

Lab session – Estimation of the reproduction number of Covid19

1 Context, model and goals

From the very beginning of the Covid19 pandemic National Health Authorities of all countries worldwide are monitoring the number of new infections each day, denoted by Z_t at day t . An example of such daily counts for five weeks in October and November 2022 in France is provided in Figure 1, as collected and made available by Johns Hopkins University¹.

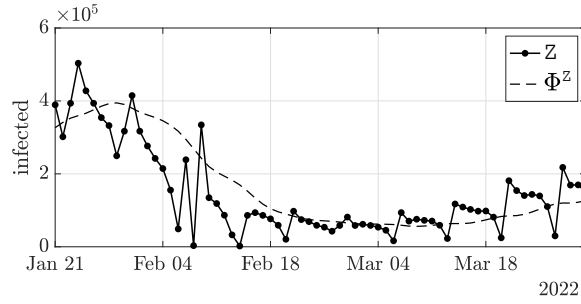


FIGURE 1 – Daily new infection counts Z in France for 10 weeks.

a. Load the MATLAB file `data_covid.mat` and plot the daily new infections Z with respect to days.

Yet, the number of new infections itself is not informative enough about the dynamics of the pandemic. Thus, looking only at Z_t does not make it possible to detect an epidemic resurgence early enough, and therefore to react quickly enough to avoid a dramatic explosion in the number of infected people.

This is why we rapidly turn to the monitoring of the *standard reproduction number*, R_0 , defined as the average number of secondary cases generated by a typical infected individual throughout its period of contagiousness [3, 4]. The reproduction number thus quantifies the intensity of the pandemic :

- when $R_0 > 1$ the virus is spreading at exponential speed ;
- when $R_0 < 1$ the epidemic is vanishing ;
- when $R_0 = 1$ the epidemic is stable.

The standard definition of the reproduction number is relaxed into a time-dependent reproduction number R_t at day t , which is linked to the number of new infections by Cori's model [3]. In this epidemiological model the number of new infections at day t depends on the past daily counts Z_1, \dots, Z_{t-1} and follow a Poisson distribution

$$Z_t | Z_1, \dots, Z_{t-1} \sim \text{Poisson}(R_t \Phi_t^Z), \quad \text{with } \Phi_t^Z = \sum_{u=1}^{\tau_\Phi} \phi(u) Z_{t-u} \quad (1)$$

where ϕ is the *serial interval function* associated to the pandemic, modeling the random delay between primary and secondary cases².

Reminder 1 (Poisson distribution and likelihood). The Poisson distribution of parameter $\mathbf{p} \in \mathbb{R}_+$ is a probability distribution on nonnegative integers. A random variable Z follows a Poisson distribution if and only if

$$\forall k \in \mathbb{N}, \quad \mathbb{P}(Z = k | \mathbf{p}) = e^{-\mathbf{p}} \frac{\mathbf{p}^k}{k!}.$$

Thus, given an observation $Z \in \mathbb{N}$ assumed to follow a Poisson model of parameter \mathbf{p} , the log-likelihood $\ln \mathcal{L}(Z | \mathbf{p})$ writes

$$\ln \left(e^{-\mathbf{p}} \frac{\mathbf{p}^Z}{Z!} \right) = -\mathbf{p} + Z \ln(\mathbf{p}) - \ln(Z!) \underset{Z \gg 1}{\simeq} -\mathbf{p} + Z \ln(\mathbf{p}) - Z \ln(Z) + Z = - \left(Z \ln \left(\frac{Z}{\mathbf{p}} \right) + \mathbf{p} - Z \right),$$

where the approximation $\ln(Z!) \simeq Z \ln(Z) - Z$, valid for $Z \rightarrow \infty$, can be derived from Stirling formula.

1. <https://coronavirus.jhu.edu/map.html>

2. For Covid19 pandemic the serial interval function is modeled by a Gamma distribution with mean 6.6 days and standard deviation 3.5 days cropped at $\tau_\Phi = 26$ days.

