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ORIGINAL PAPER

Numerical modeling of oxygen diffusion in cells with Michaelis-Menten uptake kinetics

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Abstract A class of singular boundary value problems is studied, which models the oxygen diffusion in a spherical cell with Michaelis-Menten uptake kinetics. Suitable singular Cauchy problems are considered in order to determine one-parameter families of solutions in the neighborhood of the singularities. These families are then used to construct stable shooting algorithms for the solution of the considered problems and also to propose a variable substitution in order to improve the convergence order of the finite difference methods. Numerical results are presented and discussed.

Keywords m-Laplacian · Singular Cauchy problem · Singular boundary value problem · Shooting method · Finite difference method

1 Introduction

It is known that boundary value problems of the form

$$y''(x) + \frac{2}{x} y'(x) = f(y), \quad 0 < x < 1 \tag{1}$$

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$$y'(0) = 0, \tag{2}$$
$$ay(1) + by'(1) = c, \quad a > 0, b \geq 0, c \geq 0, \tag{3}$$

model several physiological processes. In the case

$$f(y) = -\alpha e^{-\beta y}, \quad \alpha > 0, \beta > 0; \tag{4}$$

problem (1)–(3) arises in the study of the heat conduction problem in the human head (see [6,7,2,5]). Recently, in [14], a generalized model for this problem was considered, where the classical Laplacian, staying on the left-hand side of Eq. (1), was replaced by the so-called degenerate m-Laplacian:

$$L_m(y) := \left(\left|y'(x)\right|^{m-2} y'(x)\right)' + \frac{N-1}{x}\left|y'(x)\right|^{m-2} y'(x); \tag{5}$$

here, $N > 1$ is the space dimension and m is a real parameter ($m > 1$); L_m reduces to the classical Laplacian whem $m = 2$. As explained in the cited work, the physical meaning of introducing the m-Laplacian in heat conduction problems is that we replace the classical Fourier law by a generalized version of this law, which is more adequate to model heat conduction in non-homogeneous media.

The physical motivation for the present work comes also from a problem in Biosciences: oxygen diffusion in a spherical cell with Michaelis-Menten uptake kinetics. In this case, the classical governing equation is also of the form (1), but with the right-hand side function given by

$$f(y) = \delta \frac{y(x)}{y(x) + \mu}; \tag{6}$$

in this case, y represents the oxygen tension; δ and μ are positive constants involving the reaction rate and the Michaelis constant. The boundary conditions that the solution must satisfy are also given by (2) and (3), with $b > 0$, $a = c = 1$, b being a constant related with the permeability of the cell.

As far as we know, this problem was first analysed, from the mathematical point of view, in 1976 by Lin [12] and in 1978 by McElwain [13], who have carried out numerical computations using the shooting method. In 1983, Hiltman and Lory [8] have proved existence and uniqueness of solution of this problem. On the other hand, Anderson and Arthurs in 1980 have applied to this problem variational methods based on extremum principles [1]. In [3], the same authors have obtained lower and upper functions which provide a simple and efficient way to approximate the solution. In [4], the authors have considered a modified version of Eq. (1) (without the term with the first derivative) and searched for a solution that satisfies the boundary conditions $y(\pm 1) = 1$. Lower and upper bounding functions for this case were found; existence and uniqueness of solution was proved.

In [15] and [16] the authors have used a finite difference scheme to obtain the solution of a wider class of problems for the considered model: instead of the linear differential operator $Ly = y''(x) + \frac{2}{x}y'(x)$ in Eq. (1), they have considered $\frac{(p(x)y'(x))'}{p(x)}$, where $p(x) = x^{b_0}$, with $b_0 \geq 1$. This operator reduces to Ly when $b_0 = 2$.

In the present paper we also consider a generalization of Eq. (1), with the right-hand side in the form (6) and with the classical Laplacian replaced by the mentioned above degenerate m-Laplacian. This leads us to the following equation:

$$\left(\left|y'(x)\right|^{m-2} y'(x)\right)' + \frac{N-1}{x}\left|y'(x)\right|^{m-2} y'(x) = \delta \frac{y(x)}{y(x)+\mu} \quad . \tag{7}$$

When introducing the m-Laplacian operator in this model, we are allowing nonlinear diffusion in the following sense: the module of the oxygen flux is proportional to the $(m-1)$-th power of the oxygen tension gradient. As mentioned above, this reduces to the clasical situation when $m = 2$.

