Project
Parameter estimation of the SIRV model to study the spreading of COVID-19

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Contents

1 Background

It has been two years since the coronavirus pandemic has started. This global pandemic has its cause in the severe respiratory syndrome coronavirus 2 (SARS-Cov-2), a virus that was firstly identified in a Chinese city named Wuhan in December 2019. According to the coronavirus resource center of the Johns Hopkins University, the total coronavirus cases reported globally are 437.025.681, the total deaths are 5.957.572, and the total vaccine doses administered are 10.535.510.733 from the start of the pandemic to 01/03/2022. Thus, it is crucial to deeply understand the transmission dynamics of COVID-19 virus to make decisions in terms of vaccination strategies and manage future pandemics.

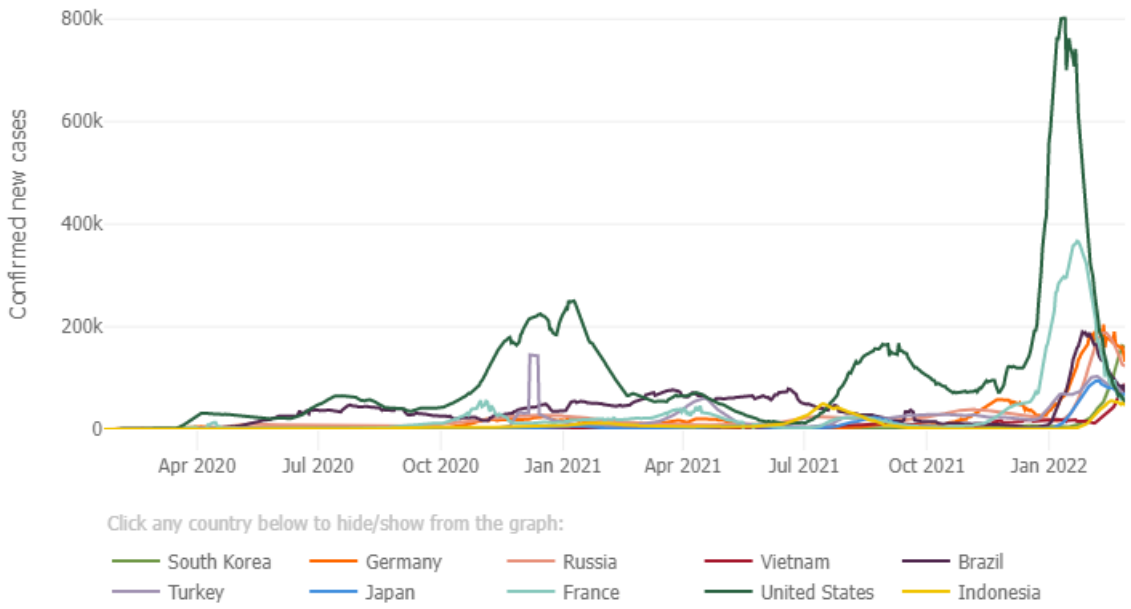


Figure 1: Daily confirmed new cases (7-day moving average).Outbreak evolution for the current most affected countries

1.1 Mathematical Modeling in Epidemiology

In the Dictionary of Epidemiology[17], epidemiology is defined as the study of the distribution and determinants of health-related states or events in specified populations and the application of this study to control health problems.Experiments are the tools for testing the validity of given hypotheses and obtain useful information. However in epidemiological studies the design of a natural experiment with control is very difficult to be carried out and sometimes it raises ethical questions. Another important point to mention is that even in the case of a well-imposed epidemiological experiment, the obtained data can be incomplete or can exhibit a chaotic behaviour. For this reason, it is essential to create mathematical models in epidemiology because they allow us to understand the transmission dynamics of a disease and suggest strategies to control the spreading.

The mathematical models in epidemiology can by divided into two main categories: Prevalence Models and Density models[18]. The Prevalence models are those that describe the number of human individuals that moving from one identical status to another. On the contrary, the Density models consider the number of parasites in a host and describe a mean parasite load. In this work we will focus on the prevalence compartmental models which are based on the idea of dividing the host population into a discrete number of small compartments. Each compartment is identical in a way that is characterized by an identical status with respect to the studied disease. One of the greatest contributions in the field of compartmental models for epidemiology was the mathematical model SIR introduced by Kermack and Mc Kendrick[3] in 1927.

The model consists of three compartments:

- S(t) is the susceptible compartment that includes susceptible individuals but not yet infected by the virus.
- I(t) is the infectious compartment that includes individuals who have been infected and are able to transmit the virus to susceptible individuals
- R(t) is the recovered compartment that counts for infectious individuals who either have recovered (developed immune response) or have died.

It is important to mention at this point that the total number of the host population is given by the expression of $N = S + I + R$. The nonlinear system of first-order ordinary differential equations proposed is the following:

$$\frac{dI}{dt} = \beta I \frac{S}{N} - \gamma I \tag{1}$$

$$\frac{dS}{dt} = -\beta I \frac{S}{N} \tag{2}$$

$$\frac{dR}{dt} = \gamma I \tag{3}$$

Parameters β and γ are positive parameters that govern the flow from one compartment to another. Parameter β represents the transmission rate and parameter γ represents the removal rate (so the mean infectious period is $1/\gamma$).One of the major assumptions of this model is that the disease lasts for a short period of time and due to that the total population remains constant. It is also assumed that the transmission rate β and the removal rate γ are constant with the time. Also, the equation for of dR/dt does not influence the dynamics of susceptible and infectious compartment. This indication shows that the removed individuals cannot affect the transmission of the disease. In the original SIR model it is hypothesized that all the individual consisting the host population are susceptible to a new disease (S(0) = N). This means that a newly infected individual is able to spread the disease to other people at the rate β*N during the expected infectious time period of $1/\gamma$. By considering that, this first infected individual is able to infect β*N*$1/\gamma$ individuals. The expression given by β*N*$1/\gamma$ is named basic reproduction number (R0) and it is a very essential number since it measures the transmission potential of a disease. More precisely, this number determines whether an epidemic can take place or not. It is important to keep in mind that R0 is always greater than 1. This can be explain by thinking that if an individual transmits a disease in a average which is less than one individual, the number of cases will reduce over time.

