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Mathematical Models in Epidemiology

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As Alfred North Whitehead, mathematician and philosopher, said:

> "No one who achieves success does so without acknowledging the help of others. The wise and confident acknowledge this help with gratitude."

Abstract

The present dissertation, entitled *Mathematical Models in Epidemiology*, is composed by two chapters. In the first one, we start by taking the Kermack-McKendrick continuous-time model and derive a discrete-time version. We follow with the study of the continuous-time model and an expression for the susceptible proportion is derived. We repeat the process for the discrete-time model, including some examples and some comparisons with the previous model. Important definitions (e.g *basic reproduction number*) are given. The next step is the study of the initial phase and of the final size in the case of discrete-time models. We start by obtaining the Euler-Lotka equation and we recognize the importance of the basic reproduction number R_0 in the existence of positive solutions. We give the compartmental formulation for two specific models in both time settings.

In the second chapter, the objective is to show how to integrate separable static heterogeneity into compartmental models. We start by reducing the Kermack-McKendrick model to a compartmental model by considering a specific form for the expected contribution to the force of infection: $A(\tau) = Ue^{\tau\Sigma}V$. We give two alternative ways of formulating compartmental models: the *integrated form* and the *standard form*. We finally consider a heterogeneous population where individuals are characterized by a certain trait. We reformulate the Kermack-McKendrick model. We consider the expected contribution to the force of infection of the form $A(\tau, \omega, \eta) = a(\omega)b(\tau)c(\eta)$, where $a(\omega)$ is the susceptibility of individuals with trait ω and $c(\eta)$ is the infectiousness of individuals with trait η. We acknowledge that it suffices to redefine a function to integrate heterogeneity into the integrated form. Next, we integrate heterogeneity into the standard form by considering the relative trait-specific susceptibility and $b(\tau) = Ue^{\tau\Sigma}V$. Some examples are given.

We leave here the following sentence, taken from the book [Müller and Kuttler, 2015]:

> "All in all, epidemiology is complex, but encloses mathematically interesting problems and very useful applications."

Keywords: epidemiology, mathematical modelling, continuous-time models, discrete-time models, heterogeneity

Resumo

Esta dissertação, cujo título é *Mathematical Models in Epidemiology* (com tradução para *Modelos Matemáticos em Epidemiologia*), é composta por dois capítulos: comparação entre modelos de tempo discreto e modelos de tempo contínuo, e inserção de heterogeneidade separável e estática em alguns casos especiais. Além disso, contém um anexo composto maioritariamente por teoremas e resultados auxiliares de Análise e Álgebra Linear (destacam-se o Teorema de Fubini, o Teorema da convergência dominada de Lebesgue e o critério de Weierstrass — na área da Análise — e resultados sobre a matriz exponencial — na área da Álgebra Linear). É também aqui que se encontram provas alternativas para resultados enunciados e demonstrados no texto principal e alguns exemplos são dados. Termina-se o anexo com uma breve descrição da transformada de Laplace — definição, condições suficientes para existência desta transformada e algumas propriedades (linearidade, primeira translação e multiplicação por variável).

Notamos que os modelos matemáticos não são precisos e que a modelação de doenças infeciosas poderá ter que incluir vacinação e/ou quarentena, ou ter que levar em conta a imprevisibilidade do comportamento humano e a sua complexidade. Além disso, não podemos esperar que os indivíduos de uma população (de uma certa espécie) sejam todos iguais: por exemplo, alguns indivíduos podem ser (parcialmente ou totalmente) imunes a uma certa doença infeciosa enquanto outros não são. É o caso da população humana, que é claramente heterogénea.

As doenças infeciosas existem no mundo há milhares e milhares de anos, antes da existência da humanidade. A ideia de que existiam criaturas vivas invisíveis e que estas eram prováveis responsáveis pela doença remonta à literatura médica mais antiga, como se pode ver, por exemplo, nos escritos de Aristóteles (384 AC – 322 AC).

Acredita-se que Daniel Bernoulli (1700 – 1782) foi o pioneiro da aplicação da matemática ao estudo das doenças infeciosas quando, em 1760, usou um método matemático para avaliar a eficácia das técnicas de variolização contra a varíola. No século seguinte, importantes contribuições a partir de uma perspetiva estatística foram dadas por William Farr (1807 – 1883) e John Brownlee (1868 – 1927). William Hamer (1862 – 1936) e Ronald Ross (1857 – 1932) foram os primeiros cientistas a formular declarações matemáticas sobre a transmissão de doenças infeciosas. Em 1906, Hamer propôs que a evolução de uma epidemia dependia da taxa de contacto entre indivíduos suscetíveis e indivíduos infeciosos (*mass action principle* — o princípio da ação das massas). O trabalho de Hamer e Ross inspirou o trabalho de muitos outros, entre eles Anderson Gray McKendrick (1876 – 1943) e William Ogilvy Kermack (1898 – 1970) que, em 1927, estabeleceram a famosa *threshold theory* — teoria do limite (ver [Kermack and McKendrick, 1927]): um surto epidémico não pode ocorrer a partir da inserção de alguns indivíduos infeciosos numa população totalmente suscetível a não ser que a densidade de indivíduos suscetíveis esteja acima de um certo valor.

O princípio da ação de massas e a teoria do limite formam a fundação da epidemiologia teórica moderna.

Kermack e McKendrick são considerados por muitos como os pioneiros de modelos epidemiológicos e o seu modelo de 1927 é até hoje um protótipo para quase todos estes modelos. Embora simples, pode ser generalizado de modo a incluir estrutura (idade, espaço) e/ou estocacidade.

No primeiro capítulo, começamos por tomar o modelo (de tempo) contínuo de Kermack-McKendrick e mostramos como obter uma versão de tempo discreto. Prosseguimos com o estudo do modelo de tempo contínuo e, em particular, derivamos uma expressão para a proporção de suscetíveis. Repetimos o processo para o modelo de tempo discreto, incluindo agora alguns exemplos, e fazemos algumas compara-

ções com o modelo anterior. Durante o estudo, definições importantes (por exemplo, *número básico de reprodução*) são dadas. No modelo contínuo, alguns resultados que se tornarão bastante úteis no próximo capítulo são já enunciados e provados. Em particular, prova-se que a força cumulativa de infeção w satisfaz uma equação de renovação que envolve o número Ψ de indivíduos não-suscetíveis na população. O próximo passo é estudar a fase inicial e o tamanho final no caso de modelos discretos. Aqui, começamos por obter a equação de Euler-Lotka e pela procura de soluções positivas. Reconhecemos a importância do número básico de reprodução R_0 na existência de soluções positivas. Terminamos este capítulo com a formulação compartimental para os modelos SIR e SEIR, começando no cenário contínuo e prosseguindo com o cenário discreto. Em particular, calculamos a contribuição esperada para a força de infeção, no caso contínuo, e a contribuição esperada para a força cumulativa de infeção, no caso discreto. Além disso, determinamos o número básico de reprodução para cada um dos dois modelos, tanto no cenário contínuo como no discreto, e vemos que, em cada cenário, o número básico de reprodução é o mesmo para o modelo SIR e para o modelo SEIR (o que é natural, já que o compartimento E, de indivíduos expostos (infetados que ainda não transmitem a doença), não contribui para a força de infeção.

No segundo e último capítulo desta dissertação, o objetivo é mostrar como integrar heterogeneidade separável e estática em modelos epidémicos compartimentais. Aqui, começamos por considerar o modelo (contínuo) de Kermack-McKendrick e depois reduzimo-lo a um modelo compartimental, bastando apenas considerar uma forma específica para a contribuição esperada para a força de infeção: $A(\tau) = Ue^{\tau\Sigma}V$. Apresentamos duas formas alternativas de formular modelos compartimentais: a *forma integrada* e a *forma padrão*. Mostramos a relação entre a equação de renovação que descreve a força cumulativa de infeção w e a forma integrada. Ao longo deste estudo, vários exemplos são dados. Calculamos o número básico de reprodução e o tempo de geração e derivamos a equação de Euler-Lotka. Em seguida, finalmente, consideramos uma população hospedeira heterogénea, onde indivíduos são caracterizados por uma determinada característica. Reformulamos o modelo (contínuo) de Kermack-McKendrick e obtemos uma equação diferencial (parcial) para descrever a proporção de indivíduos com uma determinada característica que ainda é suscetível e ainda uma equação de renovação para descrever a força de infeção. Notamos que a contribuição esperada para a força de infeção é agora uma função de três variáveis: o tempo desde infeção τ do indivíduo infetado e as características ω do indivíduo em risco de ser infetado e η do indivíduo infetado. Consideramos a contribuição esperada para a força de infeção da forma $A(\tau, \omega, \eta) = a(\omega)b(\tau)c(\eta)$, onde $a(\omega)$ é a suscetibilidade de indivíduos com característica ω e $c(\eta)$ é a infecciosidade de indivíduos com caraterística η. Afirmamos que basta redefinir uma função, definida no primeiro capítulo, para integrar heterogeneidade na forma integrada. Para isso, provamos que a força cumulativa de infeção é dada pelo produto da suscetibilidade $a(\omega)$ por uma função de tempo $w(t)$. Vemos que w satisfaz a equação de renovação obtida para a força de infeção cumulativa do modelo sem heterogeneidade quando redefinimos a função Ψ. Depois queremos integrar heterogeneidade na forma padrão e vemos que aqui o processo já não é tão simples. Para isso, consideramos a suscetibilidade relativa, específica da característica (ao escolher uma característica $\bar{\omega}$ que normaliza esta função, i.e., $a(\bar{\omega}) = 1$). Aqui, assumimos $b(\tau) = Ue^{\tau\Sigma}V$, i.e., da forma especial tomada pela contribuição esperada para a força de infeção no início do capítulo. Terminamos o capítulo e esta dissertação com alguns exemplos (um exemplo especial é o da distribuição Gamma).

Deixamos aqui a seguinte frase, tirada do livro [Müller and Kuttler, 2015]:

> "All in all, epidemiology is complex, but encloses mathematically interesting problems and very useful applications."

com tradução para

> "Em suma, a epidemiologia é complexa, mas inclui problemas matematicamente interessantes e aplicações muito úteis."

Palavras-chave: epidemiologia, modelação matemática, modelos de tempo contínuo, modelos de tempo discreto, heterogeneidade

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Important Terms

basic reproduction number expected number of secondary cases generated by a primary case in a totally susceptible host population

demographic stochasticity random variations in the size of a population that occur because the birth and death of any individual is a discrete and probabilistic event

disease vector living organism that can transmit pathogens between humans or from animals to humans

force of infection probability per unit of time at which a susceptible becomes infected

incidence number of new cases of the disease arising per unit of time

infectiousness (of an individual) measures the force with which the individual infects

pathogen/ infectious agent any organism or agent that can produce disease

susceptibility (of an individual) measures the probability that the individual has of being infected

List of Symbols

$\boldsymbol{S(t)}$ density of susceptible individuals at time t

$\boldsymbol{E(t)}$ density of exposed individuals (infected but not yet infectious) at time t

$\boldsymbol{I(t)}$ density of infectious individuals at time t

$\boldsymbol{R(t)}$ density of removed individuals at time t

$\boldsymbol{s(t)}$ proportion of susceptible individuals at time t

$\boldsymbol{e(t)}$ proportion of exposed individuals at time t

$\boldsymbol{i(t)}$ proportion of infectious individuals at time t

$\boldsymbol{r(t)}$ proportion of removed individuals at time t

$\boldsymbol{N}$ Population size

$\boldsymbol{R_0}$ basic reproduction number

$\boldsymbol{A(\tau)}$ expected contribution to the force of infection by an individual that was itself infected τ units of time ago

$\boldsymbol{A_k}$ expected contribution to the cumulative force of infection over $]t, t+1]$ by an individual who itself became infected in the time window $]t-k, t-k+1]$, k time steps earlier

$\boldsymbol{\tilde{A}_k}$ $= A_k N$

$\boldsymbol{\Lambda(t)}$ force of infection at time t

$\boldsymbol{\hat{\Lambda}(t)}$ cumulative force of infection over $]t, t+1]$

$\boldsymbol{w(t)}$ cumulative force of infection at time t (in the case of a homogeneous population)

$\boldsymbol{\Psi(t)}$ number of individuals in the (homogeneous) population that are no longer susceptible at time t

$\boldsymbol{\beta}$ per capita contribution to the force of infection

$\boldsymbol{\gamma}$ rate at which individuals leave compartment E (in the continuous SEIR model)/ probability to leave compartment E in one time step (in the SEIR model)

$\boldsymbol{\alpha}$ rate at which individuals leave compartment I (in the continuous SIR/SEIR model)/ probability to leave compartment I in one time step (in the continuous SIR/ SEIR model)

$\boldsymbol{\mathcal{M}_{m\times n}}$ set of real matrices of order $m \times n$

$\mathcal{M}^{+}_{m\times n}$ set of real matrices of order $m\times n$ with nonnegative entries and at least one positive entry

$\mathcal{OD}^{+}_{m\times n}$ set of real matrices of order $m\times n$ with nonnegative entries in the off-diagonal

Σ matrix that describes the state transitions of the infected

U row-vector such that its k-th component gives the contribution to the force of infection by an individual in the k-th infected state

V column-vector representing the probability distribution of the state-at-infection

$\sigma(M)$ spectrum of the square matrix M, i.e., the set of eigenvalues of M

$\rho(M)$ spectral radius of the square matrix M, i.e., the maximum of the absolute values of $\sigma(M)$

$\kappa(M)$ spectral abscissa of the square matrix M, i.e., the greatest real part of $\sigma(M)$

$A(\tau,\omega,\eta)$ expected contribution to the force of infection on (susceptible) individuals of trait ω by an individual of trait η that was itself infected τ units of time ago

$\Lambda(t,\omega)$ force of infection on (susceptible) individuals of trait ω at time t

$s(t,\omega)$ probability that an individual with trait ω is susceptible at time t

Ω trait space, assumed to be measurable

Φ probability measure on Ω, i.e., a measure that describes the probability distribution of the trait in the host population

$a(\omega)$ susceptibility of individuals with trait ω

$c(\eta)$ infectiousness of individuals with trait η

$b(\tau)$ function of age of infection that describes the expected contribution to the force of infection (in the heterogeneous case)

Acronyms

HIV/AIDS Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome

COVID-19 Coronavirus disease of 2019

SIR Susceptibles-Infected-Removed model

SEIR Susceptibles-Exposed-Infectious-Removed model

ODE Ordinary differential equation

Introduction

The present dissertation was written for the purpose of obtaining the Master's degree in Mathematics from the Faculty of Sciences of the University of Lisbon (FCUL). In addition, due to the writer's prominent interest in mathematical models, in particular applied to Biology, and with the aim to broaden her knowledge in the area of infectious diseases, the theme chosen was

Mathematical Models in Epidemiology.

What is Epidemiology?

Let us now introduce the concept of epidemiology. Here we follow [Müller and Kuttler, 2015].

The term **epidemiology** extends to two possible descriptions:

1. environmental or behavioural factors that increase the risk for the development of certain diseases (e.g. excessive exposure to ultraviolet radiation — present in the sunlight — can cause skin cancer while a regular consumption of alcohol can lead to cardiovascular disease);
2. the dynamics of infectious diseases (examples of infectious diseases are malaria, cholera, tuberculosis and, as we've experienced more recently, coronavirus).

For this thesis, our interest lies in the second description: the dynamics of infectious diseases.

Infectious diseases

Infectious diseases have been around for ages and ages, even longer than humankind. It is only natural that humans start to question the origins of the disease and how it transmits.

Historical Background

For more details, see [Anderson and May, 1991].

The idea that invisible living creatures might be the culprits for the disease dates back to the earliest medical literature, e.g. in the writings of Aristotle (384 BC – 322 BC). However, the emergence of "germ theory" is more prominent in the 16^{th} century, when a honourable physician of Verona by the name of Frascastorius (c. 1478 – 1553) published an article in which he distinctly exhibits the belief that invisible living organisms have the ability to generate disease and transmit it by direct or indirect contact from person to person. A century later, Antonie van Leeuwenhoek (1632 – 1723) proved the existence of micro-organisms when simple magnifying lenses were developed and the microscopes created. In 1840, the scientist Jakob Henle (1809 – 1885) stated the germ theory of disease as it is known today and, moreover, stipulated a series of required procedures which would have to be executed in order to prove

this theory. At the end of the 19th century and beginning of the 20th century, three exceptional scientists, Louis Pasteur (1822 – 1895), Joseph Lister (1827 – 1912) and Robert Koch (1843 – 1910) elaborated credible methods for accomplishing these procedures.

Henle, Pasteur and Koch — and their discoveries — extremely influenced biomedical sciences and epidemiological study, bringing a more rigorous approach to it. The work of many epidemiologists should also be noted as another influence for this new path. We mention here the fathers of epidemiology, John Snow (1813 – 1858) and Peter Panum (1820 – 1885), responsible for a exhaustive study of population patterns of disease.

There was an incredible progress in epidemiology and, with the improvement made in the fields of immunology and of cellular and molecular biology, came the tools to help in the quantification of patterns of infection within human populations.

In the table I.1 (taken from [Sampath et al., 2021]), a timeline of (a selected number of) pandemics is given. For each pandemic, we can see when it occurred, the area where it emerged, the pathogen and the vector of the disease[1], and the mortality.

Table I.1: A timeline of Infectious Diseases.

Timeline	Pandemic	Area of emergence	Pathogen	Vector	Death toll
430 BC – 426 BC	Athenian Plague	Ethiopia	Unknown	Unknown	Unknown
165 – 180	Antonine Plague	Iraq	Variola virus	Humans	5 million
541 – 543	Justinian Plague	Egypt	Yersinia pestis	Rodents' associated fleas	30–50 million
1347 – 1351	Black Death	Central Asia	Yersinia pestis	Rodents' associated fleas	200 million
1817 – Present	The Seven Cholera Pandemics	India	Vibrio cholerae	Contaminated water	40 million
1918 – 1919	Spanish Flu	USA	Influenza A (H1N1)	Avian	50 million
1957 – 1958	Asian Flu	China	Influenza A (H2N2)	Avian	>1 million
1968	Hong Kong Flu	China	Influenza A (H3N2)	Avian	1–4 million
1981 – Present	HIV/AIDS	Central Africa	HIV	—	36 million
2002 – 2003	Severe acute respiratory syndrome coronavirus	China	Severe acute respiratory syndrome coronavirus	Bats and palm civets	774
2009 – 2010	Swine Flu	Mexico	Influenza A (H1N1)	Pigs	148000–249000
2014 – 2016	Ebola	Central Africa	Ebola virus	Unknown	11000
2019 – Present	COVID-19	China	SARS-Cov-2	Unknown, maybe bats or pangolins?	>4 million

[1] A *pathogen* or *infectious agent* is any organism or agent that can produce disease. A *disease vector* is a living organism that can transmit pathogens between humans or from animals to humans.

Mathematical Epidemiology

For this brief introduction to Mathematical Epidemiology, we follow [Müller and Kuttler, 2015].

It should be noted that mathematical models are not precise and the modelling of infectious diseases might have to include vaccination, quarantine or have into account the unpredictability of human behaviour and its complexity. E.g. a small proportion of the global population is against vaccination, others refuse to isolate in the presence of a respiratory infectious disease, some people prefer to stay home while others like to go to concerts. Furthermore, one cannot expect the individuals of a (certain species) population to be equal: e.g. some individuals might be (partially or totally) immune to a certain infectious disease while others are not. The human population, for example, is clearly heterogeneous!

We leave here a quote taken from this book:

> "All in all, epidemiology is complex, but encloses mathematically interesting problems and very useful applications."

Historical Background

For more details on the historical background, see [Anderson and May, 1991]. Some details of the Kermack-McKendrick model here mentioned can be seen in [Müller and Kuttler, 2015].

It is believed that Daniel Bernoulli (1700 – 1782) was the pioneer of the application of mathematics to the study of infectious diseases when, in 1760, he used a mathematical method to evaluate the effectiveness of the techniques of variolation against smallpox. A century later, in 1840, the physician William Farr (1807 – 1883) fitted a normal curve to smoothed quarterly data on deaths from smallpox in England and Wales over the period 1837 – 1839. John Brownlee (1868 – 1927), in 1906, published a paper entitled *Statistical studies in immunity; the theory of an epidemic* in which he developed the descriptive approach given by Farr. William Hamer (1862 – 1936) and Ronald Ross (1857 – 1932) contributed with works in two particular problems: measles epidemics and the relationship between the numbers of mosquitoes and the incidence of malaria. These two scientists were the first to formulate mathematical statements about the transmission of infectious diseases. In 1906, Hamer proposed that the evolution of an epidemic depended on the rate of contact between susceptible and infectious individuals (*mass action principle*). The work of Hamer and Ross inspired the work of many others, as is the case of two famous names in mathematical epidemiology: the physician and epidemiology Anderson Gray McKendrick (1876 – 1943) and the biochemist William Ogilvy Kermack (1898 – 1970). McKendrick and Kermack, in 1927, stated the famous *threshold theory* (see [Kermack and McKendrick, 1927]): an epidemic outbreak cannot occur by the insertion of a few infectious individuals in an all susceptible population unless the density of susceptible individuals is above a certain critical value. The work of Herbert Soper (1865 – 1930) who, in 1929, deduced the fundamental mechanisms responsible for the periodicity of epidemics, was also inspired by the work of Hamer and Ross.

The *mass action principle* and the *threshold theory* form the foundation of modern theoretical epidemiology.

Moreover, Kermack and McKendrick are in fact considered by many as the pioneers of epidemiological models and their model ([Kermack and McKendrick, 1927]) is until this day a prototype of almost every epidemiological model. Generalized versions of this model include structure (age, space) and/or stochasticity.

It should be noted that, in 1927, when the original model was conceived, some questions had yet to be answered: How can an epidemic outbreak of an infectious disease vanish while susceptible individuals are still present? Is it because the infectious agent gets weaker by fighting against the immune system of each infected individual until it stops infecting or is it due to a low number of susceptibles?

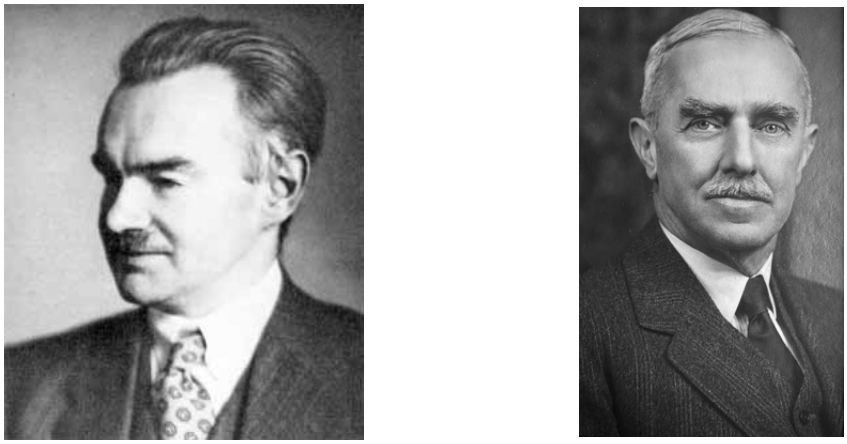

Fig. I.1. William Ogilvy Kermack (left) and Anderson Gray McKendrick (right).

The dissertation

The present dissertation, entitled *Mathematical Models in Epidemiology*, has two main points of interest: discrete-time models in comparison with continuous-time models and the insertion of separable static heterogeneity in some very special cases.

We start the thesis with the first point and there we mainly follow [Diekmann et al., 2021]. For the second point, the reference mainly used is [Diekmann and Inaba, 2023]. To complement some aspects of the first topic, particularly in the study of continuous-time models, we choose [Breda et al., 2012]. The appendix is mainly composed of some auxiliary theorems and results of Analysis and of Linear Algebra (references: [Sarrico, 2015], [Pestana da Costa, 2001], [Varga, R.S., 2000] and [Spiegel, M.R., 1965]). It is also in the appendix that one can find alternative proofs for results enunciated and proven in the main text and some examples are given.

Structure

The main part of this thesis is composed by two chapters. In both chapters, it is assumed that the disease generates permanent immunity and the host population is demographically closed as was done by Kermack and McKendrick in 1927 ([Kermack and McKendrick, 1927]).

In the first chapter, entitled **The discrete Kermack-McKendrick model versus the continuous version**, the objective is to compare the continuous Kermack-McKendrick model with a derived discrete version and, furthermore, to motivate discrete-time models.

In section 1.1, we give the assumptions that will stay valid throughout this essay. From such assumptions, we derive a continuous-time model and then we show how to obtain a discrete-time version of such model. We follow with section 1.2, where we study both the continuous and the discrete models. When studying the discrete-time models, we include some examples and we give some comparisons with the

previous model. We show the relation between the density/proportion of susceptibles and the cumulative force of infection. Here, important definitions (e.g. *basic number of reproduction*) are given. We enunciate and prove some results in the continuous model that will be very useful in the next chapter. In particular, we obtain a renewal equation for the cumulative force of infection w that involves the number Ψ of no longer susceptible individuals. Next, in section 1.3, we define the Euler-Lotka equation for the discrete case and we show the relation between the basic reproduction number R_0 and the stability of a special equilibrium. We finish the chapter with section 1.4, where we study the famous compartmental models: SIR and SEIR. We start with the continuous-time setting and then we proceed to the discrete-time setting. In particular, we calculate the expected contribution to the force of infection, in the continuous case, and the expected contribution to the cumulative force of infection, in the discrete case. Furthermore, we determine the basic number of reproduction for each one of the two models, both in the continuous-time setting and in the discrete-time setting.

In the second chapter, entitled **Compartmental epidemic models with separable static heterogeneity**, it is shown how to integrate separable static heterogeneity into compartmental epidemic models, i.e., we wish to construct a compartmental epidemic model where host individuals are characterized by some trait that does not depend on time and the host population can be separated into groups according to the trait that each individual presents.

We start with section 2.1 where we consider a special form for the expected contribution to the force of infection by an individual with age of infection τ: $A(\tau) = Ue^{\tau\Sigma}V$. Here, it is shown how to arrive to two different forms: the *integrated form* and the *standard form*. We demonstrate the relation between the renewal equation that describes the cumulative force of infection w and the integrated form. The basic reproduction number R_0, the generation time T and the Euler-Lotka equation are calculated for this special case. We follow with section 2.2 where we finally integrate heterogeneity into the model. We consider a heterogeneous host population where individuals are characterized by a certain trait. A reformulation of the Kermack-McKendrick model is given and we obtain a (partial) differential equation to describe the fraction of the individuals with a certain trait that is still susceptible and also a renewal equation to describe the force of infection. We note that the expected contribution to the force of infection is now a function of three variables: the time-since-infection τ and the trait η of the infected individual, and the trait ω of the individual at risk of being infected. We continue the study of heterogeneity for a special case: $A(\tau, \omega, \eta) = a(\omega)b(\tau)c(\eta)$, where $a(\omega)$ is the susceptibility of individuals with trait ω and $c(\eta)$ is the infectiousness of individuals with trait η. We claim that to integrate heterogeneity into the integrated form, it suffices to redefine a function: we prove that the cumulative force of infection is given by the product of the susceptibility $a(\omega)$ and a function of time $w(t)$, and we see that w satisfies the renewal equation obtained for the cumulative force of infection of the homogeneous model when we redefine Ψ. Then we want to integrate heterogeneity into the standard form and we will see that the process here is not as simple. For that, we consider the relative trait-specific susceptibility and we assume $b(\tau) = Ue^{\tau\Sigma}V$, i.e., of the special form taken by the expected contribution for the force of infection at the beginning of the chapter.

Chapter 1

The discrete Kermack-McKendrick model versus the continuous version

In this chapter, we will mainly follow [Diekmann et al., 2021] where it is shown that, at times, a discrete-time modelling framework is more powerful than a continuous-time one. The motivation for discrete-time models is simple: although the numbers of individuals varies at a continuous time, collection of data is often done at regular intervals, i.e., on a discrete-time basis. Furthermore, "numerical implementation is straightforward" in such models. For the continuous-time models, [Breda et al., 2012] is a nice tool to complement the study.

In section 1.1, we give the assumptions that will stay valid throughout this essay. From such assumptions, we derive a continuous-time model and then we show how to obtain a discrete-time version of such model. We follow with section 1.2, where we study both the continuous and the discrete models and a comparison is given. We show the relation between the density/proportion of susceptibles and the cumulative force of infection. For that [Diekmann and Inaba, 2023] is shortly used. Next, in section 1.3, we define the Euler-Lotka equation for the discrete case and we show the relation between the basic reproduction number R_0 and the stability of a special equilibrium. We finish the chapter with section 1.4, where we study the famous compartmental models: SIR and SEIR.

Important quantities in this chapter are the number of susceptibles at time t, denoted by $S(t)$, and its proportion, denoted by $s(t)$.

1.1 Introducing the discrete-time version

Here, we start with a continuous-time model and show how to go from there to a discrete-time model. We make the following assumptions:

It is considered the spread of an infectious disease in a host population when
- the disease generates permanent immunity (each individual is infected exactly once or not at all);
- the host population is demographically closed (demographic changes — births, deaths, migrations, …— happen at a much slower time scale than transmission of the disease and are thus ignored).

Let Λ be the *force of infection*, i.e., **the probability per unit of time at which a susceptible becomes**

infected. The **number of new cases per unit of time**, called *incidence*, is given by ΛS.

With the considered assumptions, the density of susceptibles S only varies due to transmission of infection, i.e., the (continuous-time) equation for the density S is given by

$$\frac{dS}{dt}(t) = -\Lambda(t)S(t)\cdot \tag{1.1}$$

Remark 1. With these assumptions, it makes perfect sense that the product $\Lambda(t)S(t)$ is bounded and therefore $\left|\frac{dS}{dt}\right|$ is bounded as well.

Integrating (1.1) over the time window $]t, t+1]$, one obtains the relation

$$S(t+1) = e^{-\hat{\Lambda}(t)}S(t) \tag{1.2}$$

where the integral

$$\hat{\Lambda}(t) \coloneqq \int_t^{t+1} \Lambda(\tau)\, d\tau \tag{1.3}$$

is called the *cumulative force of infection* over $]t, t+1]$. The equation (1.2) gives a discrete-time model under the same assumptions made for the continuous-time model given by (1.1). Notice that the factor $e^{-\hat{\Lambda}(t)}$ corresponds to the probability for a susceptible to escape from infection in time window $]t, t+1]$.

Remark 2. Equation (1.2) should <u>not</u> be replaced by its linearized form

$$S(t+1) = \left(1 - \hat{\Lambda}(t)\right) S(t), \tag{1.4}$$

even if this difference equation is a good approximation of (1.2), for small values of $\hat{\Lambda}(t)$. For sufficiently large values of $\hat{\Lambda}(t)$, this approximation might fail and, furthermore, it can lead to negative values of S, which is clearly absurd. This happens since (1.4) does not take into account the permanent immunity that follows from the first infection:

- the number of new infected individuals over the time window $]t, t+1]$ is, in this case, $\hat{\Lambda}(t)S(t)$;
- if $\hat{\Lambda}(t^*) > 1$, the number of new infected individuals over the time window $]t^*, t^*+1]$ is greater than the number of susceptibles at time t^*;
- so there must be a positive contribution to the number of susceptibles in the time window $]t^*, t^*+1]$;
- assuming that the population is demographically closed, then this positive contribution must be due to reinfection.

However, equation (1.2) takes this into account, as we will now demonstrate. To follow with this demonstration, we take a simple example and we show that the probability that a susceptible escapes from becoming infected is indeed given by an exponential. To start, let p be the probability that a susceptible becomes infected when the host population is formed by one single infectious individual and the remaining individuals are susceptibles. Then $1-p$ is the probability that a susceptible escapes infection. Now, if there are I infectious individuals and these make contacts with susceptibles independently of each other, then any susceptible escapes from becoming infected with probability $(1-p)^I$. Thus the probability of a susceptible to be infected is given by $1-(1-p)^I = 1 - e^{I\ln(1-p)}$ and not by pI as one might expect.

1.2 The General Kermack-McKendrick Model: Continuous VS Discrete

In this section, we will give some important definitions and we will state and prove some results involving the number/proportion of susceptibles. A comparison between the general continuous-time Kermack-McKendrick model and the general discrete-time version is given.

In what follows, N denotes the **population size** (constant due to the previous assumptions). Furthermore, it is clear by the given models that the quantity $S(t)$ is a monotone nonincreasing function, bounded from above by the total host population N. In particular, "in the infinite past, all host individuals were susceptible" and the limit $S(-\infty) := \lim_{t\to-\infty} S(t)$ exists and is equal to N.

The proportion of susceptibles at time t, denoted by $s(t)$, is thus defined by

$$s(t) := \frac{S(t)}{N},$$

and it is clear that $s(-\infty) := \lim_{t\to-\infty} s(t) = 1$.

The General Continuous-Time Kermack-McKendrick Model

We note that the "current force of infection is generated by individuals who were themselves infected some time ago". Kermack and McKendrick (see [Kermack and McKendrick, 1927]) translate this observation into the constitutive equation

$$\Lambda(t) = \int_0^\infty A(\tau)\Lambda(t-\tau)S(t-\tau)\,d\tau \tag{1.5}$$

where $A(\tau)$ is *the expected contribution to the force of infection by an individual that was itself infected τ units of time ago* while the product $\Lambda(t-\tau)S(t-\tau)$ is the incidence at time $t-\tau$.

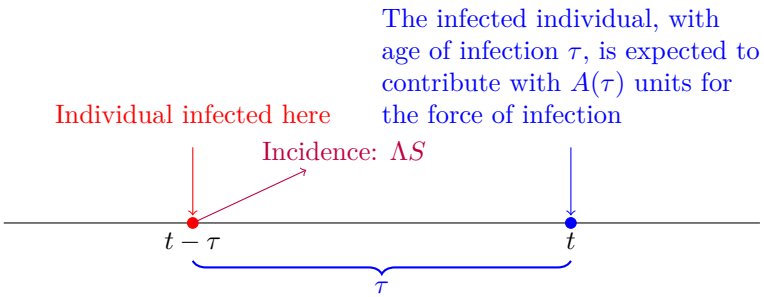

Fig. 1.1. An explanatory scheme for equation (1.5).

It is assumed that $\boldsymbol{A}$**:**$[0,+\infty[\longrightarrow [0,+\infty[$ is positive in some interval of $[0,+\infty[$ and integrable in $[0,+\infty[$, i.e.,

$$\int_0^\infty A(\tau)\,d\tau < +\infty.$$

We now give an important definition: the *basic reproduction number*. This number is of great importance for studying the evolution of an infectious disease.

Definition 1 (Basic reproduction number)**.** The **basic reproduction number** is the *expected number of cases directly generated by one case in a population where all individuals are susceptible to infection* and is given by

$$R_0 := N\int_0^\infty A(\tau)\,d\tau. \tag{1.6}$$

Remark 3. In a totally susceptible population, the expected contribution to the force of infection after the insertion of one infectious individual is equal to $\int_0^\infty A(\tau)\,d\tau$ (we can see this integral as the sum of contributions to the force of infection of the infectious individual from the moment it was infected until now). Since we assume the population to have size N, then the number of new cases is equal to $N\int_0^\infty A(\tau)\,d\tau$. This explains formula (1.6).

Before we continue, we note the following: with our assumptions, it is natural that the disease leaves the population at some point in time (either because every individual got infected or because infected individuals didn't infect others before loosing infectiousness — for example, if all individuals were put in quarantine until recovery). In other words, it is expected that the force of infection Λ reaches the value zero at some point in time. Hence we give the following result:

Proposition 1. *The force of infection defined by* (1.5) *satisfies:*

$$\lim_{t\to+\infty} \Lambda(t) = 0,$$

provided that the limit exists.

Proof. Since $t\mapsto S(t)$ is a monotone nonincreasing and bounded function, then the limit

$$S(\infty) \coloneqq \lim_{t\to+\infty} S(t)$$

exists. Now, let $n \in \mathbb{N}$. By the mean value theorem (theorem 10 in the appendix), there is $t_n \in]n, n+1[$ such that

$$\frac{dS}{dt}(t_n) = \frac{S(n+1) - S(n)}{(n+1) - n} = S(n+1) - S(n)\cdot$$

Passing to the limit as $n \to +\infty$, one has

$$\lim_{n\to+\infty} \frac{dS}{dt}(t_n) = S(\infty) - S(\infty) = 0\cdot$$

On the other hand, it is clear that $t_n \to +\infty$ when $n \to +\infty$. Since the limits $S(\infty)$ and

$$\Lambda(\infty) \coloneqq \lim_{t\to+\infty} \Lambda(t)$$

exist, then, using equation (1.1), one has the existence of the limit

$$\lim_{t\to+\infty} \frac{dS}{dt}(t) = -\lim_{t\to+\infty} \Lambda(t)S(t)$$

and this limit is equal to $-\Lambda(\infty)S(\infty)$.
Now, since $\{t_n\}_{n\in\mathbb{N}}$ is a sequence such that $t_n \to +\infty$ and the limit $\lim_{t\to+\infty} \frac{dS}{dt}(t)$ exists, then

$$-\Lambda(\infty)S(\infty) = \lim_{t\to+\infty} \frac{dS}{dt}(t) = \lim_{n\to+\infty} \frac{dS}{dt}(t_n) = 0\cdot$$

It follows that

$$\Lambda(\infty) = 0 \quad \vee \quad S(\infty) = 0\cdot$$

On the other hand, Lebesgue's dominated convergence theorem (see example 11 in the appendix) guarantees that the sequence $\{\Lambda(k)\}_{k\in\mathbb{N}}$ converges to

$$\lim_{k\to+\infty} \Lambda(k) = \Lambda(\infty)S(\infty) \int_0^\infty A(\tau)\, d\tau = \Lambda(\infty)S(\infty)\frac{R_0}{N}\cdot$$

It follows that

$$\Lambda(\infty) = 0 \quad \vee \quad S(\infty) = \frac{N}{R_0} > 0\cdot$$

Thus it has to be

$$\lim_{t\to+\infty} \Lambda(t) = 0\cdot$$

□

We intend to finish this part with a recurrence relation for the proportion of susceptibles s. We start by obtaining an alternative form for the cumulative force of infection $\hat{\Lambda}$.