Definition 1. The Kullback-Leibler between a vector $\mathbf{Z} \in \mathbb{R}^T$ and a vector $\mathbf{p} \in \mathbb{R}^T$ is defined in a fully separable manner as

$$d_{\text{KL}}(\mathbf{Z}|\mathbf{p}) = \sum_{t=1}^T d_{\text{KL}}(Z_t|\mathbf{p}_t), \text{ where } d_{\text{KL}}(Z_t|\mathbf{p}_t) = \begin{cases} Z_t \ln\left(\frac{Z_t}{\mathbf{p}_t}\right) + \mathbf{p}_t - Z_t & \text{if } Z_t > 0, \mathbf{p}_t > 0 \\ \mathbf{p}_t & \text{if } Z_t = 0, \mathbf{p}_t \geq 0 \\ \infty & \text{otherwise.} \end{cases}$$

If $\mathbf{Z} \in \mathbb{N}^T$ is a vector of nonnegative integer observations, it quantifies the discrepancy between \mathbf{Z} and a vector of Poisson random variables of parameters \mathbf{p} .

Thus, the opposite log-likelihood associated to Cori's model (2) expresses in terms of the Kullback-Leibler divergence as

$$-\ln \mathcal{L}(\mathbf{Z}|\mathbf{R}) = d_{\text{KL}}(\mathbf{Z}|\mathbf{R} \odot \Phi^{\mathbf{Z}}) \quad (2)$$

where $\mathbf{R} \odot \Phi^{\mathbf{Z}}$ denotes the component-wise vector product, $(\mathbf{R} \odot \Phi^{\mathbf{Z}})_t = R_t \Phi_t^{\mathbf{Z}}$.

- b. For Z_t fixed at $Z_t \in \{0, 10, 250\}$ plot the function $\mathbf{p}_t \mapsto d_{\text{KL}}(Z_t|\mathbf{p}_t)$.
- c. Show that the function $\mathbf{p}_t \mapsto d_{\text{KL}}(Z_t|\mathbf{p}_t)$ is convex and differentiable.
- d. Is the gradient of $\mathbf{p}_t \mapsto d_{\text{KL}}(Z_t|\mathbf{p}_t)$ Lipschitzian? Justify your answer.

2 Estimation of the reproduction number

2.1 Maximum Likelihood Estimator

- a. Given fixed Z_t and $\Phi_t^{\mathbf{Z}} = \sum_{u=1}^{\tau_{\Phi^{\mathbf{Z}}}} \Phi^{\mathbf{Z}}(u) Z_{t-u}$, compute the minimum and the minimizer of the function $d_{\text{KL}} : \mathbf{R}_t \mapsto d_{\text{KL}}(Z_t|\mathbf{R}_t \Phi_t^{\mathbf{Z}})$.
- b. Deduce the minimum and the minimizer $\hat{\mathbf{R}}^{\text{MLE}}$ of the Kullback-Leibler divergence

$$D_{\text{KL}} : \begin{cases} \mathbb{R}^T & \rightarrow \mathbb{R} \\ \mathbf{R} & \mapsto \sum_{t=1}^T d_{\text{KL}}(Z_t|\mathbf{R}_t \Phi_t^{\mathbf{Z}}). \end{cases}$$

This minimizer is denoted $\hat{\mathbf{R}}^{\text{MLE}}$ because it is the Maximum Likelihood Estimator of \mathbf{R} .

Indeed, as stated in Equation (3), the Kullback-Leibler divergence is the opposite log-likelihood of the Poisson model, thus minimizing $d_{\text{KL}}(\mathbf{Z}|\mathbf{R} \odot \Phi^{\mathbf{Z}})$ amounts to maximize the likelihood $\mathcal{L}(\mathbf{Z}|\mathbf{R})$.

- c. Compute numerically the Maximum Likelihood Estimate from the data \mathbf{Z} , named `Z` in the file `data_covid.mat`, and the global infectiousness $\Phi^{\mathbf{Z}}$, named `PhiZ` in `data_covid.mat`. Plot it and comment about its temporal behavior.
- d. Would you advocate the use of the Maximum Likelihood Estimator to monitor the Covid19 pandemic? Explain why.

