MATHEMATICAL MODEL OF GUILLAIN-BARRE SYNDROME WITH HOLLING TYPE II FUNCTIONAL RESPONSE

by Universitas Internasional Semen Indonesia

Submission date: 17-Mar-2022 08:19PM (UTC-0500)
Submission ID: 1786750487
File name: Artikel_Math_Model_GBs.pdf (381.13K)
Word count: 4431
Character count: 21804

Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2020, 2020:88
https://doi.org/10.28919/cmbn/4805
ISSN: 2052-2541

MATHEMATICAL MODEL OF GUILLAIN-BARRE SYNDROME WITH HOLLING TYPE II FUNCTIONAL RESPONSE

LISA RISFANA SARI[1], PUJI ANDAYANI[1,*], AGUS SURYANTO[2], ISNANI DARTI[2]

[1]Universitas Internasional Semen Indonesia, Gresik City 61122, Indonesia

[2]Department of Mathematics, Brawijaya University, Malang City 65145, Indonesia

Abstract. This paper studies the dynamics of the Guillain-Barre syndrome model (GB's) with Holling type II functional responses. Autoimmune disorders occur when the immune system is damaged where the immune system attacks tissues and organs. It was reported that a viral infection can be related to GB's. A mathematical model about the mechanism of autoimmunity in GB's was studied. The immune response used is assumed to follow the Holling Type II functional response. The dynamics of the model are analyzed to see system behavior. The GB's model has three equilibrium points in its conditions. The equilibrium represents health, autoimmune disease, and complications. The local stability for each equilibrium point is analyzed with certain stability conditions. Numerical simulations are also performed to observe the dynamic behavior of the model. The results of the model analysis show the factors that determine the outcome of the disease.

Keywords: dynamical behavior; functional response; Guillain-Barre syndrome; Holling tipe II; stability.

2010 AMS Subject Classification: 37N25, 34A34, 34C40.

1. INTRODUCTION

The immune system is a convoluted structure of cells and organs that defend the body. The main chore of the immune system is to identify and respond to foreign agents to protect the

*Corresponding author

E-mail address: puji.andayani@uisi.ac.id

Received June 26, 2020

body against infection. Most of the immune cells are eliminated giving a self-tolerant immune system that reacts to self-tissues [18]. This mechanism is carried out to protect the body itself. When this control mechanism is inadequate, an impaired immune function can threaten the body [17]. Recently, a scientist has proven that autoimmunity is a natural phenomenon that appears in every normal individual, with self-reactive antibodies and autoimmune cells. Previously, the problem of the immune system reactivity to autoimmunity antigens was considered a distorted response. The anti-self response that results in the process of generating an antigen response to a way to save a damaged self, but autoimmune disease only occurs if autoimmunity persists [12]. According to Rose, there are around 80 types of autoimmune diseases in the world. Autoimmune affects any site in the body so that clinical explanations vary [17]. Genetic and environmental factors become to trigger the spread of autoimmune diseases. The autoimmune diseases are not common, because they are the third most common disease category in industrialized countries, after the first and second are cardiovascular disease and cancer [13].

Guillain-Barre Syndrome (GB's) is a type of autoimmune disease that occurs when the body's immune system mistakenly attacks parts of the nervous system. According to the CDC [20], GB's can also be caused by the Zika virus which attacks humans of a certain age. This disease can also induce nerve inflammation which causes tingling, muscle weakness, paralysis, and other symptoms. It often starts with tingling and weakness starting in the legs and feet and spread to the upper body and arms (US Medical Library, 2017). People with GB's will experience the most significant weakness usually within two or four weeks after symptoms begin. GB's occur in several forms with the main types being inflammatory acute inflammatory poly radiculo neuropathy (AIDP) inflammation, Miller Fisher's syndrome (MFS), acute motor axonal neuropathy (AMAN), and acute motor-sensory axon neuropathy (AMSAN) [16].

GB's is not exactly known why, but are generally triggered by infection depending on the infection outbreak. Several events have been reported that could potentially trigger GB's. Relationships with infections include cytomegalovirus, Epstein-Barr virus, influenza A, Mycoplasma pneumonia, Hemophilus influenza, hepatitis (A, B, and E) and Zika virus (ZIKV) [21]. It has also been reported that ZIKV infection develops into neurological diseases such as microcephaly in infants and Guillain-Barre syndrome (GB's) in adults [3]. Based on Arnaud

Fontanet's study there is a possible relationship between the Zika virus and Guillain-Barre syndrome. At present, there has been a proven incidence of GB's in 24 cases per 100,000 people infected with the Zika virus [19].

