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Homoclinic and heteroclinic solutions to a hepatitis C evolution model

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Abstract: Homoclinic and heteroclinic solutions to a standard hepatitis C virus (HCV) evolution model described by T. C. Reluga, H. Dahari and A. S. Perelson, (*SIAM J. Appl. Math.*, 69 (2009), pp. 999–1023) are considered in this paper. Inverse balancing and generalized differential techniques enable derivation of necessary and sufficient existence conditions for homoclinic/heteroclinic solutions in the considered system. It is shown that homoclinic/heteroclinic solutions do appear when the considered system describes biologically significant evolution. Furthermore, it is demonstrated that the hepatitis C virus evolution model is structurally stable in the topological sense and does maintain homoclinic/heteroclinic solutions as diffusive coupling coefficients tend to zero. Computational experiments are used to illustrate the dynamics of such solutions in the hepatitis C evolution model.

Keywords: hepatitis C model, homoclinic/heteroclinic solution, generalized differential operator, inverse balancing

MSC: 34A34, 35C07, 92B05

1 Introduction

Modeling of biomedical processes using differential equations has become more and more widespread over recent years [6, 12, 29]. Various differential equation models on the use of oncolytic viruses as therapeutic agents against cancer are discussed in [28]. A clinically validated model of tumor-immune cell interactions is considered in [4]. A new mathematical model for the explanation of the failure of cancer chemotherapy treatment is presented in [22]. A mathematical model based on differential equations is used to describe the interactions between Ebola virus and wild-type Vero cells *in vitro* in [21].

Beginning with the classical paper by Neumann et al [20], various differential equation models for the modeling of hepatitis virus infection have been proposed. Global dynamics of a delay differential model of hepatitis B infection evolution are studied in [5, 27]. The transmission of hepatitis C virus (HCV) among injecting drug users is modeled using ordinary differential equations in [11]. A mathematical multi-scale

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model of the within-host dynamics of HCV infection is used to study patients under treatment with direct acting antiviral medication in [3]. The authors of [2] give a review of recent HCV kinetics models.

Reluga et al [25] present the following model of hepatitis C virus infection that explicitly includes proliferation of infected and uninfected hepatocytes:

$$\begin{aligned}
\mathcal{T}_{\hat{t}} &= \hat{s} + r_{\mathcal{T}}\mathcal{T}\left(1 - \frac{\mathcal{T}+\mathcal{I}}{\mathcal{T}_{max}}\right) - d_{\mathcal{T}}\mathcal{T} - (1-\eta)\,\beta\mathcal{V}\mathcal{T} + \hat{q}\mathcal{I};\\
\mathcal{I}_{\hat{t}} &= r_{\mathcal{I}}\mathcal{I}\left(1 - \frac{\mathcal{T}+\mathcal{I}}{\mathcal{T}_{max}}\right) + (1-\eta)\,\beta\mathcal{V}\mathcal{T} - d_{\mathcal{I}}\mathcal{I} - \hat{q}\mathcal{I};\\
\mathcal{V}_{\hat{t}} &= (1-\epsilon)\,p\mathcal{I} - c\mathcal{V},
\end{aligned} \tag{1}$$

where $\hat{t}$ is time; $\mathcal{T}\left(\hat{t}\right)$ represents uninfected hepatocytes; $\mathcal{I}\left(\hat{t}\right)$ represents infected cells and $\mathcal{V}\left(\hat{t}\right)$ represents free virus population. The parameters of (1) have the following meaning: β is the rate of infection per free virus per hepatocyte; c is the immune virus clearance rate; p is the free virus production rate per infected cell; $d_{\mathcal{T}}$, $d_{\mathcal{I}}$ are death rates for uninfected hepatocytes and infected cells respectively; $r_{\mathcal{T}}$, $r_{\mathcal{I}}$ are parameters of the logistic proliferation of $\mathcal{T}$ and $\mathcal{I}$ respectively; logistic proliferation happens only if $\mathcal{T} < \mathcal{T}_{max}$; parameters $\hat{s}$ and $\hat{q}$ represent the increase rate of uninfected hepatocytes through immigration and spontaneous cure by noncytolytic process respectively; finally the effect of antiviral treatment reduces the infection rate by a fraction η and the viral production rate by a fraction ϵ. Ranges of parameters are given in [25].

As shown in [25], $\mathcal{V}$ can be solved explicitly for patients in a steady state before treatment. Furthermore, introducing dimensionless state variables and parameters transforms (1) into:

$$\begin{aligned}
x_\tau &= x\,(1-x-y) - (1-\theta)\,bxy + qy + s;\\
y_\tau &= ry\,(1-x-y) + (1-\theta)\,bxy - dy - qy,
\end{aligned} \tag{2}$$

where x, y are dimensionless state variables for uninfected hepatocytes and infected cells respectively; $r, b, \theta, d, q, s \in \mathbb{R}$ are real parameters.

System (2) can be rewritten in a more general form:

$$\begin{aligned}
x_\tau &= a_0 + a_1x + a_2x^2 + a_3xy + a_4y; \quad x\Big|_{\tau=c} = u;\\
y_\tau &= b_0 + b_1y + b_2y^2 + b_3xy + b_4x; \quad y\Big|_{\tau=c} = v,
\end{aligned} \tag{3}$$

where $c, u, v, a_k, b_k \in \mathbb{R}$, $k = 1, \ldots, 4$.

The main objective of this paper is to study soliton-like dynamics of the system (3). Note that since (3) is not a system of nonlinear partial differential equations (PDEs), soliton (or solitary) solutions cannot exist, due to their definition being closely connected to concrete physical phenomena. However, as is demonstrated in the paper, solutions that exhibit analogous dynamics to those observed in solitary solutions, can be constructed for system (3). Since the phase trajectories of these solutions are homoclinic or heteroclinic, we refer to such solutions and homoclinic/heteroclinic solutions.

In the case $a_4 = b_4 = 0$, system (3) has already been shown to admit homoclinic/heteroclinic solutions [19], [15]. Solutions described in [19] have simple monotonous transitions from two steady states, while those found in [15] exhibit much more complicated transient effects. Because of this reason, only the latter homoclinic and heteroclinic solutions to (2), (3) are considered.

Using the inverse balancing and generalized differential operator techniques, explicit homoclinic and heteroclinic solution existence conditions are obtained in terms of the parameters of (2). These conditions, together with explicit expressions of such solutions, provide insight not only into HCV model (2), but also other models of nonlinear evolution.

Note that the application of direct techniques to compute the homoclinic/heteroclinic trajectories of (3) is not straightforward. For example, computation of the first integral requires the solution of the following first-order ODE:

$$y_x = \frac{a_0 + a_1x + a_2x^2 + a_3xy + a_4y}{b_0 + b_1y + b_2y^2 + b_3xy + b_4x}. \tag{4}$$

While the above ODE can be integrated for some parameter values, there is no general method to determine such cases. Furthermore, the generalized differential operator technique yields not only phase trajectories of (3), but also its general solution and the conditions with respect to $a_0, \ldots, a_4; b_0, \ldots, b_4$ under which homoclinic/heteroclinic solutions exist.

2 Preliminaries

2.1 Power series and their extensions

In this paper, functions of the following power series form are considered:

$$f(z) = \sum_{j=0}^{+\infty} a_j \frac{z^j}{j!}, \tag{5}$$

where $z, a_j \in \mathbb{C}$. The coefficients of power series (33) are constructed via generalized differential operator technique, described in the following sections of the paper.

We treat the convergence of series (33) as follows. If (33) converges in some ball $|z| < R$; $R > 0$, then it is possible to extend (33) to a wider complex domain (not including the singularities of (33)) via classical extension techniques. Let $t \in \mathbb{R}$ denote a real argument of this extended function. Inserting t into the extension of (33) yields a real power series $f(x)$ defined for values not necessarily in the radius $|t| < R$. For the purposes of this paper, we consider $f(x)$ and its power series representation to be congruent.

2.2 Monotonous and non-monotonous homoclinic/heteroclinic solutions

First, let us consider monotonous homoclinic and heteroclinic solutions of the following soliton-like form [23, 26]:

$$x(\tau; c, u, v) = \sigma \frac{\exp(\eta(\tau - c)) - x_1}{\exp(\eta(\tau - c)) - \tau_1^{(x)}}; \tag{6}$$

$$y(\tau; c, u, v) = \gamma \frac{\exp(\eta(\tau - c)) - y_1}{\exp(\eta(\tau - c)) - \tau_1^{(y)}}, \tag{7}$$

where $\eta \neq 0$, $\sigma, \gamma \in \mathbb{R}$ are constants; $\tau_1^{(x)}, \tau_1^{(y)}$ depend on initial conditions u, v.

The biological interpretation of (6), (7) represents the transition from the size of population of cells before therapy to the size of population after therapy. However, this transition is monotonous; the solutions shown in Fig. 1 (a) describe the difference between the sizes of populations before and after therapy, and the transition between the steady states.

