

# A Novel Crossover Variable Order (Deterministic-Stochastic) Lung Cancer and Tumor-Immune System Interaction: Numerical Simulations

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**Abstract:** The tumor-immune interaction model related to lung cancer by applying the fractional variable-order Brownian motion and hybrid variable-order fractional piecewise derivatives are presented for the first time in this paper. The variable order fractional derivative of the Caputo proportional constant is applied to extend the deterministic model, and the variable order fractional Brownian motion is applied to extend the stochastic differential equations. A parameter  $\zeta$  is presented to be consistent with the physical model problem. The stability of the proposed model is discussed. New numerical algorithms are improved to study the proposed model. These techniques are the modified nonstandard Euler Maruyama approach to study the stochastic model and the constant proportional Caputo non-standard fifth step Adams-Bashfourth method to study numerically the deterministic model of variable order derivative. Several numerical experiments verify the method's efficiency and support the theoretical results.

**Keywords:** Tumor-Immune; lung Cancer; variable order constant proportional Caputo derivative; the fifth-step proportional Caputo constant nonstandard Adams-Bashfourth method; modified nonstandard Euler Maruyama method.

## 1 Introduction

Cancer and cancer cells are the most widespread and deadliest diseases of our time. One type of disease is the lung cancer. The multiplicity of lung cancer's sub-types and the intricacy of the disease's mechanism make early diagnosis particularly challenging [1]. Lung cancer is the primary cause of cancer-related fatalities worldwide. As a result, the sickness is still deadly and hasn't been completely cured. Cancer cells, known to divide swiftly and expand uncontrollably, cause this illness [2]. Additionally, cancerous tumor cells undergo changes and rapid development. Knowing how this mechanism operates will make it simpler for us to defeat cancer from the start.

Mathematical models have proven to be invaluable in understanding the dynamics of disease spread. These models serve as powerful tools for capturing the laws, processes, and trends associated with the spread of diseases. Over the years, significant progress has been made in both the theoretical foundations and practical applications of mathematical research on disease dynamics [3, 4]. Only a few research have been done on mathematical modelling of fractional order lung cancer, for instance [5]. The paper [7] summarizes the most promising new directions addressed and improved during the scientific debate at the conference ICMAS'19, as well as noteworthy complementary fresh works. Advanced theoretical, experimental, and numerical simulations yielded novel insights in all aspects of cancer and HIV/AIDS dynamic systems. Over the recent years, fields like physics [6], quantum [8], chemistry [9], finance [10], medicine [11] and several others have all noticed an increase in their use of fractional calculus. Fractional differential equations are the most effective at describing biological phenomena [12].

Fractional-order differential equations (FODE) models have advantages over integer-order mathematical models and are more accurate and realistic. Fractional-order models are better able to explain these complicated events than integer-order models since most biological systems continue to function utilizing memory, after-effects, and hereditary features compared with Integer-order differential equation models. Because biological phenomena usually face abrupt

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changes, they cannot be included when modelling evolutionary processes that depend on short memory. The aforementioned characteristic has been thoroughly investigated using the concept of a piecewise derivative of fractional order. The authors come to the conclusion that the aforementioned fractional calculus property may be used as a powerful tool to describe a range of dynamic behaviours observed in real life.

The effects of a time-dependent system's extensive variable memory can be described using variable-order fractional derivatives (VOFDs). This unusual extension of the classical fraction computation was proposed by the reference [13]. As a result, the variable-order fractional derivatives used to define the derivative models are advantageous and suitable for the epidemic models. Fractional order and integer order results can be derived from mathematical models with variable-order fractional derivatives.

To more accurately reflect complicated behaviors encountered in some real-world problems, piecewise calculus has been developed in recent years. In many real-world phenomena, such as infectious illness, heat transfer, fluid flow, and several complex advection problems, crossover behaviors take place [14–17]. Recent studies have demonstrated that differential equations with piecewise equations, as opposed to equations with standard fractional or integer orders, are more appropriate for representing the previously indicated process. It should be mentioned that this concept of the derivative of piecewise is similar to the short memory concept in fractional calculus. Recent works in this field have been published as [18, 19].

This study's piecewise mathematical model representation of cancer revealed a feature that had never been studied or observed in previous studies that used mathematical models based on classical or other fractional derivatives. This approach of piecewise mathematical model representation of many real-world dynamic systems is eye-opening for scholars, as it has the ability to unearth hidden aspects in a system's dynamics [16]. The reference [17] incorporates a hybrid fractional operator. This novel operator outperforms Caputo's fractional derivative operator in terms of flexibility. As a particular case, we can derive a hybrid fractional derivative operator to get Caputo's fractional derivative operator, where the fractional derivative of Caputo and the Riemann-Liouville integral are combined linearly in the hybrid fractional operator.

The lung cancer and tumor-immune system interaction model [20] will be developed into a piecewise hybrid fractional variable-order and stochastic fractional variable order Brownian motion (VFBM) model in this study. This work will be the first to present this mathematical model. We shall talk about the existence of a stochastic model and the stability of the suggested model. To solve the suggested model, new numerical methods will be developed by us. The fractional variable-order hybrid derivative deterministic model is solved using the fifth-step proportional Caputo constant nonstandard Adams-Bashfourth method (PCC-NAB5SM), while the stochastic model is solved using the nonstandard modified Euler Maruyama methodology. The theoretical results will be supported by a number of numerical experiments.

The following is the paper's basic structure: Multiple definitions of the variable-order fractional-order derivative (VFOD) and background information on the Modified Euler-Maruyama approach are given in Section 2. A steady-state analysis of the hybrid variable-order fractional piecewise and variable-order stochastic Brownian motion models is explored. in 4, Section. Furthermore, this paper's Section 5 explores the stability analysis of the proposed approach and offers novel numerical techniques for analyzing the model. Numerical simulations are described in Section 6. A summary of the study's main conclusions and contributions is given in section 7.

## 2 Fundamental Definitions

In the next section, we present a number of significant definitions of the variable-order fractional that will be used throughout the text.

**Definition 1.** *The variable order fractional of the Riemann-Liouville integral's left and right (L-R) sides, where  $f(t)$  is a continuous function are defined, respectively, as follows [21]:*

$${}_a I_t^{\alpha(t)} \mathbb{F}(t) = \left[ \int_a^t (-s+t)^{-1+\alpha(t)} \mathbb{F}(s) ds \right] (\Gamma(\alpha(t)))^{-1}, \quad t > a, \quad (1)$$

$${}_t I_b^{\alpha(t)} \mathbb{F}(t) = \left[ \int_t^b (-s+t)^{-1+\alpha(t)} \mathbb{F}(s) ds \right] (\Gamma(\alpha(t)))^{-1}, \quad t < b. \quad (2)$$

**Definition 2.** *Here are the definitions of the left side Caputo derivatives of variable order fractional for a function  $\mathbb{F}(t)$  of order  $\alpha(t)$ ,  $\mathbb{F} \in AC^n[a, b]$  [21]:*

$$({}^C D_{a+}^{\alpha(t)} \mathbb{F})(t) = ({}^C D_t^{\alpha(t)} \mathbb{F})(t) = \frac{1}{\Gamma(-\alpha(t) + n)} \left( \int_a^t \frac{\mathbb{F}^{(n)}(s)}{(t-s)^{1-n+\alpha(t)}} ds \right), \quad t > a. \quad (3)$$

