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Approximating the Solution of Cell-cell Adhesion Model via the Homotopy Perturbation Method

Hasan Almefleh

Department of Mathematics
Yarmouk University
Irbid, Jordan, 21163

email: almefleh@yu.edu.jo

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Abstract

Homotopy perturbation method (HPM) is applied to approximate and simulate the cell-cell adhesion model.

1 Introduction

Cell-cell adhesion is a biological phenomenon which describes how one cell binds to another by proteins on the surface of the cell, known as cell adhesion molecules (CAMs) [1, 2, 3, 4]. Graner and Galzier in 1992-1993 [6, 5], studied this phenomena where they adopted the Pott model to a biological cell population. Armstrong et al. in 2006 have derived a mathematical model to describe this phenomenon given by the non-local reaction diffusion equation:

$$\frac{\partial}{\partial t}n(t,x) = D\frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\,K(n(t,x))), \tag{1.1}$$

where

$$K(n(t,x)) = \frac{\alpha\phi}{R}\int_{-R}^{R} g(n(t,x+y))\omega(y)dy.$$

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ϕ is viscosity constant, D is the diffusion rate, α is a positive parameter reflecting the strength of adhesion force between the cells, and R the radius of the cell sense to its ambient. The function $g(n)$ is given by

$$g(n) = \begin{cases} n(1-n/M), & n < M, \\ 0, & n \geq M, \end{cases} \tag{1.2}$$

where the constant M represents the crowding capacity of the population. $\omega(y)$ is considered to be an odd function such

$$\omega(y) = \begin{cases} 1, & 0 < y < T, \\ -1, & -R < y < 0. \end{cases} \tag{1.3}$$

Assume

$$x^* = \frac{x}{R}, \quad t^* = \frac{Dt}{R^2}, \quad n^* = \frac{n}{n_0}, \quad \alpha^* = \frac{\alpha\phi\, R\, M}{D}.$$

Then (1.1) reduces to

$$\frac{\partial}{\partial t}n(t,x) = \frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\,K(n(t,x))), \tag{1.4}$$

where

$$K(n(t,x)) = \alpha\int_{-1}^{1} g(n(t,x+y))\omega(y)dy,$$

and the non-dimensionalised logistic force function $g(n)$ is $g(n) = n(1-n)$. The authors showed that the homogeneous steady state solution U is linearly unstable provided that

$$\frac{1}{2\alpha U}k^2 < 1 - cos(k),$$

where the constant k is the wave number.

Now, the above model does not take into consideration cell division and lose. Sherratt et al. [9] add to Armstrong model the cell kinetics function $f(n)$ to represent the cell division and cell loss. The new model is given by the following non-local reaction diffusion equation:

$$\frac{\partial}{\partial t}n(t,x) = D\frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\,K(n(t,x))) + f(n), \tag{1.5}$$

where

$$K(n(t,x)) = \frac{\alpha\phi}{R}\int_{-R}^{R} g(n(t,x+y))\omega(y)dy.$$

The standard choice of the function $f(n)$ is the logistic function $f(n) = \mu\, n\,(1-n/n_0)$, where μ is a positive constant. The authors used the following scaling:

$$x^* = \frac{x}{R}, \quad t^* = \frac{Dt}{R^2}, \quad n^* = \frac{2n}{M}, \quad \alpha^* = \frac{\alpha\phi\, M}{4D}, \mu^* = \frac{\mu R^2}{D}, \quad n_0^* = \frac{2n_0}{M},$$

so the non-dimensionalised problem is given by

$$\begin{aligned} \frac{\partial n(t,x)}{\partial t} &= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha\frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1} \max\{n(t,x+y)(2-n(t,x+y)),0\}\, sign(y)\, dy\right] \\ &+ \mu n(1-n/n_0). \end{aligned} \tag{1.6}$$

If $n_0 < 2$, then $n = n_0$ is a homogeneous steady state solution for this equation. The linear stability shows that $n = n_0$ is unstable provided that

$$4\alpha n_0(1-n_0) > \frac{4\theta^2+\mu}{2\sin^2\theta},$$

where $\theta \in (0, \pi/2)$ is the solution of $\tan\theta = \frac{4\theta^2+\mu}{4\theta}$ [9].