Proposition 2. *The cumulative force of infection over* $]t, t+1]$*, defined by* (1.3)*, can be given by the alternative formula*

$$\hat{\Lambda}(t) = \int_0^\infty A(\tau)\left[S(t-\tau) - S(t+1-\tau)\right]\, d\tau\cdot \tag{1.7}$$

Proof. We start by plugging (1.1) into equation (1.5), obtaining

$$\Lambda(t) = -\int_0^\infty A(\tau)\frac{dS}{dt}(t-\tau)\, d\tau\cdot$$

and, by integration in $]t, t+1]$,

$$\int_t^{t+1} \Lambda(\nu)\, d\nu = -\int_t^{t+1}\int_0^\infty A(\tau)\frac{dS}{d\nu}(\nu-\tau)\, d\tau\, d\nu\cdot$$

By Fubini's theorem (see example 12 in appendix), we can switch the order of integration, hence:

$$\begin{aligned}\hat{\Lambda}(t) &\coloneqq \int_t^{t+1}\Lambda(\nu)\, d\nu\\ &= \int_0^\infty A(\tau)\left(-\int_t^{t+1}\frac{dS}{d\nu}(\nu-\tau)\, d\nu\right)\, d\tau\\ &= \int_0^\infty A(\tau)\left[S(t-\tau) - S(t+1-\tau)\right]\, d\tau\cdot\end{aligned}$$

□

The next step is to obtain the solution of (1.1) that satisfies $S(-\infty) = N$.

Proposition 3. *The solution of* (1.1) *that satisfies* $S(-\infty) = N$ *is given by*

$$S(t) = \exp\left\{-\int_{-\infty}^t \Lambda(\nu)\, d\nu\right\} N\cdot \tag{1.8}$$

Proof. An integrating factor of equation (1.1) is $\exp\left\{\int\limits_{-t_0}^{t}\Lambda(\nu)\, d\nu\right\}$ (for some real number t_0). Thus equation (1.1) is equivalent to:

$$\frac{d}{dt}\left(\exp\left\{\int_{-t_0}^t \Lambda(\nu)\, d\nu\right\} S(t)\right) = 0\cdot$$

Integrating in $]-t_0, t[$ (for $t > -t_0$) and multiplying by $\exp\left\{-\int\limits_{-t_0}^{t}\Lambda(\nu)\, d\nu\right\}$, it follows that

$$S(t) = \exp\left\{-\int_{-t_0}^t \Lambda(\nu)\, d\nu\right\} S(-t_0), \quad \text{i.e.,} \quad \int_{-t_0}^t \Lambda(\nu)\, d\nu = -\ln\left(\frac{S(t)}{S(-t_0)}\right)\cdot$$

Now, since $\lim\limits_{t_0\to+\infty} S(-t_0) = N$ and $t \mapsto S(t)$ is a bounded function, then the limit of the integral when $t_0 \to +\infty$ must exist and be finite. By taking the limit (of the first expression) when $t_0 \to +\infty$, we obtain (1.8). □

In particular, since $s(t)$ is the proportion of susceptibles at time t, then the previous solution can also be given as a proportion:

$$s(t) = \exp\left\{-\int_{-\infty}^{t} \Lambda(\nu)\, d\nu\right\}. \tag{1.9}$$

Furthermore, the existence of $\int_{-\infty}^{t} \Lambda(\nu)\, d\nu$ means that the force of infection Λ can be assumed to be negligible in the infinite past. As was done in [Diekmann and Inaba, 2023], one introduces the cumulative force of infection:

Cumulative force of infection

$$w(t) \coloneqq \int_{-\infty}^{t} \Lambda(\nu)\, d\nu. \tag{1.10}$$

The objective now is to find a renewal equation for the cumulative force of infection w.

We start by using (1.7) to obtain an alternative formula for w:

Lemma 1. *The cumulative force of infection w, defined in* (1.10) *can be given by:*

$$w(t) = \int_{0}^{\infty} [1 - s(t-\tau)]\, NA(\tau)\, d\tau. \tag{1.11}$$

Proof. We have

$$\begin{aligned}
w(t) &\coloneqq \int_{-\infty}^{t} \Lambda(\nu)\, d\nu \\
&= \lim_{M\to+\infty} \sum_{k=-M}^{-1} \int_{t+k}^{t+k+1} \Lambda(\nu)\, d\nu \\
&= \lim_{M\to+\infty} \sum_{k=-M}^{-1} \hat{\Lambda}(t+k) \\
&= \lim_{M\to+\infty} \sum_{k=-M}^{-1} \int_{0}^{\infty} A(\tau)\left[S(t+k-\tau) - S(t+k+1-\tau)\right] d\tau \qquad \text{[by equation (1.7)]} \\
&= \lim_{M\to+\infty} \int_{0}^{\infty} A(\tau) \underbrace{\sum_{k=-M}^{-1} \left[S(t+k-\tau) - S(t+k+1-\tau)\right]}_{=S(t-M-\tau)-S(t-\tau)} d\tau \\
&= \lim_{M\to+\infty} \int_{0}^{\infty} A(\tau)\left[S(t-M-\tau) - S(t-\tau)\right] d\tau \\
&= \int_{0}^{\infty} A(\tau)\left[S(-\infty) - S(t-\tau)\right] d\tau \qquad \text{[by example 13 (in the appendix)]} \\
&= \int_{0}^{\infty} [1 - s(t-\tau)]\, NA(\tau)\, d\tau
\end{aligned}$$

and thus we have the required result. □

Next, we rewrite the proportion s, given by (1.9), in terms of w:

Lemma 2. *The proportion of susceptibles at time t satisfies*

$$s(t) = e^{-w(t)} \tag{1.12}$$

and, furthermore, one can characterize w by

$$w(t) = -\ln\left(s(t)\right)\cdot$$

Proof. Immediate by plugging definition (1.10) into equation (1.9). □

Finally, we are ready for the intended result:

Proposition 4. *The cumulative force of infection w satisfies the following equation:*

$$w(t) = \int_0^\infty A(\tau)\Psi(w(t-\tau))\,d\tau \tag{1.13}$$

where

$$\Psi(w) \coloneqq N\left(1 - e^{-w}\right) \tag{1.14}$$

is exactly the number of individuals in the population that are no longer susceptible.

Proof. Immediate by plugging (1.12) into (1.11) and using definition (1.14). □

To follow this proposition, we give recurrence relation for the proportion $s(t)$:

Proposition 5. *The proportion of susceptibles at time t can be given by:*

$$s(t) = \exp\left\{-\int_0^\infty \left[1 - s(t-\tau)\right] NA(\tau)\,d\tau\right\}\cdot \tag{1.15}$$

Proof. The formula follows by plugging (1.11) into (1.12). □

We end this part with a proposition that will turn useful in the next chapter:

Proposition 6. *Equation* (1.13)*, with Ψ defined by* (1.14)*, has a nonzero constant solution $\bar{w}$ if and only if $R_0 \neq 1$.*

Proof. Let Ψ be defined by (1.14). We start by noting that $\bar{w}$ is a constant solution of equation (1.13) if and only if

$$\bar{w} = \int_0^\infty A(\tau)\Psi(\bar{w})\,d\tau, \quad \text{i.e.,} \quad \bar{w} = R_0(1 - e^{-\bar{w}})\cdot$$

Let $g(x) \coloneqq x + R_0 e^{-x}$, so that the problem is transformed into finding the nonzero roots of $g(x) = R_0$. We have $g'(x) = 1 - R_0 e^{-x}$. We would like to remind the reader that R_0 is a positive quantity (see definition (1.6)).
The monotonicity of g can be seen below:

Table 1.1: Monotonicity table for $g(x) = x + R_0 e^{-x}$.

x	$-\infty$	$\ln R_0$	$+\infty$
g	$\searrow$	$1 + \ln R_0$	$\nearrow$
g'	$-$	0	$+$

Now, if $R_0 = 1$, one sees that g decreases in $]-\infty, 0[$, takes the value $g(0) = 1 = R_0$ and then increases in $]0, +\infty[$. So, in this case, there are no nonzero roots.
Suppose now that $R_0 \neq 1$. It is easy to see that $1 + \ln R_0 < R_0$: if $h(x) = x - \ln x$, then $h(1) = 1$ and $h'(x) = 1 - \frac{1}{x} = \frac{x-1}{x}$, so that

- $h' < 0$ in $]0, 1[$ and h strictly decreases in $]0, 1[$;
- $h' > 0$ in $]1, +\infty[$ and h strictly increases in $]1, +\infty[$.

In both cases, $h(x) > h(1) = 1$ for $x \in \mathbb{R}^+ \setminus \{1\}$ and thus $1 + \ln R_0 < R_0$. Therefore g attains the minimum value $1 + \ln R_0 < R_0$ and, by continuity of g, one concludes that g has two distinct roots, and thus at least one nonzero root.
In conclusion, equation (1.13) has a nonzero constant solution if and only if $R_0 \neq 1$.

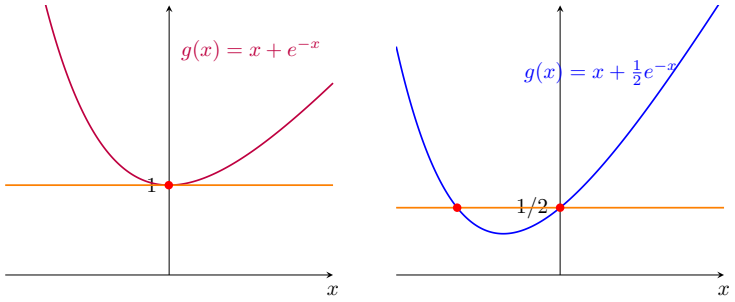

Fig. 1.2. Graph of $g(x) = x + R_0 e^{-x}$ when $R_0 = 1$ (left) and when $R_0 = \frac{1}{2} < 1$ (right).

□

The General Discrete-Time Kermack-McKendrick Model

Now let us return to the discrete-time model (1.2) and compare results. One key difference is the use of series instead of integrals as in the continuous-time case. An important ingredient will be the collection $\{A_k\}_{k\in\mathbb{N}}$ of nonnegative numbers, which we assume to be summable, i.e., such that $\sum_{k=1}^{\infty} A_k < \infty$.

The discrete-time counterpart of (1.7) reads

$$\hat{\Lambda}(t) = \sum_{k=1}^{\infty} A_k \left[S(t-k) - S(t+1-k)\right] \tag{1.16}$$

where A_k is *the expected contribution to the cumulative force of infection over* $]t, t+1]$ *by an individual who itself became infected in the time window* $]t-k, t-k+1]$, k *time steps earlier*[2].

Similarly to the continuous-time case, we define the basic reproduction number when time is seen as a discrete variable:

Definition 2 (Basic reproduction number)**.**

$$R_0 := N \sum_{k=1}^{\infty} A_k. \tag{1.17}$$

Now we will reformulate some of the previous equations in the sense of discrete-time models.

The next equation is the discrete-time version of (1.8).

Proposition 7. *The number of susceptibles at time* t *is given by:*

$$S(t) = \exp\left\{-\sum_{k=1}^{\infty} \hat{\Lambda}(t-k)\right\} N. \tag{1.18}$$

[2]Here $A_0 = 0$ since an individual who was infected in the time window $]t, t+1]$ does not contribute to the cumulative force of infection over $]t, t+1]$.

Proof. First, we iterate (1.2):

$$S(t+1) = e^{-\hat{\Lambda}(t)} S(t) = e^{-\hat{\Lambda}(t)} \underbrace{e^{-\hat{\Lambda}(t-1)} S(t-1)}_{=S(t)} = \left(\prod_{m=0}^{n} e^{-\hat{\Lambda}(t-m)} \right) S(t-n),\ n \in \mathbb{N}_0$$

or

$$S(t+1) = \exp\left\{ -\sum_{m=0}^{n} \hat{\Lambda}(t-m) \right\} S(t-n),\ n \in \mathbb{N}_0 \cdot$$

Now, one needs to justify that the exponent in the second member converges. We start by noting that one wants to take n large enough so that $S(t-n) = N$ and thus it makes sense that $S(t+1) > 0$ (otherwise $S(t) = 0$ for all $t \in \mathbb{R}$, since $\tilde{S} = 0$ is an equilibrium[3] of (1.2)). We rewrite the previous equation as

$$\frac{S(t-n)}{S(t+1)} = \exp\left\{ \sum_{m=0}^{n} \hat{\Lambda}(t-m) \right\}$$

Given that the first member converges when $n \to +\infty$, then the second must converge and, furthermore, the nonnegative series $\sum_{m=0}^{\infty} \hat{\Lambda}(t-m)$ must be convergent. Thus, passing to the limit as $n \to +\infty$ and using $S(-\infty) = N$, one obtains

$$\frac{N}{S(t+1)} = \exp\left\{ \sum_{m=0}^{\infty} \hat{\Lambda}(t-m) \right\} \cdot$$

It follows that

$$S(t+1) = \exp\left\{ -\sum_{m=0}^{\infty} \hat{\Lambda}(t-m) \right\} N$$

and thus, with $k = m+1$,

$$S(t) = \exp\left\{ -\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) \right\} N \cdot$$

□

This lemma will guarantee the convergence of very useful series in this essay[4].

Lemma 3. *Let $t \mapsto \hat{\Lambda}(t)$ be defined by* (1.16)*. Suppose that $\{A_j\}_{j\in\mathbb{N}}$ is a summable collection of nonnegative terms and that $t \mapsto S(t)$ is a nonnegative and nonincreasing function, bounded above by $N > 0$, with $S(-\infty) := \lim_{t\to-\infty} S(t) = N$. Then, for fixed t,*

$$\sum_{k=1}^{m} \hat{\Lambda}(t-k) = \sum_{j=1}^{\infty} A_j \left[S(t-m-j) - S(t-j) \right] \quad \forall m \in \mathbb{N} \cdot \tag{1.19}$$

Furthermore, the sequence $\left\{ \hat{\Lambda}(t-k) \right\}_{k\in\mathbb{N}}$ is summable and its sum is given by

$$\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) = \sum_{j=1}^{\infty} A_j \left[N - S(t-j) \right] \cdot \tag{1.20}$$

[3] $\tilde{x}$ is an equilibrium of $x(t+1) = f(t, x(t))$ if $f(t, \tilde{x}) = \tilde{x}$ for all $t \in \mathbb{R}$.

[4] A very simple proof of the convergence of this series was done while proving proposition 7. Lemma 3 gives an alternative but more complex proof and here we will obtain some useful equations.

Proof. Let t be fixed. To prove equation (1.19), one only needs to use (1.16) and switch the order of summation: for $m \in \mathbb{N}$,

$$\begin{aligned}\sum_{k=1}^{m} \hat{\Lambda}(t-k) &= \sum_{k=1}^{m}\sum_{j=1}^{\infty} A_j \left[S(t-k-j) - S(t-k+1-j)\right] \\ &= \sum_{j=1}^{\infty} A_j \underbrace{\sum_{k=1}^{m} \left[S(t-k-j) - S(t-k-j+1)\right]}_{=S(t-m-j)-S(t-j)} \\ &= \sum_{j=1}^{\infty} A_j \left[S(t-m-j) - S(t-j)\right] \cdot\end{aligned}$$

Let $f_j(m) \coloneqq A_j \left[S(t-m-j) - S(t-j)\right]$ for all $m, j \in \mathbb{N}$. Since $t \mapsto S(t)$ is a nonnegative and nonincreasing function and $A_j \geq 0$ for all $j \in \mathbb{N}$, then $|f_j(m)| \leq N A_j$ for all $m, j \in \mathbb{N}$. Furthermore, since $\{A_j\}_{j\in\mathbb{N}}$ is summable by hypothesis, then

$$\sum_{j=1}^{\infty} N A_j = N \sum_{j=1}^{\infty} A_j < +\infty\cdot$$

Then, by the Weierstrass criterion (theorem 14 in the appendix), $\sum_{j=1}^{\infty} f_j$ converges uniformly in $\mathbb{N}$. Now, uniform convergence implies that

$$\lim_{m\to+\infty} \sum_{j=1}^{\infty} f_j(m) = \sum_{j=1}^{\infty} f_j \left(\lim_{m\to+\infty} m \right)$$

i.e.,

$$\begin{aligned}\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) &\coloneqq \lim_{m\to+\infty} \sum_{k=1}^{m} \hat{\Lambda}(t-k) \\ &= \lim_{m\to+\infty} \sum_{j=1}^{\infty} A_j \left[S(t-m-j) - S(t-j)\right] \\ &= \sum_{j=1}^{\infty} A_j \left[S(-\infty) - S(t-j)\right] \\ &= \sum_{j=1}^{\infty} A_j \left[N - S(t-j)\right] \qquad \text{[since } S(-\infty) = N\text{]}.\end{aligned}$$

Given that $t \mapsto S(t)$ is a nonnegative function, then $N - S(t-j) \leq N$ for every $j \in \mathbb{N}$, and, since $A_j \geq 0$ for all $j \in \mathbb{N}$, it follows that

$$\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) = \sum_{j=1}^{\infty} A_j \left[N - S(t-j)\right] \leq \sum_{j=1}^{\infty} A_j N = N \sum_{j=1}^{\infty} A_j < +\infty,$$

since $\{A_j\}_{j\in\mathbb{N}}$ is summable. We conclude that $\left\{\hat{\Lambda}(t-k)\right\}_{k\in\mathbb{N}}$ is summable. □

Remark 4. One would like to use the previous proof to remark that, for fixed t,

$$\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) \leq R_0 \cdot$$

We use proposition 7 to obtain a recurrence relation for the proportion of susceptibles at time t. First, we define

$$\tilde{A}_k \coloneqq A_k N$$

and we note that (1.17) gives

$$R_0 = \sum_{k=1}^{\infty} \tilde{A}_k \cdot \tag{1.21}$$

The equation in the next proposition is the discrete-time version of (1.15).

Proposition 8. *The proportion of susceptibles at time* t *is given by*

$$s(t) = \exp\left\{ -\sum_{k=1}^{\infty} \tilde{A}_k \left[1 - s(t-k)\right] \right\} \cdot \tag{1.22}$$

Proof. Using equation (1.20) from lemma 3, one gets

$$\sum_{k=1}^{\infty} \hat{\Lambda}(t-k) = \sum_{j=1}^{\infty} A_j \left[N - S(t-j)\right] \cdot$$

Using (1.18), one concludes that the number of susceptibles at time t can be given by

$$S(t) = \exp\left\{ -\sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right] \right\} N \tag{1.23}$$

and its proportion by

$$s(t) = \exp\left\{ -\sum_{k=1}^{\infty} \tilde{A}_k \left[1 - s(t-k)\right] \right\} \cdot$$

□

Before we continue, we would like to give an example where the formula (1.22) is used. Here, we choose a collection $\{\tilde{A}_k\}_{k\in\mathbb{N}}$ with an infinite trail of zeros and we find $s(0)$ given certain conditions in the previous n-th terms, where $n \in \mathbb{N}$ is such that $\tilde{A}_n > 0$ and $\tilde{A}_k = 0$ for $k \in \{n+1, n+2, \ldots\}$. We will see two cases: one where $R_0 < 1$ and the other where $R_0 > 1$.

Example 1. Let $a > 0$ and define[5]

$$\tilde{A}_k \coloneqq \begin{cases} a & \text{if } k \in \{1,2\} \\ 0 & \text{otherwise} \end{cases}$$

[5]The contribution to the force of infection is not expected to be of such form. However, here the only desire is to compare the (quickness of) evolution of (the proportion of) susceptibles when $R_0 < 1$ and when $R_0 > 1$ and so a very simple expression for $\{\tilde{A}_k\}_{k\in\mathbb{N}}$ is chosen.

so that $R_0 = 2a$. Now, equation (1.22) gives, with $t = 0$,

$$s(0) = \exp\left\{-\sum_{k=1}^{\infty} \tilde{A}_k \left[1 - s(-k)\right]\right\} = e^{a[s(-1)+s(-2)-2]}.$$

Therefore it suffices to know the value of $s(-1)+s(-2)$, keeping in mind that this value must be chosen from $[0, 2]$ (since $0 \leq s(t) \leq 1$). For example, let $s(-1) + s(-2) = 1$. Then

$$s(0) = e^{-a}.$$

If $a = \frac{1}{4}$, then $R_0 = \frac{1}{2} < 1$ and

$$s(0) = \frac{1}{\sqrt[4]{e}} \approx 0.779$$

i.e., at time $t = 0$, about 77.9% of the population is susceptible. Now, if $a = 1$, then $R_0 = 2 > 1$ and

$$s(0) = \frac{1}{e} \approx 0.368$$

i.e., at time $t = 0$, about 36.8% of the population is susceptible.

Comparing the cases in the previous example, one can see that the number of susceptibles decreases faster when $R_0 > 1$ then when $R_0 < 1$, as we expected.

Remark 5. We note that, in the previous example, when $a = \frac{1}{4}$ (and $R_0 < 1$), the function $t \mapsto s(t)$ cannot be monotone nonincreasing, otherwise $s(-2) \geq s(-1) \geq s(0)$ and it follows that

$$1 = s(-1) + s(-2) \geq 2s(0) \approx 1.558.$$

Hence, in that case, s does not satisfy the assumptions that were made in section 1.1. Furthermore, this example pushes the following question: when $R_0 < 1$, what solutions satisfy the assumptions that were made initially?

The following theorem answers this question:

Theorem 1. *When $R_0 \leq 1$, the equilibrium $s \equiv 1$ is the (unique) monotone nonincreasing positive solution of equation* (1.22).

Proof. Let $R_0 \leq 1$ and suppose $t \mapsto s(t)$ is a monotone nonincreasing positive solution of (1.22). It follows that

$$s(t - k) \geq s(t) \quad k \in \mathbb{N}$$

and thus, by the nonnegativity of $\{\tilde{A}_k\}_{k\in\mathbb{N}}$,

$$\sum_{k=1}^{\infty} \tilde{A}_k \left[1 - s(t - k)\right] \leq \left[1 - s(t)\right] \sum_{k=1}^{\infty} \tilde{A}_k = R_0 \left[1 - s(t)\right].$$

Hence, since s is a solution of (1.22),

$$s(t) \geq e^{-R_0[1-s(t)]}.$$

Let $g(x) \coloneqq x + e^{-R_0 x}$. Here, we note that

$$g(1 - s(t)) = 1 - s(t) + e^{-R_0[1-s(t)]}$$

and thus

$$s(t) \geq e^{-R_0[1-s(t)]} \iff g(1-s(t)) \leq 1\cdot$$

So we start by looking for the values of x that satisfy $g(x) \leq 1$. We have $g'(x) = 1 - R_0 e^{-R_0 x}$. We would like to remind the reader that R_0 is a positive quantity (see definition (1.6)).
The monotonicity of g can be seen below:

Table 1.2: Monotonicity table for $g(x) = x + e^{-R_0 x}$.

x	$-\infty$	$\frac{\ln R_0}{R_0}$	$+\infty$
g	$\searrow$	$\frac{1+\ln R_0}{R_0}$	$\nearrow$
g'	$-$	0	$+$

If $R_0 = 1$, then $g(0) = 1$, g is strictly decreasing in $]-\infty, 0[$ and strictly increasing in $]0, +\infty[$. Thus $x = 0$ is the only solution of the inequality $g(x) \leq 1$.
If $R_0 < 1$, then $\frac{\ln R_0}{R_0} < 0$ and $g\left(\frac{\ln R_0}{R_0}\right) = \frac{1+\ln R_0}{R_0} < 1$ (we have seen in the proof of proposition 6 that $1 + \ln R_0 < R_0$ whenever $R_0 \neq 1$). Since $g(0) = 1$ and g is strictly increasing in $]0, +\infty[$, we conclude that $x = 0$ is the only nonnegative solution of the inequality $g(x) \leq 1$.
Now, we are looking for $s(t) \in [0, 1]$ such that $g(1 - s(t)) \leq 1$. Notice that $1 - s(t) \in [0, 1]$. We conclude that $s \equiv 1$ is the only monotone nonincreasing positive solution of equation (1.22).

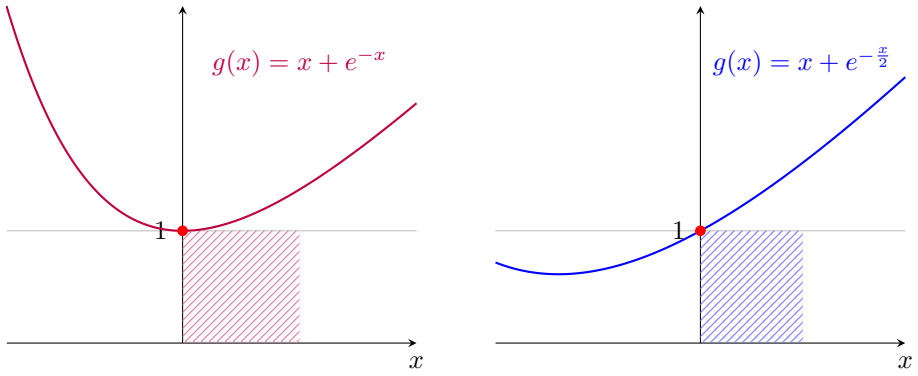

Fig. 1.3. Graph of $g(x) = x + e^{-R_0 x}$ when $R_0 = 1$ (left) and when $R_0 = \frac{1}{2} < 1$ (right).

□

Corollary 1. *If the disease generates permanent immunity and the host population is demographically closed, then equation* (1.2) *has the unique solution* $S \equiv N$ *whenever* $R_0 \leq 1$.

The next proposition gives a recurrence relation to the proportion of susceptibles:

Proposition 9. *The proportion of susceptibles satisfies:*

$$s(t+1) = s(t) \exp\left\{-\sum_{k=1}^{\infty} \tilde{A}_k \left[s(t-k) - s(t-k+1)\right]\right\}. \tag{1.24}$$

Proof. The result follows immediately by plugging (1.22) into the second side of equation (1.24). □

Remark 6. We note that, for each $k \in \mathbb{N}$, the difference $s(t-k) - s(t-k+1)$ is exactly the proportion of new cases over the time window $]t-k, t-k+1]$.

The main advantage of the equation (1.24) is that "one can provide an initial condition, say, at time 0, by prescribing $s(0)$ and the (nonnegative) incidences $\ldots, s(-3)-s(-2), s(-2)-s(-1), s(-1)-s(0)$". Furthermore, if $\tilde{A}_k = 0$ when $k > K$ (for a certain $K \in \mathbb{N}$), then it suffices to prescribe $s(0)$ and $s(-K) - s(-K+1), \ldots, s(-1) - s(0)$, so only a finite number of prescriptions.

In conclusion, one can obtain a discrete-time Kermack-McKendrick epidemic model, with a countably infinite parameter[6] $\{A_k\}_{k\in\mathbb{N}}$, by considering either equation (1.22) or equation (1.24).

To end this section, we give an example to illustrate the use of equation (1.24)

Example 2. Define

$$\tilde{A}_k := \begin{cases} \ln 2 & \text{if } k \in \{1, 2\} \\ 0 & \text{otherwise} \end{cases}.$$

Then, for each t, formula (1.24) gives

$$s(t+1) = \frac{s(t)}{2^{[s(t-1)-s(t)]+[s(t-2)-s(t-1)]}}.$$

Therefore, if one wishes to find the value of $s(k)$ for each $k \in \mathbb{N}$, it suffices to prescribe $s(0)$ and the incidences $s(-2) - s(-1)$ and $s(-1) - s(0)$. Suppose

$$s(0) = \frac{1}{4}, \qquad s(-2) - s(-1) = \frac{1}{4}, \qquad s(-1) - s(0) = \frac{1}{4}.$$

Finally one can obtain $s(1), s(2), \cdots$ using formula (1.24):

$$\begin{aligned} s(1) &= \frac{1}{4 \times 2^{\frac{1}{2}}} = \frac{\sqrt{2}}{8} \approx 0.177 \\ s(2) &= \frac{\sqrt{2}}{8 \times 2^{\frac{1}{2}-\frac{\sqrt{2}}{8}}} = \frac{2^{\frac{\sqrt{2}}{8}}}{8} \approx 0.141 \\ &\vdots \end{aligned}$$

One notes that, in this case,

$$R_0 = 2 \ln 2 > 1.$$

1.3 The Initial Phase and the Final Size

Firstly, we would like to define the term *demographic stochasticity*:

Definition 3 (Demographic stochasticity)**.** The size of a population is subject to random variations, since the birth and death of any individual is a discrete and probabilistic event. Such random variations are described by *demographic stochasticity*.

[6] One notes that, in practice, an individual does not remain infectious for an infinite period of time. Therefore it makes sense that the collection $\{A_k\}_{k\in\mathbb{N}}$ is in fact a finite parameter with an infinite trail of zeros.

In a host population where an infectious disease was just introduced, the demographic stochasticity is captured with the use of branching processes. However, once the number of infected individuals is large enough, a deterministic description can be used. Nevertheless, this large number may "still constitute only a rather small fraction of a very large host population". In this last situation, we may take $x(t)$ as the proportion of individuals that are not susceptible at time t and consider it small enough that it makes sense to replace e^x by $1+x$ (its 1st degree Taylor polynomial). Then, if we write $s(t) = 1 - x(t)$, where $s(t)$ is the proportion of individuals that have escaped infection up to time t, equation (1.22) gives

$$1 - x(t) = e^{-\sum_{k=1}^{\infty} \tilde{A}_k x(t-k)} \tag{1.25}$$

and, since $x(t)$ is assumed to be small enough, then $\sum_{k=1}^{\infty} \tilde{A}_k x(t-k)$ may be assumed to be small enough, because $\{\tilde{A}_k\}_{k\in\mathbb{N}}$ is summable and each $x(t-k)$ is even smaller than $x(t)$. The second member of (1.25) can be replaced by $1 - \sum_{k=1}^{\infty} \tilde{A}_k x(t-k)$ and one gets the relation

$$x(t) = \sum_{k=1}^{\infty} \tilde{A}_k x(t-k)\cdot \tag{1.26}$$

Before we continue, we give two important remarks about the numbers $\{A_k\}_{k\in\mathbb{N}}$, and thus about the numbers $\{\tilde{A}_k\}_{k\in\mathbb{N}}$:

Remark 7. It is quite obvious that, in the presence of an infectious disease, there is $j \in \mathbb{N}$ such that $A_j > 0$, and thus $\tilde{A}_j > 0$, otherwise the total contribution to the force of infection would be 0 and therefore we would not be in presence of an infectious disease.

Remark 8. It makes sense that $A_k = 0$, and thus $\tilde{A}_k = 0$, for large $k \in \mathbb{N}$, given that an individual who itself was infected in $]t-k, t-k+1]$ (interval in the "infinite past") does not contribute to the force of infection over $]t, t+1]$ (interval in the "present").

The objective now is to show that positive solutions of the equation (1.26) grow when $R_0 > 1$ but decrease when $R_0 < 1$. We start by looking for solutions of the form

$$x(t) = \lambda^t \tag{1.27}$$

where $\lambda > 0$. Plugging (1.27) into (1.26), one gets

$$\lambda^t = \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{t-k} = \lambda^t \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k}$$

or

$$1 = \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k}. \tag{1.28}$$

Therefore x defined by (1.27) is a solution of (1.26) if and only if λ is a real positive solution of the characteristic equation (1.28), known as the **Euler-Lotka** equation. The following theorem gives a top bound for the number of positive real solutions of the Euler-Lotka equation (1.28):

Theorem 2. *The Euler-Lotka equation* (1.28) *has at most one positive real solution.*

Proof. Let $f : \mathcal{D}_f \subseteq \mathbb{R}^+ \to \mathbb{R}$ be defined by $f(\lambda) := \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k}$, where $\mathcal{D}_f$ is the maximal subset where the series converges.

Notice that λ is a solution of (1.28) if and only if $f(\lambda) = 1$. Now, f is a strictly monotonically decreasing function, since, for all $\lambda, \mu \in \mathcal{D}_f$,

$$\mu < \lambda \implies \mu^{-k} > \lambda^{-k} \quad \forall k \in \mathbb{N} \implies f(\mu) > f(\lambda),$$

where the last implication is due to the fact that, with our assumptions, $\tilde{A}_k \geq 0$ forall $k \in \mathbb{N}$ with at least one $j \in \mathbb{N}$ such that $\tilde{A}_j > 0$.
Since f is a monotonically strictly decreasing function, the equation $f(\lambda) = 1$ has at most one solution. Therefore we conclude that the Euler-Lotka equation (1.28) has at most one positive real solution. □

The previous theorem guarantees uniqueness of positive real solution (if existent) for the Euler-Lotka equation (1.28). The next theorem guarantees existence of a positive real solution whenever $R_0 \geq 1$ and, given certain conditions in the parameters $\tilde{A}_k$ ($k \in \mathbb{N}$), when $R_0 < 1$.

Theorem 3. *If $R_0 \geq 1$, the Euler-Lotka equation given by* (1.28) *has an unique positive real solution, situated in* $[1, +\infty[$. *In the case $R_0 < 1$,* (1.28) *has an unique positive real solution, situated in* $]0, 1[$, *if* $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ *is a finite set.*

Proof. Let $f : \mathcal{D}_f \subseteq \mathbb{R}^+ \to \mathbb{R}$ be defined by $f(\lambda) \coloneqq \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k}$ as in the proof of the previous theorem. Again, notice that λ is a solution of (1.28) if and only if $f(\lambda) = 1$, and that f is a monotone decreasing function. Furthermore, the domain $\mathcal{D}_f$ contains the interval $[1, +\infty[$ (by comparison with the convergent series (1.21)) and

$$f(1) = \sum_{k=1}^{\infty} \tilde{A}_k = R_0$$

(clearly $\tilde{\rho} = 1$ is a solution of (1.28) if $R_0 = 1$) and

$$\lim_{\lambda \to +\infty} f(\lambda) = f\left(\lim_{\lambda \to +\infty} \lambda\right) = \sum_{k=1}^{\infty} \tilde{A}_k \left(\lim_{\lambda \to +\infty} \lambda\right)^{-k} = 0,$$

where the first equality follows from continuity of f on $[1, +\infty[$ (f is defined by an uniformly convergent series on $[1, +\infty[$: apply the Weierstrass criterion — theorem 14 (in the appendix) — to the sequence of functions $f_k(\lambda) \coloneqq \tilde{A}_k \lambda^{-k}$ defined on $[1, +\infty[$). Furthermore, by the intermediate value theorem (theorem 11 in the appendix), if there is $\mu \in [1, +\infty[$ such that $1 < f(\mu) < +\infty$, then there is $\tilde{\rho} > \mu$ such that $f(\tilde{\rho}) = 1$. In particular, if $R_0 > 1$, then there is $\tilde{\rho} > 1$ such that $f(\tilde{\rho}) = 1$.
Now suppose that $R_0 < 1$ and that $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is a finite set, say $\{k_1, \cdots, k_n\}$, where $k_1, \cdots, k_n \in \mathbb{N}$, then

$$f(\lambda) = \sum_{j=1}^{n} \tilde{A}_{k_j} \lambda^{-k_j}$$

which is clearly continuous in $\mathbb{R}^+$ and

$$\lim_{\lambda \to 0^+} f(\lambda) = \lim_{\lambda \to 0^+} \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k} = \lim_{\lambda \to 0^+} \sum_{j=1}^{n} \tilde{A}_{k_j} \lambda^{-k_j} = \sum_{j=1}^{n} \tilde{A}_{k_j} \lim_{\lambda \to 0^+} \lambda^{-k_j} = +\infty,$$

thus there is $\tilde{\rho} \in]0, 1[$ such that $f(\tilde{\rho}) = 1$.
The uniqueness part now follows from theorem 2. □

We now give a remark about the collection $\{\tilde{A}_k\}_{k \in \mathbb{N}}$ that will allow us to answer to the following question: what if $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is not a finite set? We keep the notation used in the proof (of

theorem 3).

