Global behavior of epidemics models in age-structured populations

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The coupling between time periodic variations and the age-structure of a single species population is investigated through a mathematical model also containing a spatial structure. Using simplifying assumptions we exhibit a threshold parameter yielding the existence and stability of non trivial stationary or periodic states. Next the propagation of a mild disease within this population is analyzed. More precisely, we look for sufficient conditions giving, for the S.I.S. model with vertical transmission, the existence and stability of a non trivial periodic endemic state under either a periodic contact rate or a periodic supply of infected individuals. Stationary solutions are investigated as well.

1 INTRODUCTION

Let \( u(x, t, a) = u \geq 0 \) be the density of individuals in a single species population having age \( a > 0 \) at time \( t > 0 \) and location \( x \) in some domain \( \Omega \) in \( \mathbb{R}^d, d = 1, 2 \) or 3 ; the usual time-space distribution i.e. the total population is thus given by

\[
P(x, t) = \int_0^\infty u(x, t, a)da
\]  

(1.1)

The dynamics of the population is run by the classical balance law of the Lotka and Sharpe form

\[
\text{net growth-rate} = \text{diffusion} - \text{death} + \text{supply} ;
\]

see Gurtin (1973), Hoppensteadt (1974) and the books of Webb (1985), Busenberg and Cooke (1993). Assuming the flux of population lies along the lines of (spatially) decreasing densities this reads

\[
\partial_t u + \partial_a u = k \Delta_x u - \mu(P(x, t), x, t, a)u + f(x, t, a).
\]

(1.2)

Herein, \( \mu = \mu(p, x, t, a) \geq 0 \) is the death rate at age \( a > 0 \), time \( t > 0 \) and location \( x \) when the size of the total population is \( p \), and \( f = f(x, t, a) \geq 0 \) the external supply of individuals ; \( k \) is the diffusion coefficient and \( \Delta_x \) the Laplace operator in the spatial variables.

The birth process is described by the renewal equation
\[ u(x, t, 0) = \int_0^\infty \beta(P(x, t), x, t, a)u(x, t, a)da, \quad (1.3) \]

\[ \beta = \beta(p, x, t, a) \geq 0 \text{ being the fertility function age } a > 0, \text{ time } t > 0 \text{ and location } x \text{ when the size of the total population is } p. \text{ One assumes } \text{ a no flux boundary condition,} \]

\[ \partial_n u(x, t, a) = 0 \text{ on the boundary of } \Omega \quad (1.4) \]

The model equations for the epidemic problem are of the Kermack and Mac Kendrick form, assuming the disease does affect neither the flux of population nor the birth and death processes. The epidemic classes are composed of susceptible, infected and removed individuals, denoted by \( s, i \) and \( r \) respectively. Thus, setting \( D = \partial_t + \partial_a - k \Delta_x \), one has

\[
\begin{align*}
Ds + \mu(P(x, t), x, t, a)s &= -\gamma(t, a)\varphi(i)s + \delta(a)i + \rho(a)r + f_s, \\
Di + \mu(P(x, t), x, t, a)i &= +\gamma(t, a)\varphi(i)s - \delta(a)i - \sigma(a)i + f_i, \\
Dr + \mu(P(x, t), x, t, a)r &= +\sigma(a)i - \rho(a)r + f_r,
\end{align*}
\]

where \( \sigma \) (resp. \( \delta \)) is the age specific recovery rate with immunization (resp. without immunization) and \( \rho \) the rate at which this immunization is lost. The force of infection \( \gamma(t, a)\varphi(i) \) will take either mass action forms

\[ \gamma(t, a)\varphi(i)(x, t, a) = \begin{cases} 
\gamma_0(t, a)i(x, t, a) & \text{intracohort model,} \\
\gamma_1(t, a)\int_0^\infty i(x, t, a)da & \text{intercohort model.}
\end{cases} \]

In the first case this says that a susceptible can get the disease only from an infected of the same age while on the second case he may catch it from any infected individuals ; \( \gamma \) is the contact rate.

