Computers, Materials & Continua DOI: 10.32604/cmc.2023.029046 Article



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Numerical Procedure for Fractional HBV Infection with Impact of Antibody Immune

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 Received: 23 February 2022; Accepted: 28 April 2022

Abstract: The current investigations are presented to solve the fractional order HBV differential infection system (FO-HBV-DIS) with the response of antibody immune using the optimization based stochastic schemes of the Levenberg-Marquardt backpropagation (LMB) neural networks (NNs), i.e., LMBNNs. The FO-HBV-DIS with the response of antibody immune is categorized into five dynamics, healthy hepatocytes (H), capsids (D), infected hepatocytes (I), free virus (V) and antibodies (W). The investigations for three different FO variants have been tested numerically to solve the nonlinear FO-HBV-DIS. The data magnitudes are implemented 75% for training, 10%for certification and 15% for testing to solve the FO-HBV-DIS with the response of antibody immune. The numerical observations are achieved using the stochastic LMBNNs procedures for soling the FO-HBV-DIS with the response of antibody immune and comparison of the results is presented through the database Adams-Bashforth-Moulton approach. To authenticate the validity, competence, consistency, capability and exactness of the LMBNNs, the numerical presentations using the mean square error (MSE), error histograms (EHs), state transitions (STs), correlation and regression are accomplished.

Keywords: Fractional order HBV differential infection system; artificial neural networks; nonlinear; Levenberg-Marquardt backpropagation; Adams-Bashforth-Moulton



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1 Introduction

The hepatitis B virus (HBV) is known as a threatening disease, which directly attacks the healthy liver. Around 257 million individuals get infected per year, among them the top disease is HBV [1]. To investigate this serious viral HBV infection, a number of mathematical systems have been introduced. Bangham and Nowak were known as the pioneer to introduce the mathematical form of the with three categories, the free virus, uninfected and infected [2–6]. It is observed that the virus adopts a certain procedure using these measures, i.e., an uninfected cell with the major points is replicated, encapsulation and decapitation [7,8]. This significant viral procedure represents a new compartment in the traditional dynamical viral system [9]. The process of humoral insusceptibility is used to decrease the intensity of the viral disease [10]. This insusceptibility frequently represents the antibodies, which are produced from B cells to attack and defuse the diseases [11]. Based on the HBV dynamics and its antibodies, several mathematical systems have been proposed using the ordinary differential equations [12].

The fractional order (FO) derivative is a significant operator to design a real apparatus. A number of the FO derivatives have been used in the nonlinear models [13–15]. The nonlocal operator makes the FO derivative different to the integer order. To calculate the FO derivative at $t = t_1$, the starting to desired time ($t = t_0$ to $t = t_1$) is reported in the literature. Therefore, the phenomena to calculate more real results of the mathematical FO derivatives has been motivated by many researchers [16]. It is also signified that the biological based FO derivatives have been analyzed to produce the rheological cell's characteristics [17]. The FO derivatives have also been used in the electrical cell's conductance based on the biological organism [18]. In the mechanical field, FO derivatives have been used to indicate the effectiveness of the complex behavior of various physical models [19,20]. Few investigations have been presented based on the FO derivatives, few of them are a local wave fractional model based on the fractal string presented by Bhatter et al. [21]. FO differential system were also used to model the Drinfeld Sokolov Wilson model, KdV and Kawahara equations [22,23]. A number of discussions that have been presented to discuss the behavior of the viral infections using the FO differential models [24,25]. The optimal control systems, immune models and tumor cells have been discussed using the FO derivatives [26,27]. FO tuberculosis and diabetes systems of optimal control have been discussed by Baleanu et al. [28]. The model based on the blood and liver using the FO derivative is presented by Jajarmi et al. [29]. Moreover, FO derivatives have been used in the spread of the dengue fever [30] and many other of utmost significance [31-38].

