FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 7 No. 5, October, 2023, pp 9 - 17
DOI: https://doi.org/10.33003/fjs-2023-0705-1990

A STOCHASTIC DIFFERENTIAL EQUATION (SDE) BASED MODEL FOR THE SPREAD OF TUBERCULOSIS

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ABSTRACT
Understanding dynamics of an infectious disease helps in designing appropriate strategies for containing its spread in a population. In this work, a deterministic and stochastic model of the transmission dynamics of Tuberculosis is developed and analyzed. The models involve the Susceptible, Exposed, Infectious and Recovered individuals. We computed the basic reproduction number R_0 and showed that for $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable. The resulting deterministic model was transformed into an equivalent stochastic model resulting in stochastic differential equation. The drift coefficient, the covariance matrix and the diffusion matrix were determined using the method proposed by Allen et al. (2008).

Keywords: Deterministic model, Stochastic model, Stochastic Differential Equation, Tuberculosis

INTRODUCTION

Tuberculosis is an infectious bacterial disease caused by Mycobacterium tuberculosis, also known as the tubercle bacillus. This disease has been affecting the human population since as far back as 2400 BC (Adetunde, 2008). It is one of the most prevalent infectious diseases and typically targets various parts of the body, including the lungs, central nervous system, lymphatic system, brain, and kidneys. Infection occurs when individuals inhale tuberculosis germs, which are released into the air when infected individuals cough, spit, sneeze, or talk. Those at high risk of infection are individuals frequently exposed to infectious individuals over extended periods. Some infected individuals may remain asymptomatic throughout their lives, a condition known as latent TB. Active TB, which is the clinical disease, can manifest in pulmonary and extra-pulmonary forms. Extra-pulmonary TB is more common in children, while pulmonary TB is more prevalent in adults. Children aged 0-5 years are particularly susceptible to developing active TB due to their less developed immune systems (World Health Organization, 2007).

Many mathematical models of disease epidemiology primarily used deterministic ordinary differential equations, which did not account for uncertainties in disease transmission. These uncertainties stem from various sources, including assumptions about disease parameters, population heterogeneity, behavioral changes, interventions, external factors, and unforeseen events. Stochastic models, on the other hand, embrace the randomness and uncertainty inherent in disease transmission. On the contrary, stochastic models take into account the randomness and uncertainty inherent in disease transmission. This approach considers the probabilistic nature of events, such as infection and recovery which can provide insights into the variability and uncertainty of disease spread. While the conventional ODE models is better for a large population, stochastic models are particularly useful for capturing the effects of small population sizes or rare events.

This work put into cognizance uncertainties that may arise in disease epidemiological models by introducing a random white noise modelled as a Wiener process which results in Stochastic Differential Equation (SDE) instead of the convention deterministic ordinary differential equations (ODE). We considered the model resulting in ODE and later formulate an equivalent SDE model for the spread of tuberculosis. The population under study is divided into four disjoint classes which change with time t using Susceptible Exposed Infected Recovered Susceptible (SEIRS) model. In the work, a deterministic model using ordinary differential equations (ODEs), and afterward transform it into a stochastic model considering the random changes and the transition probabilities, to investigate the transmission dynamics of TB is developed.

Review of Related Literature

The increasing rate of tuberculosis (TB) cases in many countries of Sub-Saharan Africa over the past decade is largely attributed to the human immunodeficiency virus (HIV) and other emerging infections. Meanwhile, Mathematical models for transmission dynamics of tuberculosis within human populations have been acknowledged in helping policy makers and epidemiologists interpret epidemiological trends and understand the dynamics of disease spread with efficiency of disease prevention and control. A number of stochastic and deterministic mathematical models have analyzed the transmission dynamics of tuberculosis.

Waller, Geser and Anderson (1962) pioneered mathematical modelling for the transmission dynamics of TB. Their model comprises of a system of linear difference equations. They divided the population in three different epidemiological classes namely, the non-infected (susceptible); latent (infected but not infectious) and infectious (infected cases). They expressed the rate of infection as a function of the number of individuals that are infectious. Their study provided many researchers with the basic starting point in Mathematical modelling of the transmission dynamics of TB in communities. Other models which were improvements on this prime approach based on factors like heterogeneity (age), mode of transmission, assumption of nonlinearity and so on has continued to emerge unabatedly over time.

Allen (2007) presented a primer on stochastic epidemic models. In her primer, she provided a brief introduction to the formulation, numerical simulation, and analysis of stochastic epidemic models for a newcomer to the field. A background in modeling with ordinary differential equations (ODEs) was assumed. The ODE epidemic models served as a framework for formulating analogous stochastic models and as a source

of comparison with the stochastic models. The primer was restricted to two types of stochastic settings, continuous-time Markov chains (CTMCs) and stochastic differential equations (SDEs). Some well-known examples were used for illustration such as an SIR epidemic model and a host-vector malaria model.

Kalu and Inyama (2012) developed a Mathematical Model of the Role of Vaccination and Treatment on the Transmission Dynamics of Tuberculosis. In their model, the role of vaccination of new born babies against tuberculosis and treatment of both latently and activity infected individuals in controlling the spread of tuberculosis was mathematically modelled based on the standard SEIR model. The disease - free equilibrium state of the model was established and its stability analyzed using the Routh-Hurwitz theorem. The result of the analysis of the stability of the disease-free equilibrium state shows that tuberculosis can totally be eradicated if effort is made to ensure that the sum of the rate of recovery of the latent class, the rate at which latently infected individuals become actively infected and the rate of natural death , must have a lower bound.

