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Research article

Analysis of a non-standard finite-difference-method for the classical target cell limited dynamical within-host HIV-model - Numerics and applications

Benjamin Wacker[1,*] **and Jan Christian Schlüter**[2,3,*]

[1] Department of Engineering and Natural Sciences, University of Applied Sciences Merseburg, Eberhard-Leibnitz-Str. 2, D-06217 Merseburg, Germany

[2] Chair of Data Science, Faculty of Management, Social Work and Construction, HAWK, Haarmannplatz 3, D-37603 Holzminden, Germany

[3] Computational Epidemiology and Public Health Research Group, Institute for Medical Epidemiology, Biometrics and Informatics, Interdisciplinary Center for Health Sciences, Martin Luther University Halle-Wittenberg, Magdeburger Str. 8, D-06112 Halle, Germany

* **Correspondence:** Email: benjamin.wacker@hs-merseburg.de (Benjamin Wacker), jan@schluetergroup.org (Jan Christian Schlüter).

Abstract: Mathematical modeling and numerical simulation are valuable tools for getting theoretical insights into dynamic processes such as, for example, within-host virus dynamics or disease transmission between individuals. In this work, we propose a new time discretization, a so-called non-standard finite-difference-method, for numerical simulation of the classical target cell limited dynamical within-host HIV-model. In our case, we use a non-local approximation of our right-hand-side function of our dynamical system. This means that this right-hand-side function is approximated by current and previous time steps of our non-equidistant time grid. In contrast to classical explicit time stepping schemes such as Runge-Kutta methods which are often applied in these simulations, the main advantages of our novel time discretization method are preservation of non-negativity, often occurring in biological or physical processes, and convergence towards the correct equilibrium point, independently of the time step size. Additionally, we prove boundedness of our time-discrete solution components which underline biological plausibility of the time-continuous model, and linear convergence towards the time-continuous problem solution. We also construct higher-order non-standard finite-difference-methods from our first-order suggested model by modifying ideas from Richardson's extrapolation. This extrapolation idea improves accuracy of our time-discrete solutions. We finally underline our theoretical findings by numerical experiments.

Keywords: Boundedness; convergence; non-negativity; non-standard finite-difference-method; numerical simulation; within-host HIV-model

1. Introduction

Differential equations, satisfying non-negativity conditions for solutions, play a key role in different areas of applied mathematics, engineering and natural sciences. In biology, different fields can be mentioned. For a general overview, we refer readers to Murray's book [1]. Ashi and Alahmadi suggested a model for the spread of brain cancer [2]. Srivastava and co-authors investigated the effect of fear on competition of two species [3]. Wacker and Schlüter described calcium-ion concentrations in different cells by differential equations [4]. Wanassi and Torres proposed a fractional-order differential equation for ethanol metabolism in the human body [5]. Another classical field where differential equations are applied is chemistry. One classical book on chemical reaction networks was written by Feinberg [6]. Non-negativity of solutions of differential equations play an important role in different settings in chemistry, see [7, 8]. Epidemiology with the classical susceptible-infected-recovered (SIR) model [9] or different generalizations by differential equations [10, 11] is another field of interest. To name a last field of application, population dynamics can be mentioned [12–14].

In this article, we propose a time-discrete formulation of the classical target cell limited dynamical within-host HIV model

$$\left.\begin{aligned} T'(t) &= r - \beta \cdot V(t) \cdot T(t) - d \cdot T(t), \\ T_i'(t) &= \beta \cdot V(t) \cdot T(t) - \delta \cdot T_i(t), \\ V'(t) &= \pi \cdot T_i(t) - c \cdot V(t), \\ T(0) &= T_0, \\ T_i(0) &= T_{i,0}, \\ V(0) &= V_0 \end{aligned}\right\} \tag{1.1}$$

by a non-standard finite-difference-method based on non-local approximation of the right-hand-side function where $T(t)$, $T_i(t)$ and $V(t)$ represent current number of target CD4+ T-cells, current amount of infected target CD4+ T-cells and current load of viral particles at the actual time point t. Here, the positive problem parameters r, β, d, δ, π and c describe constant production rate of target CD4+ T-cells, constant infection rate of target CD4+ T-cells by contact with HIV particles, constant clearance rate of target CD4+ T-cells, constant clearance rate of infected target CD4+ T-cells, constant replication rate of HIV particles and constant elimination rate of HIV particles respectively. Conclusively, T_0, $T_{i,0}$ and V_0 are non-negative initial conditions for (1.1). Regarding further information on dynamics of primary HIV infection, we refer interested readers to well-written introductory texts [15–17]. Perelson and different co-authors have also written many articles on HIV infection over the course of time [18–20]. Mathematical properties of (1.1) were mainly studied in [21].

Although our dynamical system (1.1) is a basic model on virus dynamics, it captures some important aspects of an untreated HIV-infection such as the acute phase and the asymptotic phase of such an infection [15] where asymptotical loads of CD4+ T-cells and virus particles are captured by numerical simulation and appropriate choice of parameters [22]. Recently, more sophisticated models have been proposed in order to capture even later stages of untreated HIV infection [23] by introducing further immune cells such as macrophages into the dynamical system. Even though there are more sophiscated models, introduction of appropriate time-discrete variants seem to be fewer investigated. We are going to discuss this point in a few paragraphs. Here, we shortly want to conclude our discussion on different modeling approaches by mentioning the field of fractional-order derivatives which replace typical integer-order derivatives, compare [24–26]. It can be seen from these sources that it is also of interest to examine co-infections of HIV with different other infections such as tuberculosis or hepatitis.

At this point, we want to shortly note that (1.1) is mathematically not equivalent to the classical SIR model, see e.g. Wacker and Schlüter [27],

$$\begin{aligned} S'(t) &= -\alpha \cdot S(t) \cdot I(t), \\ I'(t) &= \alpha \cdot S(t) \cdot I(t) - \beta \cdot I(t), \\ R'(t) &= \beta \cdot I(t) \end{aligned}$$

because our constant problem parameters δ and π are in general unequal. Furthermore, in contrast to the classical SIR model, population size is not conserved.

Classical explicit numerical time-stepping methods such as Runge-Kutta schemes are often applied in many branches of science [28–30]. Their traditional forms suffer from instabilities and non-preservation of important properties such as non-negativity in different situations such as epidemiology [31] or calcium-ion concentration in liver cells [32]. For these reasons, Mickens introduced his methodology of non-standard finite-difference-methods to cure these issues [33, 34]. In particular, Mickens summarized his methodology in his book [33] and also wrote an article on conservation of non-negativity in the case of discretization of differential equations [34].

Consequently, we want to construct a non-standard finite-difference method for finding approximate solutions of (1.1) and applying ideas from [35]. While those authors applied a non-standard finite-difference method to an epidemiological model, we here suggest a non-standard finite-difference method based on non-local approximations of the right-hand-side function of our dynamical system and we also use Richardson's extrapolation idea to construct higher-order numerical approximation schemes which yield higher accuracy of the time-discrete solution components. The main goal, applying this approach, is to conserve important properties such as non-negativity, boundedness or convergence towards correct equilibrium points.

Our main contributions can be summarized as follows:

- In Section 2, we suggest a new non-standard finite-difference-method for solving (1.1) numerically. A summary of its algorithm is given in Algorithm 1. Our main idea for constructing this finite-difference-method is based on a non-local approximation of the right-hand-side vectorial function of our dynamical system. This implies that we approximate this function not only by the current time point, but also by previous time points. A careful choice of these time-discrete points leads to a numerical solution scheme which conserves important properties of the time-continuous case such as non-negativity and boundedness of all solution components. This aspect seems reasonable because our mathematical model should capture properties of an untreated HIV-infection. Further, our construction yields the same equilibrium points in the time-discrete setting as in the time-continuous case.
- We describe our new non-standard finite-difference method, solely based on non-local approximations, in Section 2. In contrast to other works, we apply non-uniform meshes which means that different non-standard denominator functions in non-standard finite-difference settings, compare Mickens [33], are already included in our analysis. Hence, our results also transfer to the possibility of adaptive time-stepping strategies.
- We provide proofs of unique solvability, non-negativity, boundedness of all time-discrete solution components and convergence towards equilibria for large time step sizes of Algorithm 1 in Section

3. This underlines that our time-discrete method is capable of producing reliable results which we expect to transfer from our time-continuous model to our time-discrete variant.
- As our main technical result in Section 4, we show that our time-discrete solution components of Algorithm 1 convergence linearly towards the time-continuous solution components of (1.1).
- As our practical contribution, we stress our theoretical findings by different numerical experiments in Section 5. Furthermore, we construct higher-order non-standard finite-difference-methods based on Richardson's extrapolation [36] and we modify ideas given in [35].

2. Formulation of proposed non-standard finite-difference-method

We consider a time discretization of (1.1) on our considered time interval $[0, T]$ with final simulation time $T > 0$ where

$$t_1 = 0 < t_2 < \ldots < t_{M-1} < t_M = T,$$

represents the grid of time points t_j for all time indices $j \in \{1, 2, \ldots, M-1, M\}$. Here, f_j describe time-discrete functions

$$f : \left\{ t_j \,|\, j \in \{1, 2, \ldots, M-1, M\} \right\} \longrightarrow \mathbb{R},$$

at time points t_j for all time indices $j \in \{1, 2, \ldots, M-1, M\}$. Hence, we propose our discretization method based on non-local approximations by

$$\left.\begin{aligned} \frac{T_{j+1} - T_j}{h_j} &= r - \beta \cdot T_{j+1} \cdot V_j - d \cdot T_{j+1}, \\ \frac{T_{i,j+1} - T_{i,j}}{h_j} &= \beta \cdot T_{j+1} \cdot V_j - \delta \cdot T_{i,j+1}, \\ \frac{V_{j+1} - V_j}{h_j} &= \pi \cdot T_{i,j+1} - c \cdot V_{j+1}, \\ T_1 = T_0 \,;\; T_{i,1} &= T_{i,0} \,;\; V_1 = V_0 \end{aligned}\right\}, \tag{2.1}$$

as a time-discrete formulation of (1.1) as our non-standard finite-difference-method. $h_j := t_{j+1} - t_j$ describes a possibly non-equidistant time step size for all indices $j \in \{1, 2, \ldots, M-2, M-1\}$. We can equivalently formulate (2.1) by

$$\left.\begin{aligned} &\frac{T_{j+1}-T_j}{h_j} = r - \beta \cdot T_{j+1} \cdot V_j - d \cdot T_{j+1} \\ \iff & T_{j+1} \cdot \Big(1 + h_j \cdot \beta \cdot V_j + h_j \cdot d\Big) = T_j + h_j \cdot r \\ \iff & \boxed{T_{j+1} = \frac{T_j + h_j \cdot r}{1 + h_j \cdot \beta \cdot V_j + h_j \cdot d}}, \\ &\frac{T_{i,j+1}-T_{i,j}}{h_j} = \beta \cdot T_{j+1} \cdot V_j - \delta \cdot T_{i,j+1} \\ \iff & T_{i,j+1} \cdot \Big(1 + h_j \cdot \delta\Big) = T_{i,j} + h_j \cdot \beta \cdot T_{j+1} \cdot V_j \\ \iff & \boxed{T_{i,j+1} = \frac{T_{i,j} + h_j \cdot \beta \cdot T_{j+1} \cdot V_j}{1 + h_j \cdot \delta}}, \\ &\frac{V_{j+1}-v_j}{h_j} = \pi \cdot T_{i,j+1} - c \cdot V_{j+1} \\ \iff & V_{j+1} \cdot \Big(1 + h_j \cdot c\Big) = V_j + h_j \cdot \pi \cdot T_{i,j+1} \\ \iff & \boxed{V_{j+1} = \frac{V_j + h_j \cdot \pi \cdot T_{i,j+1}}{1 + h_j \cdot c}} \end{aligned}\right\}, \tag{2.2}$$

and obtain an explicit time-discrete solution algorithm of our time-discrete system of difference equations (1.1) for all time indices $j \in \{1, 2, \ldots, M-2, M-1\}$. By taking these explicit formulations into account, we can summarize our algorithm for our proposed non-standard finite-difference-method in Algorithm 1.

