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Modeling of HIV, SIR and SIS epidemics on time scales and oscillation theory

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MODELING OF HIV, SIR AND SIS EPIDEMICS ON TIME SCALES AND OSCILLATION THEORY

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ABSTRACT

We study higher dimensional systems of first order dynamic equations on time scales together with their applications. In particular, we focus on epidemic models such as HIV (Human Immunodeficiency Virus), SIS (Susceptible-Infected-Susceptible) and SIR (Susceptible-Infected-Recovered).

First, we generalize the early studied continuous three dimensional linear model of drug therapy for HIV-1 decline on time scales in order to derive new discrete models that predict the total concentration of plasma virus as a function of time. We compare these models to explore the impact of the theory of time scales. After fitting the models to the data collected at a clinical trial using nonlinear regression analysis, we show that the discrete systems result in the best fit. We extend our work, in which the efficacy of the drug therapy is assumed to be perfect, to the presence of combined imperfect drug therapy, and derive the unique solution for the model on time scales. We also discuss the stability of the trivial solution of this model on the set of integers.

Motivated by the fact that between discrete and continuous models of HIV-1 dynamics, the former is more appropriate, we formulate and solve two dimensional SIS and SIR epidemic models with nonlinear incidence and time dependent coefficients on time scales. Later on, we discuss the asymptotic behavior of susceptibles and infectives. In addition, we study three dimensional discrete SIR models with nonlinear incidence and time independent coefficients. Specifically, we show the local stability and global stability of equilibria by the linearization method and constructing a suitable Lyapunov function.

In all the work above, we show the applications of positive solutions of higher dimensional systems in epidemiology. Finally, we investigate four dimensional dynamic systems, in which solutions are classified based on the signs of their components, and find the criteria to ensure that these systems are oscillatory and nonoscillatory.

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1. INTRODUCTION

The theory of time scales, closed subsets of the real numbers, dates back to Ph.D. dissertation of Stefan Hilger in 1988, [27]. The main idea of studying dynamic equations on time scales is the unification and the extension of continuous and discrete analysis. Dynamic equations on time scales turn out to be ordinary differential equations if the time scale is chosen to be the set of real numbers, and difference equations if the time scale is chosen to be the set of integers. Many other time scales may also be chosen to study such as $q^{N_0} = \{q^n : n \in \mathbb{Z}\} \cup \{0\}$, $q > 1$ and $h\mathbb{Z} = \{hz : z \in \mathbb{Z}\}$, $h > 0$. Indeed, the theory of time scales helps avoid proving results individually for different time scales.

This dissertation is related to both continuous and discrete epidemic models and behavior of their solutions. In the next subsections, time scales calculus and epidemic models are presented briefly and the outline of the dissertation is given at the end of this section.

1.1. INTRODUCTION TO TIME SCALES CALCULUS

In this subsection, the basics of time scales calculus are introduced from the well-known introductory books by Bohner and Peterson [13, 14].

Let $\mathbb{T}$ be a time scale. For $t \in \mathbb{T}$, the forward jump operator $\sigma : \mathbb{T} \to \mathbb{T}$ and the backward jump operator $\rho : \mathbb{T} \to \mathbb{T}$ are defined by $\sigma(t) := \inf\{s \in \mathbb{T} : s > t\}$ and $\rho(t) := \sup\{s \in \mathbb{T} : s < t\}$. The graininess function $\mu : \mathbb{T} \to [0, \infty)$, defined by

$\mu(t) := \sigma(t) - t$ and is the distance between successive points in the time scales. Using the forward and backward jump operators, any point of a time scale can be classified as in the following table:

Table 1.1. Classification of points

$t < \sigma(t)$	t is right-scattered
$t = \sigma(t)$	t is right-dense
$\rho(t) < t < \sigma(t)$	t is isolated
$t > \rho(t)$	t is left-scattered
$t = \rho(t)$	t is left-dense
$\rho(t) < t < \sigma(t)$	t is dense

Note that $\sigma(\rho(t)) = t$ and $\rho(\sigma(t)) = t$ may not always be true. If $\mathbb{T}$ has a left-scattered maximum m, then $\mathbb{T}^\kappa = \mathbb{T} - \{m\}$. Otherwise, $\mathbb{T}^\kappa = \mathbb{T}$. The function $f^\sigma : \mathbb{T} \to \mathbb{R}$ is defined by $f^\sigma(t) = f(\sigma(t))$ for all $t \in \mathbb{T}$ and $[t_0, \infty)_\mathbb{T} := [t_0, \infty) \cap \mathbb{T}$.

The jump operator is used to define a generalized derivative f^Δ, so called the delta (or Hilger) derivative of f. For given any $\epsilon > 0$, if there exists a $\delta > 0$ such that

$$|[f^\sigma(t) - f(s)] - f^\Delta(t)[\sigma(t) - s]| \leq \epsilon|\sigma(t) - s|, \quad \text{for all } s \in (t - \delta, t + \delta),$$

then f is delta differentiable on $t \in \mathbb{T}^\kappa$. If $\mathbb{T} = \mathbb{R}$, then $f^\Delta = f'$, i.e., the delta derivative coincides with the usual derivative. If $\mathbb{T} = \mathbb{Z}$, then $f^\Delta = \Delta f$, where Δ is the usual forward difference operator.

Theorem 1.1.1. Suppose $f : \mathbb{T} \to \mathbb{R}$ and $t \in \mathbb{T}^\kappa$.

(i) If f is differentiable at t, then f is continuous at t.

(ii) If f is continuous at t and t is right-scattered, then f is differentiable at t with

$$f^\Delta(t) = \frac{f^\sigma(t) - f(t)}{\mu(t)}.$$

(iii) If t is right-dense, then f is differentiable at t iff the limit

$$\lim_{s\to t}\frac{f(t)-f(s)}{t-s}$$

exists as a finite number. In this case, the limit is equal to the delta derivative of f.

(iv) If f is differentiable at t, then $f^\sigma(t) = f(t) + \mu(t)f^\Delta(t)$.

The equation in Theorem 1.1.1 (iv) is called simple useful formula and holds for any point in $\mathbb{T}$. The product and the quotient rules on time scales are presented in the next theorem.

Theorem 1.1.2. Assume $f, g : \mathbb{T} \to \mathbb{R}$ are differentiable at $t \in \mathbb{T}^\kappa$. Then:

(i) The product $fg : \mathbb{T} \to \mathbb{R}$ is differentiable at t with

$$(fg)^\Delta(t) = f^\Delta(t)g(t) + f^\sigma(t)g^\Delta(t) = f(t)g^\Delta(t) + f^\Delta(t)g^\sigma(t).$$

(ii) If $g(t)g^\sigma(t) \neq 0$, then $\frac{f}{g}$ is differentiable at t and

$$\left(\frac{f}{g}\right)^\Delta(t) = \frac{f^\Delta(t)g(t) - f(t)g^\Delta(t)}{g(t)g^\sigma(t)}.$$

It is clear that $1^\Delta = 0$, $t^\Delta = 1$, and from Theorem 1.1.2 (i),

$$(t^2)^\Delta = (t\cdot t)^\Delta = t + \sigma(t) = \begin{cases} 2t & \text{if } \mathbb{T} = \mathbb{R} \\ 2t+1 & \text{if } \mathbb{T} = \mathbb{Z} \\ 3t & \text{if } \mathbb{T} = \{2^n : n \in \mathbb{Z}\} \cup \{0\}, \end{cases}$$

and second derivative of t^2 may not exist because the forward jump operator is not differentiable, see Example 1.56 in [13]. A function $f : \mathbb{T} \to \mathbb{R}$ is called rd-continuous provided it is continuous at right-dense points in $\mathbb{T}$ and its left-sided limit exists (finite) at left dense points in $\mathbb{T}$. The set of rd-continuous functions $f : \mathbb{T} \to \mathbb{R}$ is denoted by $C_{rd} = C_{rd}(\mathbb{T}) = C_{rd}(\mathbb{T}, \mathbb{R})$. Every rd-continuous function has an antiderivative. In particular, if $t_0 \in \mathbb{T}$, then for $t \in T$

$$F(t) := \int_{t_0}^{t} f(\tau)\Delta\tau$$

is an antiderivative of f. For $f \in C_{rd}$, $a, b \in \mathbb{T}$, if $\mathbb{T} = \mathbb{R}$, then $\int_a^b f(t)\Delta t = \int_a^b f(t)dt$, and if $\mathbb{T} = \mathbb{Z}$, then

$$\int_a^b f(t)\Delta t = \begin{cases} \sum_{i=a}^{b-1} f_i & \text{if } a < b \\ -\sum_{i=a}^{b-1} f_i & \text{if } a > b \\ 0 & \text{if } a = b. \end{cases}$$

Since there are two product rules for differentiation on time scales, one can expect two integration by parts formulations on time scales. For $f, g \in C_{rd}$ and $a, b \in \mathbb{T}$, then

$$\int_a^b f^{\sigma}(t)g^{\Delta}(t)\Delta t = (fg)(b) - (fg)(a) - \int_a^b f^{\Delta}(t)g(t)\Delta t$$

and

$$\int_a^b f(t)g^{\Delta}(t)\Delta t = (fg)(b) - (fg)(a) - \int_a^b f^{\Delta}(t)g^{\sigma}(t)\Delta t.$$

A function $f : \mathbb{T} \to \mathbb{R}$ is called regressive provided $1 + \mu(t)f(t) \neq 0$ for all $t \in \mathbb{T}^{\kappa}$. The set of all regressive and rd-continuous functions $f : \mathbb{T} \to \mathbb{R}$ is denoted by $\mathcal{R} = \mathcal{R}(\mathbb{T}) = \mathcal{R}(\mathbb{T}, \mathbb{R})$. There are two operations on $\mathcal{R}$ to simplify expressions and calculations on time scales, circle plus $\oplus$ and circle minus $\ominus$, and defined as $(p \oplus q)(t) = p(t) + q(t) + \mu(t)p(t)q(t)$ and $(p \ominus q)(t) = (p \oplus (\ominus q))(t)$ for $p, q \in \mathcal{R}$, $t \in \mathbb{T}^{\kappa}$, where $(\ominus p)(t) := -\frac{p(t)}{1+\mu(t)p(t)}$, respectively.

Theorem 1.1.3. Suppose $p \in \mathcal{R}$ and fix $t_0 \in \mathbb{T}$. Then the initial value problem

$$y^{\Delta} = p(t)y, \quad y(t_0) = 1$$

has a unique solution $e_p(\cdot, t_0)$, so called the exponential function on time scales.

Let $\alpha \in \mathcal{R}$. If $\mathbb{T} = \mathbb{R}$, then $e_\alpha(t, t_0) = e^{\alpha(t-t_0)}$ and $e_{\ominus\alpha} = e^{-\alpha(t-t_0)}$. If $\mathbb{T} = h\mathbb{Z}$, then $e_\alpha(t, t_0) = (1 + \alpha h)^{(t-t_0)/h}$ and $e_{\ominus\alpha} = (1 + \alpha h)^{-(t-t_0)/h}$.

The following theorem presents some important properties of exponential functions on time scales in which some properties are related to the delta derivative and the forward jump operator, see Theorems 2.36 and 2.38 in [13].

Theorem 1.1.4. If $p, q \in \mathcal{R}$, then

(i) $e_0(t, s) = 1$ and $e_p(t, t) = 1$

(ii) $e_p(\sigma(t), s) = (1 + \mu(t)p(t))e_p(t, s)$

(iii) $e_p(t, s) = \dfrac{1}{e_p(s, t)} = e_{\ominus p}(s, t)$

(iv) $e_p(t, s)e_p(s, r) = e_p(t, r)$

(v) $e^\Delta_{p\ominus q}(\cdot, t_0) = (p - q)\dfrac{e_p(\cdot, t_0)}{e^\sigma_q(\cdot, t_0)}$.

It is worth mentioning that if p is positively regressive, then $e_p(t, t_0)$ is positive, which is used in the discussion on stability. Since this dissertation also deals with systems of first order linear dynamic equations and the following Variation of Constants Formulas on time scales (see Theorems 2.74 and Theorem 2.77 in [13]) are needed to find the unique solution of such systems.

Suppose $p \in \mathcal{R}$ and $f \in C_{rd}$. Let t_0 and $y_0 \in \mathbb{R}$. The unique solutions of the following dynamic equations with the initial condition $y(t_0) = y_0$

$$y^\Delta = -p(t)y^\sigma + f(t) \quad \text{and} \quad y^\Delta = -p(t)y + f(t)$$

are given by the following solutions respectively

$$y(t) = e_{\ominus p}(t, t_0)y_0 + \int_{t_0}^{t} e_{\ominus p}(t, \tau)f(\tau)\Delta\tau \quad \text{and} \quad y(t) = e_p(t, t_0)y_0 + \int_{t_0}^{t} e_p(t, \sigma(\tau))f(\tau).$$

1.2. INTRODUCTION TO EPIDEMIC MODELS

An epidemic is an unusually large, short term outbreak of a disease, [26]. The first recorded epidemics occurred in the 14th century and 25 million people died in Europe due to Bubonic Plague known as Black Death. In 1665, the British were exposed to the virus known as Plague of London. Another epidemic occurred in the Aztec's population in the 16th century and smallpox killed 35 million people. A recent influenza virus broke out in 1919, killing 20 million people. At present, we still face outbreaks of epidemics such as SARS (Severe Acute Respiratory Syndrome), measles, tuberculosis, and AIDS (Acquired Immune Deficiency Syndrome). The virus that causes AIDS is HIV (Human Immunodeficiency Virus). Based on Global Health Observatory (GHO) data [1], 75 million people have been infected with the virus and about 32 million have died. Globally, 37.9 million [32.7 – 44.0] people were living with HIV at the end of 2018.

Mathematical models of infectious diseases have a tremendous impact on understanding the spread of diseases, the risk factors, the predictability and control of an epidemic and hence developing the cure. The first mathematical epidemic model regarding to smallpox was formulated by Daniel Bernoulli and published in 1760, [11]. His paper is considered to be the very first compartmental model of an infectious disease.

In this dissertation, HIV and compartmental models of SIR and SIS on time scales are proposed.

1.2.1. HIV: Basic Modeling of the Infection Dynamics. One of the two types of HIV is HIV-1, which is found worldwide. The dynamics of HIV-1 infection have been scrutinized by different mathematical models. The basic model of HIV-1 infection dynamics considers three populations: uninfected target cells T, infected cells I, and free virus V (see [36] by Nowak and May, 2000 and [42] by Perelson et. al, 1996) and is described by the system of first order differential equations

$$\begin{cases} T' = s - dT - kVT \\ I' = kVT - \delta I \\ V' = \lambda I - cV - kTV, \end{cases}$$

where uninfected cells are produced by the immune system at a constant rate s, uninfected cells become infected at a rate kVT. λ is the rate of production of free viral particles from one infected cell, δ and c are the per cell rate of productively infected cell death and the rate constant for virus clearance, respectively.

1.2.2. SIS and SIR Epidemic Models. Unlike HIV model, there are some other diseases, such as chickenpox, mumps, rubella, which are modeled at the population level. The individuals in a population are divided into compartments: susceptible S, infected I and removed/recover R. The first modern model of disease dynamics was proposed in 1927 by Kermack and McKendrick, [31], and given by the system of first order differential equations

$$\begin{cases} S' = -\beta SI \\ I' = \beta SI - \gamma I \\ R' = \gamma I, \end{cases}$$

where β and γ are the infection rate and recovery rate, respectively. When individuals become susceptible after they recover, the model is called SIS and has the form of

$$\begin{cases} S' = -\beta SI + \gamma I \\ I' = \beta SI - \gamma I. \end{cases}$$

The threshold value for a disease is determined by the reproduction number $\mathscr{R}_0$. From epidemiological perspective, the reproduction number gives the number of secondary cases of an infectious disease that one case would generate in a completely susceptible population [25]. If $\mathscr{R}_0 > 1$, then the disease becomes endemic and if $\mathscr{R}_0 < 1$, the disease dies out. Equilibrium points are constant solutions in time and play a key role in the long term behavior of the solutions. An equilibrium point is called a disease-free if the disease is not present in the population while called an endemic if the disease is present in the population. This work contains SIS and SIR models with nonlinear incidence rates on different time domain and stability analysis of the equilibrium points.

1.3. OUTLINE

The organization of this dissertation is as follows: In Paper I, the mathematical models of the dynamics of HIV-1 infection in vivo are presented on time scales. Comparison of these models to data obtained from a clinical trial when the patients were given antiretroviral drug therapy is discussed by estimating the parameters. Combination drug therapy model is also presented on time scales and the stability of the trivial solution of the discrete model is discussed. In Paper II, SIS and SIR models with nonlinear incidence rate and time dependent coefficients are formulated and solved on time scales. Moreover, asymptotic behavior of the solutions is discussed and some illustrative examples are given on different time scales. In Paper III, discrete SIR models with nonlinear incidence rate and time independent coefficients, one of which is an advanced model, are presented, and the stability of the disease-free and endemic equilibria is discussed. In Papers IV and V, oscillation and nonoscillation criteria for solutions to four dimensional systems of first order dynamic equations, that some of which are either advanced or delay, are obtained. Several examples are provided to highlight the main results. We finalize the dissertation with conclusions and future research ideas.

PAPER

I. CONTINUOUS AND DISCRETE MODELING OF HIV-1 DECLINE ON THERAPY

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ABSTRACT

Mathematical models have shed light on the dynamics of HIV- 1 infection in vivo. In this paper, we generalize continuous mathematical models of drug therapy for HIV-1 by Perelson et al. [7, 8] on time scales, i.e., a nonempty closed subset of real numbers in order to derive new discrete models that predict the total concentration of plasma virus as a function of time.

One of our main goals is to compare discrete mathematical models with the continuous model in [8] where HIV infected patients were given protease inhibitors and sampled frequently thereafter. For the comparison, we use experimental data collected in [8] and estimate the parameters such as the virion clearance rate and the rate of loss of infected cells by fitting the total concentration of plasma virus to this data set. Our results show that discrete systems describe the best fit.

In the previous models of this study, the efficacy of protease inhibitor is assumed to be perfect. Motivated by [7], we end the paper with a mathematical model of imperfect protease inhibitor and reverse transcriptase (RT) inhibitor combination therapy of HIV-1 infection on time scales with its stability analysis.

Keywords: Time scales; HIV; Dynamic equations; Difference equations; Differential equations; Systems; Mathematical modeling

1. INTRODUCTION

The human immunodeficiency virus (HIV) infects a host's $CD4^+$ T cells which play an essential role in the immune system. HIV-1 infection leads to reduction of T cells over time. Therefore, the count of T cells is used to measure advancement of HIV-1 infection. The population dynamics of $CD4^+$ T cells is modeled in [7] as follows

$$\frac{dT}{dt} = s + pT\left(1 - \frac{T}{T_{max}}\right) - d_T T,$$

where T is the concentration of $CD4^+$ T cells, s is the source of new T cells from the thymus, p is the maximum $CD4^+$ T cells proliferation rate, T_{max} is the maximum level of $CD4^+$ T concentration when T_{max} is chosen such that $d_T T_{max} > s$ and d_T is the death rate per T cell. When HIV-1 infects $CD4^+$ T cells, they become infected cells, I. Hence, the model of dynamics between the immune system and HIV-1 is given in [7] by

$$\begin{cases} \dfrac{dT}{dt} = s + pT\left(1 - \dfrac{T}{T_{max}}\right) - d_T T - kVT \\ \dfrac{dI}{dt} = kVT - \delta I \\ \dfrac{dV}{dt} = N\delta I - cV, \end{cases} \tag{1}$$

where I and V are the concentrations of infected $CD4^+$ T cells and viral particles in plasma, respectively. The term kVT denotes the infection of $CD4^+$ T cells by HIV-1 with the infection rate constant k. In this model, δ represents the death rate of infected cells, c is the virus clearance rate constant, and N is the number of new virus particles produced per infected cell.

Perelson et al. in [8] developed a mathematical model from a clinical trial where five HIV-1 infected patients were given the protease inhibitor ritonavir. After treatment, HIV-1 RNA concentrations in plasma, viral load of genetic material, were measured every 2 hours until the 6 hour, every 6 hours until day 2, and every day until day 7. In this clinical trial, 15 data points were obtained from each patient where the unit of time was in days. System (1) is assumed to be at quasi-steady state before treatment, that is, V and I are relatively constant yielding $I'(t) = 0$ and $V'(t) = 0$. Hence, $kV_0T_0 = \delta I_0$ and $N\delta I_0 = cV_0$, and so $c = NkT_0$ and $I_0 = \frac{kV_0T_0}{\delta}$, where the subscript 0 denotes a pretreatment quasi-steady state value.

After treatment, newly created virions are noninfectious while infectious virions from prior to the treatment still remain. Therefore, the total virus concentration is

$$V = V_I + V_{NI}, \tag{2}$$

where V_I and V_{NI} are the concentrations of infectious and noninfectious virions, respectively. Drug efficacy is assumed 100% and (1) becomes

$$\begin{cases} \dfrac{dT}{dt} = s + pT\left(1 - \dfrac{T}{T_{max}}\right) - d_T T - kVT \\ \dfrac{dI}{dt} = kV_I T - \delta I \\ \dfrac{dV_I}{dt} = -cV_I \\ \dfrac{dV_{NI}}{dt} = N\delta I - cV_{NI}. \end{cases} \tag{3}$$

Assuming that system (1) is at quasi-steady state before drug treatment and T remains at approximately its steady state value T_0, that is $T = constant = T_0$ for 1 week after drug treatment, (3) leads to the following system

$$\begin{cases} \dfrac{dI}{dt} = kV_I T_0 - \delta I \\ \dfrac{dV_I}{dt} = -cV_I \\ \dfrac{dV_{NI}}{dt} = N\delta I - cV_{NI} \end{cases} \tag{4}$$

with the initial conditions

$$\begin{cases} I(0) = \frac{kV_0 T_0}{\delta} \\ V_I(0) = V_0 \\ V_{NI}(0) = 0. \end{cases} \tag{5}$$

Perelson et al. in [7] also develop a mathematical model for the effects of combination therapy with both RT and protease inhibitors

$$\begin{cases} \dfrac{dI}{dt} = (1 - \eta_{RT}) kV_I T_0 - \delta I \\ \dfrac{dV_I}{dt} = (1 - \eta_{PI}) N\delta I - cV_I \\ \dfrac{dV_{NI}}{dt} = \eta_{PI} N\delta I - cV_{NI} \end{cases} \tag{6}$$

with the initial conditions (5), where η_{RT} and η_{PI} are the efficacy of the RT and protease inhibitors, respectively, on anti-HIV treatment. In particular, $\eta_{PI}, \eta_{RT} = 0$ denote a null therapy, while $\eta_{PI}, \eta_{RT} = 1$ denotes a 100% effective therapy.

The systems above are continuous models of HIV-1 dynamics in vivo. According to our knowledge, there hasn't been any study of the discrete cases of these models. Instead of considering a discrete model itself, we prefer unifying the continuous and discrete analysis in one comprehensive theory, a so called time scales theory. A time scale, denoted by $\mathbb{T}$, is an arbitrary nonempty closed subset of the real numbers. The theory of time scales was first initiated by Stefan Hilger in his PhD thesis [4] in 1988. The set of all real numbers $\mathbb{R}$, which gives rise to differential equations, the set of all integers $\mathbb{Z}$, which gives rise to difference equations, and the set of all integer powers of a number $q > 1$, including 0, which gives rise to q-difference equations, are the well known examples of time scales, see [3, 5, 6].

In this paper, we first consider a mathematical model of perfect protease inhibitor monotherapy of HIV-1 infection on time scales. One of our main purposes is to analyze patient data presented in [8] on continuous and discrete cases. The outline of this paper is as follows: In Section 2, time scales calculus is introduced briefly including essentials. In Section 3, we formulate an initial value problem (IVP) modeling the dynamics of HIV-1 on time scales generalizing the IVP (4), (5) and calculate the total concentration of plasma virions on different time scales. In addition to these models, we also introduce an alternative discrete model in Section 4. We compare all these models by using nonlinear least squares fitting in Section 5. It turns out that the alternative discrete model gives the best fit in hours. This motivates us to consider another discrete model with the step-size $h > 0$ and this model has the best fit in days. In the last section, we present a mathematical model of imperfect RT and protease inhibitors combination therapy of HIV-1 infection on time scales, and analyze the stability of the zero solution.

2. ESSENTIALS

In this section, we first include some preliminary concepts regarding the calculus on time scales without proofs. The proofs can be found in the books written by Bohner and Peterson [1, 2].

Definition 2.1. For $t \in \mathbb{T}$, the forward jump operator $\sigma : \mathbb{T} \to \mathbb{T}$ is

$$\sigma(t) := \inf\{s \in \mathbb{T} : s > t\}$$

while the backward jump operator $\rho : \mathbb{T} \to \mathbb{T}$

$$\rho(t) := \sup\{s \in \mathbb{T} : s < t\},$$

and the graininess function $\mu : \mathbb{T} \to [0, \infty)$, defined as $\mu(t) := \sigma(t) - t$.

If $\sigma(t) > t$, we say that t is *right-scattered*, while if $\rho(t) < t$ we say that t is *left-scattered*. Points that are right-scattered and left-scattered at the same time are called *isolated*. Besides, if $t < \sup \mathbb{T}$ and $\sigma(t) = t$, then t is called *right-dense*, and if $t > \inf \mathbb{T}$ and $\rho(t) = t$, then t is called *left-dense*. Points that are right-dense and left-dense at the same time are called *dense*. The function $f^\sigma : \mathbb{T} \to \mathbb{R}$ is defined by $f^\sigma(t) = f(\sigma(t))$ for all $t \in \mathbb{T}$, i.e., $f^\sigma = f \circ \sigma$ and $[t_0, \infty)_\mathbb{T} := [t_0, \infty) \cap \mathbb{T}$. If $\mathbb{T}$ has a left-scattered maximum m, then $\mathbb{T}^\kappa = \mathbb{T} - \{m\}$. Otherwise, $\mathbb{T}^\kappa = \mathbb{T}$.

Definition 2.2. Assume $f : \mathbb{T} \to \mathbb{R}$ is a function and let $t \in \mathbb{T}^\kappa$. Then, the delta (or Hilger) derivative of f, denoted by f^Δ, on $\mathbb{T}^\kappa$ is defined to be the number (provided it exists) such that for given any $\epsilon > 0$, there is a neighborhood $U = (t - \delta, t + \delta)$ for some $\delta > 0$ such that

$$|[f^\sigma(t) - f(s)] - f^\Delta(t)[\sigma(t) - s]| \leq \epsilon|\sigma(t) - s|$$

for all $s \in U$.

If $\mathbb{T} = \mathbb{R}$, then $f^\Delta = f'$, i.e., the delta derivative coincides with the usual derivative. If $\mathbb{T} = \mathbb{Z}$, then $f^\Delta(t) = \Delta f(t) = f(t+1) - f(t)$, where Δ is the usual forward difference operator.

Theorem 2.3. Assume $f : \mathbb{T} \to \mathbb{R}$ is a function and let $t \in \mathbb{T}^\kappa$. Then we have the following:

(i) If f is differentiable at t, then f is continuous at t.

(ii) If f is continuous at t and t is right-scattered, then f is differentiable at t with

$$f^\Delta(t) = \frac{f^\sigma(t) - f(t)}{\mu(t)}.$$

(iii) If t is right-dense, then f is differentiable at t iff the limit

$$\lim_{s\to t}\frac{f(t)-f(s)}{t-s}$$

exists as a finite number. In this case

$$f^{\Delta}(t)=\lim_{s\to t}\frac{f(t)-f(s)}{t-s}.$$

(iv) If f is differentiable at t, then $f^{\sigma}(t)=f(t)+\mu(t)f^{\Delta}(t)$.

Theorem 2.4. Assume $f, g:\mathbb{T}\to\mathbb{R}$ are differentiable at $t\in\mathbb{T}^{\kappa}$. Then:

(i) The sum $f+g:\mathbb{T}\to\mathbb{R}$ is differentiable at t with

$$(f+g)^{\Delta}(t)=f^{\Delta}(t)+g^{\Delta}(t).$$

(ii) The product $fg:\mathbb{T}\to\mathbb{R}$ is differentiable at t with

$$(fg)^{\Delta}(t)=f^{\Delta}(t)g(t)+f^{\sigma}(t)g^{\Delta}(t)=f(t)g^{\Delta}(t)+f^{\Delta}(t)g^{\sigma}(t).$$

(iii) If $g(t)g^{\sigma}(t)\neq 0$, then $\frac{f}{g}$ is differentiable at t and

$$\left(\frac{f}{g}\right)^{\Delta}(t)=\frac{f^{\Delta}(t)g(t)-f(t)g^{\Delta}(t)}{g(t)g^{\sigma}(t)}.$$

Definition 2.5. A function $f:\mathbb{T}\to\mathbb{R}$ is called rd-continuous provided it is continuous at right-dense points in $\mathbb{T}$ and its left-sided limit exists (finite) at left dense points in $\mathbb{T}$. The set of rd-continuous $f:\mathbb{T}\to\mathbb{R}$ is denoted by $C_{rd}=C_{rd}(\mathbb{T})=C_{rd}(\mathbb{T},\mathbb{R})$.

Every rd-continuous function has an antiderivative. In particular, if $t_0\in\mathbb{T}$, then the antiderivative of f for $t\in T$ is

$$F:=\int_{t_0}^{t}f(\tau)\Delta\tau.$$

Definition 2.6. A function $f : \mathbb{T} \to \mathbb{R}$ is called regressive provided

$$1 + \mu(t) f(t) \neq 0$$

for all $t \in \mathbb{T}^{\kappa}$. The set of all regressive and rd-continuous functions $f : \mathbb{T} \to \mathbb{R}$ is denoted by $\mathcal{R} = \mathcal{R}(\mathbb{T}) = \mathcal{R}(\mathbb{T}, \mathbb{R})$.

Definition 2.7. If $p, q \in \mathcal{R}$, then the function $\ominus p$ "circle minus" is defined by

$$(\ominus p)(t) := -\frac{p(t)}{1 + \mu(t) p(t)}$$

while the function "circle minus substraction" is defined by

$$(p \ominus q)(t) := \frac{p(t) - q(t)}{1 + \mu(t) q(t)}$$

for all $t \in \mathbb{T}^{\kappa}$.

Theorem 2.8. Suppose $p \in \mathcal{R}$ and fix $t_0 \in \mathbb{T}$. Then the initial value problem

$$y^{\Delta} = p(t) y, \quad y(t_0) = 1$$

has a unique solution $e_p(\cdot, t_0)$, the so called the exponential function on time scales.

Let $a, b \in \mathbb{T}$ with $a < b$, $f \in C_{rd}$ and $\alpha \in \mathcal{R}$. Then, if $\mathbb{T} = \mathbb{R}$

$$\int_a^b f(t) \Delta t = \int_a^b f(t) dt, \quad e_{\alpha}(t, t_0) = e^{\alpha(t - t_0)} \quad \text{and} \quad e_{\ominus \alpha} = e^{-\alpha(t - t_0)}.$$

If $\mathbb{T} = h\mathbb{Z} = \{hk : k \in \mathbb{Z}\}$, where $h > 0$ then

$$\int_a^b f(t) \Delta t = \sum_{k = a/h}^{b/h - 1} f(kh) h, \quad e_{\alpha}(t, t_0) = (1 + \alpha h)^{(t - t_0)/h} \quad \text{and} \quad e_{\ominus \alpha} = (1 + \alpha h)^{-(t - t_0)/h}.$$

We use the following properties of exponential functions on time scales in our proofs, see Theorems 2.36 and 2.38 in [1].

Theorem 2.9. If $p, q \in \mathcal{R}$, then

(i) $e_0(t, s) = 1$ and $e_p(t, t) = 1$

(ii) $e_p(\sigma(t), s) = (1 + \mu(t)p(t))e_p(t, s)$

(iii) $e_p(t, s) = \dfrac{1}{e_p(s, t)} = e_{\ominus p}(s, t)$

(iv) $e_p(t, s)e_p(s, r) = e_p(t, r)$

(v) $e^{\Delta}_{p\ominus q}(\cdot, t_0) = (p - q)\dfrac{e_p(\cdot, t_0)}{e^{\sigma}_q(\cdot, t_0)}$.

