

An Initial-Value Method for the Solution of Certain Nonlinear Diffusion Equations in Biology

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ABSTRACT

The steady-state one-dimensional diffusion equation with a nonlinear source term is a class of differential equations governing the behavior of many biological systems. As with other types of nonlinear differential equations, exact analytical solutions exist only in some very special cases. Previously, analytical solutions could be obtained only by a linearization process; moreover, the analytical solutions thus obtained approach the exact solution in a very limited range of some physical parameters. On the other hand, numerical solutions obtained by using digital computers, although exact, usually require an iteration process due to the two-point nature of the boundary conditions in such problems.

In this article a method of transformation is introduced that makes it possible to transform the governing differential equation from a boundary-value to an initial-value problem. As a result, exact numerical solutions to this class of equations can be obtained in a single step. Numerical solutions of the concentration profiles in an enzyme system are presented as an illustration of the method.

INTRODUCTION

The behavior of many biological systems can be described by the steady-state one-dimensional diffusion equation with a source term:

$$\frac{d^2C}{dr^2} + \frac{p+1}{r} \frac{dC}{dr} = f(C) \quad (1)$$

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where $f(C)$ is the source term, usually nonlinear, for biological systems and p equals -1 , 0 , or 1 , depending on whether a plane, cylindrical, or spherical system is considered. The following examples of known forms of $f(C)$ can be cited.

1. $f(C) = \exp(\beta C)$

If C is interpreted as temperature, then this form of $f(C)$ represents the heat generation in the body of the lizard [3].

2. $f(C) = (k/D)C(C_0 - C)$

This form was used by Ames *et al.* [1] to characterize the biochemical reactions in the analysis of the steady-state operation of the trickling filter in sewage treatment.

3. $f(C) = (k_2 E_0 KC)/(1 + KC)$

This form is the familiar Michaelis–Menten equation representing the consumption of substrate as a result of an enzyme–substrate reaction [2].

4. $f(C) = KC^n/(1 + KC^n)$

This is a generalization to the form of case 3 if more than one substrate molecule, n say, combine with one enzyme molecule [8].

As with other nonlinear equations, exact analytical solutions to these equations usually do not exist; the exceptions are very special cases. Until now, analytical solutions could only be obtained by a linearization process. The results approach the exact solutions only in a very limited range of some physical parameters. In order to get exact numerical solutions without such limitations, digital computers must be used. One of the difficulties usually encountered in the integration process comes from the fact that the boundary conditions are usually given at two points. Thus, the numerical integration has to be started by assuming the missing boundary condition at the initial point, and the equation must be integrated as an initial-value problem. If the assumed initial condition is correct, the solution will satisfy the boundary condition at the second point. Otherwise, another value has to be chosen and the process repeated. This trial-and-error process usually takes a great deal of computing time and the solution is frequently very sensitive to even a very small change in the assumed initial condition. Therefore, the introduction of a transformation by which the boundary-value problem could be changed to an initial-value problem would be of great importance.

To date, two entirely different approaches have been developed for transforming a boundary-value problem to an initial-value problem.

One is by the concept of *transformation groups*; the other is the *invariant imbedding* method. The former was first given by Töpfer (see [4]) in 1912, but only recently has considerable progress been made [6, 7]. The latter method was developed mainly by Bellman and Kalaba (see, for example, [5] for the basic concept). The method presented in this article is an extension of the transformation group method given in [7]. The extended method is shown to be especially suitable for problems where certain physical parameters appear in the differential equation or boundary conditions, or in both, and solutions for a range of these parameters are sought. The method is illustrated by numerically solving case 3 where the source term is the Michaelis–Menten equation [2].

GOVERNING DIFFERENTIAL EQUATION

As was stated, we illustrate the method by numerically solving case 3, in which the source term of the diffusion equation is given by the Michaelis–Menten equation [2]. The enzyme E with concentration E_0 interacts with the substrate S with concentration C to form a complex $E \cdot S$ which may either dissociate into its components or decompose to regenerate E and liberate product P [2]:



