

# Functional Law of Large Numbers and PDEs for Spatial Epidemic Models with Infection-age Dependent Infectivity

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joint work with G. Pang (Rice Univ. USA)

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# The spatial model

- We consider a population of fixed size  $N$  distributed in  $K = K^N$  locations  $x_1, \dots, x_K$  in  $\mathcal{S} = [0, 1]$ . Let  $\mathbb{I}_k^N, k = 1, \dots, K^N$  be a partition of  $[0, 1]$  such that  $x_k^N \in \mathbb{I}_k^N$  and  $|\mathbb{I}_k^N| = (K^N)^{-1}, 1 \leq k \leq K$ . Individuals do not move between the locations. There are  $B_k^N$  individuals at location  $x_k, B_1^N + \dots + B_{K^N}^N = N$ .
- In each location, individuals are categorized into three groups :  $S, I$  and  $R$ . We denote the numbers of indiv. in those compartments at time  $t$  and location  $x_k$  as  $S_k^N(t), I_k^N(t)$  and  $R_k^N(t)$ . For all  $t \geq 0, S_k^N(t) + I_k^N(t) + R_k^N(t) = B_k^N$ .
- We define the piecewise constant functions of  $x$  :

$$S^N(t, x) = \sum_{k=1}^K S_k^N(t) 1_{\mathbb{I}_k^N}(x), \quad I^N(t, x) = \sum_{k=1}^K I_k^N(t) 1_{\mathbb{I}_k^N}(x),$$
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# Varying infectivity

- In each location  $x_k$ , there are two types of individuals : those who are infected at time  $t = 0$ , there are  $I_k^N(0)$  of those, who have been infected at times  $\tau_{-j,k}^N < 0$ ,  $1 \leq j \leq I_k^N(0)$ , and those who are susceptible at time  $t = 0$ , and may get infected (i.e. jump from  $S$  to  $I$ ) at times  $\tau_{1,k}^N < \tau_{2,k}^N < \dots$ .
- Let  $\{\lambda_{j,k}, j \in \mathbb{Z} \setminus \{0\}, 1 \leq k \leq K\}$  be an i.i.d. collection of random elements of  $D(\mathbb{R}; \mathbb{R}_+)$ , which satisfy  $\lambda(t) = 0$  for  $t < 0$ . Let  $\eta_{j,k} = \sup\{t > 0, \lambda_{j,k}(t) > 0\}$ . At time  $\tau_{j,k}^N + \eta_{j,k}$ , the individual  $j$  jumps from the  $I$  to the  $R$  compartment.
- As a result, the total force of infection at time  $t$  and location  $x_k$  is

$$\mathfrak{F}_k^N(t) = \sum_{j=1}^{I_k^N(0)} \lambda_{-j,k}(t - \tau_{-j,k}) + \sum_{j=1}^{A_k^N(t)} \lambda_{j,k}(t - \tau_{j,k}),$$

where  $A^N(t)$  is the number of initially susceptible who have been infected on the time interval  $[0, t]$ . We also define

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# The propagation of the epidemic

- $\{P_k, 1 \leq k \leq K\}$  denoting mutually independent standard Poisson processes, we let

$$A_k^N(t) = P_k \left( \int_0^t \Upsilon_k^N(s) ds \right), \quad \text{where}$$

$$\Upsilon_k^N(t) = \frac{S_k^N(t)}{B_k^N} \frac{1}{K} \sum_{k'=1}^K \beta_{k,k'}^N \mathfrak{I}_{k'}^N(t).$$

- Finally we define the number of infected indiv. at location  $x_k$  and time  $t$ , who have have been infected for a duration less than  $\alpha$  :

$$\mathfrak{I}_k^N(t, \alpha) = \sum_{j=1}^{I_k^N(0)} \mathbf{1}_{\tau_{-j,k}^N + \eta_{-j,k} > t} \mathbf{1}_{-\tau_{-j,k}^N \leq (\alpha - t)^+} + \sum_{j=A_k^N((t-\alpha)^+)+1}^{A_k^N(t)} \mathbf{1}_{\tau_{j,k}^N + \eta_{j,k} > t}$$

$$\text{Also } \mathfrak{I}^N(t, \alpha, x) = \sum_{k=1}^K \mathfrak{I}_k^N(t, \alpha) \mathbf{1}_{I_k^N(x)}.$$



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# The stochastic finite population model

- We have

$$S^N(t, x) = S^N(0, x) - A^N(t, x),$$

$$I^N(t, x) = \sum_{j=1}^{I^N(0, x)} \mathbf{1}_{\tau_{-j, k}^N + \eta_{-j, k} > t} + \sum_{j=1}^{A^N(t, x)} \mathbf{1}_{\tau_{j, k}^N + \eta_{j, k} > t}, \text{ if } x \in I_k$$

$$R^N(t, x) = R^N(0, x) + \sum_{j=1}^{I^N(0, x)} \mathbf{1}_{\tau_{-j, k}^N + \eta_{-j, k} \leq t} + \sum_{j=1}^{A^N(t, x)} \mathbf{1}_{\tau_{j, k}^N + \eta_{j, k} \leq t}.$$

- We let  $\bar{X}^N(t, x) := \frac{X^N(t, x)}{B^N(x)}$ , where  $B^N(x) = \sum_{k=1}^K B_k^N \mathbf{1}_{I_k}(x)$ .
- We wish to take the limit as  $N \rightarrow \infty$  in  $(\bar{S}^N(t, x), \bar{I}^N(t, x), \bar{R}^N(t, x))$  and also in  $\bar{J}^N(t, a, x)$ .

