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Eigenvalues for HIV-1 dynamic model with two delays

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Abstract : *In this paper we provide the asymptotic expansion of the roots of nonlinear dynamic system with two delays. We develop a series expansion to solve for the roots of the nonlinear characteristic equation obtained from the HIV-1 dynamical system. Numerical calculation are carried out to explain the mathematical conclusions.*

Keywords: *Asymptotic expansion, Delay Differential equations, Eigenvalues, HIV-1.*

I. INTRODUCTION

The disease of human immunodeficiency virus (HIV) infection has become a worldwide pandemic [1,2]. Very effective treatments for HIV infected individuals have been developed. The emergence of drug resistance is one of the most prevalent reasons for treatment failure in HIV therapy. Although the correlates of immune protection in HIV infection remain largely unknown, our knowledge of viral replication dynamics and virus-specific immune responses has grown.

A number of mathematical models have been proposed to understand the effect of drug therapy on viremia [3-6]. Drugs e.g., fusion inhibitors, reverse transcriptase inhibitors and protease inhibitors have been developed so as to attack on different phases of viral life cycle during infection [7,8]. Combination of these drugs is also used in some article [9]. The eclipse phase is an important phase of virus life cycle on which the drug therapy primarily depends. Assuming that the level of target cells is constant and that the protease inhibitor is 100% effective, they obtained the expression of the viral load and explored the effect of the intracellular delay on viral load change [10].

The nonlinear characteristic equation corresponding to the HIV-1 model belongs to a well-known class of equations known as exponential polynomials [11-13] and many researchers in DDEs have (understandably) chosen to study them [14,15]. In the broader mathematics community, research into this class of algebraic equations is very active and extends to numerical schemes for computing the roots (see papers by Jarlebring such as [16]) and applications to fields afar as quantum computing [17].

In this paper we presented a new approach to solve the transcendental characteristic equation of HIV-1 infection dynamical system of DDEs, based upon the series expansion for the roots of the nonlinear eigenvalue problem. Also we provide the numerical results to support our claims of accuracy.

II. EIGENVALUES OF DELAY DIFFERENTIAL EQUATION WITH MULTI DELAY

Consider a delay differential equation with multi delay $\tau_i, i = 1,2, ...,$

$$\dot{y}(t) = a_1 y(t) + a_2 y(t-\tau_1) + a_3 y(t-\tau_2) + ... + a_i y(t-\tau_i) + \ldots ; t > 0, \tag{1}$$

$$y(t) = \varphi(t); \ t \leq 0,$$

where $\varphi(t)$ is the initial history function. The Laplace transform of (1) is

$$s = a_1 + a_2 e^{-s\tau_1} + \cdots + a_i e^{-s\tau_i} + \cdots, \tag{2}$$

a transcendental equation with an infinite number of roots $\{s_j\}$ in the complex plane. Thus the solutions are constructed as an infinite series

$$Y(t) = \sum_{j=-\infty}^{\infty} C_j e^{s_j t},$$

and we note that these basis functions $e^{s_j t} x$ form a Schauder basis for L^p functions over a finite domain. The coefficients C_j can be computed via evaluating the history function $\varphi(t)$ and the basis functions $e^{s_j t}$ at $2N+1$ time points in $[-\tau, 0]$ and then linearly solving for $2N+1$ of the C_j's.

The exponential term, $e^{-s\tau_i}$, induced by the time delay term $x(t-\tau_i)$, makes the characteristic equation transcendental (i.e., infinite dimensional and nonlinear). Thus, it is not feasible to find roots of equation (1), which has an infinite number of roots. We develop a series expansion for the roots to the nonlinear eigenvalue problem corresponding to delay differential equation with multi delay. Our goal is to make the truncated sums to be more computationally efficient to evaluate.

III. HIV-1 INFECTION MODEL WITH TWO DELAY

The general model that have been used to study [3,8,18-20], HIV-1 infection dynamics have a form similar to

$$\begin{aligned} \frac{dT}{dt} &= s - d_T T - kVT, \\ \frac{dT^*}{dt} &= kVT - \delta T^*, \\ \frac{dV}{dt} &= N\delta T^* - cV. \end{aligned} \tag{3}$$

where the notations are described below in Table-I.