The local rate of consumption of substrate can be expressed in terms of the local concentration of substrate by the Michaelis–Menten equation

$$v = \frac{K_2 E_0 \bar{K} C}{1 + \bar{K} C}$$

where $\bar{K} = K_1/(K_{-1} + K_2)$. The steady-state one-dimensional diffusion equation for the concentration of substrate can be written as [2]

$$\frac{d^2 C}{dr^2} + \frac{p + 1}{r} \frac{dC}{dr} = \frac{K_2 E_0 \bar{K} C}{D(1 + \bar{K} C)} \tag{2}$$

subject to the boundary conditions

$$r = 0: \quad \frac{dC}{dr} = 0;$$

$$r = r_0: \quad D \left(\frac{dC}{dr} \right)_{r=r_0} = H(C_0 - C_i).$$

Introducing the following dimensionless radius and concentration

$$\bar{r} = \frac{r}{r_0}, \quad \bar{C} = \frac{C}{C_0}, \quad (3)$$

we get for Eq. (2)

$$\frac{d^2\bar{C}}{d\bar{r}^2} + \frac{p+1}{\bar{r}} \frac{d\bar{C}}{d\bar{r}} = \frac{\beta\bar{C}}{1+k^*\bar{C}} \quad (4)$$

subject to the boundary conditions

$$\begin{aligned} \bar{r} = 0: \quad \frac{d\bar{C}}{d\bar{r}} &= 0; \\ \bar{r} = 1: \quad \left(\frac{d\bar{C}}{d\bar{r}}\right)_{\bar{r}=1} &= N(1 - \bar{C}_{\bar{r}=1}); \end{aligned}$$

where

$$\begin{aligned} \beta &= \frac{K_2 E_0 r_0^2 \bar{K}}{D}, \\ k^* &= \bar{K} C_0, \quad N = \frac{H r_0}{D}. \end{aligned} \quad (5)$$

Equation (4) is seen to be a boundary-value problem since its boundary conditions are specified at two points.

TRANSFORMATION TO AN INITIAL-VALUE PROBLEM

To transform Eq. (4) to an initial-value problem, a linear group of transformation is introduced:

$$\bar{r} = A^{\alpha_1} r^*, \quad \bar{C} = A^{\alpha_2} C^* \quad (6)$$

where A is the parameter of transformation and α_1 and α_2 are constants to be determined. Under this group of transformation, Eq. (4) becomes

$$\frac{d^2 C^*}{dr^{*\,2}} + \frac{p+1}{r^*} \frac{dC^*}{dr^*} = A^{2\alpha_1} \frac{\beta C^*}{1+k^* A^{\alpha_2} C^*}. \quad (7)$$

In the original method developed in [7], the first condition to be satisfied is that the differential equation be invariant under this group of transformations. However, this condition can be satisfied only when α_1 and α_2 are both zero (i.e., identical transformation). Thus, the original method cannot be applied to this problem.

The difficulty can be overcome by modifying the original method if solutions to Eq. (4) for a range of values of k^* are sought. The key to

this method lies in the introduction of one constant, namely,

$$k' = k^* A^{\alpha_2}. \tag{8}$$

With the constant k' thus defined, Eq. (7) is seen to be independent of A if α_1 takes the value of zero; that is,

$$\alpha_1 = 0. \tag{9}$$

Equation (7) now becomes

$$\frac{d^2 C^*}{d\bar{r}^2} + \frac{p+1}{\bar{r}} \frac{dC^*}{d\bar{r}} = \frac{\beta C^*}{1+k' C^*} \tag{10}$$

with its boundary condition at the initial point as

$$\bar{r} = 0: \frac{dC^*}{d\bar{r}} = 0. \tag{11}$$

It should be emphasized that although k' is still a function of A , we will reverse the process by assigning values of k' , instead of k^* , and the solution to Eq. (10) sought. After the solution based on the assigned value of k' is obtained, the value of k^* corresponding to this particular solution is determined. Other values of k' can be assigned and the process repeated until the required range of k^* is covered. This is an important step in the extended method and can be applied to a wide class of equations where certain physical parameters appear in either the differential equation or the boundary conditions and solutions are needed for a range of values of these parameters.

To get the missing boundary condition at $\bar{r} = 0$, we put

$$\bar{r} = 0: \bar{C} = A,$$

which, upon transformation, becomes

$$\bar{r} = 0: A^{\alpha_2} C^* = A;$$

the latter is seen to be independent of A if

$$\alpha_2 = 1. \tag{12}$$

We then have

$$\bar{r} = 0: C^* = 1. \tag{13}$$

Finally, the parameter of transformation A can be computed from the boundary condition at the second point, which gives

$$A \left(\frac{dC^*}{d\bar{r}} \right)_{\bar{r}=1} = N(1 - AC^*_{\bar{r}=1})$$

or

$$A = \frac{N}{(dC^*/d\bar{r})_{\bar{r}=1} + NC^*_{\bar{r}=1}}. \quad (14)$$

Thus, solution of Eq. (4) for a range of values of k^* (and constant β and N) then consists of the following steps.

