HYDRODYNAMICAL LIMITS FOR EPIDEMIC MODELS

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Abstract

Hydrodynamical limits of a spatial epidemic model are studied through the representation of the process as a projection of a higher dimensional Poisson process. The standardized process $(I_n(t))$ of infected individuals in a box of volume one at time t converges to a deterministic process $(I(t))$. Moreover, there exists a Gaussian process V such that $n^{d/2}(I_n - I)$ converges to V weakly.
Key words: Poisson point process, epidemic model, S-I-R model, predictable sets, projection method.

1 Introduction

Epidemic models can be studied through their representation as multiparameter time changes of Poisson processes. Kurtz (1981, 1983) used such representations to get a Gaussian approximation for a non-spatial epidemic model. Solomon (1987) generalized Kurtz' results for age dependent processes. Garcia (1995b) used a similar characterization for a spatial epidemic model to get Law of Large Numbers and Central Limit Theorem type results for the density process of infected individuals when the population under study is located at the points of a λn- homogeneous Poisson point process on a compact set K. In this work we obtain similar results for a standardized process when the population under study is located at the points of a λ-homogeneous Poisson process on a large compact set $K_n = [-n/2, n/2]^d \subset \mathbb{R}^d$ suggesting that if we do not have high density infectious processes on a compact set, we can get the same limit behavior observing the infection process over large areas.

We are considering the so called S-I-R models, where the individuals in this population can be of three types: susceptible, infective and removed. Assume:

(i) that at time t, the intensity that a susceptible individual in the population at site y becomes infective, when the configuration of infected individuals is in state μ, is given by $\alpha(y, \mu)$;

(ii) the lengths of the infectious period for newly infective individuals are independent ν-distributed random variables (ν is a probability measure);

(iii) removed individuals, who have had the disease, cannot contract it again (immunization or death);

(iv) For simplicity, assume that the initially infected individuals have just become infected at time zero and hence the times at which they are removed are independent, ν-distributed random variables.

A practical application of the S-I-R model described above is the focus expansion experiment used by phytopathologists to study the spread of a disease. A plant is infected at the origin and the spread of the disease from the focus is observed. The steepness of gradients of disease incidence are of interest. For example, if the disease incidence $Y(s)$ is the number of infected plants in a disk of radius s, the quantity under study is $\frac{d}{ds}Y(s)$. Van den Bosch, Zadocks and Metz (1988) describe a set of assumptions for their model that can be simplified in ours. Although they assume that for a large population size a deterministic approximation can be used, this was just a conjecture. Garcia (1995b) proved this conjecture and studied the asymptotics of such processes for high density plantations finding consistent and asymptotically normal estimators for the steepness of the gradient. A related question would be if it is possible to get asymptotic results for large plantation areas, that is, to get Law of Large Numbers and Central Limit Theorem type results for a standardized process when the population under study is located at the points of a λ-homogeneous Poisson process on a compact set $K_n = [-n/2, n/2]^d \subset \mathbb{R}^d$. It is obvious that after some time all individuals in a given compact set are removed. However, using the deterministic limit process obtained by the Law of Large Numbers, we could analyze questions of interest such as, how the intensity function α influences the infection process, how to estimate some parameter of the intensity function, how does the spatial component affect the results. The Central Limit Theorem would give asymptotic distributions of estimators.

We can think of the infection process as a birth and death process with variable birth rate and constant death rate, so that it can be constructed through the projection method, described by Garcia (1995a) and developed for epidemic models in Garcia (1995b). Let N be a Poisson processes on $\mathbb{R}^d \times [0,\infty)^3$ with mean measure $\eta = \lambda\, m^d \times m \times m \times \nu$ (m^d is a Lebesgue measure on $\mathbb{R}^d$). We need to construct a family of random sets Γ_t^n and hence of measure-valued processes $I_n(t)$ by taking the points of N that lie in Γ_t^n and projecting them onto $\mathbb{R}^d$. Consider the following system:

$$\begin{cases} I_n(t,B) = \frac{1}{n^d} N(\Gamma_t^n \cap (nB \times [0,\infty)^3)), \quad B \subset [-1/2,1/2]^d \\ \Gamma_t^n = \{(x,s,y,z); x \in [-n/2,n/2]^d, s \le t, 0 \le y \le \gamma(x,s-,I_n), z > t-s\} \\ \gamma(x,t,I_n) = \alpha(x,I_n(t)) e^{-\int_0^t \alpha(x,I_n(u))du}, \quad \gamma(x,0,I_n) = f_0(x) \end{cases} \tag{1.1}$$

where f_0 is such that the distribution of the locations of the individuals initially infected is given by $I_n(0)$. $I_n(t)$ can be interpreted as the scaled distribution of infected individuals in $[-n/2,n/2]^d$. There are several systems that would give the desired epidemic model. System (1.1) was preferred since, as it is shown in Sections 2 and 3, the sets Γ_t^n have desired properties for proving Law of Large Numbers and Central Limit Theorem type results.

