Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Study of the COVID-19 pandemic trending behavior in Israeli cities

Henrique Mohallem Paiva*1  
Rubens Junqueira Magalhães Afonso**  
Davi Gonçalves Sanches *  
Frederico José Ribeiro Pelogia*

* Universidade Federal de São Paulo (UNIFESP)  
Rua Talim, 330, São José dos Campos, SP, Brazil, 12231-280 (e-mails: hmpaiva@unifesp.br, davi.sanches@unifesp.br, fpelogia@unifesp.br)  
** Instituto Tecnológico de Aeronáutica (ITA)  
Praça Marechal Eduardo Gomes, 50, São José dos Campos, SP, Brazil, 12228-900 (e-mail: rubensjm@ita.br)

Abstract: This paper studies the trending behavior of the COVID-19 dynamics in Israeli cities. The model employed is used to describe, for each city, the accumulated number of cases, the number of cases per day, and the predicted final number of cases. The innovative analysis adopted here is based on the daily evolution of the predicted final number of infections, estimated with data available until a given date. The results discussed here are illustrative for six cities in Israel, including Jerusalem and Tel Aviv. They show that the model employed fits well with the observed data and is able to suitably describe the COVID-19 dynamics in a country strongly impacted by the disease that holds one of the most successful vaccination programs in the world.

Keywords: COVID-19, SARS-CoV-2, epidemiology, mathematical models, trend analysis, Israel

1. INTRODUCTION

In December 2019, a new coronavirus, later called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in the Chinese city of Wuhan, in the province of Hubei. Although initially associated with zoonotic transmission on a seafood market in Wuhan, the virus was quickly spread to other regions, mainly through human-to-human transmission (Li et al., 2020).

The disease caused by the SARS-CoV-2 virus is called COVID-19. Besides common pulmonary symptoms such as cough and dyspnea (Wang et al., 2020), the disease can include fever, distortion of the senses of taste (dysgeusia), and smell (anosmia) (Vaira et al., 2020) and also affect systems including the gastrointestinal (Devaux et al., 2021), musculoskeletal and even neurological (Ellul et al., 2020). Carfi et al. (2020) show that some of these symptoms may persist after the acute cases and Yuki et al. (2020) show that adults and elders are more susceptible than children.

In early 2020, the virus began spreading to other countries. In March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic (Cucinotta and Vanelli, 2020). With the number of cases and deaths rising daily, researchers worldwide tried to understand and model the virus’ transmission dynamics, anticipating that its highly contagious nature could cause overcrowding of the health system (Wu et al., 2020).

The main form of prevention from the disease is the control of the transmission of the virus, achieved through social distancing, hand washing, surface sanitizing, and the use of facial masks and other kinds of personal protective equipment (PPE) (Pradhan et al., 2020). While some countries started taking actions, such as quarantine decrees, soon to prevent the spread of the virus, others were reluctant to do so, fearing the negative impact on the economy.

After the SARS-CoV-2 genetic sequence was published in January 2020, multiple research teams, from both private and public institutions, started studying ways to produce a safe and effective vaccine as fast as possible, given that it traditionally is a long and expensive process, with multiple testing phases. Thus, new vaccine development paradigms and cutting-edge technology platforms were used to achieve faster results (Le et al., 2020; Lurie et al., 2020).

As soon as some of the vaccines had their testing phases finished, the affected countries started approving their usage and buying doses in order to start elaborating the vaccination program and the distribution to the population. Just as happened with the preventive measures, each country is taking vaccination at its own pace, according to its position in the queue for acquiring doses and to internal distribution logistics (Mills and Salisbury, 2021).

In Israel, four epidemiological waves have occurred, with the last two being significantly larger than the first two. The first wave peaked in late March 2020, followed by some months of a low and controlled number of cases and deaths. At the end of June 2020, the numbers started to rise again and the country faced two sequential peaks in July and September of 2020. The last wave started with an increase
in the number of infections in December 2020, and peaked at the end of January 2021. Since then, the numbers are decreasing, as the vaccination program, which started in December 2020, goes on at a rapid pace (Wahltinez et al., 2020; Rosen et al., 2021).

The study of the transmission dynamics of an epidemic through mathematical and computational models is crucial for the management of resources in moments of crisis. In most cases, this kind of modeling uses data from the past months to tune the parameters, testing their performance on describing the behavior of a sample of the most recent data. This way, it is possible to forecast the trend in the following weeks.

Predictions from reliable models can indicate the status of the pandemic in some regions, such as sensing a new epidemiological wave or a stabilization on the number of cases. Thus, this information can help local governments in taking action and making decisions, such as quarantine decrees, and discussing the vaccination agenda.