Since Eq. (7) may be written in the form

$$y'' = -\frac{1}{m-1}\left(\frac{N-1}{x}y' - \frac{f(y)}{|y'|^{m-2}}\right) \tag{8}$$

we easily see that problem (7), (2), (3) is singular at $x = 0$, with respect to the independent variable, due to the division by x on the first term of the right-hand side of (8), and also with respect to the dependent variable, whenever $m > 2$, due to the division by $|y'|^{m-2}$ and the boundary condition (2).

As it is known the convergence order of finite difference schemes may decrease significantly in the presence of singularities, as it happens in this case. The main goal of this paper is to avoid this problem by performing simple variable substitutions taking into account the behavior of the solution in the neighborhood of the singular points.

The paper is organized as follows: In the next section, we determine one-parameter families of solutions of suitable singular Cauchy problems describing the behavior of the solution in the neighborhood of the singularities. Based on that behavior we construct in the following sections some efficient numerical methods. In Sect. 3, we will introduce some lower and upper solutions to the considered problem, which are useful to locate the exact solution and can be also used as initial approximations for the application of iterative methods. In Sect. 4 we will introduce a shooting algorithm, using the same approach as we did in [10] and [11], by adjusting the parameter of the families of solutions in order to satisfy condition (3). In Sect. 5 we introduce a finite difference scheme and a smoothing variable substitution. Numerical results are presented and compared with those obtained by the shooting method and also with those obtained by other authors (in the case $m = 2$).

2 Behavior of the solution in the neighborhood of the singularity $x = 0$

Consider the following singular initial value problem

$$\left(\left|y'(x)\right|^{m-2} y'(x)\right)' + \frac{N-1}{x}\left|y'(x)\right|^{m-2} y'(x) = \delta \frac{y(x)}{y(x)+\mu}, \quad x > 0 \tag{9}$$

$$y(0) = y_0, \quad \lim_{x \to 0^+} xy(x) = 0, \tag{10}$$

where $\delta > 0$, $\mu > 0$, $m > 1$ and $N \geq 1$.

Let us look for a solution of this problem in the form:

$$\begin{aligned} y(x) &= y_0 + Cx^k(1 + o(1)) \\ y'(x) &= Ckx^{k-1}(1 + o(1)) \\ y''(x) &= Ck(k-1)x^{k-2}(1 + o(1)), \quad x \to 0^+ \end{aligned} \tag{11}$$

where C is a positive constant and $k > 1$. If we substitute (11) in (9) we obtain

$$k = \frac{m}{m-1}, \quad k - 1 = \frac{1}{m-1} > 0, \text{ and } C = \frac{1}{k}\left(\frac{\delta y_0}{(y_0 + \mu)N}\right)^{k-1}. \tag{12}$$

In order to improve representation (11) we perform the variable substitution

$$y(x) = y_0 + Cx^k(1 + g(x))$$

obtaining the Cauchy problem in the new unknown g:

$$\frac{(m-1)^2}{m}\left[k(k-1)(1+g) + 2kxg' + x^2g''\right]\left[1 + g + \frac{x}{k}g'\right]^{m-2} + \tag{13}$$

$$+(N-1)\left[1 + g + \frac{x}{k}g'\right]^{m-1} = \frac{N(y_0 + \mu)}{y_0}\frac{y_0 + Cx^k(1+g)}{y_0 + Cx^k(1+g) + \mu} \tag{14}$$

$$g(0) = 0, \quad \lim_{x \to 0^+} xg'(x) = 0. \tag{15}$$

Leu us seek for a particular solution of problem (14), (15) in the form

$$g_p(x, y_0) = \sum_{l=0,\, j=0,\, l+j \geq 1}^{+\infty} g_{l,j}\,(y_0)\, x^{l + j\frac{m}{m-1}}, \quad 0 \leq x \leq \delta\,(y_0)\,, \;\; \delta\,(y_0) \geq 0. \tag{16}$$

