

# Lab session – Estimation of the reproduction number of Covid19

## 1 Preliminaries : subdifferentiable and proximal operators

**Exercise 1.** Let  $f, g : \mathbb{R}^T \rightarrow \mathbb{R} \cup \{\infty\}$ , two proper, continuous functions. Show that, if  $\text{dom } f \cap \text{dom } g \neq \emptyset$ , then

$$\forall \mathbf{x} \in \mathbb{R}^T, \quad \partial f(\mathbf{x}) + \partial g(\mathbf{x}) \subset \partial(f + g)(\mathbf{x}).$$

In particular, show that if  $f$  is continuously differentiable and convex on its domain, then

$$\forall \mathbf{x} \in \mathbb{R}^T, \quad \nabla f(\mathbf{x}) + \partial g(\mathbf{x}) \subset \partial(f + g)(\mathbf{x}). \quad (1)$$

**Remark 1.** This property does not require functions  $f$  and  $g$  to be convex. Its reciprocal does (see [1, Proposition 16.42] for the exact hypotheses required and a demonstration using convex duality, out of the scope of the present course!). Yet, the above inclusion is enough to interpret mixed proximal-gradient scheme : since, due to Equation (1),  $\nabla f(\mathbf{x}^{[k]}) + \mathbf{u}^{[k]}, \mathbf{u}^{[k]} \in \partial g(\mathbf{x}^{[k]})$  is indeed one subgradient of  $f + g$  at  $\mathbf{x}^{[k]}$ .

**Exercise 2.** Given some  $\mathbf{y} \in \mathbb{R}^T$ , let

$$f : \begin{cases} \mathbb{R}^T & \rightarrow \mathbb{R} \\ \mathbf{x} & \mapsto \frac{1}{2} \|\mathbf{x} - \mathbf{y}\|_2^2. \end{cases}$$

compute the proximity operator of  $\gamma f$ , for  $\gamma > 0$ . Plot it when  $T = 1$  and comment briefly its behavior.

**Exercise 3.** Let  $f : \mathbb{R}^T \rightarrow \mathbb{R}, \mathbf{x} \mapsto \|\mathbf{x}\|_1$ , compute the proximity operator of  $\gamma f$ , for  $\gamma > 0$ . Comment briefly its behavior.

## 2 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 University<sup>1</sup>.

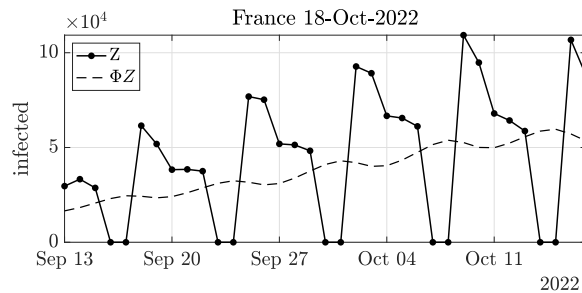


FIGURE 1 – Daily new infection counts  $Z$  in France for the past 5 weeks.

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 :

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

- 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

$$Z_t | Z_1, \dots, Z_{t-1} \sim \text{Poisson}(R_t \Phi_t), \quad \text{with } \Phi_t = \sum_{u=1}^{\tau_\Phi} \phi(u) Z_{t-u} \quad (2)$$

where  $\phi$  is the *serial interval function* associated to the pandemic, modeling the random delay between primary and secondary cases<sup>2</sup>.

**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.

**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

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

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

$$-\ln \mathcal{L}(\mathbf{Z} | \mathbf{R}) = d_{\text{KL}}(\mathbf{Z} | \mathbf{R} \odot \Phi) \quad (3)$$

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

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

### 3 Estimation of the reproduction number

#### 3.1 Maximum Likelihood Estimator

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

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

<sup>2</sup>. 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.

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  $d_{\text{KL}}(\mathbf{Z}|\mathbf{R} \odot \Phi)$  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  $\Phi$ , 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.

