# Estimation of the reproduction number of the Covid19 pandemic

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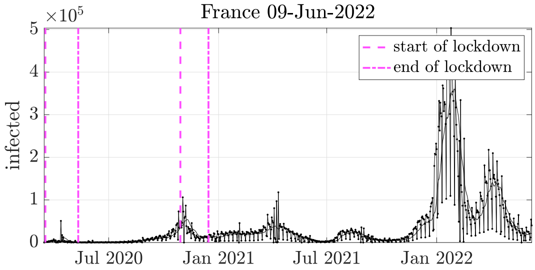
**CANUM 2020**

**Data:** number of daily new infection counts




(partial) lockdown

*data from Johns Hopkins University*

Designing adapted counter measures and evaluating their effectiveness

→ requires reliable monitoring tools *epidemiological model,*

→ which perform real-time estimation *fast algorithm,*

→ robust to low quality of the data *managing outliers.*

✗ number of cases not informative enough: need to capture the *dynamics*

# Epidemiological models

Susceptible-Infected-Recovered (SIR), among *compartmental models*

- refinement needed to get socially realistic model
- quadratic increase of the number of parameters
- Bayesian framework: heavy computational burden
- need consolidated and accurate datasets

✗ not adapted to real-time monitoring of Covid19 pandemic

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Reproduction number $R0$

*averaged number of people contaminated by one infected person*

$R0 > 1$: the virus propagates

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✓ one single indicator accounting for the overall pandemic mechanism

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✓ one single indicator accounting for the overall pandemic mechanism

$\Longrightarrow$ Taking counter-measures and evaluating their efficiency requires a **real-time**, daily, estimate $R_t$.

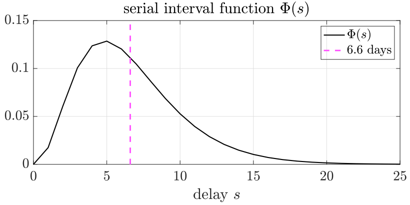
# Cori's model

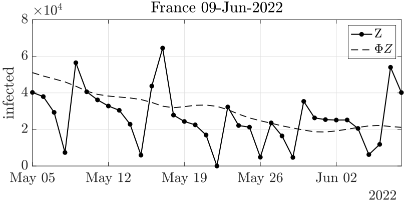
**Poisson process** accounting for random contamination (Cori, 2013)

$$Z_t \sim \mathrm{Poiss}\,(p_t)\,, \quad p_t = R_t \sum_{s=1}^{\tau_\Phi} \Phi(s) Z_{t-s}$$

$\Phi(s)$: **serial interval function** $\tau_\Phi = 26$ days

*random delay between onset of symptoms in primary and secondary cases*




$>$ modeled by a Gamma distribution with mean and variance of 6.6 and 3.5 days

Unknown parameters: $\boldsymbol{R} = (R_1, \ldots, R_T) \in \mathbb{R}_+^T$

Observed data: $\boldsymbol{Z} = (Z_1, \ldots, Z_T)$

**Poisson distribution** of parameter $p_t = R_t \sum_{s=1}^{\tau_\Phi} \Phi(s) Z_{t-s}$

$$\mathbb{P}(Z_t | \boldsymbol{Z}_{t-\tau_\Phi:t-1}, R_t) = \frac{p_t^{Z_t} \mathrm{e}^{-p_t}}{Z_t!}$$

> negative log-likelihood

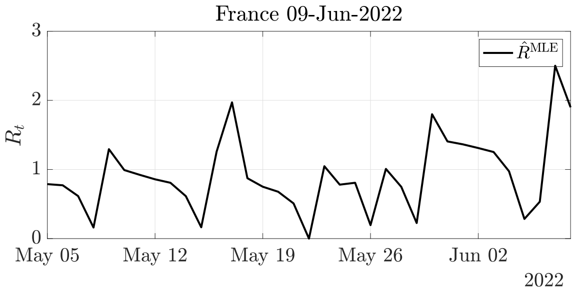
$$\begin{aligned} -\ln\left(\mathbb{P}(Z_t | \boldsymbol{Z}_{t-\tau_\Phi:t-1}, R_t)\right) &= p_t - Z_t \ln(p_t) + \ln(Z_t!) \\ &\underset{Z_t \gg 1}{\simeq} p_t - Z_t \ln(p_t) + Z_t \ln(Z_t) - Z_t \\ &\underset{\text{(def.)}}{=} \mathrm{d}_{\mathrm{KL}}(Z_t | p_t) \quad \text{Kullback-Leibler divergence} \end{aligned}$$