We need the following Variation of Constants Formulas on time scales.

Theorem 2.10. ([1], Theorem 2.74) Suppose $p \in \mathcal{R}$ and $f \in C_{rd}$. Let t_0 and $y_0 \in \mathbb{R}$. The unique solution of the initial value problem

$$y^{\Delta} = -p(t)y^{\sigma} + f(t), \quad y(t_0) = y_0$$

is given by

$$y(t) = e_{\ominus p}(t, t_0)y_0 + \int_{t_0}^{t} e_{\ominus p}(t, \tau)f(\tau)\Delta\tau.$$

Theorem 2.11. ([1], Theorem 2.77) Suppose $p \in \mathcal{R}$ and $f \in C_{rd}$. Let t_0 and $y_0 \in \mathbb{R}$. The unique solution of the initial value problem

$$y^{\Delta} = -p(t)y + f(t), \quad y(t_0) = y_0$$

is given by

$$y(t) = e_p(t, t_0)y_0 + \int_{t_0}^{t} e_p(t, \sigma(\tau))f(\tau)\Delta\tau.$$

An $n \times n$ -matrix-valued function A on a time scale $\mathbb{T}$ is called regressive provided $I + \mu(t)A(t)$ is invertible for all $t \in \mathbb{T}^{\kappa}$.

Theorem 2.12. ([1], Exercise 5.6) An $n \times n$ -matrix-valued function A is regressive iff the eigenvalues $\lambda_i(t)$ of $A(t)$ are regressive for all $1 \leq i \leq n$.

The vector dynamic equation

$$x^{\Delta} = Ax,$$

where $A \in \mathcal{R}$ is a real constant $n \times n$-matrix.

Theorem 2.13. ([1], Theorem 5.30) If λ_0, ξ is an eigenpair for the constant $n \times n - matrix$ A, then $x(t) = e_{\lambda_0}(t, t_0)\xi$ is a solution of the vector dynamic equation above on $\mathbb{T}$.

To have an alternative discrete model to the IVP (3), (5), we need the following results.

Theorem 2.14. ([6], Theorem 3.1) Let $p(t) \neq 0$ and $r(t)$ be given for $t = a, a+1, \cdots$. Then,

(i) The solutions of $u(t+1) = p(t)u(t)$ are

$$u(t) = u(a) \prod_{s=a}^{t-1} p(s), \quad (t = a, a+1, \cdots)$$

(ii) All solutions of $y(t+1) - p(t)y(t) = r(t)$ are given by

$$y(t) = u(t) \left[\sum \frac{r(t)}{Eu(t)} + C \right],$$

where E is the shift operator defined by $Eu(t) = u(t+1)$, C is a constant, and $u(t)$ is any nonzero function from part (i).

Here, an "indefinite sum" (or "antidifference") of $y(t)$, denoted $\sum y(t)$, is any function so that $\Delta \left(\sum y(t) \right) = y(t)$ for all t in the domain of y.

The following system of n linear equations:

$$
\begin{aligned}
u_1(t+1) &= a_{11}u_1(t) + a_{12}u_2(t) + \cdots + a_{1n}u_n(t)\\
u_2(t+1) &= a_{21}u_1(t) + a_{22}u_2(t) + \cdots + a_{2n}u_n(t)\\
\vdots \quad & \qquad \vdots \qquad\qquad \vdots \qquad\qquad\qquad \vdots\\
u_n(t+1) &= a_{n1}u_1(t) + a_{n2}u_2(t) + \cdots + a_{nn}u_n(t)
\end{aligned}
$$

may be written in the vector form

$$u(t+1) = Au(t), \tag{7}$$

where $u(t) = (u_1(t), u_2(t), \cdots, u_n(t))^T \in \mathbb{R}^n$, and $A = (a_{ij})$ is an $n \times n$ real nonsingular matrix. Here T indicates the transpose of a vector. System (3) is considered autonomous, or time-invariant, since the values of A are all constants. The spectral radius of A is defined as

$$r(A) = max \{|\xi| : \ \xi \text{ is an eigenvalue of A}\}.$$

The next theorem summarizes the main stability results for the linear autonomous (time-invariant) systems (3).

Theorem 2.15. ([3], Theorem 4.13) The following statements hold:

(i) The zero solution of (3) is stable if and only if $r(A) \leq 1$ and the eigenvalues of unit modulus are semisimple, i.e., if the corresponding Jordan block is diagonal.

(ii) The zero solution of (3) is asymptotically stable if and only if $r(A) < 1$.

3. DYNAMICS OF HIV-1 DECLINE DURING 100% EFFECTIVE PROTEASE INHIBITOR MONOTHERAPY

We consider one of the generalization of the IVP (4), (5)

$$\begin{cases} I^{\Delta} = kV_I^{\sigma}T_0 - \delta I^{\sigma} \\ V_I^{\Delta} = -cV_I^{\sigma} \\ V_{NI}^{\Delta} = N\delta I^{\sigma} - cV_{NI}^{\sigma} \end{cases} \tag{8}$$

on $[0, \infty)_{\mathbb{T}}$ subject to the initial conditions (5), where all parameters are positive constants such that $\delta \neq c$. Here, the forward jump operator appears in the system. In this section, our purpose is to find the total concentration of plasma virions on different time scales. To do this, we first solve the IVP (8), (5).

Theorem 3.1. The unique solution (I, V_I, V_{NI}) of the IVP (8), (5) is given by

$$\begin{cases} I(t) = e_{\ominus\delta}(t,0)kV_0T_0\left\{\frac{1}{\delta} + \frac{1}{\delta-c}\left[e_{\delta\ominus c}(t,0) - 1\right]\right\} \\ V_I(t) = e_{\ominus c}(t,0)V_0 \\ V_{NI}(t) = \frac{cV_0}{c-\delta}\left\{\frac{c}{c-\delta}\left[e_{\ominus\delta}(t,0) - e_{\ominus c}(t,0)\right] - \delta e_{\ominus c}(t,0)\displaystyle\int_0^t \frac{1}{1+\mu(\tau)c}\Delta\tau\right\}, \end{cases}$$

where all parameters are positive constants such that $\delta \neq c$.

Proof. We start with the second equation of (8) with $V_I(0) = V_0$ to solve the system. From Theorem 2.10, we obtain

$$V_I(t) = e_{\ominus c}(t,0)V_0. \tag{9}$$

Substituting V_I into the first equation of (8) yields

$$I^{\Delta}(t) = ke_{\ominus c}^{\sigma}(t,0)V_0T_0 - \delta I^{\sigma}(t). \tag{10}$$

From Theorem 2.10, the IVP (10) with $I(0) = \frac{kV_0T_0}{\delta}$ has a unique solution

$$I(t) = e_{\ominus\delta}(t,0)I(0) + kV_0T_0 \int_0^t e_{\ominus\delta}(t,\tau)e^{\sigma}_{\ominus c}(\tau,0)\Delta\tau, \quad t \geq 0.$$

Since we assume that I is in quasi-steady state before initiation of therapy, after plugging $I(0)$ into I above and using the properties of exponential functions given in Theorem 2.9, we get

$$\begin{aligned} I(t) =& e_{\ominus\delta}(t,0)\frac{kV_0T_0}{\delta} + kV_0T_0 \int_0^t e_{\ominus\delta}(t,\tau)e^{\sigma}_{\ominus c}(\tau,0)\Delta\tau \\ =& e_{\ominus\delta}(t,0)\frac{kV_0T_0}{\delta} + kV_0T_0 e_{\ominus\delta}(t,0)\int_0^t e_{\ominus\delta}(0,\tau)\frac{1}{e^{\sigma}_c(\tau,0)}\Delta\tau \\ =& e_{\ominus\delta}(t,0)\frac{kV_0T_0}{\delta} + kV_0T_0 \frac{e_{\ominus\delta}(t,0)}{\delta - c}\int_0^t e^{\Delta}_{\delta\ominus c}(\tau,0)\Delta\tau \\ =& e_{\ominus\delta}(t,0)\frac{kV_0T_0}{\delta} + kV_0T_0 \frac{e_{\ominus\delta}(t,0)}{\delta - c}\left[e_{\delta\ominus c}(t,0) - 1\right]. \end{aligned} \tag{11}$$

Therefore,

$$I(t) = e_{\ominus\delta}(t,0)kV_0T_0\left\{\frac{1}{\delta} + \frac{1}{\delta - c}\left[e_{\delta\ominus c}(t,0) - 1\right]\right\}. \tag{12}$$

To solve V_{NI}, we substitute (12) into the third equation of system (8) and obtain

$$V^{\Delta}_{NI}(t) = N\delta kV_0T_0 e^{\sigma}_{\ominus\delta}(t,0)\left\{\frac{1}{\delta} + \frac{1}{\delta - c}\left[e^{\sigma}_{\delta\ominus c}(t,0) - 1\right]\right\} - cV^{\sigma}_{NI}(t). \tag{13}$$

From Theorem 2.10 and $c = NkT_0$, the IVP (13) with $V_{NI}(0) = 0$ has a unique solution

$$V_{NI}(t) = e_{\ominus c}(t,0)V_{NI}(0) + cV_0\delta \int_0^t e_{\ominus c}(t,\tau)e^{\sigma}_{\ominus\delta}(\tau,0)\left\{\frac{1}{\delta} + \frac{1}{\delta - c}\left[e^{\sigma}_{\delta\ominus c}(\tau,0) - 1\right]\right\}\Delta\tau.$$

Using $V_{NI}(0) = 0$ and properties of exponential functions on time scales yield

$$\begin{aligned}
V_{NI}(t) =& cV_0 \left\{ \frac{c}{c-\delta} \int_0^t e_{\ominus c}(t,\tau) e^{\sigma}_{\ominus\delta}(\tau,0)\Delta\tau + \frac{\delta}{\delta-c}\int_0^t e_{\ominus c}(t,\tau) e^{\sigma}_{\ominus\delta}(\tau,0) e^{\sigma}_{\delta\ominus c}(\tau,0)\Delta\tau \right\} \\
=& cV_0 \left\{ \frac{c}{c-\delta} \left[\frac{e_{\ominus c}(t,0)}{c-\delta} \left(e_{c\ominus\delta}(t,0) - 1\right)\right] + \frac{\delta}{\delta-c}\int_0^t e_{\ominus c}(t,\tau) \frac{1}{e^{\sigma}_{\delta}(\tau,0)} \frac{e^{\sigma}_{\delta}(\tau,0)}{e^{\sigma}_{c}(\tau,0)}\Delta\tau \right\} \\
=& cV_0 \left\{ \frac{c}{(c-\delta)^2} \left[e_{\ominus\delta}(t,0) - e_{\ominus c}(t,0)\right] + \frac{\delta}{\delta-c} e_{\ominus c}(t,0) \int_0^t e_{\ominus c}(0,\tau) \frac{1}{e^{\sigma}_{c}(\tau,0)}\Delta\tau \right\} \\
=& cV_0 \left\{ \frac{c}{(c-\delta)^2} \left[e_{\ominus\delta}(t,0) - e_{\ominus c}(t,0)\right] + \frac{\delta}{\delta-c} e_{\ominus c}(t,0) \int_0^t \frac{1}{1+\mu(\tau)c}\Delta\tau \right\},
\end{aligned}$$

where the first integration above is computed as in (11). Hence,

$$V_{NI}(t) = \frac{cV_0}{c-\delta} \left\{ \frac{c}{c-\delta} \left[e_{\ominus\delta}(t,0) - e_{\ominus c}(t,0)\right] - \delta e_{\ominus c}(t,0) \int_0^t \frac{1}{1+\mu(\tau)c}\Delta\tau \right\}. \tag{14}$$

This completes the proof. □

Note that (9) and (14) imply that the total concentration of plasma virions (2) is

$$V(t) = e_{\ominus c}(t,0)V_0 + \frac{cV_0}{c-\delta} \left\{ \frac{c}{c-\delta} \left[e_{\ominus\delta}(t,0) - e_{\ominus c}(t,0)\right] - \delta e_{\ominus c}(t,0) \int_0^t \frac{1}{1+\mu(\tau)c}\Delta\tau \right\}. \tag{15}$$

In the next examples, we calculate (15) on different time scales for data analysis.

Example 3.2. The total viral concentration (15) turns out to be

$$V(t) = e^{-ct}V_0 + \frac{cV_0}{c-\delta} \left\{ \frac{c[e^{-\delta t} - e^{-ct}]}{c-\delta} - \delta t e^{-ct} \right\} \tag{16}$$

on $[0,\infty)$ which is consistent with the total viral load in [8].

Example 3.3. Now consider the isolated time scales $[0,\infty)_{h\mathbb{Z}}$, $h > 0$. In this case, the total concentration of plasma virions is

$$V(t) = \frac{1}{(1+ch)^{\frac{t}{h}}}V_0 + \frac{cV_0}{c-\delta}\left\{\frac{c[(1+ch)^{\frac{t}{h}} - (1+\delta h)^{\frac{t}{h}}]}{(c-\delta)(1+\delta h)^{\frac{t}{h}}(1+ch)^{\frac{t}{h}}} - \frac{\delta t}{(1+ch)^{\frac{t}{h}+1}}\right\}. \tag{17}$$

In the special case of $h = 1$ in (17), that is on $[0,\infty)_{\mathbb{Z}}$, we have

$$V(t) = \frac{1}{(1+c)^{t}}V_0 + \frac{cV_0}{c-\delta}\left\{\frac{c[(1+c)^{t} - (1+\delta)^{t}]}{(c-\delta)(1+\delta)^{t}(1+c)^{t}} - \frac{\delta t}{(1+c)^{t+1}}\right\}. \tag{18}$$

4. AN ALTERNATIVE DISCRETE HIV-1 MODEL

Note that system (8) turns out to be the following system

$$\begin{cases} \Delta I(t) = kV_I(t+1)T_0 - \delta I(t+1) \\ \Delta V_I(t) = -cV_I(t+1) \\ \Delta V_{NI}(t) = N\delta I(t+1) - cV_{NI}(t+1) \end{cases} \tag{19}$$

on $[0,\infty)_{\mathbb{Z}}$ and the related total concentration of plasma virions of system (19) is given by (18). In this section, we now consider an alternative discrete model

$$\begin{cases} \Delta I(t) = kV_I(t)T_0 - \delta I(t) \\ \Delta V_I(t) = -cV_I(t) \\ \Delta V_{NI}(t) = N\delta I(t) - cV_{NI}(t) \end{cases} \tag{20}$$

on $[0,\infty)_{\mathbb{Z}}$ to the HIV-1 dynamics associated with (5). Therefore, we have the following theorem where we assume $c \neq \delta$ and $c, \delta \neq 1$ in order to solve (20).

Theorem 4.1. The unique solution (I, V_I, V_{NI}) of the IVP (20), (5) is given by

$$\begin{cases} I(t) = \frac{kV_0T_0}{\delta - c}\left\{(1-c)^t - \frac{c(1-\delta)^t}{\delta}\right\} \\ V_I(t) = V_0(1-c)^t \\ V_{NI}(t) = \frac{cV_0}{c-\delta}\left\{\frac{c}{c-\delta}\left[(1-\delta)^t - (1-c)^t\right] - \delta t(1-c)^{t-1}\right\}, \end{cases}$$

where all parameters are positive constants such that $\delta \neq c$ and $c, \delta \neq 1$.

Proof. System (20) can be written as a recurrence relation

$$\begin{cases} I(t+1) = kV_I(t)T_0 + (1-\delta)I(t) \\ V_I(t+1) = (1-c)V_I(t) \\ V_{NI}(t+1) = N\delta I(t) + (1-c)V_{NI}(t). \end{cases} \tag{21}$$

Solving the second equation with $V_I(0) = V_0$ and using Theorem 2.14 (i), we obtain

$$V_I(t) = V_I(0)\prod_{s=0}^{t-1}(1-c) = V_0(1-c)^t. \tag{22}$$

Substituting (22) into the first equation of (21), one can obtain

$$I(t+1) = kV_0T_0(1-c)^t + (1-\delta)I(t).$$

By Theorem 2.14 (i), the solution of $u^*(t+1) = (1-\delta)u^*(t)$ is

$$u^*(t) = u^*(0)\prod_{s=0}^{t-1}(1-\delta) = (1-\delta)^t,$$

where $u^*(0) = 1$. Then by Theorem 2.14 (ii), we have

$$\begin{aligned} I(t) =& u^*(t)\left[\sum \frac{kV_0T_0(1-c)^t}{u^*(t+1)} + C\right] \\ =& (1-\delta)^t\left[\sum \frac{kV_0T_0(1-c)^t}{(1-\delta)^{t+1}} + C\right] \\ =& (1-\delta)^t\left[\frac{kV_0T_0(1-c)^t}{(\delta-c)(1-\delta)^t} + C\right], \end{aligned}$$

where C is an arbitrary constant. Therefore,

$$I(t) = \frac{kV_0T_0(1-c)^t}{\delta - c} + (1-\delta)^t C, \tag{23}$$

and $I(0) = \frac{kV_0T_0}{\delta}$ implies $C = -\frac{ckV_0T_0}{\delta(\delta-c)}$. Substituting C into (23), we obtain

$$I(t) = \frac{kV_0T_0}{\delta - c}\left[(1-c)^t - \frac{c(1-\delta)^t}{\delta}\right].$$

To solve V_{NI}, we first plug I into the third equation of (20) and then use the fact $NkT_0 = c$ and obtain

$$V_{NI}(t+1) = \frac{cV_0\delta}{\delta - c}\left[(1-c)^t - \frac{c}{\delta}(1-\delta)^t\right] + (1-c)V_{NI}(t).$$

By Theorem 2.14 (i), the solution of $u(t+1) = (1-c)u(t)$ is

$$u(t) = u(0)\prod_{s=0}^{t-1}(1-c) = (1-c)^t,$$

where $u(0) = 1$. Then, we have

$$
\begin{aligned}
V_{NI}(t) =&u(t)\left\{\sum \frac{\frac{cV_0\delta}{\delta-c}\left[(1-c)^t-\frac{c(1-\delta)^t}{\delta}\right]}{u(t+1)}+D\right\}\\
=&(1-c)^t\left\{\sum \frac{\frac{cV_0\delta}{\delta-c}\left[(1-c)^t-\frac{c(1-\delta)^t}{\delta}\right]}{(1-c)^{t+1}}+D\right\}\\
=&(1-c)^t\left\{\frac{cV_0\delta}{(\delta-c)(1-c)}\sum\left[1-\frac{c}{\delta}\left(\frac{1-\delta}{1-c}\right)^t\right]+D\right\}\\
=&(1-c)^t\left\{\frac{cV_0\delta}{(\delta-c)(1-c)}\left[t-\frac{c}{\delta}\left(\frac{1-\delta}{1-c}\right)^t\frac{1-c}{c-\delta}\right]+D\right\},
\end{aligned}
$$

where D is an arbitrary constant and we use Theorem 2.14 (ii). Hence,

$$
V_{NI}(t) = -\frac{cV_0\delta t(1-c)^{t-1}}{c-\delta}+\frac{c^2V_0(1-\delta)^t}{(c-\delta)^2}+(1-c)^tD.
$$

To evaluate D, we use $V_{NI}(0)=0$ yielding $D=-\dfrac{c^2V_0}{(c-\delta)^2}$, and that

$$
V_{NI}(t) = \frac{cV_0}{c-\delta}\left\{\frac{c}{c-\delta}\left[(1-\delta)^t-(1-c)^t\right]-\delta t(1-c)^{t-1}\right\}, \tag{24}
$$

and hence the proof is completed. □

In this discrete case, the total concentration of plasma virions of the IVP (20), (5) that follows from (22) and (24) is given by

$$
V(t) =V_0(1-c)^t+\frac{cV_0}{c-\delta}\left\{\frac{c}{c-\delta}\left[(1-\delta)^t-(1-c)^t\right]-\delta t(1-c)^{t-1}\right\}, \tag{25}
$$

which is not equivalent to (18).

Note that $\delta > c > 1$ and chosing t to be even guarantee the positiveness of V_I as in (22) and V_{NI} as in (24).

5. DATA ANALYSIS

In this section, we determine how well the total viral concentrations obtained from our models fit the HIV-1 RNA measurements from one reprensentative patient, namely patient 104 in [8]. Here, we use MATLAB with nonlinear least squares fitting of data to estimate the parameters of our models.

In the previous sections, we model the dynamics of HIV-1 decline in patients on protease inhibitor monotherapy by the IVPs (8), (5) and (20), (5). From the IVP (8), (5), we obtain the total viral concentrations (16), (17), (18) on $[0, \infty)_{\mathbb{T}}$ when $\mathbb{T}$ is equal to $\mathbb{R}$, $h\mathbb{Z}$ and $\mathbb{Z}$, respectively. From the alternative discrete model (20), (5), we obtain (25) on $[0, \infty)_{\mathbb{Z}}$.

In Tables 1 and 2, these total viral concentrations are represented in the second row when $\mathbb{T}$ is equal to $\mathbb{R}$, $h\mathbb{Z}$ and $\mathbb{Z}$. Estimated parameters and evaluated R^2_{adj}, SSE and $RMSE$ values from the fit of (16), (17), (18) and (25) to the HIV-1 RNA data are listed in these tables as well.

In the following subsection, we discuss the results from the fit of the total viral concentrations when the unit of time is in days and in hours.

5.1. TIME IN DAYS AND IN HOURS

In [8], HIV-1 RNA data was measured every 2 hours until the 6 hour, every 6 hours until day 2, and every day until day 7 and the unit of the original data is in days.

Note that the IVP (8), (5) when $\mathbb{T} = \mathbb{R}$ is known as the continuous case and (16) is the corresponding total viral load introducing in [8]. From Table 1, we conclude that the discrete cases (17) and (18) fit to the data as well as the continuous case (16) except for the alternative discrete case (25). (17) has the best fit when h gets very close to zero. In fact, the continuous case is obtained when $h \to 0$.

In [8], the lower and upper 68% confidence intervals are calculated and the virion clearance rate is estimated as $c = 3.68$ day^{-1} that lies between 2.53 and 6.19 day^{-1} while the rate of loss of infected cells is estimated as $\delta = 0.50$ day^{-1} that lies between 0.47 and 0.54 day^{-1}. Note that c and δ obtained from the nonlinear regression analysis for the continuous case in our study are estimated as 3.11 day^{-1} and 0.51 day^{-1}, and within those confidence intervals, respectively, see Table 1.

Table 1. Data Analysis when time is in days

IVP	(8), (5)			(20), (5)
V	(16)	(17)	(18)	(25)
$\mathbb{T}$	$\mathbb{R}$	$h\mathbb{Z}$	$\mathbb{Z}$	$\mathbb{Z}$
R^2_{adj}	0.88916	0.87808	0.87955	0.52586
SSE	3079703800	3079703900	3346799500	13174681000
$RMSE$	14328.768	14328.768	14937.201	29636.33
V_0	133956.89	133958.03	138869.87	110124.12
c	3.11582	3.11637	2.54322	0.62332867
δ	0.51553	0.51549	0.83074	0.62332868
h		0.00000007		

Since (25) results a bad fit in days, see Figure 1, this urges us to investigate a different time domain for (25). Therefore, we attempt scaling the input data by changing the unit from days to hours.

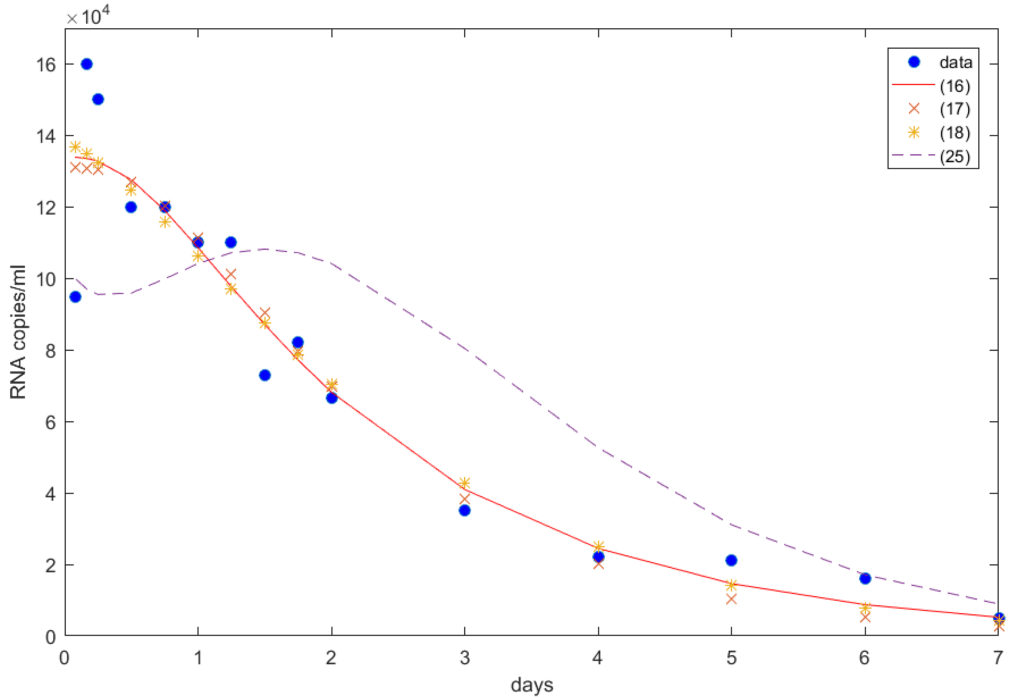

Figure 1. Fitted models in days

When changing the unit from days to hours, we note that all data was collected at times that are even when expressed in hours, i.e. t is even. We also observe that curve fittings of (16) and (17) to the data predict the same virion concentrations, see Tables 1 and 2. On the other hand, fittings of (18) and (25) to the data are improved. Indeed, fitting (25) to the data is not only improved significantly but also results in by far the highest R^2_{adj} value and smaller errors.

For all the patients in [8], HIV-1 RNA levels increase at the beginning of therapy, then drop down and keep decreasing. As seen in Figure 2, (25) is the only model capturing this behavior in hours. For t even and $1 < c < 2$, the last term in (25), $-\delta t(1-c)^{t-1}$, is positive and initially increases and then decreases for the estimated parameters. Hence, this causes the initially increasing behaviour of (25).

Table 2. Data Analysis when time is in hours

IVP	(8), (5)			(20), (5)
V	(16)	(17)	(18)	(25)
$\mathbb{T}$	$\mathbb{R}$	$h\mathbb{Z}$	$\mathbb{Z}$	$\mathbb{Z}$
R^2_{adj}	0.88916	0.87808	0.88859	0.97198
SSE	3079703800	3079703800	3095595300	778626850
$RMSE$	14328.768	14328.768	14365.689	7204.7524
V_0	133957	133956.79	134261.42	95708.735
c	0.12983	0.12982	0.12861	1.13006
δ	0.02148	0.02148	0.02189	1.98095
h		0.00000059		

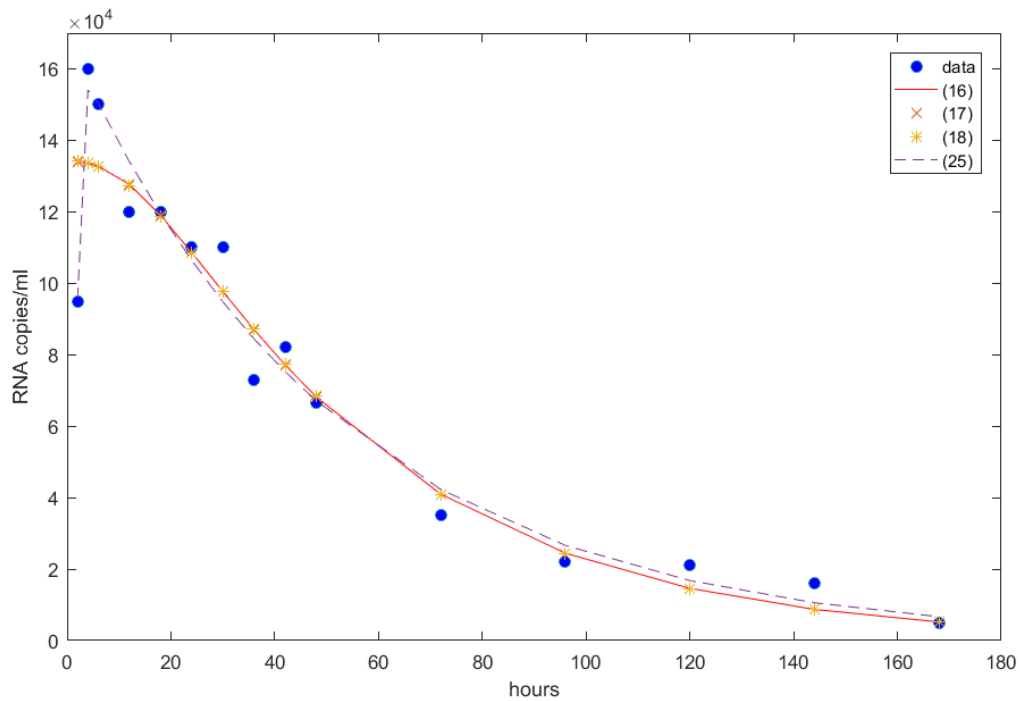

Figure 2. Fitted models in hours

We observe that by changing the unit from days to hours the alternative discrete curve (25) has the best fit. This leads to the important point of whether one should discuss more discrete models for HIV-1 dynamics. Therefore, we now want to unify and extend the continuous IVP (4), (5) and the discrete IVP (20), (5) in order to obtain the total viral load on more discrete time settings. The model is formulated as follows:

$$\begin{cases} I^{\Delta} = kV_I T_0 - \delta I \\ V_I^{\Delta} = -cV_I \\ V_{NI}^{\Delta} = N\delta I - cV_{NI} \end{cases} \tag{26}$$

subject to the initial conditions (5), where all parameters are positive constants such that $\delta \neq c$, $-c, -\delta \in \mathcal{R}$, i.e., $1 + \mu(-c) \neq 0$ and $1 + \mu(-\delta) \neq 0$.

Note that system (26) is equivalent to systems (4) and (8) on $[0, \infty)$ whereas it is equivalent to system (20) on $[0, \infty)_{\mathbb{Z}}$.

To find the total concentrations of virions, we follow similar steps of the proof of Theorem 3.1. By Theorems 2.11 and 2.9, we first obtain

$$V_I(t) = e_{-c}(t, 0)V_0$$

and

$$I(t) = kV_0 T_0 \left\{ \frac{ce_{-\delta}(t, 0) - \delta e_{-c}(t, 0)}{\delta(c - \delta)} \right\}. \tag{27}$$

Substituting (27) in the third equation of system (26) and solving for V_{NI} yield

$$V_{NI}(t) = \frac{cV_0}{c - \delta} \left\{ \frac{c\left[e_{-\delta}(t, 0) - e_{-c}(t, 0)\right]}{c - \delta} - \delta e_{-c}(t, 0) \int_0^t \frac{1}{1 - \mu(\tau)c} \Delta\tau \right\}.$$

Hence, the total concentration of plasma virions is

$$V(t) = e_{-c}(t,0)V_0 + \frac{cV_0}{c-\delta}\left\{\frac{c\left[e_{-\delta}(t,0) - e_{-c}(t,0)\right]}{c-\delta} - \delta e_{-c}(t,0)\int_0^t \frac{1}{1-\mu(\tau)c}\Delta\tau\right\}. \tag{28}$$

As a result, (28) yields the same total concentration of plasma virions (16) on $[0,\infty)$ and (25) obtained on $[0,\infty)_{\mathbb{Z}}$. One can also calculate the total concentration of plasma virions (28) on $h\mathbb{Z}$ as

$$V(t) = (1-ch)^{\frac{t}{h}}V_0 + \frac{cV_0}{c-\delta}\left\{\frac{c\left[(1-\delta h)^{\frac{t}{h}} - (1-ch)^{\frac{t}{h}}\right]}{c-\delta} - \delta t(1-ch)^{\frac{t}{h}-1}\right\}, \tag{29}$$

which is not same as (17). Tables 1 and 2 show data fitting of (16), (17), (18) and (25). Now we compare (17) obtained from the system with forward jump operator and (29) obtained from the system without forward jump operator.

