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Nita H. Shah

Mandeep Mittal *Editors*

Mathematical Analysis for Transmission of COVID-19



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Mathematical Engineering

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Editors

Mathematical Analysis for Transmission of COVID-19

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Chapter 1

Introduction to Compartmental Models in Epidemiology



Nita H. Shah and Mandeep Mittal

Abstract In this chapter, we discuss the basics of compartmental models in epidemiology and requisite analysis.

Keywords Mathematical model · Dynamics · Reproduction number · Equilibrium points · Stability

Introduction

The transmission of infections is broadly classified as vector-borne, waterborne or airborne diseases in epidemiology science. The transmission of infections can be epidemic which is a sudden outbreak of a disease, e.g. COVID-19, or endemic in which disease remains in the society, e.g. malaria. Epidemics like the 2002 outbreak of SARS, the Ebola virus, Zika virus and avian flu attracted the research community to study transmission of such diseases. The outbreak of Spanish flu caused huge human life loss. An endemic situation in epidemiology is one in which disease is always prevalent.

Our objective is to discuss mathematical epidemiology, with the formulation of mathematical models for the spread of disease and criteria for their analysis. Mathematical models in epidemiology help to understand the underlying mechanism that stimulates the spread of disease progression which can be used to develop strategies to curtail the transmission of disease. The degree of heterogeneity, usually known as “threshold” or “reproduction number”, helps to understand the behaviour of transmission of disease. The term “threshold” or “reproduction number” in epidemiological terms can be defined as follows: if the average number of secondary infections caused by an average infective, called the basic reproduction number, is less than one, then a

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disease will die out, while if it exceeds one then disease will be an epidemic, and if it exceeds one and spreads in major part of the globe then it is pandemic. This quantitative quantity can be used to estimate the effectiveness of vaccination programmes, preventive measures and likelihood that a disease may be eliminated or eradicated.

In the mathematical modelling of disease transmission, there is a trade-off between simple models, which neglects most details and is designed to focus on general qualitative behaviour and detailed models usually formulated for specific situations including short-term quantitative predictions. Sometimes, detailed models are difficult to analyse analytically, and hence their utility for theoretical purpose is limited, although their implicative value may be high.

Let us discuss mathematical models to study endemic states. We will also describe age-dependent infectivity. That means, we will try to find explicit solutions of the system of differential equations to visualize the models. We will discuss asymptomatic behaviour of the models, i.e. solutions of the models as $t \rightarrow \infty$.

Simple Epidemic Models

An epidemic can be treated as a sudden outbreak of a disease that infects a substantial fraction of the population in the region.

In compartmental models, the population under consideration is divided into compartments with assumptions about the nature and time rate of motion from one compartment to another. The independent variable in compartmental model is the time t , and the rates of transfer between compartments are expressed mathematically as derivatives with respect to time of the sizes of the compartments. Our models are formulated as system of differential equations.

Some basic terminologies required for model constitution are:

- **Susceptible:** An individual who is at a risk of catching infection though still not infected.
- **Exposed:** An individual person who is infected but not capable to transmit infection.
- **Infectious:** An infected individual capable of transmitting infection.
- **Recovered:** After treatment or due to immunity development, infection heals up and the individual does not remain infectious.
- **Epidemic:** Disease is said to be in epidemic stage if the number of cases rapidly increases within a short duration of time for said population.
- **Endemic:** Disease is said to be endemic if it persist for long time among population of particular area.
- **Incubation Period:** The duration between an individual receives an infection and having first apparent symptom of the disease.

The system of nonlinear ordinary differential equation has the form

$$\frac{d\bar{X}(t)}{dt} = f(\bar{X}) \quad (1.1)$$

where $\bar{X}(t) \in \mathbb{R}^n$ is a model compartment and time-derivative, which is also written as $\dot{\bar{X}}$ or \bar{X}' . Equation (1.1) is a dynamical system with finite-dimensional state $\bar{X}(t)$ of n -dimension. In dynamical models, the problem is divided into compartments with characteristics that variables in each compartment have homogeneous characteristics. Therefore, these models are also known as compartmental models.

In compartmental model, we write

$$\begin{aligned} \bar{X} &= (X_1, X_2, \dots, X_n) \\ \Rightarrow f(\bar{X}) &= (f_1(X_1, X_2, \dots, X_n), f_2(X_1, X_2, \dots, X_n), \dots, f_n(X_1, X_2, \dots, X_n)) \end{aligned}$$

Using the definition of $f(\bar{X})$, the system (1.1) can be replaced by

$$\begin{aligned} \frac{dX_1(t)}{dt} &= f_1(X_1, X_2, \dots, X_n) \\ \frac{dX_2(t)}{dt} &= f_2(X_1, X_2, \dots, X_n) \\ &\vdots \\ \frac{dX_n(t)}{dt} &= f_n(X_1, X_2, \dots, X_n) \end{aligned} \quad (1.2)$$

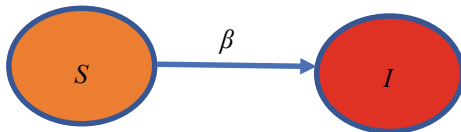
where f_1, f_2, \dots, f_n represents the rate of change of compartment with respect to time. Solving this system, realistic solution can be found but at the other end, it is more complex to solve.

Capital letters such as $S(t)$, $E(t)$, $I(t)$, $R(t)$ are state variables used to represent various compartments.