# Maximum Likelihood Estimate

$>$ maximizing the likelihood is equivalent to minimizing $-\ln \mathbb{P}$

$$\widehat{\boldsymbol{R}}^{\mathsf{MLE}} = \underset{\boldsymbol{R} \in \mathbb{R}_+^T}{\operatorname{argmin}} \sum_{t=1}^{T} \mathsf{d}_{\mathsf{KL}}\left(Z_t \,|\, R_t (\Phi Z)_t\right), \quad (\Phi Z)_t \triangleq \sum_{s=1}^{\tau_\Phi} \Phi(s) Z_{t-s}$$

**Explicit solution:** $\widehat{\boldsymbol{R}}_t^{\mathsf{MLE}} = Z_t / (\Phi Z)_t$




**not realistic!** pseudo-periodicity, irregularity, no local trend

# Penalized log-likelihood

$$\widehat{\boldsymbol{R}}^{\mathrm{PL}} = \operatorname*{argmin}_{\boldsymbol{R} \in \mathbb{R}_+^T} \sum_{t=1}^{T} \mathsf{d}_{\mathsf{KL}} \left( Z_t \,|R_t(\Phi Z)_t \right) + \lambda_{\mathrm{time}} \mathcal{P}(\boldsymbol{R})$$

with $\mathcal{P}(\boldsymbol{R})$ favoring some temporal regularity

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Total Variation $\Rightarrow$ piecewise constancy:

$$\mathcal{P}(\boldsymbol{R}) = \|\mathbf{D}_1\boldsymbol{R}\|_1, \quad (\mathbf{D}_1\boldsymbol{R})_t = R_{t+1} - R_t \text{ first order discrete derivative}$$

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Total Variation $\Rightarrow$ piecewise constancy: ✗ *not epidemiologically realistic*

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Penalized Laplacian $\Rightarrow$ piecewise linear behavior:

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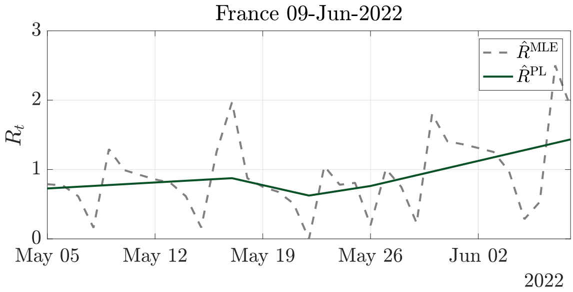

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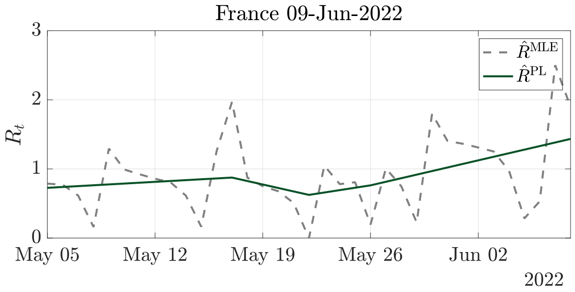
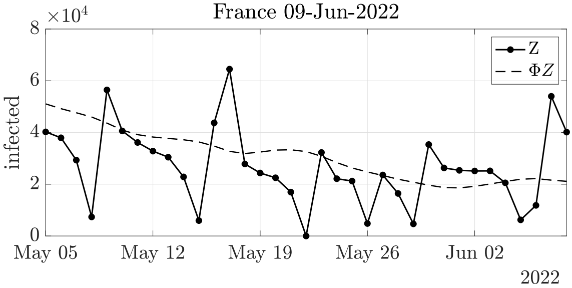



**better,** but still pseudo-oscillations

# Managing low quality of the data




New infection counts $\boldsymbol{Z} = (Z_1, \ldots, Z_T)$ are corrupted by

- missing samples,
- non meaningful negative counts,
- retrospected cumulated counts spread over few days,
- pseudo-seasonality effects, with less counts on non working days, ...

