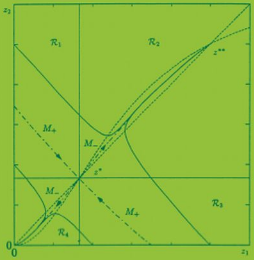
Lecture Notes in Biomathematics

97

Vincenzo Capasso

Mathematical Structures of Epidemic Systems



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Mathematical Structures of Epidemic Systems

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A chi mi ha dedicato
tutti i suoi pensieri.

Foreword

The dynamics of infectious diseases represents one of the oldest and richest areas of mathematical biology. From the classical work of Hamer (1906) and Ross (1911) to the spate of more modern developments associated with Anderson and May, Dietz, Hethcote, Castillo-Chavez and others, the subject has grown dramatically both in volume and in importance. Given the pace of development, the subject has become more and more diffuse, and the need to provide a framework for organizing the diversity of mathematical approaches has become clear. Enzo Capasso, who has been a major contributor to the mathematical theory, has done that in the present volume, providing a system for organizing and analyzing a wide range of models, depending on the structure of the interaction matrix. The first class, the quasi-monotone or positive feedback systems, can be analyzed effectively through the use of comparison theorems, that is the theory of order-preserving dynamical systems; the second, the skew-symmetrizable systems, rely on Lyapunov methods. Capasso develops the general mathematical theory, and considers a broad range of examples that can be treated within one or the other framework. In so doing, he has provided the first steps towards the unification of the subject, and made an invaluable contribution to the Lecture Notes in Biomathematics.

Simon A. Levin

Princeton, January 1993

Author's Preface to Second Printing

In the Preface to the First Printing of this volume I wrote:

> " ..[I] hope to find some reader who may appreciate the volume
> as a guided tour through the vast literature on the subject."

I am glad, after such a long time (about twenty years) to have discovered that my book received much more attention than expected.

I wish to thank Catriona Byrne, the Mathematical Editor of Springer-Heidelberg, who kindly insisted that the book be reprinted, thus making it available again after many requests that could be not satisfied, since the original printing was sold out.

I have taken the opportunity, in this second printing, to correct all detected misprints. I have also included reference data to papers in the bibliography that have meanwhile been published.

Vincenzo Capasso

Milan, May 2008

"Non con soverchie speranze ...,
né avendo nell'animo illusioni
spesso dannose, ma nemmeno con
indifferenza, deve essere accolto
ogni tentativo di sottoporre al calcolo
fatti di qualsiasi specie."
(Vito Volterra, 1901)

Author's Preface

It is now exactly twenty years since the first time I read the first edition of the now classic book by N.T.J. Bailey, The Mathematical Theory of Epidemics (Griffin, London, 1957). With my background in Theoretical Physics, I had been attracted by the possibility of analyzing with mathematical rigor an area of Science which deals with highly complex natural systems. Anyway, in the preface of his book, Bailey stated that the discipline was already old about fifty years, in the modern sense of the phrase, by dating the beginnings at the work by William Hamer (1906) and Ronald Ross (1911).

This monograph was started after a suggestion by Simon A. Levin, during an Oberwolfach workshop in 1984, to organize better my own ideas about the mathematical structures of epidemic systems, that I had been presenting in various papers and conferences. He had been very able to identify the "leit motiv" of my thoughts, that a professional mathematician can contribute in the growth of knowledge only if he is capable of building up a fair and correct interface between the core subject of a specific discipline and the most recent "tools" of Mathematics.

The scope of this monograph is then to make them available to a large audience, in a possibly accessible way, powerful techniques of modern Mathematics, without obscuring with "magic symbols" the intrinsic vitality of mathematical concepts and methods.

"I non iniziati ai segreti del Calcolo e dell'Algebra si fanno talora
l'illusione che i loro mezzi siano di natura diversa da quelli di cui
il comune ragionamento dispone." (Volterra,1901).

Clearly I did not go much further than my wishful thinking, but still hope to find some reader who may appreciate the volume as a guided tour through the vast literature on the subject. I wish to specify that the list of references includes only the ones explicitly quoted in the text. I apologize for my ignorance of papers directly related with this monograph.

The contribution of Dr. R. Caselli is warmly acknowledged for all the numerical simulations and their graphical representation included in the monograph.

It is now time to thank Si for his encouragement and patience. Also for her very gentle patience I wish to thank Dr. C. Byrne (Mathematical Editor of Springer-Verlag) who has been waiting and supporting this project for such a long time.

I shall not forget to thank the Director and the staff of the Mathematical Centre at Oberwolfach for providing me, during a wonderful month in the summer of 1990, the right scientific environment for producing the core of this monograph.

Thanks are due to the numerous Colleagues who carefully read parts of the manuscript, and gave me relevant advice ; in particular I thank Edoardo Beretta, Carlos Castillo-Chavez, Andrea di Liddo, Herb Hethcote, Mimmo Iannelli, John Jacquez, Simon Levin, Stefano Paveri-Fontana, Andrea Pugliese, Carl Simon.

I also wish to thank S. Levin and coauthors for the use of Figures 3.1, 3.3 and Tables 3.1-3.5; J. Jacquez and coauthors for Figures 3.5, 3.6; H. Hethcote and coauthors for Table 3.6.

Finally I would like to thank my research advisor at the University of Maryland (College Park) Grace Yang, for the key role played in introducing me to this very challenging area of scientific research, and Jim Murray for making me familiar with reaction-diffusion systems.

Financial assistance is acknowledged by the National Research Council of Italy (CNR) through the National Group for Mathematical Physics (GNFM) and the Institute for Research in Applied Mathematics (IRMA).

Vincenzo Capasso

Milan, October 1992

Table of Contents

"... l' universo ... é scritto in lingua matematica,
e i caratteri sono triangoli, cerchi, ed altre figure
geometriche ...; senza questi
é un aggirarsi vanamente per un oscuro laberinto"
(Galileo Galilei, Saggiatore (VI, 232), 1623).

"All epidemiology, conceived as it is with the
variation of disease from time to time and
from place to place, must be considered
mathematically, however many variables are
implicated, if it is to be considered
scientifically at all"
(Sir Ronald Ross, 1911)

1. Introduction

The main scope of mathematical modelling in epidemiology is clearly stated in the second edition (1975) of Bailey's book [19]: "we need to develop models that will assist the decision-making process by helping to evaluate the consequences of choosing one of the alternative strategies available. Thus , mathematical models of the dynamics of a communicable disease can have a direct bearing on the choice of an immunization program, the optimal allocation of scarce resources, or the best combination of control or eradication techniques."

We may like to say with Okubo [177] that "A mathematical treatment is indispensable if the dynamics of ecosystems are to be analyzed and predicted quantitatively. The method is essentially the same as that used in such fields as classical and quantum mechanics, molecular biology, and biophysics... One must not be enamored of mathematical models; there is no mystique associated with them...physics and mathematics must be considered as tools rather than sources of knowledge, tools that are effective but nonetheless dangerous if misused".

Even though I consider mathematical reasoning much more than just a tool in scientific investigation, in this monograph I have pursued the main objective of providing a companion in the scientific process of building and analyzing mathematical models for communicable diseases.

As reported in the long, but still a sample, list of references, an enormous literature is available nowadays, dealing with modelling the dynamics of infectious diseases (during the final phase of preparation of this monograph a monumental volume has appeared due to Anderson and May [9] which is further encouraging in this direction). What I personally feel is that there is a concrete possibility of classifying most of the available models according to their mathematical structure.

In this respect two main classes may be identified. One of them, composed of the quasimonotone or positive feedback systems, has attracted various mathematicians in the last twenty years to build a mathematical theory of order preserving dynamical systems. In the other case, Lyapunov methods play a central role.

The Italian main precursor in the field of biomathematics, Vito Volterra, in his pioneering work on predator-prey systems, introduced a Lyapunov functional (the Volterra-Lyapunov potential) which has been the basis for a large amount of work on the generalized Lotka-Volterra systems. As shown in this monograph, these include a large class of epidemic systems, based on the "law of mass action". (The Volterra-Lyapunov potential has been recently given an information theoretic interpretation by Capasso and Forte in [52]).

A lot of attention has been attracted in the recent years to the mathematical modelling of HIV/AIDS infection, in order to predict the evolution of this modern "plague". Actually this poses highly challenging problems, which are essentially of modelling more than of analysis. Due to the long duration of the disease in each individual, and to the fast transportation means between different geographical areas of the world, and the increased communication among different social groups, coupling at different time and "space" scales cannot be ignored. Problems of coupling at very different scales pose big challenges to mathematical analysis and computation. A chapter has been devoted to HIV/AIDS infections as a specific case study; but, in the spirit of this monograph, only simplified "educational models" have been analyzed.

Only purely deterministic models are the subject of this monograph, even though I think that in order to fit real data, stochastic fluctuations cannot be ignored, especially in connection with biological systems. Furthermore the analysis of most stochastic models is based on the common tools of the mathematical theory of evolution equations (ODE's and PDE's), so that this may provide the necessary background for stochastic modelling as well.

Who knows ? This might be the first of two volumes...

For the biological interpretation of the models which are analyzed here we refer to the literature, while for an historical development of the subject we refer to Dietz and Schenzle [83].

We shall mainly be concerned with the so called "compartmental models".

Compartmental models are most suitable for microparasitic infections (typified by most viral and bacterial, and many protozoan, infections) [163]; the duration of infection is usually short, relative to the expected life span of the host.

In a compartmental model the total population (relevant to the epidemic process) is divided into a number (usually small) of discrete categories: susceptibles, infected but not yet infective (latent), infective, recovered and immune, without distinguishing different degrees of intensity of infection.

In contrast, for macroparasitic infections, such as helminthic infections, it is relevant to know the parasite burden borne by an individual host: there can be an important distinction between infection (having one or more parasites) and disease (having a parasite load large enough to produce illness). Consequently, mathematical models for host-macroparasitic associations need to deal with the full distribution of parasites among the host population [82].

We shall not analyze this case, for which we refer to the literature (see e.g. [82, 92, 173]).

A key problem in modelling the evolution dynamics of infectious diseases is the mathematical representation of the mechanism of transmission of the contagion. The concepts of "force of infection" and "field of forces of infection" (when dealing with structured populations) which were introduced in [48], will be the guideline of this presentation.

Suppose at first that the population in each compartment does not exhibit any structure (space location, age, etc.). The infection process (S to I) is driven by a force of infection ($f.i.$) due to the pathogen material produced by the infective population and available at time t

$$(f.i.)(t) = [g(I(\cdot))]\,(t) \tag{1.1}$$

which acts upon each individual in the susceptible class. Thus a typical rate of the infection process is given by the

$$(incidence\ \ rate)(t) = (f.i.)(t)\ S(t). \tag{1.2}$$

From this point of view, the "law of mass action" simply corresponds to choosing a linear dependence of $g(I)$ upon I [132]

$$(f.i.)(t) = k\,I(t). \tag{1.3}$$

Section 2 is devoted to epidemic models based on the "law of mass action". From a mathematical point of view the evolution of the epidemic is described (in the space and time homogeneous cases) by ODE 's which contain at most bilinear terms. The major "tool" in analyzing these systems is the "Volterra-Lyapunov potential".

In Section 3 the law of mass action model has been extended to include a nonlinear dependence

$$(f.i.)(t) = g(I(t))\ ; \tag{1.4}$$

particular cases are

$$g(I) = k\ I^p \quad , \qquad p > 0 \tag{1.5}$$

$$g(I) = \frac{k\ I^p}{\alpha + \beta\ I^q}\quad , \qquad p, q\ > 0\ . \tag{1.6}$$

The general model (1.1) for the force of infection may be extended to include a nonlinear dependence upon both I and S , as discussed in the recent modelling of AIDS epidemics.

When dealing with populations which exhibit some structure (identified here by a parameter z) either discrete (e.g. social groups) or continuous (e.g. space location, age, etc.), the target of the infection process is the specific "subgroup" z in the susceptible class, so that the force of infection has to be evaluated with reference to that specific subgroup. This induces the introduction of a classical concept in physics: the "field of forces of infection" $(f.i.)(z;t)$ such that the incidence rate at time t at the specific "location" z will be given by

$$(incidence\ \ rate)(z;t) = (f.i.)(z;t)\ s(z;t). \tag{1.7}$$

We may like to remark here that this concept is not very far from the mediaeval idea that infectious diseases were induced into a human being by a flow of bad air ("mal aria" in Italian).

Anyhow in quantum field theory any field of forces is due to an exchange of particles: in this case bacteria, viruses, etc., so that the corpuscular and the continuous concepts of field are conceptually unified.

It is of interest to identify the possible structures of the field of forces of infection which depend upon the specific mechanisms of transmission of the disease among different groups. This problem has been raised since the very first models when age and/or space dependence had to be taken into account.

Section 5 is devoted to systems with space structure.

When dealing with populations with space structure the relevant quantities are spatial densities, such as $s(z;t)$ and $i(z;t)$, the spatial densities of susceptibles and of infectives respectively, at a point z of the habitat Ω, and at time $t \geq 0$.

The corresponding total populations are given by

$$S(t) = \int_\Omega s(z;t)\ dz \tag{1.8}$$

$$I(t) = \int_\Omega i(z;t)\ dz \tag{1.9}$$

In the law of mass action model, if only local interactions are allowed, the field at point $z \in \Omega$ is given by

$$(f.i.)(z;t) = k(z)\ i(z;t). \tag{1.10}$$

On the other hand if we wish to take also distant interactions into account as proposed by D.G. Kendall [130], the field at point $z \in \Omega$ is given by (see Section 5.5)

$$(f.i.)(z;t) = \int_{\Omega} k(z,z')\ i(z';t)\ dz'\ . \tag{1.11}$$

When dealing with populations with an age structure (see Section 6) we interpret the parameter z as the age-parameter so that model (1.10) is a model with intracohort interactions while model (1.11) is a model with intercohort interactions.

Section 4 and consequently large parts of Section 5 are devoted to mathematical models of communicable diseases, which exhibit a cooperative (positive feedback) structure. The common feature for this class of models is the monotonicity (order preservation) of the dynamical systems associated with the epidemic models.

The non monotone case has been also considered by means of Lyapunov functionals and the LaSalle Invariance Principle (see Section 5.6).

The emergence of travelling waves in epidemic systems with spatial structure will not be discussed here. An elegant introduction to the subject has been provided by J.D. Murray [171].

Chapter 7 contains a brief presentation on the use of mathematical models in the definition of optimal control strategies and in the key problem of identification of parameters.

Appendices A and B (more technical in nature) have been added for the ease of non professional mathematicians who may then find this monograph self consistent as an introduction to the mathematical modelling of infectious diseases.

2. Linear models

2.1. One population models

We shall start considering the evolution of an epidemic in a closed host population of total size N. One of the most elementary compartmental models is the so called SIR model which was first due to Kermack-McKendrick [132] but is reproposed here in a rather simplified structure (see also [19] and [9]).

The total population is divided into three classes:

(S) the class of susceptibles, i.e. those individuals capable of contracting the disease and becoming themselves infectives;
(I) the class of infectives, i.e. those individuals capable of transmitting the disease to susceptibles;
(R) the class of removed individuals, i.e. those individuals which, having contracted the disease, have died or, if recovered, are permanently immune, or have been isolated, thus being unable to further transmit the disease.

A model based on these three compartments is generally called a SIR model. In order to write down a mathematical formulation for the dynamics of the epidemic process we introduce differential equations for the rates of transfer from one compartment to another:

$$\begin{aligned}\frac{dS}{dt} &= f_1(I,S,R)\\ \frac{dI}{dt} &= f_2(I,S,R)\\ \frac{dR}{dt} &= f_3(I,S,R)\end{aligned} \tag{2.1}$$

Typically a "law of mass action" [105, 222] has been assumed for the infection process: the transfer process from S to I. On the other hand the transfer from I to R is considered to be a pure exponential decay.

Thus the simplest choice for f_i , $i = 1,2,3$ has been the following:

$$\begin{aligned}f_1(I,S,R) &= -kIS\\ f_2(I,S,R) &= +kIS - \lambda I\\ f_3(I,S,R) &= +\lambda I\end{aligned} \tag{2.2}$$

with k and λ positive constants.

It is easily understood that in (2.2) it is assumed that when a susceptible is infected he immediately becomes infectious, i.e. there is no latent period.

If latency is allowed, an additional class (E) of latent individuals may be included (see Section 3).

2.1.1. SIR model with vital dynamics

In the above formulation the total population

$$N = S + I + R \tag{2.3}$$

is a constant, as can be seen by simply adding the three equations in (2.2).

The invariance of the total population can be maintained if we introduce an intrinsic vital dynamics of the individuals in the total population by means of a net mortality μN compensated by an equal birth input in the susceptible class.

In this case (2.2) are substituted by:

$$\begin{aligned} f_1(I,S,R) &= -kIS - \mu S + \mu N \\ f_2(I,S,R) &= +kIS - \lambda I - \mu I \\ f_3(I,S,R) &= \lambda I - \mu R \end{aligned} \tag{2.4}$$

In fact, it is easy to check that

$$N(t) = S(t) + I(t) + R(t) \tag{2.5}$$

is again constant in time.

We shall assume model (2.4) as a convenient point of departure for subsequent analysis, since it already contains the basic features of a general epidemic system, including the possibility of a nontrivial steady state as we shall see later.

System (2.1) together with (2.4) becomes,

$$\begin{cases} \dfrac{dS}{dt} = -kIS - \mu S + \mu N \\ \dfrac{dI}{dt} = kIS - \mu I - \lambda I \\ \dfrac{dR}{dt} = \lambda I - \mu R \end{cases} \tag{2.6}$$

for $t > 0$, which has to be subject to suitable initial conditions.

In this same class other models can be introduced. We shall list the most well known. From now on, when constant in time, the total population N will be assumed equal to 1, so that we refer to fractions of the total population. For a discussion about the related values of the parameters, refer to [118].

The SIR model with vital dynamics will then be rewritten as follows:

$$(2.6') \qquad \begin{cases} \dfrac{dS}{dt} = -kIS - \delta S + \delta \\ \dfrac{dI}{dt} = kIS - \gamma I - \delta I \\ \dfrac{dR}{dt} = \gamma I - \delta R \end{cases}$$

We may notice that the first two equations may be solved independently of the third one. Thus we shall be limiting ourselves to a two-dimensional system.

The same will be done in other cases without further advice.

2.1.2. SIRS model with temporary immunity [110]

This model derives from the SIR model with vital dynamics, but recovery gives only a temporary immunity

$$(2.7) \qquad \begin{cases} \dfrac{dS}{dt} = -kIS + \delta - \delta S + \alpha R \\ \dfrac{dI}{dt} = kIS - (\gamma + \delta) I \\ \dfrac{dR}{dt} = \gamma I - \alpha R \end{cases}$$

2.1.3. SIR model with carriers [110]

A carrier is an individual who carries and spreads the infectious disease, but has no clinical symptoms. If we assume that the number C of the carriers in the population is constant, we modify accordingly the SIR model with vital dynamics,

$$(2.8) \qquad \begin{cases} \dfrac{dS}{dt} = -k(I + C)S + \delta - \delta S \\ \dfrac{dI}{dt} = k(I + C)S - (\gamma + \delta) I \\ \dfrac{dR}{dt} = \gamma I - \delta R \end{cases}$$

2.1.4. The general structure of bilinear systems

According to a recent formulation due to Beretta and Capasso [28] all of the above models can be written in the general form:

$$\frac{dz}{dt} = diag(z)(e + Az) + c \tag{2.9}$$

where

$z \in \mathbb{R}^n,$	n being the number of different compartments
$e \in \mathbb{R}^n,$	is a constant vector
$A = (a_{ij})_{i,j=1,\ldots,n}$	is a real constant matrix
$c \in \mathbb{R}^n,$	is a constant vector.

In the above examples we have in fact:

- SIR model with vital dynamics (model (2.6))

$$A = \begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix}; \quad e = \begin{pmatrix} -\delta \\ -(\delta + \gamma) \end{pmatrix}; \quad c = \begin{pmatrix} \delta \\ 0 \end{pmatrix} \tag{2.10}$$

- SIRS model with temporary immunity (model (2.7))

For our convenience, we change the variables (S, I) into $(\tilde{S}, I)$ such that $\tilde{S} = S + \dfrac{\alpha}{k}$.

Again, by taking into account that $S + R + I = 1$ (constant in time), we may ignore the equation for R.

