Step Method for Solving Nonlinear Two Delays Differential Equation in Parkinson's Disease

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Abstract—Parkinson's disease (PD) is a heterogeneous disorder with common age of onset, symptoms, and progression levels. In this paper we will solve analytically the PD model as a non-linear delay differential equation using the steps method. The step method transforms a system of delay differential equations (DDEs) into systems of ordinary differential equations (ODEs). On some numerical examples, the analytical solution will be difficult. So we will approximate the analytical solution using Picard method and Taylor method to ODEs.

Keywords—Parkinson's disease, Step method, delay differential equation, simulation.

I. Introduction

PD occurs when not enough dopamine is secreted into the nerve cells in the brain. Its causes may be be environmental, as a result of exposure to chemicals or genetic causes. It mostly affects the elderly, especially after sixty. The patient may have several movement symptoms, trembling of the hands and arms, as well as slow movement and stiffness. There are neurological symptoms such as depression and psychosis.

There are medications that reduce symptoms and help produce dopamine. Also, surgery is used for late cases, and currently deep brain stimulation is used to treat Parkinson's symptoms.

PD has been studied mathematically in [1]-[6] as in the following DDEs:

$$\frac{dx(t)}{dt} = a_1 \, x(t-\tau_1) + a_2 \, x(t-\tau_2) + a_3 \, x(t-\tau_1) x(t-\tau_2) \quad (1)$$

$$x(t) = h, \ t > 0 \ and \quad -\tau_2 < -\tau_1 < t < 0$$

where, a_1, a_2, a_3 are constant coefficients, $x(t)$ the function described PD, h history value. In [1] the time series method was used to create a model for PD. The authors in [6] discussed Claudia model in [1] and have endorsed that it is unbounded and unstable for the case of positive coefficients, but this is not true for the biodynamic systems. Moreover, the authors in [6] try to suggest some modifications for Claudia model in [1] to be bounded for this case as follows:

$$\frac{dx(t)}{dt} = a_1 \, x(t-\tau_1) + a_2 \, x(t-\tau_2) + a_3 \, x(t-\tau_1) x(t-\tau_2) - x^2 \quad (2)$$

$$x(t) = h, \ t > 0 \ and \quad -\tau_2 < -\tau_1 < t < 0$$

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with stability conditions: $a_1 + a_2 + a_3 < 1$ and for more stability by the condition:

$$a_1 + a_2 + 2\frac{a_1 + a_2}{1 - a_3} < 2$$

We will give study numerical cases for two models using step method for solving DDE. The methods of steps transform a system of DDEs into systems of ODEs.

The width of each step depends on the values of the delays, if $\tau_2 = n\tau_1$ where n are positive integer number the width for every step is τ_1, if $\tau_2 \neq n\tau_1$ the width of step is τ_1 until $\tau_2 - n\tau_1 < \tau_1$ then the width of steps is ; $\tau_2 - n\tau_1$ hence, the width will be the smallest of values of ($\tau_2 - n\tau_1$ or $(n+1)\tau_1 - \tau_2$); the smallest width will be the width of all next steps. For improving that we can give the following cases:

Case1. If $\tau_2 = n\tau_1$ then the steps will be: $[0, \tau_1]$, $[\tau_1, 2\tau_1]$, $[2\tau_1, 3\tau_1], \ldots, [(n-1)\tau_1, \tau_2]$, $[\tau_2, (n+1)\tau_1], \ldots$

Case2. If $\tau_2 < 2\tau_1$ and $\tau_2 - \tau_1 < 2\tau_1 - \tau_2$ then the steps will be: $[0, \tau_1]$, $[\tau_1, \tau_2]$, $[\tau_2, 2\tau_2 - \tau_1]$, $[2\tau_2 - \tau_1, 3\tau_2 - 2\tau_1]$, ... If $\tau_2 < 2\tau_1$ and $\tau_2 - \tau_1 > 2\tau_1 - \tau_2$ then the steps will be: $[0, \tau_1]$, $[\tau_1, \tau_2]$, $[\tau_2, 2\tau_1]$, $[2\tau_1, 4\tau_1 - \tau_2]$, $[4\tau_1 - \tau_2, 6\tau_1 - 2\tau_2]$, ...

