
Global Stability of Equilibria for a Metapopulation S–I–S Model

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1 Introduction

Standard models for the dynamics of infection disease are based on the assumption of homogeneous mixing among individuals. However, individuals are generally aggregated in patches (pieces of woodland, farms, households, villages. . .) and transmission of infection is much easier within patches than from one patch to the other.

Different approaches have been used to handle the “patchy” structure of populations, that run from individual-based simulation models (see, for instance, [11] for avian flu in Thailand) to systems of differential equations for the infection classes at each patch (see, for instance, [2]). An interesting approach is the use of “spatially implicit metapopulation models”: in these, the discrete nature of individual and patches is clearly retained, so that each patch has always an integer number of infectives; however, the spatial arrangement of patches is not considered, so that infection transmission is the same to any other patch.

Following a long tradition of stochastic models for infection transmission within and between households[5], Ball [4] has derived a deterministic system for an epidemic of SIS type spreading in a population distributed in an infinite number of households, each one of size N ; mixing outside the households is assumed to be random. The system can be obtained [9] as the limit, as M goes to infinity, of a corresponding stochastic model with a finite number M of households. This system, which is the focus of this contribution, will be presented in detail in the next Section. Ball [4] obtains complete results on the stability of the endemic equilibrium for $N = 2$ and numerical simulations are given for $N \geq 3$. Arrigoni and Pugliese [3] compute the reproduction ratio R_0 for the limiting system, and study how this depends on the household size N . Ghoshal *et al.* [12] show that R_0 is indeed the usual threshold quantity for epidemic models: for $R_0 < 1$ the infection-free equilibrium is stable, and there are no endemic equilibria; for $R_0 > 1$, the infection-free equilibrium is unstable, and there is exactly one endemic equilibrium.

In this contribution, we extend the previous results, by showing that the endemic equilibrium is globally stable for $R_0 > 1$. The result is not unexpected, because S–I–S models have been proved to be stable in populations with spatial structure [8] or with age structure [7]. The key to these proofs has been to employ methods from the theory of monotone dynamical systems (see [15] for a general treatment), thanks to the monotone properties of S–I–S epidemic models.

Here, we exploit too the monotonicity of the dynamical system (albeit relative to an appropriate stochastic ordering), together with a probabilistic interpretation, suggested in [6], of the solutions of the deterministic system.

2 The Model

The main variable in the system under study will be the vector-valued function $\underline{\xi}(t) = (\xi_0(t), \dots, \xi_N(t))$: the j -th component $\xi_j(t)$ represents the fraction of households with j infectives at time t (j will be named the state of the

household). The state space is $\Sigma = \left\{ \sum_{j=0}^N \xi_j = 1, \quad \xi_j \geq 0, \quad j = 0, \dots, N \right\}$.

When an infective recovers, her household moves from state j to $j - 1$; if γ is the recovery rate of infectives, the overall rate at which a household moves from state j to $j - 1$ is γj .

Conversely, a household moves from j to $j + 1$ when a new infection occurs. Each susceptible can get infected from an infective in the same household (at a rate proportional to the fraction of infected individuals, j/N) or from an infective everywhere in the population (at a rate proportional to the fraction

of infected individuals: $\frac{1}{N} \sum_{l=0}^N l \xi_l$). Overall (in a household at state j , there are $N - j$ susceptibles), the rate at which households move from state j to

$j + 1$ is $(N - j) \left(c \frac{j}{N} + \frac{d}{N} \sum_{l=0}^N l \xi_l \right)$, where c is the rate of within-household infection, and d is the rate of between-household infection.

Hence:

$$\begin{cases} \dot{\xi}_j(t) = - \left[(N - j) \left(c \frac{j}{N} + \frac{d}{N} \sum_{l=0}^N l \xi_l \right) + \gamma j \right] \xi_j \\ \quad + \gamma(j + 1) \xi_{j+1} + (N - j + 1) \left(c \frac{j - 1}{N} + \frac{d}{N} \sum_{l=0}^N l \xi_l \right) \\ \dot{\xi}_0(t) = \gamma \xi_1 - \xi_0 d \sum_{l=0}^N l \xi_l \end{cases} \quad (1)$$

with initial value $\xi_j(0) = y_j$, $j = 0, \dots, N$, a probability distribution, so that \underline{y} is non-negative and satisfies $\sum_{j=0}^N y_j = 1$.

