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GLOBAL PROPERTIES FOR SIR AND SEIR AGE-STRUCTURED MODELS

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Abstract. We consider global asymptotic properties for the *SIR* and *SEIR* age structured models for infectious diseases where the susceptibility depends on the age. Using the direct Lyapunov method with Volterra type Lyapunov functions, we establish conditions for the global stability of a unique endemic steady state and the infection-free steady state.

1. Introduction

The susceptibility of individuals varies significantly during their life time. These variations are firstly due to the development of the immune system. For a first few weeks or months of its life, a newly born is receiving maternal antibodies with mother milk. In contrast, with the age the immune system can degrade making an elderly individual more susceptible to infections. The individual level of susceptibility can also change following changes in the life style. Thus, the probability of being infected directly depends on the number of everyday contacts. Contacts of a newborn are usually limited to the family, medical personal and care givers. As a child grows, the number of contacts increases as well, and it explodes when a child enters a school. During the school and college years, the number of contacts remains large and approximately constant, and then it may decline depending on an occupation and a social role. For an elderly or retired person, the number of contacts may considerably drop to a rather limited group, which includes family and care givers. The age-varying susceptibility is particularly apparent for sexually transmitted diseases. For these infections, the probability of being infected directly depends on the number of sexual contacts, and hence on the sexual life style, which significantly varies with age.

The susceptibility of individuals also varies throughout their life due to immunisation. Immediately after successful and completed vaccination course, the individual susceptibility to a particular infection drops to virtually zero and remains at or near zero level for very long (for most cases, during whole life). However, for some infections the immunity acquired via vaccination can wane after some time leading to a rise in the susceptibility. Pertussis is probably the most apparent

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example [13]; however even for measles, where the vaccine is reliable, there are cases of immunity failure [13, 6]. This makes the models with age dependent susceptibility particular relevant for vaccination scheduler planning [32].

In the framework of a compartmental model, the progression through a succession of stages with different susceptibility can be modelled by a chain of susceptible compartments,

$$\longrightarrow S_1 \longrightarrow S_2 \longrightarrow \cdots \longrightarrow S_i \longrightarrow \cdots \longrightarrow S_n,$$

which are characterized by different susceptibility. The infectious individuals can be assumed either identical, or progressing though the same number of infectious compartments. The simplest examples of such models are *MSIR* and *MSEIR* models [6], where there are two susceptible compartments: a passively immune compartment M which includes the newly born infants, and the susceptible compartment S. A difficulty that is typical for this kind of models is their size, which makes their application and analysis difficult. Another approach is applying an age-structured model with the age dependent susceptibility. The latter type of models is considered in this notice.

The models with age-dependent susceptibility mirror in a certain sense the models with disease progression, where there is a single susceptible compartment whereas the infectious are assumed to progress through a succession of stages. The global asymptotic stability for the disease progression models with distributed infectivity was recently proved by C.C. McCluskey and collaborators [25, 23, 27]; the global properties of compartmental disease progression models were also established [4, 5, 29]. These proofs are based on the Volterra Lyapunov functions in the form $V(x) = x - a \ln x/a$. This function has been discovered by Volterra himself [33, p.15] and proved to be extremely successful for a broad variety of problems that arise in mathematical biology, including systems with an arbitrary number of subpopulations [1, 2, 14], systems with distributed subpopulations and delays [12, 20, 21, 26, 8, 10, 11], and systems with nonlinear functional responses [7, 9, 3, 15, 17, 16, 18, 28] (see also [30] for contemporary survey). In this notes we show that this type of Lyapunov functions can be successfully applied for analysis of the age structured models as well.