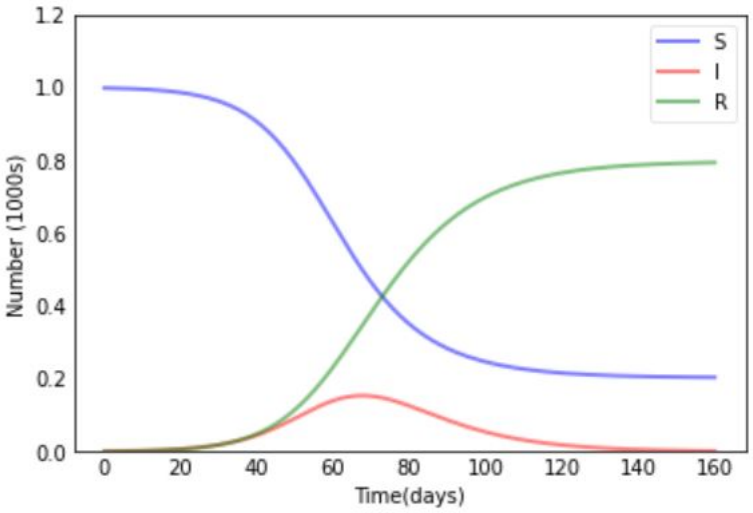


Figure 2: The original SIR model

1.2 Vaccination strategy: Concerns and challenges

Many scientists within the past two years have been used SIR model or modified SIR models to predict the transmission of COVID-19 in different countries [4] [5]. Due to the massive production of the vaccines in 2021, it is crucial to study the transmission dynamics of COVID-19 by considering the vaccination strategy and incorporating vaccination in the general SIR model.

Although several promising vaccines have now been developed there are still concerns and challenges related to vaccination.In order to respond to questions related to safety of vaccine and severity of side effects, Qutaiba et al. [1], performed a study about the post-vaccination signs and symptoms expressed by the participants vaccinated by Pfizer, AstraZeneca, and Sinopharm vaccines. Among 1736 randomized individuals participated in the study, 34.56% of them have showed side effects at the site of the injection including pain, redness, urticaria, and swelling.The percentage of participants who did not have any symptoms was equal to 40% for those who received Sinopharm vaccine, 25.71% for those received Pfizer vaccine, and 18.39% for those got vaccinated by AstraZeneca vaccine.

Another critical issue is the total duration of the acquired immunity due to infection or vaccination.In [2], Laith et al. reported that out of 133,266 confirmed COVID-19 cases, 0.18% were tested again 45 days after the first positive swab, and only 1 person was hospitalized with a relatively mild infection. Based on this data, the risk of reinfection is (0.01–0.02)% and the incidence rate of reinfection is (0.28–0.47) per 10,0 0 0 person-weeks, suggesting a strong protective immunity at least for a few months after primary infection. One of the main questions have arisen at the beginning of the pandemic was how the vaccination can reduce the transmission rate of the disease. In the scientific article of Makhoul et al. [6] a quantitative analysis of vaccination impact on COVID-19 is presented and it is reported that a vaccine with efficacy more than 70% could be efficient to control the spreading of the virus. However it is stated that an increase in the contact rate among vaccinated people can reduce the vaccination impact on the control of the pandemic. In the work made by Mukandavire et al. [7], it is emphasized that even a vaccine with efficacy greater than 70% should be related to high vaccination coverage rates around 94.44% in order to be able to reduce the transmission of COVID-19 in South Africa.

2 Problem statement and focus topic

In this research project we introduce a simple compartmental epidemiological model to study the transmission dynamics of COVID-19 considering vaccination. The main focus of our work was to estimate the parameters that are involved in our model to better understand how vaccination affects the virus spreading.

The model can be simply described by the following schematic diagram 3. The compartments that constitute the model are the susceptible, infectious, recovered and vaccinated compartment. In the vaccinated compartment we have included individuals got vaccinated by one shot of the vaccine. In the recovered compartment we have counted individuals fully immunized and individuals died after getting infected by the virus. In the current model, we have maintain the assumptions previously presented for the SIR model. The only difference is that in our model we consider the recovered population as "partially" immunized. This means that after a certain period of time those immunized individuals from the recovered population can become susceptible again. This behavior is shown by an arrow starting from the recovered population and directed to the susceptible compartment.

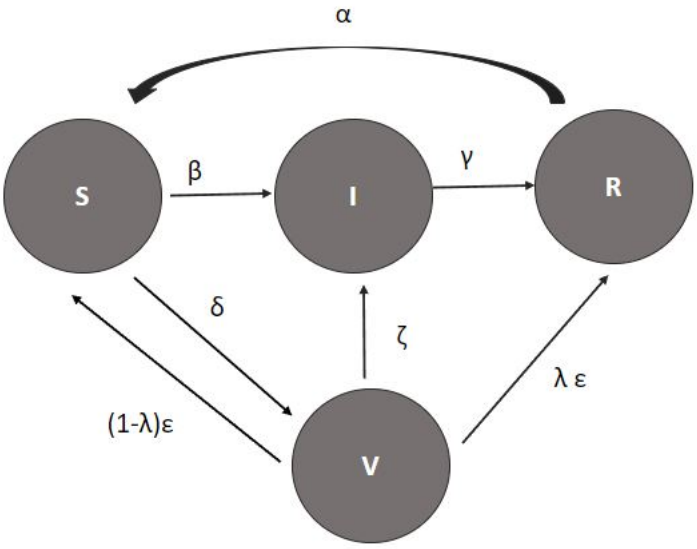


Figure 3: Illustration of the SIRV model compartments and their interdependencies denoted by incoming and outgoing arrows and relevant flow parameters.