TABLE - I: In vitro model parameters and its values which are taken from [21**Error! Reference source not found.**] and [22]

Notation	Description	Values
T[cells/mm^3]	Uninfected target cells	180
T^* [cells/mm^3]	Infected cells that are producing virus	3.6
V [virions/mm^3]	Virus (Both infectious and non-infectious virus)	134
s [cells/mm^3/day]	Rate at which new target cells are generated	1−10
d_T [/day]	Specific death rate of target cells	0.01−0.03
k[mm^3/virions/day]	Constant rate that characterizing target cell infection	$3.5 \times 10^{-5} - 4.2 \times 10^{-5}$
δ [/day]	Total death rate of target cells	0.26−0.68
N [virions/cells]	New virus particles	326−503

Models of this standard form have been adequate to summarize the effects of drug therapy on the virus concentration. Perelson [21] used this model to analyse the response to the protease inhibitor therapy. We assumed that the target cell density remained unchanged during the observed period. Also we introduced two delays τ_1 as the total intracellular delay, considered in Dixit and Perelson [23], and τ_2 as the delay representing the time necessary for a newly infected virus to become mature and then infectious.

Thus the standard model reduced to a model with delay kernal as

$$\begin{aligned} \frac{dT^*}{dt} &= kT_0 V_I(t-\tau_1) - \delta T^*(t), \\ \frac{dV_I}{dt} &= (1-n_p)N\delta T^*(t-\tau_2) - cV_I(t), \\ \frac{dV_{NI}}{dt} &= n_p N\delta T^*(t-\tau_2) - cV_{NI}(t). \end{aligned} \tag{4}$$

where T_0 is the constant level of target cells and n_p is the efficacy of the protease inhibitor scaled such that $n_p = 1$ corresponds to a completely effective drug that results only in the production of non infectious virions, V_{NI}.

IV. ASYMPTOTIC EXPANSION FOR THE EIGENVALUES

In this section, we develop our series expansion for the roots to the nonlinear characteristic equation arising from the two delay DDE. Note that for the multi delay case, the conventional approach focuses on developing bounds for the roots, whereas here, we are explicitly computing the roots.

The linearized HIV-1 equation (4) can be expressed in state space as,

$$\dot{x}(t) = ax(t) + bx(t-\tau_1) + cx(t-\tau_2) \tag{5}$$

where, $a = \begin{bmatrix} -\delta & 0 & 0 \\ 0 & -c & 0 \\ 0 & 0 & -c \end{bmatrix}$, $b = \begin{bmatrix} 0 & kT_0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$ and $c = \begin{bmatrix} 0 & 0 & 0 \\ (1-n_p)N\delta & 0 & 0 \\ n_p N\delta & 0 & 0 \end{bmatrix}$.

Defining $x = \{T^*, V_I, V_{NI}\}^T$, where ^{T} indicates transpose. a, b and c are the linearized coefficient matrix of the HIV-1 infection model and are functions of in vitro model parameters.We will rescale and rearrange terms, defining several new variables and parameters in order to reduce the equation to its essential mathematical features. We rescale time by the first delay $t = \frac{t}{\tau_1}$, the parameters so that $a_1 = a\tau_1, b_1 = b\tau_1, c_1 = c\tau_1, \tau = \frac{\tau_2}{\tau_1}$, and denote $\dot{x}(t) = \frac{d}{dt}x(t) = \tau_1 \frac{d}{dt}x(t)$ to obtain the equation

$$\dot{x}(t) = a_1 x(t) + b_1 x(t - \tau_1) + c_1 x(t - \tau_2)$$

After a Laplace transform, the corresponding nonlinear characteristic equation for $s \in C$ is, thus

$$s = a_1 + b_1 e^{-s} + c_1 e^{-s\tau}. \qquad (6)$$

We then let $\lambda = s - a_1, b_2 = b_1 e^{-a_1}, c_2 = c_1 e^{-a_1 \tau}$, and multiply through by $e^{\lambda\tau}$, equation (6) becomes much cleaner equation as,