**Definition 3.** According to ([22], [23]), the Caputo proportional constant variable order fractional operator (CPC) is defined as follows:

$$\begin{aligned}
 {}_0^{CPC}D_t^{\alpha(t)}\mathbb{F}(t) &= \left( \int_0^t (t-s)^{-\alpha(t)}\mathbb{F}'(s)(f(s)K_1(\alpha(t)) + K_0(\alpha(t)))ds \right) (\Gamma(-\alpha(t) + 1))^{-1} \\
 &= K_1(\alpha(t)) {}_0^{RL}I_t^{1-\alpha(t)}\mathbb{F}(t) + K_0(\alpha(t)) {}_0^CD_t^{\alpha(t)}\mathbb{F}(t),
 \end{aligned}
 \tag{4}$$

where the constant  $Q$  and the values of kernels  $K_0$  and  $K_1$  as in [22].

### 2.1 Euler-Maruyama approach with modification

Let  $H$  be the Hurst index, which is provided by the differential equations for stochastic (SDE) controlled by FBM

$$dy_s = \Upsilon_s(y_s, t)dB_{\eta}^H(t) + \Lambda_s(y_s, t)dt, \quad 0 < t \leq T_f, \tag{5}$$

$$y_s(t_0) = y_{s,0}, \quad \eta, s = 1, \dots, \kappa,$$

where,  $\Lambda_s(y_s, t)$  and  $\Upsilon_s(y_s, t)$  are continuous real functions, with  $y_{s,0}$  representing a deterministic initial value. Also,  $\Lambda_s(y_s, t)$  represents the mean rate of change of the system state  $y_{\kappa}$  at time  $t$ , and  $\Upsilon_{\vartheta}(y_1, y_2, \dots, y_{\kappa}, t)dB_{\eta}^H(t)$  represents the random perturbation. The word  $\Lambda_{\vartheta}(y_s, t)$  represents the average or predictable component of the issue, and  $\Upsilon_s(y_s, t)$ , represents the intensity of the random part.

The Euler-Maruyama method (EMM) is a prominent solution for Eq. (5) in the case of classical Brownian motion, i.e. when  $H = 0.5$ :

$$y_s^{n+1} = \Upsilon_s(y_s^n, t^n)\Delta B_{\eta}^n + \Lambda_s(y_s^n, t^n)\Delta t + y_s^n, \quad 0 < t \leq t_f, \quad \eta, s = 1, \dots, \kappa, \tag{6}$$

Using the Modified Euler-Maruyama Method (MEMM), equation (5) is resolved as follows:

$$\begin{aligned}
 y_s^{n+1} &= y_s^n + \Lambda_s(y_s^n, t^n)\Delta t + \Upsilon_s(y_s^n, t^n)\Delta B_{\eta}^n \\
 &\quad + 0.5\Upsilon_s(y_s^n, t^n)\Upsilon_s'(y_s^n, t^n)\Delta t^{2H}, \quad s, \eta = 1, \dots, \kappa, \quad 0 < t \leq T_f, \quad H > 0.5.
 \end{aligned}
 \tag{7}$$

For more details about this method see [24–26].

## 3 The Hybrid Picewise Variable-Order Fractional for Lung Cancer Model

In the next section, the mathematical model of the interaction between the tumor and immune system for lung cancer [20] was expanded using a piecewise differential equation system. The VFBM is used to expand the stochastic equation (SDE) in the range  $T_1 < t \leq T_f$ , and the CPC variable order operator is used to expand the deterministic model in the range  $0 < t \leq T_1$ . A new parameter  $\zeta$  is introduced to be compatible with the physical model problem. Furthermore, we avoid dimensional incompatibilities by modifying the variable order fractional model with an additional parameter  $\zeta$ . The system that is produced can be expressed as follows:

$$\begin{cases}
 \zeta^{\alpha(t)-1} {}_0^{CPC}D_t^{\alpha(t)}T(t) &= r_2T(t)\left(1 - \frac{T(t)}{k_2}\right) - \mu A(t)T(t) - \delta_1T(t)W(t), \\
 \zeta^{\alpha(t)-1} {}_0^{CPC}D_t^{\alpha(t)}A(t) &= \beta M(t)A(t) - d_2A(t), \quad 0 < t \leq T_1, \\
 \zeta^{\alpha(t)-1} {}_0^{CPC}D_t^{\alpha(t)}M(t) &= r_1M(t)\left(1 - \frac{M(t)}{k_1}\right) - \mu A(t)M(t) - d_1M(t), \\
 \zeta^{\alpha(t)-1} {}_0^{CPC}D_t^{\alpha(t)}W(t) &= r_3W(t)\left(1 - \frac{W(t)}{k_3}\right) - \delta_2T(t)W(t),
 \end{cases}
 \tag{8}$$

with initial conditions

$$T(t_0) = \tau_0 \geq 0, A(t_0) = a_0 \geq 0, M(t_0) = m_0 \geq 0, W(t_0) = w_0 \geq 0, \tag{9}$$

The model can be expressed as follows in  $T_f \geq t > T_1$ ,

$$\begin{cases}
 dT &= (r_2T(t)\left(1 - \frac{T(t)}{k_2}\right) - \mu T(t)A(t) - \delta_1W(t)T(t))dt + \sigma_1C(t)dB_1^{H(t)}, \\
 dA &= (\beta M(t)A(t) - d_2A(t))dt + \sigma_2C(t)dB_2^{H(t)}, \quad t_1 < t \leq t_f, \\
 dM &= (r_1M(t)\left(1 - \frac{M(t)}{k_1}\right) - \mu M(t)A(t) - d_1M(t))dt + \sigma_3C(t)dB_3^{H(t)}, \\
 dW &= (r_3W(t)\left(1 - \frac{W(t)}{k_3}\right) - \delta_2W(t)T(t))dt + \sigma_4C(t)dB_4^{H(t)},
 \end{cases}
 \tag{10}$$

$$T(t_1) = \tau_1 \geq 0, A(t_1) = a_1 \geq 0, W(t_1) = w_1 \geq 0, M(t_1) = m_1 \geq 0. \quad (11)$$

**Table 1:** The variables in the system (8) [20].

The variable	Description
$T$	The cells of Tumor (TCs)
$A$	Macrophages that are active
$M$	The cells of Macrophages
$W$	Cellular hosts or healthy tissue cells (NTCs)

**Table 2:** The model's parameters and their values [20]

Parameters	Description	Value
$k_1$	The macrophage's carrying capacity	$5.0785e + 07$
$k_2$	The capability of TCs to carry	$2.7785e + 05$
$k_3$	The NTCs' carrying capacity	$5.4621e + 06$
$d_1$	The number of macrophages that die	$4.3884e - 14$
$d_2$	The proportion of dying active macrophages	0.8809
$\delta_1$	The NTCs' rate of competition with TCs	0.8809
$\delta_2$	The ratio of TCs to NTCs in terms of competition	0.7609
$r_1$	The pace of cell proliferation in macrophages	0.9
$r_2$	The TCs' rate of expansion	0.5045
$r_3$	How quickly NTCs are growing	0.6169
$\mu$	The frequency of TC degradation brought on by aggressive macrophage attack	0.014
$\beta_1$	The proportion of inactive macrophages that become active	0.0937
$\beta_2$	A result of active macrophages degrading macrophage cells	0.0122