A fractional order HBV differential infection system (FO-HBV-DIS) with the response of antibody immune is classified into five modules, healthy hepatocytes (H), infected hepatocytes (I), capsids (D), free virus (V) and antibodies (W). It is examined that time-fractional derivative has numerous applications to designate the different forms of dynamical model. The derivative shows the remembrance, while the memory function represents the FO derivative. The time-fractional derivative shows the characteristics of real-world models [39,40]. The general form of the nonlinear FO-HBV-DIS with the response of antibody immune is provided along with its initial conditions (ICs) as [41]:

$$D^{\alpha}H(\tau) = S - kH(\tau)V(\tau) - \mu H(\tau), \qquad H_0 = i_1,$$

$$D^{\alpha}I(\tau) = kH(\tau)V(\tau) - \delta I(\tau), \qquad I_0 = i_2,$$

$$D^{\alpha}D(\tau) = aI(\tau) - \beta D(\tau) - \delta D(\tau), \qquad D_0 = i_3,$$

$$D^{\alpha}V(\tau) = \beta D(\tau) - uV(\tau) - qV(\tau)W(\tau), \qquad V_0 = i_4,$$

$$D^{\alpha}W(\tau) = gV(\tau)W(\tau) - hW(\tau), \qquad W_0 = i_5.$$
(1)

It is observed that the hepatocytes (H) increase, decay with the rates S and μH , while it infected through virus at the kHV rate. The infected based hepatocytes (I) reduce at δI rate. The category

of the capsids (D) is produced using the infected cells with aI rate that are unconfined in blood, got viruses with βD rate and naturally die with δD rate. The dynamics of free virus (V) reduces at uV and counteracted by antibodies with qVW. The last dynamics in the nonlinear FO-HBV-DIS is antibodies (W), which develops in the response of free virus with rate and reduces with hW rate. The ICs are represented by i_1 , i_2 , i_3 , i_4 and i_5 , respectively.

The novelty of this work is to perform the numerical simulations of the nonlinear FO-HBV-DIS with the response of antibody immune using the optimization based stochastic schemes of the Levenberg-Marquardt backpropagation (LMB) neural networks (NNs), i.e., LMBNNs. The stochastic LMBNNs measures have never applied before to solve the nonlinear FO-HBV-DIS with the response of antibody immune. The data magnitudes are implemented 75% for training, 10% for certification and 15% for testing to solve the FO-HBV-DIS with the response of antibody immune. The stochastic numerical procedures have the competence and ability to solve the linear models as well as various stiff complex nonlinear systems [42–50]. These numerical performances of the integer order motivated the authors to present the numerical simulations of FO derivatives of nonlinear equations. Therefore, a well-known mathematical FO-HBV-DIS model with antibody immune response is presented to check the reliability of the proposed stochastic LMBNNs. Few novel characteristics of the present study for solving the nonlinear FO-HBV-DIS with the response of the antibody immune are presented as:

- A fractional order nonlinear mathematical system of differential equations is numerically handled successfully using the stochastic techniques.
- The design of the artificial NNs along with the LMB method is provided first time to solve the FO-HBV-DIS with the response of the antibody immune model.
- Three different FO variations have been presented for solving the biological nonlinear FO-HBV-DIS with the response of antibody immune.
- The correctness of the stochastic scheme is observed using the comparison of the obtained and numerical Adams-Bashforth-Moulton approach.
- The calculated absolute error (AE) validates the accuracy of the designed scheme for the biological nonlinear FO-HBV-DIS with the response of antibody immune.
- The performances based on the regression, error histograms (EHs), mean square error (MSE), state transitions (STs) and correlation authorize the reliability of the designed LMBNNs procedure for the biological FO-HBV-DIS with the response of the antibody immune system.

The remaining sections are organized as: The LMBNNs procedure is described in Section 2. The numerical simulations of the FO-HBV-DIS using the LMBNNs are presented in Section 3. Concluding notes are presented in the last Section.

2 Methodology

The designed procedures for the biological nonlinear FO-HBV-DIS with the response of the antibody immune system are presented in this section. The classification of the LMBNNs procedure is provided in two steps. First, the essential executions based on the LMBNNs are provided, while the implementation process is provided in second phase. An optimization method is drawn in Fig. 1 using the multi-layer process, while Fig. 2 presents a structure of single neurons. The stochastic computing processes through 'nftool' built-in command is presented in MATLAB. The statistics proportions are pragmatic 75% for training, 10% for certification and 15% for testing to solve the FO-HBV-DIS with the response of antibody immune.