The SIRV model obeys the following system of ordinary differential equations:

$$\frac{dI}{dt} = \beta I\frac{S}{N} + \zeta I\frac{V}{N} - \gamma I \tag{4}$$

$$\frac{dS}{dt} = (1-\lambda)\varepsilon V - \delta\frac{S}{N} - \beta I\frac{S}{N} + \alpha R \tag{5}$$

$$\frac{dV}{dt} = \delta\frac{S}{N} - \zeta I\frac{V}{N} - \varepsilon V \tag{6}$$

$$\frac{dR}{dt} = \gamma I + \lambda\varepsilon V - \alpha R \tag{7}$$

The parameters used for the description of the above model are the following:

- α indicates the rate at which recovered individuals lose their immunity and move to the susceptible compartment again.
- β describes the rate at which susceptible individuals become infected (transmission rate)
- γ retains the same meaning as in the SIR model, representing the mean removal rate.
- ζ is the rate at which individuals at the vaccinated compartment enters in contact with infectious individuals.
- δ is the first dose vaccination rate.
- $1/\epsilon$ is the mean amount of time an individual spends in the vaccinated compartment before reaching immunity and moving to the Removed compartment.
- λ is the vaccine efficacy.

3 Methods

3.1 Real Data

The data used in this work, is taken by the 'Our World in Data' GitHub repository. Also, the parameters used, are extracted by the scientific article of Mattia Angeli et al. [14]. With the use of the proposed parameters we generated the data for the S,I,V and R compartments. We name these data theoretical to avoid the confusion with the real ones. We also plotted the real data to visualize the behavior of each compartment.However, the most difficult part was to estimate the parameters either by using the real or the theoretical data. Thus, in the next paragraphs we describe the two different methodologies we followed trying to achieve a good parameter fitting.

3.2 Sparse identification of nonlinear dynamical systems (SINDY)

The first method we used in order to obtain the parameters, was the one proposed by Brunton et al.[19] called Sparse identification of nonlinear dynamical systems (SINDY). A brief explanation could be that SINDY is a method of taking some time series data and extracting them to interpret-able and generalizable dynamical systems models that can describe the behavior of those data. This means that from all the possible models that are able to describe the behavior of the given data, SINDY can give a minimalistic sparse model. SINDY allows us to obtain sparse dynamical systems that have a few degrees of freedom to describe the behavior of interest. This is in a way the advantage that SINDY algorithm has compared to others such as black box models. SINDY works for dynamical systems that have a form of either an ordinary differential equation, $\frac{d}{dt}\mathbf{x}(t) = \mathbf{f}(\mathbf{x}(t))$ or a partial differential equation, of the form $\frac{\partial u}{\partial t} = N(u)$. In this project we will describe the method for the ODEs since our epidemiological compartmental model is described by a system of ODEs.

The goal is to determine the right part of the ODE which is the function $f(x(t))$. To do so, we need to either numerically compute the derivative $\dot{\mathbf{x}}(t)$ by knowing $\mathbf{x}(t)$ through time or measure it. By doing this we can finally obtain two matrices for the x(t) data and for the derivative $\dot{\mathbf{x}}(t)$. Then it comes the construction of a Θ library which includes candidates of non linear functions that can represent the right-hand side of the ODE. To constrain the freedom of nonlinearities in Θ matrix, a sparse regression problem is constructed to determine the sparse vectors of coefficients $\Xi = \begin{bmatrix} \xi_1 & \xi_2 & \cdots & \xi_n \end{bmatrix}$. So the problem can be written as $\dot{\mathbf{X}} = \Theta(\mathbf{X})\Xi$.

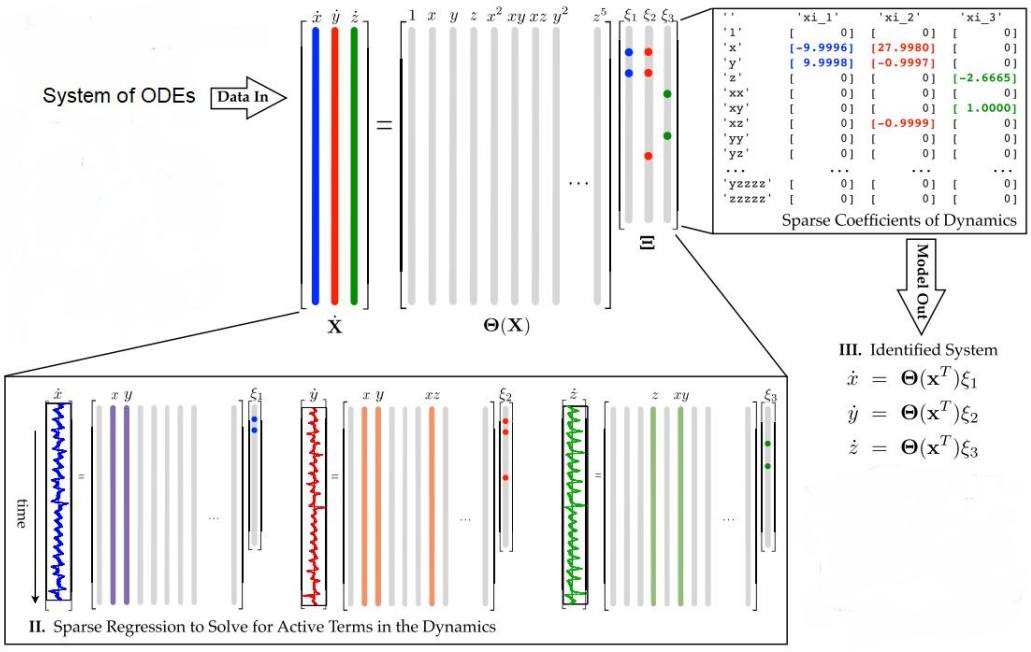


Figure 4: Sparse identification of nonlinear dynamical systems (SINDY) schematic description

3.3 Neural Networks Approach

Machine learning has been extensively used for disease modeling [8, 9, 10] and dynamical system forecasting [11, 12, 13].
In this study, a semi-supervised procedure was employed to determine the optimal set of initial conditions and parameters of the SIRV model 1, yielding solutions that best fit a given data-set.

- **Firstly, unsupervised learning procedure**
  Where a data-free (no data is used) Neural Network (NN) is trained to discover the solutions for an ODE.
  The NN takes as an input a time sequence t, a set of initial conditions Z0, and modeling parameters Θ.
  The input is then fed to a 6 layers fully connected network (FCN) to provide a prediction of the solution of the ODE.
  The quality of the learned solution (predictions of the network) is probed by the loss function L, that is then backpropagated to make the NN learns in an unsupervised way 5.

