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.

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Vincenzo Capasso

Milan, October 1992

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:

$$\left\{\begin{array}{l} \dfrac{dS}{dt} = -kIS - \delta S + \delta \\ \dfrac{dI}{dt} = kIS - \gamma I - \delta I \\ \dfrac{dR}{dt} = \gamma I - \delta R \end{array}\right. \tag{2.6'}$$

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

$$\left\{\begin{array}{l} \dfrac{dS}{dt} = -kIS + \delta - \delta S + \alpha R \\ \dfrac{dI}{dt} = kIS - (\gamma + \delta) I \\ \dfrac{dR}{dt} = \gamma I - \alpha R \end{array}\right. \tag{2.7}$$

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,

$$\left\{\begin{array}{l} \dfrac{dS}{dt} = -k(I + C)S + \delta - \delta S \\ \dfrac{dI}{dt} = k(I + C)S - (\gamma + \delta) I \\ \dfrac{dR}{dt} = \gamma I - \delta R \end{array}\right. \tag{2.8}$$

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:

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

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,

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

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,

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

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

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

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:

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

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

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

which now can be written in the form

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

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

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

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

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

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

and

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

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

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

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 $\left\{z(t), t \in \mathbb{R}_+\right\}$ of system (2.27) is contained in a bounded domain $\Omega \subset \mathbb{R}^n$:

$(A1)$ Ω 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:

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

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

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

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

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

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

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 $z^* \in \Omega \quad (z_i^* > 0, \quad i = 1, \ldots, n)$ 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

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

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

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

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

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

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

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

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

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

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

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

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

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

$$\begin{pmatrix} \frac{\theta_1 I_2}{I_1^* I_1} & \frac{\theta_2 I_1}{I_2^* I_2} - \frac{\theta_1}{I_1^*} & \frac{\theta_2}{I_2^*} \end{pmatrix} w_1 w_2 = 0 \ .$$

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

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

Consider now

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

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

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

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

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

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

$\tilde{A}$ 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 $S_i \leq 1, \quad i = 1,2,3$, from (2.34) we see that a sufficient condition for the asymptotic stability of z^* is

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

Accordingly, let us take

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

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

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

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

$$-\left[\left(\gamma_1+\delta_1\right)\left(\gamma_2+\delta_2\right)\left(\gamma_3+\delta_3\right) - \left(\gamma_3+\delta_3\right) k_{12}k_{21}\right. \tag{2.45}$$

$$\left. - \left(\gamma_1+\delta_1\right) k_{23}k_{32}\right] w_1 w_2 w_3 < 0$$

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

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

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:

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

and S_2^* is a solution of

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

where

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

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

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

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 $S_2^* = 1$, i.e. $z^* = (1, 1, 1)^T$.

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:

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

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

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

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

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

Hence consider

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

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

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 $\overset{\circ}{\Omega}$.*

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

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

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

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

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

(*A*2) $\qquad \mathbb{R}^n_+$ 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

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

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

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

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

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

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

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

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

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

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 ($W = diag\,(w_i, \quad i = 1, \ldots, n)$)

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

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

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

where z is a vector $z = (x, y, v)^T$ belonging to the non-negative orthant $\mathbb{R}^3_+$. Since $C - \frac{r}{x^*} = CS\frac{(r-k)}{\sigma}$ 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 $w_1 = \frac{\sigma}{S(r-k)}$, $\quad w_2 = w_3 = 1$. 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, $\left.\frac{dx}{dt}\right|_R = 0$, and from the first of the Eqns. (2.51) we obtain

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

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

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

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

Immediately follows

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

i.e. $y\mid_R = y^*$. 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

$$R_2^3 = \left\{ z \in \mathbb{R}^3 \mid z_i > 0, \quad i = 1, 3, \quad z_2 \geq 0 \right\}$$

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

$$R = \left\{ z \in R_2^3 \mid y = 0, \quad x = x^* \right\}.$$

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

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

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

Therefore, we obtain $v\mid_R = \left[\dfrac{(r-k)}{(\beta+k+\sigma-r)}\right] x^*$, i.e. $v\mid_R \equiv v^*$. 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

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

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 $r \leq b, \quad r > \theta + b$ 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
ϵ = excess per capita death rate of infected individuals
δ = 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
λ = 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

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

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 non-trivial 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 $\overset{\circ}{\mathcal{D}}$ which is GAS in $\overset{\circ}{\mathcal{D}}$.