2. Models with age-dependent susceptibility

We assume that the distribution of the susceptibles with respect to age a at time t is $s(t, a)$, that the susceptibility depends on the age a and this dependence is given by $\beta(a)$, and that the infectious population is homogeneous and is denoted by $I(t)$. Then an *SIR* model with the age-dependent susceptibility can be described by the following equations:

$$s(t, 0) = \Lambda,$$
$$\frac{\partial s(t,a)}{\partial t} + \frac{\partial s(t,a)}{\partial a} = -m(a)s(t, a) - \beta(a)I(t)s(t, a), \tag{1}$$

$$\frac{dI(t)}{dt} = \int_0^{+\infty} \beta(a)I(t)s(t,a)da - \delta I(t).$$

Here, Λ is the constant recruitment rate, $m(a)$ is the age-dependent mortality rate of the susceptibles, and $1/\delta$ is an average duration of the infective stage. The equation for the recovered subpopulation $R(t)$ is omitted, as we assume that the recovered are immune and do not participate in the epidemic process.

If we assume that the disease has a latent state, and the infected individuals prior to becoming infectious enter an exposed state, E, then we come to a *SEIR* model. Under the assumption of the age-dependent susceptibility, the *SEIR* model is described by the following equations:

$$\begin{aligned} s(t,0) &= \Lambda, \\ \frac{\partial s(t,a)}{\partial t} + \frac{\partial s(t,a)}{\partial a} &= -m(a)s(t,a) - \beta(a)I(t)s(t,a), \\ \frac{dE(t)}{dt} &= \int_0^{+\infty} \beta(a)I(t)s(t,a)da - \mu E(t), \\ \frac{dI(t)}{dt} &= \varepsilon E(t) - \delta I(t). \end{aligned} \tag{2}$$

Here $E(t)$ is the exposed population, ε is the rate of progression of the exposed individuals to the infectious state, and μ is the rate at which the exposed individuals leave the compartment (due to all courses including progression to the infectious stage and mortality); the other parameters are as above. The equation for the recovered is omitted.

Steady states $(s(a), E, I)$ of system (2) satisfy the equalities

$$\begin{aligned} s(0) &= \Lambda, \\ \frac{\partial}{\partial a}s(a) &= -m(a)s(a) - \beta(a)Is(a), \\ 0 &= \int_0^{+\infty} \beta(a)Is(a)da - \mu E, \\ 0 &= \varepsilon E - \delta I. \end{aligned} \tag{3}$$

From the second and third equations, we have that either $E = I = 0$, or $\int_0^{+\infty} \beta(a)s(a)da = \delta/\kappa$ (where $\kappa = \varepsilon/\mu$ for the *SEIR* model) hold at a steady state. Thus, the *SEIR* model has two kinds of steady states, namely (i) a disease-free steady state $Q^0 = (s^0(a), E^0, I^0)$, where $E^0 = I^0 = 0$, $s^0(a) = \Lambda \exp\left(-\int_0^a m(\sigma)d\sigma\right)$, and (ii) an endemic (positive) steady state $Q^* = (s^*(a), E^*, I^*)$, where $s^*(a), E^*, I^* > 0$ and the equilibrium distribution $s^*(a)$

satisfies the equality $\int_0^{+\infty} \beta(a)s^*(a)da = \delta/\kappa$. Likewise, assuming $\frac{\partial s}{\partial t} = 0$ and $\frac{dI}{dt} = 0$ in (1), we obtain the equations for steady states of (1):

$$\begin{aligned} s(0) &= \Lambda, \\ \frac{\partial}{\partial a}s(a) &= -m(a)s(a) - \beta(a)Is(a), \\ 0 &= I\left(\int_0^{+\infty} \beta(a)s(a)da - \delta\right). \end{aligned} \tag{4}$$

From the last equation, we have that either $I = 0$, or $\int_0^{+\infty} \beta(a)s(a)da = \delta/\kappa$, where $\kappa = 1$ for the *SIR* model, hold at a steady state. That is, system (1) has two steady states as well.

The existence and properties of these steady states depend on the basic reproduction number R_0, which for these models is defined as

$$R_0 = \frac{\kappa}{\delta}\int_0^{+\infty} s^0(a)\beta(a)\,da, \tag{5}$$

where $\kappa = 1$ for *SIR* model (1), or $\kappa = \varepsilon/\mu$ for *SEIR* model (2).

The local properties of these and more complicated models with age-distributed subpopulations were extensively studied; see [6, 31, 30] and bibliography therein. In this notes we address global asymptotic stability of these systems constructing appropriate Volterra type Lyapunov functions.