Note that system (1) is monotone not relatively to the usual ordering in \mathbb{R}^{N+1} but to a natural ordering for probability distributions:

$$\xi \leq^s \eta \iff \sum_{i=0}^N g(i)\xi_i \leq \sum_{i=0}^N g(i)\eta_i \text{ for all non-decreasing functions } g.$$

Alternatively, one can introduce the variables $w_j(t) = \sum_{k=j}^N \xi_k(t)$ and notice that \underline{w} satisfies the system of differential equations:

$$\dot{w}_i = \gamma i(w_{i+1} - w_i) + (N - i + 1) \left(c \frac{(i-1)}{N} + \frac{d}{N} \sum_{l=1}^N w_l \right) (w_{i-1} - w_i) \quad (2)$$

Since (2) has to be studied in the set $\{1 \geq w_1 \geq w_2 \dots \geq w_N \geq 0\}$, which is invariant, it is easy to see that the Kamke condition [15] is satisfied; hence, (2) is monotone relatively to the standard order.

The overall structure of the model is similar to that studied in [6] where $p_j(t)$ represents the fraction of local populations (within a metapopulation) with j individuals. The system considered there is

$$\left\{ \begin{array}{l} p'_i = - \left[(b_i + d_i + \lambda) i + \nu + \rho \lambda \sum_{j=0}^{\infty} j p_j \right] p_i \\ \quad + \left[b_{i-1} (i-1) + \rho \lambda \sum_{j=0}^{\infty} j p_j \right] p_{i-1} \\ \quad + [d_{i+1} + \lambda] (i+1) p_{i+1}; \quad i \geq 1 \\ p'_0 = \nu \left(\sum_{j=0}^{\infty} p_j - p_0 \right) + (d_1 + \lambda) p_1 - \rho \lambda \left(\sum_{j=0}^{\infty} j p_j \right) p_0, \end{array} \right. \quad (3)$$

where b_i and d_i represent the *per capita* birth and death rates in a patch occupied by i individuals, ν is the catastrophe rate (i.e. the rate at which all individuals in a patch are destroyed), λ is the migration rate, and ρ is the probability of a migrant to successfully reach another patch.

Under the condition that ib_i is concave and non-decreasing, and id_i is convex and non-decreasing, plus some technical assumptions, it was proved [6] that there exists a threshold quantity R for (3): when $R \leq 1$, all solutions converge to the extinction equilibrium ($p_0 = 1$, $p_i \equiv 0$ for $i \geq 1$); when $R > 1$ all non trivial solutions converge to the unique positive equilibrium.

Although (1) could be seen as a special case of (3), it is not possible to directly apply the results of [6]. Hence, we show how the methods used in [6] can be modified to handle system (1) (and, indeed, any system with similar assumptions).

The main idea is to analyse system (1) assuming that the average proportion of infectives per household is known. By setting $s = \sum_{l=1}^N l\xi_l$ in (1), we obtain a family of linear systems, indexed by the parameter s ,

$$\frac{d\underline{\xi}(t)}{dt} = A_s \underline{\xi}(t). \tag{4}$$

$$\text{with } (A_s)_{k,j} = \begin{cases} c(1 - \frac{j-1}{N})(j-1) + ds(1 - \frac{j-1}{N}) & k = j-1 \\ -c(1 - \frac{j}{N})j - ds(1 - \frac{j}{N}) - \gamma j & k = j \\ \gamma(j+1) & k = j+1 \end{cases}$$

and $(A_s)_{k,j} = 0$ for $|j - k| > 1$, where $j, k = 0, \dots, N$.

3 Probabilistic Interpretation

We adopt a probabilistic interpretation of the functions $\xi_l(t)$, used by Barbour and Pugliese [6]. In this framework, the solution $\underline{\xi}$ of system (4) represents the distribution at time t of a birth and death Markov process with finite state-space $S = \{0, 1, \dots, N\}$ and initial distribution \underline{y} . We will denote it by $X_t^{(s)}$, so that $\xi_i(t) = \mathbb{P}_{\underline{y}}[X_t^{(s)} = i] = \mathbb{P}[X_t^{(s)} = i | X_0^{(s)} \sim \underline{y}]$. Its transitions are

$$\begin{cases} j \rightarrow j+1 \text{ at rate } cj(1 - \frac{j}{N}) + ds(1 - \frac{j}{N}) \\ j \rightarrow j-1 \text{ at rate } \gamma j \end{cases}$$