The aim of this article is to employ (HPM) to approximate and simulate the solution of the model above.

2 Basics in the Homotopy Perturbation Method

Homotopy Perturbation method (HPM) was first considered by Ji-Huan He [7, 8] for solving linear and nonlinear differential equations. The basic idea of this method is to couple the perturbation method and the homotopy in topology. The method yields a very rapid convergence of the solution series in most cases [7]. To illustrate the (HPM) for solving differential equations, he [7, 8] considered the following nonlinear differential equation:

$$A(u) = f(r), \quad r \in \Omega \tag{2.1}$$

subject to the boundary condition $B(u, \frac{\partial u}{\partial n}) = 0,\ r \in \partial\Omega$. where A is a general differential operator, b is a boundary operator, $f(r)$ is a known analytic function, and $\frac{\partial u}{\partial n}$ is the differentiation along the normal vector drown outwards from Ω.

The operator A in equation (2.1) can be split as L and N, linear operator and N non-linear operators, respectively. So, equation (2.1) becomes

$$L(u) + N(u) = f(r) \quad r \in \Omega. \tag{2.2}$$

His idea is to construct a homotopy $\nu(r,\lambda) : \Omega \times [0,1] \to \mathbb{R}$ which satisfies

$$\mathcal{H}(\nu,\lambda) = (1-\lambda)\,[L(\nu) - L(u_0)] + \lambda\,[A(\nu) - f(r)] = 0, \tag{2.3}$$

where u_0 is the initial approximation of u. By substituting $A(u) = L(u) + N(u)$ in the above equation, we get

$$\mathcal{H}(\nu,\lambda) = L(\nu) - L(u_0) + \lambda L(u_0) + \lambda\,[N(\nu) - f(r)] = 0,$$

where $\lambda \in [0,1]$. Clearly, $\mathcal{H}(\nu,0) = L(\nu) - L(u_0) = 0$ and $A(\nu) - f(r) = 0$. Thus, $\mathcal{H}(\nu,0) = L(\nu) - L(u_0)$ and $A(\nu) - f(r)$ are homotopic. According to this method the parameter λ is small. Hence, the solution ν of equation (2.3) can be written as a power series in λ. Particularly,

$$\nu = \sum_{k=0}^{\infty} \nu_k \lambda^k. \tag{2.4}$$

Thus, if we let $\lambda \to 1$, then $\nu = \sum_{k=0}^{\infty} \nu_k$. Moreover, if we set $\lambda = 1$ in equation (2.3), then $A(\nu) - f(r) = 0$. This implies that $u = \lim\limits_{\lambda\to 1} \sum\limits_{k=0}^{\infty} \nu_k \lambda^k$ is approximating the solution of (2.1). For more readings about the convergence of (2.4), we refer the reader to [7, 8].

3 Approximating the Solution of Cell-Cell Adhesion Model

In this section, we employ the (HPM) to approximate the solution of

$$\begin{aligned}\frac{\partial n(t,x)}{\partial t} &= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1} \max\{n(t,x+y)(2-n(t,x+y)),0\}\, sign(y)\, dy\right] \\ &+ \mu n(1 - n/M).\end{aligned} \tag{3.1}$$

Assume that $0 \le n(t,x) \le M \le 2$. Then the above model can be reduced to

$$\begin{aligned}\frac{\partial n(t,x)}{\partial t} &= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1} n(t,x+y)(2-n(t,x+y)) sign(y)\, dy\right] \\ &+ \mu n(1 - n/M).\end{aligned} \tag{3.2}$$