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 $\overset{\circ}{\mathcal{D}}_1$, and hence of $(s^*, i^*, r^*)^T$ in $\overset{\circ}{\mathcal{D}}$.

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 $z^* \in \overset{\circ}{\mathcal{D}}_1$ exists ($\overset{\circ}{\mathcal{D}}_1$ 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 $\circ\!-\!\bullet$, and Theorem 2.3 applies to show GAS of z^* in $\overset{\circ}{\mathcal{D}}_1$.

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

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

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

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

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 $z^* \in \overset{\circ}{\mathcal{D}}_1$ exists for system (2.89) provided $R_o := \dfrac{\lambda}{c+\epsilon} > 1$ (again $\overset{\circ}{\mathcal{D}}_1$ 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 $\circ\!-\!\bullet$, and Theorem 2.3 applies to show GAS of z^* in $\overset{\circ}{\mathcal{D}}_1$.

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.

2.3.4. Multigroup models

A class of epidemic models of particular interest is related to the possibility that heterogeneous populations may participate to the epidemic process with different parameters. The case of spatially heterogeneous populations may be considered as part of this class whenever a (discrete) compartmental approach is allowed. Many authors have faced this problem to take into account socially structured populations [218]; to consider towns and villages grouping of a population [115]; to consider sexually transmitted diseases [118, 142] or other problems [114, 193, 208, 209, etc.]. But while for SIS type models a rather complete analysis of existence and global stability analysis of a nontrivial endemic state has been carried out by Lajmanovich and Yorke [142], by using techniques of monotonicity of the evolution operator (see Sect. 4.3.5), only partial results are known for SIR type models [208, 209, 29]. This is mainly due to the fact that SIR type models with vital dynamics do not show in general monotone behavior; on the contrary the trajectories spiral around the nontrivial endemic state, when this exists (see Figs. 2.1-2.3).

Anyway the SIS model for n dissimilar groups [142] can be seen as an extension of the model for two groups already discussed in Sect. 2.2.3 and Sect. 2.3.1.2.3. As such we will show that we can still put it in the general form (2.18).

2.3.4.1. SIS model for n dissimilar groups. A model for gonorrhea in an heterogeneous population [142]

The assumptions we shall make on the epidemic are the following :

(i) subpopulation $i \in \{1, \dots, n\}$ has a constant size $N_i \in \mathbb{N} - \{0\}$. The sizes of the susceptible class, and the infective class in the i-th population at time $t \geq 0$ will be denoted by $S_i(t), I_i(t)$, respectively. There is no migration among subpopulations; because of the infection process individuals are transferred among S_i and I_i classes in the i-th subpopulation but cannot be transferred to other subpopulations.

(ii) Births and deaths occur in the i-th subpopulation at equal rates for the two classes S_i, I_i and it is assumed that all newborns are susceptibles. The death process is assumed to be a linear decay with rate $\mu_i > 0$, the same for the whole i-th population, independent of the class S_i or I_i. This implies that there is no excess mortality induced by the disease. The constancy of the total size of the i-th population imposes the birth rate to be equal to μ_i.

(iii) Infective individuals of the j-th class ($j = 1, 2, \dots, n$) may transmit the disease to individuals of the i-th class ($i = 1, 2, \dots, n$); it is assumed that this occurs at a rate $\lambda_{ij} \geq 0\, (i, j = 1, \dots, n)$ according to the "law of mass action" so that the force of infection acting on the susceptibles S_i of the i-th group is given by

$$g_i(I_1,\dots,I_n)=\sum_{j=1}^{n}\lambda_{ij}I_j\,,\quad i=1,\dots,n. \tag{2.91}$$

(iv) For the i-th group the recovery process is assumed to be a linear decay from the I_i class to the S_i class at a rate $\gamma_i>0\,(i=1,\dots,n)$.
(v) All the parameters introduced above, $\mu_i,\lambda_{ij},\gamma_i\,(i,j=1,\dots,n)$ are assumed to be time independent.