Thus system (2.1) becomes:

$$\text{(2.11)} \qquad \begin{cases} \dfrac{d\tilde{S}}{dt} = -(\delta+\alpha)\tilde{S} - k\tilde{S}I + (\delta+\alpha)\left(1+\dfrac{\alpha}{k}\right) \\ \dfrac{dI}{dt} = -(\gamma+\delta+\alpha)I + k\tilde{S}I \end{cases}$$

so that

$$A = \begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix}; \quad e = \begin{pmatrix} -(\delta+\alpha) \\ -(\gamma+\delta+\alpha) \end{pmatrix}; \quad c = \begin{pmatrix} (\delta+\alpha)\left(1+\dfrac{\alpha}{k}\right) \\ 0 \end{pmatrix}$$

- SIR model with carriers (model 2.8)).

We change the variables (S, I) into $(S, \tilde{I})$, with $\tilde{I} = I + C$, so that system (2.8) becomes, ignoring the equation for R,

$$\text{(2.12)} \qquad \begin{cases} \dfrac{dS}{dt} = -\delta S - k\tilde{I}S + \delta \\ \dfrac{d\tilde{I}}{dt} = -(\gamma+\delta)\tilde{I} + k\tilde{I}S + (\gamma+\delta)C \end{cases}$$

Hence

$$A = \begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix}; \quad e = \begin{pmatrix} -\delta \\ -(\gamma+\delta) \end{pmatrix}; \quad c = \begin{pmatrix} \delta \\ (\gamma+\delta)C \end{pmatrix}$$

A further extension of the form (2.9) is needed to include the following model.

- SIR model with vertical transmission

A model has been proposed in [40] which extends the SIR model with vital dynamics to include vertical transmission and possible vaccination. It is assumed that b and b' are the rates of birth of uninfected and infected individuals respectively; r and r' are the corresponding death rates; v is the rate of recovery from infection; γ is the rate at which immune individuals loose immunity; q is the rate of vertical transmission ($p+q=1$); and m is the fraction of those born to uninfected parents which are immune because of vaccination, the rest going into a susceptible class. It has been assumed that the vaccine is not effective for the children of infected parents.

The ODE system which describes mathematically such a model is then the following,

$$\begin{cases} \dfrac{dS}{dt} = -kSI + (1-m)b(S+R) + pb'I - rS + \gamma R \\ \dfrac{dI}{dt} = kSI + qb'I - r'I - vI \\ \dfrac{dR}{dt} = vI - (r+\gamma)\,R + mb(S+R) \end{cases} \tag{2.13}$$

In order to keep a constant total population $S+I+R=1$, it is assumed that $b=r$, $b'=r'$. In this last case the above model reduces to

$$\begin{cases} \dfrac{dS}{dt} = -kSI + (1-m)b(1-I) + pb'I - rS + \gamma R \\ \dfrac{dI}{dt} = kSI - (pb'+v)I \end{cases} \tag{2.14}$$

If we set

$$A = \begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix}; \qquad e = \begin{pmatrix} -b-\gamma \\ -pb'-v \end{pmatrix}$$

$$c = \begin{pmatrix} (1-m)b+\gamma \\ 0 \end{pmatrix}; \qquad B = \begin{pmatrix} 0 & (m-1)b+pb'+\gamma \\ 0 & 0 \end{pmatrix}$$

system (2.14) can be written in the form

$$\frac{dz}{dt} = diag(z)(e+Az) + c + Bz \tag{2.15}$$

which extends equation (2.9) to include the term Bz.

This kind of approach of a unifying mathematical structure of epidemic systems can be further carried out by analyzing epidemic models in two or more interacting populations.

2.2. Epidemic models with two or more interacting populations

Typical examples of epidemics which are spread by means of the interaction between different population groups are those related to venereal diseases.

Let us refer as an example to gonorrhea (due to the bacterium "Neisseria gonorrhoeae", the gonococcus).

This disease is transmitted by sexual contacts of males and females. Thus we need to consider the two interacting populations of males (1) and females (2) each of which will be divided in the two groups of susceptibles ($S_i, i = 1, 2$) and infectives ($I_i, i = 1, 2$).

We have to take into account the fact that in this case acquired immunity to reinfection is virtually non existent and hence recovered individuals pass directly back to the corresponding susceptible pool.

Death and isolation can be ignored [118].

Models of this kind are called SIS models.

2.2.1. Gonorrhea model [71, 118]

We consider here the simple gonorrhea model proposed by Cooke and Yorke [71]. It can be seen as an SIS model for two interacting populations; if we denote by $S_i, I_i, i = 1, 2$ the susceptible and the infective populations for the two groups (males and females), we have:

$$\tag{2.16} \begin{cases} \dfrac{dS_1}{dt} = -k_{12} S_1 I_2 + \alpha_1 I_1 \\ \dfrac{dI_1}{dt} = k_{12} S_1 I_2 - \alpha_1 I_1 \\ \dfrac{dS_2}{dt} = -k_{21} S_2 I_1 + \alpha_2 I_2 \\ \dfrac{dI_2}{dt} = k_{21} S_2 I_1 - \alpha_2 I_2 \end{cases}$$

Since clearly $S_i + I_i = c_i$ (const), $i = 1, 2$, we may limit the analysis to the following system (we assume, $k_{12} = k_{21} = 1, \quad$ for simplicity)

$$\tag{2.17} \begin{cases} \dfrac{dI_1}{dt} = -I_1 I_2 - \alpha_1 I_1 + c_1 I_2 \\ \dfrac{dI_2}{dt} = -I_1 I_2 - \alpha_2 I_2 + c_2 I_1 \end{cases}$$

which now can be written in the form

$$\tag{2.18} \frac{dz}{dt} = diag(z)(e + Az) + Bz, \qquad t > 0$$

if we set $z = (I_1, I_2)^T$, and

$$A = \begin{pmatrix} 0 & -1 \\ -1 & 0 \end{pmatrix}, \quad e = \begin{pmatrix} -\alpha_1 \\ -\alpha_2 \end{pmatrix}, \quad B = \begin{pmatrix} 0 & c_1 \\ c_2 & 0 \end{pmatrix}$$

2.2.2. SIS model in two communities with migration [110]

In a SIS system with vital dynamics the population is divided into two communities; individuals migrate between the two groups. We describe each community by (S_i, I_i), $i = 1, 2$ such that

$$S_i + I_i = 1 \ , \qquad i = 1, 2 \ . \tag{2.19}$$

Hence we may limit the analysis to the following ODE system:

$$\begin{cases} \dfrac{dI_1}{dt} = k_1 I_1 (1 - I_1) - \gamma_1 I_1 - \delta_1 I_1 + \theta_1 (I_2 - I_1) \\ \dfrac{dI_2}{dt} = k_2 I_2 (1 - I_2) - \gamma_2 I_2 - \delta_2 I_2 + \theta_2 (I_1 - I_2) \end{cases} \tag{2.20}$$

Note that the migration terms $\theta_i (I_j - I_i)$, $i, j = 1, 2$, $i \neq j$, are intended to have an homogeneization effect between the two groups.

Models of this kind are used in ecological systems to describe populations that are divided in patches among which discrete diffusion occurs [148, 177, 206].

System (2.20) can be written as

$$\begin{cases} \dfrac{dI_1}{dt} = (k_1 - \gamma_1 - \delta_1 - \theta_1) I_1 - k_1 {I_1}^2 + \theta_1 I_2 \\ \dfrac{dI_2}{dt} = (k_2 - \gamma_2 - \delta_2 - \theta_2) I_2 - k_2 {I_2}^2 + \theta_2 I_1 \end{cases} \tag{2.21}$$

which can be put in the form (2.18) if we set

$$z = (I_1, I_2)^T \quad ,$$

and

$$A = \begin{pmatrix} -k_1 & 0 \\ 0 & -k_2 \end{pmatrix}, \quad e = \begin{pmatrix} k_1 - \gamma_1 - \delta_1 - \theta_1 \\ k_2 - \gamma_2 - \delta_2 - \theta_2 \end{pmatrix}, \quad B = \begin{pmatrix} 0 & \theta_1 \\ \theta_2 & 0 \end{pmatrix}$$

2.2.3. SIS model for two dissimilar groups [110, 142, 218]

In this case the population is divided into two dissimilar groups because of age, social structure, space structure, etc.. The two groups may interact with each other via the infection process; e.g. the force of infection acting on the susceptibles S_1 of the first group will given by

$$g_1(I_1, I_2) = k_{11}I_1 + k_{12}I_2$$

and the analogous for the other group.

Thus the epidemic system is described by the following set of ODE's:

$$\begin{cases} \dfrac{dI_1}{dt} = (k_{11}I_1 + k_{12}I_2)(1 - I_1) - \gamma_1 I_1 - \delta_1 I_1 \\ \dfrac{dI_2}{dt} = (k_{21}I_1 + k_{22}I_2)(1 - I_2) - \gamma_2 I_2 - \delta_2 I_2 \end{cases} \tag{2.22}$$

which can be also written as

$$\begin{cases} \dfrac{dI_1}{dt} = (k_{11} - \gamma_1 - \delta_1) I_1 - k_{11}{I_1}^2 - k_{12}I_1I_2 + k_{12}I_2 \\ \dfrac{dI_2}{dt} = (k_{22} - \gamma_2 - \delta_2) I_2 - k_{22}{I_2}^2 - k_{21}I_2I_1 + k_{21}I_1 \end{cases} \tag{2.23}$$

complemented by

$$I_1 + S_1 = 1, \quad I_2 + S_2 = 1$$

System (2.23) can be put again in the form (2.18) if we define

$$A = \begin{pmatrix} -k_{11} & -k_{12} \\ -k_{21} & -k_{22} \end{pmatrix}; \quad e = \begin{pmatrix} k_{11} - \gamma_1 - \delta_1 \\ k_{22} - \gamma_2 - \delta_2 \end{pmatrix}; \quad B = \begin{pmatrix} 0 & k_{12} \\ k_{21} & 0 \end{pmatrix}.$$

This case is a particular case (two groups) of the more general case (n groups, $n \geq 2$) analyzed by Lajmanovich and Yorke in [142]. We shall deal with this multigroup case in Section 2.3.4 , or better in Section 4.6.1 .

2.2.4. Host - vector - host model [110]

In an SIS epidemic system with vital dynamics let us suppose that a unique vector is responsible for the spread of the disease among two different hosts.

In such a case we have three classes of infectives (two hosts and one vector). The force of infection acting on the vector susceptible population (S_2) is due to the infectives I_1 and I_3 of the host.

$$g_2(I_1, I_3) = k_{21}I_1 + k_{23}I_3$$

while the force of infection acting on the two hosts S_1 and S_3 due to the vector is given, respectively, by

$$g_1(I_2) = k_{12}I_2$$

$$g_3(I_2) = k_{32}I_2$$

As a consequence , by assuming, as usual in a SIS model, that

$$S_i + I_i = \text{const} \quad (= 1), \qquad i = 1, 2, 3 \tag{2.24}$$

we have

$$\begin{cases} \dfrac{dI_1}{dt} = k_{12}I_2(1 - I_1) - \gamma_1 I_1 - \delta_1 I_1 \\ \dfrac{dI_2}{dt} = (k_{21}I_1 + k_{23}I_3)(1 - I_2) - \gamma_2 I_2 - \delta_2 I_2 \\ \dfrac{dI_3}{dt} = k_{32}I_2(1 - I_3) - \gamma_3 I_3 - \delta_3 I_3 \end{cases} \tag{2.25}$$

complemented by (2.24).

It is more convenient to rewrite system (2.24), (2.25) by emphasizing the susceptible populations $S_i = 1 - I_i$, which gives

$$\begin{cases} \dfrac{dS_1}{dt} = (-k_{12} - (\gamma_1 + \delta_1)) S_1 + k_{12}S_1S_2 + (\gamma_1 + \delta_1) \\ \dfrac{dS_2}{dt} = (-k_{21} - k_{23} - (\gamma_2 + \delta_2)) S_2 + k_{21}S_2S_1 + k_{23}S_2S_3 \\ \qquad + (\gamma_2 + \delta_2) \\ \dfrac{dS_3}{dt} = (-k_{32} - (\gamma_3 + \delta_3)) S_3 + k_{32}S_3S_2 + (\gamma_3 + \delta_3) . \end{cases} \tag{2.26}$$

System (2.26) can be put in the form (2.9) if we set

$$A = \begin{pmatrix} 0 & k_{12} & 0 \\ k_{21} & 0 & k_{23} \\ 0 & k_{32} & 0 \end{pmatrix};$$

$$e = \begin{pmatrix} -k_{12} - (\gamma_1 + \delta_1) \\ -k_{21} - k_{23} - (\gamma_2 + \delta_2) \\ -k_{32} - (\gamma_3 + \delta_3) \end{pmatrix}; \quad c = \begin{pmatrix} \gamma_1 + \delta_1 \\ \gamma_2 + \delta_2 \\ \gamma_3 + \delta_3 \end{pmatrix}.$$

2.3. The general structure

To include the models listed in Sections 2.1 and 2.2 we need to generalize (2.9) and write it in the more general form

$$\frac{dz}{dt} = diag(z)(e + Az) + b(z) \tag{2.27}$$

where now

$$b(z) = c + Bz \tag{2.28}$$

with

(i) $\quad c \in \mathbb{R}^n_+ \quad$ a constant vector

and

(ii) $\quad B = (b_{ij})_{i,j=1,\ldots,n} \quad$ a real constant matrix such that

$$b_{ij} \geq 0, \qquad i,j = 1,\ldots,n$$

$$b_{ii} = 0, \qquad i = 1,\ldots,n$$

For system (2.27) we shall give a detailed analysis of the asymptotic behavior based on recent results due to Beretta and Capasso [28].

2.3.1. Constant total population

We consider at first the case in which the total population N is constant.

A direct consequence is that any trajectory $\{z(t), t \in \mathbb{R}_+\}$ of system (2.27) is contained in a bounded domain $\Omega \subset \mathbb{R}^n$:

$$(A1) \qquad \Omega \quad \text{is positively invariant.}$$

Because of the structure of $F : \mathbb{R}^n \to \mathbb{R}^n$ defined by

$$F(z) := diag(z)(e + Az) + b(z) \tag{2.29}$$

it is clear that $F \in C^1(\Omega)$.

We shall denote by D_i the hyperplane of $\mathbb{R}^n$:

$$D_i = \{z \in \mathbb{R}^n \mid z_i = 0\}, \qquad i = 1, \ldots, n \ .$$

Clearly, for any $i = 1, \ldots, n$, $D_i \cap \Omega$ will be positively invariant if $b_i \mid_{D_i} = 0$, while $D_i \cap \Omega$ will be a repulsive set whenever $b_i \mid_{D_i} > 0$, in which case $F(z)$ will be pointing inside Ω on D_i.

Because of the invariance of Ω and the fact that $F \in C^1(\Omega)$, standard fixed point theorems [180] (Appendix B, Section B.1) assure the existence of at least one equilibrium solution of (2.27), within Ω.

Suppose now that a strictly positive equilibrium z^* exists for system (2.27) ($z_i^* > 0, \quad i = 1, \ldots, n$):

$$diag(z^*)(e + Az^*) + b(z^*) = 0$$

from which we get

$$e = -Az^* - diag\left(z^{*-1}\right) b(z^*) \tag{2.30}$$

where we have denoted by

$$z^{*-1} := \left(\frac{1}{z_1^*}, \ldots, \frac{1}{z_n^*}\right)^T$$

By substitution into (2.27), we get

$$\begin{aligned} \frac{dz}{dt} &= diag(z)\left[A + diag\left(z^{*-1}\right) B\right](z - z^*) \\ &\quad - diag(z - z^*)\, diag\left(z^{*-1}\right) b(z) \end{aligned} \tag{2.31}$$

Since (2.27) is a Volterra like system we may make use of the classical Volterra-Goh Lyapunov function [96].

$$V(z) := \sum_{i=1}^{n} w_i \left(z_i - z_i^* - z_i^* \ \ln \frac{z_i}{z_i^*} \right), \quad z \in \mathbb{R}^{n*} \tag{2.32}$$

where $w_i > 0, \quad i = 1, \ldots, n$, are real constants (the weights).

Here we denote by

$$\mathbb{R}_+^{n*} := \{z \in \mathbb{R}^n \mid z_i > 0, \quad i = 1, \ldots, n\},$$

and clearly

$$V : \mathbb{R}_+^{n*} \to \mathbb{R}_+ \quad .$$

The derivative of V along the trajectories of (2.27) is given by

$$\dot{V}(z) = (z - z^*)^T \ W\tilde{A}\,(z - z^*) - \sum_{i=1}^{n} w_i \frac{b_i(z)}{z_i z_i^*}(z_i - z_i^*)^2, \quad z \in \mathbb{R}_+^{n*} \tag{2.33}$$

which can be rewritten as

$$\dot{V}(z) = (z - z^*)^T \ W \left[\tilde{A} + diag\left(\frac{-b_1(z)}{z_1 z_1^*}, \ldots, \frac{-b_n(z)}{z_n z_n^*} \right) \right] (z - z^*) \tag{2.34}$$

We have denoted by $W := diag(w_1, \ldots, w_n)$, and by

$$\tilde{A} := A + diag\left(z^{*-1} \right) B \quad . \tag{2.35}$$

The structure of (2.33) and (2.34) stimulates the analysis of the following two cases:

(A) $\qquad \tilde{A}$ is W-skew symmetrizable

$$(B) \qquad - \left[\tilde{A} + diag\left(\frac{-b_1(z)}{z_1 z_1^*}, \ldots, \frac{-b_n(z)}{z_n z_n^*} \right) \right] \quad \in S_W \quad .$$

We say that a real $n \times n$ matrix A is "skew-symmetric" if $A^T = -A$.

We say that a real $n \times n$ matrix A is W-skew symmetrizable if there exists a positive diagonal real matrix W such that WA is skew-symmetric.

We say that a real $n \times n$ matrix A is in S_W (resp. "Volterra-Lyapunov stable") if there exists a positive diagonal real matrix W such that $WA + A^T W$ is positive definite (resp. negative definite).

In case (B)

$$\dot{V}(z) \leq 0, \qquad z \in \mathbb{R}_+^{n*}$$

and the equality applies if and only if $z = z^*$. The global asymptotic stability of z^* follows from the classical Lyapunov theorem (Appendix A, Section A.5). Thus we have proved the following

Theorem 2.1. *If system (2.27) admits a strictly positive equilibrium* $z^* \in \Omega\,(z_i > 0, i = 1, \ldots, n)$ *and condition (B) applies, then* z^* *is globally asymptotically stable within* Ω. *The uniqueness of such an equilibrium point follows from the GAS.*

Consider case (A) now. Since $W\tilde{A}$ is skew-symmetric, from (2.33) we get

$$\dot{V}(z) = -\sum_{i=1}^{n} \frac{w_i b_i(z)}{z_i z_i^*}(z_i - z_i^*)^2 \tag{2.36}$$

Since $b_i(z) \geq 0$ for any $z \in \mathbb{R}_+^{n*}$, $i = 1, \ldots, n$, we have

$$\dot{V}(z) \leq 0 \quad .$$

Denote by $R \subset \Omega$ the set of points where $\dot{V}(z) = 0$; clearly

$$R = \{z \in \Omega \mid z_i = z_i^* \quad \text{if} \quad b_i(z) > 0, \quad i = 1, \ldots, n\} \tag{2.37}$$

We shall further denote by M the largest invariant subset of R. By the LaSalle Invariance Principle [145] (Appendix A, Section A.5) we may then state that every solution tends to M for t tending to infinity.

In order to give more information about the structure of M , we refer to graph theoretical arguments [205].

Since in case (A) the elements of $\tilde{A}$ have a skew-symmetric sign distribution, we can then associate a graph with $\tilde{A}$ by the following rules.

(α) each compartment $i \in \{1, \ldots, n\}$ is represented by a labelled knot denoted by

(a.1) "$\circ$" if $b_i(z) = 0 \quad \forall z \in \Omega$

(a.2) "$\bullet$" otherwise

(β) if a pair of knots (i, j) is such that $\tilde{a}_{i,j}\tilde{a}_{j,i} < 0$ then the two knots i and j are connected by an arc (see for examples Sect. 2.3.1.1).

The following lemma holds [205].

Lemma 2.2. *Assume that $\tilde{A}$ is skew-symmetrizable. If the associated graph is either*

(a) a tree and $\rho - 1$ of the terminal knots are $\bullet$
or
(b) a chain and two consecutive internal knots are $\bullet$
or
(c) a cycle and two consecutive knots are $\bullet$

then $M = \{z^*\}$ within R.

As a consequence of this lemma and the above arguments we may state the following

Theorem 2.3. *If system (2.27) admits a strictly positive equilibrium $z^* \in \Omega$ $(z_i^* > 0, \quad i = 1, \ldots, n)$ and condition (A) applies under one of the assumptions of Lemma 2.2, then the positive equilibrium z^* is GAS within Ω (again the uniqueness of z^* follows from its GAS).*

The interest of Theorems 2.1. and 2.3. lies in the fact that they provide sufficient conditions in order that an equilibrium solution of system (2.27) be globally asymptotically stable whenever we are able to show that it exists.