Kipruto, Mung'atu, Ogila, and Mwalili (2015) sought to establish how long under different frameworks will TB disease recede to extinction. In the study, deterministic and stochastic models for the trends of tuberculosis cases over time in Kenya were developed. Susceptible Infective (SI), Susceptible Infective and Recovered (SIR) and Susceptible Exposed Infective and Recovered (SEIR) models were considered. The models were modified in order to fit the data more precisely (age structure and predisposing factors of the incident cases). The SIR and SEIR model with non-linear incidence rates were further looked at and the stability of their solutions were evaluated. The results indicated that both deterministic and stochastic models can give not only an insight but also an integral description of TB transmission dynamics.

Omame, Umana and Inyama (2015) developed a stochastic model and analyzed for the dynamics of Tuberculosis. The model, which was a multidimensional diffusion process, includes susceptible, latent, infected and treated or recovered individuals. The model used was based on a deterministic model. The model was modified by introducing a vaccination parameter and the resulting deterministic model was transformed into a stochastic model and solved with the aid of MATLAB. Real data for the simulation was based on the immunization exercise administered on 41 children at Ahmadu Bello University Teaching Hospital (ABUTH), Zaria between the months of November and December, 2003. From their work, the result showed that increased vaccination rate will lead to Tuberculosis disease reduction and possible extinction.

Umana, Omame and Inyama (2016) formulated a deterministic and stochastic model of the dynamics of drug resistant tuberculosis. In their work, they attempted to develop a mathematical model for the dynamics of drug resistant tuberculosis with the assumption that exposed individuals develop active tuberculosis due to endogenous reactivation and exogenous re-infection. They took the numerical and qualitative analyses of the model and discuss the impact of diagnosis, treatment and health education rates on the different epidemiological compartments. Results from their work showed that the disease-free equilibrium is locally asymptotically stable whenever the effective reproduction number is less than unity and the endemic equilibrium is locally asymptotically stable provided that the effective reproduction number is greater than unity. They concluded from their results that treatment of sensitive TB results in the reduction of Drug Resistant TB as most Drug Resistant TB cases come from failure to properly administer TB drugs. They further suggested that, diagnosis and health education of infectives with sensitive TB are very important in the reduction of new Drug Resistant TB cases because they lead to appropriate treatment.

Mbakoma and Oukouomi (2017), presented a Mathematical analysis of a stochastic tuberculosis model. In their model, they focused to include randomness into the model for dynamics of tuberculosis. Stochasticity to the model was introduced through perturbation of parameters which is a standard method in stochastic population modelling. The well posedness analysis of SDEs included the existence of non-negative solutions as required in the dynamics of population modelling. A detailed stability analysis of results, analytical properties and asymptotical behavior of solutions was also done. The mean reverting process was approximated for one of the variables and the mean and variance of the process was found.

Olabode, Cup and Fisher (2021) formulated a deterministic and stochastic models are proposed to study the transmission dynamics of the Coronavirus Disease 2019 (COVID-19) in Wuhan, China. The deterministic model is formulated by a system of ordinary differential equations (ODEs) that is built upon the classical SEIR framework. The stochastic model is formulated by a continuous-time Markov chain (CTMC) that is derived based on the ODE model with constant parameters. In this work, we will formulate a deterministic model using SEIRS compartment for transmission of TB. The deterministic model will then be transformed to stochastic model to study the transmission dynamics of TB epidemic.

MATERIALS AND METHODS

Assumptions of SEIRS Model

The model formulated is based on the following assumptions:

i. all unvaccinated individuals of the population are in the susceptible class;
ii. susceptible individuals has equal chances to be infected when contact with by the infectious individuals is established;
iii. recovered individuals can be re-infected;
iv. Tuberculosis induced death can occur in the infected class and
v. immigration/emigration of individuals is not taken into consideration.

Based on the assumptions above, the following parameters were use as shown in Table 1.

Table 1: Parameters used in the model and their description

Variable/Parameter	Description
S(t)	Number of susceptible individuals at time
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
ω	Recruitment rate of newborns

θ	Vaccination rate
γ	per capita natural death rate
δ	contact rate
μ	rate at which exposed individuals becomes infected
α	recovery rate for the infectious individuals
ρ	Tuberculosis induced mortality rate
ε	Waning vaccination rate

Deterministic Model of Transmission of TB

The dynamics for the transmission of TB is illustrated by Figure 1.