The coefficients $g_{l,j}$ depending on y_0 may be determined by formally inserting (16) in (14), resulting for $l = 0$ and $j = 1$:

$$g_{0,1} = \frac{CN\mu}{2(m - N + mN)y_0(y_0 + \mu)}. \tag{17}$$

Performing the variable substitutions $z_1 = g$, $z_2 = xg'$, the initial problem (14), (15) rewrites

$$\begin{aligned} xz' &= Az + F(x, z, y_0) + H(x, y_0) \\ z(0) &= 0 \end{aligned}$$

where $z = \begin{pmatrix} z_1 \\ z_2 \end{pmatrix}$, $A = \begin{pmatrix} 0 & 1 \\ -\frac{mN}{(m-1)^2} & -\frac{m+N}{m-1} \end{pmatrix}$, $F(x, z, y_0) = \begin{pmatrix} 0 \\ f(x, z_1, z_2, y_0) \end{pmatrix}$,
$H(x, y_0) = \begin{pmatrix} 0 \\ g(x, y_0) \end{pmatrix}$,

$$f(x, z_1, z_2, y_0) = \frac{mN}{(m-1)^2} \frac{y_0 + \mu}{y_0} \left[\left(1 - \frac{\mu}{y_0 + Cx^k(1+g) + \mu}\right) \left(1 + z_1 + \frac{1}{k} z_2\right)^{2-m} - \left(1 - \frac{\mu}{y_0 + Cx^k + \mu}\right) \right]$$

and

$$g(x, y_0) = \frac{mN}{(m-1)^2} \left[\frac{y_0 + \mu}{y_0} \left(1 - \frac{\mu}{y_0 + Cx^k + \mu}\right) - 1 \right].$$

Since the functions $f(x, z_1, z_2, y_0)$ and $g(x, y_0)$ satisfy the conditions of Theorem 5 of [9] and since the eigenvalues of the matrix A are $\lambda_1 = -\frac{m}{m-1} < 0$ and $\lambda_2 = -\frac{N}{m-1} < 0$, that theorem states that problem (14), (15) has a unique solution. Therefore it has no other solution than g_p.

Returning to the initial variable we easily obtain the following result.

Theorem 2.1 *For each $y_0 > 0$, problem (9), (10) has, in the neighborhood of $x = 0$, a unique holomorphic solution that can be represented by*

$$y(x, y_0) = y_0 + Cx^k \left(1 + g_{0,1} x^k + o(x^k)\right),$$

where $k = \frac{m}{m-1}$, C is given by (12) and $g_{0,1}$ by (17).

3 Lower and upper solutions

Our goal in this section is to define positive continuous upper and lower bounding functions to the solutions of the problem (7), (2), (3), with $a = c = 1, b > 0$.

We begin by remarking that if y is a solution of the considered problem, we have $0 \leq y(x) \leq 1, \forall x \in [0, 1]$. This follows from the boundary conditions and from the fact that $y'(x) > 0$, $\forall x \in]0, 1[$. (For the case $m = 2$, this result was proved in [3] and it can be proved for any $m > 1$, using similar arguments). In the cited paper, sharper lower and upper bounds were obtained for the case of the classical Laplacian. Here, we shall obtain such bounding functions for any $m > 1$, provided that the coefficients δ, μ, N, b satisfy a certain condition.

We begin by noting that the considered problem can be solved analytically in the case $f(y) = const$, that is, when the right-hand side of (7) doesn't depend on the unknown function y. In this case, taking into consideration the asymptotic expansion of the solution, given by Theorem 2.1, let us look for a solution of (7), (2), (3) in the form

$$y(x) = y_0 + A(y_0)x^{\frac{m}{m-1}}, \tag{18}$$

where A is a certain function of y_0 (to de determined). Note that in this case the boundary condition $y'(0) = 0$ is satisfied, for any value of y_0. In order to satisfy the boundary condition (3) with $a = c = 1$, $b > 0$, we substitute (18) into (3), which gives us

$$A(y_0) = \frac{1 - y_0}{1 + b\frac{m}{m-1}}. \tag{19}$$

On the other hand, if we substitute (18) into (7), with $f(y) = K$, we obtain a certain equation. If this equation can be solved with respect to the unknown y_0, and has a unique root $z \in [0, 1]$, then the problem (7), (2), (3) has a unique positive solution in the form (18), with y_0 replaced by z. If such root doesn't exist, then the considered problem has no positive solution of the mentioned form. Below we will compute some solutions of the form (18) and use them as lower (upper) bounding functions of the exact solution of the original problem.

