International Journal of Recent Technology and Engineering (IJRTE)
ISSN: 2277-3878 (Online), Volume-8 Issue-6, March 2020

A Sublime Technique to Solve DNA-Repair Model

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Abstract: ***Deoxyribonucleic acid (DNA) is an essential macromolecule for all known varieties of life and its damage is a life-threatening structure. The DNA double-strand breaks (DSBs) are considered as one of the most rigorous kinds of DNA damage and an error in its repairing mechanism stimulates cancer and also causes lethality in cells with various genetic disorders.***

In this article, we have exhibited a numerical solution of an ordinary differential equation based biological model to overcome the error for estimating the average number of DSBs per cell time. This model is called DNA repair Model (DRM) and to solve this model a Modified Adomian decomposition method with new polynomials (MADMNP) is applied. The convergence of the aforesaid method is established and the order of error is also dissertated. To solve DRM, this method provides an improved scheme to estimate the average number of DSBs per cell time in comparison to Adomain decomposition method (ADM) and Laplace ADM with Pad`e approximation (LADM-Pad`e). In this respect, a comparison table and a two-dimensional comparison graph are provided by considering a numerical example.

Keywords: Deoxyribonucleic acid, Double-strands breaks, Adomian decomposition method, New class of Adomian polynomials, Riccati differential equation.

I. INTRODUCTION

Genome integrity of an organism has the most important role in his successful healthy life and several immunological, developmental as well other health issues are also associated with it. Therefore, disintegration of genome has various lethal effects on the organism. One known major factor to disintegrate the genome is DNA double-strand breaks (DSBs). DSBs are a form of dangerous lesions which have the both broken strands of DNA duplex structure. It is also considered as a leading operator element for life threatening cancer [1], [2]. DSBs can be originated by two major ways namely exogenous and endogenous. Exogenous sources are ionizing radiation (IR) and some chemicals while endogenous sources like DNA replication, V (D)J recombination and meiotic exchange may arise DSBs [3]. Various DSB repair mechanisms are evolved by organisms to prevent their lethal effects. Unrepaired DSBs may cause of induced apoptosis, cell cycle arrest or mitotic cell death [4] while incorrectly repaired DSBs may drive cancer by inversions, deletions or translocation [5], [6]. Two extensively studied pathways to repair DSBs are homologous recombination (HR) and non-homologous end-joining (NHEJ) [7]. NHEJ characterized by blocking of 5 end resection and close vicinity of heterodimer protein Ku70-Ku80 with DSB ends.

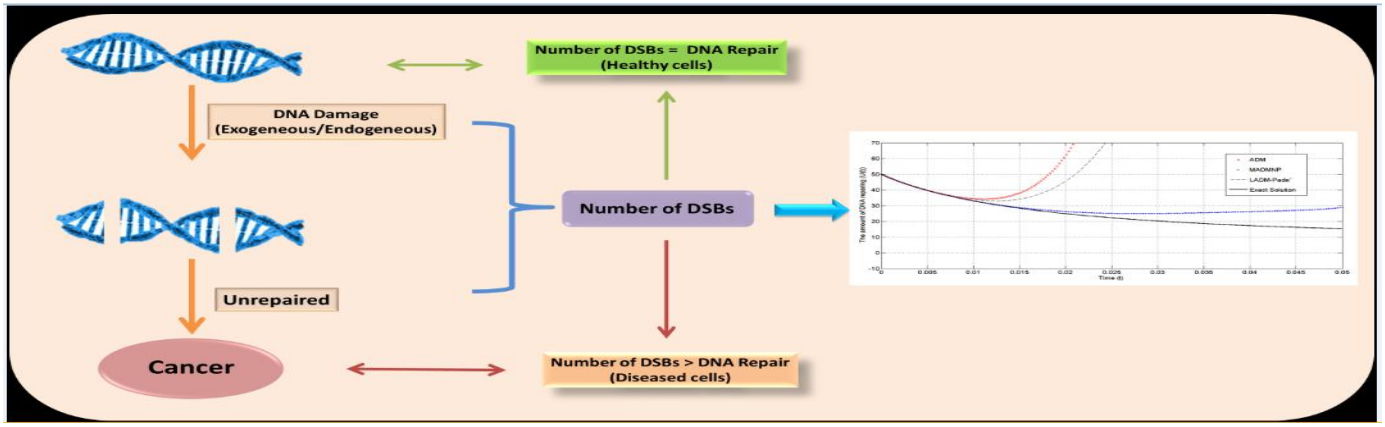

Fig.1. Schematic representation of the Riccati differential equation-based solution of DNA-repair model.

