* Journal of Biological Dynamics 4(5) (2010): pp. 478–489.

[11] M.V. Barbarossa, G. Röst: *Immuno-epidemiology of a population structured by immune status: a mathematical study of waning immunity and immune system boosting.* Journal of Mathematical Biology 71(6) (2015): pp. 1737–1770.

[12] N.D. Barlow: *Non-linear transmission and simple models for bovine tuberculosis*. Journal of Animal Ecology 69(4) (2000): pp. 703–713.

[13] N. Berglund, B. Gentz: *Geometric singular perturbation theory for stochastic differential equations*. Journal of Differential Equations 191(1) (2003): pp. 1–54.

[14] N. Berglund, B. Gentz: *Noise-Induced Phenomena in Slow-Fast Dynamical Systems*, Springer, 2006.

[15] D.P. Bertsekas: *Dynamic programming and optimal control*, Athena Scientific, Belmont MA, 1995.

[16] S. Bhattacharya, F.R. Adler: *A time since recovery model with varying rates of loss of immunity*. Bulletin of Mathematical Biology 74(12) (2012): pp. 2810–2819.

[17] M.C. Boily, R.F. Baggaley, L. Wang, B. Masse, R.G. White, R.J. Hayes, M. Alary: *Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies*. The Lancet Infectious Diseases 9(2) (2009): pp. 118–129.

[18] F. Brauer, C. Castillo-Chavez: *Mathematical models in population biology and epidemiology*, Springer, 2011.

[19] F. Brauer, P. van den Driessche, J. Wu: *Mathematical Epidemiology*, Vol. 1945, Springer, 2008.

[20] T. Britton: *Stochastic epidemic models: a survey*. Mathematical Biosciences 225(1) (2010): pp. 24–35.

[21] S. Busenberg, C. Castillo-Chavez: *A general solution of the problem of mixing of subpopulations and its application to risk-and age-structured epidemic models for the spread of AIDS*. Mathematical Medicine and Biology 8(1) (1991): pp. 1–29.

[22] S.R. Carpenter, W.A. Brock: *Rising variance: a leading indicator of ecological transition*. Ecology Letters 9(3) (2006): pp. 311–318.

[23] C. Castillo-Chavez, K. Cooke, W. Huang, S.A. Levin: *The role of long periods of infectiousness in the dynamics of acquired immunodeficiency syndrome (AIDS)*. In *Mathematical approaches to problems in resource management and epidemiology*, Springer, 1989: pp. 177–189.

[24] C. Castillo-Chavez, W. Huang, J. Li: *Competitive exclusion in gonorrhea models and other sexually transmitted diseases*. SIAM Journal on Applied Mathematics 56(2) (1996): pp. 494–508.

[25] D. Clancy, C.J. Pearce: *The effect of population heterogeneities upon spread of infection*. Journal of Mathematical Biology 67 (2012): pp. 963–978.

[26] F.A.B.Coutinho, E. Massad, L.F. Lopez, M.N. Burattini: *Modelling Heterogeneities in Individual Frailties in Epidemic Models.* Mathematical and Computer Modelling 30 (1999): pp. 97–115.

[27] T. Day, S.R. Proulx: *A general theory for the evolutionary dynamics of virulence.* The American Naturalist 163(4) (2004): E40–E63.

[28] S.Y. Del Valle, J.M. Hyman, H.W. Hethcote, S.G. Eubank: *Mixing patterns between age groups in social networks.* Social Networks 29(4) (2007): pp. 539–554.

[29] O. Diekmann, J.A.P. Heesterbeek: *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*, Wiley, Chichester, 2000.

[30] O. Diekmann, H. Heesterbeek, T. Britton: *Mathematical tools for understanding infectious disease dynamics*, Princeton University Press, 2012.

[31] O. Diekmann, J.A.P. Heesterbeek, J.A.J. Metz: *On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations.* Journal of Mathematical Biology 28(4) (1990): pp. 365–382.