Recently an important discussion which gave rise to the hypothesis that "molecular mimicry" as a causative cause of GB's. Molecular mimicry is the concept of antigens from microorganisms that are very similar to self-antigens so that the compilation of infections occurs autoimmunity is also induced [12]. Observation in GB's patients, in response to molecular mimicry that shows received antibodies. Molecular mimicry can be associated with GB's related to Zika virus because antibodies are found in 31% of patients [7].

The problem of population dynamics in autoimmune diseases has been in great demand. Iwami et al. [14] describe the dynamics of autoimmune diseases that are affected by the transition, flare, and dormancy, through mathematical modeling. In 2009, Iwami et al. [14] researched that viruses with molecular mimicry can be beneficial and also dangerous for autoimmune diseases. Elettreby et al. [11] also introduced a simple mathematical model for the stability of the Guillain-Barre Syndrome (GB's) model. The dynamics of the disease due to autoimmune are described in 4 cases. In the first two cases, the immune response is assumed to be linear, whereas in the other two cases it is assumed to be in the form of Holling type III.

This paper discusses the modification of the GB's model with cross-reactive immunity as an effort to overcome molecular mimicry as a change in virus-induced autoimmunity in GB's. In the model, we modified using the Holling type II [14] response function. We show the impact of molecular mimicry on the disease, taking into account the development of GB's.

2. Mathematical Model

In this article, we consider the GB's model presented by [11]. The GB's model is a nonlinear differential equation with two variables, which are, target cells (healthy cells) (x) and immune cells (y).

$$\begin{aligned} \frac{dx(t)}{dt} &= G(x(t)) - \beta_1 x(t) y(t) \\ \frac{dy(t)}{dt} &= F(x(t), y(t)) - \mu_2 y(t). \end{aligned} \tag{1}$$

where $G(x(t))$ is the growth function of the target cell population and $F(x(t), y(t))$ is the personal immune response function. Parameter β_1 are the efficiency of the injury process and contains the rates of immune cells to find target cells and immune cells succeed in attacking target cells. Thus β_1 x(t)y(t) represents the damage that occurred in the target cells due to their interaction with the immune system. Parameter μ_2 describes the death rate of the immune cells. In model (1), the growth rate of the target cell is assumed to be a linear growth function and logistic growth function as follows.

$$G_1(x(t)) = a - \mu_1 x(t) \tag{2}$$

$$G_2(x(t)) = a - \mu_1 x(t) + px(t)(1 - \frac{x(t)}{L}) \tag{3}$$

where a is the rate of producing new cells of the target cells, μ_1 is the natural death rate of the target cells, p is the maximum proliferation rate of the target cells and L is the target cell population density at which proliferation shuts off. The personal immune response function in the model (2) is given by the following function.

$$F_1(x(t), y(t)) = rx(t)y(t) \tag{4}$$

$$F_2(x(t), y(t)) = \frac{kx(t)^2 y(t)^2}{m^2 + x(t)^2 y(t)^2} \tag{5}$$

where r is the average magnitude of the immune activation response per-time, k is the maximum proliferation rate of immune cells created by antigen-presenting cells (APCs), and m is the number of broken cells at which the proliferation of immune cells is half of the maximum k. In ecology term, function (4) and (5) is called functional response, more precisely function (4) and (5) is called the Holling type I and III functional response respectively. In this model, the defining two types of functional response is based on the assumption that different people may have different immune response function. It depends on the personal's condition. Immunologically, antigen-presenting cells (APCs) hardly induce immune cells when only a few antigens exist. In general, the proliferation ability of immune cells is saturated for a sufficiently large amount of antigens [4] [5] [6] [1]. By considering the molecular mimicry mechanism, this implies that the proliferation of immune response is dependent on the total number of self and viral antigens.

As in one of the models in [15], the personal immune response function is regarded respectively as functional response Holling types II as follows.

$$F(D(t),V(t)) = \frac{k(D(t)+V(t))}{m+(D(t)+V(t))}, \tag{6}$$

where D and V signify the number of broken cells caused by the concentration of self-antigen, and viral agent with mimicries molecular.