- $S(t)$ Number of susceptible individuals at time t .
- $E(t)$ Number of exposed individuals at time t .
- $I(t)$ Number of infectious individuals at time t .
- $R(t)$ Number of recovered individuals at time t .
- $N(t)$ Total human population at time t .
- B Recruitment rate.
- β Transmission rate of infection from an infectious individual to a susceptible one.
- μ Natural death rate.
- α Disease-induced death rate.
- σ Rate of progression from exposed class to infectious class.
- k Recovery rate.
- θ Rate of progression from recovered class to susceptible class again.

Starting with the simplest compartmental model consisting of only two classes,

Fig. 1.1 Transmission in *SI* model



SI Model: This model is formulated by dividing total population into two compartments, namely susceptible and infected. An individual from susceptible compartment comes in contact with an infected individual from infectious compartment and joins infectious compartment. It is assumed that an individual entering in infectious compartment will remain in infectious compartment forever. Here, natural birth and natural deaths are not taken into consideration.

Figure 1.1 can be mathematically written as system of differential equations as:

$$\begin{aligned} S' &= -\beta SI \\ I' &= \beta SI - \alpha I \end{aligned}$$

SIR Model: In 1927, Kermack and McKendrick had suggested a mathematical model with three compartments, namely susceptible, infected and removed. This model was introduced with natural birth and natural death. SIR model is an extension of SI model with one more added compartment recovered. Infectious individual after getting recovery through natural immunity or by any other sources joins recovered class and remains there forever. Measles, mumps, flu and rubella are few examples of infectious diseases which follows SIR dynamics.

Figure 1.2 can be mathematically written as system of differential equations as:

$$\begin{aligned} S' &= -\beta SI \\ I' &= \beta SI - \alpha I \\ R' &= \alpha I \end{aligned} \tag{1.3}$$

The model is developed based on the following assumptions:

1. An average member of the population makes contact which is sufficient to transmit infection with βN others per unit time, i.e. mass action incidence.
2. Infectives leave the infective class at rate αI per unit time.
3. There is no entry into or exit from the population.

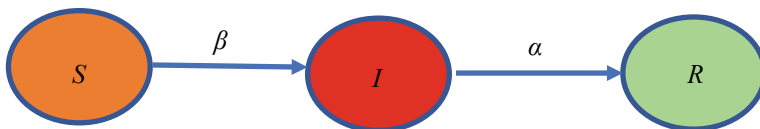


Fig. 1.2 Transmission in *SIR* model

From (1), the probability that a contact by an infective with susceptible, who can transmit an infection, is S/N , the number of new infections in unit time per infective is $(\beta N)(S/N)$, and chance that a rate of new infections is $(\beta N)(S/N)I = \beta SI$. (3) suggests that the timescale of a disease is much faster than the timescale of births and deaths resulting in ignorance of demographic effects on the population. This means we are only interested in analysing the dynamics of a single epidemic outbreak. The assumption (2) can be understood as follows:

Let us consider “cohort” of members who were all infected at one time. Let us denote it by $u(t)$. If a fraction α of this leaves the infective class in unit time, then

$$u' = -\alpha u$$

The solution of this differential equation is

$$u(t) = u(0)e^{-\alpha t}$$

Thus, the fraction of infectives are still infective at t time units after catching infection is $e^{-\alpha t}$. This suggests that the length of the infective period is distributed exponentially with mean $\int_0^\infty e^{-\alpha t} dt = 1/\alpha$ which justifies assumption (2).

We can calculate R once S and I are known. Then, Eq. (1.3) reduces to

$$\begin{aligned} S' &= -\beta SI \\ I' &= (\beta S - \alpha)I \end{aligned} \tag{1.4}$$

The nonlinearity hinders to get the closed form of the solution. WLOG, we assume that $S(t)$ and $I(t)$ are non-negative. (Note: If either $S(t)$ or $I(t)$ reaches zero, then system will terminate.) One can see that $S' < 0$ for all t and $I' > 0$ if and only if $S > \alpha/\beta$. That is, I increases till $S > \alpha/\beta$, but since S decreases for all t , I eventually decreases to zero (no epidemic), while if $S(0) > \alpha/\beta$, I attains maximum at $S = \alpha/\beta$ and then depletes to zero (epidemic). The quantity $\beta S(0)/\alpha$ is a threshold also known as basic reproduction number and is denoted by R_0 . It determines whether the disease is an epidemic or not. If $R_0 < 1$, the infection will die out, while if $R_0 > 1$, disease is epidemic. R_0 is that threshold number of secondary infections caused by a single infective entry into a wholly susceptible population of size $K \approx S(0)$ over the duration of the infection of this single infective. It means that an infective makes βK contacts in unit time, all of which are susceptible, and it produces new infectives with mean infective period $1/\alpha$. Thus, the basic reproduction number is $\beta K/\alpha$ instead of $\beta S(0)/\alpha$.

We divide equations given in (1.4), which gives

$$\frac{I'}{S'} = \frac{dI}{dS} = -1 - \frac{\alpha}{\beta S}$$

Integrating this w.r.t S gives

$$I = -S + \frac{\alpha}{\beta} \log S + c \quad (1.5)$$

This can be used to find trajectories in the (S, I) -plane. We can write

$$V(S, I) = S + I - \frac{\alpha}{\beta} \log S$$

Then, each trajectory is a curve determined by $V(S, I) = c$ for some constant c . This constant c is determined by the initial values $S(0), I(0)$ of S and I .

$$c = V(S(0), I(0)) = S(0) + I(0) - \frac{\alpha}{\beta} \log(S(0))$$

Earlier, we had seen that the maximum value of I on each of the trajectories is attained when $S = \alpha/\beta$. Note that these trajectories will never touch I -axis, $S > 0$ for all time. In particular, $S_\infty = \lim_{t \rightarrow \infty} S(t) > 0$ suggests that fraction of population does not get infection.