- **Secondly, Fitting a dataset**
  The trained NN is then used to develop a supervised pipeline for the estimation of the initial conditions and parameters, leading to solutions that fit given data.
  Starting from Z0 and a randomly selected parameters Θ in the bundles, a stochastic gradient descent optimizer then adjusts Z0 and Θ in order to minimize a loss function 7.
  This supervised learning 6 procedure will lead the NN to learn the best parameters/conditions of the SIRV model that fits given data.

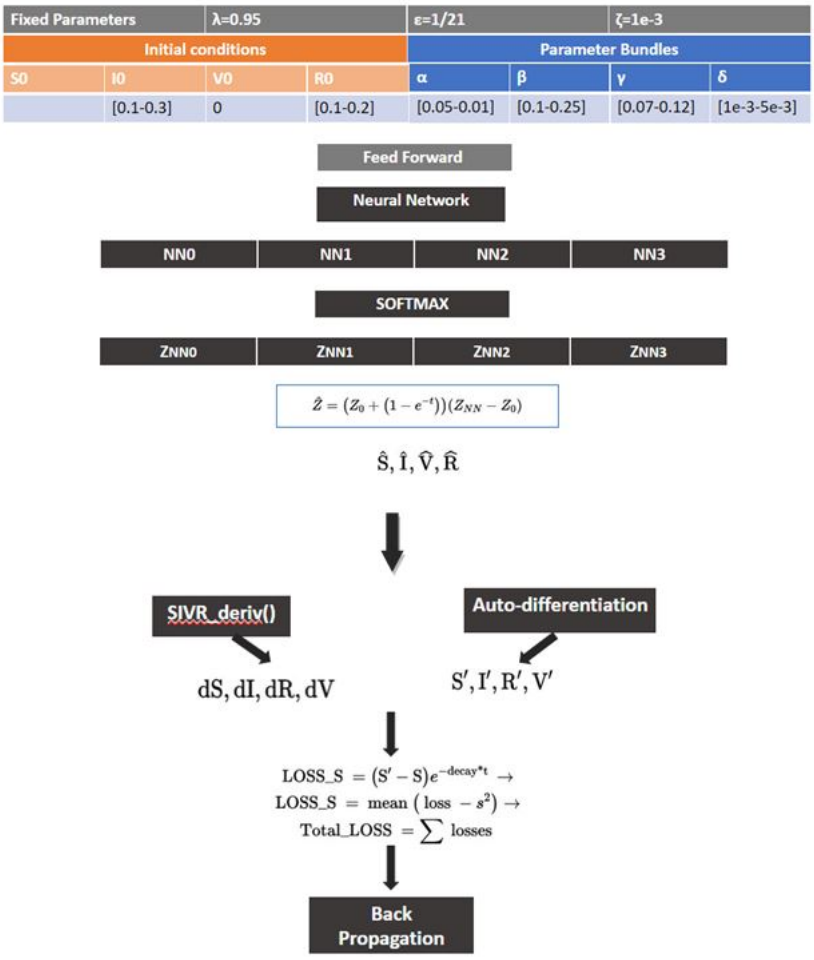


Figure 5: Unsupervised NN description

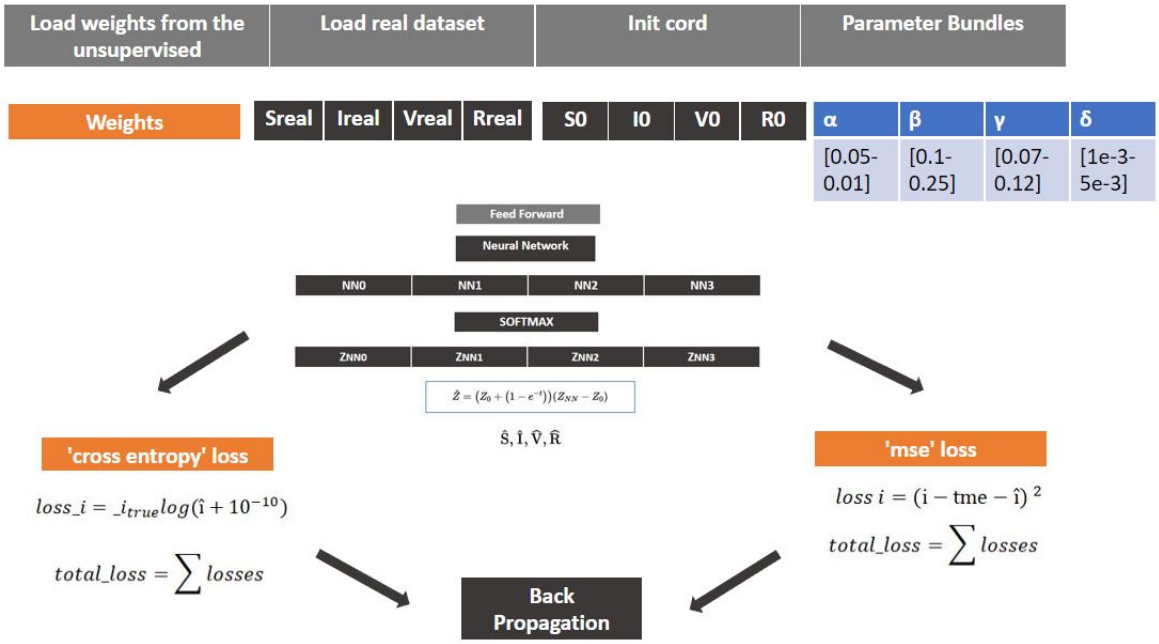


Figure 6: Supervised NN description

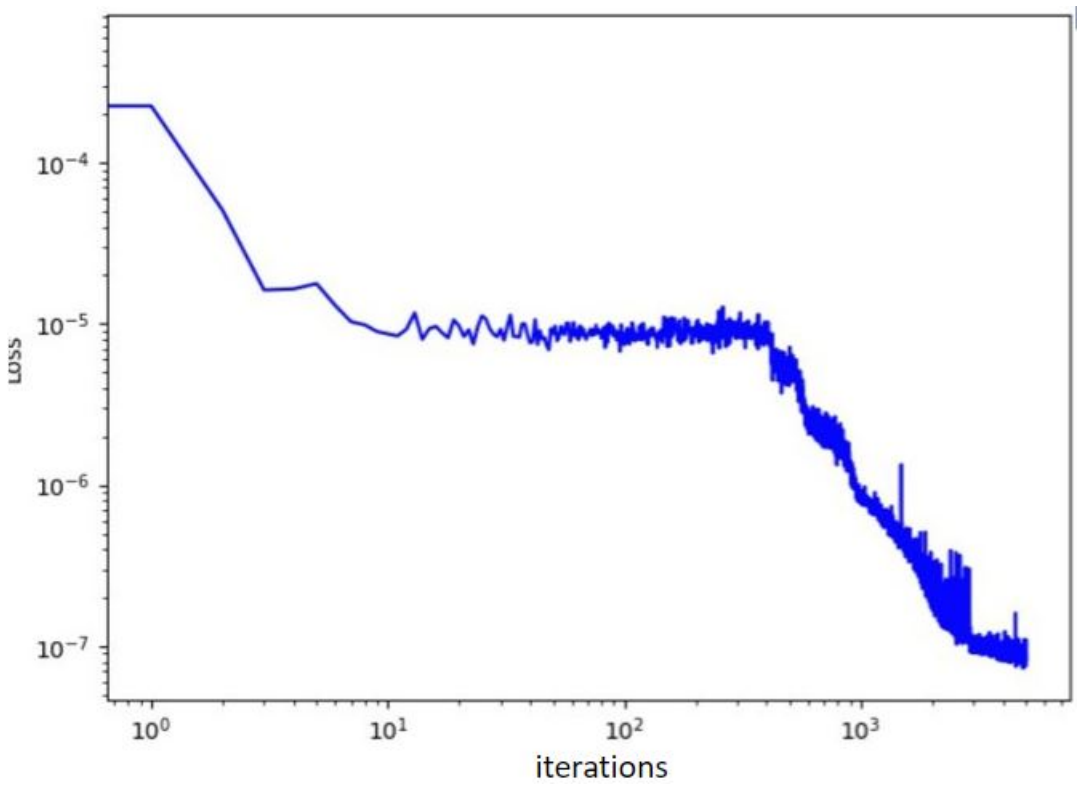


Figure 7: Loss Function

4 Results

We chose six different countries and we plotted the global real data of each to obtain the behavior of the susceptible, infected, vaccinated and recovered curves 8. The behavior of the data is quite similar for all the curves presented. We can mention in this point that the infected population as it is depicted in the curves of different countries, is almost constant and it has very low values compared to the rest populations. This can be possibly due to the existence of a vaccinated population. If for example take a look at the curves of the data of Switzerland, the infected population seems to be low when the vaccinated population increases and it starts to increase when the vaccinated population decrease. Then we generated our theoretical data by using the given coefficients which can be seen in 9b).

As we previously mentioned two different methodologies were used in order to estimate the parameters involved in our SIRV model. By using PySINDy package in Python, we obtained a very good fitting with the real data as it is shown in 11 in the case of France. By managing to design a custom made library we could obtain the right combinations of the variables S,I,V,R as they appear in the right-side of our ODE system. In figure 10a we provide the coefficient proposed in the literature as well as the coefficients we predicted by using SINDY 10b. In red boxes we indicate the coefficients that we aim to obtain using SINDY. We notice that the coefficients obtained by SINDY were different in scale, as well as new coefficients are involved.

Besides that, we performed a sensitivity analysis to better understand which parameters affect the most each compartment. In figure 11a 11b we present the histograms that show which parameters govern the most the dynamics of each population. The values of the parameters used, are the upper and lower values of the interval of each parameter as proposed in the literature [14]. For each parameter we evaluate the impact of its lower and upper bound by taking the maximum difference to a ground truth curve of what ODEi system produces using these parameters, then by calculating the ratio between the maximum value obtained using the upper and lower band per each parameter presented, we could have an estimate of the sensitivity to the parameter for each population (S,I,V,R).