The molecular mimicry mechanism has not been included in the model (1). Therefore, we propose the following model.

$$\begin{aligned} \frac{dx(t)}{dt} &= a-\mu_1 x(t)+px(t)(1-\frac{x(t)}{L}-\beta_1 x(t)y(t)) \\ \frac{dy(t)}{dt} &= \frac{k(x(t)+z(t))y(t)}{m+(x(t)+z(t))y(t)}-\mu_2 y(t) \\ \frac{dz(t)}{dt} &= (h-\mu_3-\beta_2 y(t))z(t). \end{aligned} \tag{7}$$

In this model, we assume the viral agent (z) grow with Malthusian growth rate h, decay at a rate μ_3 and is eliminated by the immune response at a rate β_2 as considered in [14]. The immune response function is assumed following the Holling types II functional response. These assumptions are dictated by our goal to simplify the mathematical analysis of the model to get some insight into the immune system and molecular mimicry mechanism in the progression of the disease symptoms.

3. Mathematical Analysis

The model (7) has three possible equilibria that represent the healthy state, the GB's state, and the GB's(autoimmune) complication state. The stability of equilibria is observed by the eigenvalues of the Jacobian matrix of the system (7) at the equilibrium point, $J(x^*,y^*,z^*)$. The eigenvalues are found by solving the characteristic equation of the matrix.

$$J(x^*,y^*,z^*) = \begin{bmatrix} J_1 & -\beta_1 x^* & 0 \\ J_2 & J_3 & J_2 \\ 0 & -\beta_2 y^* & h-\mu_3-\beta_2 y^* \end{bmatrix} \tag{8}$$

where,

$J_1 = -\mu_1 + p(1-x^*/L) - px^*/L - \beta_1 y^*$,

$$J_2 = \frac{ky^*}{m+(x^*+z^*)y^*} - \frac{k(x^*+z^*)y^{*2}}{(m+(x^*+z^*)y^*)^2},$$
$$J_3 = \frac{k(x^*+z^*)}{m+(x^*+z^*)y^*} - \frac{k(x^*+z^*)y^{*2}}{(m+(x^*+z^*)y^*)^2}.$$

3.1. Healthy State Equilibria (E_h)**.** The healthy state equilibria of system (7) describes condition where the immune cells and virus population are extinct. The system always has healthy state equilibria of the form $E_h = (\Lambda_1, 0, 0)$ where

$$\Lambda_1 = \frac{1}{2}\frac{L(p-\mu_1) + \sqrt{L^2(p-\mu_1)^2 + 4paL}}{p}. \tag{9}$$

The characteristic equation of Jacobian matrix at E_h is

$$P(\lambda) = \frac{(-\lambda m - \mu_2 m + k\Lambda_1)(-\lambda + h + \mu_3)(-\lambda L - 2p\Lambda_1 + pL - \mu_1 L)}{mL} \tag{10}$$

By solving equation (10), we have eigenvalues of $J(E_h)$ are

$$\lambda_1 = \frac{k\Lambda_1 - \mu_2 m}{m}, \tag{11}$$

$$\lambda_2 = h - \mu_3, \tag{12}$$

$$\lambda_3 = -\frac{2p\Lambda_1 - pL + \mu_1 L}{L} \tag{13}$$

Then the healthy state equilibria E_h is locally asymptotically stable under this following conditions.

$$k\Lambda_1 - \mu_2 m < 0, \tag{14}$$

$$h - \mu_3 < 0, \tag{15}$$

$$2p\Lambda_1 - pL + \mu_1 L > 0. \tag{16}$$

The simple calculation shows that the condition $2p\Lambda_1 - pL + \mu_1 L >$ is always met. Hence, E_h is locally asymptotically stable if satisfy the conditions $k\Lambda_1 - \mu_2 m < 0$ and $h - \mu_3 < 0$.

3.2. GBS (Autoimmune) State Equilibria (E_a)**.** The GB's (autoimmune) state of system (7) represent the condition where the virus population is extinct while the immune cells remain exist in the body. It shows persistent autoimmunity. The GB's (autoimmune) state equilibria is

given below,

$$E_a = (\Lambda_3, \frac{k\Lambda_3 - \mu_2 m}{\mu_2 \Lambda_3}, 0), \tag{17}$$

where,

(18)

$$\Lambda_3 = -\frac{1}{2}\frac{1}{p\mu_2}[L(-p\mu_2 + \beta_1 k + \mu_1\mu_2) - \sqrt{L^2(-p\mu_2 + \beta_1 k + \mu_1\mu_2)^2 + 4paL\mu_2^2 + 4pmL\mu_2\beta_1}].$$

The equilibrium point E_a exist if only if $k\Lambda_3 - \mu_2 m > 0$.