We do not consider here the general force of infection term of Busenberg and Cooke (1993). The vertical transmission to offsprings is

\[
\begin{align*}
s(x, t, 0) &= u(x, t, 0) - i(x, t, 0) - r(x, t, 0) \\
i(x, t, 0) &= \epsilon_i \int_0^\infty \beta(P(x, t), x, t, a)i(x, t, a)da \\
r(x, t, 0) &= \epsilon_r \int_0^\infty \beta(P(x, t), x, t, a)r(x, t, a)da
\end{align*}
\]

\( \epsilon_i \) (resp. \( \epsilon_r \)) being the constant probability that the disease (resp. the immunization) be vertically transmitted. One also requires no flux boundary conditions

\[ \partial_n s = \partial_n i = \partial_n r = 0 \text{ on the boundary of } \Omega. \quad (1.7) \]

Defining Problem (G.P.) as the set of equations (1.1)-(1.4), we shall first look at the behavior as \( t \to \infty \) of solution to (G.P.) starting from a given initial condition \( u(x, 0, a) \), under specific assumptions designed to yield explicit thresholds. Next we briefly sketch some results for the solutions to Problem (S.I.R.S.), defined as the set of relations (1.1)-(1.7). A special effort is made for the (S.I.S) model i.e. \( f_r = 0 \) and \( \sigma = 0 \), in the case of a stable and non trivial T-time periodic or stationary endemic state, generated by the contact rate or by an external supply of infected individuals.
Main assumptions and notations.

The diffusion coefficient $k$ is positive; $\Omega$ is a bounded domain in $\mathbb{R}^d$ with nice boundary. Any function introduced in our models is nonnegative and smooth enough. In order to have a simple description of the large time behaviour of the solutions one assumes:

$$(H1) \begin{cases}
\mu(p, x, t, a) = \mu_n(a) + \mu_e(p, x), \beta(p, x, t, a) = \beta_n(a)\beta_e(p, x), \\
\text{supp} \mu_n \text{ compact, supp} \beta_n \subset [0, A_1], A_1 = \max \text{supp} \beta_n.
\end{cases}$$

Herein, $\mu_n$ (resp. $\beta_n$) is the natural death-rate (resp. birth-rate) while $\mu_e$ and $\beta_e$ take care of spatial heterogeneities and density dependence, yielding a logistic effect. The external supplies $f, f_s, f_i$ and $f_r$ are such that $f = f_s + f_i + f_r$ and

$$\begin{cases}
0 \leq f_s(x, t, a), f_i(x, t, a), f_r(x, t, a) \leq f(x, t, a) \leq m < \infty \\
0 \leq F(x, t) = \int_0^\infty f(x, t, a) da \leq M < \infty.
\end{cases}$$

For the epidemic model, one also asks $\delta, \sigma$ and $\rho$ to depend only on the age variable, and supp $\delta$, supp $\sigma$, supp $\rho$ to be compact, while $\gamma$ is either independent of time: $\gamma(t, a) = \gamma(a)$ or time periodic: there is $T > 0$ such that $\gamma(t + T, a) = \gamma(t, a)$, and supp $\gamma_0 \cup$ supp $\gamma_1 \subset [0, \infty] \times [0, A_2], \quad A_2 < +\infty$.

In order to have non trivial solutions above the characteristic line $t = a$, at least when $f = 0$ on $\Omega \times [0, \infty] \times [0, A_1]$, the initial distributions of individuals at time $t = 0$ are assumed to be fertile, more precisely

$$\text{supp} u(., 0, .) \cap \Omega \times [0, A_1] \text{ non empty}.$$ 

We shall use the notation

$$\psi_\ast(a) = \inf\{\psi(p, x, t, a), p, x, t\}; \psi^\ast(a) = \sup\{\psi(p, x, t, a), p, x, t\}$$

2 SINGLE SPECIES POPULATION DYNAMICS

In this section we analyze the large time behaviour of solutions to Problem (G.P.). Specific notations are needed:

- $r$ is the root of the characteristic equation

$$1 = \int_0^\infty \beta_n(a)\pi(a)e^{-ra}da, \quad \pi(a) = \exp\left(-\int_0^a \mu_n(\alpha)d\alpha\right);$$

- $\lambda_1$ is the dominant eigenvalue of $-k\Delta + \mu_e(x)$ in $\Omega$ with Nemmann boundary conditions and $w_1$ is an associated positive eigenfunction (this makes sense when $\mu_e$ does not depend on the variable $p$).