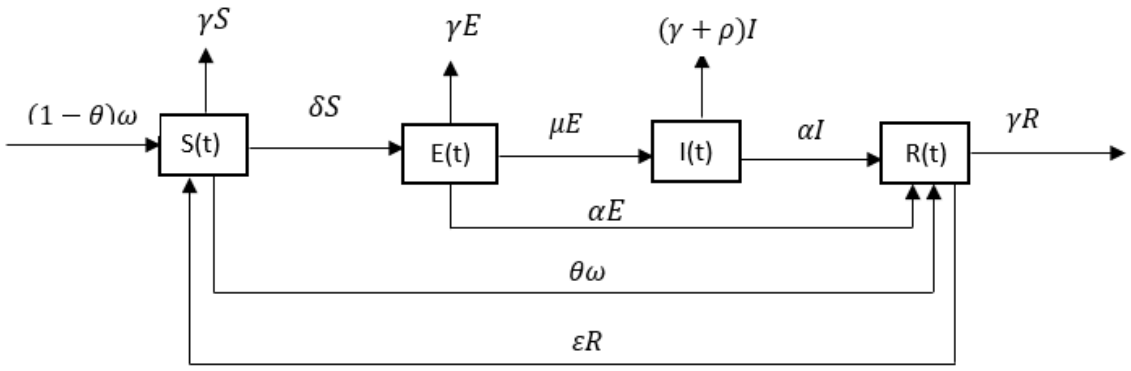


Figure 1**:** Flow diagram for the model

The population under consideration is divided into disjoint classes which change with time t as shown in Figure 1. The disjoint classes include; the Susceptible class (S), the Latent or Exposed class (E), the Infectious class (I), and the Recovered class (R). The population of susceptible individuals (S) is increased by recruitment of newborns who are not vaccinated, into the population at a rate $(1-\theta)\omega$, where ω is the recruitment rate and θ is the proportion of vaccinated newborns. It is further increased by loss of infection acquired immunity of recovered individuals into the population at a rate ε. It decreased by infection, following the effective contacts with the infected individuals at a rate δ, where $\delta = \beta SI$. It is further decreased by vaccination of susceptible at a rate θ. The susceptible population is also decreased by the natural death of susceptible at a rate γ.

Thus,

$$\frac{dS}{dt} = (1-\theta)\omega - (\delta + \theta + \gamma)S + \varepsilon R \qquad (1)$$

The population of Exposed individuals (E) is increased by the infection of susceptible individuals at a rate δ and decreased by progression of Exposed individuals into infectious at a rate μ or natural death at a rate γ. It is further decreased by the recovery of Exposed as a result of treatment and/or vaccination at a rate α.

Hence,

$$\frac{dE}{dt} = \delta S - (\mu + \gamma + \alpha)E \qquad (2)$$

The population of Infectious (I) is increased by the progression of Exposed individuals into the infectious class at a rate μ. It is decreased by the recovery of infectious individuals at a rate α. It is further decreased by natural death at a rate γ or Tuberculosis induced natural death at a rate ρ.

This implies,

$$\frac{dI}{dt} = \mu E - (\alpha + \gamma + \rho)I \qquad (3)$$

The Recovered population (R) is increased by vaccination of newborns. It is further increased by the recovery of Exposed and Infectious individuals at a rate α. It is decreased by natural death at a rate γ or loss of infection acquired immunity at a rate ε.

Hence,

$$\frac{dR}{dt} = \theta\omega + \alpha(E+I) - (\gamma + \varepsilon)R \qquad (4)$$

Based on the above assumptions and observations, the model is given by following deterministic system of non-linear differential equations.

$$\left.\begin{aligned} \frac{dS}{dt} &= (1-\theta)\omega - (\delta + \theta + \gamma)S + \varepsilon R \\ \frac{dE}{dt} &= \delta S - (\mu + \gamma + \alpha)E \\ \frac{dI}{dt} &= \mu E - (\alpha + \gamma + \rho)I \\ \frac{dR}{dt} &= \theta\omega + \alpha(E+I) - (\gamma + \varepsilon)R \end{aligned}\right\} \qquad (5)$$

Basic property of the deterministic model

Invariant PROPERTY

Theorem 3.1: The closed set $D = \left\{(S,E,I,R)\, \epsilon\, R_+^4 : N \leq \frac{\omega}{\gamma}\right\}$ is positively invariant and attracting with respect to the model (3.5).

Proof. Considering the entire population,

$$N = S + E + I + R \qquad (6)$$

Differentiating equation (3.6) with respect to time, yields;

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} \qquad (7)$$

Substituting equation (3.5) into equation (3.7) gives,

$$\begin{aligned} \frac{dN}{dt} &= (1-\theta)\omega - (\delta + \theta + \gamma)S + \varepsilon R + \delta S \\ &\quad - (\mu + \gamma + \alpha)E + \mu E - (\alpha + \gamma + \rho)I \\ &\quad + \theta\omega + \alpha(E+I) - (\gamma + \varepsilon)R \end{aligned}$$

$$\frac{dN}{dt} = \omega - \gamma S - \gamma E - \gamma I - \rho I - \gamma R$$

$$\frac{dN}{dt} = \omega - \gamma(S + E + I + R) - \rho I$$

$$\frac{dN}{dt} = \omega - \gamma N - \rho I$$

In the absence of infection, i.e., $I = 0$,

$\frac{dN}{dt} \leq \omega - \gamma N$

By separation of variable of the differential inequality,

$\frac{dN}{\omega - \gamma N} \leq dt$

Integrating both sides,

$\int \frac{dN}{\omega - \gamma N} \leq \int dt$

$\Longrightarrow -\frac{1}{\gamma}\ln(\omega - \gamma N) \leq t + k$

Multiply both sides by $-\gamma$,

$\Longrightarrow -\gamma \cdot \frac{1}{\gamma}\ln(\omega - \gamma N) \geq -\gamma(t + k)$