Let $\mathcal{M}$ be the set of Radon measures on $\mathbb{R}^d$ and identify the process I_n described above as an $\mathcal{M}$-valued process with sample paths in $D_{\mathcal{M}}[0,\infty)$; $I_n(t,B)$ is a jump process which jumps only when a birth or a death occurs. In Section 2, using a generalization of the Glivenko-Cantelli theorem

(Stute(1976)), we obtain a deterministic process $I(t)$ such that $I_n \to I$ in the Skorohod topology of $D_{\mathcal{M}}([0,\infty))$. This implies that if the observed volume is large, a deterministic model can be used. In Section 3, denoting $V_n = n^{d/2}(I_n - I)$ we obtain a Gaussian process V such that V_n converges to V weakly. Section 4 deals with applications of the above results.

2 Law of Large Numbers

Theorem 2.1 (Law of Large Numbers) *Let $\alpha : \mathbb{R}^d \times \mathcal{M} \to \mathbb{R}^+$ be a non-negative Borel function with $\alpha(x,\mu) \le M_1$ and $|\frac{\partial}{\partial x}\alpha(x,\mu)| \le M_1$ for all $x \in \mathbb{R}^d$ and $\mu \in \mathcal{M}$. If we consider $I_n(t)$ as an $\mathcal{M}$-valued process with values in the Skorohod space $D_{\mathcal{M}}([0,\infty))$, there exists a deterministic process $I(t)$ satisfying*

$$\begin{cases} I(t,B) = \eta(\Gamma_t \cap (B \times [0,\infty)^3)), \quad B \subset [-1/2,1/2]^d \\ \Gamma_t = \{(x,s,y,z); x \in [-1/2,1/2]^d, s \le t, 0 \le y \le \gamma(x,s-,I), z > t-s\} \\ \gamma(x,t,I) = \alpha(x,I(t))e^{-\int_0^t \alpha(x,I(u))du}, \quad \gamma(x,0,I) = f_0(x) \end{cases} \tag{2.1}$$

such that $I_n \to I$ in probability.

The proof of Theorem 2.1 is based on a generalization of the Glivenko-Cantelli Theorem given by Stute (1976). Define an $\mathcal{M}$-valued process

$$\tilde{I}_n(t,B) = \frac{1}{n^d}\eta(\Gamma_t^n \cap (nB \times [0,\infty)^3)) \tag{2.2}$$

and let $\mathcal{C} \subset \mathcal{B}([-1/2,1/2]^d)$ be the set of all rectangles of the form $[-1/2,a_1] \times \ldots \times [-1/2,a_d]$ with a_i rational.

Lemma 2.2 *For any $T > 0$ and $B \in \mathcal{C}$, we have that*

$$\sup_{t \le T} |I_n(t, B) - \tilde{I}_n(t, B)| \to 0 \quad a.s. \tag{2.3}$$

as $n \to \infty$.

Proof: Let M_n be the countably additive real-valued function on $\mathcal{B}(\mathbb{R}^d \times [0, \infty)^3)$ defined by

$$M_n(A) = \frac{1}{n^d} N(A) - \frac{1}{n^d} \eta(A) \tag{2.4}$$

and M_n^+ and M_n^- be the non-negative measures obtained by the Hahn-Jordan decomposition of M_n. A set A is a *lower layer* if $(x, s, y, z) \in A$ and $(x, 0, 0, 0) \le (x, s', y', z') \le (x, s, y, z)$ implies $(x, s', y', z') \in A$. Let L_α denote the collection of lower layers in $\mathbb{R}^d \times [0, \infty)^3$. If we define, for $B \in \mathcal{C}$

$$A_t^n = \{(x, s, y, z); x \in nB, s \le t, 0 \le y \le \gamma(x, s-, I_n), z \le t - s\} \tag{2.5}$$