$$\lambda e^{\lambda\tau} = b_2 e^{(\tau-1)\lambda} + c_2. \qquad (7)$$

Inspired by the original expansion in [24**Error! Reference source not found.**], we note that for $|c_2|$ near to or far from zero, we can write λ as a small perturbation u of $\ln c_2$,

$$\lambda = (\ln c_2 + u)/\tau.$$

and then safely assume that

$$|u| \ll |\ln c_2|. \qquad (8)$$

Substituting this form of λ into equation (7**Error! Reference source not found.**) we find that

$$\frac{1}{\tau}\left(1 + \frac{u}{\ln c_2}\right) c_2 e^u =$$

b2c2τ−1τlnc2 (eu)τ−1τ+ c2lnc2. *(9)*

To proceed, we will also assume that

$$\left|\frac{b_2}{c_2{}^{1/\tau} \ln c_2}\right| \ll 1, \qquad (10)$$

in addition to (8). This restriction on the coefficients is a result of the chosen rearrangement of(6) into (7). There is nothing particularly special about (10**Error! Reference source not found.**) and choosing to recast (6) differently would simply necessitate different assumptions on the parameters in order for an expansion to converge. Moving forward, we can solve (9) for u as

$$u \approx \ln \tau + \ln(1/\ln c_2),$$

which means that

$$u = \ln \tau + \ln(1/\ln c_2) + v, \qquad (11)$$

where our attention now focuses on solving for a new variable v. As discussed by Corless et al. [25**Error! Reference source not found.**], the nested logarithms in (11) need not select the same branch. As Corless et al. [25**Error! Reference source not found.**] do, we will let the outer logarithm be the principal branch and denote *Ln* as the inner logarithm for which we have not yet chosen a branch, i.e.,

$$u = \ln \tau + \ln(1/\ln c_2) + v.$$

By substituting u back into (9), we can cancel several terms and simplify our problem to one of finding the roots v to the equation

$$1 + \frac{\ln \tau}{Ln\, c_2} + \frac{\ln(1/Ln\, c_2)}{Ln\, c_2} + \frac{1}{Ln\, c_2} = \frac{b_2}{c_2}\left(\frac{c_2 \tau}{Ln\, c_2}\right)^{\frac{\tau-1}{\tau}} e^{-v/\tau} + e^{-v}.$$

If we let

$$\sigma = \frac{1}{Ln\, c_2}, \gamma = \frac{b_2}{c_2}\left(\frac{c_2 \tau}{Ln\, c_2}\right)^{\frac{\tau-1}{\tau}}, \mu = \frac{\ln \tau \ln(1/Ln\, c_2)}{Ln\, c_2} - \gamma.$$

then our efforts will focus on identifying the roots of

$$f(v) \equiv e^{-v} + \gamma e^{-v/\tau} - \sigma v - 1 - \gamma - \mu. \tag{12}$$

Note that the motivation for adding and subtracting γ will become self-evident in the proof for the following lemma.

Lemma 1 *If there exists positive numbers α and β such that $|\sigma|<\alpha$ and $|\mu|<\alpha$ then (12***Error! Reference source not found.***) has a single root inside the region $|v| \le \beta$.*

Proof. Let δ denote the lower bound of $|e^{-v}- 1|$ on $|v| = \beta$ and δ_τ denote the lower bound of $|\gamma e^{-v/\tau} - \gamma|$ on $|v| = \beta$. We can arbitrarily choose $\beta = \pi \min\{1, \tau\}$ since $e^{-v}-1$ has only one root at zero for $\beta \in (0,2\pi\tau)$ and $\gamma(e^{-v/\tau}-1)$ also has only one root at $v = 0$ for $\beta \in (0,2\pi\tau)$. Thus there is only one root at $v = 0$ for $e^{-v} -1+\gamma(e^{-v/\tau}-1)$ in the region $|v| \le \pi \min\{1, \tau\}$ and that on $|v| = \pi \min\{1, \tau\}$ we have a lower bound of $\min\{\delta,\delta_\tau\}$.