Figure 1: Workflow diagram of the designed LMBNNs procedure for the biological FO-HBV-DIS with the response of antibody immune

3 Numerical Presentations of the Nonlinear FO-HBV-DIS

In this section, the numerical presentations of the nonlinear FO-HBV-DIS are provided by using the LMBNNs. The literature values to solve the nonlinear FO-HBV-DIS are S = 2.5, $k = 1.67 \times 10^{-13}$, $\mu = 0.01$, $\delta = 0.053$, a = 150, $\beta = 0.87$, q = 0.5, $g = 1 \times 10^{-11}$, u = 3.8, h = 0.1, $i_1 = 0.1$, $i_2 = 0.2$, $i_3 = 0.3$, $i_4 = 0.1$ and $i_5 = 0.5$. Three variants of the nonlinear FO-HBV-DIS based on the FO values, 0.5, 0.7 and 0.9 have been discussed. The results comparison is performed for each class of FO-HBV-DIS, which is found in [0,1] interval with minimum step size (0.01). Twelve numbers of neurons have been used in this study and the data proportions are applied 75% for training, 10% for certification and 15% for testing to solve the FO-HBV-DIS with the response of antibody immune. The obtained results using the 12 neurons based on the LMBNNs for solving the FO-HBV-DIS are given in Fig. 3.



Figure 2: Design of proposed single neuron



Figure 3: LMBNNs structure for the FO-HBV-DIS

The graphical plots have been derived using the LMBNNs for solving the FO-HBV-DIS in Figs. 4 to 8. The MSE and STs performances have been provided for solving the FO-HBV-DIS in Fig. 4. The MSE measures for best curves, testing, training and verification are demonstrated in Figs. 4a to 4c, whereas the STs best values for solving the FO-HBV-DIS are exemplified in Figs. 4d to 4f at iterations 95, 173 and 371. The achieved presentations have been calculated at 2.1604×10^{-06} , 7.7456×10^{-07} and 1.102×10^{-08} , respectively. The gradient measures based on the proposed LMBNNs to solve the nonlinear FO-HBV-DIS are calculated 8.0165×10^{-03} , 3.1268×10^{-05} and 7.3161×10^{-06} , respectively. The achieved values in these figures represent the precision, convergence and accuracy of the proposed LMBNNs for the FO-HBV-DIS. The values of the fitting curve have been drawn in Figs. 5a to 5c for solving the FO-HBV-DIS using the proposed LMBNNs. These values have been drawn using the comparison presentations of the results. Figs. 5d to 5f is drawn using the EHs, which are found 2.173 \times 10⁻⁰³, 6.68 \times 10⁻⁰⁴ and 1.21 \times 10⁻⁰⁴ for 1st, 2nd and 3rd variation. The performances based on the regression are derived in Fig. 6. These values of the regression authenticate the performances, which lie around 1 to designate the perfect model. The performances of the verification, testing and training have been illustrated to represent the accuracy and precision of LMBNNs to solve FO-HBV-DIS. Additionally, the convergence through the MSE measure with these representations of the complexity, epochs, training, confirmation, backpropagation and testing is tabulated in Tab. 1 for the nonlinear FO-HBV-DIS.



Figure 4: MSE (a to c) and STs (d to f) for the FO-HBV-DIS using the LMBNNs



Figure 5: Valuations of the outcomes (a-c) and EHs (d-f) for the FO-HBV-DIS using the LMBNNs



Figure 6: Regression measures for the nonlinear FO-HBV-DIS using the LMBNNs



Figure 7: Result for solving the nonlinear FO-HBV-DIS using the LMBNNs



Figure 8: AE for solving the nonlinear FO-HBV-DIS using the LMBNNs

The AE plots AE have been derived using the comparisons based on the nonlinear FO-HBV-DIS in Figs. 7 to 8. The numerical values are provided for each class of the nonlinear FO-HBV-DIS with the response of antibody immune using the proposed LMBNNs. The numerical results are provided in Figs. 7a–7c, that shows the matching of proposed and reference results. These overlapping represent the accuracy and correctness of the proposed LMBNNs for nonlinear FO-HBV-DIS with the response of antibody immune.