$$B_t^n = \{(x, s, y, z); x \in nB, s \le t, 0 \le y \le \gamma(x, s-, I_n), z \ge 0\} \tag{2.6}$$

then A_t^n and B_t^n belong to L_α and by Stute (1976) we have that $\sup_{A \in L_\alpha} |M_n^+(A)| \to 0$ and $\sup_{A \in L_\alpha} |M_n^-(A)| \to 0$ as $n \to \infty$. Consequently, $\sup_{t \le T} |M_n^+(A_t^n)| \to 0$, $\sup_{t \le T} |M_n^-(A_t^n)| \to 0$, $\sup_{t \le T} |M_n^+(B_t^n)| \to 0$ and $\sup_{t \le T} |M_n^-(B_t^n)| \to 0$ a.s. for all $B \in \mathcal{C}$. Therefore, for any $B \in \mathcal{C}$ we have (2.3). $\square$

Now we are ready to prove Theorem 2.1. Given $\epsilon > 0$, with probability at least $1 - \epsilon$, we have that $\gamma(x, t, I_n)$ is equicontinuous in x and t and bounded. Considering $\{\gamma(\cdot, t, I_n), 0 \le t \le T\}$ as a process on $C_{C(\mathbb{R}^d)}[0, T]$ ($C(\mathbb{R}^d)$ is the collection of continuous functions on $\mathbb{R}^d$) we have that the sequence $\{\gamma(\cdot, t, I_n), 0 \leq t \leq T\}$ is relatively compact, that is, there exists a subsequence $\{\gamma(\cdot, t, I_{n_k}), 0 \leq t \leq T\}$ which is convergent; let $\{\bar{\gamma}(\cdot, t), 0 \leq t \leq T\}$ be the limiting process. Then, from (2.1), $\Gamma_t^{n_k} \Rightarrow \Gamma_t$, where $\Gamma_t = \{(x, s, y, z); x \in [-1/2, 1/2]^d, s \leq t, y \leq \bar{\gamma}(x, s), z > t - s\}$ and we can define the process $I(t)$ as

$$\begin{aligned} I(t, B) &= \lim_{n\to\infty} \frac{1}{n^d} \int_{nB} \int_0^t \int_0^{\bar{\gamma}(x,s)} \int_{t-s}^{\infty} \nu(dz)\, dy\, ds\, dx \\ &= \lim_{n\to\infty} \frac{1}{n^d} \int_{nB} \int_0^t \bar{\gamma}(x, s) \nu([t-s, \infty))\, ds\, dx \end{aligned} \tag{2.7}$$

for any $B \in \mathcal{B}([-1/2, 1/2]^d)$.

Let $(\mathcal{M}, \|\ \ \|)$ be the space of Radon measures on $\mathbb{R}^d$ with the total variation norm, and consider $\{\tilde{I}_{n_k}\}$ as a sequence of processes in $D_{\mathbb{R}^d}[0, T]$. We claim that the sequence $\{\tilde{I}_{n_k}\}$ is relatively compact, since it satisfies (a) and (b):

(a) We have $\mathbb{P}\ [\|\tilde{I}_{n_k}(t)\| \leq T] = 1$ for all k. If $B_m \subset [-1/2, 1/2]^d$ are such that $B_m \searrow \emptyset$, then $\tilde{I}_{n_k}(t, B_m) \leq m^d(B_m)t \to 0$ uniformly in n. Letting $\mathcal{K} = \{\mu \in \mathcal{M}; \|\mu\| \leq 1, \mu \text{ is uniformly countably additive}\}$, by Theorem IV.9.1, Dunford and Schwartz (1957), $\mathcal{K}$ is compact and $\mathbb{P}\ [\tilde{I}_{n_k} \in \mathcal{K}] = 1$.

(b) Moreover, since $|\gamma(x, s, \mu)| \leq |\alpha(x, \mu)| \leq M_1$, for all $x \in \mathbb{R}^d$, $s \geq 0$ and $\mu \in \mathcal{M}$, we have

$$\begin{aligned} &\mathbb{E}\ [\|\tilde{I}_{n_k}(t+h) - \tilde{I}_{n_k}(t)\| \|\tilde{I}_{n_k}(t) - \tilde{I}_{n_k}(t-h)\|] \\ &\leq \mathbb{E}[\frac{1}{n^d} \int_{[-n/2,n/2]^d} \int_t^{t+h} \gamma(x, s, I_n) ds dx \times \frac{1}{n^d} \int_{[-n/2,n/2]^d} \int_{t-h}^{t} \gamma(x, s, I_n) ds dx] \\ &\leq M_1 h^2. \end{aligned}$$