The characteristic equation of Jacobian matrix at E_a is

$$\lambda^3 + B_1\lambda^2 + B_2\lambda + B_3 = 0 \tag{19}$$

where,

$B_1 = \frac{(q_3)q_4}{k\Lambda_3} + \frac{Lq_1(k(\beta_1+\beta_2)+\mu_2^2) + \mu_2 q_2 q_4}{k\Lambda_3\mu_2 L}$,

$B_2 = -\frac{1}{k\Lambda_3^2\mu_2^2}(\mu_2 q_4(q_2 q_5 + L(2pq_1\beta_2 + \mu_2 q_1\beta_1)) + Lq_1{}^2(\mu_2{}^2 + k\beta_1) + \mu_2^3\Lambda_3)$,

$B_3 = \frac{q_1 q_5(\mu_2 q_2 + \beta_1 kL)}{\Lambda_3{}^2\mu_2 kL}$,

with,

$q_1 = k\Lambda_3 - \mu_2 m$,

$q_2 = 2p\Lambda_3 - pL + \mu_1 L$,

$q_3 = -(h - \mu_3)$,

$q_4 = \mu_2 m + q_1$,

$q_5 = \Lambda_3\mu_2 q_3 + \beta_2 q_1$..

Using Routh-Hurwitz criterion, we found that E_a is locally asymptotically stable if only if $B_1 > 0, B_3 > 0$, and $B_1B_2 - B_3 > 0$. This condition is satisfied if only if $q_1 > 0, q_2 > 0$, and $q_3 > 0$.

3.3. GB's Complication State Equilibria E_c. The GB's complication state depicts the condition where the immune cells and virus population exist in the body. This situation indicate persistent autoimmunity and infection. The GB's complication state equilibrium is

$$E_c = \left(\Lambda_2, \frac{h-\mu_3}{\beta_2}, \frac{m\mu_2\beta_2}{k\beta_2 - \mu_2(h-\mu_3)} - \Lambda_2\right). \tag{20}$$

where,

(21)
$$\Lambda_2 = -\frac{1}{2p\beta_2}\left[L(\mu_1\beta_2 - p\beta_2 + h\beta_1 - \mu_3\beta_1) - \sqrt{L^2(\mu_1\beta_2 - p\beta_2 + h\beta_1 - \mu_3\beta_1)^2 + 4paL\beta_2}\right].$$

The equilibrium point E_c exist if only if

(22)
$$h - \mu_3 > 0$$

(23)
$$k\beta_2 - \mu_2(h - \mu_3) > 0$$

(24)
$$\frac{m\mu_2\beta_2}{k\beta_2 - \mu_2(h-\mu_3)} - \Lambda_2 > 0$$

The characteristic equation of Jacobian matrix at E_c is

(25)
$$\lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0$$

where,
$A_1 = \frac{kg_2\beta_2 + Lg_1(k\beta_1 + \mu_2^2)}{kL\beta_2}$,
$A_2 = \frac{g_1(mg_2\beta_2^2\mu_2^2 + (\beta_1 - \beta_2)g_3^2L\Lambda_2 + L(mg_1\beta_1\beta_2\mu_2^2 + mg_3\beta_2^2\mu_2))}{kmL\beta_2^3}$,
$A_3 = \frac{g_1g_3(g_4\beta_2 + g_1\Lambda_2\mu_2)(g_2\beta_2 + g_1L\beta_1)}{kmL\beta_2^3}$.
With,
$g_1 = h - \mu_3$,
$g_2 = 2p\Lambda_2 - pL + L\mu_1$,
$g_3 = k\beta_2 - g_1\mu_2$,
$g_4 = -(k\Lambda_2 - m\mu_2)$.

Using Routh-Hurwitz criteria, we found that E_c is locally asymptotically stable if only if $A_1 > 0, A_3 > 0$, and $A_1A_2 - A_3 > 0$. This condition is satisfied if only if $g_1 > 0, g_2 > 0, g_3 > 0, g_4 > 0$ and $\beta_1 - \beta_2 > 0$.