$X_t^{(s)}$ has a stationary distribution $\pi^{(s)} = \{\pi_i^{(s)}\}_{j=0}^N$:

- if $s = 0$ then $\pi_0^{(s)} = 1$ and $\pi_j^{(s)} = 0$ for $j \geq 1$;
- if $s > 0$ then $\pi_j^{(s)} = \frac{\theta_j^{(s)}}{\sum_{j=0}^N \theta_j^{(s)}}$ where

$$\theta_0^{(s)} = 1, \quad \theta_j^{(s)} = \frac{\prod_{k=0}^{j-1} \left(1 - \frac{k}{N}\right) (ck + ds)}{\gamma^j j!}. \tag{5}$$

Moreover, we can apply to the process $X_t^{(s)}$ the following theorem (see [1]).

Theorem 1. *Let X_t be a birth-and-death process with finite state-space $S = \{0, 1, \dots, m, \dots, N\}$ such that $C = \{0, 1, \dots, m\}$ is an ergodic class and $T = \{m+1, \dots, N\}$ is a transient class, every state of which leads to all states in C . Then there exist non-negative numbers α and $\rho < 1$ such that*

$$|p_{ji}(t) - \pi_i| < \alpha\rho^t, \quad \forall j \in S. \tag{6}$$

where $\pi_i > 0, i \in C, \pi_i = 0, i \in T$ and $\sum_{i \in C} \pi_i = 1$.

Using this theorem (with $m = 0$ for $s = 0$; with $m = N$ for $s > 0$), we see that the transition probabilities $p_{ji}^{(s)} = \mathbb{P}[X_t^{(s)} = i | X_0^{(s)} = j]$ of the process $X_t^{(s)}$ attain their limit $\pi_i^{(s)}$, at an exponential rate. The vector $(\pi_0^{(s)}, \pi_1^{(s)}, \dots, \pi_N^{(s)})$ is the stationary solution of the system (4).

4 Properties of the Fixed Point Map

Our aim is to show the existence and uniqueness of a non-trivial equilibrium of the non-linear system (1), when the parameters satisfy the threshold condition shown below.

For every non-negative value of the parameter s , we have found the stationary solution $\pi^{(s)}$ of the system (4). Letting $\pi^{(s)}(f)$ be the mean of a function f relatively to the distribution $\pi^{(s)}$, we define the map G as

$$G(s) = \pi^{(s)}(e) = \sum_{i=1}^N i\pi_i^{(s)} \quad (e \text{ the identity function})$$

Note that to every positive fixed point s^* of G (that is, $G(s^*) = s^*$) corresponds an endemic equilibrium solution of the non-linear system (1). The disease-free equilibrium, instead, corresponds to the null fixed point ($G(0) = 0$).

It can be shown that G is a continuous, increasing and concave function. From this, the uniqueness of a positive fixed point follows easily.

The properties of G are established in [6]. Here, we just state some intermediate steps, together with a sketch of the proofs that require small changes.

Proposition 1. $\frac{d}{ds}\pi^{(s)}(f) = -d\pi^{(s)}(R(f))$ with

$$R(f)(j) = (1 - \frac{j}{N})(\Theta^{(s)}(f)(j+1) - \Theta^{(s)}(f)(j))$$

$$\Theta^{(s)}(f)(j) = - \int_0^{+\infty} \{\mathbb{E}^{(j)} f(Z_t^{(s)}) - \pi^{(s)}(f)\} dt$$

Proof (sketch). Let $\mathcal{A}^{(s)}$ be the generator of the Markov process $Z^{(s)}$.

$$\mathcal{A}^{(s)} f(j) = (cj(1 - \frac{j}{N}) + ds(1 - \frac{j}{N}))[f(j+1) - f(j)] + \gamma j[f(j-1) - f(j)].$$