Since the beginning of the COVID-19 pandemic, several modeling approaches have been proposed. Some, such as Cooper et al. (2020), Hou et al. (2020) and Paiva et al. (2020), used extended versions of classical epidemiological models, such as the susceptible-infected-removed (SIR). Others, among which Ardabili et al. (2020) and Punn et al. (2020), used machine learning techniques to find transmission patterns. Many other approaches were also taken, and many are still in development.

The approach introduced in (Paiva et al., 2021) allows running a trend analysis and predicting the final number of cases using mathematical functions and numerical optimization algorithms. The main innovation of such an approach lies in the study of how the predictions evolve with time. The present paper runs similar studies for the country of Israel, which has been chosen because it is one of the world most successful countries in the application of vaccines.

2. MATERIALS AND METHODS

COVID-19 contagion manifests waves, each with an acceleration and a deceleration phase. A mathematical model to represent the number of infected individuals $C(t)$ at time $t$ accurately must involve a dynamic that allows such a behavior. One such model is the Richards growth model (Smirnova and Chowell, 2017; Richards, 1959; Paiva et al., 2021), involving the following Ordinary Differential Equation (ODE)

$$\frac{dC}{dt}(t) = \frac{1}{\delta \nu} C(t) \left\{ 1 - \left[ \frac{C(t)}{A} \right]^\nu \right\}$$

(1)

The so-called intrinsic growth rate given by $(\delta \nu)^{-1}$ can be seen in (1) to be a scaling factor of the growth of $C$ with time. It can be seen from (1) that the growth rate converges to zero as $C$ approaches $A$. In fact, $A$ can be interpreted as the final number of infections.

Further examination of (1) to understand the effect of $\nu$ is on order. For the sake of illustration, let us assume that $\nu = 1$, then the growth rate is a parabola in $C$, with a peak at $A/2$. Thus, the transition from acceleration to deceleration happens at half the final amount of infections.

![Fig. 1. Illustration of the results obtained during the procedure used to determine the onset of new epidemiological waves.](image)

To find the general solution, one can differentiate (1) with respect to $C$ and search for the changes in sign to obtain:

$$1 - (\nu + 1) \left[ \frac{C(t_p)}{A} \right]^{\nu} = 0 \implies C(t_p) = A \left( \frac{1}{1 + \nu} \right)^{\frac{1}{\nu}}$$

(2)

at some instant $t_p$. From the general formula of the value of $C(t_p)$ in (2), one can see that the higher the value of $\nu$, the more infections happen before the transition to deceleration.

Given an observed $t_p$, (1)-(2) yield a boundary value problem that has a closed-form solution given by (Smirnova and Chowell, 2017; Richards, 1959; Paiva et al., 2021)

$$C(t) = \frac{A}{1 + \nu e^{-\frac{(t-t_p)}{\delta}} \nu^{\frac{1}{\nu}}}$$

(3)

under the constraints $A, t_p, \nu, \delta > 0$. Although the discussion carried herein assumes that the variables are real-valued, which is common in epidemiological models, one must stress that both $A$ and $C$ represent integer quantities, whereas in our case $t$ is given in days and is also an integer, as the infections are not reported continuously in real-time, but rather compiled in daily reports.

The daily rate of infections can be determined explicitly by differentiating (3) with respect to $t$, which yields the function

$$\frac{dC}{dt}(t) = \frac{A \delta}{\nu} \frac{e^{-\frac{(t-t_p)}{\delta}}}{\left[ 1 + \nu e^{-\frac{(t-t_p)}{\delta}} \nu^{\frac{1}{\nu}} \right]^{\frac{1}{\nu}+1}}$$

(4)

with its symmetry controlled by the value of $\nu$.

However, as mentioned beforehand, COVID-19 presented more than one wave, i.e., more than one combination
of acceleration and deceleration. We cope with this by considering the sum of $N_s$ sigmoids, each with its own set of parameters $A_j, t_{p,j}, \nu_j, \delta_j, j = 1, \ldots, N_s$. The final number of infections in this case can be determined by
\[
A = \sum_{j=1}^{N_s} A_j
\]  
This final number of infections is a parameter of interest for policy makers, as it enables one to estimate how many more infections are to come, and then adequately prepare with availability of medicine, hospital beds and personnel. Herein, the predicted value of $A$ with information up until time $t$ is represented by $\hat{A}(t)$, where the dependence in time results from the possible changes in the estimate as more data become available.