### 3.1 Existence of stochastic solutions to differential equations

Assuming that  $L^2(\Omega, F, \mathbb{P}) = L^2$  is space of containing the random processes of second order,  $y : \Omega \rightarrow \Omega \times \mathbb{R}$  and consider the equation (5). Integrate (5), then we have:

$$y(t) = y(0) + \int_0^t \Upsilon_s(y_s(\zeta), \zeta) dB_\eta^{H(t)}(\zeta) + \int_0^t \Lambda_s(y_s(\zeta), \zeta) d\zeta. \quad (12)$$

The following requirements must be met for functions  $\Upsilon_s(y_s, \zeta)$  and  $\Lambda_s(y_s, \zeta)$  to existence of a solution for (12) and satisfy the following conditions [27]:

$$\begin{aligned} |-\Upsilon_s(\bar{y}_s, t) + \Upsilon_s(y_s(t), t)| &\leq L^* |y_s(t) - \bar{y}_s(t)|, \\ |\Lambda_s(y_s(t), t) - \Lambda_s(\bar{y}_s(t), t)| &\leq L^* |y_s - \bar{y}_s(t)|, \\ |\Upsilon_s(y_s, t)| &\leq L(1 - |y_s(t)|), \\ L(1 - |y_s(t)|) &\geq |\Lambda_s(y_s(t), t)|, \end{aligned} \quad (13)$$

where  $L, L^*$  are constants.

## 4 The Equilibrium Points

To determine the system's equilibrium points (8), we write

$$D_t^{\alpha(t)} A(t) = D_t^{\alpha(t)} T(t) = D_t^{\alpha(t)} M(t) = D_t^{\alpha(t)} W(t) = 0,$$

Therefore, we have the following equilibrium points:

$$\begin{aligned}
 E_0 &= (0, 0, 0, 0), \\
 E_1 &= \left( \frac{k_2 r_3 (k_3 \delta_1 - r_2)}{k_3 k_2 \delta_2 \delta_1 - r_3 r_2}, 0, \frac{(r_1 - d_1) k_1}{r_1}, \frac{r_2 k_3 (-\delta_2 k_2 + r_2)}{-r_3 r_2 + k_3 k_2 \delta_2 \delta_1} \right), \\
 E_2 &= \left( 0, 0, \frac{(r_1 - d_1) k_1}{r_1}, 0 \right), \\
 E_3 &= \left( 0, -\frac{d_2 r_1 + k_1 \beta_1 (d_1 - r_1)}{\beta_2 \beta_1 k_1}, \frac{d_2}{\beta_1}, k_3 \right), \\
 E_4 &= \left( \frac{k_2 r_3 (k_3 \delta_1 - r_2)}{k_3 k_2 \delta_2 \delta_1 - r_3 r_2}, 0, 0, \frac{(r_1 - d_1) k_1}{r_1}, \frac{r_2 k_3 (-\delta_2 k_2 + r_2)}{-r_3 r_2 + k_3 k_2 \delta_2 \delta_1} \right), \\
 E_5 &= \left( 0, -\frac{d_2 r_1 + k_1 \beta_1 (d_1 - r_1)}{\beta_2 \beta_1 k_1}, \frac{d_2}{\beta_1}, k_3, \frac{d_2}{\beta_1}, 0 \right), \\
 E_6 &= \left( 0, 0, \frac{(r_1 - d_1) k_1}{r_1}, k_3 \right), \\
 E_7 &= \left( k_2, 0, \frac{(r_1 - d_1) k_1}{r_1}, k_3, 0 \right), \\
 E_8 &= (k_2, 0, 0, 0), \\
 E_9 &= (0, 0, 0, k_3), \\
 E_{10} &= \left( k_2 + \frac{\mu k_2 (\beta_1 (d_1 - r_1) + r_1 d_2)}{\beta_2 \beta_1 r_2 k_1}, -\frac{d_2 r_1 + k_1 \beta_1 (d_1 - r_1)}{\beta_2 \beta_1 k_1}, \frac{d_2}{\beta_1}, 0 \right), \\
 E_{11} &= (\tilde{T}, \tilde{A}, \tilde{M}, \tilde{W}),
 \end{aligned} \tag{14}$$

$$\begin{aligned}
 \tilde{T} &= \frac{k_2 r_3 \mu (r_1 d_2 - \beta_1 k_1 (-d_1 + r_1)) - r_3 k_2 k_1 \beta_2 \beta_1 (-r_2 + \delta_1 k_3)}{\beta_1 k_1} \beta_2 (r_3 r_2 - \delta_1 k_3 k_2 \delta_2), \\
 \tilde{A} &= -\frac{\beta_1 k_1 (-r_1 + d_1) + r_1 d_2}{\beta_1 k_1 \beta_2}, \\
 \tilde{M} &= \frac{d_2}{\beta_1}, \\
 \tilde{W} &= \frac{\delta_2 \mu k_3 k_2 (k_1 \beta_1 (-d_1 + r_1) - d_2 r_1) + k_1 r_2 \beta_2 \beta_1 k_3 (-\delta_2 k_2 + r_3)}{\beta_2 k_1 \beta_1 (r_3 r_2 - \delta_2 \delta_1 k_3 k_2)}.
 \end{aligned}$$

We only consider the stability of equilibrium  $E_{11}$  because our aim is to study the circumstances in which the patient can survive.

### 4.1 Local endemic equilibrium stability

The Jacobian matrix of model calculated equilibrium point  $E_{11}$ , is given by:

$$J = \zeta^{1-\alpha(t)} \begin{pmatrix} -\frac{2\tilde{T}r_2}{k_2} - r_2 - \tilde{W}\delta_1 - \tilde{A}\mu & -\mu\tilde{T} & 0 & -\tilde{T}\delta_1 \\ 0 & d_2 + \tilde{M}\beta_1 & \tilde{A}\beta_1 & 0 \\ 0 & -\tilde{M}\beta_2 & -\frac{2\tilde{M}r_1}{k_1} + r_1 - d_1 - \tilde{A}\beta_2 & 0 \\ -\tilde{W}\delta_2 & 0 & 0 & -\frac{2\tilde{W}r_3}{k_3} - \tilde{T}\delta_2 \end{pmatrix}, \tag{15}$$

