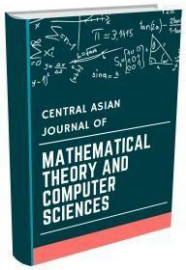

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Article

A Semi-Analytical Hybrid Methodology for Studying Mathematical Models of Cancer and Immune Dynamics

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Abstract: In this paper, we present a new method for result analytical approximate solutions to systems of cancer and immune dynamics. The new method is developed by combining the Akbari-Gangi method with an external modification of Atkin. The proposed method was tested by applying it to solve nonlinear mathematical models describing cancer and immune dynamics. To demonstrate the effectiveness of the new method in improving results, it was compared with the Akbari-Gangi method and other methods presented in the literature. The obtained results show that this method has high accuracy, good convergence, and acceptable stability, which were illustrated in the form of tables and graphical representations of the solutions and error estimates.

Keywords: Akbari-Gangi Method, Atkin's External Modification, Cancer and Immune Dynamics, Convergence and Stability.

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1. Introduction

The fundamental model used to analyze the dynamics of numerous biological systems is the tumor-immune model, inspired by the mathematical principles of chemical interactions advanced by Lotka and Volterra [1], [2], [3]. The model has extensive applicability in numerous scientific disciplines, such as chemical processes [4], [5] and bio particle granulation [6], and the interface of living organisms and ecologies [7], [8]. In recent years much research has focused on tumor-immunity models inspired by chemical reaction system [9]. Zhuoyin focused on chemical models under stochastic conditions [10]. While, Badri et al. focused on structure of these nonlinear systems and their potential equilibrium points [11].

The aim of this paper is to numerically study the dynamics of the interface between cancer cells and the immune system, which and described by following nonlinear ordinary differential equations

$$\left.\begin{aligned}\frac{dx}{dt} &= f\big(x(t), y(t), a_1(t), \dots a_n(t)\big)\\ \frac{dy}{dt} &= g\big(x(t), y(t), b_1(t), \dots b_n(t)\big)\end{aligned}\right\}, \qquad (1)$$

where $x(t)$ represents the numeral of cancer cells, and $y(t)$ represents the numeral of immune cells (such as natural killer or +CO cells) [12]. The positive function $a_i(t)$ and $b_i(t)$ typically provide measures of efficiency parameters , such as tumor growth rates, the effectiveness of immune cells in eliminating cancer cells, apoptosis rates, and effects of various treatments [13], [14]. The system's numerical solution (1) is not straightforward

because of the nonlinear and complex nature of the functions f and g therefor, it is necessary to develop reliable and efficient numerical algorithms to solve it.

Many articles have addressed the analytical approximate solution of tumor-immune systems to evaluate the efficiency and dependability of different numerical methods. For example, the Adomian method(ADM) was tested by applying it to a tumor-immune model [15], [16], [17], [18].In addition, the variational iteration method (VIM) was studied to simulate the tumor-immune system interaction [19]. These systems were analyzed using the differential transformation method (DTM). over a short time span [20], was used to approximate systems based on the ratio of treatment effects. The homotopic perturbation method (HPM) [21]. Additionally, both HPM and VIM were applied to a nonlinear tumor-immune model, along with a stability analysis [22].

Numerous studies on the traits of tumor-immune systems, including coexistence, stability, and extinction, have been presented (of either the tumor or the immune response) [23], [24], [25]. A numerical study of tumor-immune systems was presented, based on the interface rate between immune cells and tumor cells, with the addition of random temporal variation. The basic model used two methods: the forward Euler method and the finite difference method [26]. A reaction-advection tumor-immune model was demonstrated to be stable using a Holling second-type tumor functional response [27]. An epidemiological mathematical model was designed to study the interface between cancer cells and immune cells, and the stability of the resulting solution was examined using von Neumann analysis [28].

This demonstrates the importance of studying these complex dynamic system and addressing them through various techniques for simulation. In general, it is challenging to locate an exact analytical the nonlinear differential equations' solution describing tumor and immune dynamics due to their nonlinearities. Furthermore, combining analytical approximate methods with integral transformation reduces the quantity of calculations and lessens the challenge of relying solely on analytical approximation techniques, which has been the focus of recent studies [29], [30], [31]. There are numerous analytical approximate methods for solving differential equations, including the AGM developed by Akbari and Gangi [32], which is distinguished by its simplicity of use in approximating solutions to a array of nonlinear ordinary and partial differential equations. In addition, the Atkin external modification [33] is a powerful and effective tool for improving accuracy and accelerating the convergence solutions.

Since the aforementioned methods (Akbari-Gangi and Atkin's external modification) have not previously been used together in the study and analysis of cancer and immune dynamics systems, this has provided us with a strong incentive to propose an innovative method. The new method consists of integrating the Akbari-Gangi and the Atkin approximation, which we will denote as (AGAM), as an analytical-approximation tool for solving cancer and immunological problems under study. When compared with previous works addressing similar issues, the results gotten demonstrate that the proposed method is highly efficient and reliable, with high accuracy, strong convergence, and good stability, which confirms its effectiveness and suitability for handling this type of mathematical model.

This paper consists of seven sections, which is what this introduction is the first. In the second section, the construction of the suggested method is presented systematically, along with an explanation of its theoretical foundations and the main steps upon which it is based. Section 3 is devoted to applying the proposed method to a number of mathematical models describing the dynamics of the interaction between cancer cells and the immune system. Section4 presents the results obtained, along with a systematic comparison between them and the results reported in previous studies. Sections5 and 6 present an analysis of the convergence and stability of the studied systems. Finally, Section7 summarizes the most important results and conclusions reached.

2. Materials and Methods

This is an integrated mathematical tool that combines two different techniques to provide analytical approximate solutions for nonlinear systems in cancer dynamics models. The AGM forms the basis of the proposed method. This section cover the basic concepts of the Akbari-Gangi method and Atkin's external modification.

