Recent results on Epidemic Models

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Le Mans

Kermack and McKendrick, two pioneers

- In 1927, W.O. Kermack and A.G. McKendrick published a paper which proposes a SIR model of propagation of epidemic diseases with an infection–age dependent infectivity and an infection–age dependent recovery rate. In that paper, they treated also the special case of constant infectivity and constant recovery rate.

- That paper was quoted more than 10 000 times, but almost all successors of these pioneers considered only the model with constant rate, which is the following ODE model.

$$\frac{dS}{dt}(t) = -\lambda S(t)I(t),$$
$$\frac{dI}{dt}(t) = \lambda S(t)I(t) - \rho I(t),$$
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Constant vs. non–constant recovery rate

Let $\mathcal{I}$ denote the length of the infectious period of a typical individual.

- $\mathbb{P}(\mathcal{I} > t) = \exp(-\mu t)$, $t > 0$, means that $\mathcal{I}$ follows the exponential distribution with parameter μ.

- Let $t \mapsto \mu(t)$ be measurable from $\mathbb{R}_+$ into itself, s.t. $\int_0^\infty \mu(t)dt = +\infty$. Assume

$$(*) \quad \mathbb{P}(\mathcal{I} > t) = \exp\left(-\int_0^t \mu(s)ds\right), \ \ t > 0.$$

  It is easy to deduce that $\mathcal{I}$ has the density $f(t) = \mu(t)\exp\left(-\int_0^t \mu(s)ds\right).$

- Conversely, given a probability density f on $\mathbb{R}_+$, define its hazard function as $\mu(t) := \left(\int_t^\infty f(s)ds\right)^{-1} f(t)$, then we have $(*)$.

- Assuming that the individuals recover at an infection–age dependent rate allows to choose an arbitrary distribution with density for $\mathcal{I}$.

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- If $P(t)$ is a standard Poisson process, then $P(\lambda t)$ is a rate λ Poisson process, and $P(\int_0^t \lambda(s)ds)$ is a rate $\lambda(t)$ Poisson process.
- If Q is a standard PRM on $\mathbb{R}^2_+$, i.e. Q is a sum of Dirac measures at random points, the numbers of points in disjoints subsets are mutually independent, and the number of points in A follows the Poi(Leb(A)) distribution, then

$$\int_0^t \int_0^\infty 1_{u \leq \lambda(s)} Q(ds, du)$$

is a rate $\lambda(t)$ Poisson process.
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- For all $t \geq 0$, $S^N(t) + I^N(t) + R^N(t) = N$.
- Suppose that each infectious individual meets others at rate β. With probability the proportion of susceptibles in the population, i.e. $S^N(t)/N$, the individual who is met is susceptible, in which case the encounter results in a new infection with probability p. Let $\lambda := \beta p$. Assume that the durations of the infectious periods of the various individuals are i.i.d., with the law $\mathrm{Exp}(\mu)$.
- Then (with P_{inf} and P_{rec} two independent standard Poisson proc.)

$$S^N(t) = S^N(0) - P_{inf}\left(\lambda \int_0^t N^{-1} S^N(s) I^N(s) ds\right),$$

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- Let $(\bar{S}^N(t), \bar{I}^N(t), \bar{R}^N(t)) = N^{-1}(S^N(t), I^N(t), R^N(t))$.
- It follows from the LLN for Poisson processes that
  $(\bar{S}^N(t), \bar{I}^N(t), \bar{R}^N(t)) \rightarrow (\bar{S}(t), \bar{I}(t), \bar{R}(t))$, where

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SIR model with memory as LLN limit of non–Markov stochastic models

- Let us go back to the general model of Kermack–McKendrick, first with a fixed infectivity λ, during an infectious period of length $\mathcal{I}$, where $P(\mathcal{I} \le t) = F(t)$. The infection age recovery rate is the hazard function of $\mathcal{I}$, i.e. $\mu(t) := f(t)/F^c(t)$, if f if the density of F, and $F^c(t) := 1 - F(t)$, i.e. $\mathbb{P}(\mathcal{I} > t) = \exp(-\int_0^t \mu(s)ds)$.

- Then the stochastic model is non Markov, unless if F is an exponential distribution (i.e. μ is constant).

