Mathematics of Infectious Diseases, fall 2011

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1 Introduction

This text is a compilation of lecture notes from a course given by Thanate Dhirasakdanon and assisted by Ilmari Karonen at the University of Helsinki in fall 2011 on the mathematical modeling of infectious diseases. It is a work in progress, with new sections added (and earlier ones possibly revised) as the course proceeds. Each section approximately covers the material presented in one lecture session.

As its name suggests, the aim of this course is to present basic mathematical techniques for modeling the spreading of infections in a host population. This field of study is sometimes called "mathematical epidemiology", although that term really covers a wider spectrum of topics than will be touched upon in this course. In general, epidemiology means "the study of the causes, distributions and control of diseases in populations"(The American Heritage Dictionary, 2002). In this course, we will mainly focus on the distribution aspect, perhaps occasionally touching upon the effects of various disease control strategies.

The study of the mathematics of infectious diseases, as presented in this course, is essentially the study of contact processes: stochastic processes in which an infection spreads through a network of intermittent contacts among a set of hosts. However, for much of this course, we will not be dealing with the contact processes themselves — even though we formally consider an epidemic as a stochastic process, we will often approximate the dynamics of such processes with simpler models, such as deterministic differential equations.

1.1 Basic terminology

We consider a population of host individuals (humans, animals, plants, etc.) which may be infected by a disease. Typically, we divide the individual hosts into several classes, such as:

Susceptible (S): not carrying the disease but capable of contracting it, and

Infective (I): carrying the disease and capable of spreading it to susceptible individuals.

These two classes make up the simplest types of epidemic models (the "SI" and "SIS" models)[1], and are usually present in more complex models as well. In addition, several other classes may be present in the population, such as:

Latent (L), or Exposed (E): carrying the disease but not (yet) capable of spreading it,

Recovered (R): not carrying the disease and incapable of contracting it (typically due to acquired immunity after infection), or

Removed (R): infected but incapable of spreading the disease (due to death or isolation from general population).

[1] In epidemiological literature, it is common to refer to certain common classes of models using abbreviations of the sequence of states which an individual passes through over the course of the infection. Thus, a model in which susceptible individuals become permanently infective would be called an "SI" model, while one in which infective individuals eventually recover and become susceptible again would be called an "SIS" model. If the recovered individuals did not become susceptible again but remained immune, we would have an "SIR", or, if the immunity wore off after a time, an "SIRS" model.

It is somewhat confusing that the same letter "R" is traditionally used to denote both the recovered and the removed classes. Fortunately, these two classes rarely appear in the same models. Also, in many models it actually makes little if any difference whether individuals are removed from the population or remain in it in an immune, non-infective state, in which case it is safe to conflate these two classes.

Disease-causing organisms can be broadly divided into two classes: microparasites, such as viruses and bacteria, and macroparasites such as intestinal worms. The defining feature is microparasites, from the point of view of disease modeling, is that they reproduce very rapidly upon entering a new host. Thus, when modeling microparasite infections, we may reasonably classify each host individual simply as either infected or non-infected, without having to explicitly consider the number of parasites present in each infected host.

In this course, for the sake of simplicity, we will mainly consider microparasite infections.

2 Microparasite epidemic in a closed population

We consider a microparasite infection spreading in a closed population of host individuals. By "closed", we mean that we assume that no hosts will enter or leave the population during the period we consider. We also ignore host population dynamics, assuming that no new hosts will be born — this simplifying assumption is justified if the epidemic we're modeling occurs on a short timescale compared to the host life cycle, as is the case e.g. with influenza epidemics in human populations.

A model of such an epidemic was introduced by W.O. Kermack and A.G. McKendrick in 1927 (Kermack and McKendrick, 1927). Their model is formulated as a system of ordinary differential equations as

$$\frac{dS}{dt} = -\sigma SI, \qquad \frac{dI}{dt} = \sigma SI - \gamma I, \qquad \frac{dR}{dt} = \gamma I \tag{1}$$

with the initial conditions

$$S(0) \geq 0, \qquad I(0) \geq 0, \qquad R(0) \geq 0.$$

We usually only interested in the initial conditions such that $S(0) > 0$ and $I(0) > 0$.

Actually Kermack and McKendrick presented a more general model (so-called age of infection model, to be discussed later), and the above is an simplified model obtained after making certain assumptions (see Section 5).

Of course, the spreading of an actual infection is a stochastic process, but this ODE system can be interpreted as a deterministic approximation of the contact process for large host populations (formally, in the limit as the population size tends to infinity). In particular, the variables $S = S(t)$, $I = I(t)$ and $R = R(t)$ in (1) should be interpreted as the respective densities of susceptible, infective and recovered (or removed) individuals per unit area (or length or volume) in a very large, well mixed host population.

The Kermack–McKendrick model makes a number of simplifying assumptions:

- Every infective host has the same chance to recover, and every susceptible the same chance to become infected, over any given time period. Further, every infective host can spread the disease equally well.
- The host population is randomly mixed, such that each individual is equally likely to meet any other (and potentially propagate the disease) over any given time period.
- There is no latency period, i.e. infected susceptibles become immediately infective themselves.
- Once an infective is recovered or removed it is unable to become infective again. This holds, for example, if the infection gives permanent immunity against reinfection, such that no host individual can become infected more than once. Alternatively, this holds if the infection always results in death of the host.

Besides the initial conditions, the Kermack–McKendrick model has two free parameters: γ denotes the per-capita recovery rate of infective individuals per unit of time and has the unit 1/time, while σ is call "infection rate" and has the unit 1/time per density of host individuals. Note that σI can be interpreted as the per-capita rate at which susceptible individuals become infective (also called the *force of infection*), and that σS can be interpreted the per-capita rate at which infective individuals cause infection. We assume here *mass action* (also called *density-dependent* incidence, such that the total population infection rate σSI is directly proportional to both the density of susceptibles S and of the infectives I. Later on, we will consider more general forms of contact mechanism.

Determining the course of the epidemic under the Kermack–McKendrick model, given the parameters σ and γ, amounts to solving an *initial value problem* of ordinary differential equations, i.e. finding functions $S(t)$, $I(t)$ and $R(t)$ which satisfy the system of ODEs (1) and match some given initial densities $S(0)$, $I(0)$ and $R(0)$. The Kermack–McKendrick model can be shown to satisfy the following properties:

- A unique solution exists for all $t \in [0, \infty)$.
- $S(t)$, $I(t)$ and $R(t)$ are non-negative for all $t \in [0, \infty)$.
- The total population size $N = S(t) + I(t) + R(t)$ is constant (for an infection that always results in death, we should think of R as the "density" of dead individuals).
- $S(t)$ decreases monotonically towards $S_\infty := \lim_{t\to\infty} S(t) > 0$.
- If $S(0) \le \frac{\gamma}{\sigma}$, $I(t)$ decreases monotonically towards $\lim_{t\to\infty} I(t) = 0$. In this case, we say that there is *no epidemic*.
- If $S(0) > \frac{\gamma}{\sigma}$, $I(t)$ initially increases (and later decreases towards 0), in which case we say that an epidemic occurs.

Despite its simplicity and small number of free parameters (just two), the Kermack–McKendrick model provides a surprisingly good fit to measured data from many real epidemics. For example, figure 1, taken from the original 1927 paper by Kermack and McKendrick, shows a comparison of actual mortality data from a plague epidemic in Bombay in 1905–1906 with their model, with coefficients and initial conditions chosen to reproduce the observed size and duration of the epidemic. We can see that, even though the model must surely be an oversimplification of the actual disease dynamics, the shape of the curve still matches the observations remarkably well.

3 Solutions to initial value problems

This is our first mathematical interlude. All of results in this section can be found on any standard textbook on theory of ordinary differential equations. See, e.g., Hale (1970 (reprinted by Dover Publications in 2009). For brevity, we omit the proofs.

We begin with a precise definition:

Definition 3.1. Let I be a non-trivial interval in $\mathbb{R}$ and let D be a connected subset of $\mathbb{R}^n$. If $(t, x) \in I \times D$, we interpret t as time and x as state. Let $f : I \times D \to \mathbb{R}^n$ be *continuous*. Let $(t_0, x_0) \in I \times D$. The function f is called the vector field, and the point (t_0, x_0) is called the initial condition.

A function $x : J \to D$ defined on a non-trivial subinterval $J \subseteq I$ is called a solution of the initial value problem

$$\frac{dx}{dt} = f(t, x(t)), \quad x(t_0) = x_0, \tag{2}$$

if the following conditions are satisfied:

(1) $x(t) \in D$ for all $t \in J$.

(2) The function x is differentiable on J.

(3) The equation (2) is satisfied for all $t \in J$.

If a is an end-point of J, the derivative of x at a means either left- or right-derivative.

On open domain, solutions to an initial value problem always exist, at least locally:

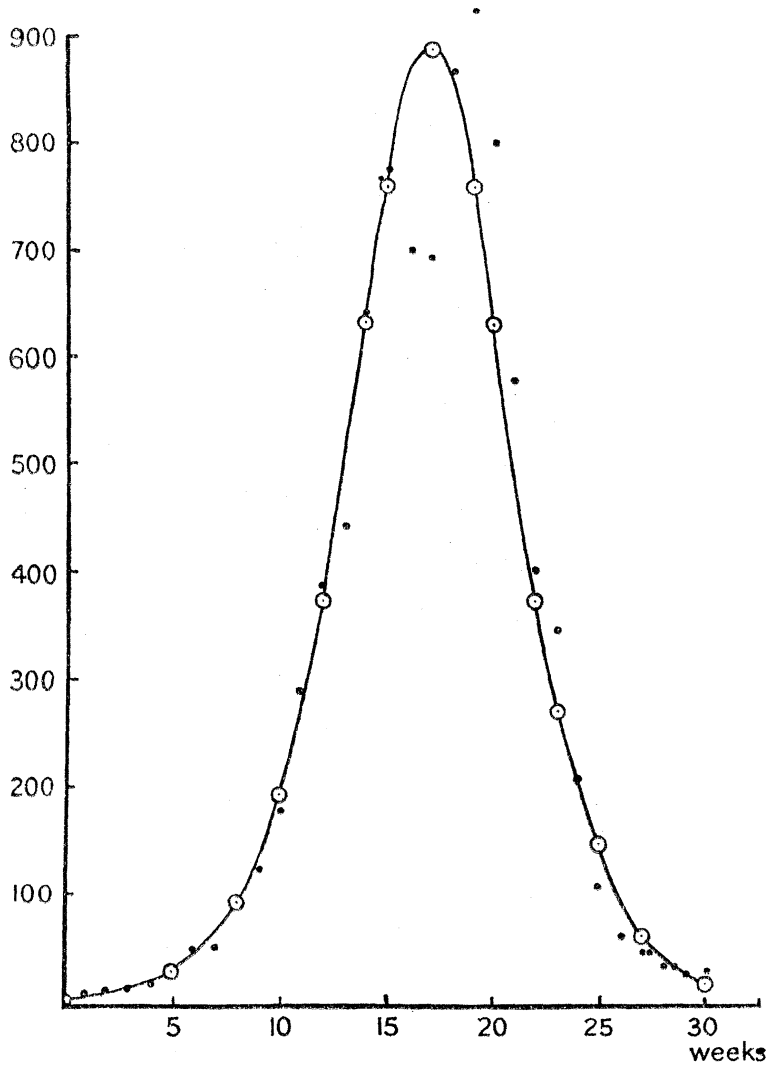

Figure 1: A chart from Kermack and McKendrick (1927), comparing recorded deaths per week from a plague epidemic in Bombay in 1905–1906 (black dots) to the Kermack–McKendrick model (line and circled dots).