Let $\alpha = \frac{\min\{\delta,\delta\tau\}}{2(\pi+1)}$ and then for $|\sigma| < \alpha$, $|\mu| < \alpha$, and $|v| = \pi \min\{1, \tau\}$, we have that

$$|\sigma v + \mu| \le |\sigma||v| + |\mu| \le \frac{\min\{\delta,\delta\tau\}}{2(\pi+1)}\pi + \frac{\min\{\delta,\delta\tau\}}{2(\pi+1)} = \frac{\min\{\delta,\delta\tau\}}{2(\pi+1)} < \min\{\delta,\delta_\tau\}.$$

Since $|e^{-v} - 1 + \gamma e^{-v/\tau} - \gamma| > \min\{\delta, \delta_\tau\}$ on the curve defined by $|v| = \pi \min\{1, \tau\}$, we have satisfied the hypotheses of Rouche` 's Theorem [26] and can therefore conclude that there is only one root to (12) inside $|v| = \pi \min\{1, \tau\}$.

□

By Cauchy's theorem, we can then compute *v* using the well-known formula from complex analysis

$$v = \frac{1}{2\pi i}\oint_{|\zeta|=\beta} \frac{f'(\zeta)\zeta}{f(\zeta)} d\zeta = \frac{1}{2\pi i}\oint_{|\zeta|=\beta} \frac{\left(-e^{-\zeta} - \gamma\frac{e^{-\zeta/\tau}}{\tau} - \sigma\right)\zeta}{e^{-\zeta} + \gamma e^{-\zeta/\tau} - \sigma\zeta - 1 - \gamma - \mu} d\zeta. \tag{13}$$

for $\beta=\pi\min\{1, \tau\}$. The $1/f(\zeta)$ can be expanded into the following (absolutely and uniformly convergent) power series

$$\frac{1}{f(\zeta)} = \sum_{k=0}^{\infty}\sum_{m=0}^{\infty}(e^{-\zeta} + \gamma e^{-\frac{\zeta}{\tau}} - 1 - \gamma)^{-k-m-1}\zeta^k \sigma^k \mu^m \alpha_m^{m+k}, \tag{14}$$

with some coefficients α_m. The substitution of (14) into (13) and evaluation of the contour integral generates a double series in *m* and *k*. Note, however, that the *m=0* term is zero because the integrand has the same number of roots (at ζ=0) in the numerator and the denominator. The doubly infinite and absolutely convergent power series for *v* in σ and μ is, thus

$$v = \sum_{k=0}^{\infty}\sum_{m=0}^{\infty} \alpha_{km}\sigma^k \mu^m \ , \tag{15}$$

where the α_{km} are coefficients independent of σ and μ. The coefficients α_{km} are computed by first computing a power series expansion in σ and then applying the Lagrange Inversion Theorem [27**Error! Reference source not found.**] to obtain *v* as a function of μ. To facilitate rearrangement of this series into the form of (15**Error! Reference source not found.**), we denote

$$f_2(w) \equiv f(w) - f(0),$$

and note that the derivative of *f*(*w*) with respect to σ is −*w*. Equation (15) can thus be written (after the power series expansion in σ around zero)

$$v = \sum_{k=0}^{\infty}\sum_{m=0}^{\infty} m^{\bar{k}} \ h_{m,k}\frac{\mu^m}{m!}\frac{\sigma^k}{k!}, \tag{16}$$

where $m^{\bar{k}}$ is a rising factorial, (We note that in the combinatorics literature, $m^{(k)}$ is more commonly used as a rising factorial, also known as the Pochhammer symbol with $\bar{k}$=(*m*+*k*−1)!−(*m*−1)!) and $h_{m,k} = \lim_{w\to 0} h_{m,k}(w)$ with

$$h_{m,k}(w) = \frac{d^{m-1}}{dw^{m-1}}\left(w^{m+k} f_2(w)^{-(m+k)}\right).$$

Straightforward application of the product rule yields that

$$h_{m,k}(w) = \sum_{l=0}^{m-1} \binom{m-1}{l} \left(\frac{d^{m-1-l}}{dw^{m-1-l}} w^{m+k}\right)\left(\frac{d^l}{dw^l} f_2(w)^{-(m+k)}\right).$$