Algorithm 1 Non-standard finite-difference-method for (2.1)

Inputs
Positive problem parameters $r, \beta, d, \delta, \pi, c \in \mathbb{R}$ and time vector $(t_1, \ldots, t_M)^T \in \mathbb{R}^M$
Initialize $\mathbf{T} := \mathbf{0}, \mathbf{T_i} := \mathbf{0}, \mathbf{V} := \mathbf{0} \in \mathbb{R}^M$
Initial conditions $\mathbf{T}_1 := T_0$, $\mathbf{T}_{\mathbf{i},1} := T_{i,0}$ and $\mathbf{V}_1 := V_0$ from (1.1)
Non-Standard Finite-Difference-Method
for $j \in \{1, \ldots, M-1\}$ **do**
  Define $h_j := t_{j+1} - t_j$ as current time step size
  Compute $T_{j+1} = \dfrac{T_j + h_j \cdot r}{1 + h_j \cdot \beta \cdot V_j + h_j \cdot d}$ by (2.2)
  Compute $T_{i,j+1} = \dfrac{T_{i,j} + h_j \cdot \beta \cdot T_{j+1} \cdot V_j}{1 + h_j \cdot \delta}$ by (2.2)
  Compute $V_{j+1} = \dfrac{V_j + h_j \cdot \pi \cdot T_{i,j+1}}{1 + h_j \cdot c}$ by (2.2)
end for
Outputs
Calculated vectors $\mathbf{T}, \mathbf{T_i}, \mathbf{V} \in \mathbb{R}^M$

3. Analytical properties of Algorithm 1

Here, we prove some important properties of Algorithm 1 such as unique solvability, non-negativity, boundedness and convergence towards correct equilibria.

Lemma 1. *The following properties hold true:*

1. *Algorithm 1 possesses a unique time-discrete solution for all time points t_j for all time indices $j \in \{1, 2, \ldots, M-1, M\}$.*
2. *The unique solution of Algorithm 1 remains non-negative for all time points t_j for all time indices $j \in \{1, 2, \ldots, M-1, M\}$.*

Proof. We devide our proof into two steps:

1. This statement is a direct consequence of (2.2).
2. We can show this assertion by induction. T_1, $T_{i,1}$ and V_1 are non-negative by assumptions on initial conditions of (1.1). If we assume T_j, $T_{i,j}$ and V_j to be non-negative for a certain time index $j \in \{1, 2, \ldots, M-2, M-1\}$, we can conclude non-negativity of T_{j+1}, $T_{i,j+1}$ and V_{j+1} by mathematical induction.

This shows both assertions. □

Proving boundedness of Algorithm 1, we need the following estimate.

Lemma 2. *It holds*

$$1 - x \leq \exp(-x)$$

for all $x \in [0, \infty)$.

Proof. Define $f(x) := \exp(-x) + x - 1$. It follows

$$f(0) = 0 \text{ and } f'(x) = 1 - \exp(-x) \geq 0,$$

for all $x \in [0, \infty)$. Consequently, $\exp(-x) \geq 1 - x$ holds for all $x \in [0, \infty)$ and this proves our assertion. □

In particular, we need the previous result mainly for all $x \in [0, 1]$. Now, we are able to discuss boundedness of solutions computed by Algorithm 1.

Theorem 3. *All solution components, calculated by Algorithm 1, remain bounded for all time indices $j \in \{1, 2, \ldots, M-1, M\}$.*

Proof. We divide our proof into multiple steps:

1. We define

$$M_{j+1} := T_{j+1} + T_{i,j+1},$$

for all $j \in \{0, 1, \ldots, M-2, M-1\}$. For all $j \in \{0, 1, \ldots, M-2, M-1\}$ by (2.1), it follows

$$\begin{aligned} M_{j+1} - M_j &= \left(T_{j+1} + T_{i,j+1}\right) - \left(T_j + T_{i,j}\right) \\ &= h_j \cdot r - h_j \cdot d \cdot T_{j+1} - h_j \cdot \delta \cdot T_{i,j+1} \end{aligned}$$

$$
\begin{aligned}
&\leq h_j \cdot r - h_j \cdot \min\{d,\delta\} \cdot \left(T_{j+1} + T_{i,j+1}\right) \\
&= h_j \cdot r - h_j \cdot \min\{d,\delta\} \cdot M_{j+1}
\end{aligned}
$$

and it implies

$$
M_{j+1} \cdot \left(1 + h_j \cdot \min\{d,\delta\}\right) \leq M_j + h_j \cdot r.
$$

Hence, it holds

$$
M_{j+1} \leq \frac{M_j}{1 + h_j \cdot \min\{d,\delta\}} + \frac{h_j \cdot r}{1 + h_j \cdot \min\{d,\delta\}}, \tag{3.1}
$$

for all $j \in \{1,2,\ldots,M-2,M-1\}$.

2. By construction, we see that

$$
\begin{aligned}
M_{j+1} &\leq \frac{M_j}{1 + h_j \cdot \min\{d,\delta\}} + \frac{h_j \cdot r}{1 + h_j \cdot \min\{d,\delta\}} \\
&\leq \frac{1}{1 + h_j \cdot \min\{d,\delta\}} \cdot \left\{\frac{M_{j-1}}{1 + h_{j-1} \cdot \min\{d,\delta\}} + \frac{h_{j-1} \cdot r}{1 + h_{j-1} \cdot \min\{d,\delta\}}\right\} \\
&\quad + \frac{h_j \cdot r}{1 + h_j \cdot \min\{d,\delta\}} \\
&= \frac{M_{j-1} + h_{j-1} \cdot r}{\left(1 + h_{j-1} \cdot \min\{d,\delta\}\right) \cdot \left(1 + h_j \cdot \min\{d,\delta\}\right)} + \frac{h_j \cdot r}{1 + h_j \cdot \min\{d,\delta\}} \\
&\leq \ldots \\
&\leq M_1 \cdot \left(\prod_{k=1}^{j} \frac{1}{(1 + h_k \cdot \min\{d,\delta\})}\right) + \sum_{k=1}^{j} \frac{h_k \cdot r}{\left(\prod_{l=k}^{j} (1 + h_l \cdot \min\{d,\delta\})\right)}
\end{aligned}
$$

holds for all $j \in \{1,2,\ldots,M-2,M-1\}$. This statement can easily be proven by mathematical induction.

3. Since

$$
\begin{aligned}
\frac{1}{1 + h_k \cdot \min\{d,\delta\}} &= 1 - \frac{h_k \cdot \min\{d,\delta\}}{1 + h_k \cdot \min\{d,\delta\}}, \\
&\leq \exp\left(-\frac{h_k \cdot \min\{d,\delta\}}{1 + h_k \cdot \min\{d,\delta\}}\right), \\
&\leq \exp\left(-\frac{\Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right),
\end{aligned}
$$

is valid for all $k \in \{1,2,\ldots,M-2,M-1\}$ by setting

$$
\Delta_{\min} := \min\{h_1,h_2,\ldots,h_{M-2},h_{M-1}\} \text{ and } \Delta_{\max} := \max\{h_1,h_2,\ldots,h_{M-2},h_{M-1}\},
$$

because

$$
f: [0,\infty) \longrightarrow [0,1) \; ; \; f(x) = \frac{x}{1+x},
$$

is a strictly monotonically increasing function, we obtain the following estimate

$$
\begin{aligned}
M_{j+1} &\leq M_1 \cdot \prod_{k=1}^{j} \exp\left(-\frac{h_k \cdot \min\{d,\delta\}}{1 + h_k \cdot \min\{d,\delta\}}\right) + \sum_{k=1}^{j} h_k \cdot r \cdot \prod_{l=k}^{j} \exp\left(-\frac{h_l \cdot \min\{d,\delta\}}{1 + h_l \cdot \min\{d,\delta\}}\right) \\
&\leq M_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) + \sum_{k=1}^{j} h_k \cdot r \cdot \exp\left(-\frac{(j-k+1) \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) \\
&\leq M_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) + \sum_{k=0}^{j} \Delta_{\max} \cdot r \cdot \exp\left(-\frac{k \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) \\
&= M_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) + \Delta_{\max} \cdot r \cdot \frac{1 - \exp\left(-\frac{(j+1) \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right)}{1 - \exp\left(-\frac{\Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right)} \\
&\leq M_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right) + \Delta_{\max} \cdot r \cdot \frac{1}{1 - \exp\left(-\frac{\Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right)},
\end{aligned}
$$

and consequently, the considered sequences $\{T_k\}_{k=1}^{j}$ and $\{T_{i,k}\}_{k=1}^{j}$ remain bounded for all time indices $k \in \{1, 2, \ldots, M-1, M\}$ with $j \leq M$.

4. At first, we see that

$$
\begin{aligned}
V_{j+1} &= \frac{V_j}{\left(1 + h_j \cdot c\right)} + \frac{h_j \cdot \pi \cdot T_{i,j+1}}{\left(1 + h_j \cdot c\right)} \\
&\leq \frac{V_{j-1}}{\left(1 + h_{j-1} \cdot c\right) \cdot \left(1 + h_j \cdot c\right)} + \frac{h_{j-1} \cdot \pi \cdot T_{i,j}}{\left(1 + h_{j-1} \cdot c\right) \cdot \left(1 + h_j \cdot c\right)} + \frac{h_j \cdot \pi \cdot T_{i,j+1}}{\left(1 + h_j \cdot c\right)} \\
&\leq V_1 \cdot \prod_{k=1}^{j} \frac{1}{(1 + h_k \cdot c)} + \sum_{k=1}^{j} \frac{h_k \cdot \pi \cdot T_{i,k+1}}{\prod_{l=k}^{j} (1 + h_k \cdot c)} \\
&\leq V_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right) + \pi \cdot \Delta_{\max} \cdot \sum_{k=1}^{j} T_{i,k+1} \cdot \prod_{l=k}^{j} \exp\left(-\frac{\Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right) \\
&\leq V_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right) + \pi \cdot \Delta_{\max} \cdot \sum_{k=1}^{j} T_{i,k+1} \cdot \exp\left(-\frac{(j-k+1) \cdot \Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right) \\
&\leq V_1 \cdot \exp\left(-\frac{j \cdot \Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right) + \pi \cdot \Delta_{\max} \cdot \left(M_1 + \frac{\Delta_{\max} \cdot r}{1 - \exp\left(-\frac{\Delta_{\min} \cdot \min\{d,\delta\}}{1 + \Delta_{\min} \cdot \min\{d,\delta\}}\right)}\right) \\
&\quad \times \frac{1}{1 - \exp\left(-\frac{\Delta_{\min} \cdot c}{1 + \Delta_{\min} \cdot c}\right)},
\end{aligned}
$$

holds for all $j \in \{1, 2, \ldots, M-2, M-1\}$ by same arguments as in Step 3. Conclusively, the sequence $\{V_k\}_{k=1}^{j}$ is a bounded sequence for all $k \in \{1, 2, \ldots, j-1, j\}$ with $j \leq M$.

Hence, all time-discrete solution components remain bounded which finishes our proof. □

For large time step sizes, i.e. $h_j \to \infty$, we want to demonstrate that Algorithm 1 converges towards the correct equilibria of the time-continuous model (1.1).