Proposition 3.2 (Local existence)**.** Let I be an *open* interval in $\mathbb{R}$ and let D be a *open* connected subset of $\mathbb{R}^n$. Let $f : I \times D \to \mathbb{R}^n$ be continuous. Let $(t_0, x_0) \in I \times D$. Then, there exist $\varepsilon > 0$ and a solution $x : (t_0 - \varepsilon, t_0 + \varepsilon) \to D$ to the initial value problem (2).

Proposition 3.2 can be strengthened considerably:

Theorem 3.3 (Maximum interval of existence)**.** Let D be an open connected subset of $\mathbb{R}^n$, I be an open interval in $\mathbb{R}$, and $f : I \times D \to \mathbb{R}^n$ be continuous. Then, for each $(t_0, x_0) \in I \times D$, there exists an open interval $J := (a, b) \subseteq I$, such that the initial value problem (2) has a solution on J but not on any proper superset of J. Furthermore, for each $c \in \{a, b\}$, at least one of the following three conditions will hold:

(1) $|c| = \infty$,

(2) $\limsup_{t \in (a,b),\, t \to c} ||x(t)|| = \infty$, or

(3) there exists an element $y \in \mathbb{R}^n \setminus D$ and a sequence (t_j) in (a, b) such that $(t_j,\, x(t_j)) \to (c, y)$ as $j \to \infty$.

In addition to the existence of solutions, we are also typically interested in their uniqueness. Theorem 3.5 below provides a sufficient and often useful condition for this. In what follows, the following definition will be central:

Definition 3.4 (Local Lipschitz continuity)**.** A function $f : I \times D \to \mathbb{R}^n$ is called *locally Lipschitz continuous* (LLC) with respect to its second argument if, for any $(t_0, x_0) \in I \times D$, there exist an $\varepsilon > 0$ and a $\Lambda > 0$ such that, for all $t \in I$, $|t - t_0| < \varepsilon$ and for all $x \in D$, $||x - x_0|| < \varepsilon$ and $x' \in D$, $||x' - x_0|| < \varepsilon$,

$$||f(t, x) - f(t, x')|| \leq \Lambda ||x - x'||.$$

Note that I and D need not be open.

This definition may seem technical, but the underlying concept is simple: if f is LLC, then around every point (t_0, x_0) we may find a neighborhood where the variation of $f(t, x)$ as a function of its second argument x is bounded, in the sense that if we move x by some distance δ (while staying within the neighborhood), then $f(t, x)$ moves at most the distance $\Lambda\delta$.

Using this definition, we may state the following sufficient criterion for the uniqueness of solutions to initial value problems:

Theorem 3.5 (Uniqueness)**.** Let D be a connected subset of $\mathbb{R}^n$ and I a non-trivial interval in $\mathbb{R}$. If $f : I \times D \to \mathbb{R}^n$ is continuous (with respect to both arguments) and LLC with respect to its second argument, then, for any $(t_0, x_0) \in I \times D$ and for any interval $J \ni t_0$, the initial value problem (2) has at most one solution on J.

Local Lipschitz continuity is a strictly stronger property than plain continuity; for example, a function cannot be LLC at a point where it has a vertical tangent. However, the following proposition can often be used to establish local Lipschitz continuity:

Proposition 3.6. Let I be a non-trivial interval in $\mathbb{R}$ and let D be an *open* connected subset of $\mathbb{R}^n$. If $f : I \times D \to \mathbb{R}^n$ is continuous and has a continuous derivative with respect to its second argument (note that the derivative is an $n \times n$ matrix), then it is locally Lipschitz continuous (with respect to its second argument).

Another useful result is:

Proposition 3.7. Let I be a non-trivial interval in $\mathbb{R}$ and let D be a connected subset of $\mathbb{R}^n$. Let $f : I \times D \to \mathbb{R}^n$. Write $f(t, x) = (f_1(t, x), \ldots, f_n(t, x))$, i.e., $f_j(t, x)$ is the jth component of $f(t, x)$. Then if each f_j is locally Lipschitz continuous, then f itself is locally Lipschitz continuous.

The following proposition is useful in many situations, especially for showing that solutions of initial value problems stay non-negative (or strictly positive) for all time.

Proposition 3.8 (Simple scalar differential inequalities)**.** Let I be a non-trivial interval in $\mathbb{R}$, and let D be a subset of $\mathbb{R}$ (*not* $\mathbb{R}^n$!). Let $f : I \times D \to \mathbb{R}$ be continuous and let $(t_0, x_0) \in I \times D$. Let $x : I \to \mathbb{R}$ be a solution of the initial value problem $\frac{\mathrm{d}x}{\mathrm{d}t} = f(t, x)$, $x(t_0) = x_0$.

- If $y : I \to \mathbb{R}$ is a continuously differentiable function such that $\frac{\mathrm{d}y}{\mathrm{d}t} \le f(t, y)$, $y(t_0) \le x_0$, then $y(t) \le x(t)$ for all $t \ge t_0$ (such that $t \in I$).
- If $y : I \to \mathbb{R}$ is a continuously differentiable function such that $\frac{\mathrm{d}y}{\mathrm{d}t} \ge f(t, y)$, $y(t_0) \ge x_0$, then $y(t) \ge x(t)$ for all $t \ge t_0$ (such that $t \in I$).

4 Properties of the simplified Kermack–McKendrick model

We now study properties of solutions of the simplified Kermack–McKendrick model (1) introduced in Section 2, which we repeat here:

$$\frac{dS}{dt} = -\sigma S I, \tag{3}$$
$$\frac{dI}{dt} = \sigma S I - \gamma I, \tag{4}$$
$$\frac{dR}{dt} = \gamma I, \tag{5}$$

with $S(0) \ge 0$, $I(0) \ge 0$, $R(0) \ge 0$, $\sigma > 0$, and $\gamma > 0$.

Proposition 4.1 (Well-posedness)**.** For each initial condition $S(0) \ge 0$, $I(0) \ge 0$, and $R(0) \ge 0$, there exists a unique solution of (3)–(5) defined on $t \in [0, \infty)$. Each component $S(t), I(t), R(t)$ of the solution is non-negative and $N := S(t) + I(t) + R(t)$ is constant. If $S(0) > 0$ and $I(0) > 0$, then $S(t) > 0$ and $I(t) > 0$ for all $t \in [0, \infty)$.

Proof. Here, the vector field is $f : (-\infty, \infty) \times \mathbb{R}^3 \to \mathbb{R}^3$ defined by

$$f(t, S, I, R) = \begin{pmatrix} -\sigma S I \\ \sigma S I - \gamma I \\ \gamma I. \end{pmatrix}$$

Since f is obviously continuous, there exists a maximal solution $(S(t), I(t), R(t))$ defined on some open interval containing 0 by Theorem 3.3, in particular, the maximal solution is defined on $[0, b)$ for some $0 < b \le \infty$. Since the derivative of f with respect to (S, I, R) is

$$f'(t, S, I, R) = \begin{pmatrix} -\sigma I & -\sigma S & 0 \\ \sigma I & \sigma S - \gamma & 0 \\ 0 & \gamma & 0. \end{pmatrix}$$

We can see that f' is continuous with respect to (S, I, R) and so f is locally Lipschitz continuous on $(-\infty, \infty) \times \mathbb{R}^3$ by Proposition 3.6. This means that the solution $(S(t), I(t), R(t))$ is uniquely defined on $[0, b)$ by Theorem 3.5. It is not hard to see that $\frac{\mathrm{d}S}{\mathrm{d}t}(t) + \frac{\mathrm{d}I}{\mathrm{d}t}(t) + \frac{\mathrm{d}R}{\mathrm{d}t}(t) = 0$, and so $N := S(t) + I(t) + R(t)$ is a constant. From (3), we have $S(t) = S(0)e^{-\sigma \int_0^t I(s)\,\mathrm{d}s} \ge 0$ for $t \in [0, b)$, and from (4), we have $I(t) = I(0)e^{\int_0^t (\sigma S(s) - \gamma)\,\mathrm{d}s} \ge 0$. The last sentence also shows that $S(t) > 0$ and $I(t) > 0$ for $t \in [0, b)$ if $S(0) > 0$ and $I(0) > 0$. From (5), we have $R(t) = R(0) + \gamma \int_0^t I(s)\,\mathrm{d}s \ge 0$. Hence the solution remains bounded on $t \in [0, b)$, i.e., $0 \le S(t) + I(t) + R(t) = N$ for $t \in [0, b)$. From Theorem 3.3, we must have $b = \infty$. □

Proposition 4.2 (Behavior of solution components)**.** Let $(S(t), I(t)), R(t))$ be the unique solution of (3)–(5). Then $S(t)$ is a non-increasing function of t, $R(t)$ is a non-decreasing function of t, and $I(t) \to 0$ as $t \to \infty$. If $S(0) > 0$ and $I(0) > 0$, then $S(t)$ is a strictly decreasing function of t, $R(t)$ is a strictly increasing function of t, and $S_\infty := \lim_{t \to \infty} S(t) < \frac{\gamma}{\sigma}$.

Proof. From equations (3) and (5), and the non-negativity of the solution, we can see that $S(t)$ is non-increasing and $R(t)$ is non-decreasing. If $I(0) = 0$, we have $I(t) = 0$ for all $t \geq 0$. If $S(0) = 0$, we have $S(t) = 0$ for all $t \geq 0$ and so $\frac{\mathrm{d}I}{\mathrm{d}t} = -\gamma I$ for all $t \geq 0$. Hence if $S(0) = 0$ or $I(0) = 0$, we have $I(t) \to 0$ as $t \in \infty$. We can now assume, for the rest of this proof, that $S(0), I(0) > 0$, and so $S(t), I(t) > 0$ for all $t \geq 0$. From equations (3) and (5) again, we can see that $S(t)$ is strictly decreasing and $R(t)$ is strictly increasing. Suppose, to get a contradiction, that $S_\infty \geq \frac{\gamma}{\sigma}$. Then $\frac{\mathrm{d}I}{\mathrm{d}t} \geq (\sigma S_\infty - \gamma)I \geq 0$. Hence $I(t) \geq I(0)$ for all $t \geq 0$. From (3), we have $\frac{\mathrm{d}S}{\mathrm{d}t} \leq -\sigma I(0)S$, and so $S(t) \leq S(0)e^{-\sigma I(0)t} \to 0$ as $t \in \infty$, contradicting the assumption that $S_\infty \geq \frac{\gamma}{\sigma}$. We therefore must have $S_\infty < \frac{\gamma}{\sigma}$. This means there exist $\varepsilon > 0$ and $t_0 > 0$ such that $S(t) \leq \frac{\gamma}{\sigma} - \varepsilon$ for $t \geq t_0$. From (4), we have $\frac{\mathrm{d}I}{\mathrm{d}t} = (\sigma S - \gamma)I \leq -\varepsilon\sigma I$ for $t \geq t_0$. Hence $I(t) \leq I(t_0)e^{-\varepsilon\sigma(t-t_0)} \to 0$ as $t \to \infty$. □

We sometimes leave out the equation (5) for R since it does not affect the dynamic of S and I in any way.

Proposition 4.3 (Constant of motion)**.** If $S(0) > 0$, then the function $V(S, I) := S + I - \frac{\gamma}{\sigma}\log S$ stays constant along the solution of (3)–(4). More precisely, $V(S(t), I(t)) = V(S(0), I(0))$ for all $t \geq 0$ if $(S(t), I(t))$ is a solution of (3)–(4) with $S(0) > 0$.