3. Properties of the models.

The natural way to introduce a Lyapunov function is to consider the global stability. The global stability of these models is given by the following Theorem:

Theorem 3.1. *(i) If* $R_0 = \frac{\kappa}{\delta}\int_0^{+\infty} s^0(a)\beta(a)\,da > 1$, *then there exists a globally asymptotically stable positive endemic steady state* Q^*.

(ii) If $R_0 \le 1$, *then disease-free equilibrium state* Q^0 *is globally asymptotically stable.*

Proof. (i) Since the explicit expressions for the endemic steady states of systems (1) and (2) are not given, we have to prove that these exist and are positive, provided $R_0 > 1$. From the first and second equations of (3) or (4), we have $s^*(a) = \Lambda\exp\left(-\int_0^a m(\sigma) + I^*\beta(\sigma)d\sigma\right)$. This equality should satisfy the rest of

equations, or, equivalently, the equality $\int_0^{+\infty} \beta(a)s^*(a)da = \delta/\kappa$. This yields

$$\frac{\kappa}{\delta} \int_0^{+\infty} \beta(a)s^0(a) \exp\left(-\int_0^a I^*\beta(\sigma)d\sigma\right) da = 1.$$

Consider the left-hand side of the last equality as a function of I^* and denote it by $f(I^*)$. It is easy to see that $\lim_{I^*\to+\infty} f(I^*) = 0$ and $f(0) = R_0$. Hence, due to the continuity, for all $R_0 > 1$ there exist $s^*(a) = \Lambda \exp\left(-\int_0^a m(\sigma) + I^*\beta(\sigma)d\sigma\right) > 0$ and $I^* > 0$ (and $E^* = \delta I^*/\varepsilon > 0$), which satisfies (3) or (4), respectively.

We introduce the notation $G(x) = x - \ln x - 1$ and start the proof of global stability from the observation that $G(x)$ is defined and positive-definite for all $x > 0$, and that it has its unique global minimum $G(x) = 0$ at $x = 1$. This fact is widely used in the proof.

Consider function

$$V(t) = \int_0^{+\infty} A(a)G(\frac{s(t,a)}{s^*(a)})\,da + BG(\frac{E(t)}{E^*}) + CG(\frac{I(t)}{I^*}),$$

where $A(a) = s^*(a)$, $B = E^*$, $C = I^*/\kappa = \mu E^*/\delta$ for system (2), and $B = 0$ for (1). It is easy to see that $V(s^*, E^*, I^*) = 0$, that the function is positive definite and is defined for all $s(a) > 0, E > 0, I > 0$, and that Q^* is the global minimum of the function. For system (2), the function satisfies

$$\begin{aligned}
\frac{d}{dt}V(t) = &\int_0^{+\infty} s^*(a)\left(\frac{1}{s^*(a)} - \frac{1}{s(t,a)}\right)\frac{\partial s(t,a)}{\partial t}\,da \\
&+ E^*\left(\frac{1}{E^*} - \frac{1}{E(t)}\right)\frac{dE(t)}{dt} + \frac{I^*}{\kappa}\left(\frac{1}{I^*} - \frac{1}{I(t)}\right)\frac{dI(t)}{dt} \\
= &-\int_0^{+\infty} s^*(a)\left(\frac{s(t,a)}{s^*(a)} - 1\right)\left(\frac{s_a(t,a)}{s(t,a)} + m(a) + \beta(a)I(t)\right)da \\
&+ E^*\left(\frac{1}{E^*} - \frac{1}{E(t)}\right)\left(\int_0^{+\infty} \beta(a)I(t)s(t,a)da - \mu E(t)\right) \\
&+ \frac{I^*}{\kappa}\left(\frac{1}{I^*} - \frac{1}{I(t)}\right)(\varepsilon E(t) - \delta I(t)) \\
= &-\int_0^{+\infty} s^*(a)\left(\frac{s(t,a)}{s^*(a)} - 1\right)\left(\frac{s_a(t,a)}{s(t,a)} + m(a) + \beta(a)I^*\right)da
\end{aligned}$$