Remark 9. If $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is not a finite set, then one can consider the subsequence $\{\tilde{A}_{k_j}\}_{j\in\mathbb{N}}$ of all the positive numbers of $\{\tilde{A}_k\}_{k\in\mathbb{N}}$ and thus, in this case,

$$f(\lambda) = \sum_{j=1}^{\infty} \tilde{A}_{k_j} \lambda^{-k_j}.$$

By comparison with the convergent series $\sum_{j=1}^{\infty} \tilde{A}_{k_j} =: R_0$, one has that the series above converges on $[1, +\infty[$. However, this series might not converge on $]0, 1[$.
Take for example $\tilde{A}_k$ with power-like behaviour for $k > K$ (for some $K \in \mathbb{N}$), i.e., $\tilde{A}_k = k^{\varepsilon}$ for some ε whenever $k > K$. Now,

i) $\sum_{k=1}^{\infty} A_k < +\infty \implies \sum_{k=1}^{\infty} \tilde{A}_k < +\infty \implies \sum_{k=K}^{\infty} k^{\varepsilon} < +\infty \implies \varepsilon < -1$;

ii) with $\nu = -\varepsilon > 1$, then

$$f(\lambda) = \sum_{k=1}^{K} \tilde{A}_k \lambda^{-k} + \sum_{k>K} k^{-\nu} \lambda^{-k}$$

that converges if and only if the $\sum_{k>K} k^{-\nu}\lambda^{-k}$ converges;

iii) the ratio test

$$\left| \frac{(k+1)^{-\nu}\lambda^{-(k+1)}}{k^{-\nu}\lambda^{-k}} \right| = \left(\frac{k}{k+1} \right)^{\nu} \frac{1}{\lambda} \xrightarrow[k\to+\infty]{} \frac{1}{\lambda}$$

guarantees that the last series converges if $\lambda > 1$ and diverges if $\lambda < 1$;

iv) if $\lambda = 1$, the series converges by hypothesis.

We can thus conclude, for $\tilde{A}_k$ with power-like behaviour for $k > K$, our function $f(\lambda)$ converges if and only if $\lambda \geq 1$ (and f is at infinity when $\lambda < 1$). This means that f jumps from infinity to $f(1) = R_0$ at $\lambda = 1$. Furthermore, if $R_0 < 1$, we conclude that f jumps from infinity to a value less than one and f is not continuous, so one does not have existence of $\tilde{\rho} \in \mathbb{R}^+$ such that $f(\tilde{\rho}) = 1$.
We conclude that, when $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is not a finite set, f might not be continuous and so it is possible that $f(\lambda) = 1$ has no root.

Before we continue, an example where $R_0 < 1$ and $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is not finite, but there is in fact a solution of $f(\lambda) = 1$, seems appropriate.

Example 3. Define

$$\tilde{A}_k := \begin{cases} 3^{-k} & \text{if } k \text{ is even} \\ 2^{-k} & \text{if } k \text{ is odd} \end{cases}.$$

Then $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\} = \mathbb{N}$, which is clearly not a finite set. On the other hand,

$$\begin{aligned} R_0 &:= \sum_{k=1}^{\infty} \tilde{A}_k \\ &= \sum_{m=1}^{\infty} 3^{-(2m)} + \sum_{m=1}^{\infty} 2^{-(2m-1)} \end{aligned}$$

$$
\begin{aligned}
&= \sum_{m=1}^{\infty} \left(\frac{1}{9}\right)^m + 2\sum_{m=1}^{\infty} \left(\frac{1}{4}\right)^m \\
&= \frac{1}{9-1} + \frac{2}{4-1} \quad \text{[two geometric series with ratio } 0 < r < 1\text{]} \\
&= \frac{19}{24}
\end{aligned}
$$

and thus $R_0 < 1$. Now,

$$
\begin{aligned}
f(\lambda) &= \sum_{k=1}^{\infty} \tilde{A}_k \lambda^{-k} \\
&= \sum_{m=1}^{\infty} (3\lambda)^{-(2m)} + \sum_{m=1}^{\infty} (2\lambda)^{-(2m-1)} \\
&= \sum_{m=1}^{\infty} \left(\frac{1}{9\lambda^2}\right)^m + 2\lambda \sum_{m=1}^{\infty} \left(\frac{1}{4\lambda^2}\right)^m
\end{aligned}
$$

and thus f is a sum of two geometric series. The first serie converges if and only if $\frac{1}{9\lambda^2} < 1$ while the second converges if and only if $\frac{1}{4\lambda^2} < 1$. Since both series have a positive ratio, then f converges if and only if both series converge and thus if and only if $\lambda > \frac{1}{2}$. In that case,

$$
f(\lambda) = \frac{1}{9\lambda^2 - 1} + \frac{2\lambda}{4\lambda^2 - 1}\cdot
$$

f is clearly continuous in $\left]\frac{1}{2}, +\infty\right[$ and one has

$$
\lim_{\lambda \to \frac{1}{2}^+} f(\lambda) = +\infty \quad \text{and} \quad f(1) = R_0 < 1\cdot
$$

By the intermediate value theorem (theorem 11 in the appendix), there is $\tilde{\rho} \in \left]\frac{1}{2}, 1\right[$ such that $f(\tilde{\rho}) = 1$. By means of a calculator, one sees that the equation

$$
\frac{1}{9\lambda^2 - 1} + \frac{2\lambda}{4\lambda^2 - 1} = 1
$$

has two real solutions: $\lambda_1 \approx 0.386$ and $\lambda_2 \approx 0.883$. Given that f is defined only in $\left]\frac{1}{2}, +\infty\right[$, one concludes that the (unique) root of $f(\lambda) = 1$ has value $\tilde{\rho} \approx 0.883$.

In what follows, we will assume $\{k \in \mathbb{N} : \tilde{A}_k \neq 0\}$ is a finite set (see remark 8). Then the root $\tilde{\rho}$ of the Euler-Lotka equation (1.28) always exists and it satisfies

$$
\operatorname{sign}(\tilde{\rho} - 1) = \operatorname{sign}(R_0 - 1), \text{ where } \operatorname{sign}\nu = \begin{cases} -1 & \text{if } \nu < 0 \\ 1 & \text{if } \nu > 0 \end{cases}\cdot
$$

Theorem 4. *The equilibrium $s(t) \equiv 1$ of (1.22) is unstable when $R_0 > 1$ and asymptotically stable when $R_0 < 1$.*

Proof. We know, from general linear theory, that positive solutions $x(t) = x_0\tilde{\rho}^t$ of (1.26) grow geometrically with rate $\tilde{\rho}$ when $\tilde{\rho} > 1$ but decline with rate $\tilde{\rho}$ when $\tilde{\rho} < 1$. General nonlinear theory guarantees that the equilibrium (steady solution) $x(t) \equiv 0$ of (1.25) is unstable for $\tilde{\rho} > 1$ (and $R_0 > 1$) but asymptotically stable for $\tilde{\rho} < 1$ (and $R_0 < 1$). The result follows. □

Now, since $s(t)$ is a bounded ($s(t) \in [0, 1] \quad \forall t \in \mathbb{R}$) and monotone nonincreasing function, then

it has a limit for $t \to \infty$. Let $s(\infty)$ denote this limit. Passing (1.22) to the limit and using (1.21), one obtains:

$$s(\infty) = e^{-R_0(1-s(\infty))}. \tag{1.29}$$

Let us study further the case when $R_0 > 1$. For that, the study of the number of fixed points[7] of a given function is a good tool:

Theorem 5. *Let $g : \mathbb{R} \to \mathbb{R}$ be a differentiable and monotonically increasing function. Furthermore, assume g is strictly concave (i.e., g' is strictly monotonically decreasing) and satisfies*

$$g(0) = 0, \quad g(1) < 1\cdot$$

Then g has no fixed points in $]0, 1[$ if $g'(0) \leq 1$ and g has an unique fixed point in $]0, 1[$ if $g'(0) > 1$.

Proof. We start by assuming that $g'(0) \leq 1$. Since g' is strictly monotonically decreasing, then $g'(x) < 1$ if $x \in]0, 1]$. Now, given that $g(0) = 0$, then $g(x) < x$ if $x \in]0, 1]$ and thus g has no fixed points in $]0, 1[$. Conversely, suppose $g'(0) > 1$. We start by noting that, since g is continuous and $g(1) < 1$, then there is $b \in]0, 1]$ (sufficiently large) such that $g(b) < b$.
Now,

$$\lim_{x\to 0} \frac{g(x)}{x} = \lim_{x\to 0} \frac{g(x) - g(0)}{x - 0} = g'(0) > 1$$

and, by definition of limit, there is $a \in]0, 1[$ (sufficiently small) such that $\frac{g(a)}{a} > 1$, i.e., $g(a) > a$.
We can assume that $a < b$. Furthermore, since $g(a) > a$ and $g(b) < b$, the intermediate value theorem (theorem 11 in the appendix) applied to the function $x \mapsto g(x) - x$ over the interval $[a, b]$ guarantees that there is $z \in]a, b[$ such that $g(z) = z$, i.e., g has a fixed point z in $]a, b[$.
To prove uniqueness of fixed point in $]0, 1[$, suppose to the contrary that g has more than one fixed point in $]0, 1[$.
It is obvious that g cannot have a semi-line $[a, b]$ $(a < b)$ of fixed points, since that would imply $g(x) = x$ whenever $x \in [a, b]$, from where $g' = 1$ in $]a, b[$ and g is not strictly concave, contradicting our hypothesis.
Now, let z_1 and z_2 be two consecutive fixed points in $]0, 1[$, with $z_1 < z_2$. By the mean value theorem (theorem 10 in the appendix), there is $c \in]z_1, z_2[$ such that

$$g'(c) = \frac{g(z_2) - g(z_1)}{z_2 - z_1} = \frac{z_2 - z_1}{z_2 - z_1} = 1\cdot$$

The mean value theorem also guarantees the existence of $z_0 \in]0, z_1[$ such that

$$g'(z_0) = \frac{g(z_1) - g(0)}{z_1 - 0} = \frac{z_1 - 0}{z_1 - 0} = 1\cdot$$

Hence $g'(z_0) = 1 = g'(c)$ and, since g' is strictly decreasing, one must have $z_0 = c$, an absurd because $z_0 < z_1 < c$. We conclude that there is at most one fixed point of g in $]0, 1[$.
g has an unique fixed point in $]0, 1[$. □

We are finally ready to give the final result of this section:

Proposition 10. *Equation* (1.29) *has an unique solution $s(\infty)$ in $]0, 1[$ when $R_0 > 1$.*

Proof. Let $x(\infty) \coloneqq 1 - s(\infty)$. Then (1.29) can be rewritten as

$$1 - e^{-R_0 x(\infty)} = x(\infty) \tag{1.30}$$

[7] z is said to be a fixed point of a function g if $g(z) = z$.

and the problem is now to find the fixed points of $g(x) \coloneqq 1 - e^{-R_0 x}$. Given that g is a differentiable, monotonically increasing and strictly concave function satisfying

$$g'(0) = R_0 > 1 \qquad g(0) = 0 \qquad g(1) = 1 - e^{-R_0} < 1,$$

then, by theorem 5, g has an unique fixed point in $]0, 1[$.

Therefore we conclude that equation (1.29) has an unique solution $s(\infty)$ in $]0, 1[$ when $R_0 > 1$. □

We end this section with the graph of the final size $1 - s(\infty)$ as a function of the basic reproduction number R_0 (adapted from [Diekmann et al., 2021]):

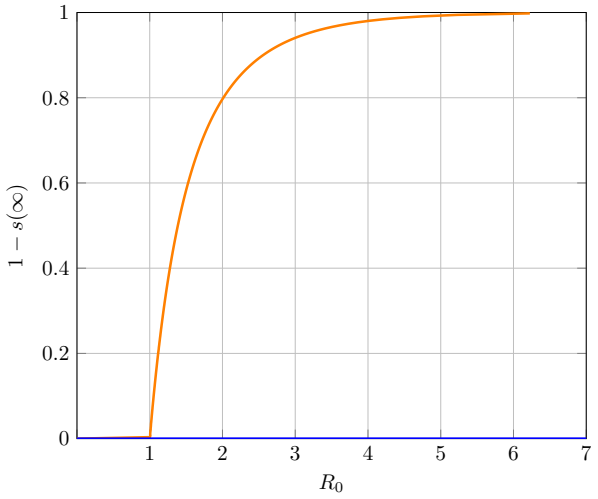

Fig. 1.4. Graph of the final size $1 - s(\infty)$ as a function of the basic reproduction number R_0 (orange), defined for $R_0 > 1$, and solution $s(\infty) = 1$ (blue), defined for $R_0 > 0$.

We explain how the graph 1.4 was obtained in the following remark:

Remark 10. When $R_0 \leq 1$, corollary 1 guarantees that $s \equiv 1$ is the only solution and thus $s(\infty) = 1$, and $1 - s(\infty) = 0$. Suppose now that $R_0 > 1$. Now $s(\infty) \equiv 1$ is a solution, but we will see that it is not unique. After some algebraic manipulations, equation (1.30) can be transformed into

$$R_0 = -\frac{\ln\left(1 - x(\infty)\right)}{x(\infty)} \tag{1.31}$$

where $x(\infty) \coloneqq 1 - s(\infty)$ is assumed to be positive. Therefore R_0 can be seen as a function of $x(\infty)$ (with domain $]0, 1[$). Let

$$g(x) \coloneqq -\frac{\ln(1-x)}{x},$$

with domain $]0, 1[$. Now,

$$\lim_{x \to 0^+} g(x) = -\lim_{x \to 0} \frac{\ln(1-x) - \ln(1-0)}{x - 0} = -\frac{d}{dx}\left(\ln(1-x)\right)\Big|_{x=0} = -\frac{-1}{1-x}\Big|_{x=0} = 1$$

and

$$\lim_{x \to 1^-} g(x) = -\lim_{x \to 1^-} \frac{\ln(1-x)}{x} = +\infty.$$

Furthermore,

$$g'(x) = \frac{\frac{x}{1-x} + \ln(1-x)}{x^2} = \frac{\frac{x}{1-x} - \ln\left(\frac{1}{1-x}\right)}{x^2} > 0,$$

since

$$\ln\left(\frac{1}{1-x}\right) < \frac{1}{1-x} - 1 = \frac{x}{1-x}$$

(we have already seen that $1 + \ln y < y$ whenever $y \in]0, +\infty[\setminus\{1\}$). Therefore g is a strictly increasing function.
The graph of the function given by (1.31) is thus given by:

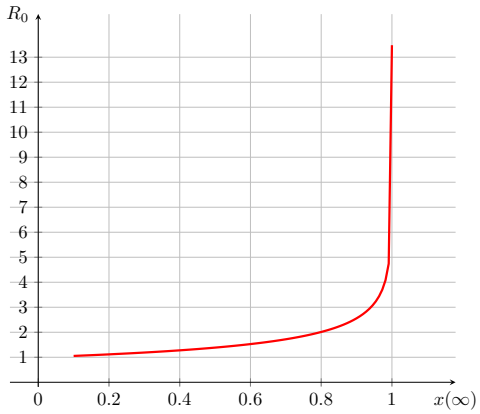

Fig. 1.5. Graph of R_0 as a function of $x(\infty)$, given by (1.31).

As we can see from this graph, the function $x(\infty) \mapsto R_0(x(\infty))$ given by (1.31) is bijective and thus invertible. The inverse is shown in the graph below:

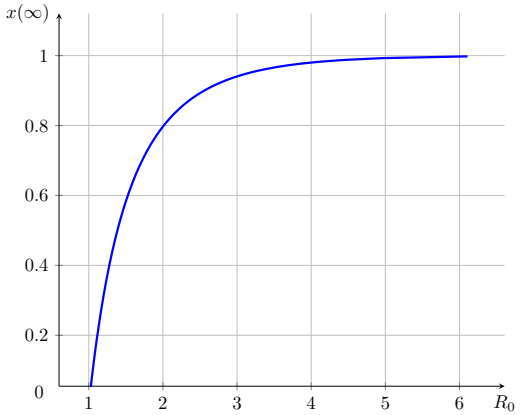

Fig. 1.6. Graph of $x(\infty)$ as a function of R_0, given by (1.30).

The sketch of figure 1.4 is now immediate.

1.4 Compartmental Formulation for Some Very Special Cases

The next step is to study some important epidemiological models: the compartmental SIR and SEIR models. The objective here is to unravel the "pattern of how to construct discrete-time models" in the setting of compartmental models.

As usual,

- S denotes the compartment of susceptible individuals;
- E denotes the compartment of exposed (infected but not yet infectious) individuals;
- I denotes the compartment of infectious individuals;
- R denotes the compartment of recovered/removed individuals.

The notation used for the number of individuals in a certain compartment is the same as for the respective compartment.

We introduce the continuous-time setting and then we move to the study of the discrete-time setting. In each setting, the first model to be studied is the SIR model since this one is simpler than the SEIR model and therefore its study is a good introduction to the study of compartmental models.

The SIR compartmental model: continuous-time setting

We make the following assumptions:

i. upon infection, individuals are transferred from the compartment S of susceptible individuals to the compartment I of infectious individuals (at a certain rate);
ii. Infectious individuals are "removed" (i.e., lose infectiousness) to compartment R of removed individuals at a rate $\alpha > 0$;
iii. the force of infection equals $\Lambda := \beta I$, i.e., $\beta > 0$ is the per capita contribution to the force of infection;
iv. immunity is permanent (and resurrection impossible).

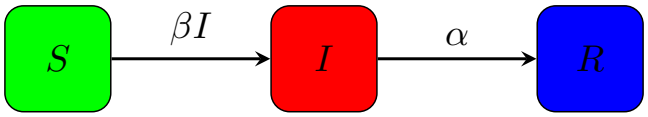

Fig. 1.7. SIR compartmental model (in the continuous-time setting) with force of infection βI and where the length of the infectious period is exponentially distributed with parameter α. Here, the host population is assumed to be demographically closed and, in particular, births and deaths (not due to the disease) are ignored.

These assumptions lead to the system of recurrence relations:

$$\begin{cases} \dfrac{dS}{dt} = -\beta IS \\ \dfrac{dI}{dt} = \beta IS - \alpha I \\ \dfrac{dR}{dt} = \alpha I \end{cases} . \tag{1.32}$$

Remark 11. Adding all equations of (1.32), we see that

$$\frac{d}{dt}\left(S + I + R\right)(t) = \frac{dS}{dt}(t) + \frac{dI}{dt}(t) + \frac{dR}{dt}(t) = 0 \quad (\forall t \in \mathbb{R})$$

and, in particular, the population size remains constant over time:

$$S(t) + I(t) + R(t) = N \quad (\forall t \in \mathbb{R})$$

where N is the population size.

Now we calculate the expected contribution $A(\tau)$ to the force of infection by an individual with age of infection τ:

Proposition 11. *The expected contribution to the force of infection by an individual with age of infection τ is given by*

$$A(\tau) = \beta e^{-\alpha\tau}. \tag{1.33}$$

Proof. Let $P_I(\tau)$ denote the probability to be in the infectious state at time τ after infection. In other words, $P_I(\tau)$ is the proportion of individuals in the population that stay infectious at time τ after infection. Furthermore β is the per capita contribution to the force of infection. Therefore one individual is expected to contribute with

$$A(\tau) = \beta P_I(\tau)$$

units to the force of infection at time τ after infection. Now, it is clear that $P_I(0) = 1$. On the other hand, since α is the rate at which individuals leave the infectious state, then P_I satisfies the Cauchy problem

$$\frac{dP_I}{d\tau} = -\alpha P_I, \quad P_I(0) = 1.$$

Easily we obtain

$$P_I(\tau) = e^{-\alpha\tau}.$$

In conclusion, the expected per capita contribution to the force of infection is given by (1.33). □

Next, we determine the value R_0.

Proposition 12. *The basic reproduction number for the SIR compartmental model* (1.32) *is given by*

$$R_0 = \frac{\beta N}{\alpha}.$$

Proof. By plugging (1.33) into definition (1.6), we obtain

$$R_0 = N \int_0^\infty \beta e^{-\alpha\tau}\, d\tau = \frac{\beta N}{\alpha}.$$

□

The SEIR compartmental model: continuous-time setting

Here, some changes in the assumptions are needed: upon infection, an individual moves from the compartment S of susceptible individuals to the compartment E of exposed (i.e. infected but not yet infectious) individuals. Individuals leave the compartment E and go to the compartment I of infectious individuals at a rate $\gamma > 0$.

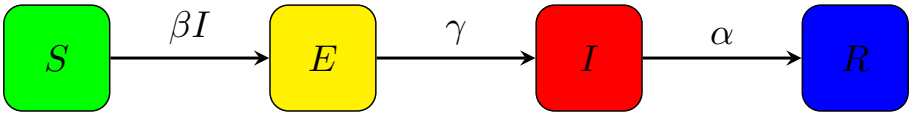

Fig. 1.8. SEIR compartmental model (in the continuous-time setting) with force of infection βI and where the lengths of the latent and infectious periods are exponentially distributed with parameters γ and α, respectively. Here, the host population is assumed to be demographically closed and, in particular, births and deaths (not due to the disease) are ignored.

Now the system is

$$\begin{cases} \dfrac{dS}{dt} = -\beta IS \\ \dfrac{dE}{dt} = \beta IS - \gamma E \\ \dfrac{dI}{dt} = \gamma E - \alpha I \\ \dfrac{dR}{dt} = \alpha I \end{cases} . \tag{1.34}$$

Remark 12. Once again, by adding all equations of (1.34), we note that

$$S(t) + E(t) + I(t) + R(t) = N \quad (\forall t \in \mathbb{R}) \cdot$$

Now we calculate the expected contribution $A(\tau)$ to the force of infection by an individual with age of infection τ:

Proposition 13. *The expected contribution to the force of infection by an individual with age of infection τ is given by*

$$A(\tau) = \begin{cases} \beta\alpha\tau e^{-\alpha\tau} & \text{if } \gamma = \alpha \\ \beta\dfrac{\gamma}{\gamma-\alpha}\left(e^{-\alpha\tau} - e^{-\gamma\tau}\right) & \text{otherwise} \end{cases} . \tag{1.35}$$

Proof. Let $P_E(\tau)$ and $P_I(\tau)$ denote, respectively, the probability to be in the latent state and the probability to be in the infectious state, at time τ after infection. In other words, $P_E(\tau)$ is the proportion of individuals in the population that are infected but not yet infectious at time τ after infection while $P_I(\tau)$ is the proportion of individuals in the population that are infectious at time τ after infection. Furthermore β is the per capita contribution to the force of infection. Therefore one individual is expected to contribute with

$$A(\tau) = \beta P_I(\tau)$$

units to the force of infection at time τ after infection. One notes that this expression was also used in the study of the SIR model. Now, in this case, $P_E(0) = 1$ and $P_I(0) = 0$. On the other hand, since γ is the rate at which individuals leave the exposed state and move to the infectious state, and α is the rate at which individuals leave the infectious state, then (P_E, P_I) satisfies the Cauchy problem

$$\begin{cases} \dfrac{dP_E}{d\tau} = -\gamma P_E, \quad P_E(0) = 1 \\ \dfrac{dP_I}{d\tau} = \gamma P_E - \alpha P_I, \quad P_I(0) = 0 \end{cases} .$$

Easily we obtain

$$P_E(\tau) = e^{-\gamma\tau}.$$

Plugging this expression into the other equation and multiplying by $e^{\alpha\tau}$, we obtain

$$\frac{d}{d\tau}\left(e^{\alpha\tau}P_I(\tau)\right) = \gamma e^{(\alpha-\gamma)\tau}.$$

It follows that

$$P_I(\tau) = e^{-\alpha\tau}\int_0^\tau \gamma e^{(\alpha-\gamma)\nu}\,d\nu = \begin{cases} \alpha\tau e^{-\alpha\tau} & \text{if } \gamma = \alpha \\ \dfrac{\gamma}{\gamma-\alpha}\left(e^{-\alpha\tau} - e^{-\gamma\tau}\right) & \text{otherwise} \end{cases} .$$

In conclusion, the expected per capita contribution to the force of infection is given by (1.35). □

Next, we determine the value R_0.

Proposition 14. *The basic reproduction number for the SEIR compartmental model* (1.34) *is given by*

$$R_0 = \frac{\beta N}{\alpha}.$$

Proof. We separate the proof in cases:

Case 1 Suppose $\gamma = \alpha$. By plugging (1.35) into (1.6), we obtain

$$R_0 = N \int_0^\infty \beta \alpha \tau e^{-\alpha\tau}\, d\tau = \beta N \left[-\tau e^{-\alpha\tau}\Big|_0^\infty + \int_0^\infty e^{-\alpha\tau}\, d\tau \right] = \frac{\beta N}{\alpha}.$$

Case 2 Suppose now that $\gamma \neq \alpha$. By plugging (1.35) into (1.6), we obtain

$$R_0 = N \int_0^\infty \beta \frac{\gamma}{\gamma - \alpha} \left(e^{-\alpha\tau} - e^{-\gamma\tau} \right) d\tau = \frac{\beta\gamma N}{\gamma - \alpha} \left(\frac{1}{\alpha} - \frac{1}{\gamma} \right) = \frac{\beta N}{\alpha}.$$

We conclude that R_0 is given by

$$R_0 = \frac{\beta N}{\alpha}.$$

□

Remark 13. The SIR and SEIR models given by (1.32) and (1.34), respectively, have the same R_0. If one thinks about this, it does not come as a surprise:

- if c is the average number of contacts of an infectious individual (generating the disease) and t_I is the average infectious period, then one infectious individual (in compartment I) in an all susceptible population is expected to infect c individuals per unit of time it is infectious, i.e., ct_I individuals in total;
- given that β is the per capita contribution to the force of infection and N the total size of the population, the infectious individual is expected to have $c = \beta N$ contacts that generate the disease;
- the average infectious period is equal to $t_I = \frac{1}{\alpha}$.

In conclusion, R_0 is not influenced by a latent compartment. In fact, by the definition of basic reproduction number, there are no individuals in compartment E when one does the calculation for R_0.

The SIR compartmental model: discrete-time setting

We make the following assumptions:

i. upon infection, an individual is transferred from the compartment S of susceptible individuals to the compartment I of infectious individuals (with a certain probability);
ii. in each time step, this infectious individual stays in compartment I with probability $1 - \alpha$ while being "removed" (i.e., losing infectiousness) to compartment R of removed individuals with probability $\alpha > 0$;
iii. the cumulative force of infection equals $\hat{\Lambda} := \beta I$, i.e., $\beta > 0$ is the per capita contribution to the force of infection, and thus $e^{-\hat{\Lambda}(t)}$ gives the fraction of those susceptible at time t that escape infection until after time $t + 1$ ($1 - e^{-\hat{\Lambda}(t)}$ will thus give the fraction of those susceptible at time t that become infected until time $t + 1$);
iv. immunity is permanent (and resurrection impossible).

Remark 14. An individual will stay removed in all the next time steps once removed at a certain time step. Therefore there is a contribution of $+R(t)$ to the number $R(t+1)$.

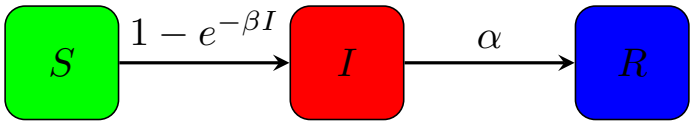

Fig. 1.9. SIR compartmental model (in the discrete-time setting) with cumulative force of infection βI and where the length of the infectious period is geometrically distributed with parameter α. Here, the host population is assumed to be demographically closed and, in particular, births and deaths (not due to the disease) are ignored.

These assumptions lead to the system of recurrence relations:

$$\begin{cases} S(t+1) = e^{-\beta I(t)} S(t) \\ I(t+1) = \left(1 - e^{-\beta I(t)}\right) S(t) + (1-\alpha) I(t) \\ R(t+1) = \alpha I(t) + R(t) \end{cases} . \tag{1.36}$$

Remark 15. Adding all equations of (1.36), we see that

$$S(t+1) + I(t+1) + R(t+1) = S(t) + I(t) + R(t) \quad (\forall t \in \mathbb{R})$$

and, in particular, the population size remains constant over time:

$$S(t) + I(t) + R(t) = N \quad (\forall t \in \mathbb{R})$$

where N is the population size.

We calculate the length of the infectious period:

Proposition 15. *The length of the infectious period is geometrically distributed with parameter α, i.e., it is expected to be equal to $\frac{1}{\alpha}$.*

Proof. Let T_I denote the time (as a random variable) at which the infectious individual stops infecting. The probability that $T_I = k$ (for $k \in \mathbb{N}_0$) is given by

$$\mathbb{P}(T_I = k) = (1-\alpha)^{k-1}\alpha,$$

since the probability distribution is geometric with parameter α: one can think of having $k-1$ fails (i.e., individual is still infectious) and 1 success (the individual stops infecting); the probability of a fail is equal to $1-\alpha$ while the probability of a success is equal to α. The average infectious period is

$$\mathbb{E}(T_I) = \sum_{k=0}^{\infty} k\mathbb{P}(T_I = k) = \sum_{k=1}^{\infty} k(1-\alpha)^{k-1}\alpha = \frac{\alpha}{[1-(1-\alpha)]^2} = \frac{1}{\alpha},$$

since this series is simply the derivative of a geometric series. □

Now we calculate the expected contribution A_k to the cumulative force of infection by an individual who itself became infected k time steps earlier:

Proposition 16. *The expected contribution to the cumulative force of infection over* $]t, t+1]$ *of an individual who itself became infected in the time window* $]t-k, t-k+1]$*, k time steps earlier, is*[8]

$$A_k = \beta(1-\alpha)^{k-1}, \quad k \in \mathbb{N}\cdot \tag{1.37}$$

Proof. We present merely a sketch for the proof.
First, notice that the expected contribution to the cumulative force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-1, t]$ (1 time step earlier) is exactly equal to the per capita contribution to the force of infection, therefore

$$A_1 = \beta\cdot$$

Now, since $1-\alpha$ can be interpreted as the proportion of individuals that remain infectious (at each time step), then

$$A_2 = \beta(1-\alpha)$$

gives the expected contribution to the cumulative force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-2, t-1]$ (2 time steps earlier).
Repeating this logic, $(1-\alpha)^2$ is the proportion of individuals that remain infectious (after 2 time steps) and thus

$$A_3 = \beta(1-\alpha)^2$$

gives the expected contribution to the cumulative force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-3, t-2]$ (3 time steps earlier).
In conclusion, the expected contribution to the cumulative force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-k, t-k+1]$, k time steps earlier, is given by (1.37). □

To continue our study, we show that $\{A_k\}_{k\in\mathbb{N}}$ given by (1.37) is a summable collection and, furthermore, we determine the value R_0.

Proposition 17. *The basic reproduction number for the SIR compartmental model* (1.36) *is given by*

$$R_0 = \frac{\beta N}{\alpha}\cdot$$

Proof. By definition (1.17),

$$R_0 = N\sum_{k=1}^{\infty}\beta(1-\alpha)^{k-1} = \frac{\beta N}{1-(1-\alpha)} = \frac{\beta N}{\alpha}$$

since this series is a geometric one with common ratio $1-\alpha \in [0, 1[$. □

Now it is shown that, choosing (1.37), then there is an equivalence between system (1.36) and the recurrence relation (1.23), given an appropriate definition for the quantity $I(t)$.

[8] Here, one allows $0^0 = 1$ for the sake of $A_1 = \beta$ when $\alpha = 1$.

Theorem 6. *Let the collection* $\{A_k\}_{k\in\mathbb{N}}$ *be given by* (1.37)*. Then the system* (1.36) *and the recurrence relation* (1.23) *are equivalent, provided that*

$$I(t) \coloneqq \sum_{k=1}^{\infty}(1-\alpha)^{k-1}\left[S(t-k)-S(t-k+1)\right]\cdot \tag{1.38}$$

Proof. We start by explaining (1.38). With (1.37), it follows that, for each $k \in \mathbb{N}$, $(1-\alpha)^{k-1}$ is the proportion of individuals that remain infectious after k time steps, while $S(t-k)-S(t-k+1)$ gives the number of new infectious individuals over the time window $]t-k, t-k+1]$. Therefore

$$(1-\alpha)^{k-1}\left[S(t-k)-S(t-k+1)\right]$$

gives the number of individuals which remain infectious after k time steps and thus it makes perfect sense to define $I(t)$ as the sum of all these terms (for $k \in \mathbb{N}$), i.e., by (1.38).
Next we show that system (1.36) can be reduced to equation (1.23). Iterating (infinitely)[9] the 1st equation of (1.36),

$$\begin{aligned} S(t+1) &= e^{-\beta I(t)}S(t) \\ &= e^{-\beta I(t)}e^{-\beta I(t-1)}S(t-1) \\ &= \cdots \\ &= \left(\prod_{j=0}^{\infty} e^{-\beta I(t-j)}\right) S(-\infty) \\ &= \exp\left\{-\beta\sum_{j=0}^{\infty} I(t-j)\right\} N\cdot \end{aligned} \tag{1.39}$$

Using the 1st equation of (1.36), we can rewrite the 2nd equation as

$$I(t+1) = S(t) - S(t+1) + (1-\alpha)I(t),$$

so that, by summation,

$$\begin{aligned} \sum_{j=0}^{\infty} I(t-j) &= \sum_{j=0}^{\infty}\left[S(t-1-j)-S(t-j)+(1-\alpha)I(t-1-j)\right] \\ &= \underbrace{\sum_{j=0}^{\infty}\left[S(t-1-j)-S(t-j)\right]}_{=S(-\infty)-S(t)} + (1-\alpha)\sum_{j=0}^{\infty} I(t-1-j) \\ &= N - S(t) + (1-\alpha)\sum_{j=0}^{\infty} I(t-1-j) \end{aligned}$$

[9] A more rigorous approach to obtain the final result is given by remark 29 (in the appendix).

and, iteratively[10], one obtains

$$\begin{aligned}\sum_{j=0}^{\infty} I(t-j) &= N - S(t) + (1-\alpha)\left[N - S(t-1) + (1-\alpha)\sum_{j=0}^{\infty} I(t-j-2)\right] \\ &= [N - S(t)] + (1-\alpha)\,[N - S(t-1)] + (1-\alpha)^2 \sum_{j=0}^{\infty} I(t-j-2) \\ &= \cdots \\ &= \sum_{m=0}^{\infty} (1-\alpha)^m\,[N - S(t-m)]\end{aligned} \tag{1.40}$$

Plugging (1.40) into (1.39), one gets

$$\begin{aligned}S(t+1) &= \exp\left\{-\beta \sum_{m=0}^{\infty} (1-\alpha)^m\,[N - S(t-m)]\right\} N \\ &= \exp\left\{-\sum_{k=1}^{\infty} \beta(1-\alpha)^{k-1}\,[N - S(t-k+1)]\right\} N \qquad \text{[with } k = m+1\text{]} \\ &= \exp\left\{-\sum_{k=1}^{\infty} A_k\,[N - S(t+1-k)]\right\} N \qquad \text{[by definition (1.37)]}\end{aligned}$$

which is exactly equation (1.23) with $t+1$ instead of t.
Conversely, starting with equation (1.23) and defining $I(t)$ by (1.38), we can arrive at system (1.36) as we show next. Choosing A_k by (1.37),

$$\begin{aligned}\sum_{k=1}^{\infty} A_k\,[N - S(t+1-k)] &= \sum_{k=1}^{\infty} \beta(1-\alpha)^{k-1}\,[N - S(t-k) + S(t-k) - S(t+1-k)] \\ &= \beta \underbrace{\sum_{k=1}^{\infty} (1-\alpha)^{k-1}\,[S(t-k) - S(t+1-k)]}_{=I(t) \quad \text{[by (1.38)]}} + \sum_{k=1}^{\infty} A_k\,[N - S(t-k)] \\ &= \beta I(t) + \sum_{k=1}^{\infty} A_k\,[N - S(t-k)]\end{aligned}$$

and thus (1.23) is equivalent to

$$\begin{aligned}S(t+1) &= \exp\left\{-\left(\beta I(t) + \sum_{k=1}^{\infty} A_k\,[N - S(t-k)]\right)\right\} N \\ &= e^{-\beta I(t)} \underbrace{\exp\left\{-\sum_{k=1}^{\infty} A_k\,[N - S(t-k)]\right\} N}_{=S(t) \quad \text{[by (1.23)]}} \\ &= e^{-\beta I(t)} S(t),\end{aligned}$$

[10] A more rigorous approach to obtain the final result is given by remark 30 (in the appendix) with $f(t) := N - S(t)$.

which is exactly the 1st equation of system (1.36). On the other hand, (1.38) gives

$$\begin{aligned}
I(t+1) &= \sum_{k=1}^{\infty}(1-\alpha)^{k-1}\left[S(t+1-k)-S(t+1-k+1)\right] \\
&= \sum_{j=0}^{\infty}(1-\alpha)^{j}\left[S(t-j)-S(t-j+1)\right] \qquad \text{[with } j=k-1\text{]} \\
&= (1-\alpha)^{0}\left[S(t-0)-S(t-0+1)\right] + (1-\alpha)\underbrace{\sum_{j=1}^{\infty}(1-\alpha)^{j-1}\left[S(t-j)-S(t-j+1)\right]}_{=I(t)\quad\text{[by (1.38)]}} \\
&= S(t)-S(t+1)+(1-\alpha)I(t) \\
&= \left(1-e^{-\beta I(t)}\right)S(t)+(1-\alpha)I(t),
\end{aligned}$$

which is exactly the 2nd equation of (1.36). Finally, since

$$S(t+1)+I(t+1)+R(t+1) = S(t)+I(t)+R(t),$$

then

$$\begin{aligned}
R(t+1) &= (S(t)+I(t)) - \underbrace{(S(t+1)+I(t+1))}_{=S(t)+(1-\alpha)I(t)} + R(t) \\
&= (\cancel{S(t)}+I(t)) - (\cancel{S(t)}+(1-\alpha)I(t)) + R(t) \\
&= \alpha I(t) + R(t)
\end{aligned}$$

and this is exactly the 3rd equation of (1.36). This concludes the proof.