This leads us to consider the following general case of (3.2):

$$\frac{\partial n(t,x)}{\partial t} = \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha\frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1} f(n(t,x+y))sign(y)\,dy\right] + \mu n(1-n/M), \tag{3.3}$$

where $f(n)$ is assumed to be $C^\infty-$function. To simplify the calculations, we rewrite (3.3) as the following:

$$\begin{aligned} n_t(t,x) &= n_{xx}(t,x) + \alpha\left[n(t,x)\left(\int_{-1}^{0} f(n(t,x+y))\,dy - \int_{0}^{1} f(n(t,x+y))\,dy\right)\right]_x \\ &+ \mu n(1-n/M), \\ &= n_{xx}(t,x) + \alpha\left[n(t,x)\left(K^-(t,x) - K^+(t,x)\right)\right]_x + \mu n(1-n/M) \\ &= n_{xx}(t,x) + \alpha n_x(t,x)\left(K^-(t,x) - K^+(t,x)\right) \\ &+ \alpha n(t,x)\left(K^-(t,x) - K^+(t,x)\right)_x + \mu n(1-n/M), \end{aligned} \tag{3.4}$$

where

$$K^-(t,x) = \int_{-1}^{0} f(n(t,x+y))\,dy = \int_{x-1}^{x} f(n(t,y))\,dy$$

and

$$K^+(t,x) = \int_{0}^{1} f(n(t,x+y))\,dy \int_{x}^{x+1} f(n(t,y))\,dy.$$

To apply the homotopy perturbation method, we assume that $n = n_0 + n_1p + n_2p^2 + n_3p^3\cdots$. Then,

$$n_t = n_{0t} + n_{1t}p + n_{2t}p^2 + n_{3t}p^3\cdots,$$

$$n_x = n_{0x} + n_{1x}p + n_{2x}p^2 + n_{3x}p^3\cdots,$$

$$n_{xx} = n_{0xx} + n_{1xx}p + n_{2xx}p^2 + n_{3xx}p^3\cdots,$$

and

$$\begin{aligned} \mu n(1-n) &= \mu n_0(1-n_0) + \mu\left(n_1(1-n_0) - n_0n_1\right)p + \mu\left(n_2(1-n_0) - n_0n_2 - n_1^2\right)p^2 \\ &+ \mu\left(n_3(1-n_0) - 2n_1n_2 - n_0n_3\right)p^3\cdots. \end{aligned}$$

To expand the terms $K^-(t,x)$ and $K^+(t,x)$ in a powers of p, we expand $f(n)$

using Taylor expansion about n_0. Particularly, we have

$$\begin{aligned} f(n) &= f(n_0) + f'(n_0)\left[n_1 p + n_2 p^2 + n_3 p^3 \cdots\right] \\ &+ \frac{f''(n_0)}{2!}\left[n_1 p + n_2 p^2 + n_3 p^3 \cdots\right]^2 \\ &+ \frac{f'''(n_0)}{3!}\left[n_1 p + n_2 p^2 + n_3 p^3 \cdots\right]^3 \\ &+ \cdots \\ &= f(n_0) + \left(f'(n_0) n_1\right) p + \left(f'(n_0) n_2 + \frac{f''(n_0)}{2!}(n_1)^2\right) p^2 \\ &+ \left(f'(n_0) n_3 + \frac{f''(n_0)}{2!}(n_1) n_2 + \frac{f'''(n_0)}{3!}(n_1)^3\right) p^3 + \cdots . \end{aligned}$$

Using this expansion of $f(n)$, we have

$$\begin{aligned} K^-(t,x) &= \int_{-1}^{0} f(n(t,x+y))dy \qquad (3.5)\\ &= \int_{-1}^{0} \Bigg(f(n_0) + \left(f'(n_0) n_1\right) p + \left(f'(n_0) n_2 + \frac{f''(n_0)}{2!}(n_1)^2\right) p^2 \qquad (3.6)\\ &+ \left(f'(n_0) n_3 + \frac{f''(n_0)}{2!}(n_1) n_2 + \frac{f'''(n_0)}{3!}(n_1)^3\right) p^3 + \cdots \Bigg) dy \qquad (3.7)\\ &= K_0^-(t,x) + K_1^-(t,x)p + K_2^-(t,x)p^2 + K_3^-(t,x)p^3 + \cdots , \qquad (3.8) \end{aligned}$$