Case		M.S.E		Performance	Mu	Gradient	Iterations	Time
	Training	Testing	Validation	_				
1	8.91×10^{-06}	9.11×10^{-06}	2.06×10^{-06}	5.63×10^{-06}	1.00×10^{-07}	8.02×10^{-03}	95	3
2	1.32×10^{-07}	1.98×10^{-08}	7.74×10^{-08}	1.19×10^{-06}	1.00×10^{-07}	3.13×10^{-05}	173	4
3	7.81×10^{-08}	2.08×10^{-08}	1.10×10^{-08}	7.72×10^{-08}	1.00×10^{-07}	7.32×10^{-06}	371	5

 Table 1: Statistical measures for solving the nonlinear FO-HBV-DIS using the LMBNNs

The AE measures for each category of the nonlinear FO-HBV-DIS with the response of antibody immune are demonstrated in Figs. 8a to 8c. The AE values for the healthy hepatocytes $H(\tau)$ lie 10^{-03} to 10^{-04} for variation 1, 10^{-03} to 10^{-06} for variation 2 and 10^{-04} to 10^{-06} for variation 3 for solving the nonlinear FO-HBV-DIS. The AE values for the infected hepatocytes $I(\tau)$ lie 10^{-03} to 10^{-05} for variation 1, 10^{-04} to 10^{-05} for variation 2 and 10^{-06} for variation 3 for solving the nonlinear FO-HBV-DIS.

The AE values for the capsids $D(\tau)$ lie around 10^{-02} to 10^{-04} , 10^{-03} to 10^{-04} and 10^{-03} to 10^{-05} for case 1 to 3 for solving the nonlinear FO-HBV-DIS. The AE values for the free virus $V(\tau)$ lie 10^{-03} to 10^{-05} for case 1 and 2, while for case 3 the AE is found around 10^{-04} to 10^{-06} for solving the nonlinear FO-HBV-DIS. The AE values for the antibodies class $W(\tau)$ lie 10^{-03} to 10^{-07} , 10^{-04} to 10^{-06} and 10^{-04} to 10^{-07} cases 1 to 3 of the nonlinear FO-HBV-DIS. The AE plots enhance the correctness and exactness of the stochastic scheme for the nonlinear biological model.

4 Conclusions

The aim of this study is to present the numerical simulations of the fractional order HBV differential infection system with the response of antibody immune using the stochastic procedures of the LMBNNs. The fractional order HBV differential infection system is implemented to solve three different deviations using different values of the fractional order. The data magnitudes are implemented 75% for training, 10% for certification and 15% for testing to solve the FO-HBV-DIS with the response of antibody immune. Twelve numbers of neurons have been implemented to solve the biological differential system. The solutions of the FO-HBV-DIS with the response of antibody immune have been presented by using the LMBNNs, however the comparative performances have been accessible through the reference results. The numerical performances of FO biological system have been simulated using the LMBNNs to lessen the MSE. To authenticate the reliability, aptitude and capability of the LMBNNs, the numerical outcomes have been plotted using the STs, regression, Ehs, MSE and correlation. The matching performances indicate the precision of the designed stochastic method. The AE in good assortments shows the correctness of the nonlinear biological fractional order system. The other performance plots signify the consistency and dependability of the proposed method.

In future work, the stochastic LMBNNs procedures have been used to achieve the numerical measures/treatments of the many potential nonlinear fractional/integer order systems [51–55]. Additionally, one may use alternative stochastic solver based on neural networks optimized with evolutionary and swarming techniques for the presented bioinformatics study for better performance in terms of accuracy and convergence. **Funding Statement:** This research received funding support from the NSRF via the Program Management Unit for Human Resources & Institutional Development, Research and Innovation (grant number B05F640092).

Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

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