Proof. We just have to show that the derivative with respect to t of $V(S(t), I(t))$ is 0. □

Proposition 4.4 (Final size)**.** Let $(S(t), I(t))$ be a solution of (3)–(4) with $S(0) > 0$ and $I(0) > 0$. Then the limit $S_\infty := \lim_{t\to\infty} S(t)$ exists and $0 < S_\infty < \frac{\gamma}{\sigma}$. This means, in particular, that there are always some susceptibles left untouched after the epidemic has passed, and that the density of susceptible after the epidemic has passed is strictly less than $\frac{\gamma}{\sigma}$.

More precisely, S_∞ is a unique solution in $(0, \frac{\gamma}{\sigma})$ of the *final size equation*:

$$S_\infty - \frac{\gamma}{\sigma}\log S_\infty = S(0) + I(0) - \frac{\gamma}{\sigma}\log S(0). \tag{6}$$

If $S(0) \leq \frac{\gamma}{\sigma}$, then $S_\infty \to S(0)$ as $I(0) \to 0$.

Proof. The facts that S_∞ exists and that $S_\infty < \frac{\gamma}{\sigma}$ are contained in the statement of Proposition 4.2. From Proposition 4.3, we have $S(t)+I(t)-\frac{\gamma}{\sigma}\log S(t) = S(0)+I(0)-\frac{\gamma}{\sigma}\log S(0)$ for all $t \geq 0$. Define $f(x) = x-\frac{\gamma}{\sigma}\log x$, $x > 0$. Then f is continuous, has a unique minimum at $x = \frac{\gamma}{\sigma}$, and is strictly decreasing on $(0, \frac{\gamma}{\sigma}]$. Since $\lim_{x\to 0^+} f(x) = \infty$ and since $f(\frac{\gamma}{\sigma}) \leq f(S(0)) < S(0) + I(0) - \frac{\gamma}{\sigma}\log S(0)$. There is a unique $S_\infty \in (0, \frac{\gamma}{\sigma})$ such that $S_\infty - \frac{\gamma}{\sigma}\log S_\infty = f(S_\infty) = S(0)+I(0)-\frac{\gamma}{\sigma}\log S(0)$. Since f is strictly decreasing on $(0, \frac{\gamma}{\sigma}]$, we can define f^{-1} with the domain $[f(\frac{\gamma}{\sigma}), \infty)$ and range $(0, \frac{\gamma}{\sigma}]$. Now if $0 < S(0) \leq \frac{\gamma}{\sigma}$, then we have $f^{-1}(f(S(0))) = S(0)$ and so $S_\infty = f^{-1}(f(S_\infty)) = f^{-1}(f(S(0)) + I(0)) \to f^{-1}(f(S(0))) = S(0)$ as $I(0) \to 0$. □

4.1 The basic reproductive number of the simplified Kermack–McKendrick model, threshold theorem

The fundamental quantity in most models in epidemiology is the *basic reproductive number*, usually denotes by $\mathcal{R}_0$, and is defined as

> the number of secondary infections caused by a single infective individual introduced into an entirely susceptible population.

For the simplified Kermack–McKendrick model, it can be shown (see Section 5) that the *mean infectious period*, i.e., the expected amount of time that a newly infected individual stays infective, is $\frac{1}{\gamma}$. Recall that σS can be interpreted the per capita rate (per unit time) at which infective individuals cause infection (see Section 2). Hence, for the simplified Kermack–McKendrick model, if an infective individual is introduced into an entirely susceptible population of initial size $S(0)$, then this infective individual will cause $\frac{\sigma S(0)}{\gamma}$ secondary infections, i.e., $\mathcal{R}_0 = \frac{\sigma S(0)}{\gamma}$.

Theorem 4.5 (Kermack–McKendrick threshold theorem)**.** Let $(S(t), I(t))$ be a solution of (1) with $S(0) > 0$ and $I(0) > 0$.

(a) If $S(0) \leq \frac{\gamma}{\sigma}$, equivalently, if $\mathcal{R}_0 \leq 1$, then $I(t)$ is strictly decreasing toward 0 as $t \to \infty$.

(b) If $S(0) > \frac{\gamma}{\sigma}$, equivalently, if $\mathcal{R}_0 > 1$, then $I(t)$ initially increases, and then decreases toward 0 as $t \to \infty$.

Define $I_{\max} = \sup_{t \in [0,\infty)} I(t) > 0$. We can now say a bit more.

(c) If $S(0) \leq \frac{\gamma}{\sigma}$, equivalently, if $\mathcal{R}_0 \leq 1$, then $I_{\max} = I(0)$, and $S_\infty \to S(0)$ as $I(0) \to 0$.

(d) If $S(0) > \frac{\gamma}{\sigma}$, equivalently, if $\mathcal{R}_0 > 1$, then $I_{\max}$ stays bounded away from 0 as $I(0) \to 0$, and $S_\infty < \frac{\gamma}{\sigma} < S(0)$ as $I(0) \to 0$.

Proof. (a) and (c): Suppose that $0 < S(0) \leq \frac{\gamma}{\sigma}$. Then $S(t) < \frac{\gamma}{\sigma}$ for $t > 0$ since $S(t)$ is strictly decreasing by Proposition 4.2. Hence $\frac{\mathrm{d}I}{\mathrm{d}t}(t) = (\sigma S(t) - \gamma)I(t) < 0$ for $t > 0$, and so $I(t)$ is strictly decreasing. Therefore, $I_{\max} = I(0)$. The limit $\lim_{t\to\infty} I(t) = 0$ by Proposition 4.2, and we have $S_\infty \to S(0)$ as $I(0) \to 0$ by Proposition 4.4.

(b) and (d): Suppose that $S(0) > \frac{\gamma}{\sigma}$. The inequalities $S_\infty < \frac{\gamma}{\sigma} < S(0)$ follows from Proposition 4.4. Since $S(t)$ is strictly decreasing by Proposition 4.2, there is $t' > 0$ such that $S(t) > \frac{\gamma}{\sigma}$ for $t \in [0, t')$, $S(t') = \frac{\gamma}{\sigma}$, and $S(t) < \frac{\gamma}{\sigma}$ for $t \in (t', \infty)$. Hence $\frac{\mathrm{d}I}{\mathrm{d}t}(t) = (\sigma S(t) - \gamma)I(t) > 0$ for $t \in [0, t')$ and $\frac{\mathrm{d}I}{\mathrm{d}t}(t) = (\sigma S(t) - \gamma)I(t) < 0$ for $t \in (t', \infty)$. This means that $I(t)$ is strictly increasing on $t \in [0, t')$ and is strictly decreasing on $t \in (t', \infty)$. The limit $\lim_{t\to\infty} I(t) = 0$ by Proposition 4.2, From Proposition 4.3, we have $I_{\max} = S(0) - \frac{\gamma}{\sigma}\log S(0) - S(t') + \frac{\gamma}{\sigma}\log S(t') + I(0) \geq S(0) - \frac{\gamma}{\sigma}\log S(0) - \frac{\gamma}{\sigma} + \frac{\gamma}{\sigma}\log\frac{\gamma}{\sigma} > 0$. The last inequality comes from the fact that the function $x \mapsto x - \frac{\gamma}{\sigma}\log x$ has a unique minimum at $x = \frac{\gamma}{\sigma}$. □

The final size equation (6) can be alternatively written as

$$\frac{S_\infty}{S(0)} - \frac{1}{\mathcal{R}_0}\log\left(\frac{S_\infty}{S(0)}\right) = 1 + \frac{I(0)}{S(0)}. \tag{7}$$

5 Age of infection Kermack–McKendrick epidemic model in closed population

The Kermack–McKendrick model described in sections 2 and 4 is based on the assumption that all infective hosts are equally likely to recover and equally effective at spreading the disease, regardless of how long ago they were infected. In most real diseases, however, infectivity and recovery (and/or mortality) rates vary considerably over the course of the infection; in particular, many infections have an initial latency period, during which infectivity is very low.

The model described in this section generalizes the simplified Kermack–McKendrick model to relax this assumption by taking into account the *age of infection*, that is to say, the amount of time since a given host was infected. This is, in fact, the model that Kermack and McKendrick proposed in (Kermack and McKendrick, 1927).

Let $S(t)$ be the density of susceptible hosts in the population at time t, and let $i : [0,\infty) \times [0,\infty) \to [0,\infty)$ be a function such that $\int_a^b i(t,\tau)d\tau$ is the density of infective hosts with *infection age* between a and b at time t, i.e., the density of infective hosts that was infected (entered infective class) between the time $t - a$ and $t - b$. Essentially, one can think of $i(t,\tau)$ as the density of infective hosts of age τ in the population at time t, although one should keep in mind that this is really a density per area *times age interval*; the actual density per area of infectives of age *exactly* τ is zero.

6 Epidemic model in closed population with general homogeneous mixing contact rate

We consider the model:

$$\frac{dS}{dt} = -C(N)\frac{SI}{N}, \tag{8}$$
$$\frac{dI}{dt} = C(N)\frac{SI}{N} - (\gamma+\alpha)I, \tag{9}$$
$$\frac{dR}{dt} = \gamma I, \tag{10}$$
$$N = S + I + R. \tag{11}$$

Here, as usual, S is the density of susceptibles, I is the density of infectives, R is the density of recovered (with permanent immunity), and N is the total population density under consideration. The parameter γ is the per-capita recovery rate of infectives, as in the simplified Kermack–McKendrick model. Unlike the simplified Kermack–McKendrick model, we distinguish between those who recover from the disease and those who die because of the disease. We let the parameter α be the per-capita mortality rate of the infectives. Notice that if $\alpha > 0$, the total population density N will not be a constant. The function $C(N)$ is a *contact rate function*, and can be interpreted as a number of contact per unit time that a typical individual makes with other individuals if the total population density is N. Note that

- if $C(N) = \sigma N$, we get the usual *mass-action incidence*, and
- if $C(N) = \sigma$ is a constant, we talk about *standard incidence*.

We make the following two assumptions:

- $\gamma \geq 0$, $\alpha \geq 0$, and $\gamma + \alpha > 0$.
- $C : (0,\infty) \to (0,\infty)$ is strictly positive, non-decreasing, and locally Lipschitz continuous function.

Note that $\lim_{N\to 0^+} C(N)$ always exists since C is non-decreasing, and we define $C(0) := \lim_{N\to 0^+} C(N)$. We will sometimes assume that $\frac{C(N)}{N}$ is a non-increasing function of N.

It is more convenience to drop the differential equation for R and to work with the differential equation for N instead. Hence we rewrite (8)–(11) as

$$\frac{dN}{dt} = -\alpha I, \tag{12}$$
$$\frac{dS}{dt} = -C(N)\frac{SI}{N}, \tag{13}$$
$$\frac{dI}{dt} = C(N)\frac{SI}{N} - (\gamma+\alpha)I. \tag{14}$$

We choose a state-space $\mathcal{S} = \{(N,S,I) \in \mathbb{R}^3 : S > 0, I > 0, S + I \leq N\}$ since we want to avoid the division by zero in (13) and (14) (this is not essential, but it helps simplify the analysis).

Proposition 6.1. The model (12)–(14) is well-defined, i.e., if $(N_0,S_0,I_0) \in \mathcal{S}$ then there is a unique solution of (12)–(14) with $N(0) = N_0$, $S(0) = S_0$, $I(0) = I_0$, and the solution is defined and stays in $\mathcal{S}$ for all $t \in [0,\infty)$.

Proof. For a moment, we work with the state-space $\mathcal{S}' := \{(N,S,I) \in \mathbb{R}^3 : N > 0, S > 0, I > 0\}$ which is an open subset of $\mathbb{R}^3$. Note that $\mathcal{S} \subseteq \mathcal{S}'$.