From the histograms we can observe that all the populations are sensitive to the changes in β value in the same way, this is because the transmission rate affects the infected compartment which has an impact on all the compartments involved. Also the parameter α seems to be important both for the susceptible and infected compartment since it is the rate at which a vaccinated by 2 shots individual moves from the recovered to the susceptible compartment. Lastly, ζ and γ parameters seem to affect more the vaccinated and the recovered population. This can be explained by the fact that those two coefficients link the vaccinated to the infected compartment as well as the infected to the recovered compartment relatively.

In figure 12 we have summarized the major results obtained using our Neural Network after 10k iterations of training. The real data are represented with a dashed line and the neural network fit with a solid line. As we can see initially the fitting of the neural network was not good enough. If we focus for example in the blue curve representing the susceptible population we can see that the fitting curve starts with very high values. To fix this we adjusted the parametric function [1] below:

$$\hat{\mathcal{Z}} = \mathcal{V}_0 + (1 - e^{-t})\,(\mathcal{V}_{NN} - \mathcal{V}_0)$$

where the function $f(t) = (1 - e^{-t})$ is a smooth, bounded function, with $f(0) = 0$, as well as f(t) rapidly tends to 1. This imposes a control on the amplitude of the output that we get from the NN, which prevents the predicted solution from exploding.

An interesting idea that we wanted to experiment was to find out whether the coefficients obtained by the Neural Network approach when used in the ODEs can capture the behavior of the real data. As it is depicted in the figure 13, the ODE curve which is represented with a dashed line, is not giving a desirable fitting.

There are many possible sources that can explain this behavior:

- A first explanation could be that the model we have formed need to be modified by taking into account more interactions between compartments in order to better describe the real data.
  For example we have not considered the scenario of including an asymptomatic compartment. By introducing this extra compartment we can experiment the interaction between the asymptomatic compartment and the vaccinated compartment. Asymptomatic individuals as they do not express

[1] In order that the learned solutions by the network $\mathcal{V}_{NN}$ to satisfy the initial conditions as well as to significantly improve the predictability of the NN solver, this form of the parametric function is considered [22].

symptoms and they are not detected by any COVID-19 diagnostic test, can take the first shot of the vaccine without knowing that have already formed antibodies against the virus.

