

# **A Mathematical Model of Dynamic Interaction Between Virus and Deleterious Immunity Response**

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## **Abstract**

The interaction between viruses and the immune system is known to be varied and complex. In particular, viruses may develop survival tactics to diminish the immune system, causing the protective immunity response to become deleterious to the host. A dynamic model is developed to depict the interaction between viruses and immune system response under this scenario. Rather general and nonlinear specifications are allowed in the growth rate of the antibodies and antibodies' kill rate. Some stylized prognosis possibilities are generated by the model. It also yields the interesting outcome in which the slightly infected may die of the disease while the seriously infected may survive. Treatment simulation is also considered.

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## 1 Introduction

The interaction between viruses and the immune system is known to be varied and complex. A virus could trigger an autoimmune response of the infected host by eliciting antiviral antibodies. Many viruses have developed survival tactics to evade or diminish the immune system that functions to protect the host. In addition, the fundamental protective response can become deleterious to the host's body. For instance, antibody response may generate cross reaction between viral and self protein, causing molecular mimicry of the host by the virus. There is convincing evidence that molecular mimicry can lead to tissue damage (see [1, 2]). Moreover, the possibility of antibody cross-reactivity between virus and host was found at the genetic level by [3]. The overlap between autoimmune and antiviral antibody gene repertoires may cause autoimmune diseases (see [4-7]). Damaging immune response to AIDS virus infection are found by [8, 9]. Deleterious immune responses are also found in malaria patients (see [10]) and mice (see [11]).

This paper develops a dynamic model to depict the interaction between viruses and the immune system response. In particular, the interaction between the virus and the host's immune system has the following characteristics. An increase in virus population or concentration increases the production of antiviral antibodies. The protective immune response causes cross reactivity between the virus and the host, and produces deleterious effects. One of these effects is that the disturbed immune system aids the growth of the virus, perhaps through mechanisms like the incorporation of cellular protein into viral protein in the course of viral replication. This translates into the scenario that increased antiviral antibodies decreases the demise rate of the virus.

The model is developed along the line of the interactive models [12-17].

Dynamic interactive models on viral infection can be found in [18-20]. In the present model, some interesting prognosis possibilities could be generated. Section 2 presents the dynamics of virus growth and immunity response. The growth trajectories of virus and antibodies are derived in Section 3. Various prognosis possibilities generated by the model are discussed in Section 4. Treatment simulation is considered in Section 5. Some concluding remarks are given in Section 6.

## 2 Dynamics of Virus Growth and Immunity Response

In this section, we formulate the dynamics of virus growth and immunity response in a mathematical model. Let  $v(t)$  denote the population or concentration of viruses at time  $t$ , and  $u(t)$  the amount of antiviral antibodies. The evolution of viruses and immunity response are hypothesized to be governed by the simultaneous equations:

$$\dot{u}(t) = \frac{du(t)}{dt} = f[v(t)] - \delta u(t), \quad (1)$$

$$\dot{v}(t) = \frac{dv(t)}{dt} = [a - g[u(t), v(t)]]v(t), \quad v(t_0) = v_0 \geq 0 \quad \text{and} \quad u(t_0) = u_0 \geq 0. \quad (2)$$

Equation (1) characterizes the growth dynamics of antibodies. The function  $f[v(t)]$  reflects the amount of antibodies induced by virus population  $v(t)$ . The positive parameter  $\delta$  represents the natural degradation rate of antibodies, and  $a$  is the nonnegative natural reproduction rate of the virus. The inducement function  $f[v(t)]$  exhibits the following characteristics:

- (i)  $f(v) > 0$ ,  $f(0) = F \geq 0$ ,
- (ii)  $f'(v) > 0$ , and  $f''(v) > 0$ . (3)

Characteristic (ii) in (3) shows that (a) the presence of viruses induces the production of antibodies, and (b) in the absence of virus antibodies may still be

generated. Characteristics (ii) demonstrates that (a) the higher the population of the virus the higher the amount of antibodies induced, and (b) the marginal rate of antibodies inducement increases with the virus population. Property (b) in (3) reflects that with cross reactivity the immune system becomes increasingly sensitive to the virus.