In NHEJ, DSB ends are directly ligated and sometimes errors make small deletions, insertions and substitutions at breaks while translocations are made by joining of DSBs from different parts of genome [8].

On the other hand, HR is considered as error free and commenced during the re-sectioning of DSBs by enzymes like helicases and nucleases. It creates 3 single stranded DNA overhangs and a complex structure forms with RAD51 recombines. Consequently, in repair DNA synthesis, a template homologous duplex DNA molecule is evaded by this complex structure [9].

Manuscript received on February 10, 2020.
Revised Manuscript received on February 20, 2020.
Manuscript published on March 30, 2020.
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The approach of mathematical modeling to handle such biological problems is a supplementary venture and various associated models of biological descriptions are presented time to time, see [10]–[12]. In addition, a few comprehensive mathematical models are also designed for DSBs [13]–[15]. However, DSBs are remaining a puzzle and the presented solutions of aforesaid models need more efficient solutions. Therefore, here still a requirement for further advancement and more specific mathematical approach to deal with DSBs in an impressive manner. For this purpose, we are using the average number of DSBs per cell at time *t* derived as elsewhere [16], [17],

$$U'(t)=\delta R-\frac{1}{\tau}U(t)-\gamma U^2(t),\quad U(a)=U_a, \tag{1}$$

Where $U(t)$ average number of DSBs per cell at time *t*, δ is average number of DSBs induced per unit dose, *R* is radiation dose rate, τ is a repair time constant, and γ is a binary reaction rate constant in the sense of mass-action chemical kinetics.
More apparently, the above mentioned DRM is a form of very common nonlinear differential equation of mathematics named Riccati differential equation. Whose closed form solution is not ingenious always. Therefore one may have to stand with the approximate solution of the discussed problem. Although there are a number of methods [18], [19] to find the approximate solution of such nonlinear problems. However, it is not essential that aforementioned methods, effective for the approximate solution of eq.(1). Therefore, a "Modified Adomian Decomposition Method with New Class of Adomian Polynomials" (MADMNP) is discussed which is a sublime technique to improve numerical solutions disposed by ADM and LADM-Pade`. This method have phenomenal accuracy and elegantly computed convergent series.
In this article, we discussed a DNA repair model (DRM), eq.(1), using a distinct ADM based approach. The approach is new to solve such kind of DRM, the discussed approach is significant because the most renowned methods are giving huge error in the comparison of MADMNP. As well, DSBs are analyzed with the MADM. In section 2, a modified Adomian decomposition method is discussed for DRM, given by (1). The convergence of this method is analyzed in section 3. In section 4, local error has been estimated for the presented approximated solution. Finally, concluding remarks are placed in section 5.

II. A MODIFIED ADOMIAN DECOMPOSITION METHOD WITH NEW POLYNOMIALS (MADMNP) FOR DRM

$$U(t)=U_a+\delta\int_a^t R(s)ds-\frac{1}{\tau}\int_a^t U(s)ds-\gamma\int_a^t U^2(s)ds. \tag{2}$$

Operator form of eq.(2) can be written as

$$U(t)=U_a+\delta\int_a^t R(s)ds-\frac{1}{\tau}\int_a^t U(s)ds-\gamma\int_a^t N(U)ds. \tag{3}$$

Basic assumption of ADM takes place with the consideration that the solution $U(t)$ and nonlinear term $U^2(t)=N(U)$ can be decomposed in an infinite series form

$$U(t)=\sum_{k=0}^{\infty}U_k(t), \tag{4}$$

$$N(U)=U^2(t)=\sum_{k=0}^{\infty}A_k(U_0,U_1,.....U_k). \tag{5}$$

Now, using eq.(4) and eq.(5) in eq.(3), recursive scheme can be defined as

$$\begin{aligned}&U_0(t)=U_a+\delta\int_a^t R(s)ds,\ and\\&U_k=-\frac{1}{\tau}\int_a^t U_{k-1}(s)ds-\gamma\int_a^t A_{k-1}(s)ds,\end{aligned} \tag{6}$$