Definition 3.1 A function $y \in C^2(0, 1] \cup C^1[0, 1]$ is said a lower solution of problem (7), (2), (3), if it satisfies the conditions

$$-L_m(y) = -\left(\left|y'(x)\right|^{m-2} y'(x)\right)' - \frac{N-1}{x}\left|y'(x)\right|^{m-2} y'(x) \le -\delta\frac{y(x)}{y(x)+\mu},$$
$$0 < x < 1; \qquad y'(0) \le 0, \qquad y(1) + by'(1) \le 1; \tag{20}$$

By reversing the sign of the inequalities we obtain the definition of an upper solution.

Let us first search for a lower solution $\bar{y}$ of (7), (2), (3) in the form (18). Since $f(y) = \frac{\delta y}{y+\mu}$ is an increasing function of y and y (given by (18)) is an increasing function of x, we have

$$f(y) \le \frac{\delta(y(1))}{y(1)+\mu} = \frac{\delta(y_0 + A(y_0))}{y_0 + A(y_0) + \mu}, \quad \forall x \in [0, 1], y \in [y_0, y_0 + A(y_0)]. \tag{21}$$

Let us now replace $f(y)$ by the right-hand side of (21) in Eq. (7) and look for a solution of problem (7), (2), (3) in the form (18). As it follows from the above arguments, such solution exists if there is a root $y_0^* \in [0, 1]$ of the equation

$$L_m\bar{y}(x) = \left(\frac{m}{m-1}\right)^{m-1} A(y_0^*)^{m-1}N = \delta\frac{y_0^* + A(y_0*)}{y_0^* + A(y_0^*) + \mu}. \tag{22}$$

where A is defined by (19). In order to analyse the solvability of Eq. (22), let us define:

$$\phi(y_0^*) = \left(\frac{m}{m-1}\right)^{m-1} A(y_0^*)^{m-1} N - \delta \frac{y_0^* + A(y_0*)}{y_0^* + A(y_0^*) + \mu}.$$

Then ϕ is obviously continuous on [0, 1] and any root of ϕ is a root of Eq. (22). Moreover, we have $\phi(1) = -\delta \frac{1}{1+\mu} < 0$. Therefore, ϕ has a root on]0, 1[, if and only if $\phi(0) > 0$. We have

$$\phi(0) = \left(\frac{m}{m-1}\right)^{m-1} A(0)^{m-1} N - \delta \frac{A(0)}{A(0) + \mu}.$$

Hence, a necessary and sufficient condition for the existence of a root $y_0^* \in]0, 1[$ of Eq. (22) is that $\phi(0) > 0$, which is equivalent to

$$\left(\frac{m}{m-1}\right)^{m-1} A(0)^{m-2} N(A(0) + \mu) - \delta > 0. \tag{23}$$

Moreover, if the condition (23) is satisfied, the Eq. (22) has a unique root on]0, 1[, since ϕ is decreasing on this interval. Finally, if y_0^* is the root of Eq. (22), then (21) is satisfied, when $y_0 = y_0^*$; this means that the function

$$\bar{y}(x) = y_0^* + A(y_0^*) x^{\frac{m}{m-1}}$$

satisfies the conditions (20) and is a lower solution of the problem (7), (2), (3). When the condition (23) is not satisfied, this is not valid and a lower solution of the considered problem in the form (18) cannot be determined. In this case, we can only use as lower bound of the solution the function $y(x) = 0$.

