



Mathematical Models for Pandemic Diseases : A Case Study of the COVID-19 Coronavirus

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ABSTRACT

In this research, we study the propagation pattern of pandemic disease such as covid-19 from a mathematical model perspective. The study is based on catastrophic outbreak of the corona virus (COVID-19). The result from such models greatly affect the use of non-pharmaceutical intervention measures management of medical resources and understanding risk factors. This paper compares popular mathematical models based on their predictive capabilities, practical validity, presumptions and drawbacks. The paper focuses on popular techniques in use for the predictive modeling of the Covid-19 pandemic.

KEYWORDS : coron virus, Disease, Mathematical Modeling, Pandemic

1. INTRODUCTION

Mathematical models are useful to understand the behavior of an infection when it enters a community and investigate under which condition it will be coiped out or continued. Since the outbreak of the COVID-19 coronavirus in early 2020, the virus has affected most countries and taken the lives of several thousands of people worldwide. By March 2020, the World Health Organization (WHO) declared the situation a pandemic, the first of its kind in our generation. To date, many countries and regions have been locked-down and applied strict social distancing measures to stop the virus propagation (Joseph et. al. 2020). From a strategic and healthcare management perspective, the propagation pattern of the disease and the prediction of its spread over time is of great importance, to save lives and to minimize the social and economic consequences of the disease. (Benjamin and Dirk, 2020).

The problem of pandemic modeling has significant practical importance for governments and decision makers. Non pharmaceutical interventions (NPIs) refer to actions and policies adopted by individuals, authorities or governments that help slowing down the spread of epidemic disease (Reza and Ndowna, 2020). NPIs are among the best ways of controlling pandemic diseases when vaccines or medications are not yet available. During the COVID-19 pandemic, several attempts have been made to categorize and quantify the various NPIs of different regions and nations. The quantification of NPI is believed to be helpful for comparing the effectiveness of regional policies in containing the pandemic spread (Barmpairs and Tsironis (2020). By using machine learning techniques, the quantified NPI can be used to forecast the future trends of the pandemic and to simulate "what if scenarios" for the better management of human

and medical controlling the pandemic. (Cheng et. al. 2020).

It should be highlighted that mathematical models supplied to real-world systems (social, biological, economical, etc.) are only valid under their assumptions and hypothesis. Therefore, this research - and similar ones - that address epidemic patterns do not convey direct clinic information and dangers for the public, but should rather be used by healthcare strategists for better planning and decision making (Jane, 2020). Hence, the study of this work is only recommended for researchers familiar with the strength points and limitations of mathematical modeling of biological systems (Tapiwa, et. al. 2020).

Mathematical models for disease epidemic are either deterministic or stochastic, where the first is considered as thermodynamic limit of the other. Mathematical modeling of epidemics broadly consists of three types, Statistical methods for epidemic surveillance, Mechanistic State-Space model and Empirical Learning models (David, et. al. 2014). Mechanistic State-Space models have outperformed the other two in describing respiratory disease such as MERS and SARS. Mechanistic state space models are classified (see Figure 1) as "Continuum" models, "Markov Chain" model, "Complex Network" models and "Agent Based Simulations".

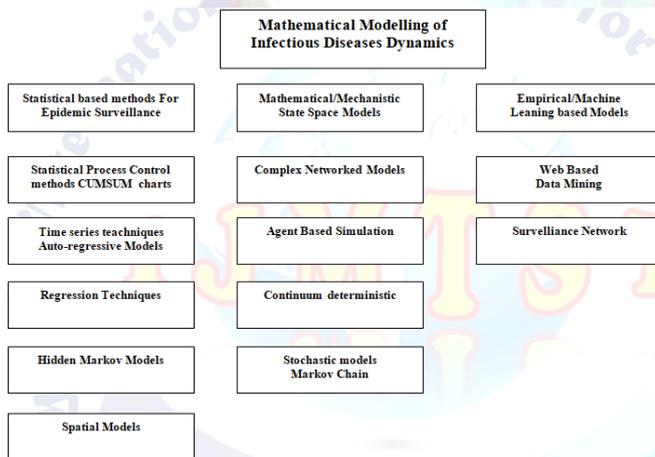


Figure 1. Classification of Mathematical Models

The most significant functions of epidemic models are monitoring, forecasting major outbreaks detection of patterns, disease characteristics that might suggest suitable measures for controlling the spread of disease (Jantin et. al 2009). Mathematics simulations have allowed rapid situation assessments for proper resource