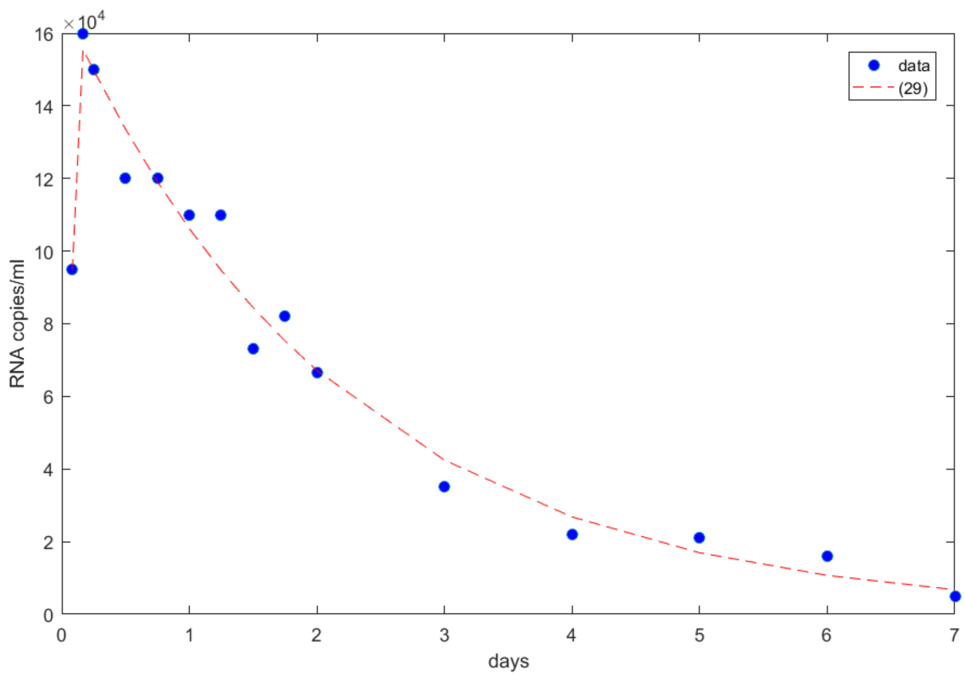

Figure 3. Fitted model in days obtained from $h\mathbb{Z}$

The data fitting of (29) is done with MATLAB fmincon and results 0.97004 R^2_{adj} value, where $SSE = 756676980$, $RMSE = 7102.4736$ and estimated initial value of virus concentration $V_0 = 151569.87$ in days. Figure 3 shows that (29) fits to the data better than other models with $c = 8.93828$, $\delta = 0.44710944$ day^{-1}, and $h = 0.11186$ in days. Note that the fittings of (29) in days and in hours result the same curve. Estimated parameters are $c = 0.35556$, $\delta = 0.01863$ hours^{-1}, $V_0 = 151082.19$, and $h = 2.81180$ in hours with 0.96996 hours^{-1} R^2_{adj} value, where $SSE = 758649430$, $RMSE = 7111.7247$.

When we compare all these models with MATLAB fmincon, we conclude that they yield consistent curve fittings as before.

6. DYNAMICS OF HIV-1 DECLINE ON COMBINATION THERAPY

In the previous sections, we formulate the models of interaction of the immune system with HIV-1 when the patients were given only protease inhibitors under the assumption of efficacy of the protease inhibitor is 100%, i.e., $\eta_{PI} = 1$. Mathematical model (6) of HIV-1 infection is studied in [7] when patients were given combination of imperfect protease inhibitor and RT inhibitors. Hence, under the assumption of $\eta_{PI} \neq 0, 1$ and $\eta_{RT} \neq 0, 1$ we generalize this model on time scales as follows:

$$\begin{cases} I^{\Delta} = (1 - \eta_{RT})kV_I T_0 - \delta I \\ V_I^{\Delta} = (1 - \eta_{PI})N\delta I - cV_I \\ V_{NI}^{\Delta} = \eta_{PI} N\delta I - cV_{NI} \end{cases} \tag{30}$$

subject to the initial conditions (5) and find the total concentration of plasma virions on different time scales by solving the IVP (30), (5).

Theorem 6.1. The unique solution (I, V_I, V_{NI}) of the IVP (30), (5) is given by

$$\begin{cases} I(t) = \dfrac{kT_0V_0(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\dfrac{\lambda_2+c\eta_{PI}}{\lambda_1+\delta}e_{\lambda_1}(t,0) - \dfrac{\lambda_1+c\eta_{PI}}{\lambda_2+\delta}e_{\lambda_2}(t,0)\right\} \\ V_I(t) = \dfrac{V_0}{\lambda_2-\lambda_1}\{(\lambda_2+c\eta_{PI})e_{\lambda_1}(t,0)-(\lambda_1+c\eta_{PI})e_{\lambda_2}(t,0)\} \\ V_{NI}(t) = \dfrac{V_0\eta_{PI}}{\lambda_2-\lambda_1}\left\{\dfrac{(\lambda_2+c\eta_{PI})e_{\lambda_1}(t,0)-(\lambda_1+c\eta_{PI})e_{\lambda_2}(t,0)}{\lambda_2-\lambda_1} - e_{-c}(t,0)\right\}, \end{cases}$$

where all parameters are positive constants and

$$\lambda_{1,2} = \frac{-(c+\delta) \pm \sqrt{(c+\delta)^2 - 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI}))}}{2}. \tag{31}$$

Proof. We first rewrite the first two equations as a vector dynamic equation and solve the obtained the two dimensional linear system of I and V_I. The vector dynamic equation is as follows

$$\begin{bmatrix} I^\Delta \\ V_I^\Delta \end{bmatrix} = \begin{bmatrix} -\delta & (1-\eta_{RT})kT_0 \\ (1-\eta_{PI})N\delta & -c \end{bmatrix}\begin{bmatrix} I \\ V_I \end{bmatrix},$$

where the characteristic equation is $\lambda^2 + (c+\delta)\lambda + \delta c(1-(1-\eta_{RT})(1-\eta_{PI})) = 0$. Here, since we assume the patient was in quasi-steady state before treatment began, then $c = NkT_0$. Hence, the eigenvalues of the coefficient matrix are given as (31). By the fact that $(\delta-c)^2 > 0$, one can get that $(\delta+c)^2 > 4\delta c$. Also, since $0 < \eta_{RT} < 1$ and $0 < \eta_{PI} < 1$, then

$$(\delta+c)^2 > 4\delta c > 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI}))$$

and this shows that these two eigenvalues are real. Furthermore,

$$0 < (c+\delta)^2 - 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI})) < (c+\delta)^2, \tag{32}$$

which implies that $-(c+\delta) + \sqrt{(c+\delta)^2 - 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI}))} < 0$. Hence,

$\lambda_1 < 0$. Note that $\lambda_2 < 0$ is negative by the definition. We have shown that λ_1 and λ_2 are real, negative and distinct eigenvalues. The vector equation is regressive for any time scale such that $1 + \lambda_{1,2}\mu(t) \neq 0$ for all $t \in \mathbb{T}^\kappa$ by Theorem 2.12. From the characteristic equation for the two dimensional I and V_I system, we have for i=1, 2

$$(1-\eta_{RT})(1-\eta_{PI}) = \frac{(\lambda_i+\delta)(\lambda_i+c)}{c\delta}. \tag{33}$$

Eigenvectors corresponding to λ_1 and λ_2 are

$$\xi_1 = \begin{bmatrix} c+\lambda_1 \\ (1-\eta_{PI})N\delta \end{bmatrix}, \quad \xi_2 = \begin{bmatrix} c+\lambda_2 \\ (1-\eta_{PI})N\delta \end{bmatrix}$$

respectively. By Theorem 2.13, it follows that

$$\begin{bmatrix} I \\ V_I \end{bmatrix} = c_1 e_{\lambda_1}(t,0) \begin{bmatrix} c+\lambda_1 \\ (1-\eta_{PI})N\delta \end{bmatrix} + c_2 e_{\lambda_2}(t,0) \begin{bmatrix} c+\lambda_2 \\ (1-\eta_{PI})N\delta \end{bmatrix}, \tag{34}$$

where c_1 and c_2 are arbitrary constants. To find c_1 and c_2, we use the initial conditions $I(0) = \frac{kV_0T_0}{\delta}$ and $V_I(0) = V_0$ with the properties of exponential functions on time scales. Hence, we get the following equations

$$\begin{aligned} kV_0T_0 &= c_1\delta(c+\lambda_1) + c_2\delta(c+\lambda_2) \\ V_0 &= c_1(1-\eta_{PI})N\delta + c_1(1-\eta_{PI})N\delta \end{aligned}$$

with the constants

$$c_1 = \frac{V_0(\lambda_2 + c\eta_{PI})}{N\delta(1-\eta_{PI})(\lambda_2-\lambda_1)} = \frac{kV_0T_0(\lambda_2+c\eta_{PI})(1-\eta_{RT})}{(\lambda_1+\delta)(\lambda_1+c)(\lambda_2-\lambda_1)}$$

and

$$c_2 = -\frac{V_0(\lambda_1 + c\eta_{PI})}{N\delta(1-\eta_{PI})(\lambda_2 - \lambda_1)} = -\frac{kV_0T_0(\lambda_1 + c\eta_{PI})(1-\eta_{RT})}{(\lambda_2+\delta)(\lambda_2+c)(\lambda_2-\lambda_1)},$$

where we use (33) to get equivalent relations for c_1 and c_2. Now, substituting c_1 and c_2 into I of (34) yields

$$\begin{aligned} I(t) &= c_1 e_{\lambda_1}(t,0)(1-\eta_{PI})N\delta + c_2 e_{\lambda_2}(t,0)(1-\eta_{PI})N\delta \\ &= e_{\lambda_1}(t,0) - \frac{kV_0T_0(\lambda_1 + c\eta_{PI})(1-\eta_{RT})}{(\lambda_2+\delta)(\lambda_2-\lambda_1)} e_{\lambda_2}(t,0). \end{aligned}$$

Therefore,

$$I(t) = \frac{kT_0V_0(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2 + c\eta_{PI}}{\lambda_1+\delta} e_{\lambda_1}(t,0) - \frac{\lambda_1 + c\eta_{PI}}{\lambda_2+\delta} e_{\lambda_2}(t,0)\right\}. \tag{35}$$

Similarly, substituting c_1 and c_2 into V_I of (34) yields

$$V_I(t) = \frac{V_0(\lambda_2 + c\eta_{PI})}{\lambda_2-\lambda_1} e_{\lambda_1}(t,0) - \frac{V_0(\lambda_1 + c\eta_{PI})}{\lambda_2-\lambda_1} e_{\lambda_2}(t,0).$$

Hence,

$$V_I(t) = \frac{V_0}{\lambda_2-\lambda_1}\Big\{(\lambda_2 + c\eta_{PI})e_{\lambda_1}(t,0) - (\lambda_1 + c\eta_{PI})e_{\lambda_2}(t,0)\Big\}.$$

Substituting (6) into the third equation of (30) results

$$V_{NI}^{\Delta}(t) = \frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2 + c\eta_{PI}}{\lambda_1+\delta} e_{\lambda_1}(t,0) - \frac{\lambda_1 + c\eta_{PI}}{\lambda_2+\delta} e_{\lambda_2}(t,0)\right\} - cV_{NI}. \tag{36}$$

From Theorem 2.11, (36) with $V_{NI}(0) = 0$ has a unique solution

$$
\begin{aligned}
V_{NI}(t) = & \int_0^t e_{-c}(t,\sigma(\tau))\frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2+c\eta_{PI}}{\lambda_1+\delta}e_{\lambda_1}(\tau,0)-\frac{\lambda_1+c\eta_{PI}}{\lambda_2+\delta}e_{\lambda_2}(\tau,0)\right\}\Delta\tau \\
= & \frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2+c\eta_{PI}}{\lambda_1+\delta}\int_0^t e_{-c}(t,\sigma(\tau))e_{\lambda_1}(\tau,0)\Delta\tau\right. \\
& \left. -\frac{\lambda_1+c\eta_{PI}}{\lambda_2+\delta}\int_0^t e_{-c}(t,\sigma(\tau))e_{\lambda_2}(\tau,0)\Delta\tau\right\} \\
= & \frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2+c\eta_{PI}}{\lambda_1+\delta}\frac{e_{-c}(t,0)}{\lambda_1+c}\int_0^t e^{\Delta}_{\lambda_1\ominus(-c)}(\tau,0)\Delta\tau\right. \\
& \left. -\frac{\lambda_1+c\eta_{PI}}{\lambda_2+\delta}\frac{e_{-c}(t,0)}{\lambda_2+c}\int_0^t e^{\Delta}_{\lambda_2\ominus(-c)}(\tau,0)\Delta\tau\right\} \\
= & \frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2+c\eta_{PI}}{\lambda_1+\delta}\frac{e_{-c}(t,0)}{\lambda_1+c}\left[e_{\lambda_1\ominus(-c)}(t,0)-1\right]\right. \\
& \left. -\frac{\lambda_1+c\eta_{PI}}{\lambda_2+\delta}\frac{e_{-c}(t,0)}{\lambda_2+c}\left[e_{\lambda_2\ominus(-c)}(t,0)-1\right]\right\}.
\end{aligned}
$$

Therefore,

$$
\begin{aligned}
V_{NI}(t) = & \frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_2+c\eta_{PI}}{(\lambda_1+\delta)(\lambda_1+c)}e_{\lambda_1}(t,0)-\frac{\lambda_2+c\eta_{PI}}{(\lambda_1+\delta)(\lambda_1+c)}e_{-c}(t,0)\right\} \\
& -\frac{V_0\delta c\eta_{PI}(1-\eta_{RT})}{\lambda_2-\lambda_1}\left\{\frac{\lambda_1+c\eta_{PI}}{(\lambda_2+\delta)(\lambda_2+c)}e_{\lambda_2}(t,0)+\frac{\lambda_1+c\eta_{PI}}{(\lambda_1+\delta)(\lambda_1+c)}e_{-c}(t,0)\right\}.
\end{aligned}
$$

Substituting (33) into the above equation and then simplifying the resulting equation, one can get

$$
V_{NI} = \frac{V_0\eta_{PI}}{\lambda_2-\lambda_1}\left\{\frac{(\lambda_2+c\eta_{PI})e_{\lambda_1}(t,0)-(\lambda_1+c\eta_{PI})e_{\lambda_2}(t,0)}{\lambda_2-\lambda_1}-e_{-c}(t,0)\right\}.
$$

This completes the proof. □

Hence, the total concentration of plasma virions is given by

$$
V(t) = \frac{V_0}{1-\eta_{PI}}\left\{\frac{(\lambda_2+c\eta_{PI})e_{\lambda_1}(t,0)-(\lambda_1+c\eta_{PI})e_{\lambda_2}(t,0)}{\lambda_2-\lambda_1}-\eta_{PI}e_{-c}(t,0)\right\}. \quad (37)
$$

System (30) with $\eta_{RT}=0$ and $\eta_{PI}=1$ reduces to (26). Note that corresponding total viral load (37) does not reduce to (28) due to the singularity.

System (30) on $[0, \infty)$ has eigenvalues $-c$ and (31) that are real, negative and distinct. Hence, the zero solution of system (30) on $[0, \infty)$ is asymptotically stable. One can also consider system (30) on $[0, \infty)_{\mathbb{Z}}$ and write it as

$$\begin{cases} I(t+1) = (1-\delta)I(t) + (1-\eta_{RT})kT_0 V_I(t) \\ V_I(t+1) = (1-\eta_{PI})N\delta I(t) + (1-c)V_I(t) \\ V_{NI}(t+1) = \eta_{PI}N\delta I(t) + (1-c)V_{NI}(t) \end{cases} \tag{38}$$

In the following theorem, we discuss the behaviour of the zero solution of system (38).

Theorem 6.2. If $c + \delta < 2$, the zero solution of system (38) is asymptotically stable.

Proof. Assume $c + \delta < 2$. An equivalent vector equation of system (38) has the companion matrix

$$A = \begin{bmatrix} 1-\delta & (1-\eta_{RT})kT_0 & 0 \\ (1-\eta_{PI})N\delta & 1-c & 0 \\ \eta_{PI}N\delta & 0 & 1-c \end{bmatrix}$$

whose characteristic equation is

$$(1-c-\xi)\left[(1-\delta-\xi)(1-c-\xi) - \delta c(1-\eta_{RT})(1-\eta_{PI})\right] = 0,$$

and the eigenvalues are $\xi_1 = 1-c$, $\xi_{2,3} = \frac{-(c+\delta-2) \pm \sqrt{(c+\delta-2)^2 - 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI}))}}{2}$. Note that ξ_i for $i = 1, 2, 3$ are real. Since $0 < c < 2$, $|\xi_1| < 1$. From (32) and the assumption, we have

$$0 < \frac{-(c+\delta-2)}{2} < \frac{-(c+\delta-2) + \sqrt{(c+\delta)^2 - 4\delta c(1-(1-\eta_{RT})(1-\eta_{PI}))}}{2} < 1.$$

Hence, $|\xi_2| < 1$. Furthermore, since $2(\delta + c) - \delta c(1 - (1 - \eta_{RT})(1 - \eta_{PI})) < 4$ and $4\delta c(1 - (1 - \eta_{RT})(1 - \eta_{PI})) < 4\delta c$, we have

$$c + \delta - 4 < -\sqrt{(c + \delta)^2 - 4\delta c(1 - (1 - \eta_{RT})(1 - \eta_{PI}))} < \delta - c$$

and so $-1 < -\delta - c + 2\sqrt{(c + \delta)^2 - 4\delta c(1 - (1 - \eta_{RT})(1 - \eta_{PI}))} < 1 - c$. The positivity of c implies that $|\xi_3| < 1$. Therefore, from Theorem 2.15 the zero solution of system (38) is asymptotically stable. This completes the proof.

□

7. CONCLUSION

In this study, one of our goals was to call attention to discrete models of the HIV-1 infection and make a comparison with the existing continuous model in [8].

We obtain the total concentration of plasma virus as a function of time for each model. Then, we test the new discrete models (17), (18) and (25) with data from a clinical trial and find the fitted new models to be as accurate as the continuous model (16) and in some cases much better.

Based on the findings, the discrete model (25) on $\mathbb{Z}$ is found to yield the best fit in hours. This motivated us to study other discrete models which have the best fit in days. It turns out that the latest proposed discrete model (29) on $h\mathbb{Z}$ achieves an almost equally good fit in both units. Moreover, in the continuous model (16) the clearance rate c and the rate of loss δ are estimated as 3.11 day^{-1} and 0.51 day^{-1}, respectively, while the clearance rate c and the rate of loss δ are estimated as 8.93 day^{-1} and 0.44 day^{-1} in the discrete model (29).

In these models, the patients were given protease inhibitor monotherapy under the assumption of the efficacy of the protease inhibitor is perfect. In addition, we consider a mathematical model of imperfect protease inhibitor and RT inhibitor combination therapy of HIV-1 infection on time scales and show that the zero solution is asymptotically stable.

By considering mathematical models on time scales, i.e. dynamic models, one can derive solutions of corresponding continuous and discrete models directly from dynamic models. This helps to avoid solving models individually on their own domain. This has shown to be significant when considering the model of HIV-1 dynamics. It is also worth to mention that not only one continuous model can be obtained from a mathematical model on time scales, but also many discrete models. In this work, one of the models on $h\mathbb{Z}$, namely (29), has an excellent fit to the data, captures the behavior of the data perfectly no matter what the unit of time and has a better fit compared to the existing continuous model in literature. Therefore, one can consider modeling on other discrete time scales such as disjoint closed intervals, the set of all integer powers of a number $q > 0$, including zero etc. which may result in better fitting.

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REFERENCES

[1] Bohner, M. and Peterson, A., *Dynamic Equations on Time Scales: An Introduction with Applications*, 2001.

[2] Bohner, M. and Peterson, A. C., *Advances in dynamic equations on time scales*, Springer, 2002.

[3] Elaydi, S. N., *An Introduction to Difference Equations*, 2005.

[4] Hilger, S., *Einßmakettenkalkül mit Anwendung auf Zentrumsmannigfaltigkeiten*, Ph.D. thesis, Ph. D. Thesis, Universität Würzburg in German, 1988.

[5] Kac, V. and Cheung, P., *Quantum calculus*, Springer Science & Business Media, 2001.

[6] Kelley, W. G. and Peterson, A. C., *Difference equations: an introduction with applications*, Academic press, 2001.

[7] Perelson, A. S. and Nelson, P. W., 'Mathematical analysis of hiv-1 dynamics in vivo,' SIAM review, 1999, **41**(1), pp. 3–44.

[8] Perelson, A. S., Neumann, A. U., Markowitz, M., Leonard, J. M., and Ho, D. D., 'Hiv-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time,' Science, 1996, **271**(5255), pp. 1582–1586.

II. ON EXACT SOLUTIONS TO EPIDEMIC DYNAMIC MODELS

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ABSTRACT

In this study, we address an SIR (susceptible-infected-recovered) model that is given as a system of first order differential equations and propose the SIR model on time scales which unifies and extends continuous and discrete models. More precisely, we derive the exact solution to the SIR model and discuss the asymptotic behavior of the number of susceptibles and infectives. Next, we introduce an SIS (susceptible-infected-susceptible) model on time scales and find the exact solution. We solve the models by using the Bernoulli equation on time scales which provides an alternative method to the existing methods. Having the models on time scales also leads to new discrete models. We illustrate our results with examples where the number of infectives in the population is obtained on different time scales.

Keywords: Dynamic equations; Time scales; Epidemic models; Asymptotic behavior

1. INTRODUCTION

Epidemic models are used for understanding infectious disease dynamics where the population dynamics is divided into compartments. In the susceptible-infected-recovered (SIR) epidemic model, susceptible individuals may become infected, and infected individuals may recover and become immune. No other transitions are considered in this model. The structure of the SIR model dates back to Kermack and McKendrick in 1927 [9] which has provided the basic framework for almost all later epidemic models ever since. In the susceptible-infected-susceptible (SIS) epidemic model, susceptible individuals may become infected, and infected individuals may recover and revert to being susceptible.

The continuous and discrete SIR and SIS models have been investigated in a number of recent works, see [3, 8, 10, 11]. One of the continuous SIR models is presented in [12] as

$$\begin{cases} S^{'} = -\beta SI - \gamma S + \gamma \\ \\ I^{'} = \beta SI - \gamma I, \end{cases} \tag{1}$$

where $S(t)$ and $I(t)$ are the number of susceptibles and the number of infectives at time t, respectively with constant population N and the average number of adequate contacts of a person per unit time, i.e, the transmission rate β and the recovery rate γ. The authors eliminate the variable S and obtain the second equation of (1) in the form of the Bernoulli equation, and by using the suitable substitution the authors find a solution to (1). According to our knowledge, the discrete case of system (1) has not been studied earlier. In this study, our purpose is to unify and extend the continuous and the discrete systems. Motivated by system (1) and the Bernoulli equation on time scales, see [1], we propose the SIR model on time scales in the following form

$$\begin{cases} S^{\Delta} = \dfrac{\gamma(t)}{\ominus(-\gamma(t))}(\ominus(\beta(t)I))S - \gamma(t)S + \gamma(t) \\ \\ I^{\Delta} = -\dfrac{\gamma(t)}{\ominus(-\gamma(t))}(\ominus(\beta(t)I))S - \gamma(t)I \end{cases} \tag{2}$$

with the initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, where $\beta, \gamma \in C_{rd}([0, \infty)_{\mathbb{T}}, \mathbb{R}^{+})$, $S, I \in C^1_{rd}([0, \infty)_{\mathbb{T}}, \mathbb{R}^{+})$. If $\mathbb{T} = \mathbb{R}$, then $\ominus p = -p$, and system (2) with positive β and γ constants turns out to be system (1). If $\mathbb{T} = \mathbb{Z}$, then $\ominus p = \frac{-p}{1+p}$ for $p \neq -1$, and system (2) is equivalent to the system of first order difference equations as follows

$$\begin{cases} S_{n+1} = \dfrac{1-\gamma_n}{1+\beta_n I_n} S_n + \gamma_n \\ \\ I_{n+1} = \dfrac{\beta_n(1-\gamma_n)}{1+\beta_n I_n} S_n I_n + (1-\gamma_n) I_n. \end{cases} \tag{3}$$

In Section 3, we find the exact number of susceptibles and infectives of system (2) and discuss their asymptotic behaviors. Furthermore, we illustrate the behavior of infectives of the continuous and the discrete SIR models by examples.

The exact solution of the following SIS model

$$\begin{cases} S^{'} = -\beta SI + \gamma I \\ \\ I^{'} = \beta SI - \gamma I \end{cases} \tag{4}$$

with the initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$ satisfying $S_0 + I_0 = N$, where β and γ are positive constants is studied in [12] while the discrete model of (4)

$$\begin{cases} S_{n+1} = S_n \left(1 - \beta I_n\right) + \gamma I_n \\ \\ I_{n+1} = I_n \left(1 - \gamma + \beta S_n\right), \end{cases} \tag{5}$$

is studied in [2]. Motivated by system (4) and the Bernoulli equation on time scales, see [1], we propose the SIS model on time scales as

$$\begin{cases} S^{\Delta} = \ominus(\beta(t)I)S - \ominus(\beta(t)I)\dfrac{\gamma(t)}{\beta(t)} \\ \\ I^{\Delta} = - \ominus (\beta(t)I)S + \ominus(\beta(t)I)\dfrac{\gamma(t)}{\beta(t)}, \end{cases} \tag{6}$$

where $\beta, \gamma \in C_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$, $S, I \in C^1_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$. If $\mathbb{T} = \mathbb{R}$, then system (6) with positive constants β and γ is equivalent to system (4). However, the discrete model of (6) when $\mathbb{T} = \mathbb{Z}$ is

$$\begin{cases} S_{n+1} = S_n \left(1 - \dfrac{\beta_n}{1+\beta_n I_n} I_n\right) + \dfrac{\gamma_n}{1+\beta_n I_n} I_n \\ I_{n+1} = I_n \left(1 - \dfrac{\gamma_n}{1+\beta_n I_n} + \dfrac{\beta_n}{1+\beta_n I_n} S_n\right), \end{cases} \tag{7}$$

which is not same as (5). Observe that continuous systems (1) and (4) are equivalent if $S + I = 1$. However, this is not true for discrete systems (5) and (7). Note that a different form of system (6) with constant coefficients is studied in [7].

In Section 4, we find the exact number of susceptibles and infectives of (6) and demostrate the behavior of the infectives on a quantum calculus with an example.

Now let us present some preliminary concepts regarding the calculus on time scales without proofs to help understanding the key points in our main results. We mainly refer readers to books by Bohner and Peterson [5, 6] and manuscripts [1, 4].

2. ESSENTIALS OF TIME SCALES

There are two important operators in $\mathbb{T}$. The forward jump operator $\sigma : \mathbb{T} \to \mathbb{T}$ is defined as $\sigma(t) := \inf\{s \in \mathbb{T} : s > t\}$ for $t \in \mathbb{T}$ while the backward jump operator $\rho : \mathbb{T} \to \mathbb{T}$ is defined as $\rho(t) := \sup\{s \in \mathbb{T} : s < t\}$. The graininess function $\mu : \mathbb{T} \to [0, \infty)$ is defined as $\mu(t) := \sigma(t) - t$. If $t < \sup \mathbb{T}$ and $\sigma(t) = t$, then t is called *right-dense*, and if $t > \inf \mathbb{T}$ and $\rho(t) = t$, then t is called *left-dense*. Besides, if $\rho(t) < t$, we say that t is *left-scattered*. If $\mathbb{T}$ has a left-scattered maximum m, then $\mathbb{T}^\kappa = \mathbb{T} - \{m\}$. Otherwise, $\mathbb{T}^\kappa = \mathbb{T}$.

Assume $f : \mathbb{T} \to \mathbb{R}$ is a function and let $t \in \mathbb{T}^\kappa$. Then, the delta (or Hilger) derivative of f, denoted by f^Δ, on $\mathbb{T}^\kappa$ is defined to be the number (provided it exists) such that for given any $\epsilon > 0$, there is a neighborhood $U = (t - \delta, t + \delta)$ for some $\delta > 0$ such that for all $s \in U$

$$|[f^\sigma(t) - f(s)] - f^\Delta(t)[\sigma(t) - s]| \le \epsilon |\sigma(t) - s|,$$

where $f^\sigma(t) = f(\sigma(t))$ for all $t \in \mathbb{T}$, i.e., $f^\sigma = f \circ \sigma$ and $[t_0, \infty)_\mathbb{T} := [t_0, \infty) \cap \mathbb{T}$. A function $f : \mathbb{T} \to \mathbb{R}$ is called rd-continuous provided it is continuous at right-dense points in $\mathbb{T}$ and its left-sided limit exists (finite) at left dense points in $\mathbb{T}$. The set of rd-continuous $f : \mathbb{T} \to \mathbb{R}$ is denoted by $C_{rd} = C_{rd}(\mathbb{T}) = C_{rd}(\mathbb{T}, \mathbb{R})$. The set of functions $f : \mathbb{T} \to \mathbb{R}$ that are differentiable and whose derivative rd-continuous is denoted by $C^1_{rd} = C^1_{rd}(\mathbb{T}) = C^1_{rd}(\mathbb{T}, \mathbb{R})$. Every rd-continuous function has an antiderivative. In particular, if $t_0 \in \mathbb{T}$, then for $t \in T$

$$F := \int_{t_0}^{t} f(\tau)\Delta\tau$$

is an antiderivative of f. The set of functions $f \in C^1_{rd}(\mathbb{T}, \mathbb{R})$, the so-called simple useful formula

$$f^\sigma(t) = f(t) + \mu(t) f^\Delta(t) \tag{8}$$

holds for all $t \in \mathbb{T}^\kappa$. For any left-dense $t_0 \in \mathbb{T}$ and any $\epsilon > 0$, let $L_\epsilon(t_0) = \{t \in \mathbb{T} : 0 < t_0 - t < \epsilon\}$, and $\bar{\mathbb{T}} = \mathbb{T} \cup \{\sup \mathbb{T}\} \cup \{\inf \mathbb{T}\}$. The following theorem is one of several L'Hôpital Rules on time scales.

Theorem 2.1. ([5], Theorem 1.120) Assume f and g are differentiable on $\mathbb{T}$ with

$$\lim_{t \to t_0^-} g(x) = \infty$$

for some left-dense $t_0 \in \bar{\mathbb{T}}$. Suppose there exists $\epsilon > 0$ with $g(t) > 0$ and $g^\Delta(t) > 0$ for all $t \in L_\epsilon(t_0)$. Then,

$$\lim_{t \to t_0^-} \frac{f^\Delta(t)}{g^\Delta(t)} = r \in \bar{\mathbb{R}}$$

implies

$$\lim_{t \to t_0^-} \frac{f(t)}{g(t)} = r.$$

A function $f : \mathbb{T} \to \mathbb{R}$ is called regressive if $1 + \mu(t)f(t) \neq 0$ for all $t \in \mathbb{T}^{\kappa}$. The set of all regressive and rd-continuous functions $f : \mathbb{T} \to \mathbb{R}$ is denoted by $\mathcal{R} = \mathcal{R}(\mathbb{T}) = \mathcal{R}(\mathbb{T}, \mathbb{R})$. Besides, $f \in \mathcal{R}$ is called positively regressive for all $t \in \mathbb{T}$ if $1+\mu(t)f(t) > 0$, and is denoted by $\mathcal{R}^{+}$. Note that $\mathcal{R}(\alpha) = \mathcal{R}$ if $\alpha \in \mathbb{N}$ and $\mathcal{R}(\alpha) = \mathcal{R}^{+}$ if $\alpha \in \mathbb{R} \setminus \mathbb{N}$. If $p, q \in \mathcal{R}$, then *circle minus* substraction is defined by

$$(\ominus p)(t) := -\frac{p(t)}{1 + \mu(t)q(t)}$$

and

$$(p \ominus q)(t) := \frac{p(t) - q(t)}{1 + \mu(t)q(t)} \tag{9}$$

for all $t \in \mathbb{T}^{\kappa}$, while *circle dot* multiplication is defined by

$$(\alpha \odot p)(t) := \alpha p(t) \int_0^1 (1 + \mu(t)p(t)h)^{\alpha-1} dh$$

to find a simple form of the derivative of p^{α} on time scales.