Let us now look for an upper solution of the considered problem in the same form. Recalling again that f is an increasing function of y, we have

$$f(y) = \delta \frac{y}{y+\mu} > \delta \frac{y0}{y_0 + \mu}, \qquad \forall y > y_0, \tag{24}$$

which can be rewritten as

$$-\delta \frac{y_0}{y_0 + \mu} > -f(y), \qquad \forall y > y_0. \tag{25}$$

Let us now determine $\tilde{y_0}$ from the condition

$$L_m \tilde{y}(x) = \left(\frac{m}{m-1}\right)^{m-1} A(\tilde{y_0})^{m-1} N = \delta \frac{\tilde{y_0}}{\tilde{y_0} + \mu} \tag{26}$$

where A is defined by (19). Using similar arguments to those we have used to analyse the solvability of Eq. (22), it can be shown that Eq. (26) has a unique root $\tilde{y_0} \in]0, 1[$,

Table 1 Coefficients of lower and upper solutions, with $N = 3$, $b = 0.2$, for different values of δ, μ, m

δ	μ	m	y_0^*	$\tilde{y}_0$
0.76129	0.03119	1.5	0.9677	0.9678
0.76129	0.03119	2	0.8280	0.8288
0.76129	0.03119	3	0.5708	0.5748
10	1	1.5	0.07501	0.4425
10	1	2	0.02657	0.3699
10	1	3	no lower sol.	0.2702

for all the considered values of b, m, δ, N, μ. Then from (25) and (26) we conclude that

$$- L_m \tilde{y}(x) \geq -f(\tilde{y}), \forall x \in [0, 1]; \tag{27}$$

from (27) it follows that $\tilde{y}$, in this case, is an upper solution of the problem (7), (2), (3).

The above results can be summarized in the following theorem.

Theorem 3.1 *The function defined by* (18)*, with A defined by* (19)*, is*

- *a lower solution of problem* (7), (2), (3) *if the condition* (23) *is satisfied and* $y_0 \leq y_0^*$*, where* y_0^* *satisfies* (22)*;*
- *an upper solution of problem* (7), (2), (3) *if* $y_0 \geq \tilde{y}_0$*, where* $\tilde{y}_0$ *satisfies* (26)*.*

In Table 1 some values of y_0^* and $\tilde{y}_0$, corresponding to different sets of parameters, are displayed. One case is reported, when no lower solution of the form (18) exists. As it follows from these results, when μ is small (that is, when the right-hand side function is close to a constant), like in the first three rows of the table, the lower and upper solution are close to each other and both give good approximations of the exact solution. The same does not happen when μ takes higher values (last three rows).

In the next section we will present examples of lower and upper solutions of the considered form and compare them with the numerical solutions, in different test cases. We remark that in the case $m = 2$ the lower and upper bounding functions determined by the method of Anderson and Arthurs [3] are, in general, better aproximations to the true solution than the ones we obtain by the present method. However, it doesn't seem possible to extend the method developped by those authors to the case of the degenerate m-Laplacian.

4 A shooting algorithm

Following the approach of [10] and [11], in this section we implement a shooting algorithm basing us on the behavior of the solution in the neighborhood of the singular point $x = 0$.

Table 2 Numerical solution of problem (7), (2), (3) for test case 1, obtained with the shooting algorithm

x	$y(x)$		
	$m = 1.5$	$m = 2$	$m = 3$
0.0	0.967753	0.828483	0.572874
0.2	0.967914	0.833375	0.602139
0.4	0.969042	0.848053	0.655708
0.6	0.972104	0.872528	0.725181
0.8	0.978069	0.906819	0.807583
1.0	0.987905	0.950946	0.901197

In order to do that, we consider the following regular initial value problem

$$\begin{aligned}
&\left(\left|y'(x)\right|^{m-2} y'(x)\right)' + \frac{N-1}{x} \left|y'(x)\right|^{m-2} y'(x) = f(y),\\
&y(d) = y_0 + Cd^k \left(1 + g_{0,1} d^k\right)\\
&y'(d) = \left[\frac{d}{dx} \left(y_0 + Cx^k \left(1 + g_{0,1} x^k\right)\right)\right]_{x=d}
\end{aligned}$$

for a certain value of $y_0 > 0$ and d small. All we have to do is to adjust the parameter y_0 in order to make the solution of the initial value problem satisfy the other boundary condition (3).