$$+\int_0^{+\infty}\beta(a)I(t)s(t,a)\,da-\mu E(t)-\int_0^{+\infty}\beta(a)I(t)s(t,a)\frac{E^*}{E(t)}\,da+\mu E^*$$

$$+\mu E(t)-\frac{\delta}{\kappa}I(t)-\mu I^*\frac{E(t)}{I(t)}+\mu E^*-\int_0^{+\infty}s(t,a)\beta(a)I(t)da$$

$$+\int_0^{+\infty}s^*(a)\beta(a)I(t)da+\int_0^{+\infty}s^*(a)\beta(a)I^*\left(\frac{s(t,a)}{s^*(a)}-1\right)da,$$

where $s_a(t,a)$ denotes $\frac{\partial}{\partial a}s(t,a)$. Note that

$$\frac{\partial}{\partial a}G(\frac{s(t,a)}{s^*(a)})=\left(\frac{s_a(t,a)}{s(t,a)}+m(a)+\beta(a)I^*\right)\left(\frac{s(t,a)}{s^*(a)}-1\right),$$

and that, by (3), $I^*\int_0^{+\infty}s^*(a)\beta(a)\,da=\mu E^*=\delta I^*/\kappa$, where $\kappa=\varepsilon/\mu$. Hence, using integration by parts,

$$\frac{d}{dt}V(t)=-\left[s^*(a)G(\frac{s(t,a)}{s^*(a)})\right]_0^{+\infty}-\int_0^{+\infty}\beta(a)I^*s^*(a)\left(\frac{s(t,a)}{s^*(a)}\frac{I(t)}{I^*}\frac{E^*}{E(t)}-1\right)da$$

$$+\int_0^{+\infty}s^*(a)\beta(a)I^*\left(\frac{s(t,a)}{s^*(a)}-1\right)da+\int_0^{+\infty}s_a^*(a)G(\frac{s(t,a)}{s^*(a)})da$$

$$-\int_0^{+\infty}\beta(a)I^*s^*(a)\left(\frac{I^*}{E^*}\frac{E(t)}{I(t)}-1\right)da.$$

The equality

$$\int_0^{+\infty}s^*(a)\beta(a)I^*\left(\ln\frac{s(t,a)}{s^*(a)}\frac{I(t)}{I^*}\frac{E^*}{E(t)}+\ln\frac{I^*}{I(t)}\frac{E(t)}{E^*}-\ln\frac{s(t,a)}{s^*(a)}\right)da=0,$$

follows from $\ln 1=0$. Adding it to $\frac{dV(t)}{dt}$ and recalling that

$$s_a^*(a)=-m(a)s^*(a)-\beta(a)I^*s^*(a)$$

and that $s(t,0)=s^*(0)=\Lambda$, we obtain

$$\frac{d}{dt}V(t)=-\left[s^*(a)G(\frac{s(t,a)}{s^*(a)})\right]_{a=+\infty}-\int_0^{+\infty}\beta(a)I^*s^*(a)G(\frac{s(t,a)}{s^*(a)}\frac{I(t)}{I^*}\frac{E^*}{E(t)})da$$

$$-\int_0^{+\infty} m(a)s^*(a)G(\frac{s(t,a)}{s^*(a)})da - \int_0^{+\infty} \beta(a)I^*s^*(a)G(\frac{I^*}{E^*}\frac{E(t)}{I(t)})da \le 0.$$

That is, positive-definite function $V(t)$ has negative-definite derivative $\frac{d}{dt}V(t)$. Furthermore, equalities $V(t) = 0$ and $\frac{d}{dt}V(t) = 0$ hold only if $s(t,a) = s^*(a)$, $I(t) = I^*$ and $E(t) = E^*$ simultaneously. Hence, by Lyapunov asymptotic stability theorem [19, 22], an endemic equilibrium state, if it exists, is globally asymptotically stable.