We get the characteristic equation as follows:

$$P(\lambda) = (\lambda^2 + \varepsilon_1 \lambda + \varepsilon_2)(\lambda^2 + \varepsilon_3 + \varepsilon_4),$$

where,

$$\begin{aligned}
 \varepsilon_1 &= -\zeta^{1-\alpha(t)} \left( r_2 + r_3 - A - \frac{2\tilde{T}r_2}{k_2} - \frac{2\tilde{W}r_3}{k_3} - \tilde{T}\delta_3 \right), \\
 \varepsilon_2 &= \zeta^{1-\alpha(t)} \left( \left( -\frac{2\tilde{T}r_2}{k_2} + r_2 - \tilde{A}\mu - \tilde{W}\delta_1 \right) \left( -\frac{2\tilde{W}r_3}{k_3} + r_3 - \tilde{T}\delta_2 \right) - \delta_2 \delta_1 \tilde{T}\tilde{W} \right),
 \end{aligned}$$

$$\varepsilon_3 = -\zeta^{1-\alpha(t)} \left( -\frac{2\tilde{M}r_1}{k_1} + r_1 - \tilde{A}\beta_2 - d_1 - d_2 + \tilde{M}\beta_1 \right),$$

$$\varepsilon_4 = \zeta^{1-\alpha(t)} \left( \left( -\frac{2\tilde{M}r_1}{k_1} - d_1 + r_1 - \tilde{A}\beta_2 \right) (-d_2 + \tilde{M}) + \beta_2\beta_1\tilde{M}\tilde{A} \right).$$

It is necessary to employ numerical methods because stationary state solutions cannot be described analytically. Consequently, long-running numerical simulations ameliorate the system for a given set of initial conditions and parameters. The parameter range is selected so that the dynamics of the non-spatial system can either occur within this range or towards its limit, where the desired dynamics difference occurs.

## 5 Numerical Techniques for Crossover Model

We provide numerical methods for solving (8-10) in this section. Our method for addressing the ensuing linear cross-over (stochastic and variable order deterministic) model is given as follows:

$${}^{\text{CPC}}D_t^{\alpha(t)} y_l = \Lambda_l(y_s, t), \quad 1 \geq \alpha(t) > 0, \quad 0 < t \leq T_1, \quad s = 1, 2, 3 \dots \kappa, \quad l = 1, 2, 3, \quad (16)$$

$$y_l(t_0) = y_{l,0},$$

$$dy_l = Y_l(y_s, t) dB_{\eta}^{H(t)}(t) + \Lambda_l(y_s, t) dt, \quad T \geq t > T_1, \quad (17)$$

$$y_{l,1} = y_l(t_1).$$

Let,

$$0 < t \leq t_1 \leq \dots \leq t_{n1} = T_1 \leq t_{n1+1} \leq t_{n1+2} \leq \dots t_{n2} = T.$$

The relation (4) can be expressed as follows:

$$\begin{aligned} {}^{\text{CPC}}D_t^{\alpha(t)} y(t) &= (\Gamma(1 - \alpha(t)))^{-1} \int_0^t (t-s)^{-\alpha(t)} (K_0(\alpha(t))y'(s) + y(s)K_1(\alpha(t))) ds, \\ &= K_1(\alpha(t)) {}_0^{\text{RL}}I_t^{1-\alpha(t)} y(t) + K_0(\alpha(t)) {}_0^{\text{C}}D_t^{\alpha(t)} y(t), \\ &= K_1(\alpha(t)) {}_0^{\text{RL}}D_t^{\alpha(t)-1} y(t) + K_0(\alpha(t)) {}_0^{\text{C}}D_t^{\alpha(t)} y(t), \end{aligned} \quad (18)$$

On  $\alpha(t)$  alone,  $K_1(\alpha(t))$ ,  $K_0(\alpha(t))$  are entirely dependent. According to Mickens in [28], the non-standard finite difference approach (NSFDM) is more dependable and accurate than the finite difference technique. We can discretize (18) in the following manner by using the discretization nonstandard finite difference Grünwald–Letnikov method:

$$\begin{aligned} {}^{\text{CPC}}D_t^{\alpha(t)} y(t)|_{t=t^{n1}} &= \frac{K_1(\alpha(t))}{(\Theta(\Delta t))^{\alpha(t)-1}} \left( y_{n1+1} + \sum_{i=1}^{1+n1} y_{n1+1-i} \omega_i \right) \\ &\quad + \frac{K_0(\alpha(t))}{(\Theta(\Delta t))^{\alpha(t)}} \left( - \sum_{i=1}^{1+n1} \mu_i y_{n1+1-i} + y_{n1+1} - q_{n1+1} y_0 \right). \end{aligned} \quad (19)$$

Now, we introduce an approximation of PCC-NAB5SM to solve (16):

$$\begin{aligned} &\frac{K_1(\alpha(t_{n1}))}{(\Theta(\Delta t))^{\alpha(t_{n1})-1}} \left( y_{n1+5} + \sum_{i=1}^{5+n1} \omega_i y_{n1+5-i} \right) + \frac{K_0(\alpha(t_{n1}))}{(\Theta(\Delta t))^{\alpha(t_{n1})}} \left( y_{n1+5} - \sum_{i=1}^{5+n1} \mu_i y_{n1+5-i} - q_{n1+5} y_0 \right) \\ &= \frac{1901}{720} \Lambda_l(y_1^{n1+4}, y_2^{n1+4}, \dots, y_{\kappa}^{n1+4}) - \frac{2774}{720} \Lambda_l(y_1^{n1+3}, y_2^{n1+3}, \dots, y_{\kappa}^{n1+3}) \\ &+ \frac{2616}{720} \Lambda_l(y_1^{n1+2}, y_2^{n1+2}, \dots, y_{\kappa}^{n1+2}) - \frac{1274}{720} \Lambda_l(y_1^{n1+1}, y_2^{n1+1}, \dots, y_{\kappa}^{n1+1}) \\ &+ \frac{521}{720} \Lambda_l(y_1^{n1}, y_2^{n1}, \dots, y_{\kappa}^{n1}). \end{aligned} \quad (20)$$

The following is an expression for the explicit solution:

$$\begin{aligned}
 y_{n_1+5} = & \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} \left( \sum_{i=1}^{n_1+5} \omega_i y_{n_1+5-i} \right) + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \left( \sum_{i=1}^{n_1+5} \mu_i y_{n_1+5-i} + q_{n_1+5} y_0 \right) \right. \\
 & - \frac{1901}{720} \Lambda_I(y_1^{n_1+4}, y_2^{n_1+4}, \dots, y_k^{n_1+4}) + \frac{2774}{720} \Lambda_I(y_1^{n_1+3}, y_2^{n_1+3}, \dots, y_k^{n_1+3}) \\
 & - \frac{2616}{720} \Lambda_I(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_k^{n_1+2}) + \frac{1274}{720} \Lambda_I(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_k^{n_1+1}) \\
 & \left. - \frac{521}{720} \Lambda_I(y_1^{n_1}, y_2^{n_1}, \dots, y_k^{n_1}) \right) / \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right). \tag{21}
 \end{aligned}$$