The *l*th derivative of $f_2(w)^{-(m+k)}$ is computed using Faă Di Bruno's formula [28**Error! Reference source not found.**] for higher derivatives of composite functions and thus

$$h_{m,k}(w) = \sum_{l=0}^{m-1} a_{klm}\ w^{k+l+1} \sum_{p=0}^{l} b_{kmp}\ f_2(w)^{-(m+k+p)}\, \mathbb{B}_{l,p}\left(f_2{}'(w), \dots, f_2{}^{(l-p+1)}(w)\right),$$

where,

$$a_{klm} = \binom{m-1}{l}\frac{(m+k)!}{(k+l+1)!}, \qquad b_{kmp} = (-1)^p (m+k)^{\overline{p}},$$

and $\mathbb{B}_{l,p}$ are the partial Bell polynomials [11,29**Error! Reference source not found.**]. Recall that for an arbitrary sequence $\{x_i\}$ and $l,p \in$N, the partial Bell polynomials are

$$\mathbb{B}_{l,p}(x_1, \dots, x_{l-p+1}) = \sum \frac{l!}{j_1!\, j_2! \dots j_{l-p+1}!}\left(\frac{x_1}{1!}\right)^{j_1}\left(\frac{x_2}{2!}\right)^{j_2} \dots \left(\frac{x_{l-p+1}}{(l-p+1)!}\right)^{j_{l-p+1}},$$

with the sum taken over all sequences $\{j_1, \dots, j_{n-k+1}\} \in$ N such that $\sum_{i=1}^{n-k+1} j_i = m$ and $\sum_{i=1}^{n-k+1} i j_i = k$ (a simple Diophantine linear system). The sets of indices $\{j_i\}$ satisfying these sums are just a way of describing all possible partitions of a set of size *k* [30**Error! Reference source not found.**].

In what follows, the argument for the Bell polynomial frequently takes the form $\{f_2{}^{(1+i)}(0)\}_{i=1}^{n}$. To improve the clarity of the formulas, we denote

$$F_n = \{f_2{}^{(1+i)}(0)\}_{i=1}^{n}; \quad n \in N,$$

to be a finite sequence of higher derivatives of f_2. Formally taking the limit for $\lim_{w\to 0} h_{m,k}(w)$ yields

$$\frac{\sum_{l=0}^{m-1} \bar{\alpha}_{klm}\ \sum_{p=0}^{l} \sum_{q=0}^{2m-2-l} \bar{\beta}_{klmpq}\ \ \mathbb{B}_{2m-2-l-q\ ,m-1-p}\ \left(F_{m-l-q+p}\right)\mathbb{B}_{l,p}^{(q)}\ (F_{l-p+1})}{f''_2\ (0)^{2m+k-1}}$$

where

$$\bar{\alpha}_{klm} = \alpha_{klm} \binom{2m+k-1}{2m-l-2}(k+l+1)!, \qquad \bar{\beta}_{klmpq} = \beta_{kmp}\binom{2m-2-l}{q}\frac{(m-1-p)!}{(2m+k-1)!}.$$

The evaluation of most terms in (17) is computationally straightforward and efficient, except the term involving $\mathbb{B}_{l,p}^{(q)}$. For example, the sum in (16) for *m* = 10 and *k* = 100 can take around one minute for computation when using Mathematica to analytically find the *q*th derivative of $\mathbb{B}_{l,p}$ and then sum the terms. In [31**Error! Reference source not found.**], Mishkov derived a formula for $\mathbb{B}_{l,p}^{(q)}$, but to implement it would consists of solving a cascade of linear Diophantine equations to obtain the correct indices for the sums. We will use a recursive property of $\mathbb{B}_{l,p}^{(k)}$ to avoid having to solve systems of Diophantine equations. Note that for an arbitrary sequence X=$\{x_j\}$

$$\frac{\partial}{\partial x_j}\mathbb{B}_{l,p}(X) = \binom{l}{j}\mathbb{B}_{l-j,p-1}(X),$$