The vector field

$$f(N,S,I) = \begin{pmatrix} -\alpha I \\ -C(N)\frac{SI}{N} \\ C(N)\frac{SI}{N} - (\gamma+\alpha)I \end{pmatrix}$$

is locally Lipschitz continuous on $\mathcal{S}'$, and so the initial value problem (12)–(14) with $(N_0, S_0, I_0) := (N(0), S(0), I(0)) \in \mathcal{S}'$ has a unique solution defined on $t \in [0, b)$ for some $b \in (0, \infty]$.

We now assume that $(N_0, S_0, I_0) \in \mathcal{S}$ for the rest of this proof.

We have $S(t) = S_0 e^{-\int_0^t C(N(s)) \frac{I(s)}{N(s)}\,\mathrm{d}s} > 0$ and $I(t) = I_0 e^{\int_0^t (C(N(s)) \frac{I(s)}{N(s)} - \gamma - \alpha)\,\mathrm{d}s} > 0$ for all $t \in [0, b)$. We also have $\dot{N} - \dot{S} - \dot{I} = \gamma I > 0$, and so $N(t) - S(t) - I(t) \geq N_0 - S_0 - I_0 \geq 0$ for all $t \in [0, b)$. Hence $(N(t), S(t), I(t)) \in \mathcal{S}$ for all $t \in [0, b)$ if $(N_0, S_0, I_0) \in \mathcal{S}$. Note also that $N(t) \leq N_0$ for all $t \in [0, b)$.

Suppose, to get a contradiction, that $b < \infty$. Then, from Theorem 3.3, either (a) $N(t) + S(t) + I(t) \to \infty$ as $t \to b^-$, or (b) there exists a sequence (t_k) in $[0, b)$ with $\lim_{k\to\infty} t_k = b$ and $\lim_{k\to\infty}(N(t_k), S(t_k), I(t_k)) := (N_b, S_b, I_b) \notin \mathcal{S}'$. (a) is impossible since $N(t)+S(t)+I(t) \leq 2N(t) \leq 2N_0$ for all $t \in [0, b)$, and (b) is impossible since $N(t) \geq S(t) + I(t)$ and since $S(t) = S_0 e^{-\int_0^t C(N(s)) \frac{I(s)}{N(s)}\,\mathrm{d}s} \geq S_0 e^{-\int_0^t C(N(s))\,\mathrm{d}s} \geq S_0 e^{-C(N_0)t} \geq S_0 e^{-C(N_0)b}$ and $I(t) = I_0 e^{\int_0^t (C(N(s)) \frac{I(s)}{N(s)} - \gamma - \alpha)\,\mathrm{d}s} \geq I_0 e^{-(\gamma+\alpha)t} \geq I_0 e^{-(\gamma+\alpha)b}$ for all $t \in [0, b)$, and so the solution is bounded away from the boundary of $\mathcal{S}'$. □

To continue, we need the following result:

Lemma 6.2 (Barbalat's Lemma)**.** Let $f : [0, \infty) \to \mathbb{R}$ be a continuously differentiable function such that $\lim_{t\to\infty} f(t)$ exists.

Suppose that $\dot{f}$ is *uniformly continuous* on $[0, \infty)$. Then $\lim_{t\to\infty} \dot{f}(t) = 0$.

In particular, if f is twice continuously differentiable and $\ddot{f}(t)$ is bounded on $t \in [0, \infty)$, then $\dot{f}$ is uniformly continuous and the conclusion of the Lemma holds.

Proof. The proof can be found in, e.g., (Thieme, 2003, Theorem A.16 and Corollary A.18). □

Proposition 6.3. $N(t)$ and $S(t)$ are strictly decreasing functions, and we have $\lim_{t\to\infty} I(t) = 0$.

Proof. It is clear that $N(t)$ and $S(t)$ are strictly decreasing since their derivatives are strictly negative.

To show that $\lim_{t\to\infty} I(t) = 0$, we consider two cases: $\alpha > 0$ and $\alpha = 0$.

Case $\alpha > 0$. We know that $N_\infty := \lim_{t\to\infty} N(t)$ exists since N is decreasing and $N(t) > 0$ for all $t \in [0, \infty)$. We also have

$$|\ddot{N}| = \alpha|\dot{I}| = \alpha\big|C(N)\frac{SI}{N} - (\gamma+\alpha)I\big| \leq \alpha\big(C(N)\frac{SI}{N} + (\gamma+\alpha)I\big) \leq \alpha\big(C(N)I + (\gamma+\alpha)I\big)$$
$$\leq \alpha\big(C(N) + (\gamma+\alpha)\big)N \leq \alpha\big(C(N_0) + (\gamma+\alpha)\big)N_0.$$

Hence $\dot{N}(t)$ is uniformly continuous on $t \in [0, \infty)$ and so $\lim_{t\to\infty} \dot{N}(t) = 0$ by Lemma 6.2. Since $I(t) = -\frac{\dot{N}(t)}{\alpha}$, we have $\lim_{t\to\infty} I(t) = 0$.

Case $\alpha = 0$. In this case, N is constant and the model reduces to the simplified Kermack–McKendrick model (with $\sigma = C(N)/N$)). Hence the claim follows from Proposition 4.2. □

In order to get the basic reproductive number for this model, we note that the initial infection rate caused by a single infective is $C(N_0)\frac{S_0}{N_0}$. The infectious period is exponentially distributed with the mean $\frac{1}{\gamma+\alpha}$. Hence, for this model, we have

$$\mathcal{R}_0 = \frac{C(N_0)S_0}{(\gamma+\alpha)N_0}. \tag{15}$$

Lemma 6.4. (a) If $C(N(t'))\frac{S(t')}{N(t')} \leq \gamma + \alpha$ for some $t' \geq 0$, then $C(N(t))\frac{S(t)}{N(t)} \leq \gamma + \alpha$ for all $t \geq t'$.

(b) If $C(N_0)\frac{S_0}{N_0} > \gamma + \alpha$, then there exists $t' > 0$ such that $C(N(t'))\frac{S(t')}{N(t')} = \gamma + \alpha$, and such that $C(N(t))\frac{S(t)}{N(t)} > \gamma + \alpha$ for all $t \in [0, t')$.

Proof. (a) Suppose, to get a contradiction, that there exists $t_1 < t_2$ such that $C(N(t_1))\frac{S(t_1)}{N(t_1)} \leq \gamma + \alpha$ and $C(N(t_2))\frac{S(t_2)}{N(t_2)} > \gamma + \alpha$. Since the function $t \mapsto C(N(t))\frac{S(t)}{N(t)}$ is continuous, we can assume that $C(N(t_1))\frac{S(t_1)}{N(t_1)} = \gamma + \alpha$, and that $C(N(t))\frac{S(t)}{N(t)} > \gamma + \alpha$ for all $t \in (t_1, t_2]$. Since $\frac{S(t)}{N(t)} < 1$, we have $C(N(t)) > \gamma + \alpha \geq \alpha$ for all $t \in (t_1, t_2]$. Since $N(t)$ is decreasing and $C(N)$ is non-decreasing, we have

$$C(N(t_2))\frac{S(t_2)}{N(t_2)} - C(N(t_1))\frac{S(t_1)}{N(t_1)} \leq C(N(t_1))\Big(\frac{S(t_2)}{N(t_2)} - \frac{S(t_1)}{N(t_1)}\Big),$$

and by the mean value theorem, there is $t \in (t_1, t_2)$ such that

$$\begin{aligned} C(N(t_2))\frac{S(t_2)}{N(t_2)} - C(N(t_1))\frac{S(t_1)}{N(t_1)} &\leq C(N(t_1))(t_2 - t_1)\Big(\frac{\dot{S}(t)}{N(t)} - \frac{S(t)}{N(t)}\frac{\dot{N}(t)}{N(t)}\Big) \\ &= C(N(t_1))(t_2 - t_1)\Big(-\frac{C(N(t))S(t)I(t)}{(N(t))^2} + \alpha\frac{S(t)I(t)}{(N(t))^2}\Big) \\ &= C(N(t_1))(t_2 - t_1)\big(-C(N(t)) + \alpha\big)\frac{S(t)I(t)}{(N(t))^2} \\ &< 0, \end{aligned}$$

contradicting $C(N(t_1))\frac{S(t_1)}{N(t_1)} = \gamma + \alpha < C(N(t_2))\frac{S(t_2)}{N(t_2)}$.

(b) If $C(N_0)\frac{S_0}{N_0} > \gamma + \alpha$, and if there does not exist $t' > 0$ such that $C(N(t'))\frac{S(t')}{N(t')} = \gamma + \alpha$, then $C(N(t))\frac{S(t)}{N(t)} > \gamma + \alpha$ for all $t \geq 0$. But then $\dot{I} = \big(C(N)\frac{S}{N} - (\gamma + \alpha)\big)I > 0$ for all $t \geq 0$, and so $I(t) \geq I_0$ for all $t \geq 0$, contradicting $\lim_{t\to\infty} I(t) = 0$. Hence there exists $t' > 0$ be such that $C(N(t'))\frac{S(t')}{N(t')} = \gamma + \alpha$, and since the function $t \mapsto C(N(t))\frac{S(t)}{N(t)}$ is continuous, we can assume that $C(N(t))\frac{S(t)}{N(t)} > \gamma + \alpha$ for all $t \in [0, t')$. □

Theorem 6.5. (a) If $\mathcal{R}_0 \leq 1$, then $I(t)$ is non-increasing and tends toward 0 as $t \to \infty$.

(b) If $\mathcal{R}_0 > 1$, then $I(t)$ initially increases, and then becomes non-increasing and tends toward 0 as $t \to \infty$.

Proof. We have $\lim_{t\to\infty} I(t) = 0$ by Proposition 6.3.

(a): Suppose that $\mathcal{R}_0 \leq 1$, and so $C(N_0)\frac{S_0}{N_0} \leq \gamma + \alpha$. By Lemma 6.4(a), we have $C(N(t))\frac{S(t)}{N(t)} \leq \gamma + \alpha$ for all $t \geq 0$, and so $\dot{I} = \big(C(N(t))\frac{S(t)}{N(t)} - (\gamma + \alpha)\big)I(t) \leq 0$ for all $t \geq 0$. Hence $I(t)$ is non-increasing.

(b): Suppose that $\mathcal{R}_0 > 0$ and so $C(N_0)\frac{S_0}{N_0} > \gamma + \alpha$. By Lemma 6.4(a,b), there exists $t' > 0$ such that such that $C(N(t))\frac{S(t)}{N(t)} > \gamma + \alpha$ for all $t \in [0, t')$, and such that $C(N(t))\frac{S(t')}{N(t)} \leq \gamma + \alpha$ for all $t \in [t', \infty)$, Since $\dot{I} = \big(C(N(t))\frac{S(t)}{N(t)} - (\gamma + \alpha)\big)I(t)$, $I(t)$ is increasing on $[0, t')$ and non-decreasing on $[t', \infty)$. □

The following proposition considers the final size of the epidemic in case where $\gamma > 0$, i.e., there are possibilities that some individuals survive the disease.

Proposition 6.6. If $\gamma > 0$, then $N_\infty > 0$ and $S_\infty > 0$ where $N_\infty := \lim_{t\to\infty} N(t)$ and $S_\infty := \lim_{t\to\infty} S(t)$.

If $\frac{C(N)}{N}$ is a non-increasing function of N, we also have a final size inequality (compare with (6)):

$$\log S_0 - \log S_\infty \geq \frac{C(N_0)}{N_0}\frac{S_0 + I_0 - S_\infty}{\gamma + \alpha}. \tag{16}$$

We can also write (16) as (compare with (7)):

$$\frac{S_\infty}{S_0} - \frac{1}{\mathcal{R}_0}\log\frac{S_\infty}{S_0} \geq 1 + \frac{I_0}{S_0}, \tag{17}$$

Proof. We again consider two cases: $\alpha > 0$ and $\alpha = 0$.