1. Assign a value of k' (instead of k^*).
2. Numerically integrate Eq. (10) as an initial-value problem with the boundary conditions given by Eqs. (11) and (13) from $\bar{r} = 0$ to $\bar{r} = 1$. The values of C^* and $dC^*/d\bar{r}$ at $\bar{r} = 1$ are then obtained.
3. The parameter of transformation A is computed from Eq. (14).
4. With A , α_1 , and α_2 known, the solution to the original equation, Eq. (4), can be computed from the transformation equation, Eq. (6), as

$$\bar{r} = \bar{r}, \quad \bar{C} = AC^*. \quad (15)$$

5. The value of k^* corresponding to this particular solution can then be computed by Eq. (8).

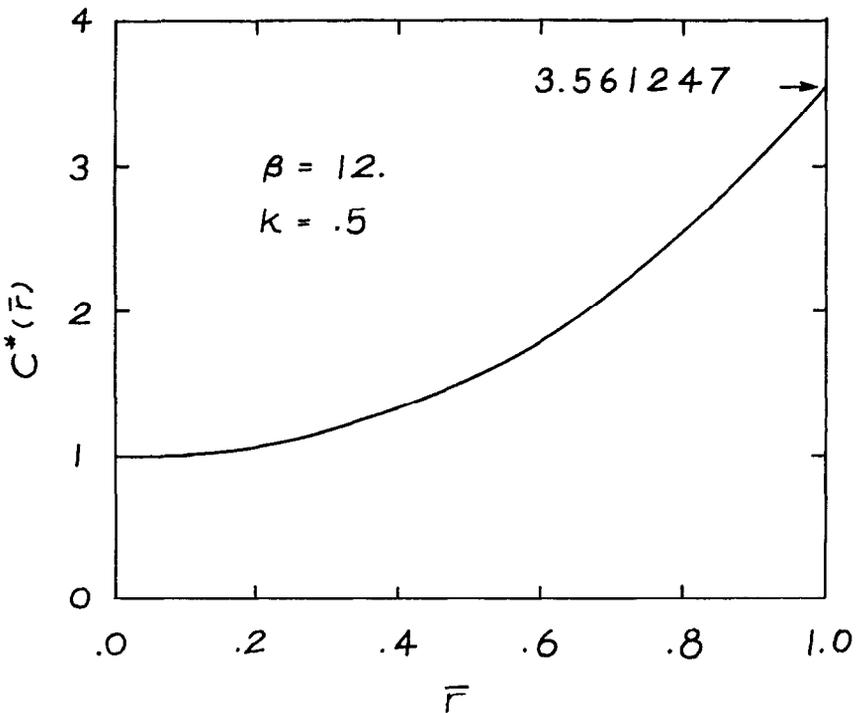


FIG. 1. Solution of Eq. (10) for $C^*(\bar{r})$.

- Other values of k' are assigned and steps 1-5 are repeated until the required range of k^* is covered.

NUMERICAL SOLUTIONS

As an illustration, consider the solution of the concentration profile of a cylinder ($p = 0$) for $\beta = 12$, $N = 1$, and $k' = 0.5$. Numerical integration of Eq. (10) subject to the boundary conditions (11) and (13) constitutes an initial-value problem. The result is shown in Figs. 1 and 2.

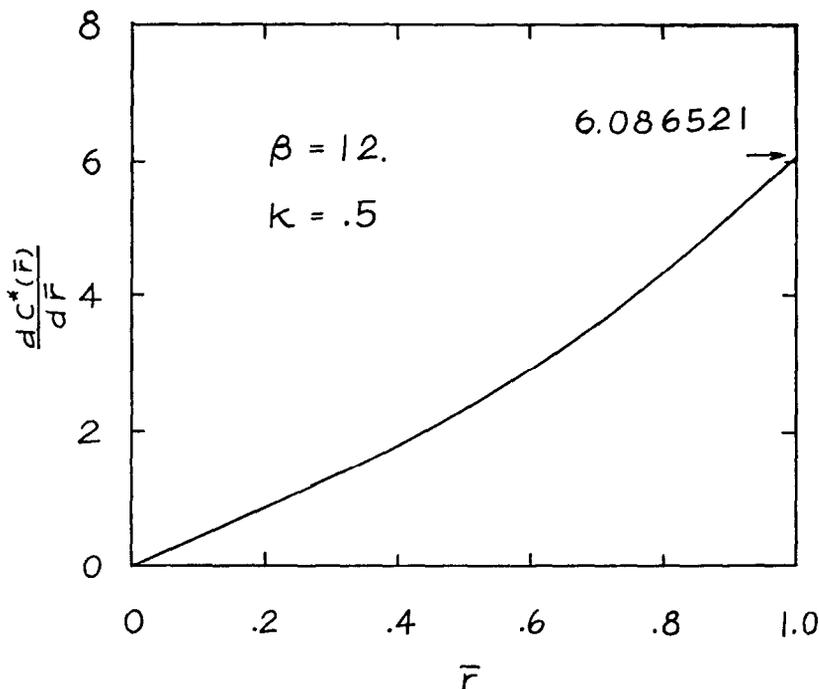


FIG. 2. Solution of Eq. (10) for $dC^*/d\bar{r}$.