(ii) If $R_0 \le 1$, we consider function

$$V(t) = \int_0^{+\infty} A(a)G(\frac{s(t,a)}{s^0(a)})da + BE(t) + CI(t),$$

where $A(a) = s^0(a)$, $B = 1$, $C = 1/\kappa$ ($\kappa = \varepsilon/\mu$) for the *SEIR* model (2); $B = 0$ and $\kappa = 1$ for the *SIR* model (1). For the *SEIR* model (2), the function satisfies

$$\begin{aligned}
\frac{d}{dt}V(t) &= \int_0^{+\infty} s^0(a)\left(\frac{1}{s^0(a)} - \frac{1}{s(t,a)}\right)\frac{\partial s(t,a)}{\partial t}\,da + \frac{d}{dt}E(t) + \frac{1}{\kappa}\frac{d}{dt}I(t)\\
&= -\int_0^{+\infty} s^0(a)\left(\frac{s(t,a)}{s^0(a)} - 1\right)\left(\frac{s_a(t,a)}{s(t,a)} + m(a) + \beta(a)I(t)\right)da\\
&\quad + \int_0^{+\infty} \beta(a)I(t)s(t,a)da - \mu E(t) + \mu E(t) - \frac{\delta}{\kappa}I(t)\\
&= -\left[s^0(a)G(\frac{s(t,a)}{s^0(a)})\right]_0^{+\infty} + \int_0^{+\infty} s^0_a(a)G(\frac{s(t,a)}{s^0(a)})da\\
&\quad + I(t)\left(\int_0^{+\infty} s^0(a)\beta(a)da - \frac{\delta}{\kappa}\right) \le I(t)\frac{\delta}{\kappa}\left(R_0 - 1\right).
\end{aligned}$$

Here we integrated by parts and used the equalities

$$\frac{\partial}{\partial a}G(\frac{s(t,a)}{s^0(a)}) = \left(\frac{s_a(t,a)}{s(t,a)} + m(a)\right)\left(\frac{s(t,a)}{s^0(a)} - 1\right),$$

$\frac{s(t,0)}{s^0(0)} = \frac{\Lambda}{\Lambda} = 1$, $s^0_a(a) = -m(a)s(a) < 0$ and the definition of R_0 (5).

Therefore, $R_0 \le 1$ ensures that $\frac{d}{dt}V(t) \le 0$ holds. Note, that the strict equality holds only if $s(t,a) - s^0(a) = 0$. Obviously, $\Omega_0 = \{s(a) - s^0(a) = 0\} \subseteq \Omega$ is not an invariant subspace in the phase space $\Omega = (s(a), E, I)$: any trajectory, starting in

$(s^0(a), E, I)$ with non-zero E or I, leaves Ω_0, since non-zero $E(t)$ leads to growth of $I(t)$, and

$$\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)\left(s(t,a)-s^0(a)\right)=-m(a)\left(s(t,a)-s^0(a)\right)-\beta(a)I(t)s(a)\neq 0.$$

That is, positive-definite function $V(t)$ has non-positive derivative $\frac{d}{dt}V(t)\leq 0$, and the only invariant subset, where $\frac{d}{dt}V(t)=0$ holds, is point $(s^0(a),0,0)$. Hence by Lyapunov-LaSalle asymptotic stability theorem, $R_0\leq 1$ ensures that the equilibrium state $(s^0(a),0,0)$ is globally asymptotically stable.

For *SIR* model (1), the calculations and conclusions are analogous, and we omit them.

Theorem 3.1 and the proof lead to a number of Corollaries.

Corollary 1. *Positive endemic steady state Q^* is unique when it exists.*

Proof. The uniqueness immediately follows from the global asymptotic stability. If this consideration is not convincing, note that $\frac{d}{dt}V(t)=0$ necessary holds at an equilibrium state, and that for both these models the sets where this equality holds contain no invariant sets of the systems other than equilibrium states Q^* or Q^0, respectively.

Corollary 2. *Any solution for (1) or (2) with a non-negative initial condition remains (i) non-negative and (ii) bounded for all $t>0$.*

Proof. Function $V(s,E,I)$ tends to infinity as either of s, E, or I tends to zero, and hence the non-negativeness follows. The surfaces $V(s,E,I)$ are closed and bounded and hence the boundedness follows.