This will reduce a problem of GAS to an "algebraic" problem. On the other hand necessary and sufficient conditions for the existence of an equilibrium solution usually include "threshold" conditions on the parameters for the existence of such a nontrivial endemic state.

Sufficient conditions for the existence of a nontrivial endemic state are given in the following corollary of Theorems 2.1. and 2.3.

Corollary 2.4. *If the vector c in (2.28) (i) is strictly positive, then the system (2.27) admits a strictly positive equilibrium $z^* \in \Omega_+$. In either cases (A) and (B), the positive equilibrium z^* is GAS (and therefore unique) with respect to Ω_+.*

An extension of these results to the space heterogeneous case can be found in Sect. 5.6.

2.3.1.1. Case A: epidemic systems for which the matrix $\tilde{A}$ is W-skew symmetrizable

2.3.1.1.1. SIR model with vital dynamics

It is clearly seen from (2.35) that, since in this case $B = 0$, we have $\tilde{A} = A$ and $b(z) = c = \begin{pmatrix} \delta \\ 0 \end{pmatrix}$.

$\tilde{A}$ is thus skew-symmetric and the associated graph is •–∘. Theorem 2.3. applies.

In this case the nontrivial equilibrium point, i.e. the nontrivial endemic state, is given by

$$S^* = \frac{\gamma + \delta}{k}; \qquad I^* = \frac{\delta}{k}\left(\frac{1}{S^*} - 1\right) \tag{2.38}$$

which exists iff

$$\sigma = \frac{k}{\gamma + \delta} > 1. \tag{2.39}$$

Note that if $\sigma \leq 1$ then the only equilibrium point of the system is $(1, 0)^T$, and this is GAS.

2.3.1.1.2. SIRS model with temporary immunity

Again in this case

$$\tilde{A} = A \quad \text{and} \quad b(z) = c$$

so that $\tilde{A}$ is skew-symmetric. The associated graph is also •–∘, and Theorem 2.3. applies.

In this case the nontrivial endemic state is given by $z^* = (S^*, I^*)^T$, where

$$S^* = \frac{\gamma + \delta}{k} =: \frac{1}{\sigma}$$

$$I^* = \frac{(\delta + \alpha)(\sigma - 1)}{k + \alpha\sigma}$$

which exists iff $\sigma > 1$.

Otherwise, for $\sigma \leq 1$, the only equilibrium point of the system is $(1, 0)^T$.

2.3.1.1.3. SIR model with carriers

In this case

$$\tilde{A} = A \quad \text{and} \quad b(z) = c.$$

Since c is positive definite and $\tilde{A}$ is skew-symmetric, we may apply Corollary 2.4 to state that a unique positive equilibrium z^* exists,which is GAS with respect to the interior of

$$\Omega := \left\{ z = \left(S, \tilde{I}\right)^T \in \mathbb{R}^2_+ \mid S + \tilde{I} \leq 1 + C \right\}$$

In this case then an endemic state always exists. Its coordinates are given by [110]

$$S^* = 1 - \frac{kI^*}{\delta\sigma}$$

$$I^* = \frac{\delta}{2k} \left(\left(\sigma - 1 - C\frac{k}{\delta} \right) + \left(\left(\sigma - 1 - C\frac{k}{\delta} \right)^2 + 4C\frac{k\sigma}{\delta} \right)^{\frac{1}{2}} \right)$$

where, as usual, $\sigma := \dfrac{k}{\gamma + \delta}$.

2.3.1.1.4. SIR model with vertical transmission

In this case $b(z) = c + Bz$.

Moreover this system admits the following equilibrium point

$$
\begin{aligned}
S^* &= \frac{pb' + v}{k} \\
I^* &= \frac{((1-m)b + \gamma)\,k - (b+\gamma)\,(pb' + v)}{(v + (1-m)\,b + \gamma)\,k}
\end{aligned}
\tag{2.40}
$$

This is a nontrivial endemic state ($I^* > 0$) iff

$$
m < \frac{(b+\gamma)\,(k - pb' - v)}{bk}. \tag{2.41}
$$

As a consequence

$$
\tilde{A} := A + diag\left(z^{*-1}\right) B = \begin{pmatrix} 0 & k\dfrac{(m-1)b - \gamma - v}{p\,b' + v} \\ k & 0 \end{pmatrix}
$$

Now, $(m-1)b, \quad -\gamma, \quad -v$ are all nonpositive quantities. We assume, to exclude extreme cases, that they are all negative. Thus a suitable positive diagonal matrix $W = diag(w_1 w_2)$ can be easily shown to exist, such that $W\tilde{A}$ reduces to $\begin{pmatrix} 0 & -k \\ k & 0 \end{pmatrix}$. We fall into case (A) Section 2.3.1. Since the associated graph is •—∘, the endemic state (2.40) (under (2.41)) is GAS.

2.3.1.2. Case B: epidemic systems for which

$$-\left[\tilde{A} + diag\left(-\frac{b_1(z)}{z_1 z_1^*}, \dots, \frac{b_n(z)}{z_n z_n^*}\right)\right] \in S_W.$$

2.3.1.2.1. Gonorrhea model

In this case (Eqn. (2.17)),

$$b(z) = Bz = \begin{pmatrix} c_1 I_2 \\ c_2 I_1 \end{pmatrix}, \qquad \tilde{A} = \begin{pmatrix} 0 & \dfrac{c_1 - I_1^*}{I_1^*} \\ \dfrac{c_2 - I_2^*}{I_2^*} & 0 \end{pmatrix}$$

consider the matrix

$$W\left[\tilde{A} + diag\begin{pmatrix} \dfrac{-c_1 I_2}{I_1^* I_1 - \dfrac{c_2 I_1}{I_2^* I_2}} \end{pmatrix}\right] = \begin{pmatrix} -w_1 \dfrac{c_1 I_2}{I_1^* I_1} & w_1 \dfrac{S_1^*}{I_1^*} \\ w_2 \dfrac{S_2^*}{I_2^*} & -w_2 \dfrac{c_2 I_1}{I_2^* I_2} \end{pmatrix} \tag{2.42}$$

which is a symmetric matrix if we choose $w_1 > 0$, and $w_2 > 0$ such that

$$w_2 \left(\frac{S_2^*}{I_2^*}\right) = w_1 \left(\frac{S_1^*}{I_1^*}\right)$$

The symmetric matrix (2.42) is negative definite. In fact the diagonal elements are negative and

$$\left(\frac{c_1 I_2}{I_1^* I_1} \frac{c_2 I_1}{I_1^* I_2} - \frac{S_1^* S_2^*}{I_1^* I_2^*}\right) w_1 w_2 = \frac{w_1 w_2}{I_1^* I_2^*} (c_1 c_2 - S_1^* S_2^*) > 0 \ ,$$

where the fact that $0 < S_i^* < c_i, \quad i = 1, 2$, is taken into account since $z^* = (I_1^*, I_2^*)^T$ is a positive equilibrium. Theorem 2.3 applies.

2.3.1.2.2. SIS model in two communities with migration

This model has been reduced to system (2.21). Hence

$$b(z) = Bz = \begin{pmatrix} \theta_1 I_2 \\ \theta_2 I_1 \end{pmatrix}, \qquad \text{and} \qquad \tilde{A} = \begin{pmatrix} -k_1 & \dfrac{\theta_1}{I_1^*} \\ \dfrac{\theta_2}{I_2^*} & -k_2 \end{pmatrix}$$

Let $\Omega \subset \mathbb{R}^2$ be defined as

$$\Omega := \left\{ z = (I_1, I_2)^T \in \mathbb{R}^2 \;\mid\; 0 \le I_i \le 1, \quad i = 1,2 \right\}$$

Because of Theorem 2.3, the sufficient condition for the asymptotic stability of a positive equilibrium z^*, with respect to Ω is

$$-\left[\tilde{A} + diag\left(-\frac{\theta_1 I_2}{I_1^* I_1}, -\frac{\theta_2 I_1}{I_2^* I_2}\right)\right] \in S_W$$

We can observe that

$$W\tilde{A} + diag\left(-w_1 \frac{\theta_1 I_2}{I_1^* I_1}, -w_2 \frac{\theta_2 I_1}{I_2^* I_2}\right) \tag{2.43}$$

$$= \begin{pmatrix} -w_1 \dfrac{\theta_1 I_2}{I_1^* I_1} & w_1 \dfrac{\theta_1}{I_1^*} \\ w_2 \dfrac{\theta_2}{I_2^*} & -w_2 \dfrac{\theta_2 I_1}{I_2^* I_2} \end{pmatrix} + diag\left(-k_1 w_1, -k_2 w_2\right)$$

The first matrix on the right hand side of (2.43) is symmetric if we choose $w_1 > 0, \quad w_2 = \dfrac{\theta_1 I_2^*}{\theta_2 I_1^*} w_1$.

This matrix is negative semidefinite since

$$\left(\frac{\theta_1 I_2}{I_1^* I_1} \quad \frac{\theta_2 I_1}{I_2^* I_2} - \frac{\theta_1}{I_1^*} \quad \frac{\theta_2}{I_2^*}\right) w_1 w_2 = 0 \ .$$

Because of the presence of the diagonal negative matrix on the right hand side of (2.43), the sufficient condition of Theorem 2.3. holds true provided that $k_1, k_2 > 0$.

Under these assumptions, if a positive equilibrium z^* exists, then it is GAS within Ω.

2.3.1.2.3. SIS model for two dissimilar groups

This model has been reduced to the form (2.23).
Hence

$$b(z) \equiv Bz = \begin{pmatrix} k_{12}I_2 \\ k_{21}I_1 \end{pmatrix}, \quad \tilde{A} = \begin{pmatrix} -k_{11} & \dfrac{k_{12}}{I_1^*}(1-I_1^*) \\ \dfrac{k_{21}}{I_2^*}(1-I_2^*) & -k_{22} \end{pmatrix}$$

Consider now

$$W\left[\tilde{A} + diag\left(-\frac{k_{12}I_2}{I_1^*I_1}, -\frac{k_{21}I_1}{I_2^*I_2}\right)\right] \tag{2.44}$$

$$= \begin{pmatrix} -w_1\dfrac{k_{12}I_2}{I_1^*I_1} & w_1\dfrac{k_{12}}{I_1^*}(1-I_1^*) \\ w_2\dfrac{k_{21}}{I_2^*}(1-I_2^*) & -w_2\dfrac{k_{21}I_1}{I_2^*I_2} \end{pmatrix} + diag\,(-k_{11}w_1, -k_{22}w_2)$$

where the first matrix on the right hand side of (2.44) is symmetric when choosing $w_1 > 0$ and w_2 such that $\left(\dfrac{k_{21}}{I_2^*}\right)(1-I_2^*)\,w_2 = \left(\dfrac{k_{12}}{I_1^*}\right)(1-I_1^*)\,w_1$. Moreover, since $0 < I_i^* < 1, \quad i = 1,2$, this matrix is negative definite. In fact,

$$\left(\frac{k_{12}I_2}{I_1^*I_1}\ \frac{k_{21}I_1}{I_2^*I_2} - \frac{k_{12}}{I_1^*}(1-I_1^*)\,\frac{k_{21}}{I_2^*}(1-I_2^*)\right) w_1w_2 > 0.$$

Hence, provided that $k_{11} \geq 0, k_{22} \geq 0$,

$$-\left[\tilde{A} + diag\left(-\frac{k_{12}I_2}{I_1^*I_1}, -\frac{k_{21}I_1}{I_2^*I_2}\right)\right] \in S_W$$

and Theorem 2.3. assures the asymptotic stability of the positive equilibrium z^* with respect to $\Omega = \left\{z \in \mathbb{R}_+^2 \mid I_i \leq 1, \quad i = 1,2\right\}$.

2.3.1.2.4. Host - vector- host model

This model has been reduced to the form (2.26).
Hence

$$b(z) \equiv c \qquad , \qquad \tilde{A} \equiv A$$

By Corollary 2.4, since c is a positive definite vector, one positive equilibrium z^* exists in $\overset{\circ}{\Omega}$, where

$$\Omega := \left\{ z \in \mathrm{IR}^3_+ \mid 0 \le S_i \le 1, \quad i = 1,2,3 \right\}.$$

$\tilde{A}$ has a symmetric sign structure. Hence, by Corollary 2.4, if

$$-\left[A + diag \left(\frac{-(\gamma_1 + \delta_1)}{S_1 S_1^*}, \frac{-(\gamma_2 + \delta_2)}{S_2 S_2^*}, \frac{-(\gamma_3 + \delta_3)}{S_3 S_3^*} \right) \right] \in S_W$$

then z^* is asymptotically stable within $\overset{\circ}{\Omega}$. If we take into account that $S_i \le 1, \quad i = 1,2,3$, from (2.34) we see that a sufficient condition for the asymptotic stability of z^* is

$$-[A + diag\,(-(\gamma_1 + \delta_1), -(\gamma_2 + \delta_2), -(\gamma_3 + \delta_3))] \in S_W.$$

Accordingly, let us take

$$W\,[A + diag\,(-(\gamma_1 + \delta_1), -(\gamma_2 + \delta_2), -(\gamma_3 + \delta_3))]$$

$$= \begin{pmatrix} -(\gamma_1 + \delta_1)\,w_1 & k_{12} w_1 & 0 \\ k_{21} w_2 & -(\gamma_2 + \delta_2)\,w_2 & k_{23} w_2 \\ 0 & k_{32} w_3 & -(\gamma_3 + \delta_3)\,w_3 \end{pmatrix}$$

This matrix is symmetric if we choose

$$w_1 > 0, \quad w_2 = \left(\frac{k_{12}}{k_{21}} \right) w_1, \quad w_3 = \left(\frac{k_{23}}{k_{32}} \right) \left(\frac{k_{12}}{k_{21}} \right) w_1.$$

It is negative definite if

$$[(\gamma_1 + \delta_1)(\gamma_2 + \delta_2) - k_{12} k_{21}]\, w_1 w_2 > 0,$$

$$-[\,(\gamma_1 + \delta_1)(\gamma_2 + \delta_2)(\gamma_3 + \delta_3) - (\gamma_3 + \delta_3)\, k_{12} k_{21} - (\gamma_1 + \delta_1)\, k_{23} k_{32}] w_1 w_2 w_3 < 0 \qquad (2.45)$$

We can observe that, if inequalities in (2.45) hold true, then

$$[(\gamma_2 + \delta_2)(\gamma_3 + \delta_3) - k_{23} k_{32}]\, w_2 w_3 > 0 \ .$$

Hence (2.45) is the sufficient condition for the asymptotic stability (and uniqueness) of the positive equilibrium z^* within $\overset{\circ}{\Omega}$.

From (2.26) the positive equilibrium z^* has the following components:

$$S_1^* = \frac{\gamma_1 + \delta_1}{k_{12}(1 - S_2^*) + (\gamma_1 + \delta_1)} \quad , \quad S_3^* = \frac{\gamma_3 + \delta_3}{k_{32}(1 - S_2^*) + (\gamma_3 + \delta_3)} \quad , \tag{2.46}$$

and S_2^* is a solution of

$$(1 - S_2)\left\{p(1 - S_2)^2 + q(1 - S_2) + r\right\} = 0 \quad , \tag{2.47}$$

where

$$p = k_{12}k_{32}\left[(k_{21} + k_{23}) + (\gamma_2 + \delta_2)\right] \quad ,$$

$$\begin{aligned} q = {} & k_{32}\left[(\gamma_1 + \delta_1)(\gamma_2 + \delta_2) - k_{12}k_{21}\right] + k_{12}\left[(\gamma_2 + \delta_2)(\gamma_3 + \delta_3) - k_{23}k_{32}\right] \\ & + k_{12}k_{21}(\gamma_3 + \delta_3) + k_{23}k_{32}(\gamma_1 + \delta_1) \end{aligned}$$

$$r = (\gamma_1 + \delta_1)(\gamma_2 + \delta_2)(\gamma_3 + \delta_3) - (\gamma_3 + \delta_3)k_{12}k_{21} - (\gamma_1 + \delta_1)k_{23}k_{32} \quad .$$

It is to be noticed that when (2.45) holds true, then $q > 0, \quad r > 0$, thus assuring that the unique asymptotically stable equilibrium is such that $S_2^* = 1, \quad$ i.e. $\quad z^* = (1, 1, 1)^T$.

When (2.45) fails to hold, by (2.47) we have another positive equilibrium for which $S_2^* < 1$ and its remaining components are given by (2.46).

To study the asymptotic stability of this equilibrium we can remember that $I_i + S_i = 1, \quad i = 1, 2, 3$, thus assuring to have a positive equilibrium $z^* = (I_1^*, I_2^*, I_3^*)^T, \quad 0 < I_i^* < 1, \quad i = 1, 2, 3$ within the subset $\overline{\Omega} = \left\{z \in \mathbb{R}_+^3 : I_i \leq 0, \quad i = 1, 2, 3\right\}$. In the old variables $I_i, \quad i = 1, 2, 3$, the positive equilibrium becomes the origin and the ODE system (2.25) can be arranged in this form:

$$\begin{aligned} \frac{dI_1}{dt} &= -(\gamma_1 + \delta_1)I_1 - k_{12}I_1I_2 + k_{12}I_2 \quad , \\ \frac{dI_2}{dt} &= -(\gamma_2 + \delta_2)I_2 - k_{21}I_2I_1 - k_{23}I_2I_3 + (k_{21}I_1 + k_{23}I_3) \quad , \\ \frac{dI_3}{dt} &= -(\gamma_3 + \delta_3)I_3 - k_{32}I_3I_2 + k_{32}I_2 \end{aligned}$$

so that

$$e = \begin{pmatrix} -(\gamma_1 + \delta_1) \\ -(\gamma_2 + \delta_2) \\ -(\gamma_3 + \delta_3) \end{pmatrix}, \quad A = \begin{pmatrix} 0 & -k_{12} & 0 \\ -k_{21} & 0 & -k_{23} \\ 0 & -k_{32} & 0 \end{pmatrix}$$

$$c = 0, \qquad B = \begin{pmatrix} 0 & k_{12} & 0 \\ k_{21} & 0 & k_{23} \\ 0 & k_{32} & 0 \end{pmatrix}$$

Thus

$$b(z) = Bz, \qquad \tilde{A} = \begin{pmatrix} 0 & \dfrac{k_{12}S_1^*}{I_2^*} & 0 \\ \dfrac{k_{21}S_2^*}{I_2^*} & 0 & \dfrac{k_{23}S_2^*}{I_2^*} \\ 0 & \dfrac{k_{32}S_3^*}{I_3^*} & 0 \end{pmatrix}$$

For the asymptotic stability of $z^* = (I_1^*, I_2^*, I_3^*)^T$ within $\overline{\Omega}$ we can apply Theorem 2.3 by requiring that

$$-\left[\tilde{A} + diag\left(-\frac{b_1(z)}{I_1 I_1^*}, -\frac{b_2(z)}{I_2 I_2^*}, -\frac{b_3(z)}{I_3 I_3^*}\right)\right] \in S_W \quad .$$

Hence consider

$$W\left[\tilde{A} + diag\left(-\frac{b_1(z)}{I_1 I_1^*}, -\frac{b_2(z)}{I_2 I_2^*}, -\frac{b_3(z)}{I_3 I_3^*}\right)\right] \tag{2.48}$$

$$= \begin{pmatrix} -\dfrac{k_{12}I_2}{I_1 I_1^*} w_1 & \dfrac{k_{12}S_1^*}{I_1^*} w_1 & 0 \\ \dfrac{k_{21}S_2^*}{I_2^*} w_2 & -\dfrac{(k_{21}I_1 + k_{23}I_3)}{I_2 I_2^*} w_2 & \dfrac{k_{23}S_2^*}{I_2^*} w_2 \\ 0 & \dfrac{k_{32}S_3^*}{I_3^*} w_3 & -\dfrac{k_{32}I_2}{I_3 I_3^*} w_3 \end{pmatrix}$$

this matrix is symmetric if we choose

$$w_1 > 0 \ , \quad w_2 = \left(\frac{k_{12}S_1^*}{k_{21}S_2^*}\right)\left(\frac{I_2^*}{I_1^*}\right) w_1 \ , \quad w_3 = \left(\frac{k_{23}S_2^*}{k_{32}S_3^*}\right)\left(\frac{I_3^*}{I_2^*}\right) w_2 \ .$$

To apply Theorem 2.3 we must require that the symmetric matrix (2.48) be negative definite. Since the diagonal elements are negative, the sufficient condition is

$$\left[\frac{k_{12}I_2}{I_1} \quad \frac{(k_{21}I_1 + k_{23}I_3)}{I_2^*} - k_{21}S_1^* k_{21}S_2^*\right] \frac{w_1 w_2}{I_1^* I_2^*} > 0 \ ,$$

$$\left[-\frac{k_{12}I_2}{I_1} \quad \frac{(k_{21}I_1 + k_{23}I_3)}{I_2} \quad \frac{k_{32}I_2}{I_3} + \frac{k_{32}I_2}{I_3} k_{12}S_1^* k_{21}S_2^* \right. \tag{2.49}$$
$$\left. + \frac{k_{12}I_2}{I_1} k_{23}S_2^* k_{32}S_3^*\right] \frac{w_1 w_2 w_3}{I_1^* I_2^* I_3^*} < 0 \ .$$

Now we observe that the sufficient condition (2.49) is always met by a positive equilibrium $z^* \in \overline{\Omega}$.