Remark 4.1 Since the performance of the shooting method depends strongly on the choice of the initial value for y_0 we proceed as in [14] to find initial approximations for that parameter, that is, we consider an approximation of the solution of the Cauchy problem (9)–(10), whose form is given by Theorem 1 (retaining only the first two terms of the series):

$$\bar{y}(x, y_0) = y_0 + Cx^k \left(1 + g_{0,1} x^k\right). \tag{28}$$

Replacing y by $\bar{y}$ in the boundary condition (3), we obtain an equation that can be solved with respect to y_0. The value of y_0 obtained as the root of this equation has proved to be a good initial guess for the shooting method. (In all the cases considered in the present paper it gives an approximation of the exact value with 2–3 correct digits). Alternatively, we can use as initial approximations the lower and upper solutions described in the previous section.

In Tables 2, 3 and Fig. 1 we display some numerical results for different values of m for two test cases (case 1: $N = 3, a = c = 1, b = 0.2, \delta = 0.76129$ and $\mu = 0.03119$; case 2: $N = 3$, $a = c = 1$, $b = 0.2$, $\delta = 10$ and $\mu = 1$). In Fig. 2, the numerical solution is compared with the corresponding lower and upper solutions, in both test cases.

Note that the results for test case 1, corresponding to $m = 2$, are in agreement with those obtained in [15] and [16]. The results for test case 2, corresponding to $m = 2$, are in agreement with the corresponding results presented in [3].

Table 3 Numerical solution of problem (7), (2), (3) for test case 2, obtained with the shooting algorithm

x	$y(x)$		
	$m = 1.5$	$m = 2$	$m = 3$
0.0	0.374783	0.285111	0.200000
0.2	0.376990	0.300081	0.245785
0.4	0.392702	0.347140	0.335995
0.6	0.437755	0.432726	0.463936
0.8	0.536136	0.567396	0.629421
1.0	0.731909	0.765232	0.832603

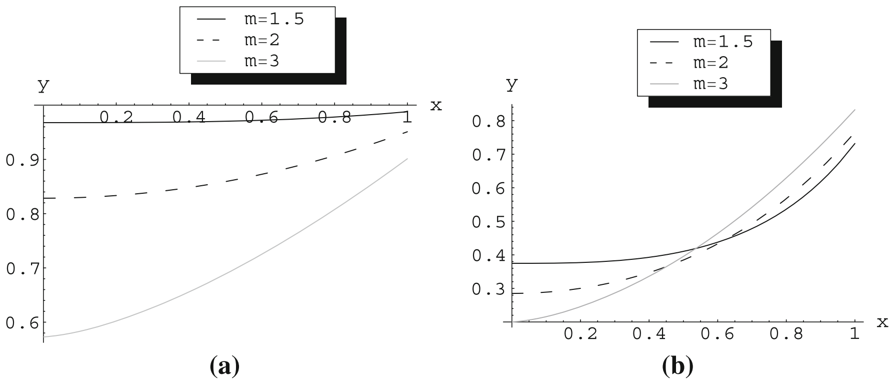

Fig. 1 Approximate solutions of problem (7), (2), (3) for (**a**) test case 1, (**b**) test case 2

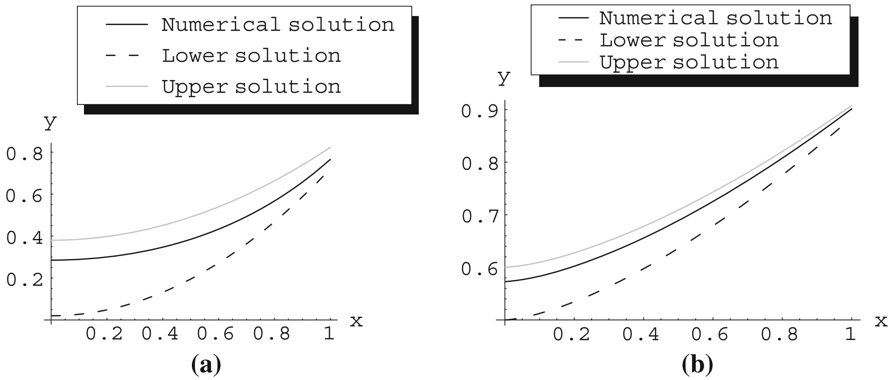

Fig. 2 Upper and lower solutions of problem (7), (2), (3) for (**a**) test case 2 with $m = 2$, (**b**) test case 1 with $m = 3$