In general, it can be compiled the sufficient conditions to guarantee the existence and stability of each equilibrium point in Table (1).

TABLE 1. Existence and Local Stability Condition of the Equilibrium

Eq.Point	Existence	Stability
E_h	always exists	$h-\mu_3<0$
		$k\Lambda_1-m\mu_2<0$
E_a	$k\Lambda_3-m\mu_2>0$	$h-\mu_3<0$
		$2\Lambda_3-L>0$
E_c	$h-\mu_3>0$	$2p\Lambda_2-pL+L\mu_1>0$
	$k\beta_2-\mu_2(h-\mu_3)>0$	$k\Lambda_2-m\mu_2<0$
	$\frac{m\beta_2\mu_2}{k\beta_2\mu_2(h-\mu_3)}-\Lambda_2>0$	$\beta_1-\beta_2>0$

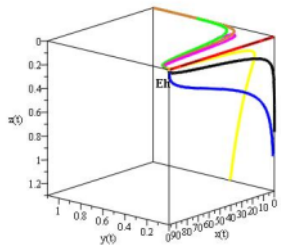
4. RESULTS AND DISCUSSION

In order to study the immune system and molecular mimicry mechanism in the progression of the disease symptoms, we analyze how the maximum value of proliferation rate of the target cells (k) and the rates of immune cells find target cells and the rate of immune cells which success attack the target cells (β_1) affect the model dynamical behavior [2]. The analysis is done by numerical simulation. Numerical simulations are performed using Maple. There are seven initial values used: (i) For normal condition IV_1, $(x(0)=1,y(0)=0,z(0)=0)$, (ii) for mild infection IV_2, $(x(0)=1.2,y(0)=0,z(0)=1)$, (iii) for severe infection IV_3, $(x(0)=0,y(0)=0,z(0)=0.8)$, (iv) for mild autoimmune IV_4, $(x(0)=0.5,y(0)=0.7,z(0)=0)$, (v) for severe autoimmune IV_5, $(x(0)=0,y(0)=1.11,z(0)=0)$, (vi) for mild complication IV_6, $(x(0)=0.3,y(0)=0.6,z(0)=0.2)$,(vii) for severe complication IV_7, $(x(0)=0,y(0)=0.4,z(0)=1.3)$.

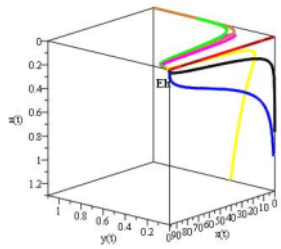
There are two cases observed, (i) when the virus cannot maintain its replication $(h-\mu_3<0)$ and (ii) when the virus can maintain its replication $(h-\mu_3>0)$. Under condition $(h-\mu_3<0)$, we found a critical rate of immune cells's proliferation (k^*), which above the endemic equilibria $E(a)$ is exists, when the other endemic equilibria is not exist.

$$k^*=\frac{2mp\mu-2}{L(-\mu_1+p)+\sqrt{L^2(-\mu_1+p)^2+4paL}} \tag{26}$$

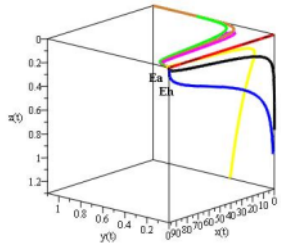
Using fixed value for parameter $a, \mu_1, p, L, m, \mu_2, \beta_1, \beta_2, h, \mu_3$ and different value for k, the numerical simulation results are shown in Figure (1).



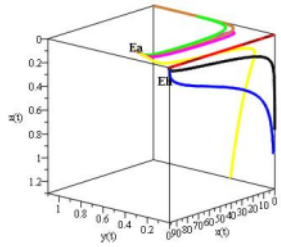
(A) $k = 0.1$



(B) $k = k^* = 0.186$



(C) $k = 0.186$, $E_a = (96.7; 1.10^{-10}; 0)$



(D) $k = 0.5, E_a = (81.24; 0.46; 0)$

FIGURE 1. Simulation with $a = 0.1; \mu_1 = 0.1; p = 3; L = 100; m = 30; \mu_2 = 0.6; \beta_2 = 1.5; \beta_1 = 1; h = 0.5; \mu_3 = 1.3$, $E_h = (96.70; 0; 0)$.