We begin with the linear case.

**Theorem 1** Assume $\beta_e = 1, \mu_e(p, x) = \mu_e(x)$ and let $f = 0$. Then any solution to Problem (G.P.) having a fertile initial condition at $t = 0$ is such that as $t \to +\infty$
- when \( r > \lambda_1 \), \( u(x, t, a) \to +\infty \) \((\text{exponentially})\),
- when \( r < \lambda_1 \), \( u(x, t, a) \to 0 \) \((\text{exponentially})\),
- when \( r = \lambda_1 \), \( u(x, t, a) \to c\pi(a)w_1(x), \ c = c(u(x, 0, a)) > 0 \),

the convergence being uniform on \( \Omega \times [0, A] \) for each \( A > 0 \).

The proof is quite similar to that in Langlais (1988), using a series expansion of \( u \) over the eigenfunctions of the diffusion operator.

When \( r < \lambda_1 \) a natural question to be asked is: can we transform the exponential decay into a stabilisation toward a non trivial state upon supplying a non trivial input of individuals? In the periodical case one finds a positive answer.

**Theorem 2** Assume \( \beta_e = 1, \mu_e(p, x) = \mu_e(x) \) and let \( f \) be a nonnegative, bounded and time periodic, with period \( T > 0 \), function, \( f(x, t, a) \neq 0 \) on \( \overline{\Omega} \times [0, T] \times [0, A_1] \). Then

- when \( r \geq \lambda_1 \) any solution to Problem (G.P.) goes to \(+\infty\) as \( t \to +\infty \) (in the way defined in Theorem 1)
- when \( r < \lambda_1 \) there exists a unique non negative time periodic, with period \( T \), solution to Problem (G.P.) and it is globally stable in the class of bounded solutions.

A proof is found in Kubo and Langlais (1991). When \( r > \lambda_1 \) it follows from a comparison argument and Theorem 1. When \( r < \lambda_1 \) the existence part uses a monotone approximation process starting from a supersolution, while uniqueness and stability are straightforward consequences of Theorem 1. Lastly the case \( r = \lambda_1 \) requires a specific calculation.

In the nonlinear setting, things get more involved, even in the autonomons case with no external supply \((f = 0)\) and no spatial structure involved \((d = 0)\) : an example given by Swick (1981) shows that a non trivial periodic solution to (G.P.) may exist when \( \beta \) depend, on both \( p \) and \( a \) but not as in (H1), while Busenberg and Iannelli (1985) proved that, when (H1) holds and \( \beta_e = 1 \), no non trivial periodic solution can exist. When no external input of individuals is supplied, an analysis of the stabilization of solutions to (GP) toward stationary states is performed in Langlais (1988) which we summarize now. By a stationary state we mean a solution to

\[
\begin{aligned}
\partial_t v - k\Delta_v + \mu(Q(x), x, a)v = g(x, a) & \quad x \in \Omega, a > 0 \\
v(x, 0) = \int_0^\infty \beta(Q(x), x, a)v(x, a)da & \quad x \in \Omega \\
\partial_\eta v = 0 & \quad x \in \partial\Omega, a > 0 \\
Q(x) = \int_0^\infty v(x, a)da & \quad x \in \Omega
\end{aligned}
\]

(SGP)

The main two ingredients are: an a priori bound for \( P(x, t) \) and some monotone dependence of \( \mu \) and \( \beta \) on the variable \( p \) ... when they do not depend on the variable \( a \) ! Under assumption(H1) this now reads

\[
0 \leq P(x, t) \leq M_1 < +\infty, x \in \Omega, t > 0,
\]
(H2) $p \rightarrow \mu_e(p, \cdot)$ non decreasing; $p \rightarrow \beta_e(p, \cdot)$ non increasing, $\beta_e(0, x) = 1$.

It is then possible to define a suitable $\omega$-limit set for $\{u(x, t, a), t > 0\}$ and to prove that each element in it is a nonnegative stationary solution.