Therefore, $\tilde{I}_{n_k} \Rightarrow I$ where I has to satisfy (2.1). By (2.3), $\sup_{t\leq T}|I_{n_k}(t,B) - \tilde{I}_{n_k}(t,B)| \to 0$, almost surely as $k\to\infty$ for all $B\in\mathcal{C}$. Then, for all ϕ bounded and continuous, $|\int\phi(y)I_{n_k}(t,dy) - \int\phi(y)I(t,dy)| \Rightarrow 0$ as $k\to\infty$. In this case, we have $I_{n_k}\Rightarrow I$ in the weak topology of $D_{\mathcal{M}}([0,\infty))$. Note that every subsequence of I_n has a further subsequence which converges to the same limit, consequently the sequence I_n converges to I. Since the limit I is deterministic, convergence in distribution is equivalent to convergence in probability. □

3 Central Limit Theorem

Theorem 3.1 *Let N be a Poisson process with mean measure $\eta = \lambda\, m^d\times m\times m\times\nu$. Consider the standardized process I_n and its deterministic limit I given by (1.1) and (2.1), respectively. Denote $V_n(t,B) = n^{d/2}(I_n(t,B) - I(t,B))$. Under conditions of Theorem 2.1 and*

$$\alpha(nx,\mu) = o\left(\frac{1}{n^{d/2}}\right) \qquad \text{as } n\to\infty, \text{ for all } \mu, \tag{3.1}$$

there is a Gaussian process V indexed by $\mathcal{B}(\mathbb{R}^d)$ with covariance $\mathbb{E}[V(t,A)V(t,B)] = I(t,A\cap B)$ such that V_n converges to V weakly.

Proof: Define

$$\begin{aligned} M_n(t,B) &= n^{d/2}(I_n(t,B) - \tilde{I}_n(t,B)) \\ &= \frac{1}{n^{d/2}}(N(\Gamma_t^n\cap nB\times[0,\infty)^3) - \eta(\Gamma_t^n\cap nB\times[0,\infty)^3)). \end{aligned} \tag{3.2}$$

Note that

$$
\begin{aligned}
V_n(t,B) &= M_n(t,B) + n^{d/2}(\eta(\Gamma_t^n \cap nB \times [0,\infty)^3) - \eta(\Gamma_t \cap nB \times [0,\infty)^3)). \\
&= M_n(t,B) + n^{d/2}(\tilde{I}_n(t,B) - I(t,B)) \qquad (3.3)
\end{aligned}
$$

Since A_t^n and B_t^n defined by (2.5) and (2.6) respectively are predictable sets as defined by Kurtz(1983) and $\Gamma_t^n = B_t^n \setminus A_t^n$, for fixed $A \in \mathcal{B}([-1/2,1/2]^d)$, $M_n(\cdot,A)$ is an $\{\mathcal{H}_u\}$-martingale with sample paths in $D_{\mathbb{R}}[0,\infty)$ where $\mathcal{H}_u = \sigma(N(A); A \in \mathcal{B}(\mathbb{R}^d \times [0,\infty)^3), A \subset \mathbb{R}^d \times [0,u] \times [0,\infty)^2))$. Moreover, if $m_n(t,A)$ is the quadratic variation of the process $M_n(t,A)$, we have

$$
\begin{aligned}
m_n(t,A) &= [M(\cdot,A)]_t \\
&= \sum_{s \le t} [M_n(s,A) - M_n(s-,A)]^2 \\
&= \frac{1}{n^d} N(\Gamma_t^n \cap (nA \times [0,\infty)^3)) = I_n(t,A) \qquad (3.4)
\end{aligned}
$$

By Theorem 2.1, $m_n(t,A) \to I(t,A)$ in probability where I is defined by (2.1). Moreover, for each $T > 0$,

$$
\mathbf{E}[\sup_{t \le T} |M_n(t,A) - M_n(t-,A)|] \le \frac{1}{n^{d/2}}.
$$

Therefore, by the Central Limit Theorem for martingales (Theorem 7.1.4, Ethier and Kurtz(1986)), there exists a process W_A depending on the set A with independent Gaussian increments and $W_A^2(t) - I(t,A)$ is martingale for each A such that $M_n(\cdot,A) \Rightarrow W_A$.