Case3. If $2\tau_1 < \tau_2 < 3\tau_1$ and $\tau_2 - 2\tau_1 < 3\tau_1 - \tau_2$ then the steps will be: $[0, \tau_1]$, $[\tau_1, 2\tau_1]$, $[2\tau_1, \tau_2]$, $[\tau_2, 2\tau_2 - 2\tau_1]$, ... If $2\tau_1 < \tau_2 < 3\tau_1$ and $\tau_2 - 2\tau_1 > 3\tau_1 - \tau_2$ then the steps will be: $[0, \tau_1]$, $[\tau_1, 2\tau_1]$, $[2\tau_1, \tau_2]$, $[\tau_2, 3\tau_1]$, $[3\tau_1, 6\tau_1 - \tau_2]$, ...

In the following sections, we will give numerical examples illustrating the step method.

II. Step Method for Model [1]

Using step method and considering $\tau_2 < 2\tau_1$ and $\tau_2 - \tau_1 > 2\tau_1 - \tau_2$:

First Interval $[0, \tau_1]$

$$\frac{dx_1(t)}{dt} = a_1 \, h + a_2 \, h + a_3 \, h^2, \qquad x_1(0) = h \quad (3)$$

Second interval $[\tau_1, \tau_2]$

$$\frac{dx_2(t)}{dt} = a_1\, x_1(t-\tau_1) + a_2\, h + a_3\, h x_1(t-\tau_1), \qquad x_2(\tau_1) = x_1(\tau_1) \quad (4)$$

Third interval $[\tau_2, 2\tau_1]$

$$\frac{dx_3(t)}{dt} = a_1\, x_1(t-\tau_1) + a_2\, x_1(t-\tau_2) + a_3\, x_1(t-\tau_1)x_1(t-\tau_2),$$
$$x_3(\tau_2) = x_2(\tau_2)$$

$$(5)$$

Fourth interval $[2\tau_1, 4\tau_1 - \tau_2]$

$$\frac{dx_4(t)}{dt} = a_1\, x_2(t-\tau_1) + a_2\, x_1(t-\tau_2) + a_3\, x_2(t-\tau_1)x_1(t-\tau_2),$$
$$x_4(2\tau_1) = x_3(2\tau_1)$$

$$(6)$$

By solving the above initial value problems we can solve the nonlinear two delays differential equation in (1) as following for first, second and third steps:

First step

$$x_1(t) = h + h_2 t$$
$$h_1 = a_1 + a_3 h$$
$$h_2 = h_1 h + a_2 h$$

Second step

$$x_2(t) = h_3 + h_4 t + h_5 t^2$$
$$h_3 = h + \frac{\tau_1^2 h_1 h_2}{2}$$
$$h_4 = h_2 - \tau_1 h_1 h_2$$
$$h_5 = \frac{h_1 h_2}{2}$$

Third step

$$x_3(t) = h_6 + h_7 t + h_8 t^2 + h_9 t^3$$
$$h_6 = h_3 + \frac{a_3 d_2^3 h_2^2}{6} + \frac{a_2 d_2^2 h_2}{2} + \frac{a_3 d_2^2 h h_2}{2} - \frac{a_3 d_1 d_2^2 h_2^2}{2}$$
$$h_7 = h_4 - a_2 d_2 h_2 + a_3 d_1 d_2 h_2^2 - a_3 d_2 h h_2$$
$$h_8 = \frac{a_1 h_2}{2} + \frac{a_2 h_2}{2} + a_3 h h_2 - \frac{a_3 d_1 h_2^2}{2} - \frac{a_3 d_2 h_2^2}{2}$$
$$h_9 = \frac{a_3 h_2^2}{3}$$

III. STEP METHOD FOR MODEL [6]

For the positive values of a_1, a_2, a_3 and h the system is unbounded and unstable. The author in [6] considers modification to the system in (1) to be bounded as follow:

$$\frac{dx(t)}{dt} = a_1\, x(t-\tau_1) + a_2\, x(t-\tau_2) + a_3\, x(t-\tau_1)x(t-\tau_2) - (x(t))^2 \quad (7)$$
$$x(t) = h,\ t > 0 \quad and \quad -\tau_2 < -\tau_1 < t < 0$$

Using step method with assuming conditions $\tau_2 < 2\tau_1$ and $\tau_2 - \tau_1 > 2\tau_1 - \tau_2$:

First interval $[0, \tau_1]$

$$\frac{dx_1(t)}{dt} = a_1\, h + a_2\, h + a_3\, h^2 - (x_1(t))^2, \qquad x_1(0) = h \quad (8)$$

Second interval $[\tau_1, \tau_2]$

$$\frac{dx_2(t)}{dt} = a_1\, x_1(t-\tau_1) + a_2\, h + a_3\, h x_1(t-\tau_1) - (x_2(t))^2, \qquad x_2(\tau_1) = x_1(\tau_1) \quad (9)$$

Third interval $[\tau_2, 2\tau_1]$

$$\frac{dx_3(t)}{dt} = a_1\, x_1(t-\tau_1) + a_2\, x_1(t-\tau_2) + a_3\, x_1(t-\tau_1)x_1(t-\tau_2) - (x_3(t))^2,$$
$$x_3(\tau_2) = x_2(\tau_2)$$

$$(10)$$

Fourth interval $[2\tau_1, 4\tau_1 - \tau_2]$

$$\frac{dx_4(t)}{dt} = a_1\, x_2(t-\tau_1) + a_2\, x_1(t-\tau_2) + a_3\, x_2(t-\tau_1)x_1(t-\tau_2) - (x_4(t))^2,$$
$$x_4(2\tau_1) = x_3(2\tau_1)$$

$$(11)$$

It is very difficult to solve initial value problem. So first we will use Picard method for solving all initial value problems; but we must satisfy Lipchitz conditions for all steps. All of the initial value problems (IVPs) satisfy existence and uniqueness theorem if the function $x(t)$ is bounded as proposed [6]:

$$\frac{dx(t)}{dt} = f(t,x), \qquad \left|\frac{\partial f(t,x)}{\partial x}\right| < l, \quad l > 0$$
$$x_n = x_0 + \int_0^t f(t, x_{n-1})dt, \quad n = 1,2,3,\dots$$

By solving the above initial value problems we can solve the nonlinear two delays differential equation in (7) as following for first, second and third steps:

For the first step: The first initial problem

$$x_{11} = h + \int_0^t \left(h_1 - h^2\right)dt, \quad h_1 = a_1 h + a_2 h + a_3 h^2$$
$$x_{11} = h + h_2\, t \qquad h_2 = h_1 - h^2$$
$$x_{12} = h + \int_0^t \left(h_1 - (x11)^2\right)dt$$

$$x_{12} = h + h_2 t - h h_2 t^2 - \frac{h_2^2}{3} t^3$$

$$x_{13} = h + \int_0^t \left(h_1 - (x_{12})^2 \right) dt$$

$$x_{13} = h + h_2\, t - h h_2\, t^2 - \frac{(h_2^2 - 2h^2 h_2)t^3}{3} + \frac{2 h h_2^2 t^4}{3} + \frac{(2 h_2^3 - 3 h^2 h_2^2)t^5}{15} - \frac{h h_2^3 t^6}{9} - \frac{h_2^4 t^7}{63}$$

Thus, the remaining approximations and the remaining steps are found.

1. Numerical Examples for Model [1]

We will provide two different examples in the steps for model [1] for considering the steps. This model is easy to integrate and we will use MATLAB code dsolve to solving every IVP.

Example1: Solve the DDE:

$$\frac{dx(t)}{dt} = 0.1x(t-2) + 0.2\,x(t-3) + 0.3x(t-2)x(t-3) \quad (12)$$

$$x(t) = 0.5 \,,\; t > 0 \quad and \quad -3 < t < 0$$

First step $[0,2]$

$$\frac{dx_1(t)}{dt} = 0.225 \quad,\quad x_1(0) = 0.5 \quad (13)$$

Second step $[2,3]$

$$\frac{dx_2(t)}{dt} = 0.25 x_1(t-2) + 0.1 \quad,\quad x_2(2) = x_1(2) \quad (14)$$

Third step $[3,4]$

$$\frac{dx_3(t)}{dt} = 0.1x_1(t-2) + 0.2x_1(t-3) + 0.3x_1(t-2)x_1(t-3) \quad,\quad x_3(3) = x_2(3)$$
$$(15)$$

Fourth step $[4,5]$

$$\frac{dx_4(t)}{dt} = 0.1x_2(t-2) + 0.2x_1(t-3) + 0.3x_2(t-2)x_1(t-3) \quad,\quad x_4(4) = x_3(4)$$
$$(16)$$