Two typical consequences concerning the stability of the trivial stationary state are

**Theorem 3** Assume (H2) hold and let $f = 0$. Let $\lambda_{10}$ be the dominant eigenvalue in $\Omega$ with Neumann boundary conditions value of $-k\Delta x + \mu_e(0, x)$ Then

- when $r \geq \lambda_{10}$ the trivial stationary state is not stable in the class of solutions of (G.P.) having a non trivial initial condition at $t = 0$.
- when $r < \lambda_{10}$ the trivial stationary state is stable in the class of solutions of (GP) having a non trivial initial condition at $t = 0$.

The structure of the solution set for (SGP) is not known in general. We now give two examples for which the existence and uniqueness of a positive and stable stationary solution can be derived.

**Example 1** Assume $\beta(p, x, a) = \beta_n(a)$; then one may show that any stationary solution is separable, i.e. $v(x, a) = \varphi(a)Q(x)$ where

$$-k\Delta Q = (r - \mu_e(Q, x))Q \text{ in } \Omega, \quad \partial_n Q = 0 \text{ on } \partial \Omega,$$

$r$ being the root of the above characteristic equation, while

$$\varphi' + (\mu_n(a) + r)\varphi = 0 \text{ in } a > 0, \varphi(0) = \int_0^\infty \beta_n(a)\varphi(a)da, \int_0^\infty \varphi(a)da = 1$$

The monotonicity property required in (H2) for $\mu_e$ implies that there is at most one non trivial and nonnegative stationary solution; furthermore it is stable from the first part of Theorem 3 as soon as it exists.

**Example 2** Assume now that $\mu_n = 0$ and $\beta(p, x, a) = \beta_n(a, x)$; then given any nonnegative and non trivial solution to (SGP) one may check upon integrating over all ages that $Q$ is a nonnegative solution to

$$-k\Delta Q = (\beta_e(Q, x) - \mu_e(Q, x))Q \text{ in } \Omega, \quad \partial_n Q = 0 \text{ on } \partial \Omega.$$

Again under condition (H2) there is at most one non trivial and nonnegative stationary solution and it is stable from the first part of Theorem 3.

Assuming a periodic input of individuals is supplied, an analysis of periodic solutions to problem (GP) is made in Kubo and Langlais (to appear); we give two simple results from it to which we refer for a more comprehensive treatment.

**Theorem 4** Assume (H2) holds; let $f$ be a time periodic, with period $T$, and nonnegative function, $f(x, t, a) \neq 0$ on $\Omega \times [0, T] \times [0, A_1]$, and let $\lambda_{10}$ be as is Theorem 3. Then

- when $r \geq \lambda_{10}$, any solution to (GP) tends to $+\infty$ as $t \to +\infty$
- when $r < \lambda_{10}$, there is at least a nonnegative, $T$-time periodic and nonnegative solution to (GP).

Again the structure of the $T$-periodic solutions set is not known in general.
3 THE S.I.R.S. MODEL

Little is known for the complete S.I.R.S. model. Most of available results are derived when \( f = 0 \) and no spatial structure involved; they concern the stabilization toward stationary solutions and the stability of the trivial endemic state. A partial uniqueness result is given in Inaba (1989) while the method in Lafaye and Langlais (manuscript) carries over to spatially structured populations.

The existence of time periodic solutions for the complete S.I.R.S. model is analyzed in Kubo and Langlais (to appear).

To conclude this short section let us say that the structure of the stationary solutions set (when \( f = 0 \)) and of the T-time periodic solution set (for T-time periodic data) for Problem (S.I.R.S.) is not known.

4 THE S.I.S. MODEL WITH VERTICAL TRANSMISSION

The S.I.S. model corresponds to the case wherein \( f_r = 0 \) and \( \sigma = 0 \) implying that the removed class is empty: \( r = 0 \). One now has \( s = u - i \) so that the model reduces to

\[
\begin{align*}
\text{(S.I.S.)} & \quad \left\{ \begin{array}{l}
D_i + [\mu(P(x,t),x,a) + \delta(a)]i = \gamma(t,a)\varphi(i)[u(x,t,a) - i] + f_i(x,t,a), \\
\quad i(x,t,0) = \epsilon_i \int_0^\infty \beta(P(x,t),x,a).i(x,t,a)da, \\
\quad \partial_{\eta}i(x,t,a) = 0 \quad \text{on the boundary of} \ \Omega.
\end{array} \right.
\end{align*}
\]

In this setting, interesting results concerning the uniqueness and stability of non trivial stationary or time periodic solutions can be derived. Most results of this section are taken from Busenberg and Langlais (in preparation).