In fact

$$\frac{k_{12}I_2}{I_1} \quad \frac{(k_{21}I_1 + k_{23}I_3)}{I_2} - k_{12}S_1^* k_{21}S_2^* > \frac{k_{12}I_2}{I_1} \quad \frac{k_{21}I_1}{I_2} - k_{12}k_{21} = 0$$

and

$$-\frac{k_{12}I_2}{I_1} \quad \frac{k_{21}I_1}{I_2} \quad \frac{k_{32}I_2}{I_3} + \frac{k_{32}I_2}{I_3} \quad k_{12}S_1^* k_{21}S_2^* - \frac{k_{12}I_2}{I_1} \quad \frac{k_{23}I_3}{I_2} \quad \frac{k_{32}I_2}{I_3}$$

$$+\frac{k_{12}I_2}{I_1} \quad k_{23}S_2^* k_{32}S_3^* =$$

$$= \frac{I_2}{I_3} k_{32} \left(-k_{12}k_{21} + k_{12}S_1^* k_{21}S_2^*\right) + \frac{k_{12}I_2}{I_1} \left(-k_{23}k_{32} + k_{23}S_2^* k_{32}S_3^*\right) < 0 \ ,$$

where, when proving the inequalities, we have taken into account that $S_i^* < 1, \quad i = 1, 2, 3.$

Hence we can conclude for the host-vector-host model that

Proposition 2.5. *If the sufficient condition (2.45) holds true, then the origin is asymptotically stable with respect to $\overline{\Omega}$. Otherwise besides the origin a positive equilibrium $z^* \in \overline{\Omega}$ exists which is GAS in $\mathring{\Omega}$.*

2.3.2. Nonconstant total population

In some relevant cases the total population

$$N(t) = \sum_{i=1}^{n} z_i(t) \tag{2.50}$$

of the epidemic system is not a constant, but rather a dynamical variable. We shall consider in the sequel specific examples of this kind.

A first model is the parasite-host system studied by Levin and Pimentel in [151]:

$$\begin{cases} \dfrac{dx}{dt} = (r-k)x - Cxy - Cxv + ry + rv \ , \\ \dfrac{dy}{dt} = -\left(\beta + k\right) y + Cxy - CSyv \ , \\ \dfrac{dv}{dt} = -\left(\beta + k + \sigma\right) v + Cxv - CSyv \end{cases} \tag{2.51}$$

The two cases $r < k$ and $r > \beta + k + \sigma$ do not give rise to nontrivial equilibrium solutions. We shall then restrict our analysis to the case $\beta + \sigma + k > r > k$ in which there is an equilibrium at

$$x^* = \frac{r}{C} \frac{\sigma}{\sigma - S(r-k)}, \quad y^* = \frac{\beta + k + \sigma}{CS} - \frac{1}{S}x^*, \quad v^* = \frac{1}{S}x^* - \frac{\beta + k}{CS} \tag{2.52}$$

The equilibrium $z^* = (x^*, y^*, v^*)$ is feasible, i.e. its components are positive if

$$\frac{r}{\beta + k + \sigma} < 1 - \frac{S(r-k)}{\sigma} < \frac{r}{\beta + k} \quad , \tag{2.53}$$

If $\sigma < \sigma_1$ where σ_1 is such that

$$\frac{r}{\beta + k + \sigma_1} = 1 - \frac{S(r-k)}{\sigma_1} \quad , \tag{2.54}$$

the first inequality in (2.53) is violated and only a partially feasible equilibrium is present given by

$$x^* = \frac{\beta + k + \sigma}{C}, \quad y^* = 0, \quad v^* = \frac{r-k}{\beta + k + \sigma + r} x^* \tag{2.55}$$

since $r < \beta + k + \sigma$. If $\sigma = \sigma_1$ then (2.52) coalesces in (2.55). If $r < \beta + k$ and $\sigma > \sigma_2$, where σ_2 is such that

$$1 - \frac{S(r-k)}{\sigma_2} = \frac{r}{\beta + k} \tag{2.56}$$

then the second inequality in (2.53) is violated and only a partially feasible equilibrium is present, given by

$$x^* = \frac{\beta + k}{C}, \quad y^* = \frac{r-k}{\beta + k - r} x^*, \quad v^* = 0 \tag{2.57}$$

since $r > k$. If $\sigma = \sigma_2$ then (2.52) coalesces in (2.57).

Concerning system (2.51), if we denote by $z = (x, y, v)^T$ and set

$$A = \begin{pmatrix} 0 & -C & -C \\ C & 0 & -CS \\ C & CS & 0 \end{pmatrix}; \quad e = \begin{pmatrix} r-k \\ -(\beta+k) \\ -(\beta+k+\sigma) \end{pmatrix}$$

$$c = 0, \quad B = \begin{pmatrix} 0 & r & r \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

we may reduce it again to the general structure (2.27), but in this case

$$\frac{dN}{dt} = (r-k)N(t) \tag{2.58}$$

and the evolution of system (2.51) has to be analyzed in the whole $\mathbb{R}^3_+$.

Local stability results were already given in [151]. Here we shall study global asymptotic stability of the feasible or partially feasible equilibrium by the Beretta-Capasso approach (see Section 2.3.2.1).

A second model that we shall analyze is the SIS model with vital dynamics, which is proposed by Anderson and May [8]

$$\begin{aligned} \frac{dS}{dt} &= (r-b)S - \rho SI + (\mu + r)\, I \\ \frac{dI}{dt} &= -\,(\theta + b + \mu)\, I + \rho SI \end{aligned} \tag{2.59}$$

If we denote by $z = (S, I)^T$ and set

$$A = \begin{pmatrix} 0 & -\rho \\ \rho & 0 \end{pmatrix}; \quad e = \begin{pmatrix} r-b \\ -\,(\theta + b + \mu) \end{pmatrix}$$

$$c = 0; \quad B = \begin{pmatrix} 0 & \mu + r \\ 0 & 0 \end{pmatrix}$$

we go back to system (2.27). In this case

$$\frac{dN}{dt}(t) = (r-b)N(t) - \theta I(t)$$

Other examples will be discussed later. It is clear that if the total population is a dynamical variable rather than a specified constant, we need to drop assumption (A1) in Section 2.3.1.

For these systems the accessible space is the whole nonnegative orthant $\mathbb{R}^n_+$ of the Euclidean space. We cannot apply then the standard fixed point theorems.

We can only assume that

$$(A2) \qquad \mathbb{R}^n_+ \quad \text{is positively invariant.}$$

We shall give now more extensive treatment of system (2.27) including the possibility of partially feasible equilibrium points.

We shall say that z^* is a partially feasible equilibrium whenever a nonempty proper subset of its components are zero. If we denote by $N = \{1, \ldots, n\}$, we mean that a set $I \subset N$ exists, such that $I \neq \emptyset, \quad I \neq N$ and $z_i^* = 0$ for any $i \in I$.

Assume from now on that this is the case; given the matrices

$$A = (a_{ij})_{i,j=1,\ldots,n} \quad \text{and} \quad B = (b_{ij})_{i,j=1,\ldots,n}$$

in system (2.27), we define a new matrix

$$\tilde{A} = (\tilde{a}_{ij})_{i,j=1,\ldots,n}$$

as follows

$$\tilde{a}_{ij} = a_{ij} + \frac{b_{ij}}{z_i^*}, \quad i \in N - I, \quad j \in N$$

$$\tilde{a}_{ij} = a_{ij}, \qquad \text{otherwise.}$$

With the above notations in mind, system (2.27) can be rewritten as

(2.60a)
$$\frac{dz_i}{dt} = z_i \sum_{j \in N} \tilde{a}_{ij} \left(z_j - z_j^*\right) - \frac{(z_i - z_i^*)}{z_i^*} b_i(z), \quad i \in N - I$$

(2.60b)
$$\frac{dz_i}{dt} = z_i \left(e_i + \sum_{j \in N} a_{ij} z_j \right), \quad i \in I$$

We introduce a new Lyapunov function suggested by Goh [94, 95, 96]

(2.61)
$$V(z) = \sum_{i \in N-I} w_i \left(z_i - z_i^* - z_i^* \ln \frac{z_i}{z_i^*} \right) + \sum_{i \in I} w_i z_i$$

where, as usual $w_i > 0, \quad i = 1, \ldots, n$.

Clearly $V \in C^1 \left(R_I^n\right)$, where we define

(2.62)
$$R_I^n := \{ z \in \mathbb{R}^n \mid z_i > 0, i \in N - I; \quad z_i \geq 0\,, \ i \in I \}$$

Let R be the subset of R_I^n defined as follows

(2.63)
$$R := \{ z \in R_I^n \mid z_i = 0, i \in I, z_i = z_i^* \text{ for any } i \in N - I \text{ s.t. } b_i(z) > 0 \}$$

and let M be the largest invariant subset of R with respect to the system (2.27).

On account of (2.60) the time derivative of V along the trajectories of system (2.27) is given by

$$\dot{V}(z) = \sum_{i \in N-I} w_i \frac{(z_i - z_i^*)}{z_i} \left\{ z_i \sum_{j \in N} \tilde{a}_{ij} \left(z_j - z_j^*\right) - \frac{(z_i - z_i^*)}{z_i^*} b_i(z) \right\}$$
$$+ \sum_{i \in I} w_i z_i \left(e_i + \sum_{j \in N} a_{ij} z_j \right)$$

or, in matrix notation ($W = diag\,(w_i, \quad i = 1, \ldots, n)$)

(2.64)
$$\dot{V}(z) = \left(z - z_i^*\right)^T W \tilde{A} \left(z - z^*\right) - \sum_{i \in N-I} w_i \frac{b_i(z)}{z_i z_i^*} \left(z_i - z_i^*\right)^2$$
$$+ \sum_{i \in I} w_i \left\{ z_i \left(e_i + \sum_{j \in N} a_{ij} z_j \right) + b_i(z) \right\}.$$

It is clear that

$$R = \left\{ z \in R_I^n \mid \dot{V}(z) = 0 \right\} .$$

We are now in a position to state the following

Theorem 2.6. *Let z^* be a partially feasible equilibrium of system (2.27), with $z_i^* = 0 \quad \text{for} \quad i \in I \subset N, \quad I \neq \emptyset, I \neq N$. Assume that*

(a) $\tilde{A}$ *is W-skew symmetrizable*

(b) $e_i + \sum_{j \in N} a_{ij} z_j^* \leq 0, \quad i \in I$

(c) $b_i(z) \equiv 0, \quad i \in I$

(d) $M \equiv \{z^*\}$

Then z^* is globally asymptotically stable within R_I^n.

Proof. Since $\tilde{A}$ is W-skew symmetrizable, the first term in (2.64) vanishes. By the assumptions (b), $\dot{V}(z) \leq 0$ in R_I^n. We can then apply LaSalle Invariance Principle [145, Theorem VI Sect. 13 (see also Appendix A, Section A.5)],to state that z^* is GAS in R_I^n.

A natural consequence of Theorem 2.6 is the following

Corollary 2.7. *Let z^* be a feasible equilibrium of (2.27) and assume that $\tilde{A}$ is W-skew symmetrizable. If $M \equiv \{z^*\}$ then z^* is globally asymptotically stable within $\mathbb{R}_+^{n*}$.*

Corollary 2.7 can be seen as a new formulation of Theorem 2.3 in the case in which $(A1)$ is substituted by $(A2)$.

Under the same conditions of this corollary we can also observe that if the graph associated with $\tilde{A}$ by means of (α) and (β) satisfies anyone of the hypotheses in Lemma 2.2, then within R we have $M \equiv \{z^*\}$.

We can now solve the two models presented in Section 2.3.1.

2.3.2.1. The parasite-host system [151]

Consider the case in which the equilibrium (2.52) is feasible, i.e. $z^* \in \mathbb{R}^3_+$. Then

$$(2.65) \qquad b(z) \equiv Bz, \quad \tilde{A} = \begin{pmatrix} 0 & -\left(C - \frac{r}{x^*}\right) & -\left(C - \frac{r}{x^*}\right) \\ C & 0 & -CS \\ 0 & CS & 0 \end{pmatrix}$$

where z is a vector $z = (x, y, v)^T$ belonging to the non-negative orthant $\mathbb{R}^3_+$. Since $C - \dfrac{r}{x^*} = CS\dfrac{(r-k)}{\sigma}$ provided that $r > k$, matrix $\tilde{A}$ is W-skew symmetrizable by the diagonal positive matrix $W = diag\,(w_1, w_2, w_3)$, where $w_1 = \dfrac{\sigma}{S(r-k)}$, $\quad w_2 = w_3 = 1$. In fact, we obtain

$$W\tilde{A} = \begin{pmatrix} 0 & -C & -C \\ C & 0 & -CS \\ C & CS & 0 \end{pmatrix}$$

Now we are in position to apply Corollary 2.7.

Since $b(z) = (r(y+z), 0, 0)^T$, the subset of all points within $\mathbb{R}^{n*}_+$ where we have $\dot{V}(z) = 0$, is

$$R = \left\{ z \in \mathbb{R}^n_+ \mid x = x^* \right\}$$

Now we look for the largest invariant subset M within R. Since $x = x^*$ for all t, $\left.\dfrac{dx}{dt}\right|_R = 0$, and from the first of the Eqns. (2.51) we obtain

$$(y + v)\mid_R = \frac{r-k}{C - \dfrac{r}{x^*}} = \frac{\sigma}{CS}, \qquad \text{for all t.}$$

Therefore, $\left.\dfrac{d(y+v)}{dr}\right|_R = 0$, and by the last two Eqns. (2.51) we obtain

$$z\mid_R = \frac{1}{\sigma}\left\{[Cx^* - (\beta + k)]\,[(y+v)]_R\right\} = \frac{1}{CS}\,[Cx^* - (\beta + k)] = \frac{x^*}{S} - \frac{\beta + k}{CS}$$

Then, by taking into account (2.52) we have $z\mid_R \equiv z^*$.

Immediately follows

$$y\,|_R = \frac{\sigma}{CS} - v^* = \frac{\beta + k + \sigma}{CS} - \frac{x^*}{S} \ ,$$

i.e. $y\,|_R = y^*$. Then the largest invariant set M within R is z^*. From Corollary 2.7 it follows the global asymptotic stability of the feasible equilibrium (2.52) within $\mathbb{R}^{3*}_+$.

It is to be noticed that the only assumptions made in this proof are $r > k$ and that equilibrium (2.52) is feasible. Under these assumptions we exclude that unbounded solutions may exist.

Suppose that $\sigma \leq \sigma_1$, i.e. the equilibrium (2.52) is not feasible and we get the partially feasible equilibrium (2.55) which belongs to

$$R^3_2 = \left\{ z \in \mathbb{R}^3 \mid z_i > 0, \quad i = 1, 3, \quad z_2 \geq 0 \right\}$$

In order to apply Theorem 2.6, hypotheses (a) and (b) must be verified. Concerning hypothesis (a), we have

$$-(\beta + k) + cx^* - cSv^* \leq 0 \ , \tag{2.66}$$

from which, by taking into account (2.55), we obtain

$$1 - \frac{S(r-k)}{\sigma} \leq \frac{r}{\beta + k + \sigma} \ , \tag{2.67}$$

Inequality (2.67) is satisfied in the whole range $\sigma \leq \sigma_1$ within which the partially feasible equilibrium (2.55) occurs. When $\sigma = \sigma_1$ the equality applies in (2.53). Hypothesis (b) is satisfied because $b(z) = (r(y+v), 0, 0)^T$ and therefore $b_2(z) \equiv 0$. Concerning hypothesis (c), consider first the case $\sigma < \sigma_1$, i.e. the inequality applies in (2.53).

Then the subset (2.63) is

$$R = \left\{ z \in R^3_2 \mid y = 0, \quad x = x^* \right\} .$$

Now we look for the largest invariant subset M within R.

Since $x = x^*, y = 0$ for all t, $\left.\dfrac{dx}{dt}\right|_R = 0$, and from the first of equation (2.51) we get

$$v\,|_R = \frac{r-k}{C-\dfrac{r}{x^*}} \quad \text{where} \quad x^* = \frac{\beta+k+\sigma}{C} \quad .$$

Therefore, we obtain $v\,|_R = \left[\dfrac{(r-k)}{(\beta+k+\sigma-r)}\right] x^*$, i.e. $v\,|_R \equiv v^*$. Thus the largest invariant set within R is

$$z^* = \left(x^* = \frac{\beta+k+\sigma}{C}, \quad y^* = 0, \quad v^* = \frac{r-k}{\beta+k+\sigma-r}x^*\right)^T .$$

When $\sigma = \sigma_1$, then equality applies in (2.53), and (2.63) becomes

$$R = \left\{z \in R_2^3 \mid x = x^*\right\} .$$

In this case, we have already proven that $M \equiv \{z^*\}$. Hence hypothesis (c) is satisfied. Then by Theorem 2.6 the partially feasible equilibrium (2.55) is globally asymptotically stable with respect to R_2^3.

If $r < \beta + k$ and $\sigma \geq \sigma_2$, then the partially feasible equilibrium (2.57) occurs. This equilibrium belongs to

$$R_3^3 = \left\{z \in \mathbb{R}_+^3 \mid z_i > 0, \quad i = 1, 2; \quad z_3 \geq 0\right\} .$$

Hypothesis (a) of Theorem 2.6 requires

$$-(\beta+k+\sigma) + Cx^* + CSy^* \leq 0 \;, \tag{2.68}$$

from which, by taking into account (2.57), we obtain

$$1 - \frac{S(r-k)}{\sigma} \geq \frac{r}{\beta+k} \quad . \tag{2.69}$$

This inequality is satisfied in the whole range of existence of the equilibrium (2.57), i.e. for all $\sigma \geq \sigma_2$.

When $\sigma = \sigma_2$, the equality applies in (2.69). Hypothesis (b) of Theorem 2.6 is obviously satisfied. Concerning hypothesis (c), at first we consider the case in which $\sigma > \sigma_2$. Therefore, the inequality applies in (2.68) and the subset (2.63) of R_3^3 is

$$R = \left\{ z \in R_3^3 \mid v = 0, x = x^* \right\}.$$

From (2.57), we are ready to prove that $M \equiv \{z^*\}$. When $\sigma = \sigma_2$, R becomes

$$R = \left\{ z \in R_3^3 \mid z = x^* \right\},$$

and we have already proven that $M \equiv \{z^*\}$. Hypothesis (c) is satisfied. Also, in this case Theorem 2.6 assures the global asymptotic stability of the partially feasible equilibrium (2.57) with respect to R_3^3.

Extensions of this model, which have raised further open mathematical problems, are due to Levin [149, 150].

2.3.2.2. An SIS model with vital dynamics

Provided that $r > b, \quad \theta > r - b$, system (2.59) has the feasible equilibrium $z^* \in \mathbb{R}_+^{2*}$:

$$S^* = \frac{\theta + b + \mu}{\rho}, \quad I^* = \frac{r - b}{\theta + b - r} S^*. \tag{2.70}$$

When $r \leq b$, or $r > \theta + b$, the equilibrium (2.70) is not feasible and the only equilibrium of (2.59) is the origin.

Here $b(z) \equiv Bz = ((\mu + r) I, 0)^T$. When z^* is a feasible equilibrium the matrix $\tilde{A} = A + diag\left(z^{*-1}\right) B$ is given by

$$\tilde{A} = \begin{pmatrix} 0 & -\left(\rho - \dfrac{\mu + r}{S^*}\right) \\ \rho & 0 \end{pmatrix}$$

Since $S^* = \dfrac{(\theta + b + \mu)}{\rho}$, provided that $\theta > r - b$ the matrix $\tilde{A}$ is skew-symmetrizable. Because $b_1(z) \geq 0$, the graph associated with $\tilde{A}$ is •—○, and by Corollary 2.7 the global asymptotic stability of z^* with respect to $\mathbb{R}_+^2$ follows.