- $(\bar{S}^N(t), \bar{I}^N(t), \bar{R}^N(t)) \to (\bar{S}(t), \bar{I}(t), \bar{R}(t))$ as $N \to \infty$, where

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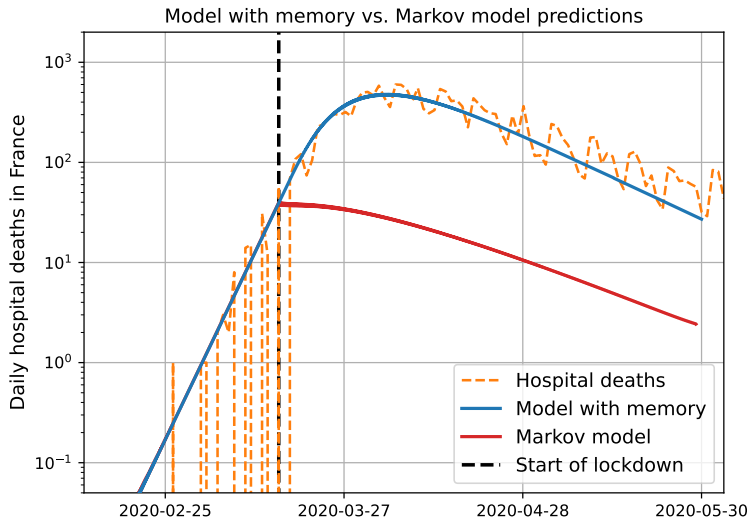# SIR model with memory as LLN limit of non–Markov stochastic models

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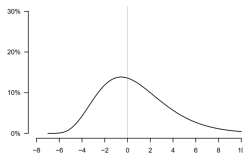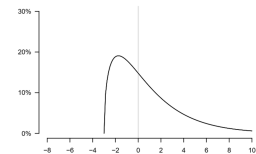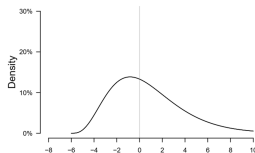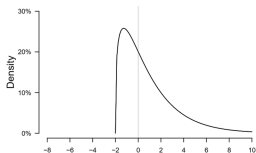$$\bar{I}(t) = \bar{I}(0)F_0^c(t) + \lambda \int_0^t F^c(t-s)\bar{S}(s)\bar{I}(s)ds,$$
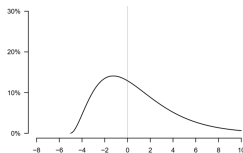
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Model with constant vs. infection age dependent recovery rate for the Covid

Model with memory vs. Markov model predictions

Varying infectivity

- Let $\{\lambda(t),\ t \geq 0\}$ be a random function with ≥ 0 values. If

$$\mathcal{E} = \inf\{t > 0, \lambda(t) > 0\} \quad \mathcal{I} = \sup\{t > 0, \lambda(\mathcal{E} + t) > 0\}.$$

Then $\mathcal{E}$ is the exposed period, $\mathcal{I}$ the infectious period.
We assume that to each individual is attached a copy $\lambda_i(t)$, where the λ_i are i.i.d. To the initially infected individuals are attached copies $\lambda_j^0(t)$ of another type of infectivity function.

- We request that λ belongs a.s. to the Skorohod space D, and that $\sup_{t \geq 0} \lambda(t) \leq \lambda^*$, where λ^* is a given constant. Then one can establish a law of large numbers as $N \to \infty$ of the corresponding individual based model. Define the total force of infection

$$\mathfrak{F}^N(t) = \sum_{j=1}^{I^N(0)} \lambda_j^0(t) + \sum_{i=1}^{A^N(t)} \lambda_i(t - \tau_i^N) = \lambda \times \# \text{ of infectious indiv.}$$

$$A^N(t) = \sum_{i \geq 1} 1_{(0,t]}(\tau_i^N) \text{ counts the number of indiv. infected on } (0, t].$$

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Varying infectivity : the LLN

- Let $S^N(t), I^N(t), R^N(t)$ denote resp. the number of susceptible, infected and recovered indiv. in the population.
  $S^N(t) + I^N(t) + R^N(t) = N$. Let $\bar{S}^N = N^{-1}S^N$, same with I and R.
- $(\bar{S}^N(t), \bar{\mathfrak{F}}^N(t), \bar{I}^N(t), \bar{R}^N(t)) \to (\bar{S}(t), \bar{\mathfrak{F}}(t), \bar{I}(t), \bar{R}(t))$ as $N \to \infty$:

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Alternative description : a PDE model

- Let us introduce the **age of infection** explicitly in our model :

$$\mu_t^N(d\mathfrak{a}) = \sum_{j=1}^{I^N(0)} 1_{\eta_j^0 > t}\delta_{\tau_{j,0}^N + t}(d\mathfrak{a}) + \sum_{i=1}^{A^N(t)} 1_{\tau_i^N + \eta_i > t}\delta_{t - \tau_i^N}(d\mathfrak{a}).$$

- Let $\bar{\mu}_t^N := N^{-1}\mu_t^N$. $\bar{\mu}^N \Rightarrow \bar{\mu}$ in $D(\mathbb{R}_+; \mathcal{M}_F(\mathbb{R}_+))$, where

$$\bar{\mu}_t(d\mathfrak{a}) = 1_{\mathfrak{a} \geq t}\frac{F^c(\mathfrak{a})}{F^c(\mathfrak{a} - t)}\bar{\mu}_0(d\mathfrak{a} - t) + 1_{\mathfrak{a} < t}F^c(\mathfrak{a})\overline{\Upsilon}(t - \mathfrak{a})d\mathfrak{a}$$

is the unique mesure valued solution of the PDE

$$\langle \partial_t \bar{\mu}_t, \varphi \rangle + \langle \partial_\mathfrak{a} \bar{\mu}_t, \varphi \rangle = \varphi(0)\overline{\Upsilon}(t) - \langle \bar{\mu}_t, h\varphi \rangle,$$

where F and h are the d.f. and the hazard rate of the duration of the infectious period, $F^c = 1 - F$.

Alternative description : a PDE model

- Let us introduce the **age of infection** explicitly in our model :

$$\mu_t^N(d\mathfrak{a}) = \sum_{j=1}^{I^N(0)} 1_{\eta_j^0 > t} \delta_{\tau_{j,0}^N + t}(d\mathfrak{a}) + \sum_{i=1}^{A^N(t)} 1_{\tau_i^N + \eta_i > t} \delta_{t - \tau_i^N}(d\mathfrak{a}).$$

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$$\partial_t \hat{\mu}_t + \partial_\mathfrak{a} \hat{\mu}_t = -h(\mathfrak{a})\hat{\mu}_t + \delta_0 \left[\hat{\Upsilon}(t) + \sqrt{\overline{\Upsilon}}(t)\frac{dW_{inf}(t)}{dt} \right] + \frac{\partial^2 W_{rec}(t, \mathfrak{a})}{\partial t \partial \mathfrak{a}}.$$

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Time of extinction of an epidemic

This is joint work with I. Drame and A. Mougabe-Peurkor.

- Suppose we are in a situation where, starting from $t = t_0$, an epidemic is declining (i.e. the mean number of susceptible individuals which an infected infects $R_{eff} < 1$), while the total number of infected individuals is $M << N =$ the size of the population. Then deterministic models are no longer valid, the epidemic is well approximated by a sub-critical branching process, which decays essentially like an exponential $e^{-\rho(t-t_0)}$.

- The approximating branching process associated to our varying infectivity model is a non–Markov continuous time branching process. We could derive an equation for the distribution function of the time of extinction, given that a unique infected individual got infected at time t_0.

- If we compare the time of extinction in our model with that of a Markov SIR model with the same R_{eff} and the same ρ, we see that the Markov model underestimates the time of extinction.