It is seen that, at $\bar{r} = 1$,

$$C^*(1) = 3.561247, \quad \frac{dC^*(1)}{d\bar{r}} = 6.086521.$$

The value of A can thus be computed as

$$A = \frac{N}{(dC^*/d\bar{r}) + NC^*(1)} = 0.103651.$$

The corresponding value of k^* is therefore

$$k^* = \frac{k'}{A} = 4.8240.$$

The value of the concentration outside the cylinder for $K = 2000$ liters/mole is

$$C_0 = \frac{k^*}{K} = 0.002412 \text{ moles/liter.}$$

As a final step, the solution to the original equation, Eq. (4), can be computed through the transformation equation, Eq. (15); the result is plotted in Fig. 3. Thus, the concentration of substrate is $0.10365C_0$ at the

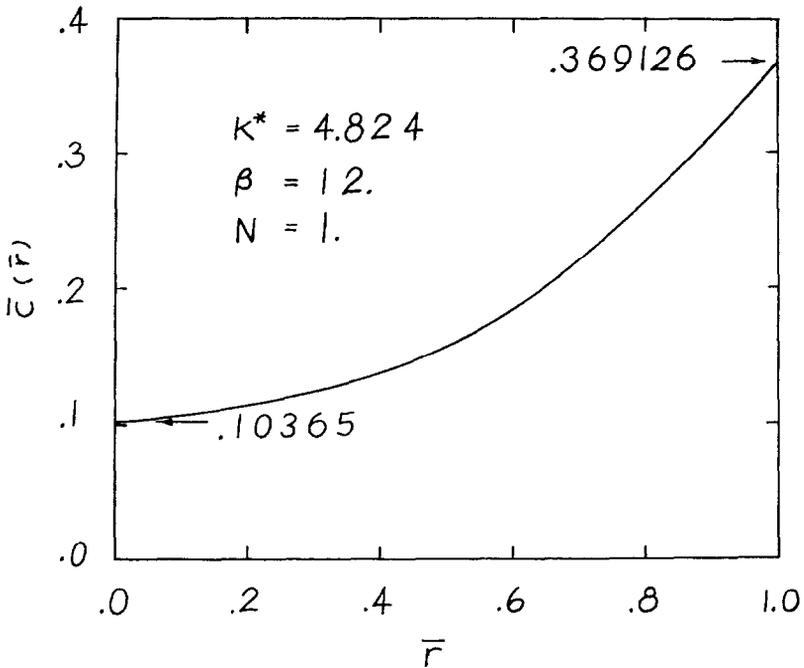


FIG. 3. Solution to Eq. (4).

center of the cylinder, increases to $0.369126C_0$ at the surface immediately inside the cylinder surface, and reaches C_0 across the cylinder surface.

Numerical solutions for a range of values of k' from 0.001 to 1000 are obtained in this manner. Table I gives a summary of the numerical
Mathematical Biosciences 6 (1970), 25-35

TABLE I
SUMMARY OF NUMERICAL SOLUTIONS ($\beta = 12$)

k'	k^*	C_0 (exact)	C_0 from Eq. (19)	C_0 from Eq. (17)
0.001	0.028	0.000014	0.000014	
0.005	0.136	0.000068	0.000070	
0.010	0.264	0.000132	0.000139	
0.050	1.114	0.000557	0.000697	
0.100	1.888	0.000944	0.001394	
0.250	3.380	0.001690		
0.500	4.824	0.002412		
1.000	6.524	0.003262		0.004994
1.500	7.676	0.003838		0.005244
2.000	8.602	0.004301		0.005498
5.000	12.684	0.006342		0.006988
10.00	18.216	0.009108		0.009480
25.00	33.612	0.016806		0.016971
50.00	58.770	0.029385		0.029448
75.00	83.802	0.041901		0.041959
100.0	108.806	0.054403		0.054447
200.0	208.756	0.104378		0.104400
500.0	508.510	0.254255		0.254264
750.0	758.288	0.379144		0.379151
1000.0	1008.064	0.504032		0.505032

results. It is seen that the solutions thus obtained correspond to a range of k^* from 0.028 to 1008. Thus, if the solutions for a range of k^* , say, from 0.1 to 1000 are sought, the data in Table I will be enough. By assigning various values of k' , instead of k^* , the equation is seen to be solvable as an initial-value problem. Figure 4 is a plot of the solutions in Table I.