[32] J. Dushoff: *Host heterogeneity and disease endemicity: A moment-based approach.* Theoretical Population Biology 56(3) (1999): pp. 325–335.

[33] J. Elstrodt: *Maß- und Integrationstheorie*, Springer, 2007.

[34] G. Feichtinger, Ts. Tsachev, and V.M. Veliov: *Maximum principle for age and duration structured systems: a tool for optimal prevention and treatment of HIV*. Mathematical Population Studies 11(1) (2004): pp. 3–28.

[35] V.V. Ganusov, C.T. Bergstrom, R. Antia: *Within-host population dynamics and the evolution of microparasites in a heterogeneous host population.* Evolution 56(2) (2002): pp. 213–223.

[36] C. Gardiner: *Stochastic Methods.* Springer, 4th edition, 2009.

[37] G.P. Garnett, R.M. Anderson: *Sexually transmitted diseases and sexual behavior: insights from mathematical models.* Journal of Infectious Diseases 174 (Supplement 2) (1996): pp. 150–161.

[38] M.A. Gilchrist, A. Sasaki: *Modeling host-parasite coevolution: a nested approach based on mechanistic models.* Journal of Theoretical Biology 218(3) (2002): pp. 289–308.

[39] B.T. Grenfell, O.N. Bjørnstad, B.F. Finkenstädt: *Dynamics of measles epidemics: scaling noise, determinism, and predictability with the TSIR model.* Ecological Monographs 72(2) (2002): pp. 185–202.

[40] T. Gross, C.J. Dommar D'Lima, B. Blasius: *Epidemic dynamics on an adaptive network.* Physical Review Letters 96 (2006): 208701.

[41] A.B. Gumel, C.C. McCluskey, P. Van den Driessche: *Mathematical study of a staged-progression HIV model with imperfect vaccine.* Bulletin of Mathematical Biology 68(8) (2006): pp. 2105–2128.

[42] W.W. Hager, H. Zhang: *Projection on a polyhedron that exploits sparsity*. (2015): Preprint available at: http://users.clas.ufl.edu/hager/papers/CG/pproj.pdf

[43] G. Hek: *Geometric singular perturbation theory in biological practice.* Journal of Mathematical Biology 60 (2010): pp. 347–386.

[44] B. Hellriegel: *Immunoepidemiology - bridging the gap between immunology and epidemiology.* Trends in Parasitology 17(2) (2001): pp. 102–106.

[45] H.W. Hethcote: *Qualitative analyses of communicable disease models.* Mathematical Biosciences 28(3) (1976): pp. 335–356.

[46] H.W. Hethcote, H.W. Stech, P. Van Den Driessche: *Nonlinear oscillations in epidemic models.* SIAM Journal on Applied Mathematics 40(1) (1981): pp. 1–9.

[47] H.W. Hethcote, J.W. Van Ark: *Epidemiological models for heterogeneous populations: proportionate mixing, parameter estimation, and immunization programs.* Mathematical Biosciences 84(1) (1987): pp. 85–118.

[48] R.I. Hickson, M.G. Roberts: *How population heterogeneity in susceptibility and infectivity influences epidemic dynamics.* Journal of Theoretical Biology 350 (2014): pp. 70–80.

[49] D.J. Higham: *An algorithmic introduction to numerical simulation of stochastic differential equations.* SIAM Review 43(3) (2001): pp. 525–546.

[50] F.M. Hilker, M. Langlais, S.V. Petrovskii, H. Malchow: *A diffusive SI model with Allee effect and application to FIV*. Mathematical Biosciences 206(1) (2007): pp. 61–80.

[51] A.N. Hill, I.M. Longini: *The critical vaccination fraction for heterogeneous epidemic models.* Mathematical Biosciences 181(1) (2003): pp. 85–106.

[52] A. Hill, D.G. Rand, M.A. Nowak, N.A. Christakis: *Emotions as infectious diseases in a large social network: the SISa model.* Proceedings of the Royal Society B 277 (2010): pp. 3827–3835.