If we assume, for simplicity, that all subpopulation sizes $N_i=S_i(t)+I_i(t)=1$, $i=1,\dots,n$, the above assumptions lead to the following family of ODE's :

$$\begin{cases}\dfrac{dI_i}{dt}=\left(\displaystyle\sum_{j=1}^{n}\lambda_{ij}I_j\right)(1-I_i)-\gamma_iI_i-\mu_iI_i\\ I_i+S_i=1\end{cases} \tag{2.92}$$

for $i=1,\dots,n$, subject to suitable initial conditions.

It is easily seen that system (2.92) can be put in the form (2.18) if we define $z:=(I_1,\dots,I_n)^T$, and

$$A:=-\Lambda\,,\quad\text{with}\quad\Lambda:=(\lambda_{ij})_{i,j=1,\dots,n} \tag{2.93}$$

$$e:=(\lambda_{ii}-\gamma_i-\mu_i)_{i=1,\dots,n} \tag{2.94}$$

$$B:=\Lambda-diag\left[(\lambda_{ii})_{i=1,\dots,n}\right] \tag{2.95}$$

For n much larger than 2 it is quite difficult to carry out the analysis of this system as we did in Sect. 2.3.1.2.3 for $n=2$ for the technical reason of the difficulty of handling by paper and pencil large matrices. So while we can conjecture that condition (B) holds for the matrix $\tilde{A}$ defined by (2.35), it is preferable to adopt monotone techniques later in Sect. 4.3.5, to show existence and global asymptotic stability of a nontrivial endemic state for system (2.92).

2.3.4.2. SIR model for n dissimilar groups [29]

Such a model is obtained if we allow disease induced immunity so that individuals in the i-th group decay from the class I_i into a removed class R_i, $i = 1, \dots, n$.

Thus now the total population N_i of the i-th group is divided into three subclasses of susceptibles S_i, of infectives I_i, and of immune (removed) R_i ;

$$N_i = S_i(t) + I_i(t) + R_i(t) \ , \qquad i = 1, \dots, n \ .$$

With respect to the SIS model in Sect. 2.3.4.1 we only need to modify assumption (iv) which now becomes

(iv') for the i-th group the recovery to immunity is assumed to be a linear decay from the I_i class to the R_i class at a rate $\gamma_i > 0 (i = 1, \dots, n)$.

If we assume for simplicity that all subpopulation sizes $N_i = S_i(t) + I_i(t) + R_i(t) = 1$, the above assumptions lead to the following family of ODE's:

$$\begin{cases} \dfrac{d}{dt} S_i = -\left(\displaystyle\sum_{j=1}^{n} \lambda_{ij} I_j \right) S_i + \mu_i - \mu_i S_i \\ \dfrac{d}{dt} I_i = \left(\displaystyle\sum_{j=1}^{n} \lambda_{ij} I_j \right) S_i - (\mu_i + \gamma_i) I_i \\ \dfrac{d}{dt} R_i = \gamma_i I_i - \mu_i R_i \end{cases} \tag{2.96}$$

for $i = 1, \dots, n$ subject to suitable initial conditions.

We shall see now that also system (2.96) can be set in the general form (2.27) with suitable transformations.

Since $S_i(t) + I_i(t) + R_i(t) = 1$, $i = 1, \dots, n$ at any time $t \geq 0$, we may ignore the third equation in (2.96).