$\Longrightarrow \ln(\omega - \gamma N) \geq -\gamma(t + k)$

Taking the exponential of both sides,

$e^{\ln(\omega - \gamma N)} \geq e^{-\gamma t} + e^{-\gamma k}$

$\Longrightarrow \omega - \gamma N \geq e^{-\gamma k} e^{-\gamma t}$

Since the exponential of a constant gives a constant, we have;

$\omega - \gamma N \geq Ae^{-\gamma t}$ where, $A = e^{-\gamma k} =$ constant

Now, for $N(0) = N_0$, it yields;

$A = \omega - \gamma N_0$

$\Longrightarrow \omega - \gamma N \geq (\omega - \gamma N_0)e^{-\gamma t}$

Solving for N,

$-\gamma N \geq -\omega + (\omega - \gamma N_0)e^{-\gamma t}$

Divide both sides by $-\gamma$,

$N \leq \frac{\omega}{\gamma} - \left(\frac{\omega - \gamma N_0}{\gamma}\right)e^{-\gamma t}$

As $t \to \infty$ in the population, $0 \leq N \leq \frac{\omega}{\gamma}$

Therefore, the model for human population from the epidemiological concept in the feasible region, enters the region $D = \left\{(S, E, I, R) \in R_+^4 : N \leq \frac{\omega}{\gamma}\right\}$.

In this case, whenever $N > \frac{\omega}{\gamma}$, then $\frac{dN}{dt} < 0$, which means that the population reduces asymptotically to the carrying capacity. Again, whenever, $N \leq \frac{\omega}{\gamma}$, every solution with initial condition in R_+^4 remains in that region for $t > 0$. Since the domain D is positively invariant, it is enough to investigate the dynamics of the flow generated by the model equations in D. Hence, the model is both mathematically and biologically modelled.

Model Analysis

In analyzing the model, the following were considered:

i. Existence of equilibrium points for non-special case

This represents a stable state in which the disease persists at a relatively constant level within the population over a long period. In the case of many infectious diseases, an endemic equilibrium occurs when the number of new infections is balanced by the number of individuals recovering from the disease. At this equilibrium point, the prevalence of the disease remains stable, neither increasing nor decreasing significantly. This is the at which the differential equations of the system (5) are equal to zero are referred to equilibrium points solutions.

$$\left(\frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt}\right) = 0$$

$$\left.\begin{aligned} (1-\theta)\omega - (\delta + \theta + \gamma)S + \varepsilon R &= 0 \\ \delta S - (\mu + \gamma + \alpha)E &= 0 \\ \mu E - (\alpha + \gamma + \rho)I &= 0 \\ \theta\omega + \alpha(E + I) - (\gamma + \varepsilon)R &= 0 \end{aligned}\right\} \quad (11)$$

Solving for equations of (3.11) above, yields;

$S^* = \frac{(1-\theta)\omega + \varepsilon R}{\delta + \theta + \gamma}$

$E^* = \frac{\delta S}{\mu + \gamma + \alpha}$

$I^* = \frac{\mu E}{\alpha + \gamma + \rho}$

$R^* = \frac{\theta\omega + \alpha(E + I)}{\gamma + \varepsilon}$

Then it is obvious to note that there is no trivial equilibrium point as long as the recruitment parameter ω is not zero. This means that $(S^*, E^*, I^*, R^* \neq (0,0,0,0))$ and the population will not be nonexistent.

ii. Local stability of the disease-free equilibrium

This represents a stable state in which the disease has been eradicated or does not exist within the population. In other words, there are no infected individuals in the population. Disease-free equilibrium is often an important goal in public health efforts to control and eliminate infectious diseases.

In the absence of infection, i.e., $(I^0 = E^0 = R^0)$, the model has a steady state E^0, called the disease-free equilibrium. This statement will reduce the system (11) to

$(1-\theta)\omega - \gamma S^0$

$\Longrightarrow S^0 = \frac{(1-\theta)\omega}{\gamma}$

$S^0 = \frac{(1-\theta)\omega}{\gamma}$ is defined as the carrying capacity of the population. Therefore, the disease- free equilibrium of the model is given by;

$E^0 = (S^0, 0,0,0) = \left(\frac{(1-\theta)\omega}{\gamma}, 0,0,0\right)$.

iii. Basic Reproduction Number R_0

The basic reproduction number R_0 is defined as the average number of secondary infections that can occur when one infected individual is introduced into an entirely susceptible human population (Van den Driessche & Watmough, 2002). R_0 is obtained by using the next generation matrix developed by Van de D. & Watmough (2002). The largest Eigenvalue or spectral radius of FV^{-1} is the R_0.

Where, F and V are $m \times m$ matrices defined as;

$F = \left[\frac{\partial F_i(E^0)}{\partial x_j}\right]$, $v = \left[\frac{\partial V_i(E^0)}{\partial x_j}\right]$

Let $x_{i=}(E, I)$, be the set of all the disease compartments. The model can be written as;

$\frac{dx_i}{dt} = F_i(x) - V_i(x)$ (12)

where, $V_i(x) = [V_i^-(x) - V_i^+(x)]$.

i is the component of disease compartment

$F_i(x)$ is the rate of appearance of new infections in the compartment i

$V_i^-(x)$ represents the rate of transfer of individuals out of component i

$V_i^+(x)$ represents the rate of transfer of individuals into compartment i by all other means.