### 3.2 Penalized likelihood

In order to enforce some regularity on the temporal behavior of  $\mathbf{R}_t$  we consider the penalized likelihood estimator

$$\hat{\mathbf{R}} \in \underset{\mathbf{R}}{\text{Argmin}} d_{\text{KL}}(\mathbf{Z}|\mathbf{R} \odot \Phi) + \lambda \|\mathbf{D}_2 \mathbf{R}\|_1, \quad (4)$$

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

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

The  $\ell_1$  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  $t \mapsto \mathbf{R}_t$  is changing.

Because of the presence of the  $\ell_1$  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  $\Phi_t = \sum_{u=1}^{\tau_\Phi} \Phi(u) \mathbf{Z}_{t-u}$ , deduce from 1. the expression of the proximity operator of  $\mathbf{R}_t \mapsto d_{\text{KL}}(\mathbf{Z}_t|\mathbf{R}_t \Phi_t)$ .
- d. Explain how to compute the proximity operator of

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

Because of the linear operator  $\mathbf{D}_2$  inside the  $\ell_1$  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

$$\|\mathbf{D}_2\|_{\text{op}}^2 = \sup_{\mathbf{R} \in \mathbb{R}^T, \mathbf{R} \neq \mathbf{0}} \frac{\|\mathbf{D}_2 \mathbf{R}\|}{\|\mathbf{R}\|}$$

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.

- e. Compute the proximity operator of the  $\ell_1$  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. Implement Algorithm 1 and run it on the data  $\mathbf{Z}$ . Plot the evolution of the objective function  $d_{\text{KL}}(\mathbf{Z}|\mathbf{R}^{[k]} \odot \Phi) + \lambda \|\mathbf{D}_2 \mathbf{R}^{[k]}\|_1$  along iterations to illustrate convergence of the scheme.
- h. Run Algorithm 1 for different values of the regularization parameter  $\lambda$  and comment on the influence of  $\lambda$ . A possibility is to consider  $\lambda \in \{0.5 \times \text{std}(\mathbf{Z}), 3.5 \times \text{std}(\mathbf{Z}), 50 \times \text{std}(\mathbf{Z}), 50 \times \text{std}(\mathbf{Z}), 250 \times \text{std}(\mathbf{Z})\}$ .

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

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

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

Max. iterations :  $k_{\max}$

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

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

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

$$\mathbf{Q}^{[k+1]} = \mathbf{Q}^{[k]} + \sigma\mathbf{D}_2\bar{\mathbf{R}}^{[k]} - \sigma\text{prox}_{\lambda\sigma^{-1}\|\cdot\|_1}(\sigma^{-1}\mathbf{Q}^{[k]} + \mathbf{D}_2\bar{\mathbf{R}}^{[k]})$$

$$\mathbf{R}^{[k+1]} = \text{prox}_{\tau\text{d}_{\text{KL}}(\mathbf{Z}|\cdot\odot\Phi)}(\mathbf{R}^{[k+1]} - \tau\mathbf{D}_2^*\mathbf{Q}^{[k+1]})$$

$$\bar{\mathbf{R}}^{[k+1]} = 2\mathbf{R}^{[k+1]} - \mathbf{R}^{[k]}$$

$k \leftarrow k + 1$

**end while**

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### 3.3 Tikhonov penalization

- a. From Exercise 2, deduce the proximity operator of  $\mathbf{x} \mapsto \|\mathbf{x}\|_2^2$ .
- b. Replace the  $\ell_1$  penalization,  $\|\mathbf{D}_2\mathbf{R}\|_1$ , by an squared  $\ell_2$  penalization  $\|\mathbf{D}_2\mathbf{R}\|_2^2$ , also called Tikhonov regularization. Implement the Chambolle-Pock algorithm replacing  $\|\cdot\|_1$  by  $\|\cdot\|_2^2$ .  
**Indication :** the convergence condition does not change.
- c. Plot the two estimates on the same graph and comment.  
**Indication :** the *optimal* parameter  $\lambda_{\mathbf{R}}$ , i.e., the one for which the estimate is regular while still reflecting the pandemic dynamics, might change depending on whether the  $\ell_1$  or  $\ell_2^2$  penalization is used.

## Références

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