If we now introduce a new family of variables

$$\chi_i(t) := S_i(t) + I_i(t) \, , \qquad t \geq 0 \tag{2.97}$$

for $i = 1, \dots, n$, system (2.96) can be rewritten as

$$
\text{(2.98)} \qquad \begin{cases} \dfrac{d}{dt}S_i = \mu_i - \mu_i S_i + \left(\displaystyle\sum_{j=1}^{n} \lambda_{ij} S_j\right) S_i - \left(\displaystyle\sum_{j=1}^{n} \lambda_{ij}\chi_j\right) S_i \\ \dfrac{d}{dt}\chi_i = -(\mu_i + \gamma_i)\chi_i + (\mu_i + \gamma_i S_i) \end{cases}
$$

for $i = 1, \ldots, n$. If we now denote

$$
\begin{aligned}
z :=& (S_1, \ldots, S_n, \chi_1, \ldots, \chi_n)^T \in \mathbb{R}^{2n} \\
c :=& (\mu_1, \ldots, \mu_n, \mu_1, \ldots, \mu_n)^T \in \mathbb{R}^{2n} \\
e :=& (-\mu_1, \ldots, -\mu_n, -(\mu_1 + \gamma_1), \ldots, -(\mu_n + \gamma_n))^T \in \mathbb{R}^{2n}
\end{aligned}
$$

$$
A := \left(\begin{array}{c|c} \Lambda & -\Lambda \\ \hline 0 & 0 \end{array}\right), \qquad \text{with} \quad \Lambda := (\lambda_{ij})_{i,j=1,\ldots,n}
$$

$$
B := \begin{pmatrix} 0 & 0 \\ \Gamma & 0 \end{pmatrix} \qquad \text{with} \quad \Gamma := diag(\gamma_1, \ldots, \gamma_n)
$$

system (2.98) becomes

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

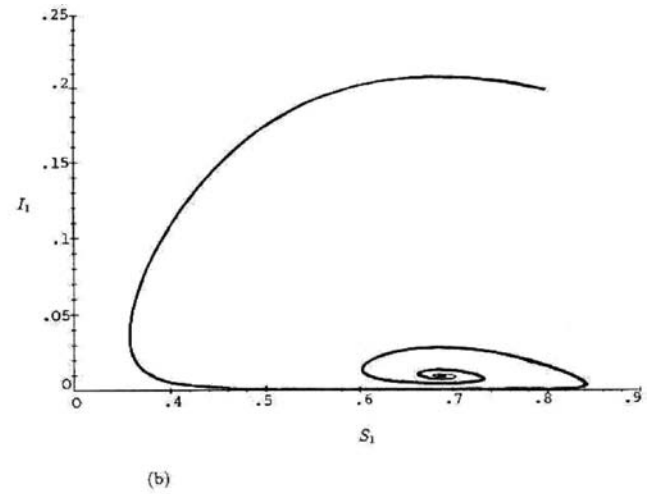
which corresponds to the general form (2.27).

We may then proceed as in Sect. 2.3.1 to prove existence and GAS of a nontrivial endemic state. By Corollary 2.4, since the vector c is strictly positive in $\mathbb{R}^{2n}$ then system (2.98) admits a strictly positive equilibrium $z^* \in \overset{\circ}{\Omega}$ where now $\Omega = \left\{ z \in \mathbb{R}^{2n}_+ \mid \sum_{i=1}^{2n} z_i \leq 2n \right\}$.

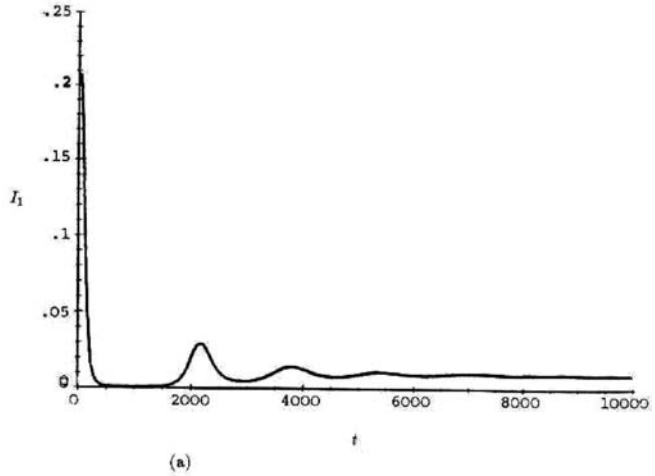
The problem which is left open (for realistic values of the parameters) is to prove that $\tilde{A}$ defined in (2.35) satisfies either the conditions of Theorem 2.1 or those of Theorem 2.3 for GAS. The problem lies in the large dimensions of $\tilde{A}$, since we already know that for $n = 1$, or for non interacting populations ($\lambda_{ij} = 0$, for $i \neq j\,, i, j = 1, \ldots, n$) a unique nontrivial endemic state exists for each group (independently of each other) provided

$$
\text{(2.99)} \qquad \lambda_{ii} > \mu_i + \gamma_i\,, \qquad i = 1, \ldots, n\ .
$$

