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GLOBAL ASYMPTOTIC PROPERTIES OF STAGED MODELS WITH MULTIPLE PROGRESSION PATHWAYS FOR INFECTIOUS DISEASES

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Abstract. We consider global asymptotic properties of compartment staged-progression models for infectious diseases with long infectious period, where there are multiple alternative disease progression pathways and branching. For example, these models reflect cases when there is considerable difference in virulence, or when only a part of the infected individuals undergoes a treatment whereas the rest remains untreated. Using the direct Lyapunov method, we establish sufficient and necessary conditions for the existence and global stability of a unique endemic equilibrium state, and for the stability of an infection-free equilibrium state.

1. **Introduction.** Mathematical modelling of infectious diseases is based on a concept adopted from chemical kinetics. According to this, a population is divided into a number of sub-populations, or compartments, and the interaction between these compartments is considered as a reaction. The whole population and each of these compartments are assumed to be homogeneously mixed, and the interaction between the compartments occurs according to the laws of chemical kinetics. In the simplest case, which goes back to the pioneering work of Kermack and McKendrick [17], the system is composed of three compartments, namely the susceptible S, the infectious I and the recovered (or removed) R, and transmission of individuals from the susceptible into the infectious compartment is assumed to occur according to the mass action law; the corresponding model is known as a *SIR* model. This simple concept is proved to be extremely successful, and mathematical models based on these assumptions brought important insight into the dynamics of infectious diseases, and in particular for childhood infections that were primary objects of modelling [2, 13]. However, these simple models lack the level of details that is

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needed, for instance, for understanding the dynamics of prolonged infections, or for studying community effects and human reaction on the threat of infection.

The diversity of individuals and conditions may be incorporated into this traditional modelling framework by introducing additional compartments for specific groups. Thus, to include the latency period (the time from infection to infectiousness) into a compartment model, an additional "exposed" compartment, that is usually denoted E, can be introduced into the model; the resulting models are known as the *SEIR* or *SEIRS* model (the latter is for the case when the recovery implies temporary immunity, and the recovered individuals after some time become susceptible again).

Additional compartments could be used to describe in detail the dynamics of long-lasting infections, where an infected individual progresses through a number of stages which significantly vary in the level of infectiousness. The most notorious example of an infection that has a variety of infectious stages is HIV infection. Typically, HIV-infected individuals are highly infectious in the acute stage that lasts for the first few weeks after infection. The acute stage is followed by a chronic asymptomatic stage of low contagiousness that in the absence of antiretroviral therapy lasts for nine to ten years on average. Then the patient becomes gradually more infectious as the immune system becomes compromised and AIDS develops. In order to model the variability of infectiousness for long infectious period, staged progression models were proposed [1, 14, 16, 26, 29]. These models usually include a succession of infectious compartments (infectious stages) that are characterised by different infectiousness, and it is assumed that an infected individual enters the first of these infectious compartments at the moment of infection and then progresses through all these compartments up to the last one. A typical transfer diagram for a staged progression model with n infectious stages is

$$S \longrightarrow I_1 \longrightarrow I_2 \longrightarrow \cdots \longrightarrow I_{n-1} \longrightarrow I_n \longrightarrow R.$$

The *SEIR* model can be considered as a particular case of a staged progression model with two infectious stages (the exposed stage E and the infectious stage I). To model amelioration, a stage progression model may include a possibility of "reversing the flow" [10, 12, 29]. More advanced models, which are sometimes termed "infection-age models", may assume a continuous distribution of infectivity as a function of the infection time instead of discrete stages [37]. These models, however, also usually assume "linear" progression from the first to the last stage.

The dynamics of the staged progression models was studied by a number of authors [7, 10, 11, 12]. Global properties of the staged progression models, including the models with amelioration, were addressed by Guo and Li [11, 12]. The global properties of models with continuous distribution of the infectivity were systematically studied by McCluskey and his collaborators [32, 34].

For a staged progression model, introduction of additional compartments is justified when the infectivity significantly varies. However, for infections with longer infectious period the level of infectivity is not necessary determined by the time of infection, and may depend on a number of other factors. Firstly, the virulence can greatly vary from case to case. For example, for Hepatitis B the infection may be entirely asymptomatic and may go unrecognized, and the level of contagiousness for asymptomatic cases is usually notably lower then that for acute infection. Clinical disease progression of HIV also varies widely between individuals, taking for progression from HIV infection to AIDS from two weeks up to 20 years [35].

Moreover, the infection could be undetected (and hence untreated), or it can be detected at very different stages. The detected infection can be properly treated, or it could be left untreated (the latter is not uncommon in developing countries), and the treatment can be either effective or non-effective. Furthermore, the level of contagiousness to a very large extend may depend of a personal attitude of an infectious individual: while some patients recognize the threat that they possess for a community and behave conscientiously restraining from potentially endangering contacts or decreasing the number of contacts to a necessary minimum, others disregard the threat and do not change their usual life style thereby effectively spreading the infection.

In the framework of a compartment model, this diversity of the possibilities can be modelled by introducing branching and alternative pathways for disease progression. A number of models with alternative pathways was developed for specific situations. For instance, tuberculosis provides an example of infection with the possibility of multiple alternative pathways, and a number of such models was considered. Thus, to model tuberculosis in Nigeria, Okuonghae and Korobeinikov [36] considered a model with two alternative pathways (detected and treated and undetected); McCluskey [30, 31] studied the dynamics of models for tuberculosis where there are alternative progressions. The global properties of *SIR* and *SEIR* models with multiple pathways were systematically considered in [24]. However, for more complex models it so far remains an open question whether the diversity of conditions can affect the qualitative dynamics of a pathogen in a population. In this paper we address this issue studying the global properties for staged progression models with multiple alternative pathways and branching. We consider two multi-staged models assuming constant recruitment and density-dependent incidence. Using the direct Lyapunov method, we prove that these models are globally asymptotically stable.

2. **Models.**

In this paper we consider two models for infectious diseases with multiple progression pathways. For the first model we assume that after infection individuals enter an exposed compartment; the exposed individuals are not infectious, and hence this compartment is assumed to be common for all pathways and hence the branching starts when the infected hosts progress to the next stage. In contrast, for the second model we assume that branching into alternative pathways starts immediately at the moment of infection. Transfer diagrams for these models are given in Fig. 1. We consider these models separately, as they require different treatment.