The above model (3.12) can also be written as; $\frac{dx}{dt} = F(x) - V(x)$

Rewriting the model equations for the disease compartments only, i.e., for (E&I) only, gives;

$\frac{dE}{dt} = \delta S - (\mu + \gamma + \alpha)E$

$\frac{dI}{dt} = \mu E - (\alpha + \gamma + \rho)I$

$F_i = \begin{bmatrix}\beta SI \\ 0\end{bmatrix}$, $V_i^- = \begin{bmatrix}(\mu + \gamma + \alpha)E \\ (\alpha + \gamma + \rho)I\end{bmatrix}$, $V_i^+ = \begin{bmatrix}0 \\ \mu E\end{bmatrix}$

$V_i = V_i^- - V_i^+ = \begin{bmatrix}(\mu + \gamma + \alpha)E \\ (\alpha + \gamma + \rho)I\end{bmatrix} - \begin{bmatrix}0 \\ \mu E\end{bmatrix}$

$$V_i = \begin{bmatrix} (\mu+\gamma+\alpha)E \\ (\alpha+\gamma+\rho)I - \mu E \end{bmatrix}$$

$$F = \begin{pmatrix} 0 & \beta S^0 \\ 0 & 0 \end{pmatrix} \; But\; S^0 = \frac{(1-\theta)\omega}{\gamma}$$

$$\therefore\; F = \begin{pmatrix} 0 & \beta\dfrac{(1-\theta)\omega}{\gamma} \\ 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \mu+\gamma+\alpha & 0 \\ -\mu & \alpha+\gamma+\rho \end{pmatrix}$$

$$V^{-1} = \frac{1}{(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)}\begin{pmatrix} \alpha+\gamma+\rho & 0 \\ \mu & \mu+\gamma+\alpha \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \dfrac{1}{(\mu+\gamma+\alpha)} & 0 \\ \dfrac{\mu}{(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)} & \dfrac{1}{(\alpha+\gamma+\rho)} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} 0 & \beta\dfrac{(1-\theta)\omega}{\gamma} \\ 0 & 0 \end{pmatrix}\begin{pmatrix} \dfrac{1}{(\mu+\gamma+\alpha)} & 0 \\ \dfrac{\mu}{(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)} & \dfrac{1}{(\alpha+\gamma+\rho)} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \dfrac{\mu\beta(1-\theta)\omega}{\gamma(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)} & \dfrac{\beta(1-\theta)\omega}{\gamma(\alpha+\gamma+\rho)} \\ 0 & 0 \end{pmatrix}$$

The eigenvalues are $\lambda_1 = \frac{\mu\beta(1-\theta)\omega}{\gamma(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)}$, $\lambda_2 = 0$

Clearly, the largest eigenvalue or spectral radius is λ_1.

Thus, $R_0 = \frac{\mu\beta(1-\theta)\omega}{\gamma(\mu+\gamma+\alpha)(\alpha+\gamma+\rho)}$.

If $R_0 \leq 1$ then the infection in the community dies out, while if $R_0 > 1$ then there is a unique positive epidemic equilibrium. Using the R_0 obtained, the following are established;

Local asymptotic stability for Disease-free equilibrium

The disease-free equilibrium E^0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$ for both special and non-special cases.

Global Asymptotic stability for disease-free equilibrium

If the reproduction number $R_0 \leq 1$, then, the disease-free equilibrium of the model is globally asymptotically stable.

Stochastic Model Formulation

The stochastic model for the deterministic model in equation (3.5) above is derived using the first modelling procedure developed by Allen et al (2008).

Let S(t), E(t), I(t) and R(t) represent the susceptible, exposed, infected and recovered class respectively. We assume that in a small time interval Δt, S(t), E(t), I(t) and R(t) can change by 1, 0 or -1 where 1 represent the likelihood of the birth of an individual into the compartment, 0 represent non-existence of birth or death in the compartment, while -1 represent the death of an individual in the compartment. The possible changes and their probabilities are shown in Table 2. For example, $[1\ 0\ 0\ 0]^T$ represent the birth of an individual into the susceptible class while $[0\quad -1\quad 1\quad 0]^T$ represent the death of an exposed individual and the birth of infected individuals.

Table 2: The possible changes and their probabilities

Change	Probability	Event
$[1\quad 0\quad 0\quad 0]^T$	$p_1 = (1-\theta)\omega\Delta t$	Susceptible dies naturally
$[-1\quad 0\quad 0\quad 0]^T$	$p_3 = \beta SI\Delta t$	Susceptible becomes Exposed
$[-1\quad 0\quad 0\quad 1]^T$	$p_4 = \theta\omega\Delta t$	Vaccination of susceptible
$[0\quad -1\quad 0\quad 0]^T$	$p_5 = \gamma E\Delta t$	Exposed dies a natural death
$[0\quad -1\quad 1\quad 0]^T$	$p_6 = \mu E\Delta t$	Exposed becomes infectious
$[0\quad -1\quad 0\quad 1]^T$	$p_7 = \alpha E\Delta t$	Exposed recovers
$[0\quad 0\quad -1\quad 0]^T$	$p_8 = (\gamma+\rho)I\Delta t$	Natural death of infectious or death of
$[0\quad 0\quad -1\quad 1]^T$	$p_9 = \alpha I\Delta t$	Infectious as a result of infection
$[0\quad 0\quad 0\quad -1]^T$	$p_{10} = \gamma R\Delta t$	Natural death of recovered
$[1\quad 0\quad 0\quad -1]^T$	$p_{11} = \varepsilon R\Delta t$	Recovered becomes susceptible