Theorem 4. *We have the following statements:*

1. *Let $h_j \to \infty$, $T_{i,1} = 0$ and $V_1 = 0$ or $\beta \cdot \pi \cdot r - c \cdot d \cdot \delta \leq 0$. Then the time-discrete equilibrium point reads*
$$\left(T_h^\star, T_{i,h}^\star, V_h^\star\right) = \left(\frac{r}{d}, 0, 0\right)$$
and it is the same equilibrium point as in the time-continuous case.
2. *Let $h_j \to \infty$ and either $T_{i,1} > 0$ or $V_1 > 0$ in the case of $\beta \cdot \pi \cdot r - c \cdot d \cdot \delta > 0$. Then the time-discrete equilibrium point reads*
$$\left(T_h^\star, T_{i,h}^\star, V_h^\star\right) = \left(\frac{c \cdot \delta}{\beta \cdot \pi}, \frac{\beta \cdot \pi \cdot r - c \cdot d \cdot \delta}{\beta \cdot \delta \cdot \pi}, \frac{\beta \cdot \pi \cdot r - c \cdot d \cdot \delta}{\beta \cdot c \cdot \delta}\right),$$
and it is the same equilibrium point as in the time-continuous case.

Proof. As a preparation step, we reformulate our Algorithm 1. Consequently, we see that

$$\left.\begin{aligned}
T_{j+1} &= \frac{T_j + h_j \cdot r}{1 + h_j \cdot \beta \cdot V_j + h_j \cdot d} \\
&= \frac{\dfrac{T_j}{h_j} + r}{\dfrac{1}{h_j} + \beta \cdot V_j + d}, \\
T_{i,j+1} &= \frac{T_{i,j} + h_j \cdot \beta \cdot T_{j+1} \cdot V_j}{1 + h_j \cdot \delta} \\
&= \frac{\dfrac{T_{i,j}}{h_j} + \beta \cdot T_{j+1} \cdot V_j}{\dfrac{1}{h_j} + \delta}, \\
V_{j+1} &= \frac{V_j + h_j \cdot \pi \cdot T_{i,j+1}}{1 + h_j \cdot c} \\
&= \frac{\dfrac{V_j}{h_j} + \pi \cdot T_{i,j+1}}{\dfrac{1}{h_j} + c}
\end{aligned}\right\}, \tag{3.2}$$

hold.

1. Since both equations $T_{i,1} = 0$ and $V_1 = 0$ hold, we notice that $T_{i,j+1} = 0$ and $V_{j+1} = 0$ for all time indices $j \in \{0, 1, 2, \ldots, M-2, M-1\}$ by (3.2). Consequently, $T^\star_{i,h} = 0$ and $V^\star_h = 0$ are valid. Additionally, we observe that

$$\begin{aligned}\lim_{h_j\to\infty} T_{j+1} &= \lim_{h_j\to\infty} \frac{\frac{T_j}{h_j} + r}{\frac{1}{h_j} + \beta \cdot V_j + d} \\ &= \lim_{h_j\to\infty} \frac{\frac{T_j}{h_j} + r}{\frac{1}{h_j} + d} \\ &= \frac{r}{d}\end{aligned}$$

holds by (3.2) which proves our first statement for zero initial conditions for $T_{i,1} = 0$ and $V_1 = 0$. Our second part under the condition $\beta \cdot \pi \cdot r - c \cdot d \cdot \delta \leq 0$ is a consequence from our following second step.

2. At first, we notice that

$$V^\star_h = \frac{\pi \cdot T^\star_{i,h}}{c} \text{ or } T^\star_{i,h} = \frac{c}{\pi} \cdot V^\star_h$$

is valid by the third equation of (3.2) for $h_j \to \infty$. Secondly, we see from the second equation of (3.2) that

$$T^\star_{i,h} = \frac{\beta \cdot T^\star_h \cdot V^\star_h}{\delta}$$

and equivalently

$$\boxed{T^\star_h = \frac{\delta}{\beta} \cdot \frac{T^\star_{i,h}}{V^\star_h} = \frac{\delta}{\beta} \cdot \frac{c}{\pi} = \frac{c \cdot \delta}{\beta \cdot \pi}},$$

hold. By the first equation of (3.2) for $h_j \to \infty$, we observe that

$$T^\star_h = \frac{r}{\beta \cdot V^\star_h + d} \iff \beta \cdot V^\star_h + d = \frac{r}{T^\star_h} = \frac{\beta \cdot \pi \cdot r}{c \cdot \delta},$$

or equivalently

$$\boxed{V^\star_h = \frac{\pi \cdot r}{c \cdot \delta} - \frac{d}{\beta} = \frac{\beta \cdot \pi \cdot r - c \cdot d \cdot \delta}{\beta \cdot c \cdot \delta}},$$

is valid. Finally, it follows

$$\begin{aligned}T^\star_{i,h} &= \frac{c}{\pi} \cdot V^\star_h \\ &= \frac{c}{\pi} \cdot \left(\frac{\beta \cdot \pi \cdot r - c \cdot d \cdot \delta}{\beta \cdot c \cdot \delta}\right)\end{aligned}$$

or equivalently

$$\boxed{T^\star_{i,h} = \frac{\beta \cdot \pi \cdot r - c \cdot d \cdot \delta}{\beta \cdot \delta \cdot \pi}},$$

and this shows our second assertion.

This completes our proof. □

4. Convergence towards time-continuous solution components

To begin with, we summarize all our assumptions for linear convergence of our time-discrete solution components of (2.2) towards the time-continuous solution components of (1.1).

(A1) We consider the time interval $[0, T]$ with partition

$$t_1 = 0 < t_2 < \ldots < t_{M-1} < t_M = T;$$

(A2) Initial conditions of the time-continuous and the time-discrete problems coincide;
(A3) Time-continuous solution components $T, T_i, V : \ [0, T] \longrightarrow [0, \infty)$ should be twice continuously differentiable;
(A4) Set $\Delta_{\max} := \max_{p \in \mathbb{N}} h_p$.

We want to shortly remark that graphs of solution components seem to be sufficiently smooth, compare [18]. However, it might seem to be of interest for future work to generalize our error analysis to Carathéodory of Lebesgue-integrable functions.

Theorem 5. *Let assumptions (A1)-(A4) be fulfilled. Then the time-discrete solution converges linearly towards the time-continuous solution if* $\Delta_{\max} \to 0$.

Proof. We briefly explain our proof's plan because it is relatively technical. Let us first assume that all time-continuous solution components coincide with all time-discrete solution components at a certain time point $t_p \in [0, T]$ for an arbitrary $p \in \{1, 2, \ldots, M-2, M-1\}$. Our first step is to examine local error propagation to a time point $t_{p+1} \in [0, T]$. Secondly, we investigate error propagation in time and finally, we inspect accumulation of these errors. Let us denote time-continuous solutions, for example, by $T\left(t_p\right)$ and time-discrete solutions, for example, by T_p at the same time point t_p.

1. For analyzing local errors, we assume that

$$\left(t_p, T_p\right) = \left(t_p, T\left(t_p\right)\right) \ ; \ \left(t_p, T_{i,p}\right) = \left(t_p, T_i\left(t_p\right)\right) \ ; \ \left(t_p, V_p\right) = \left(t_p, V\left(t_p\right)\right),$$

hold for an arbitrary $p \in \{1, 2, \ldots, M-2, M-1\}$ on the time interval $\left[t_p, t_{p+1}\right]$. As we only consider one time step, we denote corresponding time-discrete solutions by $\widetilde{T_{p+1}}$, $\widetilde{T_{i,p+1}}$ and $\widetilde{V_{p+1}}$, respectively.

1.1. We notice that

$$\begin{aligned}
\widetilde{T_{p+1}} &= \frac{T_p + h_p \cdot r}{1 + h_p \cdot \beta \cdot V_p + h_p \cdot d} \\
&= T_p + \frac{h_p \cdot r - h_p \cdot \beta \cdot V_p \cdot T_p - h_p \cdot d \cdot T_p}{1 + h_p \cdot \beta \cdot V_p + h_p \cdot d} \\
&= T\left(t_p\right) + \frac{h_p \cdot \left(r - \beta \cdot V\left(t_p\right) \cdot T\left(t_p\right) - d \cdot T\left(t_p\right)\right)}{1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d},
\end{aligned}$$

holds and we obtain

$$
\begin{aligned}
&\left|T\left(t_{p+1}\right)-\widetilde{T_{p+1}}\right| \\
&=\left|T\left(t_{p+1}\right)-T\left(t_p\right)-\frac{h_p\cdot\left(r-\beta\cdot V\left(t_p\right)\cdot T\left(t_p\right)-d\cdot T\left(t_p\right)\right)}{1+h_p\cdot\beta\cdot V\left(t_p\right)+h_p\cdot d}\right| \\
&=\left|\int_{t_p}^{t_{p+1}} T'(\tau)\ \mathrm{d}\tau-h_p\cdot\frac{\left(r-\beta\cdot V\left(t_p\right)\cdot T\left(t_p\right)-d\cdot T\left(t_p\right)\right)}{1+h_p\cdot\beta\cdot V\left(t_p\right)+h_p\cdot d}\right| \\
&\leq\underbrace{\left|\int_{t_p}^{t_{p+1}} T'(\tau)\ \mathrm{d}\tau-h_p\cdot T'\left(t_p\right)\right|}_{=:I_{T,1}} \\
&\quad+\underbrace{\left|h_p\cdot T'\left(t_p\right)-h_p\cdot\frac{\left(r-\beta\cdot V\left(t_p\right)\cdot T\left(t_p\right)-d\cdot T\left(t_p\right)\right)}{1+h_p\cdot\beta\cdot V\left(t_p\right)+h_p\cdot d}\right|}_{=:II_{T,2}}.
\end{aligned}
$$

By the mean value theorem, there exists a $\xi_{T,1}\in\left(t_p,t_{p+1}\right)$ such that

$$
\left|T''\left(\xi_{T,1}\right)\right|=\left|\frac{T'(\tau)-T'\left(t_p\right)}{\tau-t_p}\right|\leq\|T''(t)\|_\infty,
$$

is valid. It follows

$$
\begin{aligned}
I_{T,1}&=\left|\int_{t_p}^{t_{p+1}} T'(\tau)\ \mathrm{d}\tau-h_p\cdot T'\left(t_p\right)\right| \\
&=\left|\int_{t_p}^{t_{p+1}}\frac{\left(T'(\tau)-T'\left(t_p\right)\right)}{\left(\tau-t_p\right)}\cdot\left(\tau-t_p\right)\ \mathrm{d}\tau\right| \\
&\leq\frac{1}{2}\cdot h_p^2\cdot\|T''(t)\|_\infty.
\end{aligned}
$$

Furthermore, we have

$$\begin{aligned}
II_{T,2} &= \left| h_p \cdot T'\left(t_p\right) - h_p \cdot \frac{\left(r - \beta \cdot V\left(t_p\right) \cdot T\left(t_p\right) - d \cdot T\left(t_p\right)\right)}{1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d} \right| \\
&= \left| h_p \cdot T'\left(t_p\right) - h_p \cdot \frac{T'\left(t_p\right)}{1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d} \right| \\
&= \left| \frac{h_p \cdot T'\left(t_p\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right) - h_p \cdot T'\left(t_p\right)}{1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d} \right| \\
&\leq h_p \cdot \left| T'\left(t_p\right) \right| \cdot \left| h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d \right| \\
&\leq h_p^2 \cdot \|T'(t)\|_\infty \cdot \left(\beta \cdot \|V(t)\|_\infty + d\right).
\end{aligned}$$

Conclusively, by setting

$$C_{\text{loc},T} := \frac{1}{2} \cdot \|T''(t)\|_\infty + \|T'(t)\|_\infty \cdot \left(\beta \cdot \|V(t)\|_\infty + d\right),$$

we obtain

$$\begin{aligned}
&\left| T\left(t_{p+1}\right) - \widetilde{T_{p+1}} \right| \\
&\leq \frac{1}{2} \cdot h_p^2 \cdot \|T''(t)\|_\infty + h_p^2 \cdot \|T'(t)\|_\infty \cdot \left(\beta \cdot \|V(t)\|_\infty + d\right) \\
&\leq C_{\text{loc},T} \cdot h_p^2,
\end{aligned}$$

and

$$\left| T\left(t_{p+1}\right) - \widetilde{T_{p+1}} \right| \leq C_{\text{loc},T} \cdot h_p^2, \tag{4.1}$$

summarized as our first desired estimate.