where

$$K_0^-(t,x) = \int_{-1}^{0} f(n_0(t,x+y))dy,$$

$$K_1^-(t,x) = \int_{-1}^{0} \left(f'(n_0(t,x+y)) n_1(t,x+y)\right),$$

$$K_2^-(t,x) = \int_{-1}^{0} \left(f'(n_0(t,x+y)) n_2(t,x+y) + \frac{f''(n_0(t,x+y))}{2!}(n_1(t,x+y))^2 \right) dy,$$

and

$$K_3^-(t,x) = \int_{-1}^{0} \left(f'(n_0) n_3 \frac{f''(n_0)}{2!}(n_1) n_2 + \frac{f'''(n_0)}{3!}(n_1)^3 \right)\Bigg|_{(t,x+y)} dy.$$

Similarly, we have

$$K^+(t,x) = K_0^+(t,x) + K_1^+(t,x)p + K_2^+(t,x)p^2 + K_3^+(t,x)p^3 + \cdots ,$$

where

$$K_0^+(t,x) = \int_0^1 f(n_0(t,x+y))dy,$$

$$K_1^+(t,x) = \int_0^1 (f'(n_0(t,x+y))n_1(t,x+y)),$$

$$K_2^+(t,x) = \int_0^1 \left(f'(n_0(t,x+y))n_2(t,x+y) + \frac{f''(n_0(t,x+y))}{2!}(n_1(t,x+y))^2 \right) dy,$$

and

$$K_3^+(t,x) = \int_0^1 \left(f'(n_0)n_3 \frac{f''(n_0)}{2!}(n_1)n_2 + \frac{f'''(n_0)}{3!}(n_1)^3 \right)\Big|_{(t,x+y)} dy.$$

By substituting K^- and K^+ in $n_x(t,x)$, we get

$$\begin{aligned} n_x(t,x)K^-(t,x) &= n_{0x}K_0^-(t,x) + \left(n_{1x}K_0^-(t,x) + n_{0x}K_1^-(t,x)\right)p \\ &+ \left(n_{2x}K_0^-(t,x) + n_{1x}K_1^-(t,x) + n_{0x}K_0^-(t,x)\right)p^2 \\ &+ \left(n_{3x}K_0^-(t,x) + n_{2x}K_1^-(t,x) + n_{1x}K_2^-(t,x) + n_{0x}K_3^-(t,x)\right)p^3 \\ &+ \cdots, \end{aligned} \tag{3.9}$$

$$\begin{aligned} n_x(t,x)K^+(t,x) &= n_{0x}K_0^+(t,x) + \left(n_{1x}K_0^+(t,x) + n_{0x}K_1^+(t,x)\right)p \\ &+ \left(n_{2x}K_0^+(t,x) + n_{1x}K_1^+(t,x) + n_{0x}K_0^+(t,x)\right)p^2 \\ &+ \left(n_{3x}K_0^+(t,x) + n_{2x}K_1^+(t,x) + n_{1x}K_2^+(t,x) + n_{0x}K_3^+(t,x)\right)p^3 \\ &+ \cdots, \end{aligned} \tag{3.10}$$

$$\begin{aligned} n_x(t,x)(K^-(t,x))_x &= n_0K_{0x}^-(t,x) + \left(n_1K_{0x}^-(t,x) + n_0K_{1x}^-(t,x)\right)p \\ &+ \left(n_2K_{0x}^-(t,x) + n_1K_{1x}^-(t,x) + n_0K_{0x}^-(t,x)\right)p^2 \\ &+ \left(n_3K_{0x}^-(t,x) + n_2K_{1x}^-(t,x) + n_1K_{2x}^-(t,x) + n_0K_{3x}^-(t,x)\right)p^3 \\ &+ \cdots, \end{aligned} \tag{3.11}$$