- **SIRS Model:** It is further extension of SIR model adding one more situation that a recovered individual loses temporary immunity and rejoins the susceptible class.
- **SEIR Model:** Many time an infection takes a time gap (may vary from disease to disease) to make a susceptible individual infectious after catching infection from an infected individual, called incubation period. During this time period, susceptible individuals who acquired infection but still not become infectious join exposed compartment. SIR model with one more compartment added as exposed compartment suggests the dynamics of *SEIR* model.

Very basic models of mathematical epidemiology are described above. We are going to formulate more complicated models by adding more compartments and variables or parameters associated with quarantine, isolation, treatment, mass media effect and many more in this book with view of current pandemic COVID-19.

Next, we will take a closer look at characteristics of the model.

What Is Equilibrium Point and Its Existence?

An equilibrium point of a dynamical system is its fixed point which means solution that does not change with time. Equilibrium points occur when each equation of dynamical system is set to be zero, i.e. $\overline{X}'_i = f_i(X) = 0$. Hence, these equilibrium points can be said to be the root of $f_i(X)$. One can also recall that equilibrium points are constant functions which satisfy the dynamical system which means they are time-independent solutions of the model. There are at least two natures of equilibrium points:

1. Problem-free equilibrium point

2. Optimal valued equilibrium point or endemic equilibrium point or interior equilibrium point.

The equilibrium point X exists only when the stability properties are satisfied, i.e. $X > 0$.

How to Compute Threshold or Basic Reproduction Number?

The threshold is analogous to the most significant concept of the epidemiology world, and this quantity is termed as basic reproduction number and noted as R_0 . Basic reproduction number measures the maximum reproductive latent for an issue. It aids us to predict the future for an issue that whether it will remain present in atmosphere or die out soon. The concept of basic reproduction number was firstly introduced by Lotka [15] for the disease spread of Malaria. Then after, classical methods were suggested by Dublin and Lotka [7] and Kuczynski [11]. In the current scenario, the method used for calculating a basic reproduction number is through the next-generation matrix method. This was suggested by Diekmann et al. [6], and then this method came into limelight by Van den Driessche and Watmough [20]. Recently, Diekmann et al. [5] have edited this method using simplification of the Jacobian method.

The next-generation matrix method

Here, a dynamical system is to be considered which is having n -compartments at time t . It is a set of n nonlinear ordinary differential equations. The set is further separated into nonlinear and linear systems where nonlinear system $F(\bar{X})$ signifies the rate of affected components and linear system $V(\bar{X})$ represents the transfer rate of components going and coming through the respective compartment. Mathematically, the model representation is

$$\frac{d\bar{X}}{dt} = F(\bar{X}) - V(\bar{X}) \quad (1.6)$$

Now, find the Jacobian matrices of $F(\bar{X})$ and $V(\bar{X})$ about the equilibrium point, say issue-free equilibrium point E_0 and then define the next-generation matrix $f v^{-1}$ where $f = [\frac{\partial F(E_0)}{\partial X_j}]_{n \times n}$ and $v = [\frac{\partial V(E_0)}{\partial X_j}]_{n \times n}$. The spectral radius or the largest eigenvalue of the matrix $f v^{-1}$ is the basic reproduction number (threshold) of the model. If the value of threshold is less than 1, then the problem is in controllable state; otherwise, the issue will take epidemic stage in short period of time.

How to Characterize Nature of Stability?

The fundamental concept for a dynamical system is “stability”. An equilibrium point X of a system is said to be stable if for each $\varepsilon > 0$ and $t_0 \in \mathbb{R}$ there exists $\delta = \delta(\varepsilon, t_0) > 0$ such that each solution $x(t)$ having initial conditions within the distance δ , i.e. $\|x(t_0) - X\| < \delta$, then equilibrium point remains within the distance ε , i.e. $\|x(t) - X\| < \varepsilon$ for all $t \geq t_0$. In this thesis, we are focusing on a stronger condition than stability called asymptotic stability. An equilibrium point is said to be asymptotically stable if it is stable and for every $t_0 \in \mathbb{R}$ there exists $\delta_0 = \delta_0(t_0) > 0$ such that whenever $\|x(t_0) - X\| < \delta_0$ then $x(t) \rightarrow X$ as $t \rightarrow \infty$. We will study two types of stability: (1) local asymptotic stability and (2) global asymptotic stability.

1. *Local asymptotic stability*

The local asymptotic stability of a model at an equilibrium point X is that the solution of the system must approach an equilibrium point under initial condition close to the equilibrium point, i.e. at X if there is a $\delta > 0$ such that $\|x(t) - X\| < \delta \Rightarrow (x(t)) \rightarrow X$ as $t \rightarrow \infty$. The local asymptotic stability is established using Jacobian matrix of the system. If all the eigenvalues have negative real parts, then the system is locally asymptotically stable about the equilibrium point [10]. Routh–Hurwitz criteria are also well used for finding the local asymptotic stability [17]. Moreover, this stability about the interior equilibrium point can be done using curl [2–4], second-order additive compound matrix [1, 16].