1.2. It holds

$$\begin{aligned}
\widetilde{T_{i,p+1}} &= \frac{T_{i,p} + h_p \cdot \beta \cdot \widetilde{T_{p+1}} \cdot V_p}{1 + h_p \cdot \delta} \\
&= \frac{T_i\left(t_p\right) + h_p \cdot \beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right)}{1 + h_p \cdot \delta} \\
&= T_i\left(t_p\right) + \frac{h_p \cdot \beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right) - h_p \cdot \delta \cdot T_i\left(t_p\right)}{1 + h_p \cdot \delta},
\end{aligned}$$

and we obtain

$$
\begin{aligned}
&\left|T_i\left(t_{p+1}\right)-\widetilde{T_{i,p+1}}\right| \\
&=\left|T_i\left(t_{p+1}\right)-T_i\left(t_p\right)-\frac{h_p\cdot\beta\cdot\widetilde{T_{p+1}}\cdot V\left(t_p\right)-h_p\cdot\delta\cdot T_i\left(t_p\right)}{1+h_p\cdot\delta}\right| \\
&=\left|\int_{t_p}^{t_{p+1}} T_i'(\tau)\,\mathrm{d}\tau-h_p\cdot\frac{\left(\beta\cdot\widetilde{T_{p+1}}\cdot V\left(t_p\right)-\delta\cdot T_i\left(t_p\right)\right)}{1+h_p\cdot\delta}\right| \\
&\leq\left|\int_{t_p}^{t_{p+1}} T_i'(\tau)\,\mathrm{d}\tau-h_p\cdot T_i'\left(t_p\right)\right| \\
&\quad+h_p\cdot\left|T_i'\left(t_p\right)-\frac{\left(\beta\cdot\widetilde{T_{p+1}}\cdot V\left(t_p\right)-\delta\cdot T_i\left(t_p\right)\right)}{1+h_p\cdot\delta}\right| \\
&=\underbrace{\left|\int_{t_p}^{t_{p+1}} T_i'(\tau)-T_i'\left(t_p\right)\,\mathrm{d}\tau\right|}_{=:I_{T_i,1}} \\
&\quad+h_p\cdot\underbrace{\left|T_i'\left(t_p\right)-\frac{\left(\beta\cdot\widetilde{T_{p+1}}\cdot V\left(t_p\right)-\delta\cdot T_i\left(t_p\right)\right)}{1+h_p\cdot\delta}\right|}_{=:II_{T_i,2}}.
\end{aligned}
$$

Again, application of the mean value theorem yields

$$
\begin{aligned}
I_{T_i,1}&=\left|\int_{t_p}^{t_{p+1}} T_i'(\tau)-T_i'\left(t_p\right)\,\mathrm{d}\tau\right| \\
&=\left|\int_{t_p}^{t_{p+1}}\frac{\left(T_i'(\tau)-T_i'\left(t_p\right)\right)}{\left(\tau-t_p\right)}\cdot\left(\tau-t_p\right)\,\mathrm{d}\tau\right| \\
&\leq\frac{1}{2}\cdot h_p^2\cdot\|T_i''(t)\|_\infty.
\end{aligned}
$$

In addition to this result, we obtain the estimate

$$
\begin{aligned}
II_{T_i,2} &= \left| T_i'\left(t_p\right) - \frac{\left(\beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right) - \delta \cdot T_i\left(t_p\right)\right)}{1 + h_p \cdot \delta} \right| \\
&= \left| \frac{\left(\beta \cdot V\left(t_p\right) \cdot T\left(t_p\right) - \delta \cdot T_i\left(t_p\right)\right) \cdot \left(1 + h_p \cdot \delta\right) - \left(\beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right) - \delta \cdot T_i\left(t_p\right)\right)}{1 + h_p \cdot \delta} \right| \\
&= \left| \frac{\left(\beta \cdot T\left(t_p\right) \cdot V\left(t_p\right) - \beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right)\right) + h_p \cdot \delta \cdot T_i'\left(t_p\right)}{1 + h_p \cdot \delta} \right| \\
&\leq \frac{\beta \cdot \|V(t)\|_\infty}{\left(1 + h_p \cdot \delta\right)} \cdot C_{\text{loc},T} \cdot h_p^2 + \frac{\delta}{\left(1 + h_p \cdot \delta\right)} \cdot \|T_i'(t)\|_\infty \cdot h_p,
\end{aligned}
$$

by (4.1). By setting

$$
C_{\text{loc},T_i} := \frac{1}{2} \cdot \|T_i''(t)\|_\infty + \delta \cdot \|T_i'(t)\|_\infty + \beta \cdot \|V(t)\|_\infty \cdot C_{\text{loc},T} \cdot h_p,
$$

we conclude

$$
\begin{aligned}
&\left| T_i\left(t_{p+1}\right) - \widetilde{T_{i,p+1}} \right| \\
&\leq \frac{1}{2} \cdot h_p^2 \cdot \|T_i''(t)\|_\infty + h_p \cdot \left(\frac{\beta \cdot \|V(t)\|_\infty}{\left(1 + h_p \cdot \delta\right)} \cdot C_{\text{loc},T} \cdot h_p^2 + \frac{\delta}{\left(1 + h_p \cdot \delta\right)} \cdot \|T_i'(t)\|_\infty \cdot h_p \right) \\
&\leq C_{\text{loc},T_i} \cdot h_p^2.
\end{aligned}
$$

Summarizing, we obtain

$$
\left| T_i\left(t_{p+1}\right) - \widetilde{T_{i,p+1}} \right| \leq C_{\text{loc},T_i} \cdot h_p^2, \tag{4.2}
$$

as our second desired local estimate.

1.3. By setting

$$
C_{\text{loc},V} := \frac{1}{2} \cdot \|V''(t)\|_\infty + \pi \cdot \|T_i'(t)\|_\infty + c \cdot \|V'(t)\|_\infty + \pi \cdot C_{\text{loc},T_i} \cdot h_p,
$$

and using similar arguments as in the two previous steps, we obtain

$$
\left| V\left(t_{p+1}\right) - \widetilde{V_{p+1}} \right| \leq C_{\text{loc},V} \cdot h_p^2 \tag{4.3}
$$

as our last desired local estimate.

1.4. Conclusively, by setting

$$
C_{\text{loc}} := \max\left\{C_{\text{loc},T}, C_{\text{loc},T_i}, C_{\text{loc},V}\right\},
$$

we see that

$$
\begin{aligned}
A_{p+1} &:= \max\left\{ \left| T\left(t_{p+1}\right) - \widetilde{T_{p+1}} \right| ; \left| T_i\left(t_{p+1}\right) - \widetilde{T_{i,p+1}} \right| ; \left| V\left(t_{p+1}\right) - \widetilde{V_{p+1}} \right| \right\} \\
&\leq C_{\text{loc}} \cdot h_p^2,
\end{aligned} \tag{4.4}
$$

holds.

2. In general, the points $\left(t_p, T_p\right)$, $\left(t_p, T_{i,p}\right)$ and $\left(t_p, V_p\right)$ do not exactly lie on the graph of the time-continuous solution. We therefore have to examine how procedural errors such as $\left|T_p - T\left(t_p\right)\right|$, $\left|T_{i,p} - T_i\left(t_p\right)\right|$ and $\left|V_p - V\left(t_p\right)\right|$ propagate to the $(p+1)$-th time step. We further define

$$C_{\max,T} := \|T(t)\|_\infty \; ; \; C_{\max,T_i} := \|T_i(t)\|_\infty \; ; \; C_{\max,V} := \|V(t)\|_\infty,$$

by boundedness of all time-continuous solution components and

$$C_{\max,T_d} := \max_{p\in\mathbb{N}} \left|T_p\right| \; ; \; C_{\max,T_{i,d}} := \max_{p\in\mathbb{N}} \left|T_{i,p}\right| \; ; \; C_{\max,V_d} := \max_{p\in\mathbb{N}} \left|V_p\right|,$$

by boundedness of all time-discrete solution components. Additionally, we need the norms

$$B_{p+1} := \max\left\{\left|T_{p+1} - \widetilde{T_{p+1}}\right| \; ; \; \left|T_{i,p+1} - \widetilde{T_{i,p+1}}\right| \; ; \; \left|V_{p+1} - \widetilde{V_{p+1}}\right|\right\},$$

for all $p \in \{0, 1, \ldots, M-1\}$ and

$$D_p := \max\left\{\left|T_p - T\left(t_p\right)\right| \; ; \; \left|T_{i,p} - T_i\left(t_p\right)\right| \; ; \; \left|V_p - V\left(t_p\right)\right|\right\},$$

for all $p \in \{1, 2, \ldots, M\}$.

2.1. It holds

$$\begin{aligned}
&\left|T_{p+1} - \widetilde{T_{p+1}}\right| \\
&= \left|\frac{T_p + h_p \cdot r}{\left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right)} - \frac{T\left(t_p\right) + h_p \cdot r}{\left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}\right| \\
&= \left|\frac{\left(T_p + h_p \cdot r\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}{\left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}\right. \\
&\quad \left. - \frac{\left(T\left(t_p\right) + h_p \cdot r\right) \cdot \left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right)}{\left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}\right| \\
&= \left|\frac{T_p \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right) - T\left(t_p\right) \cdot \left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right)}{\left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}\right. \\
&\quad \left. + \frac{h_p^2 \cdot \beta \cdot r \cdot \left(V\left(t_p\right) - V_p\right)}{\left(1 + h_p \cdot \beta \cdot V_p + h_p \cdot d\right) \cdot \left(1 + h_p \cdot \beta \cdot V\left(t_p\right) + h_p \cdot d\right)}\right|,
\end{aligned}$$

and we further get

$$
\begin{aligned}
&\left|T_{p+1}-\widetilde{T_{p+1}}\right| \\
\leq &\left|T_p - T\left(t_p\right)\right| + h_p \cdot d \cdot \left|T_p - T\left(t_p\right)\right| + h_p \cdot \beta \cdot \left|T_p \cdot V\left(t_p\right) - T\left(t_p\right) \cdot V_p\right| \\
&+ h_p^2 \cdot \beta \cdot r \cdot \left|V\left(t_p\right) - V_p\right| \\
\leq &\left|T_p - T\left(t_p\right)\right| + h_p \cdot d \cdot \left|T_p - T\left(t_p\right)\right| + h_p \cdot \beta \cdot \left|T_p \cdot V\left(t_p\right) - T\left(t_p\right) \cdot V\left(t_p\right)\right| \\
&+ h_p \cdot \beta \cdot \left|T\left(t_p\right) \cdot V\left(t_p\right) - T\left(t_p\right) \cdot V_p\right| + h_p^2 \cdot \beta \cdot r \cdot \left|V\left(t_p\right) - V_p\right| \\
\leq &\left(1 + h_p \cdot d + h_p \cdot \beta \cdot C_{\max,V}\right) \cdot \left|T_p - T\left(t_p\right)\right| \\
&+ \left(h_p \cdot \beta \cdot C_{\max,T} + h_p^2 \cdot \beta \cdot r\right) \cdot \left|V\left(t_p\right) - V_p\right| \\
\leq &\left(1 + h_p \cdot \underbrace{\left(d + \beta \cdot (C_{\max,V} + C_{\max,T}) + h_p \cdot \beta \cdot r\right)}_{=:\widetilde{C_{\mathrm{prop},T}}}\right) \cdot D_p \\
= &\left(1 + h_p \cdot \widetilde{C_{\mathrm{prop},T}}\right) \cdot D_p.
\end{aligned}
$$