2-1 Akbari-Gangi Method (AGM)

Developed by Akbari and Gangi, this method is an excellent computational approach applicable to a wide variety of nonlinear differential equations. It assumes that the solution takes the form of a finite series; consequently, the solution is obtained by solving a set of algebraic equations. To illustrate the use of the AGM method, differential equation for the function $x(t)$ and its derivatives can be written as follows:

$$P_k = f\left(x, x', x'', \ldots, x^{(m)}\right) = 0, x = x(t), \quad \textbf{(2)}$$

where P_k symbolizes an order m nonlinear differential equation with a boundary condition.

$$\text{At } t = 0, x(t) = x_0, x'(t) = x_1, \ldots, x^{(m-1)}(t) = x_{m-1} \quad \textbf{(3a)}$$

$$\text{At } t = L, x(t) = x_{L_0}, x'(t) = x_{L_1}, \ldots, x^{(m-1)}(t) = x_{L_{m-1}}. \quad \textbf{(3b)}$$

We assume approximate solution Equation (2) in the form of a series as follows

$$x(t) = \sum_{i=0}^{n} a_i t^i \quad \textbf{(4)}$$

By applying the boundary condition to the series in Equation (4), we obtain

when $t = 0$

$$\begin{cases} x(0) = a_0 = x_0 \\ x'(0) = a_1 = x_1 \\ x''(0) = a_2 = x_2 \\ \quad\quad . \\ \quad\quad . \\ \quad\quad . \end{cases} \quad \textbf{(5)}$$

when $t = L$

$$\begin{cases} x(L) = a_0 + a_1 L + \cdots + a_n L^n = x_{L_0} \\ x'(L) = a_1 + 2a_2 L + \cdots + n a_n L^{n-1} = x_{L_1} \\ x''(L) = 2a_2 + 6a_3 L + \cdots + n(n-1) a_n L^{n-2} = x_{L_2} \\ \quad\quad\quad\quad\quad\quad . \\ \quad\quad\quad\quad\quad\quad . \\ \quad\quad\quad\quad\quad\quad . \end{cases} \quad \textbf{(6)}$$

The condition in (5) and (6) given the solution to Equation (2), which is represented by series in (4),when $n \leq m$ and when $n > m$, leaving $(n - m)$ of the coefficients of the solution series for the approximation unknown. These are calculated by substituting the solution series of the approximation of Equation (4) into Equation (2), and then applying the boundary condition to following equations.

$$P_0 = f\left(x(0), x'(0), x''(0), \ldots, x^{(m)}(0)\right) = 0$$

$$P_1 = f\left(x(L), x'(L), x''(L), \ldots, x^{(m)}(L)\right) = 0 \quad \textbf{(7)}$$

$$\vdots$$

$$P'_k: \begin{cases} f\left(x'(0), x''(0), x'''(0), \ldots, x^{(m+1)}(0)\right) = 0 \\ f\left(x'(L), x''(L), x'''(L), \ldots, x^{(m+1)}(L)\right) = 0 \end{cases} \quad \textbf{(8)}$$

$$P''_k: \begin{cases} f\left(x''(0), x'''(0), x''''(0), \ldots, x^{(m+2)}(0)\right) = 0 \\ f\left(x''(L), x'''(L), x''''(L), \ldots, x^{(m+2)}(L)\right) = 0 \end{cases} \quad \textbf{(9)}$$

By solving the resulting equations from (7-9), we have determined the values of the unknown coefficients a_i. Substituting these into Equation (4), we obtain the approximate solution to Equation (2).

2-2 Atkin Eternal Modification [33]

The mathematician Alexander Craig Atkin discovered this method in 1926, and it is surprising that the Japanese mathematician Takakazu Seki (1642-1708) had knowledge of Atkin's mothed, which accelerates the convergence of nonlinear convergent sequences that is, sequences that satisfy the condition $a \neq 1$

Atkin's eternal modification is the most well-known and oldest method. To accelerate the convergence of a given convergent sequence with values Z_n,

$$\lim_{n\to\infty} Z_n = Z \qquad (10)$$

this method transform the sequence $\{Z_n\}_n^{\infty} = 0$ into the sequence $\{T_n\}_n^{\infty} = 0$, which generally converges to Z faster than the original sequence Z_n. To illustrate the method, suppose that the sequence $\{Z_n\}_n^{\infty} = 0$ converges to Z with coefficient k

$$Z_{n+1} - Z = k(Z_n - Z) \quad , |k| < 1 \quad n = 0,1,2, \dots \dots \qquad (11)$$

The values of k and Z can be determined from Z_n , Z_{n+1},and Z_{n+2} by solving the following equation

$$Z_{n+1} - Z = k(Z_n - Z)$$
$$Z_{n+2} - Z = k(Z_{n+1} - Z) \qquad (12)$$

To be in the form

$$k = \frac{Z_{n+2} - Z_{n+1}}{Z_{n+1} - Z} \qquad (13)$$

Substituting (13) into Equation (11), where $k \neq 1$, we obtain

$$Z = \frac{(Z_n Z_{n+1} - Z_{n+1}^2)}{Z_{n+2} - 2Z_{n+1} + Z_n} \quad , \; n = 0,1, \dots \qquad (14)$$

Thus, the basic idea behind the AGAM algorithm the following is a summary of system (1) with initial conditions $x(0) = \alpha, y(0) = \beta$

Step1: Apply AGM represented as series with constant coefficients

$$x(t) = \sum_{i=0}^{n} a_i t^i \quad , \qquad y(t) = \sum_{i=0}^{n} b_i t^i \qquad (15)$$

Step2: We substitute Equation (15) into (1), that the equations take the form

$$\sum_{i=0}^{n} a_i t^i = \alpha + f\left(\sum_{i=0}^{n} a_i t^i , \sum_{i=0}^{n} b_i t^i , a_1(t), \dots a_n(t)\right)$$
$$\sum_{i=0}^{n} b_i t^i = \beta + g\left(\sum_{i=0}^{n} a_i t^i \sum_{i=0}^{n} b_i t^i , b_1(t), \dots b_n(t)\right) \qquad (16)$$

Step3: To obtain the values of the coefficients a_i and b_i in equation (16), we follow the same steps explained in equations (5-9).

Step4: Apply the Atkin eternal modification to accelerate the convergence of the solution obtain step (3).

