MACHINE LEARNING FOR EPIDEMIOLOGICAL MODELS

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WHY LEARN EPIDEMIC MODELS?

During 2020, the spread of **COVID-19** infection affected the whole world.

Some countries resorted to **non-pharmaceutical interventions** of various degrees to control the spread of the virus, such as lockdowns or imposing the use of masks.

Many countries collected vast amounts of **detailed data** about the evolution of the epidemic.

Understanding the evolution of the epidemic **from the data** can help us understand the efficacy of this interventions and predict the spread of the illness if no action is taken.

WHY LEARN EPIDEMIC MODELS?

Deterministic epidemic models, such as SIR, usually model the evolution through some **constant parameters**, such as infection rate.

Constant parameters are ill-suited to model a **dynamic phenomenon** where the spread is counter-acted by the intervention of national authorities.

Time-varying parameters are better suited, but the parameter space becomes quickly too big to be manually fine-tuned where analytical solutions do not exist.

A **Machine Learning approach** can be used to explore the parameter space and find interesting and useful models.

THE MODEL

A classical **deterministic** approach to model an epidemic is the *susceptible, infectious, removed* (SIR) model.

A population of N individuals is divided into

- $x(t) = (\#$ of susceptible at time $t)$
- $y(t) = (\#$ of infectious at time $t)$
- $z(t) = (\#$ of removed at time $t)$

We assume that the population remains **constant**, therefore:

$$x(t) + y(t) + z(t) = N.$$

THE MODEL

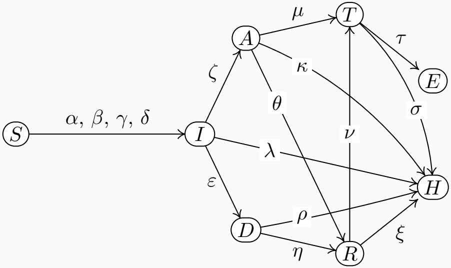
The dynamics of the epidemics then can be described by the following **system of ODEs**[1]:

$$\begin{cases} x'(t) = -\beta x(t)y(t) \\ y'(t) = \beta x(t)y(t) - \gamma y(t) \\ z'(t) = \gamma y(t) \end{cases}$$

- $\beta > 0 \rightarrow$ **infection rate**
- $\gamma > 0 \rightarrow$ **removal rate**
- $R_0 := \beta/\gamma \rightarrow$ **reproduction number**

[1] Norman TJ Bailey et al. *The mathematical theory of infectious diseases and its applications*. Charles Griffin & Company Ltd, 1975.

SIDARTHE



A more sophisticated epidemiological model is **SIDARTHE**[2], where we add **more compartments** to better describe the stages of infection. (ODEs can be found in the Appendix)

[2]Giulia Giordano et al. "Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy". In: *Nature Medicine* (2020).

SIDARTHE

Compartments:

- **S**: Susceptible
- **I**: Asymptomatic undetected infected individuals
- **D**: Aymptomatic detected infected individuals
- **A**: Symptomatic undetected infected individuals
- **R**: Symptomatic detected infected individuals
- **T**: Acutely symptomatic infected individuals
- **H**: Healed individuals
- **E**: Deceased individuals

An important difference is that we differentiate between **detected** and **undetected** individuals.

DYNAMIC PARAMETERS

The epidemiological parameters are usually considered **constant in time**.

This prevents the model from describing changes due to **non-pharmaceutical interventions** (lockdown, etc...).

We want to extend the model by allowing **daily changes** to the parameters values.

$$\beta \to \beta(t) \qquad \tau \to \tau(t)$$

In this way we can monitor how parameters (i.e. infection rate) **change** during the epidemic evolution.

The data

OFFICIAL DATA

We pre-processed the data[3] to obtain **5 time-series** which map to **5 SIDARTHE compartments**:

- $\overline{D}$: detected asymptomatic individuals
- $\overline{R}$: detected symptomatic individuals
- $\overline{T}$: acutely symptomatic individuals
- $\overline{H_d}$: portion of healed individuals that were previously detected
- $\overline{E}$: deceased individuals

We do not have access to data about the **undetected** infected individuals (of course).