When $r \leq b, \quad r > \theta + b \quad$ Theorem 2.6 cannot be applied to study attractivity of the origin because hypothesis (b) is violated.

2.3.2.3. An SIRS model with vital dynamics in a population with varying size [44]

As a generalization of the model discussed in Sect. 2.1.2 and Sect. 2.3.1.1.2, in [44] Busenberg and van den Driessche propose the following SIRS model

$$
\begin{cases}
\dfrac{dS}{dt} = bN - dS - \dfrac{\lambda}{N} IS + eR \\
\dfrac{dI}{dt} = -(d + \epsilon + c)I + \dfrac{\lambda}{N} IS \\
\dfrac{dR}{dt} = -(d + \delta + f)R + cI
\end{cases}
\tag{2.71}
$$

for $t > 0$, subject to suitable initial conditions.

In this case the evolution equation for the total population N is the following one,

$$
\frac{dN}{dt} = (b - d)N - \epsilon I - \delta R \,, \qquad t > 0 \ . \tag{2.72}
$$

We may notice that whenever $b \neq d$, N is a dynamical variable. It is then relevant to take it into explicit account in the force of infection.

If we take into account the discussion in [110] and [118], we may realize that also model (8)-(10) in [6] should be rewritten as (2.71).

The biological meaning of the parameters in (2.71) is the following :

$b =$ per capita birth rate
$d =$ per capita disease free death rate
$\epsilon =$ excess per capita death rate of infected individuals
$\delta =$ excess per capita death rate of recovered individuals
$c =$ per capita recovery rate of infected individuals
$f =$ per capita loss of immunity rate of recovered individuals
$\lambda =$ effective per capita contact rate of infective individuals with respect to other individuals.

Clearly (2.72) implies that for $b \leq d$, $N(t)$ will tend to zero so that the only possible asymptotic state for (S, I, R) is $(0, 0, 0)$.

On the other hand, for $b > d$, N may become unbounded, and the previous methods cannot directly be applied. We shall then follow the approach proposed in [44].

As usual, we may refer to the fractions

$$s(t) = \frac{S(t)}{N(t)} \ ; \quad i(t) = \frac{I(t)}{N(t)} \ ; \quad r(t) = \frac{R(t)}{N(t)} \ , \qquad t \geq 0 \tag{2.73}$$

so that

$$s(t) + i(t) + r(t) = 1 \ , \qquad t \geq 0 \ . \tag{2.74}$$

But, being $N(t)$ a dynamical variable, going from the evolution equations (2.71) for S, I, R to the evolution equations for s, i, r we need to take (2.72) into account; we have then

$$\begin{cases} \dfrac{ds}{dt} = b - bs + fr - (\lambda - \epsilon)si + \delta sr \\ \dfrac{di}{dt} = -(b + c + \epsilon)i + \lambda si + \epsilon i^2 + \delta ir \\ \dfrac{dr}{dt} = -(b + f + \delta)r + ci + \epsilon ir + \delta r^2 \end{cases} \tag{2.75}$$

for $t > 0$.

The feasibility region of system (2.75) is now

$$\mathcal{D} := \{(s, i, r)^T \in \mathbb{R}^3_+ \ | \ s + i + r = 1\} \ , \tag{2.76}$$

and it is not difficult to show that it is an invariant region for (2.75).

The trivial equilibrium $(1, 0, 0)^T$ (disease free equilibrium) always exists; we shall define

$$\mathcal{D}_o := \mathcal{D} - \{(1, 0, 0)^T\} \ . \tag{2.77}$$

Our interest is to give conditions for the existence and stability of nontrivial endemic states $z^* := (s^*, i^*, r^*)^T$ such that $i^* > 0$.

This is the content of the main theorem proven in [44]. The authors make use of the following "threshold parameters"

$$R_o := \frac{\lambda}{b+c+\epsilon} \tag{2.78}$$

$$R_1 := \begin{cases} \dfrac{b}{d}, & \text{if} \quad R_o \leq 1 \\ \dfrac{b}{d+\epsilon i^* + \delta r^*}, & \text{if} \quad R_o > 1 \end{cases} \tag{2.79}$$

$$R_2 := \begin{cases} \dfrac{\lambda}{c+d+\epsilon}, & \text{if} \quad R_o \leq 1 \\ \dfrac{\lambda s^*}{c+d+\epsilon}, & \text{if} \quad R_o > 1 \ . \end{cases} \tag{2.80}$$

Theorem 2.8. [44] *Let $b, c > 0$, and all other parameters be non negative.*

a) *If $R_o \leq 1$ then $(1,0,0)^T$ is GAS in $\mathcal{D}$*
   If $R_o > 1$ then $(1,0,0)^T$ is unstable
b) *If $R_o > 1$ then a unique nontrivial endemic state exists $(s^*, i^*, r^*)^T$ in $\mathring{\mathcal{D}}$ which is GAS in $\mathring{\mathcal{D}}$.*

Proof. It is an obvious consequence of (2.75) that the trivial solution $z^o := (1,0,0)^T$ always exists. The local stability of z^o for system (2.75) is governed by the Jacobi matrix (let $\gamma = b + c + \epsilon$)

$$J(z^o) = \begin{pmatrix} -b & -\lambda+\epsilon & f+\delta \\ 0 & \lambda-\gamma & 0 \\ 0 & c & -(b+f+\delta) \end{pmatrix} \tag{2.81}$$

whose eigenvalues are

$$(\lambda_1, \lambda_2, \lambda_3) = (-b, \gamma(R_o - 1), -(b+f+\delta)) \ . \tag{2.82}$$

Hence, if $R_o < 1$ all eigenvalues are negative and z^o is LAS. On the other hand if $R_o > 1$, $\lambda_2 > 0$ and z^o is unstable.

It can be easily seen that if $R_o \leq 1$ no nontrivial endemic state $z^* \in \mathcal{D}_o$ may exist.

By using the relation $s = 1 - i - r$ we may refer to the reduced system

$$\begin{cases} \dfrac{di}{dt} = \gamma(R_o - 1)i - (R_o\gamma - \epsilon)i^2 - (R_o\gamma - \delta)ir \\ \dfrac{dr}{dt} = -(b + f + \delta)r + ci + \epsilon ir + \delta r^2 \end{cases} \tag{2.83}$$

whose admissible region is

$$\mathcal{D}_1 := \{(i, r)^T \in \mathbb{R}^2_+ \mid i + r \leq 1\} \tag{2.84}$$

For the planar system (2.83) $\mathcal{D}_1$ is a bounded invariant region which cannot contain any other equilibrium point than $(0,0)^T$.

On the other hand $(0,0)^T$ is LAS in $\mathcal{D}$. Suppose it is not GAS, then for an initial condition outside a suitably chosen neighborhood of $(0,0)^T$, the corresponding orbit should remain in a bounded region which does not contain equilibrium points. By the Poincaré-Bendixon theorem, this orbit should spiral into a periodic solution of system (2.83). But in [44] it is proven that system (2.75) has no periodic solutions, nor homoclinic loops in $\mathcal{D}$, so this will be the case for system (2.83) in $\mathcal{D}_1$, and this leads to a contradiction.

The same holds for $R_o = 1$, so that part a) of the theorem is completely proven.

As far as part b) is concerned, from system (2.83) we obtain that a nontrivial equilibrium solution ($i^* > 0$) must satisfy

$$\begin{cases} \gamma(1 - R_o) + (\lambda - \epsilon)i + (\lambda - \delta)r = 0 \\ -(b + f + \delta)r + ci + \epsilon ir + \delta r^2 = 0 \end{cases} \tag{2.85}$$

which is proven to have a unique nontrivial solution $(i^*, r^*)^T \in \overset{\circ}{\mathcal{D}}_1$.

The local stability of this equilibrium is governed by the matrix

$$J(i^*, r^*) = \begin{pmatrix} -(R_o\gamma - \epsilon)i^* & -(R_o\gamma - \delta)i^* \\ c + \epsilon r^* & -(b + f + \delta)\epsilon i^* + 2\delta r^* \end{pmatrix}$$

By the Routh-Hurwitz criterion it is not difficult to show that $(i^*, r^*)^T$ is LAS.

Again the Poincaré-Bendixon theory, together with the nonexistence of periodic orbits for system (2.83) implies the GAS of $(i^*, r^*)^T$ in $\mathring{\mathcal{D}}_1$, and hence of $(s^*, i^*, r^*)^T$ in $\mathring{\mathcal{D}}$.

Actually for the case $\delta = 0$ we may still refer to the general structure discussed in Sect. 2.3. In fact if one considers system (2.83), it can be always reduced to the form (2.18) if we define $z = (i, r)^T$,

$$A = \begin{pmatrix} \epsilon - \lambda & -\lambda \\ \epsilon + c/r^* & 0 \end{pmatrix}, \quad e = \begin{pmatrix} \gamma(R_o - 1) \\ -(b + f) \end{pmatrix}$$

and

$$B = \begin{pmatrix} 0 & 0 \\ c & 0 \end{pmatrix}.$$

Suppose that a $z^* \in \mathring{\mathcal{D}}_1$ exists ($\mathring{\mathcal{D}}_1$ is invariant for our system), we may define $\tilde{A}$ as in (2.35) to obtain

$$\tilde{A} := A + diag(z^{*-1})B = \begin{pmatrix} \epsilon - \lambda & -\lambda \\ \epsilon + c/r^* & 0 \end{pmatrix}$$

which is sign skew-symmetric in the case $\epsilon < \lambda$. It is then possible to find a $W = diag(w_1, w_2)$, $w_i > 0$ such that $W\tilde{A}$ is essentially skew-symmetric; in fact its diagonal terms are nonpositive; we are in case (A) of Sect. 2.3. The associated graph is ∘—•, and Theorem 2.3 applies to show GAS of z^* in $\mathring{\mathcal{D}}_1$.

Altogether it has been completely proven that, for this model too, the "classical" conjecture according to which a nontrivial endemic state z^* whenever it exists is GAS, still holds.

The same conjecture was made in [166] about an AIDS model with excess death rate of newborns due to vertical transmission.

We shall analyze this model in the next section.

As far as the behavior of $N(t)$ is concerned, the following lemma holds.

Lemma 2.9. [44] *Under the assumptions of Theorem 2.8, the total population $N(t)$ for system (2.71) has the following asymptotic behavior :*

a) *if $R_1 < 1$ then* $N(t) \downarrow 0$, *as* $t \to \infty$
   if $R_1 > 1$ then $N(t) \uparrow +\infty$, *as* $t \to \infty$
b) *the asymptotic rate of decrease or increase is $d(R_1 - 1)$ when $R_o < 1$, and the asymptotic rate of increase is $(d + \epsilon i^* + \delta r^*)(R_1 - 1)$ when $R_o > 1$.*

The behavior of $(S(t), I(t), R(t))$ is a consequence of the following lemma.

Lemma 2.10. [44] *The total number of infectives $I(t)$ for the model (2.71) decreases to zero if $R_2 < 1$ and increases to infinity if $R_2 > 1$. The asymptotic rate of decrease or increase is given by* $(c + d + \epsilon)\,(R_2 - 1)$.

The complete pattern of the asymptotic behavior of system (2.71) is given in Table 2.1 .

Table 2.1. Threshold criteria and asymptotic behavior [44]

R_o	R_1	R_2	$N \to$	$(s,i,r) \to$	$(S,I,R) \to$
≤ 1	< 1	$< 1^a$	0	$(1,0,0)$	$(0,0,0)$
> 1	< 1	$< 1^a$	0	(s^*,i^*,r^*)	$(0,0,0)$
≤ 1	> 1	< 1	∞	$(1,0,0)$	$(\infty,0,0)$
≤ 1	> 1	> 1	∞	$(1,0,0)$	(∞,∞,∞)
> 1	> 1	$> 1^a$	∞	(s^*,i^*,r^*)	(∞,∞,∞)

[a] Given R_o, R_1, this condition is automatically satisfied

2.3.2.4. An SIR model with vertical transmission and varying population. A model for AIDS [166]

A basic model to describe demographic consequences induced by an epidemic has been recently proposed by Anderson, May and McLean [166], in connection with the mathematical modelling of HIV/AIDS epidemics (see also Sect. 3.4).

With our notation, the model is based on the following set of ODE's

$$\text{(2.86)} \qquad \begin{cases} \dfrac{dS}{dt} = b[N - (1-\alpha)I] - dS - \dfrac{\lambda}{N}\,IS \\ \dfrac{dI}{dt} = \dfrac{\lambda}{N}\,IS - (c+d+\epsilon)I \\ \dfrac{dR}{dt} = cI - dR \end{cases}$$

The total population $N(t)$ will then be a dynamical variable subject to the following evolution equation

$$\text{(2.87)} \qquad \frac{dN}{dt} = b(N - (1-\alpha)I) - dN - \epsilon I$$

System (2.86) can be seen as a modification of system (2.71) with $e = \delta = 0$ (no loss of immunity after the disease, no excess death rate in the recovered class), and with a total birth rate reduced by the quantity $(1-\alpha)I$, $\alpha \in [0,1]$, due to vertical transmission of the disease; a fraction α of newborns from infected mothers may die at birth.

By introducing , as in Sect. 2.3.2.3, the fractions

$$s(t) = \frac{S(t)}{N(t)} \ , \quad i(t) = \frac{I(t)}{N(t)} \ , \quad r(t) = \frac{R(t)}{N(t)}, \qquad t \geq 0 \ ,$$

we have that

$$s(t) + i(t) + r(t) = 1 \ , \qquad t \geq 0 \tag{2.88}$$

so that we may reduce our analysis to the quantities $i(t)$, $r(t)$ in addition to $N(t)$.

The evolution equations for i and r are given by

$$\begin{cases} \dfrac{di}{dt} = -(b + c + \epsilon - \lambda)i - (\lambda - \epsilon - b(1-\alpha))i^2 - \lambda ir \\ \dfrac{dr}{dt} = -br + ci + (\epsilon + b(1-\alpha))ir \end{cases} \tag{2.89}$$

for $t > 0$, while the equation for N is given by

$$\frac{dN}{dt} = (b - d)N - [b(1-\alpha) + \epsilon]I \ , \qquad t > 0 \ . \tag{2.90}$$

System (2.89) can be written in the form (2.18) if we define $z := (i, r)^T$, and

$$A = \begin{pmatrix} -\lambda + \epsilon + b(1-\alpha) & -\lambda \\ \epsilon + b(1-\alpha) & 0 \end{pmatrix}, \quad e = \begin{pmatrix} -(b + c + \epsilon - \lambda) \\ -b \end{pmatrix}$$

$$B = \begin{pmatrix} 0 & 0 \\ c & 0 \end{pmatrix}$$

The admissible space for system (2.89) is again

$$\mathcal{D}_1 := \left\{ (r,i)^T \in \mathbb{R}^2_+ \ \mid \ r+i \le 1 \right\}.$$

The trivial solution $(r,i)^T = (0,0)^T$ always exists, and it is shown in [166] that a nontrivial endemic state $z^* \in \mathring{\mathcal{D}}_1$ exists for system (2.89) provided $R_o := \dfrac{\lambda}{c+\epsilon} > 1$ (again $\mathring{\mathcal{D}}_1$ is invariant for our system).

We may define $\tilde{A}$ as in (2.35) to obtain

$$\tilde{A} := A + diag({z^*}^{-1})B = \begin{pmatrix} -\lambda + \epsilon + b(1-\alpha) & -\lambda \\ \epsilon + b(1-\alpha) + c/r^* & 0 \end{pmatrix};$$

for $\lambda > \epsilon + b(1-\alpha)$ it is sign skew-symmetric. It is then possible to find a $W = diag(w_1, w_2)$, $w_i > 0$ such that $W\tilde{A}$ is essentially skew-symmetric; in fact its diagonal terms are nonpositive; we are in case (A) of Sect. 2.3. The associated graph is ○—●, and Theorem 2.3 applies to show GAS of z^* in $\mathring{\mathcal{D}}_1$.

As far as the asymptotic behavior of $N(t)$, and of the absolute values of $(S(t), I(t), R(t))$ we refer to Table 2.1 in Sect. 2.3.2.3.

We may like to point out that model (2.86) includes, for $\alpha = 1$, the case with no vertical transmission, and corresponds to the model proposed by Anderson and May [6] for host-microparasite associations (see also [163]).

On the other hand , for $\alpha = 0$, we have complete vertical transmission.

Other models of this kind have been considered in [35, 183]. In these papers the force of infection has a more general dependence upon the total population N, so that the transformation (2.73) does not eliminate the dependence upon N; specific analysis is needed in that case. As an example we have included an outline of the results obtained in [183] in Sect. 3.3. For the other cases we refer to the literature.

Appendix A. Ordinary differential equations

A.1. The initial value problem for systems of ODE 's

We shall consider here dynamical systems defined by systems of ordinary differential equations of the form

$$\frac{dz}{dt} = f(t,z) \ , \tag{A.1}$$

with $f \in C(J \times D, \mathbb{R}^n)$, a continuous function of the variables $(t,z) \in J \times D$, where $J \subset \mathbb{R}$ is an open interval, and $D \subset \mathbb{R}^n$ is an open subset.

A function $z : J_z \to D$ is called a solution of the differential equation (A.1) (in J_z) if the following holds:

(i) $J_z \subset J$ is a nonempty interval

(ii) $z \in C^1(J_z, D)$, is continuous in J_z up to its first derivative

(iii) for any $t \in J_z$, $\frac{dz}{dt}(t) = f(t, z(t))$.

Remark. A function $z : J_z \to D$ is a solution of the differential equation (A.1) in J_z iff $z \in C(J_z, D)$ and for any $t_0 \in J_z$:

$$z(t) = z(t_0) + \int_{t_0}^{t} f(s, z(s))\, ds \ , \qquad t \in J_z \ . \tag{A.2}$$

We shall say that the function $f : J \times D \to \mathbb{R}^n$ satisfies the "Lipschitz condition" with respect to z if a constant $L > 0$ exists such that

$$\|f(t,z_1) - f(t,z_2)\| \leq L\,\|z_1 - z_2\|$$

for $t \in J$ and $z_1, z_2 \in D$. L is called the "Lipschitz constant".

Given $t_0 \in J$ and $z_0 \in D$ we say that f satisfies a "local Lipschitz condition" in (t_0, z_0) with respect to z if a, d, $L > 0$ constants exist such that

$$\|f(t,z_1) - f(t,z_2)\| \leq L\,\|z_1 - z_2\|$$

for $t \in [t_0 - a, t_0 + a]$, and $z_1, z_2 \in \overline{B}_d(z_0) := \{z \in \mathbb{R}^n \mid \|z - z_0\| \leq d\}$ (clearly a, d, L all depend upon (t_0, z_0)).

Remark. Note that f will always satisfy a local Lipschitz condition at any point of a domain $J \times D \subset \mathbb{R} \times \mathbb{R}^n$ whenever f and its partial derivatives $\partial f/\partial z_i$, $i = 1, \cdots, n$ are continuous in $J \times D$.

Theorem A.1. [85, 216] *Let* $f \in C(J \times D, \mathbb{R}^n)$, *be locally Lipschitzian in* $(t_0, z_0) \in J \times D$. *Then a* $\Delta > 0$ *exists such that the differential equation (A.1) admits a unique solution* $z \in C^1((t_0 - \Delta, t_0 + \Delta)\,,\, D)$ *satisfying*

$$(A.1o) \qquad z(t_0) = z_0 \quad .$$

Remark. It can be further shown that, with the above notations,

$$\Delta = \min\left\{a,\ \frac{d}{M}\right\}$$

where

$$M := \sup_{\substack{|t-t_0|\le a\\ \|z-z_0\|\le d}} |f(t,z)|$$

The possibility of (global) existence of the solution of problem (A.1), (A.1o) in the whole "time" interval $J \subset \mathbb{R}$ is left to the following theorem.

Theorem A.2. [3] *Let* $f \in C(J \times D, \mathbb{R}^n)$ *be locally Lipschitzian in* $J \times D$. *Then for any* $(t_0, z_0) \in J \times D$ *there exists a unique nonextendible solution*

$$z(\cdot\,;\, t_0, z_0) \ :\ J(t_0, z_0) \longrightarrow D$$

of the initial value problem (A.1), (A.1o). The maximal interval of existence $J(t_0, z_0)$ is open:

$$J(t_0, z_0) := (\tau^-(t_0, z_0), \tau^+(t_0, z_0))$$

and we either have

$$\tau^- := \tau^-(t_0, z_0) = \inf J\ , \qquad \text{resp.} \qquad \tau^+ := \tau^+(t_0, z_0) = \sup J\ ,$$

or

$$\lim_{t \to \tau^{\pm}} \min\left\{dist(z(t\,;\, t_0, z_0),\, \partial D)\ ,\ |z(t\,;\, t_0, z_0)|^{-1}\right\} = 0\ .$$

[Here of course we mean the limit as $t \to \tau^-$ when $\tau^- > \inf J$, and $t \to \tau^+$ when $\tau^+ < \sup J$, respectively. Moreover we use the convention $dist(x, \emptyset) = \infty$].

