ISSN (Online) 2456 -1304

International Journal of Science, Engineering and Management (IJSEM)
Vol 6, Issue 4, April 2021

Stability Analysis of Delay Differential Systems with Delay Dependent Parameter for Some HIV Models

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***Abstract*— In this article we study the HIV models in Delay differential Equations. The work focus on just one kind, namely those of the form using finding the bifurcation parameter in DDE for ensuing steady state using stability analysis with variable constant delays in HIV mathematical models. The objective is to ensure equilibrium by considering the parameters like local and global asymptotic states, bifurcation parameter with its sensitivity and finally concludes with the stability results. The disease free equilibrium is received with its global stability is enhanced using bifurcation and is depicted using results.**

***Keywords*— Delay Differential Equation, Bifurcation, stability, HIV**

I. INTRODUCTION

Over the period of time many mathematical models have been deployed to address human immunity with the human immune system against HIV. Such model address deals this issue in different perspective addressed using DDE [2]. The deployed DDE [4] uses both linear and non linear models addressed with the delay measures as an additional parameter. The additional parameter includes different types of cells like infective, susceptible and immune cells. Such models help to understand about HIV with its growth and the measures for recovery [12]].

Let us consider a HIV model

$$\frac{dV}{dt} = UP - cV \qquad (1.1)$$

where UP is unknown virus production with c as constant against V as variance. The virus growth pattern is not understood earlier unless or until a mathematical model details the virus population and its growth. The HIV growth population is measured using the model is evaluate by

$$P = r - dP + aP\left(1 - \frac{P}{P_{max}}\right) \qquad (1.2)$$

where r is the rate of population growth for creation new HIV cells followed dP is the depth of the population and aP is the bifurcation which is the maximum death rate of the HIV disease.

The human immune system is hardly unpredictable as it reacts to any foreign disease instantly and the P_{max} is the maximum disease spread against any vital attack against human immune system.

HIV [13] does not have the tendency to reproduce as it needs the support of human immune system for its growth. Every virus cells have the copy of DNA and its spread the DNA into the human immune system. Every human immune system acts as a host for virus reproduction in the human cell. The infection ratio is calculated using the virus population growth and the maximum certainly of the virus growth is stored in the population P. The evaluation part virus is carried out with the protein ration present in the surface of the human immune cell. Every HIV cell has a RNA that converts into DNA of the immune cell to spread it. Once after the conversion of DNA the virus started to create duplication of the host cell and thus created new version of the HIV cells. The process takes time to spread and conversion after the initial conversion the spread ration started to increase.

Hence the HIV growth chart is clearly seen and affects the immune system. The affected immune system is collapsed and it leads to death. From virus spread to person death is splitted into 4 stages. Stage 1 is the virus inclusion into body addressed using asymptotic steady state, Stage 2 is the transient addressed using bifurcation parameter, Stage 3 is latency period dealt with parameter sensitivity and finally Stage 4 is the spread ratio addressed using optimal control mechanism.

The present therapies using to address this HIV issues is widely addressed with the anti-narcotics that provides balance support to ensure stability [1] in disease prevention against its overall spread. The rapid development of the

ISSN (Online) 2456 -1304

International Journal of Science, Engineering and Management (IJSEM)
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disease is kept under control to avoid disease duplication cell by anti narcotics method like chemotherapy that convert the infected cell into recovery cell using bifurcation method. Thus a model is defined to ensure the time stability [3] of cell against HIV spread against its spread.

The disease spread is evaluated using delay system principle that calculates the overall disease spread based on the input from bifurcation methods [9]. To ensure stability of the cell, the preventing drug acts as a intruder between the plasma and its overall concentration and finally dilute it within a week time [6]. The stability is ensured by evaluating the disease cell spread ratio and kept under control during its initial phase. The ratio tends to be slow down due to the invoked therapy by considering the earlier phases that acts as a comparison measures. The stability differs based on the human immune system as its differs between humans. The invoked cell may either destroy within the person through death and it may be killed due to this suppression. The RNA plasma regenerated through the process of therapy may destroy the spreading cells and the plasma count has to be more to get rid of the spreading virus. Hence the model has to be more dynamic for understanding the cell behavior and its growth phase to invoke best practice for providing overall immune system. Overall all these process put together into the category for deactivating the infected cell by using efficient dynamic model.