2.2 Penalized likelihood

In order to enforce some regularity on the temporal behavior of R_t we consider the penalized likelihood estimator

$$\hat{\mathbf{R}} \in \underset{\mathbf{R}}{\text{Argmin}} D_{\text{KL}}(\mathbf{Z}|\mathbf{R} \odot \Phi^{\mathbf{Z}}) + \lambda \|\mathbf{D}_2 \mathbf{R}\|_1, \quad (3)$$

where $\mathbf{D}_2 : \mathbb{R}^T \rightarrow \mathbb{R}^{T-2}$ is the discrete Laplacian operator acting on \mathbb{R}^T as

$$\forall t \in \{1, 2, \dots, T-2\}, \quad (\mathbf{D}_2 \mathbf{R})_t = R_{t+2} - 2R_{t+1} + R_t.$$

The ℓ_1 penalization favors sparsity of the second order derivative of the estimate and thus $\hat{\mathbf{R}}$ is expected to be piecewise linear, with only a few days at which the slope of $t \mapsto R_t$ is changing.

Because of the presence of the ℓ_1 norm in the objective function, (4) is a nonsmooth optimization problem. Thus one has to resort to proximal operators to solve it.

- a. Based on Question 1 c. explain why it is not possible to use the *forward-backward* algorithm.

To circumvent this limitation, we will use only proximity operators.

- b. For fixed \mathbf{Z}_t , compute the proximity operator of $\mathbf{p}_t \mapsto d_{\text{KL}}(\mathbf{Z}_t | \mathbf{p}_t)$.
- c. Given \mathbf{Z}_t and $\Phi_t^{\mathbf{Z}} = \sum_{u=1}^{\tau \Phi^{\mathbf{Z}}} \Phi^{\mathbf{Z}}(u) \mathbf{Z}_{t-u}$, deduce from 1. the expression of the proximity operator of $\mathbf{R}_t \mapsto d_{\text{KL}}(\mathbf{Z}_t | \mathbf{R}_t \Phi_t^{\mathbf{Z}})$.
- d. Explain how to compute the proximity operator of

$$\mathbf{D}_{\text{KL}} : \begin{cases} \mathbb{R}^T & \rightarrow \mathbb{R} \\ \mathbf{R} & \mapsto \sum_{t=1}^T d_{\text{KL}}(\mathbf{Z}_t | \mathbf{R}_t \Phi_t^{\mathbf{Z}}). \end{cases}$$

Because of the linear operator \mathbf{D}_2 inside the ℓ_1 norm in (4), we do not have a closed-form expression of the proximity operator of the penalization $\|\mathbf{D}_2 \mathbf{R}\|_1$ and hence it is necessary to use a *splitting* scheme. We will thus turn to the primal-dual algorithm proposed in [2]. To ensure convergence of Algorithm 1, the descent steps $\tau > 0$ and $\sigma > 0$ must be chosen so that $\sigma\tau \|\mathbf{D}_2\|_{\text{op}}^2 < 1$, where $\|\mathbf{D}_2\|_{\text{op}}^2$ denotes the *operator norm* of \mathbf{D}_2 defined as

$$\|\mathbf{D}_2\|_{\text{op}} = \sup_{\mathbf{R} \in \mathbb{R}^T, \mathbf{R} \neq \mathbf{0}} \frac{\|\mathbf{D}_2 \mathbf{R}\|}{\|\mathbf{R}\|}$$

To compute the operator norm of a matrix $\mathbf{D}_2 \in \mathbb{R}^{T-2 \times T}$, you can use the Matlab function `norm(D2)`. A standard choice for the descent steps is $\sigma = \tau = 0.99 / \|\mathbf{D}_2\|_{\text{op}}$. Feel free to explore other choices satisfying the convergence condition.

Algorithm 1 Primal-dual minimization of the penalized Kullback-Leibler (4) for the estimation of reproduction numbers.