Fifth step $[5,6]$

$$\frac{dx_5(t)}{dt} = 0.1x_3(t-2) + 0.2x_2(t-3) + 0.3x_3(t-2)x_2(t-3) \quad,\quad x_5(5) = x_4(5)$$
$$(17)$$

General step $[d_{i-1}, d_i]$

$$\frac{dx_i(t)}{dt} = 0.1x_{i-2}(t-2) + 0.2x_{i-3}(t-3) + 0.3x_{i-2}(t-2)x_{i-3}(t-3),\; x_i(d_{i-1}) = x_{i-1}(d_{i-1})$$
$$(18)$$

By solving the initial value problem to every step

$$x(t) = \begin{cases} \dfrac{1}{2} & ,\, -3 \le t \le 0 \\[2mm] \dfrac{9t}{40} + \dfrac{1}{2} & ,\, 0 \le t \le 2 \quad (19) \\[2mm] \dfrac{9t^2}{320} + \dfrac{9t}{80} + \dfrac{49}{80} & ,\, 2 \le t \le 3 \\[2mm] \dfrac{81t^3}{16000} + \dfrac{189t^2}{6400} - \dfrac{261t}{8000} + \dfrac{28753}{32000} & ,\, 3 \le t \le 4 \\[2mm] \dfrac{243t^4}{512000} + \dfrac{57t^3}{128000} + \dfrac{63t^2}{1600} - \dfrac{9t}{800} + \dfrac{6309}{6400} & ,\, 4 \le t \le 5 \\[2mm] \cdots\cdots \end{cases}$$
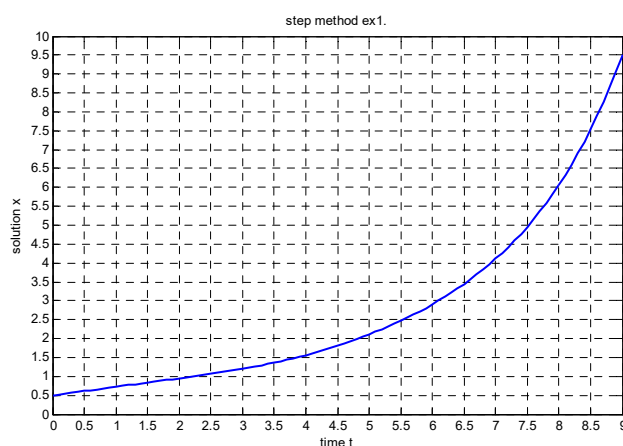

Fig. 1 Model in [1] $a_1 = 0.1, a_2 = 0.2, a_3 = 0.3, h = 0.5, \tau_1 = 2, \tau_2 = 3$ by step method
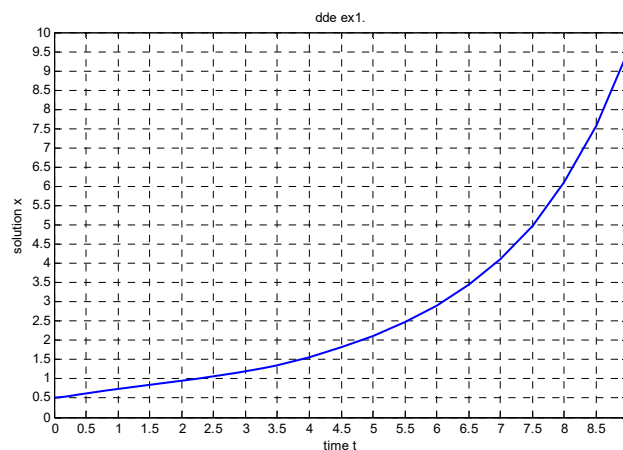

Fig. 2 Model in [1] $a_1 = 0.1, a_2 = 0.2, a_3 = 0.3, h = 0.5, \tau_1 = 2, \tau_2 = 3$ by code MATLAB dde23

Comparing Figs. 1 and 2, we find a great match between the MATLAB code dde23 and the solution using the steps method.