Non-monotonous homoclinic/heteroclinic solutions read [7, 26]:

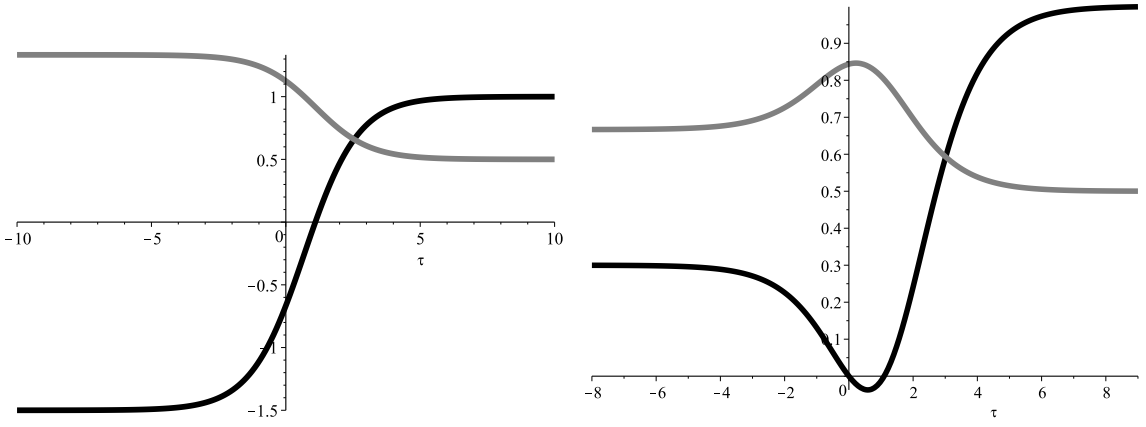
$$x(\tau; c, u, v) = \sigma \frac{\left(\exp(\eta(\tau - c)) - x_1\right)\left(\exp(\eta(\tau - c)) - x_2\right)}{\left(\exp(\eta(\tau - c)) - \tau_1^{(x)}\right)\left(\exp(\eta(\tau - c)) - \tau_2^{(x)}\right)}; \tag{8}$$

$$y(\tau; c, u, v) = \gamma \frac{\left(\exp(\eta(\tau - c)) - y_1\right)\left(\exp(\eta(\tau - c)) - y_2\right)}{\left(\exp(\eta(\tau - c)) - \tau_1^{(y)}\right)\left(\exp(\eta(\tau - c)) - \tau_2^{(y)}\right)}, \tag{9}$$

where $\eta \neq 0$, $\sigma, \gamma \in \mathbb{R}$ are constants; $\tau_k^{(x)}, \tau_k^{(y)}, x_k, y_k, k = 1, 2$ depend on initial conditions u, v.

Solutions (8), (9) describe much more complex transition processes between the steady states. The size of the population of cells during the transient process exceeds populations both at the beginning and the end of the therapy if only the considered solutions have minimum points (the black line in Fig. 1 (b)). Analogously,

Figure 1: Monotonous (a) and non-monotonous homoclinic/heteroclinic solutions (b). Black and gray lines represent $x(\tau)$ and $y(\tau)$ respectively. The parameters of solutions read: $\eta = \sigma = 1; \gamma = 1/2; c = 0; x_1 = 3; x_2 = 1; \tau_1^{(x)} = -2; \tau_2^{(x)} = -5; y_1 = -8; y_2 = -1/2; \tau_1^{(y)} = -3; \tau_2^{(y)} = -1$.



(a) (b)

solutions with maximum points describe complex transitions from the population of cells before and after the treatment (the gray line in Fig. 1 (b)).

From the biological point of view, transient processes governed by homoclinic and heteroclinic solutions highlight important phenomena. Let us consider the dynamics of uninfected cells (the black line in Fig. 1 (b)). The population of uninfected cells after the therapy becomes lower than the population before the therapy. However, the number of uninfected cells grows during the therapy and exceeds the population of uninfected cells at the beginning of the computational experiment (Fig. 1 (b)).

Note that the negative values of cell population $x(\tau)$ and $y(\tau)$ are a consequence of the non-dimensionalization of system (1).

2.3 Solution transformation

In the following derivations, the standard independent variable transformation will be used:

$$t := \exp\left(\eta\left(\tau - c\right)\right); \quad \widehat{c} := \exp\left(\eta\left(\tau - c\right)\right). \tag{10}$$

Using (10), homoclinic/heteroclinic solutions (8), (9) can be written as:

$$\widehat{x}\left(t; c, u, v\right) := x\left(\frac{1}{\eta}\ln\tau; \frac{1}{\eta}\ln c, u, v\right) = \sigma\frac{\left(t - \widehat{x}_1\right)\left(t - \widehat{x}_2\right)}{\left(t - t_1^{(x)}\right)\left(t - t_2^{(x)}\right)}; \tag{11}$$

$$\widehat{y}\left(\tau; c, u, v\right) := y\left(\frac{1}{\eta}\ln\tau; \frac{1}{\eta}\ln c, u, v\right) = \gamma\frac{\left(t - \widehat{y}_1\right)\left(t - \widehat{y}_2\right)}{\left(t - t_1^{(y)}\right)\left(t - t_2^{(y)}\right)}, \tag{12}$$

where $t_k^{(x)} = \widehat{c}\tau_k^{(x)}$, $t_k^{(y)} = \widehat{c}\tau_k^{(y)}$, $\widehat{x}_k = \widehat{c}x_k$, $\widehat{y}_k = \widehat{c}y_k$, $k = 1, 2$. Using partial fractions (11), (12) can be rewritten as:

$$\widehat{x} = \sigma + \frac{\lambda_1}{1 - \rho_1\left(t - \widehat{c}\right)} + \frac{\lambda_2}{1 - \rho_2\left(t - \widehat{c}\right)}; \tag{13}$$

$$\widehat{y} = \gamma + \frac{\mu_1}{1 - \nu_1\left(t - \widehat{c}\right)} + \frac{\mu_2}{1 - \nu_2\left(t - \widehat{c}\right)}, \tag{14}$$

where $\lambda_k, \mu_k, \rho_k, \nu_k, k = 1, 2$ are functions of u, v.

2.4 Generalized differential operator technique

In this section, a summary on the generalized differential operator technique for the construction of solutions to ordinary differential equations in presented. More detailed derivations can be found in [16].

2.4.1 Generalized differential operators

Let $P(c,u,v)$, $Q(c,u,v)$ be trivariate analytic functions. A generalized differential operator $\mathbf{D}_{cuv}$ reads:

$$\mathbf{D}_{cuv} := \mathbf{D}_c + P(c,u,v)\mathbf{D}_u + Q(c,u,v)\mathbf{D}_v, \tag{15}$$

where $\mathbf{D}_\beta := \dfrac{\partial}{\partial\beta}$ for any variable β. Standard properties of differentiation operators hold true for (15) [14]:

$$\mathbf{D}_{cuv} f\left(g(c,u,v)\right) = \frac{\mathrm{d}f}{\mathrm{d}g}\,\mathbf{D}_{c,uv} g; \tag{16}$$

$$\mathbf{D}_{cuv}\left(fg\right) = g\left(\mathbf{D}_{cuv} f\right) + f\left(\mathbf{D}_{cuv} g\right); \tag{17}$$

$$\mathbf{D}_{cuv}\frac{f}{g} = \frac{g\left(\mathbf{D}_{cuv} f\right) - f\left(\mathbf{D}_{cuv} g\right)}{g^2}, \tag{18}$$

where f, g denote arbitrary functions analytic in c,u,v.

2.4.2 Multiplicative operators

Using (15), the multiplicative operator can be constructed:

$$\mathbf{M} := \sum_{j=0}^{+\infty} \frac{t^j}{j!}\mathbf{D}_{cuv}^j, \tag{19}$$

where t is an arbitrary real variable. Operator (19) has two important properties:

$$\mathbf{M}c^m = (t+c)^m, \quad m = 0,1,\ldots; \tag{20}$$

$$\mathbf{M}f(c,s,t) = f(t+c, \mathbf{M}s, \mathbf{M}t). \tag{21}$$

Note that (20) follows immediately from the definition of (19). Without loss of generality, the proof of (21) for multiplicative operator $\mathbf{M} = \sum_{j=0}^{+\infty} \frac{t^j}{j!}\left(P(u,v)\mathbf{D}_u + Q(u,v)\mathbf{D}_v\right)^j$ is presented below.

Let $y_1 := \mathbf{M}u = y_1(t,u,v)$, $y_2 := \mathbf{M}v = y_2(t,u,v)$, $z := \mathbf{M}f(u,v) = z(t,u,v)$ and $w := f(\mathbf{M}u, \mathbf{M}v) = f(y_1,y_2)$. To prove (21), it needs to be shown that $z = w$ for all t,u,v.

Note that:

$$\mathbf{D}_t z = \mathbf{D}_t \sum_{j=0}^{+\infty} \frac{t^j}{j!}\mathbf{D}_{uv}^j f(u,v) = \sum_{j=1}^{+\infty} \frac{t^{j-1}}{(j-1)!}\mathbf{D}_{uv}^j f(u,v) = \mathbf{D}_{uv}\mathbf{M}f(u,v) = \mathbf{D}_{uv} z = P\mathbf{D}_u z + Q\mathbf{D}_v z. \tag{22}$$

Thus, the function $z(t,u,v)$ satisfies the partial differential equation:

$$\frac{\partial z}{\partial t} = P\frac{\partial z}{\partial u} + Q\frac{\partial z}{\partial v}, \tag{23}$$

with initial condition $z(0,u,v) = f(u,v)$ that follows from the definition of z.

Analogously, it is shown that:

$$\frac{\partial y_k}{\partial t} = P\frac{\partial y_k}{\partial u} + Q\frac{\partial y_k}{\partial v}; \quad k = 1,2; \tag{24}$$

with $y_1(0,u,v)=u$ and $y_2(0,u,v)=v$. Using (24) and the definition of w yields:

$$\begin{aligned}\mathbf{D}_t w = \mathbf{D}_t f(y_1,y_2) &= \left.\frac{\partial f(\alpha,\beta)}{\partial\alpha}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\left(P\frac{\partial y_1}{\partial u}+Q\frac{\partial y_1}{\partial v}\right)+\left.\frac{\partial f(\alpha,\beta)}{\partial\beta}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\left(P\frac{\partial y_2}{\partial u}+Q\frac{\partial y_2}{\partial v}\right)\\ &= P\left(\left.\frac{\partial f(\alpha,\beta)}{\partial\alpha}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\frac{\partial y_1}{\partial u}+\left.\frac{\partial f(\alpha,\beta)}{\partial\beta}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\frac{\partial y_2}{\partial u}\right)+Q\left(\left.\frac{\partial f(\alpha,\beta)}{\partial\alpha}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\frac{\partial y_1}{\partial v}+\left.\frac{\partial f(\alpha,\beta)}{\partial\beta}\right|_{\substack{\alpha=y_1\\ \beta=y_2}}\frac{\partial y_2}{\partial v}\right)\\ &= P\frac{\partial w}{\partial u}+Q\frac{\partial w}{\partial v}.\end{aligned} \tag{25}$$

Note that w satisfies the initial condition $w(0,u,v)=f\left(y_1(0,u,v),y_2(0,u,v)\right)=f(u,v)$, thus z and w coincide, which results in the proof of (21).