allocation (Kenji et. al. 2020). In situations where cost of testing restricts collection of fresh data, mathematical simulation can be game changing (Cintra and Fontinele 2020). The Covid-19 pandemic has exemplified the centrality of dynamic mathematical models in predicting and containing outbreaks, response logistical and policy making on Non Pharmaceutical Intervention (NPI).

2. MATHEMATICAL MODELS :

A. Gaussian Models

Statistical Regression models detect dynamics of epidemic outbreak by monitoring the time-series statistics of reported infected cases (Qun, 2020). One of the early works on this was published by Serfling which was incepted to analyze the deaths caused by pneumonia and influenza. Gaussian Model (GM) is one such statistical model that has outperformed its peers in reliably predicting Covid-19 outbreaks. Gaussian models are based on the control limit theorem of Statistic where the proposition consists of multiple independent and random variables, their suitably normalized sum tends towards a Gaussian distribution even if the original variables themselves aren't distributed normally (Janik et. al. 2019).

In the Gaussian model, the bell shaped Gaussian function is fitted to existing data of cumulative deaths or detected infections and extrapolate the numbers to future times. Although Gaussian Model appears to be too simple and primitive, its applicability can be substantially justified (Sang and Kim, 2017). Firstly GM appears to be a special case of continuum models as suggested by Secondly, GM is known to be compatible with an agent based epidemiological model as showcased by.

A model was developed using Gaussian error function and Monte Carlo simulation to predict the outbreak of corona virus in Italy. Based upon distribution observed in study of seasonal influenza [9], the cumulative number of detected cases and deaths in china were fitted with a Gaussian error function containing four parameters (see Figure 2). The Gaussian function used to be represented by Equation 1. Where $\text{erf}(z)$ represents Gaussian error function depicted by Equation 2.

$$a + b \text{erf}(cx + d) \quad (1)$$

$$\text{erf}(z) = \frac{2}{\pi} \int_0^z e^{-t^2} dt \quad (2)$$

The day of the Flex (i.e. the day the number of daily positive cases decelerating) in U.P. is predicted to lie between 14 April to 15 May. However, it was actually observed on 23rd April 2021. Additionally, the day with substantial reduction in the number of new cases by more than 100) was predicted to lie between April 20th and April 30th. This substantial reduction was observed on 25th and 26th April 2021.

Similar model was developed by IHME COVID-19 health services utilization forecasting team. This model forecasts the impact of COVID-19 on hospital beds and demand for ventilators in the United States. Findings from this study have been crucial in developing lockdown strategies and justifying the use of Non-Pharmaceutical Interventions (Reinhard, 2020).

Another model similar to IHME COVID-19 was developed to predict the spread of the virus in Germany and Europe. It differs from the earlier mentioned work by suggesting the use of monitored doubling times to approximate the total duration of the first wave and the point of time with peak deaths (Fernandez and Charles, 2020). This paper has concluded that higher order coefficients tend to fit noise better than the signal itself. Therefore, second order polynomial (GM) is used to fit logarithmic daily deaths. Daily fatalities as a function of time denoted by $d(t)$ and cumulative logarithmic daily deaths as a function of time denoted by $D(t)$ of degree 2

$$d(t) = d_{max} \exp \left\{ \frac{(t - t_{d,max})^2}{\omega_d^2} \right\} \quad (3)$$

$$D_m(t) = \frac{d D_m t}{dt} \quad (4)$$

$$\ln(D_m(t)) = \ln \left(d_{max} - \left(\frac{t - t_{d,max}}{\omega_d} \right)^2 \right) = c_0 + c_1 t + c_2 t^2 \quad (5)$$

$$c_0 = \ln d_{max} - \frac{t_{d,max}^2}{\omega_d^2}, c_1 = \frac{2t_{d,max}}{\omega_d^2}, c_2 = \frac{1}{\omega_d^2} \quad (6)$$

The applicability of such model can be confirmed using a holistic agent model. It is also observed that the width of GM is within 10 and 15 days, and the peak in fatalities approximately occurs below 20 deaths per million.