Numerical Experiments

This section demonstrates the application of the new method to solve three different systems of the cancer and immune dynamics model, where the first and third models have variable coefficients and an exact solution, while the second model has no exact solution and constant coefficients.

Example 1: This models depicts the dynamics of the interface between cancer cells and chemotherapy, where the treatment targets and eliminates cancer cells, while the cancer cells attempt to resist the treatment's effects and proliferate, leading to increased treatment efficacy and a decrease in cancer cell numbers in the early stages of the therapeutic response [21]. The mathematical model representing the interface between cancer cells and treatment can be expressed by the following ordinary differential equations

$$\left.\begin{aligned} X'(t) &= \alpha_1 X(t) - \alpha_2 X(t)y(t), \;\; X(0) = 2 \\ y'(t) &= -\beta_1 y(t) + \beta_2 X(t)y(t), \;\; y(0) = 2 \end{aligned}\right\} \quad (17a)$$

with

$$\alpha_1 = \alpha_2 = -t\,, \beta_1 = \beta_2 = t. \quad (17b)$$

The exact solution to the system of equation in (17a) are given by:

$$X(t) = \frac{2}{2 - e^{\frac{t^2}{2}}}\,, \;\; y(t) = \frac{2}{2 - e^{\frac{t^2}{2}}}$$

Now, applying the Akbari-Gangi rule, we substitute (15) into (17a) to obtain

$$\left.\begin{aligned} \textstyle\sum_{i=0}^{n} a_i t^i &= \left(\alpha_1 \textstyle\sum_{i=0}^{n} a_i t^i - \alpha_2 \textstyle\sum_{i=0}^{n} a_i t^i * \textstyle\sum_{i=0}^{n} b_i t^i \right) \\ \textstyle\sum_{i=0}^{n} b_i t^i &= \left(-\beta_1 \textstyle\sum_{i=0}^{n} b_i t^i + \beta_2 \textstyle\sum_{i=0}^{n} a_i t^i * \textstyle\sum_{i=0}^{n} b_i t^i \right) \end{aligned}\right\} \quad \textbf{(18)}$$

Equation (18), when choosing $n = 6$ substituting the values given in (17b), to obtain

$$f\big(x(t)\big) = -t^{13}a_6b_6 - t^{12}(a_5b_5 + 6a_6) - t^{11}(a_4b_6 + a_6b_4 + 6a_5) - t^{10}(a_3b_6 + a_5b_4 + a_6b_3 + 6a_4) - t^9(a_2b_6 + a_4b_4 + a_5b_3 + a_6b_2 + 6a_3) - t^8(a_1b_6 + a_3b_4 + a_4b_3 + a_5b_2 + a_6b_1 + 6a_2) - t^7(a_0b_6 + a_2b_4 + a_3b_3 + a_4b_2 + a_5b_1 + a_6b_0 + 6a_1 - a_6) - t^6(a_1b_4 + a_2b_3 + a_3b_2 + a_4b_1 + 6a_5b_0 + 6a_0 - a_5) - t^5(a_0b_4 + a_1b_3 + a_2b_2 + a_3b_1 + a_4b_0 + a_4 - 6a_6) - t^4(a_0b_3 + a_1b_2 + a_2b_1 + a_3b_0 - a_3 - 5a_5) - t^3(a_0b_2 + a_1b_1 + a_2b_0 - a_2 - 4a_4) - t^2(a_0b_1 + a_1b_0 - a_1 - 3a_3) - t(a_0b_0 - a_0 - 2a_2) + a_1 = 0 \quad (19)$$

$$g\big(y(t)\big) = -t^{13}a_6b_6 - t^{12}(a_5b_5 + 6a_6) - t^{11}(a_4b_6 + a_6b_4 + 6a_5) - t^{10}(a_3b_6 + a_5b_4 + a_6b_3 + 6a_4) - t^9(a_2b_6 + a_4b_4 + a_5b_3 + a_6b_2 + 6a_3) - t^8(a_1b_6 + a_3b_4 + a_4b_3 + a_5b_2 + a_6b_1 + 6a_2) - t^7(a_0b_6 + a_2b_4 + a_3b_3 + a_4b_2 + a_5b_1 + a_6b_0 + 6a_1 - a_6) - t^6(a_1b_4 + a_2b_3 + a_3b_2 + a_4b_1 + 6a_5b_0 + 6a_0 - a_5) - t^5(a_0b_4 + a_1b_3 + a_2b_2 + a_3b_1 + a_4b_0 + a_4 - 6a_6) - t^4(a_0b_3 + a_1b_2 + a_2b_1 + a_3b_0 - a_3 - 5a_5) - t^3(a_0b_2 + a_1b_1 + a_2b_0 - a_2 - 4a_4) - t^2(a_0b_1 + a_1b_0 - a_1 - 3a_3) - t(a_0b_0 - a_0 - 2a_2) + a_1 = 0 \quad (20)$$

The constant coefficients of Equation (19) and (20), namely $\{a_0, \dots, a_6 \; and \; b_0, \dots, b_6\}$, can be calculated by applying the initial conditions.

$$x(t=0) = 2 \to a_0 = 2, \quad y(t=0) = 2 \to b_0 = 2 \quad (21)$$

where the remaining coefficients are calculated by applying the initial conditions to both Equation (19) and (20) and their derivatives as follows:

$$f\big(x(t=0)\big): a_1 = 0,$$
$$g\big(y(t=0)\big): b_1 = 0,$$
$$f'(x(t=0)): -a_0b_0 + a_0 + 2a_2 = 0,$$
$$g'(y(t=0)): -a_0b_0 + b_0 + 2b_2 = 0,$$
$$f''\big(x(t=0)\big): -2a_0b_1 - 2a_1b_0 + 2a_1 + 6a_3 = 0,$$
$$g''\big(y(t=0)\big): -2a_0b_1 - 2a_1b_0 + 2b_1 + 6b_3 = 0,$$
$$f'''\big(x(t=0)\big): -6a_0b_2 - 6a_1b_1 - 6a_2b_0 + 6a_2 + 24a_4 = 0,$$
$$g'''\big(y(t=0)\big): -6a_0b_2 - 6a_1b_1 - 6a_2b_0 + 6b_2 + 24b_4 = 0,$$
$$f''''\big(x(t=0)\big): -24a_0b_3 - 24a_1b_2 - 24a_2b_1 - 24a_3b_0 + 24a_3 + 120a_5 = 0,$$
$$g''''\big(y(t=0)\big): -24a_0b_3 - 24a_1b_2 - 24a_2b_1 - 24a_3b_0 + 24b_3 + 120b_5 = 0,$$
$$f'''''\big(x(t=0)\big): -120a_0b_4 - 120a_1b_3 - 120a_2b_2 - 120a_3b_1 - 120a_4b_0 + 120a_4 + 720a_6 = 0,$$
$$g'''''\big(y(t=0)\big): -120a_0b_4 - 120a_1b_3 - 120a_2b_2 - 120a_3b_1 - 120a_4b_0 + 120b_4 + 720b_6 = 0,$$