Case $\alpha > 0$. We have $\dot{I} = -\dot{S} + \frac{\gamma+\alpha}{\alpha}\dot{N}$, and so, by integrating both side, we have $I(t) = I_0 + S_0 - S(t) + \frac{\gamma+\alpha}{\alpha}(N(t) - N_0)$. Hence

$$\begin{aligned}\dot{N}(t) &= -\alpha I(t) = -\alpha\big(I_0 + S_0 - S(t) + \frac{\gamma+\alpha}{\alpha}(N(t) - N_0)\big)\\ &= \alpha S(t) - (\gamma+\alpha)\big(N(t) - N_0\big) - \alpha(I_0 + S_0) = \alpha S(t) - (\gamma+\alpha)N(t) + \gamma N_0 + \alpha(N_0 - I_0 - S_0)\\ &\geq -(\gamma+\alpha)N(t) + \gamma N_0.\end{aligned}$$

Solving the above differential inequality, we get $N(t) \geq N_0 e^{-(\gamma+\alpha)t} + \frac{\gamma N_0}{\gamma+\alpha}\big(1 - e^{-(\gamma+\alpha)t}\big)$. Hence $N_\infty \geq \frac{\gamma N_0}{\gamma+\alpha} > 0$. Since $\frac{\dot{S}}{S} = \frac{C(N)}{N}\frac{\dot{N}}{\alpha}$, and so, by integrating both side, we have

$$\log\frac{S(t)}{S_0} = \frac{1}{\alpha}\int_0^t C(N(s))\frac{\dot{N}(s)}{N(s)}\,\mathrm{d}s = \frac{1}{\alpha}\int_{\log N_0}^{\log N(t)} C(e^s)\,\mathrm{d}s.$$

Hence $S(t) = S_0 e^{\frac{1}{\alpha}\int_{\log N_0}^{\log N(t)} C(e^s)\,\mathrm{d}s}$, and so $S_\infty = S_0 e^{\frac{1}{\alpha}\int_{\log N_0}^{\log N_\infty} C(e^s)\,\mathrm{d}s} > 0$. Now since $\dot{S} + \dot{I} = -(\gamma+\alpha)I$ we have $S(t) + I(t) - S_0 - I_0 = -(\gamma+\alpha)\int_0^t I(s)\,\mathrm{d}s$. Since $\frac{\dot{S}}{S} = -\frac{C(N)I}{N}$, we have

$$\begin{aligned}\log\frac{S_0}{S(t)} &= \int_0^t \frac{C(N(s))}{N(s)}I(s)\,\mathrm{d}s \geq \frac{C(N_0)}{N_0}\int_0^t I(s)\,\mathrm{d}s\\ &= \frac{C(N_0)}{N_0}\frac{S_0 + I_0 - S(t) - I(t)}{\gamma+\alpha}.\end{aligned}$$

Taking the limit as $t \to \infty$, we have (16).

Now since $\mathcal{R}_0 = \frac{C(N_0)S_0}{\gamma+\alpha}$, $\log\frac{S_0}{S_\infty} \geq \mathcal{R}_0\big(1 + \frac{I_0}{S_0} - \frac{S_\infty}{S_0}\big)$, and so $\frac{S_\infty}{S_0} - \frac{1}{\mathcal{R}_0}\log\frac{S_\infty}{S_0} \geq 1 + \frac{I_0}{S_0}$.

Case $\alpha = 0$. In this case, N is constant and the model reduces to the simplified Kermack–McKendrick model (with $\sigma = C(N)/N$)). Hence the claim follows from Proposition 4.4. Note that in this case (16) is an equality. □

We now consider the final size of the epidemic in case $\gamma = 0$, i.e., every infective dies because of the disease. In this case, we have $N = S + I$ since there is no recovered individual.

Proposition 6.7. Suppose that $\gamma = 0$ (and so $\alpha > 0$).

If $C(0) \geq \alpha$, then $N_\infty = S_\infty = 0$, i.e., the population goes extinct because of the disease.

If $C(0) < \alpha$, then $N_\infty = S_\infty > 0$.

Proof. We define $f(t) := \frac{I(t)}{N(t)}$, which is well-defined since $N(t) > 0$ for all t. We also have $0 < f(t) < 1$ for all t since $S(t), I(t) > 0$.

From (12) and (14), and the fact that $S(t) = N(t) - I(t)$, we have (using the quotient rule from calculus):

$$\begin{aligned}\dot{N}(t) &= -\alpha f(t)N(t),\\ \dot{f}(t) &= \big(C(N(t)) - \alpha\big)\big(1 - f(t)\big)f(t).\end{aligned}$$

Suppose that $C(0) \geq \alpha$. Then $C(N) \geq \alpha$ for all N and so $\dot{f}(t) \geq 0$. Hence $f(t) \geq f_0$ (where $f_0 = f(0)$), and so $\dot{N}(t) = -\alpha f(t)N(t) \leq -\alpha f_0 N(t)$. Hence $N(t) \leq N_0 e^{-\alpha f_0 t}$ and so $N_\infty = 0$.

Now suppose that $C(0) < \alpha$. If $C(N_\infty) \geq \alpha$, then we must have $N_\infty > 0$ since $C(0) < \alpha$ and C is non-decreasing. So we can assume that $C(N_\infty) < \alpha$. Hence there exist $T > 0$ and $\varepsilon > 0$ such that $C(N(t)) < \alpha - \varepsilon$ for $t \geq T$, and so $\dot{f}(t) = (C(N(t)) - \alpha)(1 - f(t))f(t) < -\varepsilon(1 - f(t))f(t)$. Hence $f(t)$ is decreasing for $t \geq T$ and $\dot{f}(t) < -\varepsilon(1 - f(t))f(t) < -\varepsilon(1 - f(T))f(t)$ for all $t \geq T$. This means that $f(t) \leq f(T)e^{-\varepsilon(t-T)}$ for $t \geq T$. Since $\dot{N}N = -\alpha f$, we have

$$\log N(t) - \log N(T) = -\alpha\int_T^t f(s)\,\mathrm{d}s \geq -\alpha f(T)\int_T^t e^{-\varepsilon(s-T)}\,\mathrm{d}s = -\alpha f(T)\frac{1 - e^{-(t-T)}}{\varepsilon} > -\frac{\alpha f(T)}{\varepsilon}.$$

Hence $\log N(t)$ is bounded away from $-\infty$ and so $N_\infty > 0$. □

7 Stability of equilibria for systems of ordinary differential equations

This is another mathematical interlude.

Definition 7.1. Let $f : D \to \mathbb{R}^n$ be a vector field defined on a connected subset D of $\mathbb{R}^n$. A point $x \in D$ is called an *equilibrium* of the vector field f if $f(x) = 0$.

Proposition 7.2. Let D be a connected subset of $\mathbb{R}^n$. Let $f : D \to \mathbb{R}^n$ be locally Lipschitz continuous. Let $x_0 \in D$ be an equilibrium of f. Then the "constant" function $x : (-\infty, \infty) \to D$ defined by $x(t) = x_0$ for all $t \in (-\infty, \infty)$ is a solution to the differential equation

$$\frac{dx}{dt} = f(x(t)).$$

Furthermore, x is the only solution of the differential equation that passes through the point x_0, i.e., if $y : I \to D$ is a solution of the differential equation such that $y(t_0) = x_0$ for some $t_0 \in I$, then $y = x$ on I.

Definition 7.3. Let D be a connected subset of $\mathbb{R}^n$. Let $f : D \to \mathbb{R}^n$ be locally Lipschitz continuous. Let $y \in D$ be an equilibrium of f. Then

- y is a *(locally) stable* equilibrium if for every $\varepsilon > 0$, there is $\delta > 0$ such that if $x : [0, \infty) \to D$ is a solution to the differential equation $\frac{dx}{dt} = f(x(t))$ with $\|x(0) - y\| < \delta$, then $\|x(t) - y\| < \varepsilon$ for all $t \in [0, \infty)$.
- y is a *locally asymptotically stable* equilibrium if it is a stable equilibrium and there exists $\varepsilon > 0$ such that if $x : [0, \infty) \to D$ is a solution to the differential equation $\frac{dx}{dt} = f(x(t))$ with $\|x(0) - y\| < \varepsilon$, then $\lim_{t\to\infty} x(t) = y$.
- y is an *unstable* equilibrium if it is not stable.

Proposition 7.4 (Principle of linearized stability)**.** Let D be a connected subset of $\mathbb{R}^n$. Let $f : D \to \mathbb{R}^n$ be *continuously differentiable.* Let $y \in D$ be an equilibrium of f. Let J be the Jacobian matrix of f evaluated at y. Then

- y is locally asymptotically stable if all of the eigenvalues of J have strictly negative real part.
- y is unstable if there is an eigenvalue of J that have strictly positive real part.

Proposition 7.5 (Routh-Hurwitz criteria)**.**

- Let D be a connected subset of $\mathbb{R}^2$. Let $f : D \to \mathbb{R}^2$ be continuously differentiable. Let $y \in D$ be an equilibrium of f. Let J be the Jacobian matrix of f evaluated at y.

  Then

  - y is locally asymptotically stable if $\det J > 0$ and $\operatorname{trace} J < 0$.
  - y is unstable if either $\det J < 0$ or $\operatorname{trace} J > 0$.

- Let D be a connected subset of $\mathbb{R}^3$. Let $f : D \to \mathbb{R}^3$ be continuously differentiable. Let $y \in D$ be an equilibrium of f. Let J be the Jacobian matrix of f evaluated at y.

  Then y is locally asymptotically stable if $\det J < 0$, $\operatorname{trace} J < 0$, and

  $$\det A - (\operatorname{trace} A)(A_1 + A_2 + A_3) > 0,$$

  where A_j, $j = 1, 2, 3$, are determinants of 2×2 matrices obtained from J by deleting the jth column and jth row.

8 Host limitation by infectious diseases

Consider the following model:

$$\frac{dS}{dt} = \beta N - \mu S - \sigma SI, \tag{18}$$
$$\frac{dI}{dt} = \sigma SI - (\mu + \gamma + \alpha)I, \tag{19}$$
$$\frac{dR}{dt} = \gamma I - \mu R, \tag{20}$$
$$N = S + I + R. \tag{21}$$

Here β is the per-capita birth rate of the host population. Notice that we assume that susceptibles, infectives, and recovered individual gives birth at the same rate, and that all new-borns are susceptibles. We also assume that susceptibles and recovered die at the per-capita death rate μ, and that infectives die at the per-capita death rate $\mu + \alpha$. Hence α can be thought of as an additional death rate by being infected. For simplicity, we work with the mass-action incidence (σSI). All other parameters and state variables have the same meaning as the ones in Section 6. We will assume that $\mu > 0$, $\beta > \mu$, $\alpha > 0$, $\sigma > 0$, and $\gamma \geq 0$.

It will be more convenience to rewrite (18)–(21) as

$$\frac{dN}{dt} = (\beta - \mu)N - \alpha I, \tag{22}$$
$$\frac{dS}{dt} = \beta N - \mu S - \sigma SI, \tag{23}$$
$$\frac{dI}{dt} = \sigma SI - (\mu + \gamma + \alpha)I. \tag{24}$$

We pick $\mathcal{S} = \{(N, S, I) \in \mathbb{R}^3 : S \geq 0,\ I \geq 0,\ S + I \leq N\}$ as our state-space.