Here U_a is germinated from the given initial condition, and A_i^s are defined as Adomina polynomials with a special class [20], such that

$$\begin{cases}A_0=A_0^{**}\\ \quad=N(U_0),\\ A_1=A_1^{**}\\ \quad=U_1N^{(1)}(U_0)+\frac{1}{2!}U_1^2N^{(2)}(U_0),\\ A_2=A_2^{**}\\ \quad=U_2N^{(1)}(U_0)+\frac{1}{2!}(2U_1U_2+U_2^2)N^{(2)}(U_0)+\frac{1}{3!}U_1^3N^{(3)}(U_0),\\ A_3=A_3^{**}\\ \quad=U_3N^{(1)}(U_0)+|\frac{1}{2!}(2U_1U_3+2U_2U_3+U_3^2)N^{(2)}(U_0)\\ \quad+\frac{1}{3!}(3U_1^2U_2+3U_2U_2^2+U_2^3)N^{(3)}(U_0)+\frac{1}{4!}U_1^4U_0N^{(4)}(U_0),\end{cases}$$

It is clear from the origination of Adomian polynomials that there is no unique definition for the Adomian polynomials as the Adomian series $\sum_{i=0}^{\infty}A_i$ is generalized by Taylor's series [21]. (Statement 1)
Here we define $\psi_k(t)$ as the k^{th} term approximation of the solution such that,

$$\psi_k(t)=\sum_{r=0}^{k}U_r(t),$$

where $\lim_{k\to\infty}\psi_k(t)=U(t)$.

III. CONVERGENCE OF DRM SOLVED BY MADMNP

This section explores theoretically the convergence of two series $\sum_{i=0}^{\infty}u_i$ and $\sum_{i=0}^{\infty}A_i$ for DRM. The section also exhibits an analysis of the error up the order of precision.

A. Convergence of Adomian's series of new polynomials

The convergence of a nonlinear dynamical system basically depends upon the assumption that a nonlinear operator must be contractive. Due to this consideration, a unique solution of the problem takes place, which is not possible in all the practical cases. Therefore a different approach [22] has been discussed for the convergence of DRM.

Theorem 1. *If eq.(4) supposed to be absolutely convergent also the nonlinear operator $N(U)$ is expressible in a series form eq.(5)with infinity radius of convergence, i.e.,*

$$N(U)=\sum_{I=0}^{\infty}N^{(i)}(0)\frac{U^i}{i!},|U|<\infty. \quad (7)$$

Then the series $\sum_{i=0}^{\infty}U_i$ *is the solution of eq.*(1).

Proof. Since the series defined in eq. (7) converges for any U (Using the hypothesis of radius of convergence). Also the series defined in eq.(4) is absolutely convergent with absolute convergence $\mathbb{U}_A<\infty$. Therefore using eq.(7), we have

$$N(U)=\sum_{I=0}^{\infty}N^{(i)}(0)\frac{\sum_{i=0}^{\infty}U_i}{i!},|U|<\infty. \quad (8)$$

Therefore in order to rearrange $N(U)$ we can write U^i as

$$U^i=\left(\sum_{i=0}^{\infty}U_i\right)^i=\sum_{j=0}^{\infty}\lambda_{ij}(U_0,U_1,.....U_j), \quad (9)$$

right hand side of eq.(9) can be proved through article, [23]. Now, eq.(8) can be written as

$$N(U)=\sum_{I=0}^{\infty}\left[\frac{N^{(i)}(0)}{i!}\sum_{i=0}^{\infty}\lambda_{ij}(U_0,U_1,.....U_j)\right],$$
$$=\sum_{i=0}^{\infty}\sum_{j=0}^{\infty}\frac{N^{(i)}(0)}{i!}\lambda_{ij}.$$