The major drawbacks of mathematical models involving sigmoid functions are: (i) their tendency of over-fitting the data, (ii) high sensitivity to initial condition and (iii) requiring large number of parameters. However, sigmoidal functions have been acknowledged for automatically accounting for exponential growth phase and the subsequent flattening phase that are observed in epidemic curves (Wim, 2020). Most

exponential models rely on doubling times, which demands extensive pre-processing of the data. It is important to note that GM is able to accurately fit and model data produced by agent-based approach, given that the degree of social distancing remains unchanged. Gaussian models are so simple that comprehensive understanding of neither statistics nor epidemiology is required for its implementation.

B. Continuum Models

State-Space models have been used to infuse our mechanistic understanding of disease transmission with a statistical framework by associating observed incidence disease dynamics with underlying population disease burden and susceptibility. The field of study in mechanistic modeling is described by a set of differential equations. These differential equations can be discretized to give simple difference equations. The differential equations symbolize the general state space where as the difference equations define the various states. Owing to the uncertainty related to measurement to process states, random abrupt peaks it is critical to remove measurement noise and on-line estimation to the process states for the real time deployment of this mechanistic model (Joseph and Gabriel, 2020).

Continuum models can describe the rough dynamics of the disease in the population. Continuum models can project the severity of epidemics as a function of age distributions or the evolution of disease transmission under Non-Pharmaceutical Interventions. The classical SIR model divides the population into 3 groups: susceptible individuals (S), infected individuals (I), and recovered individuals (R). Successive models SIRD, SEIRD also include dead individual (D) and exposed but asymptomatic individuals (E). The compartmental action-mass model introduced by Kermack and McKendrick in 1922, can be considered as the basis of such models. The idea behind Continuum model can be summed up in following set of equations,

$$\frac{dP_t(S)}{dt} = -\rho_{S-1} \sum_{N(S)} P_t(S, I), \quad \frac{dP_t(I)}{dt} = -\rho_{S-1} P_t(I), \quad \frac{dP_t(R)}{dt} = -\rho_{S-R} P_t(I) \quad (7)$$

$$\frac{dS}{dt} = -\alpha SI, \quad \frac{dI}{dt} = \alpha SI - \beta I, \quad \frac{dR}{dt} = \beta I \quad (8)$$

$$\frac{dS}{dt} = -\alpha SI + \gamma R, \quad \frac{dI}{dt} = \alpha SI - \beta I, \quad \frac{dR}{dt} = \beta I - \gamma R,$$

Equations 7 denote probabilities of population moving from one compartment to the other. The symbols α and

$(1/\beta)$ denote average values of the probability of disease transmission and the mean time period during which an infected person can spread the disease before completely recovering respectively.

Interesting research was carried out incorporating three variants of classical SIR model, a time dependent SIR model, a discrete time time-dependent SIR model and SIR model considering undetected infected persons. Discrete time dependent model can be represented as the following difference equations :

$$S(t+1) - S(t) = \frac{-\beta(t)S(t)X(t)}{n} \quad (10)$$

Table 2. List not Notations Used

Notation	Description
β	Disease transmission rate (stationary)
$\beta(t)$	Disease transmission rate as function of time
β_1	Disease transmission rate of detectable cases
β_2	Disease transmission rate of undetectable cases
γ	Rate or recovery (stationary)
$\gamma(t)$	Rate of recovery as function of time
γ_1	Rate of recovery for detectable cases
γ_2	Rate of recovery for undetectable cases
n	The total population
R_0	The basic reproduction number
$R_0(t)$	The basic reproduction number as function of time
$R(t)$	Number of recovered persons at time t
$S(t)$	Number of susceptible persons at time t
ω_1	Probability that an infected person is detectable
ω_2	Probability that an infected person in unde tectable
$X(t)$	Number of infected person at time t