Using Maple, the values of the unknown constant a_i and b_i were found by solving the above equations, which are of the following form:

$$a_1 = b_1 = 0\,, a_2 = b_2 = 1\,, a_3 = b_3 = 0, a_4 = b_4 = \frac{3}{4}\,, a_5 = b_5 = 0\,, \quad and \quad a_6 = b_6 = \frac{13}{24}$$

Substituting these into Equation (15), we obtain the following approximate solution

$$x(t) = y(t) = 2 + t^2 + 0.750000t^4 + 0.541666t^6 \qquad (22)$$

After applying the external adjustment to accelerate the solution in Equation (22), we obtain the solution to system (17a):

$$x_{[6,6]}(t) = y_{[6,6]}(t) = \frac{\left(t^2+2\right)\left(t^2+2+\left(\frac{3}{4}\right)t^4+\left(\frac{13}{24}\right)t^6\right)-\left(t^2+2+\left(\frac{3}{4}\right)t^4\right)^2}{-\left(\frac{3}{4}\right)t^4+\left(\frac{13}{24}\right)t^6}$$

Example 2: The second model takes into account the fact the immune system in this model is not of direct therapeutic importance. Cancer cells are constantly subjected to ablation or treatment, which does not directly affect immune system activity. The presence of cancer cells available to the immune system indirectly reduces the efficiency of the immune system. Furthermore, the number of cancer cells is expected to increase according to a logistic model [16], which represents the following system:

$$\left.\begin{array}{l} X(t) = X(t)\big(1 - X(t)\big) - bz(t) - rX(t), \;\; X(0) = 0.5 \\ y(t) = cz(t) - ey(t), \;\; y(0) = 0.3 \end{array}\right\} \qquad (23a)$$

$$z(t) = \frac{X(t)y(t)}{X(t)+y(t)}$$

Numerical values for model (23a) we take

$$b = 0.8\,,\; c = 0.2\,,\; e = 0.5\,,\; r = 0.9 \qquad (23b)$$

Now, applying the Akbari-Gangi rule, we substitute (15) into (23a) to obtain

$$\left.\begin{array}{l} \sum_{i=0}^{n} a_i t^i = \left(\sum_{i=0}^{n} a_i t^i \left(1 - \sum_{i=0}^{n} a_i t^i\right) - bz(t) - r\sum_{i=0}^{n} a_i t^i\right) \\ \sum_{i=0}^{n} b_i t^i = \left(cz(t) - e\sum_{i=0}^{n} b_i t^i\right) \end{array}\right\} \qquad (24)$$

where

$$z(t) = \frac{\sum_{i=0}^{n} a_i t^i \sum_{i=0}^{n} b_i t^i}{\sum_{i=0}^{n} a_i t^i + \sum_{i=0}^{n} b_i t^i}$$

Equation (24), when choosing $n = 3$ Substituting the values given in (23b), to obtain

$$f\big(x(t)\big) := 3t^2a_3 + 2ta_2 + a_1 - (t^3a_3 + t^2a_2 + ta_1 + a_0)(-t^3a_3 - t^2a_2 - ta_1 - a_0 + 1) + 0.8\,u + 0.9(t^3a_3 + t^2a_2 + ta_1 + a_0) = 0 \qquad (25)$$

$$g\big(y(t)\big) := 3t^2b_3 + 2tb_2 + b_1 - 0.2\,u + 0.5\,(t^3b_3 + t^2b_2 + tb_1 + b_0) = 0 \qquad (26)$$

where

$$u = \frac{(t^3a_3+t^2a_2+ta_1+a_0)(t^3b_3+t^2b_2+tb_1+b_0)}{(t^3a_3+t^2a_2+ta_1+a_0)+(t^3b_3+t^2b_2+tb_1+b_0)}$$

The constant coefficients of Equations (25) and (26), namely $\{a_0, \dots, a_3 \; and \; b_0, \dots, b_3\}$, can be calculated by applying the initial conditions

$$x(t=0) = 0.5 \to a_0 = 0.5, \quad y(t=0) = 0.3 \to b_0 = 0.3 \qquad (27)$$

where the remaining coefficients are calculated by applying the initial conditions to both Equation (25) and (26) and their derivatives as follows:

$$f\big(x(t=0)\big):\; a_1 - a_0(1-a_0) + \frac{0.8a_0b_0}{a_0+b_0} = 0$$

$$g\big(y(t=0)\big): b_1 - \frac{0.2a_0b_0}{a_0+b_0} + 0.5b_0 = 0$$

$$f'\big(x(t=0)\big): 2a_2 - a_1(1-a_0) + a_0a_1 + 0.8\left(\frac{a_2b_0}{a_0+b_0} + \frac{a_1b_1}{a_0+b_0} - \frac{a_1b_0(a_1+b_1)}{a_0+b_0}\right) + 0.9a_1 = 0$$

$$g'\big(y(t=0)\big): 2b_2 - 0.2\left(\frac{a_1b_0}{a_0+b_0} - \frac{a_0b_1}{a_0+b_0} + \frac{a_0b_0(a_1+b_1)}{(a_0+b_0)^2}\right) + 0.5b_1 = 0,$$