**Theorem 5** Let \( \gamma \) and \( f_i \) be nonnegative and T-time periodic functions; assume that there is a nonnegative T-time periodic solution \( u \) of Problem (G.P.) non trivial on \( \Omega \times [0,T] \times [0,A_1] \). Then there is a maximal T-time periodic solution of Problem (S.I.S) in the range \( 0 \leq j \leq u \).

The proof uses ideas in Langlais (manuscript) for the intracohort model whithout diffusion. Actually, a suitable modification of the partial differential equation yields the following: the semi-orbit \( \{i(x,t,a), t > 0\} \) corresponding to the initial condition \( i(x,0,a) = u(x,0,0) \) is such that \( 0 \leq i(x,t + (n+1)T,a) \leq i(x,t + nT,a) \leq u(x,t,a) \), for any \( n \geq 0 \). In the limit \( n \to +\infty \) one has a nonnegative T-periodic solution. It is the maximal solution in the desired range from a comparison principle.

When \( f_i(x,t,a) \neq 0 \) on \( \Omega \times [0,T] \times [0,\infty) \), it is quite clear that this maximal solution is not the trivial one. Otherwise, when \( f_i = 0 \) on \( \Omega \times [0,T] \times [0,A_1] \), this maximal solution is not the trivial one on that domain if one can find a non trivial and nonnegative sub-solution (as it is easily done when no spatial structure is involved) or if this assumption leads to a contradiction (see below).
Now regardless of these sufficient conditions to get a non trivial solution, a uniqueness and stability result may be proved, provided some a priori positivity result be granted. Set (see Busenberg at all (manuscript))

\[(H3) \begin{cases} & \text{either } f_i(x, t, a) \neq 0 \text{ on } \Omega \times [0, T] \times [0, A_1], \\ & \text{or } f_i = 0 \text{ and there exist } \sigma > 0 \text{ and } \gamma_{11}(a) \neq 0 \text{ on } [0, A_1] \text{ such that } \\ & \sigma \gamma_{11}(a) \leq \gamma_1(t, a) \leq \gamma_{11}(a), a > 0, \text{ in the intercohort case } , \\ & \text{or } f_i = 0 \text{ and else } \gamma_0(t, a) \neq 0 \text{ on } [0, T] \times [0, A_1] \text{ in the intracohort case .} \end{cases}\]

**Theorem 6** Let \( \gamma, f, f_i \) and \( u \) be as in Theorem 5. Assume \( 0 < \varepsilon_1 \leq 1 \) and \((H3)\) holds. Then there is at most one \( T \)-time periodic solution to Problem (S.I.S.) in the range \( 0 \leq j \leq u \) and non trivial on \( \bar{\Omega} \times [0, T] \times [0, +\infty) \). Furthermore it is globally stable in the range of solutions to Problem (S.I.S.) having a fertile initial condition, such that \( 0 \leq i(x, 0, a) \leq u(x, 0, a) \).

The proof is derived upon adapting techniques developped in Busenberg et al (manuscript) to deal with stationary solutions for a general force of infection term without spatial structure. Under assumption \((H3)\) one may show that, for the vertical transmission case, any \( T \)-time periodic solution of (S.I.S.), non trivial on \( \bar{\Omega} \times [0, T] \times [0, A_1] \) is actually positive on this domain. Uniqueness and stability follow from a concavity argument.

We now apply our results to answer three questions of relevant epidemiological interest.

**Question 1** Assuming no external supply of infected individuals, can an initial input of infected individuals generate a stationary and stable non trivial endemic state within a global population at stationary state?