Example2: Solve the DDE:

$$\frac{dx(t)}{dt} = 0.1x(t-2) + 0.2\,x(t-5) + 0.3x(t-2\,)x(t-5\,) \qquad (20)$$

$$x(t) = 1\,,\ t > 0\ \ and\ \ -5 < t < 0$$

First step $[0,2]$

$$\frac{dx_1(t)}{dt} = 0.6\quad,\quad x_1(0) = 1 \qquad (21)$$

Second step $[2,4]$

$$\frac{dx_2(t)}{dt} = 0.4x_1(t-2) + 0.2\quad,\quad x_2(2) = x_1(\,2\,) \qquad (22)$$

Third step $[4,5]$

$$\frac{dx_3(t)}{dt} = 0.4x_2(t-2) + 0.2\quad,\quad x_3(4) = x_2(\,4\,) \qquad (23)$$

Fourth step $[5,6]$

$$\frac{dx_4(t)}{dt} = 0.1x_2(t-2) + 0.2x_1(t-5) + 0.3x_2(t-2)x_1(t-5),\ x_4(5) = x_3(\,5\,) \qquad (24)$$

By solving the initial value problem to every step

$$x(t) = \begin{cases} 1 & ,\, -5 \le t \le 0 \\[4pt] \frac{3t}{5} + 1 & ,\, 0 \le t \le 2 \\[4pt] \frac{3t^2}{25} + \frac{3t}{25} + \frac{37}{25} & ,\, 2 \le t \le 4 \\[4pt] \frac{2t^3}{125} - \frac{9t^2}{125} + \frac{111t}{125} + \frac{57}{125} & ,\, 4 \le t \le 5 \\[4pt] \frac{27t^4}{5000} - \frac{26t^3}{625} + \frac{381t^2}{1250} - \frac{63t}{50} + \frac{5601}{1000} & ,\, 5 \le t \le 6 \\[4pt] \frac{9t^5}{15625} - \frac{239t^4}{25000} + \frac{344t^3}{3125} - \frac{2739t^2}{6250} + \frac{117t}{250} + \frac{516093}{125000} & ,\, 6 \le t \le 7 \\[4pt] \dots\dots \end{cases} \qquad (25)$$
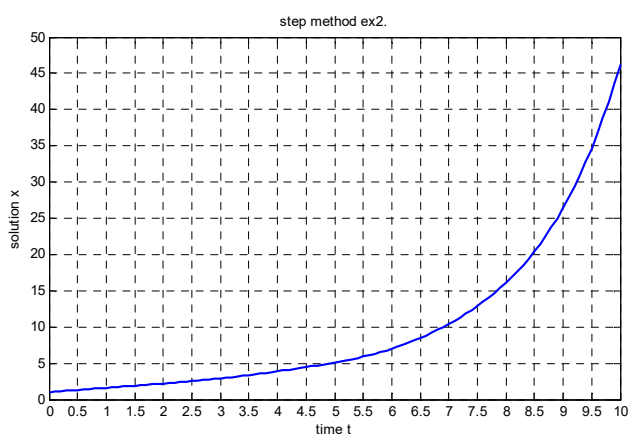

Fig. 3 Model in [1] $a_1 = 0.1\,, a_2 = 0.2\,, a_3 = 0.3\,, h = 1\,, \tau_1 = 2\,, \tau_2 = 5$ by step method
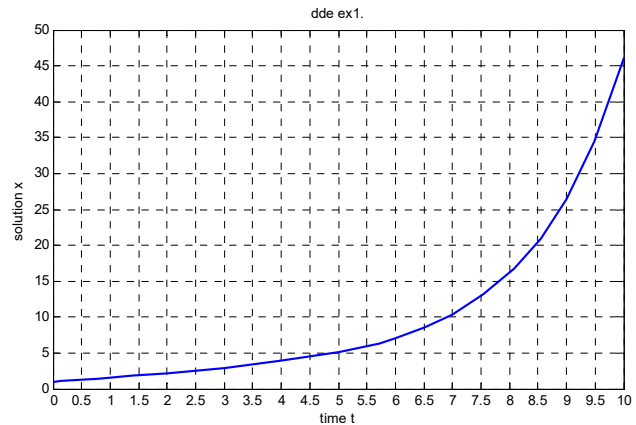

Fig. 4 Model in [1] $a_1 = 0.1\,, a_2 = 0.2\,, a_3 = 0.3\,, h = 1\,, \tau_1 = 2\,, \tau_2 = 5$ by code dde23

Comparing Figs. 3 and 4, we find a great match between the MATLAB code dde23 and the solution using the steps method.