$$X(t+1) - X(t) = \frac{\beta(t)S(t)X(t)}{n} - \gamma(t)X(t) \quad (11)$$

$$R(t+1) - R(t) = \gamma(t)X(t) \quad (12)$$

According to reports from WHO only 87.9% of Covid-19 patients have fever and only about 67.7% of them development dry cough. Other studies on the characteristics of the virus have also given similar conclusions. Therefore, it is essential of consider undetected infected persons while development mathematical. This SIR model designed to consider undetected infected person with w_1 being probability of detectable cases and w_2 being probability of undetectable cases. See Table 2 for complete list of notations used in Equations 10-16.

$$w_1 + w_2 = 1 \quad (13)$$

$$X_1(t+1) - X_1(t) = \beta_1 X_1(t) \omega_1 + \beta_2 X_2(t) \omega_2 - \gamma_1 X_1(t) \quad (14)$$

$$X_2(t+1) - X_2(t) = \beta_2 X_2(t) \omega_2 + \beta_2 X_2(t) \omega_2 - \gamma_2 X_2(t) \quad (15)$$

$$R(t+1) - R(t) = \gamma_1 X_1(t) + \gamma_2 X_2(t) \quad (16)$$

A study similar in nature carried out employing a slightly modified SIR model has yielded accurate predictions with an errors loss than 33%. Since Caussian evolution observed from China-driven Gaussian model, a standard SIR model was developed additionally which has derived similar dependence. The Gaussian function used in mentioned below. Here, α and μ are infection and recovery rates respectively. While β and γ are respective constants such that they satisfy equation.

Additionally, another observed carried out reflected a comparative analysis of SIRD and SEIRD models. The study observed that there was no difference about the accuracy of the fit to data, and both models yielded very close values for epidemiological parameters. However, the average time taken for an infected person to die was slightly lower on SIERD model. The SEIRD models indicates slower growth rate, which can be attributed to the incubation period included in its design. When it comes to predicting the impact of the epidemic kwith age distributions, SEIRD model offers more precision. But even with better predictions, the proposed SEIRD model is far more complicated than the SIRD model and the use of the latter should not compromise data analysis. The paper concludes that the age division does not alter predictions drastically, implying the case the SIRD models are useful.

During the early days of the epidemic, it was observed that the primary agents by air. To the virus from its epicenter in Wuhan to other citie4s were passengers who traveled by air. To estimate the number of infected cases exported out of Wuhan to other parts of Mainland China as well as cities the world, as alternate study was rolled out comprising a novel SEIR model.

Taking into account the known special characteristics of this virus, the existence of infected undetected cases, a novel θ - SEIHRD model was developed to consider the fraction θ of undetected cases over the real number of total infected cases, which allows the examination of this ration's impact on the epidemic. In this paper. both deterministic and stochastic versions of the model were proposed. However, the deterministic model was used considering various advantages that in offered over the later.

3. CONCLUSION

According to mathematical modelers, a good mathematical model reflects the data it uses. The major

hurdle currently faced by Mathematical models in the lack of noiseless undelayed consistent data. The adulteration of data appears to be occurring primarily due to the variation in guidelines to register cases and the uncertainty of the symptoms of covid-19 the continuum (SIR) family of models seems to be rapidly growing with ever increasing considerations and variables, subsequently increasing the complexity of differential equations involved. Challenges faced by mathematical modelers is summarized into :

On model fits to all is not applicable to devices a Mathematical model in epidemiology. The nature of the problem assists in identifying the suitable model. The key factor is not to cite which model is accurate but to identify the model caters to the requirement and in addressing the problem.

Conflict of interest statement

Authors declare that they do not have any conflict of interest.

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