□

The SEIR compartmental model: discrete-time setting

Here, some changes in the assumptions are needed: upon infection, an individual moves from the compartment S of susceptible individuals to the compartment E of exposed (i.e. infected but not yet infectious) individuals, and stays in E with probability $1-\gamma$ while moving to the compartment I of infectious individuals with probability $\gamma > 0$ (in each time step).

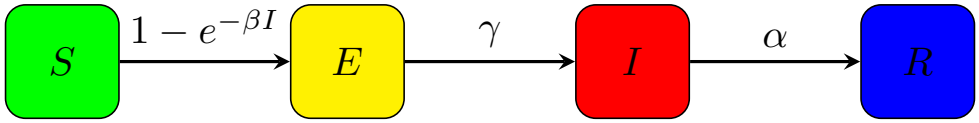

Fig. 1.10. SEIR compartmental model (in the discrete-time setting) with cumulative force of infection $-\beta I$ and where the lengths of the latent and infectious periods are geometrically distributed with parameters γ and α, respectively. Here, the host population is assumed to be demographically closed and, in particular, births and deaths (not due to the disease) are ignored.

Now the system is

$$\begin{cases} S(t+1) = e^{-\beta I(t)} S(t) \\ E(t+1) = \left(1 - e^{-\beta I(t)}\right) S(t) + (1-\gamma) E(t) \\ I(t+1) = \gamma E(t) + (1-\alpha) I(t) \\ R(t+1) = \alpha I(t) + R(t) \end{cases} . \tag{1.41}$$

Remark 16. Once again, by adding all equations of (1.41), we note that

$$S(t) + E(t) + I(t) + R(t) = N \quad (\forall t \in \mathbb{R}) \cdot$$

We calculate the lengths of the latent and infectious periods:

Proposition 18. *The lengths of the latent and infectious periods are geometrically distributed with parameters γ and α, respectively. I.e., the average latent period is equal to $\frac{1}{\gamma}$ whereas the average infectious period is equal to $\frac{1}{\alpha}$.*

Proof. Let T_E and T_I denote the time (as a random variable) at which the infected individual starts infecting and at which the infectious individual stops infecting, respectively. The probability that $T_E = k$ (for $k \in \mathbb{N}_0$) is given by

$$\mathbb{P}(T_E = k) = (1-\gamma)^{k-1}\gamma,$$

since the probability distribution is geometric with parameter γ: one can think of having $k-1$ fails (i.e., individual is still not infectious) and 1 success (the individual starts infecting); the probability of a fail is equal to $1-\gamma$ while the probability of a success is equal to γ. The average latent period is

$$\mathbb{E}(T_E) = \sum_{k=0}^{\infty} k\mathbb{P}(T_E = k) = \sum_{k=1}^{\infty} k(1-\gamma)^{k-1}\gamma = \frac{\gamma}{\left[1-(1-\gamma)\right]^2} = \frac{1}{\gamma},$$

since this series is simply the derivative of a geometric series. Similarly, the probability that $T_I = k$ (for $k \in \mathbb{N}_0$) is given by

$$\mathbb{P}(T_I = k) = (1-\alpha)^{k-1}\alpha,$$

since the probability distribution is geometric with parameter α, and the average infectious period is

$$\mathbb{E}(T_I) = \sum_{k=0}^{\infty} k\mathbb{P}(T_I = k) = \sum_{k=1}^{\infty} k(1-\alpha)^{k-1}\alpha = \frac{\alpha}{\left[1-(1-\alpha)\right]^2} = \frac{1}{\alpha},$$

since this series is simply the derivative of a geometric series. □

Now we calculate the expected contribution A_k to the cumulative force of infection by an individual who itself became infected k time steps earlier:

Proposition 19. *The expected contribution to the force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-k, t-k+1]$, k time steps earlier, is given by*[11]

$$A_k = \beta \sum_{j=1}^{k-1} \gamma(1-\gamma)^{j-1}(1-\alpha)^{k-1-j} \tag{1.42}$$

[11] Again, one allows $0^0 = 1$ for the sake of $A_2 = \beta\gamma$ when $\gamma = 1$ or $\alpha = 1$.

or, in a more explicit form,[12]

$$A_k = \begin{cases} \beta\alpha(k-1)(1-\alpha)^{k-2} & \text{if } \gamma = \alpha \\ \beta\dfrac{\gamma}{\gamma-\alpha}\left[(1-\alpha)^{k-1} - (1-\gamma)^{k-1}\right] & \text{otherwise} \end{cases}. \tag{1.43}$$

Proof. We think in terms of a stochastic process, in which an individual can be in one of four states: S, E, I and R. To find an expression for the collection $\{A_k\}_{k\in\mathbb{N}}$, one needs to "keep tabs" on an infected (infectious or not) individual. Hence, we can choose our starting and ending points as the time when the individual is infected and when it loses infection, respectively. It thus suffices to consider only 2 states: E and I. Furthermore, we consider the reduced system

$$\begin{cases} E(t+1) = (1-\gamma)E(t) \\ I(t+1) = \gamma E(t) + (1-\alpha)I(t) \end{cases}. \tag{1.44}$$

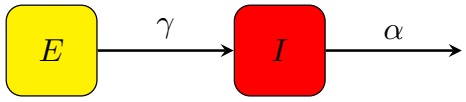

Fig. 1.11. Diagram of the compartmental system (1.44).

The probability distribution of the state-at-infection[13] can be represented by the vector $\begin{bmatrix} 1 \\ 0 \end{bmatrix}$, where the 1st index represents the state E and the 2nd the state I. Furthermore, if X_t represents the compartment where a fixed individual is at time t (as a random variable), then $\mathbb{P}(X_{t+1} = C_2 | X_t = C_1)$ denotes the (conditional) probability of going from state (compartment) C_1 to state (compartment) C_2 in 1 time step (note that these probabilities do not depend on the time t, but on the time steps between transition of compartments) and

$$\begin{aligned} \mathbb{P}(X_{t+1} = E | X_t = E) &= 1-\gamma & \mathbb{P}(X_{t+1} = E | X_t = I) &= 0 \\ \mathbb{P}(X_{t+1} = I | X_t = E) &= \gamma & \mathbb{P}(X_{t+1} = I | X_t = I) &= 1-\alpha \end{aligned}$$

by the hypothesis of the (1.41). The state transitions are described by the matrix

$$P := \begin{bmatrix} \mathbb{P}(X_{t+1} = E | X_t = E) & \mathbb{P}(X_{t+1} = E | X_t = I) \\ \mathbb{P}(X_{t+1} = I | X_t = E) & \mathbb{P}(X_{t+1} = I | X_t = I) \end{bmatrix} = \begin{bmatrix} 1-\gamma & 0 \\ \gamma & 1-\alpha \end{bmatrix}$$

and infectiousness by the vector

$$b = \begin{bmatrix} 0 & \beta \end{bmatrix}$$

(individuals at "E" are <u>not</u> yet infectious, while individuals at "I" are infectious with per capita contribution to the force of infection equal to β). Furhermore, by proposition 31 (in the appendix),

$$\begin{aligned} \mathbb{P}(X_{t+m} = E | X_t = E) &= (P^m)_{11} & \mathbb{P}(X_{t+m} = E | X_t = I) &= (P^m)_{12} \\ \mathbb{P}(X_{t+m} = I | X_t = E) &= (P^m)_{21} & \mathbb{P}(X_{t+m} = I | X_t = I) &= (P^m)_{22} \end{aligned}$$

[12] Here, in the case $\gamma = \alpha$, one ignores $(1-\alpha)^{k-2}$ when $k = 1$ and thus $A_1 = 0$. Furthermore, by allowing $0^0 = 1$, then $A_2 = \beta$ when $\alpha = 1$.

[13] An individual who was just infected (state-at-infection) is in compartment E with probability 1.

for any $m \in \mathbb{N}$. Now, the expected contribution to the force of infection over $]t, t+1]$ of an individual who itself became infected in the time window $]t-k, t-k+1]$, k time steps earlier, is

$$A_k = bP^{k-1}\begin{bmatrix}1\\0\end{bmatrix} = \beta(P^{k-1})_{21}.$$

A nice way to understand why we take $m = k-1$ is to notice that $A_k = \beta\mathbb{P}(X_t = I | X_{t-k+1} = E)$ (if the individual was infected in the time window $]t-k, t-k+1]$, then it is in compartment "E" at time $t-k+1$, i.e., $X_{t-k+1} = E$; this individual contributes to the force of infection over $]t, t+1]$ if it is in compartment "I" at time t, i.e., $X_t = I$). Now, since these probabilities depend only on the time steps between transition, one has

$$\mathbb{P}(X_t = I | X_{t-k+1} = E) = \mathbb{P}(X_{t+k-1} = I | X_t = E) = (P^{k-1})_{21}.$$

To end the proof, we need to determine P^{k-1}. To simplify this calculation, we are going to (when possible) diagonalize P, i.e., find a diagonal matrix D and an invertible matrix Q such that $P = QDQ^{-1}$. Now, the eigenvalues of P are $1-\gamma$ and $1-\alpha$. It is quite easy to see that, if $1-\gamma = 1-\alpha$, i.e., $\gamma = \alpha$, then the matrix P is not diagonalizable (the algebraic multiplicity is 2 while the geometric multiplicity is 1). However, in the case $\gamma \neq \alpha$, the two eigenvalues have algebraic and geometric multiplicities both equal to 1 and hence P is diagonalizable.
Let us start by studying the case $\gamma = \alpha$. In that case, P can be written as a sum of two commutative (and quite nice) matrices:

$$P = \begin{bmatrix}1-\alpha & 0\\ \alpha & 1-\alpha\end{bmatrix} = (1-\alpha)\underbrace{\begin{bmatrix}1&0\\0&1\end{bmatrix}}_{\text{identity}} + \alpha\underbrace{\begin{bmatrix}0&0\\1&0\end{bmatrix}}_{\text{nilpotent of index 2}}.$$

and thus we can apply the binomial theorem. One gets, for $\alpha \neq 1$:

$$\begin{aligned}
P^{k-1} &= \sum_{j=0}^{k-1}\binom{k-1}{j}\left((1-\alpha)\begin{bmatrix}1&0\\0&1\end{bmatrix}\right)^{k-1-j}\underbrace{\left(\alpha\begin{bmatrix}0&0\\1&0\end{bmatrix}\right)^{j}}_{\neq 0 \text{ iff } j\in\{0,1\}}\\
&= (1-\alpha)^{k-1}\begin{bmatrix}1&0\\0&1\end{bmatrix} + (k-1)(1-\alpha)^{k-2}\alpha\begin{bmatrix}0&0\\1&0\end{bmatrix}\\
&= (1-\alpha)^{k-2}\begin{bmatrix}1-\alpha & 0\\ \alpha(k-1) & 1-\alpha\end{bmatrix}
\end{aligned}$$

so that

$$A_k = \beta\alpha(k-1)(1-\alpha)^{k-2} \quad \forall k \in \mathbb{N},$$

which is exactly (1.43), or (1.42) with $\gamma = \alpha$. If $\alpha = 1$, then

$$P = \begin{bmatrix}0&0\\1&0\end{bmatrix}, \quad P^n = \begin{bmatrix}0&0\\0&0\end{bmatrix} \quad (n \in \mathbb{N}, n \geq 2)$$

and thus $A_k = 0$ for all $k \in \mathbb{N}\setminus\{2\}$ and $A_2 = \beta$. This is equivalent to (1.43) when $\gamma = \alpha = 1$.
Now, suppose $\gamma \neq \alpha$. Linear algebra theory guarantees that there are a diagonal matrix D and an invertible matrix Q such that $P = QDQ^{-1}$. Furthermore, the diagonal entries of D are the eigenvalues of P

and the columns of Q are the eigenvectors (in respective order). Then we can take

$$D \coloneqq \begin{bmatrix} 1-\gamma & 0 \\ 0 & 1-\alpha \end{bmatrix} \quad \text{and} \quad Q \coloneqq \begin{bmatrix} \alpha-\gamma & 0 \\ \gamma & 1 \end{bmatrix}.$$

The inverse of Q is easily calculated:

$$Q^{-1} = \frac{1}{\alpha-\gamma} \begin{bmatrix} 1 & 0 \\ -\gamma & \alpha-\gamma \end{bmatrix}.$$

Since $P = QDQ^{-1}$, then

$$P^n = QD^nQ^{-1} \quad \forall n \in \mathbb{N}_0$$

and, moreover, the n-th power of a diagonal matrix is a diagonal matrix where the entry (j,j) is given by d_{jj}^n if d_{jj} is the entry (j,j) of the original matrix. It follows that

$$D^n = \begin{bmatrix} (1-\gamma)^n & 0 \\ 0 & (1-\alpha)^n \end{bmatrix} \forall n \in \mathbb{N}_0.$$

Some simple algebraic calculations give:

$$P^n = QD^nQ^{-1} = \frac{1}{\alpha-\gamma} \begin{bmatrix} (\alpha-\gamma)(1-\gamma)^n & 0 \\ \gamma\left[(1-\gamma)^n - (1-\alpha)^n\right] & (\alpha-\gamma)(1-\alpha)^n \end{bmatrix} \quad \forall n \in \mathbb{N}_0.$$

Now, we can factorize the last factor of element $(2,1)$ as:

$$(1-\gamma)^n - (1-\alpha)^n = [(1-\gamma)-(1-\alpha)] \sum_{j=0}^{n-1} (1-\gamma)^j (1-\alpha)^{n-j-1} = (\alpha-\gamma) \sum_{j=0}^{n-1} (1-\gamma)^j (1-\alpha)^{n-1-j}$$

where the sum is equal to zero if $n < 1$ (i.e., if $n = 0$). Therefore

$$P^n = \begin{bmatrix} (1-\gamma)^n & 0 \\ \gamma \sum_{j=0}^{n-1} (1-\gamma)^j (1-\alpha)^{n-1-j} & (1-\alpha)^n \end{bmatrix} \quad \forall n \in \mathbb{N}_0$$

and, in particular,

$$P^{k-1} = \begin{bmatrix} (1-\gamma)^{k-1} & 0 \\ \gamma \sum_{j=0}^{k-2} (1-\gamma)^j (1-\alpha)^{k-2-j} & (1-\alpha)^{k-1} \end{bmatrix} \quad \forall k \in \mathbb{N}.$$

Finally,

$$A_k = \beta (P^{k-1})_{21} = \beta\gamma \sum_{j=0}^{k-2} (1-\gamma)^j (1-\alpha)^{k-2-j} = \beta\gamma \sum_{\ell=1}^{k-1} (1-\gamma)^{\ell-1} (1-\alpha)^{k-1-\ell} \qquad \forall k \in \mathbb{N}$$

where we let $\ell = j+1$ in the last equality. The previous formula is clearly equivalent to (1.42). Now, one should note that, for $\alpha \neq 1$,

$$A_k = \beta\gamma (1-\alpha)^{k-2} \sum_{j=1}^{k-1} \left(\frac{1-\gamma}{1-\alpha} \right)^{j-1}$$

and

$$\sum_{j=1}^{k-1}\left(\frac{1-\gamma}{1-\alpha}\right)^{j-1}=\frac{1-\left(\frac{1-\gamma}{1-\alpha}\right)^{k-1}}{1-\frac{1-\gamma}{1-\alpha}}=\frac{1-\alpha}{(1-\alpha)^{k-1}}\frac{(1-\alpha)^{k-1}-(1-\gamma)^{k-1}}{\gamma-\alpha},$$

because this sum is simply the sum of a geometric progression. Equation (1.43) now follows. For $\alpha=1$, one has

$$A_1=0,\quad A_k=\beta\gamma(1-\gamma)^{k-2}(k\in\mathbb{N},k\geq 2),$$

which is equivalent to (1.43) with $\gamma<\alpha=1$. □

Remark 17. The matrix P mentioned in the previous proof satisfies

$$\begin{bmatrix}E(t+1)\\I(t+1)\end{bmatrix}=P\begin{bmatrix}E(t)\\I(t)\end{bmatrix}$$

(this is exactly a matricial form for the system (1.44), present in the previous proof).

To continue our study, we show that $\{A_k\}_{k\in\mathbb{N}}$ given by (1.42) is a summable collection and, furthermore, we determine the value R_0.

Proposition 20. *The basic reproduction number for the SEIR compartmental model* (1.41) *is given by*

$$R_0=\frac{\beta N}{\alpha}\cdot$$

Proof. We separate the proof in cases:

Case 1 Suppose $\gamma=\alpha$. Then the series (1.17) for R_0 is simplified to

$$R_0=N(\beta)=\frac{\beta N}{1}$$

when $\alpha=1$ and

$$R_0=\frac{\beta\alpha N}{1-\alpha}\sum_{k=1}^{\infty}(k-1)(1-\alpha)^{k-1}=\beta\alpha N\sum_{k=1}^{\infty}(k-1)(1-\alpha)^{k-2}=\frac{\beta\alpha N}{[1-(1-\alpha)]^2}=\frac{\beta N}{\alpha}$$

when $\alpha\neq 1$ (note that the series above is simply the derivative of a geometric series).

Case 2 Suppose now that $\gamma\neq\alpha$. Then the series (1.17) for R_0 give

$$\begin{aligned}R_0&=\frac{\beta\gamma N}{\gamma-\alpha}\sum_{k=1}^{\infty}\left[(1-\alpha)^{k-1}-(1-\gamma)^{k-1}\right]\\&=\frac{\beta\gamma N}{\gamma-\alpha}\left(\frac{1}{\alpha}-\frac{1}{\gamma}\right)\\&=\frac{\beta N}{\alpha}\cdot\end{aligned}$$

We conclude that R_0 is given by

$$R_0=\frac{\beta N}{\alpha}\cdot$$

□

Remark 18. The SIR and SEIR models given by (1.36) and (1.41), respectively, have the same R_0. If one thinks about this, it does not come as a surprise:

- if c is the average number of contacts of an infectious individual (generating the disease) and t_I is the average infectious period, then one infectious individual (in compartment I) in an all susceptible population is expected to infect c individuals per unit of time it is infectious, i.e., ct_I individuals in total;
- given that β is the per capita contribution to the force of infection and N the total size of the population, the infectious individual is expected to have $c = \beta N$ contacts that generate the disease;
- by proposition 18, the average infectious period is equal to $\frac{1}{\alpha}$.

In conclusion, R_0 is not influenced by a latent compartment. In fact, by the definition of basic reproduction number, there are no individuals in compartment E when one does the calculation for R_0.

As was done for the SIR model, we now show that, with (1.42), the system (1.41) and the recurrence relation (1.23) are equivalent, given appropriate definitions for the quantities $E(t)$ and $I(t)$.

Theorem 7. *Let the collection* $\{A_k\}_{k\in\mathbb{N}}$ *be given by* (1.42)*. Then the system* (1.41) *and the recurrence relation* (1.23) *are equivalent, provided that*

$$E(t) \coloneqq \sum_{k=1}^{\infty}(1-\gamma)^{k-1}\left[S(t-k) - S(t-k+1)\right] \tag{1.45}$$

and

$$I(t) \coloneqq \sum_{k=1}^{\infty}\left([S(t-k) - S(t-k+1)]\sum_{j=1}^{k-1}\gamma(1-\gamma)^{j-1}(1-\alpha)^{k-1-j}\right). \tag{1.46}$$

Proof. We start by explaining (1.45) and (1.46). With (1.42), it follows that, for each $k \in \mathbb{N}$, the factor

$$\theta_k \coloneqq \sum_{j=1}^{k-1}\gamma(1-\gamma)^{j-1}(1-\alpha)^{k-1-j}$$

is the proportion of individuals that remain infectious (i.e., in compartment I) after k time steps. In particular, after 1 time step, this proportion is zero (and indeed $\theta_1 = 0$), since any individual is either in compartment S (it was not infected) or in compartment E (it was just infected). After 2 time steps, this proportion is equal to the probability of an individual to move from compartment E to compartment I, from where $\theta_2 = \gamma$ is the proportion of infected individuals that start transmitting the disease (at each time step). Hence, for each $k \in \mathbb{N}$, $(1-\gamma)^{k-1}$ is the proportion of individuals that remain infected but not infectious (i.e., stays in compartment E), while $S(t-k) - S(t-k+1)$ gives the number of new infected (but not infectious) individuals over the time window $]t-k, t-k+1]$. Therefore

$$(1-\gamma)^{k-1}\left[S(t-k) - S(t-k+1)\right]$$

and

$$[S(t-k) - S(t-k+1)]\sum_{j=1}^{k-1}\gamma(1-\gamma)^{j-1}(1-\alpha)^{k-1-j}$$

give the number of individuals which remain infected and infectious after k time steps, respectively. Thus it makes perfect sense to define $E(t)$ and $I(t)$ as the sum of all the (respective) terms (for $k \in \mathbb{N}$), i.e., by (1.45) and (1.46), respectively.

Next we show that system (1.41) can be reduced to equation (1.23). We can use equation (1.39), since the 1st equation (for the number for the number of susceptibles) remains the same. Similarly to what was done in the previous model, one obtains

$$\sum_{j=0}^{\infty} E(t-j) = \sum_{m=0}^{\infty} (1-\gamma)^m \left[N - S(t-m)\right] \tag{1.47}$$

(now with E instead of I). Using the 3rd equation of (1.41), one obtains

$$\begin{aligned}
\sum_{j=0}^{\infty} I(t-j) &= \sum_{j=0}^{\infty} \left[\gamma E(t-1-j) + (1-\alpha) I(t-1-j)\right] \\
&= \gamma \sum_{j=0}^{\infty} E(t-1-j) + (1-\alpha) \sum_{j=0}^{\infty} I(t-1-j) \\
&= \gamma \sum_{m=0}^{\infty} (1-\gamma)^m \left[N - S(t-1-m)\right] + (1-\alpha) \sum_{j=0}^{\infty} I(t-1-j) \qquad \text{[by (1.47)]}
\end{aligned}$$

and, by remark 30 (in the appendix) with

$$f(t) \coloneqq \gamma \sum_{m=0}^{\infty} (1-\gamma)^m \left[N - S(t-1-m)\right],$$

it follows that

$$\sum_{j=0}^{\infty} I(t-j) = \sum_{k=1}^{\infty} \left[N - S(t-k+1)\right] \sum_{\ell=1}^{k-1} \gamma (1-\gamma)^{\ell-1} (1-\alpha)^{k-1-\ell}. \tag{1.48}$$

Plugging (1.48) into (1.39), one gets

$$\begin{aligned}
S(t+1) &= \exp\left\{ -\sum_{k=1}^{\infty} \left[N - S(t-k+1)\right] \underbrace{\beta \sum_{\ell=1}^{k-1} \gamma (1-\gamma)^{\ell-1} (1-\alpha)^{k-1-\ell}}_{=A_k \quad \text{[by definition (1.42)]}} \right\} N \\
&= \exp\left\{ -\sum_{k=1}^{\infty} A_k \left[N - S(t+1-k)\right] \right\} N
\end{aligned}$$

which is exactly equation (1.23) with $t+1$ instead of t.
Conversely, starting with equation (1.23) and defining $E(t)$ and $I(t)$ by (1.45) and (1.46), respectively, we can arrive at system (1.41) as we show next. Choose A_k by (1.42). Then

$$\begin{aligned}
\sum_{k=1}^{\infty} A_k \left[N - S(t+1-k)\right] &= \sum_{k=1}^{\infty} A_k \left[N - S(t-k) + S(t-k) - S(t+1-k)\right] \\
&= \sum_{k=1}^{\infty} \left[S(t-k) - S(t+1-k)\right] \beta \sum_{\ell=1}^{k-1} \gamma (1-\gamma)^{\ell-1} (1-\alpha)^{k-1-\ell} \\
&\quad + \sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right]
\end{aligned}$$

$$= \beta \underbrace{\sum_{k=1}^{\infty} [S(t-k) - S(t+1-k)] \sum_{\ell=1}^{k-1} \gamma(1-\gamma)^{\ell-1}(1-\alpha)^{k-1-\ell}}_{=I(t) \quad \text{[by (1.46)]}}$$

$$+ \sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right]$$

$$= \beta I(t) + \sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right]$$

and thus (1.23) is equivalent to

$$S(t+1) = \exp\left\{ - \left(\beta I(t) + \sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right] \right) \right\} N$$

$$= e^{-\beta I(t)} \underbrace{\exp\left\{ - \sum_{k=1}^{\infty} A_k \left[N - S(t-k)\right] \right\} N}_{=S(t) \quad \text{[by (1.23)]}}$$

$$= e^{-\beta I(t)} S(t),$$

which is exactly the 1st equation of system (1.41). On the other hand, (1.45) gives

$$E(t+1) = \sum_{k=1}^{\infty} (1-\gamma)^{k-1} \left[S(t+1-k) - S(t+1-k+1)\right]$$

$$= \sum_{j=0}^{\infty} (1-\gamma)^{j} \left[S(t-j) - S(t-j+1)\right] \qquad \text{[with } j = k-1\text{]}$$

$$= (1-\gamma)^{0} \left[S(t-0) - S(t-0+1)\right] + (1-\gamma) \underbrace{\sum_{j=1}^{\infty} (1-\gamma)^{j-1} \left[S(t-j) - S(t-j+1)\right]}_{=E(t) \quad \text{[by (1.45)]}}$$

$$= S(t) - S(t+1) + (1-\gamma) E(t)$$

$$= \left(1 - e^{-\beta I(t)}\right) S(t) + (1-\gamma) E(t),$$

which is exactly the 2nd equation of (1.41). Now, (1.46) gives

$$I(t+1) = \sum_{k=1}^{\infty} \left(\left[S(t+1-k) - S(t+1-k+1)\right] \sum_{j=1}^{k-1} \gamma(1-\gamma)^{j-1}(1-\alpha)^{k-1-j} \right)$$

$$= \sum_{m=0}^{\infty} \left(\left[S(t-m) - S(t-m+1)\right] \sum_{j=1}^{m} \gamma(1-\gamma)^{j-1}(1-\alpha)^{m-j} \right) \qquad \text{[with } m = k-1\text{]}$$

$$= \left[S(t-0) - S(t-0+1)\right] \underbrace{\sum_{j=1}^{0} \gamma(1-\gamma)^{j-1}(1-\alpha)^{0-j}}_{=0}$$

$$+ \gamma \underbrace{\sum_{m=1}^{\infty} \left[S(t-m) - S(t-m+1)\right] (1-\gamma)^{m-1}}_{=E(t) \quad \text{[by (1.45)]}}$$

$$+ (1-\alpha) \underbrace{\sum_{m=1}^{\infty} \left([S(t-m) - S(t-m+1)] \sum_{j=1}^{m-1} \gamma(1-\gamma)^{j-1}(1-\alpha)^{m-1-j} \right)}_{=I(t) \quad \text{[by (1.46)]}}$$

$$= \gamma E(t) + (1-\alpha) I(t),$$

and this is exactly the 3rd equation of (1.41). The last equation of (1.41) is obtained in the same manner as in the case of the SIR model. This concludes the proof.

□

Chapter 2

Compartmental epidemic models with separable static heterogeneity

Next we follow [Diekmann and Inaba, 2023] where it is shown how to integrate separable static heterogeneity into compartmental epidemic models, i.e., we wish to construct a compartmental epidemic model where host individuals are characterized by some trait that does not depend on time and the host population can be separated into groups according to the trait that each individual presents.

As was done in the previous chapter, it is assumed that the disease generates permanent immunity and the host population is demographically closed.

Now, the separability condition allows the following property: the trait of an individual does not change with infection and it is constant along time.

We would like to note that compartmental models are a particular case of the general Kermack-McKendrick model, as was seen in the previous chapter: one takes $\Lambda(t) \coloneqq \beta I(t)$ in (1.1), where $\beta > 0$ is the per capita contribution to the force of infection and $I(t)$ denotes the number of infectious individuals at time t (see section 1.4).

We start with section 2.1 where we consider a special form for the expected contribution $A(\tau)$ to the force of infection by an individual with age of infection τ. Here, it is shown how to arrive to two different forms: the integrated form and the standard form. The basic reproduction number R_0, the generation time T and the Euler-Lotka equation are calculated for this special case. We follow with section 2.2 where we finally integrate heterogeneity into the model. We consider a special case for the expected contribution $A(\tau, \omega, \eta)$ to the force of infection (now a function of three variables): $A(\tau, \omega, \eta) = a(\omega)b(\tau)c(\eta)$. We finish this chapter with section 2.3, a section dedicated to show specific examples of the reduction of the general Kermack-McKendrick model to a compartmental model and of the insertion of heterogeneity into compartmental epidemic models (a special example is that of the Gamma distribution).

Here the notation used is the same as in the previous chapter. Furthermore, as usual, given a matrix M, we denote its (k, j)-th entry by M_{kj}. The transpose of M will be denoted by M^T. Furthermore, for $n \in \mathbb{N}$, we consider the set

$$[n] \coloneqq \{1, \dots, n\}.$$

Let $\mathcal{M}_{m\times n}$ be the set of real matrices of order $m \times n$ and define

$$\mathcal{M}^+_{m\times n} \coloneqq \{M \in \mathcal{M}_{m\times n} | \quad M_{kj} \geq 0 \quad \forall (k, j) \in [m] \times [n] \quad \wedge \quad \exists (k', j') \in [m] \times [n] : M_{k'j'} > 0\}$$

and

$$\mathcal{OD}^+_{m\times n} \coloneqq \{M \in \mathcal{M}_{m\times n} | \quad M_{kj} \geq 0 \quad \forall (k, j) \in [m] \times [n] \text{ with } k \neq j\}.$$

2.1 Reduction of the general (continuous) Kermack-McKendrick model to a compartmental model: a special case

In this section, we show (as was done in [Diekmann and Inaba, 2023]) how to reduce the general (continuous) Kermack-McKendrick model to a compartmental model, as long as the expected contribution $A(\tau)$ to the force of infection is defined in a certain way. Here, some of the results obtained in the first part of section 1.2 are used.

In this section, the following special case is considered:

The expected contribution to the force of infection: a special case

Let $n \in \mathbb{N}$ be the number of infected states in a certain population and suppose that the expected contribution to the force of infection at time τ after infection is given by

$$A(\tau) \coloneqq Ue^{\tau\Sigma}V, \tag{2.1}$$

where $\tau \geq 0$ and

- $\Sigma \in \mathcal{OD}^{+}_{n\times n}$ is a matrix that generates the Markov chain dynamics[14] of the infected states, i.e., it describes the *state transitions of the infected*;
- $U \in \mathcal{M}^{+}_{1\times n}$ is a (row) vector such that its k-th component gives the contribution to the force of infection by an individual in the k-th (infected) state;
- $V \in \mathcal{M}^{+}_{n\times 1}$ is a (column) vector representing the probability distribution of the state-at-infection.

As was done in the previous chapter, one assumes that $A : [0, +\infty[\longrightarrow [0, +\infty[$ is positive in some interval of $[0, +\infty[$ and integrable in $[0, +\infty[$, i.e.,

$$0 < U\left(\int_0^{\infty} e^{\tau\Sigma}\, d\tau\right)V < +\infty. \tag{2.3}$$

Now, by proposition 32 (in the appendix), the condition $\Sigma \in \mathcal{OD}^{+}_{n\times n}$ guarantees that $e^{\tau\Sigma}$ is a nonnegative[15] matrix with an all positive diagonal. This, along with the conditions $U \in \mathcal{M}^{+}_{1\times n}$ and $V \in \mathcal{M}^{+}_{n\times 1}$, guarantees that the function $A(\tau)$ is indeed nonnegative (although it does not guarantee that it is positive).

Remark 19. It is important to note that one might have $A(\tau) < 0$ for some $\tau \geq 0$ if one allows Σ to have a negative off-diagonal entry[16]. In fact, if one chooses

$$U = \begin{bmatrix} 0 & \cdots & 0 & \underbrace{1}_{k-\text{th position}} & 0 & \cdots & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} 0 & \cdots & 0 & \underbrace{1}_{j-\text{th position}} & 0 & \cdots & 0 \end{bmatrix}^T$$

[14] Consider a (finite or infinite) countable set $\mathcal{S}$ and let $\{X_m\}_{m\in\mathbb{N}}$ be a sequence of random variables with values in $\mathcal{S}$. If

$$\mathbb{P}(X_{m+1} = a_{j_{m+1}} | X_1 = a_{j_1} \wedge \ldots \wedge X_m = a_{j_m}) = \mathbb{P}(X_{m+1} = a_{j_{m+1}} | X_m = a_{j_m}) \tag{2.2}$$

for all $m \in \mathbb{N}$, where $a_{j_1}, \ldots, a_{j_m} \in \mathcal{S}$, then the sequence $\{X_m\}_{m=1}^{\infty}$ is called a Markov chain. (2.2) is known as the Markov property.

[15] Here, a matrix is said to be nonnegative if each of its entries is nonnegative.

[16] We would like to note that an off-diagonal entry Σ_{kj} $(k \neq j)$ of Σ represents the transition of an individual from the j-th infected state to the k-th infected state and thus it makes sense here to not allow Σ to have negative off-diagonal entries.

with $k \neq j$, then $A(\tau) = \left(e^{\tau\Sigma}\right)_{kj}$ and thus, if Σ has a negative off-diagonal entry in the position (k, j), then, for small $\tau > 0$,

$$e^{\tau\Sigma} \approx I_n + \tau\Sigma \quad \text{and} \quad A(\tau) = \left(e^{\tau\Sigma}\right)_{kj} \approx 0 + \tau\Sigma_{kj} < 0,$$

which contradicts the nonnegativity of $A(\tau)$.

Before we continue, we would like to give an example by showing that the SEIR model has in fact an expected contribution to the force of infection at time τ after infection of the special form (2.1).