[3] You can find the **data** following this link: https://github.com/pcm-dpc/COVID-19

TRAIN/VALIDATION/TEST SPLIT

All time-series were **split** into three sets:

- **Train Set** (size T): $0 \leq t \leq T$
- **Validation Set** (size V): $T \leq t \leq T + V$
- **Test Set** (size D): $T + V \leq t \leq T + V + D$

As usual, the training set will be used to **fit** the model, the validation set will be used to evaluate **over-fitting** and the test set will be used for the **final evaluation** of the model.

The learning problem

GENERIC STATEMENT

We call $u(t)$ the **concatenation** of all parameters at time t.

$$u(t) = (\alpha(t), \beta(t)...)$$

Problem

Learning $u(t)$ from **supervisions** on the number of people in the **detected** compartments, i.e. $\overline{D}$, $\overline{R}$, $\overline{T}$, $\overline{H_d}$ and $\overline{E}$.

PRECISE FORMULATION

Given the **supervisions** $\overline{D}$, $\overline{R}$, $\overline{T}$, $\overline{H_d}$ and $\overline{E}$

Given $\hat{D}^u$, $\hat{R}^u$, $\hat{T}^u$, $\hat{H}_d^u$ and $\hat{E}^u$ the **solutions** of SIDARTHE equations given by parameters $u(t)$.

We want to find the set of parameters $u(t)$ which minimizes the **MSE** of the prediction against the targets on samples for $t = 0 \rightarrow T$.

GRADIENT DESCENT THROUGH ODES

The learning is done through **Gradient Descent**.

The SIDARTHE equations are computed through **numeric integration**, using **Heun** method and a fixed time step.

To obtain the gradient of parameters through the integration, we have implemented the Heun method in **PyTorch** to leverage its powerful autograd framework.

Sidenote: there are strong similarities with **Neural ODEs**.

Regularization

SMOOTHNESS

In case of **overfitting**, the learned parameters could result in a discontinuous and wrinkled function of time.

To avoid this problem and reduce overfitting, we augment the loss function with a **regularization term** $R(u)$.

The penalty $R(u)$ is higher when the parameters are discontinuous and enforces a **smooth** function.

MOMENTUM

Since the solution is computed through integration, the value of parameters at initial time steps have a **bigger impact** on the solution w.r.t. values at final time steps.

This can be seen in the gradient of each parameter: for $t \to T$, gradients **approach** 0.

Hence, we augmented the Gradient Descent update rule with a *momentum* term, which manages to **distribute** the gradient throughout the u function.

Important note: the commonly known momentum carries the gradient over subsequent **epochs**; this momentum term carries the gradient over subsequent **time steps** of the parameters $u(t)$

TARGET NORMALIZATION

$\overline{D}$, $\overline{R}$, $\overline{T}$, $\overline{H_d}$ and $\overline{E}$ have very different **scales** of values.

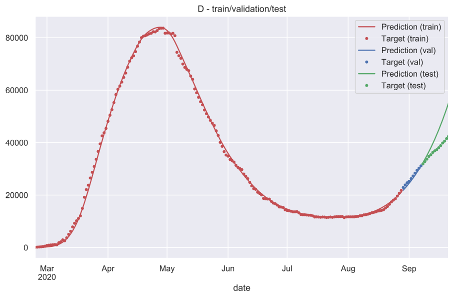
E.g. $max(\overline{H_d}) \approx 200'000$ and $max(\overline{T}) \approx 4'000$

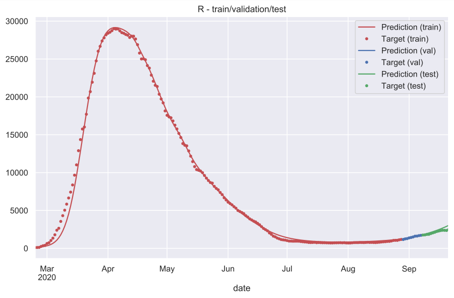
This could cause the learning to **prefer** a target at the expense of another one.

We **weight** the loss components for each target based on its scale **relative** to the other targets.