2. *Global asymptotic stability*

The global asymptotic stability of a model at an equilibrium point X is the solution of the system must approach to the equilibrium point under all initial conditions; i.e. for every $x(t)$, we have $x(t) \rightarrow X$ as $t \rightarrow \infty$. Lyapunov function [12] helps to establish that the model is globally asymptotically stable. In addition, graph theory [9] and theory of geometric method [13, 14, 19] deliberate the global asymptotic stability of the model.

What Is Bifurcation and What It Reflects?

Bifurcation is one of the important concepts for a dynamical system because it helps us to framework the qualitative change of the system. A bifurcation occurs when a small and smooth variation is made to the value of model parameter which leads to a rapid qualitative change in its nature. In other words, it reflects the qualitative change to the state of the system as a model parameter is changed. Hence, we can see the significant impact on the solution while using bifurcation analysis. The parameter which set to be varied is known as bifurcation parameter, and the curve which reflects the qualitative nature of the system is called bifurcation curve.

The dynamical system includes different bifurcations:

1. Saddle-node bifurcation
2. Flip bifurcation
3. Forward bifurcation
4. Backward bifurcation
5. Hopf bifurcation
6. Neimark–Sacker bifurcation
7. Transcritical bifurcation
8. Pitchfork bifurcation.

Backward bifurcation occurs when a branch of the system varies its stability at a point and turns into unstable state, whereas at the same time, a new branch of positive endemic steady state comes up to coincide with the initial stable state. The point from which state is changing from stable to unstable is called bifurcation point or critical threshold noted as R_C . In general, for a dynamical system, when a parameter is permissible to fluctuate within the range then the system may vary. It can result that an equilibrium can attain epidemic state and a periodic solution may happen or a unique stable equilibrium may grow up making earlier equilibrium unstable. The backward bifurcation has a characteristic: it exists only when the threshold of model is less than 1. Moreover, the critical threshold should be less than original threshold, i.e. extended characteristic $R_C < R_0 < 1$ which ensures the expulsion of problem in nearer future. In addition, bifurcation analysis reflects the global stability of a model.

How to Optimize the Issue?

Optimizing an issue is a fundamental tool in the world of dynamical modelling. Optimization can improve the results. Optimization of dynamical modelling is done through control theory. Control theory suggests that applying sufficient control at appropriate time will try to shatter the problem in sooner time. To achieve this objective, the objective function for the model along with the controls is designed as

$$J(u_i, \Omega) = \int_0^T (A_1 X_1^2 + A_2 X_2^2 + \cdots + A_n X_n^2 + w_1 u_1^2 + w_2 u_2^2 + \cdots + w_m u_m^2) dt \quad (1.7)$$

where Ω is the set consisting of all compartmental variables; A_1, A_2, \dots, A_n (non-negative weight constants for X_1, X_2, \dots, X_n , respectively); and $\omega_1, \omega_2, \dots, \omega_m$ (non-negative weight constants for u_1, u_2, \dots, u_m , respectively).

The weight constants $\omega_1, \omega_2, \dots, \omega_m$ normalized the optimal control condition. Now, measure the values of control variables from $t = 0$ and $t = T$ such that

$$J(u_1(t), u_2(t), \dots, u_m(t)) = \min \{ J(u_i^*, \Omega) / (u_1, u_2, \dots, u_m) \in \phi \}$$

where $u_i^*; i = 1, 2, \dots, m$ is optimal control, i.e. $\phi = \{u_i(t)/a_i < u_i < b_i; i = 1, 2, \dots, m\}$ is control set with a_i as a lower bound and b_i as an upper bound. Here, ϕ is a smooth function on the interval $[0, 1]$. Before finding optimal controls, some hypothesis should hold:

1. The set of control (ϕ) and state variable (Ω) are non-empty.
2. The control set ϕ is closed and convex.
3. The system is bounded by the linear function made of state and control variable including time-dependent coefficients.
4. The integrand of the objective function is convex on ϕ and bounded below by $c_1(|u_1|^2 + |u_2|^2 + \dots + |u_m|^2)^{\frac{\alpha}{2}} - c_2$ where c_1 and c_1 are positive constants and $\alpha > 1$.

Now, let us compute the optimal controls $u_i^*, i = 1, 2, \dots, m$ by accumulating all the integrands of objective function (1.7) using the lower and upper bounds described in the results of Fleming and Rishel [8].

Further, consider Pontryagin's principle from Boltyanski et al. Next, construct a Lagrangian function consisting of state equations and adjoint variables $A_i = (\lambda_1, \lambda_2, \dots, \lambda_n)$ to minimize the cost function given in objective function (1.7). The Lagrangian function is expressed as

$$L(\Omega, A_i) = A_1 X_1^2 + A_2 X_2^2 + \dots + A_n X_n^2 + w_1 u_1^2 + w_2 u_2^2 + \dots + w_m u_m^2 + \lambda_1(X_1') + \lambda_2(X_2') + \dots + \lambda_n(X_n') \quad (1.8)$$

The partial derivative of the Lagrangian function with respect to each compartment gives the adjoint equation corresponding the system, which is followed by

$$\left. \begin{aligned} \dot{\lambda}_1 &= -\frac{\partial L}{\partial X_1} \\ \dot{\lambda}_2 &= -\frac{\partial L}{\partial X_2} \\ &\vdots \\ \dot{\lambda}_n &= -\frac{\partial L}{\partial X_n} \end{aligned} \right\} \quad (1.9)$$