Four points are needed to solve (21). These points can be obtained by using the discretization of the CPC operator in the Adams-Bashforth technique's first, second, third, and fourth phases. The CPC-NAB1SM is available in the following formats:

$$\begin{aligned}
 y_{n_1+1} = & \left( (\Theta(\Delta t))^{-\alpha(t_{n_1})+1} K_1(\alpha(t_{n_1})) \left( \sum_{i=1}^{1+n_1} y_{n_1+1-i} \omega_i \right) \right. \\
 & + (\Theta(\Delta t))^{-\alpha(t)} K_0(\alpha(t_{n_1})) \left( \sum_{i=1}^{1+n_1} y_{n_1+1-i} \mu_i + q_{n_1+1} y_0 \right) \\
 & \left. - \Lambda_I(y_1^{n_1}, y_2^{n_1}, \dots, y_k^{n_1}) \right) / \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right), \tag{22}
 \end{aligned}$$

In addition, CPC-NAB2SM is:

$$\begin{aligned}
 y_{n_1+2} = & \left( (\Theta(\Delta t))^{-\alpha(t_{n_1})+1} K_1(\alpha(t_{n_1})) \left( \sum_{i=1}^{2+n_1} y_{2+n_1-i} \omega_i \right) \right. \\
 & + K_0(\alpha(t_{n_1})) (\Theta(\Delta t))^{-\alpha(t_{n_1})} \left( \sum_{i=1}^{2+n_1} \mu_i y_{n_1+2-i} + q_{n_1+2} y_0 \right) \\
 & - \frac{3}{2} \Lambda_I(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_k^{n_1+1}) - \frac{1}{2} \Lambda_I(y_1^{n_1}, y_2^{n_1}, \dots, y_k^{n_1}) \\
 & \left. / \left( (\Theta(\Delta t))^{-\alpha(t_{n_1})+1} K_1(\alpha(t_{n_1})) + (\Theta(\Delta t))^{-\alpha(t_{n_1})} K_0(\alpha(t_{n_1})) \right) \right). \tag{23}
 \end{aligned}$$

Also, CPC-NAB3SM is given as:

$$\begin{aligned}
 y_{n_1+3} = & \left( (\Theta(\Delta t))^{-\alpha(t_{n_1})+1} K_1(\alpha(t_{n_1})) \left( \sum_{i=1}^{3+n_1} y_{n_1-i+3} \omega_i \right) \right. \\
 & + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \left( \sum_{i=1}^{n_1+3} \mu_i y_{n_1+3-i} + q_{n_1+3} y_0 \right) \\
 & - \frac{23}{12} \Lambda_I(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_k^{n_1+2}) + \frac{16}{12} \Lambda_I(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_k^{n_1+1}) \\
 & \left. - \frac{5}{12} \Lambda_I(y_1^{n_1}, y_2^{n_1}, \dots, y_k^{n_1}) \right) / \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right). \tag{24}
 \end{aligned}$$

The CPC-NAB4SM is displayed as:

$$\begin{aligned}
 y_{n_1+4} = & \left( (\Theta(\Delta t))^{-\alpha(t)+1} K_1(\alpha(t_{n_1})) \left( \sum_{i=1}^{4+n_1} y_{n_1+4-i} \omega_i \right) \right. \\
 & + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \left( \sum_{i=1}^{n_1+4} \mu_i y_{n_1+4-i} + q_{n_1+4} y_0 \right) \\
 & - \frac{55}{24} \Lambda_l(y_1^{n_1+3}, y_2^{n_1+3}, \dots, y_\kappa^{n_1+3}) + \frac{59}{24} \Lambda_l(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_\kappa^{n_1+2}) \\
 & \left. - \frac{37}{24} \Lambda_l(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_\kappa^{n_1+1}) + \frac{9}{24} \Lambda_l(y_1^{n_1}, y_2^{n_1}, \dots, y_\kappa^{n_1}) \right) \\
 & / \left( \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right). \tag{25}
 \end{aligned}$$

Now, by using (22), (23), (24), and (25), We're going to get  $y(4), y(3), y(2)$ , and  $y(1)$  points. We solve (16) using these points and (21). where,  $\omega_i = \omega_{i-1}(1 - \alpha i^{-1})$ ,  $\omega_0 = 1$ ,  $n_1(\Theta(\Delta t)) = t^{n_1}$ ,  $T_1 N_n^{-1} = \Delta t$ ,  $N_n$  is a natural number,  $\alpha(1) = \mu_1$ ,  $\mu_i = (-1)^{i-1} \binom{\alpha(t)}{i}$ ,  $q_i = (\Gamma(1 - \alpha(t_{n_1})))^{-1} i^{\alpha(t)}$ ,  $i = 1, 2, \dots, n_1 + 1$ . Let [29]:

$$(\Gamma(1 - \alpha(t_{n_1}))^{-1} = q_1.$$

*Remark.* If  $K_0(\alpha(t)) = 1$  and  $K_1(\alpha(t)) = 0$  in (21), we obtain the discretization of the fifth step nonstandard Adams-Bashfourth technique with the discretization of the Caputo operator (C-NAB5M).

We extended NMEMM in this work as follows [24] in order to solve the differential stochastic equations driven by VFBM (17):

$$\begin{aligned}
 y_l^{n_2+1} = & y_l^{n_2} + \Lambda_l(y_1^{n_2}, y_2^{n_2}, \dots, y_\kappa^{n_2}, t^{n_2}) \Theta(\Delta t) + \Upsilon_l(y_1^{n_2}, y_2^{n_2}, \dots, y_\kappa^{n_2}, t^{n_2}) \Delta B_\eta^{n_2} \\
 & + 0.5 \Upsilon_l(y_1^{n_2}, y_2^{n_2}, \dots, y_\kappa^{n_2}, t^{n_2}) \Upsilon_l'(y_1^{n_2}, y_2^{n_2}, \dots, y_\kappa^{n_2}, t^{n_2}) \Theta(\Delta t)^{2H(t_{n_2})}, \quad T \geq t > T_1, \quad l = n_1, \dots, \kappa. \tag{26}
 \end{aligned}$$

### 5.1 The PCC-NAB5SM's stability

Consider the most general form of a hybrid fractional system:

$${}^{CPC} D_t^\alpha y_l(t) = \Phi_l(y_1, y_2, \dots, y_\kappa), \quad y_l(t_0) = y_{l,0}, \quad l = 1, \dots, \kappa, \tag{27}$$

$\Phi_l$  denotes continuous functions on  $\mathbb{R}^\kappa$ .