Construction of general solutions to ODEs requires one final operator which is denoted as the generalized multiplicative operator:

$$\mathbf{G}:=\sum_{j=0}^{+\infty}\frac{(t-c)^j}{j!}\mathbf{D}_{cuv}^j. \tag{26}$$

Operator $\mathbf{G}$ has two properties analogous to (20), (21):

$$\mathbf{G}c^m=t^m,\quad m=0,1,\ldots; \tag{27}$$

$$\mathbf{G}f(c,u,v)=f\left(x,\mathbf{G}u,\mathbf{G}v\right), \tag{28}$$

where f is a trivariate analytic function. The proof of (28) follows from (21):

$$\mathbf{M}f(c,u,v)=f\left(t+c,\sum_{j=0}^{+\infty}\frac{t^j}{j!}\mathbf{D}_{cuv}^j u,\sum_{j=0}^{+\infty}\frac{t^j}{j!}\mathbf{D}_{cuv}^j v\right). \tag{29}$$

Substituting t for $t-c$ yields (28).

2.4.3 Construction of solutions to ODEs

Let us consider the following system of ODEs:

$$\begin{aligned}\hat{x}_t &= P\left(t,\hat{x},\hat{y}\right);\quad \left.\hat{x}\right|_{t=\hat{c}}=u;\\ \hat{y}_t &= Q\left(t,\hat{x},\hat{y}\right);\quad \left.\hat{y}\right|_{t=\hat{c}}=v,\end{aligned} \tag{30}$$

where P, Q are analytic functions. The generalized differential operator respective to (30) reads [13]:

$$\mathbf{D}_{\hat{c}uv}:=\mathbf{D}_{\hat{c}}+P\left(\hat{c},u,v\right)\mathbf{D}_u+Q\left(\hat{c},u,v\right)\mathbf{D}_v. \tag{31}$$

Using (31), general solution to (30) is expressed as [13, 14]:

$$\hat{x}=\mathbf{G}u=\sum_{j=0}^{+\infty}\frac{\left(t-\hat{c}\right)^j}{j!}\mathbf{D}_{\hat{c}uv}^j u;\quad \hat{y}=\mathbf{G}v=\sum_{j=0}^{+\infty}\frac{\left(t-\hat{c}\right)^j}{j!}\mathbf{D}_{\hat{c}uv}^j v. \tag{32}$$

The convention $\mathbf{D}_{\hat{c}uv}^0=\mathbf{I}$, where $\mathbf{I}$ is the identity operator, is used.

Identities (32) can be proven using properties (21) and (28) derived in the previous section. Consider operators $\mathbf{M}$, $\mathbf{G}$ defined with respect to the generalized differential operator (31). First, let $z=z(t,\hat{c},u,v)=\mathbf{M}u$ and $w=w(t,\hat{c},u,v)=\mathbf{M}v$. Property (21) yields:

$$\mathbf{D}_t z=\mathbf{D}_t\mathbf{M}u=\mathbf{D}_{\hat{c}uv}\mathbf{M}u=\mathbf{M}\mathbf{D}_{\hat{c}uv}=\mathbf{M}P\left(\hat{c},u,v\right)=P\left(t+c,\mathbf{M}u,\mathbf{M}v\right)=P(t+c,z,w). \tag{33}$$

Analogously,

$$\mathbf{D}_t w = Q(t + c, z, w). \tag{34}$$

Selecting $\hat{x} = z(t - c, \hat{c}, u, v) = \mathbf{G}u$ and $\hat{y} = w(t - c, \hat{c}, u, v) = \mathbf{G}v$ yields the system (30). Furthermore, the definition of operator $\mathbf{G}$ yields that $\hat{x}\Big|_{t=\hat{c}} = u$ and $\hat{y}\Big|_{t=\hat{c}} = v$, thus (32) hold true.

In the following derivations, the notation

$$p_j = p_j(\hat{c}, u, v) := \mathbf{D}^j_{\hat{c}uv} u; \quad q_j = q_j(\hat{c}, u, v) := \mathbf{D}^j_{\hat{c}uv} v; \quad j = 0, 1, \dots \tag{35}$$

will be used, which transforms (32) into:

$$\hat{x} = \sum_{j=0}^{+\infty} \frac{(t - \hat{c})^j}{j!} p_j; \tag{36}$$

$$\hat{y} = \sum_{j=0}^{+\infty} \frac{(t - \hat{c})^j}{j!} q_j. \tag{37}$$

Furthermore, coefficients p_j, q_j satisfy recurrence relations:

$$p_{j+1} = \mathbf{D}_{\hat{c}uv} p_j; \quad q_{j+1} = \mathbf{D}_{\hat{c}uv} q_j. \tag{38}$$

3 Existence of homoclinic/heteroclinic solutions in (30)

Let $\rho_1 \neq \rho_2$. If (30) admits solutions (13), (14) then (13) and (36) must be equal. Expanding (13) in a power series and equating to (36) yields:

$$\sigma + \lambda_1 + \lambda_2 + \sum_{j=1}^{+\infty} \frac{(t - \hat{c})^j}{j!} \left(j! \lambda_1 \rho_1^j + j! \lambda_2 \rho_2^j \right) = \sum_{j=0}^{+\infty} \frac{(t - \hat{c})^j}{j!} p_j. \tag{39}$$

Note that $p_0 = u$ by (35), thus (39) yields:

$$p_0 = u; \tag{40}$$

$$p_j = j! \left(\lambda_1 \rho_1^j + \lambda_2 \rho_2^j \right), \quad j = 1, 2, \dots. \tag{41}$$

Analogous derivations with respect to y and $\nu_1 \neq \nu_2$ result in:

$$q_0 = v; \tag{42}$$

$$q_j = j! \left(\mu_1 \nu_1^j + \mu_2 \nu_2^j \right), \quad j = 1, 2, \dots. \tag{43}$$

Thus (30) admits solutions (13), (14) if and only if (41), (43) hold true.

Theorem 3.1. *System (30) admits homoclinic/heteroclinic solutions (13), (14) with $\rho_1 \neq \rho_2$ if and only if:*

$$\lambda_k = \frac{p_2 - 2\rho_l p_1}{2\rho_k (\rho_k - \rho_l)}; \qquad \mu_k = \frac{q_2 - 2\nu_l q_1}{2\rho_k (\nu_k - \nu_l)}; \tag{44}$$

$$\mathbf{D}_{\hat{c}uv} \rho_k = \rho_k^2; \qquad \mathbf{D}_{\hat{c}uv} \nu_k = \nu_k^2; \tag{45}$$

$$\mathbf{D}_{\hat{c}uv} \lambda_k = \lambda_k \rho_k; \qquad \mathbf{D}_{\hat{c}uv} \mu_k = \mu_k \nu_k; \tag{46}$$

$$3p_1^2 p_4^2 - 36 p_1 p_2 p_3 p_4 + 32 p_1 p_3^3 + 36 p_2^3 p_4 - 36 p_2^2 p_3^2 \neq 0; \tag{47}$$

$$3q_1^2 q_4^2 - 36 q_1 q_2 q_3 q_4 + 32 q_1 q_3^3 + 36 q_2^3 q_4 - 36 q_2^2 q_3^2 \neq 0, \tag{48}$$

$k, l = 1, 2;\ k \neq l.$

Proof. It will be proven that (41), (43) hold true if and only if (44)–(48) hold true.

Necessity. Let (41) hold true. Taking $j = 1, 2$ yields:

$$p_1 = \lambda_1\rho_1 + \lambda_2\rho_2; \tag{49}$$

$$p_2 = 2\left(\lambda_1\rho_1^2 + \lambda_2\rho_2^2\right). \tag{50}$$

Solving the above equations for λ_1, λ_2 results in (44).

Equation (41) yields the following determinant equality:

$$\det\begin{bmatrix} \frac{p_1}{1!} & \frac{p_2}{2!} & \frac{p_3}{3!} \\ \frac{p_2}{2!} & \frac{p_3}{3!} & \frac{p_4}{4!} \\ 1 & \rho_k & \rho_k^2 \end{bmatrix} = 0; \quad k = 1, 2. \tag{51}$$

Expanding the left side of (51) yields:

$$\Delta_2\rho_k^2 - \Delta_1\rho_k + \Delta_0 = 0; \quad k = 1, 2, \tag{52}$$

where

$$\Delta_2 = \frac{p_1p_3}{3!} - \left(\frac{p_2}{2!}\right)^2; \tag{53}$$

$$\Delta_1 = \frac{p_1p_4}{4!} - \frac{p_2p_3}{2!\cdot 3!}; \tag{54}$$

$$\Delta_0 = \frac{p_2p_4}{2!\cdot 4!} - \left(\frac{p_3}{3!}\right)^2. \tag{55}$$

Solving (52) for ρ_k results in:

$$\rho_{1,2} = \frac{\Delta_1 \pm \sqrt{\Delta_1^2 - 4\Delta_2\Delta_0}}{2\Delta_2}. \tag{56}$$

Since $\rho_1 \neq \rho_2$, the discriminant $\Delta_1^2 - 4\Delta_2\Delta_0 \neq 0$, which results in condition (47).