- The second explanation could be related to the way the NN predicts the solution by minimizing a cost function given some initial conditions and parameters bundles in its input. This involves complex interactions between the inputs, and therefore by using the parameters predicted by the network on the ODE system we have introduced 4, may not be able to obtain a good fitting. The main reason is that the network uses all the possible interactions between the terms which is a way much more complex compared to the simple interactions proposed through our equations.

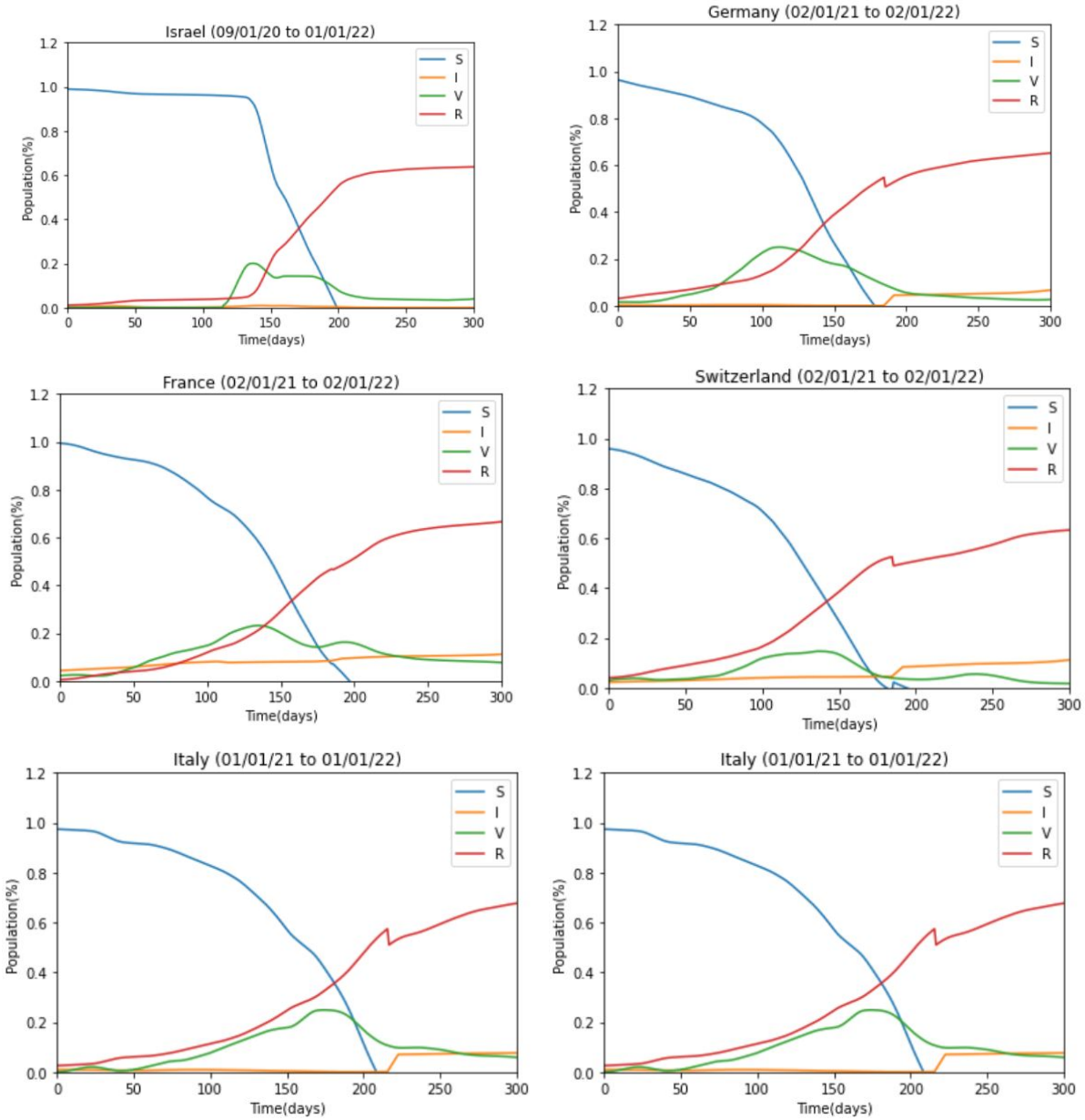
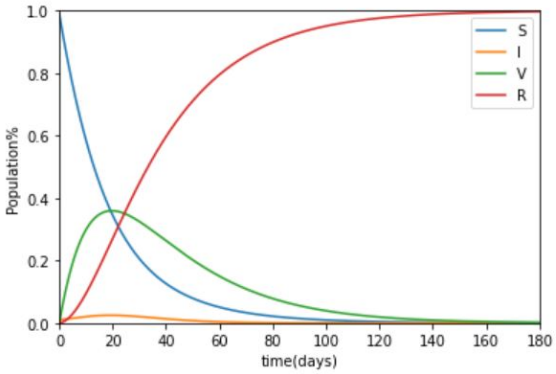
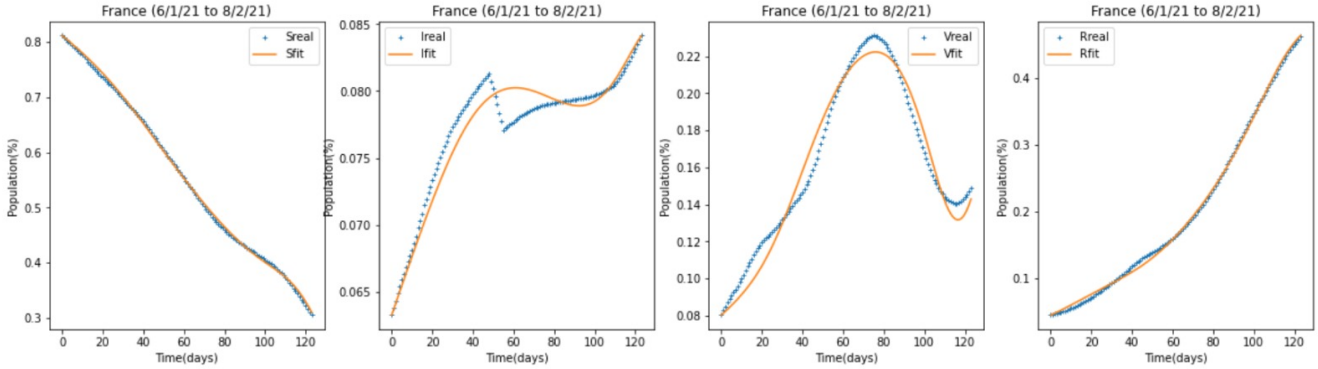