**Theorem 1.** *The CPC-NAB5S technique is stable.*

*Proof.* We have the following by approximating (8) with CPC-NAB5SM:

$$\begin{aligned}
 & \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} \left( y_{n_1+5} + \sum_{i=1}^{n_1+5} \omega_i y_{n_1+5-i} \right) + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \left( y_{n_1+5} - \sum_{i=1}^{n_1+5} \mu_i y_{n_1+5-i} - q_{n_1+5} y_0 \right) \\
 = & \frac{1901}{720} \Phi_l(y_1^{n_1+4}, y_2^{n_1+4}, \dots, y_\kappa^{n_1+4}) - \frac{2774}{720} \Phi_l(y_1^{n_1+3}, y_2^{n_1+3}, \dots, y_\kappa^{n_1+3}) \\
 & + \frac{2616}{720} \Phi_l(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_\kappa^{n_1+2}) - \frac{1274}{720} \Phi_l(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_\kappa^{n_1+1}) \\
 & + \frac{521}{720} \Phi_l(y_1^{n_1}, y_2^{n_1}, \dots, y_\kappa^{n_1}). \tag{28}
 \end{aligned}$$



Then, CPC-NAB5SM is given as:

$$\begin{aligned}
 y_{n_1+5} = & \left( K_1(\alpha(t_{n_1}))(\Theta(\Delta t))^{-\alpha(t_{n_1})+1} \left( \sum_{i=1}^{5+n_1} y_{n_1-i+5} \omega_i \right) + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \left( \sum_{i=1}^{n_1+5} \mu_i y_{n_1+5-i} + q_{n_1+5} y_0 \right) \right. \\
 & - \frac{1901}{720} \Phi_l(y_1^{n_1+4}, y_2^{n_1+4}, \dots, y_{\kappa}^{n_1+4}) + \frac{2774}{720} \Phi_l(y_1^{n_1+3}, y_2^{n_1+3}, \dots, y_{\kappa}^{n_1+3}) \\
 & - \frac{2616}{720} \Phi_l(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_{\kappa}^{n_1+2}) - \frac{1274}{720} \Phi_l(y_1^{n_1+1}, y_2^{n_1+1}, \dots, y_{\kappa}^{n_1+1}) \\
 & \left. - \frac{521}{720} \Phi_l(y_1^{n_1}, y_2^{n_1}, \dots, y_{\kappa}^{n_1}) \right) / \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right), \tag{29}
 \end{aligned}$$

$$\begin{aligned}
 y_{n_1+5} \leq & \left( K_1(\alpha(t_{n_1}))(\Theta(\Delta t))^{-\alpha(t_{n_1})a+1} \left( \sum_{i=1}^{5+n_1} y_{n_1-i+5} \omega_i \right) \right. \\
 & + K_0(\alpha(t_{n_1}))(\Theta(\Delta t))^{-\alpha(t_{n_1})} \left( \sum_{i=1}^{5+n_1} \mu_i y_{n_1+5-i} + q_{n_1+5} y_0 \right) \\
 & - \frac{1901}{720} \Phi_l(y_1^{n_1+4}, y_2^{n_1+4}, \dots, y_{\kappa}^{n_1+4}) - \frac{2616}{720} \Phi_l(y_1^{n_1+2}, y_2^{n_1+2}, \dots, y_{\kappa}^{n_1+2}) \\
 & \left. - \frac{521}{720} \Phi_l(y_1^{n_1}, y_2^{n_1}, \dots, y_{\kappa}^{n_1}) \right) / \left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right), \tag{30}
 \end{aligned}$$

because  $\frac{1}{\left( \frac{K_1(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})-1}} + \frac{K_0(\alpha(t_{n_1}))}{(\Theta(\Delta t))^{\alpha(t_{n_1})}} \right)} < 1$ , therefore

$$y_5 \leq y_0,$$

$$y_{n_1+5} \leq y_{n_1+4} \leq \dots \leq y_5 \leq y_0.$$

The suggested CPC-NAB5SM is then stable.

## 6 Numerical Simulations

In the following, we focus on the model’s simulations (8-11), using the initial conditions  $T(0) = 5, A(0) = 22, M(0) = 20, W(0) = 50000$ . The parameters’ values of this model are given in Table 2 and the denominator function  $\Theta(\Delta t) = 1 - e^{(-\Delta t)}$  and assume that  $T_1 = 10, T_f = 100$ . The numerical results of (8-11) are represented graphically at various  $\alpha(t)$  and  $H(t)$  values. NMEMM (26) and CPC-NAB5SM (21) were used to run the simulation. The dynamical behavior of the cells of Tumor, macrophages that are active, the cells of macrophages and healthy tissue cells in systems (8-11) are depicted in figures 1-4. Figure 1 illustrates the behavior of the cells of Tumor, macrophages that are active, the cells of macrophages and healthy tissue cells for (8-10) with  $\alpha(t) = 0.95 - 0.001t, \sigma_1 = 0.05, \sigma_2 = 0.05, \sigma_3 = 0.05, \sigma_4 = 0.05$ , and different values of  $H(t)$ . Figure 2 explains how solutions behave differently when the values of  $\alpha(t)$  are different and  $\sigma_1 = 0.05, \sigma_2 = 0.05, \sigma_3 = 0.05, \sigma_4 = 0.05$ . Figure 3 represents the system’s (8-10) dynamic behavior at  $H(t) = 0.70 - 0.1t, \sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = 0.05$  and various values of  $\alpha(t)$ . From Figures 1-3, we noted the crossover behavior can be clearly observed near the values of  $T_1 = 10, T_f = 100$ . Before these points dynamics show multiplicity in its behavior.

To illustrate how parameter values  $\sigma_i$ , and  $H(t)$  affect on the result Figure 4 is presented, whereand  $T_1 = 50, T_f = 100$  and  $\sigma_1 = 0.04, \sigma_2 = 0.5, \sigma_3 = 0.3, \sigma_4 = 0.09$ . We observed that after  $T_f = 50$ , the crossover system’s behavior changed. Additionally, we discovered that for solutions not covered in the reference [20], unexpected behavior arises and all variables are impacted.

## 7 Conclusion

In conclusion, A novel crossover hybrid variable order deterministic-stochastic differential equations for the interaction between the immune and tumor for lung cancer mode has been developed in this paper. In two time intervals, two distinct models of variable-order fractional and variable-order stochastic derivatives are defined. The variable order

operator CPC is used to enhance the deterministic model. By applying variable-order fractional Brownian motion, the stochastic differential equations are extended. Adams-Bashfourth fifth step method with Caputo proportional constant and non-standard modified Euler Maruyama approach are used to solve the proposed problem. For the approximation CPC fractional operator, GLNSFDM is used. It has good stability characteristics for solving the suggested system, and precise approximations are given. Moreover, it can reduce computation time when the finish time is quite long. Results for the suggested models are displayed graphically. Some phase pictures in a stochastic context are provided. Piecewise derivative concept leads us to analyze and predict the process from the beginning to the end of the tumor, as it offers the possibility to observe many behaviors from crossover to stochastic processes. Generally, we found that this study provides new insights into the interaction between the immune and tumor for lung cancer model under complex real-world conditions. Consequently, researchers can successfully capture reality by applying this operator to real-world problems.