LINEARIZED SOLUTIONS

Two limiting solutions of Eq. (4), namely, $k^* \bar{C} \gg 1$ and $k^* \bar{C} \ll 1$, are of interest since they lead to analytical solutions. For such cases, Eq. (4) can be approximated by the following linear equations. For $k^* \bar{C} \gg 1$,

$$\frac{d^2 \bar{C}}{d\bar{r}^2} + \frac{p+1}{\bar{r}} \frac{d\bar{C}}{d\bar{r}} = \frac{\beta}{k^*} \tag{16}$$

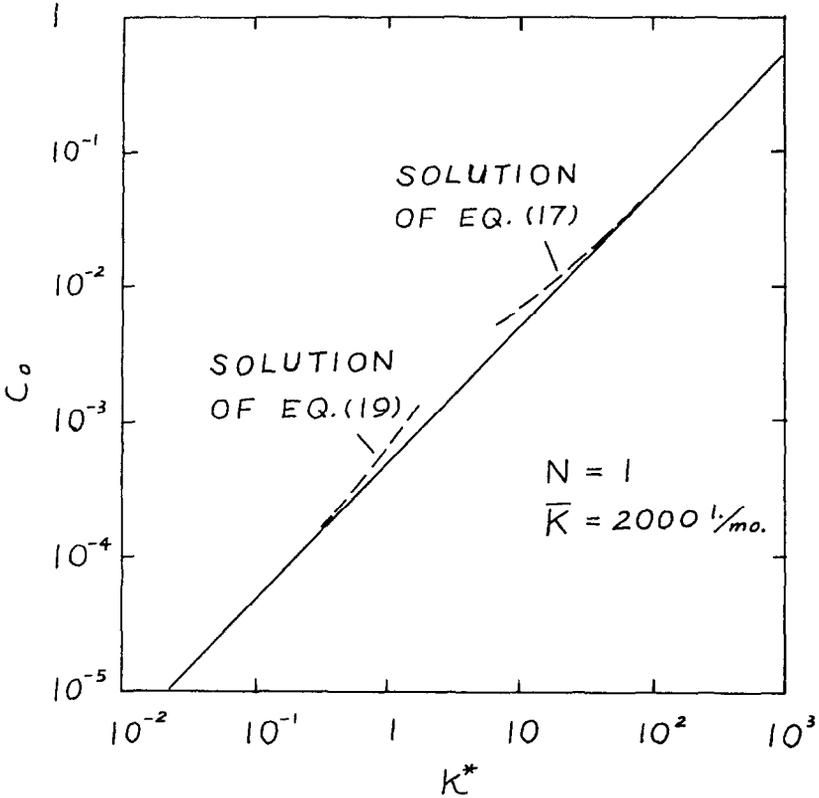


FIG. 4. The surface concentration C_0 as a function of k^* .

with the solution

$$\bar{C} = 1 - \frac{\beta}{4k^*} \left(1 + \frac{2}{N} - \bar{r}^2 \right). \tag{17}$$

For $k^* \bar{C} \ll 1$,

$$\frac{d^2 \bar{C}}{d\bar{r}^2} + \frac{p+1}{\bar{r}} \frac{d\bar{C}}{d\bar{r}} = \beta \bar{C} \tag{18}$$

with the solution

$$\bar{C} = \frac{N}{\beta I_0'(\beta) + N I_0(\beta)} I_0(\beta \bar{r}) \tag{19}$$

where $I_0(\beta \bar{r})$ is the modified Bessel function of the first kind of order zero.

Numerical data for Eqs. (17) and (19) are listed in Table I and Fig. 4. It is seen that the linearized solutions always overestimate the surface concentration and that solutions to Eqs. (17) and (19) start to deviate

from the nonlinear exact solution for k^* smaller than 80 and greater than 0.2, respectively.

CONCLUDING REMARKS

The method just described makes possible the solution of Eq. (4) as an initial-value problem. Solutions to Eq. (1) for the other forms of $f(C)$ can be obtained by following the same steps as in this example. The method is seen to be applicable to differential equations where certain parameters appear in either the differential equation or the boundary conditions, or both, and solutions for a range of these parameters are sought. No iteration is needed and the solution can be obtained in one step. This method has been applied to other problems in fluid mechanics and heat transfer with equal success. Results of this work will be reported in the near future.

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