Estimating the state of the Covid-19 epidemic in France using a non-Markovian model

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Introduction

Markovian stochastic epidemic models converge to standard ODE models as the population size tends to infinity. This requires that the time spent by each individual in each compartment (exposed, infectious) be exponentially distributed, which does not fit the observations. Non-Markovian stochastic epidemic models, with more general distributions for the time spent in each compartment, converge to a system of integral equations (*i.e.* with distributed delays) [3].

Notations

- $\lambda(t)$: contact rate in the population at time t.
- $(\overline{S}(t), \overline{E}(t), \overline{I}(t), \overline{R}(t))$: proportions of susceptible, exposed, infectious and removed individuals.
- $(\mathcal{E}, \mathcal{I})$: exposed and infectious periods of a newly infected individual.
- $(\mathcal{E}_0, \mathcal{I}_0)$: exposed and infectious periods of an initially exposed individual.
- $\mathcal{I}_1$: infectious period of an initially infectious individual.

Deterministic SEIR model with general exposed and infectious period distributions

$$\overline{S}(t) = \overline{S}(0) - \int_0^t \lambda(s)\overline{S}(s)\overline{I}(s)ds,$$

$$\overline{E}(t) = \overline{E}(0)\,\mathbb{P}(t < \mathcal{E}_0) + \int_0^t \lambda(s)\,\mathbb{P}(t-s < \mathcal{E})\,\overline{S}(s)\overline{I}(s)ds,$$

$$\overline{I}(t) = \overline{E}(0)\,\mathbb{P}(\mathcal{E}_0 \le t < \mathcal{E}_0 + \mathcal{I}_0) + \overline{I}(0)\,\mathbb{P}(t < \mathcal{I}_1) + \int_0^t \lambda(s)\,\mathbb{P}(\mathcal{E} \le t-s < \mathcal{E}+\mathcal{I})\,\overline{S}(s)\overline{I}(s)ds,$$

$$\overline{R}(t) = \overline{E}(0)\,\mathbb{P}(\mathcal{E}_0 + \mathcal{I}_0 \le t) + \overline{I}(0)\,\mathbb{P}(\mathcal{I}_1 \le t) + \int_0^t \lambda(s)\,\mathbb{P}(\mathcal{E}+\mathcal{I} \le t-s)\,\overline{S}(s)\overline{I}(s)ds.$$

Exposed and infectious periods for Covid-19

Infectiousness starts 24 to 48h before symptom onset, so $\mathcal{I} > 2$. Two types of infected individuals [2]:

- **Reported individuals** are isolated quickly, $\mathcal{E} \in [2,4]$, $\mathcal{I} \in [3,5]$,
- **Unreported individuals** are not isolated, $\mathcal{E} \in [2,4]$, $\mathcal{I} \in [8,12]$.

The distribution of $\mathcal{I}$ is thus *bimodal* to reflect these different behaviours. We take $p_R = 0.8$ for the proportion of reported individuals.

Covid-19 hospital data in France

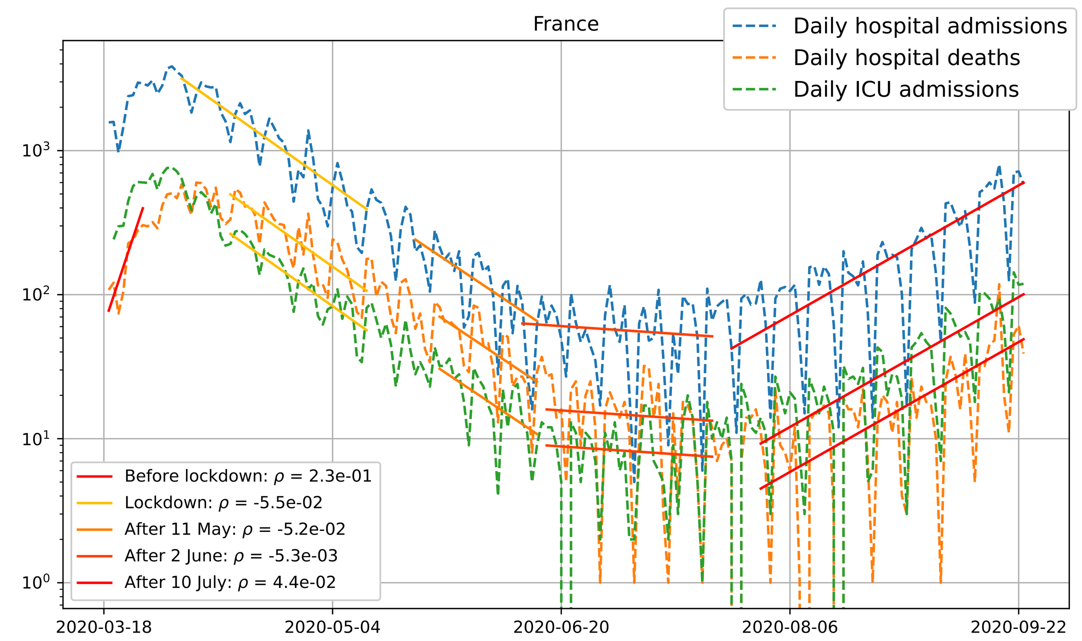

Figure 1: Exponential growth rates of the number of daily hospital admissions, ICU admissions and hospital deaths throughout the epidemic in France.