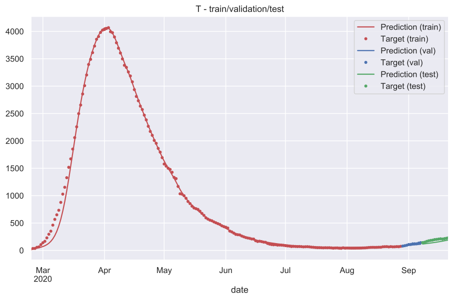
Fitting the data

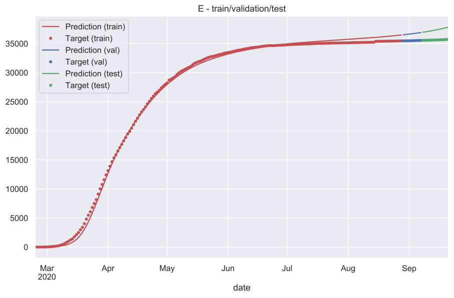
INFECTED INDIVIDUALS



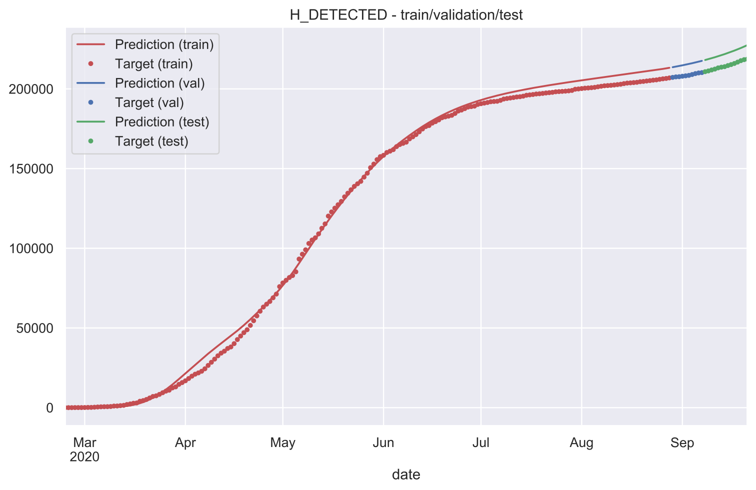


ACUTELY SYMPTOMATIC & DECEASED

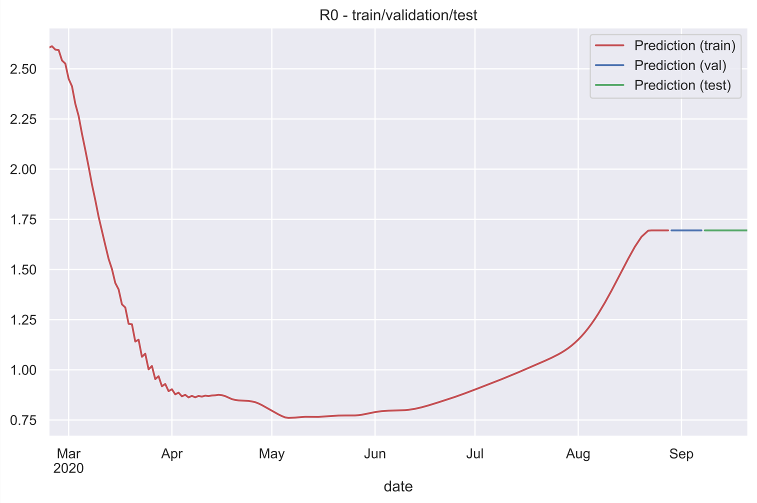




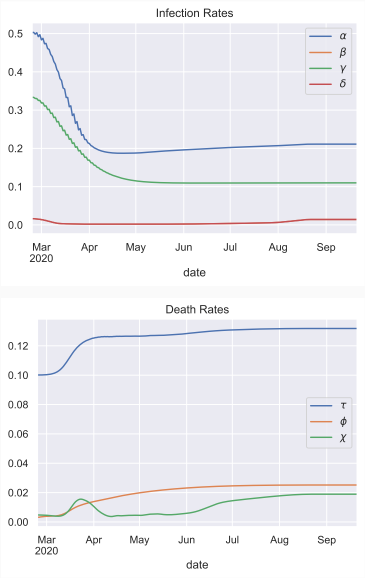
DETECTED HEALED INDIVIDUALS



R0


R0 - train/validation/test
Prediction (train)
Prediction (val)
Prediction (test)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
Mar
2020
Apr
May
Jun
Jul
Aug
Sep
date