Equation (2) characterizes the growth dynamics of the virus. The natural reproduction rate of virus is  $a$ . The term  $[g[u(t),v(t)]]$  represents the antibodies' kill rate of the virus which depends on the amount of antibodies and the virus population. The function  $g[u(t),v(t)]$  is supposed to have the following features:

- (i)  $g_u(u,v) < 0$ ,  $g_{uu}(u,v) < 0$ , and  $g(u,v) \geq 0$  for  $u \geq 0$  and  $v \geq 0$ ;
- (ii)  $g_v(u,v) > 0$ ,  $g_{vv}(u,v) = 0$  and  $g_{uv}(u,v) = 0$ ;
- (iii)  $g(0,v) > 0$ . (4)

Feature (i) in (4) shows that (a) an increase in antibodies would decrease the antibodies' kill-rate of virus because of deleterious immunological effects, (b) (the negative) increment of the antibodies' kill-rate would decrease as antibodies increase, and (c) the antibodies' kill-rate remains non-negative.

Property (b) reflects the fact that protective immune response causes cross reactivity and produces deleterious effects which aid the growth of the virus, perhaps through mechanisms like the incorporation of cellular protein into viral protein in the course of viral replication. As stated in Section 1, this translates into the scenario that increased antiviral antibodies decreases the demise rate of the virus.

Feature (ii) in (4) shows that (a) an increase in virus increases the antibodies' kill-rate due to an increase in the catch-able rate, (b) the increment of the antibodies' kill-rate brought about by an increase in virus is not affected by changes in the virus population, and (c) the (negative) increment of the antibodies' kill-rate brought about by an increase in antibodies is not affected by changes in the virus population.

Feature (iii) shows that in the absence of antibodies, the natural death rate of virus is  $g(0, v)$  which depends on its population. With  $g_v(u, v) > 0$ , the natural death rate increases as congestion increases. Moreover, we denote the level of virus such that its natural reproduction rate  $a$  equals its natural death rate  $g(0, v)$  by  $v_n$ .

One can readily verify that given nonnegative  $v_0$  and  $u_0$  at initial time  $t_0$ ,  $u(t) \geq 0$  and  $v(t) \geq 0$  for all  $t \in [t_0, \infty)$ .

### 3 Growth Trajectories of Virus and Antibodies

The growth trajectories of virus and antibodies can be analyzed in the phase space. First, the isocline  $\dot{u} = 0$  is the locus  $v = \varepsilon(u)$  which satisfies the condition  $f(v) - \delta u \equiv 0$ . The slope of isocline  $\dot{u} = 0$  in the positive quadrant of the  $u$ - $v$  phase space can be obtained readily as:

$$\left. \frac{dv}{du} \right|_{\dot{u}=0} = \frac{\delta}{f'(v)} = \frac{\delta}{f'[\varepsilon(u)]} > 0. \quad (5)$$

With  $\varepsilon'(u) = \frac{d\varepsilon(u)}{du} = \left. \frac{dv}{du} \right|_{\dot{u}=0} = \frac{\delta}{f'(v)}$ , the derivative of the slope of isocline

$\dot{u} = 0$  in (5) can be obtained as:

$$d \left( \left. \frac{dv}{du} \right|_{\dot{u}=0} \right) / du = \frac{-\delta f''[\varepsilon(u)] [\varepsilon'(u)]}{[f'[\varepsilon(u)]]^2} = \frac{-f''(v) \delta^2}{[f'(v)]^3} < 0. \quad (6)$$

Condition (6) shows that the isocline  $\dot{u} = 0$  resembles the graph of a strictly concave function in the positive quadrant of the  $u$ - $v$  phase space.