[53] A. Hill, D.G. Rand, M.A. Nowak, N.A. Christakis: *Infectious disease modeling of social contagion in networks.* PLoS Computational Biology 6(11) (2010): e1000968.

[54] T. House, M.J. Keeling: *Insights from unifying modern approximations to infections on networks.* Journal of The Royal Society Interface 8 (2011): pp. 63–73.

[55] J.M. Hyman, E.A. Stanley: *Using mathematical models to understand the AIDS epidemic.* Mathematical Biosciences 90(1) (1988): pp. 415–473.

[56] H. Inaba: *Endemic threshold results in an age-duration-structured population model for HIV infection.* Mathematical Biosciences 201(1) (2006): pp. 15–47.

[57] A.R. Ives, V. Dakos: *Detecting dynamical changes in nonlinear time series using locally linear state-space models.* Ecosphere 3(6) (2012): art58.

[58] C.K.R.T. Jones: *Geometric singular perturbation theory.* In *Dynamical Systems*, Springer, 1995: pp. 44–118.

[59] G.P. Karev: *Dynamics of Heterogeneous Populations and Communities and Evolution of Distributions.* Discrete and Continuous Dynamical Systems Supplement (2005): pp. 487–496.

[60] G.P. Karev: *On mathematical theory of selection: continuous time population dynamics.* Journal of Mathematical Biology 60 (2010): pp. 107–129.

[61] G.P. Karev: *Dynamics of inhomogeneous populations and global demography models.* Journal of Biological Systems 13(1) (2005): pp. 83–104.

[62] I. Kareva, M. Benjamin, C. Castillo-Chavez: *Resource Consumption, Sustainability, and Cancer.* Bulletin of Mathematical Biology 77(2) (2014): pp. 1–20.

[63] M.J. Keeling, K.T. Eames: *Networks and epidemic models.* Journal of the Royal Society Interface 2(4) (2005): pp. 295–307.

[64] M.J. Keeling, P. Rohani: *Modeling infectious diseases in humans and animals*, Princeton University Press, 2008.

[65] J.O. Kephart, S.R. White: *Directed-graph epidemiological models of computer viruses.* In *Proceedings. 1991 IEEE Computer Society Symposium on Research in Security and Privacy*, IEEE, 1991: pp. 343–359.

[66] W.O. Kermack, A.G. McKendrick: *A contribution to the mathematical theory of epidemics.* Proceedings of the Royal Society London A 115 (1927): pp. 700–721.

[67] D.E. Kirk: *Optimal control theory: an introduction*, Courier Corporation, 1970.

[68] M. Krupa, P. Szmolyan: *Extending slow manifolds near transcritical and pitchfork singularities.* Nonlinearity 14 (2001): pp. 1473–1491.

[69] C. Kuehn: *A mathematical framework for critical transitions: normal forms, variance and applications*. Journal of Nonlinear Science 23(3) (2013): pp. 457–510.

[70] C. Kuehn: *Multiple Time Scale Dynamics*, Springer, 2015.

[71] C. Kuehn: *Warning signs for wave speed transitions of noisy Fisher-KPP invasion fronts*. Theoretical Ecology 6(3) (2013): pp. 295–308.

[72] C. Kuehn, G. Zschaler, T. Gross: *Early warning signs for saddle-escape transitions in complex networks*. Scientific reports 5 (2015): art.nr. 13190

[73] A.B. Kurzhanski, P. Varaiya: *Optimization of output feedback control under set-membership uncertainty*. Journal of Optimization Theory and Applications 151(1) (2011): 11–32.

[74] A.B. Kurzhanski, P. Varaiya: *Dynamics and Control of Trajectory Tubes: Theory and Computation*, Vol. 85, Springer, 2014.