From the first modelling procedure by Allen et al (2008), the stochastic model equations are given by;

$$\left.\begin{aligned} d\vec{X} &= \vec{f}\big(t,\vec{X}(t)\big)dt + B\big(t,\vec{X}(t)\big)d\vec{W}(t) \\ \vec{X}(0) &= [X_1(0),\ X_2(0),\ X_3(0),\ X_4(0)]^T \end{aligned}\right\} \qquad (4.1)$$

Where B = $V^{1/2}$, $\vec{W}$(t) is a vector of Wiener processes and $\vec{f}$ is a drift vector defined by;

$$\vec{f} = \sum_{j=1}^{11} p_j\vec{\lambda}_j$$

Where $\vec{\lambda}_j$ and p_j are the random changes and the transition probabilities respectively.

$$\vec{f} = p_1\vec{\lambda}_1 + p_2\vec{\lambda}_2 + p_3\vec{\lambda}_3 + p_4\vec{\lambda}_4 + p_5\vec{\lambda}_5 + p_6\vec{\lambda}_6 + p_7\vec{\lambda}_7 + p_8\vec{\lambda}_8 + p_9\vec{\lambda}_9 + p_{10}\vec{\lambda}_{10} + p_{11}\vec{\lambda}_{11}$$

$$\vec{f} = p_1\begin{pmatrix}1\\0\\0\\0\end{pmatrix} + p_2\begin{pmatrix}-1\\0\\0\\0\end{pmatrix} + p_3\begin{pmatrix}-1\\1\\0\\0\end{pmatrix} + p_4\begin{pmatrix}-1\\0\\0\\1\end{pmatrix} + p_5\begin{pmatrix}0\\-1\\0\\0\end{pmatrix} + p_6\begin{pmatrix}0\\-1\\1\\0\end{pmatrix} + p_7\begin{pmatrix}0\\-1\\0\\1\end{pmatrix} + p_8\begin{pmatrix}0\\0\\-1\\0\end{pmatrix} + p_9\begin{pmatrix}0\\0\\-1\\1\end{pmatrix} + p_{10}\begin{pmatrix}0\\0\\0\\-1\end{pmatrix}$$

$$+\ p_{11}\begin{pmatrix}1\\0\\0\\-1\end{pmatrix}$$

$$\vec{f} = (1-\theta)\omega\begin{pmatrix}1\\0\\0\\0\end{pmatrix} + \gamma S\begin{pmatrix}-1\\0\\0\\0\end{pmatrix} + \delta S\begin{pmatrix}-1\\1\\0\\0\end{pmatrix} + \theta\omega\begin{pmatrix}-1\\0\\0\\1\end{pmatrix} + \gamma E\begin{pmatrix}0\\-1\\0\\0\end{pmatrix} + \mu E\begin{pmatrix}0\\-1\\1\\0\end{pmatrix} + \alpha E\begin{pmatrix}0\\-1\\0\\1\end{pmatrix} + (\gamma+\rho)I\begin{pmatrix}0\\0\\-1\\0\end{pmatrix} + \alpha I\begin{pmatrix}0\\0\\-1\\1\end{pmatrix} + \gamma R\begin{pmatrix}0\\0\\0\\-1\end{pmatrix} + \varepsilon R\begin{pmatrix}1\\0\\0\\-1\end{pmatrix}$$

Hence, the drift vector $\vec{f}$ of order 4×1 is;

$$\vec{f} = \begin{bmatrix}(1-\theta)\omega - \gamma S - \delta S - \theta\omega + \varepsilon R\\ \delta S - (\gamma+\mu+\alpha)E\\ \mu E - (\alpha+\gamma+\rho)I\\ \theta\omega + \alpha(E+I) - (\gamma+\varepsilon)R\end{bmatrix} \quad (13)$$

The covariance matrix V is defined by;

$$\mathrm{V} = \sum_{j=1}^{11} p_j \vec{\lambda}_j \left(\vec{\lambda}_j\right)^T$$

$$\mathrm{V} = p_1\begin{pmatrix}1\\0\\0\\0\end{pmatrix}[1\ \ 0\ \ 0\ \ 0] + p_2\begin{pmatrix}-1\\0\\0\\0\end{pmatrix}[-1\ \ 0\ \ 0\ \ 0] + p_3\begin{pmatrix}-1\\1\\0\\0\end{pmatrix}[-1\ \ 1\ \ 0\ \ 0] + p_4\begin{pmatrix}-1\\0\\0\\1\end{pmatrix}[-1\ \ 0\ \ 0\ \ 1] + p_5\begin{pmatrix}0\\-1\\0\\0\end{pmatrix}[0\ \ -1\ \ 0\ \ 0] + p_6\begin{pmatrix}0\\-1\\1\\0\end{pmatrix}[0\ \ -1\ \ 1\ \ 0] + p_7\begin{pmatrix}0\\-1\\0\\1\end{pmatrix}[0\ \ -1\ \ 0\ \ 1] + p_8\begin{pmatrix}0\\0\\-1\\0\end{pmatrix}[0\ \ 0\ \ -1\ \ 0] + p_9\begin{pmatrix}0\\0\\-1\\1\end{pmatrix}[0\ \ 0\ \ -1\ \ 1] + p_{10}\begin{pmatrix}0\\0\\0\\-1\end{pmatrix}[0\ \ 0\ \ 0\ \ -1] + p_{11}\begin{pmatrix}1\\0\\0\\-1\end{pmatrix}[1\ \ 0\ \ 0\ \ -1]$$