Denoting $\Theta := \sqrt{\Delta_1^2 - 4\Delta_2\Delta_0}$ and applying operator $\mathbf{D}_{\hat{c}uv}$ to (56) results in:

$$\mathbf{D}_{\hat{c}uv}\rho_{1,2} = \frac{(\pm\Theta - \Delta_1)\left(\mathbf{D}_{\hat{c}uv}\Delta_2\right) + \Delta_2\left(\left(\mathbf{D}_{\hat{c}uv}\Delta_1\right) \pm \left(\mathbf{D}_{\hat{c}uv}\Theta\right)\right)}{2\Delta_2^2}. \tag{57}$$

Using recursion (38) it can be obtained that:

$$\mathbf{D}_{\hat{c}uv}\Delta_2 = \frac{p_1p_4}{6} - \frac{p_2p_3}{3}; \tag{58}$$

$$\mathbf{D}_{\hat{c}uv}\Delta_1 = \frac{p_1p_5}{24} - \frac{p_2p_4}{24} - \frac{p_3^2}{12}; \tag{59}$$

$$\mathbf{D}_{\hat{c}uv}\Delta_0 = \frac{p_2p_5}{48} - \frac{5p_3p_4}{144}; \tag{60}$$

$$\mathbf{D}_{\hat{c}uv}\Theta = \frac{1}{\Theta}\left(\Delta_1\left(\mathbf{D}_{\hat{c}uv}\Delta_1\right) - 2\Delta_0\left(\mathbf{D}_{\hat{c}uv}\Delta_2\right) - 2\Delta_2\left(\mathbf{D}_{\hat{c}uv}\Delta_0\right)\right). \tag{61}$$

Relation (41) transforms (53)–(55) and Θ into:

$$\Delta_2 = \lambda_1\lambda_2\rho_1\rho_2\left(\rho_1 - \rho_2\right)^2; \tag{62}$$

$$\Delta_1 = \lambda_1\lambda_2\rho_1\rho_2\left(\rho_1 + \rho_2\right)\left(\rho_1 - \rho_2\right)^2; \tag{63}$$

$$\Delta_0 = 5\lambda_1\lambda_2\rho_1^2\rho_2^2\left(\rho_1 - \rho_2\right)^2; \tag{64}$$

$$\Theta = \lambda_1\lambda_2\rho_1\rho_2\left(\rho_1 - \rho_2\right)^3. \tag{65}$$

Furthermore,

$$\mathbf{D}_{\hat{c}uv}\Delta_2 = 4\lambda_1\lambda_2\rho_1\rho_2\left(\rho_1 + \rho_2\right)\left(\rho_1 - \rho_2\right)^2; \tag{66}$$

$$\mathbf{D}_{\hat{c}uv}\Delta_1 = \lambda_1\lambda_2\rho_1\rho_2\left(\rho_1-\rho_2\right)^2\left(5\rho_1^2+8\rho_1\rho_2+5\rho_2^2\right); \tag{67}$$

$$\mathbf{D}_{\hat{c}uv}\Delta_0 = 5\lambda_1\lambda_2\rho_1^2\rho_2^2\left(\rho_1+\rho_2\right)\left(\rho_1-\rho_2\right)^2; \tag{68}$$

$$\mathbf{D}_{\hat{c}uv}\Theta = 5\lambda_1\lambda_2\rho_1\rho_2\left(\rho_1+\rho_2\right)\left(\rho_1-\rho_2\right)^3. \tag{69}$$

Inserting (62)–(69) into (57) yields (45).

Applying operator $\mathbf{D}_{\hat{c}uv}$ to (44) and using (45) yields:

$$\mathbf{D}_{\hat{c}uv}\lambda_k = \frac{4p_1\rho_k\rho_l - p_2\left(2\rho_k+3\rho_l\right)+p_3}{2\rho_k\left(\rho_k-\rho_l\right)}. \tag{70}$$

Inserting (41) into (70) results in (46).

Sufficiency. Condition (44) yields:

$$p_1 = \lambda_1\rho_1+\lambda_2\rho_2. \tag{71}$$

Applying operator $\mathbf{D}_{\hat{c}uv}$ to (71) results in:

$$\begin{aligned}\mathbf{D}_{\hat{c}u}p_1 &= \rho_1\left(\mathbf{D}_{\hat{c}uv}\lambda_1\right)+\lambda_1\left(\mathbf{D}_{\hat{c}uv}\rho_1\right)+\rho_2\left(\mathbf{D}_{\hat{c}uv}\lambda_2\right)+\lambda_2\left(\mathbf{D}_{\hat{c}uv}\rho_2\right)\\ &= 2\left(\lambda_1\rho_1^2+\lambda_2\rho_2^2\right)=p_2.\end{aligned} \tag{72}$$

Continuing by induction yields (41).

The proof for parameters of y is analogous. □

Corollary 3.1. *If conditions of Theorem 3.1 hold true, then the third and higher order Hankel determinants of sequences* $\frac{p_j}{j!}, \frac{q_j}{j!}; j = 1, 2, \ldots$ *are equal to zero:*

$$H_p^{(n)} = \det\left[\frac{p_{j+k-2}}{(j+k-2)!}\right]_{1\leqslant j,k\leqslant n+1} = 0; \tag{73}$$

$$H_q^{(n)} = \det\left[\frac{q_{j+k-2}}{(j+k-2)!}\right]_{1\leqslant j,k\leqslant n+1} = 0, \tag{74}$$

$n = 3, 4, \ldots$.

Proof. Proof results from the derivation of Theorem 3.1 and (41), (43). □

4 Necessary homoclinic/heteroclinic solution existence conditions in (3)

The inverse balancing technique can be used to determine necessary existence conditions of solutions (8), (9) to (3). The main principle of this technique is to insert the solution ansatz into the considered equations and obtain a system of equations linear in system parameters $a_k, b_k, k = 0, \ldots, 4$. The inverse balancing technique has been successfully used to obtain necessary solution existence conditions in a variety of nonlinear ordinary and partial differential equations [10, 15, 18]. Note that the inverse balancing technique does not possess the drawbacks associated with various solution construction (or direct ansatz) methods, which have attracted a significant amount of criticism [1, 8, 9, 17, 24].

4.1 Transformation of (3)

Using the substitution (10), system (3) is transformed to:

$$\begin{aligned}\eta t\hat{x}_t &= a_0+a_1\hat{x}+a_2\hat{x}^2+a_3\hat{x}\hat{y}+a_4\hat{y};\\ \eta t\hat{y}_t &= b_0+b_1\hat{y}+b_2\hat{y}^2+b_3\hat{x}\hat{y}+b_4\hat{x},\end{aligned} \tag{75}$$

with initial conditions

$$\left.\hat{x}\right|_{t=\hat{c}} = u; \quad \left.\hat{y}\right|_{t=\hat{c}} = v. \tag{76}$$

The following notations are introduced:

$$X(t) := (t-\hat{x}_1)(t-\hat{x}_2); \quad Y(t) := (t-\hat{y}_1)(t-\hat{y}_2); \tag{77}$$

$$T_x(t) := \left(t-t_1^{(x)}\right)\left(t-t_2^{(x)}\right); \quad T_y(t) := \left(t-t_1^{(y)}\right)\left(t-t_2^{(y)}\right), \tag{78}$$

which transform solutions (11), (12) to:

$$\hat{x} = \sigma\frac{X(t)}{T_x(t)}; \quad \hat{y} = \gamma\frac{Y(t)}{T_y(t)}. \tag{79}$$

4.2 Necessary existence conditions for (79) in (75)

Following the inverse balancing technique, solution ansatz (79) is inserted into (75). After simplification, (75) reads:

$$\eta t\sigma T_y\left(X_t T_x - X\left(T_x\right)_t\right) = a_0 T_x^2 T_y + a_1\sigma T_x T_y X + a_2\sigma^2 X^2 T_y + a_3\sigma\gamma XYT_x + a_4\gamma YT_x^2; \tag{80}$$

$$\eta t\gamma T_x\left(Y_t T_y - Y\left(T_y\right)_t\right) = b_0 T_y^2 T_x + b_1\gamma T_y T_x Y + b_2\gamma^2 Y^2 T_x + b_3\sigma\gamma YXT_y + b_4\gamma XT_y^2. \tag{81}$$

Equation (78) results in:

$$T_x\left(t_1^{(x)}\right) = T_x\left(t_2^{(x)}\right) = T_y\left(t_1^{(y)}\right) = T_y\left(t_2^{(y)}\right) = 0; \tag{82}$$

$$\left(T_x\right)_t\Big|_{t=t_1^{(x)}} = t_1^{(x)} - t_2^{(x)}; \quad \left(T_x\right)_t\Big|_{t=t_2^{(x)}} = t_2^{(x)} - t_1^{(x)}; \tag{83}$$

$$\left(T_y\right)_t\Big|_{t=t_1^{(y)}} = t_1^{(y)} - t_2^{(y)}; \quad \left(T_y\right)_t\Big|_{t=t_2^{(y)}} = t_2^{(y)} - t_1^{(y)}. \tag{84}$$