[75] A.B. Kurzhanski, V.M. Veliov (Eds.): *Modeling Techniques for Uncertain Systems*, Progress in Systems and Control Theory 18, Birkhäuser, Boston, 1994.

[76] G.E. Lahodny Jr, L.J. Allen: *Probability of a disease outbreak in stochastic multipatch epidemic models*. Bulletin of Mathematical Biology 75(7) (2013): pp. 1157–1180.

[77] A. Lajmanovich, J.A. Yorke: *A deterministic model for gonorrhea in a nonhomogeneous population*. Mathematical Biosciences 28(3) (1976): pp. 221–236.

[78] H. Liu, J. Yu, G. Zhu: *Global behaviour of an age-infection-structured HIV model with impulsive drug-treatment strategy*. Journal of Theoretical Biology 253(4) (2008): pp. 749–754.

[79] P. Magal, S. Ruan (Eds.): *Structured population models in biology and epidemiology*, Springer, Berlin, 2008.

[80] M. Martcheva, S.S. Pilyugin: *An epidemic model structured by host immunity*. Journal of Biological Systems 14(02) (2006): pp. 185–203.

[81] R.M. May, R.M. Anderson: *The transmission dynamics of human immunodeficiency virus (HIV)*. Philosophical Transactions of the Royal Society B 321(1207) (1988): pp. 565–607.

[82] H. McCallum, N. Barlow, J. Hone: *How should pathogen transmission be modelled?* Trends in Ecology & Evolution 16(6) (2001): pp 295–300.

[83] L. Meyers: Contact network epidemiology: *Bond percolation applied to infectious disease prediction and control*. Bulletin of the American Mathematical Society 44(1) (2007): pp. 63–86.

[84] L.A. Meyers, M.E.J. Newman, B. Pourbohloul: *Predicting epidemics on directed contact networks.* Journal of Theoretical Biology 240(3) (2006): pp. 400–418.

[85] M. Milanese, J. Norton, H. Piet-Lahanier, É. Walter (Eds). *Bounding approaches to system identification*, Plenum Press, New York, 1996.

[86] J.C. Miller: *Epidemic size and probability in populations with heterogeneous infectivity and susceptibility*. Physical Review E 76(1) (2007): 010101.

[87] N.A. Molinari, I.R. Ortega-Sanchez, M.L. Messonnier, W.W. Thompson, P.M. Wortley, E. Weintraub, C.B. Bridges: *The annual impact of seasonal influenza in the US: measuring disease burden and costs.* Vaccine 25(27) (2007): pp. 5086–5096.

[88] Y. Moreno, R. Pastor-Satorras, A. Vespignani: *Epidemic outbreaks in complex heterogeneous networks.* The European Physical Journal B 26(4) (2002): pp. 521–529.

[89] J. Mossong, D.J. Nokes, W.J. Edmunds, M.J. Cox, S. Ratnam, C.P. Muller: *Modeling the impact of subclinical measles transmission in vaccinated populations with waning immunity*. American Journal of Epidemiology 150(11) (1999): pp. 1238–1249.

[90] I. Nasell: *The quasi-stationary distribution of the closed endemic SIS model.* Advances in Applied Probability 28(3) (1996): pp. 895–932.

[91] A.S. Novozhilov: *On the spread of epidemics in a closed heterogeneous population.* Mathematical Biosciences 215(2) (2008): pp. 177–185.

[92] A.S. Novozhilov: *Epidemiological models with parametric heterogeneity: Deterministic theory for closed populations.* Mathematical Modelling of Natural Phenomena 7(03) (2012): pp. 147–167.

[93] S.M. O'Regan, J.M. Drake: *Theory of early warning signals of disease emergence and leading indicators of elimination.* Theoretical Ecology 6(3) (2013): pp. 333–357.

[94] M.T. Osterholm: *Preparing for the next pandemic.* New England Journal of Medicine 352(18) (2005): pp. 1839–1842.

[95] A.S. Perelson, G. Weisbuch: *Immunology for physicists.* Reviews of Modern Physics 69(4) (1997): pp. 1219–1267.