Figs. 2.1-2.3 [29] show by computer experiments the existence and GAS of a non trivial endemic state in a range of parameters which is more suitable for human diseases such as influenza, mumps, measles, etc. For this range of parameters $\mu \simeq 0$, as opposed to the other parameters, making the model rather insensitive to vital dynamics. In fact $I^* \simeq 0$ and the trajectories exhibit a behavior which corresponds more to the classical Kermack-McKendrick model.

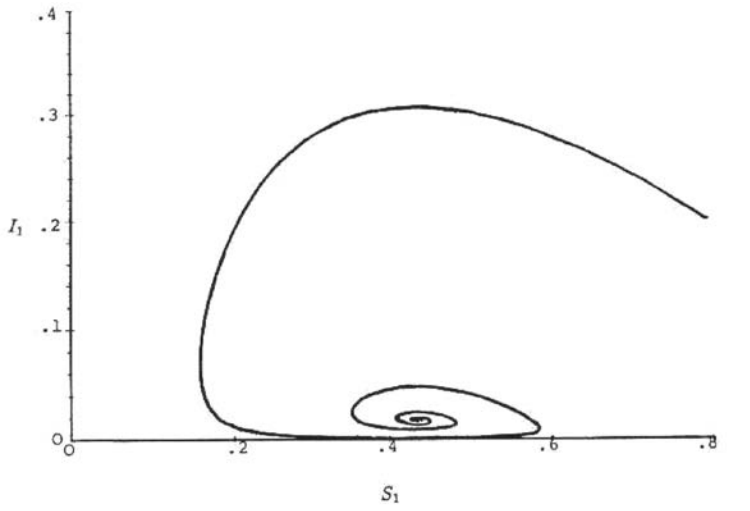


(b)

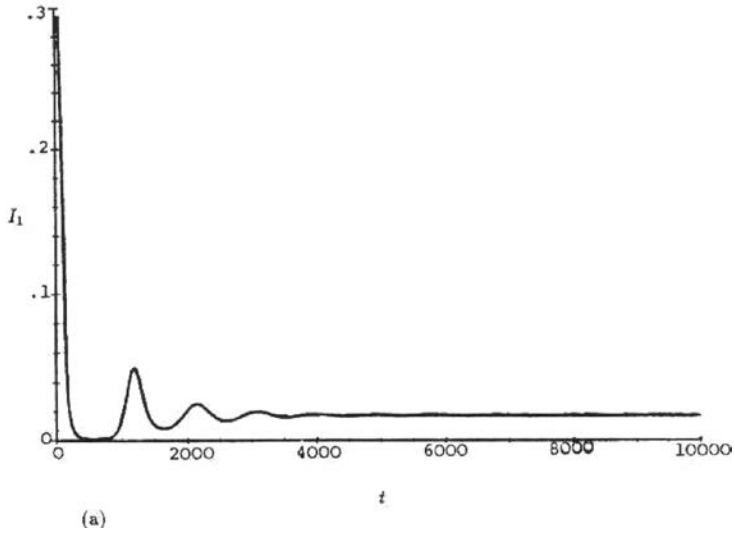


(a)

Fig. 2.1. $n = 2\,;\ \lambda_{ii} = 0.05,\ \lambda_{ij} = 0,\ \ i \neq j\,,\ i,j = 1,2\,;\ \mu_i = 10^{-3}\,,$ $\gamma_i = 30^{-1},\ i = 1,2;\ S_i^\circ = 0.8,\ I_i^\circ = 0.2,\ i = 1,2\,;$ [29].