By Dynkin’s formula [13], $\pi^{(s)}(\mathcal{A}^{(s)}g) = 0$ for all g . Hence

$$\begin{aligned} 0 &= \pi^{(s+h)}(\mathcal{A}^{(s+h)}g) = \mathbb{E}^{\pi^{(s+h)}}\left(\mathcal{A}^{(s+h)}g(Z_0^{(s)})\right) \\ &= \mathbb{E}^{\pi^{(s+h)}}\left\{\mathcal{A}^{(s)}g(Z_0^{(s)}) + dh\left(1 - \frac{Z_0^{(s)}}{N}\right)\Delta g(Z_0^{(s)})\right\} \end{aligned}$$

Set $g = \Theta^{(s)}(f)$ (as defined in the thesis, thanks to (6)) and note that $\Theta^{(s)}(f)$ satisfies the equation

$$\mathcal{A}^{(s)}(\Theta^{(s)}(f))(j) = f(j) - \pi^{(s)}(f).$$

Then

$$0 = \mathbb{E}^{\pi^{(s+h)}}\left\{f(Z_0^{(s)}) - \pi^{(s)}(f) + dh\left(1 - \frac{Z_0^{(s)}}{N}\right)\Delta\Theta^{(s)}(f)(Z_0^{(s)})\right\}$$

so that

$$|\pi^{(s+h)}(f) - \pi^{(s)}(f) + dh\pi^{(s)}(R(f))| \leq d|h|o(1)$$

and the thesis follows. \square

Applying the previous proposition to the identity function e , we obtain

$$G'(s) = d\pi^{(s)}(R(e)) = d\pi^{(s)}(g) \quad \text{with}$$

$$g(j) = \left(1 - \frac{j}{N}\right) \int_0^{+\infty} \{\mathbb{E}^{(j+1)}(Z_t^{(s)}) - \mathbb{E}^{(j)}(Z_t^{(s)})\} dt.$$

In the next Section we will prove, through coupling methods, the rather intuitive fact that $\mathbb{E}^{(j+1)}(Z_t^{(s)}) \geq \mathbb{E}^{(j)}(Z_t^{(s)})$. It will then follow that $G'(s) \geq 0$.

The quantity $G'(0) = d \int_0^{+\infty} \mathbb{E}^{(1)}(Z_t^{(0)}) dt$ will be shown to be the threshold quantity for system (1).

The following proposition can be proved with a similar technique (see [6])

Proposition 2. $G''(s) = 2d^2\pi^{(s)}(R(R(e))) = 2d^2\pi^{(s)}(h)$ where

$$\begin{aligned} h(m) &= \left(1 - \frac{m}{N}\right) \int_0^{+\infty} \left[\mathbb{E}^{(m+1)}Q(X_t^{(s)}) - \mathbb{E}^{(m)}Q(X_t^{(s)})\right] dt \\ Q(j) &= \left(1 - \frac{j}{N}\right) \int_0^{+\infty} (\mathbb{E}^{(j+1)}X_w^{(s)} - \mathbb{E}^{(j)}X_w^{(s)}) dw. \end{aligned}$$

5 Coupling Methods

In this Section, we prove by coupling methods (see, for instance, [14]) some results, needed to prove the properties of G , about rather general birth-and-death processes. We consider a birth-and-death process $X := (X_t, t \geq 0)$ with birth and death rates $\lambda(i)$ and $\mu(i)$ respectively and state space $S = \{0, 1, 2, \dots, N\}$. Assume that the function $\lambda(i)$ is concave in i and that the function $\mu(i)$ is convex and non-decreasing (and that $\mu(0) = 0$).

Proposition 3. *Let X be as above. Let $\mathbb{E}^{(m)}(X_t) = \mathbb{E}(X_t|X_0 = m)$. Then for all $m \geq 0$,*

$$\mathbb{E}^{(m+1)}X_t - \mathbb{E}^{(m)}X_t > 0$$

Proof. We consider a two-dimensional pure jump Markov process ($\underline{F}_t = (Y_t, W_t), t \geq 0$); the processes $X^1 = Y, X^2 = Y + W$ will be Markov and have the same generator as X . Setting $Y(0) = m, W(0) = 1, \mathbb{E}^{(m+1)}X_t = \mathbb{E}X_t^1$ and $\mathbb{E}^{(m)}X_t = \mathbb{E}X_t^2$, so that $\mathbb{E}^{(m+1)}X_t - \mathbb{E}^{(m)}X_t = \mathbb{E}W_t$.