2.1. **A model with a common exposed state.**

We assume, that the infection progress through n infectious stages, and that at each stage there is a possibility of alternative further progression (and hence a possibility of branching). We also assume in this subsection that after infection an individual enters the exposed compartments; the exposed individuals are non-infectious, and hence this compartment is common for all pathways. Accordingly, we assume that the total population is partitioned into following compartments: the susceptible compartment S, the exposed compartment I_0^0 (that is usually denoted by E; however we prefer notation I_0^0 for the sake of consistency of notation), the infectious compartments I_j^i (where $i = 1, 2, \dots, n$ and $j = 0, 1, \dots, m-1$) and the removed compartment R. Individuals in the exposed and the infectious compartments may die, or progress with

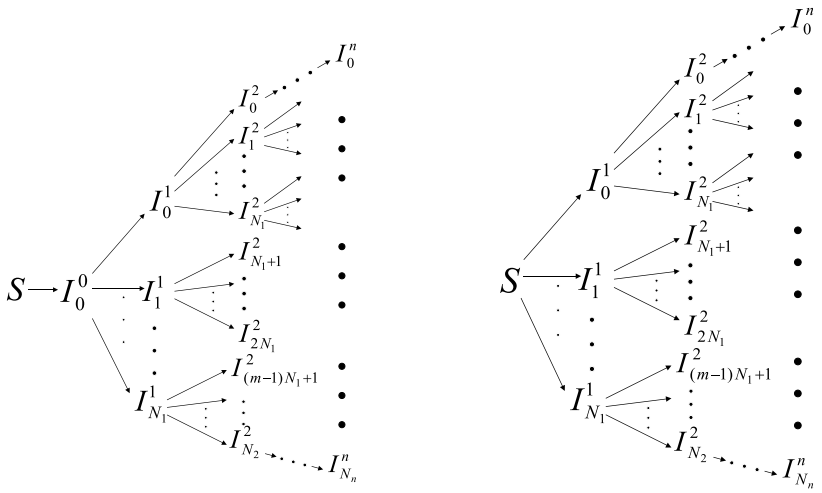

FIGURE 1. Transfer diagrams for models of infections with multiple progression pathways; left diagram is for the model with a common exposed state I_0^0, and right diagram is for the model where branching into alternative pathways starts immediately after an instance of infection.

the probability p_j (where $\sum_1^m p_j \leq 1$) into one of m next-stage compartments according to the transfer diagram (Fig. 1). Accordingly, infectious compartment I_j^i $(i = 1, \ldots, n-1)$ has a parent-compartment $I_{[j/m]}^{i-1}$ and m next stage compartments $I_{m\cdot j}^{i+1}$, $I_{m\cdot j+1}^{i+1}, \ldots, I_{m\cdot(j+1)-1}^{i+1}$ (see Fig. 2). Here and below, $[x]$ denotes the integer part of x.

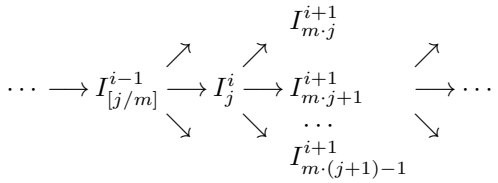

FIGURE 2. The order of numbering for the infectious compartments.

This model can be described by the following system of differential equations

$$\begin{aligned}
\frac{d}{dt}S &= \Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S - \mu S,\\
\frac{d}{dt}I_0^0 &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S - \phi_0^0 I_0^0,\\
\frac{d}{dt}I_j^i &= \omega_j^i I_{[j/m]}^{i-1} - \phi_j^i I_j^i.
\end{aligned} \tag{1}$$

Here, $i = 1, \ldots, n$, $j = 0, \ldots, N_i$; Λ is the recruitment rate into the susceptible class; $\beta_j^i I_j^i S$ is the standard density-dependent bilinear incidence rate of the infection

transmission; μ is per capita natural mortality rate; ϕ_0^0 and ϕ_j^i are the rates at which the individuals in the exposed and infectious compartments, respectively, leave their compartments due to either disease progression, or mortality (and hence duration of stage I_j^i is $1/\phi_j^i$), and ω_j^i is the average progression rate from $I_{[j/m]}^{i-1}$ to I_j^i. Equation for R is omitted as it is assumed that the individuals in this compartment are removed from the infection process. We assume that all variables are non-negative, and all coefficients are positive. It is naturally to expect that $\omega_j^i < \phi_{[j/m]}^{i-1}$ holds; however our results and conclusions do not depend on this condition. We consider system (1) in the non-negative octant $\mathbb{R}_{\geq 0} = \{(S, I_0^0, I_j^i),\ S \geq 0,\ I_0^0 \geq 0,\ I_j^i \geq 0\}$, which is the phase space for the system.

To simplify the notation, we assume without loss of generality that each of the infectious compartments has the same number of the next generation compartments. It is obvious that this assumption does not affect the generality of results and conclusions as one always can "remove" compartment I_j^i and all subsequential pathways simply assuming $\omega_j^i, \beta_j^i = 0$.

2.2. **A model where there is no common exposed state.** We assume now that branching into alternative pathways starts immediately after infection. Accordingly, there is no common compartment I_0^0, and the population is partitioned into following compartments: the susceptible compartment S, the infectious compartments I_j^i and the removed compartment R (see Fig. 1, right diagram). After infection an individual immediately moves, with the probability p_j (where $j = 0, \ldots, m-1$ and $\sum_{j=0}^{m-1} p_j = 1$) into one of m compartments I_j^1. This model can be described by the following system of differential equations:

$$\begin{aligned}
\frac{d}{dt}S &= \Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \mu S, \\
\frac{d}{dt}I_k^1 &= p_k \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \phi_k^1 I_k^1, \qquad\qquad k = 0, \ldots, N_1 \\
\frac{d}{dt}I_j^i &= \omega_j^i I_{[j/m]}^{i-1} - \phi_j^i I_j^i, \qquad \text{for} \quad i = 2, \ldots, n;\ j = 0, \ldots, N_i.
\end{aligned} \tag{2}$$

Here all parameters are defined as above; the equation for $R(t)$is omitted.

We have to stress that the absence of the common compartment I_0^0 does not necessary implies the absence of a latent state, as one can always assume that $\beta_j^1 = 0$ for any or all of j (in fact, one can assume β_j^i for any i, j as well).

3. **Properties of the models.** It is easy to see that systems (1) and (2) always have an infection-free equilibrium state with $S = \Lambda/\mu$ and $I_j^i = 0$. Apart from this equilibrium state, both models can also have an endemic equilibrium state.