and thus in the context of (17) we have that

$$\mathbb{B}_{l,p}^{(q)}(F_{l-p+1}) = \sum_{r_1=1}^{l-p+1}\binom{l}{r_1}\sum_{r_2=0}^{q-1}\binom{q-1}{r_2}\ \mathbb{B}_{l-r_1,p-1}^{q-r_2-1}(F_{l-p+1}) \tag{18}$$

recursively allows (eventual) computation of the derivatives by evaluation of the partial Bell polynomials themselves The use of Mathematica's memoization features for recursive sums substantially sped up the computation as well, naturally at the expense of increased memory usage. We now have that the principal branch of the roots of (7) is

$$\lambda = \frac{\ln c_2 + \ln\tau + \ln(1/\ln c_2) + v}{\tau}, \tag{19}$$

where

$$v = \sum_{k=0}^{\infty}\sum_{m=0}^{\infty} m^{\bar{k}} \;\; h_{m,k}\frac{\mu^m}{m!}\frac{\sigma^k}{k!}, \tag{20}$$

We note that for $i \geq 1$

$$f_2^{(1+i)}(0) = (-1)^i(1 + c\tau - i).$$

and thus $h_{m,k}$ is defined as

$$\frac{\sum_{l=0}^{m-1}\sum_{p=0}^{l}\sum_{q=0}^{2m-2-l}\hat{\alpha}_{klmpq}\;\; \mathbb{B}_{2m-2-l-q,m-1-p}\left(F_{m-l-q+p}\right)\mathbb{B}_{l,p}^{(q)}\left(F_{l-p+1}\right)}{-(1+\eta\tau^{-1})^{2m+k-1}}$$

(21)
where

$$F_n = \{(-1)^n(1 + \eta\tau^{-n})\}_{i=1}^{n},$$

$$\alpha_{klmpq} = \frac{(-1)^p(k+m)\Gamma(m)\Gamma(m-p)\Gamma(k+m+p)}{q!\,l!\,\Gamma(2+k+l)\Gamma(-l+m)\Gamma(-1-l+2m-q)},$$

$$\sigma = \frac{1}{Ln\, c_2}, \gamma = \frac{b_2}{c_2}\left(\frac{c_2\tau}{Ln\, c_2}\right)^{\frac{\tau-1}{\tau}}, \mu = \frac{\ln\tau\ln(1/Ln\, c_2)}{Ln\, c_2} - \gamma.$$

and recalling that $\mathbb{B}_{l,p}^{(q)}$ is defined recursively in (18).

The full description of the jth branch root for the characteristic equation in (6**Error! Reference source not found.**) is therefore

$$s_j = \frac{1}{\tau}\left(\ln_j c_2 + \ln\tau + \ln\left(1/\ln_j c_2\right) + v_j\right) + a_1,$$

Where $\ln_j(z) = |z| + \arg(z) + 2\pi ij$, v is defined in (20**Error! Reference source not found.**), and the subscript on the v indicates the chosen branch for the logarithms in σ,η, and μ.

V. NUMERICAL CALCULATION

In this section, we provide numerical results for the estimation of the eigenvalues. Consider the vector form of the delay differential equation (5) with two delay.

We note that the accuracy of our asymptotic expansion rests on the assumption that (10) is small and so we choose

$$b_2 = \begin{bmatrix} 0 & 5.382\times10^{-4} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},\quad c_2 = \begin{bmatrix} 1.0832 & 0 & 0 \\ 0 & 0.0068 & 0 \\ 0 & 0 & 0.0068 \end{bmatrix}, \text{ and } a_1 = \begin{bmatrix} -0.96 & 0 & 0 \\ 0 & -9 & 0 \\ 0 & 0 & -9 \end{bmatrix}.$$

$$a = \begin{bmatrix} -0.32 & 0 & 0 \\ 0 & -3 & 0 \\ 0 & 0 & -3 \end{bmatrix},\quad b = \begin{bmatrix} 0 & 0.0058 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},\quad \text{and } c = \begin{bmatrix} 0 & 0 & 0 \\ 15.36 & 0 & 0 \\ 138.24 & 0 & 0 \end{bmatrix},$$

and thus

$$\frac{b_2}{c_2^{1/\tau}\ln c_2} \approx \begin{bmatrix} 0 & 0.0782 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