Proposition 8.1. The model (22)–(24) is well-defined on the state-space $\mathcal{S}$, i.e., for every $(N_0, S_0, I_0) \in \mathcal{S}$, there exists a unique solution $(N(t), S(t), I(t)) \in \mathcal{S}$ defined on $t \in [0, \infty)$ such that $(N(0), S(0), I(0)) = (N_0, S_0, I_0)$.

If $I_0 = 0$, we have $N(t) = N_0 e^{(\beta-\mu)t}$ for $t \geq 0$, i.e., the total density of the population grows exponentially in absence of the diseases. Also if $I_0 = 0$ and $N_0 = S_0$, we have $N(t) = S(t)$ for all $t \geq 0$.

The proof will be left as a homework.

We now look for equilibria of this model, i.e., for all values of (N, S, I) that solve the following system of algebraic equations:

$$0 = (\beta - \mu)N - \alpha I, \tag{25}$$
$$0 = \beta N - \mu S - \sigma SI, \tag{26}$$
$$0 = \sigma SI - (\mu + \gamma + \alpha)I. \tag{27}$$

If $N = 0$, we have $I = 0$ from (25), and then we have $S = 0$ from (26). We can then verify that $(N, S, I) = (0, 0, 0)$ is a solution to (25)–(27). Now we assume that $N > 0$. From (25), we have $I = \frac{\beta-\mu}{\alpha}N > 0$. From (27), we have $S = \frac{\mu+\gamma+\alpha}{\sigma}$. From (26), we have $I = \frac{\beta N - \mu S}{\sigma S}$. So, $\frac{\beta-\mu}{\alpha}N = I = \frac{\beta N - \mu S}{\sigma S}$. Solving for N, we have $N = \frac{\mu S}{\beta - \frac{\beta-\mu}{\alpha}\sigma S} = \frac{\mu\frac{\mu+\gamma+\alpha}{\sigma}}{\beta - \frac{\beta-\mu}{\alpha}(\mu+\gamma+\alpha)} = \frac{\alpha\mu(\mu+\gamma+\alpha)}{\sigma(\mu(\mu+\gamma+\alpha) - \beta(\mu+\gamma))} = \frac{\alpha}{\sigma\left(1 - \frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\right)}$. So $I = \frac{\beta-\mu}{\alpha}N = \frac{\beta-\mu}{\sigma\left(1-\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\right)}$, and $S + I = \frac{(\mu+\gamma+\alpha)(1-\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}) + (\beta-\mu)}{\sigma\left(1-\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\right)} = \frac{(\mu+\gamma+\alpha) - \frac{\beta}{\mu}(\mu+\gamma) + (\beta-\mu)}{\sigma\left(1-\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\right)} = \frac{\gamma+\alpha-\frac{\beta}{\mu}\gamma}{\sigma\left(1-\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\right)}$. Notice that, to have $N > 0$ and $I > 0$, we must require that $\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} < 1$. Also, to have $S + I \leq N$, we must require that $\gamma + \alpha - \frac{\beta}{\mu}\gamma \leq \alpha$, but this last inequality is automatically satisfied because of the assumption $\beta > \mu$. We now summarize:

Proposition 8.2. $(N, S, I) = (0, 0, 0)$ is always an equilibrium. If $\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} < 1$, there is another equilibrium (N^*, S^*, I^*) where

$$N^* = \frac{\alpha}{\sigma\big(1 - \frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\big)}, \tag{28}$$

$$S^* = \frac{\mu+\gamma+\alpha}{\sigma}, \tag{29}$$

$$I^* = \frac{\beta-\mu}{\sigma\big(1 - \frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}\big)}. \tag{30}$$

If the inequality in the above Proposition is reversed, the solution is unbounded:

Proposition 8.3. If $\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} > 1$, then $\lim_{t\to\infty} N(t) = \infty$ for every solution of (22)–(24) with $N_0 > 0$.

Proof. If $I_0 = 0$, then $N(t) = N_0 e^{(\beta-\mu)t} \to \infty$ as $t \to \infty$ and the claim is true. So we can assume that $I_0 > 0$. Define $x(t) = N(t) - \frac{\alpha}{\mu+\gamma+\alpha}\big(S(t) + I(t)\big)$. Then

$$\begin{aligned}
\dot{x} &= \dot{N} - \frac{\alpha}{\mu+\gamma+\alpha}(\dot{S} + \dot{I}) = (\beta-\mu)N - \alpha I - \frac{\alpha}{\mu+\gamma+\alpha}\big(\beta N - \mu S - (\mu+\gamma+\alpha)I\big) \\
&= (\beta-\mu)N - \frac{\alpha\beta}{\mu+\gamma+\alpha}N + \frac{\alpha\mu}{\mu+\gamma+\alpha}S \geq (\beta-\mu)N - \frac{\alpha\beta}{\mu+\gamma+\alpha}N \\
&= \mu\Big(\frac{\beta}{\mu} - 1 - \frac{\alpha\beta}{\mu(\mu+\gamma+\alpha)}\Big)N = \mu\Big(\frac{\beta}{\mu}\big(1 - \frac{\alpha}{\mu+\gamma+\alpha}\big) - 1\Big)N \\
&= \mu\Big(\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} - 1\Big)N \geq \mu\Big(\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} - 1\Big)\Big(N - \frac{\alpha}{\mu+\gamma+\alpha}(S+I)\Big) \\
&\geq \mu\Big(\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} - 1\Big)x.
\end{aligned}$$

Hence $x(t) \geq x_0 e^{\mu(\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} - 1)t}$, where $x_0 = N_0 - \frac{\alpha}{\mu+\gamma+\alpha}(S_0 + I_0) > N_0 - (S_0 + I_0) \geq 0$. Hence $x(t) \to \infty$ as $t \to \infty$. Since $N(t) \geq x(t)$, we have $N(t) \to \infty$ as $t \to \infty$. □

We now study the stability of the equilibrium (N^*, S^*, I^*) (note that the equilibrium $(N, S, I) = (0, 0, 0)$ is always unstable).

The Jacobian matrix of (22)–(24) is

$$\begin{pmatrix} \beta-\mu & 0 & -\alpha \\ \beta & -\mu-\sigma I & -\sigma S \\ 0 & \sigma I & \sigma S - \mu - \gamma - \alpha \end{pmatrix} \tag{31}$$

Proposition 8.4. The equilibrium (N^*, S^*, I^*), if it exists, is locally asymptotically stable.

Proof. We use the Routh-Hurwitz criterion. At (N^*, S^*, I^*), the Jacobian matrix is

$$A = \begin{pmatrix} \beta-\mu & 0 & -\alpha \\ \beta & -\mu-\sigma I^* & -\sigma S^* \\ 0 & \sigma I^* & 0 \end{pmatrix} = \begin{pmatrix} \beta-\mu & 0 & -\alpha \\ \beta & -\beta\frac{N^*}{S^*} & -\sigma S^* \\ 0 & \sigma I^* & 0 \end{pmatrix}$$

We have

$$\begin{aligned}
\det A &= -\sigma\alpha\beta I^* + \sigma^2 S^* I^*(\beta-\mu) \\
&= \sigma I^*\big(-\alpha\beta + \sigma S^*(\beta-\mu)\big) \\
&= \sigma I^*\big(-\alpha\beta + (\mu+\gamma+\alpha)(\beta-\mu)\big) \\
&= \sigma I^*\big(-\alpha\beta + (\mu+\gamma+\alpha)\beta - (\mu+\gamma+\alpha)\mu\big) \\
&= \sigma I^*\big((\mu+\gamma)\beta - (\mu+\gamma+\alpha)\mu\big) \\
&= \sigma I^*(\mu+\gamma+\alpha)\mu\Big(\frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha} - 1\Big) < 0,
\end{aligned}$$

and

$$\text{trace } A = \beta - \mu - \beta\frac{N^*}{S^*} < -\mu < 0.$$

We have $A_1 = \sigma^2 I^* S^*$, $A_2 = 0$, $A_3 = -(\beta-\mu)\beta\frac{N^*}{S^*}$. Hence

$$\begin{aligned}
&\det A - (\text{trace } A)(A_1 + A_2 + A_3) \\
&= \sigma I^*\big(-\alpha\beta + \sigma S^*(\beta-\mu)\big) - \Big(\beta - \mu - \beta\frac{N^*}{S^*}\Big)\Big(\sigma^2 I^* S^* - (\beta-\mu)\beta\frac{N^*}{S^*}\Big).
\end{aligned}$$

Now note that $\sigma I^* = \frac{\beta N^* - \mu S^*}{S^*}$ and $\sigma S^* = \mu + \gamma + \alpha$. Hence

$$\begin{aligned}
&\det A - (\text{trace } A)(A_1 + A_2 + A_3) \\
&= \frac{\beta N^* - \mu S^*}{S^*}\big(-\alpha\beta + (\mu+\gamma+\alpha)(\beta-\mu)\big) - \Big(\beta-\mu-\beta\frac{N^*}{S^*}\Big)\Big(\frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma+\alpha) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big) \\
&= -\alpha\beta\frac{\beta N^* - \mu S^*}{S^*} + (\beta-\mu)^2\beta\frac{N^*}{S^*} + \beta\frac{N^*}{S^*}\Big(\frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma+\alpha) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big) \\
&> -\alpha\beta\frac{\beta N^* - \mu S^*}{S^*} + \beta\frac{N^*}{S^*}\Big(\frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma+\alpha) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big) \\
&= \Big(\frac{N^*}{S^*} - 1\Big)\alpha\beta\frac{\beta N^* - \mu S^*}{S^*} + \beta\frac{N^*}{S^*}\Big(\frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big).
\end{aligned}$$

Let $F = \frac{\beta}{\mu}\frac{\mu+\gamma}{\mu+\gamma+\alpha}$. Since $N^* = \frac{\alpha}{\sigma(1-F)}$ and $S^* = \frac{\mu+\gamma+\alpha}{\sigma}$, we have

$$\frac{N^*}{S^*} = \frac{\alpha}{(\mu+\gamma+\alpha)(1-F)}$$

and so

$$\begin{aligned}
\frac{N^*}{S^*} - 1 &= \frac{\alpha - (\mu+\gamma+\alpha)(1-F)}{(\mu+\gamma+\alpha)(1-F)} = \frac{\alpha - (\mu+\gamma+\alpha) + \frac{\beta}{\mu}(\mu+\gamma)}{(\mu+\gamma+\alpha)(1-F)} \\
&= \frac{-\mu(\mu+\gamma) + \beta(\mu+\gamma)}{\mu(\mu+\gamma+\alpha)(1-F)} = \frac{(\beta-\mu)(\mu+\gamma)}{\mu(\mu+\gamma+\alpha)(1-F)} \\
&= \frac{(\beta-\mu)(\mu+\gamma)}{\mu\alpha}\frac{N^*}{S^*}.
\end{aligned}$$

Hence

$$\begin{aligned}
&\det A - (\text{trace } A)(A_1 + A_2 + A_3) \\
&> \frac{(\beta-\mu)(\mu+\gamma)}{\mu\alpha}\frac{N^*}{S^*}\alpha\beta\frac{\beta N^* - \mu S^*}{S^*} + \beta\frac{N^*}{S^*}\Big(\frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big) \\
&= \beta\frac{N^*}{S^*}\Big(\frac{(\beta-\mu)(\mu+\gamma)}{\mu}\frac{\beta N^* - \mu S^*}{S^*} + \frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma) - (\beta-\mu)\beta\frac{N^*}{S^*}\Big) \\
&= \beta\frac{N^*}{S^*}\Big((\beta-\mu)\Big(\frac{(\mu+\gamma)}{\mu}\frac{\beta N^* - \mu S^*}{S^*} - \beta\frac{N^*}{S^*}\Big) + \frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma)\Big) \\
&= \beta\frac{N^*}{S^*}\Big((\beta-\mu)\Big(\frac{\beta N^*}{S^*}(\frac{\mu+\gamma}{\mu} - 1) - (\mu+\gamma)\Big) + \frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma)\Big) \\
&> \beta\frac{N^*}{S^*}\Big(- (\beta-\mu)(\mu+\gamma) + \frac{\beta N^* - \mu S^*}{S^*}(\mu+\gamma)\Big) \\
&> \beta\frac{N^*}{S^*}\Big(- (\beta-\mu)(\mu+\gamma) + (\beta-\mu)(\mu+\gamma)\Big) \\
&= 0.
\end{aligned}$$

□

9 Invariant sets, ω-limit sets, and Lyapunov-LaSalle theorem

Another mathematical interlude.