Now, the partial derivative of the Lagrangian function with respect to each control is

$$\left. \begin{aligned} \dot{u}_1 &= -\frac{\partial L}{\partial u_1} \\ \dot{u}_2 &= -\frac{\partial L}{\partial u_2} \\ &\vdots \\ \dot{u}_m &= -\frac{\partial L}{\partial u_m} \end{aligned} \right\} \quad (1.10)$$

Now, to achieve the necessary condition, set each equation of (1.10) equal to zero, we have the values of u_1, u_2, \dots, u_m . Hence, the required optimal control condition is calculated as

$$\left. \begin{aligned} u_1^* &= \max(a_1, \min(b, u_1)) \\ u_2^* &= \max(a_2, \min(b, u_2)) \\ &\vdots \\ u_m^* &= \max(a_m, \min(b, u_m)) \end{aligned} \right\} \quad (1.11)$$

Inside This Book

Chapter 2: Modelling the Impact of Nationwide BCG Vaccine Recommendations on COVID-19 Transmission, Severity and Mortality

Coronavirus disease 2019 (COVID-19) is declared as pandemic on 11 March 2020 by World Health Organization (WHO). There are apparent dissimilarities in incidence and mortality of COVID-19 cases in different parts of world. Developing countries in Asia and Africa with fragile health system are showing lower incidence and mortality compared to developed countries with superior health system in Europe and America. Most countries in Asia and Africa have national Bacillus Calmette-Guerin (BCG) vaccination programme, while Europe and America do not have such programme or have ceased it. At present, there is no known Food and Drug Administration (FDA)-approved treatment available for COVID-19. There is no vaccine available currently to prevent COVID-19. As mathematical modelling is ideal for predicting the rate of disease transmission as well as evaluating efficacy of possible public health prevention measures, we have created a mathematical model with seven compartments to understand nationwide BCG vaccine recommendation on COVID-19 transmission, severity and mortality. We have computed two basic reproduction numbers, one at vaccine-free equilibrium point and other at non-vaccine-free equilibrium point, and carried out local stability, sensitivity and numerical analysis. Our result showed that individuals with BCG vaccinations have lower risk of getting COVID-19 infection, shorter hospital stays and increased rate of recovery. Furthermore, countries with long-standing universal BCG vaccination policies have reduced incidence, mortality and severity of COVID-19. Further research will focus on exploring the immediate benefits of vaccination to healthcare workers and patients as well as benefits of BCG re-vaccination.

Chapter 3: Modeling the Spread of COVID-19 Among Doctors from the Asymptomatic Individuals

The present world is in dire straits due to the deadly SARS CoV-2 (coronavirus-2) outbreak, and the experts are trying heart and soul to discover any prevention and/or remedy. The people from all walks of life in the universe are fighting to defeat this novel coronavirus. In this case, doctors are in the front-line fighters who have put themselves at a risk. In this paper, we have formulated a nonlinear mathematical model of COVID-19 based on the tendency of doctors to be infected. The target of

this study is to take a look at the transmission of COVID-19 from asymptomatic populations to the doctors. The model is analysed with the determination of the basic reproductive ratio and related stability analysis at the disease-free and endemic equilibrium points. The graph of the basic reproductive ratio for different parameters has been drawn to show the disease behaviour. Finally, numerical simulations have been performed to illustrate the analytic results. Our study shows that the asymptomatic population increases as the disease (COVID-19) transmission rate increases and also the number of infected population increases when the infection rate increases. These increasing asymptomatic and infected populations lead the doctors to get infected by contacting with them. Thus, the whole medical service system is getting down over time.

Chapter 4: Transmission Dynamics of Covid-19 from Environment with Red Zone, Orange Zone, Green Zone Using Mathematical Modelling

The novel coronavirus or COVID-19 spread had its inception in November of 2019, and in March 2020 it was declared as a pandemic. Since its initial stage, it has now already infected over 5 million people, leading to the lockdown of countries around the world and a halt on global as well as national travel across the globe. Based on this, the research proposes a mathematical COVID-19 model to study the outcome of these classified zones under different control strategies. In the nonlinear mathematical model, the total population has been divided into seven compartments, namely susceptible, exposed, red zone, orange zone, green zone, hospitalized and recovered. The spectral radius is calculated to analyse dynamics of the COVID-19. To control the spread of the virus, the parameters of controls are medical intervention, partial lockdown and strict lockdown. This model has been validated with numerical data. The conclusion validates the implementation of lockdown in curbing COVID-19 cases.

Chapter 5: A Comparative Study of COVID-19 Pandemic in Rajasthan, India

The treatment of coronavirus diseases is not possible without any vaccine. However, spreading of the deadly virus can be controlled by various measures being imposed by government like lockdown, quarantine, isolation, contact tracing, social distancing and putting face mask on mandatory basis. As per information from the Department of Medical Health and Family Welfare of Rajasthan on 19 September 2020, COVID-19 severely affected the state of Rajasthan, resulting in cumulative positive cases 113,124, cumulative recovered 93,805 and cumulative deaths 1322. Without any appropriate treatment, it may further spread globally as it is highly communicable and because potentially affecting the human body respiratory system, which could be fatal to mankind. Therefore, to reduce the spread of infection, authors are motivated to construct a predictive mathematical model with sustainable conditions as per the ongoing scenario in the state of Rajasthan. Mathematica software has been used for numerical evaluation and graphical representation for variation of infection, recovery, exposed, susceptible and mortality versus time. Moreover, comparative analysis of results obtained by predictive mathematical model has been done with the exact data plotting by curve fitting as obtained from Rajasthan government website. As a

part of analysis and result, it is noted that due to the variation of transmission rate from person to person corresponding rate of infection goes on increasing monthly and mortality rate found high as shown and discussed numerically. Further, we can predict that the situation will become worse in the winter months, especially in the month of December due to unavailability of proper vaccine. This model may become more efficient when the researchers, experts from medical sciences and technologist work together.