Numerical investigations suggested that the series converges in m about a factor of four times faster than it converges in k. Accordingly, Figure - 1 depicts the convergence in m with $k = m^4$. We note that up to $m = 8$, the series converges nicely. For $m > 8$, however, the series exhibits a reduction of accuracy, likely due to the numerical issues inherent in evaluating such large series. Lastly, in subsequent computations of s_j, we choose to truncate the series at $m = 8$ and $k = 1000$ to maintain accuracy.

Figure - 1

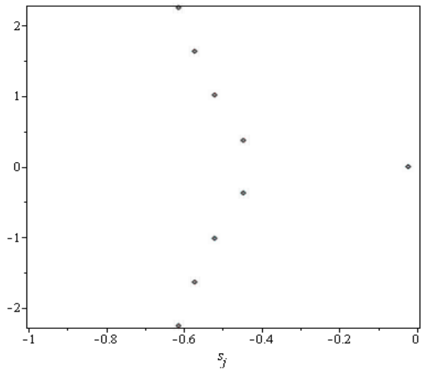

Figure - 1: Eigenvalues s_j computed using the expansion in Section 4 with the parameter values in Table-I.

VI. CONCLUSION

In this paper, the new approach for the eigenvalue of the HIV-1 infected dynamical problem, have been presented using the series expansion of the roots of the nonlinear characteristic equation. Since Asl and Ulsoy's [32**Error! Reference source not found.**] original article, the connection between DDE eigenvalues and solutions to Lambert *W* has been substantially extended and expanded [16,25,28,29,31**Error! Reference source not found.**]. These results, however, do not extend to multi delay DDEs as (to the best of our knowledge) the nonlinear eigenvalue problem can be cast as a Lambert *W* equation only when the DDE has a single delay. We have developed an asymptotic expansion for the roots to a nonlinear eigenvalue problem associated with two delay model of HIV-1 infection dynamics. We have provided numerical evidence supporting the accuracy of our expansion.

REFERENCES

[1] S. Bonhoeffer, R.M. May, G.M Shaw, M.A. Nowak, Virus dynamics and drug therapy, *Proc. Natl. Acad. Sci. USA*, 94, 1997, 6971 - 6976.

[2] X.Y. Song, A.U. Neumann, Global stability and periodic solution of the viral dynamics, *J. Math. Anal. Appl.*, 329, 2007, 281 - 297.

[3] M.A. Nowak, S. Bonhoeffer, G.M. Shaw, R.M. May, Anti-viral drug treatment: dynamics of resistance in free virus and infected cell populations, *J. Theor. Biol.*, 184, 1997, 203 - 217.

[4] T.B. Kepler, A.S. Perelson, Drug concentration heterogeneity facilitates the evolution of drug resistance, *Proc. Natl. Acad. Sci. USA*, 95, 1998, 11514 - 11519.

[5] P.K. Roya, A.N. Chatterjee, D. Greenhalgh, J.A. Khanc, Long term dynamics in a mathematical model of HIV-1 infection with delay in different variants of the basic drug therapy model, *Nonlinear Analysis: Real World Applications*, 14, 2013, 1621 - 1633.

[6] R.J. Smith, L.M. Wahl, Distinct effects of protease and reverse transcriptase inhibition in an immunological model of HIV-1 infection with impulsive drug effects, *Bull. Math. Biol.*, 66, 2004, 1259 - 1283.

[7] M. Pitchaimani, C. Monica, M. Divya, Stability analysis for HIV infection delay model with protease inhibitor, *Biosystems*, 114, 2013, 118 - 124.

[8] D. Kirschner, Using mathematics to understand HIV immune dynamics, *Notices Am. Math. Soc*., 43, 1996, 191 - 202.

[9] P.W. Nelson, A.S. Perelson, Mathematical Analysis of delay differential equation models of HIV-1 infection, *Math. Biosci*., 179, 2002, 73 - 94.