Example 4 (The expected contribution to the force of infection of the SEIR model)**.** Here one only needs to consider the ODEs of the infected states:

$$\begin{cases} \dfrac{dE}{dt} = \beta IS - \gamma E \\ \dfrac{dI}{dt} = \gamma E - \alpha I \end{cases},$$

where β is the per capita contribution to the force of infection, γ is the rate at which individuals leave the exposed compartment and α is the rate at which individuals leave the infectious compartment.
As was done in section 1.4, for the SEIR model, one represents the state E with the 1st index and the state I with the 2nd index. The state transition matrix of the infected states is given by

$$\Sigma := \begin{bmatrix} -\gamma & 0 \\ \gamma & -\alpha \end{bmatrix}$$

while $U = \begin{bmatrix} 0 & \beta \end{bmatrix}$ (individuals at state E do not contribute to the force of infection while any individual in state I has a contribution equal to β) and $V = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$ (at state-of-infection, infected individuals are not yet infectious). To calculate the exponential $e^{\tau\Sigma}$, one considers two cases:

Case 1 $\gamma = \alpha$

In this case,

$$\Sigma = -\gamma \underbrace{\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}}_{\text{identity}} + \gamma \underbrace{\begin{bmatrix} 0 & 0 \\ 1 & 0 \end{bmatrix}}_{\text{nilpotent of index 2}},$$

so that

$$\begin{aligned} e^{\tau\Sigma} &= \exp\left\{\tau\left(-\gamma\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} + \gamma\begin{bmatrix} 0 & 0 \\ 1 & 0 \end{bmatrix}\right)\right\} \\ &= \exp\left\{-\gamma\tau\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}\right\}\exp\left\{\gamma\tau\begin{bmatrix} 0 & 0 \\ 1 & 0 \end{bmatrix}\right\} \quad \text{[the matrices are commutative]} \\ &= \left(e^{-\gamma\tau}\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}\right)\left(\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} + \gamma\tau\begin{bmatrix} 0 & 0 \\ 1 & 0 \end{bmatrix}\right) \\ &= \begin{bmatrix} e^{-\gamma\tau} & 0 \\ \gamma\tau e^{-\gamma\tau} & e^{-\gamma\tau} \end{bmatrix} \end{aligned}$$

and thus

$$A(\tau) = Ue^{\tau\Sigma}V = \begin{bmatrix} 0 & \beta \end{bmatrix} \begin{bmatrix} e^{-\gamma\tau} & 0 \\ \gamma\tau e^{-\gamma\tau} & e^{-\gamma\tau} \end{bmatrix} \begin{bmatrix} 1 \\ 0 \end{bmatrix} = \beta\gamma\tau e^{-\gamma\tau}.$$

One can see that

$$R_0 = \beta N \int_0^\infty \gamma\tau e^{-\gamma\tau}\, d\tau = \beta N \left[\cancel{-\tau e^{-\gamma\tau}\Big|_0^\infty} - \int_0^\infty -e^{-\gamma\tau}\, d\tau \right] = \frac{\beta N}{\gamma}.$$

Case 2 $\gamma \neq \alpha$

In this case, one can diagonalize Σ, since this matrix has two distinct eigenvalues, $-\gamma$ and $-\alpha$, with associated eigenvectors $\begin{bmatrix} \alpha - \gamma \\ \gamma \end{bmatrix}$ and $\begin{bmatrix} 0 \\ 1 \end{bmatrix}$, respectively. Therefore, one can consider

$$D := \begin{bmatrix} -\gamma & 0 \\ 0 & -\alpha \end{bmatrix} \quad \text{and} \quad P := \begin{bmatrix} \alpha - \gamma & 0 \\ \gamma & 1 \end{bmatrix},$$

so that $\Sigma = PDP^{-1}$ and

$$\begin{aligned} e^{\tau\Sigma} &= Pe^{\tau D}P^{-1} \\ &= \begin{bmatrix} \alpha - \gamma & 0 \\ \gamma & 1 \end{bmatrix} \begin{bmatrix} e^{-\gamma\tau} & 0 \\ 0 & e^{-\alpha\tau} \end{bmatrix} \frac{1}{\alpha - \gamma} \begin{bmatrix} 1 & 0 \\ -\gamma & \alpha - \gamma \end{bmatrix} \\ &= \begin{bmatrix} e^{-\gamma\tau} & 0 \\ \dfrac{\gamma}{\alpha - \gamma}\left(e^{-\gamma\tau} - e^{-\alpha\tau}\right) & e^{-\alpha\tau} \end{bmatrix}, \end{aligned}$$

and, finally,

$$A(\tau) = Ue^{\tau\Sigma}V = \begin{bmatrix} 0 & \beta \end{bmatrix} \begin{bmatrix} e^{-\gamma\tau} & 0 \\ \dfrac{\gamma}{\alpha - \gamma}\left(e^{-\gamma\tau} - e^{-\alpha\tau}\right) & e^{-\alpha\tau} \end{bmatrix} \begin{bmatrix} 1 \\ 0 \end{bmatrix} = \frac{\beta\gamma}{\alpha - \gamma}\left(e^{-\gamma\tau} - e^{-\alpha\tau}\right).$$

One can see that

$$R_0 = \frac{\beta N\gamma}{\alpha - \gamma}\left(\int_0^\infty e^{-\gamma\tau}\, d\tau - \int_0^\infty e^{-\alpha\tau}\, d\tau\right) = \frac{\beta N\gamma}{\alpha - \gamma}\left(\frac{1}{\gamma} - \frac{1}{\alpha}\right) = \frac{\beta N\gamma}{\alpha - \gamma}\frac{\alpha - \gamma}{\gamma\alpha} = \frac{\beta N}{\alpha}.$$

One concludes that

$$A(\tau) = \begin{cases} \beta\gamma\tau e^{-\gamma\tau} & \text{if } \gamma = \alpha \\ \dfrac{\beta\gamma}{\alpha - \gamma}\left(e^{-\gamma\tau} - e^{-\alpha\tau}\right) & \text{otherwise} \end{cases}$$

and, furthermore,

$$R_0 = \frac{\beta N}{\alpha}.$$

The objective in this section is to show that the renewal equation (1.13), equipped with definition (1.14)[17], reduces to an ODE system when (2.1) holds (with some appropriate assumptions on the transition matrix Σ). Furthermore, it is also shown that, given an appropriate ODE and an appropriate definition of the cumulative force of infection w, one easily obtains (1.13).

[17]The renewal equation (1.13) and the definition (1.14) are present, for the first time, in the first part of section 1.2.

The first step is to note the following:

Proposition 21. *If the cumulative force of infection is defined by* (1.13) *and* (2.1) *holds, then*

$$w(t) = UZ(t), \tag{2.4}$$

where one defines the n-th vector valued function Z by

$$Z(t) \coloneqq \int_0^\infty e^{\tau\Sigma} V \Psi(w(t-\tau))\, d\tau\cdot \tag{2.5}$$

Proof. Immediate by plugging (2.1) into (1.13) and then using definition (2.5). □

Remark 20. Although $w(t)$ (if nonnegative) is bounded if equations (2.4) and (1.14) hold, the function Z might not be so lucky as we will see in the next example.

Example 5. Let

$$\Sigma = \begin{bmatrix} -1 & 1 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, \quad U = \begin{bmatrix} 6 & 0 & 0 \end{bmatrix}, \quad V = \frac{1}{6}\begin{bmatrix} 5 \\ 0 \\ 1 \end{bmatrix}\cdot$$

Then Σ is a Jordan canonical form[18], with two Jordan blocks:

$$\Sigma = \begin{bmatrix} \Sigma_1 & \mathbf{0_{2\times 1}} \\ \mathbf{0_{1\times 2}} & \Sigma_2 \end{bmatrix}$$

where

$$\Sigma_1 \coloneqq \begin{bmatrix} -1 & 1 \\ 0 & -1 \end{bmatrix} \text{ and } \Sigma_2 \coloneqq \begin{bmatrix} 1 \end{bmatrix}\cdot$$

From linear algebra theory, one knows that

$$e^{\tau\Sigma} = \begin{bmatrix} e^{\tau\Sigma_1} & \mathbf{0_{2\times 1}} \\ \mathbf{0_{1\times 2}} & e^{\tau\Sigma_2} \end{bmatrix}\cdot$$

We start by noting that

$$e^{\tau\Sigma_2} = \begin{bmatrix} e^{\tau} \end{bmatrix}\cdot$$

On the other hand, one notes that Σ_1 can be written as a sum of two commutative matrices:

$$\Sigma_1 = \begin{bmatrix} -1 & 0 \\ 0 & -1 \end{bmatrix} + \begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix}\cdot$$

It is clear that the first matrix is the symmetric of the identity matrix while the second is a nilpotent matrix of index 2. Therefore

$$e^{\tau\Sigma_1} = \exp\left\{\tau\begin{bmatrix} -1 & 0 \\ 0 & -1 \end{bmatrix}\right\}\exp\left\{\tau\begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix}\right\} = e^{-\tau}\left(\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} + \begin{bmatrix} 0 & \tau \\ 0 & 0 \end{bmatrix}\right) = \begin{bmatrix} e^{-\tau} & \tau e^{-\tau} \\ 0 & e^{-\tau} \end{bmatrix}\cdot$$

So

$$e^{\tau\Sigma} = \begin{bmatrix} e^{-\tau} & \tau e^{-\tau} & 0 \\ 0 & e^{-\tau} & 0 \\ 0 & 0 & e^{\tau} \end{bmatrix}$$

[18] A more detailed explanation of the Jordan canonical form can be found in [Pestana da Costa, 2001].

and

$$e^{\tau\Sigma}V = \frac{1}{6}\begin{bmatrix} 5e^{-\tau} \\ 0 \\ e^{\tau} \end{bmatrix}\cdot$$

One notes that $\tau \mapsto A(\tau)$ is a positive and integrable function in $[0, +\infty[$:

$$A(\tau) = Ue^{\tau\Sigma}V = 5e^{-\tau} > 0 \text{ and } \int_0^\infty A(\tau)\,d\tau = 5\int_0^\infty e^{-\tau}\,d\tau = 5 < +\infty\cdot$$

Now, if N denotes the total number of individuals in the population (and $N \in \mathbb{N}$), one has that

$$R_0 \coloneqq N\int_0^\infty A(\tau)\,d\tau = 5N > 1$$

and thus, by proposition 6, equation (1.13) has a nonzero root $\bar{w}$ provided that Ψ is given by (1.14). One can therefore assume that $w(t) = \bar{w}$ is a nonzero root of (2.4), where Ψ is defined by (1.14).
Defining $Z(t)$ by (2.5), one gets

$$Z(t) = \int_0^\infty e^{\tau\Sigma}V\Psi(\bar{w})\,d\tau = N(1 - e^{-\bar{w}})\int_0^\infty e^{\tau\Sigma}V\,d\tau\cdot$$

The third component of Z is given by

$$Z_3(t) = \underbrace{N(1 - e^{-\bar{w}})}_{\neq 0}\int_0^\infty \frac{1}{6}e^{\tau}\,d\tau,$$

which clearly diverges.

For our main result, some conditions on the matrix Σ are needed. First, a definition (of Linear Algebra) is given:

Definition 4. Let $m \in \mathbb{N}$ and consider M, a $m \times m$ square matrix. The *spectrum* of M is the set of eigenvalues of M and is denoted by

$$\sigma(M) \coloneqq \{\lambda \in \mathbb{C} : Mv = \lambda v \quad \text{for some} \quad v \in \mathbb{C}^{m\times 1} \setminus \{\mathbf{0_{m\times 1}}\}\}\cdot$$

The *spectral radius* of M is then defined as the maximum of the absolute values of its eigenvalues and will be denoted by

$$\rho(M) \coloneqq \max_{\lambda\in\sigma(M)} |\lambda|,$$

while the *spectral abscissa* of M is defined as the greatest real part of the matrix spectrum and will be denoted by

$$\kappa(M) \coloneqq \max_{\lambda\in\sigma(M)} \Re(\lambda)\cdot$$

Finally, we are ready to give the main result. The following ODE system plays an important role in this result:

Definition 5. The ODE system

$$\frac{dZ}{dt} = \Sigma Z + V\Psi(UZ), \tag{2.6}$$

where $Z = Z(t)$ is given by (2.5), is called the *integrated form* of the compartmental model corresponding to Σ, U and V.

Theorem 8. *Let Ψ be given by* (1.14)*. Suppose that* (2.1) *holds and that Σ is such that $\kappa(\Sigma) < 0$. Then the renewal equation* (1.13)*, equipped with the conditions $w(t) \geq 0$ for all $t \in \mathbb{R}$ and $\lim_{t\to-\infty} w(t) = 0$, reduces to the ODE system* (2.6)*. Conversely, if Z is a solution of* (2.6) *such that $UZ(t) \geq 0$ for all $t \in \mathbb{R}$ and $\lim_{t\to-\infty} UZ(t) = 0$, and one defines w by* (2.4)*, then* (1.13) *holds.*

Proof. We start by noting that, since $\kappa(\Sigma) < 0$, then proposition 33 (in the appendix) guarantees that $\lim_{t\to+\infty} e^{t\Sigma} = \mathbf{0_{n\times n}}$. Furthermore, Σ is clearly invertible and one notes that

$$\int_0^\infty e^{\tau\Sigma}\, d\tau = \left(\int_0^\infty e^{\tau\Sigma}\Sigma\, d\tau\right)\Sigma^{-1} = \big(\underbrace{\lim_{\tau\to\infty} e^{\tau\Sigma}}_{=\mathbf{0_{n\times n}}} - e^{0\cdot\Sigma}\big)\,\Sigma^{-1} = -\Sigma^{-1}.$$

One should also remember that $e^{\tau\Sigma}$ is a nonnegative matrix whenever $\tau \geq 0$ (see proposition 32 in the appendix).

Suppose that (1.13) holds and define Z by (2.5). Letting $\nu = t - \tau$ in the integral in (2.5), one obtains

$$Z(t) = e^{t\Sigma}\int_{-\infty}^{t} e^{-\nu\Sigma}V\Psi(w(\nu))\, d\nu,$$

i.e.,

$$Z(t) = e^{t\Sigma}\left(\int_{-\infty}^{t_0} e^{-\nu\Sigma}V\Psi(w(\nu))\, d\nu + \int_{t_0}^{t} e^{-\nu\Sigma}V\Psi(w(\nu))\, d\nu\right),$$

for $t_0 \in \mathbb{R}$. Differentiation gives

$$\frac{dZ}{dt}(t) = \Sigma Z(t) + e^{t\Sigma}\left(0 + e^{-t\Sigma}V\Psi(w(t))\right),$$

i.e.,

$$\frac{dZ}{dt} = \Sigma Z + V\Psi(w)\cdot \tag{2.7}$$

Now, by proposition 21, one has that (2.4) holds. Finally, by plugging (2.4) into (2.7), one gets the ODE system (2.6), as desired.

Conversely, assume Z is a solution of (2.6) such that $UZ(t) \geq 0$ for all $t \in \mathbb{R}$ and $\lim_{t\to-\infty} UZ(t) = 0$. Define w by (2.4) and note that, since (1.14) and (2.1) hold, (1.13) is equivalent to

$$U\left[Z(t) - \int_0^\infty e^{\tau\Sigma}V\Psi(UZ(t-\tau))\, d\tau\right] = 0,$$

so, if one defines f as the $n \times 1$ vector-valued function by

$$f(t) \coloneqq Z(t) - \int_0^\infty e^{\tau\Sigma}V\Psi(UZ(t-\tau))\, d\tau,$$

then our objective is to prove that $Uf(t) = 0$ for all $t \in \mathbb{R}$. One starts by noting that the integral is convergent (it suffices to repeat the argument given in the justification that Z is bounded in each of its entries, done for the reciprocal implication). Therefore, one can differentiate $f(t)$. First, one can note that $f(t)$ can be rewritten as

$$f(t) = Z(t) - e^{t\Sigma}\int_{-\infty}^{t} e^{-\nu\Sigma}V\Psi(UZ(\nu))\, d\nu,$$

and now, by differentiating:

$$\begin{aligned}\frac{df}{dt}(t) &= \frac{dZ}{dt}(t) - \Sigma e^{t\Sigma}\int_{-\infty}^{t} e^{-\nu\Sigma}V\Psi(UZ(\nu))\,d\nu - V\Psi(UZ(t)) \\ &= \frac{dZ}{dt}(t) + \Sigma\left[f(t) - Z(t)\right] - V\Psi(UZ(t)) \\ &= \underbrace{\frac{dZ}{dt}(t) - \Sigma Z(t) - V\Psi(UZ(t))}_{=0} + \Sigma f(t) \\ &= \Sigma f(t),\end{aligned}$$

i.e., $f(t)$ satisfies

$$\frac{df}{dt} = \Sigma f\cdot$$

By proposition 34, for each $k \in \{1,\dots,n\}$, the k-th entry of f is of the form

$$f_k(t) = e^{\lambda_{\ell_k} t}p_k(t) \tag{2.8}$$

where $\lambda_{\ell_k} \in \sigma(\Sigma)$ and p_k is a polynomial in t.
Next, one uses the definition to prove that $\lim_{t\to-\infty} Uf(t) = 0$. We have

$$\begin{aligned}\lim_{t\to-\infty} Uf(t) &= \lim_{t\to-\infty}\left[UZ(t) - \int_0^{\infty} Ue^{\tau\Sigma}V\Psi(UZ(t-\tau))\,d\tau\right] \\ &= -\lim_{t\to-\infty}\int_0^{\infty} A(\tau)\Psi(UZ(t-\tau))\,d\tau,\end{aligned}$$

since $\lim_{t\to-\infty} UZ(t) = 0$ by hypothesis. Consider the sequence of functions

$$y_m(\tau) \coloneqq A(\tau)\Psi(UZ(t_m - \tau)) \quad \forall m \in \mathbb{N}$$

where $t_m \to -\infty$ when $m \to +\infty$. Now, since $\tau \mapsto A(\tau)$ and Ψ are continuous functions, then y_m is continuous (and thus measurable) for each $m \in \mathbb{N}$. On the other hand,

$$\lim_{m\to+\infty} y_m(\tau) = \lim_{m\to+\infty} A(\tau)\Psi(UZ(t_m-\tau)) = NA(\tau)\lim_{m\to+\infty}\left(1 - e^{-UZ(t_m-\tau)}\right) = 0$$

where the last equality follows from the hypothesis $\lim_{t\to-\infty} UZ(t) = 0$ (since the limit exists, then every sequence $\{x_m\}_{m\in\mathbb{N}}$ with $x_m \to -\infty$ satisfies $UZ(x_m) \to -\infty$). Now, since $UZ(t) \geq 0$ for all $t \in \mathbb{R}$, then $0 \leq \Psi \leq N$ and

$$|y_m(\tau)| \leq NA(\tau),$$

i.e., the sequence is dominated by $\tau \mapsto NA(\tau)$ and this last one is integrable by assumption. Lebesgue's dominated convergence theorem (theorem 12 in the appendix) guarantees that

$$\lim_{m\to+\infty}\int_0^{\infty} y_m(\tau)\,d\tau = \int_0^{\infty}\lim_{m\to+\infty} y_m(\tau)\,d\tau = 0\cdot$$

This proves that

$$\lim_{t\to-\infty} Uf(t) = -\lim_{t\to-\infty}\int_0^{\infty} A(\tau)\Psi(UZ(t-\tau))\,d\tau = 0\cdot$$

Now, one notes that

$$Uf(t) = \sum_{k=1}^{n} U_k f_k(t) = \sum_{k=1}^{n} U_k e^{\lambda_{\ell_k} t} p_k(t).$$

Suppose Σ has m distinct eigenvalues $\mu_1, \ldots, \mu_m$. For each $j \in \{1, \ldots, m\}$, denote

$$K_j \coloneqq \{k \in \{1, \ldots, n\} : \quad \lambda_{\ell_k} = \mu_j\}.$$

Therefore

$$Uf(t) = \sum_{j=1}^{m} e^{\mu_j t} \left[\sum_{k \in K_j} U_k p_k(t) \right].$$

Since $\mu_1, \ldots, \mu_n$ are distinct eigenvalues, then:

$$\lim_{t \to -\infty} Uf(t) = 0$$

if and only if, for each $j \in \{1, \ldots, m\}$,

$$\lim_{t \to -\infty} e^{\mu_j t} \left[\sum_{k \in K_j} U_k p_k(t) \right] = 0.$$

Now, for each $j \in \{1, \ldots, m\}$,

$$\lim_{t \to -\infty} \left| e^{\mu_j t} \left[\sum_{k \in K_j} U_k p_k(t) \right] \right| = \lim_{t \to -\infty} e^{\Re(\mu_j) t} \left| \sum_{k \in K_j} U_k p_k(t) \right|$$

and it is clear that $\sum_{k \in K_j} U_k p_k(t)$ is a polynomial in t. Furthermore, $\Re(\mu_j) < 0$, since $\mu_j \in \sigma(\Sigma)$ and $\kappa(\Sigma) < 0$. Therefore

$$\lim_{t \to -\infty} \left| e^{\mu_j t} \left[\sum_{k \in K_j} U_k p_k(t) \right] \right| = +\infty \tag{2.9}$$

if $\sum_{k \in K_j} U_k p_k(t) \neq 0$ for some $t \in \mathbb{R}$. It follows that, for each $j \in \{1, \ldots, m\}$,

$$\sum_{k \in K_j} U_k p_k(t) = 0 \quad \forall t \in \mathbb{R}.$$

We conclude that $Uf(t) = 0$ for all $t \in \mathbb{R}$ and finally equation (1.13) now follows. □

Now we give a lemma with some results on equation (2.6). Some fundamental theorems on the theory of ordinary differential equations are used (see, for example, [Pestana da Costa, 2001]).

Lemma 4. *The set*

$$\mathbb{R}^n_+ \coloneqq \{(x_1, \ldots, x_n) \in \mathbb{R}^n : \quad x_k > 0 \quad \forall k \in \{1, \ldots, n\}\}$$

is positively invariant for (2.6)*, i.e.,*

$$Z(t_0) = q \in \mathbb{R}^n_+ \implies Z(t) \in \mathbb{R}^n_+ \quad \forall t \geq t_0.$$

Proof. We start by noting that $Z \equiv \mathbf{0}_{n \times 1}$ is an equilibrium of (2.6). By uniqueness of solution, for each $t \in \mathbb{R}$, there is $k \in \{1, \ldots, n\}$ such that $Z_k(t) \neq 0$ for every other solution Z. If $n = 1$, the conclusion

is immediate. So we assume $n \in \mathbb{N}, n > 1$.
Suppose $Z(t_0) = q$ with $q_j > 0$ for all $j \in \{1, \dots, n\}$. Then, for each $t \in \mathbb{R}$, there exists always some $k \in \{1, \dots, n\}$ such that $Z_k(t) \neq 0$.
Let us assume, by way of contradiction, that $Z_1, \dots, Z_m$ (for some $m \in \{1, \dots, n-1\}$) are the first that arrive at zero (and at the same time). Take

$$t_1 := \min\{t > t_0 : \quad Z_1(t_1) = 0\},$$

i.e.,

$$\begin{cases} Z_j(t_1) = 0 & \text{if } j \in \{1, \dots, m\} \\ Z_j(t_1) > 0 & \text{if } j \in \{m+1, \dots, n\} \end{cases}.$$

It is obvious that, for $k \in \{1, \dots, m\}$, Z_k decreases in $]t_1 - \delta, t_1]$ for some sufficiently small $\delta > 0$. Therefore,

$$\frac{dZ_k}{dt} \leq 0 \quad (k \in \{1, \dots, m\}).$$

Now Z satisfies (2.6), so, for each $k \in \{1, \dots, n\}$, one has

$$\frac{dZ_k}{dt} = \sum_{j=1}^{n} \Sigma_{kj} Z_j + V_k \Psi \left(\sum_{j=1}^{n} U_j Z_j \right)$$

and, for $k \in \{1, \dots, m\}$

$$\frac{dZ_k}{dt}(t_1) = \sum_{j=m+1}^{n} \underbrace{\Sigma_{kj}}_{\geq 0} \underbrace{Z_j(t_1)}_{>0} + \underbrace{V_k}_{\geq 0} \underbrace{\Psi \left(\sum_{j=m+1}^{n} \underbrace{U_j}_{\geq 0} \underbrace{Z_j(t_1)}_{>0} \right)}_{\geq 0} \geq 0.$$

We conclude that

$$\frac{dZ_k}{dt}(t_1) = 0 \quad (k \in \{1, \dots, m\}),$$

from where $\Sigma_{kj} = 0$ for all $j \in \{m+1, \dots, n\}$ and either $V_k = 0$ or $U_j = 0$ for all $j \in \{m+1, \dots, n\}$ ($k \in \{1, \dots, m\}$). It follows that

$$\frac{dZ_k}{dt} = \sum_{j=1}^{m} \Sigma_{kj} Z_j \quad \text{i.e.} \quad \frac{d}{dt}\left(e^{-\Sigma_{kk} t} Z_k(t)\right) = e^{-\Sigma_{kk} t} \sum_{\substack{j=1 \\ j \neq k}}^{m} \Sigma_{kj} Z_j(t)$$

for each $k \in \{1, \dots, m\}$. Now, if, for some $k \in \{1, \dots, m\}$, there is some $j \in \{1, \dots, m\} \setminus \{k\}$ such that $\Sigma_{kj} > 0$, then it is clear that

$$\frac{d}{dt}\left(e^{-\Sigma_{kk} t} Z_k(t)\right)(t) > 0 \quad \text{whenever} \quad t_0 \leq t < t_1$$

and $t \mapsto e^{-\Sigma_{kk} t} Z_k(t)$ increases in all $[t_0, t_1[$. In particular,

$$e^{-\Sigma_{kk} t_0} Z_k(t_0) < e^{-\Sigma_{kk} t} Z_k(t) \quad \text{whenever} \quad t_0 < t < t_1$$

and, by continuity,

$$e^{-\Sigma_{kk} t_0} Z_k(t_0) \leq e^{-\Sigma_{kk} t_1} Z_k(t_1) = 0,$$

which is absurd since $Z_k(t_0) > 0$ by hypothesis. Since Σ is nonnegative off-diagonal, we conclude that

$\Sigma_{kj} = 0$ whenever $k, j \in \{1, \dots, m\}$ with $k \neq j$. Then

$$Z_k(t) = e^{\Sigma_{kk} t} Z_k(t_0) \quad (k \in \{1, \dots, m\}).$$

In particular, $Z_k(t_1) = e^{\Sigma_{kk} t_1} Z_k(t_0) > 0$ for $k \in \{1, \dots, m\}$, a contradiction as desired. □

Remark 21. Given that $w(t)$ denotes the cumulative force of infection at time t, it makes perfect sense to consider it approximates 0 in the infinite past (at the beginning of the infection), i.e.,

$$\lim_{t \to -\infty} w(t) = 0.$$

On the other hand, for each $k \in \{1, \dots, n\}$, one has that U_k denotes the contribution to the force of infection of an individual in the k-th state, while $Z_k(t)$ denotes the number of individuals that were, at some time $t_1 \leq t$, in the k-th state:

- for each $\tau \geq 0$, $\Psi(w(t-\tau))$ denotes the number of individuals that are no longer susceptible at time $t - \tau$ (i.e., that were infected at some time $t_0 \leq t - \tau$;
- for each $\tau \geq 0$ and $j \in \{1, \dots, n\}$, the (k, j) entry of $e^{\tau \Sigma}$ denotes the probability to go from the j-th state to the k-th state at time τ after infection, so that $\left(e^{\tau \Sigma}\right)_{kj} V_j$ denotes the proportion of individuals in the k-th state at time τ after infection, descendant from the j-th state, and

$$\left(e^{\tau \Sigma} V\right)_k = \sum_{j=1}^{n} \left(e^{\tau \Sigma}\right)_{kj} V_j$$

  denotes the (total) proportion of individuals in the k-th state at time τ after infection;
- hence, for each $\tau \geq 0$, $\left(e^{\tau \Sigma} V\right)_k \Psi(w(t-\tau))$ gives the number of individuals that were in the k-th (infected) state before/at time t with age of infection τ;
- viewing the integral as a sum, one concludes that $Z_k(t)$ is counting the number of individuals that were in the k-th (infected) state at some time $t_1 \leq t$ (and that were infected since the infinity past until t).

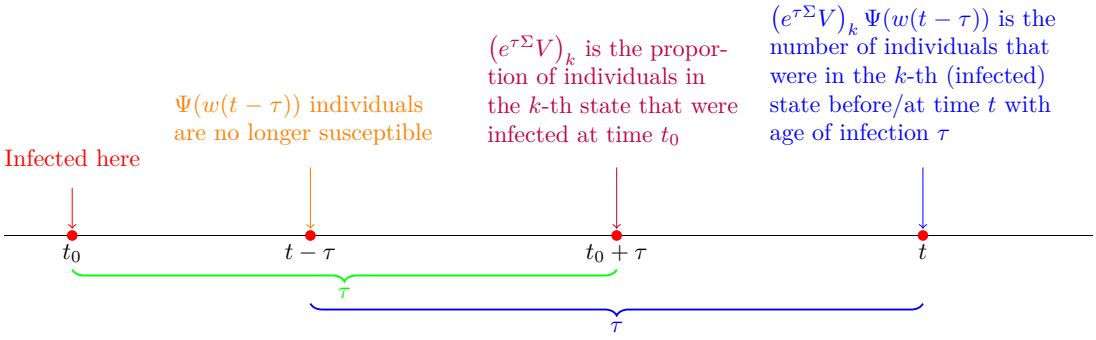

Fig. 2.1. Scheme explaining why Z defined by (2.5) counts the number of individuals that were infected at some time $t_1 \leq t$.

Hence $U_k Z_k(t)$ is the contribution to the cumulative force of infection at time t of the k-th state (for each $k \in \{1, \dots, n\}$) and so

$$UZ(t) = \sum_{k=1}^{n} U_k Z_k(t)$$

is the cumulative force of infection at time t, so that $UZ(t) = w(t)$.

Furthermore, if one defines the expected contribution to the force of infection at time τ after infection by (2.1), one can easily calculate some basic indices for the Kermack-McKendrick model:

Proposition 22. *Suppose that the expected contribution to the force of infection at time τ after infection is given by* (2.1) *and that Σ is such that $\kappa(\Sigma) < 0$. Then:*

1. *the basic reproduction number is given by*

$$R_0 = -NU\Sigma^{-1}V; \tag{2.10}$$

2. *the Euler-Lotka equation is*

$$1 = NU(\lambda I_n - \Sigma)^{-1}V \tag{2.11}$$

   and the intrinsic growth rate $\tilde{\rho}$ is given by its real root;

3. *the generation time T is given by*

$$T = -\frac{U\Sigma^{-2}V}{U\Sigma^{-1}V}. \tag{2.12}$$

Proof. One starts by noting that Σ is invertible, since $\kappa(\Sigma) < 0$. It now follows easily that

$$\int_0^\infty e^{\tau\Sigma}\,d\tau = \left(\int_0^\infty e^{\tau\Sigma}\Sigma\,d\tau\right)\Sigma^{-1} = \Big(\underbrace{\lim_{\tau\to\infty} e^{\tau\Sigma}}_{=\mathbf{0_{n\times n}}} - I_n\Big)\Sigma^{-1} = -\Sigma^{-1}$$

and

$$\int_0^\infty A(\tau)\,d\tau = U\left(\int_0^\infty e^{\tau\Sigma}\,d\tau\right)V = -U\Sigma^{-1}V.$$

With definition (1.6), one now obtains (2.10). Before we continue with the proof, note that $\Sigma \in \mathcal{OD}^+_{n\times n}$ and thus proposition 32 (in the appendix) guarantees that $e^{\tau\Sigma}$ is a nonnegative matrix with positive diagonal entries for every $\tau \geq 0$. The integral of this matrix is therefore a nonnegative matrix with positive diagonal entries. It follows that Σ^{-1} is a nonpositive matrix with negative diagonal entries.
Now, using integration by parts,

$$\int_0^\infty \tau e^{\tau\Sigma}\,d\tau = \left(\int_0^\infty \tau e^{\tau\Sigma}\Sigma\,d\tau\right)\Sigma^{-1} = \left(\underbrace{\lim_{\tau\to\infty} \tau e^{\tau\Sigma}}_{=\mathbf{0_{n\times n}}} - 0\times I_n - \int_0^\infty e^{\tau\Sigma}\,d\tau\right)\Sigma^{-1} = \Sigma^{-2},$$

so that

$$\int_0^\infty \tau A(\tau)\,d\tau = U\left(\int_0^\infty \tau e^{\tau\Sigma}\,d\tau\right)V = U\Sigma^{-2}V$$

and thus the generation time is

$$T \coloneqq \frac{\int_0^\infty \tau A(\tau)\,d\tau}{\int_0^\infty A(\tau)\,d\tau} = -\frac{U\Sigma^{-2}V}{U\Sigma^{-1}V},$$

which corresponds to (2.12). Now, the Euler-Lotka equation is given by

$$1 = N\int_0^\infty e^{-\lambda\tau}A(\tau)\,d\tau,$$

i.e.,

$$1 = NU\left(\int_0^\infty e^{-\tau(\lambda I_n - \Sigma)}\,d\tau\right)V.$$

If $\lambda \in \sigma(\Sigma)$, then $0 \in \sigma(\lambda I_n - \Sigma)$ and $1 \in \sigma\left(e^{-\tau(\lambda I_n - \Sigma)}\right)$ for each $\tau \geq 0$. In this case, the integral diverges and thus λ cannot be a solution of the Euler-Lotka equation. We conclude that $\lambda \notin \sigma(\Sigma)$ and

thus $\lambda I_n - \Sigma$ is invertible. It is now easy to integrate:

$$\begin{aligned}\int_0^\infty e^{-\tau(\lambda I_n - \Sigma)}\, d\tau &= \left(\int_0^\infty e^{-\tau(\lambda I_n - \Sigma)}\,(\lambda I_n - \Sigma)\, d\tau\right)(\lambda I_n - \Sigma)^{-1} \\ &= \left(I_n - \lim_{\tau\to\infty} e^{\tau(\Sigma - \lambda I_n)}\right)(\lambda I_n - \Sigma)^{-1}\,.\end{aligned}$$

We will prove that $\kappa(\Sigma - \lambda I_n) < 0$. First, if $\kappa(\Sigma - \lambda I_n) > 0$, then proposition 33 (in the appendix) guarantees that $\tau \mapsto e^{\tau(\Sigma - \lambda I_n)}$ diverges when $\tau \to +\infty$. Now we will see that $\kappa(\Sigma - \lambda I_n) = 0$ implies that $\lambda \in \sigma(\Sigma)$ and thus λ could not be a solution of the Euler-Lotka equation. We start by noting that $\mu \in \sigma(\Sigma - \lambda I_n)$ if and only if there is a nonzero vector $v \in \mathbb{C}^{n\times 1}$ such that

$$(\Sigma - \lambda I_n)v = \mu v$$

or, equivalently,

$$\Sigma v = (\lambda + \mu)v$$

i.e., $\lambda + \mu \in \sigma(\Sigma)$. Then

$$k(\Sigma - \lambda I_n) = \max_{\mu\in\sigma(\Sigma - \lambda I_n)} \Re(\mu) = \max_{\lambda+\mu\in\sigma(\Sigma)} \Re(\lambda + \mu) - \lambda = \max_{\vartheta\in\sigma(\Sigma)} \Re(\vartheta) - \lambda = \kappa(\Sigma) - \lambda\cdot$$

Next, we prove that $\kappa(\Sigma)$ is the greatest real eigenvalue of Σ:

1. let $m \coloneqq \max\{|\Sigma_{kk}| :\ k \in \{1,\dots,n\}\}$, so that $\tilde{\Sigma} = \Sigma + mI_n$ is a nonnegative matrix;
2. by Perron-Frobenius theory (see [Varga, R.S., 2000, Chapter 2.3.]), one has that $\rho(\tilde{\Sigma}) \in \sigma(\tilde{\Sigma})$ and thus $\rho(\tilde{\Sigma})$ is a real eigenvalue of $\tilde{\Sigma}$;
3. it follows that $\rho(\tilde{\Sigma}) \in \{\Re(\tilde{\mu}) :\ \tilde{\mu} \in \sigma(\tilde{\Sigma})\}$ and, by definition of $\kappa(\cdot)$, $\rho(\tilde{\Sigma}) \le \kappa(\tilde{\Sigma})$;
4. on the other hand, also by definition of $\kappa(\cdot)$, there is $\tilde{\mu} \in \sigma(\tilde{\Sigma})$ such that $\Re(\tilde{\mu}) = \kappa(\tilde{\Sigma})$ and thus

   $$\kappa(\tilde{\Sigma}) = \Re(\tilde{\mu}) \le |\tilde{\mu}| \le \rho(\tilde{\Sigma}),$$

   where the last inequality follows by definition of $\rho(\cdot)$;
5. we conclude that $\kappa(\tilde{\Sigma}) = \rho(\tilde{\Sigma}) \in \sigma(\tilde{\Sigma})$;
6. furthermore, with the same logic as for $\Sigma - \lambda I_n$ (just let $m = -\lambda$), one has that
   (a) $\mu \in \sigma(\tilde{\Sigma})$ if and only if $\mu - m \in \sigma(\Sigma)$;
   (b) $\kappa(\tilde{\Sigma}) = \kappa(\Sigma) + m$;
7. in particular, $\kappa(\Sigma) = \kappa(\tilde{\Sigma}) - m \in \sigma(\Sigma)$, i.e., $\kappa(\Sigma)$ is an eigenvalue of Σ and thus, by definition of $\kappa(\cdot)$, $\kappa(\Sigma)$ is the greatest real eigenvalue of Σ.