Figure 8: Plots of real global data for different countries



(a) Theoretical Data



(b) Fitting Real Data of France

Figure 9: (a) Generating data by using the coefficients provided in the literature.(b) Fitting real data with SINDY

The coeffecient found in the literature

	S	I	V	R	S*I	I*V
S	-0.005	0.00	0.002381	0.005556	-0.2	0.000
I	0.000	-0.08	0.000000	0.000000	0.2	0.001
V	0.005	0.00	-0.047619	0.000000	0.0	-0.001
R	0.000	0.08	0.045238	-0.005556	0.0	0.000

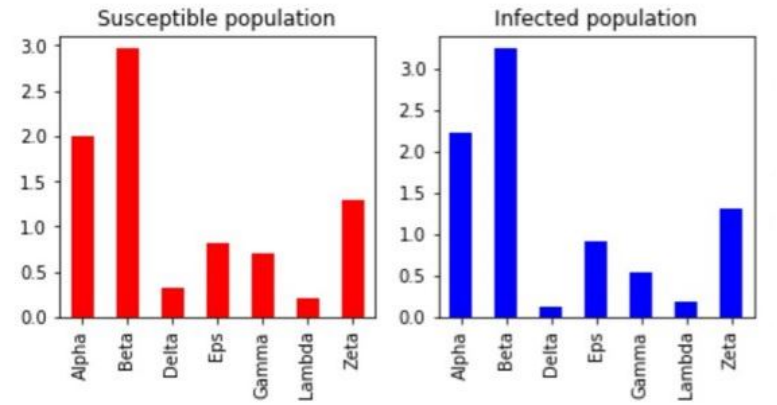
(a) Coefficients found in the literature

The coeffecient found by SINDy

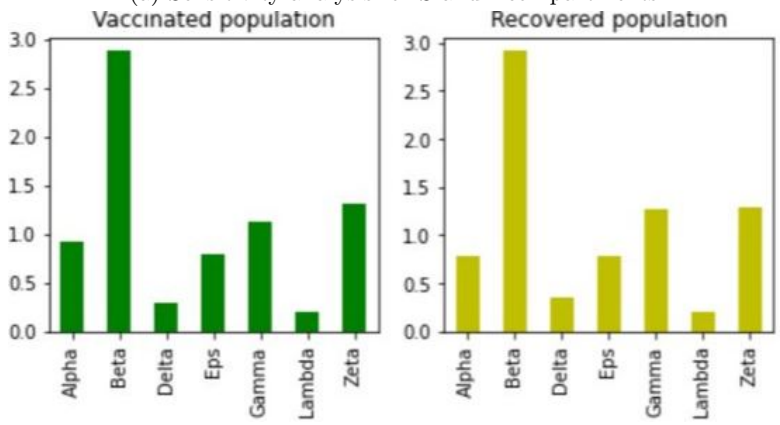
	S	I	V	R	S*I	I*V
S	0.0	-2.731069	-0.267435	0.239287	2.903503	6.186918
I	0.0	0.008742	0.000000	0.000000	0.002628	-0.048617
V	0.0	5.039310	0.484463	-0.454713	-5.417534	-11.442631
R	0.0	-2.536032	-0.263914	0.234519	2.754966	6.117804

(b) Coefficients predicted by SINDY

Figure 10: Tables shown the comparison between the coefficients found in the literature and the predicted ones by SINDY



(a) Sensitivity analysis for S and I compartments



(b) Sensitivity analysis for V and R compartments

Figure 11: Sensitivity analysis to determine which parameters affect the most each compartment of the model