[10] V. Herz, S. Bonhoeffer, R. Anderson, R. May, M. Nowak, Viral dynamics in vivo: limitations on estimations on intracellular delay and virus decay, *Proc. Nat. Acad. Sci.*, 93, 1996, 7247.

[11] E.T. Bell, Exponential Polynomials, *The Analysis of Mathematics*, 35(2), 1934, 258 - 277.

[12] C.J. Moreno, The zeros of exponential polynomials (I), *Compositio Mathematica*, 26(1), 1973, 69 - 78.

[13] J.F. Ritt, On the Zeros of Exponential Poylnomials, *Transactions of the American Mathematical Society*, 31(4), 1929, 680 - 686.

[14] C.E. Avellar, J.K. Hale, On the Zeros of Exponential Polynomials, *Journal of Mathematical Analysis and Applications*, 73, 1980, 434 - 452.

[15] K.L. Cooke, P. Van Den Driessche, On zeros of some transcendental functions, *Eunkcialaj Ekvacioj*, 29, 1986, 77 - 90.

[16] E. Jarlebring, Critical delays and polynomial eigenvalue problems, *Journal of Computational and Applied Mathematics*, 224(1), 2009, 296- 306.

[17] Y. Sasaki, On zeros of exponential polynomials and quantum algorithms, *Quantum Information Processing*, 9(3), 2009, 419 - 427.

[18] A. Perelson, D. Kirschner, R. De Boer, Dynamics of HIV infection of CD4+ T cells, *Math. Biosci*., 114, 1993, 81 - 90.

[19] A. McLean, S. Frost, Ziduvidine and HIV: mathematical models of within-host population dynamics, *Rev. Med. Virol*., 5, 1995, 141 - 145.

[20] M. Nowak, R. Anderson, M. Boerlijst, S. Bonhoeffer, R. May, A. McMichael, HIV-1 evolution and disease progression, *Science,* 274 1996, 1008 - 1011.
[21] A. Perelson, A. Neumann, M. Markowitz, J. Leonard, D. Ho, HIV-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time, *Science*, 271, 1996, 1582 - 1585.
[22] P.K. Srivastava, M. Banerjee, P. Chandra, Modeling the drug therapy for HIV infection, *J. Biol. systems*, 17, 2009, 213 - 223.
[23] N.M. Dixit, A.S. Perelson, Complex patterns of viral load decay under antiretroviral therapy: in
uence of pharmacokinetics and intracellular delay, *J. Theor. Biol.*, 226m 2004, 95 - 109.
[24] N.D. De Bruijn, Asymptotic Methods in Analysis, North Holland Publishing Company, Amsterdam, The Netherlands, Dover Edition, 1958.
[25] R.M. Corless, G.H. Gonnet, D.E.G. Hare, D.J. Jerey, and D.E. Knuth, On Lambert's W function, *Advances in Computational Mathematics*, 5, 1996, 329 - 359.
[26] J.K. Hale, Theory of Functional Differential Equations, *Springer-Verlag, New York*, 1977.
[27] M. Abramowitz, I.A. Stegun, Handbook of Mathematical Functions, Dover, New York, NY, 1972.
[28] W.P. Johnson, The Curious History of Fa di Bruno's Formula, *The American Mathematical Monthly*, 109(3), 2002, 217 - 222.
[29] Wheeler, F. S., 1987. Bell polynomials, *ACM SIGSAM Bulletin*, 21(3): 44 - 53.
[30] L.H. Encinas, A.M. Del Rey, J.M. Masque, Faa di Bruno's formula, lattices, and partitions, *Discrete Applied Mathematics*, 148(3), 2005, 246 - 255.
[31] R.L. Mishkov, Generalization of the formula of Fa di Bruno for acomposite function with a vector argument, *International Journal of Mathematics and Mathematical Sciences*, 24(7), 2000, 481 - 491.
[32] F.M. Asl, A.G. Ulsoy, Analysis of a system of linear delay differential equations, ASME. *J. Dyn. Syst. Meas. Cont.*, 125, 2003, 215 - 223.