II. PROPERTIES OF DYNAMIC MODEL

The model to be implemented satisfies the following criteria (i) Stability (ii) Delay (iii) Affected rate and (iv) Cure rate.

While proposing model the infection ratio is set for the stability impact by the equation given below

$$\frac{dP}{dt} = s - dP + aP\left(1 - \frac{P}{P_{max}}\right) - \beta PV + \rho I, \quad (2.1)$$

$$\frac{dI}{dt} = \beta PV - (\delta + \rho)I, \quad (2.2)$$

$$\frac{dV}{dt} = qI - cV, \quad (2.3)$$

Where P is overall population, I is the cell infected and finally V is the Volume. The disease infection rate is βPV where β rate of infection. The density of infected cell is calculated with δ that gives the linear rate of virus spread.

The use of delay systems are widely used in many applications especially in engineering science

This work deals with DDE using variable discrete delays [8]. DDE is distinguished as bounded and unbounded with the variable or fixed time delay adapts to the change state based on the past and future variables [5]. Such application reflects to the mechanism of machine processing, control unit, dynamics. All these systems are exposed to time delay and its leads to poor performance [11], unstable system and also reflect in other notable damages caused due to instability.

Generally the time delay systems are adhered to dynamics and are exposed using DDE for evaluating its performance [7]. The results of such system are its stability flow explained using stability lobe diagram that measures its stability along with the control segment. More analytical and numerical derivations are focused to deal this issue to maintain the stability in every control systems. The stability control parameters are its (i) disease spread speed and (ii) disease depth parameter.

2.1 DISEASE SPREAD SPEED

In order to categorize the stability based on its subdivision, the stability criteria are detailed using scalar and frequency domain approaches.

The concept of shifted polynomial approrimization gives a new approach to the system by representing the stability in monodromy matrix.

The spread speed is measures using the delay parameter, where β, δ are spread rate and depth rate respectively.

$$\frac{dP}{dt} = s - dP + aP\left(1 - \frac{P}{P_{max}}\right) - \beta P(t-i)V(t-i) + \rho I \quad (2.4)$$

$$\frac{dI}{dt} = \beta P(t-i)V(t-i) - (\delta + \rho)I, \quad (2.5)$$

$$\frac{dV}{dt} = qI - cV, \quad (2.6)$$

Based on the overall population, the delay [14] and spread is measured with the frequency virus spreading ratio and the non infected cells are traced based on the spread value. In the above equation t-i is the times versus infection ratio with respect to the overall population. The 'i' value gives the time period between infected and non infected cell with i as positive constant. The delay is also measures using t-i terms satisfying the initial value.

III. DISEASE DEPTH PARAMETER

The depth is measures using disease depth with the uninfected cells. The uninfected stage starts with the initial value θ. Hence P_0, V_0 and I_0 are the initial value of population, velocity and 'i' is the infection period. All these values are set for the early stage of inspection to assume the cell are free from virus. $\overline{P_0}$ $\overline{V_0}$ $\overline{I_0}$ declares the infected cell ratio based on its previous observed values. To give state priority the initial value and the final values are monitored and the state is fixed to measure its stability.

While measuring the cell stability, the equilibrium is measured based on local and global asymptotic states [Krol, Katja]. Let E be the equilibrium. Then the local and global parameters are measured as follows

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$E^0 = P_0, V_0, I_0$ (3.1)

$E^1 = \overline{P_0}, \overline{V_0}, \overline{I_0}$ (3.2)

The cell population is measures by

Where

$P_0 = \left(\frac{P_{max}}{2t}\right)(t - d + \sqrt{(t-d)^2 + 4ts/P_{max}})$ (3.3)

$\overline{P_0} = c(\delta + \rho)/\beta\rho$ (3.4)

$\overline{V_0} = \left(\frac{1}{\delta}\right)[s - d\overline{P_0} + a\overline{P_0}(1 - {\overline{P_0}}/{P_{max}})$ (3.5)

$\overline{I_0} = ({q}/{c})\overline{V_0}$ (3.6)

Let us assume the relation R as ${P_0}/{\overline{P_0}}$ as is the basis stability ration for the relation. Using R the newly generated cells that are in the level two are monitored and observation. Such monitoring and observation gives the cell changing ratio by which non infected cells are converted to infected cells. The change ratio is evaluated using the relation R. It determines the overall infection period calculated using stability equilibrium change ratio between the initial and final state.