Theorem 2.2. Suppose $p \in \mathcal{R}$ and fix $t_0 \in \mathbb{T}$. Then the initial value problem

$$y^{\Delta} = p(t)y, \quad y(t_0) = 1$$

has a unique solution $e_p(\cdot, t_0)$, so called the exponential function on time scales.

Let $\alpha \in \mathcal{R}$ be constant and $t_0 \in \mathbb{T}$. If $\mathbb{T} = \mathbb{R}$, then

$$e_{\alpha}(t, t_0) = e^{\alpha(t-t_0)}. \tag{10}$$

For the discrete time scales $\mathbb{T} = \mathbb{Z}$,

$$e_{\alpha}(t, t_0) = (1 + \alpha)^{t-t_0} \tag{11}$$

and $\mathbb{T} = q^{\mathbb{N}_0} = \{q^n : n \in \mathbb{N}\}$, where $q > 1$ and $q \in \mathbb{R}$, i.e., the quantum calculus

$$e_\alpha(t, t_0) = \prod_{s \in [t_0, t)_{q^{\mathbb{N}_0}}} [1 + (q-1)\alpha s], \quad t > t_0. \tag{12}$$

We use the following properties of exponential functions on time scales in our proofs, see Theorems 2.36, 2.39 and 2.44 in [5].

Theorem 2.3. If $p, q \in \mathcal{R}$ and $t_0, t, s \in \mathbb{T}$, then

(i) $e_0(t, s) = 1$ and $e_p(t, t) = 1$

(ii) $e_p(t, s) = \dfrac{1}{e_p(s, t)} = e_{\ominus p}(s, t)$

(iii) $e_p(t, s) e_p(s, r) = e_p(t, r)$

(iv) $\displaystyle\int_{t_0}^{t} p(\tau) e_p(s, \sigma(\tau)) \Delta\tau = e_p(s, t_0) - e_p(s, t)$

(v) If $p \in \mathcal{R}^+$ on $\mathbb{T}^\kappa$, then $e_p(t, t_0) > 0$ for all $t \in \mathbb{T}$.

One of the Variation of Constants Formulas in [5, Theorem 2.77] states the following.

Theorem 2.4. Suppose $p \in \mathcal{R}$ and $f \in C_{rd}$. Then the unique solution of the initial value problem

$$y^\Delta = p(t) y + f(t), \quad y(t_0) = y_0$$

is given by

$$y(t) = e_p(t, t_0) y_0 + \int_{t_0}^{t} e_p(t, \sigma(\tau)) f(\tau) \Delta\tau,$$

where t_0 and $y_0 \in \mathbb{R}$.

As we mention in the introduction, our main results are based on solutions of the Bernoulli equation on time scales of the form

$$x^\Delta = \left[p(t) \ominus \left(\frac{1}{\alpha} \odot (f(t) x^\alpha) \right) \right] x, \tag{13}$$

where $\alpha \in \mathbb{R} \setminus 0$, and the proof of the existence of solutions of (13) can be found in [1, Theorem 6.1].

Theorem 2.5. Suppose $\alpha \in \mathbb{R} \setminus 0$, $p \in \mathcal{R}(\alpha)$ and $f \in C_{rd}$. If

$$\frac{1}{x_0^\alpha} + \int_{t_0}^{t} e_p^\alpha(\tau, t_0) f(\tau) \Delta\tau > 0$$

for all $t \in \mathbb{T}$, then

$$x(t) = \frac{e_p(t, t_0)}{\left[\frac{1}{x_0^\alpha} + \int_{t_0}^{t} e_p^\alpha(\tau, t_0) f(\tau) \Delta\tau\right]^{1/\alpha}}$$

solves the Bernoulli equation (13) with $x(t_0) = x_0$.

Note that in the case of $\alpha = 1$ in (13), we have

$$(1 \odot fx)(t) := f(t)x \int_0^1 (1 + \mu(t) f(t) x h)^0 dh = f(t)x. \tag{14}$$

Hence, the Bernoulli equation (13) is equivalent to

$$x^\Delta = \left[\frac{p(t) - f(t)x}{1 + \mu(t) f(t) x}\right] x, \tag{15}$$

where we use (9) and (14), and the solution of (15) with $x(t_0) = x_0$ is

$$x(t) = \frac{e_p(t, t_0)}{\frac{1}{x_0} + \int_{t_0}^{t} e_p(\tau, t_0) f(\tau) \Delta\tau} \tag{16}$$

by Theorem 2.5.

The following inequalities, see [4, Lemma 2] and [4, Remark 2], are necessary to show the asymptotic behavior of solutions of systems (2). For nonnegative f if $-f \in \mathcal{R}^+$, then

$$1 - \int_s^t f(u) \Delta u \le e_{-f}(t, s) \le \exp\left\{-\int_s^t f(u) \Delta u\right\}, \tag{17}$$

and if f is rd-continuous, then

$$1+\int_s^t f(u)\Delta u \le e_f(t,s) \le \exp\left\{\int_s^t f(u)\Delta u\right\}, \tag{18}$$

for all $t \ge s$.

3. AN SIR MODEL ON TIME SCALES

In this section, we find the exact solution to SIR model (2) with the initial conditions (S_0, I_0). Then, we discuss the asymptotic behavior of the solutions and illustrate the behavior of infectives on continuous and discrete time scales.

Theorem 3.1. Let $\beta, \gamma \in C_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$ and $-\gamma \in \mathcal{R}^+$. Then the unique solution (S, I) of SIR model (2) with the initial conditions (S_0, I_0) is given by

$$\begin{cases} S = e_{-\gamma}(t,0)\,(D_0-1)+1-\dfrac{e_p(t,0)}{\dfrac{1}{I_0}+\displaystyle\int_0^t \beta(\tau)e_p(\tau,0)\Delta\tau} \\ I = \dfrac{e_p(t,0)}{\dfrac{1}{I_0}+\displaystyle\int_0^t \beta(\tau)e_p(\tau,0)\Delta\tau}, \end{cases} \tag{19}$$

where $S, I \in C^1_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$, $D = S + I$ with $D(0) = D_0$, and

$$p(t) = \beta(t)D(t)(1-\mu(t)\gamma(t)) - \gamma(t) \quad for \quad t \in [0,\infty)_{\mathbb{T}}. \tag{20}$$

Proof. Suppose $\beta, \gamma \in C_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$ and $-\gamma \in \mathcal{R}^+$. First of all, from the assumption $-\gamma \in \mathcal{R}^+$, $1+\mu(t)p(t) = 1+\mu(t)\left[\beta(t)D(t)(1-\mu(t)\gamma(t))-\gamma(t)\right] > 1-\mu(t)\gamma(t) > 0$, that is $p \in \mathcal{R}^+$. Note that $S^\Delta + I^\Delta = -\gamma(t)(S+I)+\gamma(t)$, that is

$$D^\Delta = -\gamma(t)D + \gamma(t), \quad t \in [0,\infty)_{\mathbb{T}}. \tag{21}$$

Since $-\gamma \in \mathcal{R}^+$, from Theorem 2.4, the solution to (21) with $D(0) = D_0$ is

$$\begin{aligned}
D(t) =& e_{-\gamma}(t,0)D_0 + \int_0^t e_{-\gamma}(t,\sigma(\tau))\gamma(\tau)\Delta\tau \\
=& e_{-\gamma}(t,0)D_0 - e_{-\gamma}(t,0)\int_0^t (-\gamma(\tau))e_{-\gamma}(0,\sigma(\tau))\Delta\tau \\
=& e_{-\gamma}(t,0)D_0 - e_{-\gamma}(t,0)\left[e_{-\gamma}(0,0) - e_{-\gamma}(0,t)\right] \\
=& e_{-\gamma}(t,0)D_0 - e_{-\gamma}(t,0) + 1 \\
=& e_{-\gamma}(t,0)(D_0 - 1) + 1 \qquad (22)
\end{aligned}$$

for $t \in [0,\infty)_{\mathbb{T}}$, where we use Theorem 2.3 (iv). Note that SIR model (2) on time scales can be rewritten as

$$\begin{cases}
S^\Delta = -\dfrac{\beta(t)(1-\mu(t)\gamma(t))}{1+\mu(t)\beta(t)I}SI - \gamma(t)S + \gamma(t), \\
I^\Delta = \dfrac{\beta(t)(1-\mu(t)\gamma(t))}{1+\mu(t)\beta(t)I}SI - \gamma(t)I.
\end{cases} \qquad (23)$$

By plugging $S = D - I$ into the second equation of (1), we have

$$\begin{aligned}
I^\Delta =& \frac{\beta(t)(1-\mu(t)\gamma(t))}{1+\mu(t)\beta(t)I}I[D(t) - I] - \gamma(t)I \\
=& \frac{\beta(t)(1-\mu(t)\gamma(t))[D(t)-I]I - [1+\mu(t)\beta(t)I]\gamma(t)I}{1+\mu(t)\beta(t)I} \\
=& \frac{[\beta(t)D(t) - \beta(t)D(t)\mu(t)\gamma(t) - \gamma(t) - \beta(t)I]I}{1+\mu(t)\beta(t)I} \\
=& \left[\frac{p(t) - \beta(t)I}{1+\mu(t)\beta(t)I}\right]I, \qquad (24)
\end{aligned}$$

where p is defined as in (20). Note that (24) is a Bernoulli equation in the form of (15). Therefore, by Theorem 2.5 when $\alpha = 1$, we obtain I as in (19). This implies that $S = D - I$ is obtained as in (19). Therefore, the proof is completed. □

We now consider system (2) with positive β and γ constants for the following examples.

Example 3.2. Let $\mathbb{T} = [0, \infty)$ and $D = 1$ in system (2). Then, since $\mu = 0$, we have $p = \beta - \gamma$ from (20). From Theorem 3.1, the number of infectives to the continuous SIR model with initial conditions S_0 and I_0 is given by

$$I(t) = \frac{1}{\dfrac{1}{I_0} + \beta t}, \quad t \in [0, \infty) \tag{25}$$

if $p = 0$, that is $\beta = \gamma$. Moreover, if $p \neq 0$ then

$$\begin{aligned} I(t) =& \frac{e^{\int_0^t (\beta-\gamma) du}}{\frac{1}{I_0} + \frac{\beta}{\beta-\gamma} e^{(\beta-\gamma)t} - \frac{\beta}{\beta-\gamma}} \\ =& \frac{e^{(\beta-\gamma)t}}{\frac{1}{I_0} + \frac{\beta}{\beta-\gamma}\left[e^{(\beta-\gamma)t} - 1\right]}, \quad t \in [0, \infty), \end{aligned} \tag{26}$$

where we use (10), and so $S = 1 - I$.

Example 3.3. Let $\mathbb{T} = \mathbb{Z}_0^+$ and $D = 1$ in system (2). Then, since $\mu = 1$ and $-\gamma \in \mathcal{R}^+$, we have $p = \beta - \beta\gamma - \gamma$ from (20) and so $1 + \mu p = 1 - \gamma + \beta(1 - \gamma) = (1 - \gamma)(1 + \beta) > 0$, i.e. $p \in \mathcal{R}^+$. Theorem 3.1 states that the number of infectives to discrete SIR model (3) with initial conditions S_0 and I_0 is given by

$$I_n = \frac{1}{\dfrac{1}{I_0} + \beta n}, \quad n \in \mathbb{Z}_0^+ \tag{27}$$

if $p = 0$. Moreover, if $p \neq 0$, then from (11)

$$\begin{aligned} I_n =& \frac{(1 + p)^n}{\dfrac{1}{I_0} + \beta \displaystyle\sum_{k=0}^{n-1} (1 + p)^k} \\ =& \frac{(1 + p)^n}{\dfrac{1}{I_0} + \beta \left[\dfrac{(1 + p)^n - 1}{p}\right]} \\ =& \frac{(1 + p)^n p I_0}{p + \beta I_0 \left[(1 + p)^n - 1\right]}, \quad n \in \mathbb{Z}_0^+. \end{aligned} \tag{28}$$

Remark 3.4. Since $\gamma > 0$ and $-\gamma \in \mathcal{R}^+$, from Theorem 2.3 (v) and (17) we have

$$0 < e_{-\gamma}(t,0) \leq e^{-\int_0^t \gamma \Delta u} = e^{-\gamma t}, \quad t \in [0,\infty)_{\mathbb{T}}.$$

This implies that $e_{-\gamma}(t,0) \to 0$ as $t \to \infty$. Therefore, $D(t) \to 1$ as $t \to \infty$ by (22). Note that $D^{\Delta}(t) = -\gamma e_{-\gamma}(t,0)(D_0 - 1)$ for all $t \in [0,\infty)_{\mathbb{T}}$. Hence, $D^{\Delta}(t) > 0$ if $0 < D_0 < 1$ and $D^{\Delta}(t) < 0$ if $D_0 > 1$ for $t \in [0,\infty)_{\mathbb{T}}$.

The results in Remark 3.4 are important to analyze the asymptotic behavior of infectives and susceptibles to system (2) with positive constants β and γ in the following theorem.

Theorem 3.5. Consider system (2) with positive constants β and γ. Let $-\gamma \in \mathcal{R}^+$ and p be as in (20).

1. If $p(t) = 0$ on $[0,\infty)_{\mathbb{T}}$, then all solutions (S,I) of system (2) with $D_0 = S_0 + I_0$ converge to $(1,0)$.
2. If $p(t) < 0$ on $[0,\infty)_{\mathbb{T}}$ and $\gamma > k\beta$ for some $k > 0$, then all solutions (S,I) of system (2) with $D_0 = S_0 + I_0$ converge to $(1,0)$.
3. If $p(t) > 0$ for $t \in [0,\infty)_{\mathbb{T}}$ with the constant graininess μ, then all solutions (S,I) of system (2) with $D_0 = S_0 + I_0$ converge to $(\gamma\mu + \frac{\gamma}{\beta}, 1 - \gamma\mu - \frac{\gamma}{\beta})$.

Proof. Assume that β and γ are positive constants, $-\gamma \in \mathcal{R}^+$, and p is as in (20) for $t \in [0,\infty)_{\mathbb{T}}$. In the proof of Theorem 3.1, we show that $p \in \mathcal{R}^+$.

1. Let $p(t) = 0$ on $[0,\infty)_{\mathbb{T}}$. Then, $e_p(t,0) \equiv 1$ and by Theorem 3.1 the number of infectives is (25) and so $I(t) \to 0$ as $t \to \infty$. Since $D(t) \to 1$ as $t \to \infty$ by Remark 3.4 and $D = S + I$, then $S(t) \to 1$ as $t \to \infty$.

2. Suppose $p(t) < 0$ on $[0,\infty)_{\mathbb{T}}$ and $\gamma > k\beta$ for some $k > 0$. Since $p \in \mathcal{R}^+$, then $e_p(t,0) > 0$ for all $t \in [0,\infty)_{\mathbb{T}}$ by Theorem 2.3 (v). Therefore, we have

$$0 < I(t) \leq e_p(t,0)I_0, \quad t \in [0,\infty)_{\mathbb{T}}, \tag{29}$$

where we use Theorem 3.1. If $0 < D_0 \leq 1$, then $D(t) \leq 1$ for $t \in [0,\infty)_{\mathbb{T}}$ by Remark 3.4. Therefore, $p(t) \leq \beta D - \gamma \leq \beta - \gamma < 0$ for $t \in [0,\infty)_{\mathbb{T}}$. Now let $-f = p < 0$, then $f > 0$ and $-f \in \mathcal{R}^+$. We can apply (17) for nonnegative f as follows

$$0 < e_p(t,0) \leq e^{\int_0^t p(u)\Delta u} \leq e^{\int_0^t (\beta-\gamma)\Delta u} = e^{(\beta-\gamma)t} \to 0 \quad \text{as} \quad t \to \infty.$$

Hence, $e_p(t,0) \to 0$ as $t \to \infty$. This concludes that $I(t) \to 0$ because of (29) and so $S(t) \to 1$ as $t \to \infty$. If $D_0 > 1$, then there exist $\eta > 1$ and $t_0 \in [0,\infty)_{\mathbb{T}}$ such that $D(t) \leq \eta$ for $t \in [t_0,\infty)_{\mathbb{T}}$ by Remark 3.4. Besides, $p(t) \leq \beta D - \gamma \leq \beta\eta - \gamma < 0$ by assumption. Again, by letting $-f = p < 0$ such that $-f \in \mathcal{R}^+$, we can apply (17) for nonnegative f and obtain

$$0 < e_p(t,0) \leq e^{\int_0^t p(u)\Delta u} \leq e^{\int_0^t (\beta\eta-\gamma)\Delta u} = e^{(\beta\eta-\gamma)t} \to 0 \quad \text{as} \quad t \to \infty.$$

Therefore, $e_p(t,0) \to 0$ as $t \to \infty$. This implies that $I(t) \to 0$ as $t \to \infty$ because of (29) and so $S(t) \to 1$ as $t \to \infty$.

3. Let $p(t) > 0$ for $t \in [0,\infty)_{\mathbb{T}}$ with the constant graininess μ. Then, $e_p(t,0) \to \infty$ as $t \to \infty$ and we have

$$e_p(t,0) \geq 1 + \int_0^t p(u)\Delta u, \quad t \in [0,\infty)_{\mathbb{T}}$$

by (18). Integrating the above inequality from 0 to ∞ gives $\int_0^\infty e_p(u,0)\Delta u = \infty$. For the limit of I, we apply L'Hôpital Rule. Let $g(t) = \frac{1}{I_0} + \beta\int_0^t e_p(\tau,0)\Delta\tau > 0$ and $f(t) = e_p(t,0) > 0$ on $[0,\infty)_{\mathbb{T}}$ in Theorem 2.1. Hence, $\lim_{t\to\infty} g(t) = \infty$, $g^\Delta = \beta e_p > 0$ by Theorem 2.3 (v) and $f^\Delta = pe_p$. Therefore,

$$\lim_{t\to\infty}\frac{f^\Delta(t)}{g^\Delta(t)} = \lim_{t\to\infty}\frac{p(t)e_p(t,0)}{\beta e_p(t,0)} = \lim_{t\to\infty}\frac{p(t)}{\beta}.$$

Since $D(t)\to 1$ as $t\to\infty$, $\lim_{t\to\infty} p(t) = \beta(1-\gamma\mu)-\gamma$. This implies that

$$\lim_{t\to\infty} I(t) = \lim_{t\to\infty}\frac{f(t)}{g(t)} = \lim_{t\to\infty}\frac{p(t)}{\beta} = 1-\gamma\mu-\frac{\gamma}{\beta},$$

and so $S(t)\to\gamma\mu+\frac{\gamma}{\beta}$ as $t\to\infty$.

□

The following examples illustrate Theorem 3.5, where the number of infectives is obtained for the continuous and discrete SIR models.

Example 3.6. Consider SIR model (2) with $(S_0, I_0) = (0.8, 0.2)$ on $[0,\infty)$. In Example 3.2, we obtain the number of infectives from (25) and (26) for all $t\in[0,\infty)$. If $\beta=\gamma=0.5$, then $p=0$. Hence, $I\to 0$ as $t\to\infty$. If $\beta=0.3$ and $\gamma=0.4$ are chosen, then $p=-0.1<0$ and in this case, $I(t)\to 0$ as $t\to\infty$. On the other hand, choosing $\beta=0.4$ and $\gamma=0.3$ yields $p=0.1>0$. Hence, $I(t)\to\frac{1}{4}$ as $t\to\infty$. Figure 1 shows the number of infectives for all $t\in[0,50]$ based on the sign of p.

Example 3.7. Now consider SIR model (2) with $(S_0, I_0) = (0.8, 0.2)$ on $[0,\infty)_{\mathbb{Z}}$. In Example 3.3, we compute the number of infectives for all $n\in[0,\infty)_{\mathbb{Z}}$ from (27) and (28). If $\beta=0.25$ and $\gamma=0.2$, then $p=0$ and so $I_n\to 0$ as $n\to\infty$. Letting $\beta=0.1$ and $\gamma=0.4$ yields $p=-0.34<0$. Hence, $I_n\to 0$ as $n\to\infty$. Now let $\beta=1.5$ and $\gamma=0.5$. Then, $p=0.25>0$ and $I_n\to\frac{1}{6}$ as $n\to\infty$. Number of infectives on $[0,25]_{\mathbb{Z}}$ for these cases are demostrated in Figure 2.

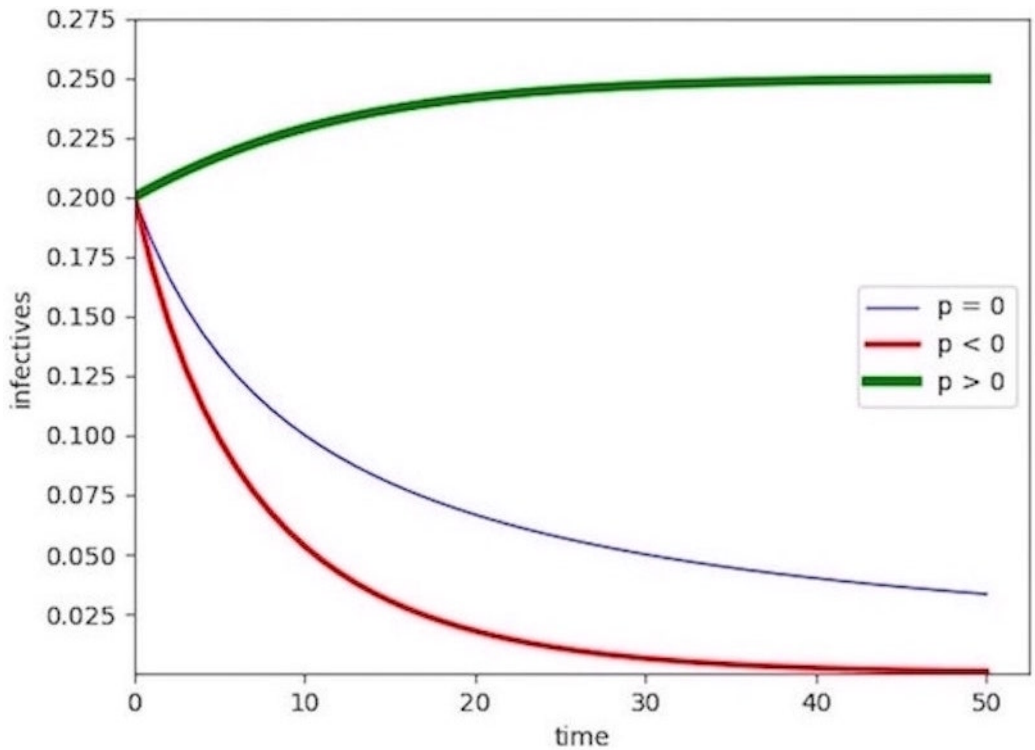

Figure 1. Number of infectives on $[0, 50]$

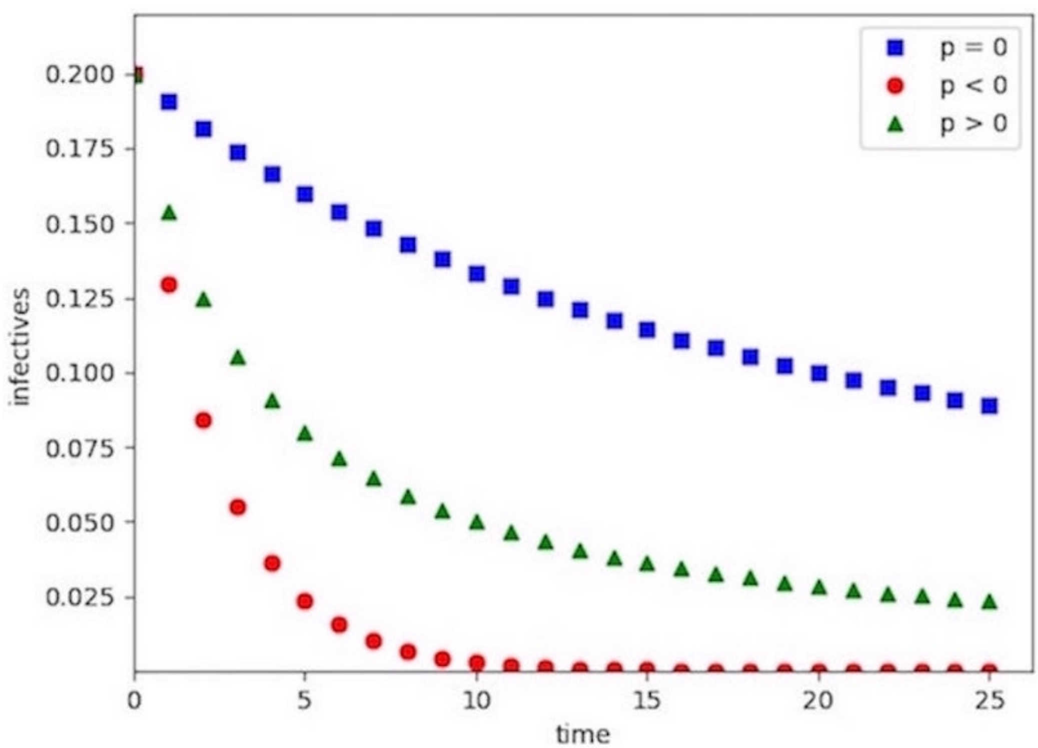

Figure 2. Number of infectives on $[0, 25]_{\mathbb{Z}}$

4. AN SIS MODEL ON TIME SCALES

We now find the exact solution to SIS model (6) with the initial conditions (S_0, I_0) where the population size is constant. An example on quantum calculus is presented at the end of this section.

Theorem 4.1. Let $\beta, \gamma \in C_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$ and $q(t) = \beta(t)N - \gamma(t) \in \mathcal{R}^+$. Then the unique solution (S, I) of SIS model (6) is given by

$$\begin{cases} S(t) = N - \dfrac{e_q(t,0)}{\dfrac{1}{I_0} + \displaystyle\int_0^t \beta(\tau)e_q(\tau,0)\Delta\tau} \\ I(t) = \dfrac{e_q(t,0)}{\dfrac{1}{I_0} + \displaystyle\int_0^t \beta(\tau)e_q(\tau,0)\Delta\tau}, \end{cases} \tag{30}$$

with the initial conditions $S(0) = S_0$ and $I(0) = I_0$, where $S, I \in C^1_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$ and $N = S_0 + I_0$.

Proof. Suppose $\beta, \gamma \in C_{rd}([0,\infty)_{\mathbb{T}}, \mathbb{R}^+)$ and $q(t) = \beta(t)N - \gamma(t) \in \mathcal{R}^+$. First, adding dynamic equations of system (6) yields $S^\Delta + I^\Delta = 0$. This implies that the total population size $N = S + I$ is constant in time and hence $N = S_0 + I_0$. Note that (6) can be rewritten as

$$\begin{cases} S^\Delta = -\dfrac{\beta(t)}{1+\mu(t)\beta(t)I}SI + \dfrac{\gamma(t)}{1+\mu(t)\beta(t)I}I \\ I^\Delta = \dfrac{\beta(t)}{1+\mu(t)\beta(t)I}SI - \dfrac{\gamma(t)}{1+\mu(t)\beta(t)I}I. \end{cases} \tag{31}$$

By plugging $S = N - I$ into the second equation of (31), we have

$$\begin{aligned} I^\Delta =& \frac{\beta(t)}{1+\mu(t)\beta(t)I}(N-I)I - \frac{\gamma(t)}{1+\mu(t)\beta(t)I}I \\ =& \frac{[\beta(t)N - \gamma(t) - \beta(t)I]I}{1+\mu(t)\beta(t)I} \\ =& \left[\frac{q(t) - \beta(t)I}{1+\mu(t)\beta(t)I}\right] I, \end{aligned} \tag{32}$$

where $q(t) = \beta(t)N - \gamma(t) \in \mathcal{R}^+$ for all $t \in [0, \infty)_{\mathbb{T}}$. Therefore, we obtain I as in (30) by Theorem 2.5 when $\alpha = 1$. The number of susceptibles can be found by $S = N - I$ as in (30). This completes the proof. $\square$

Remark 4.2. In the proof of Theorem 4.1, it is mentioned that SIS model (6) can be rewritten as (31). Furthermore, if $\beta, \gamma \in C_{rd}([0, \infty)_{\mathbb{T}}, \mathbb{R}^+)$, then from the first equation of (31), one can obtain

$$S^\Delta(1 + \mu(t)\beta(t)I) = -\beta(t)SI + \gamma(t)I, \quad t \in [0, \infty)_{\mathbb{T}}$$

and from (8)

$$S^\Delta + (S^\sigma - S)\beta(t)I = -\beta(t)SI + \gamma(t)I, \quad t \in [0, \infty)_{\mathbb{T}}.$$

This implies that

$$S^\Delta = -\beta(t)S^\sigma I + \gamma(t)I, \quad t \in [0, \infty)_{\mathbb{T}}. \tag{33}$$

Now from the second equation of (31), we get

$$\begin{aligned}
I^\Delta =& \beta(t)\left[1 - \frac{\mu(t)\beta(t)I}{1 + \mu(t)\beta(t)I}\right]SI - \gamma(t)\left[\frac{\mu(t)\beta(t)I}{1 + \mu(t)\beta(t)I} - 1\right]I \\
=& \beta(t)SI - \mu(t)\beta(t)I\left[\frac{\beta(t)SI}{1 + \mu(t)\beta(t)I}\right] - \mu(t)\beta(t)I\left[\frac{\gamma(t)I}{1 + \mu(t)\beta(t)I}\right] - \gamma(t)I \\
=& \beta(t)SI + \mu(t)\beta(t)I\left[-\frac{\beta(t)}{1 + \mu(t)\beta(t)I}SI + \frac{\gamma(t)I}{1 + \mu(t)\beta(t)I}\right] - \gamma(t)I \\
=& \beta(t)SI + \mu(t)\beta(t)S^\Delta I - \gamma(t)I \\
=& \beta(t)(S + \mu(t)S^\Delta)I - \gamma(t)I \\
=& \beta(t)S^\sigma I - \gamma(t)I, \quad t \in [0, \infty)_{\mathbb{T}},
\end{aligned} \tag{34}$$

where we use (8) in the last step. Note that when β and γ are positive constants, (33) and (34) give SIS model (3.1) in [7].

Remark 4.3. Let β and γ be positive constants and $\mathscr{R}_0 = \frac{\beta N}{\gamma}$ be the reproduction number. If $q = 0$, i.e. $\mathscr{R}_0 = 1$, then Theorem 4.1 states that the number of susceptibles is $S = N - I$, where I is given as in (25). If $q \neq 0$, i.e. $\mathscr{R}_0 \neq 1$, then the number of infectives is

$$I(t) = \frac{qI_0 e_q(t,0)}{q - \beta I_0 + \beta I_0 e_q(t,0)}. \tag{35}$$

Remark 4.4. Consider SIS model (6) when β and γ are positive constants. If $q = 0$, i.e. $\mathscr{R}_0 = 1$, then $I(t) \to 0$ and $S(t) \to N$ as $t \to \infty$ from (25). Hence, the disease dies out. The asymptotic behavior of infectives is discussed in [7, Theorem 3.2] when $q \neq 0$, i.e. $\mathscr{R}_0 < 1$ and $\mathscr{R}_0 > 1$.