Early phase of the epidemic

At the beginning of the epidemic, $\overline{S}(t) \approx 1$, and

$$(N\overline{E}(t), N\overline{I}(t), N\overline{R}(t)) \approx (E(t), I(t), R(t)),$$

with

$$E(t) = \lambda \int_{-\infty}^t \mathbb{P}(t-s < \mathcal{E})\, I(s)ds,$$

$$I(t) = \lambda \int_{-\infty}^t \mathbb{P}(\mathcal{E} \le t-s < \mathcal{E}+\mathcal{I})\, I(s)ds, \quad (1)$$

$$R(t) = \lambda \int_{-\infty}^t \mathbb{P}(\mathcal{E}+\mathcal{I} \le t-s)\, I(s)ds.$$

Solution of the linearised system

The system (1) admits solutions of the form

$$E(t) = \boldsymbol{e}\, e^{\rho t}, \quad I(t) = \boldsymbol{i}\, e^{\rho t}, \quad R(t) = \boldsymbol{r}\, e^{\rho t},$$

with $\rho > 0$ if

$$\lambda = \frac{\rho}{\mathbb{E}[e^{-\rho\mathcal{E}}(1 - e^{-\rho\mathcal{I}})]}. \quad (2)$$

Formula (2) provides a relation between the **observed** growth rate of the number of infected individuals, and the **unknown** contact rate in the population. In turn, this yields the following relation between the growth rate ρ and the basic reproduction number R_0:

$$R_0 = \frac{\rho\,\mathbb{E}[\mathcal{I}]}{\mathbb{E}[e^{-\rho\mathcal{E}}(1 - e^{-\rho\mathcal{I}})]}.$$

p_R	Before lockdown	During lockdown	Second wave
0.2	4.7	0.66	1.4
0.8	3.5	0.73	1.3

Table 1: Values of R_0 during the different phases of the Covid-19 epidemic for two values of the proportion of reported individuals p_R.

Calibrating the SEIR model

- f: proportion of infected individuals who die in hospitals (infection fatality ratio).
- $\mathcal{D}$: delay between infection and hospital death.
- $\Lambda_D(t)$: cumulative number of hospital deaths related to Covid-19 at time t.

Then, during the initial growth phase of the epidemic,

$$\Lambda_D(t) = f\,\mathbb{E}[e^{-\rho_0\mathcal{D}}]\,e^{\rho_0 t}.$$

In addition, after lockdown restrictions are introduced at the **unknown** time t_L,

$$\Lambda_D(t) = f\,e^{\rho_0 t_L}\left(C_1 + C_2\,\mathbb{E}[e^{-\rho_1\mathcal{D}}]\,e^{\rho_1 t}\right), \quad t \gg t_L,$$

for some constants C_1 and C_2, with $\rho_1 < 0$.

Assuming $\mathcal{D} \sim \Gamma(k, \theta)$, we can solve for (t_L, k, θ) for a **known value of** f.

The IFR f has been estimated to be of the order of 0.5% [4].

Delay distributions

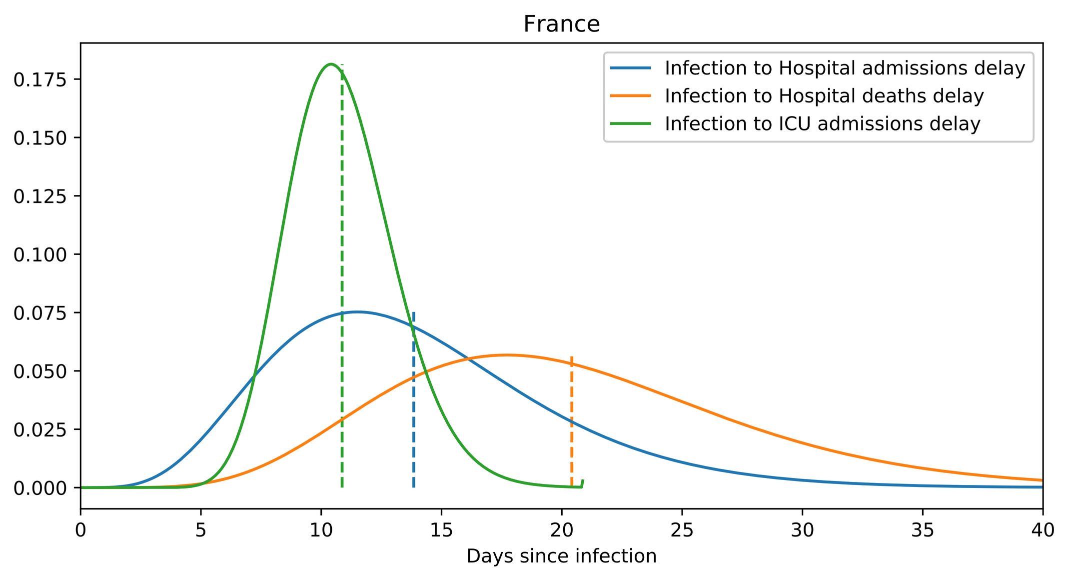

Figure 2: Distributions of the delays between infection and hospital admission, ICU admission and hospital death, estimated from the hospital data.