2.2. Furthermore, we obtain

$$
\begin{aligned}
&\left|T_{i,p+1}-\widetilde{T_{i,p+1}}\right| \\
= &\left|\frac{T_{i,p} + h_p \cdot \beta \cdot T_{p+1} \cdot V_p}{1 + h_p \cdot \delta} - \frac{T_i\left(t_p\right) + h_p \cdot \beta \cdot \widetilde{T_{p+1}} \cdot V\left(t_p\right)}{1 + h_p \cdot \delta}\right| \\
\leq &\left|T_{i,p} - T_i\left(t_p\right)\right| + h_p \cdot \beta \cdot \left|T_{p+1} \cdot V_p - \widetilde{T_{p+1}} \cdot V\left(t_p\right)\right| \\
\leq &\left|T_{i,p} - T_i\left(t_p\right)\right| + h_p \cdot \beta \cdot \left|T_{p+1} \cdot V_p - T_{p+1} \cdot V\left(t_p\right)\right| \\
&+ h_p \cdot \beta \cdot \left|T_{p+1} \cdot V\left(t_p\right) - \widetilde{T_{p+1}} \cdot V\left(t_p\right)\right| \\
\leq &\left|T_{i,p} - T_i\left(t_p\right)\right| + h_p \cdot \beta \cdot C_{\max,T_d} \cdot \left|V_p - V\left(t_p\right)\right| + h_p \cdot \beta \cdot C_{\max,V} \cdot \left|T_{p+1} - \widetilde{T_{p+1}}\right| \\
\leq &\left(1 + h_p \cdot \beta \cdot C_{\max,T_d}\right) \cdot D_p \\
&+ h_p \cdot \beta \cdot C_{\max,V} \cdot \left(1 + h_p \cdot \underbrace{\left(d + \beta \cdot (C_{\max,V} + C_{\max,T}) + h_p \cdot \beta \cdot r\right)}_{=:\widetilde{C_{\mathrm{prop},T}}}\right) \cdot D_p \\
= &\left(1 + h_p \cdot \underbrace{\left(\beta \cdot C_{\max,T_d} + \beta \cdot C_{\max,V} + h_p \cdot \beta \cdot C_{\max,V} \cdot \widetilde{C_{\mathrm{prop},T}}\right)}_{=:\widetilde{C_{\mathrm{prop},T_i}}}\right) \cdot D_p \\
= &\left(1 + h_p \cdot \widetilde{C_{\mathrm{prop},T_i}}\right) \cdot D_p.
\end{aligned}
$$

2.3. Additionally, it follows

$$\begin{aligned}
&\left|V_{p+1} - \widetilde{V_{p+1}}\right| \\
&= \left|\frac{V_p + h_p \cdot \pi \cdot T_{i,p+1}}{1 + h_p \cdot} - \frac{V\left(t_p\right) + h_p \cdot \pi \cdot \widetilde{T_{i,p+1}}}{1 + h_p \cdot}\right| \\
&\leq \left|V_p - V\left(t_p\right)\right| + h_p \cdot \pi \cdot \left|T_{i,p+1} - \widetilde{T_{i,p+1}}\right| \\
&\leq \left|V_p - V\left(t_p\right)\right| + h_p \cdot \pi \cdot \left(1 + h_p \cdot \widetilde{C_{\text{prop},T_i}}\right) \cdot D_p \\
&\leq \left(1 + h_p \cdot \underbrace{\left(\pi + h_p \cdot \pi \cdot \widetilde{C_{\text{prop},T_i}}\right)}_{=:\widetilde{C_{\text{prop},V}}}\right) \cdot D_p \\
&= \left(1 + h_p \cdot \widetilde{C_{\text{prop},V}}\right) \cdot D_p.
\end{aligned}$$

2.4. Let us define

$$C_{\text{prop}} := \max\left\{\widetilde{C_{\text{prop},T}}\ ;\ \widetilde{C_{\text{prop},T_i}}\ ;\ \widetilde{C_{\text{prop},V}}\right\}.$$

Conclusively, we obtain

$$B_{p+1} \leq \left(1 + h_p \cdot C_{\text{prop}}\right) \cdot D_p. \tag{4.5}$$

3. Finally, we see that

$$\begin{aligned}
D_{p+1} &\leq B_{p+1} + A_{p+1} \\
&\leq \left(1 + h_p \cdot C_{\text{prop}}\right) \cdot D_p + h_p^2 \cdot C_{\text{loc}} \\
&\leq \left(1 + h_p \cdot C_{\text{prop}}\right) \cdot \left(\left(1 + h_{p-1} \cdot C_{\text{prop}}\right) \cdot D_{p-1} + h_{p-1}^2 \cdot C_{\text{loc}}\right) + h_p^2 \cdot C_{\text{loc}},
\end{aligned}$$

is valid by (4.4) and (4.5). Inductively, we can conclude that

$$D_{p+1} \leq \exp\left(C_{\text{prop}} \cdot T\right) \cdot D_1 + \exp\left(C_{\text{prop}} \cdot T\right) \cdot C_{\text{loc}} \cdot T \cdot \Delta_{\max}, \tag{4.6}$$

holds. Since our initial conditions of our time-continuous and our time-discrete model coincide, we can further simplify this result and obtain

$$D_{p+1} \leq \exp\left(C_{\text{prop}} \cdot T\right) \cdot C_{\text{loc}} \cdot T \cdot \Delta_{\max}, \tag{4.7}$$

as our estimate because of $D_1 = 0$.

This completes our proof. □

5. Numerical experiments

Here, we want to underline our theoretical findings of our previous investigations. In all numerical simulations, we use the following positive constant problem parameters and all initial conditions summarized in Table 1. Additionally, we perform our calculations on the time interval $[0, T]$ where the final time T is defined later in our examples.

Table 1. Constant problem parameters and initial conditions for (1.1) in Examples 1–4 which are taken from Table 1 of [15]

Parameter	Value	Unit
r	0.17	$\frac{\text{cells}}{\mu\text{L} \cdot \text{day}}$
β	0.00065	$\frac{\mu\text{L}}{\text{virions} \cdot \text{day}}$
d	0.01	$\frac{1}{\text{day}}$
δ	0.39	$\frac{1}{\text{day}}$
π	850	$\frac{\text{virions}}{\text{cells} \cdot \text{day}}$
c	3	$\frac{1}{\text{day}}$
T_0	10	$\frac{\text{cells}}{\mu\text{L}}$
$T_{i,0}$	0	$\frac{\text{cells}}{\mu\text{L}}$
V_0	0.000001	$\frac{\text{virious}}{\mu\text{L}}$

In our first example, we want to stress non-negativity of our proposed non-standard finite-difference-method from Algorithm 1. We demonstrate that, even for moderately equidistant time step sizes such as $h = 1$, only our numerical scheme preserves non-negativity in contrast to the explicit Eulerian time stepping method and a second-order Runge-Kutta scheme. Secondly, we demonstrate for large time step sizes that our numerical schemes converges towards the correct endemic equilibrium point. Furthermore, we underline our theoretical finding of linear convergence with regard to a fourth-order Runge-Kutta scheme. In addition to that, we numerically show higher-order convergence of constructed methods based on Richardson's extrapolation. We further demonstrate that we obtain qualitatively similar results to previous studies in HIV-dynamics and finally, we compare our non-standard finite-difference-method with classical denominator function with one method where a non-standard denominator function is applied.

5.1. Example 1: Non-negativity

Here, $T \approx 250$. In Figure 1, we can see the comparison of three different numerical discretization schemes for (1.1). We solely display the solution component $T(t)$. Clearly, we observe that, even for $h = 1$, which is an equidistant time step size, only our proposed non-standard finite-difference-method from Algorithm 1 is capable of capturing preservation of non-negativity. In case of $h = 0.1$, we notice that all schemes are able to do so, compare Figure 2. In case of $h = 0.6$, the Eulerian time-stepping method becomes unstable, while the other two method remain stable. In case of $h = 0.75$, both Runge-Kutta methods, namely the Eulerian method and the second-order Runge-Kutta scheme, produce negative values and become unstable. We do not show graphs of these solutions. It is well

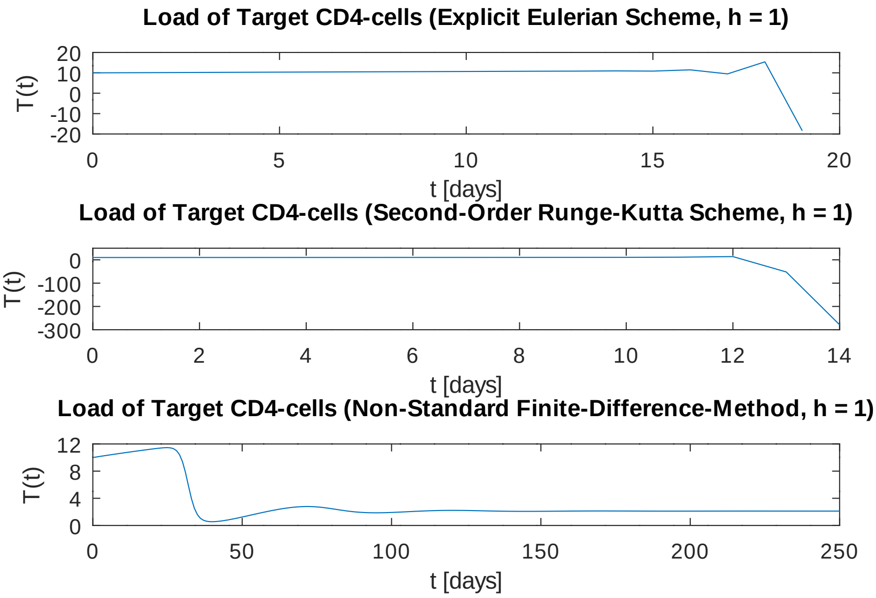

Figure 1. Numerical simulations of $T(t)$ for Explicit Eulerian, second-order Runge-Kutta and our proposed non-standard finite-difference-method in case of $h = 1$.

known that explicit Runge-Kutta time-stepping methods only remain stable for sufficiently small time step sizes. This is a clear advantages of our proposed non-standard finite-difference-method which preserves non-negativity on the time-discrete level for arbitrary positive time step sizes. However, we observe that the steep decline in target cells is located a bit differently, depending on the choice of discretization method, compare Figure 3.

5.2. *Example 2: Convergence towards endemic equilibrium*

Here, $T \approx 10000$ and $h = 100$. The endemic equilibrium point with conditions from Table 1 reads

$$T^\star \approx 2.1176 \; ; \; T_i^\star \approx 0.3816 \; ; \; V^\star \approx 108.12.$$

In Figure 4, we see that this equilibrium point is even reached for high time step sizes such as $h = 100$. The absolute differences between the solution components and the respective components of the equilibrium are depicted in Figure 5. We can clearly see that these differences vanish for large t.