The global bifurcation is measured using the differential equation is measured and the results are received based on the observation.

Lemma 1: Let the relation R <1, $E^0 = P_0, V_0, I_0$ is set to be locally stable and when R > 1, $E^0 = P_0, V_0, I_0$ is set be globally stable.

Lemma 2: Let us assume a balanced form of global and local variables F > 0, are fully depended on P(t), V(t) and I(t) where t is the time proportion that fluctuate between the initial and final state variables.

By considering Lemma 1 and Lemma 2, Lemma 3 is derived with the following assumption

(i) R > 1,

(ii) (c + δ + ρ + d – t + $2t\overline{P}/P_{max}$)

(iii) (-d + t –$2t\,\overline{P}/P_{max}$)(c + δ + ρ) + $\beta\bar{I}(c + \delta) < 0$

IV. ENSURING DELAY METRICS IN HIV PREDICTION

The disease free equilibrium is evaluated using DDE model, and the stability is evaluated with R>1 and R<1.

Lemma1: The disease predication is measured using the conversion rate with the infected cell that is converted from the non infected cell to infected cell. The asymptotic stability is measures with R<1 with the unstable equilibrium of R>1.

In order to prove the above mentioned prediction by implementing few negative solution with the following characteristics

$\partial_1 = t - d - 2t\frac{P_0}{P_{max}}$ (4.1)

Using the equation (4.1) the equilibrium E^0 declares the disease identification proportion that gives eigen solution of the same.

$\partial^2 + (\delta + \rho + c)\partial + c(\delta + \rho) - q\beta P_0 e^{-\partial\tau} = 0$ (4.2)

The disease infection equilibrium τ

$-w + i(\delta + \rho + c)w + c(\delta + \rho) - q\beta P_0 \cos w\tau + iq\beta P_0 \sin w\tau = 0$ (4.3)

While separating the cells as infected and noninfected, that is denoted by

$-w^2 + c(\delta + \rho) = q\beta P_0 \cos w\tau,$ (4.4)

$(\delta + \rho + c)w = -q\beta P_0 \sin w\tau$ (4.5)

Squaring on both the equation 4.4 and 4.5 that results eqn 4.6

$w4 + [(\delta + \rho + c)2 + 2c(\delta + \rho)]w2 + c2(\delta + \rho)2 - q2\beta2P\,2 = 0$ (4.6)

To narrow down the results, it result in the following quadratic functions with the following assumptions

$T_{10} = (\delta + \rho + c)2 + 2c(\delta + \rho)$ (4.7)

$T_{20} = C^2(\delta + \rho)^2 - q^2\beta^2P_0^2$ (4.8)

The eqn (4.6) is rewritten as

$x^2 + T_{10}x + T_{20} = 0$ (4.9)

The coefficient of the quadratic equation by squaring T_{10} based on the squaring of T_{20}. The results obtained are

$T_{10} = (\delta + \rho + c)2 + 2c(\delta + \rho) > 0$ (4.10)

$T_{20} = C^2(\delta + \rho)^2 - q^2\beta^2P_0^2 = c(\delta + \rho)[c(\delta + \rho) + \beta P_0][1 - R\,]$ (4.11)

Eqn 4.9 has positive product which is complex and real with the same sign. The negative sign reflects on real or negative and the Eqn do not have real roots whose sign is positive. Finally there is no such negative equilibrium. Hence Eqn 4.9 equals Eqn 4.2

V. BIFURCATION BREAKDOWN

The bifurcation breakdown is measured using the time delay proportion τ and is considered as its parameter for ensuring and evaluating time delay. While addressing the delay proposition the value of R>1 is assumed as the equilibrium E that exists as the stability parameter. E is considered as stability equilibrium that results in linear equation resulting in the following equation

$\partial^3 + t_1\partial^2 + t_2\partial + t_3 = e^{-\partial\tau}(u_1\partial^2 + u_2\partial + u_3)$ (4.12)

Coefficients of the equation are represented by

$t_1 = c + \delta + d - t + \frac{2t\bar{P}}{P_{max}} - \rho$ (4.13)

$t_2 = c(\delta + \rho) + (c + \delta + \rho)\left(d - a + \frac{2t\bar{P}}{P_{max}} - \rho\right)$ (4.14)

$t_3 = c(\delta + \rho) + \left(d - a + \frac{2t\bar{P}}{P_{max}} - \rho\right)$ (4.15)