Therefore solutions of the Euler-Lotka equation satisfy $\kappa(\Sigma - \lambda I_n) < 0$ (if solutions exist). Proposition 33 (in the appendix) is applicable and now one can easily obtain (2.11).
Now, it is obvious that

$$f(\lambda) \coloneqq NU(\lambda I_n - \Sigma)^{-1}V$$

is a continuous function in $]\kappa(\Sigma), +\infty[$ satisfying

$$\lim_{\lambda\to\kappa(\Sigma)^+} f(\lambda) = +\infty \quad \text{and} \quad \lim_{\lambda\to+\infty} f(\lambda) = 0\text{:}$$

- continuity of f follows from continuity of the function that maps any invertible matrix to its inverse:
  - the function $\lambda \mapsto \lambda I_n - \Sigma$ is clearly continuous;
  - the function $M \in \mathcal{M}_{n\times n} \mapsto \det M$ is continuous, since it is a polynomial in the coefficients of M, and, if M_{kj} denotes the $(n-1)\times(n-1)$ matrix obtained from M by removing the k-th

row and the j-th column, then the function $M \mapsto \operatorname{adj} M \coloneqq \left[(-1)^{k+j} \det(M_{kj})\right]_{j,k=1,\ldots,n}$ is continuous (each entry is a polynomial);
  - in the set of invertible matrices, one has that the determinant is always nonzero and thus the map $M \mapsto M^{-1} \coloneqq \frac{1}{\det M} \operatorname{adj} M$ is continuous, since both the numerator and denominator are continuous functions and the denominator is never zero (in fact, this map is a rational function);
  - it follows that $\lambda \mapsto (\lambda I_n - \Sigma)^{-1}$ is a composition of continuous functions, hence continuous;
- if one looks at the integral form of f, i.e.,

$$f(\lambda) = NU\left(\int_0^\infty e^{-\tau(\lambda I_n - \Sigma)}\, d\tau\right) V,$$

then continuity of f implies that

$$\lim_{\lambda \to \kappa(\Sigma)^+} f(\lambda) = NU\left(\int_0^\infty e^{-\tau(\kappa(\Sigma) I_n - \Sigma)}\, d\tau\right) V = +\infty$$

(one has that the integral is nonnegative and that it diverges for every $\lambda \in \sigma(\Sigma)$).
- Lebesgue's dominated convergence theorem (theorem 12 in the appendix) guarantees that

$$\lim_{k \to +\infty} \int_0^\infty f_k(\tau)\, d\tau = 0$$

where the sequence $(f_k)_{k \in \mathbb{N}}$ is defined by $f_k : [0, +\infty[\to \mathbb{R}$, $\tau \mapsto Ue^{-\tau(kI_n - \Sigma)}V$ (these functions are clearly continuous, thus measurable, and one can easily see that they are bounded by the integrable function $\tau \mapsto A(\tau)$; furthermore, one can rewrite these functions as $f_k(\tau) = e^{-k\tau} U e^{\tau\Sigma} V$ and conclude easily that $f_k \to 0$ when $k \to +\infty$). Then

$$\lim_{k \to +\infty} f(k) = N \lim_{k \to +\infty} \int_0^\infty f_k(\tau)\, d\tau = 0$$

and, since f is a positive nonincreasing function (demonstrated ahead), the limit exists (see e.g. [Sarrico, 2015]) and thus

$$\lim_{\lambda \to +\infty} f(\lambda) = 0 \cdot$$

The intermediate value theorem (theorem 11 in the appendix) guarantees that the Euler-Lotka equation $f(\lambda) = 1$ has a real root $\tilde{\rho}$ in $]\kappa(\Sigma), +\infty[$. One can see that

$$f'(\lambda) = -NU(\lambda I_n - \Sigma)^{-2} V \cdot$$

It is obvious that $\Sigma - \lambda I_n$ and Σ have the same off-diagonal entries, and so $\Sigma - \lambda I_n \in \mathcal{OD}^+_{n \times n}$ (since $\Sigma \in \mathcal{OD}^+_{n \times n}$). Proposition 32 (in the appendix) guarantees that $e^{\tau(\Sigma - \lambda I_n)} \in \mathcal{OD}^+_{n \times n}$ with a positive diagonal. Then

$$(\lambda I_n - \Sigma)^{-1} = \int_0^\infty e^{\tau(\lambda I_n - \Sigma)}\, d\tau$$

is a nonnegative matrix with a positive diagonal. Now, there is $\tilde{\tau} \in [0, +\infty[$ such that $A(\tilde{\tau}) > 0$. One notes that

$$A(\tau) = Ue^{\tau\Sigma}V = \sum_{k=1}^n \sum_{j=1}^n U_k \left(e^{\tau\Sigma}\right)_{kj} V_j$$

is a sum of nonnegative terms. Thus there is $m, \ell \in \{1, \dots, n\}$ such that

$$U_m \left(e^{\tilde{\tau}\Sigma}\right)_{m\ell} V_\ell > 0,$$

i.e.,

$$U_m > 0, \quad \left(e^{\tilde{\tau}\Sigma}\right)_{m\ell} > 0, \quad V_\ell > 0.$$

By continuity, there is an open subset $\mathcal{O} \subseteq [0, +\infty[$ containing $\tilde{\tau}$ such that

$$\left(e^{\tau\Sigma}\right)_{m\ell} > 0 \quad \text{if } \tau \in \mathcal{O}.$$

It follows that

$$\begin{aligned}
\left((\lambda I_n - \Sigma)^{-1}\right)_{m\ell} &= \left(\int_0^\infty e^{-\tau(\lambda I_n - \Sigma)}\, d\tau\right)_{m\ell} \\
&= \int_0^\infty e^{-\lambda\tau} \left(e^{\tau\Sigma}\right)_{m\ell} d\tau \\
&= \underbrace{\int_{\mathcal{O}} \underbrace{e^{-\lambda\tau}}_{>0} \underbrace{\left(e^{\tau\Sigma}\right)_{m\ell}}_{>0} d\tau}_{>0} + \underbrace{\int_{[0,+\infty[\setminus\mathcal{O}} \underbrace{e^{-\lambda\tau}}_{>0} \underbrace{\left(e^{\tau\Sigma}\right)_{m\ell}}_{\geq 0} d\tau}_{\geq 0} \\
&> 0
\end{aligned}$$

and thus

$$\begin{aligned}
\left((\lambda I_n - \Sigma)^{-2}\right)_{m\ell} &= \sum_{j=1}^n \left((\lambda I_n - \Sigma)^{-1}\right)_{mj} \left((\lambda I_n - \Sigma)^{-1}\right)_{j\ell} \\
&= \underbrace{\sum_{\substack{j=1 \\ j\neq\ell}}^n \underbrace{\left((\lambda I_n - \Sigma)^{-1}\right)_{mj}}_{\geq 0} \underbrace{\left((\lambda I_n - \Sigma)^{-1}\right)_{j\ell}}_{\geq 0}}_{\geq 0} + \underbrace{\underbrace{\left((\lambda I_n - \Sigma)^{-1}\right)_{m\ell}}_{>0} \underbrace{\left((\lambda I_n - \Sigma)^{-1}\right)_{\ell\ell}}_{>0}}_{>0} \\
&> 0.
\end{aligned}$$

Finally

$$\begin{aligned}
f(\lambda) &= NU(\lambda I_n - \Sigma)^{-1} V \\
&= N \left(\underbrace{U_m \left((\lambda I_n - \Sigma)^{-1}\right)_{m\ell} V_\ell}_{>0} + \underbrace{\sum_{\substack{k=1 \\ k\neq m}}^n \sum_{\substack{j=1 \\ j\neq\ell}}^n \underbrace{U_k \left((\lambda I_n - \Sigma)^{-1}\right)_{kj} V_j}_{\geq 0}}_{\geq 0} \right) \\
&> 0
\end{aligned}$$

and

$$\begin{aligned}
f'(\lambda) &= -NU(\lambda I_n - \Sigma)^{-2} V \\
&= -N \left(\underbrace{U_m \left((\lambda I_n - \Sigma)^{-2}\right)_{m\ell} V_\ell}_{>0} + \underbrace{\sum_{\substack{k=1 \\ k\neq m}}^n \sum_{\substack{j=1 \\ j\neq\ell}}^n \underbrace{U_k \left((\lambda I_n - \Sigma)^{-2}\right)_{kj} V_j}_{\geq 0}}_{\geq 0} \right) \\
&< 0.
\end{aligned}$$

Therefore f (is a positive function and) is a strictly decreasing function. One concludes that the Euler-Lotka equation has exactly one real root $\tilde{\rho}$ in $]\kappa(\Sigma), +\infty[$. □

2.1.1 An alternative way of formulating compartmental models

Here, the starting point is the differential equation (1.1), where the force of infection Λ satisfies the renewal equation (1.5). One makes the same assumptions as in section 1.1 and assumes that the expected contribution to the force of infection at time τ after infection is given by (2.1) and that $\kappa(\Sigma) < 0$ (all eigenvalues of Σ have negative real part). One introduces the $n \times 1$ vector-valued function

$$Y(t) \coloneqq \int_0^\infty e^{\tau\Sigma} V \Lambda(t-\tau) S(t-\tau)\, d\tau \tag{2.13}$$

to count the individuals that are infected at time t: for each $t \in \mathbb{R}$,

- the quantity $\Lambda(t)S(t)$ gives the number of new cases per unit of time at time t;
- for each $\tau \geq 0$ and $j \in \{1, \ldots, n\}$, we saw in the previous section that $\left(e^{\tau\Sigma}V\right)_k$ denotes the (total) proportion of individuals in the k-th state at time τ after infection;
- hence, for each $\tau \geq 0$, $\left(e^{\tau\Sigma}V\right)_k \Lambda(t-\tau)S(t-\tau)$ gives the number of individuals in the k-th state at time t that were infected at time $t-\tau$;
- viewing the integral as a sum, one concludes that $Y_k(t)$ is counting the number of individuals that are in the k-th (infected) state at time t (and that were infected since the infinity past until this time).

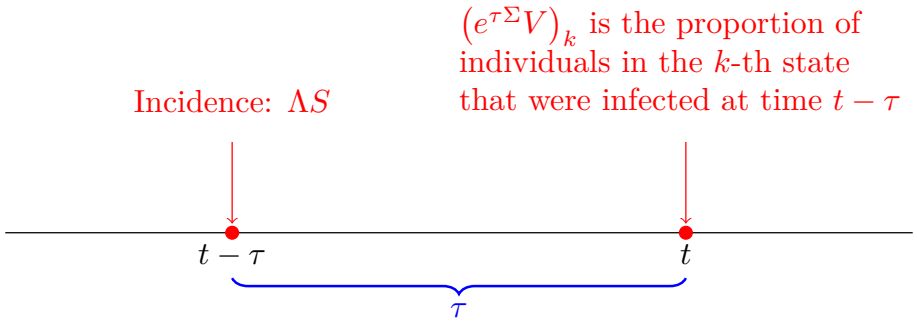

Fig. 2.2. Scheme explaining why Y defined in (2.13) counts the number of individuals that are infected at time t.

One will now prove that Y satisfies an ODE (as was done for Z in the first part of this section):

Proposition 23. *The quantity $Y(t)$ given by* (2.13) *is a bounded function and satisfies the ordinary differential equation*

$$\frac{dY}{dt} = \Sigma Y + (\Lambda S)V\cdot \tag{2.14}$$

Proof. Let $k \in \{1, \ldots, n\}$. It is clear that $Y_k(t) \geq 0$ for all $t \in \mathbb{R}$ (note that $\Lambda \geq 0$, $S \geq 0$, V is a vector with nonnegative entries and, by proposition 32 in the appendix, $e^{\tau\Sigma}$ is a matrix with nonnegative entries). On the other hand, one knows from section 1.1 that $t \mapsto \Lambda(t)S(t)$ is a bounded function, i.e.,

$$\Lambda(t)S(t) = |\Lambda(t)S(t)| \leq C \quad \forall t \in \mathbb{R}$$

for some scalar $C > 0$. It follows that

$$Y_k(t) \leq C\left(\left(\int_0^\infty e^{\Sigma\tau}\, d\tau\right) V\right)_k = C\left(\left(\lim_{\tau\to\infty} e^{\tau\Sigma} - e^{0\cdot\Sigma}\right)\Sigma^{-1}V\right)_k = -C\left(\Sigma^{-1}V\right)_k$$

for every $t \in \mathbb{R}$. Hence $\|Y(t)\| \leq C\|\Sigma^{-1}V\|$ for all $t \in \mathbb{R}$ and thus Y is a bounded function.

Letting $\nu = t - \tau$ in the integral, one obtains

$$Y(t) = e^{t\Sigma} \int_{-\infty}^{t} e^{-\nu\Sigma} V \Lambda(\nu) S(\nu)\, d\nu,$$

and now, by differentiating, it follows that Y satisfies the differential equation

$$\frac{dY}{dt}(t) = \Sigma \underbrace{e^{t\Sigma} \int_{-\infty}^{t} e^{-\nu\Sigma} V \Lambda(\nu) S(\nu)\, d\nu}_{=Y(t)} + \cancel{e^{t\Sigma} e^{-t\Sigma}} V \underbrace{\Lambda(t) S(t)}_{\text{scalar quantity}}$$

i.e., we obtain equation (2.14). □

The following proposition shows a relation between the number (in fact a vector with numbers) of infected individuals Y and the force of infection Λ:

Proposition 24. *The quantity $Y(t)$ given by* (2.13) *is such that $\Lambda(t) = UY(t)$.*

Proof. Immediate by plugging (2.1) into (1.5). □

Definition 6. The ODE system

$$\begin{cases} \dfrac{dS}{dt} = -\Lambda S \\ \dfrac{dY}{dt} = \Sigma Y + (\Lambda S) V \\ \Lambda = UY \end{cases} \tag{2.15}$$

is called the *standard form* of the compartmental model corresponding to Σ, U and V.

Next, we go back to the first part of this section and show that the vector-valued function Z is in fact the integral of Y:

Proposition 25. *The function Z, defined in* (2.5)*, is the integral of Y, i.e.,*

$$Z(t) = \int_{-\infty}^{t} Y(\nu)\, d\nu. \tag{2.16}$$

Proof. Integrating the expression (2.13), that defines $Y(t)$, in $]-t_0, t[$ $(t > -t_0)$, one has

$$\begin{aligned} \int_{-t_0}^{t} Y(\nu)\, d\nu &= \int_{-t_0}^{t} \int_{0}^{\infty} e^{\tau\Sigma} V \Lambda(\nu - \tau) S(\nu - \tau)\, d\tau\, d\nu \\ &= \int_{0}^{\infty} e^{\tau\Sigma} V \left(\int_{-t_0}^{t} -\frac{dS}{d\nu}(\nu - \tau)\, d\nu \right) d\tau \\ &= \int_{0}^{\infty} e^{\tau\Sigma} V \left[S(-t_0 - \tau) - S(t - \tau) \right] d\tau \end{aligned}$$

where in the second line, the change in the order of the integrals follows from Fubini's theorem (theorem 13 in the appendix) applied to each coordinate [19] and one used equation (1.1). Assuming, for simplicity, that $t_0 \in \mathbb{N}$ (the case $t_0 \in \mathbb{R}$ follows by the existence of the limit[20]), one can now apply Lebesgue's

[19] One should use the fact that $t \mapsto \Lambda(t)S(t)$ is a bounded function and the existence of Σ^{-1} to prove integrability (in the product space).

[20] Let $f(t_0) := \int_{-t_0}^{t} Y(\nu)\, d\nu$. It's easy to see that the $k-th$ coordinate of f is bounded above: $f_k \leq -N \left(\Sigma^{-1} V\right)_k$. Furthermore, each coordinate of f is nondecreasing: $f_k'(t_0) = Y_k(-t_0) \geq 0$. Thus the limit $\lim_{t_0 \to +\infty} f(t_0)$ exists (see e.g. [Sarrico, 2015]).

dominated convergence theorem (theorem 12 in the appendix) to each coordinate and obtain

$$\begin{aligned}
\int_{-\infty}^{t} Y(\nu)\,d\nu &\coloneqq \lim_{t_0\to+\infty}\int_{-t_0}^{t} Y(\nu)\,d\nu \\
&= \lim_{t_0\to+\infty}\int_0^{\infty} e^{\tau\Sigma}V\left[S(-t_0-\tau)-S(t-\tau)\right]\,d\tau \\
&= \int_0^{\infty} e^{\tau\Sigma}V\left[\lim_{t_0\to+\infty} S(-t_0-\tau)-S(t-\tau)\right]\,d\tau \\
&= \int_0^{\infty} e^{\tau\Sigma}V\left[N-S(t-\tau)\right]\,d\tau \\
&= \int_0^{\infty} e^{\tau\Sigma}VN\left(1-s(t-\tau)\right)\,d\tau \quad \text{[by the definition of the proportion } s\text{]} \\
&= \int_0^{\infty} e^{\tau\Sigma}V\Psi(w(t-\tau))\,d\tau \quad \text{[using (1.12) and then (1.14)]} \\
&= Z(t) \quad \text{[by equation (2.5)].}
\end{aligned}$$

□

We can now use (the proof of) proposition 25 to arrive at the integrated form (2.6): since

$$Z(t) = \int_0^{\infty} e^{\tau\Sigma}V\Psi(w(t-\tau))\,d\tau$$

and the change of variable $\nu = t-\tau$ leads to

$$Z(t) = e^{t\Sigma}\int_{-\infty}^{t} e^{-\nu\Sigma}V\Psi(w(\nu))\,d\nu,$$

then one only needs to differentiate and use equation (2.4) to obtain the integrated form.

Remark 22. One should note that the integrated form (2.6) has dimension n while the standard form (2.15) has dimension $n+1$. So, in terms of dimensions, the integrated form has the advantage. Furthermore, one can extend immaculately the integrated form to the separable heterogeneous setting (while it is not as easy for the standard form, as we will see in the next section).

Now, we follow with two basic examples to illustrate the integrated formalism: the SIR model and the SEIR model.

Example 6 (SIR model)**.** The standard form of the SIR model is given by

$$\begin{cases} \dfrac{dS}{dt} = -\beta IS \\ \dfrac{dI}{dt} = \beta IS - \alpha I \end{cases},$$

where β is the per capita contribution to the force of infection and α is the rate at which individuals leave the infected compartment. Here, there is only one infected state I, so that $n=1$ and $Y(t)=I(t)$. The force of infection is clearly $\Lambda(t)=\beta I(t)$, the state transition matrix is $\Sigma=-\alpha$ and one has clearly $U=\beta$ and $V=1$. The expected contribution to the force of infection is

$$A(\tau) = Ue^{\tau\Sigma}V = \beta e^{-\alpha\tau}.$$

The integrated form is

$$\frac{dZ}{dt} = -\alpha Z + \Psi(\beta Z) \tag{2.17}$$

where $Z(t) = \int_{-\infty}^{t} I(\nu)\, d\nu$. One can see that

$$w(t) = \int_{-\infty}^{t} \Lambda(\nu)\, d\nu = \beta \int_{-\infty}^{t} I(\nu)\, d\nu = \beta Z(t) = UZ(t)\cdot$$

Example 7 (SEIR model)**.** The standard form of the SEIR model is given by

$$\begin{cases} \dfrac{dS}{dt} = -\beta IS \\ \dfrac{dE}{dt} = \beta IS - \gamma E \\ \dfrac{dI}{dt} = \gamma E - \alpha I \end{cases},$$

where β is the per capita contribution to the force of infection, γ is the rate at which individuals leave the exposed compartment and α is the rate at which individuals leave the infectious compartment. Here, there are two infected states E and I, so that $n = 2$ and $Y(t) = \begin{bmatrix} E(t) \\ I(t) \end{bmatrix}$. The force of infection is $\Lambda(t) = \beta I(t)$, the state transition matrix is $\Sigma = \begin{bmatrix} -\gamma & 0 \\ \gamma & -\alpha \end{bmatrix}$ and one has clearly $U = \begin{bmatrix} 0 & \beta \end{bmatrix}$ and $V = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$. The expected contribution to the force of infection is

$$A(\tau) = Ue^{\tau\Sigma}V = \begin{cases} \beta\gamma e^{-\gamma\tau} & \text{if } \gamma = \alpha \\ \dfrac{\beta\gamma}{\alpha - \gamma}\left(e^{-\gamma\tau} - e^{-\alpha\tau}\right) & \text{if } \gamma \neq \alpha \end{cases}$$

(one can see the calculations in example 4, in the first part of this section). The integrated form is

$$\frac{dZ}{dt} = \begin{bmatrix} -\gamma & 0 \\ \gamma & -\alpha \end{bmatrix} Z + \begin{bmatrix} 1 \\ 0 \end{bmatrix} \Psi\left(\begin{bmatrix} 0 & \beta \end{bmatrix} Z\right) \tag{2.18}$$

i.e.,

$$\begin{cases} \dfrac{dZ_1}{dt} = -\gamma Z_1 + \Psi(\beta Z_2) \\ \dfrac{dZ_2}{dt} = \gamma Z_1 - \alpha Z_2 \end{cases}$$

where

$$Z(t) = \begin{bmatrix} Z_1(t) \\ Z_2(t) \end{bmatrix} = \begin{bmatrix} \int_{-\infty}^{t} E(\nu)\, d\nu \\ \int_{-\infty}^{t} I(\nu)\, d\nu \end{bmatrix}.$$

One can see that

$$w(t) = \int_{-\infty}^{t} \Lambda(\nu)\, d\nu = \beta \int_{-\infty}^{t} I(\nu)\, d\nu = \beta Z_2(t) = UZ(t)\cdot$$

2.2 Taking heterogeneity into account

Here we consider a host population where individuals are characterized by a certain trait[21], say $\omega \in \Omega$ with Ω a measurable space. With this formulation, one has that ω may be a discrete variable, a continuous variable or a mixture of these two (i.e., ω may have both a discrete and a continuous component). Now the expected contribution to the force of infection, A, has three arguments:

- ω: trait value of the individual that is at risk of becoming infected;
- η: trait value of the infected individual;
- τ: time-since-infection of the infected individual;

i.e., $A = A(\tau, \omega, \eta)$ is the *expected contribution to the force of infection on (susceptible) individuals of trait ω by an individual of trait η that was itself infected τ units of time ago*.

The objective is to study the implementation of heterogeneity whether the trait set Ω is discrete (e.g., a finite set) or continuous. For this generalization, one considers that the population composition is described by:

- a probability measure[22] Φ on Ω;
- for any $t \in \mathbb{R}$, a bounded measurable function $s(t, \cdot)$ such that a fraction $s(t, \omega)$ of the individuals with trait ω is still susceptible at time t (i.e., $s(t, \omega)$ is the probability that an individual with trait ω is susceptible at time t and $s(-\infty, \omega) \coloneqq \lim_{t \to -\infty} s(t, \omega) = 1$).

The differential equation that describes the number (or rather the proportion) of susceptibles is but just a reformulation of ODE (1.1):

$$\frac{\partial s}{\partial t}(t, \omega) = -\Lambda(t, \omega) s(t, \omega) \tag{2.19}$$

where $\Lambda(t, \omega)$ is the force of infection on (susceptible) individuals of trait ω at time t. In the same manner, the renewal equation (1.5), that describes the force of infection, can be rewritten as

$$\Lambda(t, \omega) = N \int_0^\infty \int_\Omega A(\tau, \omega, \eta) \Lambda(t - \tau, \eta) s(t - \tau, \eta)\, \Phi(d\eta)\, d\tau. \tag{2.20}$$

A special case

Assume that there are nonnegative measurable functions (not identically 0) a, b and c such that

$$A(\tau, \omega, \eta) \coloneqq a(\omega) b(\tau) c(\eta) \cdot \tag{2.21}$$

Here, one has

- $a(\omega)$ is the susceptibility of individuals with trait ω;
- $c(\eta)$ is the infectiousness of individuals with trait η.

Remark 23. One can assume that b is integrable in $[0, \infty[$, and a and c are integrable in Ω with respect to the measure Φ.

[21] An individual keeps the same trait throughout its life.

[22] The measure Φ describes the probability distribution of the trait in the host population. In particular, if Ω is a discrete space and Φ is a discrete measure, then $\Phi(\{\omega\})$ can be seen as the proportion of individuals with trait $\omega \in \Omega$.

One starts by obtaining a simpler formula for the cumulative force of infection, in this special case.

Proposition 26. *The force of infection on susceptible individuals of trait ω is a product of the susceptibility $a(\omega)$ and a function of time. Furthermore, the cumulative force of infection on susceptible individuals of trait ω is of the form*

$$\int_{-\infty}^{t} \Lambda(\nu, \omega)\, d\nu = a(\omega) w(t), \tag{2.22}$$

for some function w of t.

Proof. With (2.21), the renewal equation (2.20) gives

$$\Lambda(t, \omega) = N \int_0^\infty \int_\Omega a(\omega) b(\tau) c(\eta) \Lambda(t - \tau, \eta) s(t - \tau, \eta)\, \Phi(d\eta)\, d\tau,$$

i.e.,

$$\Lambda(t, \omega) = a(\omega) \cdot \underbrace{N \int_0^\infty \int_\Omega b(\tau) c(\eta) \Lambda(t - \tau, \eta) s(t - \tau, \eta)\, \Phi(d\eta)\, d\tau}_{=:W(t),\ \text{a function of time } t} \cdot$$

Hence

$$\Lambda(t, \omega) = a(\omega) W(t)$$

and (2.22) follows by taking w as the integral of W, i.e.,

$$w(t) \coloneqq \int_{-\infty}^{t} W(\nu)\, d\nu.$$

□

Now, one gets a really nice expression for the solution of (2.19) that satisfies $s(-\infty, \omega) = 1$ for all $\omega \in \Omega$:

Proposition 27. *The solution of* (2.19) *that satisfies $s(-\infty, \omega) = 1$ for all $\omega \in \Omega$ is given by:*

$$s(t, \omega) = e^{-a(\omega) w(t)}. \tag{2.23}$$

Proof. From (2.19), it is clear that

$$s(t, \omega) \exp\left\{ \int_{t_0}^{t} \Lambda(\nu, \omega)\, d\nu \right\} = s(t_0, \omega)$$

for some real number t_0. Now, by hypothesis,

$$s(-\infty, \omega) \coloneqq \lim_{t \to -\infty} s(t, \omega) = 1 \quad \forall \omega \in \Omega,$$

and thus the second side of the obtained expression converges when $t_0 \to -\infty$. We conclude that the first side must converge when $t_0 \to -\infty$. Hence one can take the limit when $t_0 \to -\infty$ and obtain

$$s(t, \omega) \exp\left\{ \int_{-\infty}^{t} \Lambda(\nu, \omega)\, d\nu \right\} = s(-\infty, \omega),$$

i.e.,

$$s(t, \omega) \exp\left\{ \int_{-\infty}^{t} \Lambda(\nu, \omega)\, d\nu \right\} = 1 \cdot$$

Therefore

$$s(t,\omega) = \exp\left\{-\int_{-\infty}^{t} \Lambda(\nu,\omega)\, d\nu\right\}$$

and, with (2.22), one obtains (2.23). □

Finally, a proposition very similar to proposition 4 is given:

Proposition 28. *The function w defined in proposition 26 satisfies:*

$$w(t) = \int_0^\infty b(\tau)\Psi(w(t-\tau))\, d\tau \tag{2.24}$$

with Ψ now defined by

$$\Psi(w) \coloneqq N\int_\Omega c(\eta)\left(1 - e^{-a(\eta)w}\right)\Phi(d\eta)\cdot \tag{2.25}$$

Proof. Choosing $t_0 \in \mathbb{N}$, integrating W in $]-t_0, t]$ (for $t > -t_0$) and using (2.19), one obtains

$$\int_{-t_0}^{t} W(\nu)\, d\nu = N\int_{-t_0}^{t}\int_0^\infty\int_\Omega b(\tau)c(\eta)\left[-\frac{\partial s}{\partial \nu}(\nu-\tau,\eta)\right]\Phi(d\eta)\, d\tau\, d\nu\cdot$$

Now, Φ is a probability measure in Ω and so $\Phi(\Omega) = 1$. By example 15 (in the appendix),

$$\int_{-t_0}^{t} W(\nu)\, d\nu = N\int_0^\infty\int_\Omega b(\tau)c(\eta)[s(-t_0-\tau,\eta) - s(t-\tau,\eta)]\,\Phi(d\eta)\, d\tau\cdot$$

By example 16 (in the appendix),

$$\lim_{k\to+\infty}\int_{-k}^{t} W(\nu)\, d\nu = \int_0^\infty\int_\Omega b(\tau)c(\eta)[1 - s(t-\tau,\eta)]\, d(\Phi(\eta),\tau)\cdot$$

By the existence of the limit[23], we conclude that

$$\int_{-\infty}^{t} W(\nu)\, d\nu \coloneqq \lim_{t_0\to+\infty}\int_{-t_0}^{t} W(\nu)\, d\nu = N\int_0^\infty\int_\Omega b(\tau)c(\eta)[1 - s(t-\tau,\eta)]\,\Phi(d\eta)\, d\tau\cdot$$

Finally, by using (2.23), one has

$$\int_{-\infty}^{t} W(\nu)\, d\nu = N\int_0^\infty b(\tau)\left(\int_\Omega c(\eta)\left[1 - e^{a(\omega)w(t-\tau)}\right]\Phi(d\eta)\right) d\tau$$

and, with (2.25), one obtains (2.24). □

Remark 24. Equations (1.13) and (2.24) are essentially the same.

Remark 25. When a and c are identically equal to 1 (homogeneous case), (2.25) reduces to (1.14).

Remark 26. When a is identically equal to 1, definition (2.25) gives

$$\Psi(w) = N(1 - e^{-w})\int_\Omega c(\eta)\,\Phi(d\eta)$$

and thus one can work with the average value of c.

[23] Let $f(t_0) = \int_{-t_0}^{t} W(\nu)\, d\nu$. Since b and c are nonnegative and integrable in their domains, then is easy to see that f is bounded above. On the other hand, $f_k'(t_0) = W_k(-t_0) \geq 0$ and thus f_k is a nondecreasing function. We conclude that the limit $\lim_{t_0\to+\infty} f(t_0)$ exists (see e.g. [Sarrico, 2015].

Remark 27. When $b(\tau) = Ue^{\tau\Sigma}V$ with the same assumptions as (2.1), then the study done in section 2.1 is valid for this case (just switch $A(\tau)$ by $b(\tau)$ and redefine Ψ). Therefore **to integrate separable heterogeneity into the integrated formulation of a compartmental model, it suffices to redefine the function Ψ.**

Next one sees that incorporation of heterogeneity into the standard form is not as simple as in the integrated form. Here, it is assumed that $b(\tau)$ is of the form (2.1), i.e.,

Let $n \in \mathbb{N}$ be the number of infected states in a certain population and suppose

$$b(\tau) \coloneqq Ue^{\tau\Sigma}V,$$

where $\tau \geq 0$ and

- $\Sigma \in \mathcal{OD}^{+}_{n\times n}$ is a matrix that generates the Markov chain dynamics of the infected states, i.e., it describes the *state transitions of the infected*;
- $U \in \mathcal{M}^{+}_{1\times n}$ is a (row) vector such that its k-th component gives the contribution to the force of infection of an individual in the k-th (infected) state;
- $V \in \mathcal{M}^{+}_{n\times 1}$ is a (column) vector representing the probability distribution of the state-at-infection.

The objective now is to take the standard form (2.15) and incorporate separable static heterogeneity as described by

- the trait space Ω;
- the trait distribution Φ;
- the relative trait-specific susceptibility a;
- the trait-specific infectiousness c.

Here *relative* means that one chooses a representative $\bar{\omega} \in \Omega$ such that $a(\bar{\omega}) = 1$, always possible if one swaps the function $a(\omega)$ by

$$\frac{a(\omega)}{a(\bar{\omega})}$$

where $\bar{\omega} \in \Omega$ is such that $a(\bar{\omega}) \neq 0$ (existent by hypothesis).

With this choice, one obtains the following result:

Proposition 29. *Let $\omega \in \Omega$. The fraction of the individuals with trait ω that escaped infection until time t is given by*

$$s(t,\omega) = \bar{s}(t)^{a(\omega)}, \tag{2.26}$$

where $\bar{s}(t) \coloneqq s(t,\bar{\omega})$. Furthermore,

$$w(t) = -\ln \bar{s}(t)\cdot \tag{2.27}$$

Proof. By proposition 27, the fraction of the individuals with trait ω that are still susceptible until time t is given by (2.23). In particular,

$$s(t,\bar{\omega}) = e^{-a(\bar{\omega})w(t)}$$

and, given that $a(\bar{\omega}) = 1$ by hypothesis, one obtains

$$\bar{s}(t) = e^{-w(t)}.$$

Equations (2.26) and (2.27) now follow. □

Remark 28. The previous proposition shows that to determine $s(t,\omega)$ or $w(t)$, it suffices to know $\bar{s}(t)$.

Corollary 2. *The total proportion of susceptibles at time* t *is given by*

$$s_{total}(t) = \int_\Omega \bar{s}(t)^{a(\omega)} \Phi(d\omega). \tag{2.28}$$

Now, in analogy with (2.13), one introduces the trait-specific $n \times 1$ vector-valued function

$$y(t,\eta) \coloneqq \int_0^\infty e^{\tau\Sigma} V \Lambda(t-\tau,\eta) s(t-\tau,\eta)\, d\tau \tag{2.29}$$

to count the number of infected individuals with trait η at time t, and then one defines the weighted average

$$Y(t) \coloneqq N \int_\Omega c(\eta) y(t,\eta) \Phi(d\eta). \tag{2.30}$$

As was done in the previous section, define the $n \times 1$ vector-valued function Z by (2.5), where Ψ is given by (2.25). Then Z is the integral of Y, i.e.:

Proposition 30. *Let* Y *be defined by* (2.30)*, where* y *is defined by* (2.29)*. The function* Z*, defined in* (2.5)*, where* Ψ *is given by* (2.25)*, is the integral of* Y*, i.e.,*

$$Z(t) = \int_{-\infty}^t Y(\nu)\, d\nu.$$

Proof. The proof is very similar to the proof of proposition 25: one starts with the same integral, applies Fubini's theorem (theorem 13 in the appendix) to each coordinate two times and obtains, after integrating in order to ν,

$$\int_{-t_0}^t Y(\nu)\, d\nu = N \int_\Omega c(\eta) \left[\int_0^\infty e^{\tau\Sigma} V \left(s(-t_0-\tau,\eta) - s(t-\tau,\eta) \right) d\tau \right] \Phi(d\eta).$$

Now, as was done there, one applies Lebesgue's dominated convergence theorem (theorem 12 in the appendix) to each coordinate and uses (2.23) to obtain

$$\int_{-\infty}^t Y(\nu)\, d\nu \coloneqq \int_{-t_0}^t Y(\nu)\, d\nu = N \int_\Omega c(\eta) \left[\int_0^\infty e^{\tau\Sigma} V \left(1 - e^{-a(\eta) w(t-\tau)} \right) d\tau \right] \Phi(d\eta).$$

Applying Fubini's theorem to each coordinate, using (2.25) and (2.5), one obtains the desired result. □

We are finally prepared to formulate the standard form which takes into account the separable static heterogeneity:

Theorem 9. *The heterogeneous compartmental model system consisting of the integrated form* (2.6)*, with* Ψ *defined by* (2.25)*, has the standard form representation*

$$\begin{cases} \dfrac{d\bar{s}}{dt} = -\bar{\Lambda}\bar{s} \\ \dfrac{dY}{dt} = \Sigma Y + \left(\bar{\Lambda} \Psi'(-\ln \bar{s}) \right) V \\ \bar{\Lambda} = UY \end{cases} \tag{2.31}$$

where $\bar{s}(t) = s(t,\bar{\omega})$ *and* $\bar{\Lambda}(t) = \Lambda(t,\bar{\omega})$*. Furthermore,*

$$\Psi'(w) = N \int_\Omega c(\eta) a(\eta) e^{-a(\eta)w}\, \Phi(d\eta). \tag{2.32}$$

Proof. Using equation (2.19),

$$\frac{d\bar{s}}{dt} = \left(\frac{\partial s}{\partial t}(t,\omega)\right)\Big|_{\omega=\bar{\omega}} = (-\Lambda(t,\omega)s(t,\omega))|_{\omega=\bar{\omega}} = -\Lambda(t,\bar{\omega})s(t,\bar{\omega}) = -\bar{\Lambda}(t)\bar{s}(t)\cdot$$

Now,

$$A(\tau,\bar{\omega},\eta) = \underbrace{a(\bar{\omega})}_{=1} b(\tau)c(\eta) = Ue^{\tau\Sigma}Vc(\eta)$$

and, by applying Fubini's theorem (theorem 13 in the appendix) to each coordinate,

$$\begin{aligned}
\bar{\Lambda}(t) &= \Lambda(t,\bar{\omega}) \\
&= U \cdot N \int_0^\infty \int_\Omega c(\eta) e^{\tau\Sigma} V \Lambda(t-\tau,\eta) s(t-\tau,\eta)\, \Phi(d\eta)\, d\tau \\
&= U\left[N \int_\Omega c(\eta) \underbrace{\left(\int_0^\infty e^{\tau\Sigma} V \Lambda(t-\tau,\eta) s(t-\tau,\eta)\, d\tau\right)}_{=y(t,\eta)} \Phi(d\eta)\right] \\
&= U\left[N \int_\Omega c(\eta) y(t,\eta)\, \Phi(d\eta)\right] \\
&= UY(t)
\end{aligned}$$

where definitions (2.29) and (2.30) were used.
Finally, by proposition 30, one has that Z is the integral of Y and thus

$$Y = \frac{dZ}{dt}\cdot$$

Now, since Z satisfies (2.6), one has

$$Y = \Sigma Z + V\Psi(UZ)$$

and, differentiating,

$$\frac{dY}{dt} = \Sigma\frac{dZ}{dt} + \left(U\frac{dZ}{dt}\Psi'(UZ)\right)V = \Sigma Y + \left(UY\Psi'(UZ)\right)V\cdot$$

It is already proven that $\bar{\Lambda} = UY$. On the other hand, by proposition 21 and by equation (2.27), one has the following identity $UZ = -\ln \bar{s}$. It follows that

$$\frac{dY}{dt} = \Sigma Y + \left(\bar{\Lambda}\Psi'(-\ln \bar{s})\right)V\cdot$$

Equation (2.32) follows by differentiating equation (2.25). □

2.3 Examples

The Gamma Distribution

Take $\Omega =]0,\infty[$ and let Φ be the Gamma Distribution with mean 1 and variance p^{-1} (for some $p > 0$), i.e., the density of Φ is given by

$$\phi :]0,\infty[\to]0,\infty[, \quad \omega \mapsto \frac{p^p}{\Gamma(p)}\omega^{p-1}e^{-p\omega}$$

Assume that the trait corresponds directly to the relative susceptibility, i.e., $a(\omega) = \omega$. Then, by

definition (2.25),

$$\Psi(w) = N \int_0^\infty c(\eta) \left(1 - e^{-\eta w}\right) \Phi(d\eta) = N \int_0^\infty c(\eta) \left(1 - e^{-w\eta}\right) \phi(\eta)\, d\eta.$$

Choose $c(\eta) = c_1\eta + c_2$ for some $c_1, c_2 \geq 0$ with $c_1 \neq 0$ or $c_2 \neq 0$. In this case, one will see that Ψ is easily calculated with the use of the Laplace Transform (see the last part of the appendix for more details) $\hat{\Phi}$ of ϕ. One has:

$$\Psi(w) = N \left[\int_0^\infty (c_1\eta + c_2)\phi(\eta)\, d\eta - \int_0^\infty (c_1\eta + c_2)\phi(\eta) e^{-w\eta}\, d\eta \right].$$

Now, for $\lambda \in \mathbb{C}$,

$$\begin{aligned}
\int_0^\infty (c_1\eta + c_2)\phi(\eta) e^{-\lambda\eta}\, d\eta &= \mathcal{L}\left\{(c_1\eta + c_2)\phi(\eta)\right\}(\lambda) \\
&= c_1 \mathcal{L}\left\{\eta\phi(\eta)\right\}(\lambda) + c_2 \mathcal{L}\left\{\phi(\eta)\right\}(\lambda) \\
&= -c_1 \frac{d\hat{\Phi}}{d\lambda}(\lambda) + c_2 \hat{\Phi}(\lambda)
\end{aligned}$$

where $\mathcal{L}\{f\}(\lambda)$ denotes the Laplace Transform of f at $\lambda \in \mathbb{C}$. One has

$$\begin{aligned}
\hat{\Phi}(\lambda) &:= \mathcal{L}\left\{ \frac{p^p}{\Gamma(p)} \eta^{p-1} e^{-p\eta} \right\}(\lambda) \\
&= \frac{p^p}{\Gamma(p)} \mathcal{L}\left\{\eta^{p-1} e^{-p\eta}\right\}(\lambda) \\
&= \frac{p^p}{\Gamma(p)} \mathcal{L}\left\{\eta^{p-1}\right\}(\lambda + p) \\
&= \frac{p^p}{\cancel{\Gamma(p)}} \frac{\cancel{\Gamma(p)}}{(\lambda + p)^p} \\
&= \left(\frac{\lambda}{p} + 1\right)^{-p}
\end{aligned}$$

for $\lambda \in \mathbb{C}$ such that $\Re(\lambda) > -p$. Differentiating, one gets

$$\frac{d\hat{\Phi}}{d\lambda}(\lambda) = -p \frac{1}{p} \left(\frac{\lambda}{p} + 1\right)^{-p-1} = -\left(\frac{\lambda}{p} + 1\right)^{-p-1}.$$

It follows that

$$\int_0^\infty (c_1\eta + c_2)\phi(\eta) e^{-\lambda\eta}\, d\eta = c_1 \left(\frac{\lambda}{p} + 1\right)^{-p-1} + c_2 \left(\frac{\lambda}{p} + 1\right)^{-p}$$

for $\lambda \in \mathbb{C}$ such that $\Re(\lambda) > -p$.