5.3. *Example 3: Linear convergence towards time-continuous solution*

Here, our final simulation time reads $T = 10$ and we use a fourth-order Runge-Kutta scheme with $h = 0.0001$ for comparison reasons. We apply four different time step sizes $h \in \{0.1, 0.05, 0.025, 0.0125\}$ for our proposed non-standard finite-difference-method. Let us denote our solutions by T_{NSFDM} and T_{RK4} respectively at same time points t_j. Our error norm reads

$$\text{error} := \max_j \Big\{ \left| T_{\text{NSFDM}}\left(t_j\right) - T_{\text{RK4}}\left(t_j\right) \right| \; ; \; \left| T_{i,\text{NSFDM}}\left(t_j\right) - T_{i,\text{RK4}}\left(t_j\right) \right| \; ; \\ \left| V_{\text{NSFDM}}\left(t_j\right) - V_{\text{RK4}}\left(t_j\right) \right| \Big\} .$$

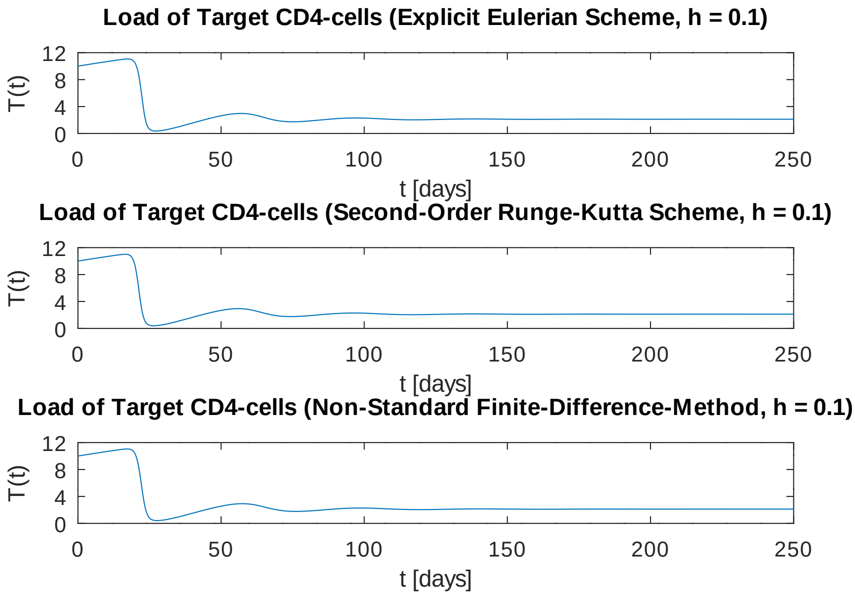

Figure 2. Numerical simulations of $T(t)$ for Explicit Eulerian, second-order Runge-Kutta and our proposed non-standard finite-difference-method in case of $h = 0.1$. where we notice that these results are qualitatively equivalent.

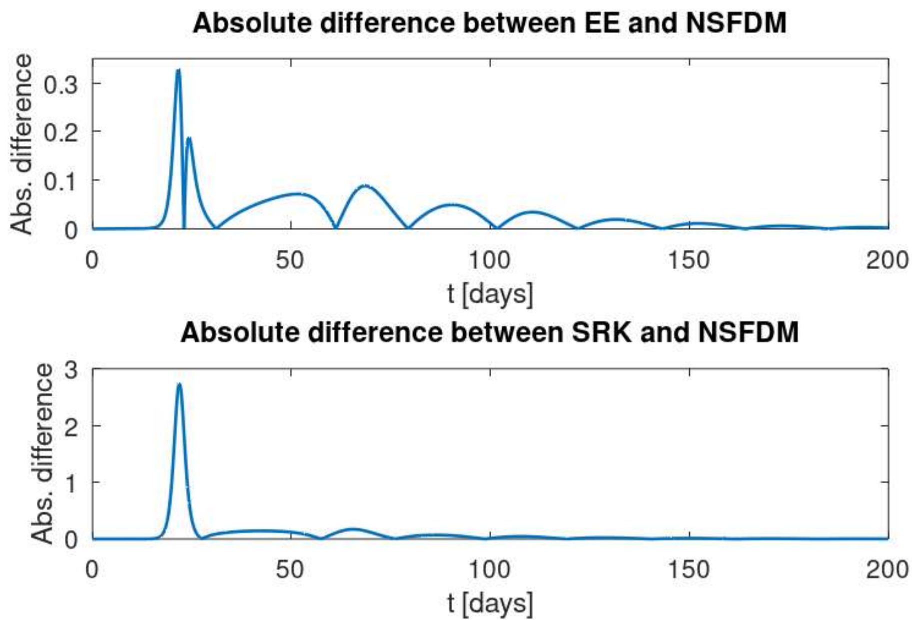

Figure 3. Absolute differences of $T(t)$ for Explicit Eulerian (EE), second-order Runge-Kutta (SRK) and our proposed non-standard finite-difference-method (NSFDM) in case of $h = 0.1$ where we notice that especially the steep decline in target cells is located a bit differently.

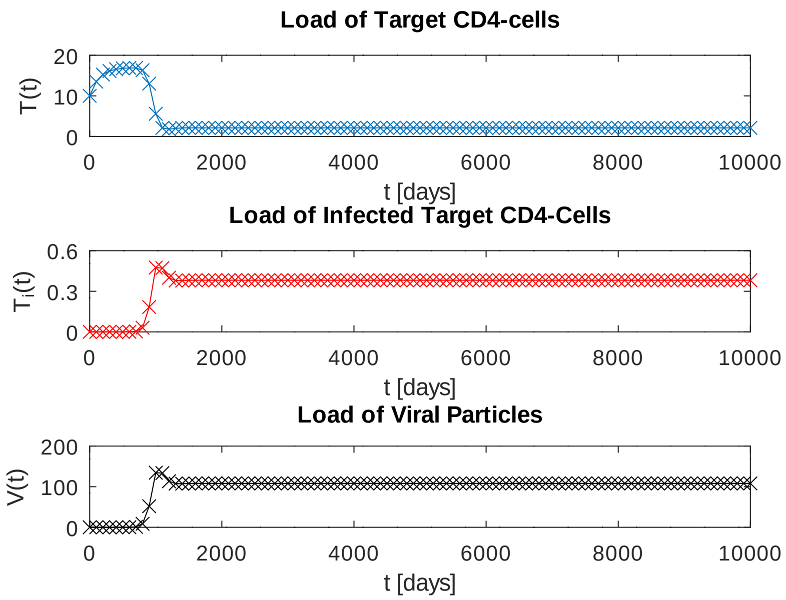

Figure 4. Numerical simulations of endemic equilibrium point for $h = 100$ by our proposed non-standard finite-difference-method.

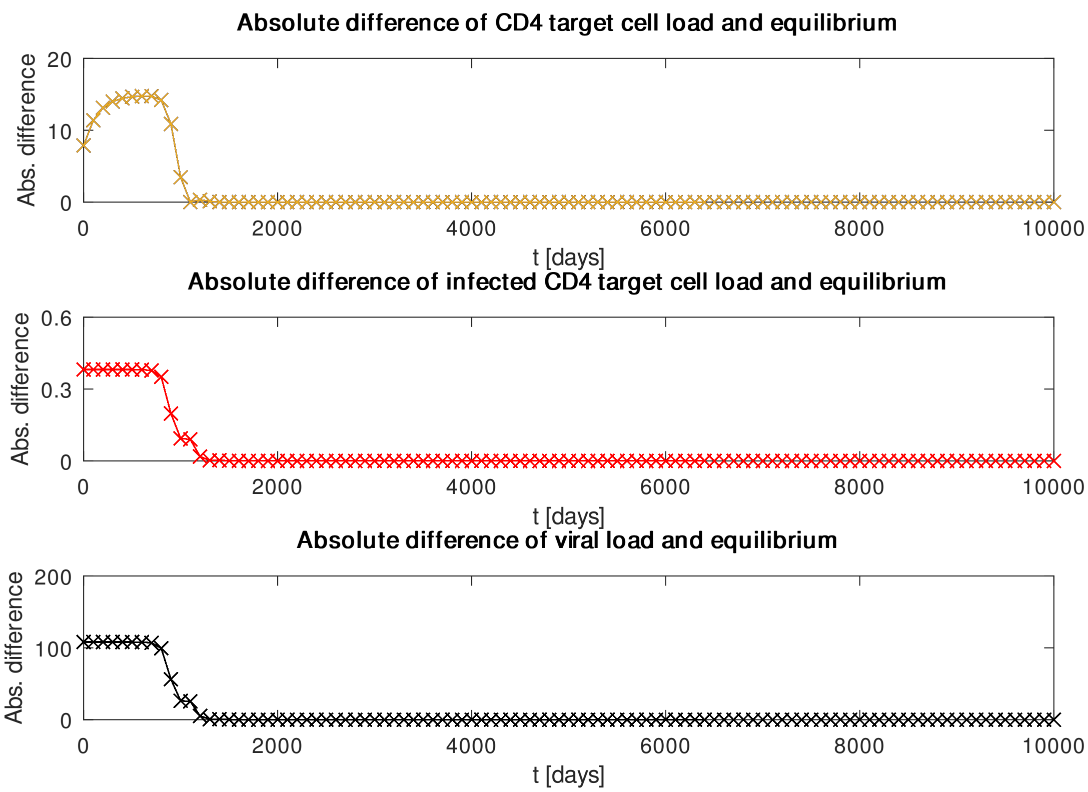

Figure 5. Absolute differences of solution components and endemic equilibrium point for $h = 100$ by our proposed non-standard finite-difference-method.

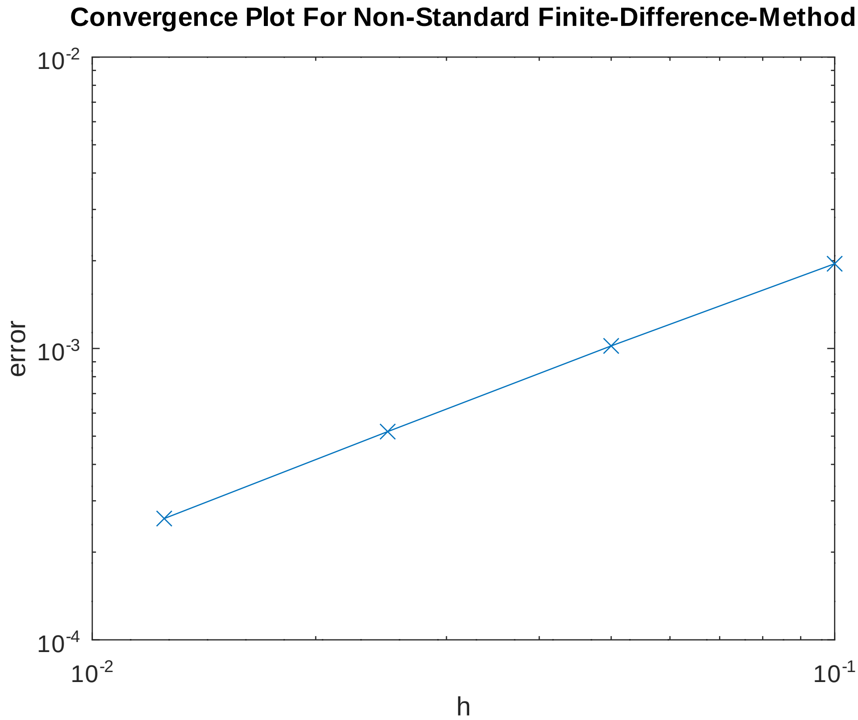

Figure 6. Numerical simulations for linear convergence of our proposed non-standard finite-difference-method towards the time-continuous solution.

In Figure 6, we can clearly observe that our proposed non-standard finite-difference-method converges linearly towards the time-continuous solution in a double-logarithmic plot, where time-continuous solution components are represented by a fine-scale fourth-order Runge-Kutta solution. The linear convergence is also stressed by our results in Table 2.

Table 2. Results of error norm for different equidistant time step sizes for Figure 6.

h	0.0125	0.025	0.05	0.1
error	$2.6079E-4$	$5.1840E-4$	$1.0203E-3$	$1.9532E-3$

5.4. Example 4: Construction of higher-order non-standard finite-difference-methods

Following ideas from [35], we apply methods presented in that work to construct high-order non-standard finite-difference-methods from our proposed model (2.1) by Algorithm (1). For our comparison, we again take error norms of our previos example.

Here, we briefly define two higher-order non-standard finite-difference-methods by using adopted ideas of Richardson's extrapolation [36]. An extrapolated value is denoted by $y\,(\widehat{x_0 + h})$ and $y_h\,(x_0 + h)$ represents numerical solution on meshes with time-step sizes h. Hence, a second-order scheme is given by

$$y\,(\widehat{x_0 + h}) = 2 \cdot y_{h/2}\,(x_0 + h) - y_h\,(x_0 + h)\,,$$

while a third-order scheme reads

$$y\widehat{(x_0+h)} = \frac{9 \cdot y_{h/4}(x_0+h) - 8 \cdot y_{h/2}(x_0+h) + y_h(x_0+h)}{2},$$

The results of our first-order, second-order and third-order non-standard finite-difference-methods by Richardson's extrapolation can be seen in Figure 7.