Chapter 6: A Mathematical Model for COVID-19 in Italy with Possible Control Strategies

Italy faced the COVID-19 crisis in the early stages of the pandemic. In the present study, a SEIR compartment mathematical model has been proposed. The model considers four stages of infection: susceptible (S), exposed (E), infected (I) and recovered (R). Basic reproduction number R_0 which estimates the transmission potential of a disease has been calculated by the next-generation matrix technique. We have estimated the model parameters using real data for the coronavirus transmission. To get a deeper insight into the transmission dynamics, we have also studied four of the most pandemic affected regions of Italy. Basic reproduction number stood differently for different regions of Italy, i.e. Lombardia (2.1382), Veneto (1.7512), Emilia Romagna (1.6331), Piemonte (1.9099) and for Italy at 2.0683. The sensitivity of R_0 corresponding to various disease transmission parameters has also been demonstrated via numerical simulations. Besides, it has been demonstrated with the help of simulations that earlier lockdown and rapid isolation of infective individuals would have been helpful in a dual way, by substantially decreasing transmission of COVID-19.

Chapter 7: Effective Lockdown and Plasma Therapy for COVID-19

COVID-19 is a major pandemic threat of 2019–2020 which originated in Wuhan. As of now, no specific antiviral medication is available. Therefore, many countries in the world are fighting to control the spread by various means. In this chapter, we model COVID-19 scenario by considering compartmental model. The set of dynamical system of nonlinear differential equation is formulated. Basic reproduction number R_0 is computed for this dynamical system. Endemic equilibrium point is calculated, and local stability for this point is established using Routh–Hurwitz criterion. COVID-19 has affected more than 180 countries in several ways like medically, economy, etc. It necessitates the effect of control strategies applied by various governments worldwide to be analysed. For this, we introduce different types of time-dependent controls (which are government rules or social, medical interventions) in order to control the exposure of COVID-19 and to increase recovery rate of the disease. By using Pontryagin's maximum principle, we derive necessary optimal conditions which depicts the importance of these controls applied by the government during this epidemic.

Chapter 8: Controlling the Transmission of COVID-19 Infection in Indian Districts: A Compartmental Modelling Approach

The widespread of the novel coronavirus (2019-nCoV) has adversely affected the world and is treated as a Public Health Emergency of International Concern by the World Health Organization. Assessment of the basic reproduction number with the help of mathematical modelling can evaluate the dynamics of virus spread and facilitate critical information for effective medical interventions. In India, the disease control strategies and interventions have been applied at the district level by categorizing the districts as per the infected cases. In this study, an attempt has been made to estimate the basic reproduction number R_0 based on publicly available data at the district level in India. The susceptible-exposed-infected-critically infected-hospitalization-recovered (SEICHR) compartmental model is constructed to understand the COVID-19 transmission among different districts. The model relies on the twelve kinematic parameters fitted on the data for the outbreak in India up to 15 May 2020. The expression of basic reproduction number R_0 using the next generating matrix is derived and estimated. The study also employs three time-dependent control strategies to control and minimize the infection transmission from one district to another. The results suggest an unstable situation of the pandemic that can be minimized with the suggested control strategies.

Chapter 9: Fractional SEIR Model for Modelling the Spread of COVID-19 in Namibia

In this chapter, a fractional SEIR model and its robust first-order unconditionally convergent numerical method are proposed. Initial conditions based on Namibian data as of 4 July 2020 were used to simulate two scenarios. In the first scenario, it is assumed that proper control mechanisms for curbing the spread of COVID-19 are in place. In the second scenario, a worst-case scenario is presented. The worst case is characterized by ineffective COVID-19 control mechanisms. Results indicate that, if proper control mechanisms are followed, Namibia can contain the spread of COVID-19 in the country to a lowest level of 1, 800 positive cases by October 2020. However, if no proper control mechanisms are followed, Namibia can hit a potentially unmanageable level of over 14, 000 positive cases by October 2020. From a mathematical point of view, results indicate that the fractional SEIR model and the proposed method are appropriate for modelling the chaotic nature observed in the spread of COVID-19. Results herein are fundamentally important to policy- and decision-makers in devising appropriate control and management strategies for curbing further spread of COVID-19 in Namibia.

Chapter 10: Impact of COVID-19 in India and Its Metro Cities: A Statistical Approach

The infectious coronavirus disease is spreading at an alarming rate, not only in India but globally too. The impact of coronavirus disease 2019 (COVID-19) outbreak needs to be analysed statistically and modelled to know its behaviour so as to predict the same for future. An exhaustive statistical analysis of the data available for the spread

of this infection specifically on the number of positive cases, active cases, death cases and recovered cases and connection between them could probably suggest some key factors. This has been achieved in this paper by analysing these four dominant cases. This helped to know the relationship between the current and the past cases. Hence, in this paper an approach of statistical analysis of COVID-19 data specific to metropolitan cities of India is done. A regression model has been developed for prediction of active cases with 10 lag days in four metropolitan cities of India. The data used for developing the model is considered from 26 April to 31 July (97 days), tested for the month of August. Further, an artificial neural network (ANN) model using back-propagation algorithm for active cases for all India and Bangalore has been developed to see the comparison between the two models. This is different from the other existing ANN models as it uses the lag relationships to predict the future scenario. In this case, data is divided into training, validation and testing sets. Model is developed on the training sets, is checked on the validation set, is tested on the remaining and is implemented for prediction.