Example 4.5. Consider SIS model (6) on $[0,\infty)_{2^{\mathbb{N}_0}}$ with $N = 1$, and positive constants β, γ. Let $s = 2^n$ and $t = 2^k$, $n, k \in \mathbb{N}$ and $q = \beta - \gamma \in \mathcal{R}^+$. From Remark 4.3, the unique solution to the discrete SIS model with initial conditions S_0 and I_0 is given by

$$I(t) = \frac{1}{\dfrac{1}{I_0} + \beta t} \tag{36}$$

if $q = 0$. Moreover, if $q \neq 0$, then $e_q(t,0) = \prod_{s \in [0,t)_{2^{\mathbb{N}_0}}} (1 + qs) = \prod_{n=0}^{k-1} (1 + q2^n)$ by (12). Hence, (35) implies that the number of infectives can be found as

$$I(t) = \frac{qI_0 \prod_{n=0}^{k-1} (1 + q2^n)}{q - \beta I_0 + \beta I_0 \prod_{n=0}^{k-1} (1 + q2^n)}, \tag{37}$$

and $S(t) = 1 - I(t)$ for $t \in [0,\infty)_{\mathbb{T}}$.

Example 4.6. Consider SIS model (6) with $(S_0, I_0) = (0.6, 0.4)$ on $[0, \infty)_{2^{\mathbb{N}_0}}$. If $\beta = \gamma = 0.3$, then $q = 0$ and $I(t) \to 0$ as $t \to \infty$. Choosing $\beta = 0.0008$ and $\gamma = 0.0016$ yields $q = -0.0008 < 0$ and $I(t) \to 0$ as $t \to \infty$. If $\beta = 0.5$ and $\gamma = 0.4$ are chosen, then $q = 0.1 > 0$. Hence, $I(t) \to \frac{q}{\beta} = 0.2$ as $t \to \infty$. Figure 3 illustrates the behavior of infectives on $[0, 1024)_{2^{\mathbb{N}_0}}$ based on the sign of q. Here, the number of infectives is computed from (36) and (37) in Example 4.5.

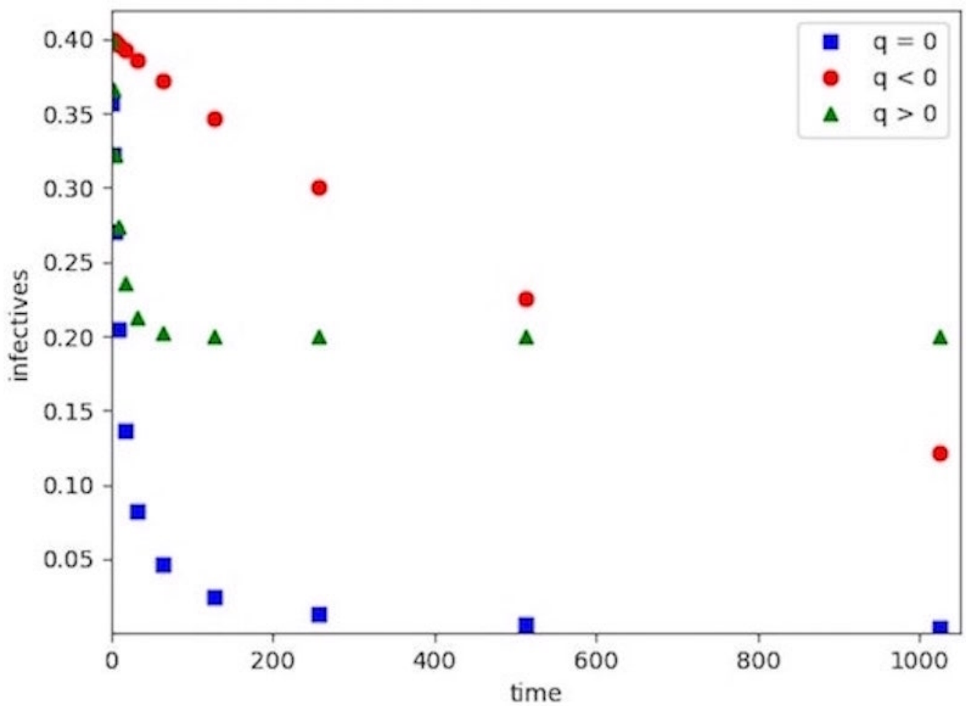

Figure 3. Number of infectives on $[0, 1024)_{2^{\mathbb{N}_0}}$

REFERENCES

[1] Elvan Akın-Bohner and Martin Bohner. Miscellaneous dynamic equations. *Methods and applications of analysis*, 10(1):011–030, 2003.

[2] Linda JS Allen. Some discrete-time si, sir, and sis epidemic models. *Mathematical biosciences*, 124(1):83–105, 1994.

[3] Pablo G Barrientos, J Ángel Rodríguez, and Alfonso Ruiz-Herrera. Chaotic dynamics in the seasonally forced sir epidemic model. *Journal of mathematical biology*, 75(6-7):1655–1668, 2017.

[4] Martin Bohner. Some oscillation criteria for first order delay dynamic equations. *Far East J. Appl. Math*, 18(3):289–304, 2005.

[5] Martin Bohner and Allan Peterson. *Dynamic Equations on Time Scales: An Introduction with Applications*. 2001.

[6] Martin Bohner and Allan C Peterson. *Advances in dynamic equations on time scales*. Springer, 2002.

[7] Martin Bohner and S Streipert. The sis-model on time scales. *Pliska Stud. Math. Bulgar*, 26:11–28, 2016.

[8] Martin Bohner, Sabrina Streipert, and Delfim FM Torres. Exact solution to a dynamic sir model. *Nonlinear Analysis: Hybrid Systems*, 32:228–238, 2019.

[9] William Ogilvy Kermack and Anderson G McKendrick. A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character*, 115(772):700–721, 1927.

[10] Seong-Hun Paeng and Jonggul Lee. Continuous and discrete sir-models with spatial distributions. *Journal of mathematical biology*, 74(7):1709–1727, 2017.

[11] Kaori Saito. On the stability of an sir epidemic discrete model. In *International Conference on Difference Equations and Applications*, pages 231–239. Springer, 2016.

[12] G Shabbir, H Khan, and MA Sadiq. A note on exact solution of sir and sis epidemic models. *arXiv preprint arXiv:1012.5035*, 2010.

III. STABILITY OF DISCRETE SIR MODELS

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ABSTRACT

In this study, we present discrete SIR (susceptible-infected-recovered) epidemic models. We discuss the stability of the disease free and endemic equilibrium points by using the linearization method and Lyapunov function.

Keywords: SIR epidemic model; Difference equations; Equilibrium points; Local stability; Global stability; Lyapunov

1. INTRODUCTION

In this paper, we consider a disease transmission model when the population is divided into three epidemiological classes as the susceptibles S, the infectives I, and the removed/recovered R, SIR in short. A basic continuous SIR model is studied by Hethcote [9]:

$$\begin{cases} S' = -\beta SI - \gamma S + \alpha \\ I' = \beta SI - (\gamma + \lambda)I \\ R' = \lambda I - \gamma R, \end{cases}$$

where the transmission rate β is the average number of adequate contacts per unit time, and γ and λ are the death rates of the population and the recovery rate of infectives, respectively. The birth rate of susceptibles is denoted by α. The incidence rate βSI can be considered in a nonlinear form as $\frac{\beta SI}{1+\alpha I}$ in [4] and as $\frac{\beta S(t)I(t-\tau)}{1+\alpha I(t-\tau)}$ in [5, 13, 14]. Here, τ indicates the delay needed for the force of infection. McCluskey in [14] considers the system above with $\frac{\beta S(t)I(t-\tau)}{1+\alpha I(t-\tau)}$ incidence rate and establishes global stability analysis of the endemic equilibrium by constructing Lyapunov functions.

In [1], the unification of continuous and discrete models of SIR is formulated on an arbitrary closed subset of real numbers, so called a time scale. The model in [1] is given as a system of two nonlinear dynamic equations, and the exact solution is derived by the approach of the Bernoulli equation on time scales, see [2]. In a number of works, some other continuous and discrete SIR models have been investigated, see [3, 7, 8, 10, 12, 15].

Motivated by [1], we consider the following discrete SIR (susceptible-infected-recovered) epidemic model of the form

$$\begin{cases} \Delta S_n = -\dfrac{\beta(1-\gamma)}{1+\beta I_n} S_n I_n - \gamma S_n + \alpha \\ \\ \Delta I_n = \dfrac{\beta(1-\gamma)}{1+\beta I_n} S_n I_n - (\gamma+\lambda) I_n \\ \\ \Delta R_n = \lambda I_n - \gamma R_n \end{cases} \tag{1}$$

with initial conditions $S_0 > 0$, $I_0 > 0$ and $R_0 \geq 0$. The numbers of susceptibles, infectives and recovered for $n \geq 0$ are denoted by S_n, I_n, and R_n respectively. It is assumed that all parameters are positive such that $\gamma < 1$.

We first introduce the prelimary results for the system of difference equations and discrete stability analysis. Later, we find the equilibrium points that are classified as disease free and endemic. We show the necessary conditions for their local stability. By the fact that system (1) and the following system with the initial conditions $S_0 > 0$, $I_0 > 0$ and $R_0 \geq 0$

$$\begin{cases} \Delta S_n = -\dfrac{\beta(1-\gamma)}{1+\beta I_{n+1}} S_{n+1} I_{n+1} - \gamma S_{n+1} + \alpha \\ \\ \Delta I_n = \dfrac{\beta(1-\gamma)}{1+\beta I_{n+1}} S_{n+1} I_{n+1} - (\gamma+\lambda) I_{n+1} \\ \\ \Delta R_n = \lambda I_{n+1} - \gamma R_{n+1} \end{cases} \tag{2}$$

have same equilibrium points, we construct a Lypunov fuction to show the global stability of the endemic equilibrium, see Section 4.

2. PRELIMINARIES

In this paper, we discuss the stability analysis of systems (1) and (2). Therefore, we first present some necessary definitions and results related to stability theory from the books written by Peterson and Elaydi [6, 11].

The following system of n linear equations:

$$\begin{aligned} x_1(n+1) &= a_{11}x_1(n) + a_{12}x_2(n) + \cdots + a_{1m}x_m(n) \\ x_2(n+1) &= a_{21}x_1(n) + a_{22}x_2(n) + \cdots + a_{2m}x_m(n) \\ &\vdots \qquad\qquad \vdots \qquad\qquad \vdots \qquad\qquad \vdots \\ x_m(n+1) &= a_{m1}x_1(n) + a_{m2}x_2(n) + \cdots + a_{mm}x_m(n) \end{aligned}$$

may be written in the vector form

$$x(n+1) = Ax(n), \tag{3}$$

where $x(n) = (x_1(n), x_2(n), \cdots, x_m(n))^T \in \mathbb{R}^n$, and $A = (a_{ij})$ is an $m \times m$ real nonsingular matrix. System (3) is considered autonomous or time-invariant, since the values of A are all constants. The spectral radius of A is defined as

$$r(A) = \max \{|\xi| : \xi \text{ is an eigenvalue of A}\}.$$

We consider the vector difference equation

$$x(n+1) = f(x(n)), \tag{4}$$

with $x(n_0) = x_0$, where $x(n) \in \mathbb{R}^k$, $f : \mathbb{R}^k \to \mathbb{R}^k$ is continuous. A point x^* in $\mathbb{R}^k$ is called an equilibrium point of (4) if $f(x^*) = x^*$ for all $n \geq n_0$.

Definition 2.1. ([6], Definition 4.2) The equilibrium point x^* of (4) is said to be:

(i) Stable if given $\epsilon > 0$ and $n_0 \geq 0$, there exists $\delta = \delta(\epsilon, n_0)$ such that $\|x_0 - x^*\| < \delta$ implies $\|x(n, n_0, x_0) - x^*\| < \epsilon$ for all $n \geq n_0$.

(ii) Attracting if there exists $\mu = \mu(n_0)$ such that $\|x(n, n_0, x_0) - x^*\| < \mu$ implies $\lim_{n\to\infty} x(n, n_0, x_0) = x^*$.

(iii) Asymptotically stable if it is stable and attracting.

(iv) Globally asymptotically stable if $\mu = \infty$ in parts (ii) and (iii).

The next theorem summarizes the main stability results for the linear autonomous system (3).

Theorem 2.2. ([6], Theorem 4.13) The following statements hold:

(i) The zero solution of (3) is stable if and only if $r(A) \leq 1$ and the eigenvalues of unit modulus are semisimple, i.e., if the corresponding Jordan block is diagonal.

(ii) The zero solution of (3) is asymptotically stable if and only if $r(A) < 1$.

For two dimensional systems, if

$$|\mathrm{tr}A| < 1 + \det A < 2 \tag{5}$$

holds, then the zero solution of (3) is asymptotically stable, see [6].

Let x^* be an equilibrium point of f in (4). A real-valued continuous function V on some ball B about x^* is called a "Lyapunov function" for f at x^* provided $V(x^*) = 0$, $V(x) > 0$ for $x \neq x^*$ in B, and

$$\Delta_n V(x) \equiv V(f(x)) - V(x) \leq 0 \tag{6}$$

for all x in B. If the inequality (6) is strict for $x \neq x^*$, then V is a "strict Lyapunov function". We have the following theorem, which plays an important role in showing the global stability of an equilibrium of the system of autonomous difference equations.

Theorem 2.3. (Lyapunov Stability Theorem) Let x^* be a equilibrium point of f, and assume f is continuous on some ball about x^*. If there is a Lyapunov function for f at x^*, then x^* is stable. If there is a strict Lyapunov function for f at x^*, then x^* is asymptotically stable. Moreover, if $V(x) \to \infty$ as $\|x\| \to \infty$, then x^* is globally asymptotically stable.

2.1. EQUILIBRIUM POINTS

The first two equations of the SIR epidemic model (1) can be rewritten as

$$\begin{cases} S_{n+1} = -\dfrac{\beta(1-\gamma)}{1+\beta I_n} S_n I_n + (1-\gamma)S_n + \alpha \\[2ex] I_{n+1} = \dfrac{\beta(1-\gamma)}{1+\beta I_n} S_n I_n + (1-\gamma-\lambda)I_n. \end{cases} \tag{7}$$

It is clear that the equilibrium solution of (2) has

$$S^* = \frac{\alpha + \alpha\beta I^*}{\gamma + \beta I^*}. \tag{8}$$

From the second equation of (2), one can get $\beta(1-\gamma)S^*I^* + (1-\gamma-\lambda)I^*(1+\beta I^*) = (1+\beta I^*)I^*$. Simplifying yields $I^*\left(\beta I^*(\gamma+\lambda) + \gamma + \lambda - \beta S^* + \beta\gamma S^*\right) = 0$. Therefore,

$$I^* = 0 \quad \text{or} \quad \beta I^*(\gamma+\lambda) + \gamma + \lambda - \beta S^* + \beta\gamma S^* = 0. \tag{9}$$

Now we want to solve (8) and (9). If $I^* = 0$, then $S^* = \frac{\alpha}{\gamma}$. If $\beta I^*(\gamma+\lambda)+\gamma+\lambda-\beta S^*+\beta\gamma S^* = 0$, then

$$I^{*2} + \left(\frac{\gamma+1}{\beta} + \frac{\alpha(\gamma-1)}{\gamma+\lambda}\right) I^* + \left(\frac{\gamma}{\beta^2} + \frac{\alpha(\gamma-1)}{\beta(\gamma+\lambda)}\right) = 0. \tag{10}$$

Solving the algebraic equation (10) gives

$$I^*_{1,2} = \frac{-\left(\frac{\gamma+1}{\beta} + \frac{\alpha(\gamma-1)}{\gamma+\lambda}\right) \pm \sqrt{\left(\frac{\gamma+1}{\beta} + \frac{\alpha(\gamma-1)}{\gamma+\lambda}\right)^2 - 4\left(\frac{\gamma}{\beta^2} + \frac{\alpha(\gamma-1)}{\beta(\gamma+\lambda)}\right)}}{2}.$$

To find I^*_1 and I^*_2 values, the expression in the square root needs to be simplified as follows

$$\begin{aligned} \left(\frac{\gamma+1}{\beta} + \frac{\alpha(\gamma-1)}{\gamma+\lambda}\right)^2 - 4\left(\frac{\gamma}{\beta^2} + \frac{\alpha(\gamma-1)}{\beta(\gamma+\lambda)}\right) &= (\gamma-1)^2\left[\frac{1}{\beta^2} + \frac{2\alpha}{\beta(\gamma+\lambda)} + \frac{\alpha^2}{(\gamma+\lambda)^2}\right] \\ &= (\gamma-1)^2\left[\frac{1}{\beta} + \frac{\alpha}{(\gamma+\lambda)}\right]^2. \end{aligned}$$

Using the fact that $\gamma < 1$, we get

$$I_{1,2}^* = \frac{-\left(\frac{\gamma+1}{\beta} + \frac{\alpha(\gamma-1)}{\gamma+\lambda}\right) \pm (1-\gamma)\left[\frac{1}{\beta} + \frac{\alpha}{(\gamma+\lambda)}\right]}{2}.$$

Hence,

$$I_1^* = -\frac{\gamma}{\beta} + (1-\gamma)\frac{\alpha}{\gamma+\lambda} \quad \text{and} \quad I_2^* = -\frac{1}{\beta}.$$

If $I^* = I_1^*$, then substituting I^* into (8) gives $S^* = \frac{\alpha+\alpha\beta I^*}{\gamma+\beta I^*} = \frac{\gamma+\lambda}{\beta} + \alpha$ immediately. Therefore, system (2) with initial conditions has a disease free equilibrium $E_0 = (S_0^*, I_0^*, R_0^*)$, where

$$S_0^* = \frac{\alpha}{\gamma}, \quad I_0^* = 0, \quad \text{and} \quad R_0^* = 0 \tag{11}$$

and a positive endemic equilibrium $E^+ = (S^*, I^*, R^*)$, where

$$S^* = \frac{\gamma+\lambda}{\beta} + \alpha, \quad I^* = -\frac{\gamma}{\beta} + (1-\gamma)\frac{\alpha}{\gamma+\lambda}, \quad R^* = \frac{\lambda}{\gamma}\left(-\frac{\gamma}{\beta} + (1-\gamma)\frac{\alpha}{\gamma+\lambda}\right). \tag{12}$$

Now define the basic reproduction number for system (1) as

$$\mathscr{R}_0 = \frac{(1-\gamma)\alpha\beta}{\gamma} + 1 - (\gamma+\lambda). \tag{13}$$

We analyze the stability of the equilibria of system (1) based on the basic reproduction number.

3. LOCAL STABILITY OF EQUILIBRIUM POINTS OF SYSTEM (1)

In this section, we show that if $\mathscr{R}_0 < 1$, then all solutions of system (1) approach $E_0 = (S_0^*, 0, 0)$ as in (11). For the proof, it is sufficient to consider system (7).

Theorem 3.1. If $\mathscr{R}_0 < 1$, then the disease free equilibrium E_0 of system (1) is locally asymptotically stable. And if $\mathscr{R}_0 > 1$, then E_0 is unstable.

Proof. The Jacobian matrix for the variables of system (7) is

$$J(S,I) = \begin{bmatrix} \frac{1-\gamma}{1+\beta I} & \frac{\beta(\gamma-1)S}{(1+\beta I)^2} \\ \\ \frac{\beta(1-\gamma)I}{1+\beta I} & \frac{\beta(1-\gamma)S}{(1+\beta I)^2} + 1 - \gamma - \lambda \end{bmatrix}. \tag{14}$$

For the disease free equilibrium $(S_0^*, 0)$ of system (7), the Jacobian matrix is given by

$$J(S_0^*, 0) = \begin{bmatrix} 1-\gamma & \frac{(\gamma-1)\alpha\beta}{\gamma} \\ \\ 0 & \frac{(1-\gamma)\alpha\beta}{\gamma} + 1 - \gamma - \lambda \end{bmatrix}$$

whose eigenvalues are

$$\xi_1 = 1 - \gamma \quad \text{and} \quad \xi_2 = \frac{(1-\gamma)\alpha\beta}{\gamma} + 1 - \gamma - \lambda. \tag{15}$$

It follows that if $\mathscr{R}_0 < 1$, then $\xi_1 < 1$ and $\xi_2 < 1$. Therefore, $(S_0^*, 0)$ is locally asymptotically stable. If $\mathscr{R}_0 > 1$, then $\xi_2 > 1$ and thus $(S_0^*, 0)$ is unstable. Now one can consider system (1), where $R_{n+1} = \lambda I_n + (1-\gamma)R_n$. In this case, the Jacobian matrix for E_0 is given by

$$J(E_0 = (S_0^*, 0, 0)) = \begin{bmatrix} 1-\gamma & \frac{(\gamma-1)\alpha\beta}{\gamma} & 0 \\ \\ 0 & \frac{(1-\gamma)\alpha\beta}{\gamma} + 1 - \gamma - \lambda & 0 \\ \\ 0 & \lambda & 1-\gamma \end{bmatrix}$$

whose eigenvalues are ξ_1, ξ_2 given as in (15), and $\xi_3 = 1 - \gamma$. Since $\gamma < 1$, $\xi_3 < 1$. Therefore, if $\mathscr{R}_0 < 1$, then E_0 is locally asypmtotically stable, and unstable if $\mathscr{R}_0 > 1$ by Theorem 2.2. Hence, the proof is completed. □

Following similar steps as in the previous theorem, in this section we show that if $\mathscr{R}_0 > 1$, then all solutions of system (1) approach $E^+ = (S^*, I^*, R^*)$ as in (12). Note that one can get the disease free equilibrium, i.e., $S_0^* = \frac{\alpha}{\gamma}$, $I_0^* = 0$, and $R_0^* = 0$ if $\mathscr{R}_0 = 1$.

Theorem 3.2. If $\mathscr{R}_0 > 1$, then the endemic equilibrium point E^+ of system (1) is locally asymptotically stable.

Proof. Assume $\mathscr{R}_0 > 1$. In the proof of Theorem 3.1, the Jacobian matrix for the variables of system (7) is computed as in (14). Hence, for the endemic equilibrium (S^*, I^*), the Jacobian matrix is

$$\begin{aligned} J(S^*, I^*) &= \begin{bmatrix} \frac{1-\gamma}{1+\beta I^*} & \frac{\beta(\gamma-1)S^*}{(1+\beta I^*)^2} \\ \\ \frac{\beta(1-\gamma)I^*}{1+\beta I^*} & \frac{\beta(1-\gamma)S^*}{(1+\beta I^*)^2} + 1 - \gamma - \lambda \end{bmatrix} \\ &= \begin{bmatrix} \frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta} & -\frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma+\lambda+\alpha\beta)} \\ \\ -\gamma + \frac{\alpha\beta}{\gamma+\lambda+\alpha\beta} & \frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma+\lambda+\alpha\beta)} + 1 - \gamma - \lambda \end{bmatrix}. \end{aligned}$$

To show that (S^*, I^*) is locally asymptotically stable, condition (5) needs to be held for $J(S^*, I^*)$, i.e.,

$$|\mathrm{tr}J(S^*, I^*)| < 1 + \det J(S^*, I^*) < 2. \tag{16}$$

First, note that

$$\begin{aligned} \det J(S^*, I^*) &= \frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma+\lambda+\alpha\beta)} \left(\frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta} + \frac{\alpha\beta}{\gamma+\lambda+\alpha\beta} - \gamma \right) \\ &+ \frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta}(1-\gamma-\lambda) \\ &= \frac{(\gamma+\lambda)^2}{\gamma+\lambda+\alpha\beta} + \frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta}(1-\gamma-\lambda) \\ &= \frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta}. \end{aligned} \tag{17}$$

The assumption $\mathscr{R}_0 > 1$ implies that

$$\frac{\gamma + \lambda}{(1-\gamma)(\gamma + \lambda + \alpha\beta)} - 1 < 0. \tag{18}$$

Therefore,

$$\begin{aligned} |\mathrm{tr}J(S^*, I^*)| &= |\frac{\gamma + \lambda}{\gamma + \lambda + \alpha\beta} + \frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma + \lambda + \alpha\beta)} + 1 - (\gamma + \lambda)| \\ &= 1 + \frac{\gamma + \lambda}{\gamma + \lambda + \alpha\beta} + (\gamma + \lambda)\left(\frac{\gamma + \lambda}{(1-\gamma)(\gamma + \lambda + \alpha\beta)} - 1\right) \\ &< 1 + \mathrm{det}J(S^*, I^*) \end{aligned} \tag{19}$$

by (17) and (18). Furthermore,

$$1 + \mathrm{det}J(S^*, I^*) = 1 + \frac{\gamma + \lambda}{\gamma + \lambda + \alpha\beta} = 1 + \frac{1}{1 + \frac{\alpha\beta}{\gamma+\lambda}} < 2. \tag{20}$$

Hence, (16) holds from (19) and (20). For system (1), the characteristic equation is

$$\det(J(E^+ = (S^*, I^*, R^*)) - rI_{3\times 3}) = \begin{vmatrix} \frac{\gamma+\lambda}{\gamma+\lambda+\alpha\beta} & -\frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma+\lambda+\alpha\beta)} & 0 \\ -\gamma + \frac{\alpha\beta}{\gamma+\lambda+\alpha\beta} & \frac{(\gamma+\lambda)^2}{(1-\gamma)(\gamma+\lambda+\alpha\beta)} + 1 - \gamma - \lambda & 0 \\ 0 & -\lambda & 1-\gamma-r \end{vmatrix}$$

$$= \det(J((S^*, I^*)) - rI_{2\times 2}) \times (1 - \gamma - r) = 0,$$

where $I_{i\times i}$ is the $i \times i$ unit matrix for $i = 2, 3$. We already have the eigenvalues r_1 and r_2 of $\det(J((S^*, I^*)) - rI_{2\times 2})$, and $r_3 = 1 - \gamma$. Thus, by (16) and the Schur-Cohn Criterion in [6], we have $|r_1| < 1$, $|r_2| < 1$, and $|r_3| < 1$. By Theorem 2.2, the positive endemic equilibrium E^+ is locally asymptotically stable if $\mathscr{R}_0 > 1$. □

Remark 3.3. From Theorems 3.1 and 3.2, $\mathscr{R}_0 < 1$ guarantees that the disease free equilibrium is locally asymptotically stable. On the other hand, $\mathscr{R}_0 > 1$ guarantees that the endemic equilibrium is locally asymptotically stable while the disease free equilibrium is unstable.

4. GLOBAL STABILITY OF THE ENDEMIC EQUILIBRIUM FOR SYSTEM (2)

By the fact that systems (1) and (2) have the same equilibrium points under the same conditions, we show the global stability of the endemic equilibrium $E^+ = (S^*, I^*, R^*)$ of system (2) when $\mathscr{R}_0 > 1$. Note that $\mathscr{R}_0 > 1$ guarantees the positivity of I^* of E^+.

Theorem 4.1. If $\mathscr{R}_0 > 1$, then the endemic equilibrium E^+ of system (2) is globally asymptotically stable.

Proof. Let $f(x) = \frac{x}{1+\beta x}$ and $g(x) = x - 1 - \ln x$, $x > 0$. It is clear that g has minimum at $x = 1$ such that $g(1) = 0$ and $g(x) \geq 0$ for $x > 0$. We define the following Lyapunov function

$$V_n = V(S_n, I_n, R_n) = \frac{1}{\beta(1-\gamma) f(I_0^*)} V_{S_n} + \frac{I^*}{\beta(1-\gamma) S^* f(I^*)} V_{I_n}, \tag{21}$$

where

$$V_{S_n} = g\left(\frac{S_n}{S^*}\right), \quad V_{I_n} = g\left(\frac{I_n}{I^*}\right). \tag{22}$$

Now we calculate ΔV_{S_n} and ΔV_{I_n} in order to show $\Delta V_n < 0$.

$$\begin{aligned}
\Delta V_{S_n} &= g\left(\frac{S_{n+1}}{S^*}\right) - g\left(\frac{S_n}{S^*}\right) \\
&= \frac{S_{n+1} - S_n}{S^*} + \ln \frac{S_n}{S_{n+1}} \\
&\leq (S_{n+1} - S_n)\left(\frac{S_{n+1} - S^*}{S^* S_{n+1}}\right) \\
&= -\gamma \frac{(S_{n+1} - S^*)^2}{S^* S_{n+1}} - \beta(1-\gamma) f(I^*)\left(\frac{S_{n+1} f(I_{n+1})}{S^* f(I^*)} - 1\right)\left(1 - \frac{S^*}{S_{n+1}}\right),
\end{aligned} \tag{23}$$

where we use $\ln(1-x) \le -x$ for $x < 1$ and replace α by $\beta(1-\gamma)S^* f(I^*) + \gamma S^*$. Similarly,

$$\begin{aligned}
\Delta V_{I_n} &= g\left(\frac{I_{n+1}}{I^*}\right) - g\left(\frac{I_n}{I^*}\right) \\
&= \frac{I_{n+1} - I_n}{I^*} + \ln \frac{I_n}{I_{n+1}} \\
&\le (I_{n+1} - I_n)\left(\frac{I_{n+1} - I^*}{I^* I_{n+1}}\right) \\
&= \frac{\beta(1-\gamma)S^* f(I^*)}{I^*}\left(\frac{S_{n+1} f(I_{n+1})}{S^* f(I^*)} - \frac{I_{n+1}}{I^*}\right)\left(1 - \frac{I^*}{I_{n+1}}\right),
\end{aligned} \tag{24}$$

since $(\gamma + \lambda)I^* = \beta S^* f(I^*)$. Therefore, from (23) and (24)

$$\begin{aligned}
\Delta V_n &= V_{n+1} - V_n \\
&\le -\gamma \frac{(S_{n+1} - S^*)^2}{\beta(1-\gamma) f(I^*) S^* S_{n+1}} - \left(\frac{S_{n+1} f(I_{n+1})}{S^* f(I^*)} - 1\right)\left(1 - \frac{S^*}{S_{n+1}}\right) \\
&+ \left(\frac{S_{n+1} f(I_{n+1})}{S^* f(I^*)} - \frac{I_{n+1}}{I^*}\right)\left(1 - \frac{I^*}{I_{n+1}}\right).
\end{aligned} \tag{25}$$

For simplicity, let $x_{n+1} = \dfrac{S_{n+1}}{S^*}$, $y_{n+1} = \dfrac{I_{n+1}}{I^*}$ and $F(y_{n+1}) = \dfrac{f(I_{n+1})}{f(I^*)}$. Then, (25) becomes

$$\Delta V_n \le -\gamma \frac{(S_{n+1} - S^*)^2}{\beta(1-\gamma) f(I^*) S^* S_{n+1}} + F(y_{n+1}) - \frac{x_{n+1}}{y_{n+1}} F(y_{n+1}) - \frac{1}{x_{n+1}} - y_{n+1} + 2. \tag{26}$$

Adding and subtracting $\ln \dfrac{x_{n+1}}{y_{n+1}} F(y_{n+1})$ in (26) yields

$$\begin{aligned}
\Delta V_n \le -\gamma \frac{(S_{n+1} - S^*)^2}{\beta(1-\gamma) f(I^*) S^* S_{n+1}} - g\left(\frac{1}{x_{n+1}}\right) - g\left(\frac{x_{n+1}}{y_{n+1}} F(y_{n+1})\right) \\
+F(y_{n+1}) - y_{n+1} + \ln y_{n+1} - \ln F(y_{n+1}).
\end{aligned} \tag{27}$$

Let $h(z) = F(z) - z + \ln z - \ln F(z)$, where $z = y_{n+1}$. Then, $h(1) = 0$ and $h'(z) = (1-z)\left(\frac{2\beta I^* + (\beta I^*)^2 z}{(1+\beta I^* z)^2}\right)$. Hence, $h'(z) > 0$ if $z < 1$ and $h'(z) < 0$ if $z > 1$.