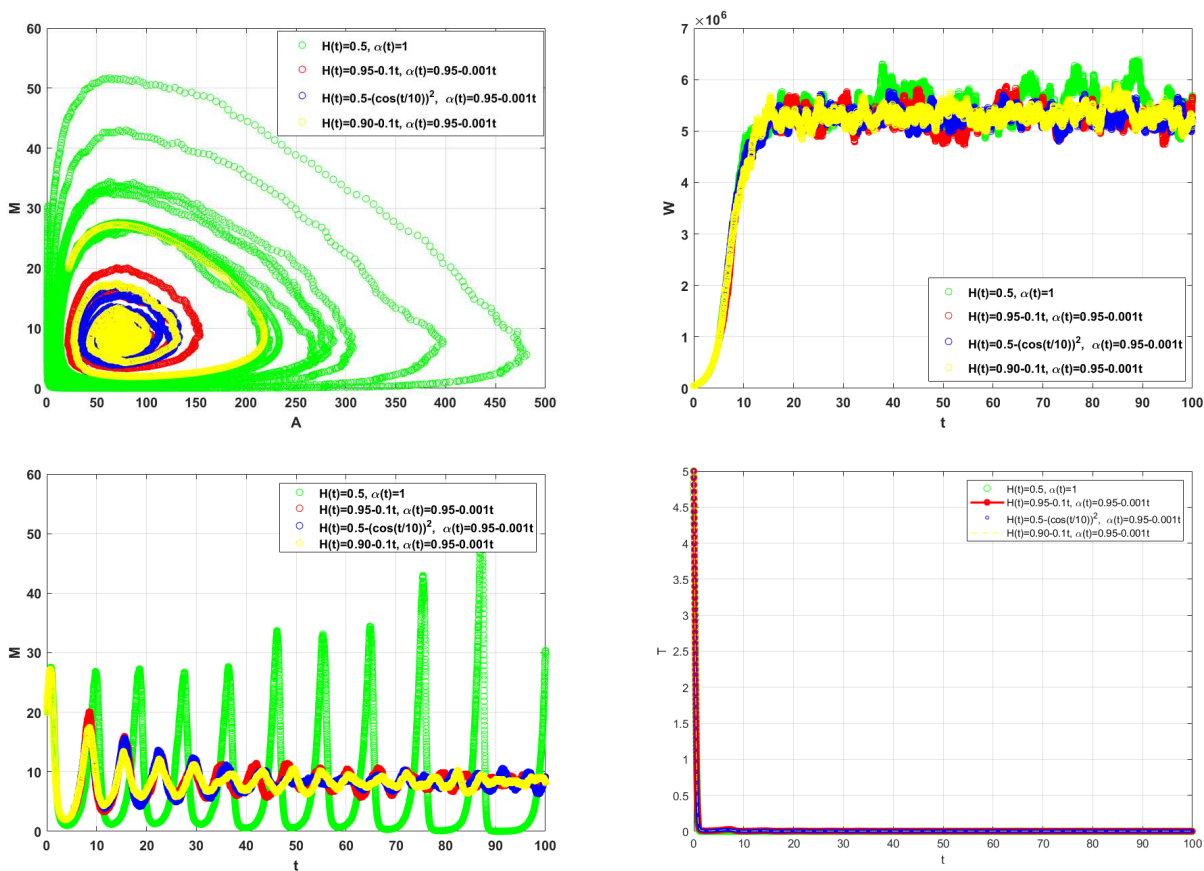
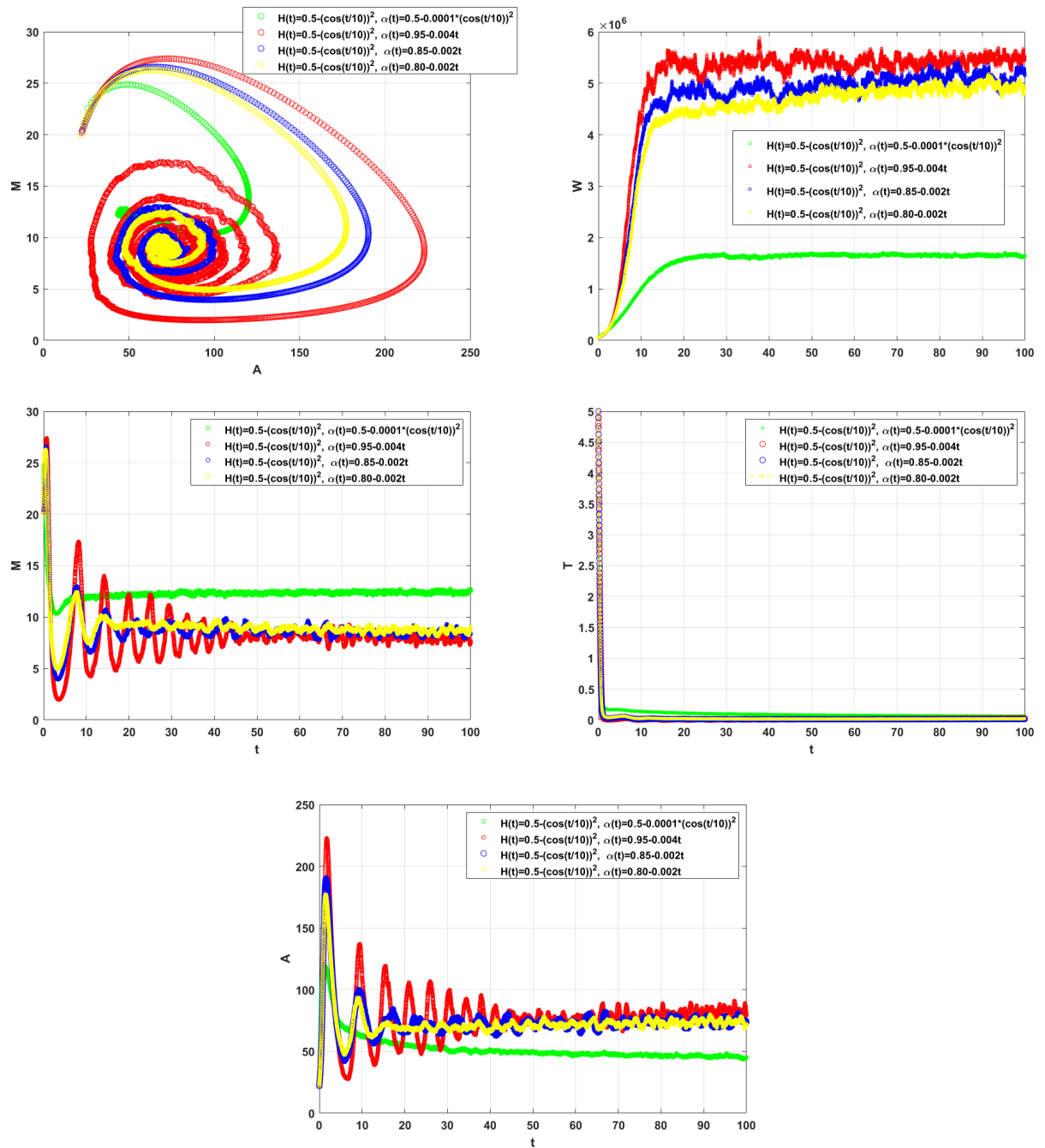


Fig. 1: Simulation for (8-10),  $\alpha(t) = 0.95 - 0.001t$ .