At an equilibrium state of the model (1), the equalities

$$\Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \mu S = 0, \tag{3}$$

$$\sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \phi_0^0 I_0^0 = 0, \tag{4}$$

$$\omega_j^i I_{[j/m]}^{i-1} - \phi_j^i I_j^i = 0, \tag{5}$$

hold for all $i = 1, \dots, n,\ j = 0, \dots, N_i$. At an equilibrium state of model (2), the equalities

$$\Lambda - \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i S - \mu S = 0, \tag{6}$$

$$p_k \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i S - \phi_k^1 I_k^1 = 0, \tag{7}$$

$$\omega_j^i I_{[j/m]}^{i-1} - \phi_j^i I_j^i = 0, \tag{8}$$

where $k = 0, \dots, N_1$, $i = 2, \dots, n$ and $j = 0, \dots, N_i$, hold. Equalities (5) and (8) imply that the equilibrium level for each of I_j^i can be expressed as a fraction of the equilibrium level for I_k^1. Let

$$\varkappa_j^1 = \beta_j^1, \qquad \varkappa_j^i = \beta_j^i \prod_{l=0}^{i-2} \frac{\omega_{[j/m^l]}^{i-l}}{\phi_{[j/m^l]}^{i-l}}, \qquad \varkappa_k = \sum_{i=1}^{n} \sum_{j=k\cdot m^{i-1}}^{(k+1)m^{i-1}-1} \varkappa_j^i, \tag{9}$$

where $i \geq 2$ and $k = 0, \dots, N_1$. Then $\beta_j^i I_j^i = \varkappa_j^i I_{[j/m^{i-1}]}^1$. Furthermore, for any k, l such that $p_k, p_l \neq 0$, equality (7) implies that

$$\frac{\phi_k^1}{p_k} I_k^1 = \frac{\phi_l^1}{p_l} I_l^1.$$

For model (2) we denote $\phi_0^0 = 1$, $\omega_k^1 = p_k$ and

$$\frac{\phi_k^1}{p_k} I_k^1 = \frac{\phi_l^1}{p_l} I_l^1 = I_0^0. \tag{10}$$

Then

$$\sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i S = \sum_{k=0}^{N_1} \varkappa_k I_k^1 S = \varkappa \phi_0^0 I_0^0 S, \qquad \text{where } \varkappa = \sum_{k=0}^{N_1} \frac{\varkappa_k \omega_k^1}{\phi_k^1 \phi_0^0},$$

hold at an equilibrium state for both systems. Substituting these into (3–5), or into (6–8) yields

$$\Lambda - \mu S = \varkappa I_0^0 S, \qquad I_0^0 \phi_0^0 (\varkappa S - 1) = 0, \qquad \omega_j^i I_{[j/m]}^{i-1} = \phi_j^i I_j^i.$$

The second equation has two solutions: either $I_0^0 = 0$, or $S = \varkappa^{-1}$ holds. Substituting either of these into the first equation, we obtain that either $S = \frac{\Lambda}{\mu}$, or $I_0^0 = \frac{1}{\phi_0^0}\left(\Lambda - \frac{\mu}{\varkappa}\right)$, respectively, holds. Since in either case I_0^0 is known, we can now find sequentially all I_j^i from (5), or (8) and (10). Hence, the equilibrium states of the systems are found.

Either of the systems has two equilibrium states:

(i) disease-free equilibrium state $Q_0 = (\widetilde{S}, \widetilde{I_0^0}, \widetilde{I_j^i})$, where $\widetilde{S} = \frac{\Lambda}{\mu}$ and $\widetilde{I_0^0} = \widetilde{I_j^i} = 0$ for all i, j; and

(ii) endemic equilibrium state $Q^* = (S^*, I^{*0}_0, I^{*i}_j)$, where $S^* = \varkappa^{-1}$, $I^{*0}_0 = \frac{1}{\phi_0^0}(\Lambda - \frac{\mu}{\varkappa})$, $I^{*i}_j = \frac{\omega_j^i}{\phi_j^i} I^{*i-1}_{[j/m]}$ $(i = 1, \dots, n,\ j = 0, \dots, N_i)$ for (1), or $S^* = \varkappa^{-1}$, $I^{*1}_k = \frac{p_k}{\phi_k^1}\left(\Lambda - \frac{\mu}{\varkappa}\right)$, $I^{*i}_j = \frac{\omega_j^i}{\phi_j^i} I^{*i-1}_{[j/m]}$ $(i = 2, \dots, n,\ j = 0, \dots, N_i)$ for (2).

Note that while the disease-free equilibrium state Q_0 always exists, the endemic equilibrium state Q^* exists if and only if $R_0 = \Lambda\varkappa/\mu > 1$; if $R_0 \le 1$ then Q_0 is the only equilibrium state of the systems (1) and (2). Here $R_0 = \Lambda\varkappa/\mu$ is the basic reproduction number for these systems [6, 39].

The following theorem addresses the properties of the equilibrium states.

Theorem 3.1. *Systems (1) and (2) are globally asymptotically stable. That is,*

(i) if $R_0 > 1$, then the endemic equilibrium state Q^* exists and is globally asymptotically stable in $\mathbb{R}_+$;

(ii) if $R_0 \le 1$, then disease-free equilibrium state Q_0 is globally asymptotically stable in $\mathbb{R}_{\ge 0}$.

4. Proof of the Theorem.

4.1. Global stability of endemic equilibrium state Q^* when $R_0 > 1$. Let $R_0 > 1$, and hence $S^*, I^{*0}_0, I^{*i}_j > 0$. We consider a function

$$V(S, I^0_0, I^i_j) = S - S^* \ln S + A(I^0_0 - I^{*0}_0 \ln I^0_0) + \sum_{i=1}^{n}\sum_{j=0}^{N_i} B^i_j (I^i_j - I^{*i}_j \ln I^i_j). \tag{11}$$

Here $A = 1$ for model (1), or $A = 0$ for (2), and B^i_j satisfy

$$B^n_j \phi^n_j = \beta^n_j S^*, \quad j = 0, \dots, N_n, \tag{12}$$

$$B^i_j \phi^i_j = \beta^i_j S^* + \sum_{k=0}^{m-1} B^{i+1}_{m\cdot j+k} \omega^{i+1}_{m\cdot j+k}, \tag{13}$$

$$\text{for} \quad j = 0, \dots, N_i, \ i = 1, \dots, n-1.$$

The coefficients B^i_j obviously exist and are non-negative. It is easy to see that function $V(S, I^0_0, I^i_j)$ is continuously differentiable in $\mathbb{R}_+$, and that point Q^* is its global minimum in $\mathbb{R}_+$.

For model (2) we note, that, by (13) and (8),

$$\begin{aligned} \sum_{j=0}^{N_i} B^i_j \phi^i_j I^{*i}_j &= \sum_{j=0}^{N_i} \beta^i_j S^* I^{*i}_j + \sum_{j=0}^{N_i}\sum_{k=0}^{m-1} B^{i+1}_{m\cdot j+k} \omega^{i+1}_{m\cdot j+k} I^{*i}_j \\ &= \sum_{j=0}^{N_i} \beta^i_j S^* I^{*i}_j + \sum_{j=0}^{N_i}\sum_{k=0}^{m-1} B^{i+1}_{m\cdot j+k} \phi^{i+1}_{m\cdot j+k} I^{*i+1}_{m\cdot j+k}. \end{aligned} \tag{14}$$