The demarcation lines yielding  $\dot{v} = 0$  include (i) the axis  $v = 0$ , and (ii) the isocline  $\dot{v} = 0$  represented by the locus  $v = \mathcal{G}(u)$  which satisfies the condition  $a - g(u)v \equiv 0$  in the positive quadrant of the  $u$ - $v$  phase space. The slope of the

isocline  $\dot{v} = 0$  represented by the locus  $v = \mathcal{G}(u)$  can be obtained readily as:

$$\left. \frac{dv}{du} \right|_{\dot{v}=0} = \frac{-g_u(u, v)}{g_v(u, v)} = \frac{-g_u[u, \mathcal{G}(u)]}{g_v[u, \mathcal{G}(u)]} > 0. \quad (7)$$

With  $\mathcal{G}'(u) = \frac{d\mathcal{G}(u)}{du} = \left. \frac{dv}{du} \right|_{\dot{v}=0} = \frac{-g_u(u, v)}{g_v(u, v)}$ , the derivative of the slope of isocline

$\dot{u} = 0$  in (7) can be obtained as:

$$\begin{aligned} & d\left(\left. \frac{dv}{du} \right|_{\dot{v}=0}\right) / du \\ &= -\frac{g_{uu}[u, \mathcal{G}(u)] + g_{uv}[u, \mathcal{G}(u)]\mathcal{G}'(u) - g_{vu}[u, \mathcal{G}(u)] - g_{vv}[u, \mathcal{G}(u)]\mathcal{G}'(u)}{[g_v[u, \mathcal{G}(u)]]^2} \\ &= -\frac{g_{uu}[u, \mathcal{G}(u)]}{[g_v[u, \mathcal{G}(u)]]^2} = -\frac{g_{uu}(u, v)}{[g_v[u, \mathcal{G}(u)]]^2} > 0. \end{aligned} \quad (8)$$

Condition (8) shows that the isocline  $\dot{v} = 0$  resembles the graph of a strictly convex function in the positive quadrant of the  $u$ - $v$  phase space.

Given that both isoclines are positively sloped while the isocline  $\dot{u} = 0$  is strictly concave and the isocline  $\dot{v} = 0$  is strictly convex, they may (a) intersect with each other twice, or (b) intersect just once, or (c) never intersect with each other. At the point where the isoclines intersect, both the virus and antibodies cease to grow, and a stationary point (steady state) appears. In the following two subsections, we first consider the prime case in which the isoclines intersect twice and depict various dynamics and outcomes generated. Then we consider the peripheral case in which the isoclines intersect once or do not intersect at all.

### 3.1. The prime case -- isoclines intersect twice

In the case when the isoclines  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect with each other twice the two stationary points (steady states) are denoted as  $(u^*, v^*)$  and

$(u^{**}, v^{**})$  in Figure 1. The types of steady state these stationary points represent are provided in Property 1 below.

**Property 1.** The point  $(u^*, v^*)$  is a stable node and  $(u^{**}, v^{**})$  is a saddle point.

**Proof.** The variational matrix of system (1)-(2) is:

$$V = \begin{bmatrix} -\delta & f'(v) \\ -g_u(u, v) & a - g_v(u, v)v - g(u, v) \end{bmatrix}. \quad (9)$$

At a stationary point,  $a - g(u, v) = 0$ , and the trace of  $V$  is

$$Tr(V) = -\delta - g_v(u, v)v < 0, \quad (10)$$

which is always negative; and the determinant of  $V$  is

$$|V| = \delta g_v(u, v)v + f'(v)g_u(u, v). \quad (11)$$

Furthermore, at a stationary point, the term:

$$\begin{aligned} [Tr(V)]^2 - 4|V| &= [-\delta - g_v(u, v)v]^2 - 4[\delta g_v(u, v)v + f'(v)g_u(u, v)] \\ &= [\delta - g_v(u, v)v]^2 - 4f'(v)g_u(u, v) > 0. \end{aligned} \quad (12)$$

At  $(u^*, v^*)$ , the slope of the isocline  $\dot{u} = 0$  is steeper than that of the isocline  $\dot{v} = 0$ , therefore

$$\left. \frac{dv}{du} \right|_{\dot{u}=0} = \frac{\delta}{f'(v)} > \left. \frac{dv}{du} \right|_{\dot{v}=0} = \frac{-g_u(u, v)}{g_v(u, v)}, \text{ and}$$

the determinant of  $V$  is

$$|V| = \delta g_v(u, v)v + f'(v)g_u(u, v) > 0. \quad (13)$$

Given that  $Tr(V) < 0$  and  $|V| > 0$  and  $[Tr(V)]^2 - 4|V| > 0$ , both eigenvalues of  $V$  are real and negative. Hence, the stationary point  $(u^*, v^*)$  is a stable node.