and

$$\begin{aligned} n_x(t,x)(K^+(t,x))_x &= n_0K_{0x}^+(t,x) + \left(n_1K_{0x}^+(t,x) + n_0K_{1x}^+(t,x)\right)p \\ &+ \left(n_2K_{0x}^+(t,x) + n_1K_{1x}^+(t,x) + n_0K_{0x}^+(t,x)\right)p^2 \\ &+ \left(n_3K_{0x}^+(t,x) + n_2K_{1x}^+(t,x) + n_1K_{2x}^+(t,x) + n_0K_{3x}^+(t,x)\right)p^3 \\ &+ \cdots. \end{aligned} \tag{3.12}$$

By substituting the perturbed formula of $n_t,\ n_x$, and n_{xx} in (3.4), we get

$$\begin{aligned}
n_{0t}+n_{1t}p &+ n_{2t}p^2+n_{3t}p^3\cdots = p\left[n_{0xx}+n_{1xx}p+n_{2xx}p^2+n_{3xx}p^3\cdots\right]\\
&+ \alpha p\left[n_{0x}K_0^-(t,x)+\left(n_{1x}K_0^-(t,x)+n_{0x}K_1^-(t,x)\right)p+\right.\\
&\left(n_{2x}K_0^-(t,x)+n_{1x}K_1^-(t,x)+n_{0x}K_0^-(t,x)\right)p^2+\\
&\left(n_{3x}K_0^-(t,x)+n_{2x}K_1^-(t,x)+n_{1x}K_2^-(t,x)+n_{0x}K_3^-(t,x)\right)p^3+\\
&\left.\cdots\right]\\
&+ \alpha p\left[n_0K_{0x}^-(t,x)+\left(n_1K_{0x}^-(t,x)+n_0K_{1x}^-(t,x)\right)p+\right.\\
&\left(n_2K_{0x}^-(t,x)+n_1K_{1x}^-(t,x)+n_0K_{0x}^-(t,x)\right)p^2+\\
&\left(n_3K_{0x}^-(t,x)+n_2K_{1x}^-(t,x)+n_1K_{2x}^-(t,x)+n_0K_{3x}^-(t,x)\right)p^3+\\
&\left.\cdots\right]\\
&- \alpha p\left[n_{0x}K_0^-(t,x)+\left(n_{1x}K_0^-(t,x)+n_{0x}K_1^-(t,x)\right)p+\right.\\
&\left(n_{2x}K_0^-(t,x)+n_{1x}K_1^-(t,x)+n_{0x}K_0^-(t,x)\right)p^2+\\
&\left(n_{3x}K_0^-(t,x)+n_{2x}K_1^-(t,x)+n_{1x}K_2^-(t,x)+n_{0x}K_3^-(t,x)\right)p^3+\\
&\left.\cdots\right]\\
&- \alpha p\left[n_0K_{0x}^-(t,x)+\left(n_1K_{0x}^-(t,x)+n_0K_{1x}^-(t,x)\right)p+\right.\\
&\left(n_2K_{0x}^-(t,x)+n_1K_{1x}^-(t,x)+n_0K_{0x}^-(t,x)\right)p^2+\\
&\left(n_3K_{0x}^-(t,x)+n_2K_{1x}^-(t,x)+n_1K_{2x}^-(t,x)+n_0K_{3x}^-(t,x)\right)p^3+\\
&\left.\cdots\right]\\
&+ \mu p\left[n_0(1-n_0)+\left(n_1(1-n_0)-n_0n_1\right)p+\left(n_2(1-n_0)-n_0n_2-n_1^2\right)p^2+\right.\\
&\left.\left(n_3(1-n_0)-2n_1n_2-n_0n_3\right)p^3\cdots\right]. \qquad (3.13)
\end{aligned}$$