Chapter 11: A Fractional-Order SEQAIR Model to Control the Transmission of nCOVID 19

The ensuing paper expounds a new mathematical model for a pandemic instigated by novel coronavirus (COVID-19) with influence of quarantine on transmission of COVID-19, using Caputo fractional-order derivative for various fractional orders. Basic reproduction number for the SEQAIR model has been calculated in the study, additionally, proving the existence and uniqueness of the solution using the fixed-point theorem. Furthermore, numerical solution is revealed using the Adams–Bashforth–Moulton method, and its application for real-world data is deliberated.

Chapter 12: Analysis of Novel Corona Virus (COVID-19) Pandemic with Fractional-Order Caputo–Fabrizio Operator and Impact of Vaccination

In a very short time period, the coronavirus disease 2019 (COVID-19) has created a global emergency situation by spreading worldwide. This virus has dissimilar effects in different geographical regions. In the beginning of the spread, the number of new cases of active coronavirus has shown exponential growth across the globe. At present, for such infection, there is no vaccination or antiviral medicine specific to the recent coronavirus infection.

Mathematical formulation of infection models is exceptionally successful to comprehend epidemiological models of ailments, just as it causes us to take vital proportions of general well-being interruptions to control disease transmission and spread. This work based on a new mathematical model analyses the dynamic behaviour of novel coronavirus (COVID-19) using Caputo–Fabrizio fractional derivative. A new modified SEIRQ compartment model is developed to discuss various dynamics. The COVID-19 transmission is studied by varying reproduction number. The basic reproduction number R_0 is determined by applying the next-generation matrix. The equilibrium points for disease-free and endemic states are computed with the help of basic reproduction number R_0 and check the stability

property. The Picard approximation and Banach fixed-point theorem based on iterative Laplace transform are useful in establishing the existence and stability behaviour of the fractional-order system. Finally, numerical computations of the COVID-19 fractional-order system are presented to analyse the dynamical behaviour of the solutions of the model. Also, a fractional-order SEIRQ COVID-19 model with vaccinated people has also been formulated and its dynamics with impact on the propagation behaviour is studied.

Chapter 13: Compartmental Modelling Approach for Accessing the Role of Non-pharmaceutical Measures in the Spread of COVID-19

Epidemic diseases are well known to be fatal and cause great loss worldwide—economically, socially and mentally. Even after around nine months, since the coronavirus disease 2019 began to spread, people are getting infected all over the world. This is one of the areas where human medical advancements fail because by the time the disease is identified and its treatment is figured out, most of the population is already exposed to it. In such cases, it becomes easier to take steps if the dynamics of the disease and its sensitivity to various factors is known. This chapter deals with developing a mathematical model for the spread of coronavirus disease, by employing a number of parameters that affect its spread. A compartmental modelling approach using ordinary differential equation has been used to formulate the set of equations that describe the model.

We have used the next-generation method to find the basic reproduction number of the system and proved that the system is locally asymptotically stable at the disease-free equilibrium for $R_0 < 1$. Stability and existence of endemic equilibrium have been discussed, followed by sensitivity of infective classes to parameters like proportion of vaccinated individuals and precautionary measures like social distancing. It is expected that after the vaccine is developed and is available to use, as the proportion of vaccinated individuals will increase, the infection will decrease in the population which can gradually lead to herd immunity. Since the vaccine is still under development, non-intervention measures play a major role in coping with the disease. The disease generally transmits when the water droplets from an infected individual's mouth or nose are inhaled by a healthy individual. The best measures that should be adopted are social distancing, washing one's hands frequently and covering one's mouth with mask, quarantine and lockdowns. Thus, as more and more precautionary measures are taken, it would gradually reduce the infection which has also been proved numerically by the sensitivity analysis of “w” in our dynamical analysis.

Chapter 14: Impact of ‘COVID-19’ on Education and Service Sectors

Coronavirus disease is an infectious disease which is caused by a virus called coronavirus. The people who are infected with this disease will experience respiratory illness. This disease has been declared pandemic by “World Health Organization (WHO)”. There are many sectors that have been affected due to the lockdown practised in the entire country, among agricultural sector, manufacturing sector, service sector, education sector, business sector, etc. In our research, we examined the impact of COVID-19 in India vis-a-vis different sectors. For the purposes of this research,

we shortlisted two particular sectors, i.e. education and service sectors. These two sectors form the backbone of our country. While the impact on education sector has led to many young minds and vulnerable school kids being affected in an adverse way and have left them to cope with new practices such as online classes during the lockdown period and on the other hand, in the service sector, employees are working from home which in some case has had an impact on the effectiveness and efficiency of their work. In this paper, we assessed the impact on these two sectors on Indian economy by analysing the responses given by our respondents through the questionnaires (Google form) and we then combined the data points to study how students and employees are being affected during the present lockdown period, imposed due to COVID-19. This chapter will help the readers to get to know more about the thinking of the students and employees in lockdown and how much they are affected by this pandemic. Towards the trailing part of our research, we have discussed the possible steps that can be adopted in future, by the employers and educational institutions, in order to limit the damage to the sector and to make recovery in future.