The transitions of the process \underline{F}_t are the following, letting $\mathbf{n} = (i, j)$ and $\mathbf{e}^{(i)}$ the i -th coordinate vector. :

$$\begin{aligned} \mathbf{n} &\rightarrow \mathbf{n} - \mathbf{e}^{(1)} && \text{at rate } \mu(i) \\ \mathbf{n} &\rightarrow \mathbf{n} - \mathbf{e}^{(2)} && \text{at rate } \mu(i + j) - \mu(i) \\ \mathbf{n} &\rightarrow \mathbf{n} + \mathbf{e}^{(1)} && \text{at rate } \min(\lambda(i), \lambda(i + j)) \\ \mathbf{n} &\rightarrow \mathbf{n} + \mathbf{e}^{(2)} && \text{at rate } \lambda(i + j) - \min(\lambda(i), \lambda(i + j)) \\ \mathbf{n} &\rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(2)} && \text{at rate } \lambda(i) - \min(\lambda(i), \lambda(i + j)). \end{aligned}$$

It is easy to see that X^1 and X^2 have the required properties, and that $V(t) \geq 0$.

Propositions 1 and 3 show that the function G , defined in the previous Section, is non-decreasing.

The assumptions on the concavity and convexity of birth and death rates play a key-role in the proof of the following proposition. This rather long construction represents the main paper of this contribution relatively to [6].

Proposition 4. *Let X as above. Then, for all $m \geq 0$,*

$$\mathbb{E}^{(m+1)}X_t - \mathbb{E}^{(m)}X_t > \mathbb{E}^{(m+2)}X_t - \mathbb{E}^{(m+1)}X_t.$$

Proof. We consider a four dimensional pure jump Markov process ($\underline{D}_t = (Y_t, W_t, U_t, V_t), t \geq 0$); the aim of this construction is to have four processes $X^1 = Y, X^2 = Y + W, X^3 = Y + U, X^4 = Y + W + V$ which are Markov and have the same generator as the process X . Setting $Y(0) = m, W(0) = U(0) = V(0) = 1$, we will have $X^1(0) = m, X^2(0) = X^3(0) = m + 1, X^4(0) = m + 2$.

The state-space of the four dimensional process is

$$S = \{(i, j, k, l) : i \geq 0, j \geq 0, k \geq l \geq 0, \}$$

Letting $\mathbf{n} = (i, j, k, l)$, we describe the transitions of the process \underline{D}_t together with the relative rates. First those representing deaths

- if $k \neq l$

$$\begin{aligned} \mathbf{n} &\rightarrow \mathbf{n} - \mathbf{e}^{(1)} \Big| \mu(i) && \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(2)} \Big| \mu(i + j) - \mu(i) \\ \mathbf{n} &\rightarrow \mathbf{n} - \mathbf{e}^{(3)} \Big| \mu(i + k) - \mu(i) && \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(4)} \Big| \mu(i + j + l) - \mu(i + j) \end{aligned}$$

- if $k = l$

$$\begin{array}{l} \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(1)} \\ \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(3)} - \mathbf{e}^{(4)} \\ \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(4)} \end{array} \left| \begin{array}{l} \mu(i) \\ \mu(i+k) - \mu(i) \\ \mu(i+j+k) - \mu(i+j) - \mu(i+k) + \mu(i) \end{array} \right. \mathbf{n} \rightarrow \mathbf{n} - \mathbf{e}^{(2)} \left| \mu(i+j) - \mu(i) \right.$$

The transition rates representing births are as follows:

- if $k > l$
 - if $j, k, l > 0$

$$\begin{array}{l} \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(2)} - \mathbf{e}^{(3)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(2)} - \mathbf{e}^{(4)} \end{array} \left| \begin{array}{l} \lambda(i) \\ \lambda(i+j) \end{array} \right. \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} \left| \lambda(i+k) \right. \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(4)} \left| \lambda(i+j+l) \right.$$
 - if $0 = j < l < k$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(4)} \left| \lambda(i+l) \right. \quad \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(3)} - \mathbf{e}^{(4)} \left| \lambda(i) \right. \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} \left| \lambda(i+k) \right.$$
 - if $0 = l < j, k$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(2)} \left| \lambda(i+j) \right. \quad \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(2)} - \mathbf{e}^{(3)} \left| \lambda(i) \right. \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} \left| \lambda(i+k) \right.$$
 - if $j = l = 0 < k$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(3)} \left| \lambda(i) \right. \quad \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} \left| \lambda(i+k) \right.$$
- if $k = l$
 - if $j, k > 0$