From the above discussion and the fact that g is nonnegative, if $(S_{n+1}, I_{n+1}) = (S^*, I^*)$, then $h = 0$ and $\Delta V_n = 0$. If $(S_{n+1}, I_{n+1}) \neq (S^*, I^*)$, then $h < 0$ and hence $\Delta V_n < 0$ for any $n \geq 0$ from (27). Since V is a monotone decreasing sequence, $\lim_{n\to\infty} V_n \geq 0$ and $\lim_{n\to\infty} (V_{n+1} - V_n) = 0$. Therefore, (26) implies that

$$\lim_{n\to\infty} S_{n+1} = S^*. \tag{28}$$

By solving the first equation of system (2) for I_{n+1} and using (28), we have

$$\lim_{n\to\infty} I_{n+1} = \lim_{n\to\infty} \frac{\alpha - (\gamma + 1)S_{n+1} + S_n}{\beta(2S_{n+1} - S_n - \alpha)} = \frac{\alpha - \gamma S^*}{\beta(S^* - \alpha)} = I^*. \tag{29}$$

From the third equation of system (2) and (29), $\lim_{n\to\infty} R_n = R^*$ can be shown similarly. Hence, we obtain $\lim_{n\to\infty} (S_n, I_n, R_n) = (S^*, I^*, R^*)$. Therefore, the endemic equilibrium E^+ of system (2) is asymptotically stable and since $V(x) \to \infty$ as $\|x\| \to \infty$, where $x = (S_n, I_n, R_n)$, E^+ is globally asymptotically stable by Theorem 2.3. □

5. CONCLUSION

In this paper, we propose discrete SIR epidemic models (1) and (2) with nonlinear incidence rate. The stability of disease-free and endemic equilibria is determined by the reproduction number, $\mathscr{R}_0$. We show the local stability of disease-free and endemic equilibria of system (1) by the linearizarion method, yet the global stability is left as an open problem. On the other hand, we successfully show the global stability of the endemic equilibrium of system (2) by constructing a suitable Lyapunov function. Note that since the first two equations of system (2) is independent from the last equation, $R_n \to R^*$ as $n \to \infty$ can be also obtained in Theorem 4.1 if the right-side of last equation has the form of $\lambda I_{n+1} - \gamma R_n$. To investigate an application of discrete models (1) and (2) from the epidemiological perspective, the authors would like fit these models to a clinical data.

REFERENCES

[1] Elvan Akın and Gülşah Yeni. On exact solutions to epidemic dynamic models. *Submitted*, 2019.

[2] Elvan Akın-Bohner and Martin Bohner. Miscellaneous dynamic equations. *Methods and applications of analysis*, 10(1):011–030, 2003.

[3] Linda JS Allen. Some discrete-time si, sir, and sis epidemic models. *Mathematical biosciences*, 124(1):83–105, 1994.

[4] Vincenzo Capasso and Gabriella Serio. A generalization of the kermack-mckendrick deterministic epidemic model. *Mathematical Biosciences*, 42(1-2):43–61, 1978.

[5] Kenneth L Cooke. Stability analysis for a vector disease model. *The Rocky Mountain Journal of Mathematics*, 9(1):31–42, 1979.

[6] Saber N. Elaydi. *An Introduction to Difference Equations*. 2005.

[7] Yoichi Enatsu, Yukihiko Nakata, and Yoshiaki Muroya. Global stability for a class of discrete sir epidemic models. *Math. Biosci. Eng*, 7(2):347–361, 2010.

[8] Yoichi Enatsu, Yukihiko Nakata, Yoshiaki Muroya, Giuseppe Izzo, and Antonia Vecchio. Global dynamics of difference equations for sir epidemic models with a class of nonlinear incidence rates. *Journal of Difference Equations and Applications*, 18(7):1163–1181, 2012.

[9] Herbert W Hethcote. The mathematics of infectious diseases. *SIAM review*, 42(4):599–653, 2000.

[10] Sophia Jang and Saber Elaydi. Difference equations from discretization of a continuous epidemic model with immigration of infectives. 2003.

[11] Walter G Kelley and Allan C Peterson. *Difference equations: an introduction with applications*. Academic press, 2001.

[12] William Ogilvy Kermack and Anderson G McKendrick. A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character*, 115(772):700–721, 1927.

[13] C Connell McCluskey. Complete global stability for an sir epidemic model with delay distributed or discrete. *Nonlinear Analysis: Real World Applications*, 11(1):55–59, 2010.

[14] C Connell McCluskey. Global stability for an sir epidemic model with delay and nonlinear incidence. *Nonlinear Analysis: Real World Applications*, 11(4):3106–3109, 2010.

[15] Kaori Saito. On the stability of an sir epidemic discrete model. In *International Conference on Difference Equations and Applications*, pages 231–239. Springer, 2016.

IV. OSCILLATION CRITERIA FOR FOUR-DIMENSIONAL TIME-SCALE SYSTEMS

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ABSTRACT

In this paper, we obtain oscillation and nonoscillation criteria for solutions to four dimensional systems of first order dynamic equations on time scales. Especially, we are interested in the conditions which insure that every solution is oscillatory in the sub-linear, half-linear, and super-linear cases. Our approach is based on the sign of the components of nonoscillatory solutions. Several examples are included to highlight our main results.

Keywords: Time scales; Oscillation; Nonoscillation; Four-dimensional systems

1. INTRODUCTION

We investigate four dimensional dynamic systems of the form

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(\sigma(t)) \end{cases} \tag{1}$$

on a time scale $\mathbb{T}$, i.e., a closed subset of real numbers, where the coefficient functions $a, b, c, d \in C_{rd}([t_0, \infty)_{\mathbb{T}}, (0, \infty))$ and $\alpha, \beta, \gamma, \lambda$ are the ratios of odd positive integers. Here, C_{rd} is the set of rd-continuous functions and $[t_0, \infty)_{\mathbb{T}} := [t_0, \infty) \cap \mathbb{T}$. Throughout this paper, we assume

$$\int_{t_0}^{\infty} a(t)\Delta t = \int_{t_0}^{\infty} b(t)\Delta t = \int_{t_0}^{\infty} c(t)\Delta t = \infty \tag{2}$$

and consider time scales unbounded. By a solution (x, y, z, w) of system (1), we mean that functions x, y, z, w are delta-differentiable, their first delta-derivatives are rd-continuous, and satisfy system (1) for all $t \geq t_0$. We call (x, y, z, w) a *proper* solution if it is defined on $[t_0, \infty)_{\mathbb{T}}$ and for $t \geq t_0$, $\sup\{|x(s)|, |y(s)|, |z(s)|, |w(s)| : s \in [t, \infty)_{\mathbb{T}}\} > 0$. A solution (x, y, z, w) of system (1) is said to be *oscillatory* if all of its components x, y, z, w are oscillatory, i.e., neither eventually positive nor eventually negative. Otherwise, it is said to be *nonoscillatory*. Obviously, if one component of a solution of system (1) is eventually of one sign, then all its components are eventually of one sign and so nonoscillatory solutions have all components nonoscillatory. We are also interested in system (1) in the sub-linear case, half-linear case, and super linear case, that is, when $\alpha\beta\gamma\lambda < 1$, $\alpha\beta\gamma\lambda = 1$, and $\alpha\beta\gamma\lambda > 1$, respectively.

Motivated by [5] and [7], we establish some oscillation results for system (1) on time scales. In the next section, we present some auxiliary lemmas which are needed in the proof of our results and we consider two types of nonoscillatory solutions: one type when all components have the same sign, the other type when the third component has a different sign. In the following sections, we consider the properties of these types including the asymptotic behaviors. Our approach is based on the integral conditions of the coefficient functions a, b, c and d with the products of $\alpha, \beta, \gamma, \lambda$. We also illustrate the results by examples. Finally, we introduce the conditions which insure that every solution of system (1) is oscillatory in the sub-linear, half-linear and super-linear cases.

2. PRELIMINARY RESULTS

We only include preliminary results in this section. Nevertheless, we suggest readers the books by Bohner and Peterson [3, 4] for an introduction to time scales calculus.

The following lemma is essential to establish our main theorems for the sub-linear, half-linear and super-linear cases. Its proof follows from the chain rule on a time scale, see [1].

Lemma 2.1. Let $x \in C_{rd}\left(\mathbb{T}, \mathbb{R}^+\right)$.

(i) If $0 < \eta < 1$ and $x^{\Delta}(t) < 0$ on $\mathbb{T}$, then

$$\int_T^\infty -\frac{x^{\Delta}(t)}{x^{\eta}(t)}\Delta t < \infty, T \in \mathbb{T}.$$

(ii) If $\eta > 1$ and $x^{\Delta}(t) > 0$ on $\mathbb{T}$, then

$$\int_T^\infty \frac{x^{\Delta}(t)}{x^{\eta}(\sigma(t))}\Delta t < \infty, T \in \mathbb{T}.$$

Using the sign of the components, one can observe the following: let (x, y, z, w) be a nonoscillatory solution of system (1). Without loss of generality, assume that $x(t) > 0$ for $t \geq t_0$, $t_0 \in \mathbb{T}$. From the fourth equation of system (1), w is strictly decreasing. Hence, it is of one sign. Continuing by the same argument, we get z and y are monotone and of one sign for large t too. The remaining cases when any of the components y, z, w are eventually positive or negative are proved similarly. Therefore, if one of the components of a solution (x, y, z, w) is eventually of one sign, then all of its components are eventually of one sign. In other words, any nonoscillatory solution of system (1) has all components nonoscillatory.

The next lemma shows that any nonoscillatory solution (x, y, z, w) of system (1) has two types when (2) holds.

Lemma 2.2. Any nonoscillatory solution (x, y, z, w) of system (1) such that $x(t) > 0$ for large $t \in \mathbb{T}$ is one of the following types:

Type (a): $x > 0,\ y > 0,\ z > 0,\ w > 0$ eventually

Type (b): $x > 0,\ y > 0,\ z < 0,\ w > 0$ eventually.

Proof. Let (x, y, z, w) be a nonoscillatory solution of system (1). Without loss of generality, assume that $x(t) > 0$ for $t \geq T$, $T \in \mathbb{T}$. Then we first assume that there exists a solution such that $y(t) > 0$, $z(t) < 0$, and $w(t) < 0$ for $t \geq T$. The negativity of w and the third equation of system (1) show that $z(t)$ is nonincreasing for $t \geq T$. Therefore, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $k > 0$ such that $z(t) \leq -k$ for $t \geq t_0$. Plugging this inequality in the integration of the second equation from t_0 to t we get

$$y(t) - y(t_0) \leq -k^{\beta} \int_{t_0}^{t} b(s)\Delta s, \quad t \geq t_0.$$

Then $y(t) \to -\infty$ as $t \to \infty$, but this contradicts the fact that $y(t) > 0$ for large t. The case when $y(t) < 0$, $z(t) > 0$, and $w(t) > 0$ is similar and hence is eliminated. Now assume that there exists a nonoscillatory solution of system (1) such that $y(t) < 0$, $z(t) < 0$ for $t \geq T$. The negativity of z and the second equation of system (1) yield $y(t)$ is nonincreasing for $t \geq T$. Hence, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $l > 0$ such that $y(t) \leq -l$ for $t \geq t_0$. Plugging this inequality in the integration of the first equation from t_0 to t yields

$$x(t) - x(t_0) \leq -l^{\alpha} \int_{t_0}^{t} a(s)\Delta s, \quad t \geq t_0.$$

Then $x(t) \to -\infty$ as $t \to \infty$, but this contradicts the fact that $x(t) > 0$ for large t. Next, assume that there exists a nonoscillatory solution of system (1) such that $z(t) > 0$, $w(t) < 0$ for $t \geq T$. The positivity of x and the fourth equation of system (1) yield $w(t)$ is nonincreasing for $t \geq T$. Hence, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $m > 0$ such that $w(t) \leq -m$ for $t \geq t_0$. Using this inequality and integrating the third equation from t_0 to t, we get

$$z(t) - z(t_0) \leq -m^{\gamma} \int_{t_0}^{t} c(s)\Delta s, \quad t \geq t_0.$$

Then $z(t) \to -\infty$ as $t \to \infty$, but this contradicts the assumption $z(t) > 0$ for large t. □

In order to show that system (1) is oscillatory, we first try the divergence of the single integral of d.

Lemma 2.3. System (1) is oscillatory if

$$\int_{t_0}^{\infty} d(t)\Delta t = \infty. \tag{3}$$

Proof. By Lemma 2.2, any nonoscillatory solution of system (1) is either Type (a) or Type (b). Let (x, y, z, w) be of a Type (a) solution of system (1) such that $x(t) > 0$ for $t \geq T$. The positivity of y and the first equation of system (1) show that $x(t)$ is nondecreasing for $t \geq T$. Therefore, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $k > 0$ such that $x(t) \geq k$ for $t \geq t_0$. Then using this inequality and the integration of the fourth equation from t_0 to t give us

$$w(t) \leq -k^{\lambda} \int_{t_0}^{t} d(s)\Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $w(t) \to -\infty$ by (3). But, this is a contradiction because of the assumption $w(t) > 0$ for large t. The discussion above is also valid for Type (b) solutions because the sign of z is not needed in this proof. Therefore, system (1) does not have any nonoscillatory solutions and so the proof is completed. □

Now as a result of the discussion above, from now on we will assume that

$$\int_{t_0}^{\infty} d(t)\Delta t < \infty. \tag{4}$$

3. TYPE (A) SOLUTIONS

In this section, we investigate not only nonoscillatory criteria, but also the asymptotic behavior of Type (a) solutions. The following property of Type (a) solutions in the discrete case can be found in [6].

Proposition 3.1. Every solution (x, y, z, w) of Type (a) of system (1) satisfies

$$I\left(\int_t^\infty d(s)\Delta s\right)^{\gamma\beta\alpha} \leq x^{1-\lambda\gamma\beta\alpha}(\sigma(t)), \tag{5}$$

where $t \in \mathbb{T}$ is sufficiently large and

$$I = \int_{t_0}^t a(s)\left(\int_{t_0}^s b(r)\left(\int_{t_0}^r c(\eta)\Delta\eta\right)^\beta \Delta r\right)^\alpha \Delta s. \tag{6}$$

Proof. Let (x, y, z, w) be of a Type (a) solution of system (1) such that $x(t) > 0$ for $t \geq T$. Then integrating the third equation from t_0 to t yields

$$z(t) \geq \int_{t_0}^t c(s)w^\gamma(s)\Delta s, \quad t \geq t_0. \tag{7}$$

Since $w(t)$ is nonincreasing for $t \geq T$, (7) yields

$$z^\beta(t) \geq w^{\gamma\beta}(t)\left(\int_{t_0}^t c(s)\Delta s\right)^\beta, \quad t \geq t_0.$$

Now integrating of the second equation of system (1) from t_0 to t and plugging the above inequality into the resulting inequality yield

$$y^\alpha(t) \geq w^{\gamma\beta\alpha}(t)\left(\int_{t_0}^t b(s)\left(\int_{t_0}^s c(r)\Delta r\right)^\beta \Delta s\right)^\alpha, \quad t \geq t_0, \tag{8}$$

where we use the monotonicity of w. Integrating the first equation of system (1) from t_0 to t and substituting (8) in the resulting integration give us

$$x(\sigma(t)) \geq w^{\gamma\beta\alpha}(t)I, \tag{9}$$

where we use the monotonicities of x and w, and I is defined as in (6). Integrating the fourth equation of system (1) from t to ∞ and using the monotonicity of x yield

$$w(t) \geq \int_t^\infty d(s)x^\lambda(\sigma(s))\Delta s \geq x^\lambda(\sigma(t)) \int_t^\infty d(s)\Delta s \tag{10}$$

and this implies

$$w^{\gamma\beta\alpha}(t) \geq x^{\lambda\gamma\beta\alpha}(\sigma(t)) \left(\int_t^\infty d(s)\Delta s\right)^{\gamma\beta\alpha}. \tag{11}$$

Therefore, from (9) and (11) we have

$$x(\sigma(t)) \geq I x^{\lambda\gamma\beta\alpha}(\sigma(t)) \left(\int_t^\infty d(s)\Delta s\right)^{\gamma\beta\alpha}$$

which proves the desired result (5). □

Theorem 3.1. Every nonoscillatory solution of system (1) is of Type (a) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^\infty c(t)\left(\int_t^\infty d(s)\Delta s\right)^\gamma \Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^\infty b(t)\left(\int_t^\infty c(r)\left(\int_r^\infty d(\tau)\Delta\tau\right)^\gamma \Delta r\right)^\beta \Delta s = \infty;$

(iii) $\alpha\beta\gamma\lambda < 1$ and $\displaystyle\int_{t_0}^\infty b(t)\left(\int_{t_0}^t a(s)\Delta s\right)^{\lambda\gamma\beta}\left(\int_t^\infty c(r)\left(\int_r^\infty d(\tau)\Delta\tau\right)^\gamma \Delta r\right)^\beta \Delta t = \infty;$

(iv) $\lambda\gamma\beta\alpha > 1$ and $\displaystyle\int_{t_0}^\infty a(t)\left(\int_{\sigma(t)}^\infty b(s)\left(\int_s^\infty c(r)\left(\int_r^\infty d(\eta)\Delta\eta\right)^\gamma \Delta r\right)^\beta \Delta s\right)^\alpha \Delta t = \infty.$

Proof. Since (2) holds, every nonoscillatory solution of system (1) is of either Type (a) or Type (b) by Lemma 2.2. Assume that (x, y, z, w) is of a Type (b) solution of system (1) such that $x(t) > 0$ for $t \geq T$.

Assume (i) holds. Since the monotonicities and the signs of x and w are same for both types, (10) holds not only for Type (a) solutions but also for Type (b) solutions of system (1). Substituting (10) in the integration of the third equation from t_0 to t yields

$$-z(t_0) \geq x^{\lambda\gamma}(t_0) \int_{t_0}^{t} c(s) \left(\int_{s}^{\infty} d(r)\Delta r \right)^{\gamma} \Delta s, \quad t \geq t_0 \tag{12}$$

following from the monotonicity of x. As $t \to \infty$, the right-hand side of (12) approaches to ∞ by (i), but then this contradicts the boundedness of z. Therefore, (x, y, z, w) is of Type (a) solution.

Assume that (ii) holds. Since w is positive, from the third equation of system (1) we have that $z(t)$ is nondecreasing for $t \geq T$. Therefore, by integrating the third equation of system (1) from t to ∞ and using the inequality (10), we have

$$-z(t) \geq x^{\lambda\gamma}(t) \int_{t}^{\infty} c(s) \left(\int_{s}^{\infty} d(r)\Delta r \right)^{\gamma} \Delta s, \quad t \geq t_0, \tag{13}$$

where we use the monotonicity of x. The negativity of z and the second equation of system (1) give us that $y(t)$ is nonincreasing for $t \geq T$. Therefore, integrating the second equation from t_0 to t and plugging (13) into the resulting integration yield

$$y(t_0) \geq x^{\lambda\gamma\beta}(t_0) \int_{t_0}^{t} b(s) \left(\int_{s}^{\infty} c(r) \left(\int_{r}^{\infty} d(\tau)\Delta\tau \right)^{\gamma} \Delta r \right)^{\beta} \Delta s. \tag{14}$$

As $t \to \infty$, the right hand side of the inequality (14) approaches to ∞ by (ii). On the other hand, this contradicts the boundedness of y. Hence, we have shown that (x, y, z, w) is of Type (a) solution.

Assume that (iii) holds. By integrating the first equation of system (1) from t_0 to t and using the monotonicity of y, we get

$$x(t) \geq \int_{t_0}^{t} a(s) y^{\alpha}(s) \Delta s \tag{15}$$

$$\geq y^{\alpha}(t) \int_{t_0}^{t} a(s) \Delta s, \quad t \geq t_0. \tag{16}$$

Substituting (13) in the second equation of system (1) yields for $t \geq t_0$

$$-y^{\Delta}(t) = b(t)(-z^{\beta}(t)) \geq x^{\lambda\gamma\beta}(t) b(t) \left(\int_{t}^{\infty} c(s) \left(\int_{s}^{\infty} d(r) \Delta r \right)^{\gamma} \Delta s \right)^{\beta}.$$

Finally, substituting (16) in the above inequality gives us

$$-y^{\Delta}(t) \geq b(t) y^{\lambda\gamma\beta\alpha}(t) \left(\int_{t_0}^{t} a(s) \Delta s \right)^{\lambda\gamma\beta} \left(\int_{t}^{\infty} c(s) \left(\int_{s}^{\infty} d(r) \Delta r \right)^{\gamma} \Delta s \right)^{\beta}.$$

Dividing both sides of the inequality above by $y^{\lambda\gamma\beta\alpha}$ and integrating both sides of the resulting inequality from t_0 to t yield

$$\int_{t_0}^{t} -\frac{y^{\Delta}(s)}{y^{\lambda\gamma\beta\alpha}(s)} \Delta s \geq \int_{t_0}^{t} b(s) \left(\int_{t_0}^{s} a(\eta) \Delta \eta \right)^{\lambda\gamma\beta} \left(\int_{s}^{\infty} c(r) \left(\int_{r}^{\infty} d(\tau) \Delta \tau \right)^{\gamma} \Delta r \right)^{\beta} \Delta s.$$

As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} -\frac{y^{\Delta}(s)}{y^{\lambda\gamma\beta\alpha}(s)} \Delta s = \infty$ by (iii). However, $\displaystyle\int_{t_0}^{\infty} -\frac{y^{\Delta}(s)}{y^{\lambda\gamma\beta\alpha}(s)} \Delta s < \infty$ by Lemma 2.1 (i) so this gives a contradiction and completes the proof. Therefore, (x, y, z, w) is of Type (a) solution.

Assume that (iv) holds. Integrating the second equation of system (1) from $\sigma(t)$ to ∞ and the monotonicity of y yield

$$y(t) \geq y(\sigma(t)) \geq \int_{\sigma(t)}^{\infty} b(s)(-z^{\beta}(s)) \Delta s. \tag{17}$$

Substituting (13) and (17) gives

$$y(t) \geq x^{\lambda\gamma\beta}(\sigma(t)) \int_{\sigma(t)}^{\infty} b(s) \left(\int_{s}^{\infty} c(r) \left(\int_{r}^{\infty} d(\tau)\Delta\tau \right)^{\gamma} \Delta r \right)^{\beta} \Delta s, \tag{18}$$

where we use the monotonicity of x. Now after plugging (18) into the first equation system (1), dividing both sides of the resulting inequality by $x^{\lambda\gamma\beta\alpha}(\sigma(t))$ and then integrating from t_0 to t, we obtain

$$\int_{t_0}^{t} \frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(\sigma(s))}\Delta s \geq \int_{t_0}^{t} a(s) \left(\int_{\sigma(s)}^{\infty} b(r) \left(\int_{r}^{\infty} c(\tau) \left(\int_{\tau}^{\infty} d(\eta)\Delta\eta \right)^{\gamma} \Delta\tau \right)^{\beta} \Delta r \right)^{\alpha} \Delta s.$$

As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} \frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(s)}\Delta s = \infty$ by (iv). However, $\displaystyle\int_{t_0}^{\infty} \frac{x^{\Delta}(t)}{x^{\lambda\gamma\beta\alpha}(\sigma(t))}\Delta t < \infty$ by Lemma 2.1 (ii). So this gives a contradiction and shows that (x, y, z, w) has to be of Type (a) solution of system (1). □

Since $\displaystyle\int_{t_0}^{\infty} d(t)\Delta t < \infty$, we have

$$\int_{t_0}^{\infty} c(t) \left(\int_{t}^{\infty} d(s)\Delta s \right) \Delta t = \int_{t_0}^{\infty} d(t) \left(\int_{t_0}^{\sigma(t)} c(s)\Delta s \right) \Delta t,$$

see [2]. Therefore, in the special case of $\gamma = 1$ in part (i) of Theorem 3.1, we get the following nonoscillation criteria.

Remark 3.2. If $\displaystyle\int_{t_0}^{\infty} d(t) \left(\int_{t_0}^{\sigma(t)} c(s)\Delta s \right) \Delta t = \infty$, then every nonoscillatory solution of system (1) is of Type (a).

Finding an integral condition for Type (a) solutions when $\lambda\gamma\beta\alpha = 1$ is still open for discussion. Nevertheless, we have the following corollary.

Corollary 3.1. Every nonoscillatory solution of system (1) is of Type (a) if $\lambda\gamma\beta\alpha = 1$ and

$$\limsup_{t\to\infty} \left(\int_{\sigma(t)}^{\infty} b(s) \left(\int_{s}^{\infty} c(r) \left(\int_{r}^{\infty} d(\eta)\Delta\eta \right)^{\gamma} \Delta r \right)^{\beta} \Delta s \right)^{\alpha} \left(\int_{t_0}^{t} a(s)\Delta s \right) > 1. \tag{19}$$

Proof. Let $\alpha\beta\gamma\lambda = 1$. Since (2) holds, every nonoscillatory solution of system (1) is of either Type (a) or Type (b) by Lemma 2.2. Assume (19) holds and (x, y, z, w) is of a Type (b) solution of system (1) such that $x(t) > 0$ for $t \geq T$. Then (16) and (18) hold. Plugging (18) into (16) yields

$$x(t) \geq x^{\lambda\gamma\beta\alpha}(\sigma(t))\left(\int_{\sigma(t)}^{\infty} b(s)\left(\int_{s}^{\infty} c(r)\left(\int_{r}^{\infty} d(\tau)\Delta\tau\right)^{\gamma}\Delta r\right)^{\beta}\Delta s\right)^{\alpha}\int_{t_0}^{t} a(s)\Delta s. \quad (20)$$

Hence, after dividing the inequality above by $x^{\lambda\gamma\beta\alpha}(\sigma(t))$ and taking the lim sup of the resulting inequality, we get

$$\limsup_{t\to\infty}\left(\int_{\sigma(t)}^{\infty} b(s)\left(\int_{s}^{\infty} c(r)\left(\int_{r}^{\infty} d(\eta)\Delta\eta\right)^{\gamma}\Delta r\right)^{\beta}\Delta s\right)^{\alpha}\left(\int_{t_0}^{t} a(s)\Delta s\right) \leq 1$$

which contradicts (19). Therefore, (x, y, z, w) is of a Type (a) solution of (1). □

Remark 3.3. Any Type (a) solution (x, y, z, w) of system (1) satisfies the following:

(i) $\lim_{t\to\infty} x(t) = \infty$;

(ii) $\lim_{t\to\infty} y(t) = \infty$.

Proof. Let (x, y, z, w) be of a Type (a) solution of system (1) such that $x(t) > 0$ for $t \geq T$. Since z is positive, from the second equation of system (1) we have that $y(t)$ is nondecreasing for $t \geq T$. Hence, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $k > 0$ such that $y(t) \geq k$ for $t \geq t_0$. Then (15) holds. This implies that

$$x(t) \geq k^{\alpha}\int_{t_0}^{t} a(s)\Delta s, \quad t \geq t_0. \quad (21)$$

As $t \to \infty$, we get $\lim_{t\to\infty} x(t) = \infty$.

Now since w is positive, from the third equation of system (1) we have that $z(t)$ is nondecreasing for $t \geq T$. Hence, there exist $t_0 \geq T$, $t_0 \in \mathbb{T}$ and $k > 0$ such that $z(t) \geq k$ for $t \geq t_0$. Integrating the second equation from t_0 to t and using this inequality give us

$$y(t) \geq \int_{t_0}^{t} b(s) z^{\beta}(s) \Delta s \tag{22}$$

$$\geq k^{\beta} \int_{t_0}^{t} b(s) \Delta s, \quad t \geq t_0. \tag{23}$$

As $t \to \infty$, we have $\lim_{t\to\infty} y(t) = \infty$. $\square$

Let us consider the following example to illustrate Theorem 3.1.

Example 3.4. Let $\mathbb{T} = \mathbb{Z}$ and $t_0 = 1$. Consider the system

$$\begin{cases} \Delta x_n = \dfrac{19.3^n}{2^{n+3}} y_n \\ \Delta y_n = \dfrac{5.3^{\frac{9n}{5}}}{2^{2n+2}} z_n^{\frac{1}{5}} \\ \Delta z_n = \dfrac{2^{n+1}}{3^{1-n}} w_n \\ \Delta w_n = -\dfrac{1}{3^n} x_{n+1}^{\frac{1}{3}} \end{cases} . \tag{24}$$

Then $\int_1^{\infty} a(t)\Delta t = \lim_{T\to\infty} \sum_{n=1}^{T-1} \frac{19.3^n}{2^{n+3}} = \sum_{n=1}^{\infty} \frac{19.3^n}{2^{n+3}} = \frac{19}{8} \sum_{n=1}^{\infty} \left(\frac{3}{2}\right)^n = \infty$ by geometric series. Similarly, $\int_1^{\infty} b(t)\Delta t = \int_1^{\infty} c(t)\Delta t = \infty$, and $\int_1^{\infty} d(t)\Delta t < \infty$. Furthermore,

$$\begin{aligned} \int_1^{\infty} c(t)\left(\int_t^{\infty} d(s)\Delta s\right)\Delta t &= \lim_{T\to\infty} \sum_{n=1}^{T-1} c_n \left(\sum_{k=n}^{\infty} d_n\right) = \sum_{n=1}^{\infty} \frac{2^{n+1}}{3^{1-n}} \left(\sum_{k=n}^{\infty} \frac{1}{3^k}\right) \\ &= \frac{2}{3} \sum_{n=1}^{\infty} 6^n \left(\sum_{k=n}^{\infty} \frac{1}{3^k}\right) = \frac{2}{3} \sum_{n=1}^{\infty} 6^n \frac{1}{3^n} \frac{3}{2} = \sum_{n=1}^{\infty} 2^n \\ &= \infty. \end{aligned}$$

Therefore, every nonoscillatory solution of system (24) is of Type (a) by Theorem 3.1 (i). In fact, one can also show that $\left(\left(\frac{3}{2}\right)^{3n}, \left(\frac{3}{2}\right)^{2n}, 3^n, \frac{3}{2^n}\right)$ is of a Type (a) solution of (24).

4. TYPE (B) SOLUTIONS

The following property of Type (b) solutions in the discrete case is shown by Došlá and Krejčová in [6] and its proof follows from (20) immediately.

Proposition 4.1. Every solution (x, y, z, w) of Type (b) of system (1) satisfies

$$J^{\alpha}\int_{t_0}^{t} a(s)\Delta s \leq \frac{x(t)}{x^{\lambda\gamma\beta\alpha}(\sigma(t))},$$

where $t \in \mathbb{T}$ is sufficiently large and

$$J = \int_{\sigma(t)}^{\infty} b(s)\left(\int_{s}^{\infty} c(r)\left(\int_{r}^{\infty} d(\eta)\Delta\eta\right)^{\gamma}\Delta r\right)^{\beta}\Delta s.$$

Theorem 4.1. Every nonoscillatory solution of system (1) is of a Type (b) solution if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{t} a(s)\Delta s\right)^{\lambda}\Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\Delta r\right)^{\alpha}\Delta s\right)^{\lambda}\Delta t = \infty;$

(iii) $\alpha\beta\gamma\lambda < 1$ and $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda}\Delta t = \infty;$

(iv) $\alpha\beta\gamma\lambda = 1$ and $0 < \varepsilon < 1$
$$\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda(1-\varepsilon)}\Delta t = \infty;$$

(v) $\alpha\beta\gamma\lambda > 1$ and $\displaystyle\int_{t_0}^{\infty} a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(\tau)\Delta\tau\right)^{\beta}\Delta s\right)^{\alpha}\left(\int_{\sigma(t)}^{\infty} d(\eta)\Delta\eta\right)^{\gamma\beta\alpha}\Delta t = \infty.$

Proof. Since (2) holds, every nonoscillatory solution of system (1) is of either Type (a) or Type (b) by Lemma 2.2. Assume that (x, y, z, w) is a Type (a) solution of system (1) such that $x(t) > 0$ for $t \geq T$.

Assume that (i) holds. Then (21) holds. Now integrating the fourth equation of system (1) from t_0 to t and plugging (21) into the resulting integration yield for $t \geq t_0$,

$$w(t) - w(t_0) = -\int_{t_0}^{t} d(s)x^\lambda(\sigma(s))\Delta s \leq -k^\alpha \int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} a(r)\Delta r\right)^\lambda \Delta s$$

following from the monotonicity of x. Then as $t \to \infty$, $w(t) \to -\infty$ by (i). But this contradicts the boundedness of w. Therefore, (x, y, z, w) is of a Type (b) solution of system (1).