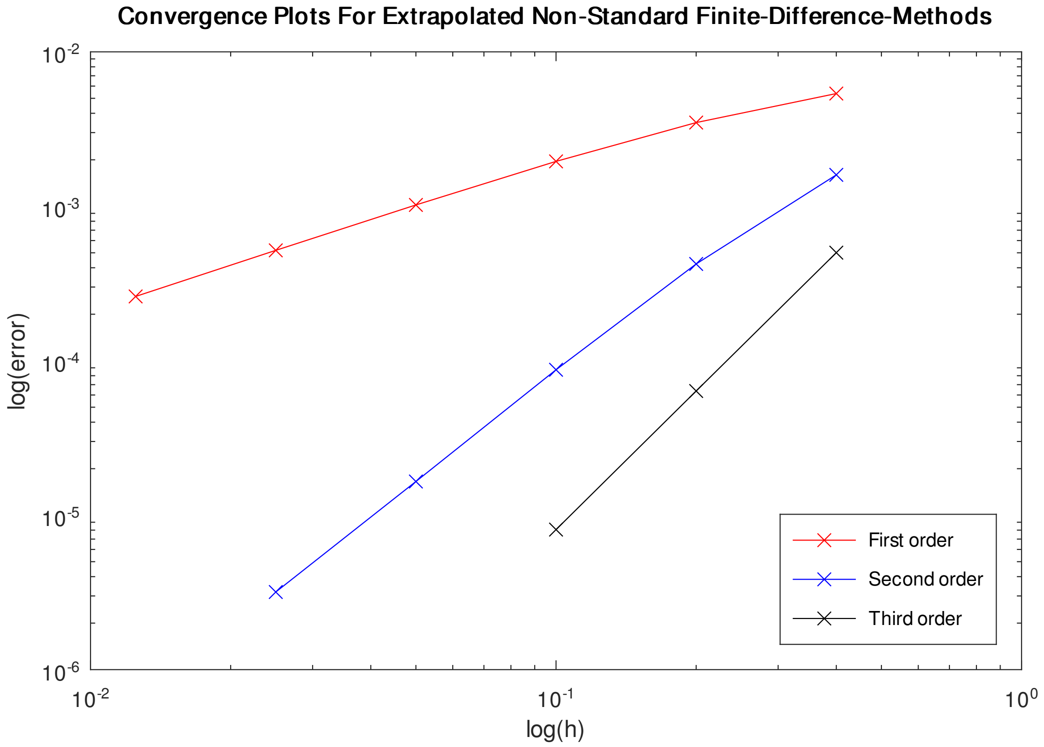

Figure 7. Numerical simulations for our different proposed non-standard finite-difference-method (red: first order, blue: second order, black: third order) towards the time-continuous solution.

In addition to Figure 7, we present theoretical results in the following Table 3.

By taking logarithms to the basis 2, we can indeed conclude that our proposed schemes are of first (red), second (blue) and third (black) order as suggested by [35]. We want to note that we apply Richardson's extrapolation to our dynamical system while those aforementioned authors apply Richardson's idea to their non-standard finite-difference discretization of an epidemiological model. Additionally, all extrapolation schemes conserve non-negativity of all solution components numerically.

5.5. *Example 5: Qualitative comparison with results from [18]*

Conclusively, we show that we obtain qualitatively comparable results as given in Figure 2 of [18] by an appropriate choice of problem parameters. Our chosen parameters can be seen in Table 4 which is inspired by Table 1 of [18]. However, even those authors stated finding acceptable parameters for the in-vivo situation is difficult.

Table 3. Results of error norm for different equidistant time step sizes for Figure 7. Error factors, given in brackets, are computed by the division of previous error dived the current error.

j	h	Error (red)	Error (blue)	Error (black)
1	0.4	5.3689E-03 (-)	1.5973E-03 (-)	5.0081E-04 (-)
2	0.2	3.4831E-03 (1.54)	4.2320E-04 (3.77)	6.3683E-05 (7.86)
3	0.1	1.9532E-03 (1.78)	8.7406E-05 (4.84)	8.0665E-06 (7.89)
4	0.05	1.0203E-03 (1.91)	1.6521E-05 (5.29)	-
5	0.025	5.1840E-04 (1.97)	3.1806E-06 (5.19)	-
6	0.0125	2.6079E-04 (1.99)	-	-

Table 4. Constant problem parameters and initial conditions for (1.1) in Example 5.

Parameter	Value
r	10
β	0.0000065
d	0.01
δ	0.39
π	340
c	4.4
T_0	1000
$T_{i,0}$	0
V_0	0.001

Results for $T = 5000$ and $h = 10$ can be seen in Figure 8.

We clearly observe that our results show similar qualitative behavior compared to the computed solutions of Figure 2 from [18]. In particular, a steep decrease in the amount of uninfected CD4+ T-cells and a steep increase in the load of virus particles can be observed after a certain amount of time. This result is in accordance with the acute and the asymptotic phase of an untreated HIV infection, see [18] and [15].

5.6. Example 6: Comparison between two different non-standard finite-difference schemes

Let us take the same problem parameters as defined in Example 5. Let us define our suggested non-standard finite-difference method by the standard denominator function

$$\varphi(h) = h$$

and let us, for reasons of comparison, define another non-standard finite-difference method by replacing h_n by

$$\varphi(x) = \frac{1 - \exp(-0.25 \cdot x)}{0.25}.$$

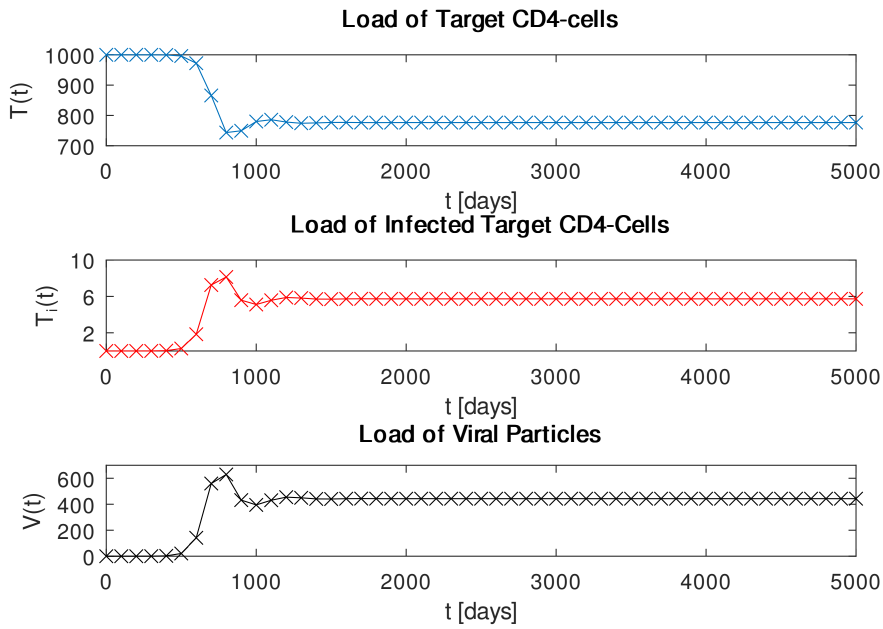

Figure 8. Numerical simulatons for $h = 10$ by our proposed non-standard finite-difference-method to compare the qualitative behavior with Figure 2 of [18] graphically.

We want to remark that a continuously differentiable non-standard denominator function is just a rescaling of our standard denominator function because

$$\begin{aligned}\varphi(h) &= \frac{\varphi(h) - \varphi(0)}{h - 0} \cdot h \\ &= \varphi'(\xi) \cdot h,\end{aligned}$$

holds for one $\xi \in (0, h)$ due to $\varphi(0) = 0$ by application of the mean value theorem. The results are presented in Figure 9.

6. Conclusion and outlook

In this work, we proposed a novel non-standard finite-difference-method for numerical approximation of (1.1). At first, we showed important properties of our proposed numerical scheme such as non-negativity, boundedness and convergence towards correct endemic equilibria. Secondly, we proved linear convergence towards the time-continuous solution of dynamical system (1.1). Finally, we underlined our theoretical results by numerical simulations.

We also want to shortly comment on other numerical solution schemes such as implicit solvers or adaptive time-stepping schemes. Let us first comment on adaptive time-stepping methods. Although they control local errors based on a time-stepping strategy, they are not as straight-forward to implement as our proposed non-standard finite-difference-method. Since explicit solution schemes are normally used, we still have to face the problem of sufficiently small time-step sizes to preserve non-negativity in contrast to our suggested non-standard finite-difference scheme. Additionally, our numerical solution scheme is easy to implement. Let us now consider implicit solvers. Generally, a

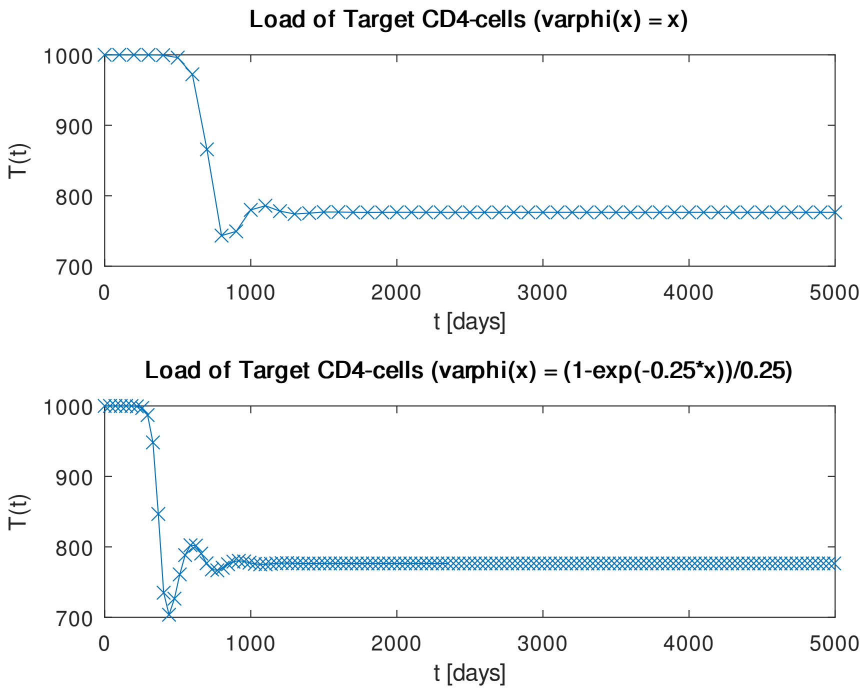

Figure 9. Numerical simulations for the first time-step size $h_1 = 10$ by our proposed non-standard finite-difference-method to compare with the non-standard finite-difference method for the second time-step size $h_2 = \dfrac{1 - \exp(-0.25 \cdot 10)}{0.25}$.

non-linear system of equation has to solved in each time step. This implies higher computation times as compared to our non-standard finite-difference method. Hence, our suggested numerical solution scheme is an attractive alternative and it preserves many important qualitative features of the time-continuous solution.

In contrast to other works on non-standard finite-difference methods, we applied standard denominator functions

$$\varphi(h) = h$$

instead of non-standard denominator functions such as

$$\varphi(h) = \frac{1 - \exp(-a \cdot h)}{a}.$$

for a positive constant a. The advantage of this standard denominator, in contrast to non-standard ones, is that we do not have restrictions on time-step sizes such as $\varphi(h) < b$ for a positive constant b.

Regarding future research directions, we believe that possible directions might be the following:

- Since Korobeinikov demonstrated stability analysis of equilibrium points in the time-continuous case [37], a proof of global asymptotic stability of the equilibrium states in the time-discrete case might be of interest for a future research article.
- As mentioned in [35] as well, we only observe preservation of non-negativity of our extrapolation schemes numerically. It would be of interest if there is a possibility to show analytically non-negativity in these higher-order methods based on Richardson's extrapolation.