5 A finite difference scheme

In order to discretize (7), (2), (3), we introduce in the interval [0, 1] a uniform grid of stepsize $h = \frac{1}{n}$ defined by the gridpoints $x_i = ih$, $i = 0, \ldots, n$. At every point x_i, $i = 1, \ldots, n-1$, an approximation for the first and second derivative of the solution

Table 4 Approximate solution of y_0 for test case 1, for different values of h

	$h = \frac{1}{100}$	$h = \frac{1}{200}$	$h = \frac{1}{400}$	$h = \frac{1}{800}$
$m = 1.5$	0.967755620	0.967753296	0.967752704	0.967752554
$m = 2$	0.828483352	0.828483306	0.828483294	0.828483291
$m = 3$	0.572896104	0.572881224	0.572876419	0.572874834
$m = 4$	0.409120467	0.409036715	0.409004044	0.408991218
$m = 5$	0.301244898	0.301096645	0.301034968	0.301009195
$m = 6$	0.225698288	0.225517722	0.225440008	0.225406391

will be given by the first and second central differences formulas:

$$y'(x_i) \simeq \frac{y(x_{i+1}) - y(x_{i-1})}{2h} = y'_i,$$
$$y''(x_i) \simeq \frac{y(x_{i+1}) - 2y(x_i) + y(x_{i-1})}{h^2} = y''_i,$$

respectively.

The derivatives at the endpoints $x = 0$ and $x = 1$ are approximated by the second order formulae

$$y'(0) = \frac{1}{2h}\left(-3y(0) + 4y(h) - y(2h)\right) + O(h^2)$$
$$y'(1) = \frac{1}{2h}\left(3y(1) - 4y(1-h) + y(1-2h)\right) + O(h^2).$$

In this way, we obtain the discretized problem which is solved by the Newton method. In order to choose an initial approximation, we took into consideration the behavior of the solution in the neighborhood of $x = 0$ (see Theorem 2.1) an used the function

$$y_0 + Cx^k\left(1 + g_{0,1}x^k\right),$$

where y_0 could be determined by using the procedure described in the last section, see Remark 4.1.

In order to estimate the convergence order of the finite difference method, we have carried out several experiments for different values of the step size h (see Tables 4 and 5) and used the formula

$$c_{y_0} = -\log_2 \frac{|y_0^{h_3} - y_0^{h_2}|}{|y_0^{h_2} - y_0^{h_1}|}, \tag{29}$$

to estimate the convergence order at $x = 0$, where $y_0^{h_i}$ is the approximate value of y_0 obtained with stepsize $h_i = \frac{h_{i-1}}{2}$. The results are presented in Tables 6 and 7.

Table 5 Approximate solution of y_0 for test case 2, for different values of h

	$h = \frac{1}{100}$	$h = \frac{1}{200}$	$h = \frac{1}{400}$	$h = \frac{1}{800}$
$m = 1.5$	0.374847260	0.374799255	0.374787047	0.374783966
$m = 2$	0.285129177	0.285115517	0.285112100	0.285111246
$m = 3$	0.173352644	0.173319070	0.173319070	0.173306095
$m = 4$	0.108720354	0.108611151	0.108570866	0.108555629
$m = 5$	0.066668783	0.066497900	0.066431412	0.066404783
$m = 6$	0.037316134	0.037106889	0.037025796	0.036993155

Table 6 Estimates of the convergence order at $x = 0$ (in test case 1) for different values of m

	$m = 1.5$	$m = 2$	$m = 3$	$m = 4$	$m = 5$	$m = 6$
$h_1 = \frac{1}{200}$	2.00	2.00	1.59	1.35	1.26	1.21
$h_1 = \frac{1}{100}$	1.95	1.94	1.63	1.36	1.27	1.22

Table 7 Estimates of the convergence order at $x = 0$ (in test case 2) for different values of m

	$m = 1.5$	$m = 2$	$m = 3$	$m = 4$	$m = 5$	$m = 6$
$h_1 = \frac{1}{200}$	1.99	2.00	1.74	1.40	1.32	1.31
$h_1 = \frac{1}{100}$	1.98	1.67	1.77	1.44	1.36	1.37