By matching the coefficients of p^i, we get

$$\begin{aligned}
p^0 &: \quad n_{0t}=0\\
p^1 &: \quad n_{1t}=n_{0xx}-\alpha n_0K_{0x}-\alpha n_{0x}K_0+\mu n_0(1-n_0)\\
p^2 &: \quad n_{2t}=n_{1xx}-\alpha\left(n_0K_{1x}+n_1K_{0x}\right)-\left(n_{1x}K_0+n_{0x}K_1\right)+\mu\left(n_1(1-n_0)-n_0n_1\right)\\
p^3 &: \quad n_{3t}=n_{2xx}-\alpha\left(n_0K_{2x}+n_1K_{1x}+n_2K_{0x}\right)-\alpha\left(n_{2x}K_0+n_{1x}K_1+n_{0x}K_2\right)+\\
&\qquad \mu\left(n_2(1-n_0)-n_0n_2-n_1^2\right),\\
\vdots &\qquad\qquad \vdots
\end{aligned}$$

where the initial data to solve the above system of differential equations are $n_0(0,x)=f(x)$ and $n_1(0,x)=n_2(0,x)=n_3(0,x)=\cdots=0$. Thus, the solution of (3.1) by using the (HPM) is given by

$$n(t,x)=\lim_{p\to 1}\left(n_0(t,x)+n_1(t,x)p+n_2(t,x)p^2+\cdots\right).$$

Example 3.1. *Consider* (3.1) *with the initial data* $n(0,x) = M$ *where* M *is a positive constant such that* $0 < M < 2$. *Then, simple calculations show that* $n_0(t,x) = M,\ n_1(t,x) = M(1-M)t,\ n_2(t,x) = M(1-M)(1-2M)\frac{t^2}{2!}$, *and* $n_3(t,x) = M(1-M)(1-2M)(1-6m+6M^2)\frac{t^3}{3!}$. *Thus,*

$$\begin{aligned} n(t,x) &= M + M(1-M)t + M(1-M)(1-2M)\frac{t^2}{2!} + M(1-M)(1-2M)(1-6m+6M^2)\frac{t^3}{3!}\cdots \\ &= \frac{Mt^t}{1-M+Me^t}. \end{aligned}$$

In the following section, we use the above approximations along with a numerical simulation to approximate the solution of (3.1) with the initial data $n(0,x) = \exp\{-\frac{x^2}{2}\}$.

4 Numerical Simulation

In this section, we apply a numerical scheme for our perturbation method to simulate the solution of the reaction diffusion equation (1.6) with the initial data $n(0,x) = \exp\{-\frac{x^2}{2}\}$ and the parameters $\alpha = 1,\ \mu = 1$ and $n_0 = 1.8$. Thus,

$$n_0(t,x) = \exp\{-\frac{x^2}{2}\}$$

and the first approximation is given by

$$n_1 = \frac{1}{2}\sqrt{\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}(1-x) + \sqrt{2\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}\left(\frac{x-1}{\sqrt{2}}\right) + \sqrt{\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}(x) -$$

$$2\sqrt{2\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}\left(\frac{x}{\sqrt{2}}\right) - \frac{1}{2}\sqrt{\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}(x+1) + \sqrt{2\pi}te^{-\frac{x^2}{2}}x\mathrm{erf}\left(\frac{x+1}{\sqrt{2}}\right) + te^{-\frac{x^2}{2}}x^2 - 2te^{-\frac{3x^2}{2}} +$$

$$\frac{7}{2}te^{-x^2} + te^{-\frac{x^2}{2}-(1-x)^2} - 2te^{-\frac{x^2}{2}-\frac{1}{2}(1-x)^2} + te^{-\frac{x^2}{2}-(x+1)^2} - 2te^{-\frac{x^2}{2}-\frac{1}{2}(x+1)^2}.$$

This approximation is given in the following figure which shows a good stability for the solution when the time is relatively small.