$$\begin{array}{l} \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(2)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(3)} - \mathbf{e}^{(4)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} + \mathbf{e}^{(4)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(2)} \\ \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(2)} - \mathbf{e}^{(4)} \end{array} \left| \begin{array}{l} \lambda(i+j+k) - \min(\lambda(i+k), \lambda(i+j+k)) \\ \lambda(i+k) - \min(\lambda(i) + \lambda(i+j+k), \lambda(i+k)) \\ \lambda(i) + \min(\lambda(i+k), \lambda(i+j+k)) \\ - \min(\lambda(i) + \lambda(i+j+k), \lambda(i+k)) \\ \min(\lambda(i+k), \lambda(i+j+k)) \\ \min(\lambda(i) + \lambda(i+j+k), \lambda(i+k)) \\ - \min(\lambda(i+k), \lambda(i+j+k)) \\ \lambda(i+j) + \min(\lambda(i) + \lambda(i+j+k), \lambda(i+k)) \\ - \lambda(i) - \lambda(i+j+k) \end{array} \right.$$

- if $0 = j < k$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(3)} - \mathbf{e}^{(4)} \left| \lambda(i) \right. \quad \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(3)} + \mathbf{e}^{(4)} \left| \lambda(i+k) \right.$$
- if $0 = k < j$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} - \mathbf{e}^{(2)} \left| \lambda(i) \right. \quad \mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(2)} \left| \lambda(i+j) \right.$$
- if $j = k = 0$

$$\mathbf{n} \rightarrow \mathbf{n} + \mathbf{e}^{(1)} \left| \lambda(i) \right.$$

Note that all transitions are within the state space S , and that the assumptions on μ and λ guarantee that all rates are nonnegative.

We obtain $\mathbb{E}^{(m+1)}X_t - \mathbb{E}^{(m)}X_t = \mathbb{E}U_t$ and $\mathbb{E}^{(m+2)}X_t - \mathbb{E}^{(m+1)}X_t = \mathbb{E}V_t$. By construction, $U_t \geq V_t$, and we obtain the thesis. \square

These two propositions allow us to conclude that G is concave. In fact, we can compute $h(m)$, defined in Proposition 2, using the process (Y_t, W_t) used in the proof of Proposition 3. We obtain, in the notation of Proposition 2 and with $g(j, w) = \mathbb{E}^{(j)}X_w^{(s)}$:

$$\begin{aligned} &\mathbb{E}^{(m+1)}Q(X_t^{(s)}) - \mathbb{E}^{(m)}Q(X_t^{(s)}) = \mathbb{E}(Q(Y_t + W_t) - Q(Y_t)) \\ &= \mathbb{E} \int_0^\infty \left[\left(1 - \frac{Y_t + W_t}{N}\right) (g(Y_t + W_t + 1, w) - g(Y_t + W_t, w)) \right. \\ &\quad \left. - \left(1 - \frac{Y_t}{N}\right) (g(Y_t + 1, w) - g(Y_t, w)) \right] dw \\ &= \mathbb{E} \int_0^\infty [(g(Y_t + W_t + 1, w) - g(Y_t + W_t, w)) - (g(Y_t + 1, w) - g(Y_t, w))] dw \\ &\quad \times \left(1 - \frac{Y_t}{N}\right) - \mathbb{E} \int_0^\infty \frac{W_t}{N} (g(Y_t + W_t + 1, w) - g(Y_t + W_t, w)) dw. \end{aligned}$$

Proposition 4 yields $g(m+k+1, w) - g(m+k, w) - (g(m+1, w) - g(m, w)) < 0$ for all $m, k \geq 0$ and $w \geq 0$; hence the first integral is negative. Similarly Proposition 3 shows that $g(m+1, w) - g(m, w) > 0$. Hence $h(m) < 0$ for all $m \geq 0$ and $G''(s) < 0$.

6 Equilibria and Asymptotic Behavior

The results of Section 4 show that the function G is continuous and differentiable and satisfies $G(0) = 0$. Moreover, Propositions 1 and 2, together with Propositions 3 and 4 show that G is non-decreasing and concave.