$>$ parametric modeling out of reach

# Extended model accounting for measurement noise

**Nonstationary Poisson process** with *outliers*

$$Z_t \sim \mathrm{Poiss}\left(R_t(\Phi Z)_t + O_t\right), \quad \underbrace{\widetilde{p}_t = R_t \sum_{s=1}^{\tau_\Phi} \Phi(s) Z_{t-s} + O_t}_{\text{new instant Poisson intensity}}$$

$O_t$: significant values, concentrated on specific days (Sundays, day-offs, ...)

$\Rightarrow$ unknown parameters: $(\boldsymbol{R}, \boldsymbol{O}) = (R_1, \ldots, R_T, O_1, \ldots, O_T) \in \mathbb{R}_+^T \times \mathbb{R}^T$

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**Extended penalized log-likelihood**

$$\left(\widehat{\boldsymbol{R}}, \widehat{\boldsymbol{O}}\right) = \underset{(\boldsymbol{R},\boldsymbol{O}) \in \mathbb{R}_+^T \times \mathbb{R}^T}{\operatorname{argmin}} \sum_{t=1}^{T} \mathrm{d}_{\mathrm{KL}}\left(Z_t \,|\, R_t(\Phi Z)_t + O_t\right) + \lambda_{\mathrm{time}} \|\mathbf{D}_2 \boldsymbol{R}\|_1 + \iota_{\geq 0}(\boldsymbol{R}) + \lambda_{\mathrm{O}} \|\boldsymbol{O}\|_1$$

$>$ favors piecewise linear non-negative reproduction number and sparse outliers

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**Existence and uniqueness of the solution** (Pascal et al., 2022)

> There exists at least one solution $\left(\widehat{\boldsymbol{R}}, \widehat{\boldsymbol{O}}\right)$.

> The estimated Poisson intensity $\widehat{\boldsymbol{p}} = \widehat{\boldsymbol{R}} \cdot \boldsymbol{\Phi} \boldsymbol{Z} + \widehat{\boldsymbol{O}}$ is unique.

**Estimation of reproduction numbers and *outliers***

$$\left(\widehat{\boldsymbol{R}}, \widehat{\boldsymbol{O}}\right) = \underset{(\boldsymbol{R},\boldsymbol{O})\in\mathbb{R}_+^T\times\mathbb{R}^T}{\operatorname{argmin}} \; \mathrm{D}_{\mathrm{KL}}\left(\boldsymbol{Z}\,|\,\boldsymbol{R}\cdot\Phi\boldsymbol{Z}+\boldsymbol{O}\right) + H(\mathbf{L}(\boldsymbol{R},\boldsymbol{O}))$$

- $\mathbf{L}(\boldsymbol{R},\boldsymbol{O}) = (\lambda_{\mathrm{time}}\mathbf{D}_2\boldsymbol{R}, \boldsymbol{R}, \lambda_{\mathrm{O}}\boldsymbol{O})$ a linear operator
- $H(\boldsymbol{Q}_1, \boldsymbol{Q}_2, \boldsymbol{Q}_3) = \|\boldsymbol{Q}_1\|_1 + \iota_{\geq 0}(\boldsymbol{Q}_2) + \|\boldsymbol{Q}_3\|_1$ convex, **nonsmooth**