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# Assumptions

- $K^N \rightarrow \infty$  as  $N \rightarrow \infty$ ,  $\inf_k B_k^N \rightarrow \infty$ , and  $\sup_{N,k,k'} \frac{B_k^N}{B_{k'}^N} < \infty$ .
- We assume that the initial conditions converge towards appropriate limits, namely for all  $\alpha > 0$ , as  $N \rightarrow \infty$ ,

$$\|\bar{S}^N(0, \cdot) - \bar{S}(0, \cdot)\|_1 + \|\bar{J}^N(0, \alpha, \cdot) - \bar{J}(0, \alpha, \cdot)\|_1 + \|\bar{R}^N(0, \cdot) - \bar{R}(0, \cdot)\|_1 \rightarrow 0$$

- $\sup_{N,k,k'} \beta_{k,k'}^N < \infty$  and  $\beta^N(x, x') \rightarrow \beta(x, x')$  in  $L^1([0, 1]^2)$ , where

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- $\lambda(t) \leq \lambda^*$  a.s. for all  $t \geq 0$ ,  $\lambda$  has at most a given finite number of jumps and is uniformly continuous between its jumps. Notation :  $\bar{\lambda}(t) = \mathbb{E}[\lambda(t)]$ .

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# The limiting quantities

- Consider the system (with  $F(t) = \mathbb{P}(\eta_{1,1} \leq t)$ ,  $F^c(t) = 1 - F(t)$ )

$$\bar{S}(t, x) = \bar{S}(0, x) - \int_0^t \bar{\Upsilon}(s, x) ds,$$

$$\bar{\mathfrak{F}}(t, x) = \int_0^\infty \bar{\lambda}(a+t) \bar{\mathfrak{J}}(0, da, x) + \int_0^t \bar{\lambda}(t-s) \bar{\Upsilon}(s, x) ds,$$

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$$\bar{R}(t, x) = \bar{R}(0, x) + \int_0^\infty \left(1 - \frac{F^c(a'+t)}{F^c(a')}\right) \bar{\mathfrak{J}}(0, da', x) + \int_0^t F(t-s) \bar{\Upsilon}(s, x) ds$$

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# The convergence result

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## Theorem

$$\|\bar{S}^N(t, \cdot) - \bar{S}(t, \cdot)\|_1 \rightarrow 0, \quad \|\bar{\mathfrak{F}}^N(t, \cdot) - \bar{\mathfrak{F}}(t, \cdot)\|_1 \rightarrow 0, \quad \|\bar{R}^N(t, \cdot) - \bar{R}(t, \cdot)\|_1 \rightarrow 0 \\ \|\bar{\mathfrak{J}}^N(t, \mathbf{a}, \cdot) - \bar{\mathfrak{J}}(t, \mathbf{a}, \cdot)\|_1 \rightarrow 0$$

*in probability as  $N \rightarrow \infty$ , locally uniformly in  $t$  and  $\mathbf{a}$ , where the limits are given by the unique solution to the above set of integral equations.*

- In fact the pair  $(\bar{S}, \bar{\mathfrak{F}})$  is the unique solution of an integral equation, and the other quantities are then expressed in terms of that solution.
- The result follows from the proof that as  $N \rightarrow \infty$ , locally uniformly in  $t$ ,

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*in probability as  $N \rightarrow \infty$ , locally uniformly in  $t$  and  $\mathfrak{a}$ , where the limits are given by the unique solution to the above set of integral equations.*

- In fact the pair  $(\bar{S}, \bar{\mathfrak{F}})$  is the unique solution of an integral equation, and the other quantities are then expressed in terms of that solution.
- The result follows from the proof that as  $N \rightarrow \infty$ , locally uniformly in  $t$ ,

$$\|\bar{S}^N(t, \cdot) - \bar{S}(t, \cdot)\|_1 \rightarrow 0, \quad \|\bar{\mathfrak{F}}^N(t, \cdot) - \bar{\mathfrak{F}}(t, \cdot)\|_1 \rightarrow 0$$