By condition (3.1) and the Dominated Convergence Theorem, we have

$n^{d/2}(\tilde{I}_n(t,A) - I(t,A)) \to 0$ in probability and

$$V_n(\cdot, A) \Rightarrow W_A. \tag{3.5}$$

Analogously, for fixed $A_1, \ldots A_n \in \mathcal{B}([-1/2, 1/2]^d)$, $(M_n(\cdot, A_1), \ldots, M_n(\cdot, A_n))$ is an $\{\mathcal{H}_u\}$-martingale with sample paths in $D_{\mathbb{R}^n}[0,\infty)$ where $\mathcal{H}_u = \sigma(N(A); A \in \mathcal{B}(\mathbb{R}^d \times [0,\infty)^3), A \subset \mathbb{R}^d \times [0,u] \times [0,\infty)^2)))$. Moreover, if $(m_n^{ij}(t))$ is the quadratic variation matrix of the process M_n, we have

$$\begin{aligned} m_n^{ij}(t) &= [M_n(\cdot, A_i), M_n(\cdot, A_j)]_t \\ &= \sum_{s \le t} [M_n(s, A_i) - M_n(s-, A_i)][M_n(s, A_j) - M_n(s-, A_j)] \\ &= \frac{1}{n^d} N(\Gamma_t^n \cap (n(A_i \cap A_j) \times [0,\infty)^3)) = I_n(t, A_i \cap A_j) \end{aligned} \tag{3.6}$$

By Theorem 2.1, $m_n^{ij}(t) \to I(t, A_i \cap A_j)$ in probability where I is defined by (2.1). Therefore, by the Central Limit Theorem for martingales, there exists an n-dimensional process $(W_1, \ldots, W_n)$ with independent Gaussian increments and $W_i(t)W_j(t) - I(t, A_i \cap A_j)$ is martingale and

$$(V_n(\cdot, A_1), \ldots, V_n(\cdot, A_n)) \Rightarrow (W_1, \ldots, W_n). \tag{3.7}$$

Equation (3.7) gives the convergence of the finite dimensional distribution of the process V_n, however, by Theorem 9.1.VI, Daley and Vere-Jones (1988) , this is enough to prove weak convergence. $\square$

4 Applications

In this section three consequences of Theorem 2.1 and Theorem 3.1 are presented in order to give the reader some idea of the useful information that can be extracted out of the limiting results.

1.- It is immediate to see that after some time all infected individuals in a compact set A are removed, indeed we can quantify this time. Denote by $N_t(A)$ the number of infectives in a compact set A. By Theorem 2.1, for any given $\delta > 0$

$$\mathbb{P}(-\delta\|A\| \leq N_t(A) - n^d I(t, \frac{A}{n}) \leq \delta\|A\|) \to 1$$

as $n \to \infty$. For each $\epsilon > 0$, take $\delta > 0$ such that $\delta(\|A\|+1) < 1$ and let N_0 and T_0 the minimum values of n and t that satisfy:

$$\begin{cases} \mathbb{P}(-\delta\|A\| \leq N_t(A) - n^d I(t, \frac{A}{n}) \leq \delta\|A\|) > 1-\epsilon, \\ n^d I(t, \frac{A}{n}) = \lambda \int_A \int_0^t \alpha(x, I(s)) e^{-\int_0^s \alpha(x, I(u))du} \nu([t-s, \infty)) ds\, dx < \delta. \end{cases} \tag{4.1}$$

In this case, it is easy to see that

$$\mathbb{P}(N_{T_0}(A) = 0) > 1-\epsilon.$$

Note that T_0 is finite, since at each compact set there is only a finite number of possible infected individuals, and the infection times are independent random variables with common distribution ν.

2.- For the special case where $\alpha(x,\mu) = \int \rho(|x-y|)\mu(dy)$ we can characterize the limit process I. Note that

$$I(t, B) = \lambda \int_B \int_0^t \int \rho(|x-y|) I(s, dy) e^{-\int_0^s \int \rho(|x-y|) I(u,dy) du} \nu([t-s, \infty)) ds\, dx$$

that is, for every $t > 0$, $I(t, \cdot)$ is an absolutely continuous measure with respect to the Lebesgue measure on $[-1/2, 1/2]^d$ and, if we denote $\phi(t, \cdot)$ its

Radon-Nikodym derivative, it satisfies the integral equation

$$\phi(t,x) = \lambda \int_0^t (\int \rho(|x-y|)\phi(y,s)\, dy)\, e^{-\int_0^s \int \rho(|x-y|)\phi(u,y)\, dy\, du} \nu([t-s,\infty))ds. \tag{4.2}$$

3.- A practical application to phytopathology as described in Section 1 can be done, similarly to Garcia (1995b), considering the focus expansion experiment used to study the spread of a disease. In this paper a question of interest would be if instead of considering high density plantations, we observe the process over a large region. We investigate whether the estimators are consistent and asymptotically normal.