$$V = (1-\theta)\omega\begin{pmatrix}1\\0\\0\\0\end{pmatrix}[1\ \ 0\ \ 0\ \ 0] + \gamma S\begin{pmatrix}-1\\0\\0\\0\end{pmatrix}[-1\ \ 0\ \ 0\ \ 0] + \delta S\begin{pmatrix}-1\\1\\0\\0\end{pmatrix}[-1\ \ 1\ \ 0\ \ 0] + \theta\omega\begin{pmatrix}-1\\0\\0\\1\end{pmatrix}[-1\ \ 0\ \ 0\ \ 1] + \gamma E\begin{pmatrix}0\\-1\\0\\0\end{pmatrix}[0\ \ -1\ \ 0\ \ 0] + \mu E\begin{pmatrix}0\\-1\\1\\0\end{pmatrix}[0\ \ -1\ \ 1\ \ 0] + \alpha E\begin{pmatrix}0\\-1\\0\\1\end{pmatrix}[0\ \ -1\ \ 0\ \ 1] + (\gamma+\rho)I\begin{pmatrix}0\\0\\-1\\0\end{pmatrix}[0\ \ 0\ \ -1\ \ 0] + \alpha I\begin{pmatrix}0\\0\\-1\\1\end{pmatrix}[0\ \ 0\ \ -1\ \ 1] + \gamma R\begin{pmatrix}0\\0\\0\\-1\end{pmatrix}[0\ \ 0\ \ 0\ \ -1] + \varepsilon R\begin{pmatrix}1\\0\\0\\-1\end{pmatrix}[1\ \ 0\ \ 0\ \ -1]$$

Multiplying the covariance matrix, it yields;

$$\mathrm{V} = \begin{bmatrix}(1-\theta)\omega & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}\gamma S & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}\delta S & -\delta S & 0 & 0\\ -\delta S & \delta S & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}\theta\omega & 0 & 0 & -\theta\omega\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ -\theta\omega & 0 & 0 & \theta\omega\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & \gamma E & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & \mu E & -\mu E & 0\\ 0 & -\mu E & \mu E & O\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & \alpha E & 0 & -\alpha E\\ 0 & 0 & 0 & 0\\ 0 & -\alpha E & 0 & \alpha E\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & (\gamma+\rho)I & 0\\ 0 & 0 & 0 & 0\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & \alpha I & -\alpha I\\ 0 & 0 & -\alpha I & \alpha I\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & \gamma R\end{bmatrix} + \begin{bmatrix}\varepsilon R & 0 & 0 & -\varepsilon R\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ -\varepsilon R & 0 & 0 & \varepsilon R\end{bmatrix}$$

Hence, the covariance matrix V of order 4×4 is;

$$V = \begin{bmatrix}(1-\theta)\omega + \gamma S + \delta S + \theta\omega + \varepsilon R & -\delta S & 0 & -\theta\omega - \varepsilon R\\ -\delta S & \delta S + \gamma E + \mu E + \alpha E & -\mu E & -\alpha E\\ 0 & -\mu E & \mu E + (\gamma+\rho)I + \alpha I & -\alpha I\\ -\theta\omega - \varepsilon R & -\alpha E & -\alpha I & \theta\omega + \alpha E + \alpha I + (\gamma+\varepsilon)R\end{bmatrix}$$

The resulting SDE is therefore

$$\left.\begin{aligned} d\vec{X} &= \vec{f}\left(t, \vec{X}(t)\right)dt + V\left(t, \vec{X}(t)\right)d\vec{W}(t)\\ \vec{X}(0) &= [X_1(0),\ X_2(0),\ X_3(0),\ X_4(0)]^T\end{aligned}\right\}$$

Numerical Simulation

The Milstein numerical method for of SDEs was used for the simulation. The method is a numerical scheme used for approximating the solutions of stochastic differential equations (SDEs). It is designed for simulating systems that involve both deterministic and stochastic components. It is a more accurate and refined method compared to Euler-Maruyama, particularly when dealing with SDEs that have strong or nonlinear stochastic terms. It is an extension of the Euler-Maruyama method. It introduces a correction term for the stochastic part. The method can be implemented through the following steps:

i. Choose a time step Δt and divide the interval [0, T] into smaller time steps: 0 = t0 < t1 < t2 < ... < tn = T.
ii. Initialize the process at t0 with an initial value X_0
iii. For each time step i from 1 to n, do the following:
   a. Calculate the deterministic drift term $f(X(t_{i-1}), t_{i-1})$
   b. Calculate the stochastic diffusion term $V(X(t_{i-1}), t_{i-1})$
   c. Generate a random increment $\Delta W(t_{i-1}) \sim N(0, \Delta t)$ where $N(0, \Delta t)$ represents a normal distribution with mean 0 and variance Δt.
   d. Calculate the correction term $\frac{\partial V}{\partial X} * V(X(t_{i-1}), t_{i-1}) * \Delta W(t_{i-1})^2 - \Delta t$
   e. Update the process value at ti:

$$X(t_i) = X(t_{i-1}) + f(X(t_{i-1}), t_{i-1}) * \Delta t + V(X(t_{i-1}), t_{i-1}) * \Delta W(t_{i-1}) + \frac{\partial V}{\partial X} * V(X(t_{i-1}), t_{i-1}) * \Delta W(t_{i-1})^2 - \Delta t$$

The correction term $\frac{\partial V}{\partial X} * V(X(t_{i-1}), t_{i-1}) * \Delta W(t_{i-1})^2 - \Delta t$ accounts for the second-order expansion of the stochastic term, resulting in increased accuracy compared to the Euler-Maruyama method.