In case $\hat{A}(t)$ presents only slight variations in an interval $t_1 \leq t \leq t_2$, then it may be considered that the prediction is stable and the disease spread is under control. On the other hand, a sudden or a continuing growth in $\hat{A}(t)$ may indicate the onset of a new wave or the inefficiency of the measures under application.

2.1 Determination of new epidemiological waves

Each sigmoid describes an acceleration and a deceleration phase. A new epidemiological wave is associated with a new acceleration behavior. Hence, the onset of a new wave can be detected by observing when the second derivative of the number of accumulated infections with respect to time changes from negative to positive values.

The number of accumulated infections is normalized by its maximum value and its derivative is calculated numerically, using the forward Euler approximation. It is known that numeric derivatives are extremely prone to noise effects. In order to overcome this sensitivity, a filtering process is adopted to the first derivative, involving the following operations in series:

i) a moving-average filter with a 21-day window;

ii) a second-order lowpass filter with damping coefficient of 0.7 and period of 14 days;

iii) a median filter with a 14-day window;

The filtered first derivative is then differentiated, once more with the forward Euler approximation, obtaining an estimate of the second derivative. Also to overcome sensitivity to noise, a threshold of $\pm 3 \times 10^{-5}$ normalized cases/day$^2$ is adopted. A transition from a deceleration to an acceleration phase is detected when this function changes from a value smaller than the lower threshold to a value greater than the upper threshold (representing that the sign of the second derivative was negative and became positive).

This filtering process is very aggressive. On the other hand, it causes no loss in the representation of the system dynamics, for it is used exclusively to determine the points of transition to new waves.

The procedure to determine the occurrences of new waves is illustrated in Figure 1: Fig. 1-(a) indicates the number of accumulated cases; Fig. 1-(b) represents the raw first derivative, calculated from (a) using the Euler approximation, as well as the filtered signal; finally, Fig. 1-(c) represents the second derivative, calculated from the filtered signal in (b). In this particular case, there are two transition points indicating new epidemiological waves; these two points are highlighted in the figure and were used as a reference to draw the vertical lines in Figs. 1-(a), 1-(b), and 1-(c)

2.2 Parameter estimation

Estimating $A_j, t_{p,j}, \nu_j, \delta_j, j = 1, \ldots, N_s$ from real-world reports can be done by constrained optimization. In view
of the constraints and the nonlinearity of the expression in (3) with respect to the parameters, nonlinear numerical algorithms have to be used to find an optimal set of parameters that minimize the residues between observed and fitted data. In the present paper, the Sequential Quadratic Programming (SQP) method is used (Gill and Wong, 2012), which solves nonlinear programming problems by iterative linearization and solution of a Quadratic Programming problem.

2.3 Data source

This paper used data updated until March 21st, 2020, and downloaded from (Wahltinez et al., 2020).

3. RESULTS AND DISCUSSION

Figure 2 presents the results of this study for the city of Jerusalem: (a) shows the number of accumulated cases, where it is possible to see how the model output matched the observed data until March 2021, and what is expected for the following months of the year; (b) shows the number of cases per day; (c) shows the predicted final number of cases in the city. From the results of Figure 2, it is possible to say that the last wave of COVID-19 in Jerusalem in early January 2021 was indeed much greater than its predecessor waves, but the results for the following months confirmed a trend of decrease in the number of new cases in the city, which can be associated with the success of the national vaccination program of the country.

The same analysis was applied for five other important cities in Israel, each of them being represented in the following Figures. For each Figure: subfigure (a) shows the number of accumulated cases; (b) shows the number of cases per day, and (c) shows the final number of cases in the city.

Figure 3 presents the results for the city of Tel Aviv, the country’s capital. In Tel Aviv, the last wave did not have a much higher peak than its predecessor wave, but it lasted longer, as shown in Figure 3(b). The trend analysis used by this study also showed a stabilization of the predicted final number of cases since February (Figure 3(c)), indicating that the vaccination of the population is finally controlling the epidemic and preventing new outbreaks.

Figure 4 presents the results for the city of Petah Tikva, which showed the same pattern as for the city of Jerusalem: The number of new cases was much greater during the December-January wave, but a decrease was observed since February 2021, after the intensification of the national vaccination program. The model output also matched well with the observed data for the city of Petah Tikva.

Figures 5, 6, and 7 present the results for Beersheba, Haifa, and Rishon LeZion cities, respectively. For all of them, the model output matched well with the observed data (Figures 5(a), 6(a), and 7(a)), predicting a stabilization of the curve of the accumulated cases since March 2021. The last wave of COVID-19 cases lasted longer in those three different cities, but in Beersheba, its peak was smaller and its decrease was slower, which led to a longer wave of infections in the city, according to the trend analysis here discussed. The model still shows stabilization of the epidemic, though.