It is clear that $\Re(0) > -p$. Then

$$\int_0^\infty (c_1\eta + c_2)\phi(\eta)\, d\eta = \int_0^\infty (c_1\eta + c_2)\phi(\eta) e^{-0\cdot\eta}\, d\eta = c_1 \left(\frac{0}{p} + 1\right)^{-p-1} + c_2 \left(\frac{0}{p} + 1\right)^{-p} = c_1 + c_2.$$

Now, for $w \geq 0$, one has $\Re(w) = w > -p$ and so

$$\int_0^\infty (c_1\eta + c_2)\phi(\eta) e^{-w\eta}\, d\eta = c_1 \left(\frac{w}{p} + 1\right)^{-p-1} + c_2 \left(\frac{w}{p} + 1\right)^{-p}.$$

Therefore

$$\Psi(w) = N\left[(c_1+c_2) - \left(c_1\left(\frac{w}{p}+1\right)^{-p-1} + c_2\left(\frac{w}{p}+1\right)^{-p}\right)\right],$$

i.e.,

$$\Psi(w) = N\left[c_1\left(1-\left(\frac{w}{p}+1\right)^{-p-1}\right) + c_2\left(1-\left(\frac{w}{p}+1\right)^{-p}\right)\right].$$

In particular, if the trait has no influence on infectiousness, i.e., with $c \equiv 1$ ($c_1 = 0, c_2 = 1$), we have

$$\Psi(w) = N\left[1-\left(\frac{w}{p}+1\right)^{-p}\right],$$

while if infectiousness too is correspondent to the trait, i.e., with $c(\eta) = \eta$ ($c_1 = 1, c_2 = 0$), we have

$$\Psi(w) = N\left[1-\left(\frac{w}{p}+1\right)^{-p-1}\right].$$

Now we obtain easily an expression for the total proportion of susceptibles s_{total} in terms of $\bar{s}$:

$$s_{\text{total}} = \int_0^\infty \bar{s}^\omega\, \Phi(d\omega) = \int_0^\infty \phi(\omega) e^{-(-\ln \bar{s})\omega}\, d\omega = \hat{\Phi}(-\ln \bar{s}) = \left(\frac{-\ln \bar{s}}{p}+1\right)^{-p}$$

where in the last equality we use the fact that $p > 0$ and $\bar{s} < 1$, and so $\Re(-\ln \bar{s}) = -\ln \bar{s} > 0 > -p$. Differentiating

$$\frac{ds_{\text{total}}}{dt} = \cancel{-p}\left(\frac{-\ln \bar{s}}{p}+1\right)^{-p-1}\left(\cancel{-\frac{1}{p}}\frac{1}{\bar{s}}\frac{d\bar{s}}{dt}\right) = \underbrace{\frac{1}{\bar{s}}\frac{d\bar{s}}{dt}}_{=-\hat{\Lambda}}\underbrace{\left(\frac{-\ln \bar{s}}{p}+1\right)^{-p-1}}_{=s_{\text{total}}^{-\frac{1}{p}}} = -\hat{\Lambda} s_{\text{total}}^{1+\frac{1}{p}}.$$

We can thus obtain the standard form using s_{total} instead of $\bar{s}$.

The next step is to differentiate the expression for Ψ:

$$\begin{aligned}\Psi'(w) &= N\left[-c_1(-p-1)\frac{1}{p}\left(\frac{w}{p}+1\right)^{-p-2} - c_2(-p)\frac{1}{p}\left(\frac{w}{p}+1\right)^{-p-1}\right] \\ &= N\left(\frac{w}{p}+1\right)^{-p-1}\left[c_2 + c_1\left(1+\frac{1}{p}\right)\left(\frac{w}{p}+1\right)^{-1}\right]\end{aligned}$$

and

$$\Psi'(-\ln \bar{s}) = N\left(-\frac{\ln \bar{s}}{p}+1\right)^{-p-1}\left[c_2 + c_1\left(1+\frac{1}{p}\right)\left(-\frac{\ln \bar{s}}{p}+1\right)^{-1}\right].$$

It is clear that

$$-\ln \bar{s} = p s_{\text{total}}^{-\frac{1}{p}} - p.$$

Now, by defining $\Upsilon(s) \coloneqq \Psi'\left(p s^{-\frac{1}{p}} - p\right)$, one gets

$$\Upsilon(s) = N\left(s^{-\frac{1}{p}}\right)^{-p-1}\left[c_2 + c_1\left(1+\frac{1}{p}\right)\left(s^{-\frac{1}{p}}\right)^{-1}\right],$$

i.e.,

$$\Upsilon(s) = N s^{1+\frac{1}{p}}\left[c_2 + c_1\left(1+\frac{1}{p}\right)s^{\frac{1}{p}}\right].$$

In particular,

$$\Upsilon(s) = \begin{cases} N s^{1+\frac{1}{p}} & \text{if } c \equiv 1 \\ N\left(1+\frac{1}{p}\right) s^{1+\frac{2}{p}} & \text{if } c(\eta) = \eta \end{cases}.$$

One should note that $\Upsilon\left(s_{\text{total}}\right) = \Psi'(-\ln \bar{s})$.

Therefore the standard form (2.31) is, in this particular case, given by

$$\begin{cases} \dfrac{ds_{\text{total}}}{dt} = -\bar{\Lambda} s_{\text{total}}^{1+\frac{1}{p}} \\ \dfrac{dY}{dt} = \Sigma Y + \left(\bar{\Lambda}\Upsilon\left(s_{\text{total}}\right)\right) V \\ \bar{\Lambda} = UY \end{cases}$$

with s_{total} instead of $\bar{s}$.

Other examples

Example 8 (SEIR model with asymptomatic infection and quarantine)**.** Here we show the relation between the model ingredients U, Σ and V and the diagram that represents the model. It is shown the relation between the compartmental model, the standard form (2.15) and the integrated form (2.6). We will also calculate some basic indices for the model (see proposition 22): the basic reproduction number R_0, the generation time T and the Euler-Lotka equation.

In the following scheme, it is represented a SEIR model with asymptomatic infection and quarantine:

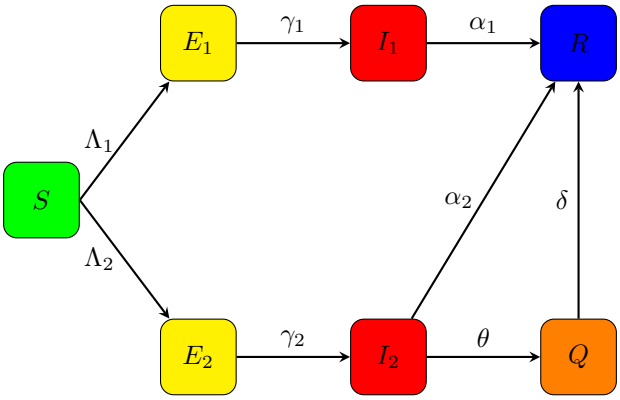

Fig. 2.3. SEIR compartmental model with asymptomatic infection and quarantine. Upon infection, individuals are separated into two subgroups: asymptomatic (with index 1) and symptomatic (with index 2). The force of infection responsible for infected individuals of type j is Λ_j (for $j \in \{1,2\}$). Individuals move from the j-th latent compartment E_j to the j-th infectious compartment I_j at a rate γ_j and move from this to compartment R at a rate α_j ($j \in \{1,2\}$). Furthermore, symptomatic infectious individuals (I_2) go to quarantine (Q) at a rate θ. From Q, individuals go to compartment R at a rate δ. Here, the host population is assumed to be demographically closed and, in particular, births and deaths (not due to the disease) are ignored.

We denote asymptomatic individuals by index 1 and symptomatic by index 2, and we assume they occur with ratio $p : 1-p$, with $p \in]0,1[$ a parameter. I.e., if Λ is the force of infection, then the force of infection responsible for asymptomatic infectious individuals is $\Lambda_1 = p\Lambda$ whereas the force of infection responsible for symptomatic infectious individuals is $\Lambda_2 = (1-p)\Lambda$. The asymptomatic individuals follow the "usual" model whereas the symptomatic individuals may be put in quarantine as the symptoms

appear. Here, the compartment of quarantined individuals is denoted by Q. Furthermore, for $j \in \{1, 2\}$,

- individuals move from E_j to I_j at a rate γ_j;
- individuals move from I_j to R at a rate α_j;
- individuals move from I_2 to Q at a rate θ;
- individuals move from Q to R at a rate δ.

We define the 4-vector Y by

$$Y = \begin{bmatrix} E_1 \\ E_2 \\ I_1 \\ I_2 \end{bmatrix}$$

to count the number of infected individuals that are not quarantined (for $k \in \{1, 2, 3, 4\}$, the $k - th$ infected state is the k-th component of Y). We note that

$$S + E_1 + E_2 + I_1 + I_2 + Q + R$$

is constant along time. Furthermore, from the diagram, we see that $\frac{dQ}{dt} = \theta I_2 - \delta Q$ and thus one can obtain an expression for Q if given an expression for I_2. Therefore it is irrelevant to include Q in our vector Y. Now, an individual who was just infected is not yet infectious and so the probability to enter the compartment I_1 or I_2 is 0; for $j \in \{1, 2\}$, the probability to enter compartment E_j is given by $\frac{\Lambda_j}{\Lambda}$. Hence the vector V, that represents the probability distribution of the state-at-infection, can be defined by

$$V = \begin{bmatrix} p \\ 1 - p \\ 0 \\ 0 \end{bmatrix}.$$

The matrix Σ, that describes the state transitions of the infected, is defined by

$$\Sigma = \begin{bmatrix} -\gamma_1 & 0 & 0 & 0 \\ 0 & -\gamma_2 & 0 & 0 \\ \gamma_1 & 0 & -\alpha_1 & 0 \\ 0 & \gamma_2 & 0 & -(\alpha_2 + \theta) \end{bmatrix},$$

since each element $\Sigma_{k\ell}$ ($k \neq \ell$) represent the transition rate from state ℓ to state k while $-\Sigma_{kk}$ represent the rate at which individuals leave state k.

Now, since individuals in compartments E_1 and E_2 are not yet infectious, then the vector U, that gives the contribution to the force of infection by an individual, can be defined by

$$U = \begin{bmatrix} 0 & 0 & \beta_1 & \beta_2 \end{bmatrix},$$

where β_j is the per capita contribution to the force of infection Λ_j ($j \in \{1, 2\}$).

The standard form (2.15) leads to the system of equations

$$\begin{cases} \Lambda & = \beta_1 I_1 + \beta_2 I_2 \\ \dfrac{dS}{dt} & = -(\beta_1 I_1 + \beta_2 I_2) S \\ \dfrac{dE_1}{dt} & = -\gamma_1 E_1 + p(\beta_1 I_1 + \beta_2 I_2) S \\ \dfrac{dE_2}{dt} & = -\gamma_2 E_2 + (1-p)(\beta_1 I_1 + \beta_2 I_2) S \\ \dfrac{dI_1}{dt} & = \gamma_1 E_1 - \alpha_1 I_1 \\ \dfrac{dI_2}{dt} & = \gamma_2 E_2 - (\alpha_2 + \theta) I_2 \end{cases}$$

which, with $\frac{dQ}{dt} = \theta I_2 - \delta Q$ and $\frac{dR}{dt} = \alpha_1 I_1 + \alpha_2 I_2 + \delta Q$, is exactly the compartmental model schematized in figure 2.3.

Now, by defining Z by (2.16), one obtains the integrated form (2.6). Indeed, one has

$$Z(t) = \int_{-\infty}^{t} Y(\nu)\, d\nu = \begin{bmatrix} \int_{-\infty}^{t} E_1(\nu)\, d\nu \\ \int_{-\infty}^{t} E_2(\nu)\, d\nu \\ \int_{-\infty}^{t} I_1(\nu)\, d\nu \\ \int_{-\infty}^{t} I_2(\nu)\, d\nu \end{bmatrix}$$

and

$$UZ(t) = \int_{-\infty}^{t} \left(\beta_1 I_1(\nu) + \beta_2 I_2(\nu)\right)\, d\nu = \int_{-\infty}^{t} -\frac{1}{S}\frac{dS}{dt}\, dt = \ln S(-\infty) - \ln S(t) = \ln \frac{N}{S(t)};$$

then, since Ψ is the number of individuals that are no longer susceptible,

$$\Psi(UZ(t)) = N - S(t) = \int_{-\infty}^{t} \left(-\frac{dS}{d\nu}(\nu)\right)\, d\nu = \int_{-\infty}^{t} \left(\beta_1 I_1(\nu) + \beta_2 I_2(\nu)\right) S(\nu)\, d\nu$$

and now one easily sees that

$$\Sigma Z(t) + V\Psi(UZ(t)) = \begin{bmatrix} \int_{-\infty}^{t} \left(\frac{dE_1}{d\nu}(\nu)\right) d\nu \\ \int_{-\infty}^{t} \left(\frac{dE_2}{d\nu}(\nu)\right) d\nu \\ \int_{-\infty}^{t} \left(\frac{dI_1}{d\nu}(\nu)\right) d\nu \\ \int_{-\infty}^{t} \left(\frac{dI_2}{d\nu}(\nu)\right) d\nu \end{bmatrix} = \begin{bmatrix} E_1(t) - \cancel{E_1(-\infty)} \\ E_2(t) - \cancel{E_2(-\infty)} \\ I_1(t) - \cancel{I_1(-\infty)} \\ I_2(t) - \cancel{I_2(-\infty)} \end{bmatrix} = Y(t) = \frac{dZ}{dt}(t).$$

We follow with the calculation of some basic indices. It is not difficult to calculate

$$\Sigma^{-1} = \begin{bmatrix} -\frac{1}{\gamma_1} & 0 & 0 & 0 \\ 0 & -\frac{1}{\gamma_2} & 0 & 0 \\ -\frac{1}{\alpha_1} & 0 & -\frac{1}{\alpha_1} & 0 \\ 0 & -\frac{1}{\alpha_2+\theta} & 0 & -\frac{1}{\alpha+\theta} \end{bmatrix}$$

and

$$\Sigma^{-2} = \begin{bmatrix} \frac{1}{\gamma_1^2} & 0 & 0 & 0 \\ 0 & \frac{1}{\gamma_2^2} & 0 & 0 \\ \frac{1}{\alpha_1}\left(\frac{1}{\gamma_1}+\frac{1}{\alpha_1}\right) & 0 & \frac{1}{\alpha_1^2} & 0 \\ 0 & \frac{1}{\alpha_2+\theta}\left(\frac{1}{\gamma_2}+\frac{1}{\alpha_2+\theta}\right) & 0 & \frac{1}{(\alpha+\theta)^2} \end{bmatrix}.$$

Definition (2.10) leads to

$$R_0 = N\left[p\frac{\beta_1}{\alpha_1} + (1-p)\frac{\beta_2}{\alpha_2+\theta}\right].$$

Furthermore, definition (2.12) leads to

$$T = \frac{p\frac{\beta_1}{\alpha_1}\left(\frac{1}{\gamma_1}+\frac{1}{\alpha_1}\right) + (1-p)\frac{\beta_2}{\alpha_2+\theta}\left(\frac{1}{\gamma_2}+\frac{1}{\alpha_2+\theta}\right)}{p\frac{\beta_1}{\alpha_1} + (1-p)\frac{\beta_2}{\alpha_2+\theta}}.$$

Now, in this case, $\kappa(\Sigma) = -\min\{\gamma_1, \gamma_2, \alpha_1, \alpha_2+\theta$. For $\lambda > \kappa(\Sigma)$, one has

$$(\lambda I_4 - \Sigma)^{-1} = \begin{bmatrix} \frac{1}{\lambda+\gamma_1} & 0 & 0 & 0 \\ 0 & \frac{1}{\lambda+\gamma_2} & 0 & 0 \\ \frac{\gamma_1}{(\lambda+\gamma_1)(\lambda+\alpha_1)} & 0 & \frac{1}{\lambda+\alpha_1} & 0 \\ 0 & \frac{\gamma_2}{(\lambda+\gamma_2)(\lambda+(\alpha_2+\theta))} & 0 & \frac{1}{\lambda+(\alpha_2+\theta)} \end{bmatrix}$$

and

$$U(\lambda I_4 - \Sigma)^{-1}V = p\frac{\beta_1\gamma_1}{(\lambda+\gamma_1)(\lambda+\alpha_1)} + (1-p)\frac{\beta_2\gamma_2}{(\lambda+\gamma_2)(\lambda+(\alpha_2+\theta))},$$

so the Euler-Lotka equation (2.11) is given by

$$N\left[p\frac{\beta_1\gamma_1}{(\lambda+\gamma_1)(\lambda+\alpha_1)} + (1-p)\frac{\beta_2\gamma_2}{(\lambda+\gamma_2)(\lambda+(\alpha_2+\theta))}\right] = 1.$$

Example 9 (Immune system related heterogeneity)**.** We distinguish between standard individuals, which we label 1, and partially immune individuals, which we label 2. The relative susceptibility of type 2 individuals is given by the parameter a_2 while the infectiousness is given by the parameter c_2. With our notation,

$$\Omega = \{1,2\}, \quad a(\omega) = \begin{cases} 1 & \text{if } \omega = 1 \\ a_2 & \text{if } \omega = a_2 \end{cases}, \quad c(\eta) = \begin{cases} 1 & \text{if } \eta = 1 \\ c_2 & \text{if } \eta = c_2 \end{cases}.$$

Furthermore, since $\bar{\omega}$ is chosen such that $a(\bar{\omega}) = 1$, we can take $\bar{\omega} = 1$.
Let N_1 and N_2 be the size of the subpopulation of individuals of type 1 and 2, respectively, so that $N = N_1 + N_2$. Thus Φ has components N_1 and N_2, i.e., for an integrable function (relatively to the measure Φ) f,

$$\int_\Omega f(\omega)\, d\Phi(\omega) = f(1)\frac{N_1}{N} + f(2)\frac{N_2}{N}$$

and

$$\int_{\{j\}} f(\omega)\, d\Phi(\omega) = f(j)\frac{N_j}{N} \quad (j \in \Omega).$$

Equation (2.25) gives

$$\Psi(w) = N\left[c(1)\left(1-e^{-a(1)w}\right)\frac{N_1}{N} + c(2)\left(1-e^{-a(2)w}\right)\frac{N_2}{N}\right] = N_1\left(1-e^{-w}\right) + N_2c_2\left(1-e^{-a_2w}\right)$$

and, differentiating,

$$\Psi'(w) = N_1e^{-w} + N_2a_2c_2e^{-a_2w},$$

which corresponds to equation (2.32). One can now assume we are in a population described by an SEIR model with asymptomatic infection and quarantine, and use U, Σ and V, determined in the previous example, to obtain the integrated form and the standard form.

Example 10 (Heterosexually transmitted disease and the impact of promiscuity)**.** In our results, we have considered $A(\tau)$ as a scalar function. In this example, we will see that it can be useful to consider $A(\tau)$ as a matrix function.

We start by noting that here one should consider two subgroups of the population: males (denoted by index 1) and females (denoted by index 2). First we consider these subpopulations to be homogeneous. Later, we will introduce a trait representing promiscuity.

Let Λ_j be the force of infection of the subpopulation j ($j \in \{1,2\}$). The expected contribution to the force of infection can be defined by

$$A(\tau) \coloneqq \begin{bmatrix} 0 & A_{12}(\tau) \\ A_{21}(\tau) & 0 \end{bmatrix},$$

where the (k,j)-th element $A_{kj}(\tau)$ is the expected contribution to the force of infection Λ_k by an individual of type j with age of infection τ. A female cannot infect a female and a male cannot infect a male. Hence $A(\tau)$ is a matrix with 0 on the diagonal entries.

Let S_j denote the size of the susceptible population of type j ($j \in \{1,2\}$). As usual, the size of the susceptible population follows the model

$$\frac{dS_j}{dt} = -\Lambda_jS_j$$

where

$$\begin{bmatrix}\Lambda_1(t)\\ \Lambda_2(t)\end{bmatrix} \coloneqq \int_0^\infty A(\tau)\begin{bmatrix}\Lambda_1(t-\tau)S_1(t-\tau)\\ \Lambda_2(t-\tau)S_2(t-\tau)\end{bmatrix}d\tau,$$

i.e.,

$$\Lambda_1(t) = \int_0^\infty A_{12}(\tau)\Lambda_2(t-\tau)S_2(t-\tau)\,d\tau \quad \text{and} \quad \Lambda_2(t) = \int_0^\infty A_{21}(\tau)\Lambda_1(t-\tau)S_1(t-\tau)\,d\tau\cdot$$

The cumulative force of infection is now a vector and can be defined as

$$w(t) = \begin{bmatrix}w_1(t)\\ w_2(t)\end{bmatrix} \coloneqq \begin{bmatrix}\int_{-\infty}^t \Lambda_1(\nu)\,d\nu\\ \int_{-\infty}^t \Lambda_2(\nu)\,d\nu\end{bmatrix}.$$

We obtain the renewal equation

$$w(t) = \int_0^\infty A(\tau)\Psi(w(t-\tau))\,d\tau,$$

with

$$\Psi(w) \coloneqq \begin{bmatrix} N_1\,(1-e^{-w_1}) \\ N_2\,(1-e^{-w_2}) \end{bmatrix}$$

where N_1 denotes the total size of the male population and N_2 denotes the total size of the female population. I.e.,

$$w_1(t) = N_2 \int_0^\infty A_{12}(\tau)\left(1-e^{-w_2(t-\tau)}\right)\,d\tau \quad \text{and} \quad w_2(t) = N_1 \int_0^\infty A_{21}(\tau)\left(1-e^{-w_1(t-\tau)}\right)\,d\tau\cdot$$

As was done at the beginning of the chapter, we reduce the model to the compartmental case by considering $A_{12}(\tau)$ and $A_{21}(\tau)$ of the form (2.1). Since A_{kj} is the expected contribution to the force of infection by an individual of type j, we define

$$A_{kj}(\tau) = U_{kj}e^{\tau\Sigma_j}V_j \quad (k,j\in\{1,2\} : k\neq j)$$

where

- $\Sigma \in \mathcal{OD}^+_{n_j\times n_j}$ is a matrix that describes the state transitions of the infected states of the subpopulation of type j;
- $U_{kj} \in \mathcal{M}^+_{1\times n_j}$ is a (row) vector such that its ℓ-th component gives the contribution to the force of infection Λ_k by an individual of type j in the ℓ-th (infected) state;
- $V_j \in \mathcal{M}^+_{n_j\times 1}$ is a (column) vector representing the probability distribution of the state-at-infection of the subpopulation of type j.

Now we can define vectors Z_1 (of size $n_1\times 1$) and Z_2 (of size $n_2\times 1$), using form (2.5):

$$Z_j(t) = \int_0^\infty e^{\tau\Sigma_j}V_j\Psi_j(w_j(t-\tau))\,d\tau \quad (j\in\{1,2\})\cdot$$

It suffices to look to the renewal equation satisfied by the cumulative force of infection to conclude that

$$w_1 = U_{12}Z_2, \quad w_2 = U_{21}Z_1\cdot$$

Now, each vector Z_j satisfies (2.7):

$$\frac{dZ_j}{dt} = \Sigma_j Z_j + V_j\Psi_j(w_j)\cdot$$

Therefore we obtain

$$\begin{cases} \dfrac{dZ_1}{dt} = \Sigma_1 Z_1 + V_1\Psi_1(U_{12}Z_2) \\ \dfrac{dZ_2}{dt} = \Sigma_2 Z_2 + V_2\Psi_2(U_{21}Z_1) \end{cases}.$$

This is the integrated version of the following standard form:

$$\begin{cases} \dfrac{dS_j}{dt} = -\Lambda_j S_j \\ \dfrac{dY_j}{dt} = \Sigma_j Y_j + \Lambda_j S_j V_j \qquad\qquad (j\in\{1,2\}), \\ \Lambda_1 = U_{12}Y_2, \quad \Lambda_2 = U_{21}Y_1 \end{cases}$$

obtained by defining the vectors Y_1 and Y_2 by (2.13), i.e.,

$$Y_j(t) \coloneqq \int_0^\infty e^{\tau\Sigma_j}V_j\Lambda_j(t-\tau)S_j(t-\tau)\,d\tau\cdot$$

Finally, we introduce heterogeneity into the subpopulations. It should be noted that the functions defined previously will be redefined. We let ω represent promiscuity and we assume males and females are characterized with the same trait space Ω.
We leave the compartmental case and we assume

$$A_{kj}(\tau,\omega,\eta) = \begin{cases} a_k(\omega)b_j(\tau)c_j(\eta) & \text{if } k{\neq}j \\ 0 & \text{otherwise} \end{cases} \qquad (k,j \in \{1,2\})\cdot$$

Indeed, since A_{kj} is the expected contribution to the force of infection Λ_k by an individual of type j, it makes sense to consider the susceptibility a_k of individuals of type k and the infectiousness c_j of individuals of type j ($k{\neq}j$) Furthermore, the function of time since infection depends on the individuals of type j.
By proposition 26,

$$\int_{-\infty}^{t} \Lambda_k(\nu,\omega)\, d\nu = a_k(\omega)w_k(t) \quad (k \in \{1,2\})\cdot$$

By proposition 28, with $w = \begin{bmatrix} w_1 \\ w_2 \end{bmatrix}$, one has

$$w(t) = \int_0^{\infty} b(\tau)\Psi(w(t-\tau))\, d\tau$$

where

$$b(\tau) = \begin{bmatrix} 0 & b_2(\tau) \\ b_1(\tau) & 0 \end{bmatrix}$$

and Ψ is redefined as

$$\Psi(w) \coloneqq \begin{bmatrix} N_1 \int_\Omega c_1(\eta)\left(1 - e^{-a_1(\eta)w_1}\right)\, \Phi_1(d\eta) \\ N_2 \int_\Omega c_2(\eta)\left(1 - e^{-a_2(\eta)w_2}\right)\, \Phi_2(d\eta) \end{bmatrix},$$

where Φ_j is the measure that describes the probability distribution of the trait in the subpopulation of type j ($j \in \{1,2\}$). Thus we obtain

$$\begin{cases} w_1(t) = N_2 \int_0^{\infty} b_2(\tau) \int_\Omega c_2(\eta)\left(1 - e^{-a_2(\eta)w_2(t-\tau)}\right)\, \Phi_2(d\eta)\, d\tau \\ w_2(t) = N_1 \int_0^{\infty} b_1(\tau) \int_\Omega c_1(\eta)\left(1 - e^{-a_1(\eta)w_1(t-\tau)}\right)\, \Phi_1(d\eta)\, d\tau \end{cases}.$$

Returning to the compartmental case, we define

$$b_1(\tau) \coloneqq U_{21}e^{\tau\Sigma_1}V_1 \quad \text{and} \quad b_2(\tau) \coloneqq U_{12}e^{\tau\Sigma_2}V_2,$$

and we obtain the same integrated form, with a redifinition of Ψ.

Conclusion

We have finally arrived at the finish line of this dissertation. Writing

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has been a long process but nevertheless it has allowed us to grow as mathematicians and has most certainly broaden our horizons in the topic of mathematics applied to epidemiology and infectious diseases.

The main objectives of this dissertation are:

1. to compare continuous-time models and discrete-time models;
2. to insert heterogeneity into compartmental models.

The motivation for discrete-time models is simple: although the numbers of individuals varies at a continuous time, collection of data is often done at regular intervals, i.e., on a discrete-time basis. Furthermore, "numerical implementation is straightforward" in such models. As was shown in chapter 1 of this dissertation (and in [Diekmann et al., 2021]), the continuous-time Kermack-McKendrick model (see [Kermack and McKendrick, 1927]) is easily transformed into a discrete-time version. The proportion of susceptibles satisfies equation (1.15) in the continuous case and equation (1.22) in the discrete case. These equations have the same form if one recalls the connection between integrals and sums. In the discrete case, we went even further and we obtained equation (1.24). This equation has the main advantage that an initial condition (at time 0), can be provided by prescribing $s(0)$ and the incidences $\ldots, s(-3) - s(-2), s(-2) - s(-1), s(-1) - s(0)$. Furthermore, one predicts the expected contribution to the force of infection A_k (by an individual who itself was infected k steps earlier) to be zero from a certain order $\ell \in \mathbb{N}$, since an individual does not remain infectious for an infinite period of time. In that case, a finite number of prescriptions is sufficient: it suffices to prescribe $s(0)$ and $s(-\ell+1) - s(-\ell), \ldots, s(-1) - s(0)$.

In chapter 2, we saw how to reduce a continuous-time Kermack-McKendrick model to a compartmental model when the expected contribution to the force of infection by an individual with age of infection τ is of the form (2.1). Two alternative processes were given and we obtained to possible forms for the compartmental model: the *integrated form* (2.6) and the *standard form* (2.15). Introducing heterogeneity into the integrated form is straightforward: one only needs to redefine the function Ψ that counts the number of individuals that are no longer susceptible. The insertion of heterogeneity into the standard form is not as immediate and involves choosing a representative $\bar{\omega}$ of the trait space Ω such that the susceptibility $a(\omega)$ satisfies $a(\bar{\omega}) = 1$; with this choice, we say that $a(\omega)$ is the relative trait-specific susceptibility.

Future work

We are of the opinion that writing this essay was a first step to study a larger class of epidemiological (discrete or continuous) models with heterogeneity. In fact the two chapters describe and analyze tools and concepts which can be useful in future work. In particular the impact of altering traits on the heterogeneity can be a future topic of study.

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Appendix

Here we will present some theorems and propositions, that are very useful for the main essay. We also present some alternative proofs for some of the results given in the main text. Furthermore, we illustrate some of these results with examples.

The appendix is organized as follows: results/ examples are presented according to when they are used (for the first time) in the main text, with the exception of the next four theorems which we have chosen to present right away for their great usefulness in the area of Calculus.

We start by presenting two of the most prominent theorems of introductory Calculus, the **mean value theorem** and the **intermediate value theorem**, also known as **Lagrange theorem** and **Bolzano's theorem**, respectively.

Theorem 10 (Mean value theorem/ Lagrange theorem)**.** *Let f be continuous on the closed interval $[a, b]$ $(a < b)$ and differentiable on the open interval $]a, b[$. Then:*

$$\exists\, c \in]a, b[: \quad f'(c) = \frac{f(b) - f(a)}{b - a}.$$

Theorem 11 (Intermediate value theorem/ Bolzano's theorem)**.** *Let $a, b \in \mathbb{R}$ with $a < b$ and consider a continuous function $f : [a, b] \to \mathbb{R}$. If $(f(a) - u)(f(b) - u) < 0$, then there is $c \in]a, b[$ such that $f(c) = u$.*

Now we present another well known theorem from Calculus, the **Lebesgue's dominated convergence theorem**:

Theorem 12 (Lebesgue's dominated convergence)**.** *Let $\{f_n\}_{n\in\mathbb{N}}$ be a sequence of measurable functions on a measure space $(X, \mathcal{A}, \mu)$. Suppose that the sequence converges pointwise to a function f and is dominated by some integrable function g, i.e.,*

$$|f_n(x)| \leq g(x)$$

for all $n \in \mathbb{N}$ and all $x \in X$. Then f is (Lebesgue) integrable and

$$\lim_{n\to+\infty} \int_X f_n(x)\, dx = \int_X f(x)\, dx.$$

The following theorem is a well known theorem in the area of Multivariable Calculus and is known as **Fubini's theorem**.

Theorem 13 (Fubini)**.** *Let X and Y be two σ-finite measure spaces, and let f be a measurable function on $X \times Y$ such that*

$$\int_{X\times Y} |f(x, y)|\, d(x, y) < +\infty,$$

where $X \times Y$ is given the product measure. Then:

$$\int_X \left[\int_Y f\, dy\right] dx = \int_{X\times Y} f\, d(x,y) = \int_Y \left[\int_X f\, dx\right] dy$$

To chapter 1

To the first part of section 1.2

Here, we present some applications of the Lebesgue's dominated convergence theorem and the Fubini's theorem, enunciated above.

The next example is an application of the Lebesgue's dominated convergence theorem 12 and is useful in the proof of proposition 1 (in the main text).

Example 11. The space $X \coloneqq [0, +\infty[$ is a measure space and, furthermore, $f_k : [0, +\infty[\to \mathbb{R}$ defined by

$$f_k(\tau) \coloneqq A(\tau)\Lambda(k-\tau)S(k-\tau)$$

are measurable functions: $A(\tau)$ is integrable and, for $k \in \mathbb{N}$, $\Lambda(k-\tau)S(k-\tau)$ is continuous, hence they are both measurable and thus their product is measurable. Furthermore, since $t \mapsto \Lambda(t)S(t)$ is a bounded function and $\tau \mapsto A(\tau)$ is a nonnegative function, then there exists $C > 0$ such that $|\Lambda S| \leq C$ and

$$|f_k(\tau)| \leq CA(\tau),$$

so that f_k is dominated by an integrable function: $g(\tau) \coloneqq CA(\tau)$ is integrable because $\tau \mapsto A(\tau)$ is integrable. The sequence $\{f_k\}_{k\in\mathbb{N}}$ converges pointwise to the function

$$f(\tau) \coloneqq A(\tau)\Lambda(\infty)S(\infty),$$

with the assumption that the limits

$$\Lambda(\infty) \coloneqq \lim_{t\to+\infty} \Lambda(t) \quad \text{and} \quad S(\infty) \coloneqq \lim_{t\to+\infty} S(t)$$

exist. By Lebesgue's dominated convergence theorem 12, f is integrable and

$$\lim_{k\to+\infty} \int_0^\infty f_k(\tau)\, d\tau = \int_0^\infty f(\tau)\, d\tau = \Lambda(\infty)S(\infty) \int_0^\infty A(\tau)\, d\tau\cdot$$

For applications of the Fubini's theorem, we have the following example that is useful for proving proposition 2 (in the main text).

Example 12. The spaces $X \coloneqq]t, t+1]$ and $Y \coloneqq [0, +\infty[$ are σ-finite measure spaces: if μ is the Lebesgue measure, then

$$\mu(]t, t+1])) = (t+1) - t = 1 < +\infty$$

and

$$[0, +\infty[= \bigcup_{n\in\mathbb{N}_0} [n, n+1[$$

is a countable union of measurable sets with finite measure ($\mu([n, n+1[) = (n+1) - n = 1 < +\infty$).