$u_1 = -\beta\bar{I}$ (4.16)

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$$u_2 = -\beta\bar{I}(c+\delta) \quad (4.17)$$
$$u_3 = -\beta\bar{I}(c\delta) \quad (4.18)$$

While $\tau = 0$ the characteristics matches with the DDE equation by proving all eigen values satisfies negative equilibrium based on Lemma 1. The asymptotic stability satisfies $\tau = 0$ when local stability results in equilibrium. When $\tau > 0$ it does not balances non negative solution based on equilibrium stability. Hence forth $t_1 > 0$, $t_2 > 0$, $t_3 > 0$ followed by $u_1 > 0, u_2 > 0, u_3 > 0$ to justify overall equilibrium. Based on the results, it proves it cannot be zero or negative and thus it concludes the result is non-negative to ensure its equilibrium.

$$-iw^3 - t_1w^2 + it_2w + t_3 \quad (4.19)$$
$$-u_1w^2\cos w\tau + iu_2w\cos w\tau + u_3\cos w\tau - iu_3w^2\sin w\tau - u_3w\sin w\tau + iu_3\sin w\tau \quad (4.20)$$

While separating both real, imaginary part from the equation and it is derived by

$$t_3 - t_1w^2 = (u_3 - u_1w^2)\cos w\tau - t_2w\sin w \quad (4.21)$$
$$t_2w - w3 = u_2w\cos w\tau + (u_3 - u_1w2)\sin w\tau \quad (4.22)$$

By squaring on both sides the equation becomes a trigonometry functions resulting in

$$w^6 + (t_1^2 . - 2t_2 - u_1^2)w^4 + (t_2^2 . - 2t_1t_3 + 2u_1u_3 - u_3^2)w^2 + t_3^2 - u_3^2 . = 0$$

The even power of w is assuming the fact z = w^2 and the third order of equation is

$$z^3 + m_1z^2 + m_2z + m_3 = 0 \quad (4.23)$$

Where

$$m_1 = t_1^2 . - 2t_2 - u_1^2 \quad (4.24)$$
$$m_2 = t_2^2 . - 2t_1t_3 + 2u_1u_3 - u_3^2 \quad (4.25)$$
$$m_3 = t_3^2 - u_3^2 \quad (4.26)$$

Equation 4.23 does not have any negative solution by squaring w that does not provide positive imaginary solution. Supporting the above mentioned results the lemma below satisfies the condition

Lemma 3: The real roots positivity is checked with the condition when m_1, m_2 and m_3 >=0

Let us assume

$$z = h(z) = z^3 + m_1z^2 + m_2z + m_3 = 0, \quad (4.27)$$

Then the derivative with respect to z proves that h(z) = h′(z). As z>0 then h>0 and hence prove that h'(z) which is also >0. Therefore

$$h'(z) = 3z2 + 2m1z + m \quad (4.28)$$

where h(z) has no positive real roots and thus proves the lemma.

The above lemma proves that there is no w where iw is said to be eigen value. Hence proves the theorem for all real eigen values is said to be negative when $\tau \geq 0$. Consolidation of the above theorems the conclusions lead to the following assumption

Assume that

a) m_1, m_2 and m_3 >=0
b) $R_0 > 1$

The above two assumption states that a) is ensuring real positive values and b) ensures equilibrium stability

Where E is asymptotically stable based on delay$\tau \geq 0$

Both the assumption tends to satisfy both a) and b) where E is the equilibrium tend to be stable when there is a delay, and such delay does not impact on the asymptotic stability as delay is ensured with ≥ 0 .

Let us assume that if the condition a) and b) are not stable and does not reacts to the stability then the delay is measured and its tend to vary not satisfying the condition $\tau \geq 0$. In the case of instability the results tends to oscillate.

When $m_3 < 0$ then the value of h(0) is also < 0 based on the limit $\lim_{z\to\infty} h(z) = \infty$ and inorder to achieve least positive root from the equation 4.23 then resultant becomes $w = \sqrt{z}$.

In this situation bifurcation analysis is introduced in order to prove the results with least positive root.