The above result can be expressed somewhat imprecisely as : either the solution exists for all time, or it approaches the boundary of D (where the boundary of D includes the "point at infinity" ($\|z\| = \infty$)).

A slight refinement of the above result is given by the following corollary.

Corollary A.3. [223] *Under the same assumption of Theorem A.2, assume further that given* $(t_0, z_0) \in J \times \mathbb{R}^n$ *there is a function* $m \in C\left([t_0, \sup J)\,,\, \mathbb{R}_+\right)$ *such that, for any* $t \in [t_0, \tau^+(t_0, z_0))$ *:*

$$\|z(t\,;\, t_0, z_0)\| \le m(t)\ ,$$

then

$$\tau^{+}(t_0, z_0) = \sup J \ .$$

A useful criterion, implying the boundedness of all solutions of the differential equation (A.1) (for finite time), is given by the following proposition.

Proposition A.4. [3] *Assume there exist* $\alpha, \beta \in C(J, \mathbb{R}_+) \cap L^1(J, \mathbb{R})$ *such that*

$$\|f(t,z)\| \le \alpha(t)\,\|z\| + \beta(t) \ , \qquad (t,z) \in J \times D \ .$$

Then for any $(t_0, z_0) \in J \times D$, we have $\tau^{+}(t_0, z_0) = \sup J$.

A particular case of Proposition A.4 is given by linear systems of differential equations.

Theorem A.5. [3, 223] *Let* $A \in C\left(J, \mathbb{R}^{n\times n}\right)$, *and* $b \in C(J, \mathbb{R}^n)$. *Then the linear (nonhomogeneous) IVP*

$$(A.3) \qquad \dot{z} = A(t)\,z + b(t) \quad ; \quad z(t_0) = z_0$$

has a unique global solution for every $(t_0, z_0) \in J \times \mathbb{R}^n$.

For any choice of $(t_0, z_0) \in J \times D$, Theorem A.2 defines a solution $\{z(t\,;\,t_0, z_0)\ ,\ t \in (\tau^{-}(t_0, z_0)\ ,\ \tau^{+}(t_0, z_0))\}$.

Now $z = z(t\,;\,t_0, z_0)$ may be seen as a function of the $2+n$ variables (t, t_0, z_0) ; its domain of definition is

$$\Omega := \bigcup_{(t_0,z_0)\in J\times D} I(t_0, z_0) \subset \mathbb{R}\times\mathbb{R}\times\mathbb{R}^n$$

where

$$I(t_0, z_0) := \left\{(t, t_0, z_0) \mid \tau^{-}(t_0, z_0) < t < \tau^{+}(t_0, z_0)\right\} \subset \mathbb{R}\times\mathbb{R}\times\mathbb{R}^n \ .$$

Theorem A.6. [223] *The domain of definition* Ω *of the (maximal) solution function* $z(t\,;\,t_0, z_0)$ *of system (A.1), (A.1o) is an open set in* $\mathbb{R}\times\mathbb{R}\times\mathbb{R}^n$ *and* z *is continuous on* Ω.

Further regularity of the solution function $z(t\,;\,t_0, z_0)$ is induced by the regularity of f [3, 223].

For any $(t_0, z_0) \in J \times D$, the set of points in $\mathbb{R}^{n+1}$ given by

$$\{(t\ ,\ z(t\,;\,t_0, z_0)) \mid t \in I(t_0, z_0)\}$$

will be called the "trajectory" through (t_0, z_0).

The "path" or "orbit" of a trajectory is the projection of the trajectory into $\mathbb{R}^n$, the space of dependent variables in (A.1). The space of dependent variables is usually called the "state space" or "phase space" [104].

Suppose, for simplicity, that system (A.1), (A.1o) possesses a forward-unique solution $z(\cdot) = z(\cdot\,; t_0, z_0)$ defined on the forward interval $J(t_0) = [t_0, +\infty)$, for every $(t_0, z_0) \in \mathbb{R} \times D$. Then, defining $\varphi(\tau, t_0, z_0) := z(\tau + t_0, t_0, z_0)$, $\tau \in \mathbb{R}_+$, we see that the mapping $\varphi : \mathbb{R}_+ \times \mathbb{R} \times D \longrightarrow \mathbb{R}^n$ satisfies

(i) $\varphi(0\,; t_0, z_0) = z_0$, for any $(t_0, z_0) \in \mathbb{R} \times D$

(ii) $\varphi(\tau+s\,; t_0, z_0) = \varphi(\tau\,; s+t_0, \varphi(s\,; t_0, z_0))$, for any $\tau, s \in \mathbb{R}_+$, $(t_0, z_0) \in \mathbb{R} \times D$

(iii) φ is continuous on $\mathbb{R}_+ \times \mathbb{R} \times D$.

Because of (i), (ii), (iii), we say that system (A.1) generates a "process" φ [215, 223].

A.1.1. Autonomous systems

In this section we refer to the case in which the function f of system (A.1) does not depend explicitly upon t; namely we consider the "autonomous" system

$$(A.4) \qquad \frac{dz}{dt} = f(z) \ .$$

Now $f \in C(D)$, a continuous function of $z \in D$, with D an open subset of $\mathbb{R}^n$.

A basic property of autonomous systems is the following : if $z(t)$ is a solution of (A.4) on an interval $(a, b) \subset \mathbb{R}$, then, for any real number τ, the function $z(t - \tau)$ is a solution of (A.4) on the interval $(a + \tau, b + \tau)$. This is clear since the differential equation remains unchanged by a translation of the independent variable.

In particular we have

$$z(t\,; t_0, z_0) = z(t - t_0\,; 0, z_0)$$

for any $t \in J(t_0, z_0)$.

Moreover

$$J(t_0, z_0) = J(0, z_0) + t_0$$

for any $(t_0, z_0) \in J \times D$ (this means that $J(t_0, z_0)$ is obtained by shifting the interval $J(0, z_0)$ of the quantity t_0).

Thus the family of solutions of (A.4) subject to the initial condition

$$(A.4o) \qquad z(0) = z_0$$

completely defines the set of solutions of (A.4) subject to initial conditions of the more general form (A.1o).

For $z_0 \in D$ we now set

$$\begin{aligned} \tau^{\pm}(z_0) &:= \tau^{\pm}(0, z_0) \\ J(z_0) &:= J(0, z_0) = (\tau^-(z_0), \tau^+(z_0)) \end{aligned}$$

and we define

$$\varphi(t, z_0) := z(t\,;\, 0, z_0)$$

We now let

$$\Omega := \left\{(t, z) \in \mathbb{R} \times D \mid \tau^-(z) < t < \tau^+(z)\right\} \ .$$

By specializing Theorem A.6 to the autonomous case, Ω is an open subset of $\mathbb{R}^{n+1}$, and φ is continuous on Ω.

Moreover

(i) $\varphi(0; z_0) = z_0$, for any $z_0 \in D$

(ii) $\varphi(t + s\,;\, z_0) = \varphi(t\,;\, \varphi(s, z_0))$, for any $z_0 \in D$ and for all $s \in J(z_0)$, and $t \in J(\varphi(s\,;\, z_0))$.

Because of properties (i) and (ii) we say that system (A.4) generates a "(local) flow" or a "(local) dynamical system" on $D \subset \mathbb{R}^n$.

If $\Omega = \mathbb{R} \times D$, that is $\tau^-(z_0) = -\infty$ and $\tau^+(z_0) = +\infty$ for all $z_0 \in D$, then φ is called a "global flow" or a "global dynamical system".

For any $z_0 \in D$ we call

$$\begin{aligned} \Gamma_+(z_0) &:= \left\{\varphi(t\,;\, z_0) \mid t \in \left[0, \tau^+(z_0)\right)\right\} \ , \\ \Gamma_-(z_0) &:= \left\{\varphi(t\,;\, z_0) \mid t \in \left(\tau^-(z_0), 0\right]\right\} \ , \\ \Gamma(z_0) &:= \{\varphi(t\,;\, z_0) \mid t \in J(z_0)\} \ , \end{aligned}$$

the "positive semiorbit", the "negative semiorbit", the "orbit" through z_0 respectively.

Note that each point of D belongs exactly to one orbit.

In the context of autonomous systems the family of vectors $\{f(z)\ ,\ z \in D\}$ or better the family $\{(z, f(z))\ ,\ z \in D\}$ is called the "vector field" defining system (A.4).

A point $z^* \in D$ is called an "equilibrium point" or "critical point" or "singularity point" or "stationary point" of an n-dimensional vector field $f \in C^1(D, \mathbb{R}^n)$ if

$$f(z^*) = 0 \ .$$

If $z^* \in D$ is an equilibrium point then clearly

$$z(t) = z^* \ , \qquad t \in \mathbb{R}$$

is a (global) solution of system (A.4).

The trajectory of the critical point z^* is the line in $\mathbb{R}^{n+1}$ given by $\mathbb{R} \times \{z^*\}$. The orbit of a critical point z^* is $\Gamma(z^*) = \{z^*\} \subset \mathbb{R}^n$.

With the notations introduced above, the following proposition holds true.

Proposition A.7. [223] *Let $z_0 \in D$; if $\varphi(t\,;\,z_0)$ approaches a point a in D as $t \to \tau^+(z_0)$ then $\tau^+(z_0) = +\infty$ and a is a critical point.*

Let C_ψ denote a curve in $\mathbb{R}^n$ parametrized by a continuous function $\psi \in C\left([a,b], \mathbb{R}^n\right)$. If C_ψ does not intersect itself, that is, if ψ is one-to-one (injective) then it is called a "simple curve" or "arc".

If $\psi(a) = \psi(b)$, but still $\psi(t_1) \neq \psi(t_2)$ for every $t_1 \neq t_2$ in $[a,b)$, then C_ψ is called a "simple closed curve" or "Jordan curve".

Theorem A.8. [104, 223] *Let C denote the orbit of the autonomous system (A.4). The following statements are equivalent*

(i) C intersects itself in at least one point.
(ii) C is the orbit of a periodic solution.
(iii) C is a simple, closed (Jordan) curve.

Because of Theorem A.8 an orbit which is a Jordan curve is sometimes called a "periodic orbit".

Note that if Γ is a closed orbit of (A.4) and $z_0 \in \Gamma$, there is a $\tau \neq 0$ such that $\varphi(\tau\,;\,z_0) = z_0 = \varphi(0\,;\,z_0)$. By uniqueness of solutions $\varphi(t+\tau\,;\,z_0) = \varphi(t\,;\,z_0)$ for all $t \in \mathbb{R}$, which says that $\{\varphi(t\,;\,z_0)\ ,\ t \in \mathbb{R}\}$ has period τ.

If Γ is a closed path, not reducing to an equilibrium point, there exists a smallest positive period $T > 0$, which is called the "minimal" or "fundamental period" of $\varphi(t\,;\,z_0)$ for any $z_0 \in \Gamma$; i.e., any $z_0 \in \Gamma$ is a fixed point of the map $\varphi(T\,;\,\cdot) : D \longrightarrow D$.

The map $\varphi(T\,;\,\cdot)$ is usually called the "monodromy operator" of our dynamical system.

It can be shown [3] that there exist exactly three types of orbits for the autonomous system (A.4) in $\mathbb{R}^n$: (i) stationary points; (ii) periodic orbits; (iii) "open" simple curves. Clearly in cases (i) and (ii) $\tau^+(z_0) = +\infty$ and $\tau^-(z_0) = -\infty$, for any point z_0 of the orbit.

A.1.1.1. Autonomous systems. Limit sets, invariant sets

In this section we consider system (A.4) and assume that f satisfies enough conditions on D, an open subset of the space $\mathbb{R}^n$, to ensure that there exists a unique global solution $\{\varphi(t\,;\,z_0)\ ,\ t\in\mathbb{R}\}$ for any $z_0\in D$.

A point $p\in\mathbb{R}^n$ is called an "ω-limit point" of the solution $\varphi(t\,;\,z_0)$ iff there is a sequence $(t_k)_{k\in\mathbb{N}}$ of times such that

$$\begin{aligned}(i)&\quad \lim_{k\to\infty} t_k = +\infty\\ (ii)&\quad \lim_{k\to\infty}\varphi(t_k\,;\,z_0)=p\end{aligned}$$

Similarly a point $q\in\mathbb{R}^n$ is called an "α-limit point" of the solution $\varphi(t\,;\,z_0)$ iff there is a sequence of real numbers $(t_k)_{k\in\mathbb{N}}$ such that

$$\begin{aligned}(i)'&\quad \lim_{k\to\infty} t_k = -\infty\\ (ii)'&\quad \lim_{k\to\infty}\varphi(t_k\,;\,z_0)=q\ .\end{aligned}$$

The "ω-limit set" of an orbit Γ associated with the dynamical system φ is the set of all its ω-limit points

$$\omega(\Gamma) := \bigcap_{z_0\in\Gamma}\overline{\Gamma_+(z_0)}\ .$$

Similarly the "α-limit set" of an orbit Γ associated with the dynamical system φ is the set of all its α-limit points

$$\alpha(\Gamma) := \bigcap_{z_0\in\Gamma}\overline{\Gamma_-(z_0)}$$

A set $M\subset\mathbb{R}^n$ is called an "invariant set" of (A.4) if, for any $z_0\in M$, the solution $\{\varphi(t\,;\,z_0)\ ,\ t\in\mathbb{R}\}$ belongs to M :

$$\varphi(t\,;\,M)\subset M\ ,\quad \text{for any}\quad t\in\mathbb{R}\ .$$

Any orbit is obviously an invariant set of (A.4).

A set $M\subset\mathbb{R}^n$ is called "positively (negatively) invariant" if for each $z_0\in M$, $\{\varphi(t\,;\,z_0)\ ,\ t\in\mathbb{R}_+\}$ ($\{\varphi(t\,;\,z_0)\ ,\ t\in\mathbb{R}_-\}$) belongs to M.

Theorem A.9. [104] *The α- and ω-limit sets of an orbit Γ are closed and invariant. Furthermore if for some $z_0\in D$, $\Gamma_+(z_0)$ (resp. $\Gamma_-(z_0)$) is bounded, then $\omega(\Gamma(z_0))$ (resp. $\alpha(\Gamma(z_0))$) is nonempty, compact and connected. Moreover $dist(\varphi(t\,;\,z_0)\ ,\ \omega(\Gamma(z_0)))\longrightarrow 0\ ,\ $ as $t\to+\infty$ (resp. $dist(\varphi(t\,;\,z_0),$ $\alpha(\Gamma(z_0)))\longrightarrow 0\ ,\ $ as $t\to-\infty$).*

A.1.1.2. Two-dimensional autonomous systems

We specialize to the case of a two-dimensional autonomous system

$$(A.5) \qquad \begin{cases} \dfrac{dz_1}{dt} = f_1(z_1, z_2) \\ \dfrac{dz_2}{dt} = f_2(z_1, z_2) \ , \end{cases}$$

where $f := (f_1, f_2)$ is a real continuous vector function defined on a bounded open subset D of the real plane $\mathbb{R}^2$.

We assume further that for each real $t_0 \in \mathbb{R}$ and each point $z_0 \in D$ there exists a unique solution $\varphi(t\,;\,z_0)$ of (A.5) such that $\varphi(t_0\,;\,z_0) = z_0$.

The theory ensures that φ is a continuous function of (t_0, z_0) for all t for which φ is defined, and for all $z_0 \in D$.

For autonomous systems with phase space $D \subset \mathbb{R}^2$, it can be proved that every limit set is a critical point, a closed path, or a combination of solution paths and critical points joined together. In case $n = 2$ the phase space is often called the "Poincaré phase plane".

Theorem A.10. [223] *If the ω-limit set Ω for a solution of the system (A.5) contains a closed path C, then $\Omega = C$.*

Theorem A.11. [223] *If a path C of system (A.5) contains one of its own ω-limit points, then C is either a critical point or a closed path.*

Proposition A.12. *If Γ_+ and $\omega(\Gamma_+)$ have a regular point in common, then Γ_+ is a periodic orbit.*

It is clear that if the ω-limit set of a solution consists of precisely one closed path C, then the ω-limit set contains no critical point.

The converse of this statement is contained in the following

Theorem A.13. (Poincaré-Bendixson) [104] *If Γ_+ is a bounded positive semiorbit and $\omega(\Gamma_+)$ does not contain a critical point, then either*

(i) $\Gamma_+ = \omega(\Gamma_+)$

or

(ii) $\omega(\Gamma_+) = \overline{\Gamma_+} - \Gamma_+$

In either case the ω-limit set is a periodic orbit, and in the latter case it is referred to as a limit cycle.

Hence, a closed path which is a limit set of a path other than itself is called a "limit cycle".

If a closed path is a limit cycle, then an other path must approach it spirally.

Theorem A.14. [104] *A closed path of system (A.5) must have a critical point in its interior.*

Another important test for the non existence of periodic solutions is provided by the following

Theorem A.15. (Bendixson negative criterion) [210] *Let* f *in system (A.5) have continuous first partial derivatives on an open simply connected subset* $D \subset \mathbb{R}^2$. *System (A.5) cannot have periodic solutions in* D *if* $div f = \frac{\partial}{\partial x} f_1 + \frac{\partial}{\partial y} f_2$ *has the same sign throughout* D.

The Bendixson negative criterion can be extended in the following form.

Theorem A.16. (Bendixson-Dulac criterion) [216] *Under the same assumptions as in Theorem A.15, suppose further that there exists a continuously differentiable function* $\beta : D \longrightarrow \mathbb{R}$ *such that the function* $\frac{\partial}{\partial x}(\beta f_1) + \frac{\partial}{\partial y}(\beta f_2)$ *does not change sign in* D. *Then there are no periodic solutions of system (A.5) in the region* D.

A.2. Linear systems of ODE 's

A.2.1. General linear systems

Consider the linear system of $n \in \mathbb{N} - \{0\}$ first order equations

$$(A.6) \qquad \frac{d}{dt} z_j = \sum_{k=1}^{n} a_{jk}(t)\; z_k + b_j(t) \;, \qquad j = 1, \cdots, n$$

where the a_{jk} and b_j for $j, k = 1, \cdots, n$ are continuous real valued functions on an interval $J \subset \mathbb{R}$. In matrix notation, system (A.6) can be rewritten as

$$(A.7) \qquad \frac{dz}{dt} = A(t)\, z + b(t)$$

where $A(t) = (a_{jk}(t))\;,\;\; j, k = 1, \cdots, n$ and $b(t) = (b_1(t), \cdots, b_n(t))^T$.

Thanks to Theorem A.5, system (A.7) admits a unique global solution in J, subject to the initial condition

$$(A.7o) \qquad z(t_0) = z_0$$

for any choice of $(t_0, z_0) \in J \times \mathbb{R}^n$.

The basic characteristic property of linear systems of the form (A.7) is the so called "Principle of Superposition": If $z(t)$ is any solution of (A.7) corresponding to the "forcing term" $b(t)$, and $y(t)$ is a solution of (A.7) corresponding to the forcing term $h(t)$, then for any choice of real (or complex) numbers c and d, $c\, z(t) + d\, y(t)$ is a solution of (A.7) corresponding to the forcing term $c\, b(t) + d\, h(t)$.

In particular if $b = h\,,\;\; z(t) - y(t)$ is a solution of the homogeneous system

$$(A.8) \qquad \frac{dz}{dt} = A(t)\, z \;.$$

Thus if $z(t)$ is a solution of (A.8) and $z_p(t)$ is a solution of (A.7) then $z(t) + z_p(t)$ is again a solution of (A.7).

We may then confine our analysis in the search of the "general" solution of the homogeneous system (A.8).

Theorem A.17. [104, 216] *Every linear combination of solutions of (A.8) is a solution of (A.8).*

Suppose now that we have n solution vectors $z^{(i)}(t)\;,\;\; i = 1, \cdots, n$ of (A.8) defined on $J \subset \mathbb{R}$.

We can form a matrix $X(t)$ whose columns are these solutions :

$$X(t) := \left[z^{(1)}(t), \cdots, z^{(n)}(t) \right] \;, \qquad t \in J \;.$$

Clearly, in J,

$$\dot{X}(t) = A(t)\, X(t) \ . \tag{A.9}$$

Furthermore, if $c \in \mathbb{R}^n$ is any constant vector, then $X(t)\, c$ is a solution of (A.8).

Lemma A.18. [104] *If $X(t)$ is a $n \times n$ matrix solution of (A.9), then either $detX(t) = 0$, for all $t \in J$, or $detX(t) \neq 0$ for all $t \in J$.*

An $n \times n$ matrix $X(t)$ solution of (A.9) such that $detX(t) \neq 0$ for all $t \in J$, will be called a "fundamental matrix solution" of system (A.7).