At  $(u^{**}, v^{**})$ , the slope of the isocline  $\dot{v} = 0$  is steeper than that of the isocline  $\dot{u} = 0$ , therefore

$$\left. \frac{dv}{du} \right|_{\dot{u}=0} = \frac{\delta}{f'(v)} < \left. \frac{dv}{du} \right|_{\dot{v}=0} = \frac{-g_u(u, v)}{g_v(u, v)} \text{ and}$$

the determinant of  $V$  is

$$|V| = \delta g_v(u, v)v + f'(v)g_u(u, v) < 0. \quad (14)$$

Given that  $Tr(V) < 0$  and  $|V| < 0$  and  $[Tr(V)]^2 - 4|V| > 0$ , the eigenvalues of  $V$  are real but of opposite signs. Hence, the stationary point  $(u^{**}, v^{**})$  is a saddle point.

Since  $(u^{**}, v^{**})$  is a saddle point, there exists a separatrix in the form of a pair of stable branches,  $v = \underline{\phi}(u)$  and  $v = \bar{\phi}(u)$ , along which points will move towards the saddle point (see [21]). These stable branches are depicted by the dotted line arrows in Figure 1.

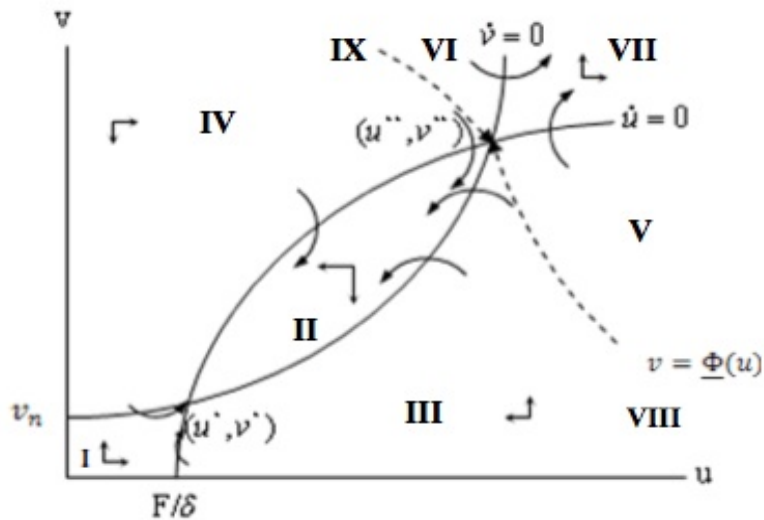


Figure 1: Phase portrait of virus concentration and antibodies level, where  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect with each other twice

The movements of virus population and antibodies level are depicted by the arrows in Figure 1. We use  $v = \phi(u)$  to denote the locus of the separatrix. Trajectories starting in the region to the left of the separatrix  $v = \phi(u)$  will



eventually settle at the stable node  $(u^*, v^*)$ . Trajectories starting in the region to the right of the separatrix  $v = \phi(u)$  will eventually go out of bounds. Trajectories starting along the stable branches will eventually settle at the saddle point  $(u^{**}, v^{**})$ .

### 3.2. Peripheral case – one or no intersection

In this subsection, we first consider the case in which  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect just once, and then the case in which the isoclines do not intersect with each other.