Since, $\sum_{j=0}^{\infty}\lambda_{ij}\le\mathbb{U}_A{}^i$, then $|N(U)|$ will be

$$|N(U)|\le\sum_{i=0}^{\infty}\left|\frac{N^{(i)}(0)}{i!}\right|\mathbb{U}_A^i,$$

which is convergent by the hypothesis of eq.(7). Now using rearrangement theorem [24], absolutely convergent series defined by $N(U)$, can be rearranged with the series $\sum_{i=0}^{\infty}A_i$. Therefore, in the contrast of the convergence of the series $\sum_{i=0}^{\infty}U_i$, we have to prove U_i's satisfy eq.(6). Now using, Statement 1 (Discussed above), we substitute $\sum_{i=0}^{\infty}U_i$, and $\sum_{i=0}^{\infty}A_i$ in eq.(3). it can be observed identically

$$\begin{cases}U_0(t)=U_\alpha+\delta\int_\alpha^t R(s)\,ds,\\ U_1(t)=\frac{1}{\tau}\int_\alpha^t U_0(s)\,ds-\gamma\int_\alpha^t A_0\,ds\\ \vdots\\ U_k(t)=-\frac{1}{\tau}\int_\alpha^t U_{K-1}(s)\,ds-\gamma\int_\alpha^t A_{k-1}\,ds.\end{cases} \quad (10)$$

Which is the relationship given in eq.(6), and the scheme discussed in eq.(6) is the solution of eq.(1).

B. Error Estimation

Error estimation of any numerical scheme depends on the number of solution components. In this section, we shall discuss, what will be the effect on error locally over a particular interval of time with the increase of series terms.
Let E is the maximum error, defined for the truncated series is,

$$E=\left|U-\sum_{r=0}^{k}U_r\right|$$
$$=\left|U-\sum_{r=k+1}^{\infty}U_r\right|.$$

Now, using eq.(5), we have

$$U_k=-\frac{1}{\tau}\int_\alpha^t U_{k-1}(s)ds-\gamma\int_\alpha^t A_{k-1}(s)ds, \quad (11)$$

It can be manifest that up to $\frac{N^{k+1}(U_0)(U-U_0)^{k+1}}{(n+1)!}$ terms in Taylor's series expansion of $N(U)$ about point U_0 gives the k^{th} Adomian polynomial $A_{k.}$ Therefore, there will be an error of order $(U-U_0)^{k+1}$ in the calculation of $A_{k.}$ Hence in eq.(11) the order of error of U_k will be equal to the order of error in A_{K-1},
Hereby, order of local error can be defined as,

$$E_{Local}=\left|\sum_{r=k+1}^{\infty}U_r\right|\equiv O(U-U_0)^{k+1}. \quad (12)$$

IV. APPLICATION

In this section, we demonstrate a numerical example based on the discussed theory.

Example 1. *Consider the DSBs per cell at time* t

$$U'(t)=150-5U-U^2,\ U(0)=50,\ 0\le t\le 0.05. \quad (13)$$

The exact solution of eq.(13) *is*

$$U(t)=\frac{130e^{25t}+120}{13e^{25t}-8}.$$

Solution. Now, using iterative scheme eq.(6), approximated series solution S_4 will be,

$$S_4(t)=\sum_{i=0}^{4}U_i(t),$$
$$=50-2600x+136500x^2-\ldots-\frac{4449462890625\times10^{16}}{74431}x^{31}.$$

For the further study of the proposed MADMNP, a comparison is made with ADM and LADM-Pade` in figure 1 and table 1.

Table 1: A comparison table of the absolute error (AE) functions with ADM, LADM, and MADMNP

t	Exact Solution	AE using ADM	AE using LADM-Pad`e	AE using MADMNP
0	50	0	0	0
0.01	33.0088	1.45638	0.942944	0.0984
0.02	24.8883	36.7988	20.6048	1.39011
0.03	20.2454	235.713	114.286	4.81608
0.04	17.3159	873.227	367.069	8.87806
0.05	15.3512	2409.95	879.377	12.2321