# Nonsmooth convex optimization for the estimation of $\boldsymbol{R}$

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nonsmooth regularization $\Rightarrow$ proximal operator

$$\operatorname{prox}_{\tau F}(\boldsymbol{Y}) = (\mathbf{I}+\tau\partial F)^{-1}(\boldsymbol{Y}) = \underset{\boldsymbol{X}}{\operatorname{argmin}}\ \frac{1}{2}\|\boldsymbol{X}-\boldsymbol{Y}\|^2 + \tau F(\boldsymbol{X})$$

| gradient descent | proximal algorithm |
|---|---|
| $\boldsymbol{X}^{[t+1]} = \boldsymbol{X}^{[t]} - \tau\nabla F(\boldsymbol{X}^{[t]})$ | $\boldsymbol{X}^{[t+1]} = \operatorname{prox}_{\tau F}(\boldsymbol{X}^{[t]})$ |

**Estimation of reproduction numbers and *outliers***

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data fidelity $\quad \widetilde{\boldsymbol{P}} \mapsto \mathrm{D}_{\mathrm{KL}}(\boldsymbol{Z}|\widetilde{\boldsymbol{P}})$ strictly convex, differentiable and proximable

penalization $\quad (\boldsymbol{R},\boldsymbol{O}) \mapsto H(\mathbf{L}(\boldsymbol{R},\boldsymbol{O}))$ convex, with $H$ proximable

✗ $\widetilde{\boldsymbol{P}} \mapsto \nabla\mathrm{D}_{\mathrm{KL}}(\boldsymbol{Z}|\widetilde{\boldsymbol{P}})$ not Lipschitz $\Rightarrow$ proximal gradient not suitable

**Estimation of reproduction numbers and *outliers***

$$\left(\widehat{\boldsymbol{R}}, \widehat{\boldsymbol{O}}\right) = \underset{(\boldsymbol{R},\boldsymbol{O}) \in \mathbb{R}_+^T \times \mathbb{R}^T}{\operatorname{argmin}} \ \mathsf{D}_{\mathsf{KL}}\left(\boldsymbol{Z} \,|\, \boldsymbol{R} \cdot \Phi \boldsymbol{Z} + \boldsymbol{O}\right) + H(\mathbf{L}(\boldsymbol{R}, \boldsymbol{O}))$$

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Primal-dual minimization of the penalized Kullback-Leibler:

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

**Choose** descent parameters: $\tau, \sigma > 0$, max. iterations: $k_{\max}$

**Initialization** $\boldsymbol{R}^{[0]} = \boldsymbol{Z}$, $\boldsymbol{O}^{[0]} = \mathbf{0}$, $\boldsymbol{Q}^{[0]} = \mathbf{L}(\boldsymbol{R}^{[0]}, \boldsymbol{O}^{[0]})$, $\overline{\boldsymbol{R}}^{[0]} = \boldsymbol{R}^{[0]}$, $\overline{\boldsymbol{O}}^{[0]} = \boldsymbol{O}^{[0]}$

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

Update the dual, primal and auxiliary variables

$$\boldsymbol{Q}^{[k+1]} = \operatorname{prox}_{\sigma H^*}(\boldsymbol{Q}^{[k]} + \sigma \mathbf{L}(\overline{\boldsymbol{R}}^{[k]}, \overline{\boldsymbol{O}}^{[k]}))$$

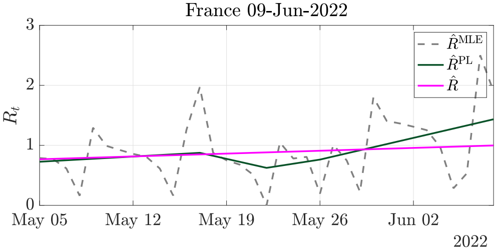
$$(\boldsymbol{R}^{[k+1]}, \boldsymbol{O}^{[k+1]}) = \operatorname{prox}_{\tau \mathsf{D}_{\mathsf{KL}}(\boldsymbol{Z}|\cdot \Phi \boldsymbol{Z} + \cdot)}((\boldsymbol{R}^{[k+1]}, \boldsymbol{O}^{[k+1]}) - \tau \mathbf{L}^* \boldsymbol{Q}^{[k+1]})$$

$$(\overline{\boldsymbol{R}}^{[k+1]}, \overline{\boldsymbol{O}}^{[k+1]}) = 2(\boldsymbol{R}^{[k+1]}, \boldsymbol{O}^{[k+1]}) - (\boldsymbol{R}^{[k]}, \boldsymbol{O}^{[k]})$$