Definition 9.1. Let D be a connected subset of $\mathbb{R}^n$, and let $f : D \to \mathbb{R}^n$ be locally Lipschitz continuous. A set $A \subseteq D$ is called an *invariant set* for the vector field f (or for the differential equation $\dot{x} = f(x)$) if for each $x_0 \in A$, the (unique) solution $x : (-\infty, \infty) \to D$ to the initial value problem $\dot{x} = f(x)$, $x(0) = x_0$ exists and is defined for all $t \in (-\infty, \infty)$ (not just for $t \in [0, \infty)$!), and furthermore, the solution stays in the set A for all $t \in (-\infty, \infty)$, i.e., $x(t) \in A$ for all $t \in (-\infty, \infty)$.

Examples of invariant sets are sets consisting of equilibria. Another example is the so-called periodic orbit.

Definition 9.2. Let $A \subseteq \mathbb{R}^n$ be non-empty and let $x \in \mathbb{R}^n$. We define the *distance between the point x and the set A* as

$$d(x, A) = \inf\{\|x - y\| \, : \, y \in A\}. \tag{32}$$

Note that if A consists of just one point y, then $d(x, A) = \|x - y\|$.

Proposition 9.3 (ω-limit set)**.** Let D be a connected subset of $\mathbb{R}^n$, and let $f : D \to \mathbb{R}^n$ be locally Lipschitz continuous. Let $x : [0, \infty) \to D$ be a solution to the differential equation $\dot{x} = f(x)$ (which is defined for all non-negative time). If x is bounded, i.e., if there exists $M > 0$ such that $\|x(t)\| \le M$ for all $t \in [0, \infty)$, then there is a unique non-empty, *compact*, *connected*, and *invariant* set $A \subseteq \overline{D}$ such that $d(x(t), A) \to 0$ as $t \to \infty$. That is, A "attracts" the solution x.

The set A is called the ω-limit set of the solution x.

Definition 9.4. Let D be a open connected subset of $\mathbb{R}^n$, and let $f : D \to \mathbb{R}^n$ be continuously differentiable. Assume that for each $x_0 \in D$, the (unique) solution to the initial value problem $\dot{x} = f(x)$, $x(0) = x_0$ exists and is defined for all $t \in [0, \infty)$. Let $V : D \to \mathbb{R}$ be a continuously differentiable function. Define the directional derivative of V at $x \in D$ in the direction of vector field f by

$$\langle \nabla V(x), f(x) \rangle.$$

Here, $\nabla V(x) = \left(\frac{\partial V}{\partial x_1}(x), \ldots, \frac{\partial V}{\partial x_1}(x)\right)^T$ and $\langle \, , \, \rangle$ is the usual inner product in $\mathbb{R}^n$.

Then V is called a *Lyapunov function* for the vector field f (or for the differential $\dot{x} = f(x)$) if

- $V(x) \to \infty$ as $\|x\| \to \infty$ (note that we require that x stays in D).
- The directional derivative of V in the direction of f exists and is non-positive for all $x \in D$, i.e.,

$$\langle \nabla V(x), f(x) \rangle \le 0, \quad \text{for all} \quad x \in D.$$

Theorem 9.5 (Lyapunov-LaSalle)**.** Let D be an open connected subset of $\mathbb{R}^n$, and let $f : D \to \mathbb{R}^n$ be continuously differentiable. Assume that for each $x_0 \in D$, the (unique) solution to the initial value problem $\dot{x} = f(x)$, $x(0) = x_0$ exists and is defined for all $t \in [0, \infty)$. Suppose that $V : D \to \mathbb{R}$ is a Lyapunov function for f. Then

- Every solution is bounded.
- The ω-limit set of every solution (which exists by Proposition 9.3) is contained in the set $\{x \in D : \langle \nabla V(x), f(x) \rangle = 0\}$.

10 Stability of the equilibria of a simple SI model with demographic

In Homework #5, we consider the model

$$\frac{dS}{dt} = B - \mu S - \sigma SI, \tag{33}$$
$$\frac{dI}{dt} = \sigma SI - (\mu + \alpha)I. \tag{34}$$

We assume that there is no recovery from the diseases, and there is a constant stream of new susceptibles, with rate B, coming into the system. All other parameters have the same meaning as the model in Section 8.1, and all parameters are assume to be strictly positive. The state-space is $\mathcal{S} = \{(S, I) \in \mathbb{R}^2 : S \geq 0, \ I \geq 0\}$.

We first find all equilibria of the model. If (S, I) is an equilibrium of the model, then we must have

$$B - \mu S - \sigma SI = 0, \tag{35}$$
$$\sigma SI - (\mu + \alpha)I = 0. \tag{36}$$

If $I = 0$, then we must have $B - \mu S = 0$, and so $S = \frac{B}{\mu}$. We can then check that $(S^o, I^o) = (\frac{B}{\mu}, 0)$ is an equilibrium. If $I \neq 0$, we must have $\sigma S - (\mu + \alpha) = 0$, and so $S = \frac{\mu+\alpha}{\sigma}$, and so we must have $I = \frac{B-\mu S}{\sigma S} = \frac{B-\mu\frac{\mu+\alpha}{\sigma}}{\sigma\frac{\mu+\alpha}{\sigma}} = \frac{B}{\mu+\alpha} - \frac{\mu}{\sigma} = \frac{\mu}{\sigma}(\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} - 1)$. To be relevant, we must have $I > 0$, and so we must have $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} > 1$. We can then check that $(S^*, I^*) = \big(\frac{\mu+\alpha}{\sigma}, \frac{\mu}{\sigma}(\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} - 1)\big)$ is an equilibrium provided that $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} > 1$.

In summary, $(S^o, I^o) = (\frac{B}{\mu}, 0)$ is always an equilibrium and

$$(S^*, I^*) = \Big(\frac{\mu+\alpha}{\sigma}, \frac{\mu}{\sigma}(\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} - 1)\Big) \tag{37}$$

is an equilibrium if and only if $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} > 1$. We call (S^o, I^o) the disease-free equilibrium and (S^*, I^*) the endemic (or interior) equilibrium.

Next, we study the stability of (S^o, I^o) and (S^*, I^*) (when it exists). The Jacobian matrix of (33)–(34) is

$$J = \begin{pmatrix} -\mu - \sigma I & -\sigma S \\ \sigma I & \sigma S - \mu - \alpha \end{pmatrix} \tag{38}$$

At (S^o, I^o), the Jacobian matrix becomes,

$$J^o = \begin{pmatrix} -\mu & -\sigma\frac{B}{\mu} \\ 0 & \sigma\frac{B}{\mu} - \mu - \alpha \end{pmatrix} \tag{39}$$

We have $\det J^o = -\mu\big(\sigma\frac{B}{\mu} - \mu - \alpha\big)$, and trace $J^o = \sigma\frac{B}{\mu} - 2\mu - \alpha$. By the Routh-Hurwitz criteria, (S^o, I^o) is locally asymptotically stable if $\det J^o > 0$ and trace $J^o < 0$, and is unstable if either $\det J^o < 0$ or trace $J^o > 0$. Hence (S^o, I^o) is locally asymptotically stable if $\sigma\frac{B}{\mu} - \mu - \alpha < 0$, which is equivalent to $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} < 1$, and (S^o, I^o) is unstable if $\sigma\frac{B}{\mu} - \mu - \alpha > 0$, which is equivalent to $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} < 1$. At (S^*, I^*), if it exists, the Jacobian matrix becomes,

$$J^o = \begin{pmatrix} -\mu - \sigma I^* & -\sigma S^* \\ \sigma I^* & \sigma S^* - \mu - \alpha \end{pmatrix} = \begin{pmatrix} -\mu - \sigma I^* & -\mu - \alpha \\ \sigma I^* & 0 \end{pmatrix} \tag{40}$$

We have $\det J^* = (\mu + \alpha)\sigma I^* > 0$, and trace $J^* = -\mu - \sigma I^* < 0$. By the Routh-Hurwitz criteria again, we can see that (S^*, I^*) is locally asymptotically stable whenever it exists.

In summary, if $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} < 1$, then (S^o, I^o) is the only equilibrium of the system, and it is locally asymptotically stable. If $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} > 1$, then (S^o, I^o) is unstable and there is another equilibrium (S^*, I^*) which is locally asymptotically stable.

By using Lyapunov-LaSalle Theorem, we will now show that, in fact, the equilibria are "globally" asymptotically stable whenever it is locally asymptotically stable, in a sense that is to be made precise below.

Assume first that $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} < 1$, and so $(S^o, I^o) = (B/\mu, 0)$ is locally asymptotically stable. Let $\mathcal{S}^o = \{(S, I) \in \mathbb{R}^2 : S > 0, I \geq 0\}$. Define a function $V : \mathcal{S}^o \to \mathbb{R}$ by

$$V(S, I) = S - S^o \log S + I. \tag{41}$$

We can see that $V(S, I) \to \infty$ as S or I goes to infinity. To show that V is a Lyapunov function, we find the directional derivative of V along the vector field defined by (33)–(34).

$$\begin{aligned}
\frac{\partial V}{\partial S}\dot{S} + \frac{\partial V}{\partial I}\dot{I} &= \big(1 - \frac{S^o}{S}\big)\big(B - \mu S - \sigma SI\big) + \sigma SI - (\mu + \alpha)I \\
&= B - \mu S - \sigma SI - S^o\big(\frac{B}{S} - \mu - \sigma I\big) + \sigma SI - (\mu + \alpha)I \\
&= (S - S^o)\big(\frac{B}{S} - \mu\big) + \big(\sigma S^o - \mu - \alpha\big)I \\
&= (S - \frac{B}{\mu})\big(\frac{B}{S} - \mu\big) + \big(\sigma\frac{B}{\mu} - \mu - \alpha\big)I \\
&= -\frac{1}{\mu S}(\mu S - B)^2 + \frac{1}{\mu + \alpha}\big(\frac{B}{\mu}\frac{\sigma}{\mu + \alpha} - 1\big)I \\
&\leq 0.
\end{aligned} \tag{42}$$

Hence, V is a Lyapunov function. From Theorem 9.5, the ω-limit set of every solution starting in $\mathcal{S}^o$ is contained in the set

$$\Big\{(S, I) \in \mathcal{S}^o : -\frac{1}{\mu S}(\mu S - B)^2 + \frac{1}{\mu + \alpha}\big(\frac{B}{\mu}\frac{\sigma}{\mu + \alpha} - 1\big)I = 0\Big\} = \big\{(B/\mu, 0)\big\}. \tag{43}$$

By Proposition 9.3, every solution that starts in $\mathcal{S}^o$ converges to $(B/\mu, 0) = (S^o, I^o)$. It is also not hard to see that a solution starts in $\mathcal{S} \setminus \mathcal{S}^o = \{(S, I) \in \mathcal{S} : I = 0\}$ also converges to $(B/\mu, 0)$. Hence we have

Proposition 10.1. If $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} < 1$, then (S^o, I^o) is the only equilibrium of the model (33)–(34). It is locally asymptotically stable, and also globally asymptotically stable in a sense that for every solution $(S(t), I(t))$, we have $\lim_{t\to\infty}(S(t), I(t)) = (S^o, I^o)$.