# Main idea of the proof

- We have

$$[\bar{S}^N - \bar{S}](t, x) = [\bar{S}^N - \bar{S}](0, x) - \int_0^t [\bar{\Upsilon}^N - \bar{\Upsilon}](s, x) ds + M_A^N(t, x),$$

$$[\bar{\mathfrak{F}}^N - \bar{\mathfrak{F}}](t, x) = [\bar{\mathfrak{F}}_0^N - \bar{\mathfrak{F}}_0](t, x) + \int_0^t \bar{\lambda}(t-s) [\bar{\Upsilon}^N - \bar{\Upsilon}](s, x) ds + \mathcal{E}_{\bar{\mathfrak{F}}}^N(t, x).$$

- An important step is to show that  $M_A^N$ ,  $\bar{\mathfrak{F}}_0^N - \bar{\mathfrak{F}}_0$  and  $\mathcal{E}_{\bar{\mathfrak{F}}}^N$  tend to 0 in probability, in  $L^1([0, 1])$ , locally uniformly in  $t$ .
- Moreover

$$\begin{aligned} [\bar{\Upsilon}^N - \bar{\Upsilon}](t, x) &= \bar{S}^N(t, x) \int_0^1 \beta^N(x, x') \bar{\mathfrak{F}}^N(t, x') dx' \\ &\quad - \bar{S}(t, x) \int_0^1 \beta(x, x') \bar{\mathfrak{F}}(t, x') dx'. \end{aligned}$$

Thanks to a priori estimates on  $\sup_{N, t \leq T, x} \{\bar{S}^N(t, x) + \bar{\mathfrak{F}}^N(t, x)\}$ , and  $\sup_{t \leq T, x} \{\bar{S}(t, x) + \bar{\mathfrak{F}}(t, x)\}$ , we deduce the wished convergence by standard inequalities and Gronwall's Lemma.

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Thanks to a priori estimates on  $\sup_{N, t \leq T, x} \{\bar{S}^N(t, x) + \bar{\mathfrak{F}}^N(t, x)\}$ , and  $\sup_{t \leq T, x} \{\bar{S}(t, x) + \bar{\mathfrak{F}}(t, x)\}$ , we deduce the wished convergence by standard inequalities and Gronwall's Lemma.

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Thanks to a priori estimates on  $\sup_{N, t \leq T, x} \{ \bar{S}^N(t, x) + \bar{\mathfrak{F}}^N(t, x) \}$ , and  $\sup_{t \leq T, x} \{ \bar{S}(t, x) + \bar{\mathfrak{F}}(t, x) \}$ , we deduce the wished convergence by standard inequalities and Gronwall's Lemma.



# PDE models 1

We suppose that  $F$  is absolutely continuous, with the density  $f(t)$ . We define the associated hazard function :  $\mu(a) = \frac{f(a)}{F^c(a)}$ . We have

## Proposition

Assume that for each  $x \in [0, 1]$ ,  $a \mapsto \bar{\mathcal{J}}(0, a, x)$  is absolutely continuous, and let  $\bar{i}(0, a, x) = \bar{\mathcal{J}}_a(0, a, x)$ . Then for all  $t, a > 0$ , a.e.  $x \in [0, 1]$ ,  $a \mapsto \bar{\mathcal{J}}(t, a, x)$  is absolutely continuous, and  $\bar{i}(t, a, x) := \bar{\mathcal{J}}_a(t, a, x)$  satisfies

$$\frac{\partial \bar{i}(t, a, x)}{\partial t} + \frac{\partial \bar{i}(t, a, x)}{\partial a} = -\mu(a)\bar{i}(t, a, x),$$

with the initial condition  $\bar{i}(0, a, x) = \bar{\mathcal{J}}_a(0, a, x)$  and the boundary condition

$$\bar{i}(t, 0, x) = \bar{S}(t, x) \int_0^1 \beta(x, x') \int_0^{t+\bar{a}} \frac{\bar{\lambda}(a')}{\frac{F^c(a')}{F^c(a'-t)}} \bar{i}(t, a', x') da' dx'.$$

Note that  $\bar{\mathcal{J}}(0, \infty, x) = \bar{\mathcal{J}}(0, \bar{a}, x)$ .





Moreover, we have  $\frac{\partial \bar{S}(t, x)}{\partial t} = -\bar{i}(t, 0, x)$ , the above PDE has a unique solution given as follows :

$$\bar{i}(t, a, x) = 1_{a \geq t} \frac{F^c(a)}{F^c(a-t)} \bar{i}(0, a-t, x) + 1_{a < t} F^c(a) \bar{i}(t-a, 0, x),$$





where the boundary function is the unique solution of the integral equation

$$\begin{aligned} \bar{i}(t, 0, x) = & \left( \bar{S}(0, x) - \int_0^t \bar{i}(s, 0, x) ds \right) \\ & \times \int_0^1 \beta(x, x') \left( \int_0^\infty \bar{\lambda}(a+t) \bar{i}(0, a, x') da + \int_0^t \bar{\lambda}(t-s) \bar{i}(s, 0, x') ds \right) dx'. \end{aligned}$$

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THANK YOU FOR  
YOUR ATTENTION!