Letting $t = t_1^{(x)}, t_2^{(x)}$ in (80), $t = t_1^{(y)}, t_2^{(y)}$ in (81) and using (82)–(84) yields the following equations:

$$T_y\left(t_1^{(x)}\right)\left(a_2\sigma^2 X^2\left(t_1^{(x)}\right) + \eta\sigma t_1^{(x)}\left(t_1^{(x)} - t_2^{(x)}\right)X\left(t_1^{(x)}\right)\right) = 0; \tag{85}$$

$$T_y\left(t_2^{(x)}\right)\left(a_2\sigma^2 X^2\left(t_2^{(x)}\right) + \eta\sigma t_2^{(x)}\left(t_2^{(x)} - t_1^{(x)}\right)X\left(t_2^{(x)}\right)\right) = 0; \tag{86}$$

$$T_x\left(t_1^{(y)}\right)\left(b_2\gamma^2 Y^2\left(t_1^{(y)}\right) + \eta\gamma t_1^{(y)}\left(t_1^{(y)} - t_2^{(y)}\right)Y\left(t_1^{(y)}\right)\right) = 0; \tag{87}$$

$$T_x\left(t_2^{(y)}\right)\left(b_2\gamma^2 Y^2\left(t_2^{(y)}\right) + \eta\gamma t_2^{(y)}\left(t_2^{(y)} - t_1^{(y)}\right)Y\left(t_2^{(y)}\right)\right) = 0. \tag{88}$$

Equations (85)–(88) have nontrivial solutions only if:

$$t_1^{(x)} = t_1^{(y)}; \quad t_2^{(x)} = t_2^{(y)}, \tag{89}$$

thus (75) (and conversely (3)) only admits homoclinic/heteroclinic solutions with equal denominators. Let $t_1 := t_1^{(x)} = t_1^{(y)}$ and $t_2 := t_2^{(x)} = t_2^{(y)}$. Equation (89) transforms (79) into:

$$\hat{x} = \sigma\frac{X(t)}{T(t)}; \quad \hat{y} = \gamma\frac{Y(t)}{T(t)}, \tag{90}$$

where $T(t) := (t-t_1)(t-t_2)$.

4.3 Necessary existence conditions for (90) in (75)

If (89) holds true, (80), (81) read:

$$\eta t\sigma\left(X_t T - X T_t\right) = a_0 T^2 + a_1 \sigma X T + a_2 \sigma^2 X^2 + a_3 \sigma\gamma X Y + a_4 \gamma Y T; \tag{91}$$

$$\eta t\gamma\left(Y_t T - Y T_t\right) = b_0 T^2 + b_1 \gamma Y T + b_2 \gamma^2 Y^2 + b_3 \sigma\gamma X Y + b_4 \sigma X T. \tag{92}$$

Note that

$$T(t_1) = T(t_2) = X(\hat{x}_1) = X(\hat{x}_2) = Y(\hat{y}_1) = Y(\hat{y}_2) = 0, \tag{93}$$

and

$$T_t = 2t - t_1 - t_2; \quad X_t = 2t - \hat{x}_1 - \hat{x}_2; \quad Y_t = 2t - \hat{y}_1 - \hat{y}_2. \tag{94}$$

Taking $t = t_1, t_2$ in (91) and using (93), (94) yields:

$$\eta t_1\left(t_2 - t_1\right) = \sigma X(t_1) a_2 + \gamma Y(t_1) a_3; \tag{95}$$

$$\eta t_2\left(t_1 - t_2\right) = \sigma X(t_2) a_2 + \gamma Y(t_2) a_3. \tag{96}$$

Analogous computations with respect to (92) result in:

$$\eta t_1\left(t_2 - t_1\right) = \gamma Y(t_1) b_2 + \sigma X(t_1) b_3; \tag{97}$$

$$\eta t_2\left(t_1 - t_2\right) = \gamma Y(t_2) b_2 + \sigma X(t_2) b_3. \tag{98}$$

Solution of (95)–(98) with respect to a_2, a_3, b_2, b_3 reads:

$$a_2 = b_3 = \frac{\eta}{\sigma} \frac{\left(t_2 - t_1\right)\left(t_1 Y(t_2) + t_2 Y(t_1)\right)}{\left(X(t_1) Y(t_2) - X(t_2) Y(t_1)\right)}; \tag{99}$$

$$b_2 = a_3 = \frac{\eta}{\gamma} \frac{\left(t_1 - t_2\right)\left(t_2 X(t_1) + t_1 X(t_2)\right)}{\left(X(t_1) Y(t_2) - X(t_2) Y(t_1)\right)}. \tag{100}$$

Similarly, taking $t = \hat{x}_1, \hat{x}_2$ in (91) and $t = \hat{y}_1, \hat{y}_2$ in (92) yields the following solutions for a_0, a_4, b_0, b_4:

$$a_0 = \frac{\eta\sigma\left(\hat{x}_1 - \hat{x}_2\right)\left(\hat{x}_1 Y(\hat{x}_2) + \hat{x}_2 Y(\hat{x}_1)\right)}{T(\hat{x}_1) Y(\hat{x}_2) - T(\hat{x}_2) Y(\hat{x}_1)}; \tag{101}$$

$$a_4 = \frac{\eta\sigma\left(\hat{x}_2 - \hat{x}_1\right)\left(\hat{x}_1 T(\hat{x}_2) + \hat{x}_2 T(\hat{x}_1)\right)}{\gamma\left(T(\hat{x}_1) Y(\hat{x}_2) - T(\hat{x}_2) Y(\hat{x}_1)\right)}; \tag{102}$$

$$b_0 = \frac{\eta\gamma\left(\hat{y}_1 - \hat{y}_2\right)\left(\hat{y}_1 X(\hat{y}_2) + \hat{y}_2 X(\hat{y}_1)\right)}{T(\hat{y}_1) X(\hat{y}_2) - T(\hat{y}_2) X(\hat{y}_1)}; \tag{103}$$

$$b_4 = \frac{\eta\gamma\left(\hat{y}_2 - \hat{y}_1\right)\left(\hat{y}_1 T(\hat{y}_2) + \hat{y}_2 T(\hat{y}_1)\right)}{\sigma\left(T(\hat{y}_1) X(\hat{y}_2) - T(\hat{y}_2) X(\hat{y}_1)\right)}. \tag{104}$$

Finally, taking $t = 0$ in (91), (92) yields a_1, b_1:

$$a_1 = -\frac{1}{\sigma}\left(a_0 + \sigma^2 a_2 + \sigma\gamma a_3 + \gamma a_4\right); \tag{105}$$

$$b_1 = -\frac{1}{\gamma}\left(b_0 + \gamma^2 b_2 + \sigma\gamma b_3 + \sigma b_4\right). \tag{106}$$

Note that there are 10 parameters in (75) and (91), (92) yields a non-degenerate system of 10 linear balancing equations, thus no constraints on the parameters of solution (90) needs to be imposed. However, as shown by (99), (100) conditions $a_3 = b_2$ and $b_3 = a_2$ must hold if (75) admits solution (90).

The results of this section are summarized in the following Lemma.

Lemma 4.1. *System (3) admits homoclinic/heteroclinic solutions (8), (9) only if:*

$$\tau_1^{(x)} = \tau_1^{(y)}; \quad \tau_2^{(x)} = \tau_2^{(y)}; \tag{107}$$

$$a_3 = b_2; \quad b_3 = a_2. \tag{108}$$

Note that condition (107) results from (89) and substitution (10). Also, $\rho_k = \nu_k$; $k = 1, 2$ in (13), (14) when (107) holds true.

5 Construction of homoclinic/heteroclinic solutions to (3)

In this section, explicit expressions of homoclinic and heteroclinic solutions to (3) are constructed. It is assumed that the necessary existence conditions (107), (108) hold true.

5.1 Derivation of parameter η

Parameter η is derived using Corollary 3.1. Consider the following Hankel determinants:

$$H_p^{(3)} = \begin{vmatrix} \frac{p_1}{1!} & \frac{p_2}{2!} & \frac{p_3}{3!} \\ \frac{p_2}{2!} & \frac{p_3}{3!} & \frac{p_4}{4!} \\ \frac{p_3}{3!} & \frac{p_4}{4!} & \frac{p_5}{5!} \end{vmatrix}; \quad H_q^{(3)} = \begin{vmatrix} \frac{q_1}{1!} & \frac{q_2}{2!} & \frac{q_3}{3!} \\ \frac{q_2}{2!} & \frac{q_3}{3!} & \frac{q_4}{4!} \\ \frac{q_3}{3!} & \frac{q_4}{4!} & \frac{q_5}{5!} \end{vmatrix}. \tag{109}$$

Parameter η must be chosen to satisfy

$$H_p^{(3)} = 0; \quad H_q^{(3)} = 0. \tag{110}$$

Furthermore, η can only depend on coefficients $a_0, \ldots, a_4; b_0, \ldots, b_4$, otherwise Theorem 3.1 does not hold true and obtained solutions would not be valid for all initial conditions.

It can be observed that:

$$H_p^{(3)} = \frac{1}{\eta^9 \widehat{c}^9} \left(A_6(u,v)\eta^6 + A_4(u,v)\eta^4 + A_2(u,v)\eta^2 + A_0(u,v) \right); \tag{111}$$

$$H_q^{(3)} = \frac{1}{\eta^9 \widehat{c}^9} \left(B_6(u,v)\eta^6 + B_4(u,v)\eta^4 + B_2(u,v)\eta^2 + B_0(u,v) \right). \tag{112}$$

Thus, roots of equations (111), (112) with respect to η that do not depend on u, v must be found. Note that:

$$A_6 = \left(\frac{1}{2160} \right)^{1/3} K^3, \quad K := \left(u^2 a_2 + (a_3 v + a_1) u + a_4 v + a_0 \right); \tag{113}$$

and

$$A_4 = F(u,v) K, \tag{114}$$

where F is a polynomial in u, v.