Now assume that $\frac{B}{\mu}\frac{\sigma}{\mu+\alpha} > 1$, and so (S^o, I^o) is unstable and (S^*, I^*) exists and is locally asymptotically stable. Let $\mathcal{S}^* = \{(S, I) \in \mathbb{R}^2 : S > 0, I > 0\}$. Define a function $V : \mathcal{S}^* \to \mathbb{R}$ by

$$V(S, I) = S - S^* \log S + I - I^* \log I. \tag{44}$$

Again, we can see that $V(S, I) \to \infty$ as S or I goes to infinity. To show that V is a Lyapunov function, we find the directional derivative of V along the vector field defined by (33)–(34).

$$\begin{aligned}
\frac{\partial V}{\partial S}\dot{S} + \frac{\partial V}{\partial I}\dot{I} &= \big(1 - \frac{S^*}{S}\big)\big(B - \mu S - \sigma SI\big) + \big(1 - \frac{I^*}{I}\big)\big(\sigma S - \mu - \alpha\big)I \\
&= (S - S^*)\big(\frac{B}{S} - \mu - \sigma I\big) + (I - I^*)\big(\sigma S - \mu - \alpha\big).
\end{aligned} \tag{45}$$

Since $B - \mu S^* - \sigma S^* I^* = 0$ and $\sigma S^* - \mu - \alpha = 0$, we have

$$\begin{aligned}
\frac{\partial V}{\partial S}\dot{S} + \frac{\partial V}{\partial I}\dot{I} &= (S - S^*)\big(\frac{B}{S} - \frac{B}{S^*} - \sigma(I - I^*)\big) + (I - I^*)\sigma(S - S^*) \\
&= (S - S^*)\big(\frac{B}{S} - \frac{B}{S^*}\big) = -\frac{B}{SS^*}(S - S^*)^2 \leq 0.
\end{aligned} \tag{46}$$

Hence, V is a Lyapunov function. From Theorem 9.5, the ω-limit set of every solution starting in $\mathcal{S}^*$ is contained in the set

$$\Big\{(S, I) \in \mathcal{S}^* : -\frac{B}{SS^*}(S - S^*)^2 = 0\Big\} = \big\{(S, I) \in \mathcal{S}^* : S = S^*\big\}. \tag{47}$$

We claim that the ω-limit set is the singleton $\{(S^*, I^*)\}$. So let $(S(t), I(t))$ be a solution that starts in $\mathcal{S}^*$ with the ω-limit set A. We know that $A \subseteq \{(S, I) \in \mathcal{S}^* : S = S^*\}$. Suppose that $A \neq \{(S^*, I^*)\}$, then there is $I' \neq I^*$ such that $(S^*, I') \in A$. Let $(\tilde{S}(t), \tilde{I}(t))$ be the solution that starts from (S^*, I'). Since A is invariant, we have $(\tilde{S}(t), \tilde{I}(t)) \in A$ for all $t \in [0, \infty)$. In particular, $\tilde{S}(t) = S_I^*$ for all $t \in [0, \infty)$, and so $0 = \frac{\mathrm{d}\tilde{S}}{\mathrm{d}t} = B - \mu S^* - \sigma S^* \tilde{I}(t)$ for all $t \in [0, \infty)$ by (33). This is only possible if $\tilde{I}(t) = I^*$ for all $t \in [0, \infty)$, but since we assume that $\tilde{I}(0) = I' \neq I^*$, this is a contradiction.

By Proposition 9.3, every solution that starts in $\mathcal{S}^*$ converges to (S^*, I^*). Note that a solution that starts in $\mathcal{S} \setminus \mathcal{S}^o = \{(S, I) \in \mathcal{S} : I = 0\}$ converges instead to $(S^o, I^o) = (B/\mu, 0)$. Hence we have

Proposition 10.2. If $\frac{B}{\mu} \frac{\sigma}{\mu+\alpha} > 1$, then (S^o, I^o) is unstable and there exists a unique locally asymptotically stable endemic equilibrium (S^*, I^*). For every solution $(S(t), I(t))$ with $I(0) = 0$, we have $\lim_{t\to\infty}(S(t), I(t)) = (S^*, I^*)$. For every solution $(S(t), I(t))$ with $S(0) > 0$ and $I(0) > 0$, we have $\lim_{t\to\infty}(S(t), I(t)) = (S^*, I^*)$.

11 Host limitation model revisited: global stability of the endemic equilibrium

We revisit the model (22)–(24) of Section 8. We now rewrite the model in term of N, $f_S := \frac{S}{N}$, and $f_I := \frac{I}{N}$. Using the quotient rule from calculus, the model becomes

$$\frac{dN}{dt} = N(\beta - \mu - \alpha f_I), \tag{48}$$

$$\frac{df_S}{dt} = \beta(1 - f_S) - \sigma N f_S f_I + \alpha f_S f_I, \tag{49}$$

$$\frac{df_I}{dt} = \sigma N f_S f_I - \alpha f_I(1 - f_I) - (\beta + \gamma) f_I. \tag{50}$$

For this section, we will assume that $\gamma = 0$, i.e., there is no recovered class. Then $N = S + I$, and so $f_S + f_I = \frac{S}{N} + \frac{I}{N} = 1$. Hence we can eliminate the equation (49) and rewrite (48)–(50) as

$$\frac{dN}{dt} = N(\beta - \mu - \alpha f_I), \tag{51}$$

$$\frac{df_I}{dt} = (\sigma N - \alpha)(1 - f_I) f_I - \beta f_I. \tag{52}$$

The state-space then becomes $\mathcal{S} = \{(N, f_I) \in \mathbb{R}^2 : N \geq 0,\ 0 \leq f_I \leq 1\}$. From Section 8, we know that the interior equilibrium $(N^*, f_I^*) \in \mathcal{S}$ exists with $N^* > 0$ and $f_I^* > 0$ if and only if $\frac{\beta}{\mu} \frac{\mu}{\mu+\alpha} < 1$, and that the interior equilibrium is locally asymptotically stable whenever it exists.

Define $\mathcal{S}^o = \{(N, f_I) \in \mathcal{S} : N > 0,\ 0 < f_I < 1\}$.

Proposition 11.1. Suppose that the equilibrium (N^*, f_I^*) exists. Then (N^*, f_I^*) is *globally* asymptotically stable in a sense that every solution that starts in $\mathcal{S}^o$ converges to (N^*, f_I^*).

Proof. We prove this by showing that the ω-limit set of every solution $(N(t), f_I(t))$ that starts in $\mathcal{S}^o$ is the singleton $\{(N^*, f_I^*)\}$, and so by Proposition 9.3, $\|(N(t), f_I(t)) - (N^*, f_I^*)\| = d\big((N(t), f_I(t)), \{(N^*, f_I^*)\}\big) \to 0$ as $t \to \infty$.

We have

$$0 = \beta - \mu - \alpha f_I^*, \tag{53}$$

$$0 = (\sigma N^* - \alpha) f_I^*(1 - f_I^*) - \beta f_I^*. \tag{54}$$

Define a function V on $\mathcal{S}^o$ as

$$V(N, f_I) = \sigma\big(N - N^* \log N\big) - \alpha\big(f_I^* \log f_I + (1 - f_I^*) \log(1 - f_I)\big). \tag{55}$$

It is easy to see that $V(N, f_I) \to \infty$ when $(N, f_I) \in \mathcal{S}^o$ and $\|(N, f_I)\| \to \infty$. To show that V is a Lyapunov function, we find the directional derivative of V along the vector field defined by (51)–(52).

$$\begin{aligned}
\frac{\partial V}{\partial N}\dot{N} + \frac{\partial V}{\partial f_I}\dot{f}_I &= \frac{\partial V}{\partial N}\big(N(\beta-\mu-\alpha f_I)\big) + \frac{\partial V}{\partial f_I}\big((\sigma N-\alpha)(1-f_I)f_I - \beta f_I\big) \\
&= \sigma\Big(1-\frac{N^*}{N}\Big)\big(N(\beta-\mu-\alpha f_I)\big) - \alpha\Big(\frac{f_I^*}{f_I} - \frac{1-f_I^*}{1-f_I}\Big)\big((\sigma N-\alpha)(1-f_I)f_I - \beta f_I\big) \\
&= \sigma(N-N^*)(\beta-\mu-\alpha f_I) - \alpha\frac{f_I^*-f_I}{f_I(1-f_I)}\big((\sigma N-\alpha)(1-f_I)f_I - \beta f_I\big) \\
&= \sigma(N-N^*)(\beta-\mu-\alpha f_I) + \alpha(f_I-f_I^*)\big(\sigma N-\alpha-\frac{\beta}{1-f_I}\big).
\end{aligned} \tag{56}$$

Using (53)–(54), we have

$$\begin{aligned}
\frac{\partial V}{\partial N}\dot{N} + \frac{\partial V}{\partial f_I}\dot{f}_I &= \sigma(N-N^*)(-\alpha f_I+\alpha f_I^*) + \alpha(f_I-f_I^*)\big(\sigma N - \frac{\beta}{1-f_I} - \sigma N^* + \frac{\beta}{1-f_I^*}\big) \\
&= -\alpha\sigma(N-N^*)(f_I-f_I^*) + \alpha\sigma(f_I-f_I^*)(N-N^*) - \alpha\beta\Big(\frac{1}{1-f_I} - \frac{1}{1-f_I^*}\Big) \\
&= -\alpha\beta(f_I-f_I^*)\frac{f_I-f_I^*}{(1-f_I)(1-f_I^*)} \le 0.
\end{aligned} \tag{57}$$

This shows that V is a Lyapunov function for our system. Hence from Theorem 9.5, the ω-limit set of every solution that starts in $\mathcal{S}^o$ is contained in the set $\{(N, f_I) \in \mathcal{S}^o : f_I = f_I^*\}$.

We claim that the ω-limit set of every solution is the singleton $\{(N^*, f_I^*)\}$. So let $(N(t), f_I(t))$ be a solution that starts in $\mathcal{S}^o$ with the ω-limit set A. We know that $A \subseteq \{(N, f_I) \in \mathcal{S}^o : f_I = f_I^*\}$. Suppose that $A \neq \{(N^*, f_I^*)\}$, then there is $N' \neq N^*$ such that $(N', f_I^*) \in A$. Let $(\tilde{N}(t), \tilde{f}_I(t))$ be the solution that starts from (N', f_I^*). Since A is invariant, we have $(\tilde{N}(t), \tilde{f}_I(t)) \in A$ for all $t \in [0, \infty)$. In particular, $\tilde{f}_I(t) = f_I^*$ for all $t \in [0, \infty)$, and so $0 = \frac{\mathrm{d}\tilde{f}_I}{\mathrm{d}t} = (\sigma\tilde{N}(t) - \alpha)(1-f_I^*)f_I^* - \beta f_I^*$ for all $t \in [0, \infty)$ by (52). This is only possible if $\tilde{N}(t) = N^*$ for all $t \in [0, \infty)$, but since we assume that $\tilde{N}(0) = N' \neq N^*$, this is a contradiction. $\square$

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