Figure (1a) dan (1b) presents the tolerance of the immune response of equilibrium point E_h is locally asymptotically stable. When a healthy cell (target cell) attacked the key effector cell, the immune cells cannot be activated and the patient does not develop autoimmune disease. Based on Figure (1c) dan (1d) we can see that the maximum proliferation rate of immune cells (k) is higher than k^*, which is results in the development of autoimmune disease symptoms. If an effector cell's key is attacks a healthy cell (target cell), then the immune cells will be activated, and the end of the autoimmune disease is developed by patients. However, this depends on

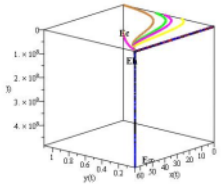
the patient's initial condition. Patients with an autoimmune disease with or without viral infection will develop the autoimmune symptom, while others can maintain the immune tolerant condition.

When the virus persists in the host ($h - \mu_3 > 0$), we have one more equilibrium E_c which represents complication state. It results in the more complex population dynamics are obtained. Figure (2) shows patients with a higher k tend to have more severe disease symptoms. Figure (2b) indicates that if the maximum proliferation rate of immune cells (k) is relatively small then autoimmune complications associated with a viral infection will occur (E_c). On the other hand, in Figure (2d) if k is large enough then the autoimmunity occurs without viral infection (E_a). In addition, the number of viral agents can blast under $h - \mu_3 > 0$. The dynamics of model (7) converges to the infection state E_{inf}, for initial value 2 and 3. This describes patient with an infection will develop the more serious infectious disease, but it will not progress to autoimmunity or complication state. Hence as in the previous simulation, the patient's state affects the development of the disease's symptoms.

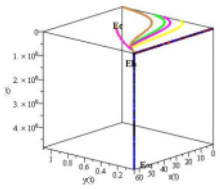
Then the simulation in case 3 are defined at the following : Simulation with various value of β_1 in Figure (3) shows strong immune affinities with self antigen, with the increasing rates at which immune cells find target cells and immune cells succeed in attacking target cells, will reduce the population of target cells as well as the population of immune cells and increase the virus population. Therefore, it engender the development of autoimmune disease with viral infection, but also reduces autoimmune disease progression.

5. Conclusion

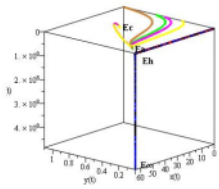
According to the whole analysis, we can conclude that in the system of autoimmune (GB's) disease the role of the maximum proliferation rate of immune cells caused by the antigen-presenting cells (APC's) and immune affinities with self-antigen. The parameter value of the symptoms of autoimmune disease and the mathematical form effectively changes. This implies that to understand the mechanism of autoimmune disease, it is important to interpret the phenomena associated with the parameter.



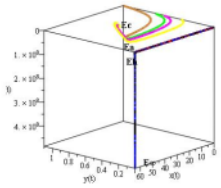
(A) $k = 0.05$



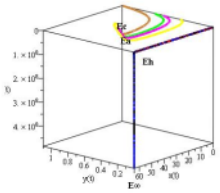
(B) $k = 0.08; E_c = (32.62; 0.67; 417.38)$



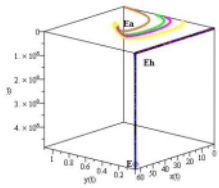
(C) $k = 0.186, \quad E_a = (96.7; 1.10^{-10}; 0)$



(D) $k = 0.11, E_c = (32.62; 0.67; 105.84), E_a = (59.66; 0.09; 0)$



(E) $k = 0.2, E_c = (32.62; 0.67; 12.38), E_a = (40.10; 0.05; 0)$

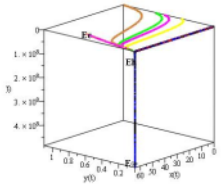


(F) $k = 0.26, E_a = (31.445; 0.69; 0)$.

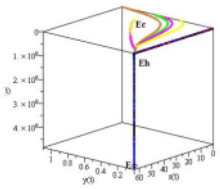
FIGURE 2. Simulation with $a = 0.9; \mu_1 = 0.3; p = 0.8; L = 100; m = 60; \mu_2 = 0.1; \beta_2 = 0.3; \beta_1 = 0.4; h = 0.4; \mu_3 = 0.2.; E_\infty = (\hat{x}; 0; \infty); E_h = (64.25; 0; 0)$.