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Varying infectivity + immunity/susceptibility

- Kermack and McKendrick already in 1932 discussed progressive loss of immunity.
- Let $\mathfrak{s}_k(t)$ be the susceptibility of the k–th indiv. at time t. The total susceptibility is $\mathfrak{S}^N(t) = \sum_{k=1}^{N} \mathfrak{s}_k(t)$. If someone gets infected at time t, the probability that k is chosen equals $\left(\mathfrak{S}^N(t)\right)^{-1} \mathfrak{s}_k(t)$.
- We assume that the i–th infected individual after time 0 has at time t the susceptibility

$$\gamma_i(t - \tau_i^N),$$

while the j–th individual infected at time 0 has at time t the susceptibility

$$\gamma_j^0(t),$$

where $\gamma_i(t)$, $i \in \mathbb{N}$, are i.i.d. $[0, 1]$–valued random functions, which are non–decreasing and satisfy

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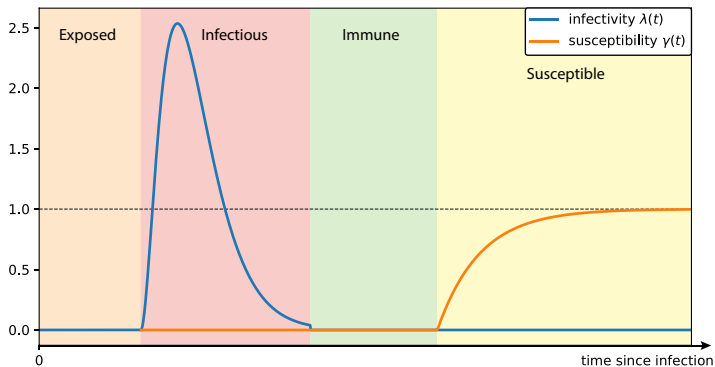
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FIGURE – Illustration of the infectivity and susceptibility of an individual from the time of becoming infected, to the time of recovery, and then to time of losing immunity and becoming fully susceptible. The blue curve represents the function $\lambda(t)$ which increases to a certain value and then decreases to zero, and the orange curve represents the function $\gamma(t)$ which gradually increases to 1.

$$\mathfrak{S}^N(t) = \sum_{k=1}^{N} \gamma_k^0(t) 1_{t < \eta_k^{N,0}} + \sum_{i=1}^{A^N(t)} \gamma_i(t - \tau_i^N) 1_{t < \eta_i^N},$$

$$\mathfrak{F}^N(t) = \sum_{j=1}^{I^N(0)} \lambda_j^0(t) + \sum_{i=1}^{A^N(t)} \lambda_i(t - \tau_i^N),$$

$$A^N(t) = \int_0^t \int_0^\infty 1_{u \le \Upsilon^N(s^-)} Q(ds, du), \Upsilon^N(t) = N^{-1} \mathfrak{S}^N(t) \mathfrak{F}^N(t),$$

where $\eta_k^{N,0}$ is the time of (re)infection of the k–th individual, who is either initially susceptible (then $\gamma_k^0(t) \equiv 1$), or initially infected (then $\gamma_k^0(0) = 0$), and η_i^N is the time of reinfection of the i–th newly infected individual. Q is a standard PRM on $\mathbb{R}_+^2$, τ_i^N's = jump times of $A^N(t)$ i.e. the times of the "new" infections, those which happen after time 0.

- Define $(\overline{\mathfrak{S}}^N(t), \bar{\bar{\mathfrak{F}}}^N(t)) = (N^{-1}\mathfrak{S}^N(t), N^{-1}\mathfrak{F}^N(t))$.
- Our main result is

Theorem

As $N \to \infty$, $(\overline{\mathfrak{S}}^N(t), \bar{\bar{\mathfrak{F}}}^N(t))$ converges in probability, locally uniformly in t, to the unique solution of

$$\overline{\mathfrak{S}}(t) = \mathbb{E}\left[\gamma^0(t)\exp\left(-\int_0^t \gamma^0(r)\overline{\mathfrak{F}}(r)dr\right)\right]$$
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- We combine the exposed and infectious individuals into unique compartment of "infected individuals". Similarly, we put the Susceptible and Recovered individuals into a unique compartment of susceptible individuals, where the recovered have susceptibility 0. The limits as $N \to \infty$ of the proportions of susceptible and infected individuals are given by the following formulas, where F (resp. F_0) denote the d.f. of the duration of the infected period of newly infected individuals (resp. of initially infected individuals).

$$\overline{S}(t) = \overline{S}(0) + \overline{I}(0)F_0(t) - \int_0^t [1 - F(t-s)]\overline{\mathfrak{S}}(s)\overline{\mathfrak{F}}(s)ds,$$

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HAPPY BIRTHDAY AND LONG LIFE TO THE LMM !