Corollary 3. *If $R_0>1$, then systems (1) and (2) are uniformly persistent.*

In other words, for $R_0>1$ any solution for (1) or (2) with positive initial condition remains positive indefinitely.

4. Lyapunov function and global asymptotic stability for the Von Foerster equation

The global stability for the Von Foerster equation immediate follows from Theorem 3.1. The Von Foerster equation

$$\begin{aligned}\frac{\partial x(a,t)}{\partial t}+\frac{\partial x(a,t)}{\partial a}&=-m(a)x(a,t),\\ x(0,t)&=\Lambda,\qquad t>0,\end{aligned}\tag{6}$$

where $x(a,t)$ is the population of age a at time t, $m(a)$ is the age-dependent mortality rate, and Λ is the constant newborn inflow rate, describes the dynamics of an age-structured population [6]. Assuming that $\frac{\partial}{\partial t}x(a,t)=0$, we obtain the

steady state distribution $x^*(a) = \Lambda e^{-\int_0^a m(s)ds}$. The global asymptotic stability of system (6) can be proved using Lyapunov function

$$V(t) = \int_0^{+\infty} x^*(a) G(\frac{x(t,a)}{x^*(a)}) da.$$

It is easy to see that $V(t)$ is positive definite. Its derivative satisfies

$$\begin{aligned}
\frac{d}{dt}V(t) &= \int_0^{+\infty} x^*(a) \frac{d}{dt} G(\frac{x(a,t)}{x^*(a)}) da \\
&= \int_0^{+\infty} x^*(a) \left(\frac{1}{x^*(a)} - \frac{1}{x(a,t)}\right) \frac{\partial x(a,t)}{\partial t} da \\
&= -\int_0^{+\infty} x^*(a) \left(\frac{1}{x^*(a)} - \frac{1}{x(a,t)}\right) (x_a(a,t) + m(a)x(a,t))\, da \\
&= -\int_0^{+\infty} x^*(a) \left(\frac{x_a(a,t)}{x^*(a)} + m(a)\frac{x(a,t)}{x^*(a)} - \frac{x_a(a,t)}{x(a,t)} - m(a)\right) da.
\end{aligned} \tag{7}$$

Recalling that

$$\frac{\partial}{\partial a} G(\frac{x(t,a)}{x^*(a)}) = \frac{x_a(t,a)}{x^*(a)} + m(a)\frac{x(t,a)}{x^*(a)} - \frac{x_a(t,a)}{x(t,a)} - m(a)$$

and that $x_a^*(a) = -m(a)x^*(a) < 0$, we have

$$\begin{aligned}
\frac{dV(t)}{dt} &= -\int_0^{+\infty} \frac{\partial}{\partial a} \left[x^*(a) G(\frac{x(t,a)}{x^*(a)})\right] da + \int_0^{+\infty} x_a^*(a) G(\frac{x(t,a)}{x^*(a)}) da \\
&= -\left[x^*(a) G(\frac{x(t,a)}{x^*(a)})\right]_{a=0}^{a=+\infty} - \int_0^{+\infty} m(a)x^*(a) G(\frac{x(t,a)}{x^*(a)}) da
\end{aligned}$$

Here, $G(y) \geq 0$ for all $y > 0$, and $\frac{x(t,0)}{x^*(0)} = \frac{\Lambda}{\Lambda} = 1$ for all $t \geq 0$ thus giving $G(\frac{x(t,0)}{x^*(0)}) = 0$. Hence $\frac{dV(t)}{dt} \leq 0$. That is, $V(t) \geq 0$ and $\frac{d}{dt}V(t) \leq 0$ hold for any $t \geq 0$, and hence the steady state $x^*(a)$ of system (6) is globally asymptotically stable.

We have to note that the solutions of the Von Foerster equation converge to the steady state very fast making a range of Lyapunov functions applicable; thus, a straightforward quadratic functional of the form $\int_0^{+\infty} u(a)(x(t,a) - x^*(a))^2 da$ can be immediately employed for this equation [24].

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