Model predictions

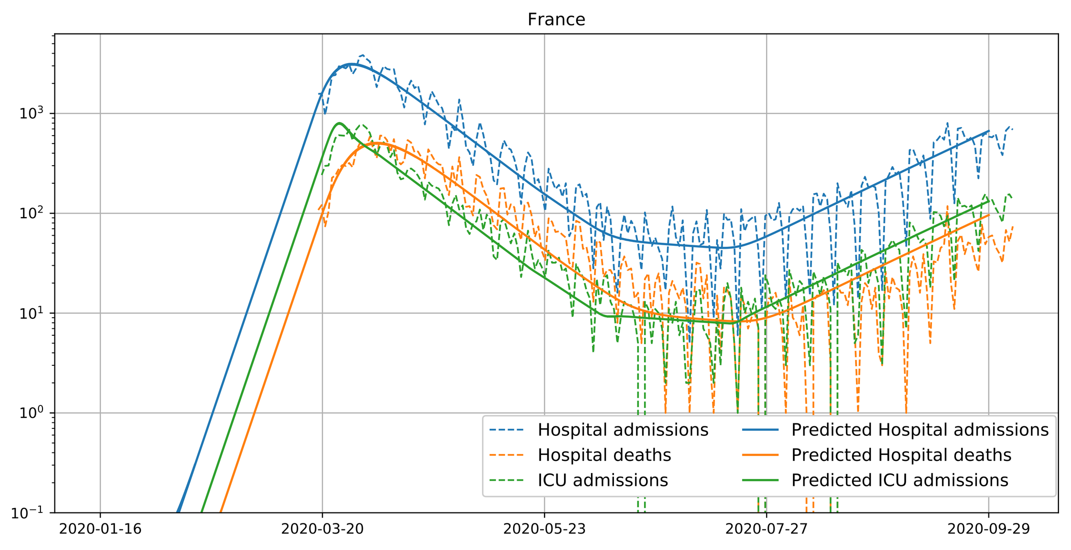

Figure 3: Comparison of the data to model predictions.

The second wave is growing more slowly than the first one, but still has the potential to overwhelm public hospitals if nothing is done.

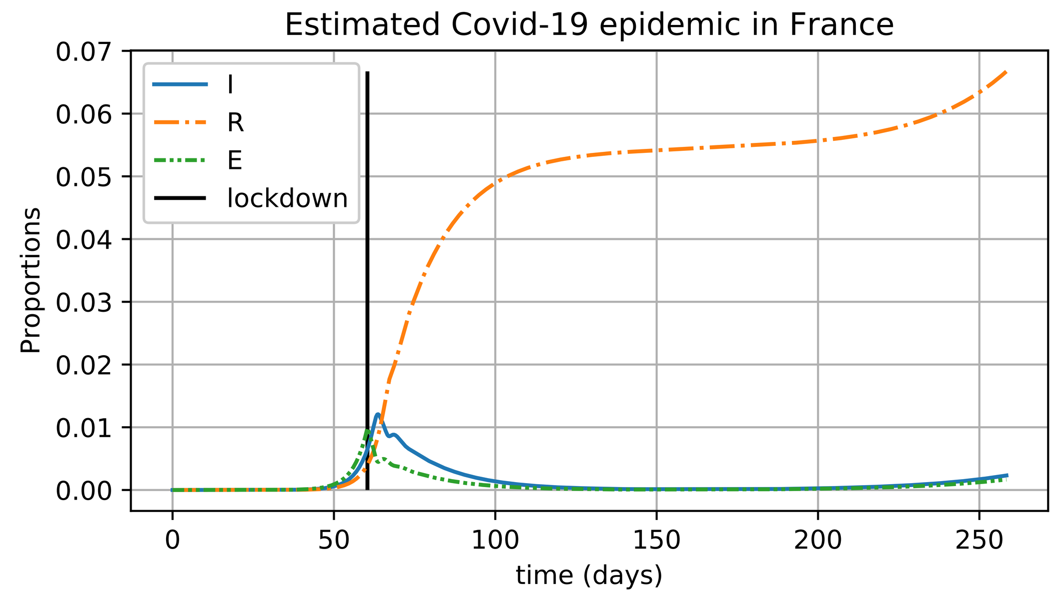

Figure 4: Estimated trajectories of $\overline{E}(t)$, $\overline{I}(t)$ and $\overline{R}(t)$.

References

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