$$f''\big(x(t=0)\big): 6a_3 - 2a_2(1-a_0) + a_1^2 + 2a_0a_2 + 0.6\left(\frac{a_1b_0}{a_0+b_0} + \frac{a_0b_1}{a_0+b_0} - \frac{a_0b_0(a_1+b_1)}{(a_0+b_0)^2} + \frac{a_0b_2}{a_0+b_0} - \frac{a_0b_1(a_1+b_1)}{(a_0+b_0)^2} + \frac{a_0b_0(a_1+b_1)^2}{(a_0+b_0)^3}\right) - 0.8\frac{a_0b_0(2a_0+2b_2)}{(a_0+b_0)^2} + 1.8a_2 = 0$$

$$g''\big(y(t=0)\big): 6b_3 - \ 0.4\left(\frac{a_2b_0}{a_0+b_0} - \frac{a_1b_1}{a_0+b_0} + \frac{a_1b_0(a_1+b_1)}{(a_0+b_0)^2} - \frac{a_0b_2}{a_0+b_0} - \frac{a_0b_1(a_1+b_1)}{(a_0+b_0)^2} + \frac{a_0b_0(a_1+b_1)^2}{(a_0+b_0)^3}\right) + \ 0.2\frac{a_0b_0(2a_1+2b_1)}{(a_0+b_0)^2} + 1.0b_2 = 0\,,$$

Using Maple, the values of the unknown constant a_i and b_i were found by solving the above equations, which are of the following form:

$a_1 = -0.35000,\ b_1 = -0.112500\,,\ a_2 = 0.194765,\ b_2 = 0.018808\,,\ a_3 = -0.107288,\ b_3 = -0.001128,$

Substituting these into Equation (15), we obtain the following approximate solution

$$\left.\begin{aligned} x(t) &= 0.5 - 0.35000t + 0.194765t^2 - 0.107288t^3 \\ y(t) &= 0.3 - 0.112500t + 0.018808t^2 \ - 0.001128\,t^3 \end{aligned}\right\} \qquad (28)$$

After applying the external adjustment to accelerate the solution in Equation (28), we obtain the solution to system (23a):

$$x_{[3,3]}(t) = \frac{(0.5-0.35t)\left(0.5-0.35t+0.19476t^2-0.10728t^3\right)-\left(0.5-0.35t+0.19476t^2\right)^2}{-0.19476t^2-0.10728t^3}$$

$$y_{[3,3]} = \frac{(0.3-0.1125t)\left(0.3-0.1125t+0.018808t^2-0.0011284t^3\right)-\left(0.3-0.1125t+0.018808et^2\right)^2}{-0.018808t^2-0.0011284et^3}$$

Example 3: This model describes the ordinary differential equation of the tumor-immune model, which describes the interactive dynamics between cancer cells and immune responses. In this model, time-varying values are taken into account for: the growth rate of cancer cells; the effectiveness of immune cells in attacking and eliminating cancer cells; the death rate of immune cells; and the rate of activation and proliferation of immune cells in response to the presence of the tumor. It is important to note that great attention must be paid to the fact that the parameters of this problem are time-dependent, in order to obtain a system of recurrence equations appropriate for the model that reflects the dynamic and time-dependent nature of both tumor development and fluctuations in the immune response. In other works [18], [21], the mathematical model representing the interaction between cancer cells and therapy can be expressed by the following ordinary differential equation.

$$\left.\begin{aligned} X'(t) &= \alpha_1 X(t) - \alpha_2 X(t)y(t),\ \ X(0) = -4 \\ y'(t) &= -\beta_1 y(t) + \beta_2 X(t)y(t),\ \ y(0) = 4 \end{aligned}\right\}, \qquad (29a)$$

with

$$\alpha_1 = 4 + \tan(t), \alpha_2 = \exp(2t)\ , \beta_1 = -2\ , \beta_2 = \cos(t), \qquad (29b)$$

The exact solution to the system of equation in (17a) are given by:

$$X(t) = \frac{-4}{\cos(t)}\ ,\ \ y(t) = 4\cos(-2t)$$

Now, applying the Akbari-Gangi rule, we substitute (15) into (29b) to obtain

$$\left.\begin{aligned} \textstyle\sum_{i=0}^{n} a_i t^i &= \left(\alpha_1 \textstyle\sum_{i=0}^{n} a_i t^i - \alpha_2 \textstyle\sum_{i=0}^{n} a_i t^i * \textstyle\sum_{i=0}^{n} b_i t^i\right) \\ \textstyle\sum_{i=0}^{n} b_i t^i &= \left(-\beta_1 \textstyle\sum_{i=0}^{n} b_i t^i + \beta_2 \textstyle\sum_{i=0}^{n} a_i t^i * \textstyle\sum_{i=0}^{n} b_i t^i\right) \end{aligned}\right\} \qquad (30)$$

Equation (30), when choosing $n = 4$ substituting the values given in (29b), to obtain

$$f\big(x(t)\big) := \ 4t^3a_4 + 3t^2a_3 + 2ta_2 + a_1 - (4 + tan(t))(t^4a_4 + t^3a_3 + t^2a_2 + ta_1 + a_0) + exp(2t)(t^4a_4 + t^3a_3 + t^2a_2 + ta_1 + a_0)(t^4b_4 + t^3b_3 + t^2b_2 + tb_1 + b_0) \ = \ 0 \qquad (31)$$

$$g\big(y(t)\big) := \ 4t^3b_4 + 3t^2b_3 + 2tb_2 + b_1 - 2t^4b_4 - 2t^3b_3 - 2t^2b_2 - 2tb_1 - 2b_0 - \cos(t)\,(t^4a_4 + t^3a_3 + t^2a_2 + ta_1 + a_0)(t^4b_4 + t^3b_3 + t^2b_2 + tb_1 + b_0) \ = \ 0 \qquad (32)$$