The setting is \( f_i = 0, u(x, t, a) = v(x, a) \) and \( P(x, t) = Q(x) \) a non trivial solution to Problem (S.G.P.), while \( \gamma_0(t, a) = \gamma_0(a) \) and \( \gamma_1(t, a) = \gamma_1(a) \). From Theorem 6, one has at most one non trivial stationary solution if either \( \gamma_1(a) \neq 0 \) or \( \gamma_0(a) \neq 0 \) on \( [0, A_1] \), and it is stable in a suitable range. Hence one are left with finding a non trivial solution. Let us consider the intracohort case. Going back to the sketched proof of Theorem 5, the maximal stationary solution is obtained as the decreasing limit as \( t \to +\infty \) of \( \{i(x, t, a), t > 0\} \) provided \( i(x, 0, a) = v(x, a) \); arguing as in Lafaye and Langlais (1993) one may prove that this convergence is uniform on any compact domain \( \bar{\Omega} \times [0, A], A > 0 \). Given any small positive \(\alpha\), if this maximal solution is the trivial one there exists \( T(\alpha) > 0 \) such that

\[ 0 \leq i(x, t, a) \leq \alpha, t \geq T(\alpha), x \in \Omega, 0 \leq a \leq \max \text{ supp } \gamma_0. \]

From a comparison principle one may show \( 0 \leq w(x, t, a) \leq i(x, t, a) \), \( w \) being the solution to the linear problem in \( \Omega \times [T(\alpha), \infty) \times [0, \infty) \):

\[
\begin{cases}
D\omega + [\mu_e(P(x), x) + \mu_n(a) + \delta(a) - \gamma_0(v_*(a) - \alpha)]\omega = 0, \\
\omega(x, t, 0) = \varepsilon_1 \int_0^\infty \beta_*(a)\omega(x, t, a)da, \\
\partial_\eta \omega(x, t, a) = 0,
\end{cases}
\]
and such that \( \omega(x, T(\alpha), a) = i(x, T(\alpha), a) \). Setting \( \lambda_{11} \) the dominant eigenvalue of \(-k\Delta + \mu_{e}(P(x), x)\) in \( \Omega \) with Neumann boundary conditions and \( r_{*} \) the root of the characteristic equation (see section 2) with \( \beta(a) = \epsilon_{i}\beta_{e}(a) \) and \( \mu_{e} \) replaced by \( \mu_{\eta} + \delta - \gamma_{0}\nu_{*} \), if follows from Theorem 1, that \( r_{*} > \lambda_{11} \) implies \( \omega(., t, .) \to +\infty \) as \( t \to +\infty \) a contradiction to the maximal solution being the trivial one. Hence when \( r_{*} > \lambda_{11} \) the answer is positive; conversely if \( r_{*} < \lambda_{11} \) (with obvious notations), one may show that the maximal solution is the trivial one and the answer is negative.

Question 2 Assuming no external supply of infected individuals, can a \( T \)-time periodic force of infection generate a stable and non trivial \( T \)-time periodic endemic state within a population at stationary state?

The setting is as in Question 1 for \( f_{i} \) and (\( u, P \)) but now \( \gamma \) is a \( T \)-time periodic function. Again, Theorem 6 yields at most one non trivial \( T \)-periodic endemic state when (\( H3 \)) holds and it is stable. A positive subsolution may be constructed upon using a non trivial stationary solution for Problem (S.I.S), the contact rate being given by either \( \gamma_{0*} \) or \( \gamma_{1*} \) : in that case the answer is positive. Conversely if there is no non trivial stationary solutions when the contact rate is given by \( \gamma_{0} \) or \( \gamma_{1} \), then the answer is negative.

Question 3 Can a \( T \)-time periodic supply of infected individuals generate a \( T \)-time periodic and stable non trivial endemic state within a \( T \)-time periodic (or stationary) global population?

The setting is now \( f \) \( T \)-time periodic (resp. time independent), (\( u, P \)) a \( T \)-time periodic solution of (G.P.) (resp. non trivial solution to (S.G.P.)) and \( f_{i} \) a \( T \)-time periodic function. From Theorem 5 and 6 it follows that the answer is positive as soon as \( f_{i}(x, t, a) \not\equiv 0 \) on \( \overline{\Omega} \times [0, T] \times [0, A_{1}] \), regardless of the contact rate term.

References


This work is partially supported by the CNRS, Programme Environnement, ”Méthodes, Modèles et Théories”, projet, ”Populations structurées et environnement".