Theorem A.19. [104, 216] *If $X(t)$ is any fundamental matrix solution of (A.8) in $J \subset \mathbb{R}$, then every solution of (A.8) in J can be written as $X(t)\, c$ for an appropriate constant vector $c \in \mathbb{R}^n$.*

We shall say that $\{z(t;c) = X(t)\, c \ ; \ c \in \mathbb{R}^n\}$ is a "general integral" of system (A.8).

In order to obtain the solution passing through the point $(t_0, z_0) \in J \times \mathbb{R}^n$, we need to choose $c = X^{-1}(t_0)\, z_0$, so that we get

$$z(t\,;\, t_0, z_0) = X(t)\, X^{-1}(t_0)\, z_0 \ , \qquad t \in J \tag{A.10}$$

Remark. In order to obtain a fundamental matrix solution of system (A.8) it suffices to select n linearly independent initial vectors ${z_0}^{(i)}\ ,\ i = 1, \cdots, n$, and finding the corresponding n linearly independent solutions of system (A.8).

If we now go back to the nonhomogeneous system (A.7) we may state that if $z_p(t)$ is a particular solution of (A.7), the general solution of (A.7) is given by

$$\{z(t;c) = X(t)\, c + z_p(t) \ , \quad c \in \mathbb{R}^n\}$$

provided $X(t)$ is a fundamental matrix solution of (A.8).

Theorem A.20. [104] *If $X(t)$ is a fundamental matrix solution of (A.8) then every solution of (A.7) is given by the formula*

$$z(t) = X(t) \left[X^{-1}(\tau)\, z(\tau) + \int_\tau^t X^{-1}(s)\, b(s)\, ds \right]$$

for any choice of $\tau \in J$.

The above theorem (known as the "variation of constants formula") gives us in particular the solution passing through the point $(t_0, z_0) \in J \times \mathbb{R}^n$:

$$z(t\,;\, t_0, z_0) = X(t)\, X^{-1}(t_0)\, z_0 + \int_{t_0}^t X(t)\, X^{-1}(s)\, b(s)\, ds \tag{A.11}$$

Note that $X(t,t_0) := X(t)\,X^{-1}(t_0)$ is such that $X(t_0,t_0) = I$. It is the unique solution of (A.9) such that this happens. The matrix $X(t,t_0)$ is known as the "principal matrix solution" of (A.7) at initial time $t_0 \in J$.

It can be easily shown that

$$(A.12) \qquad X(t,\tau) = X(t,s)\,X(s,\tau)$$

for any choice of τ, s, t in J. Thus the variation of constants formula (A.11) can be rewritten as

$$(A.13) \qquad z(t\,;\,t_0,z_0) = X(t,t_0)\,z_0 + \int_{t_0}^{t} X(t,s)\,b(s)\,ds.$$

A.2.2. Linear systems with constant coefficients

In this section we consider the homogeneous equation

$$(A.14) \qquad \dot z = Az$$

where A is an $n \times n$ real constant matrix. In this case we may assume $J = \mathbb{R}$.

Since system (A.14) is autonomous we may reduce (A.11) to considering only the case $t_0 = 0$:

$$(A.15) \qquad z(t;z_0) = X(t)\,X^{-1}(0)\,z_0 + \int_0^t X(t)\,X^{-1}(s)\,b(s)\,ds\ ,\ t \in \mathbb{R}\ .$$

The principal matrix solution of (A.14) $P(t) := X(t,0)$ is such that $P(0) = I$. In this case equation (A.12) becomes

$$(A.16) \qquad P(t+s) = P(t)\,P(s)$$

for any s, $t \in \mathbb{R}$.

This relation suggests the notation e^{At}, for $P(t)$, $t \in \mathbb{R}$.

As a consequence of the definition the $n \times n$ matrix e^{At} , $t \in \mathbb{R}$ satisfies the following properties

(i) $e^{A0} = I$

(ii) $e^{A(t+s)} = e^{At}\,e^{As}\ , \quad s,\, t \in \mathbb{R}$

(iii) $\left(e^{At}\right)^{-1} = e^{-At}\ , \quad t \in \mathbb{R}$

(iv) $\dfrac{d}{dt}e^{At} = A\,e^{At} = e^{At}\,A\ , \quad t \in \mathbb{R}$

(v) a general solution of (A.14) is $\left\{ e^{At}\, c \;,\; c \in \mathbb{R}^n \right\}$

(vi) if $X(t)$ $(\, det X(0) \neq 0\,)$ is a fundamental matrix solution of (A.14) then

$$e^{At} = X(t)\, X^{-1}(0) \;\; .$$

With these notations, equation (A.15) may be rewritten as

$$z(t; z_0) = e^{At}\, z_0 + \int_0^t e^{A(t-s)}\, b(s)\, ds \qquad t \in \mathbb{R} \tag{A.17}$$

In addition to the above properties e^{At} can be obtained as the sum of a convergent power series of matrices which resembles structurally the scalar case [216]

$$e^{At} = \sum_{k=0}^{\infty} \frac{(A\,t)^k}{k\;!} \tag{A.18}$$

Note that for any $t \in \mathbb{R}$, e^{At} is always nonsingular, i.e. $det\left(e^{At}\right) \neq 0$.

But, what is an effective means for computing e^{At} ? To find it we need to introduce the concepts of eigenvalue and eigenvector of a matrix [38, 3].

A complex number λ is called an "eigenvalue" of an $n \times n$ real matrix A if there exists a nonzero vector v such that

$$(A - \lambda I)\, v = 0 \tag{A.19}$$

Any nonzero solution $v \in \mathbb{R}^n$ of equation (A.19) is called an "eigenvector" associated with the eigenvalue λ.

It is well known that (A.19) admits (for a fixed λ) a nontrivial solution v iff the matrix $(A - \lambda I)$ is singular. Thus λ needs to satisfy the "characteristic equation"

$$det(A - \lambda I) = 0 \;\; . \tag{A.20}$$

This equation is a (real) polynomial of degree n in λ and, therefore, admits n solutions in $\mathbf{C}$, not all of which may be distinct.

On the other hand, if $\lambda_1, \cdots, \lambda_k$ are $k \leq n$ distinct eigenvalues of the matrix A and $v^1, \cdots, v^k$ are corresponding eigenvectors, then $v^1, \cdots, v^k$ are linearly independent.

The set of all eigenvalues of A is called the "spectrum" of A and is denoted by $\sigma(A)$.

Lemma A.21. *If λ is an eigenvalue of the matrix A and v is an eigenvector associated with λ, then the function*

$$z(t) = e^{\lambda t}\, v \;\; , \qquad t \in \mathbb{R}$$

is a solution of system (A.14).

If now A admits n distinct eigenvalues $\lambda_1, \cdots, \lambda_n$ and $v^1, \cdots, v^n$ are corresponding eigenvectors, we may claim, as stated above, that these eigenvectors are linearly independent.

We may then proceed as suggested in the Remark following Theorem A.19.

Let $V(t)$ be the solution of (A.9) (with $A(t) \equiv A$) such that $V(0) = \left[v^1, \cdots, v^n\right]$. Due to Lemma A.21, we have

$$V(t) = \left[e^{\lambda_1 t}\, v^1, \cdots, e^{\lambda_n t}\, v^n\right] \quad ,$$

and since $V(0)$ is nonsingular, $V(t)$ is a fundamental matrix of (A.14).

Thus a general solution of (A.14) is given by

$$z(t; c) = V(t)\, c \quad , \qquad c \in \mathbb{R}^n$$

and, due to (vi)

$$e^{At} = V(t)\, V^{-1}(0) \quad .$$

If the eigenvalues are not all distinct, it may be still possible to determine a set of n linearly independent eigenvectors of A and proceed as before to find a fundamental matrix of (A.14).

However the technique will fail if the eigenvectors do not form a basis for $\mathbb{R}^n$. Then there may be solutions of (A.14) which cannot be expressed in terms of only exponential functions and constant vectors.

To determine the form of e^{At} when A is an $n \times n$ arbitrary real matrix, compute the distinct eigenvalues $\lambda_1, \cdots, \lambda_k$ $(k \leq n)$ of A, with respective multiplicities $n_1, \cdots, n_k$, such that $n_1 + \cdots + n_k = n$.

Corresponding to each eigenvalue λ_j of multiplicity n_j consider the system of linear equations

$$(A.21) \qquad (A - \lambda_j I)^{n_j}\, v = 0 \quad , \qquad j = 1, \cdots, k \quad .$$

The linear algebraic system (A.21) has n_j linearly independent solutions, that span a subspace X_j of $\mathbb{R}^n$ $(j = 1, \cdots, k)$.

Moreover, for every $z \in \mathbb{R}^n$ there exists a unique set of vectors $z_1, \cdots, z_k$, with $z_j \in X_j$, such that

$$(A.22) \qquad z = z_1 + z_2 + \cdots + z_k \quad .$$

In the language of linear algebra, this means that $\mathbb{R}^n$ can be represented as the direct sum of subspaces X_j , $j = 1, \cdots, k$

$$\mathbb{R}^n = X_1 \oplus \cdots \oplus X_k \quad .$$

Each of the subspaces X_j is invariant under A, that is $A\, X_j \subset X_j$, $j = 1, \cdots, n$, hence, it is invariant under e^{At} and for system (A.14).

We look for a solution of system (A.14) subject to the initial condition $z(0) = z_0 \in \mathbb{R}^n$.

We know that

$$z(t; z_0) = e^{At}\, z_0 \ ,$$

but our objective is to give an explicit representation of $e^{At}\, z_0$.

In accordance with (A.22) there will exist a unique set of vectors $v_1, \cdots, v_k$, $v_j \in X_j$, such that

$$z_0 = v_1 + \cdots + v_k \ .$$

Hence

$$e^{At}\, z_0 = \sum_{j=1}^{k} e^{At}\, v_j = \sum_{j=1}^{k} e^{\lambda_j t}\, e^{(A-\lambda_j I)t}\, v_j \ .$$

Now, by using the series expansion of e^{At}

$$e^{(A-\lambda_j I)t}\, v_j = \Big[I + t(A-\lambda_j I) + \frac{t^2}{2!}(A-\lambda_j I)^2 + \cdots + \frac{t^{n_j-1}}{(n_j-1)!}(A-\lambda_j I)^{n_j-1} \Big] v_j$$

since, because of (A.21), all other terms will vanish.

Thus, for any $t \in \mathbb{R}$,

$$\begin{aligned} z(t; z_0) &= e^{At}\, z_0 \\ &= \sum_{j=1}^{k} e^{\lambda_j t} \left[\sum_{i=0}^{n_j-1} \frac{t^i}{i!}\, (A-\lambda_j I)^i \right] v_j \end{aligned} \tag{A.23}$$

We note that it may happen that a $q_j < n_j$ exists such that

$$(A-\lambda_j I)^{q_j} = 0 \qquad\qquad (j = 1, \cdots, n) \ ;$$

in such case the corresponding sum in (A.23) will contain only q_j terms instead of n_j terms.

We are now in a position to state the following

Theorem A.22. [38] *Given the linear system (A.14) if $\rho \in \mathbb{R}$ is such that*

$$\rho > \max_{\lambda \in \sigma(A)} \mathcal{R}e\ \lambda$$

then there exists a constant $k > 0$ such that for any $z_0 \in \mathbb{R}^n$:

$$\|e^{At}\, z_0\| \le k\, e^{\rho t}\, \|z_0\| \ , \qquad t \in \mathbb{R}_+ \ ,$$

or simply

$$\|e^{At}\| \le k\, e^{\rho t} \ , \qquad t \in \mathbb{R}_+ \ .$$

Remark. In Theorem A.22, the constant ρ may be chosen as any number greater than or equal to the largest of $\mathcal{R}e\ \lambda$, $\lambda \in \sigma(A)$, whenever every eigenvalue whose real part is equal to this maximum is itself simple. In particular, this is always true if A has no multiple eigenvalues.

Corollary A.23. *If all eigenvalues of A have negative real parts, then there exist constants $k > 0$, $\sigma > 0$ such that , for any $z_0 \in \mathbb{R}^n$*

$$\|e^{At} z_0\| \le k\, e^{-\sigma t}\, \|z_0\| \ , \qquad t \in \mathbb{R}_+$$

or simply

$$\|e^{At}\| \le k\, e^{-\sigma t} \ , \qquad t \in \mathbb{R}_+ \ .$$

Corollary A.24. *If all eigenvalues of A have real part negative or zero and if those eigenvalues with zero real part are simple, then there exists a constant $k > 0$ such that*

$$\|e^{At}\| \le k \ , \qquad t \in \mathbb{R}_+$$

i.e., for any $z_0 \in \mathbb{R}^n$,

$$\|e^{At} z_0\| \le k\, \|z_0\| \ , \qquad t \in \mathbb{R}_+ \ ,$$

hence any solution is bounded on $\mathbb{R}_+$.

A.3. Stability

Suppose $f \ : \ \mathbb{R} \times D \longrightarrow \mathbb{R}^n$, $D \subset \mathbb{R}^n$ be such to ensure existence, uniqueness and continuous dependence on parameters; e.g. $f \in C^1(\mathbb{R} \times D, \mathbb{R}^n)$.

Consider the (nonautonomous) system of ODE's

$$\frac{dz}{dt} = f(t, z) \ , \tag{A.24}$$

and let $\phi(t)$ be some solution of (A.24) existing for $t \in \mathbb{R}$.

As usual we shall denote by $z(t\,;\,t_0, z_0)$, a solution of (A.24) passing through $z_0 \in D$ at time $t_0 \in \mathbb{R}$ ($z(t_0\,;\,t_0, z_0) = z_0$).

The solution $\{\phi(t)\ ,\ t \in \mathbb{R}\}$ of (A.24) is said to be "stable" if for every $\epsilon > 0$ and every $t_0 \in \mathbb{R}$ there exists a $\delta > 0$ (δ may depend upon ϵ and t_0) such that whenever $\|z_0 - \phi(t_0)\| < \delta$, the solution $z(t\,;\,t_0, z_0)$ exists for any $t > t_0$ and satisfies

$$\|z(t\,;\,t_0, z_0) - \phi(t)\| < \epsilon \ , \qquad \text{for} \quad t \ge t_0 \ .$$

This definition may be extended as follows.

The solution $\{\phi(t)\ ,\ t \in \mathbb{R}\}$ is said to be "asymptotically stable" if it is stable and if there exists a $\delta_0 > 0$ (δ_0 may again depend upon t_0) such that whenever $\|z_0 - \phi(t_0)\| < \delta_0$, the solution $z(t\,;\,t_0, z_0)$ approaches $\phi(t)$ as t tends to $+\infty$; i.e.

$$\lim_{t\to+\infty} \|z(t\,;\,t_0, z_0) - \phi(t)\| = 0 \ .$$

In the same context as above, we speak of "uniform stability" of ϕ if δ does not depend upon t_0; we speak of "uniform asymptotic stability" if also δ_0 does not depend upon t_0.

Suppose now that f does not depend upon t, so that we consider the autonomous system

$$\frac{dz}{dt} = f(z) \ . \tag{A.25}$$

Let $z^* \in D$ be a critical point of f $(f(z^*) = 0)$, hence an equilibrium of (A.25). We may specialize the previous definitions to the stability of z^*.

The equilibrium solution z^* of (A.25) is said to be "stable" if for each number $\epsilon > 0$ we can find a number $\delta > 0$ (depending upon ϵ) such that whenever $\|z_0 - z^*\| < \delta$, the solution $z(t; z_0)$ exists for all $t \geq 0$ and $\|z(t; z_0) - z^*\| < \epsilon$ for $t \geq 0$.

The equilibrium solution z^* is said to be asymptotically stable if it is stable and if there exists a number $\delta_0 > 0$ such that whenever $\|z_0 - z^*\| < \delta_0$, then $\lim_{t\to+\infty} \|z(t; z_0) - z^*\| = 0$.

The equilibrium solution z^* is said to be unstable if it is not stable.

Note that because system (A.25) is autonomous the numbers δ , δ_0 are independent of the initial time which can always be chosen to be $t_0 = 0$.

Thus the stability and asymptotic stability are always uniform.

The above definitions raise the problem of finding the region of asymptotic stability of a solution $\phi(t)$, i.e. the subset $\tilde{D} \subset D$ such that, for a given t_0, for all $z_0 \in \tilde{D}$ one has

$$\lim_{t\to\infty} \|z(t\,;\,t_0, z_0) - \phi(t)\| = 0 \ .$$

We shall speak of "global asymptotic stability in $\tilde{D}$" when $\tilde{D}$ is a known subset of D. When $\tilde{D} = D$ we shall simply say "global asymptotic stability".

A.3.1. Linear systems with constant coefficients

Let A be a real $n \times n$ matrix and consider the system

$$\frac{dz}{dt} = Az \ . \tag{A.26}$$

Clearly the zero solution is an equilibrium solution of (A.26).

It is an immediate consequence of Theorem A.22 and Corollaries A.23, A.24, the following

Theorem A.25. [38, 216] *If all the eigenvalues of A have nonpositive real parts and all those eigenvalues with zero real parts are simple, then the solution $z^* = 0$ of (A.26) is stable. If and only if all eigenvalues of A have negative real parts, the zero solution of (A.26) is asymptotically stable. If one or more eigenvalues of A have a positive real part, the zero solution of (A.26) is unstable.*

The reader should observe that actually, for linear systems, the stability properties are global in $\mathbb{R}^n$.

A.3.2. Stability by linearization

Theorem A.26. (Poincaré-Lyapunov) [210] *Consider the equation*

$$\frac{dz}{dt} = Az + B(t)\,z + f(t,z) \ . \tag{A.27}$$

Let A be a real constant $n \times n$ matrix with all eigenvalues having negative real parts; $B(t)$ is a continuous real $n \times n$ matrix with the property

$$\lim_{t \to +\infty} \|B(t)\| = 0 \ ;$$

the vector function $f \in C(J \times D, \mathbb{R}^n)$ is Lipschitz continuous in a neighborhood of $0 \in D$, an open subset of $\mathbb{R}^n$; it is such that

$$\lim_{\|z\| \to 0} \frac{\|f(t,z)\|}{\|z\|} = 0 \ , \quad \text{uniformly in} \quad t \in \mathbb{R} \ . \tag{A.28}$$

Then the solution z^* of (A.27) is asymptotically stable.

Note that in this case we do not necessarily have global asymptotic stability.

Theorem A.27. [210] *Under the same assumptions of Theorem A.26 if now A admits at least one eigenvalue with positive real part, then the trivial solution of (A.27) is unstable.*

Theorems A.26 and A.27 play a central role in the analysis of the local behavior of a nonlinear autonomous system.

Suppose we are given the system

$$\frac{dz}{dt} = F(z) \tag{A.29}$$

where $F \in C^1(D)$, D an open subset of $\mathbb{R}^n$.

Suppose that $z^* \in D$ is an equilibrium of (A.29) so that $F(z^*) = 0$.

If $\{z(t)\ ,\ t \in \mathbb{R}_+\}$ is any solution of (A.29) we may write it in the form

$$z(t) = z^* + y(t)\ , \qquad t \in \mathbb{R}_+$$

so that

$$\begin{aligned}\frac{d}{dt} y(t) &= F(z^* + y(t)) \\ &= F(z^*) + J_F(z^*)\, y(t) + g(y(t)) \\ &= J_F(z^*)\, y(t) + g(y(t))\end{aligned}$$

with $g(0) = 0$. Here $J_F(z^*)$ is the Jacobi matrix of F at z^*, i.e. the constant matrix whose (i, j) elements are

$$\frac{\partial F_i}{\partial z_j}(z^*)\ , \qquad i, j = 1, \cdots, n\ .$$

Thus the displacement $y(t)$ of $z(t)$ from the equilibrium z^* satisfies the equation

$$\frac{dy}{dt} = J_F(z^*)\, y + g(y) \tag{A.30}$$

which is of the form (A.27).

A.4. Quasimonotone (cooperative) systems

In this section we shall deal with systems of ODE's of the form

$$\frac{dz}{dt} = f(t, z) \tag{A.31}$$

where $f \in C^1\left(J \times \mathbb{R}^n_+\ ,\ \mathbb{R}^n\right)$ is a quasimonotone (cooperative) function for any $t \in J \subset \mathbb{R}$.

This means that, for any $t \in J$, the off-diagonal terms of the Jacobi matrix $J_f(t; z)$ at any point $z \in \mathbb{R}^n_+$ are nonnegative

$$\frac{\partial f_i}{\partial z_j}(t; z) \geq 0\ , \qquad i \neq j$$

for $i, j = 1, \cdots, n$.