The constant coefficients of Equation (31) and (32), namely $\{a_0, \dots, a_3\ and\ b_0, \dots, b_3\}$, can be calculated by applying the initial conditions

$$x(t=0) = -4 \to a_0 = -4, \quad y(t=0) = 4 \to b_0 = 4 \qquad (33)$$ where the remaining coefficients are calculated by applying the initial conditions to both Equation (31) and (32) and their derivatives as follows:

$$f\big(x(t=0)\big) : :\ a_0b_0 - 4a_0 + a_1 = \ 0$$

$$g\big(y(t=0)\big)::\ -a_0b_0-2b_0+b_1=0$$
$$f'\big(x(t=0)\big):2a_0b_0+a_0b_1+a_1b_0-a_0-4a_1+2a_2=0$$
$$g'\big(y(t=0)\big):-a_0b_1-a_1b_0-2b_1+2b_2=0,$$
$$f''\big(x(t=0)\big):4a_0b_0+4a_0b_1+2a_0b_2+4a_1b_0+2a_1b_1+2a_2b_0-2a_1-8a_2+6a_3=0$$
$$g''\big(y(t=0)\big):2a_0b_0-2a_0b_2-2a_1b_1-2a_2b_0-4b_2+6b_3=0\,,$$
$$f'''\big(x(t=0)\big):8a_0b_0+12a_0b_1+12a_0b_2+6a_0b_3+12a_1b_0+12a_1b_1+6a_1b_2+12a_2b_0+6a_2b_1\ 8a_2+6a_3b_0-2a_0-6a_2-24a_3+24a_4=0,$$
$$g'''\big(y(t=0)\big):3a_0b_1-6a_0b_3+3a_1b_0-6a_1b_2-6a_2b_1-6a_3b_0-12b_3+24a_4=0$$

Using Maple, the values of the unknown constant a_i and b_i were found by solving the above equations, which are of the following form:

$$a_1=0,\quad b_1=4\,,\quad a_2=-2,\quad b_2=8\,,\quad a_3=0,\quad b_3=-\frac{16}{3},\quad a_4=-\frac{5}{6},\quad b_4=\frac{8}{3}$$

Substituting these into Equation (15), we obtain the following approximate solution

$$\left.\begin{aligned}x(t)&=-4-2t^2-0.8333333333t^4\\ y(t)&=4-8t+8t^2-5.333333333\,t^3+2.666666667\,t^4\end{aligned}\right\}\qquad(34)$$

After applying the external adjustment to accelerate the solution in Equation (34), we obtain the solution to system (29a):

$$x_{[4,4]}(t)=\frac{16+8t^2+\left(\frac{10}{3}\right)t^4-\left(-2t^2-4\right)^2}{2t^2-\left(\frac{5}{6}\right)t^4}\qquad y_{[4,4]}=\frac{\left(8t^2-8t+4\right)\left(8t^2-8t+4-\left(\frac{16}{3}\right)t^3+\left(\frac{8}{3}\right)t^4\right)-\left(8t^2-8t+4-\left(\frac{16}{3}\right)t^3\right)^2}{\left(\frac{16}{3}\right)t^3+\left(\frac{8}{3}\right)t^4}$$

3. Results and Discussion

Table 1. Comparison of error, CUP time, and order among the AGAM, AGPM, AGM, and ADM methods, when $t \in [0,1]$ for Example 1.

Functions	Error	AGAM	AGPM	AGM	ADM [16]
$x(t)=y(t)$	L_2	0.001321932973	0.004164659849	0.2814243556	0.9305855326
	L_∞	0.006515496	0.020801213	1.401817837	11.81992953
	cup	0.015	0.015	0.016	0.032
	order	0.972	0.878	0.820	------

Based on the results presented in Table (1), it can be concluded that the AGAM methods is the optimal and moat effective method for solving the cancer and immune dynamics models under study, significantly outperforming the traditional AGM and ADM methods and achieving a substantial improvement over the AGPM method. This confirms the importance of the modification introduced in this study (using the external Atkin modification) in developing a robust mathematical tool capable of handling the nonlinear complexities of these biological systems.

Table 2. Comparison of error, CUP time, and order among the AGAM ,AGPM, AGM, and ADM methods, when $t \in [0,5]$ for Example 2.

Functions	Error	AGAM	AGPM	AGM	ADM [18]
x(t)	L_2	0.00004546821	0.010993560	12.331800	12.33086147

	L_∞	0.0004538867	0.009627453	13.411020	13.41000000
	cup	0.016	0.015	0.032	0.031
	order	0.671	0.593	0.342	--------
y (t)	L_2	0.00015311570	0.017978380	0.1297084	0.129722317
	L_∞	0.0016294452	0.012261689	0.1410598	0.141075000
		0.016	0.015	0.032	0.031
	L_∞	0.695	0.589	0.551	-------

The results in Table (2) confirm the sustained superior performance of the AGAM method when analyzing the system functions separately to solve the problems under study, significantly outperforming the traditional AGM and ADM methods, and achieving a substantial improvement compared to the AGPM method. This confirms the importance of the modification introduced by the study in developing a powerful mathematical tool capable of handling the numerical complexities of these systems**.**

Table 3- Comparison of error, CUP time, and order among the AGAM, AGPM, AGM, and ADM methods, when $t \in [0,5]$ for Example 3.

Functions	Error	AGAM	AGPM	AGM	ADM [18]
x(t)	L_2	0.0009336806348	0.02399586585	0.02248765066	0.06355437342
	L_∞	0.025308557	0.596737128	0.569929539	1.403262872
	cup	0.016	0.015	0.016	0.015
	order	0.888	0.762	0.716	--------
y (t)	L_2	0.01437782998	0.9644026933	0.9872679555	0.2027234285
	L_∞	0.2586588676	8.000000000	8.736596206	3.458658867
	cup	0.016	0.015	0.016	0.015
	order	0.705	0.549	0.374	--------

Table (3) highlights the superiority of the AGAM method over the traditional AGM, ADM, and AGPM methods in terms of accuracy and stability in solving the problems under study, which proves the significance of the modification introduced by the study in developing a robust mathematical tool capable of handling the numerical complexities of these systems.

where q_A the order of accuracy, is computed using the formula [34],

$$q_A = \frac{\ln(\frac{O_2}{O_1})}{\ln 2}$$

where the errors are described as

$$O_1 = |\mu_e - \mu_f| \ , \qquad O_2 = |\mu_e - \mu_c|$$

In this case, μ_e stands for the exact solution, μ_f for the solution with the fine grid, and μ_c for the solution with the coarser grid.