Assume that (ii) holds. After integrating the first equation from t_0 to t and using (23), we obtain

$$x^\lambda(\sigma(t)) \geq k^{\alpha\beta\lambda}\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\Delta r\right)^\alpha \Delta s\right)^\lambda, \quad t \geq t_0. \tag{25}$$

Integrating the fourth equation of system (1) from t_0 to t and plugging (25) into it, one can get

$$w(t) - w(t_0) \leq -k^{\alpha\beta\lambda}\int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} a(r)\left(\int_{t_0}^{r} b(\tau)\Delta\tau\right)^\alpha \Delta r\right)^\lambda \Delta s, \quad t \geq t_0. \tag{26}$$

As $t \to \infty$, the right hand side of (26) approaches to $-\infty$ by (ii). Therefore, $w(t) \to -\infty$. However, this contradicts the boundedness of w and completes the proof. Hence, (x, y, z, w) is of a Type (b) solution of system (1).

Assume that (iii) holds. Taking the λ power of (9) and then multiplying both sides of the inequality by $-d$ give us the right hand side of the inequality of (9) being w^Δ, as follows

$$w^\Delta(t) \leq -w^{\gamma\beta\alpha\lambda}(t)d(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\eta)\Delta\eta\right)^\beta \Delta r\right)^\alpha \Delta s\right)^\lambda.$$

Now dividing both sides of this inequality by $-w^{\gamma\beta\alpha\lambda}$ and integrating both sides of the resulting inequality from t_0 to t yield

$$\int_{t_0}^{t} -\frac{w^{\Delta}(s)}{w^{\gamma\beta\alpha\lambda}(s)}\Delta s \geq \int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} a(r)\left(\int_{t_0}^{r} b(\tau)\left(\int_{t_0}^{\tau} c(\eta)\Delta\eta\right)^{\beta}\Delta\tau\right)^{\alpha}\Delta r\right)^{\lambda}\Delta s.$$

As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{\gamma\beta\alpha\lambda}(s)}\Delta s = \infty$ by (iii). However, $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{\gamma\beta\alpha\lambda}(s)}\Delta s < \infty$ by Lemma 2.1 (i). So this gives a contradiction and hence (x, y, z, w) is of a Type (b) solution of system (1).

Assume that (iv) holds. Taking the $\lambda(1-\epsilon)$ power of both sides of (9) implies that

$$x^{\lambda(1-\epsilon)}(\sigma(t)) \geq w^{1-\epsilon}(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\eta)\Delta\eta\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda(1-\epsilon)}. \qquad (27)$$

Since x is nondecreasing, there exists $k > 0$ such that $x^{\lambda}(\sigma(t)) \geq k$ for large t. This yields

$$x^{\lambda(1-\epsilon)}(\sigma(t)) \leq \frac{x^{\lambda}(\sigma(t))}{k^{\epsilon}} \text{ for large } t.$$

Now using the above inequality together with (27) and multiplying both sides of the resulting inequality by d give us

$$-w^{\Delta}(t) \geq k^{\epsilon}w^{1-\epsilon}(t)d(t)\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} a(\eta)\Delta\eta\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda(1-\epsilon)}.$$

Dividing this inequality by $w^{1-\epsilon}$ and integrating both sides of the resulting inequality from t_0 to t yield

$$\int_{t_0}^{t} -\frac{w^{\Delta}(s)}{w^{1-\epsilon}(s)}\Delta s \geq k^{\epsilon}\int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} a(r)\left(\int_{t_0}^{r} b(\tau)\left(\int_{t_0}^{\tau} c(\eta)\Delta\eta\right)^{\beta}\Delta\tau\right)^{\alpha}\Delta r\right)^{\lambda(1-\epsilon)}\Delta s.$$

As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{1-\epsilon}(s)}\Delta s = \infty$ by (iv). However, by Lemma 2.1 (i) we obtain $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{1-\epsilon}(s)}\Delta s < \infty$, $0 < \varepsilon < 1$. This gives a contradiction and hence (x, y, z, w) is of a Type (b) solution of system (1).

Assume (v) holds. Integrating the fourth equation of system (1) from $\sigma(t)$ to ∞ and using the monotonicity of x give us

$$w(\sigma(t)) \geq x^{\lambda}(\sigma(t)) \int_{\sigma(t)}^{\infty} d(s)\Delta s. \tag{28}$$

After subtituting (22) in the first equation of system (1) and then substituting (7) in the resulting inequality, we get

$$\begin{aligned} x^{\Delta}(t) &\geq a(t)\left(\int_{t_0}^{t} b(s)z^{\beta}(s)\Delta s\right)^{\alpha} \\ &\geq a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)w^{\gamma}(r)\Delta r\right)^{\beta}\Delta s\right)^{\alpha}, \quad t \geq t_0. \end{aligned}$$

From the monotonoticity of w, this inequality becomes

$$x^{\Delta}(t) \geq w^{\gamma\beta\alpha}(\sigma(t))a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\Delta r\right)^{\beta}\Delta s\right)^{\alpha}, \quad t \geq t_0. \tag{29}$$

Now plugging (28) into (29),

$$x^{\Delta}(t) \geq x^{\lambda\gamma\beta\alpha}(\sigma(t))a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\Delta r\right)^{\beta}\Delta s\right)^{\alpha}\left(\int_{\sigma(t)}^{\infty} d(s)\Delta s\right)^{\gamma\beta\alpha}\Delta t$$

dividing both sides by $x^{\lambda\gamma\beta\alpha}(\sigma(t))$ and integrating the resulting inequality from t_0 to t yield

$$\int_{t_0}^{t} \frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(\sigma(s))}\Delta s \geq \int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\left(\int_{\sigma(s)}^{\infty} d(\eta)\Delta\eta\right)^{\gamma\beta\alpha}\Delta s.$$

As $t \to \infty$, we get $\displaystyle\int_{t_0}^{\infty} \frac{x^{\Delta}(t)}{x^{\lambda\gamma\beta\alpha}(\sigma(t))}\Delta t = \infty$ by (v). However, $\displaystyle\int_{t_0}^{\infty} \frac{x^{\Delta}(t)}{x^{\lambda\gamma\beta\alpha}(\sigma(t))}\Delta t < \infty$ by Lemma 2.1 (ii) so it contradicts. Therefore, (x, y, z, w) is of a Type (b) solution of system (1). □

From changing the order of integration in part (i) of Theorem 4.1 when $\lambda = 1$, we obtain

$$\int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} a(r)\Delta r\right)\Delta s = \int_{t_0}^{t} a(s)\left(\int_{\sigma(s)}^{t} d(r)\Delta r\right)\Delta t,$$

see [2]. Therefore, we have the following result.

Remark 4.2. If $\displaystyle\int_{t_0}^{\infty} a(s)\left(\int_{\sigma(s)}^{\infty} d(r)\Delta r\right)\Delta s = \infty$, then every nonoscillatory solution of system (1) is of Type (b).

Remark 4.3. Any Type (b) solution (x, y, z, w) of (1) satisfies $\lim_{t\to\infty} z(t) = 0$.

Proof. Let (x, y, z, w) be of a Type (b) solution of system (1) such that $x(t) > 0$ for large $t \in \mathbb{T}$. Then z is eventually negative increasing. Therefore, $\lim_{t\to\infty} z(t) = l \leq 0$. Suppose that $l < 0$, then from the monotonicity of z, we have $z(t) \leq l$ for large t. Integrating the second of system (1) from t_0 to t yields,

$$y(t) - y(t_0) \leq l^{\beta} \int_{t_0}^{t} b(s)\Delta s, \quad t \geq t_0.$$

Letting $t \to \infty$ implies $\lim_{t\to\infty} y(t) = -\infty$. But, this contradicts the positivity of y. Hence, $\lim_{t\to\infty} z(t) = 0$. □

Corollary 4.1. Every nonoscillatory solution of system (1) is of Type (b) if $\alpha\beta\gamma\lambda = 1$ and

$$\limsup_{t\to\infty}\left(\int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)\left(\int_{t}^{\infty} d(s)\Delta s\right)^{\gamma\beta\alpha} > 1. \qquad (30)$$

Proof. Since (2) holds, every nonoscillatory solution of system (1) is of either Type (a) or Type (b) by Lemma 2.2. Assume (30) holds and (x, y, z, w) is of a Type (a) solution of system (1) such that $x(t) > 0$ for $t \geq T$. Let $\alpha\beta\gamma\lambda = 1$. Then, by (5) we have

$$I\left(\int_t^\infty d(s)\Delta s\right)^{\gamma\beta\alpha} \leq 1,$$

where I is given as in (6). Therefore,

$$\limsup_{t\to\infty} I\left(\int_t^\infty d(s)\Delta s\right)^{\gamma\beta\alpha} \leq 1$$

which contradicts (30). Therefore, (x, y, z, w) is of a Type (b) solution of system (1). $\square$

Example 4.4. We consider the quantum time scale $\mathbb{T} = q^{\mathbb{N}_0} = \{q^n : n \in \mathbb{N}\}$, where $q > 1$, $q \in \mathbb{R}$ and let $t_0 = 1$, $s = q^m$, and $t = q^n$ for $m, n \in \mathbb{N}_0$ for the system

$$\begin{cases} x^\Delta(t) = t^3 y^3(t) \\ y^\Delta(t) = \frac{1}{q} t z^3(t) \\ z^\Delta(t) = \frac{1}{q} t^8 w^5(t) \\ w^\Delta(t) = -\frac{1+q}{q^3 t^4} x(tq). \end{cases} \tag{31}$$

Then we have $\displaystyle\int_1^T t^3\Delta t = \sum_{t\in[1,T)_{q^{\mathbb{N}_0}}} t^3 t(q-1) = (q-1)\sum_{t\in[1,T)_{q^{\mathbb{N}_0}}} t^4$, and so $\displaystyle\int_1^\infty a(t)\Delta t = (q-1)\sum_{n=0}^\infty (q^4)^n = \infty$. It can be shown similary that $\displaystyle\int_1^\infty b(t)\Delta t = \int_1^\infty c(t)\Delta t = \infty$. Also, $\displaystyle\int_1^T \frac{1+q}{q^3 t^4}\Delta t = \frac{(q^2-1)}{q^3}\sum_{t\in[1,T)_{q^{\mathbb{N}_0}}} \frac{1}{t^3}$ implies $\displaystyle\int_1^\infty d(t)\Delta t = \frac{(q^2-1)}{q^3}\sum_{n=0}^\infty \frac{1}{(q^3)^n} < \infty$.

Besides,

$$\int_1^T \frac{1+q}{q^3t^4}\left(\int_1^t s^3\Delta s\right)\Delta t = \sum_{t\in[1,T)_{q^{\mathbb{N}_0}}} \frac{1+q}{q^3t^4}\left(\sum_{s\in[1,t)_{q^{\mathbb{N}_0}}} s^4(q-1)\right)(q-1)t$$
$$= \frac{(1-q)}{(1+q^2)q^3}\sum_{t\in[1,T)_{q^{\mathbb{N}_0}}} \frac{1}{t^3}\left(1-t^4\right)$$

and so

$$\int_1^\infty d(t)\left(\int_1^t a(s)\Delta s\right)\Delta t = \frac{(1-q)}{(1+q^2)q^3}\sum_{n=0}^{\infty}\left(\frac{1}{(q^3)^n}-q^n\right) = \infty$$

by geometric series. This shows that every nonoscillatory solution of system (31) is of a Type (b) by Theorem 4.1 (i). One can see that $\left(t, \frac{1}{t}, -\frac{1}{t}, \frac{1}{t^2}\right)$ is a nonoscillatory solution and hence it is of a Type (b) solution of system (31).

5. CONCLUSION

In this study, we present oscillation criteria for system (1). Condition (2) guarantees that any nonoscillatory solution (x, y, z, w) of system (1) is either of Type (a) or of Type (b), see Lemma 2.2. We show that system (1) is oscillatory when (3) holds. Then, we assume condition (4) instead of condition (3) to find oscillation criteria for system (1). In addition to condition (2), if (4) holds, Theorems 3.1 and 4.1 eliminate all Type (b) and Type (a) solutions of system (1), respectively. To achieve our goal, we use the integral conditions of the coefficient functions a, b, c and d and the product $\alpha\beta\gamma\lambda$. Furthermore, this discussion gives us the following theorem:

Theorem 5.1. If one of the conditions of Theorem 3.1 and one of the conditions of Theorem 4.1 are assumed, then system (1) is oscillatory.

We also observe that system (1) is oscillatory in the sub-linear, half-linear and super-linear cases.

Corollary 5.1. System (1) satisfies the following:

(i) Assume Theorem 3.1 (iii) and Theorem 4.1 (iii) hold, then sub-linear system (1) is oscillatory.

(ii) Assume Corollary 3.1 and Theorem 4.1 (iv) hold, then half-linear system (1) is oscillatory.

(iii) Assume Theorem 3.1 (iv) and Theorem 4.1 (v) hold, then super-linear system (1) is oscillatory.

Note that an integral condition for a Type (a) solution in the half-linear system is still to be found.

As a consequence of our proofs, it is worth to mention that by the monotonicity of the first component all the results we have gotten in this study are also valid for the advanced systems

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(k(t)), \end{cases}$$

where $k(t) \geq t$, $k \in C_{rd}\left([t_0,\infty)_{\mathbb{T}},[t_0,\infty)_{\mathbb{T}}\right)$ and $t \in \mathbb{T}$. At this point, one can consider the delay system

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(\tau(t)), \end{cases}$$

where $\tau(t) \leq t$, $\lim_{t\to\infty} \tau(t) = \infty$, and $\tau \in C_{rd}\left([t_0, \infty)_{\mathbb{T}}, [t_0, \infty)_{\mathbb{T}}\right)$. Therefore, our question is now whether or not the same results are valid for the above delay system when (2) holds.

Note that without assuming (2), there are six more types of nonoscillatory solutions of system (1). As a result of this study, we also would like to find the oscillation conditions to eliminate other types.

REFERENCES

[1] E Akın-Bohner, Z Došlá, and Bonita Lawrence. Oscillatory properties for three-dimensional dynamic systems. *Nonlinear Analysis: Theory, Methods & Applications*, 69(2):483–494, 2008.

[2] Elvan Akın-Bohner, Zuzana Došlá, and Bonita Lawrence. Almost oscillatory three-dimensional dynamical system. *Advances in Difference Equations*, 2012(1):46, 2012.

[3] Martin Bohner and Allan Peterson. *Dynamic Equations on Time Scales: An Introduction with Applications*. 2001.

[4] Martin Bohner and Allan C Peterson. *Advances in dynamic equations on time scales*. Springer, 2002.

[5] Zuzana Došlá and Jana Krejčová. Oscillation of a class of the fourth-order nonlinear difference equations. *Advances in Difference Equations*, 2012(1):99, 2012.

[6] Zuzana Došlá and Jana Krejčová. Asymptotic and oscillatory properties of the fourth-order nonlinear difference equations. *Applied Mathematics and Computation*, 249:164–173, 2014.

[7] Takasi Kusano, Manabu Naito, and Fentao Wu. On the oscillation of solutions of 4-dimensional emden-fowler differential systems (qualitative theory of functional equations and its application to mathematical science). 2001.

V. OSCILLATION AND NONOSCILLATION CRITERIA FOR FOUR DIMENSIONAL ADVANCED AND DELAY TIME-SCALE SYSTEMS

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ABSTRACT

We obtain oscillation and nonoscillation criteria for solutions to four-dimensional advanced and delay systems of first order dynamic equations on time scales. To establish oscillation criteria, we eliminate nonoscillatory solutions of the systems based on the sign of components of the solutions. Furthermore, some of our results are new in the discrete case.

Keywords: Time scales; Nonoscillation; Oscillation; Advanced and delay; Four-dimensional systems

1. INTRODUCTION

In this study, we consider the following systems on a time scale $\mathbb{T}$, i.e., arbitrary nonempty closed subset of the real numbers, see [6, 7]

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(t), \end{cases} \tag{1}$$

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(k(t)), \end{cases} \tag{2}$$

and

$$\begin{cases} x^{\Delta}(t) = a(t)y^{\alpha}(t) \\ y^{\Delta}(t) = b(t)z^{\beta}(t) \\ z^{\Delta}(t) = c(t)w^{\gamma}(t) \\ w^{\Delta}(t) = -d(t)x^{\lambda}(g(t)), \end{cases} \tag{3}$$

where $k, g \in C_{rd}\left([t_0, \infty)_{\mathbb{T}}, [t_0, \infty)_{\mathbb{T}}\right)$, $t \in [t_0, \infty)_{\mathbb{T}} := [t_0, \infty) \cap \mathbb{T}$ such that $g(t) \leq t \leq k(t)$ and $\lim_{t\to\infty} g(t) = \infty$. Here, C_{rd} is the set of rd-continuous functions. Systems (2) and (3) are so called advanced and delay systems, respectively. We also assume that the coefficient functions $a, b, c, d \in C_{rd}\left([t_0, \infty)_{\mathbb{T}}, \mathbb{R}^+\right)$, $\alpha, \beta, \gamma, \lambda$ are the ratios of odd positive integers, and $\mathbb{T}$ is unbounded. By a solution (x, y, z, w) of system (1)((2) or (3)), we mean that functions x, y, z, w are delta-differentiable, their first delta-derivatives are rd-continuous, and satisfy system (1) ((2) or (3)) for all $t \geq t_0$. We call (x, y, z, w) a *proper* solution if it is defined on $[t_0, \infty)_{\mathbb{T}}$ and $sup\{|x(s)|, |y(s)|, |z(s)|, |w(s)| : s \in [t, \infty)_{\mathbb{T}}\} > 0$ for $t \geq t_0$. A solution (x, y, z, w) of system (1) is said to be *oscillatory* if all of its components are oscillatory, i.e., neither eventually positive nor eventually negative. Otherwise, it is said to be *nonoscillatory*. Obviously, if one component of a solution is eventually of one sign, then all its components are eventually of one sign and so nonoscillatory solutions have all components nonoscillatory.

In [3], oscillation and nonoscillation criteria of system (2) where $k(t) = \sigma(t)$, $t \in \mathbb{T}$ are investigated under the following condition

$$\int_{t_0}^{\infty} a(t)\Delta t = \int_{t_0}^{\infty} b(t)\Delta t = \int_{t_0}^{\infty} c(t)\Delta t = \infty. \tag{4}$$

Assuming (4) shows that system (2) has two types of nonoscillatory solutions, namely

$$\text{Type } (a)\text{: } x > 0,\ y > 0,\ z > 0,\ w > 0 \text{ eventually,}$$
$$\text{Type } (b)\text{: } x > 0,\ y > 0,\ z < 0,\ w > 0 \text{ eventually.}$$

In other words, if (x, y, z, w) is any nonoscillatory solution of system (2) such that $x > 0$, then (4) eliminates the rest of other nonoscillatory solutions of system (2), namely

$$\text{Type } (c)\text{: } x > 0,\ y < 0,\ z > 0,\ w > 0 \text{ eventually}$$
$$\text{Type } (d)\text{: } x > 0,\ y < 0,\ z < 0,\ w > 0 \text{ eventually}$$
$$\text{Type } (e)\text{: } x > 0,\ y > 0,\ z > 0,\ w < 0 \text{ eventually}$$
$$\text{Type } (f)\text{: } x > 0,\ y < 0,\ z < 0,\ w < 0 \text{ eventually}$$
$$\text{Type } (g)\text{: } x > 0,\ y > 0,\ z < 0,\ w < 0 \text{ eventually}$$
$$\text{Type } (h)\text{: } x > 0,\ y < 0,\ z > 0,\ w < 0 \text{ eventually.}$$

In [9] and [10], Došlá and Krejčová consider a class of fourth order difference equations

$$\Delta(a_n(\Delta b_n(\Delta c_n(\Delta x_n)^{\gamma})^{\beta})^{\alpha}) + d_n x_{n+\tau}^{\lambda} = 0 \tag{5}$$

with $\tau \in \mathbb{Z}$, $\{a_n\}$, $\{b_n\}$, $\{c_n\}$ and $\{d_n\}$ are positive real sequences and present the oscillatory properties of the solutions of equation (5). The continuous analogue of (5) can be found in [12].

As a unification of the studies above with the special case of $\alpha = \beta = \gamma = \lambda = 1$, Zhang et al. [17] consider oscillatory behavior of the fourth order delay dynamic equation

$$(c(t)(b(t)(a(t)x^{\Delta}(t))^{\Delta})^{\Delta})^{\Delta} + p(t)x(\tau(t)) = 0,$$

where $\tau \in C_{rd}(\mathbb{T},\mathbb{T})$ such that $\tau(t) \leq t$ and $\tau(t) \to \infty$ as $t \to \infty$, and the fourth order advanced dynamic equation

$$(p(t)x^{\Delta^3}(t))^{\Delta} + q(t)f(x(\sigma(t))) = 0$$

is considered in Zhang et al. [18], where $p, q \in C_{rd}(\mathbb{T},\mathbb{R}^+)$ and there exists $L > 0$ constant such that $\frac{f(y)}{y} > L$ for all $y \neq 0$. Previous of this study, Agarwal et al. [1] consider oscillatory behavior of an advanced nonlinear dynamic equation

$$(p(t)(x^{\Delta^2})^{\alpha})^{\Delta^2}(t) + q(t)f(x(\sigma(t))) = 0,$$

where α is the ratio of two positive odd integers, $p, q \in C_{rd}(\mathbb{T},\mathbb{R}^+)$, and $f \in C_{rd}(\mathbb{R},\mathbb{R})$ such that $xf(x) > 0$ and $f'(x) \geq 0$ for all $x \neq 0$.

Motivated by these studies, we establish some oscillation and nonoscillation results for systems (1), (2) and (3) without assuming (4). For the entire paper, we investigate the integral conditions of the coefficient functions a, b, c and d in each subsection in order to eliminate the indicated types above.

The proof of following auxiliary lemma which plays a key role to obtain nonoscillatory criteria for systems (1)-(3) in sublinear case, that is, $\alpha\beta\gamma\lambda < 1$ follows from the chain rule on a time scale, see [4].

Lemma 1.1. Let $f \in C_{rd}(\mathbb{T},\mathbb{R}^+)$. If $0 < \eta < 1$ and $f^{\Delta} < 0$ on $\mathbb{T}$, then

$$\int_T^{\infty} -\frac{f^{\Delta}(t)}{f^{\eta}(t)}\Delta t < \infty, T \in \mathbb{T}.$$

2. ELIMINATION OF NONOSCILLATORY SOLUTIONS

Note that the condition

$$\int_{t_0}^{\infty} d(t)\Delta t = \infty \tag{6}$$

eliminates Type (a) and Type (b) nonoscillatory solutions of systems (1)-(3), see Lemma 2.3 in [3]. On the other hand, if

$$\int_{t_0}^{\infty} d(t)\Delta t < \infty, \tag{7}$$

then one can find necessary conditions in Theorem 3.1 and Theorem 4.1 in [3] to eliminate Type (b) and Type (a) nonoscillatory solutions of systems (1) and (2), respectively. The elimination criteria of these types for system (3) are stated in the next section.

In the following each subsection, we obtain nonoscillatory criteria to eliminate all the types from Type (c) to Type (h) for systems (1)-(3).

2.1. TYPE (C) SOLUTIONS

Theorem 2.1. Systems (1) and (3) have no solutions of Type (c) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} b(t)\Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^{\infty} a(t)\left(\int_{t}^{\infty} b(s)\Delta s\right)^{\alpha}\Delta t = \infty;$

(iii) $\alpha\beta\gamma\lambda < 1$ and
$$\int_{t_0}^{\infty} d(s)\left(\int_{t_0}^{s} c(r)\Delta r\right)^{\beta\alpha\lambda}\left(\int_{s}^{\infty} a(r)\left(\int_{r}^{\infty} b(\tau)\Delta\tau\right)^{\alpha}\Delta r\right)^{\lambda}\Delta s = \infty.$$

Proof. Assume that (x, y, z, w) is of a Type (c) solution of system (1). By the monotonicity of z, there exist $t_0 \in \mathbb{T}$ and $m > 0$ such that

$$z(t) \geq m, \quad t \geq t_0. \tag{8}$$

Assume (i) holds. Plugging (8) into the integration of the second equation from t_0 to t yields

$$y(t) - y(t_0) = \int_{t_0}^{t} b(s)z^{\beta}(s)\Delta s \geq m^{\beta}\int_{t_0}^{t} b(s)\Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $y(t) \to \infty$ by (i). However, this contradicts the negativity of y for large t. Hence, we have shown that system (1) has no solution of Type (c). Assume (ii) holds. Integrating the second equation of system (1) from t to ∞, we get

$$-y(t) \geq z^{\beta}(t) \int_t^{\infty} b(s)\Delta s, \quad t \geq t_0, \tag{9}$$

where we use the monotonicity of z. Now integrating the first equation from t_0 to t, plugging (9) into the resulting inequality, and (8) yield

$$\begin{aligned} x(t) - x(t_0) &\leq - \int_{t_0}^{t} a(s) \left(\int_s^{\infty} b(r) z^{\beta}(r) \Delta r \right)^{\alpha} \Delta s \\ &\leq -m^{\beta\alpha} \int_{t_0}^{t} a(s) \left(\int_s^{\infty} b(r)\Delta r \right)^{\alpha} \Delta s, \quad t \geq t_0. \end{aligned}$$

As $t \to \infty$, $x(t) \to -\infty$ by (ii). But this contradicts the positivity of x for large t. Therefore, system (1) has no solution of Type (c). Assume (iii) holds. By integrating the third equation of system (1) from t_0 to t, we have

$$z(t) \geq \int_{t_0}^{t} c(s) w^{\gamma}(s)\Delta s, \quad t \geq t_0. \tag{10}$$

Now integrating the first equation of system (1) from t to ∞ and plugging (9) into the resulting inequality give us

$$x(t) \geq \int_t^{\infty} a(s)(-y(s))^{\alpha} \Delta s \geq z^{\beta\alpha}(t) \int_t^{\infty} a(s) \left(\int_s^{\infty} b(r)\Delta r \right)^{\alpha} \Delta s$$

for $t \geq t_0$, where we use the monotonicity of z. By plugging (10) into the equality above, taking λ power of both sides of the resulting inequality, and using the monotonicity of w, we get

$$x^{\lambda}(t) \geq w^{\alpha\beta\gamma\lambda}(t) \left(\int_{t_0}^{t} c(s)\Delta s \right)^{\beta\alpha\lambda} \left(\int_t^{\infty} a(s) \left(\int_s^{\infty} b(r)\Delta r \right)^{\alpha} \Delta s \right)^{\lambda} \tag{11}$$

for $t \geq t_0$. Multiplying (11) by $-d$, dividing both sides of the resulting inequality by $w^{\alpha\beta\gamma\lambda}$, and integrating from t_0 to t yield

$$\int_{t_0}^{t} -\frac{w^{\Delta}(s)}{w^{\alpha\beta\gamma\lambda}(s)}\Delta s \geq \int_{t_0}^{t} d(s)\left(\int_{t_0}^{s} c(r)\Delta r\right)^{\beta\alpha\lambda}\left(\int_{s}^{\infty} a(r)\left(\int_{r}^{\infty} b(\tau)\Delta\tau\right)^{\alpha}\Delta r\right)^{\lambda}\Delta s.$$

As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{\alpha\beta\gamma\lambda}(s)}\Delta s = \infty$ by (iii). However, $\displaystyle\int_{t_0}^{\infty} -\frac{w^{\Delta}(s)}{w^{\alpha\beta\gamma\lambda}(s)}\Delta s < \infty$ by Lemma 1.1 and so this gives a contradiction and completes the proof for system (1). Note that the proof for system (3) can be shown similarly. □

Remark 2.2. If (i) or (ii) holds in Theorem 2.1, then system (2) has no solution of Type (c) either.

Since $\displaystyle\int_{t_0}^{\infty} b(t)\Delta t < \infty$ in Theorem 2.1 (ii), from changing the order of integration, see [5], we obtain the following nonoscillation criteria.

Remark 2.3. If $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t_0}^{\sigma(t)} a(s)\Delta s\right)\Delta t = \infty$, then systems (1), (2) and (3) with $\alpha = 1$ have no solutions of Type (c).

2.2. TYPE (D) SOLUTIONS

Theorem 2.4. Systems (1) and (3) have no solutions of Type (d) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} a(t)\Delta t = \infty$;

(ii) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t}^{\infty} a(s)\Delta s\right)^{\lambda}\Delta t = \infty$;

(iii) $\displaystyle\int_{t_0}^{\infty} c(t)\left(\int_{t}^{\infty} d(s)\left(\int_{s}^{\infty} a(r)\Delta r\right)^{\lambda}\Delta s\right)^{\gamma}\Delta t = \infty$.

Proof. Assume that (x, y, z, w) is of a Type (d) solution of system (1). By the monotonicity of y, there exist $t_0 \in \mathbb{T}$ and $l < 0$ such that $y(t) \leq l$ for $t \geq t_0$. Assume (i) holds. Plugging this inequality into the integration of the first equation of system (1) from t_0 to t yields

$$x(t) - x(t_0) \leq l^{\alpha} \int_{t_0}^{t} a(s)\Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $x(t) \to -\infty$ by (i). But, this contradicts the positivity of x. Hence, system (1) has no solution of Type (d). Assume (ii) holds. Integrating the first equation from t to ∞ yields

$$-x(t) \leq l^{\alpha} \int_{t}^{\infty} a(s)\Delta s, \quad t \geq t_0. \tag{12}$$

Now integrating the fourth equation from t_0 to t and substituting (12) in the resulting integration shows that

$$w(t) - w(t_0) \leq l^{\alpha\lambda} \int_{t_0}^{t} d(s) \left(\int_{s}^{\infty} a(r)\Delta r \right)^{\lambda} \Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $w(t) \to -\infty$ by (ii). But, this contradicts the positivity of w. Hence, system (1) has no solution of Type (d). Assume (iii) holds. Substituting (12) in the integration of the fourth equation from t to ∞ yields

$$w(t) \geq -l^{\alpha\lambda} \int_{t}^{\infty} d(s) \left(\int_{s}^{\infty} a(r)\Delta r \right)^{\lambda} \Delta s, \quad t \geq t_0. \tag{13}$$

By integrating the third equation of system (1) from t_0 to t and plugging (13) into the resulting integration, we get

$$z(t) - z(t_0) \geq -l^{\alpha\lambda} \int_{t_0}^{t} c(s) \left(\int_{s}^{\infty} d(r) \left(\int_{r}^{\infty} a(\tau)\Delta \tau \right)^{\lambda} \Delta r \right)^{\gamma} \Delta s$$

for $t \geq t_0$. As $t \to \infty$, $z(t) \to \infty$ by (iii). But, this contradicts the negativity of z. Therefore, system (1) has no solution of Type (d). When (i) holds, the proof for system (3) can be done similarly. The monotonicity of x is used in the proof of system (3) for (ii) and (iii). $\square$

Since $\int_{t_0}^{\infty} a(t)\Delta t < \infty$ in Theorem 2.4 (ii), from changing the order of integration, see [5], we get the following result.

Remark 2.5. If $\int_{t_0}^{\infty} a(t)\left(\int_{t_0}^{\sigma(t)} d(s)\Delta s\right)\Delta t = \infty$, then systems (1) and (3) with $\lambda = 1$ have no solutions of Type (d).

Remark 2.6. If (i) holds in Theorem 2.4, then system (2) has no solution of Type (d) either.

In the following theorem, we introduce double and triple integral conditions to eliminate Type (d) solutions for system (2).

Theorem 2.7. System (2) has no solution of Type (d) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{k(t)}^{\infty} a(s)\Delta s\right)^{\lambda}\Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^{\infty} c(t)\left(\int_{t}^{\infty} d(s)\left(\int_{k(s)}^{\infty} a(r)\Delta r\right)^{\lambda}\Delta s\right)^{\gamma}\Delta t = \infty.$

Proof. Assume that (x, y, z, w) is of a Type (d) solution of system (2). By the monotonicity of y, there exist $t_0 \in \mathbb{T}$ and $l < 0$ such that $y(t) \leq l$ for $t \geq t_0$. Plugging this inequality into the integration of the first equation from $k(t)$ to ∞ yields

$$-x(k(t)) \leq l^{\alpha}\int_{k(t)}^{\infty} a(s)\Delta s, \quad t \geq t_0.$$

The rest of the proofs of (i) and (ii) can be completed similarly as in the proof of Theorem 2.4 (ii) and (iii), respectively. $\square$

2.3. TYPE (E) SOLUTIONS

Theorem 2.8. Systems (1), (2) and (3) have no solutions of Type (e) if any of the following conditions holds:

(i) $\int_{t_0}^{\infty} c(t)\Delta t = \infty$;

(ii) $\int_{t_0}^{\infty} c(t)\left(\int_{t_0}^{t} d(s)\Delta s\right)^{\lambda} \Delta t = \infty$.