Applying this equality recurrently and recalling (12) yields

$$B^i_j \phi^i_j I^{*i}_j = B^i_j \omega^i_j I^{*i-1}_{[j/m]} = \sum_{l=i}^{n} \sum_{k=jm^{l-i}}^{(j+1)m^{l-i}-1} \beta^l_k I^{*l}_k S^*, \tag{15}$$

$$\sum_{j=0}^{N_i} B^i_j \phi^i_j I^{*i}_j = \sum_{l=i}^{n}\sum_{j=0}^{N_l} \beta^l_j I^{*l}_j S^*, \tag{16}$$

and hence

$$\sum_{i=1}^{n}\sum_{j=0}^{N_i} B^i_j \phi^i_j I^{*i}_j = \sum_{i=1}^{n}\sum_{j=0}^{N_i} i\beta^i_j I^{*i}_j S^*. \tag{17}$$

We now observe that for B^i_j the following equalities hold:

$$\sum_{k=0}^{N_1} B^1_k p_k = 1, \tag{18}$$

$$B^1_k p_k \varkappa_q I^{*1}_q = B^1_q p_q \varkappa_k I^{*1}_k, \quad k = 0, \ldots, N_1;\ q = 0, \ldots, N_1. \tag{19}$$

Indeed, (17) holds for coefficients B^1_k, and, by (7), $\sum\limits_{i=1}^{n}\sum\limits_{j=0}^{N_i} \beta^i_j I^{*i}_j S = \dfrac{\phi^1_k}{p_k} I^{*1}_k = \dfrac{\phi^1_q}{p_q} I^{*1}_q$. Hence

$$\sum_{k=0}^{N_1} B^1_k p_k = \sum_{k=0}^{N_1} B^1_k \phi^1_k I^{*1}_k \frac{p_k}{\phi^1_k I^{*1}_k} = \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^{*i}_j S^* \Big/ \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^{*i}_j S^* = 1,$$

and

$$\begin{aligned} B^1_k p_k \varkappa_q I^{*1}_q &= B^1_k \phi^1_k I^{*1}_k \frac{p_k}{\phi^1_k I^{*1}_k} \varkappa_q I^{*1}_q = \sum_{i=1}^{n} \sum_{j=m^{i-1}k}^{m^{i-1}(k+1)-1} \beta^i_j I^{*i}_j S^* \cdot \frac{p_k}{\phi^1_k I^{*1}_k} \varkappa_q I^{*1}_q \\ &= \varkappa_k I^{*1}_k S^* \cdot \frac{p_k}{\phi^1_k I^{*1}_k} \varkappa_q I^{*1}_q = \varkappa_k I^{*1}_k \cdot \frac{p_q}{\phi^1_q I^{*1}_q} \varkappa_q I^{*1}_q S^* \\ &= \varkappa_k I^{*1}_k \frac{p_q}{\phi^1_q I^{*1}_q} \sum_{i=1}^{n} \sum_{j=m^{i-1}q}^{m^{i-1}(q+1)-1} \beta^i_j I^{*i}_j S^* = \varkappa_k I^{*1}_k B^1_q p_q. \end{aligned}$$

Using (6) and (18), the derivative $\dfrac{dV}{dt}$ for model (2) satisfies

$$\begin{aligned} \frac{d}{dt}V &= \Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^i_j S - \mu S - \Lambda \frac{S^*}{S} + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^i_j S^* + \mu S^* \\ &\quad + \sum_{k=0}^{N_1} \left(B^1_k p_k \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^i_j S \left(1 - \frac{I^{*1}_k}{I^1_k}\right) - B^1_k \phi^1_k I^1_k + B^1_k \phi^1_k I^{*1}_k \right) \\ &\quad + \sum_{i=2}^{n}\sum_{j=0}^{N_i} \left[B^i_j \omega^i_j I^{i-1}_{[j/m]} - B^i_j \phi^i_j I^i_j - B^i_j \omega^i_j I^{i-1}_{[j/m]} \frac{I^{*i}_j}{I^i_j} + B^i_j \phi^i_j I^{*i}_j \right] \\ &= \mu S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^i_j S^* \\ &\quad - \sum_{k=0}^{N_1} B^1_k \phi^1_k I^1_k - \sum_{i=2}^{n}\sum_{j=0}^{N_i} B^i_j \phi^i_j I^i_j + \sum_{i=2}^{n}\sum_{j=0}^{N_i} B^i_j \omega^i_j I^{i-1}_{[j/m]} \\ &\quad + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^{*i}_j S^* + \sum_{k=0}^{N_1} B^1_k \phi^1_k I^{*1}_k + \sum_{i=2}^{n}\sum_{j=0}^{N_i} B^i_j \phi^i_j I^{*i}_j - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta^i_j I^{*i}_j S^* \frac{S^*}{S} \\ &\quad - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\sum_{k=0}^{N_1} B^1_k p_k \beta^i_j I^i_j S \frac{I^{*1}_k}{I^1_k} - \sum_{i=2}^{n}\sum_{j=0}^{N_i} B^i_j \omega^i_j I^{i-1}_{[j/m]} \frac{I^{*i}_j}{I^i_j} \\ &= \mu S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + X + Y. \end{aligned}$$

Here,

$$\begin{aligned} X &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S^* - \sum_{i=1}^{n}\sum_{j=0}^{N_i} B_j^i\phi_j^i I_j^i + \sum_{i=2}^{n}\sum_{j=0}^{N_i} B_j^i\omega_j^i I_{[j/m]}^{i-1} \\ &= \sum_{i=1}^{n-1}\sum_{j=0}^{N_i} I_j^i\left[\beta_j^i S^* + \sum_{k=0}^{m-1} B_{jm+k}^{i+1}\omega_{jm+k}^{i+1} - B_j^i\phi_j^i\right] + \sum_{j=0}^{N_n} I_j^n\left(\beta_j^n S^* - B_j^n\phi_j^n\right), \end{aligned}$$

and hence, by definition of B_j^i (12), (13), $X = 0$.

$$\begin{aligned} Y &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I^{*i}{}_j S^* + \sum_{i=1}^{n}\sum_{j=0}^{N_i} i\beta_j^i I^{*i}{}_j S^* - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I^{*i}{}_j S^*\frac{S^*}{S} \\ &\quad - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\sum_{k=0}^{N_1} B_k^1 p_k\beta_j^i I_j^i S\frac{I^{*1}_k}{I_k^1} - \sum_{i=2}^{n}\sum_{j=0}^{N_i}\sum_{l=0}^{i-2}\beta_j^i I^{*i}{}_j S^*\frac{I^{*i-l}_{[j/m^l]}}{I^{i-l}_{[j/m^l]}}\frac{I^{i-(l+1)}_{[j/m^{l+1}]}}{I^{*i-(l+1)}_{[j/m^{l+1}]}} \\ &= \sum_{j=0}^{N_1}\sum_{k=0}^{N_1} B_k^1 p_k\beta_j^1 I^{*1}{}_j S^*\left(2 - \frac{S^*}{S} - \frac{I_j^1}{I^{*1}_j}\frac{I^{*1}_k}{I_k^1}\frac{S}{S^*}\right) + \\ &\quad + \sum_{k=0}^{N_1}\sum_{i=2}^{n}\sum_{j=0}^{N_i} B_k^1 p_k\beta_j^i I^{*i}{}_j S^*\left(1 + i - \mathfrak{C}_{i,j}^k\right), \end{aligned}$$

where $\mathfrak{C}_{i,j}^k = \frac{S^*}{S} + \frac{I_j^i I^{*1}_k S}{I^{*i}_j I_k^1 S*} + \sum_{l=0}^{i-2}\frac{I^{*i-l}_{[j/m^l]} I^{i-(l+1)}_{[j/m^{l+1}]}}{I^{i-l}_{[j/m^l]} I^{*i-(l+1)}_{[j/m^{l+1}]}}$, for any $k = 0,\ldots,N_1$, $i = 2,\ldots,n$, $j = 0,\ldots,N_i$.