Furthermore, the function $f :]t, t+1] \times [0, +\infty[\to \mathbb{R}$ defined by

$$f(\nu, \tau) \coloneqq A(\tau) \frac{dS}{d\nu}(\nu - \tau)$$

is a measurable function, since it is a product of measurable functions: $A(\tau)$ is integrable[24] and $\frac{dS}{d\nu}(\nu - \tau)$ is continuous, hence they are both measurable. Now, since $\tau \mapsto A(\tau)$ is a nonnegative integrable function and $\left|\frac{dS}{d\nu}\right|$ is bounded, then

$$\int_{X \times Y} |f(\nu, \tau)| \, d(\nu, \tau) < +\infty.$$

Fubini's theorem 13 is applicable and thus

$$\int_t^{t+1} \int_0^{\infty} A(\tau) \frac{dS}{d\nu}(\nu - \tau) \, d\tau \, d\nu = \int_0^{\infty} \int_t^{t+1} A(\tau) \frac{dS}{d\nu}(\nu - \tau) \, d\nu \, d\tau.$$

The following example is another application of the Lebesgue's dominated converge theorem 12 and is useful in the proof of lemma 1 (in the main text).

Example 13. The space $X \coloneqq [0, +\infty[$ is a measure space and, furthermore, $f_M : [0, +\infty[\to \mathbb{R}$ defined by

$$f_M(\tau) \coloneqq A(\tau) \left[S(-M - \tau) - S(t - \tau) \right]$$

(for t fixed) are measurable functions: $A(\tau)$ is integrable and, for $M \in \mathbb{N}$, $S(-M - \tau)$ is continuous, hence they are both measurable and thus their product is measurable. Furthermore, since

$$|S(-M - \tau) - S(t - \tau)| \leq N,$$

and $\tau \mapsto A(\tau)$ is a nonnegative function, then

$$|f_M(\tau)| \leq N A(\tau),$$

so that f_M is dominated by an integrable function: $g(\tau) \coloneqq N A(\tau)$ is integrable because $\tau \mapsto A(\tau)$ is integrable. The sequence $\{f_M\}_{M \in \mathbb{N}}$ converges pointwise to the function

$$f(\tau) \coloneqq A(\tau) \left[N - S(t - \tau) \right],$$

since $S(-\infty) = N$. By Lebesgue's dominated convergence theorem 12, f is integrable and

$$\lim_{M \to +\infty} \int_0^{\infty} f_M(\tau) \, d\tau = \int_0^{\infty} f(\tau) \, d\tau.$$

[24] Since $A(\tau)$ is not dependent on ν, one gets

$$\int_{X \times Y} A(\tau) \, d(\nu, \tau) = \underbrace{\mu(]t, t+1])}_{=1} \underbrace{\int_0^{+\infty} A(\tau) \, d\tau}_{<+\infty \text{ by hypothesis}} < +\infty.$$

To the second part of section 1.2

The following theorem can be found in [Sarrico, 2015] and gives sufficient conditions for uniform convergence of a given series of functions.

Theorem 14 (Weierstrass criterion)**.** *Suppose that* $\{f_n\}_{n\in\mathbb{N}}$ *is a sequence of complex-valued functions defined on a nonempty set* $X \subseteq \mathbb{R}$ *and that there is a sequence* $\{a_n\}_{n\in\mathbb{N}}$ *of nonnegative numbers such that*

a) $|f_n(x)| \leq a_n$*, for every* $x \in X$*, whenever* $n \geq n_0$ *for some order* $n_0 \in \mathbb{N}$*;*

b) $\sum_{n=1}^{\infty} a_n$ *is convergent.*

Then $\sum_{n=1}^{\infty} f_n$ *converges uniformly on* X*.*

The previous theorem will be very useful to prove convergence of the series $\sum_{k=1}^{\infty} \hat{\Lambda}(t-k)$, with the function $t \mapsto \hat{\Lambda}(t)$ given by (1.16) (see lemma 3 in the main text). To illustrate such convergence, we follow with an example. One should note that, in this example, the function $t \mapsto S(t)$ is given. However, the main objective of the series $\sum_{k=1}^{\infty} \hat{\Lambda}(t-k)$ is to find a formula for the number $S(t)$, as one can see from proposition 7 in the main essay. Furthermore, if the function $t \mapsto S(t)$ is given, the collection $\{A_j\}_{j\in\mathbb{N}}$ might not be summable (note that this collection and the function S are related), and thus proposition 7 cannot be applied. The reason for this is simple: if an individual is infected, then the number of susceptibles will decrease, not only because of this individual, but also because of all the individuals it infects.

Example 14. Define the function $t \mapsto S(t)$ as

$$S(t) = \frac{S_0 N}{S_0 + (N - S_0)e^t} \tag{A.1}$$

where $N \in \mathbb{N}$ and $0 < S_0 < N$. The function $t \mapsto S(t)$ is a solution of the famous logistic differential equation[25]

$$\frac{dP}{dt} = rP\left(1 - \frac{P}{N}\right),$$

where $r = -1$, provided with the initial condition $P(0) = S_0$. This function is nonnegative and nonincreasing, and is bounded above by N, with $\lim_{t\to-\infty} S(t) = N$. The graph below exemplifies the behaviour of such function (the parameters chosen were $N = 500$ and $S_0 = 200$):

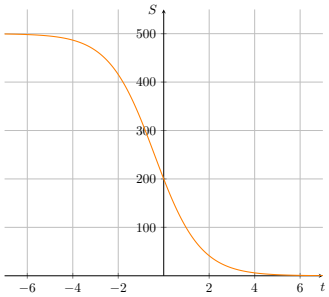

Fig. A.1. Graph of the function $t \mapsto S(t)$ given by (A.1) with $N = 500$ and $S_0 = 200$.

[25] Although it is usual to consider a positive growth rate r, here we consider $r < 0$ so that one can have a bounded positive solution that decreases with time.

Next, we show that $\left\{\hat{\Lambda}(t-k)\right\}_{k\in\mathbb{N}}$ is summable (for fixed t). Using equation (1.20),

$$\begin{aligned}\sum_{k=1}^{\infty}\hat{\Lambda}(t-k) &= \sum_{j=1}^{\infty}A_j\left[N-\frac{S_0N}{S_0+(N-S_0)e^{t-j}}\right]\\ &= N\sum_{j=1}^{\infty}A_j\frac{\left[\cancel{S_0}+(N-S_0)e^{t-j}\right]-\cancel{S_0}}{S_0+(N-S_0)e^{t-j}}\\ &= N\sum_{j=1}^{\infty}A_j\frac{(N-S_0)e^{t-j}}{S_0+(N-S_0)e^{t-j}}\\ &\leq N\sum_{j=1}^{\infty}A_j\end{aligned}$$

and, assuming $\{A_j\}_{j\in\mathbb{N}}$ is summable, one concludes that $\{\hat{\Lambda}(t-k)\}_{k\in\mathbb{N}}$ is summable (for fixed t).
Before we end this example, we would like to show why one should not give an expression to $S(t)$ and then make assumptions on the collection $\{A_j\}_{j\in\mathbb{N}}$. Equation (1.18) in proposition 7 can be rewritten as

$$\sum_{k=1}^{\infty}\hat{\Lambda}(t-k)=\ln\left(\frac{N}{S(t)}\right).$$

With $S(t)$ given by (A.1), one obtains

$$N\sum_{j=1}^{\infty}A_j\frac{(N-S_0)e^{t-j}}{S_0+(N-S_0)e^{t-j}}=\ln\left(\frac{S_0+(N-S_0)e^{t}}{S_0}\right)$$

i.e., with $K\coloneqq\frac{N-S_0}{S_0}$,

$$N\sum_{j=1}^{\infty}\frac{A_j}{e^{-t+j}+K}=\frac{\ln\left(1+Ke^{t}\right)}{K}.$$

Now, letting $f_j(t)\coloneqq\frac{A_j}{e^{-t+j}+K}$, one easily sees that $|f_j(t)|\leq\frac{A_j}{K}$ and, by hypothesis,

$$\sum_{j=1}^{\infty}\frac{A_j}{K}=\frac{1}{K}\sum_{j=1}^{\infty}A_j<+\infty.$$

Therefore, by theorem 14 (in the appendix), one has uniform convergence of $\sum_{j=1}^{\infty}f_j$ and, in particular, passing the series to the limit as $t\to+\infty$, one obtains

$$\lim_{t\to+\infty}N\sum_{j=1}^{\infty}\frac{A_j}{e^{-t+j}+K}=N\sum_{j=1}^{\infty}\frac{A_j}{e^{-\lim_{t\to+\infty}t+j}+K}=N\sum_{j=1}^{\infty}\frac{A_j}{K}=\frac{R_0}{K}.$$

However

$$\lim_{t\to+\infty}\ln\left(1+Ke^{t}\right)=+\infty$$

from where $R_0=+\infty$, i.e., in fact, the collection $\{A_j\}_{j\in\mathbb{N}}$ is not summable.
We conclude that, with $S(t)$ given by (A.1), one cannot find a summable collection $\{A_j\}_{j\in\mathbb{N}}$ such that equation (1.18), with $t\mapsto\hat{\Lambda}(t)$ given by (1.16), is satisfied.
One might wonder the reason for this. Now, if $S(t)$ is defined by (A.1), then $S(t)$ converges to zero when $t\to+\infty$. Speaking in terms of biology, in the (infinite) future, the population tends to a state where no

more individuals are susceptible, i.e., all individuals were infected. So indeed it makes perfect sense that the total contribution of an infected individual to the cumulative force of infection is large enough in such a manner that all individuals in the population get infected.

To section 1.4

The next remark is an alternative proof of the expression (1.39) obtained for the susceptibles density.

Remark 29. If $S(t+1) = e^{-\beta I(t)} S(t)$ and $M \in \mathbb{N}_0$, then

$$\prod_{j=0}^{M} S(t-j+1) = \prod_{j=0}^{M} \left[e^{-\beta I(t-j)} S(t-j) \right] = \exp\left\{ -\beta \sum_{j=0}^{M} I(t-j) \right\} \left[\prod_{j=0}^{M} S(t-j) \right]$$

but, on the other hand, assuming M is large enough so that $S(t-M) > 0$,

$$\prod_{j=0}^{M} S(t-j+1) = \frac{S(t+1)}{S(t-M)} \left[\prod_{j=1}^{M+1} S(t-(j-1)) \right] = \frac{S(t+1)}{S(t-M)} \left[\prod_{k=0}^{M} S(t-k) \right],$$

where $k = j-1$. Comparison gives

$$S(t+1) = \exp\left\{ -\beta \sum_{j=0}^{M} I(t-j) \right\} S(t-M)\cdot$$

Letting $M \to \infty$, we finally obtain (1.39).

The next remark is an alternative proof of the expression (1.40) obtained for the series with terms given by the infectious density.

Remark 30. Suppose

$$\sum_{j=0}^{\infty} I(t-j) - (1-\alpha) \sum_{j=0}^{\infty} I(t-1-j) = f(t)\cdot$$

Let $J(t) \coloneqq (1-\alpha)^{-t} \sum_{j=0}^{\infty} I(t-j)$. Then we can rewrite the previous recurrence relation as

$$J(t) - J(t-1) = \frac{f(t)}{(1-\alpha)^t}$$

and

$$\sum_{m=0}^{\infty} [J(t-m) - J(t-m-1)] = \sum_{m=0}^{\infty} \frac{f(t-m)}{(1-\alpha)^{t-m}} = (1-\alpha)^{-t} \sum_{m=0}^{\infty} (1-\alpha)^m f(t-m)\cdot$$

On the other hand, given $M \in \mathbb{N}_0$,

$$\begin{aligned} \sum_{m=0}^{M} [J(t-m) - J(t-m-1)] &= [J(t) - \cancel{J(t-1)}] + \cdots + [\cancel{J(t-M)} - J(t-M-1)] \\ &= J(t) - J(t-M-1) \end{aligned}$$

and, letting $M \to \infty$,

$$\sum_{m=0}^{\infty} [J(t-m) - J(t-m-1)] = J(t) - J(-\infty) = J(t),$$

where the last equality comes from

$$J(-\infty) \coloneqq \lim_{t\to-\infty} J(t) = \lim_{t\to-\infty} \left[\underbrace{(1-\alpha)}_{\in]0,1[}^{-t} \sum_{j=0}^{\infty} I(t-j) \right] = 0\cdot$$

Comparison gives

$$J(t) = (1-\alpha)^{-t} \sum_{m=0}^{\infty} (1-\alpha)^m f(t-m)$$

and we conclude

$$\sum_{j=0}^{\infty} I(t-j) = \sum_{m=0}^{\infty} (1-\alpha)^m f(t-m)\cdot$$

The next proposition deals with probability matrices and is useful for the proof of proposition 19 (in the main text).

Proposition 31. *Let $n \in \mathbb{N}$ and consider the set of states $\Omega = \{1, \dots, n\}$. Let X_t denote the state at time t and P the $n \times n$ probability matrix that describes the state transitions: the entry (i,j) of P is $P_{ij} = \mathbb{P}(X_{t+1} = i | X_t = j)$. Then, for each $m \in \mathbb{N}$,*

$$\mathbb{P}(X_{t+m} = i | X_t = j) = (P^m)_{ij}\cdot \tag{A.2}$$

Proof. We prove (A.2) by induction on m. The basis step $m = 1$ follows from definition of P. Now, if (A.2) is true for a certain $m \in \mathbb{N}$, then

$$\begin{aligned}
\mathbb{P}(X_{t+m+1} = i | X_t = j) &= \sum_{k=1}^{n} \mathbb{P}(X_{t+m+1} = i | X_{t+m} = k \wedge X_t = j) \mathbb{P}(X_{t+m} = k | X_t = j) \\
&= \sum_{k=1}^{n} \mathbb{P}(X_{t+m+1} = i | X_{t+m} = k) \mathbb{P}(X_{t+m} = k | X_t = j) \\
&= \sum_{k=1}^{n} P_{ik} (P^m)_{kj} \\
&= (P^{m+1})_{ij}
\end{aligned}$$

where the first equality follows from the partition theorem, the second from the memoryless property of any stochastic process, and the third by definition of P and by the hypothesis. We conclude that (A.2) is true for all $m \in \mathbb{N}$. □

To chapter 2

To section 2.1

The following proposition was based on [Varga, R.S., 2000, Chapter 8.2.].

Proposition 32. *Let $n \in \mathbb{N}$ and let $M \in \mathcal{OD}^{+}_{n\times n}$. Then $e^M \in \mathcal{OD}^{+}_{n\times n}$ and, furthermore, it has an all positive diagonal.*

Proof. Let $m = \max\{|M_{kk}| \, | k \in [n]\}$. Then $\widetilde{M} = M + mI_n$ is a real matrix where all entries are nonnegative. In particular, every power of $\widetilde{M}$ has only nonnegative entries and hence

$$e^{\widetilde{M}} = \sum_{k=0}^{\infty} \frac{1}{k!}\widetilde{M}^k = I_n + \widetilde{M} + \frac{1}{2}\widetilde{M}^2 + \cdots$$

has only nonnegative entries. Since $\widetilde{M}$ and $-mI_n$ commute, then

$$e^M = e^{\widetilde{M}-mI_n} = e^{-m}e^{\widetilde{M}}$$

and thus e^M has only nonnegative entries. Furthermore, it is quite obvious that each entry of the diagonal of $e^{\widetilde{M}}$ is positive (due to the 1s in the identity matrix) and thus e^M has only positive entries in the diagonal. □

Next, a proposition involving the spectral abscissa and the exponential matrix is given:

Proposition 33. *Let $n \in \mathbb{N}$ and consider M, a $n \times n$ square matrix. If $\kappa(M) < 0$, then*

$$\lim_{t\to+\infty} e^{tM} = \mathbf{0_{n\times n}}.$$

Proof. Let M be a $n \times n$ square matrix and $\lambda_1, \ldots, \lambda_q$ its eigenvalues (not necessarily distinct). Now, from Linear Algebra theory (see, for example, [Pestana da Costa, 2001]), we know that M is similar to a Jordan normal form, i.e., there is an invertible matrix P such that $M = PJP^{-1}$ and J is a block diagonal matrix

$$J = \begin{bmatrix} J_1 & & \\ & \ddots & \\ & & J_q \end{bmatrix}, \tag{A.3}$$

where, for each $k \in \{1, \ldots, q\}$, J_k is a square matrix of the form

$$J_k = \begin{bmatrix} \lambda_k & 1 & & \\ & \ddots & \ddots & \\ & & \ddots & 1 \\ & & & \lambda_k \end{bmatrix} \tag{A.4}$$

(every entry on the main diagonal is equal to λ_k and every entry on the superdiagonal is equal to 1, while the remaining entries are equal to 0). In particular, if J_k has order 1, then $J_k = \begin{bmatrix}\lambda_k\end{bmatrix}$. It follows that

$$e^{tM} = Pe^{tJ}P^{-1} = P \begin{bmatrix} e^{tJ_1} & & \\ & \ddots & \\ & & e^{tJ_q} \end{bmatrix} P^{-1}$$

and thus it suffices to study the form of each e^{tJ_k} (for each $k \in \{1, \dots, q\}$). For each $k \in \{1, \dots, q\}$, let n_k be the order of J_k and notice that $\sum_{k=1}^{q} n_k = n$. One notes that, for each $k \in \{1, \dots, q\}$,

$$J_k = \lambda_k I_{n_k} + N_k,$$

where I_{n_k} is the identity matrix of order n_k and N_k is the matrix with each entry on the superdiagonal equal to 1 and every other entry equal to 0. One can see that, for each $k \in \{1, \dots, q\}$, N_k is a nilpotent matrix with index n_k, i.e.,

$$n_k = \min\{m \in \mathbb{N} : \quad N_k^m = \mathbf{0_{n_k \times n_k}}\},$$

and, if $m \in \{1, \dots, n_k - 1\}$, then N_k^m has $n_k - m$ entries equal to 1,

$$(1, m+1), \dots, (n_k - m, n_k),$$

and the remaining entries equal to 0.
Therefore, for each $k \in \{1, \dots, q\}$,

$$e^{tN_k} = \sum_{m=0}^{\infty} \frac{t^m}{m!} N_k^m = I_{n_k} + tN_k + \cdots + \frac{t^{n_k-1}}{(n_k-1)!} N_k^{n_k-1} = \begin{bmatrix} 1 & t & \frac{t^2}{2} & \cdots & \frac{t^{n_k-2}}{(n_k-2)!} & \frac{t^{n_k-1}}{(n_k-1)!} \\ 0 & 1 & t & \cdots & \frac{t^{n_k-3}}{(n_k-3)!} & \frac{t^{n_k-2}}{(n_k-2)!} \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & t & \frac{t^2}{2} \\ 0 & 0 & 0 & \cdots & 1 & t \\ 0 & 0 & 0 & \cdots & 0 & 1 \end{bmatrix}$$

and, finally, since $\lambda_k I_{n_k}$ and N_k commute, then

$$e^{tJ_k} = e^{t(\lambda_k I_{n_k} + N_k)} = e^{t\lambda_k} e^{tN_k} = \begin{bmatrix} e^{t\lambda_k} & te^{t\lambda_k} & \frac{t^2}{2}e^{t\lambda_k} & \cdots & \frac{t^{n_k-2}}{(n_k-2)!}e^{t\lambda_k} & \frac{t^{n_k-1}}{(n_k-1)!}e^{t\lambda_k} \\ 0 & e^{t\lambda_k} & te^{t\lambda_k} & \cdots & \frac{t^{n_k-3}}{(n_k-3)!}e^{t\lambda_k} & \frac{t^{n_k-2}}{(n_k-2)!}e^{t\lambda_k} \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & te^{t\lambda_k} & \frac{t^2}{2}e^{t\lambda_k} \\ 0 & 0 & 0 & \cdots & e^{t\lambda_k} & te^{t\lambda_k} \\ 0 & 0 & 0 & \cdots & 0 & e^{t\lambda_k} \end{bmatrix}.$$

Now it suffices to note that, for $p \geq 0$, if $\lambda \in \mathbb{C}$ is such that $\Re(\lambda) < 0$, then

$$\lim_{t \to +\infty} \left| t^p e^{\lambda t} \right| = \lim_{t \to +\infty} |t|^p e^{\Re(\lambda) t} = 0$$

and thus

$$\lim_{t \to +\infty} t^p e^{\lambda t} = 0.$$

Given that $\kappa(M) < 0$, then $\Re(\lambda) < 0$ for each $\lambda \in \sigma(M)$ and we conclude that, for each $k \in \{1, \dots, q\}$,

$$\lim_{t \to +\infty} e^{tJ_k} = \mathbf{0_{n_k \times n_k}}$$

and therefore

$$\lim_{t\to+\infty} e^{tM} = \mathbf{0}_{\mathbf{n}\times\mathbf{n}}.$$

□

The following proposition (see [Pestana da Costa, 2001]) will be useful for obtaining a explicit formula for the solution of a linear system of ODEs:

Proposition 34. *Let M be a $n\times n$ matrix and consider the linear system of ODEs*

$$y' = My, \tag{A.5}$$

where $y = y(t)$ is a $n \times 1$ vector-valued function. Any solution of (A.5) *is of the form*

$$y(t) = \Upsilon(t)\mathbf{C}$$

where Υ is a fundamental matrix of (A.5) *(i.e., the columns of Υ form a basis for the set of solutions of* (A.5)*) and $\mathbf{C}$ is a $n \times 1$ matrix. In particular, if $\lambda_1, \ldots, \lambda_q$ are the (not necessarily distinct) eigenvalues of M, then the k-th entry of y is of the form*

$$y_k(t) = e^{\lambda_{\ell_k} t} p_k(t)$$

for some $\ell_k \in \{1, \ldots, q\}$, where p_k is a polynomial in t (for each $k \in \{1, \ldots, n\}$).

Proof. Any solution of (A.5) is of the form

$$y(t) = e^{tM}\mathbf{B}$$

where $\mathbf{B}$ is a $n \times 1$ matrix. As was done in the proof of the previous theorem, one notes that M is similar to a Jordan normal form, i.e., there is an invertible matrix P such that $M = PJP^{-1}$. Furthermore, the columns of P are composed by eigenvectors and generalized eigenvectors of M (it suffices to note that $MP = JP$ and the main diagonal of J is composed by the eigenvalues of M). Let J be of the form (A.3), where, for each $\ell \in \{1, \ldots, q\}$, J_ℓ is a $n_\ell \times n_\ell$ square matrix of the form (A.4). It follows that

$$e^{tM} = Pe^{tJ}P^{-1} \quad \text{i.e.} \quad e^{tM}P = Pe^{tJ},$$

from where one sees that $\Upsilon(t) = e^{tJ}P$ is a fundamental matrix for (A.5). Hence

$$y(t) = Pe^{tJ}P^{-1}\mathbf{B}$$

and thus

$$y(t) = \Upsilon(t)\mathbf{C}$$

where $\mathbf{C} = P^{-1}\mathbf{B}$. It follows that, for each $k \in \{1, \ldots, n\}$, $y_k(t) = \Upsilon_k^*(t)\mathbf{C}$, where Υ_k^* denotes the k-th row of Υ. On the other hand,

$$\Upsilon_k^*(t) = \left(e^{tJ}\right)_k^* P$$

where $\left(e^{tJ}\right)_k^*$ denotes the k-th row of e^{tJ}.

Suppose $k = \sum_{j=1}^{\ell-1} n_j + m_\ell$ for some $\ell = \ell_k \in \{1, \ldots, q\}$ (with $1 = \ell_1 \leq \ldots \leq \ell_n = q$ such that $\ell_{k+1} = \ell_k$ or $\ell_{k+1} = \ell_k + 1$) and some $m_\ell \in \{1, \ldots, n_\ell\}$ (note that $k \in \{1, \ldots, n\}$). The k-th row of

e^{tJ} is the m_ℓ row in the $n_\ell \times n$ submatrix

$$\begin{bmatrix} \mathbf{0}_{\mathbf{n_\ell \times c_{\ell-1}}} & e^{tJ_\ell} & \mathbf{0}_{\mathbf{n_\ell \times (n-c_\ell)}} \end{bmatrix}$$

where $c_\ell = \sum_{j=1}^{\ell} n_j$. On the other hand,

$$e^{tJ_\ell} = e^{\lambda_\ell t} \begin{bmatrix} 1 & t & \frac{t^2}{2} & \cdots & \frac{t^{n_\ell-2}}{(n_\ell-2)!} & \frac{t^{n_\ell-1}}{(n_\ell-1)!} \\ 0 & 1 & t & \cdots & \frac{t^{n_\ell-3}}{(n_\ell-3)!} & \frac{t^{n_\ell-2}}{(n_\ell-2)!} \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & t & \frac{t^2}{2} \\ 0 & 0 & 0 & \cdots & 1 & t \\ 0 & 0 & 0 & \cdots & 0 & 1 \end{bmatrix}$$

and one notes that the m_ℓ-th row of e^{tJ_ℓ} is

$$e^{\lambda_\ell t} \begin{bmatrix} \underbrace{0 \quad \cdots \quad 0}_{m_\ell - 1 \text{ columns}} & 1 & t & \cdots & \frac{t^{n_\ell-m_\ell-1}}{(n_\ell-m_\ell-1)!} & \frac{t^{n_\ell-m_\ell}}{(n_\ell-m_\ell)!} \end{bmatrix}.$$

Therefore

$$\left(e^{tJ}\right)_k^* = e^{\lambda_\ell t} \begin{bmatrix} \mathbf{0}_{\mathbf{1 \times c_{\ell-1}}} & \underbrace{0 \quad \cdots \quad 0}_{m_\ell - 1 \text{ columns}} & 1 & t & \cdots & \frac{t^{n_\ell-m_\ell-1}}{(n_\ell-m_\ell-1)!} & \frac{t^{n_\ell-m_\ell}}{(n_\ell-m_\ell)!} & \mathbf{0}_{\mathbf{1 \times (n-c_\ell)}} \end{bmatrix},$$

i.e.,

$$\left(e^{tJ}\right)_k^*(t) = e^{\lambda_\ell t} \begin{bmatrix} \mathbf{0}_{\mathbf{1 \times (k-1)}} & 1 & t & \cdots & \frac{t^{c_\ell-k-1}}{(c_\ell-k-1)!} & \frac{t^{c_\ell-k}}{(c_\ell-k)!} & \mathbf{0}_{\mathbf{1 \times (n-c_\ell)}} \end{bmatrix}$$

where one used $c_{\ell-1} + m_\ell = k$ and $n_\ell - m_\ell = c_\ell - k$. Let P_j denote the j-th column of P and C_j denote the j-th entry of $\mathbf{C}$ ($j \in \{1, \ldots, n\}$). Then

$$y_k(t) = e^{\lambda_\ell t} \begin{bmatrix} \mathbf{0}_{\mathbf{1 \times (k-1)}} & 1 & t & \cdots & \frac{t^{c_\ell-k}}{(c_\ell-k)!} & \mathbf{0}_{\mathbf{1 \times (n-c_\ell)}} \end{bmatrix} P\mathbf{C}$$

and it is clear that

$$p_k(t) \coloneqq \begin{bmatrix} \mathbf{0}_{\mathbf{1 \times (k-1)}} & 1 & t & \cdots & \frac{t^{c_\ell-k}}{(c_\ell-k)!} & \mathbf{0}_{\mathbf{1 \times (n-c_\ell)}} \end{bmatrix} P\mathbf{C}$$

is a polynomial in t. □

To section 2.2

The following examples are very useful for proving proposition 28.

We start with another application of the Fubini's theorem 13.

Example 15. Let Ω be a measurable set with finite measure Φ.
$X_1 \coloneqq]-t_0, t]$ and $X_2 \coloneqq [0, +\infty[\times \Omega$ are σ-finite measure spaces, since

$$\mu(X_1) = t - (-t_0) < +\infty$$

where μ is the Lebesgue measure, and

$$X_2 = \left(\bigcup_{n \in \mathbb{N}_0} [n, n+1[\right) \times \Omega$$

is the Cartesian product of a countable union of measurable sets with finite measure and a measurable set with measure 1. Furthermore,

$$(\nu, (\tau, \eta)) \mapsto g(\nu, (\tau, \eta)) \coloneqq b(\tau)c(\eta) \left[-\frac{\partial s}{\partial \nu}(\nu - \tau, \eta) \right]$$

is a measurable function on $X_1 \times X_2$ since it is a product of measurable functions. Now, $\left| -\frac{\partial s}{\partial \nu} \right|$ is a bounded function, from where

$$K \coloneqq \sup_{(\nu,(\tau,\eta)) \in X \times Y} \left| \frac{\partial s}{\partial \nu}(\nu - \tau, \eta) \right| < +\infty$$

and

$$\int\limits_{X_1 \times X_2} |g(\nu, (\tau, \eta))| \; d(\nu, (\tau, \Phi(\eta))) \leq K\mu(X_1) \left(\int_0^\infty b(\tau) \, d\tau \right) \left(\int_\Omega c(\eta) \, \Phi(d\eta) \right) < +\infty,$$

since b and c are integrable in $[0, \infty[$ and Ω, respectively. By Fubini's theorem (theorem 13),

$$\begin{aligned}
&\int_{-t_0}^{t} \int_0^\infty \int_\Omega b(\tau)c(\eta) \left[-\frac{\partial s}{\partial \nu}(\nu - \tau, \eta) \right] \, \Phi(d\eta) \, d\tau \, d\nu \\
&= \int_0^\infty \int_\Omega b(\tau)c(\eta) \int_{-t_0}^{t} \left[-\frac{\partial s}{\partial \nu}(\nu - \tau, \eta) \right] \, d\nu \, \Phi(d\eta) \, d\tau \\
&= \int_0^\infty \int_\Omega b(\tau)c(\eta) \left[s(-t_0 - \tau, \eta) - s(t - \tau, \eta) \right] \, \Phi(d\eta) \, d\tau \cdot
\end{aligned}$$

The next example is another application of the Lebesgue's dominated convergence theorem 12.

Example 16. Let Ω be a measurable set and Φ a finite measure on Ω. Then $X \coloneqq [0, +\infty[\times \Omega$ is a measure space (consider the product measure $\mu \times \Phi$ where μ is the Lebesgue measure). Now, consider the sequence $\{g_k(\eta, \tau)\}_{k \in \mathbb{N}}$ of measurable functions defined by

$$g_k(\eta, \tau) \coloneqq b(\tau)c(\eta)[s(-k - \tau, \eta) - s(t - \tau, \eta)],$$

where $(\eta, \tau) \in X$. One has that

$$\lim_{k \to +\infty} g_k(\eta, \tau) = b(\tau)c(\eta)[1 - s(t - \tau, \eta)] \cdot$$

Furthermore the sequence is dominated by an integrable function:

$$|g_k(\eta, \tau)| = b(\tau)c(\eta)|s(-k - \tau, \eta) - s(t - \tau, \eta)| \leq 2b(\tau)c(\eta) \cdot$$

By Lebesgue's dominated convergence theorem (theorem 12), one has

$$\lim_{k \to +\infty} \int_X g_k(\eta, \tau) \, d(\Phi(\eta), \tau) = \int_X \lim_{k \to +\infty} g_k(\eta, \tau) \, d(\Phi(\eta), \tau)$$

i.e.,

$$\lim_{k\to+\infty}\int_0^\infty\int_\Omega b(\tau)c(\eta)[s(-k-\tau,\eta)-s(t-\tau,\eta)]\;d(\Phi(\eta),\tau)$$
$$=\int_0^\infty\int_\Omega b(\tau)c(\eta)[1-s(t-\tau,\eta)]\,d(\Phi(\eta),\tau)\cdot$$

To section 2.3

Here, it will be useful to introduce the notion of **Laplace transform** and a few of its properties. The following definitions and results were taken from [Spiegel, M.R., 1965].

Definition 7 (Laplace Transform)**.** Let $f(t)$ be a function of t specified for $t>0$. Then the **Laplace transform** of $f(t)$, denoted by $\mathcal{L}\{f(t)\}$, is defined by

$$\mathcal{L}\{f(t)\}(\lambda)\coloneqq\int_0^\infty e^{-\lambda t}f(t)\,dt\cdot$$

Remark 31. The Laplace transform is said to exist if the integral above converges for some λ.

We thus should give some sufficient conditions for the existence of the Laplace transform. First, a definition is necessary:

Definition 8 (Exponential order)**.** A function $f(t)$ is said to be of exponential order θ if there exists constants $\theta, M>0, t_0>0$ such that

$$|f(t)|\le Me^{\theta t}\quad\forall t>t_0\cdot$$

Proposition 35 (Sufficient conditions for existence of Laplace transforms)**.** *If $f(t)$ is piecewise continuous in every finite interval $[0,t_0]$ ($t_0>0$) and of exponential order θ for $t>t_0$, then its Laplace transform exists for $\Re(\lambda)>\theta$.*

Proof. For every $t_0>0$,

$$\int_0^\infty e^{-\lambda t}f(t)\,dt=\int_0^{t_0}e^{-\lambda t}f(t)\,dt+\int_{t_0}^\infty e^{-\lambda t}f(t)\,dt\cdot\tag{A.6}$$

Since $f(t)$ is piecewise continuous in every finite interval $[0,t_0]$, the first integral on the right exists. On the other hand, since $f(t)$ is of exponential order θ for $t>t_0$,

$$\begin{aligned}\left|\int_{t_0}^\infty e^{-\lambda t}f(t)\,dt\right|&\le\int_{t_0}^\infty\left|e^{-\lambda t}\right||f(t)|\,dt\\&\le\int_0^\infty e^{-\Re(\lambda)t}\left(Me^{\theta t}\right)\,dt\\&=M\int_0^\infty e^{(\theta-\Re(\lambda)t}\,dt\end{aligned}$$

and thus the last integral of (A.6) converges whenever $\Re(\lambda)>\theta$. Therefore the Laplace transform exists for $\Re(\lambda)>\theta$. □

Finally, we give some properties:

Proposition 36. *Let $\delta, c_1, c_2 \in \mathbb{C}$ and consider $f(t)$ and $g(t)$, functions of t specified for $t > 0$. We have the following properties:*

Linearity $\mathcal{L}\{c_1 f(t) + c_2 g(t)\} = c_1 \mathcal{L}\{f(t)\} + c_2 \mathcal{L}\{g(t)\}$;

First translation $\mathcal{L}\left\{e^{\delta t} f(t)\right\}(\lambda) = \mathcal{L}\{f(t)\}(\lambda - \delta)$;

Multiplication by t $\mathcal{L}\{tf(t)\}(\lambda) = -\frac{d}{d\lambda}\left(\mathcal{L}\{tf(t)\}\right)$.

Proof. The linearity property follows by the linearity of the integral. For the first translation property, one notes that

$$\mathcal{L}\left\{e^{\delta t} f(t)\right\}(\lambda) = \int_0^\infty e^{-\lambda t} e^{\delta t} f(t)\, dt = \int_0^\infty e^{-(\lambda-\delta)t} f(t)\, dt \mathcal{L}\{f(t)\}(\lambda - \delta).$$

Now, differentiating the Laplace transform gives

$$\begin{aligned}
\frac{d}{d\lambda}\left(\mathcal{L}\{f(t)\}(\lambda)\right) &= \frac{d}{d\lambda}\int_0^\infty e^{-\lambda t} f(t)\, dt \\
&= \int_0^\infty -te^{-\lambda t} f(t)\, dt \\
&= -\int_0^\infty e^{-\lambda t}\left(tf(t)\right)\, dt \\
&= -\mathcal{L}\{tf(t)\}(\lambda).
\end{aligned}$$

□

To end this study, we give the Laplace transform of a particular function.

Lemma 5. *Let $q > -1$. The Laplace transform of $f(t) = t^q$ is given by*

$$\mathcal{L}\{t^q\}(\lambda) = \frac{\Gamma(q+1)}{\lambda^{q+1}}$$

for $\Re(\lambda) > 0$.

Proof. f is clearly of exponential order $\theta > 0$ for every $t > 0$. One concludes that the Laplace transform of f exists for $\Re(\lambda) > 0$.
We focus merely on the case $\lambda \in \mathbb{R}$, so that we can present a simple proof. We assume $\lambda = \Re(\lambda) > 0$. One has

$$\mathcal{L}\{t^q\}(\lambda) = \int_0^\infty e^{-\lambda t} t^q\, dt.$$

Let $u = \lambda t$. Then

$$\mathcal{L}\{t^q\}(\lambda) = \int_0^\infty e^{-u}\left(\frac{u}{\lambda}\right)^q \frac{1}{\lambda}\, dt = \frac{1}{\lambda^{q+1}} \underbrace{\int_0^\infty u^{(q+1)-1} e^{-u}\, du}_{=\Gamma(q+1)} = \frac{\Gamma(q+1)}{\lambda^{q+1}}$$

where Γ denotes the Gamma function defined by

$$\Gamma(z) = \int_0^\infty t^{z-1} e^{-t}\, dt \quad \text{for} \quad \Re(z) > 0.$$

□