The results show that the model can represent with high accuracy the data with the accumulated cases and also the general trend of the data with the daily number of cases.

The vaccination program in Israel started during the acceleration phase of the most recent wave in the country. Thus, the next three months were marked by a race between the wave, which peaked in late January, and the
mass vaccination, which progressed rapidly. As a result, as shown in the figures, in all of the studied cities the last wave was wider than its predecessor, with a less steep climb to the peak of cases and also a slower deceleration. Less sudden peaks are more manageable for the health system to deal with, avoiding problems like hospital overcrowding and, therefore, reducing the number of deaths.

One of the main contributions of the trend analysis here presented is the result of the predicted cases of COVID-19 for each city, showed in Figures 2-7(c). Since the asymmetric sigmoid fits well the data for all six cities, it is possible to say that the convergence to stabilization of cases starting in February 2021 is accurate and indicates that the pandemic is near its end in those cities after the fourth wave of infections in Israel. During the peak of new cases in January 2021, the prediction of the final number of cases varied in all cities, but a stabilizing trend can be observed after the initiation of the vaccination campaign in the country along with the social restraint measures adopted in February.

Another interesting result from Figures 2-7(c) is the stabilization of their curves between two peaks of COVID-19 infections, meaning that until a new epidemiological wave is identified, the model predicts a final number of cases based on the stable sanitary scenario in the region. In fact, the plot with the predicted final number of cases remains almost constant when a wave is decelerating and that once the numbers start to rise again, a sudden increase in the prediction is manifested, alerting this behavior. This can be seen in the figures, where, some weeks before the peak of the last wave, the prediction of the final number of cases grows abruptly for most of the cities.

New variants or big changes in social behavior (gatherings during important holidays, for example) can cause a strong disturbance in the system, making the model recalculate the final prediction of cases in a city. The stabilization of final cases in Israel after the world’s fastest vaccination program can indicate how successful vaccines can be in the fight against COVID-19, leading countries closer to the end of the pandemic.

From the results above, it is possible to observe that the trend analysis here discussed presents itself as a good model for the forecasting of new cases since it has matched well with the observed data for all the six different cities in Israel. The model confirmed the pattern of the last wave in the country, which represented the worst sanitary scenario during the pandemic so far, and also showed how the national vaccination program for COVID-19, one of the most successful programs in the world, contributed to contain new outbreaks and to control the pandemic in all regions of the country since February 2021. These results show how vaccines can represent a significant change in the fight against COVID-19, reducing new infections, and consequently reducing also the hospitalizations and deaths.

4. CONCLUSION

This work presented an application of a mathematical model based on a sum of asymmetric sigmoids for different cities in Israel, which provided useful information about the COVID-19 pandemic in the country, especially after the most recent epidemiological wave in January 2021.

The results obtained from the model fitted well with the observed data for all six cities, showing how accurate the methodology here described can be when forecasting the trend of the COVID-19 pandemic in a certain region. The accumulated number of cases and the number of cases per day are two important results from the method, which showed how strong the fourth wave of infections in Israel was and also how the pandemic decelerated after February.
2021 for most cities, when social restraint measures and the national vaccination program took place.

The model adopted in this paper does not rely on any assumption regarding the localities for which it is adjusted. In fact, the model parameters are a function only of the data given in terms of daily cases. In turn, this renders the approach directly adaptable to any region in the world. Moreover, the choice of Israel for the present paper indicates that the presence of a change in the scenario with the introduction of mass vaccination did not compromise the ability to fit the data and perform accurate predictions. Consequently, applying this methodology to other localities is both possible and also of interest to the research community.

The most important contribution of this work is the prediction of the final number of cases, which can effectively tell when a region is stabilizing the pandemic and reaching its end. For all the cities studied in Israel, convergence to stabilization of cases was observed after the vaccination program in February took place.

The predictions run for Israel in this work are important to show how effective a mass vaccination program can be when fighting a pandemic such as the COVID-19 outbreak since the country leads the world’s vaccination race to protect people from the disease. The results obtained in this work were positive since they illustrate how successful the Israeli vaccination program was, pointing out a possible solution for the global sanitary crisis.

REFERENCES

Ardabili, S.F., Mosavi, A., Ghamisi, P., Ferdinand, F., Varkonyi-Koczy, A.R., Reuter, U., Rabczuk, T., and Atkinson, P.M. (2020). COVID-19 outbreak prediction with machine learning. *Algorithms*, 13(10), 249.