The subset of pairs (i,j), $i = 2,\ldots,n$, $j = 0,\ldots,N_i$ that satisfy $j/m^{i-1} = q$, $q = 0,\ldots,N_1$ (or, what is the same, $q\cdot m^{i-1} \le j \le (q+1)m^{i-1} - 1$) is denoted by $\mathfrak{D}(q)$. Note, that if $(i,j) \in \mathfrak{D}(q)$ then the product of terms of $\mathfrak{C}_{i,j}^k$,

$$prod(\mathfrak{C}_{i,j}^k) = \frac{S^*}{S}\cdot\frac{I_j^i I^{*1}_k S}{I^{*i}_j I_k^1 S*}\cdot\prod_{l=0}^{i-2}\frac{I^{*i-l}_{[j/m^l]} I^{i-(l+1)}_{[j/m^{l+1}]}}{I^{i-l}_{[j/m^l]} I^{*i-(l+1)}_{[j/m^{l+1}]}} = \frac{I^{*1}_k I_q^1}{I_k^1 I^{*1}_q}.$$

In particular, $prod(\mathfrak{C}_{i,j}^k) = 1$ if only $(i,j) \in \mathfrak{D}(k)$. Now,

$$\begin{aligned} Y =& \sum_{k=0}^{N_1}\sum_{q=0}^{N_1} B_k^1 p_k\left(\beta_q^1 I^{*1}{}_q S^*\left(2 - \frac{S^*}{S} - \frac{I_q^1}{I^{*1}_q}\frac{I^{*1}_k}{I_k^1}\frac{S}{S^*}\right)\right. \\ &\left. + \sum_{(i,j)\in\mathfrak{D}(q)}\beta_j^i I^{*i}{}_j S^*\left(1 + i - \mathfrak{C}_{i,j}^k\right)\right) \\ =& \sum_{k=0}^{N_1} B_k^1 p_k\left(\beta_k^1 I^{*1}{}_k S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + \sum_{(i,j)\in\mathfrak{D}(k)}\beta_j^i I^{*i}{}_j S^*\left(1 + i - \mathfrak{C}_{i,j}^k\right)\right) \\ &+ \sum_{k=1}^{N_1}\sum_{q=0}^{k-1} Z_{k,q} \\ \le& \sum_{k=1}^{N_1}\sum_{q=0}^{k-1} Z_{k,q}. \end{aligned}$$

Here

$$Z_{k,q} = B_k^1 p_k S^* \left(\beta_q^1 I^{*1}_q \left(2 - \frac{S^*}{S} - \frac{I_q^1}{I^{*1}_q} \frac{I^{*1}_k}{I_k^1} \frac{S}{S^*} \right) + \sum_{(i,j)\in\mathfrak{D}(k)} \beta_j^i I^{*i}_j \left(1 + i - \mathfrak{C}^k_{i,j}\right) \right)$$
$$+ B_q^1 p_q S^* \left(\beta_k^1 I^{*1}_k \left(2 - \frac{S^*}{S} - \frac{I_k^1}{I^{*1}_k} \frac{I^{*1}_q}{I_q^1} \frac{S}{S^*} \right) + \sum_{(i,j)\in\mathfrak{D}(k)} \beta_j^i I^{*i}_j \left(1 + i - \mathfrak{C}^q_{i,j}\right) \right).$$

By (9) and (19), we have for any $k = 0, \ldots, N_1$, $q = 0, \ldots, N_1$

$$B_k^1 p_k \beta_q^1 I^{*1}_q S^* + \sum_{(i,j)\in\mathfrak{D}(k)} B_k^1 p_k \beta_j^i I^{*i}_j S^* = B_q^1 p_q \beta_k^1 I^{*1}_k S^* + \sum_{(i,j)\in\mathfrak{D}(k)} B_q^1 p_q \beta_j^i I^{*i}_j S^*. \tag{20}$$

Furthermore, obviously, the following equalities hold:

$$\begin{aligned}
\frac{S^*}{S} \cdot \frac{I_q^1}{I^{*1}_q} \frac{I^{*1}_k}{I_k^1} \frac{S}{S^*} \cdot \frac{S^*}{S} \cdot \frac{I_k^1}{I^{*1}_k} \frac{I^{*1}_q}{I_q^1} \frac{S}{S^*} &= 1, \\
prod(\mathfrak{C}^k_{i,j}) \cdot prod(\mathfrak{C}^q_{\tilde{i},\tilde{j}}) &= 1, \quad (i,j) \in \mathfrak{D}(q), \quad (\tilde{i},\tilde{j}) \in \mathfrak{D}(k), \\
\frac{S^*}{S} \cdot \frac{I_q^1}{I^{*1}_q} \frac{I^{*1}_k}{I_k^1} \frac{S}{S^*} \cdot prod(\mathfrak{C}^q_{\tilde{i},\tilde{j}}) &= 1, \quad (i,j) \in \mathfrak{D}(q), \\
prod(\mathfrak{C}^k_{i,j}) \cdot \frac{S^*}{S} \cdot \frac{I_k^1}{I^{*1}_k} \frac{I^{*1}_q}{I_q^1} \frac{S}{S^*} &= 1, \quad (\tilde{i},\tilde{j}) \in \mathfrak{D}(k).
\end{aligned}$$

This guarantees that $Z_{k,q} \le 0$ for any k, q (for clarification, see Appendix), and hence $\dfrac{dV}{dt} \le 0$ holds in $\mathbb{R}_+$, provided that $S^*, I^{*i}_j > 0$. Furthermore, $\dfrac{dV}{dt} = 0$ holds only on the straight line $S = S^*$, $\dfrac{I^i_j}{I^{*i}_j} = \dfrac{I^1_k}{I^{*1}_k}$, $i = 2, \ldots, n-1$, $j = 0, \ldots, N_i$, $k = 0, \ldots, N_1$. Moreover, it is easy to see that point Q^* is the only invariant set of system (2) in the set $S = S^*$, $\dfrac{I^i_j}{I^{*i}_j} = \dfrac{I^1_k}{I^{*1}_k}$, and hence by Lyapunov-LaSalle asymptotic stability theorem [3, 25, 27], the equilibrium state Q_* is globally asymptotically stable.