- It might be of interest to analyze more complex dynamical systems for HIV infections such as given in [18] with latently and actively infected T cells and [16]. Here, an appropriate choice of non-standard finite-difference approximations seems of interest to preserve different dynamical properties such as non-negativity of solutions or correct numerical approximations of equilibrium states. This extension also includes identifying compartmental delay differential equations [38] or ordinary differential equations with more solution components [15] or partial differential equations [39] incorporating spatial tissue inhomogeneities. For reasons of numerical approximation, we need good analytical results to construct appropriate simulation methods.
- Furthermore, a generalization of our error analysis to Carathéodory or Lebesgue-integrable functions might be of interest as well.
- As an addition to our previous proposition, development of numerical simulation schemes might be interesting as well. For example, non-standard finite-difference-methods [33, 34] or finite-element-methods [40] for conservation of important properties such as non-negativity or settlement to correct equilibria are an active area of research [41–43].

Overall, we observe that there are still interesting numerical and theoretical gaps with regard to mathematical or numerical analysis of HIV infections.

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Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare there is no conflict of interest.

References

1. J. D. Murray, *Mathematical Biology I: An Introduction*, 3^{rd} edition, Springer-Verlag, New York, 2002. https://doi.org/10.1007/b98868
2. H. A. Ashi, D. M. Alahmadi, A mathematical model of brain tumor, *Math. Method. Appl. Sci.*, **46** (2023), 10137–10150. https://doi.org/10.1002/mma.9107
3. V. Srivastava, E. M. Takyi, R. D. Parshad, The effect of ”fear” on two species competition, *Math. Biosci. Eng.*, **20** (2023), 8814–8855. https://doi.org/10.3934/mbe.2023388
4. B. Wacker, J. C. Schlüter, Qualitative analysis of two systems of non-linear first-order ordinary differential equations for biological systems, *Math. Meth. Appl. Sci.*, **45** (2022), 4597–4624. https://doi.org/10.1002/mma.8056

5. O. K. Wanassi, D. F. M. Torres, Modeling blood alcohol concentration using fractional differential equations based on Ψ-Caputo derivative, *Math. Meth. Appl. Sci.*, **47** (2024), 7793–7803. https://doi.org/10.1002/mma.10002

6. M. Feinberg, *Foundations of Chemical Reaction Network Theory*, 1^{st} edition, Springer-Verlag, Cham, 2019. https://doi.org/10.1007/978-3-030-03858-8

7. L. Formaggia, A. Scotti, Positivity and Conservation Properties of some Integration Schemes for Mass Action Kinetics, *SIAM J. Numer. Anal.*, **49** (2011), 1267–1288. https://doi.org/10.1137/100789592

8. M. Mincheva, D. Siegel, Nonnegativity and positiveness of solutions to mass action reaction-diffusion systems, *J. Math. Chem.*, **42** (2007), 1135–1145. https://doi.org/10.1007/s10910-007-9292-0

9. M. Bohner, S. Streipert, D. F. M. Torres, Exact solution to a dynamic SIR model, *Nonlinear Anal. Hybrid Syst.*, **32** (2019), 228–238. https://doi.org/10.1016/j.nahs.2018.12.005

10. F. Brauer, Discrete epidemic models, *Math. Biosci. Eng.*, **7** (2010), 1–15. https://doi.org/10.3934/mbe.2010.7.1

11. M. Martcheva, *An Introduction to Mathematical Epidemiology*, 1^{st} edition, Springer-Verlag, New York, 2015. https://doi.org/10.1007/978-1-4899-7612-3

12. T. Cuchta, S. Streipert, Dynamic gompertz model, *Appl. Math. Inf. Sci.*, **14** (2020), 9–17. https://doi.org/10.18576/amis/140102

13. M. T. Hoang, J. C. Valverde, A generalized model for the population dynamics of a two stage species with recruitment and capture using a nonstandard finite difference scheme, *Comput. Appl. Math.*, **43** (2024), 54. https://doi.org/10.1007/s40314-023-02539-9

14. S. H. Streipert, G. S. K. Wolkowicz, Derivation and dynamics of discrete population models with distributed delay in reproduction, *Math. Biosci.*, **376** (2024), 109279. https://doi.org/10.1016/j.mbs.2024.109279

15. S. Alizon, C. Magnus, Modelling the Course of an HIV Infection: Insights from Ecology and Evolution, *Viruses*, **4** (2012), 1984–2013. https://doi.org/10.3390/v4101984

16. I. D'Orso, C. V. Forst, Mathematical Models of HIV-1 Dynamics, Transcription, and Latency, *Viruses*, **15** (2023), 2119. https://doi.org/10.3390/v15102119

17. D. E. Kirschner, Using Mathematics to Understand HIV Immune Dynamics, *Notices Amer. Math. Soc.*, **43** (1996), 191–202. Available from: `https://www.ams.org/journals/notices/199602/kirschner.pdf`

18. A. S. Perelson, D. E. Kirschner, R. De Boer, Dynamics of HIV infection of $CD4^+$ T cells, *Math. Biosci.*, **114** (1993), 81–125. https://doi.org/10.1016/0025-5564(93)90043-A

19. A. S. Perelson, A. U. Neumann, M. Markowitz, J. M. Leonard, D. D. Ho, HIV-1 Dynamics in Vivo: Virion Clearance Rate, Infected Cell Life-Span, and Viral Generation Time, *Science*, **271** (1996), 1582–1586. https://doi.org/10.1126/science.271.5255.1582

20. A. S. Perelson, Modelling viral and immune system dynamics, *Nat. Rev. Immunol.*, **2** (2002), 28–36. https://doi.org/10.1038/nri700

21. B. Wacker, Revisiting the classical target cell limited dynamical within-host HIV model - Basic mathematical properties and stability analysis, *Math. Biosci. Eng.*, **21** (2024), 7805–7829. https://doi.org/10.3934/mbe.2024343

22. M. A. Stafford, L. Corey, Y. Cao, E. S. Daar, D. D. Ho, A. S. Perelson, Modeling plasma virus concentration during primary HIV infection, *J. Theor. Biol.*, **203** (2000), 285–301. https://doi.org/10.1006/jtbi.2000.1076

23. C. Clarke, S. Pankavich, Three-stage modeling of HIV infection and implications for antiretroviral therapy, *J. Math. Biol.*, **88** (2024), 34. https://doi.org/10.1007/s00285-024-02056-1

24. X. Liu, S. Ahmad, M. ur Rahman, Y. Nadeem, A. Akgül, Analysis of a TB and HIV co-infection model under Mittag-Leffler fractal-fractional derivative, *Phys. Scr.*, **97** (2022), 054011. https://doi.org/10.1088/1402-4896/ac645e

25. M. ur Rahman, Y. Karaca, R. P. Agarwal, S. A. David, Mathematical modelling with computational fractional order for the unfolding dynamics of the communicable diseases, *Appl. Math. Sci. Eng.*, **32** (2024), 2300330. https://doi.org/10.1080/27690911.2023.2300330

26. A. Saleem, M. ur Rahman, S. Boulaaras, R. Guefaifia, D. Baleanu, Exploring the dynamics of HIV and HCV co-infection through piecewise modified Mittag-Leffler fractional derivatives, *Appl. Math. Sci. Eng.*, **33** (2025), 2478038. https://doi.org/10.1080/27690911.2025.2478038

27. B. Wacker, J. C. Schlüter, Time-continuous and time-discrete SIR models revisited: Theory and applications, *Adv. Differ. Equ.*, **2020** (2020), 556. https://doi.org/10.1186/s13662-020-02995-1

28. E. Hairer, G. Wanner, S. P. Nørsett, *Solving Ordinary Differential Equations I - Nonstiff problems*, 1^{st} edition, Springer-Verlag, Berlin, 1993. https://doi.org/10.1007/978-3-540-78862-1

29. E. Hairer, G. Wanner, *Solving Ordinary Differential Equations II - Stiff and Differential-Algebraic Problems*, 1^{st} edition, Springer-Verlag, Berlin, 1996. https://doi.org/10.1007/978-3-642-05221-7

30. H. Ranocha, M. Sayyari, L. Dalcin, M. Parsani, D. I. Ketcheson, Relaxation Runge-Kutta methods: Fully discrete explicit entropy-stable schemes for the compressible Euler and Navier-stokes equations, *SIAM J. Sci. Comput.*, **42** (2020), A612–A638. https://doi.org/10.1137/19M1263480

31. B. Wacker, J. C. Schlüter, A non-standard finite-difference-method for a non-autonomous epidemiological model: analysis, parameter identification and applications, *Math. Biosci. Eng.*, **20** (2023), 12923–12954. https://doi.org/10.3934/mbe.2023577

32. B. Wacker, Framework for solving dynamics of Ca^{2+} ion concentrations in liver cells numerically: Analysis of a non-negativity-preserving non-standard finite-difference method, *Math. Meth. Appl. Sci.*, **46** (2023), 16625–16643. https://doi.org/10.1002/mma.9464

33. R. E. Mickens, *Nonstandard Finite Difference Models of Differential Equations*, 1^{st} edition, World Scientific, Singapore, 1993. https://doi.org/10.1142/2081

34. R. E. Mickens, Calculation of denominator functions for nonstandard finite difference schemes for differential equations satisfying a positivity condition, *Numer. Meth. Part. Differ. Equ.*, **23** (2007), 672–691. https://doi.org/10.1002/num.20198

35. J. Martín-Vaquero, A. Martín del Rey, A. H. Encinas, J. D. Hernández Guillén, A. Queiruga-Dios, G. Rodríguez Sánchez, Higher-order nonstandard finite difference schemes for a

MSEIR model for a malware propagation, *J. Comput. Appl. Math.*, **317** (2017), 146–156. https://doi.org/10.1016/j.cam.2016.11.044

36. L. F. Richardson, The approximate arithmetical solution by finite differences of physical problems including differential equations, with an application to the stresses in a masonry dam, *Phil. Trans. R. Soc. A*, **210** (1911), 307–357. https://doi.org/10.1098/rsta.1911.0009
37. A. Korobeinikov, Global properties of basic virus dynamics models, *Bull. Math. Biol.*, **66** (2004), 879–883. https://doi.org/10.1016/j.bulm.2004.02.001
38. J. Yang, X. Wang, F. Zhang, A Differential Equation Model of HIV Infection of $CD4^+$ T-Cells with Delay, *Discrete Dyn. Nat. Soc.*, **2008** (2008), 903678. https://doi.org/10.1155/2008/903678
39. E. B. S. Marinho, F. S. Bacelar, R. F. S. Andrade, A model of partial differential equations for HIV propagation in lymph nodes, *Physica A Stat. Mech. Appl.*, **391** (2012), 132–141. https://doi.org/10.1016/j.physa.2011.08.023
40. A. Ern, J. L. Guermond, *Theory and Practice of Finite Element Methods*, 1^{st} edition, Springer-Verlag, New York, 2004. https://doi.org/10.1007/978-1-4757-4355-5
41. M. T. Hoang, M. Ehrhardt, A dynamically consistent nonstandard finite difference scheme for a generalized SEIR epidemic model, *J. Differ. Equ. Appl.*, **30** (2024), 409–434. https://doi.org/10.1080/10236198.2023.2291151
42. M. T. Hoang, M. Ehrhardt, A second-order nonstandard finite difference method for a general Rosenzweig-MacArthur predator-prey model, *J. Comput. Appl. Math.*, **444** (2024), 115752. https://doi.org/10.1016/j.cam.2024.115752
43. B. Wacker, J. C. Schlüter, An age- and sex-structured SIR model: Theory and an explicit-implicit numerical solution algorithm, *Math. Biosci. Eng.*, **17** (2020), 5752–5801. https://doi.org/10.3934/mbe.2020309

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