Proof. Assume that (x, y, z, w) is of a Type (e) solution of system (1). Assume (i) holds. By the monotonicity of w, there exist $t_0 \in \mathbb{T}$ and $l < 0$ such that

$$w(t) \leq l, \quad t \geq t_0. \tag{14}$$

Plugging (14) into the integration of the third equation from t_0 to t yields

$$z(t) - z(t_0) = \int_{t_0}^{t} c(s)w^{\gamma}(s)\Delta s \leq l^{\gamma} \int_{t_0}^{t} c(s)\Delta s, \quad t \geq t_0. \tag{15}$$

Then as $t \to \infty$, $z(t) \to -\infty$ by the assumption, but this contradicts the positivity of z. Hence, it is shown that system (1) has no solution of Type (d). Assume (ii) holds. By the monotonicity of x, there exist $t_0 \in \mathbb{T}$ and $m > 0$ such that $x(t) \geq m$ for $t \geq t_0$. Substituting this inequality in the integration of the fourth equation from t_0 to t and plugging the resulting inequality into the integration of the third equation from t_0 to t yields

$$z(t) - z(t_0) = \int_{t_0}^{t} c(s)w^{\gamma}(s)\Delta s \leq -m^{\lambda\gamma} \int_{t_0}^{t} c(s)\left(\int_{t_0}^{s} d(r)\Delta r\right)^{\gamma} \Delta s$$

for $t \geq t_0$. As $t \to \infty$, $z(t) \to -\infty$ by (ii). But, we get a contradiction with the fact that $z(t) > 0$ for large t. Therefore, system (1) has no solution of Type (e). Note that the proof for systems (2) and (3) can be done similarly. $\square$

2.4. TYPE (F) SOLUTIONS

Theorem 2.9. Systems (1) and (3) have no solutions of Type (f) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} a(t)\Delta t = \infty$;

(ii) $\displaystyle\int_{t_0}^{\infty} a(t)\left(\int_{t_0}^{t} b(s)\Delta s\right)^{\alpha} \Delta t = \infty$;

(iii) $\alpha\beta\gamma\lambda < 1$ and $\displaystyle\int_{t_0}^{\infty} a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\left(\int_{t_0}^{r} d(\tau)\Delta\tau\right)^{\gamma} \Delta r\right)^{\beta} \Delta s\right)^{\alpha} \Delta t = \infty.$

Proof. Suppose that (x, y, z, w) is of a Type (f) solution of system (1). The proof of (i) follows from the proof of Theorem 2.4 (i). Assume (ii) holds. There exist $t_0 \in \mathbb{T}$ and $l < 0$ such that

$$z(t) \leq l, \quad t \geq t_0. \tag{16}$$

Integrating the second equation of system (1) from t_0 to t, using (16), and plugging the resulting inequality into the integration of the first equation of system (1) from t_0 to t give us

$$x(t) - x(t_0) \leq l^{\beta\alpha} \int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\Delta r\right)^{\alpha} \Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $x(t) \to -\infty$ by (ii). However, we get a contradiction with the fact that $x(t) > 0$ for large t. Assume (iii) holds. Integrating the fourth equation of system (1) from t_0 to t and the monotonicity of x yield

$$w(t) \leq -x^{\lambda}(t) \int_{t_0}^{t} d(s)\Delta s, \quad t \geq t_0. \tag{17}$$

Plugging (17) into the integration of the third equation of system (1) from t_0 to t, and then plugging the resulting inequality into the integration of the second equation of system (1) from t_0 to t yield

$$y^{\alpha}(t) \leq -x^{\lambda\gamma\beta\alpha}(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\left(\int_{t_0}^{r} d(\tau)\Delta\tau\right)^{\gamma}\Delta r\right)^{\beta}\Delta s\right)^{\alpha},$$

$t \geq t_0$, where we again use the monotonicity of x. After multiplying the above inequality by a, dividing the resulting inequality by $-x^{\lambda\gamma\beta\alpha}$, and integrating from t_0 to t, we obtain

$$\int_{t_0}^{t} -\frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(s)}\Delta s \geq \int_{t_0}^{t} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\left(\int_{t_0}^{\tau} d(\eta)\Delta\eta\right)^{\gamma}\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s$$

for $t \geq t_0$. As $t \to \infty$, $\displaystyle\int_{t_0}^{\infty} -\frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(s)}\Delta s = \infty$ by (iii). However, $\displaystyle\int_{t_0}^{\infty} -\frac{x^{\Delta}(s)}{x^{\lambda\gamma\beta\alpha}(s)}\Delta s < \infty$ by Lemma 1.1. This gives a contradiction and completes the proof. Therefore, (x, y, z, w) is not of Type (f) solution of system (1). The proof for system (3) can be shown in the same way. □

By the fact that the fourth equation is not used in the proof of Theorem 2.9 (i) and (ii), we have the following result for system (2).

Remark 2.10. If (i) or (ii) holds in Theorem 2.9, then system (2) has no solution of Type (f) either.

2.5. TYPE (G) SOLUTIONS

Theorem 2.11. Systems (1) and (2) have no solutions of Type (g) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} b(t)\Delta t = \infty$;

(ii) $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t_0}^{t} c(s)\Delta s\right)^{\beta}\Delta t = \infty$;

(iii) $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t_0}^{t} c(s)\left(\int_{t_0}^{s} d(r)\Delta r\right)^{\gamma}\Delta s\right)^{\beta}\Delta t = \infty$;

(iv) $\alpha\beta\gamma\lambda < 1$ and $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t_0}^{t} c(s)\left(\int_{t_0}^{s} d(r)\left(\int_{t_0}^{r} a(\tau)\Delta\tau\right)^{\lambda}\Delta r\right)^{\gamma}\Delta s\right)^{\beta}\Delta t = \infty$.

Proof. Assume that (x, y, z, w) is of a Type (g) solution of system (1) and (i) holds. Plugging (16) into the integration of the second equation of system (1) from t_0 to t yields

$$y(t) - y(t_0) \leq l^{\gamma}\int_{t_0}^{t} b(s)\Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $y(t) \to -\infty$ by (i). But, this contradicts the positivity of y for large t. Hence, we have shown that system (1) has no solution of Type (g). Assume (ii) holds. Then, (15) holds and substituting (15) into the integration of the second equation of system (1) from t_0 to t yields

$$y(t) - y(t_0) \leq l^{\gamma\beta}\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\Delta r\right)^{\beta}\Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $y(t) \to -\infty$ by (ii). Assume (iii) holds. There exist $t_0 \in \mathbb{T}$ and $n < 0$ such that $x(t) \geq n$ for $t \geq t_0$. Plugging this inequality into the integration of the fourth equation of system (1) from t_0 to t yields

$$w(t) \leq -n^{\lambda}\int_{t_0}^{t} d(s)\Delta s, \quad t \geq t_0. \tag{18}$$

After substituting (18) into the integration of the third equation from t_0 to t and then substituting the resulting inequality into the integration of the second equation of system (1) from t_0 to t, we obtain

$$y(t) - y(t_0) \leq -n^{\lambda\gamma\beta}\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\left(\int_{t_0}^{r} d(\tau)\Delta\tau\right)^{\gamma}\Delta r\right)^{\beta}\Delta s.$$

As $t \to \infty$, $y(t) \to -\infty$ by (iii). However, we get a contradiction with the positivity of y. Therefore, system (1) has no solution of Type (g). Assume (iv) holds. The proof can be treated similarly as the proof of Theorem 2.9 (iii). First, substituting the integration of the first equation of system (1) from t_0 to t into the integration of the fourth equation of system (1) from t_0 to t, then substituting the resulting inequality into the integration of the third equation of system (1) from t_0 to t yield

$$z^{\beta}(t) \leq -y^{\alpha\lambda\gamma\beta}(t)\left(\int_{t_0}^{t} c(s)\left(\int_{t_0}^{s} d(r)\left(\int_{t_0}^{r} a(\tau)\Delta\tau\right)^{\lambda} \Delta\tau\right)^{\gamma} \Delta s\right)^{\beta},$$

where we use the monotonicity of y. Multiplying the above inequality by b, dividing the resulting inequality by $-y^{\alpha\lambda\gamma\beta}$ and integrating from t_0 to t, we get

$$\int_{t_0}^{t} -\frac{y^{\Delta}(s)}{y^{\alpha\lambda\gamma\beta}(s)}\Delta(s) \geq \int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\left(\int_{t_0}^{r} d(\tau)\left(\int_{t_0}^{\tau} a(\eta)\Delta\eta\right)^{\lambda} \Delta\tau\right)^{\gamma} \Delta r\right)^{\beta} \Delta s.$$

As $t \to \infty$, $\int_{t_0}^{\infty} -\frac{y^{\Delta}(s)}{y^{\alpha\lambda\gamma\beta}(s)}\Delta s = \infty$ by (iv). However, $\int_{t_0}^{\infty} -\frac{y^{\Delta}(s)}{y^{\alpha\lambda\gamma\beta}(s)}\Delta s < \infty$ by Lemma 1.1. This gives a contradiction and completes the proof. Therefore, (x, y, z, w) is not of Type (g) solution of system (1). The proof for system (2) can be shown similarly. □

Remark 2.12. If (i) or (ii) holds in Theorem 2.11, then system (3) has no solution of Type (g) either.

Theorem 2.13. Let $\alpha\beta\gamma\lambda < 1$. System (3) has no solution of Type (g) if

$$\int_{t_0}^{\infty} a(t)\left(\int_{t_0}^{t} b(s)\left(\int_{t_0}^{s} c(r)\left(\int_{t_0}^{g(r)} d(\tau)\Delta\tau\right)^{\gamma} \Delta r\right)^{\beta} \Delta s\right)^{\alpha} \Delta t = \infty. \tag{19}$$

Proof. Assume that (x, y, z, w) is of a Type (g) solution of system (3) and (19) hold. Integrating the first equation from t_0 to $g(t)$ and using the monotonicity of y yield

$$x(g(t)) \geq y^{\alpha}(g(t)) \int_{t_0}^{g(t)} a(s)\Delta s, \quad g(t) \geq t_0. \tag{20}$$

The rest of the proof can be completed similarly as in the proof of Theorem 2.11 (iv). Therefore, (x, y, z, w) is not of Type (g) solution of system (3). □

2.6. TYPE (H) SOLUTIONS

Theorem 2.14. Systems (1), (2) and (3) have no solutions of Type (h) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} c(t)\Delta t = \infty$;

(ii) $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t}^{\infty} c(s)\Delta s\right)^{\beta} \Delta t = \infty$.

Proof. Assume that (x, y, z, w) is of a Type (h) solution of system (1). The proof of (i) follows from Theorem 2.8 (i). Assume (ii) holds. Then substituting (14) in the integration of the third equation from t to ∞ yields

$$z(t) \geq -l^{\gamma} \int_{t}^{\infty} c(s)\Delta s. \tag{21}$$

Plugging (21) into the integration of the second equation from t_0 to t yields

$$y(t) - y(t_0) \geq -l^{\gamma\beta} \int_{t_0}^{t} b(s)\left(\int_{s}^{\infty} c(r)\Delta r\right)^{\beta} \Delta s, \quad t \geq t_0.$$

As $t \to \infty$, $y(t) \to \infty$ by (ii). But, this contradicts the boundedness of $y(t)$ for large t. Hence, (x, y, z, w) is not of Type (h) solution of system (1). Note that the proof for systems (2) and (3) can be done similarly. □

In Theorem 2.14 (ii), since $\displaystyle\int_{t_0}^{\infty} c(t)\Delta t < \infty$, we get the following nonoscillation criteria in the special case of $\beta = 1$ by changing the order of integration, see [5].

Remark 2.15. If $\displaystyle\int_{t_0}^{\infty} c(t)\left(\int_{t_0}^{\sigma(t)} b(s)\Delta s\right)\Delta t = \infty$, then systems (1), (2) and (3) with $\beta = 1$ have no solutions of Type (h).

3. OSCILLATORY SYSTEMS

In this section, we first introduce oscillation criteria for systems (1), (2) and then for system (3). We also finish this section with some open problems.

System (2) where $k(t) = \sigma(t)$, $t \in \mathbb{T}$ is considered in [3]. By the monotonicity of the first component of nonoscillatory solutions, all the results in [3] are valid for systems (1) and (2).

If (4) holds, then there are two types of nonoscillatory solutions of systems (1) and (2), namely Type (a) and Type (b). Assuming (6) is sufficient to eliminate these types. Therefore, this implies that systems (1) and (2) are oscillatory, see Lemma 2.3 in [3]. If (7) holds, then Theorems 3.1 and 4.1 in [3] eliminate Type (b) and Type (a) solutions of systems (1) and (2), respectively. In this case, if one of the conditions of Theorems 3.1 and Theorem 4.1 hold, then systems (1) and (2) are oscillatory.

If (4) does not hold, the theorems related with systems (1) and (2) in the previous section of this paper are to eliminate all nonoscillatory solutions from Type (c) to Type (h). In order to eliminate Type (a) and Type (b) solutions of systems (1) and (2), we have to assume one of the conditions of Theorems 3.1 and Theorem 4.1 in [3] or (6). From the discussions above, one can investigate oscillation criteria for systems (1) and (2).

In order to show that system (3) is oscillatory, we will make similar arguments. If (4) holds, system (3) does not have nonoscillatory solutions from Type (c) to Type (h). In addition, if (6) holds, then system (3) is oscillatory, see Lemmas 2.2 and 2.3 in [3]. If (7) holds, we need the following theorems to eliminate Type (a) and Type (b) solutions in order to show that system (3) is oscillatory. Note that these theorems follow from the proofs of Theorems 4.1 and 3.1 in [3], respectively. However, we must assume that g is nondecreasing in (ii) and (iii) of Theorem 3.2.

Theorem 3.1. System (3) has no solutions of Type (a) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{t} a(s)\Delta s\right)^{\lambda}\Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{g(t)} a(s)\left(\int_{t_0}^{s} b(r)\Delta r\right)^{\alpha}\Delta s\right)^{\lambda}\Delta t = \infty;$

(iii) $\alpha\beta\gamma\lambda < 1$ and $\displaystyle\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{g(t)} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda}\Delta t = \infty;$

(iv) $\alpha\beta\gamma\lambda = 1$ and $0 < \varepsilon < 1$
$$\int_{t_0}^{\infty} d(t)\left(\int_{t_0}^{g(t)} a(s)\left(\int_{t_0}^{s} b(r)\left(\int_{t_0}^{r} c(\tau)\Delta\tau\right)^{\beta}\Delta r\right)^{\alpha}\Delta s\right)^{\lambda(1-\varepsilon)}\Delta t = \infty.$$

Theorem 3.2. System (3) has no solutions of Type (b) if any of the following conditions holds:

(i) $\displaystyle\int_{t_0}^{\infty} c(t)\left(\int_{t}^{\infty} d(s)\Delta s\right)^{\gamma}\Delta t = \infty;$

(ii) $\displaystyle\int_{t_0}^{\infty} b(t)\left(\int_{t}^{\infty} c(r)\left(\int_{r}^{\infty} d(\tau)\Delta\tau\right)^{\gamma}\Delta r\right)^{\beta}\Delta s = \infty;$

(iii) $\alpha\beta\gamma\lambda < 1$ and
$$\int_{t_0}^{\infty} b(t)\left(\int_{t_0}^{g(t)} a(s)\Delta s\right)^{\lambda\gamma\beta}\left(\int_{t}^{\infty} c(r)\left(\int_{r}^{\infty} d(\tau)\Delta\tau\right)^{\gamma}\Delta r\right)^{\beta}\Delta t = \infty.$$

If (4) does not hold, similarly theorems related with system (3) are to eliminate all types of nonoscillatory solutions except for Type (a) and Type (b). In order to eliminate Type (a) and Type (b) nonoscillatory solutions, we have to assume one of the conditions of Theorems 3.1 and 3.2 or (6). Hence, under these assumptions, one can show that system (3) is oscillatory.

As a continuation of this study, first we would like to consider the oscillation and nonoscillation criteria of time-scale systems (1)-(3) in which the fourth dynamic equation does not have a negative sign, see [8] for the discrete case.

We also would like to consider nonoscillatory solutions of four-dimensional nonlinear neutral time-scale systems, see [11] for the discrete case.

There have been studies for the existence of nonoscillatory solutions of two and three dimensional dynamic systems, see [2, 13, 14, 15, 16]. As a future work, one can consider the following system

$$\begin{cases} x^{\Delta}(t) = a(t)f(y(t)) \\ y^{\Delta}(t) = b(t)g(z(t)) \\ z^{\Delta}(t) = c(t)h(w(t)) \\ w^{\Delta}(t) = \lambda d(t)l(x(t)), \end{cases}$$

where $\lambda = \pm 1$ in order to show the existence and nonexistence of nonoscillatory solutions.

REFERENCES

[1] Ravi P Agarwal, Elvan Akın, and Shurong Sun. Oscillation criteria for fourth order nonlinear dynamic equations. 2011.

[2] Elvan Akın and Özkan Öztürk. Limiting behaviors of nonoscillatory solutions for two-dimensional nonlinear time scale systems. *Mediterranean Journal of Mathematics*, 14(1):34, 2017.

[3] Elvan Akın and Gülşah Yeni. Oscillation criteria for four-dimensional time-scale systems. *Mediterranean Journal of Mathematics*, 15(5):200, 2018.

[4] E Akın-Bohner, Z Došlá, and Bonita Lawrence. Oscillatory properties for three-dimensional dynamic systems. *Nonlinear Analysis: Theory, Methods & Applications*, 69(2):483–494, 2008.

[5] Elvan Akın-Bohner, Zuzana Došlá, and Bonita Lawrence. Almost oscillatory three-dimensional dynamical system. *Advances in Difference Equations*, 2012(1):46, 2012.

[6] Martin Bohner and Allan Peterson. *Dynamic Equations on Time Scales: An Introduction with Applications*. 2001.

[7] Martin Bohner and Allan C Peterson. *Advances in dynamic equations on time scales*. Springer, 2002.

[8] Zuzana Došlá and Jana Krejčová. Nonoscillatory solutions of the four-dimensional difference system. *Proc. 9th Coll. QTDE*, (4):1–11, 2012.

[9] Zuzana Došlá and Jana Krejčová. Oscillation of a class of the fourth-order nonlinear difference equations. *Advances in Difference Equations*, 2012(1):99, 2012.

[10] Zuzana Došlá and Jana Krejčová. Asymptotic and oscillatory properties of the fourth-order nonlinear difference equations. *Applied Mathematics and Computation*, 249:164–173, 2014.

[11] Jana Krejčová. Nonoscillatory solutions of the four-dimensional neutral difference system. In *International Conference on Differential & Difference Equations and Applications*, pages 215–224. Springer, 2015.

[12] Takasi Kusano, Manabu Naito, and Fentao Wu. On the oscillation of solutions of 4-dimensional emden-fowler differential systems (qualitative theory of functional equations and its application to mathematical science). 2001.

[13] Özkan Öztürk. On the existence of nonoscillatory solutions of three-dimensional time scale systems. *Journal of Fixed Point Theory and Applications*, 19(4):2617–2628, 2017.

[14] Özkan Öztürk and Elvan Akın. Nonoscillation criteria for two-dimensional time-scale systems. *Nonautonomous Dynamical Systems*, 3(1):1–13, 2016.

[15] Özkan Öztürk and Elvan Akın. On nonoscillatory solutions of two dimensional nonlinear delay dynamical systems. *Opuscula Mathematica*, 36(5), 2016.

[16] Mahmut Reyhanoglu. *Dynamical Systems: Analytical and Computational Techniques*. BoD–Books on Demand, 2017.

[17] ChengHui Zhang, Ravi P Agarwal, Martin Bohner, and TongXing Li. Oscillation of fourth-order delay dynamic equations. *Science China Mathematics*, 58(1):143–160, 2015.

[18] Chenghui Zhang, Tongxing Li, Ravi P Agarwal, and Martin Bohner. Oscillation results for fourth-order nonlinear dynamic equations. *Applied Mathematics Letters*, 25(12):2058–2065, 2012.

SECTION

2. CONCLUSION AND FUTURE WORK

One of the main purposes of this dissertation is to provide a novel approach to epidemic models. We propose some epidemic models on time scales and introduce some new discrete models to the literature.

In the first paper, we introduce a three dimensional linear model of drug therapy for HIV-1 decline on time scales. Apart from the existing continuous model, we obtain different discrete models of the HIV-1 dynamics. This helps us calculate the total concentration of plasma virus as a function of time for each model. Fitting our models to the data from a clinical trial, we conclude that discrete models result in the best fit. It would be interesting to find out not only other discrete models, which we have not considered in this paper, but also other data that validate our results better. In these models, the patients were given protease inhibitor monotherapy and the efficacy of the protease inhibitor is assumed perfect. We also study the model in presence of imperfect protease inhibitor and reverse transcriptase (RT) inhibitor combination therapy on time scales and find the total concentration of plasma virus as a function of time for this model as well. Moreover, we consider the imperfect model on the set of integers and we show that the trivial solution is asymptotically stable. Stability of trivial solution on time scales is left as an open problem. In our study, we have assumed that our systems are in quasi-steady state before drug treatment and hence, the concentration of $CD4^+$ T cells is assumed to be constant. On the other hand, T cells can be described by either a linear function or an exponential function. This is left as an open problem. In particular, if a mathematical model of HIV-1 dynamics is not considered in quasi-steady state, the model turns out to be nonlinear. Besides, since the selective depletion of $CD4^+$ T cells is one of the consequences of infection by HIV-1, it would be also interesting to study the dynamics of HIV-1 infection of $CD4^+$ T cells on time scales.

Since our results in the first paper indicate the importance of discrete modeling of HIV-1 in data analysis, they motivate us to consider other epidemic models on time scales. In the second paper, we introduce SIS (Susceptible-Infected-Susceptible) and SIR (Susceptible-Infected-Recovered) models with nonlinear incidence rate as two dimensional systems of first order dynamic equations. Because there might be factors affecting the population dynamics in time, we present these models with time dependent coefficients, which is more accurate from the biological perspective. To derive the explicit solution for each model, we use the Bernoulli equation on time scales. Although we analyze the long term behavior of susceptibles and infectives theoretically and demostrate our results on different time scales, it would be interesting to have a data set to verify these results with.

It is worth mentioning that formulating epidemic models to derive explicit solutions on time scales is challenging. Motivated by the SIR model in the second paper, we study SIR models with nonlinear incidence rate and time independent coefficients as three dimensional systems of first order difference equations, one of which is an advanced model, in the third paper. We determine the stability of disease-free and endemic equilibria depending on the reproduction number $\mathscr{R}_0$. We show the local stability of equilibria of the first system by the linearization method, yet the global stability is left as an open problem. On the other hand, we successfully show the global stability of the endemic equilibrium of the second system by constructing a suitable Lyapunov function. We would like to fit all these models to H1N1 swine flu data.

The technique we use in these papers could be expanded to other discrete epidemic and disease outbreak models such as SIRS (Susceptible-Infected-Recovered-Susceptible), SPIR (Susceptible-Potential-Infected-Recovered), SEIR (Susceptible-Exposed-Infected- Recovered), and SEIRS (Susceptible-Exposed-Infected-Recovered-Susceptible).

Throughout the first three papers, we are mainly interested in the applications of positive solutions of dynamical systems. In the fourth and fifth papers, we investigate four dimensional systems of first order dynamic equations, where there are not only positive solutions but also other types of nonoscillatory solutions. We show the conditions to ensure that these systems are oscillatory and nonoscillatory. Showing the existence of nonoscillatory solutions is left as an open problem.

REFERENCES

[1] 'Global health observatory (gho) data,' https://www.who.int/gho/hiv/en/, Accessed: 2019-10-21.

[2] Agarwal, R. P., Akın, E., and Sun, S., 'Oscillation criteria for fourth order nonlinear dynamic equations,' 2011.

[3] Akın, E. and Öztürk, Ö., 'Limiting behaviors of nonoscillatory solutions for two-dimensional nonlinear time scale systems,' Mediterranean Journal of Mathematics, 2017, **14**(1), p. 34.

[4] Akın, E. and Yeni, G., 'Oscillation criteria for four-dimensional time-scale systems,' Mediterranean Journal of Mathematics, 2018, **15**(5), p. 200.

[5] Akın, E. and Yeni, G., 'On exact solutions to epidemic dynamic models,' Submitted, 2019.

[6] Akın-Bohner, E. and Bohner, M., 'Miscellaneous dynamic equations,' Methods and applications of analysis, 2003, **10**(1), pp. 011–030.

[7] Akın-Bohner, E., Došlá, Z., and Lawrence, B., 'Oscillatory properties for three-dimensional dynamic systems,' Nonlinear Analysis: Theory, Methods & Applications, 2008, **69**(2), pp. 483–494.

[8] Akın-Bohner, E., Došlá, Z., and Lawrence, B., 'Almost oscillatory three-dimensional dynamical system,' Advances in Difference Equations, 2012, **2012**(1), p. 46.

[9] Allen, L. J., 'Some discrete-time si, sir, and sis epidemic models,' Mathematical biosciences, 1994, **124**(1), pp. 83–105.

[10] Barrientos, P. G., Rodríguez, J. Á., and Ruiz-Herrera, A., 'Chaotic dynamics in the seasonally forced sir epidemic model,' Journal of mathematical biology, 2017, **75**(6-7), pp. 1655–1668.

[11] Bernoulli, D., 'De la mortalité causée par la petite vérole, et des avantages de l'inoculation pour la prévenir,' Mem. Acad. Roy. Set, 1760.

[12] Bohner, M., 'Some oscillation criteria for first order delay dynamic equations,' Far East J. Appl. Math, 2005, **18**(3), pp. 289–304.

[13] Bohner, M. and Peterson, A., *Dynamic Equations on Time Scales: An Introduction with Applications*, 2001.

[14] Bohner, M. and Peterson, A. C., *Advances in dynamic equations on time scales*, Springer, 2002.

[15] Bohner, M. and Streipert, S., 'The sis-model on time scales,' Pliska Stud. Math. Bulgar, 2016, **26**, pp. 11–28.

[16] Bohner, M., Streipert, S., and Torres, D. F., 'Exact solution to a dynamic sir model,' Nonlinear Analysis: Hybrid Systems, 2019, **32**, pp. 228–238.

[17] Capasso, V. and Serio, G., 'A generalization of the kermack-mckendrick deterministic epidemic model,' Mathematical Biosciences, 1978, **42**(1-2), pp. 43–61.

[18] Cooke, K. L., 'Stability analysis for a vector disease model,' The Rocky Mountain Journal of Mathematics, 1979, **9**(1), pp. 31–42.

[19] Došlá, Z. and Krejčová, J., 'Nonoscillatory solutions of the four-dimensional difference system,' Proc. 9th Coll. QTDE, 2012, (4), pp. 1–11.

[20] Došlá, Z. and Krejčová, J., 'Oscillation of a class of the fourth-order nonlinear difference equations,' Advances in Difference Equations, 2012, **2012**(1), p. 99.

[21] Došlá, Z. and Krejčová, J., 'Asymptotic and oscillatory properties of the fourth-order nonlinear difference equations,' Applied Mathematics and Computation, 2014, **249**, pp. 164–173.

[22] Elaydi, S. N., *An Introduction to Difference Equations*, 2005.

[23] Enatsu, Y., Nakata, Y., and Muroya, Y., 'Global stability for a class of discrete sir epidemic models,' Math. Biosci. Eng, 2010, **7**(2), pp. 347–361.

[24] Enatsu, Y., Nakata, Y., Muroya, Y., Izzo, G., and Vecchio, A., 'Global dynamics of difference equations for sir epidemic models with a class of nonlinear incidence rates,' Journal of Difference Equations and Applications, 2012, **18**(7), pp. 1163–1181.

[25] Heesterbeek, J. and Dietz, K., 'The concept of ro in epidemic theory,' Statistica neerlandica, 1996, **50**(1), pp. 89–110.

[26] Hethcote, H. W., 'The mathematics of infectious diseases,' SIAM review, 2000, **42**(4), pp. 599–653.

[27] Hilger, S., *Einßmakettenkalkül mit Anwendung auf Zentrumsmannigfaltigkeiten*, Ph.D. thesis, Ph. D. Thesis, Universität Würzburg in German, 1988.

[28] Jang, S. and Elaydi, S., 'Difference equations from discretization of a continuous epidemic model with immigration of infectives,' 2003.

[29] Kac, V. and Cheung, P., *Quantum calculus*, Springer Science & Business Media, 2001.

[30] Kelley, W. G. and Peterson, A. C., *Difference equations: an introduction with applications*, Academic press, 2001.

[31] Kermack, W. O. and McKendrick, A. G., 'A contribution to the mathematical theory of epidemics,' Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character, 1927, **115**(772), pp. 700–721.

[32] Krejčová, J., ‘Nonoscillatory solutions of the four-dimensional neutral difference system,’ in ‘International Conference on Differential & Difference Equations and Applications,’ Springer, 2015 pp. 215–224.

[33] Kusano, T., Naito, M., and Wu, F., ‘On the oscillation of solutions of 4-dimensional emden-fowler differential systems (qualitative theory of functional equations and its application to mathematical science),’ 2001.

[34] McCluskey, C. C., ‘Complete global stability for an sir epidemic model with delay distributed or discrete,’ Nonlinear Analysis: Real World Applications, 2010, **11**(1), pp. 55–59.

[35] McCluskey, C. C., ‘Global stability for an sir epidemic model with delay and nonlinear incidence,’ Nonlinear Analysis: Real World Applications, 2010, **11**(4), pp. 3106–3109.

[36] Nowak, M. and May, R. M., *Virus dynamics: mathematical principles of immunology and virology: mathematical principles of immunology and virology*, Oxford University Press, UK, 2000.

[37] Öztürk, Ö., ‘On the existence of nonoscillatory solutions of three-dimensional time scale systems,’ Journal of Fixed Point Theory and Applications, 2017, **19**(4), pp. 2617–2628.

[38] Öztürk, Ö. and Akın, E., ‘Nonoscillation criteria for two-dimensional time-scale systems,’ Nonautonomous Dynamical Systems, 2016, **3**(1), pp. 1–13.

[39] Öztürk, Ö. and Akın, E., ‘On nonoscillatory solutions of two dimensional nonlinear delay dynamical systems,’ Opuscula Mathematica, 2016, **36**(5).

[40] Paeng, S.-H. and Lee, J., ‘Continuous and discrete sir-models with spatial distributions,’ Journal of mathematical biology, 2017, **74**(7), pp. 1709–1727.

[41] Perelson, A. S. and Nelson, P. W., ‘Mathematical analysis of hiv-1 dynamics in vivo,’ SIAM review, 1999, **41**(1), pp. 3–44.

[42] Perelson, A. S., Neumann, A. U., Markowitz, M., Leonard, J. M., and Ho, D. D., ‘Hiv-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time,’ Science, 1996, **271**(5255), pp. 1582–1586.

[43] Reyhanoglu, M., *Dynamical Systems: Analytical and Computational Techniques*, BoD–Books on Demand, 2017.

[44] Saito, K., ‘On the stability of an sir epidemic discrete model,’ in ‘International Conference on Difference Equations and Applications,’ Springer, 2016 pp. 231–239.

[45] Shabbir, G., Khan, H., and Sadiq, M., ‘A note on exact solution of sir and sis epidemic models,’ arXiv preprint arXiv:1012.5035, 2010.

[46] Zhang, C., Agarwal, R. P., Bohner, M., and Li, T., ‘Oscillation of fourth-order delay dynamic equations,’ Science China Mathematics, 2015, **58**(1), pp. 143–160.

[47] Zhang, C., Li, T., Agarwal, R. P., and Bohner, M., 'Oscillation results for fourth-order nonlinear dynamic equations,' Applied Mathematics Letters, 2012, **25**(12), pp. 2058–2065.

VITA

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