Likewise, for model (1), using equality $\Lambda = \sum\limits_{i=1}^{n} \sum\limits_{j=0}^{N_i} \beta_j^i I^{*i}_j S^* + \mu S^*$, the derivative of function $V(S, I^0_0, I^i_j)$ satisfies:

$$\begin{aligned}
\frac{d}{dt}V &= \Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \mu S - \Lambda \frac{S^*}{S} + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S^* + \mu S^* \\
&\quad + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S - \phi_0^0 I_0^0 - \sum_{i=1}^{n}\sum_{j=0}^{N_i} \beta_j^i I_j^i S \frac{I^{*0}_0}{I_0^0} + \phi_0^0 I^{*0}_0 \\
&\quad + \sum_{i=1}^{n}\sum_{j=0}^{N_i} \left[B_j^i \omega_j^i I^{i-1}_{[j/m]} - B_j^i \phi_j^i I_j^i - B_j^i \omega_j^i I^{i-1}_{[j/m]} \frac{I^{*i}_j}{I_j^i} + B_j^i \phi_j^i I^{*i}_j \right] \\
&= \mu S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*} \right) + X + Y,
\end{aligned}$$

where

$$X = \sum_{i=1}^{n}\sum_{j=0}^{N_i}\left(\beta_j^i I_j^i S^* + B_j^i \omega_j^i I_{[j/m]}^{i-1} - B_j^i \phi_j^i I_j^i\right) - \phi_0^0 I_0^0$$

and

$$\begin{aligned} Y = &\sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i {I^*}_j^i S^* + \phi_0^0 {I^*}_0^0 + \sum_{i=1}^{n}\sum_{j=0}^{N_i} B_j^i \phi_j^i {I^*}_j^i \\ &- \sum_{i=1}^{n}\sum_{j=0}^{N_i}\left[\beta_j^i {I^*}_j^i S^* \frac{S^*}{S} - \beta_j^i I_j^i S \frac{{I^*}_0^0}{I_0^0} - B_j^i \omega_j^i I_{[j/m]}^{i-1}\frac{{I^*}_j^i}{I_j^i}\right]. \end{aligned}$$

Obviously, $\mu S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) \le 0$ holds for all $S, S^* > 0$. Furthermore, by (5), (16) and (4),

$$\sum_{j=0}^{N_1} B_j^1 \omega_j^1 = \frac{1}{{I^*}_0^0}\sum_{j=0}^{N_1} B_j^1 \phi_j^1 {I^*}_j^1 = \frac{1}{{I^*}_0^0}\sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i {I^*}_j^i S = \phi_0^0, \tag{21}$$

and hence, by (12), (13) and (21), $X = 0$.

In order to prove that $Y \le 0$ holds in $\mathbb{R}_+$, we firstly note that if all $S^*, {I^*}_0^0, {I^*}_j^i \ge 0$, then, by the theorem that the arithmetic mean is greater than or equal to the geometric mean,

$$W_j^i(S, I_0^0, I_j^i) = 2 + i - \frac{S^*}{S} - \frac{{I^*}_0^0}{I_0^0}\frac{I_j^i}{{I^*}_j^i}\frac{S}{S^*} - \sum_{k=0}^{i-1}\frac{{I^*}_{[j/m^k]}^{i-k}}{I_{[j/m^k]}^{i-k}}\frac{I_{[j/m^{k+1}]}^{i-(k+1)}}{{I^*}_{[j/m^{k+1}]}^{i-(k+1)}} \le 0$$

holds for all $(S, I_0^0, I_j^i) \in \mathbb{R}_+$ and for all $i = 1, \ldots, n$, $j = 0, \ldots, N_i$. Our intention is to prove that $Y = \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i {I^*}_j^i S^* W_j^i$, and hence $Y \le 0$. By (15),

$$\begin{aligned} \sum_{i=1}^{n}\sum_{j=0}^{N_i}\sum_{k=0}^{i-1}\beta_j^i {I^*}_j^i S^* \frac{{I^*}_{[j/m^k]}^{i-k}}{I_{[j/m^k]}^{i-k}}\frac{I_{[j/m^{k+1}]}^{i-(k+1)}}{{I^*}_{[j/m^{k+1}]}^{i-(k+1)}} &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\sum_{l=i}^{n}\sum_{k=m^{l-i}j}^{m^{l-i}(j+1)-1}\beta_k^l {I^*}_k^l S^* \frac{I_{[j/m]}^{i-1}}{{I^*}_{[j/m]}^{i-1}}\frac{{I^*}_j^i}{I_j^i} \\ &= \sum_{i=1}^{n}\sum_{j=0}^{N_i} B_j^i \omega_j^i {I^*}_{[j/m]}^{i-1}\frac{I_{[j/m]}^{i-1}}{{I^*}_{[j/m]}^{i-1}}\frac{{I^*}_j^i}{I_j^i}. \end{aligned}$$

Using this, (4) and (17), we obtain

$$\begin{aligned} \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i {I^*}_j^i S^* W_j^i &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\left[2 + i - \frac{S^*}{S} - \frac{{I^*}_0^0}{I_0^0}\frac{I_j^i}{{I^*}_j^i}\frac{S}{S^*}\right]\beta_j^i {I^*}_j^i S^* \\ &\quad - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\sum_{k=0}^{i-1}\frac{{I^*}_{[j/m^k]}^{i-k}}{I_{[j/m^k]}^{i-k}}\frac{I_{[j/m^{k+1}]}^{i-(k+1)}}{{I^*}_{[j/m^{k+1}]}^{i-(k+1)}}\beta_j^i {I^*}_j^i S^* \\ &= \sum_{i=1}^{n}\sum_{j=0}^{N_i}\left[2\beta_j^i {I^*}_j^i S^* + B_j^i \phi_j^i {I^*}_j^i - \beta_j^i {I^*}_j^i S^*\frac{S^*}{S}\right] \\ &\quad - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\left[\beta_j^i I_j^i S\frac{{I^*}_0^0}{I_0^0} + B_j^i \omega_j^i I_{[j/m]}^{i-1}\frac{{I^*}_j^i}{I_j^i}\right] = Y. \end{aligned}$$

Therefore, $\frac{d}{dt}V = \mu S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + X + Y \le 0$ holds for all $(S, I_0^0, I_j^i) \in \mathbb{R}_+$. Furthermore, $\frac{d}{dt}V = 0$ holds only on the straight line $S = S^*$, $\frac{I_j^i}{I^{*i}_j} = \frac{I_0^0}{I^{*0}_0}$, $i = 1, \ldots, n-1$, $j = 0, \ldots, N_i$. This line is transversal to the phase flow everywhere except Q^*, and point Q^* is the only invariant set of the system on the line. Hence by Lyapunov-LaSalle asymptotic stability theorem, the equilibrium state Q_* is globally asymptotically stable.