Chapter 15: Global Stability Analysis Through Graph Theory for Smartphone Usage During COVID-19 Pandemic

During the pandemic due to coronavirus disease 2019 (COVID-19), technology is regarded as a boon as well as a curse to human life which has a great impact on surroundings, people and the society. One of the innovative, however, perilous (if misused) inventions of humans is the smartphone which is becoming more and more alarmingly common yet an urgent question to be addressed. A wide application of smartphone technology is observed during this pandemic. It has both positive and negative impacts on the prominent areas which include education, business, health, social life and furthermore. Moreover, the impact of such an addiction is observed not only among youngsters but has influenced all age groups. This scenario is modelled in this research through nonlinear ordinary differential equations where individuals susceptible to smartphone use will be either positively or negatively infected/addicted, and may suffer from health issues procuring medication. Threshold is calculated using the next-generation matrix method. Stability analysis is done using graph theory, and for the validation of data, numerical simulation is carried out. This study gives results explaining positive and negative issues on health due to excessive use of smartphone.

Chapter 16: Modelling and Sensitivity Analysis of COVID-19 Under the Influence of Environmental Pollution

The ongoing COVID-19 pandemic emerged as one of the biggest challenges of recent times. Efforts have been made from different corners of the research community to understand different dimensions of the disease. Some theoretical works have reported that disease becomes severe in the presence of environmental pollution. In this work, we propose a nonlinear mathematical model to study the influence of air pollution on the dynamics of the disease. The basic reproduction number plays a vital role in predicting the future of an epidemic. Therefore, we obtain the expression of the

basic reproduction number and performed a detailed sensitivity and uncertainty analysis. The values of partial rank correlation coefficient (PRCC) have been calculated corresponding to six critical parameters. The positive values of PRCC for pollution-related parameters depict that pollution enhances the chances of a rapid spread of COVID-19.

Chapter 17: Bio-waste Management During COVID-19

Since December 2019, coronavirus through human to human hit the world. As this disease is spreading every day, hospitalization of individuals increased. Consequence of this, there is a sudden surge of millions of gloves, masks, hand sanitizers and the other essential equipment in each month. Disposal of these commodities is a big challenge for hospitals and COVID centre, as they may become the reason of creating pollution and infect the surroundings. Increasing hospitalization cases of COVID-19 results in raising bio-waste which creates pollution. Observing the scenario, a mathematical model with four compartments is constructed in this article. The threshold value indicates the intensity of pollution that emerged from bio-waste. Stability of the equilibrium point gave the necessary condition. Optimal control theory is outlined to achieve the purpose of this chapter by reducing pollution. Outcomes are analytically proven and also numerically simulated.

Chapter 18: Mathematical Modelling of COVID-19 in Pregnant Women and Newly Born

Enlightened by the coronavirus, the present paper deals with a mathematical model of COVID-19 to investigate the impact of S-I-R-M model on the pregnant women and the newly born due to the influence of availability of suitable conditions. The rates of infection, rate of recovery, rate of mortality for pregnant women before and after delivery and for newly born babies due to the transmission rate have been discussed for the present observed data. The numerical illustrations have been carried out for the parameters and functions and represented graphically by Mathematica software. Moreover, some comparisons have been shown in the figure to estimate the impact of susceptible conditions and represent the particular cases of S-I-R-M model.

Chapter 19: Sensor and IoT-Based Belt to Detect Distance and Temperature of COVID-19 Suspect

Owing to the pandemic issue of the coronavirus disease 2019 (COVID-19), it is imperative to keep up more than 1 m of social distancing and 37.5 °C temperature to stop the transmission of COVID-19 from human to human. Therefore, it is utmost requirement to make the smart belt installed with ultrasonic and LM35 sensors for distance and temperature measurements to reduce the transmission of COVID-19, respectively. The embedded sensors with NodeMCU show that once anything come in the proximity of 1 m near to the smart belt or helmet fixed to human body, it automatically makes an alarm for distance contact as well as temperature of incoming/outgoing body and sends an email to the controller with the help of Blynk application through Internet of things (IoT). This data can be stored in the

cloud for the future purpose. However, the distance sensor has detected the movement of a person from 3 cm up to around 240 cm. The LM35 temperature sensor measures the actual temperature of the host body, i.e. 35.4 °C with time. With the help of this research, it is possible to interface a camera module which detects the suspects. It could be interfaced with global positioning system (GPS) which can give location-wise data and help us to obtain the probability of suspects at a particular region. It is cost effective, i.e. \$14/belt, which can help to control the transmission of coronavirus from human to human.

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Chapter 2

Modelling the Impact of Nationwide BCG Vaccine Recommendations on COVID-19 Transmission, Severity and Mortality



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Abstract Coronavirus Disease 2019 (COVID-19) is declared as pandemic on 11 March 2020 by World Health Organization (WHO). There are apparent dissimilarities in incidence and mortality of COVID-19 cases in different parts of world. Developing countries in Asia and Africa with fragile health system are showing lower incidence and mortality compared to developed countries with superior health system in Europe and America. Most countries in Asia and Africa have national Bacillus Calmette-Guerin (BCG) vaccination programme, while Europe and America do not have such programme or have ceased it. At present, there is no known Food and Drug Administration (FDA)-approved treatment available for COVID-19 disease. There is no vaccine available currently to prevent COVID-19 disease. As mathematical modelling is ideal for predicting the rate of disease transmission as well as evaluating efficacy of possible public health prevention measures, we have created

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