Since the roots η must not depend on initial conditions, any values of u, v can be chosen and inserted into (111). Let

$$v = f(u) = -\frac{a_2 u^2 + a_1 u + a_0}{b_2 u + a_4}, \tag{115}$$

then $A_6 = A_4 = 0$ and using (111), η^2 can be expressed as:

$$\eta^2 = -\frac{A_0(u, f(u))}{A_2(u, f(u))}. \tag{116}$$

The numerator and denominator of (116) depend linearly on u:

$$\eta^2 = \frac{\alpha_1 u + \alpha_0}{\beta_1 u + \beta_0}, \tag{117}$$

where α_k, β_k are functions of $a_0, \ldots, a_4; b_0, \ldots, b_4$.

Analogous computations with respect to $H_q^{(3)}$ lead to:

$$u = g(v) = -\frac{b_2 v^2 + b_1 v + b_0}{a_2 v + b_4}; \tag{118}$$

$$\eta^2 = -\frac{B_0(g(v), v)}{B_2(g(v), v)} = \frac{\widehat{\alpha}_1 v + \widehat{\alpha}_0}{\widehat{\beta}_1 v + \widehat{\beta}_0}. \tag{119}$$

Parameter η does not depend on u, v only if:

$$\alpha_1\beta_0 - \alpha_0\beta_1 = 0; \tag{120}$$

$$\widehat{\alpha}_1\widehat{\beta}_0 - \widehat{\alpha}_0\widehat{\beta}_1 = 0. \tag{121}$$

Note that:

$$\frac{1}{a_0 b_2^2 - a_1 a_4 b_2 + a_2 a_4^2}\left(\alpha_1\beta_0 - \alpha_0\beta_1\right) = \frac{1}{b_0 a_2^2 - b_1 b_4 a_2 + b_2 b_4^2}\left(\widehat{\alpha}_1\widehat{\beta}_0 - \widehat{\alpha}_0\widehat{\beta}_1\right), \tag{122}$$

which leads to the following sufficient existence condition for homoclinic/heteroclinic solutions to (3):

$$\begin{aligned} &9a_0a_1a_2 + 9b_0b_1b_2 - 18a_0a_2b_1 - 18b_0b_2a_1 + 3a_1b_1^2 + 3b_1a_1^2 - 2a_1^3 - 2b_1^3 \\ &- 9a_1a_4b_4 - 9b_1b_4a_4 + 27a_0b_2b_4 + 27b_0a_2a_4 = 0. \end{aligned} \tag{123}$$

If (123) holds true, η can be computed from either (117) or (119). Furthermore, if (123) holds true, the parameter η does not depend on initial conditions c, u, v.

5.2 Necessary and sufficient existence conditions for homoclinic/heteroclinic solutions to (3)

Theorem 3.1, Lemma 4.1 and condition (123) together with computer algebra computations result in the following theorem.

Theorem 5.1. *System (3) admits homoclinic/heteroclinic solutions (8), (9) if and only if conditions (107), (108) and (123) hold true.*

Note that

$$\rho_k = \frac{\rho_k^*}{\widehat{c}}; \quad k = 1, 2, \tag{124}$$

where $\rho_k^* = \rho_k^*(u, v)$.

Relations between parameters of (13), (14) and (8), (9) read:

$$\tau_k = 1 + \frac{1}{\rho_k^*}; \quad k = 1, 2; \tag{125}$$

$$x_{1,2} = \frac{1}{2}\left(A_x \pm \sqrt{A_x^2 - 4B_x}\right); \tag{126}$$

$$y_{1,2} = \frac{1}{2}\left(A_y \pm \sqrt{A_y^2 - 4B_y}\right), \tag{127}$$

where

$$A_x := \frac{\lambda_1}{\sigma\rho_1^*} + \frac{\lambda_2}{\sigma\rho_2^*} + \tau_1 + \tau_2; \tag{128}$$

$$B_x := \tau_1\tau_2 + \frac{\lambda_1\tau_2}{\sigma\rho_1^*} + \frac{\lambda_2\tau_1}{\sigma\rho_2^*}; \tag{129}$$

$$A_y := \frac{\mu_1}{\gamma\rho_1^*} + \frac{\mu_2}{\gamma\rho_2^*} + \tau_1 + \tau_2; \tag{130}$$

$$B_y := \tau_1\tau_2 + \frac{\mu_1\tau_2}{\gamma\rho_1^*} + \frac{\mu_2\tau_1}{\gamma\rho_2^*}. \tag{131}$$

Parameters σ, γ read:

$$\sigma = u - \lambda_1 - \lambda_2; \quad \gamma = v - \mu_1 - \mu_2. \tag{132}$$

Note that (117) yields two values for η, however, it is sufficient to consider only the positive or negative root of (117) to obtain the general solution to (3) when Theorem 5.1 holds true, because the sign of η can be interchanged:

$$\begin{aligned} x &= \sigma\frac{\left(\exp\left(\eta\left(\tau - c\right)\right) - x_1\right)\left(\exp\left(\eta\left(\tau - c\right)\right) - x_2\right)}{\left(\exp\left(\eta\left(\tau - c\right)\right) - \tau_1\right)\left(\exp\left(\eta\left(\tau - c\right)\right) - \tau_2\right)} \\ &= \sigma\frac{x_1x_2\left(\exp\left(-\eta\left(\tau - c\right)\right) - \frac{1}{x_1}\right)\left(\exp\left(-\eta\left(\tau - c\right)\right) - \frac{1}{x_2}\right)}{\tau_1\tau_2\left(\exp\left(-\eta\left(\tau - c\right)\right) - \frac{1}{\tau_1}\right)\left(\exp\left(-\eta\left(\tau - c\right)\right) - \frac{1}{\tau_2}\right)}. \end{aligned} \tag{133}$$

As demonstrated in [15], the value $\frac{x_1x_2}{\tau_1\tau_2}$ does not depend on initial conditions, which proves that changing the sign of η does not yield new solutions.

6 Homoclinic/heteroclinic solutions to hepatitis C model (2)

6.1 Existence conditions

Comparing (2) to (3) it can be observed that:

$$a_0 = s; \quad a_1 = 1; \quad a_2 = -1; \quad a_3 = b\left(\theta - 1\right) - 1; \quad a_4 = q; \tag{134}$$

$$b_0 = 0; \quad b_1 = r - d - q; \quad b_2 = -r; \quad b_3 = b\left(1 - \theta\right) - r; \quad b_4 = 0. \tag{135}$$

To preserve biological significance of system (2), the parameters (134), (135) must satisfy $q, s, r \geqslant 0$; $b \in \left[10^{-2}; 10^3\right]$; $d \in \left[10^{-3}; 10^2\right]$ [25].

Using Theorem 5.1 conditions for the existence of homoclinic/heteroclinic solutions to (2) can be derived. Note that only homoclinic/heteroclinic solutions with $\tau_k^{(x)} = \tau_k^{(y)}$ can be considered. Inserting (134), (135) into (108) yields two congruent equations:

$$\left(1 - \theta\right)b - r = -1; \quad b\left(\theta - 1\right) - 1 = -r. \tag{136}$$

Both equations are satisfied if parameter r reads:

$$r = b\left(1 - \theta\right) + 1. \tag{137}$$

Let (137) hold true. Denote $\Omega := b\left(1 - \theta\right) + 1 - d - q = r - d - q$. Inserting (134), (135) into condition (123) yields:

$$s = \frac{1}{9}\left(\Omega^2 - \Omega - 2\right). \tag{138}$$

Equations (137) and (138) result in the following corollary.

Corollary 6.1. *Hepatitis C model (2) admits homoclinic/heteroclinic solutions if and only if $\tau_k^{(x)} = \tau_k^{(y)}$, (137) and (138) hold true.*

Computer algebra computations prove that when Corollary (6.1) holds true, parameters $y_1 = y_2 = 0$.

6.2 Equilibria

Let (137) and (138) hold true. The equilibria of (2) read:

$$x_*^{(1)} = \frac{2}{3} - \frac{\Omega}{3}; \quad y_*^{(1)} = 0; \tag{139}$$

$$x_*^{(2)} = \frac{1}{3} + \frac{\Omega}{3}; \quad y_*^{(1)} = 0; \tag{140}$$

$$x_*^{(3)} = \frac{(1-\theta)(s+q)b - q^2 + (1-d)q + s}{(1-\theta)^2 b^2 - (1-\theta)(d+q-1)b - d}; \tag{141}$$

$$y_*^{(3)} = \frac{2(2\Omega-1)^2}{9\left((1-\theta)^2 b^2 - (1-\theta)(d+q-1)b - d\right)}. \tag{142}$$

Equilibrium point (141), (142) is a stable node as $\tau \to +\infty$:

$$\lim_{\tau\to+\infty}\left(x(\tau), y(\tau)\right) = (\sigma, \gamma). \tag{143}$$

Equilibrium point (139) is an unstable node as $\tau \to -\infty$:

$$\lim_{\tau\to-\infty}\left(x(\tau), y(\tau)\right) = \left(\sigma\frac{x_1 x_2}{\tau_1\tau_2}, 0\right). \tag{144}$$

The remaining equilibrium point (140) is a saddle point.

6.3 Computational experiment

Let us consider the following system:

$$x_\tau = x(1-x-y) + 18xy + 4y + \frac{4}{9}; \qquad x\Big|_{\tau=c} = u; \tag{145}$$

$$y_\tau = 19y(1-x-y) - 18xy - 16y; \qquad y\Big|_{\tau=c} = v. \tag{146}$$

The above system corresponds to (2) with the following parameters:

$$b = 24; \quad \theta = \frac{1}{4}; \quad q = 4; \quad d = 12; \quad r = 19; \quad s = \frac{4}{9}. \tag{147}$$

Note that parameters (147) satisfy the guidelines given in [25] for biologically significant systems. Furthermore, conditions of Corollary 6.1 are satisfied, thus homoclinic/heteroclinic solutions to (145), (146) do exist.