Then the equation based on the stability condition it referred to

$$\frac{dRe\lambda(P)}{d_P} \mid P = P_0 > 0 \quad (4.29)$$

Table 1: Parameters for Disease spread

Parameters and variables	
Dependent variables	
P	Infected cell population size
I	Cell intensity for spread
V	Cell Volume
Parameters and constantss	Source Cells
i	Infection rate
a	Growth rate cell population
β	Infected with virus
ρ	Rate of cure
δ	Affected rate of infected cells
q	Reproductively rate of the infected
c	Death rate of free virus
τ	infection equilibrium

Lemma 4: While considering w_0 is the largest positive root then the equation is balanced with $iw(\tau_0) = iw_0$ satisfying the assumption $\partial(\tau) + iw(\tau)$ is differentiated with τ as neighborhood of τ_0.

ISSN (Online) 2456 -1304

International Journal of Science, Engineering and Management (IJSEM)
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After analysis of the above differential equation by assuming h_1, h_2, and h_3 are considered as the root of the equation then $f(h) = h^3 + m_1h^2 + m_2h = 0$ with (m_2< 0) and h_3 is the highest positive value.

$$\left(\frac{dh(x)}{dx}\Big| > 0\right) \quad (4.30)$$

Hence the above eqn proof is omitted.

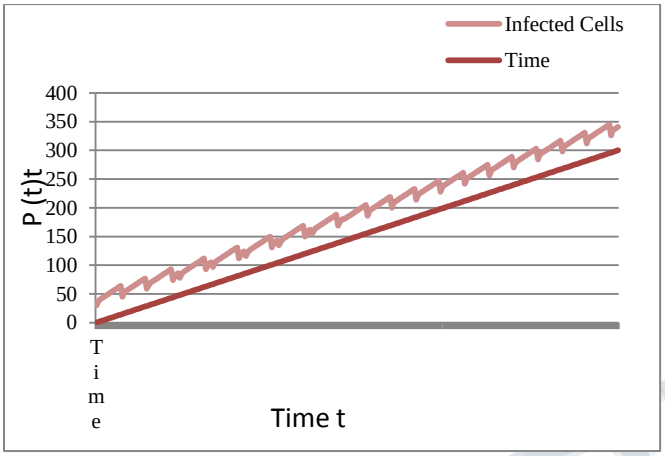

Fig 1: HIV virus infection rate vs Time

Fig 1 shows the time correlation difference between the disease spread based on the time. Such measures will assist in assumption of overall virus cells over the period of time, against the non infection and infection rate.

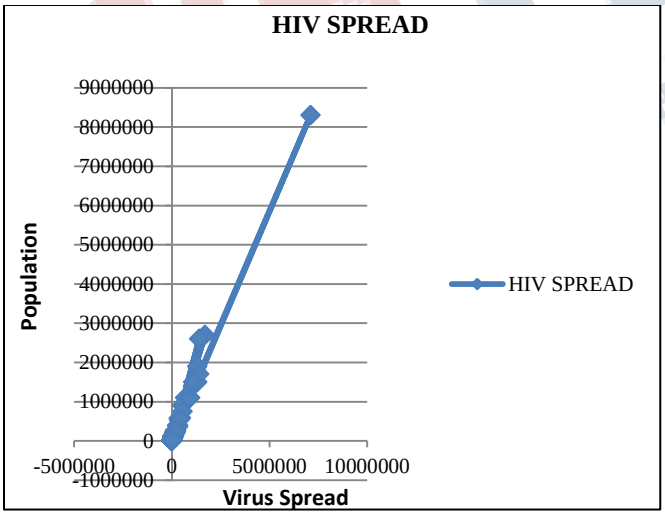

Fig2: Disease spread Ratio

Fig 2 gives the representation of the disease spread without implementing with the overall mathematical model that suggest the virus growth rate with towards acceleration and deceleration as many model fail to address two parameters as valid aspects against disease wide spread. The overall population is set for evaluation the wide spread of the spreading virus against the virus spread with the overall population represented in x axis and y axis. The Fig 3 is evaluated based on the result achieved from the overall population with that of the increasing virus spreading ratio, hence estimated HIV growth spread is shown using