Also, by implementation the numerical scheme for this method on equation (1.6) with the Dirichlet boundary conditions and the parameters $R = \pi,\ \mu = 1,\ \alpha = 0.01,$ and $n_0 = 1$, we get the following figure:

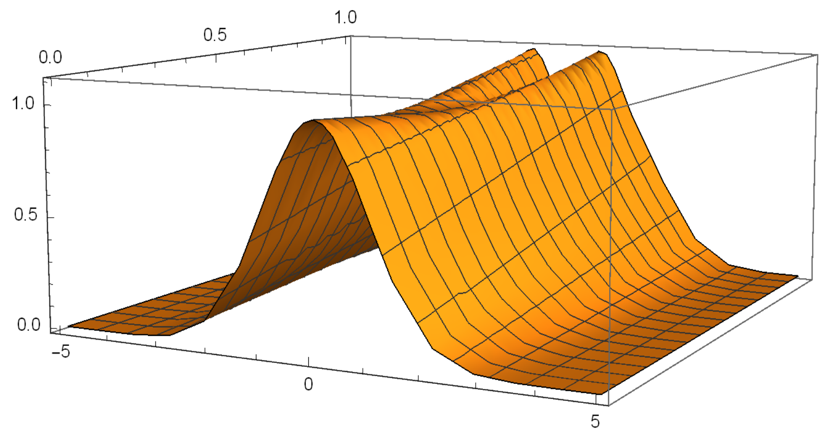

Figure 1: The values of the parameters are $R = 5,\ \mu = 1,\ \alpha = 1,$ and $n_0 = 1.8$. The initial data is $n(0, x) = \exp\{-\frac{x^2}{2}\}$.

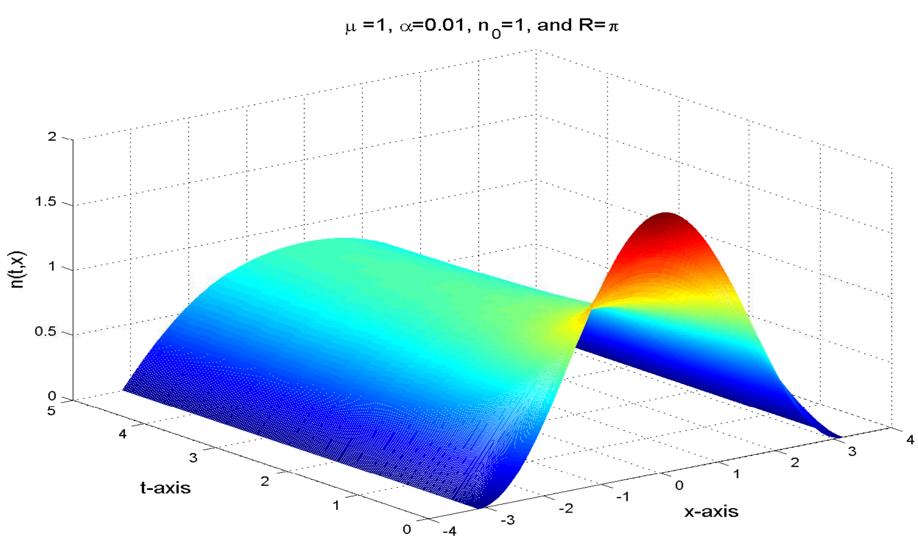

Figure 2: Dirichlet boundary conditions case. The values of the parameters are $R = \pi,\ \mu = 1,\ \alpha = 0.01,$ and $n_0 = 1$. The initial condition is $\phi(x) = 1 + \sin(\frac{\pi}{2} - x),\ -\pi \le x \le \pi$. In this case, the solution $n(t, x)$ converges to a nonnegative and not identically zero solution for large time t.

The figure shows that equation (1.6) admits a non-negative and not identically zero steady state solution, also showing that the steady state solution is asymptotically stable. Thus, it is an interesting problem to study, analytically, the existence and the global stability of such steady state solution. Instantly, this problem is very complicated and it needs more analysis. As such, we leave it as an open problem for a future work.

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