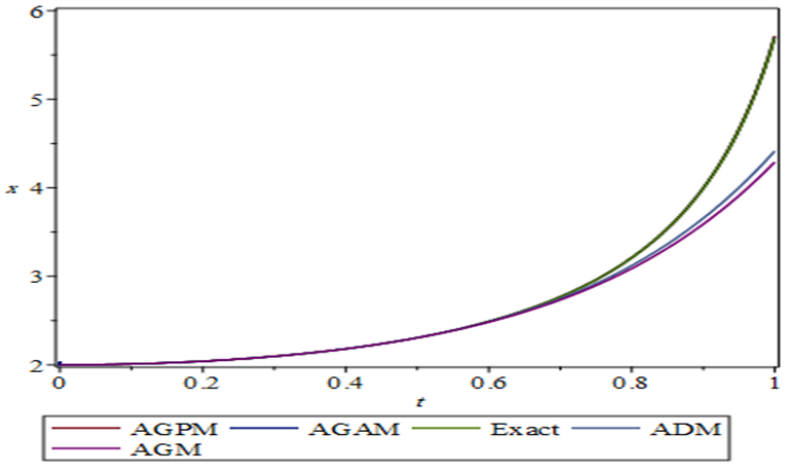

Figure 1. Comparison between the approximate solution obtained using AGAM, AGPM, and AGM, with the exact solution for Example 1 $x(t) = y(t)$.

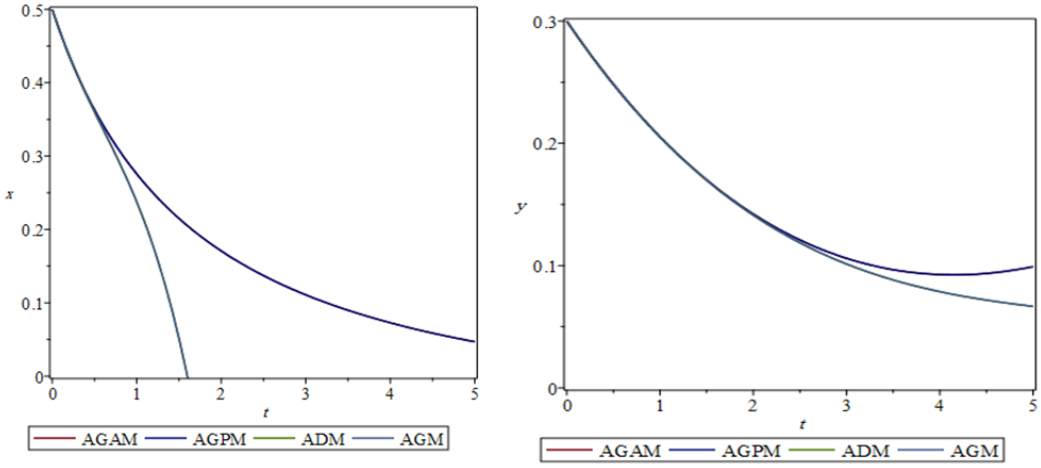

Figure 2. Comparison between the approximate solution obtained using AGAM, AGPM, and AGM, for Example 2 $x(t)$ *and* $y(t)$.

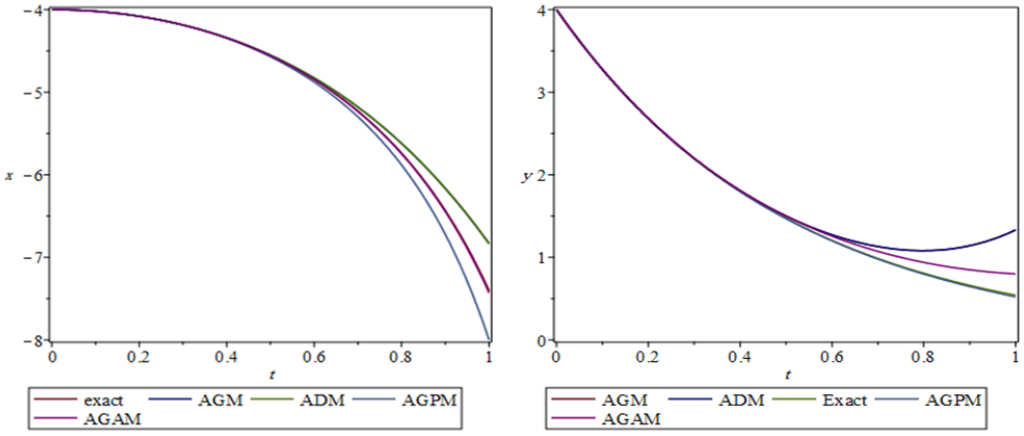

Figure 3. Comparison between the approximate solution obtained using AGAM, AGPM, and AGM, with the exact solution for Example 3 $x(t)$ *and* $y(t)$.

Analysis of the SAGAM convergence

This section illustrates how the analytical approximate solutions obtained using the AGAM method converge when solving systems (17a), (23a), and (29a).

Consider the following system of equations

$$\left.\begin{aligned} x &= F(x,y) \\ y &= G(x,y) \end{aligned}\right\}$$

where F and G are nonlinear effects. The solution using this current approach is equivalent to the following sequence

$$S_n = \sum_{j=0}^{n} x_j = \sum_{j=0}^{\infty} a_j \frac{t^j}{(j)^!}$$

$$K_n = \sum_{j=0}^{n} y_j = \sum_{j=0}^{\infty} b_j \frac{t^j}{(j)^!}$$

Definition [29]: For every n ∈ N ∪ {0},we define

$$p_j = \begin{cases} \dfrac{\|x_{j+1}\|}{\|x_j\|} \\ 0 \end{cases}, \quad \|x_j\| \neq 0 \quad and \quad q_j = \begin{cases} \dfrac{\|y_{j+1}\|}{\|y_j\|} \\ 0 \end{cases}, \quad \|y_j\| \neq 0$$

In the first example, for t∈[0,0.9] and x_1=x_2, we obtain.