When the virus cannot control its reproduction, then the system has two possible steady-state, they are a healthy state and autoimmune state. There is a critical proliferation rate of immune cells which functions as a threshold for the existence and stability of the autoimmune steady state. In different circumstances, if the virus controls its replication in the host, then there is one more steady-state which represents a complication of autoimmune disease with the viral infection.

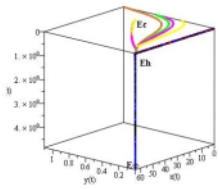
The rate of maximum proliferation of immune cells caused by antigen-presenting cells (APC's) k influence the symptoms of autoimmune disease. If k is small, then there is tolerance regardless of the number of antigens and the disease is inactive. However, if k is relatively large then immune cells are activated regardless of the number of antigens and disease develops. A certain range value of k gives a result in autoimmune disease with the viral infection.



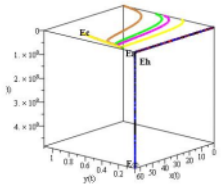
(A) $k = 0.05$



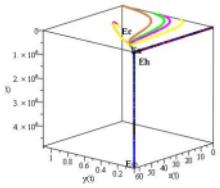
(B) $k = 0.08; E_c = (32.62; 0.67; 417.38)$



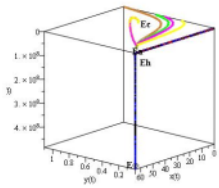
(C) $k = 0.186$, $E_a = (96.7; 1.10^{-10}; 0)$



(D) $k = 0.11, E_c = (32.62; 0.67; 105.84), E_a = (59.66; 0.09; 0)$



(E) $k = 0.2, E_c = (32.62; 0.67; 12.38), E_a = (40.10; 0.05; 0)$



(F) $k = 0.26, E_a = (31.445; 0.69; 0)$.

FIGURE 3. Simulation with $a = 0.9; \mu_1 = 0.3; p = 0.8; L = 100; m = 60; \mu_2 = 0.1; \beta_2 = 0.3; h = 0.4; \mu_3 = 0.2; E_h = (64.25; 0; 0), E_\infty = (\hat{x}; 0; \infty)$.

The strong immune affinities with self-antigen β_1 induce the development of autoimmune disease with a viral infection but reduce autoimmune disease progression. Therefore, there should be an investigation about the appropriate value of the immune affinity with self-antigen so delay autoimmune disease progression.

The progression of autoimmune disease can include autoimmunity without persistent infection, depending on the patient's state in which it related to the initial number of the antigen (target cell and virus population). When we choose a small initial number of antigens, then the autoimmune disease symptoms are tolerance, although the maximum proliferation rate of immune cells, k, is large. Nevertheless, when the initial value of antigens is high, then immune cells are activated. Finally, the patient develops the autoimmune disease although the disease progression includes the viral infection.

6. ACKNOWLEDGEMENT

The authors express the big gratitude to Direktorat Riset dan Pengabdian Masyarakat (DRPM), Direktorat Jenderal Penguatan Riset dan Pengembangan, the minister of Research, Technology, and Higher Education, Indonesia for the funding support. We also impressed the gratefulness to LPPM Universitas Internasional Semen Indonesia(UISI), for Informatics Department UISI, and Mathematics Department, Brawijaya University for the big supports.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

REFERENCES

[1] P. Andayani, The effect of social media for a Zika virus transmission with Beddington DeAngelis incidence rate: Modeling and analysis, in: Istanbul, Turkey, 2019: p. 090003.

[2] P. Andayani, L.R. Sari, A. Suryanto, I. Darti, Numerical study for Zika virus transmission with Beddington-DeAngelis incidence rate. Far East J. Math. Sci. 111(2019), 145-157.

[3] L. Barbi, A.V.C. Coelho, L.C.A. de Alencar, S. Crovella, Prevalence of Guillain-Barré syndrome among Zika virus infected cases: a systematic review and meta-analysis, Brazil. J. Infect. Dis. 22 (2018), 137–141.

[4] J.A. Borghans, R.J. De Boer, A minimal model for T-cell vaccination. Proc. R. Soc. Lond. Ser. B., Biol. Sci. 259(1355) (1995), 173-178.