Require: Infection counts : $\mathbf{Z} \in \mathbb{R}^T$ and $\Phi^{\mathbf{Z}} \in \mathbb{R}^T$

Choose descent parameters : $\tau, \sigma > 0$ such that $\sigma\tau \|\mathbf{D}_2\|_{\text{op}}^2 < 1$

Max. iterations : k_{max}

Initialization $\mathbf{R}^{[0]} = \mathbf{Z} / \Phi^{\mathbf{Z}}$

$\mathbf{Q}^{[0]} = \mathbf{D}_2 \mathbf{R}^{[0]}, \bar{\mathbf{R}}^{[0]} = \mathbf{R}^{[0]}$

while $k < k_{\text{max}}$ **do**

$$\begin{aligned} \mathbf{Q}^{[k+1]} &= \mathbf{Q}^{[k]} + \sigma \mathbf{D}_2 \bar{\mathbf{R}}^{[k]} - \sigma \text{prox}_{\lambda \sigma^{-1} \|\cdot\|_1} \left(\sigma^{-1} \mathbf{Q}^{[k]} + \mathbf{D}_2 \bar{\mathbf{R}}^{[k]} \right) \\ \mathbf{R}^{[k+1]} &= \text{prox}_{\tau \mathbf{D}_{\text{KL}}(\mathbf{Z} | \cdot \odot \Phi^{\mathbf{Z}})} (\mathbf{R}^{[k]} - \tau \mathbf{D}_2^* \mathbf{Q}^{[k+1]}) \\ \bar{\mathbf{R}}^{[k+1]} &= 2\mathbf{R}^{[k+1]} - \mathbf{R}^{[k]} \end{aligned}$$

$k \leftarrow k + 1$

end while

- e. Compute the proximity operator of the ℓ_1 norm multiplied by a scalar $\lambda \sigma^{-1}$, that is of $\lambda \sigma^{-1} \|\cdot\|_1 : \mathbf{Q} \in \mathbb{R}^N \mapsto \sum_{n=1}^N \lambda \sigma^{-1} |\mathbf{Q}_n| \in \mathbb{R}$ and explain how to compute it in practice.
- f. Construct the $T - 2 \times T$ matrix of the discrete Laplacian \mathbf{D}_2 .
- g. Show that by setting $\tilde{\mathbf{Z}} := \mathbf{Z} / \alpha$ for some $\alpha > 0$,

$$D_{\text{KL}}(\tilde{\mathbf{Z}} | \mathbf{R}^{[k]} \odot \Phi^{\tilde{\mathbf{Z}}}) = \frac{1}{\alpha} D_{\text{KL}}(\mathbf{Z} | \mathbf{R}^{[k]} \odot \Phi^{\mathbf{Z}}). \quad (4)$$

Justify that running Algorithm 1 with \mathbf{Z} and $\Phi^{\mathbf{Z}}$ as input, with a given λ vs. with $\tilde{\mathbf{Z}}$ and $\Phi^{\tilde{\mathbf{Z}}}$ with $\tilde{\lambda} := \lambda / \text{std}(\mathbf{Z})$ give the same reproduction number estimate $\hat{\mathbf{R}}$.

From now on, when running Algorithm 1, replace \mathbf{Z} by $\mathbf{Z} / \text{std}(\mathbf{Z})$ and $\Phi^{\mathbf{Z}}$ by $\Phi^{\mathbf{Z}} / \text{std}(\mathbf{Z})$. Take into account that this amounts to replace λ by $\tilde{\lambda} := \lambda / \text{std}(\mathbf{Z})$. This normalization of input data improve the numerical robustness of the algorithmic scheme : it is to be seen as a purely numerical trick.

- h. Implement Algorithm 1 and run it on the data \mathbf{Z} . Plot the evolution of the objective function

$$k \mapsto D_{\text{KL}}(\mathbf{Z} | \mathbf{R}^{[k]} \odot \Phi^{\mathbf{Z}}) + \lambda \|\mathbf{D}_2 \mathbf{R}^{[k]}\|_1 \quad (5)$$

along iterations to illustrate convergence of the scheme.

- i. Run Algorithm 1 for different values of the regularization parameter $\tilde{\lambda}$ and comment on its influence. A possibility is to consider $\tilde{\lambda} \in \{0.5, 3.5, 15, 50, 150, 250\}^3$.

3. This correspond to non normalized regularization parameters $\lambda \in \{0.5 \times \text{std}(\mathbf{Z}), 3.5 \times \text{std}(\mathbf{Z}), 15 \times \text{std}(\mathbf{Z}), 50 \times \text{std}(\mathbf{Z}), 150 \times \text{std}(\mathbf{Z}), 250 \times \text{std}(\mathbf{Z})\}$.

Références

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