#### (a) *Isoclines intersect just once*

Consider the case in which the isoclines  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect with each other just once at  $(u^z, v^z)$  as in Figure 2. Note that at  $(u^z, v^z)$ , where the slopes

of the isoclines are equal, that is  $\left. \frac{dv}{du} \right|_{\dot{u}=0} = \frac{\delta}{f'(v)} = \left. \frac{dv}{du} \right|_{\dot{v}=0} = \frac{-g_u(u, v)}{g_v(u, v)}$ , the

determinant of the variational matrix  $V$  is

$$|V| = \delta g_v(u, v)v + f'(v)g_u(u, v) = 0. \quad (15)$$

Therefore one of the eigenvalues of  $V$  is zero while the other is negative, hence  $(u^z, v^z)$  is neither a stable node nor a saddle point. Instead, it is an improper node (unstable steady state) at which  $\dot{u} = 0$  and  $\dot{v} = 0$ . The movements of virus population and antibodies level are depicted by the arrows in Figure 2.

There are trajectories moving towards the stationary point  $(u^z, v^z)$  and there are also trajectories that will go out of bounds.

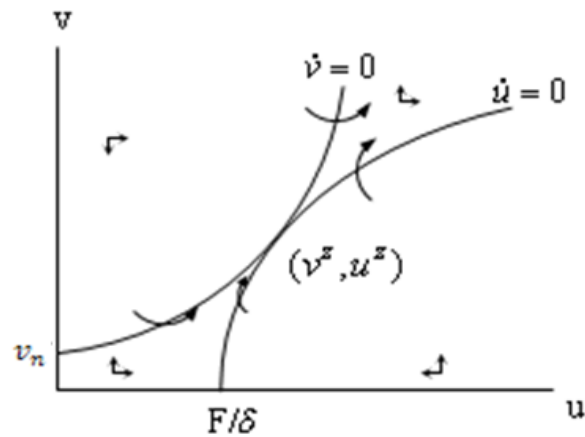


Figure 2: Phase portrait of virus concentration and antibodies level, where  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect with each other once

**(b) Isoclines do not intersect**

In the case when  $\dot{u} = 0$  and  $\dot{v} = 0$  do not intersect with each other, the movements of virus population and antibodies level are depicted by the arrows in Figure 3.

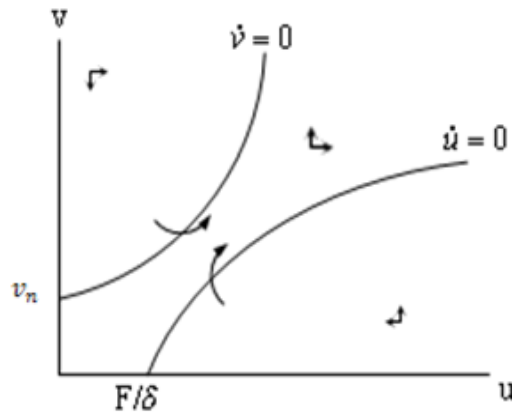


Figure 3: Phase portrait of virus concentration and antibodies level, where  $\dot{u} = 0$  and  $\dot{v} = 0$  do not intersect with each other

Any trajectory starting in the interior of the positive quadrant of the  $u$ - $v$  phase space will eventually go out of bounds.

## 4 Prognosis Possibilities

The course of development of many virus infections could be very complex and varied due to deleterious immunity response of the infected host subject. In the sequel, we use the dynamic interactive model of viruses and deleterious immunity response in (1) – (2) to generate outcomes which reflects some stylized prognoses.

Consider first the prime case when  $\dot{u} = 0$  and  $\dot{v} = 0$  intersect twice. The  $u$ - $v$  phase space in Figure 1 can be divided into nine regions: I, II, III, IV, V, VI, VII, VIII and IX.