**Fig. 2:** Simulation for (8-10),  $H(t) = 0.5 - (\cos(t/10))^2$ .

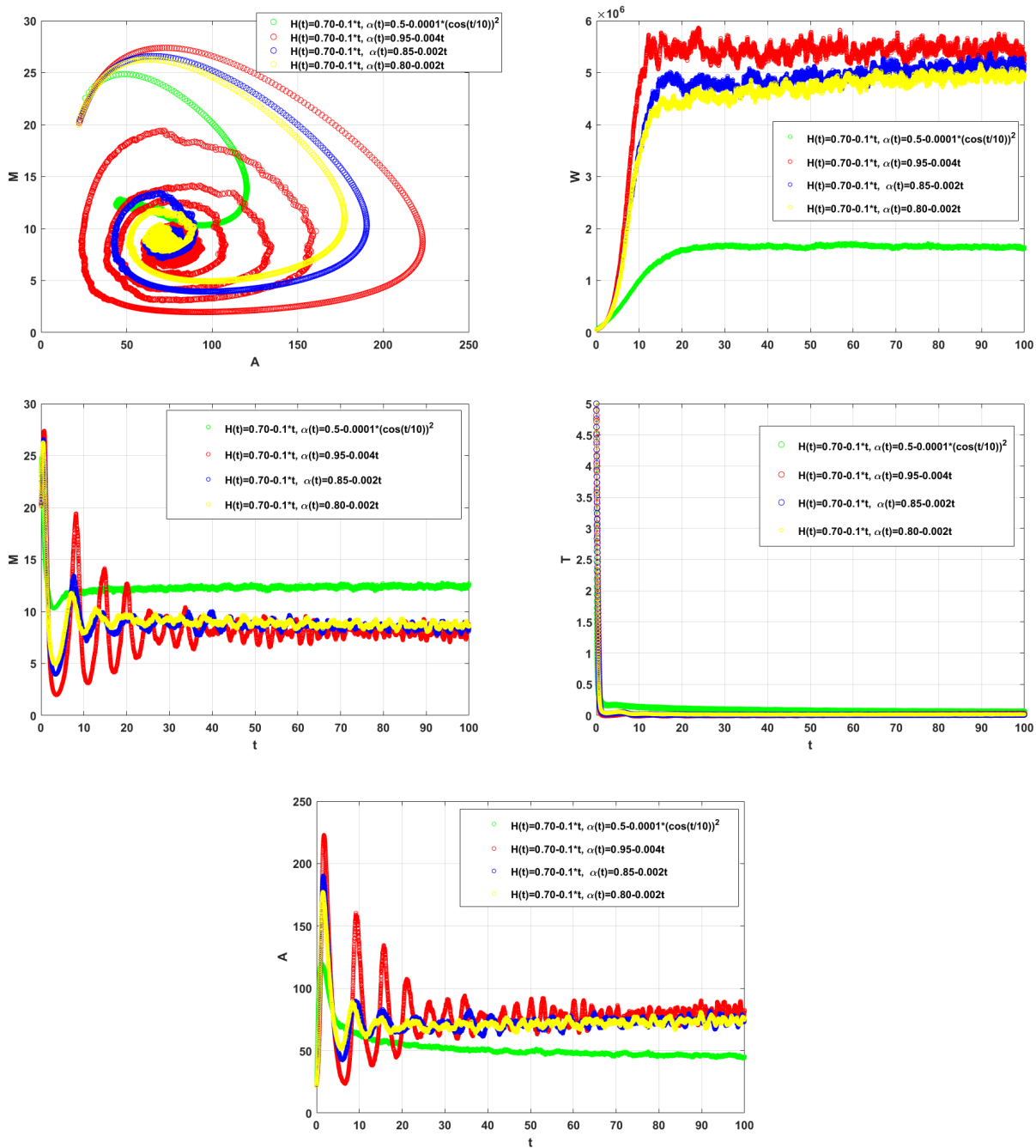
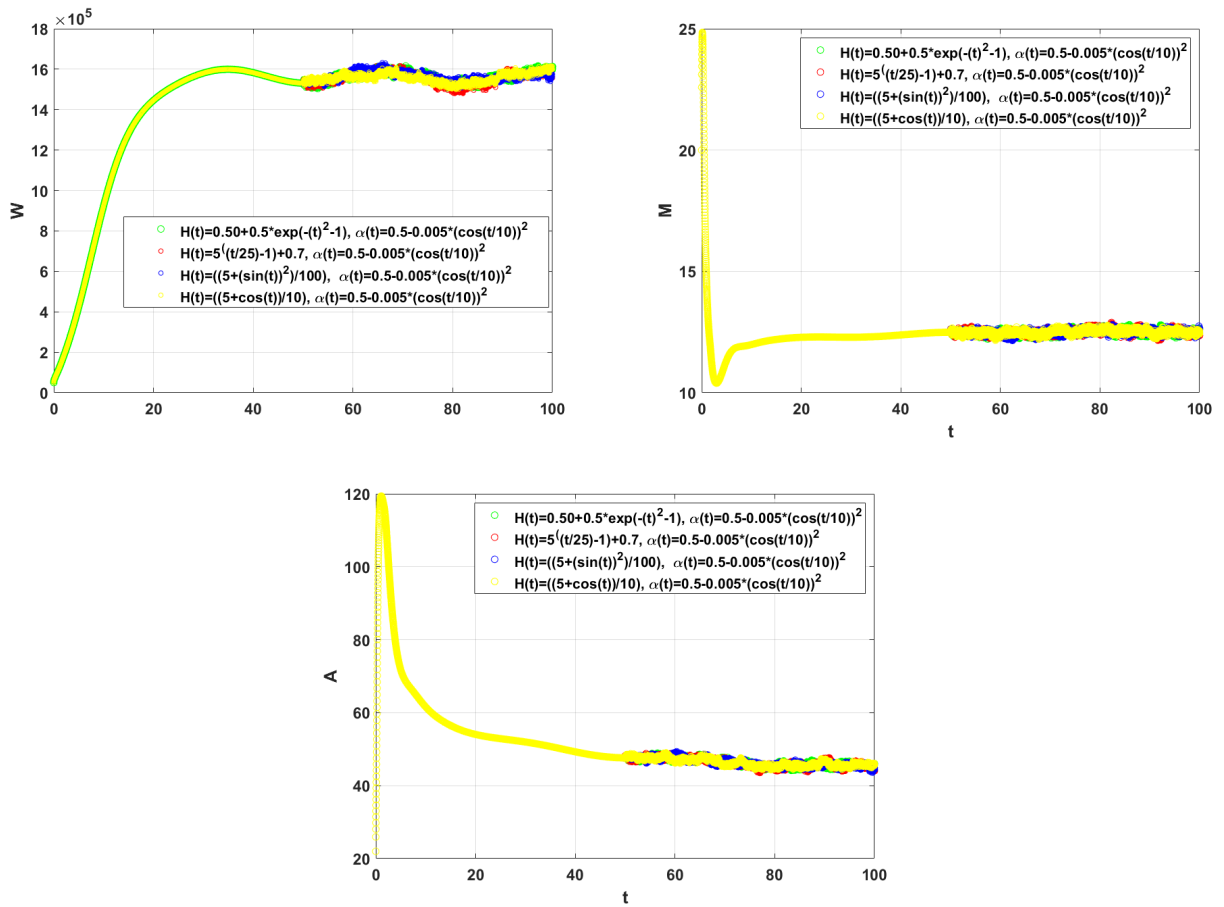


Fig. 3: Simulation for (8-10),  $H(t) = 0.70 - 0.1t$ .



**Fig. 4:** Simulation for (8-10),  $\alpha(t) = 0.5 - 0.005(\cos(t/10))^2$ .

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