[5] J.A.M. Borghans, R.J. de Boer, E. Sercarz, V. Kumar, T cell vaccination in experimental autoimmune encephalomyelitis: a mathematical model. J. Immunol. 161 (1998), 1087-1093.

[6] J.A.M. Borghans, L.S. Taams, M.H.M. Wauben, R.J. de Boer, Competition for antigenic sites during T cell proliferation: A mathematical interpretation of in vitro data, Proc. Nat. Acad. Sci. 96 (1999), 10782–10787.

[7] P.R. Bourque, J.W. Chardon, R. Massie, Autoimmune peripheral neuropathies, Clinica Chimica Acta. 449 (2015), 37–42.

[8] R.J. De Boer, A.S. Perelson, Towards a general function describing t cell proliferation, J. Theor. Biol. 175 (1995), 567–576.

[9] R. Deboer, A. Perelson, I. Kevrekidis, Immune network behavior—I. From stationary states to limit cycle oscillations, Bull. Math. Biol. 55 (1993), 745–780.

[10] R.J. de Boer, M.C. Boerlijst, B. Sulzer, A.S. Perelson, A new bell-shaped function for idiotypic interactions based on cross-linking, Bull. Math. Biol. 58 (1996), 285–312.

[11] M.F. Elettreby, E. Ahmed, M. Safan, A simple mathematical model for Guillain–Barré syndrome, Adv. Differ. Equ. 2019 (2019), 208.

[12] D. Fairweather, R. Root-Bernstein, Autoimmune Disease: Mechanisms, in: John Wiley & Sons Ltd (Ed.), ELS, John Wiley & Sons, Ltd, Chichester, UK, 2015: pp. 1–7.

[13] S.M. Hayter, M.C. Cook, Updated assessment of the prevalence, spectrum and case definition of autoimmune disease, Autoimmun. Rev. 11 (2012), 754–765.

[14] S. Iwami, Y. Takeuchi, K. Iwamoto, Y. Naruo, M. Yasukawa, A mathematical design of vector vaccine against autoimmune disease, J. Theor. Biol. 256 (2009), 382–392.

[15] S. Iwami, Y. Takeuchi, Y. Miura, T. Sasaki, T. Kajiwara, Dynamical properties of autoimmune disease models: Tolerance, flare-up, dormancy, J. Theor. Biol. 246 (2007), 646–659.

[16] National Institute of Neurological Disorders and Stroke, Guillain-Barré Syndrome Fact Sheet. http://www.ninds.nih.gov/disorders/gbs/detail_gbs.htm. 2018. (accessed Jun. 27, 2019).

[17] N.R. Rose, Autoimmune Diseases, in: International Encyclopedia of Public Health, Elsevier, 2008: pp. 267–271.

[18] A.M. Silverstein, Autoimmunity, in: The Autoimmune Diseases, Elsevier, 2014: pp. 11–17.

[19] A. Uncini, N. Shahrizaila, S. Kuwabara, Zika virus infection and Guillain-Barré syndrome: a review focused on clinical and electrophysiological subtypes, J. Neurol. Neurosurg. Psychiatry. 88 (2017), 266–271.

[20] U.S. National Library of Medicine, Guillain-Barre syndrome. https://medlineplus.gov/ency/article/000684.htm. 2017. (accessed Jun. 27, 2019).

[21] E.F.M. Wijdicks, C.J. Klein, Guillain-Barré Syndrome, Mayo Clinic Proc. 92 (2017), 467–479.

MATHEMATICAL MODEL OF GUILLAIN-BARRE SYNDROME WITH HOLLING TYPE II FUNCTIONAL RESPONSE

ORIGINALITY REPORT

11%	9%	12%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Shingo Iwami, Yasuhiro Takeuchi, Yoshiharu Miura, Toru Sasaki, Tsuyoshi Kajiwara. "Dynamical properties of autoimmune disease models: Tolerance, flare-up, dormancy", Journal of Theoretical Biology, 2007 Publication	6%
2	advancesindifferenceequations.springeropen.com Internet Source	5%

Exclude quotes	Off	Exclude matches	< 3%
Exclude bibliography	On		

MATHEMATICAL MODEL OF GUILLAIN-BARRE SYNDROME WITH HOLLING TYPE II FUNCTIONAL RESPONSE

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9

PAGE 10

PAGE 11

PAGE 12

PAGE 13

PAGE 14

PAGE 15