Nine different prognoses can be obtained as follows:

- (i) **Region I.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, both virus concentration and antibodies level will grow until they reach the stable steady state  $(u^*, v^*)$ .
- (ii) **Region II.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, both virus concentration and antibodies level will decline until they reach the stable steady state  $(u^*, v^*)$ .
- (iii) **Region III.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, virus concentration will grow and antibodies level will drop until either (a) they arrive at a point on the isocline  $\dot{v} = 0$  and then both of them will decline until the stable steady state  $(u^*, v^*)$  is reached, or (b) they arrive at a point on the isocline  $\dot{u} = 0$  and then both of them will rise until the stable steady state  $(u^*, v^*)$  is reached.
- (iv) **Region IV.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, virus concentration will drop and the level of antibodies will rise until either (a) they arrive at a

point on the isocline  $\dot{v} = 0$  and then both of them will decline until the stable steady state  $(u^*, v^*)$  is reached, or (b) they arrive at a point on the isocline  $\dot{u} = 0$  and then both of them will rise until the stable steady state  $(u^*, v^*)$  is reached.

- (v) **Region V.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, virus concentration will grow and antibodies level will drop until they arrive at a point on the isocline  $\dot{u} = 0$ . Then both of them will rise continuously and go out of bounds eventually.
- (vi) **Region VI.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, virus concentration will drop and antibodies level will rise until they arrive at a point on the isocline  $\dot{v} = 0$ . Then both of them will rise continuously and eventually go out of bounds.
- (vii) **Region VII.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region, both virus concentration and antibodies level will rise continuously and go out of bounds eventually.
- (viii) **Region VIII.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region – that is the lower stable branch, virus concentration will rise and antibodies level will drop until they reach the saddle point steady state  $(u^{**}, v^{**})$ .
- (ix) **Region IX.** If the infected host is diagnosed to have virus concentration and antibodies level belonging to states in this region – that is upper stable branch, virus concentration will drop and antibodies level will rise until they reach the saddle point steady state  $(u^{**}, v^{**})$ .

Thus, for virus-antibodies combinations in regions I to IV, they will eventually settle at the stable node  $(u^*, v^*)$ . For virus-antibodies combinations in

regions V to VII, they will grow out of bounds eventually. For with virus-antibodies combinations in region VIII or region IX, their conditions will settle at the saddle point steady state  $(u^{**}, v^{**})$  eventually.

Once a steady state is reached, virus concentration and antibodies level will remain there until new virus infection occurs. Consider the case when the stable steady state  $(u^*, v^*)$  has been attained and there was a new virus infection leading to a change in the virus-antibodies combination. If the virus-antibodies combination after the new infection is within regions I to IV, the stable node will be restored eventually. If the virus-antibodies combination after the new infection is in regions V to VII, the virus-antibodies combination will either go out-of-bounds. Finally, if the virus-antibodies combination after the new infection is along the stable arms it will eventually settling at the saddle point  $(u^{**}, v^{**})$ .

Interesting results mimicking actual cases can be generated by the model. For instance, some hosts with initially mild infection (with low level of virus) may die of the disease eventually. This would happen if the initial virus-antibodies combination of the host is in the low virus part of Region V. Similarly, some hosts who are initially seriously infected (with high virus concentration) may eventually survive. This would happen if the initial virus-antibodies combination of the host is in the high virus part of Region IV.

Next we consider the peripheral case when the isoclines intersect once or do not intersect. We first examine the case when the isoclines intersect only once as in the  $u$ - $v$  phase space in Figure 2. The following prognoses can be made.

- (x) Depending on the starting point, initially virus concentration and antibodies level may rise together or move in opposite directions, and subsequently both of them will rise and eventually go out of bounds.
- (xi) Depending on the starting point, initially virus concentration and antibodies level may rise together or move in opposite directions, and eventually both of them will rise together towards the steady state

$$(u^z, v^z).$$

Now, we consider the case when the isoclines  $\dot{u} = 0$  and  $\dot{v} = 0$  do not intersect with each other. Since all trajectories in the interior of the positive quadrant of the  $u$ - $v$  phase space will eventually go out of bounds, the following prognoses can be made.

- (xii) The viral infection is absolutely fatal. Irrespective to the starting point, the virus concentration and antibodies level will go out of bounds eventually.