$k \leftarrow k + 1$

**end while**

# Denoised infection counts

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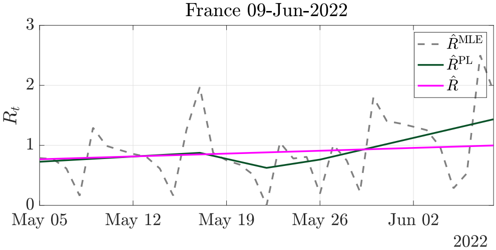


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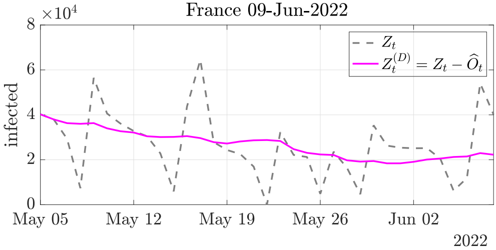
As a byproduct $\widehat{\boldsymbol{Z}}^{(\mathrm{D})} = \boldsymbol{Z} - \widehat{\boldsymbol{O}}$



New infection counts per county: $\boldsymbol{Z} = \left\{ Z_t^{(d)},\ d \in [1, D],\ t \in [1, T] \right\}$

$\Rightarrow$ multivariate reproduction number $R_t^{(d)}$

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**Multivariate penalized log-likelihood**

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$$+ \lambda_{\mathsf{time}} \|\mathbf{D}_2 \boldsymbol{R}\|_1 + \iota_{\geq 0}(\boldsymbol{R}) + \lambda_{\text{space}} \|\mathbf{G}\boldsymbol{R}\|_1 + \lambda_{\mathrm{O}} \|\boldsymbol{O}\|_1$$

$>$ $\|\mathbf{G}\boldsymbol{R}\|_1$ favors piecewise constancy in space

# Multivariate estimation: spatial regularization

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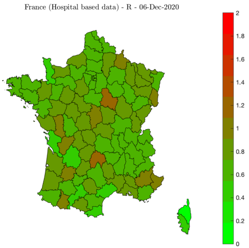
<u>Graph Total Variation</u>

$$\|\mathbf{G}\boldsymbol{R}\|_1 = \sum_{t=1}^{T} \sum_{d_1 \sim d_2} \left| R_t^{(d_1)} - R_t^{(d_2)} \right|$$

sum over neighboring counties

here: $d_1 \sim d_2 \Leftrightarrow$ share terrestrial border

$$\widetilde{\mathbf{L}}(\boldsymbol{R}, \boldsymbol{O}) = (\lambda_{\text{time}} \mathbf{D}_2 \boldsymbol{R}, \boldsymbol{R}, \lambda_{\text{space}} \mathbf{G}\boldsymbol{R}, \lambda_{\mathrm{O}} \boldsymbol{O})$$



# Conclusion

**Achieved:**

*(in this presentation)* (Pascal et al., TSP, 2022)

- estimation and regularization of multivariate reproduction number $R_t^{(d)}$
  - piecewise linearity in time
  - piecewise constancy in space
- manage low quality of reported data
  - extended epidemiological model
  - sparsity of *outliers*

https://perso.ens-lyon.fr/patrice.abry/

(preprint available) (Fort et al., arXiv:2203.09142, 2022)

- real-time credibility interval estimate of $R_t$
  - leverage connection between *variational* and *Bayesian* formulations
  - using nonsmooth optimization tools smarter than random walk

https://perso.math.univ-toulouse.fr/gfort/

**Perspective:**

- automated selection of regularization parameters $(\lambda_{\text{time}}, \lambda_{\text{space}}, \lambda_{\text{O}})$
- data on graph: alternative connectivity function $d_1 \sim d_2$
- adaptive serial interval function $\Phi$ depending on pandemic phase