It is then easy to obtain

Theorem 2. *If $G'(0) > 1$, then there exists a unique positive fixed point s^* of G ; if $G'(0) \leq 1$, then $G(s) < s$ for all $s > 0$.*

Proof. The proof is straightforward. If $G'(0) \leq 1$, from the concavity of G it follows that $G(s) < s$. Otherwise, since it is clear that $G(s) < N$ for all s , there exists a unique $s \in (0, N)$ such that $G(s) = s$. \square

The quantity

$$G'_+(0) = d \int_0^\infty \mathbb{E}^{(1)} Z_t^{(0)} dt.$$

is then the threshold quantity for (1), and will be named R_0 (see [3] for a derivation of this quantity following the lines of [10]).

Remark 1. It is possible to obtain an explicit expression for $G'(0)$. In fact from

$$G'(s) = \sum_{j=1}^N j \frac{d}{ds} \left(\pi_j^{(s)} \right) \text{ and using (5), we obtain, after lengthy computations,}$$

$$R_0 = G'_+(0) = \sum_{j=1}^N j \pi'_j(0) = \frac{d}{c} \sum_{j=1}^N \left(\frac{c}{\gamma N} \right)^j \binom{N}{j} j!.$$

In [6], stochastic comparison arguments, together with arguments from the theory of the dynamical systems are used to prove that all solutions converge to an equilibrium: the trivial equilibrium for $R_0 \leq 1$, the positive equilibrium for $R_0 > 1$. The same arguments would apply (more easily, because the system is finite-dimensional) to (1). It is, however, easier to use results from the theory of monotone dynamical systems either to (1) (relatively to $\overset{s}{\leq}$) or to (2) (relatively to the standard order).

Indeed, Theorem 2.3.1 from [15] shows that, for $R_0 \leq 1$, all solutions converge to the infection-free equilibrium. For $R_0 > 1$, one can use Theorem 2.3.2 from [15] to see that all solutions converge to an equilibrium; further, studying the linearization of (1) (restricted to the components 1 to N) at the infection-free equilibrium, it is easy to see that no solution starting with a non-zero fraction of infectives can converge to the infection-free equilibrium. This proves the main result of this paper:

Theorem 3. *If $R_0 \leq 1$, all solutions of (1) converge to the infection-free equilibrium; if $R_0 > 1$, all solutions of (1) with $\sum_{j=1}^N y_j > 0$ converge to the unique positive equilibrium.*

7 Different Household Sizes

The modelling assumption that all households are of the same size N seems rather unrealistic. More reasonably, we can let $n_i, i = 1, \dots, N$ be the fraction of households with i individuals. Now N is the maximum number of individuals per household: this assumption allows us to deal with a finite-dimensional space, and is reasonable from the biological point of view.

We introduce the variables $\xi_l^i, i = 1, \dots, N, l = 0, \dots, i$: $\xi_l^i(t)$ is the fraction of households of size i that at time t have l infectives, so that $\sum_{l=0}^i \xi_l^i = 1$.

In this framework, the system of differential equations (1) becomes

$$\begin{cases} \dot{\xi}_j^i(t) = -[(i-j)(c_{\frac{i}{j}}^j + ds(t)) + \gamma j] \xi_j^i \\ \quad + \gamma j \xi_{j+1}^i + (i-j+1)(c_{\frac{i}{i-j}}^{j-1} + ds(t)) \xi_{j-1}^i \\ \dot{\xi}_0^i(t) = \gamma \xi_1^i - \xi_0^i ds(t) \end{cases} \quad (7)$$

with initial value $\xi_j^i(0) = y_j^i$ where $\sum_{j=0}^i y_j^i = 1$ and $y_j^i \geq 0$. The term

$$s(t) = \frac{\left(\sum_{i=1}^N n_i \sum_{l=0}^i \xi_l^i(t) l \right)}{\sum_{i=1}^N i n_i}$$

represents the average infective fraction in the population, and drives the infection transmission among different households. It is the only nonlinear term in the system, and indeed is the only term that ‘mixes’ the equations for households of different sizes.

If we assume that the quantity s is known, we deal with N different systems: each of them has the same structure as system (4) with $d_i = di$ instead of d :

$$\frac{d\xi^i(t)}{dt} = A_s^i \xi^i(t), \quad i = 1, \dots, N. \tag{8}$$

The i -th system (8) has an equilibrium solution $\pi^{(s)i}$ and the function $G^i(s) = \sum_{l=0}^i l \pi_l^{(s)i}$ is increasing and concave.