PARAMETERS



Infection Rates
α
β
γ
δ
0.5
0.4
0.3
0.2
0.1
0.0
Mar
2020
Apr
May
Jun
Jul
Aug
Sep
date
Detection Rates
0.35
0.30
0.25
0.20
0.15
ε
θ
Mar
2020
Apr
May
Jun
Jul
Aug
Sep
date
Death Rates
0.12
0.10
0.08
0.06
0.04
0.02
0.00
τ
ϕ
χ
Mar
2020
Apr
May
Jun
Jul
Aug
Sep
date
Symptoms Development Rates
η
ζ
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Mar
2020
Apr
May
Jun
Jul
Aug
Sep
date

Thank you for listening!

References

Bailey, Norman TJ et al. *The mathematical theory of infectious diseases and its applications*. Charles Griffin & Company Ltd, 1975.

Giordano, Giulia et al. "Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy". In: *Nature Medicine* (2020).

Appendix

SIDARTHE EQUATIONS

$$
\begin{cases}
\dot{S}(t) = -S(t)\big(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)\big); \\
\dot{I}(t) = S(t)\big(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)\big) - (\varepsilon + \zeta + \lambda) I(t); \\
\dot{D}(t) = \varepsilon I(t) - (\eta + \rho) D(t); \\
\dot{A}(t) = \zeta I(t) - (\theta + \mu + \kappa + \phi) A(t); \\
\dot{R}(t) = \eta D(t) + \theta A(t) - (\nu + \xi + \chi) R(t); \\
\dot{T}(t) = \mu A(t) + \nu R(t) - (\sigma + \tau) T(t); \\
\dot{H}(t) = \lambda I(t) + \rho D(t) + \kappa A(t) + \xi R(t) + \sigma T(t); \\
\dot{E}(t) = \phi A(t) + \chi R(t) + \tau T(t)
\end{cases}
$$

LOSS FUNCTION

The loss function $F(u)$ has **5 components**, one for each target.

Each target is weighted by the **normalizing weight** W_x, which takes into account the difference in scale relatively to other targets.

Reminder: $\hat{X}$ is the target, $\overline{X}^u$ is the **solution** computed by the model using parameters $u(t)$

$$F(u) = \frac{1}{T}\sum_{t=0}^{T} \frac{W_D}{2}\left(\overline{D}(t) - \hat{D}^u(t)\right)^2 + \frac{W_R}{2}\left(\overline{R}(t) - \hat{R}^u(t)\right)^2 +$$

$$\frac{W_T}{2}\left(\overline{T}(t) - \hat{T}^u(t)\right)^2 + \frac{W_H}{2}\left(\overline{H_d}(t) - \hat{H}_d^u(t)\right)^2 + \frac{W_E}{2}\left(\overline{E}(t) - \hat{E}^u(t)\right)^2$$

SMOOTHNESS

The smoothness regularization term depends on the **derivative** of the parameters.

It is also weighted with the hyper-parameter W_R to better tune the **regularizing effect** of the term.

$$R(u) = \frac{W_R}{T} \sum_{t=0}^{T} \frac{\dot{u}(t)^2}{2}$$

MOMENTUM

The momentum term is added to the well-known **update rule** of **Gradient Descent**.

$$u_t^{k+1} = \begin{cases} u_t^k - \nabla_t f(u^k) & \text{if} \quad t = 0 \\ u_t^k - \nabla_t f(u^k) + \mu_t (u_{t-1}^{k+1} - u_{t-1}^k) & \text{if} \quad t > 0 \end{cases}$$

Where k is the epoch number, $\nabla_t f(u^k)$ is the **gradient** of parameter u at **time** t and **epoch** k, $\mu(t) = sigmoid(mt)$ and m is a hyper-parameter.

LINKS

SAILab: https://sailab.diism.unisi.it/

Code: https://github.com/sailab-code/learning-sidarthe

Data: https://github.com/pcm-dpc/COVID-19

Speaker webpage: https://enricomeloni.github.io