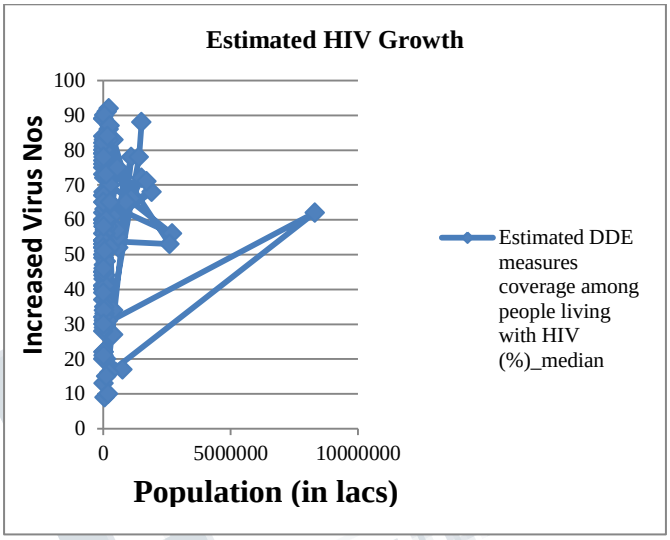

Fig 3: HIV Growth against population and infection

The infection ratio is calculated against specific population then by applying DDE as mathematical model addressing the infection growth rate by considering on virus stability equilibrium by non-considering on negative occurrence of the increasing virus volumes.

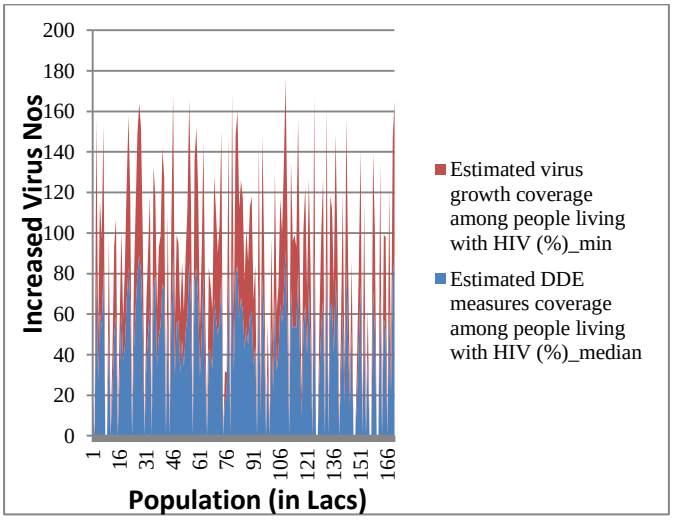

Fig 4: Min and Max Virus Growth Rate

ISSN (Online) 2456 -1304

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Fig 4 gives out the Minimum and Maximum growth rate where the increasing growth of virus against overall population is ensured and gives clarity of the growth stability analysis dealing with asymptotic states of the virus spread and its classification.

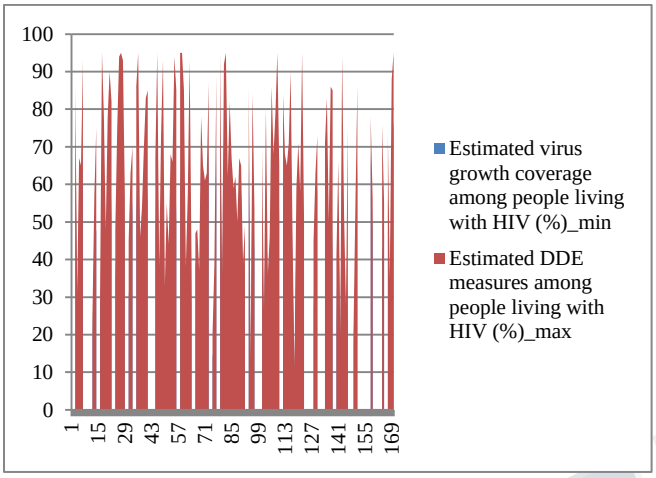

Fig 5: Virus asymptotic growth rate

Fig 5 gives the note towards asymptotic stability rate of the virus growth against growing population. The results provide trade off analysis between virus growth and DDE model analysis for ensuring maximum stability for Virus asymptotic growth rate. When applying DDE model, the stability is ensured based on virus growth against its growing population and tries to balance it using asymptotic stability analysis. The relation is ensured using asymptotic stability checks for the maximum positivity for providing consistent virus growth and gives clear analysis of its growth stability.