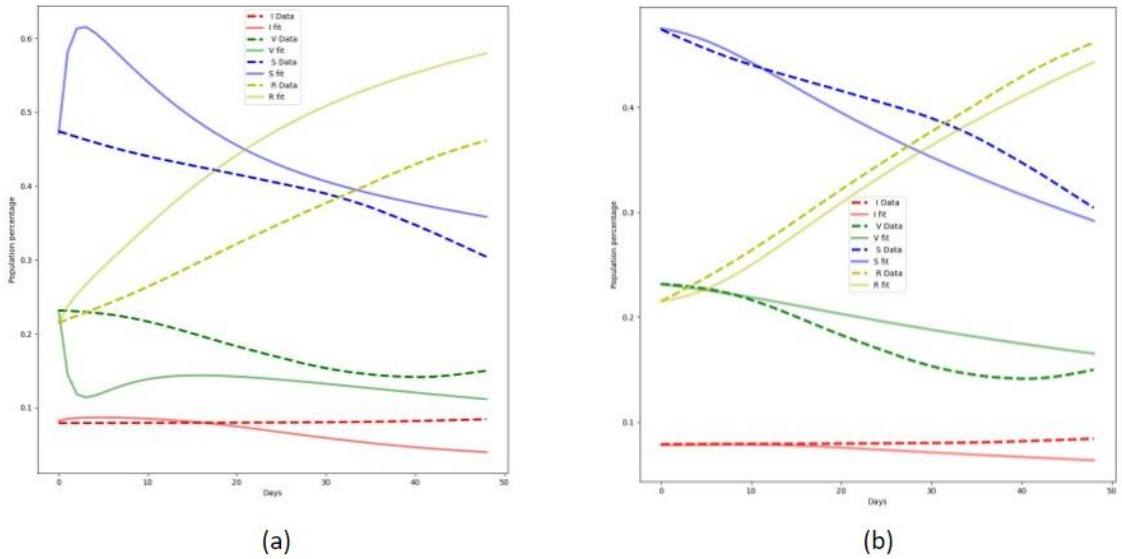
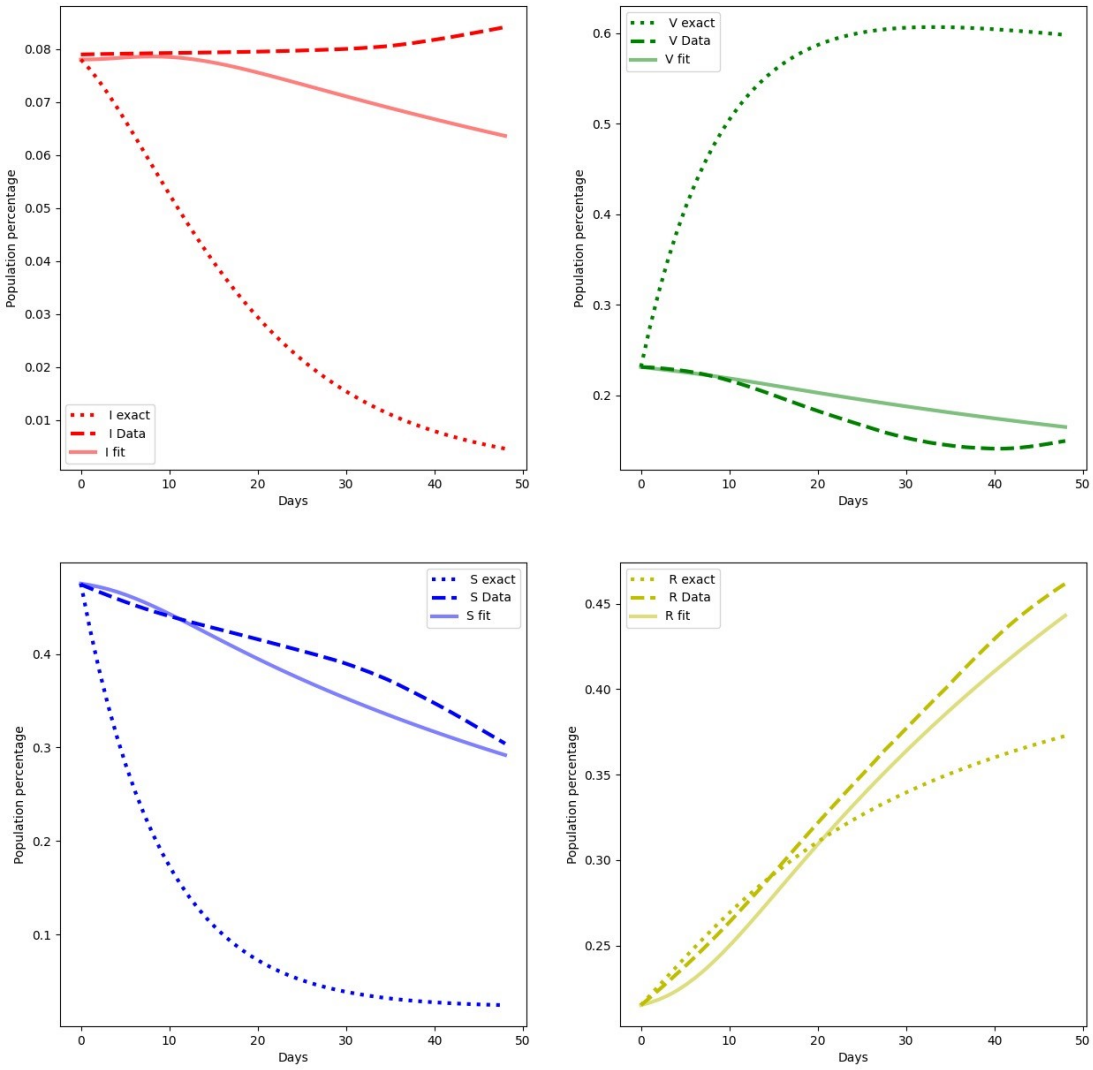


Figure 12: Fitting of real data by using our neural network.(a) An undesired fitting was firstly obtained by NN. (b) NN provides a good fitting after changing the weight of the z function



s_0=4.80e-01, i_0=8.00e-02, v_0=2.30e-01, r_0=0.22, Beta_1=0.10, γ=0.07, δ=1.00e-01

Figure 13: Comparison between Neural Network Fitting and ODE fitting

5 Discussion

5.1 Future work

In the description of our model we assumed that the entire population remains constant. This assumption was made based on the idea that the disease lasts for a small period of time which is not exactly the case with COVID-19. Additionally, in our SIRV model we do not consider individuals that are infected without expressing symptoms. This could also give us a better understanding of the transmission of the disease since it has been reported that asymptomatic individuals play a key role in the spreading of COVID-19 [20].

Apart from the limitations originating from the assumption made for the description of our SIRV model, we also have to deal with the limitations linked to the methodologies used to resolve the system of ODEs and fit the model to the real data. In terms of the SINDY method, there are many limitations that can affect the performance of this algorithm and so the results that we receive. Among them the most important are: the length of training data, the steps to estimate the predicted error, the design of the chosen library, the initial conditions, the chosen threshold and the calculation of the derivatives [21]. Considering that we have access to a big amount of global data and the length of the S,I,V,R data is equal, the major limitation for the neural network technique is the high computational cost. This means that a complex network that contains a big size of data takes a lot of time to be trained. Finally, the time length as well as the possible fluctuations that can appear in the real data cannot be captured by the neural network. Thus, this is an important limitation to take into account.

5.2 Limitations of current work

Despite the results we have presented before, there are still many important avenues for future work in this model. A future plan would be to enhance the methods described before in order to obtain an optimal set of parameters. More precisely in order to improve the SINDY method and obtain both a good fitting and a desirable set of equations we have two possible ways. First of all, we can impose some constraints on the coefficients by imposing an upper bound for each coefficient. Secondly, we can constrain the derivatives such that they sum up to zero. By fixing this two issues we think that SINDY will be a powerful way to experiment/test new hypothesis on the interaction between the different compartment, thus finding the best equations that governs the behavior of the data. Lastly, we would like to investigate the reason why parameters obtained by the Neural network approach when used with the ODE method do not give a good description of the real data.

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[23] The link to the repository that contains the code we used in this project: https://github.com/slimaneaymen/Parameter-estimation-of-the-SIRV-model-to-study-the-spreading-of-COVID-19

List of Figures