From the results displayed in Tables 6 and 7 we conclude that the convergence order estimates decrease when $m > 2$. This is not surprising if we take into account the behavior of the solution in the neighborhood of $x = 0$. When $m = 2$, according to Theorem 2.1, the solution behaves as the function $y_0 + Cx^2$, as x approaches zero. When $m < 2$, then $k = \frac{m}{m-1} > 2$ and therefore the solution in the neighborhood of the origin behaves as $y_0 + Cx^k$, with $k > 2$, so its second derivative is finite for small values of x.

The same can not be said whenever $m > 2$. As it can be easily seen, in this case the solution behaves as $y_0 + Cx^k$, with $k < 2$, near the origin, and then the second derivative of the solution becomes unbounded on that points. In order to overcome this problem, we set

$$t = x^{\frac{k}{2}}, \quad k = \frac{m}{m-1}. \tag{30}$$

The solution in the new variable t will always behave as $y_0 + Ct^2$ as t approaches zero. So, we expect to maintain the quadratic convergence estimates if we perform the

Table 8 Approximate values of y_0 (in test case 1) for different step sizes of the finite difference scheme with variable substitution

	$h = \frac{1}{100}$	$h = \frac{1}{200}$	$h = \frac{1}{400}$	$h = \frac{1}{800}$
$m = 1.5$	0.967752507	0.967752505	0.967752504	0.967752504
$m = 2$	0.828483352	0.828483306	0.828483294	0.828483291
$m = 3$	0.572874295	0.572874093	0.572874043	0.572874030
$m = 4$	0.408983292	0.408982965	0.408982884	0.408982863
$m = 5$	0.300991148	0.300990726	0.300990621	0.3009905944
$m = 6$	0.225381267	0.225380762	0.225380636	0.225380605

Table 9 Approximate values of y_0 (in test case 2) for different step sizes of the finite difference scheme with variable substitution

	$h = \frac{1}{100}$	$h = \frac{1}{200}$	$h = \frac{1}{400}$	$h = \frac{1}{800}$
$m = 1.5$	0.374799140	0.374786998	0.374783951	0.374783188
$m = 2$	0.285129177	0.285115517	0.285112100	0.2851112458
$m = 3$	0.173322059	0.173309025	0.173305769	0.1733049558
$m = 4$	0.108562160	0.108550040	0.108547012	0.1085462558
$m = 5$	0.066401439	0.066389992	0.066387132	0.0663864171
$m = 6$	0.036984212	0.036973181	0.036970423	0.0369697333

Table 10 Estimates of the convergence order at $x = 0$ (for test case 1) of the finite difference scheme with variable substitution

	$m = 1.5$	$m = 2$	$m = 3$	$m = 4$	$m = 5$	$m = 6$
$h_1 = \frac{1}{200}$	2.58	1.99	2.00	2.00	2.00	1.58
$h_1 = \frac{1}{100}$	1.94	2.00	2.00	2.00	2.00	2.09

Table 11 Estimates of the convergence order at $x = 0$ (for test case 2) of the finite difference scheme with variable substitution

	$m = 1.5$	$m = 2$	$m = 3$	$m = 4$	$m = 5$	$m = 6$
$h_1 = \frac{1}{200}$	2.00	2.00	2.00	2.00	2.00	1.99
$h_1 = \frac{1}{100}$	2.00	2.00	2.00	2.00	2.00	2.00

variable substitution (30). Some numerical results using the finite difference method after this variable substitution are presented in Tables 8 and 9. The estimates of the convergence order, using Eq. (29), are presented in Tables 10 and 11.

6 Conclusions and future work

In this paper, for a class of singular boundary value problems arising in physiology, numerical methods where implemented based on the asymptotic behavior of the solution in the neighborhood of the singular point $x = 0$: a shooting algorithm and a finite difference scheme whose convergence order is increased by a simple variable substitution. Numerical results are presented confirming the efficiency of the methods. As future work, we intend to prove that the finite difference method, after the variable substitution, has second order convergence, as it is suggested by the numerical results.

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