It is easy to see that the function $G(s) = \frac{d \sum_{i=1}^N i n_i G^i(s)}{\sum_{i=1}^N i n_i}$ shares the same properties. Theorem 2 guarantees that, if $G'(0) > 1$, there exists a unique positive fixed point s^* , and, thus, an endemic equilibrium for the system (7). On the other hand, when $G'(0) \leq 1$, there is no positive equilibrium.

As in the previous Section, arguments from the theory of monotone dynamical systems (or the same arguments used in [6]) guarantee that all solutions of (7) converge to the infection-free equilibrium, below the threshold, and to the endemic equilibrium, above the threshold.

8 Discussion

We have shown here how the monotone structure of S–I–S epidemic models can be used, also in a metapopulation setting, to prove global convergence to the equilibria, thus yielding a sharp threshold result.

In order to obtain complete results, we had to establish the uniqueness of positive equilibria. This has been proved interpreting the solutions of the equations as the probabilities of a birth-and-death process; the required properties were obtained by studying the stationary distributions of the processes, extending the results of [6]. On the other hand, Ghoshal *et al.* [12] had proved uniqueness by direct computation.

We believe that our approach is more general, being easy to extend to the case of households of different size (Section 7), to nonlinear infection rules, and possibly to S–I–R models. The last extension would require us to consider the properties not of birth-and-death processes, but of two-dimensional stochastic epidemic models. Clearly, these have no monotonicity properties, but perhaps the fact that the function G is non-decreasing and concave might still hold.

A great limitation of this kind of metapopulation models is that the transmission of infection is the same among all patches. This is, however, an assumption inherent to the method, and cannot be relaxed. At the moment,

metapopulation models with a real spatial (or network) structure can be studied only through simulations. The study of spatially implicit metapopulation models may shed some light on the relevance of the discrete nature of individuals and patches for the overall epidemic dynamics, and constitute a standard, against which to compare the result of spatially structured metapopulation simulation models.

References

1. Adke, S.R., Manjunath, S. M.: An introduction to finite Markov processes. Wiley, New York (1984)
2. Arino, J., van den Driessche, P., A multi-city epidemic model. *Math. Pop. Studies*, **10**, 175-193 (2003)
3. Arrigoni, F., Pugliese, A., Limits of a multi-patch SIS epidemic model, *J. Math. Biol.* **45**, 419-440 (2002)
4. Ball, F. Stochastic and deterministic models for SIS epidemics among a population partitioned into households, *Math. Biosci.* **156**, 41-67 (1999)
5. Ball, F., Mollison, D., Scalia-Tomba, G. Epidemics with two levels of mixing, *Annals Appl. Prob.* **7**, 46-89 (1997)
6. Barbour, A.D., Pugliese, A., Asymptotic behavior of a metapopulation model, *Annals Applied Probability* **15**, 1306-1338 (2005)
7. Busenberg, S., Iannelli, M., Thieme, H. Global behavior of an age-structured S-I-S epidemic model. *SIAM J. Math. Anal.* **22**, 1065-1080 (1991)
8. Capasso, V. *Mathematical structures of epidemic systems*. Springer, Berlin (1993)
9. Ethier, S. N., Kurtz, T. G.: *Markov processes*. Wiley, New York (1986)
10. Diekmann, O., Heesterbeek, J.A.P.. *Mathematical Epidemiology of Infectious Diseases*. Wiley, New York (2000)
11. Ferguson, N.M., Cummings, D.A.T., Cauchemez, S., Fraser, C., Riley, S., Meechai, A., Iamsirithaworn, S., Burke, D.S. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature*, **437**, 209-214 (2005)
12. Ghoshal, G., Sander, L. M., Sokolov, I. M. SIS epidemics with household structure: the self-consistent field method, *Math. Biosci.* **190**, 71-85 (2004)
13. Hamza, K., and Klebaner, F.C. Conditions for integrability of Markov chains., *J. Appl. Prob.* **32**, 541-547 (1995)
14. Lindvall, T.: *Lectures on the coupling method*. Wiley, New York, 1992.
15. Smith, H.: *Monotone dynamical systems*. American mathematical society, Providence, USA (1995)