(b)



(a)

Fig. 2.2. $n = 2\,;\ \lambda_{ii} = 0.05,\ \lambda_{ij} = 0.03,\ i \neq j\,,\ i,j = 1,2\,;\ \mu_i = 10^{-3}\,,$ $\gamma_i = 30^{-1},\ i = 1,2;\ S_i^\circ = 0.8,\ I_i^\circ = 0.2,\ i = 1,2\,;$ [29].

Anyway "zooming" (Fig. 2.3) clearly show the spiraling of trajectories about the nontrivial endemic state that always exists.

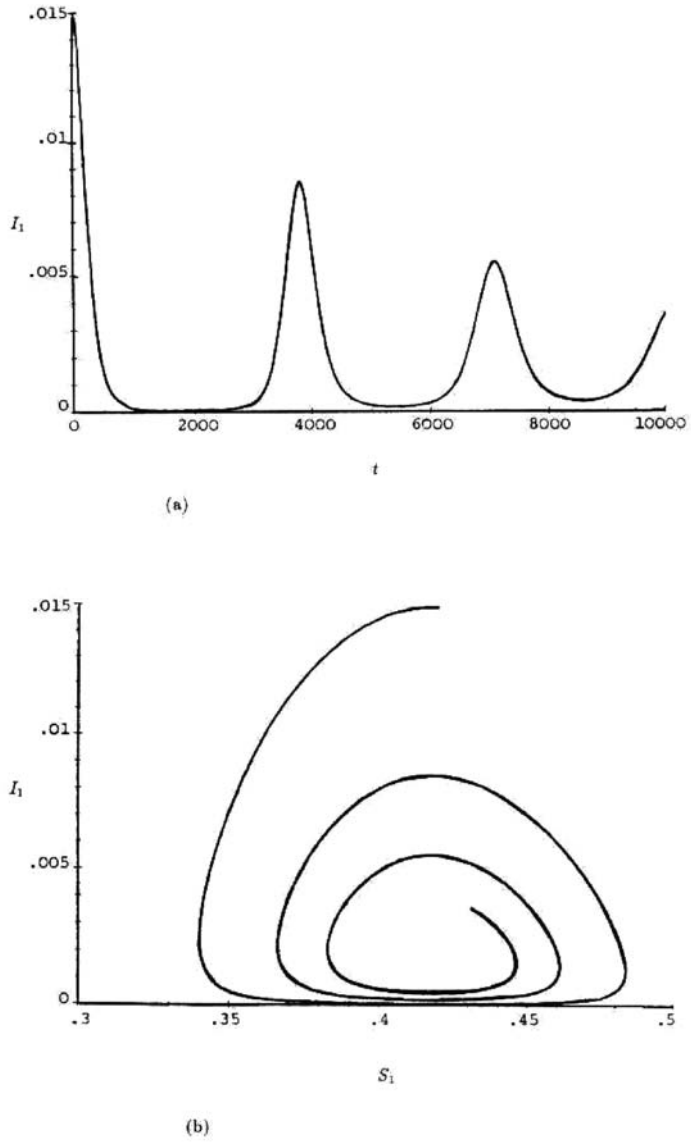


Fig. 2.3. $n = 2\,;\ \lambda_{ii} = 0.05,\ \lambda_{ij} = 0.03,\ i \neq j\,,\ i,j = 1,2\,;\ \mu_i = 10^{-4}\,,$ $\gamma_i = 30^{-1},\ i = 1,2;\ S_i^\circ = 0.8,\ I_i^\circ = 0.2,\ i = 1,2\,;$ [29].

Clearly, by continuous dependence of the solutions on the parameters, the same should hold for sufficiently small interactions $\lambda_{ij} \simeq 0$ for $i \neq j$ $(i, j = 1, \ldots, n)$, once (2.99) is satisfied.

The most interesting case would be to prove that even if $\lambda_{ii} = 0$, $i = 1, \ldots, n$, i.e. (2.99) is violated for each group, but the interaction between groups are so strong that anyway

$$\sum_{j=1}^{n} \lambda_{ij} > \mu_i + \gamma_i \,, \qquad i = 1, \ldots, n \ , \tag{2.100}$$

then still a nontrivial endemic state $z^* \gg 0$ exists which is globally asymptotically stable.