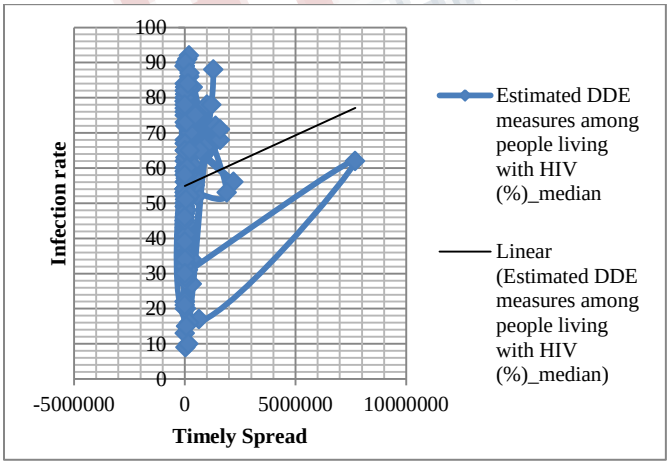

Fig 6: DDE HIV virus stability

Fig 6 gives the stability comparison of virus with its growing population against the time with the infection rate. While implementing these two coefficients into DDE model the stability is ensure against virus spread against population.

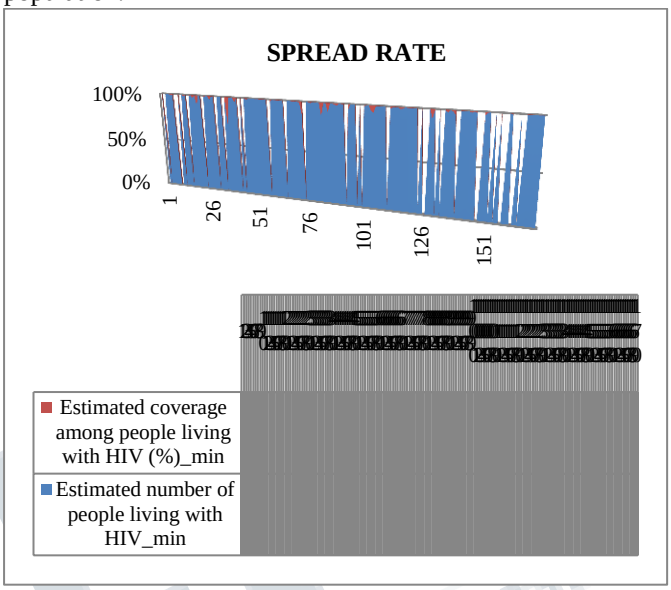

Fig 7: Virus Spread Rate with its Stability

Fig 7 gives out the stability against maximum and minimum rate of virus spread and the asymptotic stability is ensured based on the estimated growth and its overall population.

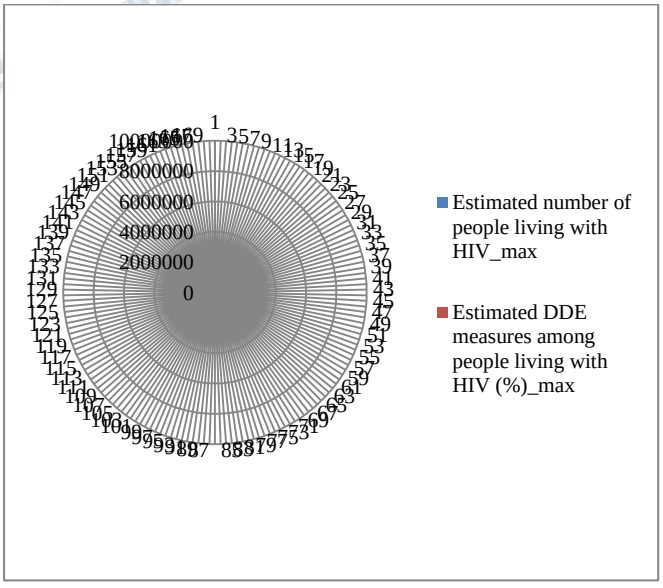

Fig 8: Bifurcation Breakdown

Fig 8 gives out Bifurcation analysis for ensuring stability by satisfying eqn 4.30. Thus concludes the stability

condition of the results by evaluating the virus population growth with the Bifurcation analysis breakdown.

VI. CONCLUSION

The work addresses the HIV virus growth stability using bifurcation parameter in DDE for ensuring the steady state by avoid the overall delay. The equilibrium considers the local and global parameter and thus ensures overall stability in growth rate. Finally the result ensure disease free equilibrium along with global stability and asymptotic bifurcation analysis breakdown.

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