[96] E. Polak: *Computational methods in optimization*, Academic press, 1971

[97] V. Rouderfer, N.G. Becker, H.W. Hethcote: *Waning immunity and its effects on vaccination schedules.* Mathematical Biosciences 124(1) (1994): pp. 59–82.

[98] S. Schecter: *Persistent unstable equilibria and closed orbits of a singularly perturbed equation.* Journal of Differential Equations 60(1) (1985): pp.131–141.

[99] M. Scheffer, J. Bascompte, W.A. Brock, V. Brovkhin, S.R. Carpenter, V. Dakos, H. Held, E.H. van Nes, M. Rietkerk, G. Sugihara: *Early-warning signals for critical transitions.* Nature 461(7260) (2009): pp. 53–59.

[100] G. Schneckenreither, F. Breitenecker, N. Popper, G. Zauner: *Cellular Automata Models for SIR-type Epidemics.* Simulation Notes Europe 16(3) (2006): pp. 27–36.

[101] L.B. Shaw, I.B. Schwartz: *Fluctuating epidemics on adaptive networks.* Physical Review E 77(6) (2008): 066101.

[102] H. Shi, Z. Duan, G. Chen : *An SIS model with infective medium on complex networks.* Physica A 387(8) (2008): pp. 2133–2144.

[103] B. Skritek: *On the Optimal Control of Heterogeneous Systems*, Dissertation, Vienna University of Technology, 2015.

[104] H.R. Thieme, P. Van Den Driessche: *Global stability in cyclic epidemic models with disease fatalities (Proceedings of the conference on Differential Equations with Applications to Biology).* Fields Institute Communications 21 (1999): pp. 459–472

[105] Ts. Tsachev, V.M. Veliov, A. Widder: *Set-membership estimations for the evolution of infectious diseases in heterogeneous populations.* Submitted. Available as *Research Report* 2015-11, ORCOS, TU Wien, 2015, http://orcos.tuwien.ac.at/research/research_reports.

[106] P. Van Mieghem, E. Cator: *Epidemics in networks with nodal self-infection and the epidemic threshold.* Physical Review E 86(1) (2012): 016116.

[107] V.M. Veliov: *On the effect of population heterogeneity on dynamics of epidemic diseases.* Journal of Mathematical Biology 51 (2005): pp. 123–143.

[108] V.M. Veliov: *Optimal Control of Heterogeneous Systems: Basic Theory*. Journal of Mathematical Analysis and Applications 346 (2008): pp. 227–242.

[109] V.M. Veliov. A. Widder: *Aggregation and asymptotic analysis of an SI-epidemic model for heterogeneous populations.* Mathematical Medicine and Biology, Advance Access published May 26, 2015, doi: 10.1093/imammb/dqv018.

[110] E. Volz: *SIR dynamics in random networks with heterogeneous connectivity*. Journal of Mathematical Biology 56(3) (2008): 293–310.

[111] L.J. White, G.F. Medley: *Microparasite population dynamics and continuous immunity*. Proceedings of the Royal Society of London B 265(1409) (1998): pp. 1977–1983.

[112] K. Wiesenfeld: *Noisy precursors of nonlinear instabilities.* Journal of Statistical Physics 38(5-6) (1985): pp. 1071–1097.

[113] J.C. Wierman, D.J. Marchette: *Modeling computer virus prevalence with a susceptible-infected-susceptible model with reintroduction.* Computational statistics & data analysis 45(1) (2004): pp. 3–23.

[114] M. Yang, G. Chen, X. Fu: *A modified SIS model with an infective medium on complex networks and its global stability.* Physica A 390(12) (2011): pp. 2408–2413.

[115] J.A. Yorke, H.W. Hethcote, A. Nold: *Dynamics and control of the transmission of gonorrhea.* Sexually transmitted diseases 5(2) (1978): pp 51–56.

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