$$p_1 = q_1 = \frac{\|x_{1_1}\|}{\|x_{1_0}\|} = 0.1811215062$$

$$p_2 = q_2 = \frac{\|x_{1_2}\|}{\|x_{1_1}\|} = 0.8201250002e-1$$

$$p_3 = q_3 = \frac{\|x_{1_3}\|}{\|x_{1_2}\|} = 0.3991953699e-1$$

In the second example, for t∈[0,1] and x_1, x_2, we get

$$p_1 = \frac{\|x_{1_1}\|}{\|x_{1_0}\|} = 0.4041451884 \qquad q_1 = \frac{\|x_{2_1}\|}{\|x_{2_0}\|} = 0.2165063509$$

$$p_2 = \frac{\|x_{1_2}\|}{\|x_{1_1}\|} = 0.1742031118 \qquad q_2 = \frac{\|x_{2_2}\|}{\|x_{2_1}\|} = 0.2803731101\text{e}-1$$

$$p_3 = \frac{\|x_{1_3}\|}{\|x_{1_2}\|} = 0.8110210476\text{e}-1 \qquad q_3 = \frac{\|x_{2_3}\|}{\|x_{2_2}\|} = 0.1421146419\text{e}-2$$

In the third example, for t∈[0,0.7] and x_1, x_2, we get

$$p_1 = \frac{\|x_{1_1}\|}{\|x_{1_0}\|} = 0.1811215062 \qquad q_1 = \frac{\|x_{2_1}\|}{\|x_{2_0}\|} = 1.039230485$$

$$p_2 = \frac{\|x_{1_2}\|}{\|x_{1_1}\|} = 0.4556250001e-1 \qquad q_2 = \frac{\|x_{2_2}\|}{\|x_{2_1}\|} = 0.7244860247$$

$$p_3 = \frac{\|x_{1_3}\|}{\|x_{1_2}\|} = 0.2234694226 \qquad q_3 = \frac{\|x_{2_3}\|}{\|x_{2_2}\|} = 0.2234694226$$

Analysis of Stability

Any dynamical system's evolution, a stable phenomenon, can be used to characterize its future state. When attempting to study the behavior of the system under investigation, stability is typically the first and most crucial step to address. The objective of this section is to analyze the stability of the solutions obtained using the proposed AGAM method, which is used to solve cancer and immune dynamics systems. For most dynamical systems, the equilibrium points of the system of nonlinear differential equations have a significant impact on the model's analysis.

Figure 4 (A) when both x_1, x_2 are greater than zero, let me know if you need it merged with the previous sentence to form a full paragraph (1,1). We start with very small numbers of both cancer cells and immune cells. We observe from the figure that the number of cancer cells increases first because the immune response is still weak. After a while, the number of immune cells increases in response to the presence of cancer cells. This leads to a decrease in cancer cells, as seen in the figure. As the number of cancer cells decreases, the system begins to return to its initial state as the immune response gradually subsides. Then the process begins to repeat itself. As t→0 approaches the critical point (0,0), some solutions appear in Figure 4(B). We have observed that the critical point is unhinged and

the solutions are unhinged in the vicinity of this point (0,0) (the absence of both cancer and immune cells). If the critical point is stable, this attracts solutions toward it, indicating complete tumor eradication. Therefore, the stability of this point is very important in cancer treatment. However, reaching this point is difficult to achieve in practice if you want it as a complete sentence is an unstable equilibrium point in most realistic models. Complete tumor eradication requires intensive therapeutic strategies that drive the system toward this stable point. In Figure 4 (c). Let me know if you need it connected to the previous sentences (0,0) when t→∞ , indicating that the immune system has gained control over the tumor. As anticipated, we see that the route corresponding to our own initial condition likewise moves in the direction of the critical point, which is stable. Stated differently, the solutions are stable around this point. In the meantime, because the point (-2, 3.5) is unstable, the solutions are unstable close to it.

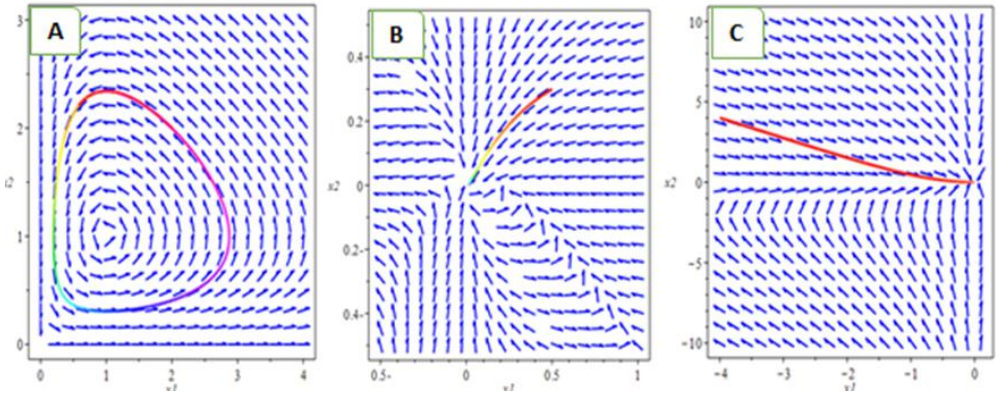

Figure 4. The direction and trajectory fields for systems (17a), (23a), and (29a), using the coefficient values $\alpha_1 = \alpha_2 and\ \beta_1 = \beta_2 in\ (A), \alpha_1 = -4, \alpha_2 = 2, \beta_1 = 7, \beta_2 = 2\ in\ (B)$.

4. Conclusion

A new analytical approximate method for solving cancer-immune dynamics systems was successfully developed and applied in this study. Compared to existing methods such as the ADM, AGPM, HPM, and AGM, The numerical outcomes from the cases under study demonstrate how accurate the new method is. Additionally, we found that the new approach is a useful mathematical tool for resolving models involving constant or variable coefficients that describe how cancer cells interact with the immune system. Additionally, it is an effective method for resolving initial and border value issues that come up in a variability of applied science domains, including computational biology, physics, mechanics, and applied mathematics. The tables and graphs showed that, in comparison to other approaches, the suggested method is distinguished by quick convergence and excellent accuracy. Moreover, the new method can be considered an extension of the AGM approach.

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