## 5 Treatment Simulation

In this section, we consider simulated effects of medical treatment on the growth of the virus and antibodies. Consider the simple scenario that medication can reduce the natural reproduction rate of virus. Equation (1) becomes:

$$\dot{v}(t) = [a - \varpi[m_1(t)] - g[u(t), v(t)]] v(t), \quad (16)$$

where  $m_1(t)$  is the level of medication applied to reduce virus growth at time  $t$ , and  $\varpi[m_1(t)]$  is the effect of the medication on the natural reproduction rate of the virus. It is assumed that  $0 \leq \varpi(m_1) \leq a$  for all possible levels of  $m_1$ .

Simultaneously, another medication can be used to reduce the sensitivity of the immune system in producing antibodies in response to virus intrusion. Equation (2) becomes:

$$\dot{u}(t) = \theta[m_2(t)]f[v(t)] - \delta u(t), \quad (17)$$

where  $m_2(t)$  is the level of medication applied to alleviate immunity sensitivity at time  $t$ , and  $\theta[m_2(t)] \in [0,1)$  represents the effect of medication on the sensitivity of the immune system.

Consider the case where constant dosages of medication,  $\hat{m}_1$  and  $\hat{m}_2$ , are applied. Therefore  $\varpi[m_1(t)] = \varpi(\hat{m}_1) = \hat{\varpi}$  and  $\theta[m_2(t)] = \theta(\hat{m}_2) = \hat{\theta}$  for all time  $t$  within the treatment period.

With medical treatment being applied to reduce the virus growth, the isocline  $\dot{v} = 0$  is on the locus  $[a - \hat{\omega} - g[u(t), v(t)]] = 0$ . While the isocline  $\dot{v} = 0$  before medication is on the locus  $[a - g[u(t), v(t)]] = 0$ . Given that  $g_v(u, v) > 0$ , the after-medication isocline  $\dot{v} = 0$  is below the before-medication isocline  $\dot{v} = 0$  in the  $u - v$  phase space in Figure 1. The term  $v_{\bar{w}}$  is used to denote the level of virus such that its after-medication reproduction rate  $a - \hat{\omega}$  equals its natural death rate  $g(0, v)$ .

After medical treatment has been applied to alleviate immunity sensitivity,  $u = \hat{\theta} f(v) / \delta$  along the isocline  $\dot{u} = 0$ . Before treatment,  $u = f(v) / \delta$  along the isocline  $\dot{u} = 0$ . Hence, after-medication, at every value of  $v$ , the value of  $u$  shrinks by the proportion  $\hat{\theta}$ . Therefore, after medical treatment is applied to alleviate immunity sensitivity, the after-medication isocline  $\dot{u} = 0$  will shift to the left of the before-medication isocline  $\dot{u} = 0$  in the  $u - v$  phase space in Figure 1.

Moreover, the slopes of the after-medication isoclines,  $\left. \frac{dv}{du} \right|_{\dot{v}=0}^{Med} = \frac{-g_u(u, v)}{g_v(u, v)}$

and  $\left. \frac{dv}{du} \right|_{\dot{u}=0}^{Med} = \frac{\delta}{\hat{\theta} f'(v)}$ , are again positive.

Following the analysis in Section 3, one can readily show that the isocline  $\dot{u} = 0$  is strictly concave and the isocline  $\dot{v} = 0$  is strictly convex. The movements of virus population and antibodies level after medication are depicted by the arrows in Figure 4. Again following the analysis in section 3 one can establish that the point  $(\bar{u}^*, \bar{v}^*)$  is a stable node and  $(\bar{u}^{**}, \bar{v}^{**})$  is a saddle point.

Since  $(\bar{u}^{**}, \bar{v}^{**})$  is a saddle point, there exists a separatrix  $v = \psi(u)$ , along which points will move towards the saddle point. Trajectories starting in the region to the right of  $v = \psi(u)$  will eventually go out of bounds. Trajectories starting in the region to the left of  $v = \psi(u)$  will eventually settle at the stable

node  $(\bar{u}^*, \bar{v}^*)$ .