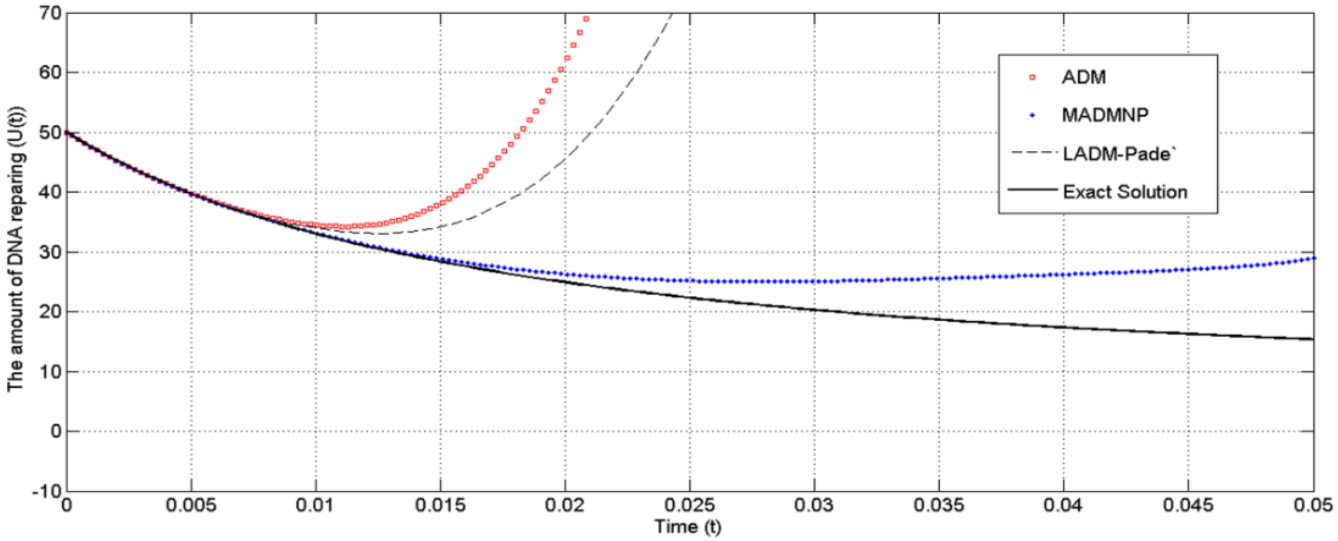

Fig. 2. A comparison graph between ADM, MADMNP, LADM-Pad`e, and Exact Solution with for k = 0 to 4.

V. RESULT AND DISCUSSION

DRM is one of the complicated and important biological problems, which has to be solved numerically. To solve this we have applied MADMNP. In example 1 a problem is considered and the average number of DSBs per cell time t are computed numerically in the interval $[0, 0.05]$ using ADM, LADM-Pade, and MADMNP. In table 1, absolute error calculations are shown for the solutions obtained by ADM, LADM-Pade`, and MADMNP with respect to per cell time $t$ from point 0 to 0.05 with time difference 0.01. For $t = 0.005$, figure 1 elaborates that the graphs of the obtained solution by ADM, LADM-Pade`, and MADMNP are identical and coincide with the exact solution. As well, for $t = 0.01$, the graphs of the solutions by ADM and LADM-Pade` start deviating from the exact solution, however, the graph of the solution by MADMNP is in the direction of exact solution. We see that the MADMNP improves the accuracy of the numerical solution of DRM in comparison to ADM and LADM-Pade for the given interval and converges to the exact solution.

VI. CONCLUSION

A different form of Adomian polynomials is used for computation of the components of the scheme given by eq.(6). This results as the MADMNP and applied to solve DRM. The main advantage of MADMNP is that it obtains a more explicit approximated solution in a given interval for DRM with the least number of components. The error analysis, comparison table, and solution graphs show that MADMNP results in the form of more promising results as compared to ADM and LADM-Pade`. As well, the convergence analysis of MADMNP is also discussed. In addition, the MADMNP can be applied in a suitably large interval by increasing the number of components.

ACKNOWLEDGMENT

The authors are thankful to Mr. Dharm Prakash Singh, (Research scholar, Department of Applied Mathematics, Gautam Buddha University, Greater Noida, 201310, India) for his valuable suggestions in manuscript writing and formatting.

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