4.2. **Stability of the disease-free equilibrium state.** Let $R_0 \le 1$ and consider a function

$$V(S, I_0^0, I_j^i) = S - \widetilde{S}\ln S + AI_0^0 + \sum_{i=1}^{n}\sum_{j=0}^{N_i} B_j^i I_j^i,$$

where $A = 1$ for model (1) and $A = 0$ for model (2), and B_j^i are defined as following:

$$B_j^n \phi_j^n = \beta_j^n \widetilde{S}, \quad j = 0, \ldots, N_n, \tag{22}$$

$$B_j^i \phi_j^i = \beta_j^i \widetilde{S} + \sum_{k=0}^{m-1} B_{m\cdot j+k}^{i+1} \omega_{m\cdot j+k}^{i+1}, \tag{23}$$

$$\text{for} \quad j = 0, \ldots, N_i, \ i = 1, \ldots, n-1.$$

We prove that if $R_0 < 1$ then the derivative of this function $\dfrac{dV}{dt} \le 0$. We note that

$$\begin{aligned} B_k^1\phi_k^1 &= \beta_k^1\tilde{S} + \frac{\omega_{m\cdot k+l}^2}{\phi_{m\cdot k+l}^2}\sum_{l=0}^{m-1} B_{m\cdot k+l}^2\phi_{m\cdot k+l}^2 = \ldots \\ &= \sum_{i=1}^{n}\sum_{j=k\cdot m^{i-1}}^{(k+1)m^{i-1}-1} \beta_j^i\tilde{S}\prod_{l=0}^{i-2}\frac{\omega_{[j/m^l]}^{i-l}}{\phi_{[j/m^l]}^{i-1}} = \sum_{i=1}^{n}\sum_{j=k\cdot m^{i-1}}^{(k+1)m^{i-1}-1} \varkappa_j^i\tilde{S} = \varkappa_k\tilde{S}, \end{aligned}$$

and hence

$$\sum_{k=0}^{N_1} B_k^1 p_k = \tilde{S}\sum_{k=0}^{N_1}\frac{p_k}{\phi_k^1}\varkappa_k = \frac{\Lambda}{\mu}\varkappa = R_0. \tag{24}$$

Then, for model (2), using (6) and (22–24), the derivative $\dfrac{dV}{dt}$ satisfies

$$\begin{aligned} \frac{d}{dt}V &= \Lambda - \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S - \mu S - \Lambda\frac{\tilde{S}}{S} + \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i\tilde{S} + \mu\tilde{S} - \sum_{i=2}^{n}\sum_{j=0}^{N_i} B_j^i\phi_j^i I_j^i \\ &\quad + \sum_{k=0}^{N_1} B_k^1 p_k \sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S - \sum_{k=0}^{N_1} B_k^1\phi_k^1 I_k^1 + \sum_{i=2}^{n}\sum_{j=0}^{N_i} B_j^i\omega_j^i I_{[j/m]}^{i-1} \\ &= \Lambda\left[2 - \frac{\tilde{S}}{S} - \frac{S}{\tilde{S}}\right] + \left[\sum_{k=0}^{N_1} B_k^1 p_k - 1\right]\sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S \\ &\quad + \sum_{i=1}^{n-1}\sum_{j=0}^{N_i} I_j^i\left[\beta_j^i\tilde{S} + \sum_{k=0}^{m-1} B_{jm+k}^{i+1}\omega_{jm+k}^{i+1} - B_j^i\phi_j^i\right] + \sum_{j=0}^{N_n} I_j^n\left(\beta_j^n\tilde{S} - B_j^n\phi_j^n\right) \\ &= \Lambda\left[2 - \frac{\tilde{S}}{S} - \frac{S}{\tilde{S}}\right] - (1 - R_0)\sum_{i=1}^{n}\sum_{j=0}^{N_i}\beta_j^i I_j^i S. \end{aligned}$$

Thus, $\frac{d}{dt}V \leq 0$ holds in $\mathbb{R}_{\geq 0}$, and $\frac{d}{dt}V = 0$ holds only if $S = \tilde{S}$, $I_j^i = 0$ or $S = \tilde{S}$, $R_0 = 1$. The equilibrium state Q_0 is the only invariant set of (2) in set $M = \left\{(S, I_j^i) \in \mathbb{R}_{\geq 0} \mid S = \widetilde{S}\right\}$ (where $\frac{d}{dt}V = 0$ holds). Hence by Lyapunov-LaSalle asymptotic stability theorem, the equilibrium state Q_0 is globally asymptotically stable when $R_0 \leq 1$.

For model (1) note, that

$$\sum_{j=0}^{N_1} B_j^1 \omega_j^1 = \sum_{j=0}^{N_1} B_j^1 \phi_j^1 \frac{\omega_j^1}{\phi_j^1} = \sum_{j=0}^{N_1} \beta_j^i \widetilde{S} \frac{\omega_j^1}{\phi_j^1} + \sum_{j=0}^{N_1} \frac{\omega_j^1}{\phi_j^1} \sum_{k=0}^{m-1} B_{m\cdot j+k}^2 \omega_{m\cdot j+k}^2.$$

$B_l^2 \omega_l^2$ can be likewise represented in terms of $B_p^3 \omega_p^3$, then $B_p^3 \omega_p^3$ in terms of $B_q^4 \omega_q^4$, and so on. Hence, applying this equality recurrently,

$$\begin{aligned} \sum_{j=0}^{N_1} B_j^1 \omega_j^1 &= \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i \widetilde{S} \prod_{l=0}^{i-1} \frac{\omega_{[j/m^l]}^{i-l}}{\phi_{[j/m^l]}^{i-1}} \\ &= \sum_{i=1}^{n} \sum_{j=0}^{N_i} \varkappa_j^i \widetilde{S} = \varkappa \widetilde{S} \phi_0^0 = R_0 \phi_0^0. \end{aligned} \tag{25}$$

Using (3), (22), (23) and (25), we have for derivative dV/dt:

$$\begin{aligned} \frac{d}{dt}V &= \Lambda - \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i S - \mu S - \Lambda \frac{\widetilde{S}}{S} + \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i \widetilde{S} + \mu \widetilde{S} \\ &\quad + \sum_{i=1}^{n} \sum_{j=0}^{N_i} \beta_j^i I_j^i S - \phi_0^0 I_0^0 + \sum_{i=1}^{n} \sum_{j=0}^{N_i} B_j^i \omega_j^i I_{[j/m]}^{i-1} - \sum_{i=1}^{n} \sum_{j=0}^{N_i} B_j^i \phi_j^i I_j^i \\ &= \Lambda \left[2 - \frac{\widetilde{S}}{S} - \frac{S}{\widetilde{S}}\right] + I_0^0 \left(\sum_{j=0}^{N_1} B_j^1 \omega_j^1 - \phi_0^0\right) \\ &\quad + \sum_{i=1}^{n} \sum_{j=0}^{N_i} I_j^i \left[\beta_j^i \widetilde{S} + \sum_{k=0}^{m-1} B_{jm+k}^{i+1} \omega_{jm+k}^{i+1} - B_j^i \phi_j^i\right] + \sum_{j=0}^{N_n} I_j^n \left(\beta_j^n \widetilde{S} - B_j^n \phi_j^n\right) \\ &= \Lambda \left[2 - \frac{\widetilde{S}}{S} - \frac{S}{\widetilde{S}}\right] - I_0^0 \phi_0^0 \left(1 - R_0\right). \end{aligned}$$