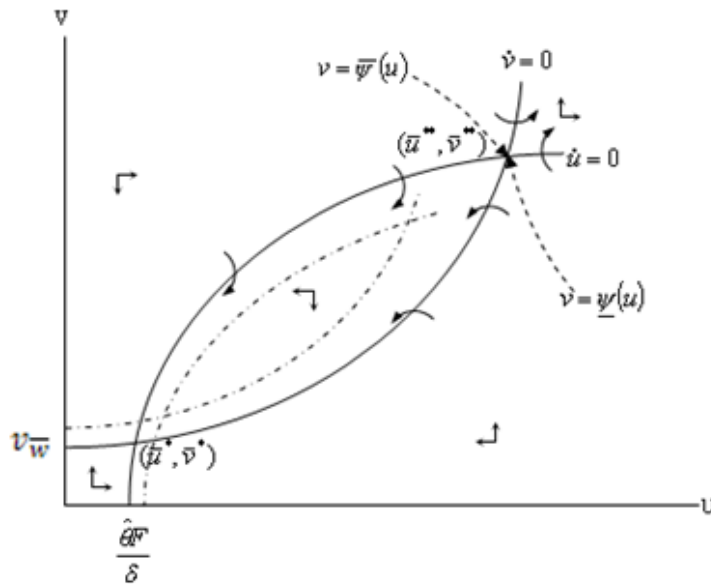


Figure 4: Phase portrait of after-medication virus concentration and antibodies level

The main objective of medication is to stop virus concentration from going out of bounds (assuming that the virus-antibodies combination of the infected host is already in an area that will send both virus concentration and antibodies level out of bounds). A necessary condition for medication to be effective is that the virus-antibodies combination is on the left of the after-medication separatrix. Once the virus-antibodies combination has been restored to the region on the left of the before-medication separatrix, medication can be taken off and the virus-antibodies combination will settle at the natural stable steady-state  $(u^*, v^*)$  in Figure 1.

## 6 Concluding Remarks

In this paper, we developed a dynamic model depicting the interaction



between viruses and the immune system response. Rather general and nonlinear specifications are allowed in the growth rate of the antibodies and antibodies' kill rate. Some interesting prognosis possibilities generated by the model are examined and treatment simulation is considered. In sum, the model developed leads to phase diagrams which yield interesting features that reflect the behaviors of viruses and antibodies.

In addition, the evolutionary dynamics of viruses and immunity response can take on more general structures with:

$$\dot{u}(t) = \hat{f}[u(t), v(t)], \quad (18)$$

$$\dot{v}(t) = \hat{g}[u(t), v(t)], \quad v(t_0) = v_0 \geq 0, \quad u(t_0) = u_0 \geq 0, \quad (19)$$

satisfying

$$\left. \frac{dv}{du} \right|_{\dot{u}=0} > 0, \quad d \left( \left. \frac{dv}{du} \right|_{\dot{u}=0} \right) / du < 0; \quad \left. \frac{dv}{du} \right|_{\dot{v}=0} > 0, \quad d \left( \left. \frac{dv}{du} \right|_{\dot{v}=0} \right) / du > 0; \text{ and}$$

the isocline  $\dot{u} = 0$  has a positive intercept along the  $u$ -axis and the isocline  $\dot{v} = 0$  has a positive intercept along the  $v$ -axis,  $\hat{f}[u, v] < 0$  for the set of  $(u, v)$  below the isocline  $\dot{u} = 0$ ,  $\hat{f}[u, v] > 0$  for the set of  $(u, v)$  above the isocline  $\dot{u} = 0$ ,  $\hat{g}[u, v] > 0$  for the set of  $(u, v)$  below the isocline  $\dot{v} = 0$ , and  $\hat{g}[u, v] < 0$  for the set of  $(u, v)$  above the isocline  $\dot{v} = 0$ ,

Last but not least, the diagrammatic result in the analysis provides a nontrivial addition to the existing two interacting species portrays in population biology like the classic Lotka-Volterra predator-predator cycles and limit cycles.

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