Carfi, A., Bernabei, R., and Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. *JAMA*, 324(6), 603–605.

Cooper, I., Mondal, A., and Antonopoulos, C.G. (2020). A SIR model assumption for the spread of COVID-19 in different communities. *Chaos, Solitons and Fractals*, 139, 110057.

Cucinotta, D. and Vanelli, M. (2020). WHO declares COVID-19 a pandemic. *Acta Bio Medica Atenei Parmensis*, 91(1), 157–160.

Devaux, C.A., Lagier, J.C., and Raoult, D. (2021). New insights into the physiopathology of COVID-19: SARS-CoV-2-associated gastrointestinal illness. *Frontiers in Medicine*, 8, 99.

Ellul, M.A., Benjamim, L., Singh, B., Lant, S., Michael, B.D., Easton, A., Kneen, R., Defres, S., Sejvar, J., and Solomon, T. (2020). Neurological associations of COVID-19. *The Lancet Neurology*, 19(9), 767–783.

Gill, P.E. and Wong, E. (2012). Sequential quadratic programming methods. In *Mixed integer nonlinear programming*, 147–224. Springer.

Hou, C., Chen, J., Zhou, Y., Hua, L., Yuan, J., He, S., Guo, Y., Zhang, S., Jia, Q., Zhao, C., et al. (2020). The effectiveness of quarantine of Wuhan city against the Coronavirus Disease 2019 (COVID-19): A well-mixed SEIR model analysis. *Journal of medical virology*, 92(7), 841–848.

Le, T.T., Andreadakis, Z., Kumar, A., Román, R.G., Tollefsen, S., Saville, M., Mayhew, S., et al. (2020). The COVID-19 vaccine development landscape. *Nat Rev Drug Discov*, 19(5), 305–306.

Li, Q., Guan, X., Wu, P., Wang, X., and Zhou, Lei, e.a. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England Journal of Medicine*, 382(13), 1199–1207.

Lurie, N., Saville, M., Hatchett, R., and Halton, J. (2020). Developing COVID-19 vaccines at pandemic speed. *New England Journal of Medicine*, 382(21), 1969–1973.

Mills, M.C. and Salisbury, D. (2021). The challenges of distributing COVID-19 vaccinations. *EClinicalMedicine*, 31. doi:10.1016/j.eclinm.2020.100674.

Paiva, H.M., Afonso, R.J.M., Alvarenga, F.M.S.L., and Velasquez, E. (2021). A computational tool for trend analysis and forecast of the COVID-19 pandemic. *Applied Soft Computing*, 107289.

Paiva, H.M., Afonso, R.J.M., Oliveira, I.L., and Garcia, G.F. (2020). A data-driven model to describe and forecast the dynamics of COVID-19 transmission. *PloS One*, 15(7), e0236386.

Pradhan, D., Biswasroy, P., Kumar Naik, P., Ghosh, G., and Rath, G. (2020). A review of current interventions for COVID-19 prevention. *Archives of Medical Research*, 51(5), 363–374.

Punn, N.S., Soubhadra, S.K., and Agarwal, S. (2020). COVID-19 epidemic analysis using machine learning and deep learning algorithms. *MedRxiv*.

Richards, F. (1959). A flexible growth function for empirical use. *Journal of Experimental Botany*, 10(2), 290–301. Publisher: Oxford University Press.

Rosen, B., Waitzberg, R., and Israeli, A. (2021). Israel’s rapid rollout of vaccinations for COVID-19. *Israel journal of health policy research*, 10(1), 1–14.

Smirnova, A. and Chowell, G. (2017). A primer on stable parameter estimation and forecasting in epidemiology by a problem-oriented regularized least squares algorithm. *Infectious Disease Modelling*, 2(2), 268–275. Publisher: Elsevier.

Vaira, L.A., Salzano, G., Deiana, G., and De Riu, G. (2020). Anomia and ageusia: common findings in COVID-19 patients. *The Laryngoscope*.

Wahltinez, O. et al. (2020). COVID-19 open-data: curating a fine-grained, global-scale data repository for SARS-CoV-2. URL https://goo.gle/covid-19-open-data. Work in progress. Accessed on 09th Apr 2021.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y., et al. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*, 323(11), 1061–1069.

Wu, J.T., Leung, K., and Leung, G.M. (2020). Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *The Lancet*, 395(10225), 689–697.

Yuki, K., Fujiogi, M., and Koutsogiannaki, S. (2020). COVID-19 pathophysiology: A review. *Clinical Immunology*, 215, 108427.