Equation (117) yields:

$$\eta = \pm\frac{5}{3}. \tag{148}$$

As noted previously, it is sufficient to consider one value of η to obtain the general solution to (145), (146). In subsequent computations the value $\eta = \frac{5}{3}$ is used.

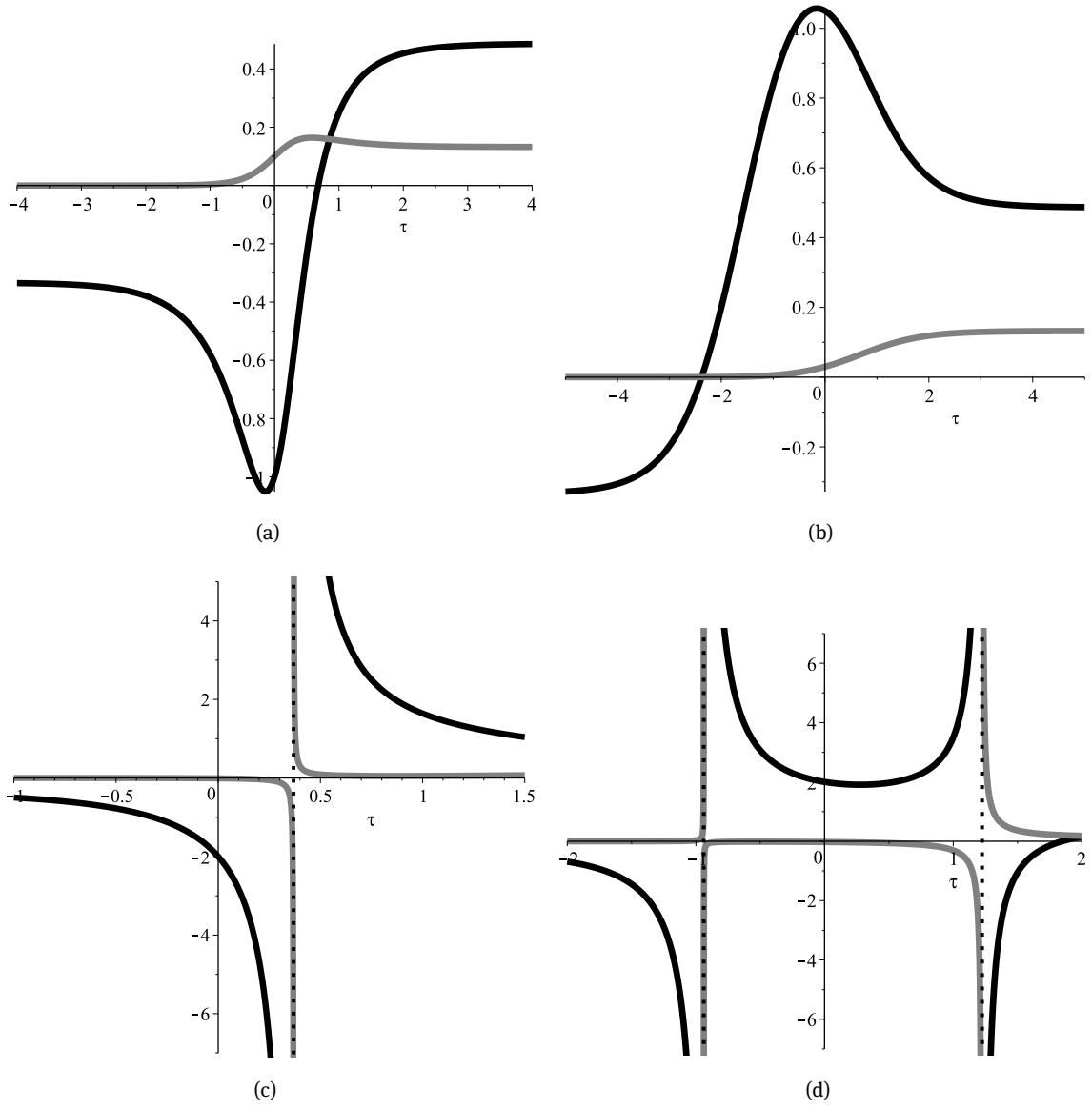
Theorem 3.1 yields the following parameters of homoclinic/heteroclinic solutions:

$$\rho_{1,2} = \frac{1}{10\widehat{c}}\left(-3u - 57v - 1 \pm \sqrt{\Phi}\right); \tag{149}$$

$$\lambda_{1,2} = \frac{3\left(\frac{\sqrt{\Phi^3}}{3} - \left(1083v^2 + (57u-202)v + 5u + \frac{5}{3}\right)\sqrt{\Phi} \mp 3648v^2 \mp (570u-760)v \mp \left(u-\frac{4}{3}\right)\Phi\right)}{\sqrt{\Phi}\left(9u + 171v + 3 \mp 3\sqrt{\Phi}\right)}; \tag{150}$$

$$\mu_{1,2} = \frac{v\left((3u+57v-9)\sqrt{\Phi} \mp (A - 30u - 192v + 40)\right)}{\sqrt{\Phi}\left(3u + 57v + 1 - \sqrt{\Phi}\right)}, \tag{151}$$

Figure 2: Homoclinic/heteroclinic solutions to (145), (146). Black and gray lines correspond to x and y respectively. Dotted lines denote singularity points in (c) and (d). Initial conditions are $u = -1, v = 1/10$ in (a); $u = 105/100, v = 3/100$ in (b); $u = -2, v = -1/100$ in (c); $u = -3; v = 2/100$ in (d). Labels (a), (b), (c), (d) correspond to respectively labeled phase plane trajectories in Fig. 3.



where

$$\Phi = \Phi(u, v) := 9u^2 + 342uv + 3249v^2 + 6u - 642v + 1. \tag{152}$$

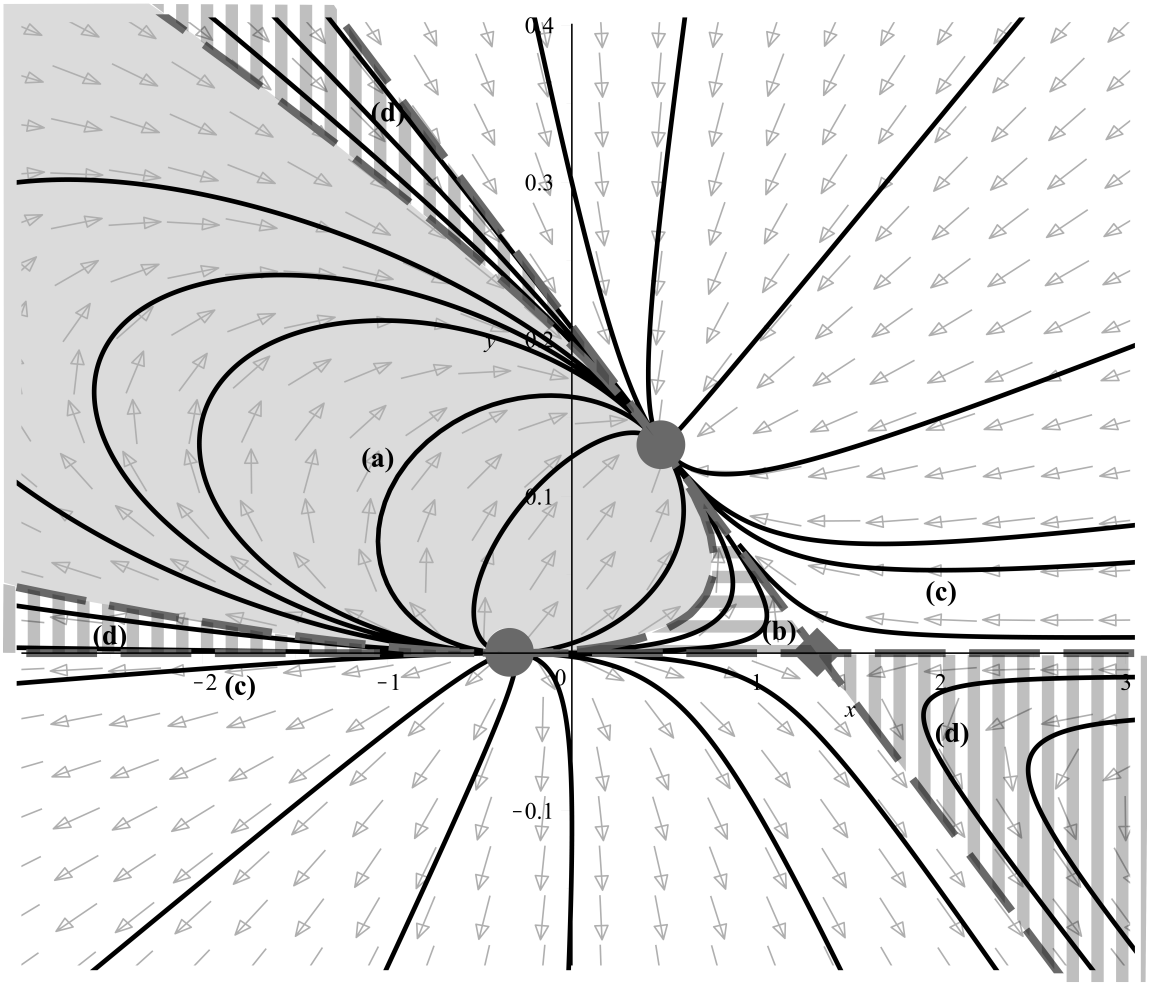
Derivations given in Subsection 5.2 result in:

$$\sigma = \frac{92}{189}; \quad \gamma = \frac{29}{189}; \tag{153}$$

$$\tau_{1,2} = \frac{\sqrt{\Phi} \mp (3u + 57v - 9)}{\sqrt{\Phi} \mp (3u + 57v + 1)}; \tag{154}$$

$$x_{1,2} = \frac{v^3}{138}\left(-15u + 93v - 5 \pm \sqrt{\Phi}\right); \quad y_{1,2} = 0. \tag{155}$$

Figure 3: Phase portrait of (145), (146). Gray circles denote the stable and unstable nodes; diamond denotes the saddle point. Solid black lines correspond to solution trajectories. Dashed gray parabola corresponds to the separatrix between solutions with elliptic and hyperbolic trajectories. Dashed gray lines denote stable and unstable manifolds of the saddle point. Labels (a), (b), (c), (d) correspond to respective parts of Fig. 2. Trajectories in the solid gray and horizontally striped filled regions are elliptic and hyperbolic respectfully and do not have singularities. Trajectories in the unfilled regions are hyperbolic and have one singularity. Trajectories in vertically striped regions are hyperbolic and have two singularities.