A.4.1. Quasimonotone linear systems

Notations. Let $\mathbb{K}$ denote the positive cone of $\mathbb{R}^n$, i.e. its nonnegative orthant,

$$\mathbb{K} := \mathbb{R}^n_+ := \{z \in \mathbb{R}^n \mid z_i \geq 0\ ,\ i = 1, \cdots, n\}\ .$$

This cone induces a partial order in $\mathbb{R}^n$ via

$$y \leq x \qquad \text{iff} \qquad x - y \in \mathbb{K}\ .$$

In addition we shall use the notation

$$y < x \qquad \text{iff} \qquad x - y \in \mathbb{K}\ , \qquad \text{and} \quad x \neq y$$

$$y \ll x \qquad \text{iff} \qquad x - y \in \mathring{\mathbb{K}} \quad (\text{the interior of } \mathbb{K}\ )\ .$$

A nonnegative matrix B is a matrix with nonnegative entries $b_{ij} \geq 0\ ,\ i, j = 1, \cdots, n$. It is such that it leaves $\mathbb{K}$ invariant:

$$B(\mathbb{K}) \subset \mathbb{K}$$

A positive matrix B is a matrix with positive entries $b_{ij} > 0\ ,\ i, j = 1, \cdots, n$.

It satisfies the equivalent property that

$$B(\mathbb{K} - \{0\}) \subset \mathring{\mathbb{K}}\ .$$

In this section we shall analyze linear systems

$$\frac{dz}{dt} = Az \tag{A.32}$$

where A is a (nonnegative) "quasimonotone" $n \times n$ real matrix, i.e. such that all nondiagonal elements of A are nonnegative:

$$a_{ij} \geq 0\ , \qquad i \neq j\ ;\ i, j = 1, \cdots, n\ . \tag{A.33}$$

Clearly for a certain $\alpha > 0$ the matrix $B = A + \alpha I$ will be a nonnegative matrix, i.e. all its elements will be nonnegative.

Theorem A.28. [93] *A necessary and sufficient condition that all the eigenvalues of the quasi-monotone matrix A should have negative real parts, is that the following inequalities be satisfied*

$$\begin{aligned} &a_{11} < 0 \\ &det \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} > 0 \\ &\cdot \\ &\cdot \\ &\cdot \\ &(-1)^n\ det A > 0 \end{aligned} \tag{A.34}$$

Theorem A.29. [31, 93] *A quasimonotone matrix A always admits a real eigenvalue μ such that for any other $\lambda \in \sigma(A)$*

$$\mu \geq \mathcal{R}e\ \lambda \ ;$$

thus

$$\mu = \max\{\mathcal{R}e\ \lambda \mid \lambda \in \sigma(A)\} \ .$$

To this dominant eigenvalue μ there corresponds a nonnegative eigenvector $\eta \in \mathbb{K}$

$$A\eta = \mu\eta \ .$$

An $n \times n$ matrix B is "reducible" if for some permutation matrix P

$$P\,B\,P^T = \begin{pmatrix} B_1 & C \\ 0 & B_2 \end{pmatrix} \ ,$$

where B_1 and B_2 are square matrices. Otherwise B will be said "irreducible".

Theorem A.30. (Perron-Frobenius) [31, 93] *If A is an irreducible quasi-monotone matrix its dominant eigenvalue μ is a simple eigenvalue of A. To μ there corresponds a positive eigenvector*

$$\eta \in \overset{\circ}{\mathbb{K}} \qquad (\eta \gg 0) \ .$$

Theorem A.31. [31] *Let A be a quasi-monotone matrix. Then*

$$(i) \qquad e^{At}\,\mathbb{K} \subset \mathbb{K} \ , \quad \text{for any} \quad t \geq 0 \ .$$

Moreover

$$(ii) \qquad e^{At}\,(\mathbb{K} - \{0\}) \subset \overset{\circ}{\mathbb{K}} \ , \quad \text{for any} \quad t > 0 \ , \quad \text{iff } A \text{ is irreducible} \ ,$$

Assume A is a quasimonotone matrix.

As a consequence of (i) and (ii) in Theorem A.31 we have the following.

If z_1, $z_2 \in \mathbb{K}$, and $z_1 \leq z_2$ we have $z_2 - z_1 \in \mathbb{K}$ so that $e^{At}\,(z_2 - z_1) \in \mathbb{K}$; hence

$$(A.35) \qquad z_1 \ , \ z_2 \in \mathbb{K} \ , \ z_1 \leq z_2 \implies e^{At}\,z_1 \leq e^{At}\,z_2 \ , \qquad t \in \mathbb{R}_+ \ .$$

We shall say that a quasimonotone (nonnegative) matrix A induces a "monotone flow" on system (A.32).

Further, if in addition A is irreducible, we have

$$(A.36) \qquad z_1 \ , \ z_2 \in \mathbb{K} \ , \ z_1 < z_2 \implies e^{At}\,z_1 \ll e^{At}\,z_2 \ , \qquad t > 0 \ .$$

i.e. A induces a "strongly monotone flow" [72, 139].

A.4.2. Nonlinear autonomous quasimonotone systems

Differential inequalities can be used to show that the flow generated by the differential system

$$\frac{dz}{dt} = f(z) \tag{A.37}$$

is monotone.

Theorem A.32. [128, 72] *Suppose* $f \in C^1(\overset{\circ}{\mathbb{K}}\ ,\ \mathbb{R}^n)$ *, and that* f *is a quasimonotone (cooperative) vector function. If* $\{z(t)\ ,\ t \in \mathbb{R}_+\}$ *satisfies*

$$\frac{dz}{dt} \leq f(z)\ ; \tag{A.38}$$

if $\{y(t)\ ,\ t \in \mathbb{R}_+\}$ *satisfies*

$$\frac{dy}{dt} \geq f(y) \tag{A.39}$$

and if

$$z(0) = z_0 \leq y_0 = y(0) \tag{A.40}$$

then,

$$z(t) \leq y(t)\ , \qquad \text{for all} \quad t \in \mathbb{R}_+\ . \tag{A.41}$$

In particular if both $z(t; z_0)$ and $y(t; z_0)$ are solutions of the ODE system (A.37) but their initial conditions satisfy (A.40), then (A.41) still holds. We may again state that system (A.37) is order preserving, or that it generates a monotone flow.

Whenever f is such that its Jacobi matrix $J_f(z)$ at any $z \in \overset{\circ}{\mathbb{K}}$ is irreducible, then for any $z_0\ ,\ y_0 \in \mathbb{K}$

$$z_0 < y_0 \implies z(t) \ll y(t)\ , \qquad t > 0\ ,$$

i.e. system (A.37) generates a "strongly monotone flow".

In particular, if we assume for $f \in C^1(\overset{\circ}{\mathbb{K}}, \mathbb{R}^n)$ the following hypotheses

(F1) $f(0) = 0$

(F2) f is quasimonotone (cooperative) in $\mathbb{K}$

(F3) for any $\xi \in \mathbb{K}$ a $\xi_0 \in \mathbb{K}$ exists, $\xi_0 \gg 0$ such that $\xi \leq \xi_0$ and $f(\xi_0) \ll 0$, we may claim that for any choice of $z_0 \in \mathbb{K}$, a unique global solution of system (A.37) exists, subject to the initial condition z_0 at $t = 0$.

We may denote such a solution by $\{V(t)\, z_0\ ,\ t \in \mathbb{R}_+\}$ so that a (nonlinear) C_o-semigroup of evolution operators $\{V(t)\ ,\ t \in \mathbb{R}_+\}$ is defined for system (A.37) (see Appendix B; Section B.1.4).

In fact, thanks to the above mentioned comparison theorem we may state that the evolution operator satisfies the following properties.

(i) $V(0) = I$

(ii) $V(t+s) = V(t)\, V(s)\ , \qquad s\,,\ t \geq 0$

(iii) $V(t)\, 0 = 0\ , \qquad t \geq 0$

(iv) for any $t \geq 0$, the mapping $z_0 \in \mathbb{K} \longrightarrow V(t)\, z_0 \in \mathbb{R}^n$ is continuous, uniformly in $t \in [t_1, t_2] \subset \mathbb{R}_+$

(v) for any $z_0 \in \mathbb{K}$, the mapping $t \in \mathbb{R}_+ \longrightarrow V(t)\, z_0 \in \mathbb{K}$ is continuous

(vi) for any $z_1\ ,\ z_2 \in \mathbb{K}$, $z_1 \leq z_2 \Longrightarrow V(t)\, z_1 \leq V(t)\, z_2$, for any $t \in \mathbb{R}_+$

(vii) for any $t \in \mathbb{R}_+\ :\ V(t)\, \mathbb{K} \subset \mathbb{K}$

The following lemma is a consequence of Theorem A.31 and of Theorem A.32.

Lemma A.33. *Under the assumptions (F1)-(F3) for f, if further a quasimonotone irreducible $n \times n$ matrix B exists for which a $\delta > 0$ exists such that*

$$\text{for any} \quad \xi \in \mathbb{K}\ ,\ |\xi| \leq \delta \quad : \quad f(\xi) \geq B\xi \tag{A.42}$$

then the evolution operator $V(t)$ of system (A.37) is strongly positive for any $t > 0$; i.e.

$$z_0 \in \mathbb{K}\ ,\ z_0 \neq 0 \quad \Longrightarrow \quad V(t)\, z_0 \gg 0\ , \quad t > 0$$

or

$$V(t)\left(\dot{\mathbb{K}}\right) \subset \overset{\circ}{\mathbb{K}}\ , \quad t > 0 \tag{A.43}$$

(we have denoted by $\dot{\mathbb{K}} := \mathbb{K} - \{0\}$).

Suppose now that the Jacobi matrix $J_f(z)$ of f be irreducible for any $z \in \mathbb{K}$, and nonincreasing in z, i.e.

$$0 \leq \eta \leq \xi \quad \Longrightarrow \quad (J_f(\eta))_{ij} \geq (J_f(\xi))_{ij}\ , \qquad i, j = 1, \cdots, n\ .$$

This implies that

(F4) for any $R > 0$ there exists a quasimonotone positive irreducible matrix C_R such that

$$0 \leq \eta \leq \xi \ , \ \ \|\xi\| \, , \, \|\eta\| \leq R \implies f(\xi) - f(\eta) \geq C_R \, (\xi - \eta)$$

Lemma A.34. [161] *Under assumptions (F4) for f in system (A.37), if $z_0 \, , \, y_0 \in \mathbb{K}$,*

$$z_0 < y_0 \implies V(t) \, z_0 \ll V(t) \, y_0 \ , \qquad t > 0 \ .$$

Finally if we introduce the property of strict sublinearity for f

(F5) for any $z \in \mathbb{K}$ and for any $\tau \in (0,1)$

$$\tau \, f(z) < f(\tau z)$$

the following lemma holds.

Lemma A.35. [161] *Under assumptions (F4) and (F5) for f the evolution operator $V(t)$ of system (A.37) is strongly concave for any $t > 0$. This means that*

(*A*.44) *for any $z_0 \in \overset{\circ}{\mathbb{K}}$, and for any $\sigma \in (0,1)$ an $\alpha = \alpha(z_0, \sigma) > 0$ exists such that*

$$V(t) \, (\sigma z_0) \geq (1 + \alpha) \, \sigma \, V(t) \, z_0 \ , \qquad t > 0$$

We anticipate here the following theorem (see Section B.1.1 for definitions):

Theorem A.36. [137] *Let E be a real Banach space with cone $\mathbb{K}$. If an operator A on E is strongly positive, strongly monotone and strongly concave with respect to $\mathbb{K}$, then A cannot have two distinct nontrivial fixed points in the cone $\mathbb{K}$.*

Remark. Clearly Theorem A.36 excludes the existence of more than one nontrivial equilibrium for system (A.37) under assumptions of Lemmas A.33-A.35, since in this case $V(t)$ is, for any $t > 0$, a strongly positive, strongly monotone and strongly concave operator, and any equilibrium of system (A.37) is a fixed point for any $V(t)$, $t > 0$.

A.4.2.1. Lower and upper solutions, invariant rectangles, contracting rectangles

We say that z^* is an equilibrium solution for system (A.37) if it satisfies the system

$$f(z) = 0 \tag{A.45}$$

We shall say that $\underline{z} \in \mathbb{K}$ is a "lower (upper) solution" for (A.45) if

$$f(\underline{z}) \geq 0 \qquad (\leq 0) \ . \tag{A.46}$$

Theorem A.37. (Invariant Rectangles) [39] *Under the assumptions of Theorem A.32, if* $\underline{z}\,,\,\overline{z}$ *are a lower solution, respectively an upper solution, of system (A.45), then*

$$\mathcal{R} := [\underline{z}\,,\,\overline{z}] = \{z \in \mathbb{K} \ \mid \ \underline{z} \leq z \leq \overline{z}\}$$

is an invariant rectangle for system (A.37).

Remark. Note that the existence of an invariant rectangle $\mathcal{R}$ for system (A.37) insures the global existence of solutions with initial condition in $\mathcal{R}$.

Theorem A.38. (Nested Invariant Rectangles) [39] *Let* z^* *be an equilibrium for (A.37) in* $\overset{\circ}{\mathbb{K}}$, *and let* $\theta\mathcal{R}$ *be the following rectangle in* $\mathbb{K}$

$$\theta\mathcal{R} := \{z \in \mathbb{K} \ \mid \ |z_i - z_i^*| \leq \theta a_i \ , \quad i = 1, \cdots, n\} \tag{A.47}$$

with $\theta \in [0,1]$, *and* $a_i \in \mathbb{R}_+$, $i = 1, \cdots, n$. *If, for any* $\theta \in [0,1]$, $\theta\mathcal{R}$ *is an invariant rectangle, then* z^* *is stable as an equilibrium solution of system (A.37).*

We shall say that a bounded rectangle $\mathcal{R} \subset \mathbb{K}$ is "contracting" for the vector field f if at every point $z \in \partial\mathcal{R}$ we have

$$f(z) \cdot \nu_z < 0 \tag{A.48}$$

where ν_z is the outward pointing normal at z.

Theorem A.39. (Nested Contracting Rectangles)[185, 39] *Under the assumptions of Theorem A.38, if further, for any* $\theta \in (0,1]$, *the rectangle (A.47) is contracting for the vector field* f, *then* z^* *is asymptotically stable as an equilibrium solution of system (A.37); globally in* $\mathcal{R}$.

Actually the proof of Theorem A.39 is based on the Lyapunov's direct method which will be introduced later.

A.5. Lyapunov methods, LaSalle Invariance Principle

In the previous section the concepts of stability and asymptotic stability of an equilibrium solution of an ODE system were introduced.

Actually, apart from the quasimonotone case, the only technical tool to show that stability holds was based on the knowledge of the eigenvalues of the Jacobi matrix of the function f at the equilibrium. But this provides only information on the local behavior at equilibrium in the case of nonlinear systems.

The methods due to Lyapunov provide a means for identifying the region of attraction of a critical point.

We shall assume that 0 is a critical point for our system. Concepts can be easily extended to any other point.

Let $\Omega \subset \mathbb{R}^n$ be an open set in $\mathbb{R}^n$ such that $0 \in \Omega$.

A scalar function

$$V : \Omega \longrightarrow \mathbb{R}$$

is "positive semidefinite" on Ω if it is continuous on Ω, $V(0) = 0$ and

$$V(z) \geq 0 \ , \qquad z \in \Omega \ .$$

A scalar function V is "positive definite" on Ω if it is positive semidefinite on Ω and

$$V(z) > 0 \ , \qquad z \in \Omega - \{0\} \ .$$

A scalar function V is "negative semidefinite (negative definite)" on Ω if $-V$ is positive semidefinite (positive definite) on Ω.

Lemma A.40. (Sylvester) [27] *The quadratic form*

$$z^T A\, z = \sum_{i,j=1}^{n} a_{ij} z_i z_j \ , \qquad z \in \mathbb{R}^n$$

associated with the $n \times n$ symmetric matrix $A = A^T$ is positive definite iff

$$det\,(a_{ij} \ ; \ i,j = 1, \cdots, s) > 0$$

for any $s = 1, \cdots, n$.

Consider the differential equation

$$\frac{dz}{dt} = f(z) \qquad (A.49)$$

where $f \in C\,(D\,, \mathbb{R}^n)$ satisfies enough smoothness properties to ensure that a solution of (A.49) exists through any point in D, is unique and depends continuously upon the initial data (we shall assume that $0 \in D$ and that $f(0) = 0$ so that 0 is an equilibrium solution of (A.49)).

Let $\Omega \subset D$ be an open subset of D in $\mathbb{R}^n$ and let $V \in C^1(\Omega, \mathbb{R})$. We define $\dot{V}$ with respect to system (A.49) as

$$\dot{V}(z) = grad\, V(z) \cdot f(z) \ , \qquad z \in \Omega \ . \tag{A.50}$$

If $z(t)$ is a solution of (A.49), then the total derivative of $V(z(t))$ with respect to $t \in \mathbb{R}_+$ is

$$\frac{d}{dt}V(z(t)) = \dot{V}(z(t)) \ ;$$

that is $\dot{V}$ is the derivative of V along the trajectories of (A.49).

Theorem A.41. (Lyapunov) [104] *If there is a positive definite function $V \in C^1(\Omega, \mathbb{R})$ on the open subset $\Omega \subset D$, such that $0 \in \Omega$, with $\dot{V}$ negative semidefinite in Ω, then the solution $z = 0$ is stable for system (A.49). If, in addition, $\dot{V}$ is negative definite on Ω, then the solution $z = 0$ is asymptotically stable for system (A.49), globally in Ω.*

Lemma A.42. (Lyapunov) [104, 38] *Let A be an $n \times n$ real matrix. The matrix equation*

$$A^T B + BA = -C \tag{A.51}$$

has a positive definite solution B (which is symmetric), for every positive definite symmetric matrix C, iff A is a stable matrix, i.e. $\mathcal{R}e\, \lambda < 0$ for any $\lambda \in \sigma(A)$.

As an application of Lemma A.42, consider the linear differential system

$$\frac{dz}{dt} = Az \tag{A.52}$$

and the scalar function

$$V(z) = z^T\, B\, z \qquad z \in \mathbb{R}^n$$

where B is a positive definite symmetric matrix then, with respect to (A.52)

$$\dot{V}(z) = z^T \, (A^T B + BA)\, z \ , \qquad z \in \mathbb{R}^n$$

According to Lemma A.42, if A is stable we may choose B so that $A^T B + BA$ is negative definite.

Thus the stability of A implies the (global) asymptotic stability of 0 for system (A.52), as already known by direct argument.

Let $V \in C^1(\Omega, \mathbb{R})$ be a positive definite function on the open set $\Omega \subset D$ such that $0 \in D$. We say that V is a "Lyapunov function" for system (A.49) if

$$(A.53) \qquad \dot{V}(z) = grad\, V(z) \cdot f(z) \leq 0 \ , \qquad \text{in} \quad \Omega \ .$$

Theorem A.43. (LaSalle Invariance Principle)[104, 216] *Let V be a Lyapunov function for system (A.49) in an open subset $\Omega \subset D$, and let V be continuous on $\overline{\Omega}$, the closure of Ω. Let*

$$E := \left\{ z \in \overline{\Omega} \mid \dot{V}(z) = 0 \right\}$$

and let M be the largest invariant subset of (A.49) in E. Suppose that for any initial point $z_0 \in \Omega$ the positive orbit $\Gamma_+(z_0)$ of (A.49) lies in Ω and is bounded. Then the ω-limit set of $\Gamma_+(z_0)$, $\omega(\Gamma_+(z_0)) \subset M$, so that

$$\lim_{t \to +\infty} dist\,(z(t; z_0) \ , \ M) = 0$$

Corollary A.44. *Under the same assumptions as in Theorem A.43 if $M = \{z^*\}$, with $f(z^*) = 0$, then the equilibrium solution z^* is a global attractor in Ω, for system (A.49).*

Corollary A.45. [104] *If V is a Lyapunov function on*

$$\Omega = \{ z \in \mathbb{R}^n \mid V(z) < \rho \}$$

and Ω is bounded, then every solution of (A.49) with initial value in Ω approaches M as $t \to +\infty$.

Corollary A.46. [104] *If V is a Lyapunov function in $\mathbb{R}^n$, bounded from below, and such that $V(z) \to +\infty$ as $\|z\| \to +\infty$, then every positive orbit of (A.49) is bounded and approaches the largest invariant subset M of $E' := \{z \in \mathbb{R}^n \mid \dot{V}(z) = 0\}$, as $t \to +\infty$. In particular if $M = \{z^*\}$, with $f(z^*) = 0$, then the equilibrium solution z^* is globally asymptotically stable in $\mathbb{R}^n$ for system (A.49).*