Hence $R_0 \leq 1$ ensures that $\dfrac{dV}{dt} \leq 0$ holds in $\mathbb{R}_{\geq 0}$, and $\frac{d}{dt}V = 0$ holds only if either $S = \widetilde{S}$, $I_0^0 = 0$, or $S = \widetilde{S}$, $R_0 = 1$. Furthermore, point Q_0 is the only invariant set of the system in the subspace $S = \widetilde{S}$, where $\frac{d}{dt}V = 0$ holds. Hence, by Lyapunov-LaSalle asymptotic stability theorem, the equilibrium state Q_0 is globally asymptotically stable when $R_0 \leq 1$. This completes the proof.

We have to remark that in the first part of the proof it was assumed that $I^{*i}_j > 0$, and we considered only the trajectories starting in $I_j^i > 0$ for all i, j. Let us consider the case, when some (but not all) of I_j^i or I^{*i}_j are zero. In this case, some expressions do not have sense, since I_j^i and I^{*i}_j occur in denominator. However, it suffices to make a few reservations to extend the proof to this case. Note that, by (8), $I^{*i}_j = 0$ holds if and only if $\omega_j^i \cdot \omega_{[j/m]}^{i-1} \cdots \omega_{[j/m^{i-1}]}^1 = 0$ holds. Furthermore, $I^{*i-1}_{[j/m]} = 0$ implies $I^{*i}_j = 0$. If $I^{*i}_j \neq 0$, then it is possible to consider the asymptotic behaviour

of trajectories, which start in $I_j^i = 0$, since $\omega_j^i, \omega_{[j/m]}^{i-1}, \ldots, \omega_{[j/m^{i-1}]}^1 > 0$ and $I_j^i > 0$ at $t = t_0 + \varepsilon$. If ${I^*}_j^i = 0$ for some (i, j), then we simply exclude the corresponding terms ${I^*}_j^i \ln I_j^i$ from Lyapunov function (11). Thus, any term containing such ${I^*}_j^i$ in numerator or denominator will disappear from our calculations, which remains valid.

It is easy to see, that any transfer diagram, which has no cycles, can be constructed from our tree-like transfer diagram by eliminating excess compartments. To "eliminate" compartment I_j^i, we put $\beta_j^i = \omega_j^i = 0$, and this implies ${I^*}_j^i = 0$. Therefore, the model with a common latent state can be considered as a subcase of the model without common exposed state with parameters $p_1 = 1$, $p_k = 0$, $\beta_j^i = \omega_j^i = 0$, $\forall (i, j) \in \mathfrak{D}(k)$, $k = 2, \ldots, N_1$. Hence, Theorem 3.1 holds for system (1) as well.

5. **Conclusion.** In this paper, we considered the global dynamics of models for infectious diseases with several infectious stages and with possibility for alternative progression pathways. The motivation for this study was the question whether this diversity of stages and pathways can affect the global dynamics of a pathogen-population system. Using the direct Lyapunov method, we proved that the considered systems are glob ally asymptotically stable and possess the only globally stable equilibrium state. Depending on the basic reproduction number, this steady state is either the endemic, or the disease-free, so that the infection fades out for $R_0 \leq 1$. This result actually implies that the global dynamics of a pathogen in population is robust, and that the diversity of specific conditions of the infected individuals does not affect its basic qualitative properties. To establish the global stability for these models, we applied the direct Lyapunov method with a remarkable Lyapunov function of the form

$$V = \sum a_i \left(x_i - x_i^* \ln x_i\right).$$

Lyapunov functions of this type were applied with a great success to a variety of models in mathematical epidemiology [4, 5, 11, 12, 19, 24, 36] and in biology in general [9, 38], and these were recently extended to models with nonlinear functional responses [8, 20, 21, 22, 23], models with delays [15, 28, 33, 40] and systems of PDE [32, 34].

Appendix. Let x_k, y_l be non-negative-valued functions and $a_i, b_j \in \mathbb{R}$, where $i = 1, \ldots, n$; $j = 1, \ldots, m$. Then

$$\begin{aligned} \sum_{i=1}^{n} a_i &= \sum_{j=1}^{m} b_j, \\ \prod_{k=\underline{k}(i)}^{\bar{k}(i)} x_k \cdot \prod_{l=\underline{l}(j)}^{\bar{l}(j)} y_l &\equiv 1, \quad \forall i, j, \end{aligned}$$

implies

$$\sum_{i=1}^{n} a_i \left(\left(\bar{k}(i) - \underline{k}(i) + 1\right) - \sum_{k=\underline{k}(i)}^{\bar{k}(i)} x_k \right) + \sum_{j=1}^{m} b_j \left(\left(\bar{l}(i) - \underline{l}(i) + 1\right) - \sum_{l=\underline{l}(j)}^{\bar{l}(j)} y_l \right) \leq 0.$$

The set c_q, where $q = 1, \ldots, q_{max}$, such that

$$\sum_{i=1}^{n} a_i \left(\bar{k}(i) - \underline{k}(i) + 1 - \sum_{k=\underline{k}(i)}^{\bar{k}(i)} x_k \right) + \sum_{j=1}^{m} b_j \left(\bar{l}(j) - \underline{l}(j) + 1 - \sum_{l=\underline{l}(j)}^{\bar{l}(j)} y_l \right)$$
$$= \sum_{q=1}^{q_{max}} c_q \left(\left(\bar{k}(i_q) - \underline{k}(i_q) + \bar{l}(j_q) - \underline{l}(j_q) + 2 \right) - \sum_{k=\underline{k}(i_q)}^{\bar{k}(i_q)} x_k - \sum_{l=\underline{l}(j_q)}^{\bar{l}(j_q)} y_l \right) = K,$$

exists. The principle of it's construction is illustrated by scheme (Fig. 5).

a_1		a_2			a_3	a_4		...	a_n
c_1	c_2	c_3	c_4	c_5	c_6	c_7	c_8	... $c_{q_{max}-1}$	$c_{q_{max}}$
b_1	b_2		b_3		b_4	b_5	...	b_m	

FIGURE 3. Principle of construction c_q

And therefore $K \leq 0$ because of inequality of arithmetic and geometric means, and $K = 0$ holds only if $x_k = y_l = 1, \quad \forall k, l$.

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