Solutions with parameters (153)–(155) are pictured in Fig. 2. Note that there are three types of solutions – non-singular solutions (a), (b); solutions with one singularity (c) and solutions with two singularities (d).

The phase plane of (145), (146) can be seen in Fig. 3. Note that labels (a), (b), (c), (d) on the phase plane correspond to respectively labeled solutions pictured in Fig. 2. System (145), (146) has the following equilibria $\left(\frac{92}{189}, \frac{29}{189}\right)$ – stable node; $\left(-\frac{1}{3}, 0\right)$ – unstable node; $\left(\frac{4}{3}, 0\right)$ – saddle point.

It has been proven in [15] that homoclinic/heteroclinic solutions of the form (8), (9) correspond to phase plane trajectories that satisfy the general conic section equation:

$$Ax^2 + Bxy + Cy^2 + Ex + Fy + G = 0; \quad A, B, C, E, F, G \in \mathbb{R}. \tag{156}$$

Solution Fig. 3 (a) corresponds to an elliptic trajectory, while the remaining (b), (c), (d) have hyperbolic trajectories. Furthermore, there is a single solution that satisfies the parabola equation:

$$\Phi(x, y) = 0. \tag{157}$$

Curve (157) is a separatrix that separates solutions with and without singularities in the phase plane (see dashed gray parabola in Fig. 3).

Stable and unstable manifolds of the saddle point are obtained by setting the numerator and denominator of $\tau_{1,2}$ to zero [15]. This yields that the stable manifold of the saddle point is the x-axis, while the unstable manifold lies on the straight line $y = -\frac{5}{32}x + \frac{5}{24}$. Manifolds of the saddle point correspond to dashed gray lines in Fig. 3.

7 Concluding remarks

Homoclinic and heteroclinic solutions to hepatitis C evolution model (2) have been constructed in this paper. Inverse balancing and generalized differential operator techniques have enabled the derivation of explicit necessary and sufficient homoclinic and heteroclinic solution existence conditions with respect to the parameters of system (2). Furthermore, it has been shown that these existence conditions are satisfied when (2) described a biologically significant system of HCV evolution.

It has been demonstrated that transient processes of the derived solutions to (2) reveal important phenomena for understanding hepatitis C virus infection dynamics. Even though antiviral therapy reduces the number of infected cells (comparing the beginning to the end of treatment), due to the transient processes during the therapy, population size of infected cells is higher than before or after therapy – if only the considered solutions are heteroclinic with maxima. Analogous biological interpretations can be made for heteroclinic solutions with minima. The population of healthy cells is lower than before or after treatment during antiviral therapy – if the number of uninfected hepatocytes is described by a heteroclinic solution possessing minima.

The main mathematical advancements of this paper can be characterized by new applications of inverse balancing technique and the development of generalized differential operator method for the solution of coupled differential equations with multiplicative and diffusive terms. As noted in Section 4, direct balancing techniques may yield wrong solutions; inverse balancing of such a complex system of nonlinear differential equations poses a number of technical problems. On the other hand, derivation of closed-form homoclinic/heteroclinic solutions and explicit conditions of their existence poses serious mathematical challenges. One of the main contributions of this paper are the necessary and sufficient conditions for the existence of these solutions in the hepatitis C evolution model.

Comparing the results of this paper with [15] it can be concluded that system (3) (and, by extension (2)) is structurally stable in the topological sense – when a_4, b_4 tend to zero, the phase plane continuously converges to the phase plane described in [15]. Moreover, structural stability can also be observed in homoclinic/heteroclinic solution existence condition (123) – in the case $a_4, b_4 \to 0$, such solutions also exist and the condition (123) is maintained. Since such effects are observed in systems with biological significance, they provide valuable insight not only into (2) but also other nonlinear evolution models.

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References

[1] Aslan Í, Marinakis V., Some remarks on Exp-function method and its applications, *Commun Theor Phys*, 2011, 56, 397–403.
[2] Chatterjee A., Guedj J., Perelson A.S., Mathematical modeling of HCV infection: what can it teach us in the era of direct antiviral agents? *Antivir Ther*, 2012, 17, 1171–1182.
[3] Clausznitzer D., Harnisch J., Kaderali L., Multi-scale model for hepatitis C viral load kinetics under treatment with direct acting antivirals, *Virus Res*, 2016, 218, 96–101.
[4] de Pillis L.G., Radunskaya A.E., Wiseman C.L., A validated mathematical model of cell-mediated immune response to tumor growth, *Cancer Res*, 2005, 65, 7950–7958.

[5] Gourley S.A., Kuang Y., Nagy J.D., Dynamics of a delay differential equation model of hepatitis B virus infection, *J Biol Dyn*, 2:140–153, 2008.
[6] Hoppensteadt F.C., Peskin C., Eds., *Modeling and Simulation in Medicine and the Life Sciences*, 2002, Springer, New York.
[7] Kudryashov N.A., On new travelling wave solutions of the KdV and the KdV-Burgers equation, *Commun Nonlinear Sci Numer Simul*, 2009, 14, 1891–1900.
[8] Kudryashov N.A., Seven common errors in finding exact solutions of nonlinear differential equations, *Commun Nonlinear Sci Numer Simul*, 2009, 14, 3507–3529.
[9] Kudryashov N.A., Loguinova N.B., Be careful with Exp-function method, *Commun Nonlinear Sci Numer Simul*, 2009, 14, 1891–1900.
[10] Marcinkevicius R., Navickas Z., Ragulskis M., Telksnys T., Solitary solutions to a relativistic two-body problem, *Astrophys Space Sci*, 2016, 361, 201.
[11] Martin N.K., Pitcher A.B., Vickerman P., Vassall A., Hickman M., Optimal control of hepatitis C antiviral treatment programme delivery for prevention amongst a population of injecting drug users, *Plos One*, 2011, 6, e22309.
[12] Mierke C.T., Ed., *Physics of Cancer*, 2015, IOP Publishing, Bristol.
[13] Navickas Z., Bikulciene L., Expressions of solutions of ordinary differential equations by standard functions, *Math Model Anal*, 2006, 11, 399–412.
[14] Navickas Z., Bikulciene L., Ragulskis M., Generalization of Exp-function and other standard function methods, *Appl Math Comput*, 2010, 216, 2380–2393.
[15] Navickas Z., Marcinkevicius R., Telksnys T., Ragulskis M., Existence of second order solitary solutions to Riccati differential equations coupled with a multiplicative term, *IMA J Appl Math*, 2016, 81, 1163–1190.
[16] Navickas Z., Ragulskis M., How far can one go with the Exp-function method? *Appl Math Comput*, 2009, 211, 522–530.
[17] Navickas Z., Ragulskis M., Bikulciene L., Be careful with the Exp-function method – additional remarks, *Commun Nonlinear Sci Numer Simul*, 2010, 15, 3874–3886.
[18] Navickas Z., Ragulskis M., Telksnys T., Existence of solitary solutions in a class of nonlinear differential equations with polynomial nonlinearity, *Appl Math Comput*, 2016, 283, 333–338.
[19] Navickas Z., Vilkas R., Telksnys T., Ragulskis M., Direct and inverse relationships between Riccati systems coupled with multiplicative terms, *J Biol Dyn*, 2016, 10, 297–313.
[20] Neumann A.U., Lam N.P., Dahari H., Gretch D.R., Wiley T.E., Layden T.J., Perelson A.S., Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy, *Science*, 1998, 282, 103–107.
[21] Nguyen V.K., Binder S.C., Boianelli A., Meyer-Hermann M., Hernandez-Vargas E.A., Ebola virus infection modeling and identifiability problems, *Front Microbiol*, 2015, 6, 257.
[22] Pang L., Shen L., Zhao Z., Mathematical modelling and analysis of the tumor treatment regimens with pulsed immunotherapy and chemotherapy, *Comput Math Methods Med*, 2017, 6260474, 12.
[23] Polyanin A.D., Zaitsev V.F., *Handbook of Exact Solutions for Ordinary Differential Equations*, 2003, Chapman and Hall/CRC.
[24] Popovych R.O., More common errors in finding exact solutions of nonlinear differential equations: Part I, *Commun Nonlinear Sci Numer Simul*, 2010, 15, 3887–3899.
[25] Reluga T.C., Dahari H., Perelson A.S., Analysis of hepatitis c virus infection models with hepatocyte homeostasis, *SIAM J Appl Math*, 2009, 69, 999–1023.
[26] Scott A., Ed., *Encyclopedia of Nonlinear Science*, 2004, Routledge, New York.
[27] Wang J., Tian X., Global stability of a delay differential equation of hepatitis B virus infection with immune response, *Electron J Differential Equations*, 2013, 1–11.
[28] Wodarz D., Computational approaches to study oncolytic virus therapy: insights and challenges, *Gene Ther Mol Biol*, 2004, 8, 137–146.
[29] Wodarz D., Komarova N.L., Eds. *Dynamics of Cancer*, 2014, World Scientific, Singapore.