2. Numerical Examples for Model [6]

We will solve numerical example with higher approximation as following:

$$\frac{dx(t)}{dt} = 0.1x(t-2) + 0.2\,x(t-3) + 0.3x(t-2\,)x(t-3) - (x(t))^2 \quad (26)$$

$$x(t) = 0.5\,,\ t > 0\ \ and\ \ -3 < t < 0$$

First step $[0,2]$

$$\frac{dx_1(t)}{dt} = 0.1 \times 0.5 + 0.2 \times 0.5 + 0.3 \times 0.5 \times 0.5 - (x_1(t))^2\quad, x_1(\,0\,) = 0.5$$

Second step $[2,3]$

$$\frac{dx_2(t)}{dt} = 0.1 \times x_1(t-2) + 0.2 \times 0.5 + 0.3 \times x_1(t-2) \times 0.5 - (x_2(t))^2\quad, x_2(\,2\,) = x_1(\,2\,)$$

Third step $[3,4]$

$$\frac{dx_3(t)}{dt} = 0.1x_1(t-2) + 0.2x_1(t-3) + 0.3x_1(t-2\,)x_1(t-3) - (x_3(t))^2\quad, x_3(\,3\,) = x_2(\,3\,)$$

By using MATLAB program for solving every step we get the solution in Fig. 5.

By comparison of Figs. 5 and 6, we find that there is a great match between using the steps method with solving IVP of every step using the Piccard method and solving it with the MATLAB command.

IV. CONCLUSION

As explained in [6] under the condition of positive values for $a_1\,, a_2\,, a_3$ and h the system in [1] will be unstable and unbounded which does not exist in biological systems. The modification in [6] adds square term with coefficient -1. The

solution of the system is bounded under the condition in [6] and we use step method to solve the problem with different delays and explain how to use it.
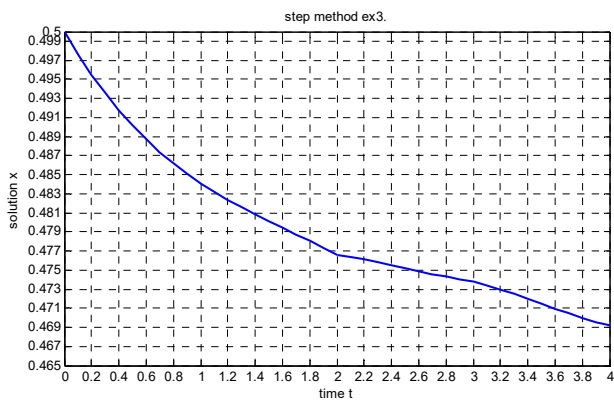

Fig. 5 Model in [6] $a_1 = 0.1$, $a_2 = 0.2$, $a_3 = 0.3$, $h = 0.5$, $\tau_1 = 2$, $\tau_2 = 3$ by step method using Picard approximation
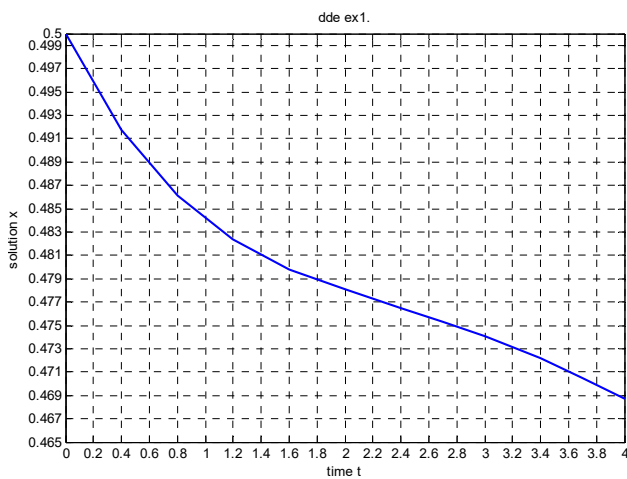

Fig. 6 Model in [6] $a_1 = 0.1$, $a_2 = 0.2$, $a_3 = 0.3$, $h = 0.5$, $\tau_1 = 2$, $\tau_2 = 3$ by MATLAB code dde23

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