Although the Milstein method is known to improve accuracy, especially for SDEs with nonlinear or strong stochastic terms, it is however computationally more expensive than the Euler-Maruyama method due to the additional calculations involved in estimating the correction term. The choice between the Euler-Maruyama and Milstein methods depends on the specific characteristics of the SDE and the desired level of accuracy in the simulation.

The algorithm for the method is as follows:

Algorithm for the Milstine Method

Function MilsteinMethod(a, b, X0, T, dt):

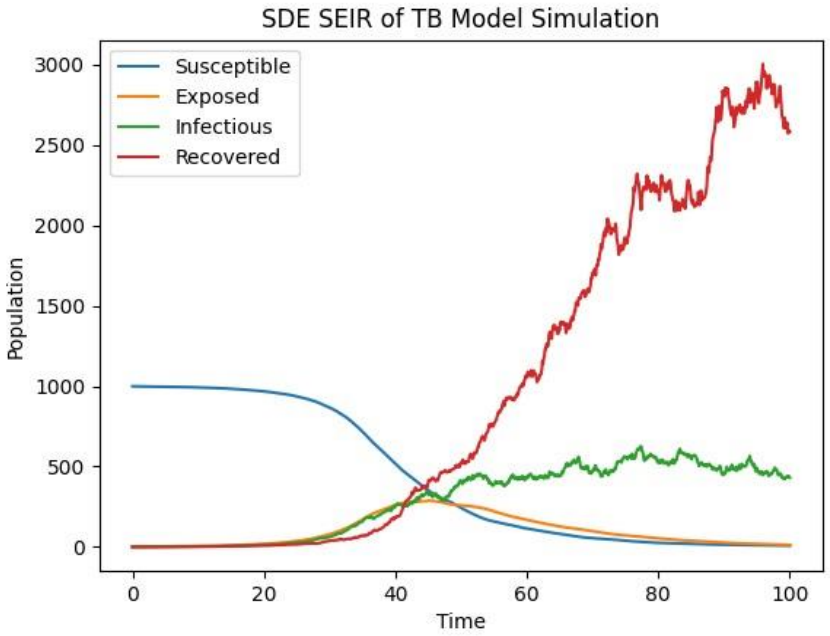
1. Input the following:
   $f(t, X(t))$- Drift term function
   $V(t, X(t))$ - Diffusion term function
   X_0- Initial value of the process
   T- Total simulation time
   dt- Time step size
2. Determine the number of time steps
   $num_{steps} = int(\frac{T}{dt})$
3. Initialize arrays to store the time and process values
   times = [0.0] * (num_steps + 1)
   X = [0.0] * (num_steps + 1)
4. Set initial values
   times[0] = 0.0
   X[0] = X0
5. Perform the Milstein simulation

for i in range(1, num_steps + 1):

   a. Current time
      t = i * dt
      times[i] = t
   b. Calculate the deterministic and stochastic terms
      drift_term = $f(t, X(t)$
      diffusion_term = $V(t, X(t))$-
   c. Generate a random increment (sampled from N(0, dt))
   d. $dW = sqrt(dt) * rand\_normal(\ )$
      Calculate the correction term due to second-order expansion
      correction_term = $0.5 * f(t, X(t_{i-1}) * V(t, X(t_{i-1}) * dW^2 - dt$
      Update the process value using the Milstein scheme
      $X_i = X_{i-1} + drift\_term * dt + diffusion\_term * dW + correction\_term$

6. return times, X

The algorithm was implemented in Python programing language. The following values were used for the parameters



Deterministic and stochastic models for the transmission dynamics of tuberculosis were studied. A deterministic mathematical model for the transmission dynamics was formulated. An equivalent stochastic model resulting in a system stochastic differential equations was derived. The population under consideration was divided into four compartments namely, the Susceptible, the Exposed, the Infected and the Recovered compartment leading to a typical SEIR model. The existence of equilibrium points for non-special case, local stability of the disease free -equilibrium and reproduction number R_0 were determined It was observed that for $R_0 < 1$, the disease free-equilibrium is locally stable and unstable if $R_0 > 1$ for both special and non-special cases. In transforming the deterministic model to the equivalent SDE model, both the drift vector and the co-variance matrix for the SDE were determined resulting to a system of SDE.

CONCLUSION

This work has shown that the transmission of tuberculosis can be studied through the use of mathematical model. The work further demonstrated that an equivalent stochastic differential equation model for the dynamics of the remission of tuberculosis can be formulated. The procedure proposed by Allen *et.al.* (2008) can be adequately used to formulate a stochastic model for transmission of diseases from its equivalent deterministic model. This work can be used in interactive workshops with health planners and other stakeholders in TB control so that participants could gain a better understanding of how BCG could be used to control the disease.

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