Consider (as done in Garcia (1995b)) as a measure of infection the density number of victims (infective and removed individuals) up to time t,

$$Y_n(t,[-1/2,1/2]^d) = \frac{1}{n^d} \int_{[-n/2,n/2]^d} \int_0^t \int_0^{\gamma(x,s,I_n)} N(dx,ds,dy,dz).$$

By Theorem 2.1, we have

$$Y_n(t,[-1/2,1/2]^d) \to \lambda \int_{[-1/2,1/2]^d} \int_0^t \alpha(x,I(s)) e^{-\int_0^s \alpha(x,I(u))du} ds\, dx$$

in probability as $n \to \infty$. For the particular case as
$\alpha(x,\mu) = \int \rho(\beta|x-y|)\mu(dy)$, we have

$$Y_n(t,[-1/2,1/2]^d) \to \lambda \int_{[-1/2,1/2]^d} (1 - e^{-\int_0^t \int \rho(\beta|x-y|)\phi(u,y)dy\, du}) dx$$

as $n \to \infty$, where ϕ is defined by (4.2) and β is a measure of the steepness of the gradient. Estimating β by the martingale method, that is, choosing $\hat{\beta}_n$ such that

$$Y_n(t,[-1/2,1/2]^d) - \lambda \int_{[-1/2,1/2]^d} (1 - e^{-\int_0^t \int \rho(\hat{\beta}_n|x-y|)I_n(s,dy)ds}) dx = 0, \tag{4.3}$$

we obtain an analogous expression as Garcia (1995b) and the estimator $\hat{\beta}_n$ is consistent and asymptotically normal with $n^{d/2}(\hat{\beta}_n - \beta) \Rightarrow \sigma M$ where M is a Gaussian process with $Var(M(t)) = I(t, [-1/2, 1/2]^d)$ and

$$\sigma^{-1} = \int_{[-1/2,1/2]^d} (\int_0^t \int |x-y| \rho'(\beta |x-y|) I(s, dy) ds) e^{-\int_0^t \int \rho(\beta|x-y|) I(s,dy) ds} \, dx. \tag{4.4}$$

Although there are difficulties in solving expressions (4.1), (4.2), (4.3) and (4.4), it is promising to have results that can be used for inference purposes in a problem very much studied by the phytopathologists.

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References

[1] Daley, D.J. and Vere-Jones, D. (1988). *An Introduction to the Theory of Point Processes.* Springer-Verlag, New York, NY.

[2] Dunford, N. and Schwartz, J.T. (1957). *Linear Operators. Part I: General Theory.* Interscience Publishers, Inc, New York, NY.

[3] Ethier, S.N. and Kurtz,T.G. (1986). *Markov Processes: Characterization and Convergence.* John Wiley & Sons.

[4] Garcia, N.L. (1995a). Birth and Death Processes as Projections of Higher Dimensional Poisson Processes. *Advances in Applied Probability*, **27**, No. 4, pp. 911-930.

[5] Garcia, N.L. (1995b). Large Population Results for Epidemic Models. *Stochastic Processes and their Applications*, **60**, No. 1, pp. 147-160.

[6] Kurtz, T.G. (1981). *Approximation of Population Processes.* CBMS-NSF Regional Conference in Applied Mathematics, SIAM.

[7] Kurtz, T.G. (1983). Gaussian approximations for Markov chains and counting processes. *Bulletin of the International Statistical Institute, Proceedings of the 44th Session, Invited Paper*, **1**, pp. 361-376.

[8] Solomon, W. (1987). Representation and approximation of large population age distributions using Poisson random measures. *Stochastic Processes and their Applications*, **26**, pp.237-255.

[9] Stute, W. (1976). On a generalization of the Glivenko-Cantelli theorem, *Z. Wahrsch. Verw. Geb.*, **35**, pp. 167-175.

[10] Van den Bosch, F., Zadoks, J.C, and Metz,J.A.J. (1988). Focus expansion in plant disease. I: The constant rate of focus expansion. *Phytopathology*, **78**, pp. 54-58.