Conjecture (2.100) has been shown to hold by computer experiments (see Figs. 2.4-2.6 , [51]).

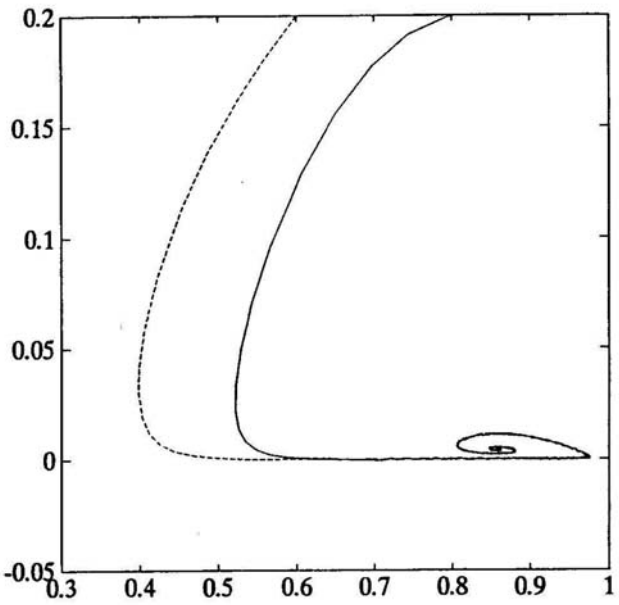


Fig. 2.4. $n = 2\,;\ \lambda_{ii} = 0,\ \lambda_{ij} = 0.04,\ i \neq j\,,\ i, j = 1, 2\,;\ \mu_i = 0.001\,,$ $\gamma_i = 0.033\,,\ i = 1, 2;\ S_1^\circ = 0.8,\ S_2^\circ = 0.6;\ I_i^\circ = 0.2,\ i = 1, 2\,;$ [51].

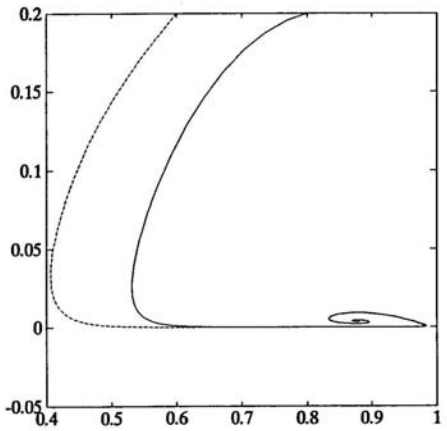


Fig. 2.5. $n = 2\,;\ \lambda_{ii} = 10^{-4},\ \lambda_{ij} = 0.039,\ \ i \neq j\,,\ i,j = 1,2\,;\ \mu_i = 0.001\,,$ $\gamma_i = 0.033\,,\ i = 1,2;\ S_1^\circ = 0.8,\ S_2^\circ = 0.6;\ I_i^\circ = 0.2,\ i = 1,2\,;$ [51].

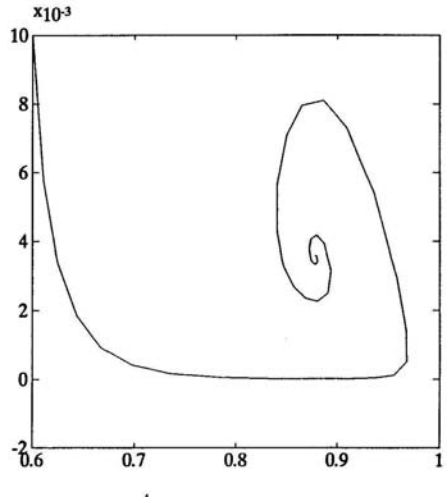


Fig. 2.6. $n = 2\,;\ \lambda_{ii} = 10^{-4},\ \lambda_{ij} = 0.039,\ \ i \neq j\,,\ i,j = 1,2\,;\ \mu_i = 0.001\,,$ $\gamma_i = 0.033\,,\ i = 1,2;\ S_i^\circ = 0.6;\ I_i^\circ = 0.01,\ i = 1,2\,;$ [51].